1

EFFECT OF HEMISPHERIC DOMINANT VERSUS NON-DOMINANT INSULAR DAMAGE ON SMOKING BEHAVIORS.

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Aims: Recent evidence suggests that damage to the insular cortex (IC), the cerebral cortex beneath the sylvian fissure, disrupts nicotine-induced cravings and is associated with a greater likelihood of cessation relative to non-IC damage. The role hemispheric dominance may play in regulating these changes, however, has not yet been explored. We hypothesized that current smokers with damage to their dominant IC would experience less withdrawal and cravings and be more likely to quit than those with non-dominant IC damage.
Methods: A total of 37 smokers with unilateral IC strokes (17 dominant and 20 non-dominant) were recruited from 3 acute care hospitals in Rochester, NY. Validated questionnaires were administered during admission to assess urge (Questionnaire on Smoking Urges) before and during admission and 3 months post-stroke, withdrawal intensity (Wisconsin Smoking Withdrawal Scale) during admission, and continuous abstinence at 3 months post-stroke. Bivariate statistics and multivariable linear regression were used to evaluate differences in urge, withdrawal, and cessation between dominant and non-dominant damaged groups, controlling for covariates.
Results: On average, smokers with dominant IC lesions had a larger decrease in urge from baseline to hospitalization (β = -0.82, 95% CI: -2.08, 0.44) but slight increase from baseline to 3-month follow-up (β = 0.55, 95% CI: -0.69, 1.79) compared to those with non-dominant damage. Dominant IC damage was also associated with a lower withdrawal score during hospitalization (β = -2.33, 95% CI: -5.48, 0.82) relative to non-dominant damage. Dominance did not seem to play a role in continuous abstinence at 3 months post-stroke (OR = 0.87, 95% CI: 0.18, 4.14).
Conclusions: Although limited by sample size, these results suggest little impact of dominant insular adaptations in regulating urge, withdrawal, and cessation.
Financial Support: This study was supported in part by the NHLBI Grant # T32 HL007937 and by CTSI Grant # UL1 RR024160 from the NIH.

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SEX, DRUGS, AND VIOLENCE: AN ANALYSIS OF WOMEN IN DRUG COURT.

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Aims: This analysis examines exposure to violence and substance use disorders among women in drug court who are: current sex traders (CST), former sex traders (FST), or women who have never traded sex.
Methods: Data comes from 319 women recruited from a Municipal Drug Court System in the Midwest. Women were interviewed about sex trading, violence, and drug use. Women who traded sex in the past 4 months for drugs, alcohol, or other resources were classified as CST, while women who previously traded sex but not in the past 4 months were classified as FST. Multinomial logistic regression determined the association between DSM-IV substance use disorder, violence, and current sex trading.
Results: Women were equally divided by trading status: 31% CST, 35% FST, and 34% never traded. Being physically attacked and emotionally abused in the past 4 months were significantly associated with sex trading status-whereas CST reported the highest rates. DSM-IV alcohol, opioid, and cocaine use disorders were also significantly associated with sex trading status and greater in CST. In an adjusted multinomial model, having at least one instance of violence increased the odds of CST (AOR 27.7) and FST (AOR 9.9) compared to those who did not report an instance of violence. Meeting the DSM-IV criteria for alcohol use disorder (CST: AOR 2.60; FST AOR: 2.59) and cocaine use disorder (CST: AOR 22.24; FST: AOR 22.17) also predicted sex trading status. Other significant variables were: having less than a high school diploma (CST: AOR 4.54; FST AOR: 2.41), 75+ lifetime sexual partners (CST: AOR 27.70; FST AOR: 9.78), and unstable housing (CST: AOR 4.33; FST AOR: 3.60).
Conclusions: Future interventions should take into account the uneven rates of alcohol/drug use and violence in this population. Interventions tailored specifically to CST and FST are needed.
Financial Support: McKnight Doctoral Fellowship, R01NR09180 (PI: Cottler)

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FUNCTIONAL CONNECTIVITY IN AN INSULA-BASED NETWORK IS ASSOCIATED WITH SMOKING CESSATION OUTCOMES.

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Aims: Tobacco addiction is a chronic condition with a high risk of relapse. Little is known regarding the neurobiological differences between smokers who can maintain abstinence compared to those who cannot. Cigarette craving and urges to smoke are believed to be significant contributors to relapse vulnerability, and evidence supports the role of the insula in connecting interoceptive awareness of craving with cognitive control regions of the brain. We investigated differences in functional connectivity between smokers who maintained 10 weeks of abstinence during a quit attempt versus those who relapsed.
Methods: Smokers (n = 85) underwent a resting-state functional connectivity scan prior to their target quit-date. Participants' smoking behavior was observed for 10 weeks following the quit-date, and participants were subsequently grouped as Abstinent (n = 44) or Relapsed (n = 41) at the end of the observation period. The right and left insula, as well as insula subdivisions (posterior, ventroanterior, and dorsoanterior) were used as seed regions of interest in the functional connectivity analysis.
Results: Using the right and left insula as seed regions, the Abstinent Group had greater functional connectivity than the Relapse Group with the bilateral pre- and postcentral gyri. This distribution of connectivity was maintained by the left and right posterior insula, but not by the other insula subdivisions.
Conclusions: Our results suggest that relapse vulnerability is associated with decreased connectivity between the posterior insula and primary sensorimotor cortices. It may be the case that greater connectivity in this network improves the ability to inhibit a motor response to cigarette cravings when those cravings conflict with a goal to remain abstinent.
Financial Support: R01 DA025876 (FJM) and K01 DA033347 (MAA).

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LOW THRESHOLD METHADONE PROTECTS AGAINST HIV INCIDENCE IN A CANADIAN SETTING.

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Aims: Hypothesis: HIV infection among persons who inject drugs (PWID) is a major international public health concern with the identification of novel protective factors of utmost importance. We hypothesized that methadone maintenance therapy, when delivered in a low-threshold setting, protects against HIV infection among PWID.
Procedure: Observational cohort study with semi-annual HIV testing.
Methods: Analysis: Data were derived from a prospective cohort of PWID in Vancouver, Canada where methadone is widely available through family physician's offices and dispensed by community pharmacies. We examined the role of methadone maintenance treatment on time to HIV incidence while adjusting for potential confounders.
Results: Results: Overall, 1639 HIV-negative individuals were recruited between May 1996 and May 2013 among whom there were 138 cases of HIV seroconversion during a median of 75.5 (interquartile range: 33.4 – 115.3) months of follow up. In multivariate Cox regression analyses, methadone maintenance therapy (adjusted relative hazard: 0.64 [95% confidence interval: 0.41 – 0.98]) remained independently associated with a reduced hazard of HIV infection after adjusting for socio-demographic characteristics and drug use patterns.
Conclusions: Conclusions: In this setting, where a low threshold program has made methadone widely available through primary care physicians, the use of methadone was independently associated with a reduced rate of HIV infection. These data reinforce the benefits of low threshold methadone on public health endpoints like reducing the spread of HIV.
Financial Support: The study was supported by the US National Institutes of Health (VIDUS: R01DA011591). This research was undertaken, in part, thanks to funding for a Tier 1 Canada Research Chair in Inner City Medicine, which supports Dr. Evan Wood.

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HEALTHCALL: TECHNOLOGY USE TO REDUCE NON-INJECTION DRUG USE IN HIV PRIMARY CARE.

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Aims: The HIV epidemic is increasingly connected with non-injecting drug use (NIDU), and in HIV-infected individuals, drug use is associated with poor adherence and sexual transmission of HIV. Drug abuse treatment is usually unavailable in HIV primary care, and many patients are uninterested in referral. We developed an innovative, technologically-based intervention 'HealthCall' designed to extend brief MI to reduce drug use in a way that would fit into busy, often understaffed HIV primary care settings.
Methods: 237 non-injection drug users actively enrolled in HIV primary care clinic were randomized to MI-only group (75), MI+HealthCall (79) and DVD control group (83). Mean age was 46.5 (s.d., 9.3), 83% male, 55% African-American, 67.7% had HS grad/GED. At baseline, mean days of drug use in the past 30 days was 8.83 (s.d., 6.7). The study is ongoing. Here we present preliminary results.
Results: At end of treatment (60 days), mean days of primary drug use (pDU) in the past 30 days was 4.25 (s.d., 6.40). The overall reduction in pDU from baseline to end of treatment was significant (p<.0001). Mean days of pDU at baseline and end-of-treatment: among cocaine users (n=48), 8.52 (s.d. 7.5) and 3.84 (s.d 6.1); among crack users (n= 118), 8.68 (s.d. 5.9) and 3.81 (s.d. 5.3). Among heroin users (n=23), 11.48 (s.d 8.9) and 6.95 (s.d. 10.2); among meth-amphetamine users (n=48) 8.33 (s.d. 6.5) and 4.53 (s.d. 6.84). All differences between baseline and end-of-treatment days used were significant (p<.05). Retention was very good: 82.4% were retained at end of treatment, and 84.1% were retained at 12 month follow-up.
Conclusions: Preliminary results from this large sample of NIDU enrolled in HIV care indicate significant drug use reductions, overall and by primary drug type. The majority of patients were highly engaged during treatment and follow-up visits. These results are promising as they indicate substance abusers can be treated at HIV primary cares with methods of brief behavioral interventions.
Financial Support: R01DA024606, K05 AA014223, NYSPI

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IDENTIFYING PREDICTIVE PROFILES OF AMPHETAMINE, HEROIN, AND POLYSUBSTANCE DEPENDENCE USING MACHINE LEARNING APPROACHES.

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Aims: Recent animal and human studies reveal distinct cognitive and neurobiological differences between addictions to different classes of drugs. However, we still know little about specific risk profiles associated with different addictions. To identify substance-specific predictive profiles, we applied a machine learning algorithm to a variety of measures from "pure" amphetamine-dependent (AD; N=46), "pure" heroin-dependent (HD; N=48), and polysubstance dependent individuals (PD; N=63) in protracted abstinence, and healthy controls (HC; N=95).
Methods: We used the elastic net algorithm to identify predictors of group membership that are generalizable to new samples. Predictors included demographic, personality, psychiatric, and neurocognitive measures.
Results: HC group membership was predicted by lower scores on externalizing personality (aggression, sensation seeking [SS], impulsivity) and psychiatric (antisocial personality, psychopathy) measures, and better neurocognitive performance on the Iowa Gambling Task and the Go/No-Go task. AD group membership was predicted by lower state anxiety, higher aggression, and higher SS, whereas HD group membership was predicted by the opposite pattern (i.e., higher state anxiety, lower aggression, and lower SS). Higher delay discounting uniquely predicted AD group membership, whereas higher delay aversion predicted HD group membership. History of childhood conduct disorder and higher anxiety sensitivity uniquely predicted PD group membership.
Conclusions: These results suggest that different mechanisms may underlie stimulant, opiate, and polysubstance dependence. This line of work may shed light on the development of objective diagnostic tests and more effective treatment programs.
Financial Support: Supported by R01DA021421 from the National Institute on Drug Abuse (NIDA) and the Fogarty International Center.

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LIFETIME VICTIMIZATION AND SEXUAL RELATIONSHIP POWER AMONG SUBSTANCE-ABUSING AFRICAN-AMERICAN WOMEN.

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Aims: The goal of the current study was to assess the associations between lifetime victimization (physical, adult sexual, and child sexual abuse) and sexual relationship power in substance abusing African American (AA) women. It is hypothesized that women who endorse any form of victimization would also report less relationship control (RC) and decision-making dominance (DMD), two subtypes sexual relationship power (SRP).
Methods: The current study was a secondary analysis of baseline data collected from the National Institute on Drug Abuse Clinical Trials Network 0019 (CTN 0019) (Tross, Campbell, Cohen, Calsyn, Pavlicova, Miele, et al., 2008). The CTN 0019 protocol was a multi-site randomized clinical trial that assessed the intervention of Safer Sex Skills Building (SSSB) in women substance abusers on reducing HIV sexual risk. The current study consists of 124 AA women from the CTN 0019 dataset. Participation eligibility required women to be at least 18 years of age, proficient in English, enrolled in substance abuse treatment, and to acknowledge unprotected heterosexual intercourse within the past 6 months.
Results: In the current sample, over 90% of the women endorsed some form of abuse (adult physical, child sexual, and adult sexual abuse) in their lifetime. Seventy percent of the participants (N=87) endorsed lifetime physical abuse from a male sexual partner. Sixty-three percent (N=79) of the women endorsed adult sexual abuse, and 52.4% (N=65) of the sample endorsed child sexual abuse.
Multiple regression analyses suggests that two (child and adult sexual abuse) of the three types of abuse in the model predicted SRP (R^2=.078, F (3, 120) = 3.4, p<.05) but not adult physical abuse.
Conclusions: The current study is among the first to examine the relationship between victimization and SRP among substance-abusing AA women. The findings from this study provide evidence that substance abuse interventions may benefit from activities promoting the development of sexual relationship power in substance-abusing AA women who have experienced victimization.
Financial Support: No financial support was provided for the current study.

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PREVALENCE OF NONMEDICAL USE OF PRESCRIPTION OPIOIDS AMONG ADOLESCENTS IN SUBSTANCE USE TREATMENT.

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Aims: Nonmedical use of prescription opioids (NMPO) is a significant public health problem in the United States that often begins in adolescence. We sought to describe the prevalence of NMPO in a sample of adolescents in substance treatment.
Methods: Adolescents in two outpatient substance treatment programs were recruited for participation between 2009 and 2013. Most patients were referred to treatment by social services or juvenile justice for serious conduct and substance use disorders. Inclusion criteria were: in substance treatment; 13-18 years of age; IQ ≥ 80; and valid written consent for 18 year olds or parental consent and assent for those ≤ 17 years. The Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM) was administered by trained nonclinical interviewers to assess substance use patterns, including onset, duration and intensity of use.
Results: A total of 382 adolescents completed the CIDI-SAM: mean age 16.1 (SD=1.1), 78% male, 50% white, non-Hispanic. Of the 382 adolescents, 121 (32%) reported nonmedical use of prescription opioids 〉5 times. Mean age at first use was 14.3 (SD=1.5). A total of 37 (31%) reported oral ingestion only, 4 (3%) smoking only, 5 (4%) snorting only, and 64 (53%) reported all three routes of administration. Only 4 (3%) reported injecting prescription opioids. Approximately 75% reported NMPO at least once a week. Of 24 youth who reported heroin use 〉5 times, 18 (75%) also reported NMPO. A total of 62 (16%) were diagnosed with opiate (prescritpion opioids and heroin) abuse or dependence according to DSM-IV criteria. Among the 121 reporting NMPO, 92 (76%) were diagnosed with alcohol abuse or dependence, 103 (85%) with cannabis abuse or dependence, 58 (48%) with club drug abuse or dependence, and 44 (36%) with amphetamine abuse or dependence.
Conclusions: NMPO is quite prevalent among adolescents receiving substance use treatment. Intervention to interrupt NMPO from progressing to injection or developing into a disorder is critical.
Financial Support: K01DA036452, R01DA035804, K24DA032555, P60DA011015, R01DA34604

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CANNABIS USE, SCHIZOTYPY, AND ATTENTIONAL INHIBITION.

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Aims: As the association between cannabis use and psychosis becomes more clear, especially in adolescence, this study aims to explore how cannabis use interacts with age to influence negative priming in adolescents and young adults.
Methods: A sample of n=124 young people (aged 15-24) participated in this experiment to examine the effects of cannabis use and schizotypy on location-based negative priming, and explore whether the effects of cannabis use on negative priming vary according to age. The experiment was run over the internet. Participants completed a number of measures of substance use, an inventory of feelings and experiences and 24 negative priming trials.
Results: Participants had a mean age of 20.3 years (SD 2.5) and 58% were female. Across all participants there was on average a slowed responding to probe displays of negative priming compared with controls ($p<.001$). The schizotypy dimension of Impulsive Nonconformity was found to have a significant effect on negative priming. Further, there was a significant age by cannabis use interaction indicating that younger, frequent users of cannabis may be more susceptible to its effects on attentional inhibition and perhaps at greater risk of developing a disorder on the psychosis dimension.
Conclusions: Higher scores on the Impulsive Nonconformity dimension of schizotypy were related to reduced negative priming, suggesting that more impulsive participants show greater deficits in cognitive control and cannabis use interacting with age to influence negative priming, implying that the effectiveness of inhibitory cognitive control processes was impaired in younger cannabis users compared with older cannabis users if they used cannabis frequently. Longitudinal research examining changes in negative priming over time among frequent adolescent cannabis users would be useful to determine the factors involved in the maintenance, as opposed to improvement in, changes in priming with age.
Financial Support: NCPIC is supported by the Australian Government Department of Health.

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AN EPIDEMIOLOGICAL TEST OF THE KANDEL-KANDEL HYPOTHESIS OF SEPT 2014: U.S. 2002-13.

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Aims: Kandel & Kandel (Sept 2014) aver a nicotine 'priming effect' with accelerated cocaine (COC) use. We offer initial epidemiological tests of K-K hypothesis.
Methods: Data are from 2002-13 US National Surveys on Drug Use and Health, yielding nationally representative samples of newly incident COC users (n>4K NICU), who completed confidential computer-assisted self-interviews. Stratification is by timing of nicotine exposure, measured by months of 1st & last tobacco cigarette smoking (TS), and tobacco dependence (TD). We estimated rapid-onset COC dependence transition probabilities (CDTP), attending to analysis weights and Taylor series variances.
Results: In aggregate, among 206 NICU with no TS, CDTP estimate = 7.4% (95%CI=0.1%,14.6%). The CDTP estimate is 4.0% for 413 NICU with past TS >12 months before test date (95%CI=1.8%,6.1%). As K-K might predict, larger CDTP estimates are seen when TS occurred during the COC onset interval (CDTP=7.5%; 95%CI= 6.2%,8.6%). These subgroup estimates are >10% for TS initiates with concurrent rapid-onset TD (CDTP=11.8%; 95%CI= 3.9%,30.4%) and for past-onset persistent TS with TD during COC onset interval (CDTP=10.0%; 95% CI= 7.8%,12.2%).
Conclusions: In initial estimates, NICU with active TS and TD have larger CDTP, tending to support K-K 'priming' hypothesis. We now seek more refined NSDUH data to increase estimate precision, include other nicotine products, and clarify timelines to identify the nature of 'nicotine pre-treatment' in this epidemiological context. In humans, rapid-onset TD might be more important than TS pre-treatment, *per se*, although time from 1st to 2nd nicotine use and time from 1st to 2nd COC use deserve attention as individual-level markers of a subject-specific reinforcing function of these compounds.
Financial Support: NIDA KCA (T32DA021129); JCA (K05DA015799)

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CONSUMPTION OF ANABOLIC STEROIDS IN ATHLETES: A BIBLIOMETRIC APPROACH (2006-2012).

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Aims: Consumption of anabolic steroids by professionals and amateurs athletes is a serious problem of public health that requires having all information to let know the state of research in this field. Anabolic steroids are substances synthesized in laboratories that mimic the testosterone effects, producing androgenic actions. Its use in sporting activity seeks to increase the muscle mass, physical strength and resistance to fatigue. Our purpose is to describe the research articles on the abuse of anabolic steroids in athletes through bibliometric analysis.
Methods: Searches were performed in Science Citation Index-Expanded and Social Science Citation Index in 2006-2012 period. A search profile that combined 36 terms related to physical activity and 61 terms related to the use of steroids in sports was used.
Results: 1,011 articles were identified, most of them published in the last few years. Drug Testing and Analysis, Analytical and Bioanalytical Chemistry, and International Journal of Sports Medicine were the most productive journals. Among Social Science journals highlights International Review for the Sociology of Sport. The most productive scientific areas in Science and Technology were Analytical Chemistry and Biochemistry, and Sport Sciences, Substance Abuse, Sociology and Ethics within Social Sciences. Doping, its control, attitudes, values, behaviors and dependence were the leading thematic contents. Research institutions from USA, Germany, Italy and Switzerland produced most of the works.
Conclusions: A mean of 144 papers per year have been published, with a wide multidisciplinarity, and participation of Biomedical, Biochemical, Sports and Sociological areas.
Financial Support: Plan Municipal de Drogodependencias, Concejalía de Sanidad, Ayuntamiento de Valencia, Spain.

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DETERMINING MENSTRUAL PHASE IN SUBSTANCE USE RESEARCH: A REVIEW WITH RECOMMENDATIONS.

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Aims: Menstrual phase is significantly associated with a several substance use related outcomes, including withdrawal, pharmacokinetics, and cessation. Unfortunately, identification of menstrual phase in biobehavioral clinical research has not been standardized. Thus, we aimed to review the current strategies being used to identify menstrual phase and provide recommendations that will enhance methodological uniformity.
Methods: We conducted a literature review via PubMed for "menstrual cycle" and "menstrual phase." We excluded articles that focused on exogenous hormones, postpartum, menstrual-related problems, and infertility. We also excluded articles that included either younger (<18) or older (>45) study samples.
Results: A total of 370 articles were initially identified. After exclusionary criteria were applied 32 articles remained, among which six different methods (self-report of onset of menses, basal body temperature (BBT), urinary luteinizing hormone (LH) testing, sex hormones via saliva samples, sex hormones via blood samples, and transvaginal ultrasound). Most articles employed more than one method (22/33 articles). The most common method used was self-report of onset of menses (31/32 articles). The least common methods used were BBT (1/32 articles) and transvaginal ultrasound (1/32 articles).
Conclusions: There is a lack of consistency in methodology used to determine menstrual phase. We recommend combining several methods to improve accuracy of phase identification, minimize costs and burden, and reduce selection bias and confounding. The adoption of these recommendations will yield a decrease in misclassification bias and facilitate cross-study comparisons.
Financial Support: P50-DA033942, P50-DA016511, P50-DA033945, K24DA038240, K12HD055887

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CANNABIS SMOKING, CARDIOMETABOLIC HEALTH, AND CARDIOVASCULAR DISEASE: UNITED STATES NHANES, 2005-2010.

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Aims: At CPDD 2014, we reported meta-analyses showing an inverse association of diabetes mellitus and cannabis smoking (CS), although case reports gave us reason to expect CS to have medical complications in other domains of cardiometabolic health (CMH) and cardiovascular disease (CVD). For example, case reports of 'pot heart attack' and other acute cardiovascular events after cannabis smoking have appeared in the clinical literature. However, the few population-based studies in this area seem to show that CS *per se* does not influence CVD. We aim to add new epidemiological evidence on CS-CMH-CVD associations.
Methods: Data are from 20-59 year old participants in the 2005-2010 US National Health and Nutrition Examination Survey (NHANES; n=9135), with standardized clinical examinations, lab workup, and self-report assessments, including CS. Multiple logistic regressions produced estimates for a profile of CMH-CVD responses, including coronary heart disease, angina, heart attack and stroke, with statistical adjustment for age, sex, ethnic self-identification, educational attainment, poverty income ratio, tobacco cigarette smoking, alcohol drinking, body mass index (Kg/m^2), glycohemoglobin levels (%), high density lipoprotein-cholesterol (mg/dL) and C - reactive protein (mg/dL).
Results: Except for stroke, estimates from these univariate-response regression models before and after statistical adjustment for covariates disclosed no CS association with these CVD outcomdes. Recently active cannabis smokers were more likely to have had stroke (covariate-adjusted OR= 2.8, 95% CI=1.2, 6.8).
Conclusions: We observe a CS-stroke association that is independent of the alternative CVD predictors studied here. We are pursuing these leads about potential CS medical complications with new multivariate response modeling approaches and a profile of cardiometabolic health indicators that might be on pathways leading from CS to CVD outcomes.
Financial Support: Supported by NIDA T32DA021129 (OA); K05DA015799 (JCA).

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ADOLESCENT OXYCODONE SELF ADMINISTRATION ALTERS SUBSEQUENT ANTINOCICEPTIVE EFFECT OF OXYCODONE IN C57BL/6J MICE IN ADULTHOOD.

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Aims: Non-medical use of oxycodone and prescription opioids in adolescence is a public health concern. The effect of adolescent oxycodone self-administration on the effects of the drug upon subsequent exposure in adulthood is unknown. The aim of this study is to examine how chronic adolescent oxycodone self administration affects the antinociceptive effect of the drug upon subsequent exposure in mice.
Methods: Groups of male adolescent mice (n=6-7) acquired oxycodone self administration (0.25mg/kg/infusion), or served as yoked saline controls (2hrs daily for 14 days) and were then withdrawn from oxycodone in their home cages for fifteen days. The mice were examined in early adulthood for the antinociceptive effects of oxycodone (5 or 7.5 mg/kg i.p., one dose per group), using a standard hot-plate assay (55°C). Nociceptive responses were measured before oxycodone (baseline) and 10, 30 and 60 min after oxycodone administration. Data were calculated as % maximal possible effect (%MPE), and area under the curve (AUC) for oxycodone %MPE was analyzed for the 10-60 min period.
Results: Mice that self-administered oxycodone during adolescence showed significant reduction in % MPE (AUC) when exposed to oxycodone in adulthood, compared to the yoked saline control group (Main effect of adolescent treatment: $F[1,23]=11.0$, $p<0.01$).
Conclusions: Mice that underwent chronic oxycodone self-administration in adolescence had decreased pharmacodynamic effects of oxycodone in adulthood, when tested after a 15-day drug-free period. These results suggest that adolescent oxycodone exposure may cause long-lasting alterations in the brain, and affect responses to prescription opioids in adulthood.
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CAMKII AND β-ACTIN ARE ACTIVATED BOTH IN STRIATUM AND HIPPOCAMPUS IN OPIOID-INDUCED CONDITIONED PLACE PREFERENCE.

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Aims: To investigate if neuronal processes coupled to learning and memory are activated by a behavioral model of the development of drug abuse. We studied the activation of Calcium/calmodulin-dependent protein kinase II (CamKII) and β-actin in striatum and hippocampus of mice subjected to Conditioned Place Preference after administration of morphine or morphine-6-glucuronide (M6G). CamKII and β-actin are intraneuronal protein known to be essential for synaptic plasticity, central for learning and memory.
Methods: Levels of cFos, CamKII, phosphorylated CaMKII (pCamKII), and β-actin in dorsal and ventral striatum, and in hippocampus were analyzed by western blotting after s.c. injection of 10 or 30 μmol/kg morphine or M6G, or saline to mice; using three different drug regimes:1) acute, 2) in combination with Conditioned Place Preference (CPP), 3) repeated mimicking the administration in CPP without exposition to the apparatus. The CPP consisted of 20 min conditioning sessions with the drug in the morning and saline in the afternoon for three days and a 20 min test session on the fourth day after saline.
Results: Both doses of morphine and 10 μmol/kg M6G induced significant CPP. Morphine and M6G increased cFos, CamKII, pCamKII and β-actin in both striatal areas after the acute and CPP treatments, especially in the animals subjected to the CPP. In the hippocampus, an increase in in these proteins was detected only in the animals exposed to the CPP.Decreases in pCamKII were observed after the repeated treatment in the three areas.
Conclusions: The results show that opioids preferentially stimulate striatal neurons after both the acute and CPP treatment. When the opioid administration is coupled to a learning paradigm like CPP, the hippocampus is also recruited. The changes in CamKII and -actin are likely connected to activation of neuronal processes involved in synaptic plasticity in these areas. The decrease in pCamKII after the repeated treatment can be related to negative cognitive effects of chronic opioids.
Financial Support: Norwegian Research Council 196621/V50

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REDUCING UNDERAGE DRINKING THROUGH COMPREHENSIVE COMMUNITY INTERVENTIONS: THE STRATEGIC PREVENTION FRAMEWORK.

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Aims: The present study examines the effects of Strategic Prevention Framework implementation on underage drinking outcomes in seven Kansas communities.
Methods: Seven Kansas community coalitions implemented a five-phase comprehensive community intervention to address disparate rates of underage drinking. The intervention components consisted of intensive community assessments, enhancing skills to bring about environmental change, developing strategic plans to guide coalition efforts, implementation of evidence-based prevention strategies, and evaluation of implemented strategies. The coalitions facilitated the administration of the Kansas Communities That Care (CTC) Survey to students in grades 6, 8, 10, and 12; the CTC survey is a validated instrument used to measure substance abuse and associated risk factors.
Results: One-way repeated measures ANOVAs indicated that between 2006 and 2012, there were significant improvements in outcomes related to past 30-day use ($p < .001$, partial eta-squared = .959), social norms ($p = .001$, partial eta-squared = .262), social access from adults ($p < .004$, partial eta-squared = .523), and enforcement of existing underage drinking laws ($p < .001$, partial eta-squared = .519).
Conclusions: The findings provide empirical support for the Strategic Prevention Framework as approach for implementing comprehensive interventions to reduce and prevent underage drinking in communities.
Financial Support: This research was funded in part by the Kansas SPF-SIG awarded by the Substance Abuse and Mental Health Services Administration to the Kansas Department of Social and Rehabilitation Services. Research reported in this publication was also supported by the National Institute on Drug Abuse of the National Institutes of Health under award number DA07272. 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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METHYLPHENIDATE FOR METHAMPHETAMINE USE DISORDERS IN PARTICIPANTS WITH AND WITHOUT ADHD.

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Aims: Methylphenidate (MPH) is a stimulant that is widely used to treat ADHD in adolescents and adults. Previous studies show that MPH provided to stimulant abusers with ADHD results in improvement in ADHD symptoms and reduces illicit drug use. A recently completed NIDA-funded study investigated the effectiveness of MPH for the treatment of methamphetamine (MA) use disorder. This secondary analysis examines the association between ADHD and treatment outcome.
Methods: 110 methamphetamine-dependent participants in Honolulu and Los Angeles were randomized to MPH (n=55) or placebo (n=55) for 10 weeks of double-blind medication followed by a 4-week return-to-baseline period in which all participants received placebo. Twice weekly clinic visits included observed dosing, urine collection for drug screens (UDS), take-home meds, psychosocial assessments, and motivational incentives for MA-negative UDS. Participants were also provided with weekly CBT. The Connors Adult ADHD scale was used at baseline to assess adult and childhood symptoms of ADHD to determine adult ADHD status. MA use at week 10 was measured by self-report and UDS.
Results: At baseline, the ADHD group reported more MA use days in the past 30 days compared to the non-ADHD group (p=0.04). For the MPH treatment condition only, after adjusting for baseline differences at week 10,, MA use was significantly less for those without ADHD (n=37) compared to the ADHD group (n=18)(p=0.045). No difference was found in MA use between the MPH and Placebo treatment conditions for those with ADHD. For retention, ADHD participants were less likely to complete the study compared to the group without ADHD (p=0.002), however no difference in treatment completion was found between treatment conditions for only those with ADHD (p=0.79).
Conclusions: Those with ADHD reported more MA use at baseline, and had poorer treatment outcome regardless of the treatment they received. These results suggest that, although MPH may be safe for the treatment of MA-dependent individuals with ADHD, it may not be effective in reducing MA use for this group.
Financial Support: DA015084

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A NEW STUDY METHODOLOGY: ADAPT, THE SHORT, STAGED TRIAL.

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Aims: The costs in time, effort, and funding for randomized clinical trials (RCT), especially given reductions in government research funding, suggests that a new model of research methodology and design for substance use trials is needed to test early phase treatment interventions. A strategy to quickly test and eliminate ineffective pharmacotherapies would enable research to move on to other test medications, similar to designs used in cancer treatment trials.
Methods: The Accelerated Development of Additive Pharmacotherapy (ADAPT) trial conducted under the auspices of the NIDA Clinical Trials Network uses a study design that reduces typical study costs and shortens the time to start-up. A 2-stage design is being used to investigate the effectiveness and safety of a combination of extended-release depot naltrexone plus extended-release bupropion as a potential pharmacotherapy for methamphetamine (MA) use disorder. The design requires meeting "success" criteria from Stage 1 before launching Stage 2. Both stages include a 30-day screening period to confirm sufficient MA use as measured by urine drug screens (UDS), followed by an 8 week medication phase that includes monthly injections of naltrexone and daily oral dosing of buproprion.
Results: Having met Stage 1 criteria of at least 3 "responders" out of 20 participants (defined as 6+ MA-negative UDS during the last 4 weeks of the medication phase, including the final test in week 8), Stage 2 enrolled an additional 29 participants. Meeting "responder" success in the pre- defined number of participants of the total enrolled (9 of 49) will suggest an adequate signal to pursue funding for a large RCT.
Conclusions: Use of this model can accelerate clinical trial implementation and findings, and reduce time, efforts, and costs necessary for large RCTs, which will only be pursued when results suggest the effectiveness of the treatment examined.
Financial Support: DA13045

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ASSOCIATIONS BETWEEN ISOMERIC SERUM METHDONE LEVELS, TOTAL SUGAR INTAKE, AND OREXIN-A.

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Aims: Methadone maintenance treatment (MMT) is an effective aid in opioid addiction recovery. However, reports indicate significant changes in weight and sugar preference for established MMT patients. Few studies explore interactions between serum methadone levels, nutritional intake, and orexin-A (a hormone associated with feeding behavior). Isomeric analysis could identify pharmacodynamic differences within a racemic methadone mixture. This study aimed to explore the relationship between serum methadone isomer levels, macronutrient intake, and orexin-A levels in MMT patients.
Methods: 76 MMT participants (minimum 6 months treatment) were consented. Demographic variables, serum samples, and a 24-hour recall of nutritional intake (ASA24™) were collected. Serum samples were analyzed for quantitative levels of (d, l) methadone and orexin-A. Nutritional intake data generated a Healthy Eating Index score (HEI-2005), a standardized measure of diet quality. A correlational analysis was conducted between methadone isomer levels, total macronutrients consumed, HEI-2005 score, and serum orexin-A levels.
Results: Mean age was 48 years (s.d., 9.8); 57% male, 54% Caucasian. The correlation between methadone d-isomer levels and total sugar intake was significant (r=0.237, p<.05). There were no other statistically-significant correlations between serum methadone isomers and serum orexin-A levels, HEI-2005 score, or total 24-hour consumption of carbohydrates, fat, protein, or calories.
Conclusions: These data suggest that serum levels of d-methadone (an NMDA antagonist), but not l-methadone (an opioid agonist) are associated with increased total sugar intake. Serum (d, l) methdone levels were not associated with serum orexin-A levels, diet quality or total 24-hour consumption of carbohydrates, fat, protein, or calories. Further research should confirm and explore underlying mechanisms and potential associations between sugar intake and NMDA antagonism.
Financial Support: NIDA K24DA023186

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INCIDENT ALCOHOL USE AMONG ADULT ARAB REFUGEES AND IMMIGRANTS.

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Aims: Incident alcohol use among adult U.S. immigrants from countries with low alcohol use may reflect increased access, acculturation, or poor mental health. The aims were to assess incidence among immigrants and determine how incident users may differ from prevalent users and abstainers,
Methods: We analyzed a random sample of newly-arrived adult Iraqi refugees (N=298) and a sample of nonIraqi Arab adult immigrants (N=314, <1 year in US) to Southeastern Michigan. Most (95.8%) were interviewed one year later. Participants were categorized into abstaining (never consumed alcohol at both times; 74.4%), prevalent (alcohol use at baseline, 20.6%), and incident (never at baseline and current at follow-up; 4.9%). Measures included PTSD checklist, modified Hassles Scale and Arab Acculturation Scale, Hospital Anxiety and Depression Scale, and trauma events from Harvard Trauma Questionnaire.
Results: The incident group was mostly male (69%), immigrant (69%), and Christian (79.3%) with mean age of 36.6 years compared to 47.0%, 48.9%, 47.0% and 31.6 years among abstainers; and 84.3%, 51.2%, 76.9%, and 36.9 years among the prevalent group. In analysis controlling for gender and religion, the incident group had highest mean scores on PTSD symptoms at baseline and follow-up, acculturation at baseline, and hassles at follow-up. There were no significant differences on other variables examined including pre-migration trauma exposure.
Conclusions: Incident alcohol use among Arab refugees and immigrants to a region with readily available alcohol was rare but associated with acculturation and poor mental health. Limitations include under-reporting due to stigma and fear of deportation, and lack of information on social monitoring. As alcohol use may worsen poor mental health, it is important to recognize that incident drinking occurs in this community, and prevention and outreach efforts are needed.
Financial Support: NIMH (R01 085793) and Lycaki-Young Funds (state of Michigan)

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CORRESPONDENCE BETWEEN SELF-REPORTED AND BIOCHEMICAL MEASURES OF SMOKING IN OPIOID-DEPENDENT PREGNANT WOMEN.

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Aims: Smoking exacerbates adverse outcomes among opioid-dependent pregnant women (e.g., a more severe neonatal abstinence syndrome in exposed neonates). Vermont birth certificate data for opioid-dependent pregnant women indicates a significant decrease in their self-reported smoking rate over the course of pregnancy, from a mean of 17.9 cigarettes per day (CPD) prior to pregnancy to 13.8, 10.9, and 9.7 in the first, second and third trimesters, respectively. This study examined self-reported smoking rate and biochemical measures of smoking to test whether self-reported decreases in smoking were paralleled by decreases in biochemical measures.
Methods: Participants were 18 opioid-dependent pregnant women enrolled in clinical trials for smoking cessation. All women continued to smoke throughout their pregnancies. Self-reported CPD prior to pregnancy were collected at the Intake Assessment. CPD, breath CO, and urine cotinine were collected at intake, at a second assessment 1 month later (Early Pregnancy Assessment), and again at the end of pregnancy (≥ 28 weeks gestation; Late Pregnancy Assessment).
Results: Like birth certificate data, self-reported smoking rates decreased from a mean of 22.6 prior to pregnancy to 15.5 at intake. During pregnancy, self-reported CPD decreased significantly from 15.5, 7.5, and 9.0 at Intake and Early and Late Pregnancy Assessments, respectively ($p < .001$). However, parallel changes were not evident in biochemical measures of smoking. Mean CO was 13.3, 10.0, and 12.3 ppm ($p = .11$) and mean urine cotinine was 1422.8, 1387.8, and 1294.1 ng/ml ($p = .71$) at the three assessments.
Conclusions: Discrepancies between self-report and biochemical measures may be explained by misrepresentation of self-reported smoking or reductions in CPD offset by changes in smoking topography (i.e., compensatory smoking). Further research is needed to understand changes in smoking among opioid-dependent pregnant women.
Financial Support: NICHD R01 HD075669, NIDA R01 DA014028 and R01 DA031928, and FDA/NIDA P50 DA036114

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IS OPIOID USE ASSOCIATED WITH T CELL DYSFUNCTION?

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Aims: To determine whether opioid use is associated with T cell dysfunction among antiretroviral-therapy (ART) naïve HIV+ individuals.
Methods: We conducted a cross-sectional analysis of baseline data from the Russia ARCH Cohort, a prospective study of HIV+ individuals living in St. Petersburg, Russia, recruited from 11/2012 through 10/2014. Demographics and clinical characteristics were determined based on surveys; T cell characteristics were determined using flow cytometry. Separate multivariable linear regression models were constructed to determine the association between any opioid use and % naïve (defined as CD45RA+CD45RO-) and memory (defined as CD45RA-CD45RO+) CD4 and CD8 T cells and the CD4/CD8 ratio. We adjusted for age, gender, log HIV viral load, time since HIV diagnosis, depressive symptoms, co-morbid infections, and substance use (smoking, heavy drinking and stimulant use over the prior 30 days).
Results: Among 149 participants with detectable HIV viral load, the mean age was 33 (SD 5), 77% male, and 40% reported opioid use. In adjusted models, opioid use was associated with altered T cell function as measured by an increase in naïve CD4 (adjusted mean difference 1.35 [95% confidence interval -4.21, 6.92]) and CD8 (adjusted mean difference 3.10 [-2.04, 8.25]) T cell %, although the results were not statistically significant. In contrast, opioid use was associated with a non-significant decrease in memory CD4 (adjusted mean difference -1.17 [-7.11, 4.77]), CD8 (adjusted mean difference -2.53 [-7.49, 2.43]) T cell % and CD4/CD8 ratio (adjusted mean difference -0.05 [-0.21, 0.12]) compared to no opioid use.
Conclusions: Opioids did not significantly alter naive or memory T cell levels among ART naïve HIV+ Russians. Longitudinal analyses, including examinations of CD28 and CD57 expression, in larger sample sizes are indicated.
Financial Support: U01AA020780, U24AA020779, U24AA020778, R25DA013582, K12DA033312, U01AA020780-02S1

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REPEATED EXPOSURE TO THE 5-HT$_{1B/1A}$ AGONIST, RU 24969, FACILITATES THE ACQUISITION OF MDMA SELF-ADMINISTRATION.

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Aims: The primary aim was to determine the effect of repeated exposure to RU 24969 on the acquisition of MDMA self-administration in rats.
Methods: RU 24969 (3.0 mg/kg), or vehicle, was administered twice per day during a three day pretreatment phase. Acquisition of MDMA self-administration was then tested in some groups. Other groups were tested to determine effects of the pretreatment on RU 24969-produced hyperactivity or adipsia.
Results: RU 24969 pretreatment increased the percentage of rats that met a criterion for acquisition of MDMA self-administration and the latency to acquire self-administration was markedly decreased by the pretreatment. Repeated exposure to RU 24969 failed to alter the adipsic response to RU 24969, but produced a decrease in the motor activating effects of the drug.
Conclusions: Because we have previously shown that RU 24969-produced adipsia reflects activation of the 5-HT$_{1B}$ receptor, while the locomotor response was due to 5-HT$_{1A}$ receptor activation, the data are consistent with the hypothesis that downregulation of 5-HT$_{1A}$ receptors facilitates the reinforcing effects of MDMA.
Financial Support: Dane Aronsen received funding from a VUW PhD scholarship and a 2015 Claude McCarthy Fellowship for travel expenses.

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DESIGN CONSIDERATIONS FOR INTEGRATING VIDEO INTO TABLET-BASED MHEALTH INTERVENTIONS ADDRESSING HIV AND SUBSTANCE USE.

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Aims: To improve the reach and effectiveness of tablet-based mHealth interventions.
Methods: mHealth interventions via tablet computer can reach patients who might otherwise be missed, and video may be especially effective with low literacy populations. However, tablets may not readily accommodate video. Understanding technical limitations, and how to address them, can potentially lead to more effective mHealth tools. The following considerations apply to interventions addressing HIV, drug use, and other behavioral health issues.
Consider the Internet connection. Many tablets require Internet connections to play video. Older iPads could *cache*, or store video, after an initial Internet connection. This meant they could play video *offline* beyond the reach of WIFI or mobile broadband. Newer iPads and Android tablets do not play video without an active Internet connection. This may limit the locations in which they can be used for mHealth. Tablets that use the Windows operating system can play video from removable media, i.e. an SD card, so they can be used in locations where Internet access is not available.
Develop a hybrid design. Flexible mHealth interventions can be created to work in situations where Internet connections may available sporadically or not at all. Interventions that can play video without a connection and then transmit data asynchronously when an Internet connection is available (possibly in another location) may address barriers to access.
Think about scale. Successful mHealth interventions can be offered simultaneously in many locations. Designing for multiple contingencies may facilitate wider adoption.
Evaluate using mixed methods. Examining how many participants complete an intervention, and whether participants stop at the same point, may provide measures of feasibility. Qualitative interviews with participants and staff may inform more successful future interventions.
Conclusions: Technology issues that could otherwise emerge as barriers can be used to optimize designs for a specific setting, population, or behavioral health issue.
Financial Support: NIDA R34DA037129; P30 DA011041

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MARIJUANA USE TRAJECTORIES DURING COLLEGE PREDICT HEALTH OUTCOMES NINE YEARS POST-MATRICULATION.

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Aims: Amid increasingly tolerant policies toward marijuana use, information about its long-term health effects is critically needed. We hypothesized that marijuana use trajectories during college would predict health outcomes 9 years after college entry.
Methods: Data were analyzed from a 10-year study of 1,253 college students interviewed annually. Marijuana use frequency during the six years following college entry was categorized into 6 distinct trajectories (Non-Use, Low-Stable, Late-Increase, Early-Decline, College-Peak, Chronic) using growth mixture modeling. Nine health outcomes assessed in Year 10 (modal age 28) were regressed on a group membership variable for the 6 marijuana trajectories, holding constant Year 1 health, demographics, and two additional trajectory group membership variables for alcohol and tobacco.
Results: Marijuana trajectory groups differed significantly on 7 self-reported outcomes (functional impairment due to injury, illness, or emotional problems; psychological distress; subjective well-being; and service utilization for physical and mental health problems), all *p*s<.001, but not on general health rating or body mass index. Both the Late-Increase and Chronic groups fared significantly worse than the Non-Use group on most outcomes, and the Late-Increase group fared significantly worse than the Chronic group. Despite converging to low levels of marijuana use by Year 6, both the Low-Stable and Early-Decline groups fared significantly worse than the Non-Use group on several outcomes. The College-Peak group had better well-being and distress ratings but worse physical health outcomes than the Non-Use, Low-Stable, and Early-Decline groups.
Conclusions: Results indicate that even occasional or time-limited marijuana use may have adverse effects on physical and mental health, perhaps enduring after several years of moderation or abstinence. Young adults whose marijuana use escalates in their early twenties may be at especially high risk for adverse outcomes.
Financial Support: NIH R01DA014845

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PREVALENCE AND CORRELATES OF DRUG USE IN WOMEN PATIENTS OF COMMUNITY HEALTH CENTERS IN TIJUANA, MEXICO AND LOS ANGELES, USA.

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Aims: To describe the prevalence of, and sociodemographic and health correlates associated with, illicit drug use and nonmedical use of prescription drugs among women patients of community health centers in LA and Tijuana.
Methods: Adult patients 18 and over who came in for a visit were asked to take a self-administered version of the WHO ASSIST (Alcohol, Smoking and Substance Involvement Screening Test) on a touchscreen tablet computer. We present an adjusted multinomial regression model for levels of drug use and was limited to those born in the US or Mexico.
Results: All Tijuana women were Latina as were 94% of LA women. Most were 45 years old or younger. 20% had ever used drugs. Living in LA was associated with a higher prevalence of drug use. As compared to women who were born and lived in Mexico, women living in Los Angeles who were born in the US had the highest odds of risky drug use (OR=20, CI=13.61-109.67), women living in the US but born in Mexico also had higher odds of risky drug use (OR=2).
Conclusions: While women in both cities were similar in terms of their cultural origins, living in LA was associated with higher prevalence of most substance use indicators. These differences point to the importance of the social environment in shaping the epidemiology of substance use. The results are consistent and extend to those of the general and immigrant populations. It is imperative to develop and evaluate strategies to detect the at-risk women population as early as possible and offer them preventive strategies. The primary care centers are places for early detection and implementing prevention services, especially for women where drug use prevention should be included as part of routine reproductive healthcare.
Financial Support: NIDA DA 022445, NIDA 3P30DA027828-02S1 and -02S2

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ASSOCIATION BETWEEN DRUG USE AND SUICIDAL IDEATION AND ATTEMPT AMONG AT-RISK PRIMARY CARE PATIENTS.

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Aims: The purpose of this study was to assess associations between drug use and suicide-related thoughts and suicide attempts among veterans who received a comprehensive assessment of psychiatric symptoms after referral from primary care.
Methods: Veterans who screened positive for depression, PTSD, and/or substance use in primary care and were contacted via telephone to further assess psychiatric symptoms participated (N=3004). Veterans completed measures of suicidal thoughts and behavior, illicit drug use, and prevalent mental disorders.
Results: More than one-third of the sample reported that "life was not worth living" in the last year and 2% reported a suicide attempt in the past year. Bivariate analysis revealed that illicit drug use was significantly higher among those with increased suicide-related thoughts (5.7% vs. 3.0%, p<.0001), but not in multivariate analyses adjusting for mental disorders. However, in the multivariate analyses of past-year suicide attempts, Veterans who reported illicit drug use in the last year were over three times more likely to have attempted suicide (Odds ratio=3.36, 95% Confidence Intervals=1.41-7.99).
Conclusions: After adjusting for mental disorders and other covariates, there was a strong association between illicit drug use and suicide attempt, but not suicide-related thoughts. The findings are potentially attributable to the unique contribution of illicit drug use to impulsive suicidal behavior, but not to more enduring suicidal thoughts that are mediated by symptoms of depression and other mental disorders.
Financial Support: This work was supported, in part, by the Advanced Fellowship Program in Mental Health Illness Research and Treatment, VISN 2 Center of Excellence for Suicide Prevention at the Canandaigua VA Medical Center, and the Mental Health Illness Research, Education, and Clinical Center at the Philadelphia VA.

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IMPULSIVITY AND MARIJUANA DEMAND AMONG FREQUENT MARIJUANA USERS.

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Aims: Aims: Distinct impulsivity domains, including traits and delay discounting, have been implicated in the development of drug dependence. Another determinant of addictive behavior may be drug demand, or high perceived drug value. Little is known about the relationship between these risk factors and their association with cannabis dependence. This study explored associations among marijuana demand, delay discounting, trait impulsivity, and cannabis dependence symptoms.
Methods: Methods: Trait impulsivity (BIS-11) and demand indices from a Marijuana Purchase Task (MPT) were completed by participants at baseline (*n*=99, 37.4% female, 15.2% cannabis dependent); a delay discounting questionnaire was completed twice following administration of a placebo and 2.8%THC cigarette on different days.
Results: Results: Increases in discounting from placebo to marijuana sessions (β=1.09; sr^2=0.06; p<.05) and greater persistence in marijuana purchase at high prices (MPT breakpoint) were independently associated with greater number of current DSM-IV cannabis dependence symptoms (β=0.05; sr^2=0.05; p<.05). Together, change in discounting (β=1.29; sr^2=0.09; p<.01), trait impulsivity (β=0.03; sr^2=0.17; p<.0001), and breakpoint (β=0.06; sr^2=0.05; p<.05) predicted current DSM-IV symptoms ($F(3,79)=10.76$, $p<0.0001$, $R^2=0.29$). Change in discounting was negatively correlated with breakpoint (*r*=-.27) and trait impulsivity was not associated with discounting (*r*=-.005) or breakpoint (*r*=.02).
Conclusions: Conclusions: These results provide support for demand, discounting, and impulsivity as independent risk factors for cannabis dependence symptomology. These findings signal the importance of considering related yet distinct pathways in the development of addiction.
Financial Support: 2T32AA007459 (Aston), R03DA27484 (Metrik, Knopik), and K23AA016936 (MacKillop)

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FACTORS ASSOCIATED WITH HISTORY OF DRUG AND PSYCHIATRIC TREATMENT AMONG ACTIVE HEROIN USERS.

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Aims: Access to care is a major contributor of health among heroin users. It is important that we identify factors that may act as barriers to drug abuse and psychiatric treatment. This study assessed several variables (e.g., race, age, mental status) that may affect history of care among active heroin users, then sought to identify which of these variables were associated with previous exposure to treatment.
Methods: Data were obtained from self-report questionnaires and clinician-administered inventories of the Opioid Research Laboratory that recruits active heroin users for research. The variables of interest were tested with a regression analysis to identify which were associated with prior drug and psychiatric treatment.
Results: Data from 69 heroin users were used in this analysis and included several racial groups (49% Afri-Amer, 29% Latino, 20% Caucasian, 2% Amer-Indian). On average the sample was 44.9 years of age, used 5.5 bags of heroin per day, and had been using heroin for 17.3 years. 43% were also abusing stimulants, and 49% alcohol. The average mini-mental score was 28.9 (of 30). When entered into the regression model, only years of heroin use and co-occurring stimulant use were positively associated with history of drug treatment (p's<0.01). IN heroin use was the only variable found to be significantly associated with previous psychiatric treatment (p<0.01).
Conclusions: Co-occurring abuse of cocaine may lead heroin users to seek drug abuse treatment, possibly due to added financial burden. Although psychiatric symptoms did not differ between IN and IV heroin users, history of psychiatry treatment did, possibly indicating a difference in accessibility of or willingness to initiate treatment. This study suggests that there may be unique factors affecting the healthcare of active opioid abusers.
Financial Support: NIDA grants: DA016759, DA030446, and DA035161

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VALIDITY OF THE EATING SECTION FOR THE MODIFIED ADDICTION SEVERITY INDEX.

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Aims: To assess the validity of the Eating section of the modified Addiction Severity Index (mASI).
Methods: Within the Aquitaine Addiction Cohort (an ongoing cohort of addiction treatment seeking patients) we selected participants who reported at least one day of food problem past 30 days at intake; and randomly selected participants who did not report food problem but sought treatment in the same time period. They were assessed with the mASI, a craving scale, DSM-5 criteria for eating disorders and putative Food Addiction (FA) criteria modeled on DSM-5 substance use disorder criteria, and Body Mass Index (BMI) was calculated.
Results: 313 subjects were included, 46.2% males, 40.9 y.o. (SD=10.9), seeking treatment for alcohol (24.0%), polysubstance (22.0%), cannabis (11.2%), tobacco (10.5%), opiates (7.3%), cocaine (1.9%), eating disorder (11.8%), gambling (5.8%). Although a minority sought treatment for eating disorder, 49.5% reported at least one day of eating problem past 30 days, They were more likely women (c^2= 60.58, p<.0001), younger (t=2.92, p=.004), and more likely to exhibit an abnormal BMI (c^2= 6.78, p=.03). Subjects who received an Eating severity score of the mASI higher than 4 (need for additional treatment) reported significantly more days (t=16.79, p<.0001) and more years of food problem (t= 11.44, p<.0001), were more bothered by food problem (t=25.19, p<.0001), and were more likely to report craving for food (c^2= 9.85, p=.002). They met significantly more often DSM-5 eating disorder diagnoses (c^2= 166.34, p<.0001) and FA criteria (c^2= 7.62, p=.006).
Conclusions: The mASI appeared to be a useful and valid tool to evaluate eating behavior in substance-related or addictive disordered patients.
Financial Support: France (PHRC 2006, MILDT 2010), Brazil (CSF, CNPq, CAPES)

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SEQUENCES OF SUBSTANCE USE INITIATION AMONG ADOLESCENT NONMEDICAL USERS OF PRESCRIPTION OPIOIDS AND STIMULANTS.

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Aims: Aims: Researchers have argued that youth tend to initiate nonmedical use of prescription stimulants after initiating other types of substance use. This research project tests the hypothesis that adolescent nonmedical users of prescription opioids (NMUPO) or stimulants (NMUPS) are equally likely to initiate such use after other types of substance use as compared with before or concurrently.
Methods: Methods: Retrospective data were gathered between 2009-2012 from Detroit area secondary school students (n=5185). Modal age at last assessment was 17 years. Characteristics of the study sample were: 49.6% female; 60.7% white, 33.8% black, and 5.5% Hispanic and other. One-sample chi-square tests examined whether adolescents were equally likely to start NMUPO or NMUPS before or at the same age as another substance, compared to at least one year in age after.
Results: Results: A greater proportion of the 620 NMUPO initiates started NMUPO before or concurrent with: nonmedical use of prescription stimulants, anxiolytics, and sleep medicines; alcohol, tobacco, marijuana, LSD, other psychedelics, ecstasy, cocaine, heroin, or meth. NMUPO was not more likely to be initiated after other substances. A greater proportion of the 127 NMUPS initiates started NMUPS after alcohol, tobacco, and marijuana, but before or concurrent with: nonmedical use of opioids and anxiolytics; and LSD, other psychedelics, ecstasy, and cocaine.
Conclusions: Conclusions: Adolescents who started to nonmedically use prescription opioids or stimulants were at greater risk of initiating other types of substances at least one year in age later. This risk was observed across 11 classes of substances for opioid initiates compared to across 6 classes of substances for stimulant initiates. Earlier interventions may be needed to prevent adolescent nonmedical use of opioids and stimulants as part of a larger substance use prevention program. Research limitations will be discussed.
Financial Support: Financial Support: National Institutes of Health awards: R01DA024678, R01DA031160, T32DA007267, and 2UL1TR000433.

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HISTORY OF TRAUMA ASSOCIATED WITH POST-DEPLOYMENT RELATIONSHIP DYSFUNCTION IN MILITARY VETERANS WITH CONCURRENT PTSD AND SUBSTANCE USE DISORDERS.

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Aims: To examine correlates of interpersonal relationship dysfunction among Veterans with concurrent Post Traumatic Stress Disorder (PTSD) and Substance Use Disorder (SUD).
Methods: Participants (N=112) were treatment-seeking Veterans who met DSM-IV-TR criteria for current PTSD and SUD (average age = 41.2 years old, 91% male, 60.7% Army). Clinician-administered and self-report surveys were used to collect baseline data as part of a larger study: the Mini-International Neuropsychiatric Interview, Clinician-Administered PTSD Scale, Addiction Severity Index, Lite version, Dyadic Adjustment Scale, Interpersonal Support Evaluation List, and Deployment Risk and Resilience Inventory.
Results: Over half (56.3%, n = 63) of the sample experienced divorce or separation from a partner during post-deployment. Veterans who did vs. did not experience post-deployment divorce or separation reported significantly higher rates of lifetime physical abuse (45.2% vs. 19.1%, p = .005), lifetime sexual abuse (29.0% vs. 10.6%, p = .03) and being physically injured by another person (65.1% vs. 38.8%, p = .006). Rates of lifetime emotional abuse (43.5% vs. 30.6%, NS) and past-month suicidal ideation were similar across groups (59.7% vs. 51.0%, NS). Veterans who did vs. did not experience post-deployment divorce or separation smoked significantly more cigarettes per day (p = .03), endorsed more years of alcohol intoxication (p = .04), and reported a greater number of hospitalizations for medical problems (p = .03).
Conclusions: The findings reveal high rates of relationship dysfunction following deployment in PTSD/SUD Veterans. In addition, high rates of physical and sexual abuse, as well as increased substance use were associated with post-deployment relationship dysfunction. The findings provide useful clinical information and may help inform the development of effective treatment interventions for Veterans with PTSD and SUD.
Financial Support: NIDA R01 DA030143 (SEB)

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EXAMINATION OF THE BEHAVIORAL EFFECTS OF ORAL CANNABIDIOL ALONE AND IN COMBINATION WITH SMOKED MARIJUANA.

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Aims: Cannabidiol (CBD), a naturally occurring phytocannabinoid, is being explored as a pharmacotherapy for marijuana dependence. There is some evidence from the human laboratory that CBD displays limited abuse liability and mitigates the anxiogenic, psychotomimetic and performance-impairing effects of smoked marijuana. The aim of this laboratory study was to examine the pharmacodynamic profile of a dose range of CBD alone and in combination with smoked marijuana.
Methods: Healthy marijuana smokers (*n*=27) were enrolled in this multi-site, within-subject, double blind, placebo-controlled, randomized outpatient study. Eight 7.5 hr weekly sessions were completed during which oral cannabidiol (0, 200, 400, 800 mg) was administered 1.5 hrs prior to smoked marijuana (0, 5.6% THC). An array of participant-rated, performance and physiological measures was collected.
Results: Active marijuana reliably produced abuse-related subjective effects (high, good drug effect) compared to placebo marijuana ($p<.05$), but did not consistently produce aversive drug effects or impair performance on cognitive or psychomotor tasks ($p>.05$). CBD was placebo-like and did not produce signals of abuse liability. Further, CBD did not produce any measureable behavioral or performance effects and did not modulate any marijuana subjective effects ($p>.05$).
Conclusions: Oral CBD in doses up to 800 mg were safely tolerated in a population of frequent marijuana smokers. Previous correlational data suggested that CBD attenuates the performance-impairing and aversive subjective effects of marijuana; however, these effects were not observed here. Overall, CBD appears to have limited abuse liability, does not modulate the abuse-related effects of marijuana and produces overall placebo-like effects in a cannabinoid-tolerant population.
Financial Support: UL1RR033173; KL2TR000116; U10DA013732

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IDENTIFYING TREATMENT RESPONSE SUBGROUPS FOR ADOLESCENT CANNABIS USE DISORDERS.

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Aims: Response to treatment for substance abuse is typically heterogeneous across participants. The present study utilized cluster analysis to identify subgroups of treatment responders among adolescents enrolled in a randomized clinical trial evaluating behavioral treatments for cannabis use disorders.
Methods: Analyses were performed on a sample of 153 adolescents (ages 12-18) who met DSM-IV criteria for cannabis abuse or dependence. Cluster analysis groups individuals into categories based on pattern level (mean), scatter (variance), and shape. Clustering based on cannabis use at 5 time periods (intake, end of treatment, 3, 6, and 9 months post-treatment) was performed using Ward's minimum variance clustering and a squared Euclidean distance metric. Participants in the identified subgroups were then compared across a number of variables not involved in the clustering (e.g., demographics, psychopathology, cognitive functioning) to establish external validity.
Results: A 4-cluster solution was found based on statistical indices and visual inspection. These subtypes were: low users (n=81, low initial level of use and sustained decrease from intake); rapid relapsers (n=33, decreased use from intake to end of treatment followed by sharp increase); non-responders (n=20; consistently high level of use); and responders (n=19, decreased use from intake to 3 months post-treatment followed by gradual increase). Comparisons across clusters supported external validity. Age, for example, was disproportionate across clusters, $\chi 2=43.84$ (18), $p<.001$, with older adolescents more likely to be non-responders; associations among other variables will be discussed.
Conclusions: Cluster analysis empirically identified different patterns of treatment response over time and revealed heterogeneous trends with adolescent cannabis use disorders. Investigating subgroups of participants provides insight into study outcomes, and variables that demonstrate relations across clusters have potential utility to enhance treatment through tailoring.
Financial Support: Research supported by T32DA037202 and R01DA015186.

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CIGARETTE SMOKING AND THE ONSET AND PERSISTENCE OF PANIC ATTACKS DURING MID-ADULTHOOD IN THE UNITED STATES: 1994-2005.

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Aims:
The current study examined the relationship between daily cigarette smoking and risk of onset and persistence of panic attacks over a 10-year period among adults in mid-adulthood in the United States, and whether quitting reduced the risk for subsequent panic attacks.
Methods:
Data were drawn from the Midlife Development in the United States Survey (MIDUS; N=2,101), a nationally representative sample of adults ages 25 and over at baseline (Wave I; 1994) and who were followed up ten years later at Wave II (2005). Logistic regressions were used to evaluate the associations between smoking status and the onset and persistence of panic attack after controlling for demographic characteristics and substance use problems.
Results:
Daily smoking in 1994 (OR=1.9 (1.1-3.3)) and persistent daily smoking (in 1994 and 2005) (OR=2.6 (1.4-4.8)) were associated with a significantly increased likelihood of panic attacks in 2005. However, for daily smoking in 1994, the association did not remain significant after controlling for substance use problems. Moreover, abstinence from smoking significantly reduced the risk of new onset panic attacks by 2005 (OR=0.6 (0.4-0.97)) and persistence of panic attacks (in 1994 & 2005; (OR=0.2 (0.1-0.5)).
Conclusions:
The present data provide novel evidence about the role of smoking in the onset and persistence of panic attacks among those in mid-adulthood. Specifically, smoking is associated with an increased risk of panic attacks and quitting helps to reduce such risk. These findings suggest that targeting smoking may also help reduce the risk of panic attacks.
Financial Support: Work on this study was funded in part by grant #DA20982-A1 (Dr. Goodwin) from NIDA.

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POPPERS: A SYSTEMATIC REVIEW.

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Aims: The aim of this work is to make a review of the literature on volatile nitrites considering the clinical, epidemiological and historical questions in order to facilitate the understanding of this substance which has been increasingly used nowadays.
Methods: We screened all articles that discuss any aspect related to nitrite use, published on scientific sites such as MEDLINE, Web of Science, Cochrane, and SCIELO. Our search strategy included the terms *poppers* OR *nitrites*, to be as broad as possible.
Results: Our search resulted in 169 articles. Twenty six papers were excluded and 143 went under a thorough analysis. Papers were divided into five groups, considering their common characteristics, which were: literature review, epidemiology, HIV/AIDS, side effects and miscellaneous (that did not belong to the previous groups). This work showed the need of deep studies on inhalants in general, and on poppers in particular, because of their relation to important side effects, such as metahemoglobinemias and blindness, and risk situations, both sexual and related to the use of other drugs. The studies on poppers pointed out the evolution of what is known about HIV/AIDS and how the risk factor may influence the scientific thoughts of a time. The use of volatile nitrites is getting more frequent nowadays, and should be considered in the clinical practice.
Conclusions: This work showed the need of deep studies on inhalants in general, and particularly on poppers, because of their relation to important side effects and risk situations, sexual or related to the use of other drugs. The studies on poppers, in an interesting way, pointedout the evolution of what is known about HIV/AIDS and also, how the risk factor may influence the scientific thoughts of a time. The use of volatile nitrites is getting more frequent nowadays, and should be considered in the clinical practice. This study is relevant because it gathers what has already been published on a subject which is becoming more current each day.
Financial Support: No financial support

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INCIDENT NON-MEDICAL USE OF PRESCRIPTION OPIOIDS IS ASSOCIATED WITH HEROIN INITIATION AMONG U.S. VETERANS: A PROSPECTIVE COHORT STUDY.

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Aims: We assessed whether incident non-medical use of prescription opioids (NMUPO) is associated with heroin initiation among U.S. veterans in primary care who had no prior history of NUMPO or heroin use.
Methods: The Veterans Aging Cohort Study (VACS) is a prospective cohort study of HIV-infected and uninfected veterans in care. We restricted our analysis to subjects who reported no prior history of injection drug use, heroin use, or NMUPO at baseline. Incident NMUPO and date of heroin initiation were ascertained from surveys administered over six follow up interviews (2002-2012). We used Cox regression to examine the relationship between incident NMUPO and heroin use, adjusting for HIV status, sociodemographics, pain interference, receipt of chronic opioid therapy, and previous diagnosis of PTSD and major depression.
Results: Among 3,430 eligible participants, the mean age was 49.7 (SD = 10.6) and 2,203 (66.4%) were African American. Over the 10-year study period, the incidence of heroin initiation was 2.76 per 100 person-years, and greater among those who reported any NMUPO (log-rank p-value < 0.001). In a multivariable model, incident NMUPO was positively and independently associated with heroin initiation (adjusted hazard ratio = 5.25, 95%CI: 4.20, 6.57).
Conclusions: NMUPO is a strong risk factor for heroin initiation among veterans seen in primary care. Most reported new onset NMUPO prior to or concurrent with heroin initiation. Strategies are needed to identify and address NMUPO among veterans.
Financial Support: K12DA033312, U01AA13566, K23AG00826, VA HSR&D CDA08-276, F31DA035567

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GENETIC AND ENVIRONMENTAL INFLUENCES ON INITIATION AND HEAVINESS OF SMOKING FROM ADOLESCENCE TO ADULTHOOD.

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Aims: Previous studies examining the genetic architecture of adolescent cigarette use initiation and its relationship to subsequent heaviness of cigarette use have been primarily focused on adults and few have examined developmental changes during a vulnerable time for the initiation of substance use. The aim of the present study was to examine how additive genetic, shared and non-shared environmental influences on smoking initiation and smoking quantity change across adolescent and young adult development.
Methods: Data came from 740 adolescent twin pairs (age14-33) from the National Longitudinal Study of Adolescent to Adult Health. We ran a series of age specific causal-contingent-common pathway models to examine whether additive genetic, shared and unique environmental influences on smoking initiation are shared with those on smoking quantity, if sex differences exist in the role of genes and environment and if their contributions change across adolescence and into young adulthood.
Results: For each age group, we fitted saturated models and tested twin model assumptions. The results indicate no sex differences in the genes/environment contribution to the variance in smoking initiation for males and females or in the magnitude of additive genetic effects. For the youngest age group (ages 14-15) genetic and environmental influences on smoking initiation were independent of those that contribute to heaviness of smoking. During late adolescence (ages 16-17), the shared environment contributed to smoking initiation and to smoking quantity through the common pathway. In adulthood, however, genetic factors influenced smoking initiation and smoking quantity and their influence was correlated.
Conclusions: These findings provide evidence of the causal process underlying the liability to smoke. With age, there is greater overlap in the gene/environment factors that influence the initiation of smoking and the number of cigarettes that are smoked.
Financial Support: Research reported in this abstract was supported by the National Institute of Drug Abuse of the National Institutes of Health under award numbers: R01DA025109 and K01DA036681.

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CEFTRIAXONE ATTENUATES ACUTE COCAINE EVOKED MOTOR ACTIVITY AND DOPAMINERGIC NEUROTRANSMISSION IN THE DORSAL AND VENTRAL STRIATUM.

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Aims: The present studies tested the hypothesis that pretreatment with ceftriaxone disrupts acute cocaine-evoked dopaminergic neurotransmission in the nucleus accumbens.
Methods: Separate groups of adult male Sprague –Dawley rats (N=60) were pretreated with ceftriaxone (200mg/kg,ip ×10 days) and then challenged with cocaine (15mg/kg, ip). Motor activity, dopamine efflux (via *in vivo* microdialysis), or protein levels of tyrosine hydroxylase, dopamine transporter, and organic cation transporter were analyzed in the dorsal and ventral striatum.
Results: Rats pretreated with ceftriaxone and then challenged with cocaine displayed reduced locomotor activity (F1, 98 = 37.31; P <0.001) and striatal dopamine efflux (F1, 121 = 7.98; P= 0.016) compared with vehicle pretreated controls challenged with cocaine. Pretreatment with ceftriaxone also reduced levels of the dopamine transporter (t16=2.626P =0.0184) and tyrosine hydroxylase (t18=2.644, P=0.0165) in the ventral striatum (nucleus accumbens). Reduced cocaine-evoked dopamine was not rescued by GLT-1 blockade in the nucleus accumbens indicating that the effect of ceftriaxone on dopamine was not dependent on GLT-1.
Conclusions: The results of these studies are the first to demonstrate that ceftriaxone has actions on dopaminergic transmission in addition to its well-described effects of glutamate, and indicate that ceftriaxone attenuation of cocaine-induced behaviors produced by acute cocaine exposure is in part due to reduced dopaminergic neurotransmission in the ventral striatum.
Financial Support: Support: T32 DA007237 & P30 DA013429 & R21 DA030676

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VALIDATION OF THE REVISED MYSTICAL EXPERIENCES QUESTIONNAIRE IN EXPERIMENTAL SESSIONS WITH PSILOCYBIN.

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Aims: The Mystical Experiences Questionnaire (MEQ) was previously developed to evaluate discrete mystical-type experiences occasioned by the classic hallucinogen psilocybin. The 30-item revised MEQ (MEQ30) was previously psychometrically validated through factor analysis of retrospective accounts of profound experiences with psilocybin-containing mushrooms. We psychometrically validated the MEQ30 using data from experimental laboratory studies with controlled doses of psilocybin.
Methods: We applied confirmatory factor analysis to MEQ30 responses provided immediately after moderate/high oral psilocybin dose (≥ 20 mg/70 kg) sessions (n=184) from five laboratory experiments. We used structural equation modeling to regress MEQ30 factor scores on the rated intensity of drug effects and ratings provided 3 to 8 weeks post-session of persisting effects attributed to the moderate to high dose psilocybin session.
Results: Confirmatory factor analyses support the reliability and internal validity of the MEQ30. Structural equation models demonstrate the external and convergent validity of the MEQ30 by showing that latent variable scores on the MEQ30 positively predict persisting change in attitudes, behavior, and well-being attributed to experiences with psilocybin while controlling for the contribution of the participant-rated intensity of drug effects.
Conclusions: Validation of the MEQ30 in experimental data constitutes an important step in developing this questionnaire instrument for use in pharmacological studies of mystical-type experiences. Further experimental work should validate the MEQ30 in studies of mystical-type experiences encountered through other means. On the basis of our findings, we recommend use of the MEQ30 for future investigations of individual episodes of mystical-type experiences.
Financial Support: NIH T32DA007209, R01DA003889, the Heffter Research Institute, and the Council on Spiritual Practices.

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ALCOHOL AND DRUG USE AMONG PATIENTS OF HIV SERVICES IN HANOI, VIETNAM.

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Aims: In countries where the HIV epidemic is driven by drug use, early screening of drug use among patients of HIV services may be a useful first step in intervening to improve HIV clinical outcomes. This study describes prevalence of alcohol and substance use among patients of HIV services who were screened with ASSIST, the instrument developed by WHO.
Methods: 592 patients (62.3% males, 37.7% females) of one voluntary testing center (VCT, n = 200) and two HIV outpatient clinics (OPC, n = 392) were recruited. The study translated and used the instrument Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) to ask about their alcohol and substance use during their lifetime and 30 days before the screening. Patients recorded their responses on PC tablets that were specifically programmed for this study.
Results: Use of alcohol, amphetamine type stimulant (ATS), and opioid during past 30 days among VCT patients (66.8%, 13.1%, and 17.1%, respectively) was higher compared to OPC patients (60.4%, 5.33%, 6.85%). Higher percentage of VCT patients reportedly used alcohol at hazardous levels (36.7%) as compared to OPC patients (24.11%). This difference also applied to ATS, but not to opioid. Multivariate analyis showed that during past 30 days men had higher risk of using alcohol (aOR: 2.77; 95%CI: 1.73 - 4.43), ATS (aOR: 2.32; 95%CI: 1.12-4.81), and opioid (aOR: 3.87; 95%CI:2.1-7.14) than women. Unemployment and experiences with compulsory drug rehabilitation were factors that increase use of opioid (aOR: 5.79; 95%CI:3.42-9.81) and amphetamine (aOR: 2.66; 95%CI: 1.42-4.99).
Conclusions: Alcohol and substance use are major issues at both HIV testing and HIV care settings in Vietnam. It is essential for doctors and health care professionals to provide routine assessment of drug and alcohol use among patients, and provide effective intervention to address these problems.
Financial Support: This study was supported by a supplement to NIDA Grant DA032733

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PSYCHOSOCIAL SYNDEMIC AFFECTING WOMEN LIVING WITH AND AT-RISK FOR HIV.

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Aims: Women in the U.S. continue to be affected by HIV, particularly through heterosexual contact. High-risk sexual behaviors are hypothesized to be associated with syndemic, or mutually reinforcing, problems including childhood sexual abuse, emotional distress, illicit substance use, violence and financial hardship. We evaluate relationships between the aforementioned syndemic problems and the number of self-reported sexual risk behaviors (e.g., unprotected and transactional sex) over the past 6 months and interactions between problems. We hypothesized that violence would interact with substance use to predict rate of endorsed risk behaviors.
Methods: Using baseline data from a cohort of women with and at-risk for HIV (n=620; 52% HIV+), we conducted Poisson regression to assess the associations of syndemic problems with rate of risk behaviors and interactions between significant predictors, controlling for age and HIV-status.
Results: Endorsing illicit substance use in the past 6 months (Incidence Rate Ratio [IRR] = 1.5; 95%CI:1.4-1.6), reporting a history of childhood sexual abuse (IRR = 1.1; 95%CI:1.0-1.2), and history of physical violence as an adult (IRR = 1.1; 95%CI:1.0-1.2) were associated with greater rates of risk behaviors. Endorsement of both recent substance use and violence was associated with a 27% elevated rate of risk behaviors over the past 6 months (IRR = 1.3; 95%CI:1.1-1.5). HIV-status did not moderate this relationship.
Conclusions: The co-occurrence of substance use and trauma are important drivers of risk behavior among women. Together illicit substance use and violence are associated with a higher rate of risk behaviors, beyond either problem separately. Within a syndemic framework, interventions targeting substance use and trauma should be prioritized to more effectively reduce HIV-related sexual risk behaviors among underserved urban women with and at-risk for HIV.
Financial Support: R01DA13564 & T32AT00399

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SMOKING AND NON-ALCOHOL SUBSTANCE USE IN VETERANS WITH PTSD AND ALCOHOL USE DISORDER.

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Aims: To describe co-occurring non-alcohol substance use in veterans with PTSD and alcohol use disorder (AUD) entering controlled trials of topiramate.
Methods: Baseline psychological, alcohol and non-alcohol substance use (NASU) measures are reported for 77 veterans with comorbid AUD and PTSD entering trials of topiramate treatment. PTSD, anxiety, and depression, as well as smoking, non-alcohol substance use (NASU) and NASU disorder diagnoses (NASUDs) were calculated. Subjects with and without smoking or NASU were compared on alcohol use, PTSD, depression, and anxiety severity.
Results: Mean age was 50.4±12.6, 93.5% were male. 41.6% were Vietnam era and 23.4% were Iraq/Afghanistan veterans. All met criteria for DSM-IV alcohol dependence and PTSD. 58.4% had combat-related PTSD. Mean Clinician Administered PTSD Scale (CAPS) score was 77.9±17.2; mean Beck Depression and Anxiety scores were 22.2±12.3 and 24.4±11.5 respectively. During the past 90 days prior to screening, participants had on average 5.4 drinking days per week, 4.5 heavy drinking days per week and consumed 63.7 drinks per week and 12.9 drinks per drinking day. 57.1% were smokers and 41.6% reported NASU in the past 30 days: 36.4% cannabis, 16.9% cocaine, 5.2% amphetamines, and 3.9% opioids. Urine drug screens were positive for cannabis in 23.4%, cocaine in 6.5%, amphetamines in 3.9%, and opiates in 7.6%. 28.6% met SCID NASUD criteria. Compared to nonsmokers, smokers had more drinks per week (72.7 vs 51.4, p=.048) and more drinks per drinking day (15.7 vs 9.4, p=.011) in the past 90 days. Smokers did not have higher mean CAPS, BDI, or BAI scores than nonsmokers. Patients with NASU also had more drinks per week (74.1 vs 53.5, p=.05); but not higher CAPS, BDI or BAI scores than those negative for NASU.
Conclusions: Smoking and other non-alcohol substance use were related with higher amounts of alcohol use but not greater PTSD, depression and anxiety severity in veterans with PTSD and AUD entering pharmacotherapy clinical trials.
Financial Support: W81XWH-05-2-0094, W81XWH-11-2-0245, W81XWH-12-2-0137

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NEUROPHARMACOLOGY OF REPLACEMENT ANALOGS OF THE DESIGNER DRUG 3,4-METHYLENEDIOXYMETHCATHINONE.

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Aims: The abuse of synthetic cathinones, known as “bath salts” or “research chemicals”, is a public health concern. 3,4-Methylenedioxymethcathinone (methylone) is a popular drug that is now illegal, but new analogs are being marketed as replacements. The purpose of the present investigation was to examine the interaction of methylone analogs with transporters for dopamine (DAT) and 5-HT (SERT).
Methods: β-Keto-*N*-methylbenzodioxolylbutanamine (butylone) and β-keto-*N*-methylbenzodioxolylpentanamine (pentylone) were the analogs studied. In vitro assays were carried out in rat brain synaptosomes to assess drug-induced effects on transporter-mediated uptake and release. In vivo microdialysis was carried out in rat n. accumbens to assess drug-induced changes in extracellular dopamine and 5-HT.
Results: Methylone, butylone and pentylone were fully efficacious uptake blockers at DAT and SERT, but pentylone was more DAT-selective than the other drugs. Methylone was a substrate-type releaser at both transporters, while butylone evoked release at SERT but not at DAT. Pentylone failed to evoke release at either transporter. Intravenous administration of butylone (1-3 mg/kg) increased extracellular 5-HT more than extracellular dopamine in the n. accumbens, while pentylone (1-3 mg/kg) increased both transmitters to the same extent.
Conclusions: Each of the compounds examined displays a unique profile of in vitro transporter activity. Butylone has “hybrid” transporter effects, acting as a substrate at SERT but a blocker at DAT. Pentylone is a DAT-preferring uptake blocker which lacks substrate activity. Overall, the data show that increasing the α-carbon chain length of methylone creates compounds with reduced releasing activity, converting them to DAT blockers. All of the compounds elevate extracellular dopamine in brain reward circuits, suggesting the drugs possess a significant risk for abuse.
Financial Support: This research was generously supported by the Intramural Research Program of NIDA, NIH, DHHS.

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WITHDRAWN

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SOCIAL PROCESSING IN AGING COCAINE SMOKERS.

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Aims: Deficits in social processing, the neurobiological and psychological processes underlying social behavior, are documented in several psychiatric disorders. Although drug abusers often have social problems, little is known about their social processing capacities. We aimed to characterize dimensions of social processing in a growing group of drug users about whom little is known – aging, long-term cocaine smokers – relative to controls. Domains assessed included facial affect recognition and social threat/reward processing. Self and peer reports of daily social function were also collected. We expected social processing to be reduced in cocaine smokers relative to controls.

Methods: Healthy cocaine smokers (≥ 2x/week; use for ≥ 20 years), aged 50 to 60, completed a three-day inpatient stay to ensure abstinence before undergoing an fMRI scan including social reward and threat tasks, and a behavioral facial affect recognition task. Participants and a friend/relative provided an assessment of the participant's daily social function. Demographically-matched controls also completed these assessments. Data were compared with *t*-tests.

Results: Data collection is ongoing. To date, 21 cocaine smokers (17M; 4F; all AA) and 13 controls (10M; 3F; all AA) have participated. Initial analyses indicate that cocaine smokers less accurately identified facial sadness than did controls (p=0.04), with no difference in other emotions. Cocaine users also experienced more daily social problems, as indicated by both self (p=0.001) and peer (p=0.02) report. fMRI data are not yet available.

Conclusions: Results to date suggest that aging cocaine users have lower social cognition and more problems in daily social function than non-users. Deficits in social processing may contribute to functional difficulties, problems accessing relationships as alternative rewards, and reduced success in psychotherapy. Further characterization of social processing difficulties in cocaine users may lead to development of more targeted interventions.

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SUBSTANCE USE OUTCOMES OF GIRLS WITH ADHD IN A 10-YEAR FOLLOW-UP OF A PROSPECTIVE LONGITUDINAL STUDY.

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Aims: To compare differences in substance use among young women with different patterns of attention-deficit/hyperactivity disorder (ADHD) in a 10-year prospective follow-up.

Methods: A diverse childhood-ascertained sample of girls with (n=124) and without (n=86) ADHD was followed 10 years later (ages 17-24 years; 95% retention rate). Childhood ADHD status was measured via structured interview; adult hyperactive/impulsive (HI) symptom severity was measured by self- and maternal-report on a validated rating scale. Substance use was measured by clinician-assisted administration of the Substance Use Questionnaire, assessing onset, frequency, and quantity of substances (alcohol, nicotine, marijuana, other illicit drugs, misuse of prescription drugs) used in the last 12 months.

Results: Girls with childhood ADHD were more likely than girls without to try smoking cigarettes (p<0.01), to smoke more cigarettes when they smoke (p<0.05), to have been daily smokers (p<0.01) and to have seriously tried to quit cigarettes (p<0.05). Girls with persistent ADHD were more likely to be daily cigarette smokers (p<0.01), smoke more often (p<0.01), and smoke more cigarettes (p<0.05). In addition, girls with ADHD showing higher levels of adult HI symptoms consumed a more alcohol per drinking occasion (p = 0.05), drank alcohol more frequently (p < 0.05), binge drank more frequently (p < 0.05), were more likely to be drunk (p < 0.05) and were drunk more often (p < 0.05) than girls with lower HI symptoms. HI was also associated with earlier age of first marijuana use (p < 0.05), lifetime cocaine use (p < 0.05), selling stimulant medication (p < 0.05), using narcotics without a prescription (p < 0.05), and seeking drug treatment (p < 0.05).

Conclusions: Childhood ADHD and persistent ADHD are associated with smoking behaviors in girls; HI severity is associated with more severe substance use in girls. Future studies should examine symptom persistence and severity to identify young women who may be susceptible to negative substance use outcomes.

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NON-FATAL OVERDOSE AMONG RECENT VETERANS: LESSONS LEARNED FROM A MIXED METHODS ANALYSIS.

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Aims: This presentation focuses on veterans' experiences of non-fatal overdose in order to better understand and address overdose risk among the veteran population. Veterans who experience non-fatal overdose can teach us much about precursors and onset of overdose.

Methods: The project conducted 50 in-depth interviews with veteran overdose survivors, and has conducted 180 out of a planned 250 quantitative baseline and overdose risk assessments thus far with veterans who reported past month misuse of opioids (heroin and/or prescription opioids) recruited using venue based, chain referral sampling.

Results: Quantitative results from the baseline indicate that using opioids alone (46%), rx off label use (46%) and mixing drugs (43%) are the most common overdose risks veterans face. Qualitative findings reveal the mechanisms and processes underlying these risks and the challenges veterans face in these three risk categories.

Conclusions: Qualitative and quantitative data suggest veterans' experiences with overdose and overdose risk are associated with social factors such as isolation, and pharmacological factors such as poly substance use and off label use. This presents implications for outreach programs such as expanded opioid safety and naloxone provision programs targeting veterans, their peers and family members. It also highlights the need for a veteran "buddy system" and additional forms of support.

Financial Support: This research was funded in part by grants from the National Institutes of Health (R01 DA036754, R01 AA020178).

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SOCIAL SUPPORT, CANNABIS MISUSE, AND POST-DEPLOYMENT DEPRESSION IN RETURNING VETERANS.

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Aims: More than two million American soldiers have served in Iraq and Afghanistan, and returning home from deployment has proven to be a difficult task (Hinojosa & Hinojosa, 2011). Although social support may be a healthy means of relieving post-deployment distress (Campbell et al., 2007), marijuana use has become a common mechanism for coping with reintegration difficulties (Boden et al., 2013; Golub and Bennett, 2014) and is prevalent in returning veterans (Bonn-Miller et al., 2012). This study examined the associations between marijuana-related problems, DSM-IV cannabis dependence, and post-deployment social support and distress in OIF/OEF/OND veterans.
Methods: Returning veterans (n=152, mean age (SD)=32.30 (9.09); 93% male) who deployed post 9/11/01 completed self-report measures of current depression (CES-D), marijuana use problems (MPS), and perceived social support (DRRI). Structured Clinical Interviews for DSM-IV were conducted to determine past year cannabis dependence diagnosis.
Results: 41% of veterans reported marijuana use in the past year, and 28% reported use in the past month. Of past year marijuana users, 22% met criteria for DSM-IV cannabis dependence diagnosis. Post-deployment social support (B=-0.71, 95% CI[-0.84, -0.58], sr^2=0.43, p<.001), marijuana-related problems (B=2.31, 95% CI[0.76, 3.86], sr^2=0.03, p<.01), and number of current cannabis dependence symptoms (B=3.0, 95% CI[0.72, 5.28], sr^2=0.02, p<.05) independently predicted CES-D depression. Marijuana problems and dependence symptoms did not moderate the relationship between social support and depression.
Conclusions: Social support and marijuana-related problems and dependence were independently associated with depression. Findings suggest that veterans may benefit from increased social support as a way of coping with post-deployment distress. Engagement in interventions and treatments focused on reducing marijuana use may help improve post-deployment outcomes.
Financial Support: R01 DA033425 (Metrik, Borsari)

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SURVEYING LACTATION PROFESSIONALS REGARDING BREASTFEEDING AND MARIJUANA USE.

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Aims: Guidelines state that women who use illicit drugs should not breastfeed (ABM, 2009; AAP, 2012). While this recommendation has traditionally included marijuana, this drug's changing legal status and the limited scientific research regarding marijuana's effect on breastfeeding (Hale & Rowe, 2014) leave it unclear what recommendations lactation professionals make to clients who use marijuana. In addition, to our knowledge, there are no data estimating the prevalence of marijuana use among breastfeeding women, making it difficult to assess how significant a problem it is. To begin understanding this issue, we will (1) assess recommendations around breastfeeding and marijuana use and (2) calculate an estimate of the prevalence of marijuana use among breastfeeding women.
Methods: A convenience sample of lactation professionals who practice throughout New England and were attending the 2014 Vermont Lactation Consultant Association conference were offered the opportunity to complete a 5-item survey.
Results: Of 120 conference attendees, 74 completed the survey. Of these, 39% percent reported that they recommend continued breastfeeding because the benefits outweigh the harms. Another 43% said their recommendation depended on factors like the severity of maternal marijuana use. The remaining 18% reported recommending that a woman should stop breastfeeding if she cannot stop using marijuana. Participants estimated that 16% (1203/7843) of their breastfeeding clients in the past year used marijuana.
Conclusions: Lactation professionals vary widely in their recommendations to breastfeeding clients who use marijuana. The estimate of prevalence also suggests this is a relatively common issue. More research is needed to validate and assess the generalizability of these findings.
Financial Support: Funding: T32 DA00742-33, P50 DA036114

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ULTRAHIGH CHRONIC OPIOID THERAPY SUBJECTS: A POPULATION DESCRIPTION.

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Aims: Concerns regarding chronic opioid therapy (COT) are growing in the US. The trend of increased opioid prescriptions and misuse of those medications is contributing to this concern. High dose COT is associated with overdose, a form of misuse. An accepted definition of high dose COT is COT of >100mg morphine equivalents (ME)/day. However, many COT cohorts include patients receiving much higher doses. The population description of "ultrahigh" COT (>200mg ME/day) has not been fully defined. The objective of this study is to describe this population of ultrahigh COT subjects.
Methods: After IRB approval, we identified patients who received at least 3 consecutive, monthly opioid prescriptions during a 90 day period at the Cincinnati VAMC and defined them as COT patients. For each subject, we obtained patient demographic data and all ICD-9 diagnosis codes. We then determined the average daily dose of opioids in morphine equivalents (ME). Subjects were stratified by age, gender, tobacco use, body mass index (BMI), military sexual trauma (MST) history, and psychiatric diagnosis.
Results: Complete dosing data for 815 subjects was obtained. Of these, 51 (6.3%) met criteria for "ultrahigh" dose COT. The median (IQR) and mean (SD) age for this population was 58 (51, 62) and 57.9 (9.5), respectively. One female (1.96%) was in this population. Thirty-three (64.7%) were tobacco users. The median (IQR) and mean (SD) BMI for this population was 29 (25, 32) and 28.7 (5.8), respectively. In terms of psychiatric diagnosis, we found: 1 subject (1.96%) with schizophrenia, 1 subject (1.96%) with anxiety, and 2 subjects (3.92%) with a history of substance use disorder. No subjects were found with mood disorders, psychosexual diagnoses, or PTSD.
Conclusions: Among patients on COT, a substantial number are on "ultrahigh" opioid doses (defined as >200mg ME/day). Characteristics of this population have not been fully defined. This study supports the contention that further studies are needed to define this population and to clarify the needs and associated health implications of "ultrahigh" opioid use.
Financial Support: Research in Addiction Medicine Scholars Program, R25DA033211.

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CORRELATES OF SPECIFIC PERSONALITY AND ALCOHOL USE WITH NONMEDICAL USE OF PRESCRIPTION STIMULANTS IN COLLEGE STUDENTS.

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Aims: To identify personality predictors that might place a person at increased risk for nonmedical prescription stimulant (NPS) use.
Methods: Participants (N = 521; M age = 18.51; 34.8% male; 82.4% Caucasian) were recruited through a psychology research pool at a large southeastern university. Following consent, participants were directed to an external website (surveymonkey.com) to complete the survey. Participants completed demographics, AUDIT, Goldberg's Big 5, and answered questions about personal NPS use. Participation lasted one hour and participants were awarded class credit.
Results: Findings revealed that 16.7% of students reported lifetime NPS use with 72.1% reporting use in the past six months and 62.8% reporting future plans to use NPS. Approximately 8% of students who did not endorse NPS history stated they would likely use NPS in the future. Participants with a history and desire for future use were labeled as "at-risk." Demographic characteristics, including gender and Greek membership, correlated with risk status and used as covariates in all analyses. AUDIT scores were significantly higher for the at-risk group compared to the low risk group, $F(25, 494) = 5.01$, $p < .001$. At-risk students were more likely to know a person with NPS history comparatively, $F(2, 515) = 10.76$, $p < .001$.
Conclusions: Findings support prior research linking increased alcohol and NPS use, along with correlations between NPS, gender and Greek membership. With the knowledge that students who use NPS obtain the drugs from peers, findings suggest that at-risk individuals are more likely to abuse stimulants because of the increased acceptability of peer NPS use. Interestingly, Big 5 personality factors did not differentiate between the groups. Future research should continue to identify personality factors that correlate with NPS use to create help deter at-risk students from using.
Financial Support: No funding was received.

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OVERDOSE EDUCATION AND NALOXONE FOR PATIENTS PRESCRIBED OPIOIDS IN PRIMARY CARE: A QUALITATIVE STUDY.

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Aims: The rate of fatal pharmaceutical opioid poisonings has increased substantially since the 1990s. Naloxone is an effective opioid antidote that can be prescribed to patients for bystander use in an overdose. Primary care clinics represent settings in which large populations of patients prescribed opioids could be reached for overdose education and naloxone prescription to prevent overdose fatalities. We investigated the knowledge, attitudes and beliefs of primary care staff about overdose education and naloxone.
Methods: We conducted 10 focus groups across 3 large Colorado health systems: a network of community health centers, a managed care organization, and an academic medical center. A focus group guide was developed based on behavioral theory. Focus group transcripts were coded and analyzed for themes.
Results: We enrolled 56 participants, including 31 MDs, 8 nurses/NPs, 7 pharmacists, and 10 other staff members. Clinical staff had substantial knowledge gaps about naloxone and its use in outpatient settings. Themes emerged in three constructs: knowledge, barriers and benefits. There was uncertainty about who to prescribe naloxone to and a range of logistical barriers to its use in practice. Clinical staff expressed fears about offending patients and concerns about increasing risk behaviors in people prescribed naloxone. When considering naloxone, some providers reflected critically and with discomfort on their own opioid prescribing. These barriers were balanced by beliefs that prescribing naloxone could prevent death and result in safer opioid use behaviors.
Conclusions: Logistical barriers and attitudinal barriers among clinical staff will need to be addressed to enhance uptake of overdose education and naloxone prescription for patients prescribed opioids for pain.
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COCAINE USE AND SEXUAL RISK AMONG INDIVIDUALS WITH A SEVERE MENTAL ILLNESS: A NARRATIVE REVIEW.

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Aims: This review examined the literature on the relationship between cocaine use and high-risk sexual behavior among individuals diagnosed with a severe mental illness (SMI).
Methods: A literature search was conducted using the PsycINFO and PsycARTICLES databases. Articles were included if they reported sexual risk (vaginal or anal sex without a condom), cocaine use, were peer-reviewed, written in English, and included participants diagnosed with SMI (schizophrenia, schizoaffective, or bipolar disorder).
Results: The 8 articles that met criteria had a mean sample size of 122. Participants were predominantly male (63%), outpatients (7/8 articles), and had a history of homelessness (71%). Cocaine use was typically reported as either frequency of use or presence of a cocaine use disorder. Three studies collapsed condom use into a sexual risk composite variable. Cocaine use was collapsed into a general substance use variable in 4/8 articles. Studies that collapsed cocaine use into a composite variable consistently found that substance use was associated with elevated rates of high-risk sex. In contrast, 67% of studies that did not use composite variables for either cocaine or condom use showed that cocaine was unrelated to likelihood of high-risk sex.
Conclusions: The direct relationship between illicit drug use and risky sexual behavior observed in other populations appears to also occur among those with a SMI. However, methodological limitations of the literature, particularly retrospective, global association study design and proclivity for using composite variables, preclude stronger conclusions regarding the relationship between cocaine and high-risk sexual behavior.
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THE EVOLUTION OF ILLICIT OPIOID USE AMONG HIV-INFECTED OPIOID USERS IN RUSSIA (2004-2014).

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Aims: In Russia, opioid use had been mostly limited to heroin use since the 1990s, the onset of the current Russian opioid epidemic. However, in recent years, illicit use of opioids other than heroin has emerged (e.g., methadone manufactured in underground labs). This study provides data documenting the evolution of illicit opioid use among people living with HIV in St. Petersburg, Russia since early in the Russian HIV epidemic.
Methods: We examined data from four NIH-supported research studies conducted in St. Petersburg, Russia from 2004 to 2014. We included current HIV-infected opioid users from PREVENT (2004-2005, n=17), HERMITAGE (2007-2010, n=281), LINC (2013-2014, n=119) and ARCH (2012-2014, n=91) studies. Descriptive statistics were calculated for key demographic variables. Recent use (i.e., past 30 days) of heroin and other opioids was assessed in each cohort with either the Addiction Severity Index, Timeline Follow Back or modified Risk Behavior Survey.
Results: These studies included members of similar birth cohorts (mean age was 24.5 years in 2004 and 33.7 in 2014). Use of any illicit opioids other than heroin increased from 6% (95% CI 0.15% - 29%) in 2004-2005 to 30% (95% CI: 25% - 36%) in 2007-2010 to 73% (95% CI: 63% - 82%) in 2012-2014, whereas use of any heroin decreased from 100% (95% CI: 80% - 100%) in 2004-2005 to 96% (95% CI: 93% - 98%) in 2007-2010 to 65% (95% CI: 55% - 75%) in 2012-2014.
Conclusions: Among HIV-infected opioid users from St. Petersburg, Russia, many of whom were born around 1980, illicit use of opioids other than heroin appears to have eclipsed heroin use in the current era.
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EFFICACY OF COMPUTER AND THERAPIST BRIEF INTERVENTIONS FOR DRUG USERS.

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Aims: The effectiveness of screening, brief interventions, and referral to treatment (SBIRT) strategies for illegal drug users in the Emergency Department (ED) has not been established. Among patients at an urban ED, we examined the effectiveness of several motivational-based SBIRT strategies to reduce illegal drug use.
Methods: This study tested two ED-based SBIRT strategies, computer-delivered brief intervention (CBI) or therapist-delivered brief intervention (TBI), compared to Enhanced Usual Care (EUC). Randomization to these three conditions in the ED was fully crossed with randomization to a therapist-delivered "booster" session 3 months post-ED visit or a control condition. Outcomes were number of days using drugs, number of weighted-drug days, and number of days using marijuana, measured at 6 and 12 months post-baseline. We used negative binomial regression with generalized estimating equations (GEE) to evaluate intervention effects over time.
Results: 780 ED patients with drug use in the prior 3 months were randomized. Results of the negative binomial models found that TBI compared to EUC had significant effects on the number of days using drugs (Effect size: -0.24, 95% Confidence Interval (CI): -0.41, -0.07, p=0.04) and weighted drug-days (Effect size: -0.24, 95% CI: -0.41, -0.08, p=0.03). For the number of days using marijuana, both CBI and TBI had significant effects compared to EUC among patients with marijuana use at baseline (CBI Effect size: -0.17, 95% CI: -0.34, -0.01, p=0.04; TBI Effect size: -0.24, 95% CI: -0.42, -0.06, p=0.01). For all three main outcomes, receiving the "booster" session at 3 months was not associated with drug use level overall.
Conclusions: Results suggest that both computerized and therapist-delivered motivational brief interventions given to patients in the ED can be effective in reducing drug use.
Financial Support: R01 DA026029

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DOES TYPE OF DRUG LEAD TO QUICKER ONSET OF INJECTION?

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Aims: Injection drug use has serious health consequences. We need more information about factors related to injection onset, including whether some drugs lead to quicker injection use uptake. In the following, we examine factors associated with drug specific time-to-injection (TTI) among people who inject drugs (PWID).

Methods: PWID in California participated in a cross-sectional study on injection initiation from 2011 to 2013 (N = 777). Interviews included items on age at first use and age of first injection for heroin, methamphetamine, opiate prescription misuse, and powder cocaine among others. Drug-specific TTI was calculated by subtracting age at first use of a drug from age of first injection of that drug. For those who did not inject a drug, the injection risk period was calculated by subtracting current age from age at first use of drug. Descriptive statistics and retrospective survival analysis techniques were used to describe drug-specific TTI and to examine demographic factors associated with drug specific TTI.

Results: Injection onset was reported by 99% of heroin users, 85% of methamphetamine users, 80% of powder cocaine users, and 48% of opiate prescription users. Hazard ratios for first year injection onset by drug were: 1.39 for heroin (median survival time [MST]=0.61 years), 0.67 for methamphetamine (MST=1.00 years), 0.50 for powder cocaine (MST=2.98 years), and 0.23 for opiate prescription misuse (MST=16.98 years). Among powder cocaine and methamphetamine users, TTI was shorter for men (p=0.003, 0.02, respectively). Among heroin users, TTI was shorter for Latinos (p=0.01). Among methamphetamine and opiate prescription misuse users, TTI was shorter for whites (p=0.007, <0.001, respectively).

Conclusions: The first year of drug use generated the highest risk for transition to injection for all drugs. However, first year risk and TTI was much lower for heroin and methamphetamine users. Better understanding of drug-specific factors could lead to improved interventions to prevent injection initiation.

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A COMPUTATION OPPONENT PROCESS MODEL DESCRIBES AND PREDICTS COCAINE SELF-ADMINISTRATION AMONG NAïVE RATS.

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Aims: To develop, calibrate and validate a computational opponent process model to cocaine self-administration data in rats.

Methods: Outcomes. Numbers of injections per session and time between injections

Data. We used data from 2 30-day rat cocaine self administration experiments (Mihindou et al., 2011, 2013). Daily sessions lasted for 6 hours in one and 3 hour in another experiment.

Model. We used a control theory computational model (4 difference equations) that simulates self-administration controlled by an adaptive self-stimulating threshold (Newlin et al. 2012). The threshold is modeled as a function of both: the drug effect and the delayed opponent process (allostatic adjustment).

Calibration and analysis. We calibrated the model to a time series based on 6-hour sessions. We used a non-linear fit algorithm and mean square error (between the data and the model-generated trajectories) as the goodness of fit criterion. We used this calibrated model to predict the numbers of injections in the 3-hour session time series. We examined variance of times between the injections among 3-hour and 6-hour sessions.

Results: The model calibrated to the 6-hour session almost perfectly predicted long-term (after 5 days) numbers of injections in 3-hour sesions. In the first 5 days, experimental data showed qualitative differences in stabilization of the variances of times between injections between the 3-hour the 6-hour sessions. The patterns of increase in daily numbers of injections in the first 5 days were also qualitatively different (concave vs. convex). This differences could be potentially attributed to the longer time the rats needed to reach stable allostatic process (learn the effect of the drug). Model improvement is proposed to capture these differences.

Conclusions: A computational model of self-administration well describes and predicts long-term cocaine self-administration of initially naïve rats. Accounting for the initial learning of drug effects (first 1-7 days) is the next step in model improvement.

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A RANDOMIZED CLINICAL TRIAL OF A BEHAVIORAL INTERVENTION TO REDUCE OPIOID OVERDOSE RISK BEHAVIOR.

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Aims: Prescription opioid overdose represents a significant public health problem, but strategies to prevent overdose risk behavior have not been studied. This study compared a motivational enhancement-based brief intervention to an educational enhanced usual care condition in a clinical trial conducted in the emergency department (ED).

Methods: Participants were approached and screened via tablet computer while waiting in the ED and were eligible if they reported prescription opioid misuse in the prior 3 months; individuals with a prior overdose experience were purposely over-sampled (76%). In total, 204 patients were randomized, and 86% were retained at 6 months follow-up. The intervention was delivered during the ED visit by master's-level therapists. The two primary outcomes were composite measures of prescription opioid misuse and overdose risk behaviors. Poisson regression was used to account for the outcome measure distributions.

Results: Patients in the intervention condition reported lower levels of overdose risk behaviors at follow-up compared to controls; incidence rate ratio (IRR) = 0.78, 95% CI: 0.65-0.94. The intervention condition was also associated with significantly lower levels of prescription opioid misuse at follow-up compared to controls; IRR = 0.85, 95% CI: 0.74-0.99).

Conclusions: This study represents the first clinical trial of a behavioral overdose prevention intervention and indicates that a motivational enhancement-based approach can reduce prescription opioid overdose risk behavior. Because the effect sizes were relatively modest, future research should explore methods to amplify the impact of the intervention.

Financial Support: CDC grant R49 CE002099

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ASSOCIATIONS BETWEEN AGE AND CANNABIS USE PROBLEMS AMONG MEDICAL CANNABIS PATIENTS.

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Aims: 23 States and the District of Columbia have passed legislation allowing for the use of cannabis for those with qualifying medical conditions. Despite the increasing number of States legalizing medical cannabis in recent years, understanding of medical cannabis patients is limited, including the extent to which patients experience problems related to cannabis use. Moreover, young people may be particularly vulnerable for such problems. In this pilot study, we estimate the prevalence of problems related to cannabis use among medical cannabis patients, as well as examine potential age differences associated with the report of specific problems.

Methods: This study includes adults 18 years and older from a convenience sample of patients from one medical cannabis clinic in Michigan. Of the 370 individuals who were approached in the waiting area of the clinic, 348 (94.1%) consented to participate. This analysis includes the 288 (82.8%) participants who reported cannabis use in the past 3 months. Problems related to past 3-month cannabis use were assessed via a modified version of the World Health Organization's Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). Bivariate logistic regression models were used to evaluate associations between age and specific problems related to cannabis use in the past 3 months.

Results: Prevalence estimates of problems related to cannabis use in the past 3 months ranged from 9.3% for failing to control, cut down or stop using cannabis to 80.2% for having a strong desire to use cannabis. Significant age associations were detected for the problems of cannabis use leading to health, social, financial, or legal problems (Odds Ratio (OR)=0.96, 95% Confidence Interval (CI)=0.92, 0.99) and failure to do what was normally expected because of cannabis use (OR=0.96, 95% CI=0.93, 0.99), such that increasing age was associated with lower odds of each of the two problems.

Conclusions: Young adult medical cannabis patients may be more likely to experience cannabis-related problems than older patients.

Financial Support: Pilot funding from the University of Michigan and NIDA R01-DA033397

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HEROIN METABOLISM IN BLOOD AND NOT IN BRAIN IS CRITICAL TO ITS ACUTE EFFECTS.

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Aims: After intravenous (i.v.) administration heroin is rapidly converted to 6-monoacetylmorphine (6MAM) which slowly metabolizes to morphine. We have shown that 6MAM, and not morphine, mediates the acute heroin effects measured as increased locomotion in mice and striatal dopamine increase in rats. The present aim of study was whether 6MAM present in brain extracellular fluid (bECF) reflected metabolism from heroin that had crossed the blood brain barrier (BBB) or uptake of 6MAM formed from heroin in the blood.
Methods: Six Sprague-Dawley rats were inserted with two catheters, in the femoral vein and in the carotid artery, and with a 4 mm cerebral microdialysis probe aimed at the striatum. Heroin was given via the femoral vein, followed by frequent sampling of blood and microdialysate. In vitro studies were performed with freshly drawn rat and human blood, and with freshly prepared rat brain homogenate. Heroin was added, and incubations were performed at 37° C with frequent sampling. The samples were analyzed for opioids by LC-MS-MS. Kinetica v.5.1 was used for all pharmacokinetic calculations.
Results: Pharmacokinetic modeling showed that metabolic conversion of heroin to 6MAM in blood was far more rapid than its transfer to bEFC, rate constants 3.26 min^{-1} and 0.15 min^{-1}, respectively. The metabolic conversion of heroin to 6MAM in bECF was much slower than in blood. The transfer of 6MAM across BBB was similar to heroin. As found in vivo, in vitro experiments showed slow heroin metabolism in brain homogenates and rapid heroin metabolism in blood. Preliminary studies demonstrated heroin metabolism rates in human blood comparable to those in rat blood.
Conclusions: By pharmacokinetic analysis it could be estimated that approximately 90% of 6MAM in bECF mediating acute effects of heroin, originated from 6MAM that had been transferred from blood. Therefore factors influencing the formation/degradation of 6MAM in blood as well as sequestration of 6MAM in the blood compartment with e.g. antibodies, could change the acute effects of heroin, and possibly have a therapeutic potential.
Financial Support: NRC196621/V50

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INFLUENCE OF BUSPIRONE MAINTENANCE ON THE PHARMACODYNAMIC EFFECTS OF COCAINE AND SEXUAL RISK TAKING IN COCAINE USERS.

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Aims: Buspirone may have promise as a putative pharmacotherapy for cocaine dependence. Buspirone may also reduce impulsive sexual decision-making that underlies sexual risk-taking behavior, a significant risk factor for HIV infection among cocaine users. This study evaluated buspirone as a candidate cocaine pharmacotherapy. Buspirone was hypothesized to reduce the reinforcing effects of cocaine and improve impulsive risky sexual decision-making in cocaine users.
Methods: Nine current cocaine users (N=9) completed a double-blind, placebo-controlled, repeated-measures protocol in which the reinforcing, subject-rated, and physiological effects of placebo and intranasal cocaine (15 and 45 mg) were assessed during maintenance on placebo or buspirone (30 mg/day) in counterbalanced order. Sexual delay discounting was assessed following buspirone and placebo maintenance. Self-administration data were analyzed as the average maximum number of drug choices. Subject-rated and physiological outcomes were analyzed as time course. Sexual delay-discounting data were analyzed as average total area under the delay-discounting curve. All data were analyzed with one-tailed *t*-tests or repeated-measures ANOVAs with post hoc tests where appropriate.
Results: Cocaine functioned as a reinforcer and increased positive subject-rated effects and cardiovascular outcomes in a dose- and time-related manner. Buspirone was well tolerated alone and in combination with cocaine. Buspirone blunted cocaine-induced increases on cardiovascular indices and decreased impulsive sexual decision-making under select conditions. Buspirone did not impact the reinforcing and subjective effects of cocaine.
Conclusions: These data indicate that buspirone may be useful for managing impulsive sexual-risk behavior associated with cocaine use.
Financial Support: Grants R21DA034095, T32DA035200, K02DA031766, TL1TR000115.

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DAILY PATTERNS OF SUBSTANCE USE AND SEXUAL BEHAVIOR AMONG URBAN ADOLESCENTS AND EMERGING ADULTS.

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Aims: Daily process studies of young people's substance use and sexual behavior are limited, and often focus on college students, reducing generalizability to other at-risk groups. Among 16 to 27-year-olds, we examined daily associations between substance use and sexual intercourse. We hypothesized that poly-substance use would be related to increased likelihood of sex.
Methods: Participants (N = 224; M age=22, SD=2.5) completed surveys and a 90-day Timeline Follow-back interview at a follow-up visit for youth who initially came to an emergency room for assault-related injury (N=159) or other reasons (N=65) and had previously used drugs. Over half were male (53.1%) and African American (62.5%). Controlling for demographics, multilevel models assessed daily relationships among substance use and intercourse over 90 days.
Results: Over the 90-day period, participants had sexual intercourse on M=16.8 days (SD=23.7; range =0-90), for a total of 3,756 days of sex out of 20,160 total daily reports. Among 20,160 daily reports, participants' substance use included: 64.2% no use, 1.5% alcohol use only (AU), 31.3% single drug use only (SDU; 96.4% cannabis), and 3.0% poly-substance use (PSU, alcohol and at least one drug). Older age (OR = 1.02, p <.05) was related to having sex. Compared to non-use days, AU (OR = 1.11), SDU (OR = 1.06), and PSU (OR = 1.22) were related to having sex (ps<.05). Compared to AU, SDU and PSU were not significantly related to odds of reporting sex. Compared to SDU only, PSU was related to increased odds of sex (OR = 1.15, p<.001).
Conclusions: Substance use is associated with increased odds of having intercourse. PSU where alcohol is also involved may be related to increased odds of sex more than SDU (primarily cannabis). Future analyses will examine relationships between daily substance use and sexual risk behaviors (e.g., unprotected sex with casual and regular partners, separately).
Financial Support: NIDA# 024646, 036008

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EVALUATION OF THE ABUSE POTENTIAL OF AN HYDROCODONE EXTENDED-RELEASE BITARTRATE TABLET FORMULATED WITH ABUSE-DETERRENCE TECHNOLOGY IN NONDEPENDENT, RECREATIONAL OPIOID USERS.

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Aims: To examine the relative abuse potential of hydrocodone extended-release (ER) bitartrate tablets formulated with CIMA® Abuse-Deterrence Technology vs. immediate-release (IR) hydrocodone.
Methods: Healthy adults with a history of recreational opioid use who were not dependent on opioids were enrolled. Subjects able to tolerate a 45-mg dose of IR hydrocodone and differentiate the effects of hydrocodone from placebo were randomized to the double-blind, crossover portion of the study. Subjects received each of the following (all orally administered) separated by a 14-day washout: intact 45-mg hydrocodone ER tablet, finely crushed 45-mg hydrocodone ER tablet, 45-mg IR hydrocodone powder in a noncarbonated beverage, and finely crushed placebo. The primary endpoint was maximum effect (E_{max}) of "at the moment" drug liking based on Drug Liking and Effects Questionnaire (DLEQ) question 1. Overall Drug Liking Visual Analog Scale (VAS) score was a secondary endpoint.
Results: Forty-five subjects were evaluable for relative abuse potential. Intact hydrocodone ER was associated with significantly (P<0.001) lower drug liking vs. IR hydrocodone (DLEQ E_{max} 53.9 vs. 85.2 and Overall Drug Liking VAS 49.2 vs. 75.0). Crushed hydrocodone ER also was associated with significantly (P<0.001) lower drug liking vs. IR hydrocodone (DLEQ E_{max} 66.9 vs. 85.2 and Overall Drug Liking VAS 59.0 vs. 75.0). Drug liking after administration of placebo was comparable to that of intact hydrocodone ER (DLEQ E_{max} 53.2 vs. 53.9 and Overall Drug Liking VAS 51.1 vs. 49.2). No new safety signals were observed with hydrocodone ER.
Conclusions: When administered orally, the most common route of abuse, this hydrocodone ER formulation (intact or crushed) had a lower abuse potential compared with IR hydrocodone. When administered intact orally, liking scores for hydrocodone ER were similar to those of placebo.
Financial Support: Study sponsored by Teva Pharmaceuticals (Frazer, PA).

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DEVELOPMENT OF A BRIEF CANNABIS USE DISORDER SCREENING TOOL: THE CUDIT SHORT-FORM.

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Aims: The aim of the present study was to develop and test the diagnostic utility of a shortened 3-item version of the Cannabis Use Disorder Identification Test-Revised (CUDIT-R) for the purpose of brief and effective screening within primary care and other medical settings.
Methods: A short form of the CUDIT-R was developed using Item Response Theory (IRT) and traditional statistical methods, with data from two community samples of cannabis users representing two countries. Four item selection methods (Rasch Regression, Test Characteristic Curve, Logistic Regression, Discriminant Function Analysis) were employed to identify the most optimal 3-item shortened version. The diagnostic ability of the short forms was evaluated using receiver operating characteristic curves.
Results: Using a cut score of 2, the 3-item CUDIT-Short Form (reliability alpha = .66 sample 1; .80 sample 2) identified 78.26% of participants in sample 1 and 78.31% of participants in sample 2 who met DSM-5 criteria for CUD, with 98% agreement in sample 1 and 93% agreement in sample 2 with the full CUDIT-R on CUD classifications using a cut score of 13. Specificity was 76.70 and 78.00 in sample 1 and 2, respectively.
Conclusions: The CUDIT-Short Form (CUDIT-SF) may be useful in busy clinical settings for a stepwise screening. Further validation of this shortened version with larger samples and in different settings is warranted.
Financial Support: This work was supported by a VA Rehabilitation Research and Development (RR&D) Career Development Award-2 (CDA-2) granted to Dr. Heinz. Additionally, funding for the conduct of the present study (i.e. materials, study travel costs, participant payment) was provided by the San Francisco Patient and Resource Center.

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DESIGNING A HUMAN ABUSE POTENTIAL STUDY FOR A DRUG WITH A NOVEL MECHANISM OF ACTION.

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Aims: The FDA safety evaluation of a CNS-active new molecular entity under the 21st Century Review process requires that the drug undergo an abuse potential assessment. If there are positive signals from abuse-related preclinical studies or abuse-related adverse events in clinical studies, it is typically necessary for the drug to be tested in a human abuse potential study. When a test drug has a novel mechanism of action, there are scientific challenges in designing the protocol for such a study.
Methods: In a human abuse potential study, individuals with a history of recreational drug use are evaluated using abuse-related subjective measures in a crossover design in which they receive single doses of a test drug, a placebo, and a positive control drug. When the test drug has similarity in mechanism of action to FDA-approved controlled substances, protocol design will be based on standard procedures developed over the past 30 years. But when the test drug has a novel pharmacology, methodological choices may be complicated but will still hold to the principles delineated in the 2010 FDA *Guidance for Industry: Assessment of the Abuse Potential of Drugs.*
Results: This presentation will discuss the necessary considerations regarding each aspect of a human abuse potential study design when a test drug that has a novel mechanism of action. We will focus on issues such as appropriate selection of the positive control drug, the specific drug history of subjects, the subjective measures to be used, the number/gender/race of subjects, and adverse events that should be monitored.
Conclusions: It is critical to correctly design a human abuse potential study with a drug that has a novel mechanism of action, in order to adequately evaluate the safety of the test drug for regulatory purposes. Although there are challenges, an appropriate design with these unusual drugs is possible using the principles of regulatory science.
Financial Support: FDA

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BUPRENORPHINE-ASSISTED TREATMENT OF OPIOID-DEPENDENT ADOLESCENTS: STATE OF THE SCIENCE.

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Aims: Opioid dependence among adolescents is a significant public health issue; however, few evidence-based treatment programs for opioid-dependent youth exist. Clinical trials have shown buprenorphine (BUP) to be a promising medication for treating this cohort. To better inform treatment strategies, outcome data were compared from three randomized trials evaluating different BUP dosing strategies.
Methods: A systematic search of the literature revealed three trials that investigated this issue: Marsch et al. 2005, Woody et al. 2008 and Marsch et al. 2014 (unpublished). BUP duration, dosing strategies, and clinical outcomes were compared.
Results: Across the trials, 241 youth aged 15 to 24 were enrolled in treatment. Prevalence of injecting behavior ranged from 33% to 60% and use of heroin as the primary drug of abuse ranged from 41% to 82% (others primarily used prescription opioids). Two studies compared different taper strategies and one study compared a taper to maintenance. All studies provided behavior therapy. Length of treatment with BUP ranged from 14 to 84 days. BUP dose ranged from 4 to 24 mg. All studies favored either BUP treatment (compared to non-opioid treatment) or longer BUP treatment (compared to shorter) in promoting retention and abstinence (based on opioid negative urinalysis). Marsch et al. 2005 (n=36) observed 72% (28 day BUP taper) vs 39% (28 day clonidine taper) retained at 28 days and 64% vs 32% abstinent at 28 days. Woody et al. 2008 (n=152) found 70% (12 week BUP maintenance) vs 20.5% (14 day BUP taper) retained at 12 weeks and 57% vs 49% abstinent at 12 weeks. Marsch et al. 2014 (n=53) found 36% (63 day BUP taper) vs 17% (28 day BUP taper) retained at 63 days and 35% vs 17% abstinent at 63 days.
Conclusions: Though trial designs differ, these data suggest that longer treatment with BUP improves clinical outcomes for opioid dependent youth. These results may guide clinicians seeking to implement science-based treatment models for this population.
Financial Support: 1T32DA037202-01

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EARLY CAREER AWARD IN CHEMISTRY OF DRUG ABUSE AND ADDICTION.

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Aims: There are four research areas of particular interest for this program. They are as follows:
1.Development of new and innovative molecular probes/ligands for receptors, transporters, ion channels, enzymes or other justifiable neurobiological targets associated with drug addiction and pain.
2.The development of novel ligands for use in neuroimaging studies of addiction is sought (e.g., PET ligands for receptors, ion channels, enzymes, transporters, etc.).
3.The application of newer areas of research, and their associated technologies. This would include areas such as genomics, transcriptomics (e.g., microarrays), proteomics, metabolomics, or lipidomics in the discovery and identification of new endogenous ligands that play a role in the underlying mechanisms of substance use disorders (SUDs).
4.Research projects aimed at isolating, identifying, purifying and characterizing new lipid ligands, receptors, transporters, enzymes, etc. for the cannabinoid, vanilloid or other lipid-based targets, would also be supported.
Conclusions: — NIDA has a concerted effort to support basic chemists through the ECHEM program
— ECHEM awardees have been highly productive and the body of work has impacted the chemistry field
— ECHEM provides new-to-NIH basic chemists 4-5 years of milestone-driven support necessary to establish a productive research program in medicinal or biological chemistry
— ECHEM awards allow young investigators the chance to become more established basic chemistry PI's
— ECHEM resources provide investigators the opportunity to discover novel and innovative potential targets and probes for complex substance use disorders
Financial Support: Not applicable.

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OVEREXPRESSION OF GRP78 CONFERS PROTECTION AGAINST NEUROCOGNITIVE IMPAIRMENT IN HIV-INFECTED POLYDRUG USERS.

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Aims: Due to the high prevalence of stress and neurocognitive impairment (NCI) in HIV infected and drug abuse patients worldwide, there is a need to study these disorders and their impact on the immune response. We hypothesize that HIV polydrug users (PDU) will have greater impact in stress and NCI leading to Endoplasmic Reticulum (ER) stress related T-lymphocyte protein and pro-inflammatory cytokine expression. To test this hypothesis, we will 1) identify stress levels and cytokine profiling in NCI in HIV+ and HIV- PDU, 2) Detect biomarkers associated with NCI, stress and HIV Polydrug Use.
Methods: The initial population analysis in this study was: 10 HIV+PDU+ and 10 HIV-PDU+. NCI and stress were respectively measured physiologically (homocysteine and cortisol levels) and psychologically (MOCA, IHDS and modified PERI scale) in HIV+PDU. Immunoproteomics and flow cytometry were used to detect ER stress markers and cytokine profiling. Gene expression and western blots were used to validate the ER stress gene and protein expression.
Results: HIV+PDU+ had elevated cortisol levels (1.25 μg/dL) as compared to HIV-PDU+ (0.107 μg/dL). Moreover, HIV+PDU+ with no NCI had an increase expression of proinflammatory cytokines. Immunoproteomics revealed the overexpression of ER stress marker GRP78 in HIV+PDU+NCI- participants. To compare significant differences between the HIV+PDU+NCI-/NCI+ groups, two-way ANOVA statistical analysis with 0.05 p value was used.
Conclusions: Our findings showed that HIV infection in PDU contributes negatively in NCI, moreover, identification of GRP78 overexpression in HIV+PDUs with no NCI highlights its cytoprotective role and the identification of ER stress markers that may serve as candidates for early diagnostic of NCI HIV+, and polydrug use.
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CORTICAL THINNING IN ADOLESCENT FEMALES WITH SUBSTANCE AND CONDUCT PROBLEMS.

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Aims: Some individuals have onset of substance use disorders early in adolescence, develop multiple substance use disorder diagnoses, and have severe persistent courses. Although such youths exhibit more impulsivity, risk-taking, and problems of inhibition, relatively little is known about brain differences seen in such youths. This is especially true of adolescent females. The aim of this study was to investigate potential brain differences in cortical thickness.
Methods: We recruited 22 patients from a university-based treatment program for youths with serious substance and conduct problems and 21 community controls, all female and aged 14-19 years. We obtained T1 structural brain images using a 3T MRI scanner and assessed for group differences in cortical thickness across the entire brain using FreeSurfer's QDEC program and for 3 regions-of-interest (ROI) bilaterally (6 comparisons). These regions of interest were defined by the Desikan's atlas, chosen based on a priori predictions from the literature, and included: 1) medial orbitofrontal cortex; 2) rostral anterior cingulate cortex; 3) middle frontal gyrus. Age and IQ were entered as nuisance factors for all analyses.
Results: Using a vertex-level threshold of p=0.005 and Monte Carlo Simulation-determined cluster threshold (250mm^2) we demonstrated on whole-brain analyses that one region, including the left pregenual rostral anterior cingulate cortex extending into the left medial orbitofrontal region (356 mm^2 in size) was significantly thinner in patients. ROI analyses yielded no group differences.
Conclusions: Adolescent females with serious substance and conduct problems may have reduced cortical thickness in pregenual regions of the left rostral anterior cingulate and medial orbitofrontal cortex These regions have been associated with poor behavioral control in past studies.
Financial Support: NIDA grants DA009842, DA011015, R25DA033219, DA031761, DA034604, the Kane and Hewit Family Foundations.

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TRAJECTORIES OF NONMEDICAL PRESCRIPTION MEDICATION USE AMONG YOUTH.

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Aims: To identify trajectories of nonmedical prescription medication use (NMU) of four scheduled drug classes among youth.
Methods: We used an accelerated longitudinal design to examine changes in NMU over time among youth. Participants were middle- and high-school students enrolled in five schools in two school districts in Southeastern Michigan. Data were collected at four time points approximately one year apart. At each wave, all students in grades 7-12 were eligible to complete the web-based, self-administered Secondary Student Life Survey, which included questions about past 12-months NMU. The cumulative sample size was **5,217**. The sample ranged from 12.7 years to 17.9 years old; about 50% were female; 61% were Caucasian, and 34% were African American. Among participants in the prospective panel cohort, 75.2% completed all four waves of data collection.
Results: We conducted repeated measures latent class analysis (RMLCA) using the SAS PROC LCA procedure to examine longitudinal changes in past 12-months NMU from grades 7 to 12. Results from a series of RMLCAs indicated that a 2-class solution best fit the data: 1) the No NMU group had very low probabilities of any NMU across all grades, and 2) the Any NMU group showed a roughly linear increase in the probability of any NMU over time. Multiple groups RMLCA showed that the 2-class solution was invariant across gender and race/ethnicity. White females were more likely to be in the Any NMU class (20.4%), followed by non-white females (16.9%), white males (9.4%), and non-white males (9.3%). For white females and males, the probability of any NMU increased with age, with a sharp rise during the transition from middle- to high-school.
Conclusions: Results identified two subgroups of youth based on any NMU that were invariant by gender and race. Among the NMU class, patterns of change in NMU were discontinuous and suggest that school-based prevention efforts should start in middle school.
Financial Support: This research was supported by the National Institute on Drug Abuse, National Institutes of Health (research grant nos. R01DA024678 and R01DA031160).

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LIMITATIONS TO PARTICIPATION IN OPIOID MAINTENANCE TREATMENT IN EUROPE.

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Aims: Our aim was to identify areas of improvement for current Opioid Maintenance Treatment (OMT) approaches, by analysing European Quality Audit of Opioid Treatment (EQUATOR) data from 8 European countries (Austria, Denmark, France, Germany, Norway, Portugal, Sweden, UK).
Methods: A standardised face-to-face survey was administered to OMT patients (OMT-P) and active opioid user (AOU). Reasons for entering and staying out of OMT, rules pertaining to OMT, and factors facilitating OMT retention were compared between countries, and between OMT-P and AOU groups. Both groups were divided into those who never had OMT before [un-experienced OMT-P (n=573) and AOU (n=360)] and those who had been maintained at least once [experienced OMT-P (n=746) and AOU (n=377)].
Results: *Motives for starting OMT* vary distinctly ($p \leq 0.001$) between countries. Transnationally, experienced AOU reported concerns about their ability to follow treatment rules and negative treatment experiences as decisive *reasons for staying out of OMT*. Greater flexibility, less pressure to reduce their treatment dose and greater treatment structure were ranked significantly higher by experienced compared to un-experienced OMT-P as *factors that might facilitate treatment retention* ($p \leq 0.05$).
Conclusions: The major strength of this investigation was the homogenous methodology applied in all countries and the high external validity, which enabled new insights in variations between treatment systems and their impact on patient outcome. Results indicate, that treatment systems need to aim an optimal balance between flexibility and structure. In addition, standardised approaches that still permit tailoring treatment to individual patient needs are crucial to yield maximum benefit for patients, and reduce the considerable societal economic burden of addiction.
Financial Support: Financial support for implementation of the survey was provided by Reckitt Benckiser Pharmaceuticals.

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HOSPITAL ADMISSIONS FOR ALCOHOL USE DISORDERS IN PREGNANCY.

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Aims: To examine hospital admissions for alcohol use disorders (AUD) during pregnancy over a decade in NSW, Australia.
Methods: Population based cohort study using linked routinely collected population data from the NSW Perinatal Data Collection (PDC) and the NSW Admitted Patients Data Collection (APDC). All women who gave birth in NSW between 1 January 2001 and 31 December 2010 were included (n=560 987). All hospital admissions for AUD in pregnancy were identified. Descriptive statistics and logistic regression were used to calculate hospital admission rate, difference over time and to analyse risk factors associated with AUDs.
Results: In the ten year study period, there were 509 women with a total of 759 hospital admissions for any AUD diagnosis in pregnancy. The majority of the women (82%) and over half of admissions (61%) did not have a principal diagnosis of AUD. Admission rates for AUD remain low with no significant change over time for principal diagnosis of AUD.There was a decreasing but variable trend for all diagnosis of AUD in pregnancy. Readmission for AUD during pregnancy is high and admissions are accounted for by minority of women: approximately 10% of women had three or more admissions, accounting for 42% and 30% of admissions for principal and all diagnoses respectively. Factors associated with AUD in pregnancy include previous psychiatric disorder (including substance use), smoking, being unmarried, being over 30 and living in remote or regional locations.
Conclusions: Despite a reported increase in the proportions of women abstaining from alcohol consumption during pregnancy in the past decade, this data suggests little change among those most at risk. The rate of admission to hospital for a principal diagnosis of AUD during pregnancy has remained stable and the readmission rate is high. Improvements in the detection and treatment of women with AUD are required to reduce the impacts of alcohol exposed pregnancies.
Financial Support: The National Drug and Alcohol Research Centre at the University of NSW is supported by funding from the Australian Government.

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THE PARENT'S MODULAR TOOLKIT: DEVELOPMENT OF AN ONLINE CRAFT PROGRAM FOR PARENTS OF EMERGING ADULTS WITH SUD.

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Aims: The purpose of the Parent's Modular Toolkit is to provide information and training to parents of emerging adults based on Community Reinforcement and Family Training (CRAFT); an empirically-supported treatment (EST) which facilitates treatment entry in treatment-resistant individuals with substance use disorders. The online toolkit addresses the needs of parents who want to receive an EST, but do not have access to a CRAFT therapist. The toolkit consists of six modules addressing different skills. The first module provides an introduction to CRAFT and trains parents how to recognize the signs that their child is currently intoxicated. The Communication module trains parents in seven communication skills. The Roadmap module conducts a functional analysis to help parents outline their child's pattern of drug use, occasioning situations and reinforcers. The Positive Reinforcement module teaches parents to identify their child's desirable behaviors and then identify and deliver reinforcers when their child is sober or when a desirable behavior occurs. The Planned Ignoring and Natural Consequences module teaches parents to avoid interaction with their child when he or she is intoxicated and teaches them to allow negative consequences to occur. In the final module, parents will learn when and how to encourage their child to enter treatment. Modules contain videos of a therapist introducing key concepts and parent/child interactions to display the concepts. In addition, there are training exercises throughout modules to allow parents to practice skills and receive feedback. The online toolkit is being developed through a partnership with the Treatment Research Institute and Cadence Online, Inc.
Conclusions: Modules will be evaluated through focus groups with the goal of evaluating the completed toolkit through randomized, controlled trials.
Financial Support: P50DA027841 & Cadence Online, Inc.

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VARENICLINE FOR THE TREATMENT OF METHAMPHETAMINE DEPENDENCE.

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Aims: The primary objective of this study is to determine the efficacy of varenicline 1 mg BID for preventing relapse to methamphetamine (MA) use.
Methods: Treatment-seeking MA-dependent adults (n=52) were enrolled in this randomized, double-blind phase 2 clinical trial. Participants received varenicline or placebo for 9 weeks and adjunct cognitive-behavioral therapy, with some (n=18) also completing an inpatient detoxification during week 2. The primary outcome was continuous MA abstinence for two weeks at end of treatment (EOT), confirmed by urine drug screens during weeks 8 and 9. Secondary outcome was the treatment effectiveness score (TES), defined as the number of MA-free urine specimens provided during the medication phase (weeks 1-9). Analyses controlled for treatment group, inpatient detox, gender, age, and pre-treatment MA use.
Results: In the full sample, 17% achieved EOT and the mean TES was 8.4 (*SD*= 9.1). The mean TES was significantly greater (*IRR* = 2.18, $p < .001$) in participants that received inpatient detox (12.4, SD=9.3) compared to than those who did not receive inpatient detox (6.3, SD=8.4); but there was no difference in EOT. There was no significant improvement in EOT abstinence (*OR* = 0.05, $p = .61$) in varenicline (15%) compared to placebo (20%). Also, the mean TES was not significantly different (*IRR* = 1.05, $p = .61$) in varenicline (8.6) vs. placebo (8.1). There were no Serious Adverse Events and adverse events were mild to moderate and typical of methamphetamine clinical trials.
Conclusions: Varenicline was well tolerated, but was not efficacious for achieving MA abstinence in this Phase 2 clinical trial.
Financial Support: R01 DA030577

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CANNABIDIOL AND TETRAHYDROCANNABINOL INTERACTIONS ON ANTINOCICEPTION IN MALE AND FEMALE RATS.

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Aims: The purpose of this study is to determine how cannabidiol (CBD) and tetrahydrocannabinol (THC) interact on tests of acute nociception in male and female rats.
Methods: Adult Harlan Sprague Dawley rats, 60-90 days old were used (N=156). Intraperitoneal injection of vehicle or CBD (10 or 30 mg/kg) was followed 15 min later by an intraperitoneal injection of vehicle or THC (1.8, 3.2, 5.6 or 10 mg/kg). Rats were tested for antinociception using warm water (50 degrees F) tail withdrawal and paw pressure tests, at 15, 30, 60, 120, 240 and 360 min post-THC injection. Locomotor activity was also measured for 10 min after nociceptive testing at each time point.
Results: CBD alone produced no effects on tests of antinociception or locomotor activity. THC produced dose- and time-dependent antinociceptive and sedative effects; THC's effects were significantly greater in females than in males on the tail withdrawal test. Overall, CBD slightly enhanced THC's antinociceptive effects on both tail withdrawal and paw pressure tests and significantly enhanced THC-induced sedation (locomotor test). CBD enhancement of THC effect tended to be greater in males than in females, but sex differences in CBD-THC interactions were not statistically significant.
Conclusions: The present results suggest that, although THC tends to be more potent in female than in male rats, CBD enhancement of THC's effects is comparable between the sexes.
Financial Support: This research was supported by funds from the National Institute on Drug Abuse (DA016644, J. Wiley, PI).

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

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Aims: Adapting evidence-based protocols for dissemination to treatment programs while still retaining clinical effectiveness is a challenge. We translated 12-Step Facilitation (12SF) into a multimedia curriculum toolkit to help counselors deliver group sessions that convey 12SF core elements, and tested the toolkit's conceptual fidelity and clinical utility.
Methods: In this randomized, controlled, Pre-Post-6 month follow-up training study, counselors (N=87) were 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 and 6-mo follow-up observations of 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 = 307) for six months following toolkit exposure.
Results: TK counselors demonstrated very large Pre- to Post-Training adherence improvements in core curriculum techniques (F=55.49, p <.0001; d = 2.07) and moderate improvements in 12-Step content (F = 4.66, p = .011; d = .55) relative to counselors in the AC condition. These effects were consistent and durable at 6-months. There were no main effects of TK exposure on self-reported 12-step attendance and substance use. Among clients actively using at baseline (35%), TK clients reported significantly fewer drinking days (p = .024; d = .52) and a trend towards fewer drug use days (p = .076; d = .49) relative to AC clients at 3 months. These differences were attenuated and no longer significant at 6 months.
Conclusions: Multimedia toolkits are an easily disseminated approach to durably improve group counseling outcomes in community treatment for key client subgroups with minimal training and supervision.
Financial Support: NIAAA R01 AA017867

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PHYSICAL AND SELF-REPORTED RESPONSE AND THE PHARMACOKINETICS OF E-CIGARETTES COMPARED TO CIGARETTES IN SUBSTANCE-ABUSING PARTICIPANTS.

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Aims: The primary aim of this study was to examine the pharmacokinetics and the physical and self-reported response to nicotine in e-cigarettes versus cigarettes in substance-abusing sample.
Methods: Our sample included non-substance abusing (n=5), methamphetamine abusing (n=2), and prescription opioid abusing smokers (n=5). Participants from each group were randomized to either an e-cigarette or cigarette condition that lasted approximately 1 hour. After a 1 hour clearance phase, participants were exposed to the opposite condition for 1 hour. During each condition participants had repeated blood draws in addition to physical (e.g., heart rate, blood pressure) and subjective measures (e.g., visual analog scales (VAS)) taken.
Results: There was an 11.9 fold-difference difference in nicotine concentration change from baseline to C_{max} in the e-cigarette condition (11.3%) compared to the cigarettes condition (134.8%). There was a statistically significant difference (F=13.18, p<0.01) in heart rate such that participants exposed to cigarettes had a significantly higher heart rate than those in the e-cigarette condition, and there was a statistically significant (t=-3.48, p<0.01) difference on the Direct Effects of Smoking Scale such that participants were more affected by cigarettes compared to e-cigarettes. No other differences in physical or self-reported measures were observed.
Conclusions: There was a sizable difference in the dose of nicotine received between the e-cigarettes and cigarettes, but the only physical difference was increased heart rate self-reported greater affect in response to this different dose.
Financial Support: Life Science Discovery Fund, Department of Justice, Bureau of Justice Affairs (Roll, PI).

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ARE EARLY-ONSET USERS OF INHALANTS AT EXCESS RISK OF DEVELOPING INHALANTS DEPENDENCE SOON AFTER ONSET OF INHALANT USE: ESTIMATES FOR THE UNITED STATES, 2002-2011.

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Aims: Use of inhalant drugs often is been viewed as a transitory feature of the childhood and adolescent years, of little public health importance. Nonetheless, a dependence syndrome attributed to use of inhalant drugs has been described and estimated. Here, the aim is to study newly incident cases of inhalant drug use (InhDU) occurring soon after InhDU onset, with a hypothesized excess risk of InhDU dependence when use starts before age 16 years.
Methods: Data are from the United States (US) National Surveys of Drug Use and Health conducted 2002-2011, each with a nationally representative sample of non-institutionalized civilians age 12 years and older (n>50,000 each year, with cumulative total of ~7500 newly incident inhalant users). Weighted data with complex survey variance estimates yield year-specific 95% confidence intervals (CI). Meta-analysis is used to summarize estimates from year-pairs across 2002-2011.
Results: Meta-analyses disclosed emergence of excess risk of inhalant dependence among early-onset inhalant users who started before age 16 (2.5%; 95% CI = 1.8%, 3.1%) relative to 0.9% with onset between the 16th and 20th birthdays (95% CI = 0.4%, 1.4%), and 1.1% for 20-24 year old initiates (95% CI = 0.04%, 2.1%), with p < 0.05. Statistically robust male-female differences are found as well, when contrasting newly incident female inhalant users (3.2%; 95% CI = 2.2%, 4.1%) versus males (1.0%; 95% CI = 0.5%, 1.5%).
Conclusions: This epidemiological evidence projects light into a black box of possibilities. Is it possible that NSDUH assessments of inhalant dependence do not have measurement equivalence across earlier- versus later-onset users, or across male and female subgroups of new initiates? Supposing measurement artifacts can be set aside, there are some underlying sex-associated neurobiological and neuropsychopharmacological mechanisms to be discussed in relation to this facet of inhalants epidemiology. Clearly, there is an agenda for future research.
Financial Support: Supported by K05DA015799 (JCA)

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USE OF TELEMEDICINE TO TREAT HEPATITIS C AT A MEDICATION-ASSISTED OPIOID TREATMENT PROGRAM.

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Aims: START Treatment & Recovery Centers is an outpatient medication-assisted opioid treatment program that also provides primary medical care. Half of our 3000 largely minority patients are infected with hepatitis C virus (HCV). To date, very few have received HCV treatment. Based on studies showing that co-location of substance abuse treatment with other co-occurring conditions results in improved outcomes for both conditions, we developed a protocol to treat HCV utilizing telemedicine.
Methods: We initially had to determine patient interest in on-site treatment. We surveyed 320 patients to determine HCV knowledge level and receptivity to attending educational sessions as a prelude to treatment. The response was overwhelmingly positive, providing impetus to move forward. Currently, we have provided HCV education to all treatment staff and 114 patients. Fifty patients are HCV infected; of which 23 have had on-site linkage to specialized medical services and evaluation for treatment. Compliance with referral to medical specialists in conventional health care settings is poor. Reasons include fears or doubts, lack of knowledge or interest, and physical limitations. Telemedicine is a simple, cost-effective way to assure timely HCV care, i.e. the hepatologist comes to our clinics (via telemedicine); instead of patients being referred offsite.
Conclusions: The process of implementing the infrastructure to provide the educational training and telemedicine capabilities presented a number of challenges involving patients, providers, technology, and reimbursement that we have successfully navigated to create a viable model for telemedicine-based delivery of HCV services in a substance use facility.
Financial Support: CDC Foundation, Gilead Sciences, Vertex Pharmaceuticals, Abbvie & Abbott Molecular

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PREGNANCY, TOBACCO USE, AND ACCESS TO HEALTH CARE.

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Aims: Access to health insurance may reduce tobacco use among pregnant women via prenatal visits, which represent opportunities to engage in smoking cessation programs and other anti-smoking resources covered by health insurance. This study assessed 1) if pregnant women with health insurance were less likely to use tobacco in the past month (e.g. cigarettes, cigars) and 2) if type of insurance matters.
Methods: Pregnant women (n=2,505) were sampled from three years (2010-2012) of the National Survey of Drug Use and Health. Logistic regressions were used to test the hypothesis that insurance coverage (i.e., any insurance, Medicaid/CHIP, military/VA insurance, private insurance) is inversely associated with past month tobacco use controlling for demographic (e.g., age, race) and other substance use variables.
Results: About 17% of pregnant women in the US used tobacco in the past month. Most pregnant women were insured (90%), 37% had Medicaid/CHIP, 50% private insurance, and 4% had VA or military insurance. Any insurance versus no insurance (adjusted odds ratio [aOR]=1.97; 95% confidence interval [CI]=1.15, 3.36) and Medicaid/CHIP versus any insurance or no insurance (aOR=2.21; 95% CI=1.43, 3.40) were associated with increased odds of past month tobacco use, while military/VA (aOR=1.91, 95% CI=0.62, 5.91) and private insurance (aOR=0.64, 95% CI=0.34, 1.21) were not associated with past month tobacco use controlling for past year alcohol, marijuana, other drug use, education, income and other demographics.
Conclusions: Insurance type is differentially associated with tobacco use among pregnant women. Further research is needed to understand why tobacco use is pervasive among pregnant women, especially women receiving Medicaid/CHIP. Failure to engage pregnant women in smoking cessation programs would be an opportunity missed, especially given insurance coverage.
Financial Support: NIDA grant T32DA031099 (P.I. Hasin).

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THE IMPACT OF CO-MORBID BORDERLINE PERSONALITY DISORDER AND SUBSTANCE USE DISORDER ON HPA AXIS REACTIVITY TO SOCIAL STRESSORS.

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Aims: Substance Use Disorder (SUD) is a detrimental co-occurring condition in individuals with Borderline Personality Disorder (BPD), their co-morbidity is associated with worsened treatment outcomes and suicidal behavior. Both BPD and SUD are associated with hypersensitivity to social stressors, often attributed to a dysregulated hypothalamic pituitary adrenal axis. The similar symptoms between these two disorders like emotional instability, impulsivity and interpersonal difficulties suggest their co-occurrence can impact an individual's ability to regulate social stress. We hypothesize individuals with BPD and SUD will have a faster rate of cortisol increase from baseline as well as a more elevated and longer lasting cortisol response to social stressors compared to BPD without SUD.
Methods: We compared two groups of Borderline Personality Disorder patients without a history of substance abuse (N=41) and were current users or in full remission (N=37). Each participant underwent a modified version of the Trier Social Stress Test where participants gave a five minute speech followed by a five minute speeded mental arithmetic task. Salivary cortisol levels were measured throughout the procedure: once at baseline and four times following the stressor at 0, 15, 20, 30 and 40 minutes.
Results: There was a main effect of time on cortisol response in both groups (ANOVA; $F=10.16$, $df=1$, $p < 0.01$). BPD patients without an SUD showed an expected linear rise in cortisol response to stressor. However, BPD patients with SUD showed a decrease, then rapid increase and leveling off in cortisol response to stressor, indicating a different trajectory of cortisol response in participants in BPD and SUD (ANOVA; $F=3.95$, $df=1$, $p=0.05$).
Conclusions: Unlike those with BPD alone, individuals with BPD and SUD had a rapid and nonlinear cortisol response to social stressors. These findings show that the dual diagnosis of SUD and BPD changes responsiveness to social stress and can improve the understanding and treatment of this co-morbidity.
Financial Support: NIH R21 grant

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ARE DSM-5 PHARMACEUTICAL OPIOID USE DISORDER CONTINUA CONSISTENT ACROSS CHRONIC PAIN AND INJECTING DRUG USE SAMPLES?

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Aims: Little work has examined the syndrome structure of DSM-5 pharmaceutical opioid use disorder; that which exists has yielded conflicting information about which symptoms are the most and least severe. With some controversy, DSM-5 use disorder criteria restrict the presence of physiological signs to situations where individuals are using opioids outside the boundaries specified by their prescriber
Methods: Lifetime DSM-5 pharmaceutical opioid use disorder was assessed using the Composite International Diagnostic Interview in 1409 people prescribed strong pharmaceutical opioids for chronic non-cancer pain and 575 people tampering with pharmaceutical opioids by injecting. Disorder driteria psychometrics were examined using Confirmatory Factor Analysis and Item-Response Theory models
Results: Rates of DSM-5 opioid use disorder varied greatly: 20.8% (4.8% severe) in the pain cohort; 96.5% (77.9% severe) in the injecting sample. CFA demonstrated good fit for a unidimensional disorder in both samples (CFI and TLI >0.92; RMSEA ≤ 0.07). IRT demonstrated divergent patterns of symptom severity, with quit/control, larger/longer and activities given up the least severe among the pain sample; and withdrawal, larger/longer and tolerance least severe among injectors
Conclusions: While diagnostic restrictions on physiological symptoms does not adversely affect the unifactorial nature of the syndrome in those prescribed opioids, this effectively makes these more 'difficult' items (use disorder needing to be more severe before these are regarded as symptoms). Consistent with prior work, most symptoms lie in a narrow band of severity, raising the possibility of streamlining of diagnoses, as proposed for ICD-11
Financial Support: National Health & Medical Research Council; Mundipharma untied educational grant

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THE EPIDEMIC THAT NEVER HAPPENED:ZOHYDRO ER AND THE IMPACT OF MEDIA COVERAGE.

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Aims: The launch of an extended-release hydrocodone (Zohydro ER) in February 2014 was publically criticized by members of Congress, state attorneys general, and other experts. Governors of two states sought to ban or restrict its use. Extensive media coverage often described Zohydro as "Super Potent" and more powerful than any other opioid. We examined actual reports of abuse cases and discussion of Zohydro in online drug abuse forums during the 6 months following Zohydro's release in the context of media coverage at the time.
Methods: From February through September 2014, we examined self-reports of past 30-day abuse of Zohydro ER and comparators in the ASI-MV®, a computerized, clinical interview for adults in substance abuse treatment. Data were also collected from online drug-abuse discussion forums to capture the level of interest expressed by this high-risk sentinel population. Media coverage of Zohydro was assessed using Google Trends news search. Correlations among data sources were conducted.
Results: During the timeframe examined, 48,386 ASI-MV assessments yielded only 20 reports of Zohydro abuse, compared with 1,594 cases for any abuse deterrent formulation (ADF), 5,867 used any ER opioid, and 6,279 used any IR opioid. A Google Trends search yielded 252 Zohydro news references. 182 unique online posts discussed Zohydro. Spearman correlations revealed high correlations between monthly Google searches and cases reported in the ASI-MV (rsp=.82). Monthly counts of Internet posts were also related to Google Trends data (rsp=.94). Content of posts by some suggested interest in abusing Zohydro, while many questioned the media coverage since other products are stronger and more easily obtained/abused.
Conclusions: Excessive media coverage peaked at the launch of a single product and subsequently declined; a pattern that was mirrored in measures of abuse and abuse-interest in the product. Although news coverage of Zohydro was high, actual levels of abuse of Zohydro remained very low and went to almost zero when the news subsided.
Financial Support: Inflexxion, Inc

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NO PLACE TO CALL HOME: WHAT HOMELESSNESS MEANS FOR PEOPLE WHO USE DRUGS.

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Aims: Substance use disorders are consistently the most prevalent mental health diagnosis amongst homeless populations in Western countries. Although research has examined substance use among people experiencing homelessness, very few studies have looked at the nature of homelessness in people who use drugs and whether the state of homelessness infers particular risks to this group. Given this present study examined the prevalence and correlates of homelessness in an Australian national sample of people who inject drugs (PWID).
Methods: Cross-sectional face-to-face interviews were conducted in 2014 with 898 Australians who injected drugs at least monthly in teh past six months.
Results: Three-quarters (74%) of the sample reported a lifetime history of homelessness. Of these, one-in-five were homeless at the time of interview and one-third reported a chronic homelessness history. The study also showed the majority of these participants had experienced a number of different forms of homelessness in their lifetimes, including rough sleeping (81%), couch surfing (77%), and staying in crisis accommodation (68%) or boarding houses/hostels (55%). Approximately one-quarter (27%) of participants reported being victims of violence during their most recent homelessness episode, most commonly in the form of being physically attacked or stood over.
Conclusions: Episodes of homelessness among PWID are common and often chronic. Given that participants had experienced multiple forms of homelessness, further research examining the efficacy of supported housing programs for this group is warranted, particularly as a means of breaking the cycle of homelessness by providing stable housing and reducing the harms associated with substance use and homelessness. Further examination of the associations between risk factors and variables of homelessness, including forms and duration, among PWID are warranted.
Financial Support: Financial support provided by Australian Department of Health

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ACUTE EFFECTS OF CANNABIS ON YOUNG DRIVERS' PERFORMANCE OF DRIVING-RELATED SKILLS.

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Aims: Young drivers are more likely to drive after smoking cannabis than after drinking alcohol. This study examines the impact of an acute dose of cannabis on driving-related skills among young drivers who use cannabis regularly.
Methods: Data are based on a double-blind, placebo-controlled mixed-design study. Participation consists of an eligibility screen and four sessions on consecutive days: practice, drug administration, and 24 and 48 hours post-dose. The sample consists of individuals aged 19 to 25 who use cannabis 1-4 times per week who were screened as eligible to participate. Measures of driving simulator performance, cognition, mood, and motor skills were collected before and after a single dose of smoked cannabis (approximately 12.5% THC). Quantification of THC and metabolites in blood and subjective drug effects were collected prior to drug administration, then repeated eleven times over the next 48 hours. This analysis focuses on the time between baseline and six hours post-dose.
Results: Preliminary results (n=42, average age=22.3, 42% female, 58% male) show significant interaction between time (pre- or post-drug) and condition (placebo or active) in all subjective drug effects reported in the Visual Analogue Scale ($p<0.001$). Drug effects also were also seen in the Addiction Research Center Inventory score for the Lysergic Acid Diethylamide scale, which measures dysphoria ($p=0.022$). Confusion as measured by the Profile of Mood States approaches significance ($p=0.069$), with higher values in the active group. Impairment of motor skills in the active group approached significance on the Grooved Pegboard Test for the non-dominant hand ($p=0.060$). Mean speed on the driving simulator is significantly reduced in the active group when driving under a dual task condition ($p=0.025$).
Conclusions: The preliminary findings of this study show that cannabis may affect driving behavior.
Financial Support: Funding was provided by Canadian Institutes of Health Research.

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HEALTH SERVICE USE IN A RANDOMIZED CLINICAL TRIAL COMPARING THREE METHODS OF EMERGENCY DEPARTMENT INTERVENTIONS FOR OPIOID DEPENDENCE.

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Aims: We previously demonstrated in a randomized clinical trial that Emergency Department (ED)-initiated buprenorphine (Bup) with primary care follow-up (BupPC) was superior to standard referral to community-based treatment (RT) and Screening, Brief Intervention with a facilitated referral (SBIRT) in increasing treatment engagement and reducing opioid use at 30-days. We aim to evaluate health service use 30 days following enrollment in this clinical trial.
Methods: We randomized 329 opioid dependent patients presenting to a large, urban ED to RT (n=104), SBIRT (n=111) or BupPC (n=114). RT patients received a referral to a substance Use Disorder (SUD) provider, SBIRT patients received a Brief Negotiation Interview and a facilitated referral to a SUD provider, BupPC patients received SBIRT, ED-initiated Bup and ongoing Bup in primary care. We assessed use of SUD treatment services in outpatient settings, EDs, and inpatient settings using the Treatment Services Review. Analyses were conducted using chi-square and MIXED models.
Results: The groups were similar: 76% male; mean age 31; 78% had insurance (43% Medicaid); and 45% reported no usual source of care. There was no difference in number of outpatient SUD visits between groups: 4.99 (95% CI 3.14-6.84), 5.67 (95% CI 3.98-7.37) and 3.71 (95% CI 2.12-5.30) in the RT, SBIRT and BupPC groups. There were no differences in ED use for SUD across the three groups: RT (15/69; 22%); SBIRT (12/82; 15%); and BupPC (18/93; 19%); $p=0.51$. Patients in the RT and SBIRT groups utilized inpatient SUD treatment services at higher rates (37%, 95% CI 27-48 and 35%, 95% CI 25-37) compared the BupPC group (11%, 95% CI 6-19); $p<0.001$.
Conclusions: Patients in the BupPC group were less likely to use inpatient SUD treatment and had similar numbers of outpatient visits, suggesting more efficient, less costly resource use.
Financial Support: NIDA-5R01DA025991, 5K12DA033312

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INTERNATIONAL STANDARDS ON THE TREATMENT OF DRUG USE DISORDERS.

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Aims: Substance abuse and dependence is a public health, developmental and security problem both in industrialized and developing countries. In the framework of the UNODC-WHO Programme on Drug Dependence Treatment and Care, UNODC and WHO together with their international partners have initiated a process to develop International Standards for the Treatment of Drug Use Disorders. The Standards will build on existing publications such as the UNODC-WHO Principles of Drug Dependence Treatment (2009) and incorporate evidence and experience gathered worldwide. The aim is to provide UN Member States with a practical and comprehensive technical tool that will help to guide policy development; plan, organize and manage drug treatment services within and beyond the health system; develop the capacity of human resources; and evaluate service and system level interventions. The International Standards for the Treatment of Drug Use Disorders will promote treatment strategies that are based on the best available science, humane, and respect human rights and dignity and this way improve the service for individuals affected by drug use disorders.
Conclusions: A first outline will be presented for discussion with the international scientific community.
Financial Support: UNODC receives voluntary and regular budget contributions from Member States.
The International Standards on the Treatment of Drug Use Disorders have received funding from the US/INL.

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HEPATITIS C AND ASSOCIATED RISK BEHAVIOURS IN PEOPLE WHO INJECT DRUGS.

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Aims: The primary objectives of this study were to (1) determine the extent of Hepatitis C (HCV) testing among a group of people who inject drugs (PWID) regularly, (2) to compare the drug use and risk behaviours of PWID who reported screening positive for HCV antibodies (HCVAb) and those who tested negative for HCVAb.
Methods: The Illicit Drug Reporting System (IDRS) is an annual sentinel surveillance system involving survey interviews with ~900 PWID in all capital cities of Australia.
Results: The majority (90%) of participants had undergone HCVAb testing and of those who had been tested, two-thirds (69%) returned a positive result. Participants who returned a positive HCVAb result were older, had longer injecting histories, and were more likely to be in current opioid substitution treatment therapy compared to the HCVAb negative group. They were also more likely to nominate heroin as their drug of choice and the drug they injected most often in the last month. Those who were positive for HCVAb were significantly more likely to use a needle after someone else than those who were HCVAb negative. However there was no significant difference between those who are HCVAb positive and those who are HCVAb negative among people who lent a needle to someone else after using it themselves.
Conclusions: The majority of participants were actively engaged in their health care and most had undergone antibody screening for HCV. While previous studies, Kwiatkowski, et al. (2002) suggest that knowledge of one's serostatus prompts individuals to modify their behaviour to avoid infecting others; results shown here suggest that rather than prompting protective behaviours (lending 'used' needles to others), individuals with a positive result for HCVAb are more likely to use a needle after someone else. Other findings from this data (not presented here) have found an ambivalent attitude towards treatment efficacy among this group which may explain, in part, a lack of concern regarding additional exposure post-diagnosis.
Financial Support: Australian Government under the Substance Misuse Prevention & Service Improvement Grant

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CHANGES IN ABUSE PREVALENCE OF PRESCRIPTION OPIOIDS AND HEROIN ACROSS SIX YEARS IN THE ASI-MV NETWORK FOR DIFFERENT PATIENT SUBGROUPS.

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Aims: In recent years, abuse of prescription (Rx) opioids has been directly addressed by certain interventions, including drug monitoring programs, abuse deterrent formulations, and a Class-wide REMS for extended-release (ER) and long-acting (LA) Rx opioids. Since 2009, the ASI-MV® network has been tracking relative prevalence of past 30-day opioid abuse (Rx and heroin) in a high-risk population of individuals evaluated for treatment. The heterogeneous nature of ASI-MV treatment programs and patients allow examination of how different subgroups of patients may be responding to these interventions.
Methods: The ASI-MV®, a computerized, clinical interview for adults in substance abuse treatment, collected self-report of past 30-day abuse of any prescription opioid and/or heroin.
Results: 391,674 unique ASI-MV assessments were collected from 2009 through Q3 2014 (approximately 65,000 per quarter). For all patients, any Rx opioid abuse increased from about (17%) in 2009 to peak at 24% in 2013 and reduced to 21% in 2014. This general pattern was observed in subgroups of those in traditional substance abuse treatment (SA Tx), criminal justice (CJ Tx) and those in methadone maintenance (MM) settings, as well as in individuals with medium and high ASI drug severity ratings. Rx opioid abuse prevalence for those rated as low severity increased somewhat from 2009 to 2010, but declined steadily since then. Past 30-day heroin use for all ASI-MV respondents increased from 5.3% in 2009 to peak at 8.7% in 2013, dropping only slightly to 8.0% in 2014. Patients in MM settings showed a dramatic increase in heroin use, from 39.6% in 2012 to 50.1% in 2013 and 59.5% in 2014. Abuse of heroin by low and moderate drug severity patients also peaked in 2013, while heroin abuse prevalence in high severity patients continued to climb. A "consistent site" analysis yielded the same results.
Conclusions: Not all substance abusers are alike. Analysis of subgroups may reflect different reactions to the interventions intended to limit Rx opioid abuse.
Financial Support: Inflexxion, Inc.

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TRENDS IN PRESCRIPTION OPIOID MISUSE AMONG YOUNG ADULT MULTIDRUG USERS IN MIAMI, 2006-2014.

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Aims: To examine the impact of Florida's 2010 and 2011 legislative interventions (prescription drug monitoring program; pill mill regulation) on prescription (Rx) opioid misuse among young adult multidrug users in Miami.
Methods: Data are drawn from baseline assessments collected as part of a natural history study in 2006-2008 (Study 1; N=600) and an ongoing behavioral intervention trial in 2011-2014 (Study 2; N=471). Eligible participants from both studies were 18-39 and reported recent (past 90 days) and regular use of club drugs (cocaine, ecstasy, LSD, GHB, ketamine, or methamphetamine) and Rx drug misuse.
Results: Participants were White (17.3%; 12.1%), Black (20.7%; 20.1%), Hispanic (58.4%; 65.2%), and female (40.0%; 45.2%) in Study 1 and Study 2 respectively. Mean ages were 22 (Study 1) and 25 (Study 2). Participants reporting recent Rx opioid misuse increased from 59.5% in Study 1 to 89.6% in Study 2. Mean frequency of recent Rx opioid misuse during Study 1 was 27.8 days, compared to 37.5 days in Study 2. Mean amount of recent Rx opioid misuse, in pills or liquid doses, was 33.1 in Study 1 and 75.8 in Study 2. While 51.6% of Study 1 participants believed Rx drug misuse is associated with moderate/high risk of harm, this increased to more than 65% in Study 2.
Conclusions: The data indicate that young adult multidrug users in Miami maintained access to Rx opioids from 2006-2014, despite Florida's legislative interventions in 2010 and 2011. Moreover, the frequency and amount of Rx opioid misuse increased from Study 1 to Study 2. Yet, more participants believed Rx drug misuse is associated with harm in Study 2 than in Study 1, indicating a potential avenue for intervention and prevention efforts.
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REGULATORY CHALLENGES IN EVALUATING THE ABUSE DETERRENT PROPERTIES OF NOVEL OPIOID PRODUCTS.

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Aims: Provide an overview of FDA's evaluation of novel abuse deterrent (AD) opioid products.
Methods: Abuse and misuse of opioid drug products is a public health concern. One approach for managing the problem is reformulation of the products to make them safer and less euphorigenic. Current efforts focus primarily on making the products more difficult to "manipulate" for injection, insufflation and inhalation. The development, assessment, and regulation of AD formulations of opioid products that are less prone to abuse or misuse is a policy priority. The FDA Center for Drug Evaluation and Research developed guidance to evaluate and label AD opioid formulations (2013), and held public meetings
Results: Premarket assessment of AD products involves three categories of studies. The first category consists of in-vitro manipulation and extraction studies to evaluate whether the AD features of a new formulation can be compromised under experimental conditions. Pharmacokinetic (PK)/pharmacodynamic (PD) studies (second category) are designed to understand the in vivo properties of the new formulation by comparing the PK profiles of the "manipulated" formulation with the intact formulation and other drugs by one or more routes of administration, and to collect PD data such as adverse events due to administration of the manipulated formulation. In the third category, the relative abuse potential of the AD formulation (intact and manipulated) is studied in human abuse potential studies. Results of the premarket assessment are used for labeling. As FDA gains experience in the evaluation of AD products, questions arise regarding science-based approaches to appropriately characterize the deterrent properties and to support labeling of the products.
Conclusions: Abuse-deterrent technologies and evaluation methodology are rapidly changing. FDA recognizes the need to identify the best approaches to characterize these products to support labeling
Financial Support: N/A

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IMPACTS OF DRINKING-AGE LEGISLATION ON ARRESTS FOR ALCOHOL-IMPAIRED DRIVING AMONG YOUNG PEOPLE IN CANADA, 2009-2012.

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Aims: International debates are occurring about the effectiveness of minimum legal drinking-age (MLDA) legislation. In Canada, the MLDA is 18 years of age in Alberta, Manitoba and Québec, and 19 in the rest of the country. Even though national Canadian public-health organizations and expert-panel working groups not only have recommended increasing the MLDA in Canada to 19 years, but also have identified 21 years as the ideal, relatively little Canadian evidence informs the current debate. This study aims to assess the impacts of Canadian drinking-age laws on national patterns of police-reported alcohol-impaired-driving (AID) arrests.
Methods: Methods. The study used data from 2009-2012 from the Uniform Crime Reporting Survey, Canada's national crime database comprising near-census records of all police-reported crimes in the country. Regression-discontinuity analyses were used to estimate MLDA effects.
Results: Results. In comparison to males slightly younger than the minimum legal drinking age, young men just older than the MLDA had abrupt and significant increases of 27.7% ($p < 0.001$; 95% CI, 16.6%-39.3%) in national AID arrests immediately following the MLDA. There was only weak evidence of increases in AID arrests immediately following the MLDA among females: in provinces with a MLDA of 18 years [34.7% (95% CI, -0.4%-71.2%)] increase; $p = 0.077$), and at the national level [15.6% (95% CI, -1.6%-33.4%] increase; $p = 0.053$).
Conclusions: Conclusion. These findings indicate that drinking-age laws continue to serve as an important component of alcohol-control strategies designed to reduce driving-related harms among Canadian young people, especially males.
Financial Support: This study was supported by a open operating research grant (MOP-133699) from the Canadian Institutes of Health Research (CIHR). The funder had no role in the data collection, data analyses, interpretation of the statistical results, or preparation of this conference material.

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PREDICTORS OF YOUTH USE OF E-CIGARETTES FOR SMOKING CESSATION.

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Aims: This study examines predictors of adolescents' and young adults' use of e-cigarettes for smoking cessation.
Methods: We conducted school-wide surveys in 2 middle (n=1166) and 4 high schools (n=3614) in fall 2013 and 1 public college (n=625) in spring 2014. We restricted the analysis to 675 students who reported lifetime use of both e-cigarettes and cigarettes (52.3% female, 79.6% White, M_{age} 17.0 (SD=2.4)). Logistic regression assessed associations of using e-cigarettes to quit smoking with demographic characteristics and tobacco use.
Results: Overall, 52.8 % of students reported past-month e-cigarette use and 47.3% reported lifetime but not past-month use. Additionally, 53.9% reported past-month cigarette use, and 46.1% reported lifetime but not past-month use. 19.9% (n=134) reported that they "have used an e-cigarette to quit smoking". White race (OR 2.33; 95% CI 1.32- 4.14) and smoking 100 cigarettes in their lifetime (OR 7.19; 95% CI 4.73-10.95) was associated with using e-cigarettes to quit smoking. Students who had used e-cigarettes to quit smoking reported more frequent e-cigarette (mean days per month 13.9 vs. 5.2; p<0.001) and cigarette (mean days per month 4.8 vs. 2.2; p<0.001) use. Lifetime smokeless tobacco use (OR 1.71; 95% CI 1.15-2.52), but not cigar, blunts, or hookah use, was associated with using e-cigarettes for smoking cessation.
Conclusions: Only 19.9% of our sample who reported lifetime use of both e-cigarettes and cigarettes has used e-cigarettes to quit cigarette smoking. Adolescents and young adults with heavier cigarette and e-cigarette use are more likely to use e-cigarettes for cessation.
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PHARMACEUTICAL OPIOID USE AND DEPENDENCE AMONG PEOPLE LIVING WITH CHRONIC PAIN: ASSOCIATIONS OBSERVED WITHIN THE PAIN AND OPIOIDS IN TREATMENT COHORT.

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Aims: The current paper examines pharmaceutical opioid dose and dependence and examines the correlates of both opioid consumption, and opioid dependence
Methods: Baseline data from a national sample of 1,424 people across Australia (median 58 years, 55% female and in pain for a median of 10 years), being prescribed opioids for CNCP. Current opioid dose was estimated in oral morphine equivalent (OME) mg, and ICD-10 pharmaceutical opioid dependence was assessed using the Composite International Diagnostic Interview.
Results: Current opioid dose varied widely: 8.8% were taking <20mg OME per day, 52.1% were taking 21-90mg OME, 24.3% were taking 91-199mg OME and 14.8% were taking >=200mg OME. Higher daily OME dose was associated with higher odds of multiple physical and mental health issues, non-adherent opioid use, problems associated with opioid medication and opioid dependence. A significant minority, 8.5% met criteria for lifetime ICD-10 pharmaceutical opioid dependence and 4.7% reported past year symptoms. Multivariable analysis found past-year dependence was independently associated with being younger, a greater number of non-adherence behaviours and a history of benzodiazepine dependence.
Conclusions: Consumption of higher opioid doses is associated with increased risk of problematic behaviours, and is more likely among people with a complex profile of physical and mental health problems.
Financial Support: This study received funding from the Australian National Health and Medical Research Council (NHMRC, #1022522).

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CHARACTERISTICS OF SMOKING PREGNANT WOMEN IN GUADALAJARA, MEXICO.

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Aims: The aim of this study was to examine the pattern of smoking in a group of pregnant women in a major pre-natal care clinic of a large university hospital in Guadalajara, Mexico.
Methods: We interviewed 235 women who smoked to investigate the pattern of tobacco use, out of 1481 women screened for tobacco use.Randon urine cotinine tests were performed in a group of patients.Patients were referred to a tobacco cessation program and follow up was carried out.
Results: Most of the women were non-working unmarried women with a low educational background with a mean age of 23.5 (± 6.5) years. Mean duration of their pregnancy was 6.6 (±1.9) months. Smoking commonly first started between 13 to 17 yrs (68.6 % cases), and was often motivated by friends (34.5 %) and curiosity (33 %). Current smoking was every day (2.1 %), some days (14.5 %) and don't smoke (82.1 %) and 14.5 % had smoked more than 100 cigarettes in their lifetime. Preferred type of cigarettes were: regular (78.7 %), light (11.9 %); menthol (20.9 %); 5.5 % smoked their first cigarette within 5 min after waking up; most of the women (82.1 %) defined as smokers here stopped smoking when they knew they were pregnant without treatment (92 %), of which 44.4 % did it during the first month of pregnancy. A large number of women were exposed to second hand smoke from relatives at home (64.3 %) while 43.8% worked or socialized with smokers. There was no history of major obstetric or pediatric complication in 98% of them.
Conclusions: Our results suggest low prevalence of smoking. Most patients did not have signs of major nicotine dependence nor of previous complications. However, a large group were exposed to second hand smoke as well as other factors which could influence smoking. As the smoking prevalence is increasing among the females, prevention programs should be directed to groups like pregnant women.
Financial Support: Funding was obtained from PROMEP Program of the Mexican Education department (SEP).

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EFFECTS OF CULTURAL CONGRUITY ON ALCOHOL USE SEVERITY AMONG HISPANIC EMERGING ADULTS IN COLLEGE.

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Aims: Aim 1 examined direct associations of behavioral acculturation, behavioral enculturation, and cultural congruity (the perception of cultural fit between the values of the academic institution and the student's personal values) with alcohol use severity. Aim 2 tested if gender moderated those associations.
Methods: Participants voluntarily consented and completed self-report measures in an anonymous online survey. A hierarchical linear regression and moderation analyses were conducted on a sample of 167 Hispanic emerging adults (ages 18 to 25) enrolled in institutions of higher education. Gender was dummy coded (0) for men and (1) for women.
Results: 20.9% of the variance in alcohol use severity was accounted for by all predictor variables entered in the regression model. After controlling for demographic variables and depressive symptoms, behavioral acculturation and enculturation did not have statistically significant associations with alcohol use severity. Further, gender did not moderate either of these associations. Conversely, greater perceptions of cultural congruity were associated with lower scores of alcohol use severity (β = -.20, p < .05). A moderation analysis with 10,000 bootstrap iteration indicated that cultural congruity had a beneficial effect in lowering alcohol use severity for men (β = -.20, $p \leq .001$, 99% CI [-.35, -.05]), but not among women (β = -.04, p > .05, 99% CI [-.13, .05]).
Conclusions: This was the first known study to examine the association of cultural congruity with alcohol use. Findings highlight the value of examining contextual factors of culture and moving beyond reductive measures of cultural orientation.
Financial Support: None.

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EFFECTS OF PARENTAL ALCOHOL VS. TOBACCO AND MARIJUANA USE ON EARLY ADOLESCENT ONSET OF ALCOHOL USE.

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Aims: Aim: Studies of effects of parental substance use on offspring alcohol use have predominantly focused on effects from parental alcohol use only, rather than also examining effects of use of other substances. Further, effects of both maternal and paternal substance use are rarely examined together. The present study examined whether use of tobacco and marijuana by fathers or mothers predicted onset of alcohol use in their offspring over and above effects of parental alcohol use.
Methods: Method: The study included 146 children of 93 parents (n = 90 fathers and n = 85 mothers). The fathers were originally recruited as boys to the Oregon Youth Study (OYS), a study of community, familial, and individual risk factors for delinquency. Children were interviewed regularly in adolescence and five binary variables were created denoting alcohol use onset response patterns for onset prior to age 11 years and onset during four periods of adolescence (ages 11-13, 13-15, 15-17, and 17-19 years). Children's alcohol use onset across adolescence was modeled using discrete-time survival analyses.
Results: Results: Only mothers' but not fathers' alcohol use was associated with children's age of onset. Mothers' tobacco use predicted children's age of onset and fathers' marijuana use interacted with their alcohol use to do so. These effects were observed when controlling for parent education, child gender, and child antisocial behavior, a general developmental risk factor for substance use onset in adolescence.
Conclusions: Conclusions: Mothers' substance use played a major role in child onset of alcohol use, yet the role of maternal substance use as a risk factor for their children has previously received less attention than the role of paternal substance use. Also, the findings imply that it may be important to identify children of polysubstance using parents for targeted prevention programs.
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COMPARATIVE PHENOMENOLOGY OF PSILOCYBIN EXPERIENCES IN RESEARCH AND NON-RESEARCH SETTINGS.

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Aims: This study sought to compare questionnaire ratings of subjective experiences after psilocybin when administered in controlled research settings vs. uncontrolled, non-research settings.
Methods: Two internet-based surveys were conducted in reference to participants' single most mystical/spiritual/meaningful experience (ME; n=1602) or to their single most psychologically difficult/challenging experience (CE; n=1993) after ingesting psilocybin mushrooms. Data from these surveys were compared to data from 3 laboratory studies conducted in healthy volunteers (LS; n=110-126) who received a high dose of psilocybin (30 mg/70 kg). Data were the percent of participants endorsing various questionnaire items.
Results: The CE group was more likely to endorse negative feelings such as fear (81% of participants), isolation (69%), physical distress (57%), and insanity (64%) than the ME or LS groups (range 21 to 30%). The ME and LS groups, respectively, were more likely to endorse positive and spiritual feelings of peace (88, 86%), awe (93, 90%), joy (91, 90%), spiritual height (76, 77%), and "All is One" (75, 70%) than the CE group (range 43 to 64%). ME and LS groups, respectively, also were more likely to endorse that the experience was among the 5 most spiritually significant of their lives (62, 67%) and that it increased well-being/life satisfaction (94, 94%) than those in the CE group (31% for spiritually significant; 76% for well-being).
Conclusions: The phenomenology of psilocybin experiences in the LS group was more similar to that in the ME group than the CE group, suggesting that laboratory procedures are effective at minimizing negative experiences and maximizing positive experiences.
Financial Support: NIH grants T32DA007209 and R01DA003889, the Heffter Research Institute and the Council on Spiritual Practices

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CHILDHOOD TRAUMA AND INITIATION OF DRUG USE IN ADOLESCENCE.

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Aims: Potentially traumatic events (PTEs) in childhood are known risk factors for drug abuse among adults. Less is known about how these events relate to initiation of drug use in adolescence. We examined whether 23 types of PTEs were associated with ever having used illicit drugs among a representative sample of U.S. adolescents (N=9,956). We hypothesized that childhood trauma would be associated with higher odds of drug use.
Methods: Following exploratory analyses, weighted logistic regression models estimated odds ratios for drug use, controlling for demographic factors and history of psychopathology (i.e. fear, distress, and behavior disorders).
Results: Exposure to any PTE before the age of 11 was reported by 36% of the sample (n=3,627). Twenty-three percent (n=2,241) had ever used marijuana, 2% (n=234) cocaine, 5% (n=483) prescription drugs nonmedically, and 3% (n=302) other drugs (e.g. heroin, LSD). Experiencing any PTE before age 11 was significantly associated with higher odds for marijuana use (aOR=1.53, 95% CI: 1.29-1.80), cocaine use (aOR=2.12, 95% CI: 1.49-3.01), nonmedical prescription drug use (aOR=1.53, 95% CI: 1.08-2.17), and other drug use (aOR=1.54, 95% CI: 1.11-2.12). Specific types of PTEs, notably exposure to violence, were consistently associated with higher odds for drug use, controlling for other PTEs. For example, being sexually assaulted was associated with a 2.83 higher odds for using marijuana (95% CI: 1.69-4.74), being beaten by parents with a 4.10 higher odds for using cocaine (95% CI: 1.97-8.53), and witnessing fighting at home with a 1.77 higher odds for using prescription drugs nonmedically (95% CI: 1.01-3.10).
Conclusions: Childhood trauma, particularly interpersonal violence, may be associated with the initiation of multiple types of illicit drug use in adolescence. Future work should explore whether adolescents with a trauma history are more likely develop chronic or harmful drug use than their peers.
Financial Support: NIDA grant T32DA031099

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PREDICTORS OF TRANSITION TO OPIOID DEPENDENCE AMONG ILLICIT PHARMACEUTICAL OPIOID USERS.

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Aims: Aims: This natural history study identifies the predictors of transition to opioid dependence among 362 young adults (aged 18-23) who were illicit pharmaceutical opioid users, but not opioid dependent at baseline.
Methods: Methods: Participants were recruited using respondent-driven sampling in the Columbus, Ohio, area and interviewed every 6 months for 3 years. Cox regression was used to test for associations between selected demographic and substance use covariates and the hazard of transition to opioid dependence.
Results: Results: Over 36 months, 163 (45.0%) participants transitioned to opioid dependence. Of these, 49.7% were male, 49.1% were white, 44.8% were Black, and the mean age at baseline was 21 years. Use of extended-release oxycodone (HR=1.5), non-oral use of pain pills (HR=2.2), sedative abuse or dependence (HR=2.2), alcohol dependence (HR=1.6), marijuana dependence (HR=1.5), and frequency of pain pill use (HR=1.5) were each significantly associated with transition to opioid dependence. Participants who were younger (HR=.83), those without post-high school education (HR=.63), and those who never used alcohol (HR=.39), sedatives (HR=.56), or MDMA/ecstasy (HR=.65), were more likely to transition to dependence. Length of pharmaceutical opioid use was not significantly associated with transition to dependence.
Conclusions: Conclusion: Although our sample is limited to one region in the Midwest, the results suggest that almost 50% who become involved with illicit pharmaceutical opioid use transition to dependence over three years. The variables associated with transition to dependence provide important insights for targeted interventions.
Financial Support: Financial support was provided by the National Institute on Drug Abuse (R01DA023577; Carlson, PI)

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THE RISKS OF GANG ASSOCIATION AMONG DRUG-USING WOMEN IN CAPE TOWN, SOUTH AFRICA.

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Aims: Western Cape has an entrenched gang culture that is strongly associated with drug trafficking and manufacture. There is concern that women who are associated with gangs are more likely to be exposed to violence, and have substance use problems, but little research has been conducted on this.
Methods: Baseline data on 720 disadvantaged drug-using women in Cape Town was collected as part of a randomized controlled trial. We compared the proportion of women who lived near gang members and had a main sexual partner who was a gang member to those that did not on substance use variables.
Results: The findings indicated that women who lived near gang members were significantly more likely to use methamphetamine (X^2=83.19, p<0.001), report having a drug problem (X^2=11.08, p<0.001), have previously gone to drug treatment (X^2=13.47, p<0.01), and used alcohol or drugs the last time they had sex (X^2=67.59, p<0.001) than women who did not live near gang members. Women who had main partners who were gang members were significantly more likely to have used methamphetamine (X^2=32.72, p<0.01) and to report using alcohol or drugs the last time they had sex (X^2=16.21, p<0.001) relative to women whose partners were not gang-affiliated.
Conclusions: Findings show that women living near gang members or in a sexual relationship with a gang member were more likely to use methamphetamine and report drug-related sex risks relative to women who were not as exposed to gangs. Future interventions that target substance-using women should also consider addressing environment risk factors, including gang activity.
Financial Support: N/A

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COCAINE SELF-ADMINISTRATION IN MALE AND FEMALE MONKEYS, TREATMENT WITH PROGESTERONE AND ENRICHED ENVIRONMENT.

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Aims: The first study examined sex differences in oral cocaine self-administration in male and female rhesus monkeys and compared cocaine intake in females during the follicular and luteal phases of their menstrual cycle to males. The effect of environmental enrichment was also studied by comparing concurrent access to a nondrug reward, saccharin (SACC) vs. water. In a second study male and female monkeys were treated with im injections of progesterone while self-administering oral cocaine.
Methods: Cocaine and water were concurrently available during daily 3-hr sessions from two drinking spouts under concurrent fixed-ratio (FR) 2, 4, or 8 schedules. Cocaine self-administration was then tested when SACC (vs. water) was concurrently available with cocaine. In the second study progesterone (0.3 mg/kg) was administered prior to the cocaine session for 4 days in males and in females during the luteal and follicular phase.
Results: Cocaine deliveries were similar in males and females during the females' luteal phase, but they were higher in females during the follicular phase. Concurrent SACC and water deliveries did not vary by cocaine concentration, sex, or hormonal conditions. SACC reduced cocaine deliveries in the follicular phase in females and cocaine intake (mg/kg) in males and in females during both phases of the menstrual cycle. Treatment with progesterone reduced cocaine self-administration in females in both menstrual phases and in males.
Conclusions: Females in the follicular phase of their cycle consumed more cocaine than in the luteal phase or than males. Treatment with the nondrug reward, SACC (vs. water), reduced cocaine intake (mg/kg) in females during both phases and in males. These effects were specific to cocaine self-administration and were not reflected in SACC or water intake. Treatment with a nondrug reward for cocaine self-administration varied by sex and menstrual cycle phase in females, while progesterone reduced oral cocaine self-administration in both males and females.
Financial Support: R01-DA002486-38, DP1-DA031340-05, University of Minnesota Medical Foundation

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EVENT-LEVEL ANALYSIS OF ANTECEDENTS TO FIREARM VIOLENCE AMONG DRUG-USING ED YOUTH.

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Aims: To examine/compare antecedents (substance use, motivations) of firearm violence (FV) and non-weapon (NFV) peer violence events among drug-using ED youth utilizing an event-level analysis
Methods: 14-24-y/o youth screening positive for past 6-mo drug use and seeking ED care for assault (AIG) or as part of a proportionally sampled comparison group (non-assault injured) were enrolled (n=599) in a 2-year longitudinal study. TLFB substance use/aggression modules were completed at baseline, 6, 12, 18 and 24-mos. FV (aggression/victimization; threats/use) and NFV events were combined across timepoints and analyzed cross-sectionally. Generalized linear mixed modeling (GLMM) using event-level data, nested by individual/timepoint, analyzed antecedents of FV events as compared to NFV events.
Results: 139 youth (mean age=19.7; 82% male; 78% African-American; 73% public assistance; 84% AIG) reported 196 FV events and 243 youth (mean age=19.9; 57% male; 61% African-American; 73% public assistance; 65% AIG) reported 592 NFV events. 24% of FV events involved aggression/93% victimization, with 37% of youth in FV events endorsing firearm possession (90% illegally). Most common motivation for firearm aggression was retaliation (53%), while "personal belongings" (25%) and "got shot for no reason" (30%) were the most common reasons for firearm victimization. 38% of FV events were preceded (within 3 hrs) by marijuana use, 17% by alcohol use, 10% by binge drinking. 61% of FV events resulted in injury requiring medical care. GLMM identified male gender (OR=4.63), African-American (OR=3.49), AIG (OR=4.32), marijuana (OR=2.22), retaliation (OR=3.75) and personal belongings (OR=2.79) as more likely correlated with FV when compared to NFV.
Conclusions: Drug-using youth have high rates of FV events with differential motivations & types of drug/alcohol use preceeding the event. Tailored interventions specifically addressing marijuana use and retaliation as precursors to FV may decrease high firearm violence rates among drug-using youth.
Financial Support: NIDA R01 024646; CDCP 1R49CE002099

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UP IN SMOKE?: MARIJUANA INITIATION AND PREVALENCE TRENDS IN COLORADO: 2008 TO 2014.

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Aims: Colorado (CO) passed laws approving medical marijuana in 2000 and legal recreation use of marijuana in 2012. Using data from individuals 18 and older from the Addiction Severity Index Multimedia Version (ASI-MV) post-marketing surveillance system, we assessed trends in initiation and prevalence of marijuana use in CO from 2008 to 2014.
Methods: Data included unique responses from 13,945 clients being assessed with the ASI-MV for treatment need in 35 CO substance abuse treatment centers from January 1, 2008 to September 30, 2014. Descriptive statistics and generalized estimating equation models explored trends over time in past year initiation and prevalence of marijuana use, controlling for age, gender, race, and 3-digit ZIP code. We also tested for associations with nonmedical prescription opioid use (NMPU).
Results: 48% of respondents were under 34, 40% were female, 51% were non-White minority, and the primary substance of abuse was 45.2% alcohol, 14.7% marijuana, 11.5% cocaine, 7.1% prescription opioids, and 6.8% heroin. There was no statistically significant increase in initiation of marijuana use over the study period. Initiation was 12.2% (95% CI: 3.4%, 35.6%) in Q12008 and 17.8% (95% CI: 13.4%, 23.4%) in Q32014. Initiation was associated (all p<.0005) with younger age (adjusted odds ratio (aOR) 3.53 for <21; 1.63 for age 21-34), Black race (aOR 1.66) and NMPU (aOR 1.5). There was a statistically significant increase (p<.0001) in prevalence of marijuana use over the study period. Prevalence was 21.3% (95% CI: 12.0%, 34.8%) in Q12008 and 32.8% (95% CI: 28.5%, 37.5%) in Q32014. Prevalent use was associated (all p<.0005) with younger age (aOR 3.11 for <21; 1.63 for age 21-34; 0.67 for age 55+), NMPU (aOR 2.15), and use of prescription opioids as prescribed (aOR 1.50).
Conclusions: Among people being assessed for substance use treatment need, prevalence but not initiation of marijuana use increased over time in Colorado, despite more permissive marijuana use laws. Findings suggest important motivations for use and highlight health disparities.
Financial Support: Supported by Inflexxion, Inc.

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DIMENSIONAL AND CATEGORICAL PHENOTYPES USING TOBACCO USE DISORDER CRITERIA: INVESTIGATING SOCIO-DEMOGRAPHIC, PSYCHIATRIC AND CLINICAL CORRELATES.

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Aims: To identify continuous and categorical phenotypes of DSM-5 Tobacco Use Disorder(TUD) among lifetime weekly smokers(n=1,388). Data came from São Paulo Megacity Mental Health Survey collected between 2005-2007 which is part of World Mental Health Survey.
Methods: Exploratory factor analysis(EFA) and latent class analysis(LCA) of 8 DSM-5 TUD symptoms were performed using Mplus software taking into account complex survey design features. Socio-demographic, psychiatric and clinical correlates were examined via weighted logistic regression models.
Results: A unidimensional model was the best EFA fit with high loadings (>60%) of all 8 symptoms tested. The best LCA model was a three-class model: a "non-symptomatic class"(32.0%), a "larger amounts moderate-low symptomatic class"(34.9%) - with high probabilities of "use in larger amounts" criterion, and a "high-moderate symptomatic class"(33.1%). Those in the "larger amounts moderate-low symptomatic class" were more likely to have higher household income than those in the "non-symptomatic class". Those in the "high-moderate symptomatic class" were more likely to have past-year depressive, anxiety, impulsive disorders and insomnia, and less likely to be lifetime pipe/cigar daily users than those in the "non-symptomatic class".
Conclusions: This study shows a continuum of DSM-5 TUD symptoms. Lifetime weekly smokers are divided into two different symptomatic phenotypes within this continuum. The most symptomatic class has a high psychiatric comorbidity, which would indicate that integrated clinical/psychiatric treatment is warranted. We found an intermediate class without comorbidities, with difficulties in controlling tobacco use, comprised by high SES respondents.
Financial Support: State of São Paulo Research Foundation, Brazil (FAPESP Grant 03/00204-3).

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PRENATAL TOBACCO EXPOSURE PREDICTS CHILD'S INTERNALIZING BEHAVIOR.

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Aims: Prenatal tobacco exposure (PTE) often has long-term, negative effects on child development. This may be expected given nicotine's teratological effects, but not all children with PTE have the same poor responses. One outcome of particular interest is internalizing behavior, a summary of children's depressed, anxious and withdrawn behaviors. Variety may be from timing and dose of exposure, as well as environmental factors, such as maternal depression (MD). This work examines whether PTE predicts greater internalizing behavior, and if so, whether MD acts as a moderator.
Methods: The nationally-representative, longitudinal dataset *The Fragile Families and Child Wellbeing Study* was used. Internalizing behavior was measured with Achenbach's Child Behavior Checklist, and MD was measured using the Composite International Diagnostic Interview; both were assessed at children's ages 3, 5 and 9. For children with PTE, multilevel modeling was used to determine if there was a dose response between PTE and higher maternal reports of children's internalizing behavior (N=306). Further, we examined if MD moderated the association between PTE and child internalizing problems. Maternal race, income, education, age and relationship status were used as covariates to account for oversampling of ethnic minorities and single-parent families.
Results: PTE significantly predicted greater internalizing scores. This association was significantly moderated by MD. MD exacerbates the effect of PTE, such that children with greater PTE and increased MD had the greatest internalizing behaviors.
Conclusions: Results indicate that greater PTE is predictive of greater internalizing behaviors in children, and that a synergistic effect exists with PTE and MD. These results provide insight into the relationship between tobacco addiction and maternal depression on children's outcomes, and may allow providers to address patients at risk for internalizing behaviors.
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HEALTHCARE UTILIZATION AND INSURANCE STATUS OF SUBSTANCE USING EX-OFFENDERS IN PRIMARY CARE.

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Aims: Individuals with criminal justice histories often have significant health needs and utilize expensive healthcare services at a high rate, which some have suggested stems from poor access to primary care and lack of insurance. However, there is little research on the healthcare utilization of those with both a criminal justice history and substance use. We examined the healthcare utilization and insurance status of primary care patients with a history of incarceration and current substance use.
Methods: As part of a clinical trial, patients in three primary care clinics were screened for risky substance use during regular appointments. Patients who met criteria and consented were randomized to receive one of two brief interventions. Participants completed assessments at baseline, 3 months, and 6 months that examined legal, medical, and behavioral indicators.
Results: Analyses were run on baseline data (n = 575) and follow-up data through 6 months (n = 308). Participants with a history of incarceration (41.7% of sample) were more likely to report a hospitalization within the past 30 days at baseline (10.8%) than those with no history of incarceration (4.5%) (x^2 [1], p=0.003), and they were also more likely to be hospitalized in the 6-month follow-up (23.2% vs. 13.5%) (x^2 [1], p=0.028). Paradoxically, ex-offenders were *more* likely to have insurance (87% vs. 72.2%)(x^2 [1], p=0.002).
Conclusions: Connection to primary care and insurance may not be sufficient to prevent hospitalizations for individuals with criminal justice histories and substance use. As the Affordable Care Act expands coverage for this population, primary care and correctional facilities should examine additional ways to address the unique health needs of these individuals.
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IS CANNABIS SMOKING HARMFUL? A MUTOSCOPE VIEW DISCLOSES PATTERNED MATURATION OF YOUTHFUL RISK PERCEPTIONS.

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Aims: We use a 'mutoscope' approach (Seedall & Anthony, 2014; http://www.ncbi.nlm.nih.gov/pubmed/25429727) to estimate the degree to which United States youth cohorts show patterned maturation in ratings of cannabis smoking harms.

Methods: Data are from the National Survey on Drug Use and Health (NSDUH) 2-year Restricted Data Analysis (RDAS) file. A nationally representative sample of non-institutionalized youth between 12-25 years of age are analyzed (unweighted aggregate *n*~447,401 across age and year pairs). Youthful participants answered standardized items on cannabis harm. Mutoscope estimates are produced cohort-by-cohort across year pairs such that participants aged 12-13 years in 2002-03 become 14-15 year olds in 2004-05, 16-17 years in 2006-07 and so on. Similarly, the cohort aged 14-15 years in 2002-03 turn 16-17 years old in 2004-05 and so on until the year 2010-11.

Results: Viewed cross-sectionally, cannabis harm ratings drop across early-mid adolescence, then show flat slopes. Mutoscope estimates disclose cohort-specific patterned maturation, with sustained downward slopes into young adult years ($p<0.05$).

Conclusions: The mutoscope approach sheds new light on maturation in ratings of cannabis harm. Our results indicate the necessity of examining cohort specific effects of youthful risk perceptions regarding the use of cannabis in addition to cross-sectional estimates.

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DO CONSUMERS SUBSTITUTE BETWEEN CANNABIS AND OPIUM? EVIDENCE FROM BRITISH INDIA.

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Aims: To test whether consumers of cannabis and opium treat the two substances as substitutes or complements and whether the consumption of these substances displays properties of dependence, price sensitivity, and income sensitivity.

Methods: Models of cannabis and opium consumption are estimated using econometric methods for the analysis of panel data. The data consist of annual population-level consumption and prices of cannabis (in the form of *bhang* and *charas* (hashish)) and opium, and control variables for 23 districts of the Punjab province in British India spanning 1908-1919 (n=276), obtained from annual provincial reports. Consumption of each drug is estimated as a function of its own price, the price of other drugs, and control variables. Dependence is incorporated into the model by including a lagged dependent variable. The models are estimated using the generalized method of moments. The null hypothesis that the consumption of a drug is not associated with the price of the other drug is tested. A positive association indicates a substitution effect, and a negative association is indicative of complementarity.

Results: For both opium and charas, there is evidence of dependence (β_C=0.39, $p < 0.01$; β_O=0.45, $p < 0.01$), price sensitivity (β_C=-0.74, $p < 0.01$; β_O=-0.28, $p < 0.01$), and income sensitivity (β_C=0.66, $p < 0.01$; β_O=0.46, $p < 0.01$). The evidence of interactions between the price of one drug and the consumption of another drug are, however, mixed, and drug-specific.

Conclusions: The behavior of populations that simultaneously consume cannabis and opium suggests that consumers treat them as substitutes or complements for each other. A key implication of this finding is that the control of one drug may simply lead to consumers switching to or reducing the consumption of the other drug.

Financial Support: This research benefited from funding from the NIH under NIDA grants 1R21 DA025917 and 1R21 DA020160.

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ESTIMATION OF LIFE EXPECTANCY AND THE EXPECTED YEARS OF LIFE LOSS AMONG HEROIN USERS IN THE ERA OF OPIATE SUBSTITUTION TREATMENT IN TAIWAN.

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Aims: To determine the life expectancy (LE) and expected years of life loss (EYLL) in a cohort of heroin users stratified by Opiate substitution treatment (OST) for comparison.

Methods: A cohort of heroin users (N=1283) were recruited during 2006-2008. Among them, 983 received OST, while 300 did not. They were followed till December 31, 2011 through record linkage to the National Mortality Registry and identify the deceased. Kaplan-Meier estimation for survival was performed, and it was extrapolated to 50 years to obtain the life expectancy by a semi-parametric method with an assumption of constant excess hazard. We further estimated the expected years of life lost (EYLL) for both cohorts by subtracting their life expectancies from the age- and sex- matched referents of the general population of Taiwan. Cause-specific standardized mortality (SMRs) were calculated and compared with the national cohort to validate the representativeness of this sample.

Results: The estimated average LE and EYLL were 27.4, 10.6 for patients receiving OST, while those of the non-OST were 20.2 and 18.4 years. The all-cause mortality rates (per 1000 person-years) in the 6 years period of OST and non-OST group were 15.5 and 23.9, respectively, representing 7.5- and 10.2-fold SMR compared to the general population, indicating a high representativeness for our sample.

Conclusions: The life-years (LY) saved by OST are substantial. Further detailed outcome assessments are needed to illustrate the overall benefit and cost-utility of this treatment.

Financial Support: This study was supported by grants MOHW-10250 from the Taiwan Ministry of Health and Welfare.

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ENERGY DRINK COMPOUNDS DIFFERENTIALLY AFFECT ANXIETY, LOCOMOTION, DEPRESSION AND COGNITION IN ADOLESCENT AND ADULT FEMALE RATS.

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Aims: In the US, nearly 75% of children under the age of 18 consume caffeine, not just in coffee, soda and tea, but also in energy drinks that also contain taurine. Energy drinks promise to improve mood, cognition and motor performance. More recently, energy drinks have been shown to decrease the subjective effects of impairment and increase binge drinking. This study aimed to determine the individual and combined effects of caffeine and taurine on locomotion, anxiety and depression, cognitive function in adolescent and adult female rats.

Methods: 32 adolescent and 32 adult female subjects were randomly divided into four groups (1) caffeine (20mg/kg/day; ip), (2) taurine (100mg/kg/day; ip), (3) caffeine & taurine (as a cocktail/day; ip) or (4) saline (ip/day). Treatment was initiated on PND 33 in adolescent females and PND 68 in adult females. One week after treatment began; consecutive behavioral assessments were performed while the females continued to be exposed to these compounds.

Results: Two-way ANOVAs determined adolescent females treated with caffeine showed increased locomotor activity ($P < 0.05$) and decreased anxiety ($P < 0.001$), while taurine and the cocktail had no effects. In adults, the compounds found in energy drinks increased anxiety ($P < 0.001$). In both age groups, caffeine alone, and combined with taurine, decreased depression ($P < 0.001$).

Conclusions: Working memory remained unaffected. These data suggest that active compounds found in energy drinks can have differential effects on emotional regulation, dependent on time of exposure, which in turn can impact behavioral outcomes related to addiction.

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CONSIDERATIONS ON DESIGNS OF INTRANASAL STUDIES FOR ABUSE-DETERRENT PRODUCTS.

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Aims: Abuse and misuse of prescription opioids is a serious and growing public health concern. Prescription opioid analgesic products can be manipulated for abuse. The Center for Drug Evaluation and Research at FDA published guidance regarding the development, evaluation and labeling of products that are less susceptible to abuse and misuse in 2013. The guidance proposes a three "Category" approach to the premarketing evaluation of abuse deterrent (AD) products. These studies include in vitro studies (Category 1), pharmacokinetic studies (Category 2), and human abuse potential studies (Category 3). Human abuse potential studies are intended to be predictive of the likelihood that the AD product will deter or reduce the abuse of the product through the oral, intranasal, or intravenous route, but the relationship between these studies and effects on abuse has yet to be confirmed. The preferred design of these studies is a randomized, double-blind, placebo- and positive comparator-controlled crossover study. However, several methodological challenges arise when evaluating the AD properties of these products for the intranasal route of administration. For example, some AD products have a much larger weight and/or volume or may, upon crushing, result in a powder of a different particle size distribution than the positive control used in the study. Because of these differences, a large sequence effect and period by treatment interaction may be observed. Some pros and cons of the current accepted designs for intranasal studies will be discussed, and a modified Williams square design will be proposed.
Conclusions: To address methodological challenges when evaluating the intranasal deterrent properties of AD opioid products in human abuse potential studies a modified Williams square design is proposed. The proposed design does not require weight matching across treatments and allows for the evaluation of whether weight itself is an abuse-deterrent factor in a proposed abuse-deterrent product.
Financial Support: N/A

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EFFECTS OF NON-PHARMACOLOGICAL TREATMENT OF SUBSTANCE USE IN MEDICARE ELDERLY WITH PROSTATE CANCER.

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Aims: To analyze the effects of non-pharmacological treatment of substance use on mortality in Medicare elderly with advanced prostate cancer and substance use disorder.
Methods: SEER-Medicare linked database for 2000 to 2009. Among men diagnosed with advanced prostate cancer between 2001 and 2004, we identified those with substance use using ICD-9 codes of 291 (Alcoholic psychosis); 292 (Drug psychoses); 303 (Alcohol dependence syndrome); 304 (Drug dependence); and 305 (Non-dependent use of drugs). For this cohort of elderly with prostate cancer and substance use, we determined the extent of non-pharmacological treatment for substance use using outpatient and provider claims. We analyzed the effects of treatment for substance use on five-year mortality using Cox regression.
Results: Of the 1509 elderly with advanced prostate cancer and substance use disorder, only 10% had a claim related to non-pharmacological treatment of substance use in the five-year post cancer diagnosis period. Demographic and clinical attributes of those treated for substance use were comparable to those not treated for substance use. Cox regression results showed that those treated for substance use had lower hazard of all-cause mortality, compared to those not treated for substance use (Hazard Ratio 0.63 ; 95% CI 0.46, 0.86).
Conclusions: Treatment for substance appears to have beneficial effect on mortality in elderly prostate cancer patients. However, the utilization of substance use treatment in this group was low. Prostate cancer incidence increases with age and substance use disorder remains a neglected co-morbidity in elderly prostate cancer patients. In addition to policies to screen and treat substance use in elderly prostate cancer patients, strategies for increasing utilization of substance use treatment by elderly cancer patients are needed.
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CHANGES IN AGE-SPECIFIC RATES OF DOCTOR-SHOPPING FOR OPIOIDS FOLLOWING INTRODUCTION OF REFORMULATED OXYCONTIN® TABLETS.

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Aims: To characterize and estimate changes in age-specific rates of doctor-shopping for OxyContin (oxycodone HCL extended-release) and other opioids before and after introduction of OxyContin reformulated with abuse deterrent properties in Aug 2010. Rates were compared for OxyContin and other single-entity (SE) opioid products, often abused through non-oral routes (eg, snorting and injecting), and combination opioid products (with acetaminophen), often abused orally by ingesting intact tablets.
Methods: The study used IMS LRx longitudinal patient data for >150 million patients covering approximately 65% of prescriptions filled in the US. Doctor shopping was defined as overlapping prescriptions with ≥2 prescribers and ≥3 pharmacies in a 6-month period. Age-specific rates were estimated by dividing the number of individuals doctor shopping in six-month periods by number of individuals prescribed for each age group. Rates of doctor-shopping were estimated for one year before (Jul 2009 - Jun 2010 and 2.5 years after (Jan 2011 - Jun 2013.
Results: Pre-reformulation, the age-specific doctor shopping profile was different for SE versus combination opioid products. Young adults (18-29 years old) had the highest rates for SE opioids (including OxyContin), whereas 30-44 and 45-54 year-olds had the highest rates for combination opioid products. After reformulation, rates of doctor-shopping declined overall for OxyContin (-50%), with the largest decline observed for 18-29 year-olds (-73%), intermediate declines for 30-44 and 45-54 year-olds (-51% and -46%) and smaller declines for 55-64 and 65+ year-olds (-25% and -29%). Post-reformulation, OxyContin age-specific rates were similar to those of opioid combination products. Declines in doctor-shopping rates were larger for OxyContin than other SE or combination opioids.
Conclusions: Large declines pre- to post- reformulation in doctor-shopping rates among young adults for OxyContin resulted in a change in its age-specific doctor-shopping distribution..
Financial Support: Support for this research was provided by Purdue Pharma, L.P.

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"DANGEROUS LIAISONS": HEIGHTENED INTRA-LIMBIC CONNECTIVITY DURING SUBLIMINAL COCAINE CUES IS A RELAPSE-VULNERABLE ENDOPHENOTYPE.

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Aims: Our laboratory has shown that even "unseen" 33 msec cocaine cues are sufficient to activate limbic motivational circuitry in cocaine patients. Heightened connectivity between the amygdala and other motivational nodes during these subliminal cues may reflect a 'dangerous liaison' – increasing cocaine relapse risk. We tested this hypothesis in a new cocaine cohort, examining (pre-treatment) amygdala connectivity for patients with GOOD vs. POOR cocaine use outcomes.
Methods: We analyzed (SPM 8) amygdala connectivity for cocaine-related and other 33 msec cues (48 per per category), presented subliminally with "fast" event-related BOLD fMRI for cocaine inpts (n=34, ongoing) — later separated into GOOD (< 30% cocaine pos/missing; n=8); vs. POOR (>90% cocaine pos/missing; n=12) outcome (2x/wk urines -12 wks).
Results: POOR pts. evidenced dramatic, widespread connectivity between the r. amygdala and multiple limbic nodes (l. amygdala, midbrain, bliateral striatum, pallidum, and insula (peak [24,6,-20] t = 40.9; p<0.000, FWE corrected) during cocaine cue exposure. In contrast, GOOD pts. showed connectivity restricted to the amygdalae and temporal poles.
Conclusions: Heightened intra-limbic connectivity to subliminal cocaine cues is indeed linked to future cocaine use, revealing a "cue-vulnerable" endophenotype. Conscious behavioral strategies may be of limited use for this vulnerability, underscoring the need for brain-targeted pharmacotherapies. The "unseen" cue paradigm may be useful both for screening medications, and for identifying the "cue-vulnerable" patients who will need these medications to achieve sustained recovery.
Financial Support: CURE Ctr; NIDA U54 Ctr.

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BSAFER: A WEB INTERVENTION FOR WOMEN IN THE ED WITH DRUG USE AND IPV.

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Aims: In a pilot RCT of BSAFER, an intervention for women with drug use and intimate partner violence (IPV) in the emergency department (ED), our aims were to:
1) Demonstrate the technical usability of the Web program and the feasibility and acceptability of the Web program and telephone booster;
2) Evaluate how well the Web program and booster adhered to the principles of motivational interviewing (MI)
Methods: We recruited adult female patients in an urban ED who screened positive for recent drug use and IPV. Participants randomized to BSAFER self-administered a brief Web program that gave feedback on drug use, linked drug use to core values, led to selection of a change goal, advised support for IPV, and offered referrals to community resources and video testimonials by women with drug use and IPV. Those randomized to control took a time-matched Web program on home fire safety. Within 2 weeks, participants received an interventionist-led telephone booster. Usability measures (SUS) were obtained after the Web program and measures of satisfaction (CSQ-8) and adherence to MI principles (12-item instrument) after the Web program and booster.
Results: Of 40 participants, 21 were randomized to BSAFER. Mean age was 30 years, 50% were non-White and 28% Hispanic. The most common drugs were marijuana (88%) and cocaine (30%); 45% reported physical abuse and 33% severe combined physical/sexual abuse. 39 (98%) completed the ED program; 20 (75%) completed the booster. Among BSAFER participants, average SUS score for the Web program was 83.5 (95%CI 78.1-88.9) of 100; average CSQ-8 score was 27.7 (95%CI 26.3-29.1) of 32; and adherence to MI principles was high (≥80% agreed with 9 of 12 MI characteristics). For the booster, average CSQ-8 score was 29.2 (95%CI 27.7-30.7);≥80% agreed with 9 of 12 MI characteristics.
Conclusions: A Web program and telephone booster intervention was feasible and acceptable to women in the ED with drug use and IPV and maintained most key elements of MI.
Financial Support: Supported by NIDA grant K23 DA031881

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EVALUATION OF COGNITIVE FUNCTIONING OF INDIVIDUALS WITH CO-OCCURRING OPIATE AND AMPHETAMINE-TYPE STIMULANTS USE DISORDERS IN MALAYSIA.

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Aims: Investigations of combined effects of opiate and ATS use on cognitive functioning are limited. We conducted a pilot evaluation of changes in cognitive functioning during medication-assisted treatment for co-occurring opioid and ATS use disorders in Malaysia.
Methods: Participants (N=50) enrolled in 18-week buprenorphine/naloxone (Bup/Nx) maintenance treatment with or without atomoxetine completed cognitive assessments at baseline and at months 2 and 4. Assessments included The Rey-Osterrieth Complex Figure (ROCF), Raven's Progressive Matrices (RPM), Trail Making Task (TMT) and backward digit span (DS-B).
Results: Among patients who completed all three assessments (n=22), lifetime duration of ATS use correlated negatively with RPM score at baseline ($p<0.05$), and RPM score at baseline correlated significantly with ROCF total recall and time taken to complete TMT at all three time points (all *p values* < 0.05). Those who tested negative for opiates and ATS on at least 50% of their urine tests during outpatient care (n=15) showed significantly greater improvements ($p<0.05$) on ROCF total recall and TMT compared to those who had less than 50% of negative tests (n=7). However, these improvements were no longer significant when baseline RPM and lifetime duration of ATS use were included as covariates.
Conclusions: Study results suggest that greater reductions of drug use during treatment may be associated with greater recovery of some cognitive functions among patients with co-occurring ATS and opioid use.
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EXAMINING DIFFERENT CHOICE PROCEDURES TO STUDY COCAINE VS. FOOD REWARD.

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Aims: Using preclinical models, a growing literature has begun to study the relationship between drugs of abuse and an alternative non-drug reward, studying how alternative reinforcers can compete with drug reinforcers. Herein, we examined different parameters in drug-food choice paradigms to assess the relative value of cocaine versus a sucrose pellet reinforcer.
Methods: Male Sprague Dawley rats were initially trained to lever press (FR1) for sucrose pellets. Rats were then catheterized and trained to lever press (FR1) for cocaine (0.3 mg/kg/inf). Rats were then placed on one of three choice paradigms consisting of 5 blocks, where cocaine dose increased by block (0, 0.1, 0.3, 0.56, and 1.0 mg/kg/inf). One paradigm consisted of 20-minute blocks where rats could distribute choices across drug and food options to earn a total of 15 reinforcers within each block. Another paradigm consisted of 4 forced trials (2 drug and 2 food) and 5 choice trials across blocks. Finally, a dependent schedule was used to assess drug and food preference while keeping experience equivalent across each reinforcer (3 drug and 3 food) where allocation of reinforcement across alternatives was randomized.
Results: Linear mixed-effects modeling was performed on the percent of cocaine choices made across block. Cocaine choices were significantly dose-dependent. However, under all procedures, there were individual differences in cocaine preference with some rats showing greater dose-dependency of drug choices. When using the combination of forced and choice trials, individual preferences tended to be exclusive to either the drug or food alternative. Under the fixed-time (20 min), fixed-reinforcer (15) procedure and the dependent schedule, individual preference for the drug option was more dose-dependent. Additionally, the dependent schedule also controlled for differential experience with each reinforcer as a possible determinant of preference.
Conclusions: Collectively, these results suggest that using different choice paradigms can produce differential sensitivity to drug reinforcers, relative to a non-drug alternative.
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POLY-SUBSTANCE USE PROFILES AMONG PEOPLE WHO INJECT DRUGS IN LOS ANGELES AND SAN FRANCISCO.

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Aims: Most PWID use more than one substance regularly, yet poly-substance use is an understudied phenomenon among PWID. We aim to classify poly-substance use profiles of PWID and to examine differences in these profiles in Los Angeles (LA) and San Francisco (SF).
Methods: Between 2011 and 2013, PWID in SF and LA participated in a cross-sectional study on injection initiation (N = 777). Interviews included questions on demographics, drugs used and route of administration for the past month. Drug use items were dichotomized into yes/no responses and those with responses greater than 15% prevalence were used as indicators in city-based latent class analyses to identify classes of substance use profiles. Demographic covariates were used as predictors for class membership.
Results: The total sample was racially/ethnically diverse, a quarter female, and split evenly between cities (SF N = 380, LA N = 397). Different sets of three classes were identified to describe substance use profiles in each region. In SF, the classes were "Heroin and Crack" (41%), "Primarily Methamphetamine" (40%), and "Heroin and poly-substance use" (18%). In LA, the classes were "Primarily Heroin" (59%), "Primarily Methamphetamine" (13%), and "Heroin and nonmedical use of prescription drugs" (28%). Age; gay, lesbian, or bisexual (GLB) identification; homelessness, and race/ethnicity were significant predictors of class membership in LA sample; in contrast, only age, GLB, and race/ethnicity were significant predictors of latent class in SF sample.
Conclusions: Our analyses of poly-substance use profiles in SF and LA suggests that they can be classified for PWID and differ by city and for various demographic covariates. Future research should examine the associations between poly-substance use with health behaviors and outcomes. Better understanding of poly-substance use profiles can be used to better inform intervention efforts.
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NATIONAL TRENDS IN HOSPITALIZATIONS FOR OPIOID PILL- AND HEROIN-RELATED OVERDOSE, 2005-2012.

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Aims: There is mounting concern of rising heroin misuse intertwined with the opioid pill misuse epidemic of the last decade. This presentation aims to:
1. Report on trends in hospitalizations for opioid pill-related overdose (OPOD) and heroin-related overdose (HOD)
2. Describe changes in the populations at risk for OPOD and HOD
3. Discuss the potential drivers of the heroin epidemic and HOD.

Methods: For years 2005-2012 heroin-related and opioid-related overdose hospitalizations were constructed from the Nationwide Inpatient Sample (NIS) data. National population estimates for hospitalizations were constructed by incorporating complex survey design into the estimates. Descriptive findings are below; analytic findings are pending.

Results: Rates of OPOD hospitalizations continued to increase nationally from 2005 to 2010. A novel finding is the decline in the OPOD rate after reaching its apogee in 2011; 2012 represents is the first year in our longer time series dataset (20 years) that a decline in OPOD hospitalizations is seen. However, rates for HOD hospitalization have risen dramatically: 8%/yr since 2005. The rates of HOD have risen the greatest among 20-35 y.o.; more than doubling from 2005 to 2012. For certain ages the rise has been more dramatic; eg HOD rates for 21 y.o. increased from 1.89 to 8.43/100000. The peak age of hospitalization for HOD is younger than for OPOD and is increasing younger by calendar year. In 2012, for the first time, rates of HOD (rising) and OPOD (declining) among 18 to 23 y.o. are converging.

Conclusions: The rise in heroin-related overdose underscores a nascent heroin epidemic in the US. Structural drivers of this epidemic include the over-supply of opioid pills and a rise in Mexican-sourced heroin. Additional pressures may stem from successful restrictions on the opioid pill supply including new laws and regulations on prescribing practices; shuttering "pill mills"; and the reformulation of OxyContin. Public policies to address this tide will be presented.

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IMPULSIVENESS AND SEX TRADING FOR DRUGS, MONEY, BOTH, OR NEITHER.

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Aims: The authors hypothesized that different patterns of results will emerge between those who sex trade for drugs, money, both, or neither.

Methods: 1,060 females were recruited in Long Beach, CA and were administered the Risk Behavioral Assessment and the Barratt Impulsivity Scale. Sex trading was categorized by sex trading for drugs only (n = 35), money only (n =124), or both drugs and money (n =275). Those who did not sex trade for drugs or money (n = 626) were used as the reference category.

Results: The generalized logit model included four factors: Sex trading for drugs only: impulsiveness (OR=2.33) crack use in the last month (OR=3.60), amphetamine use in the last month (OR=3.77) history of drug treatment (OR=4.91); Sex trading for money only: impulsiveness (OR=2.42), crack use in the last month (OR=3.10), and history of drug treatment (OR=1.9); Sex trading for both drugs and money: impulsiveness (OR=2.41), crack use in the last month (OR=5.89), history of drug treatment (OR=5.75).

Conclusions: This is the first study that models sex trading that uses those who do not sex trade as comparison. Amphetamine was only in the model for those only trading sex for drugs.

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WEB-BASED TREATMENT FOR SUBSTANCE USE DISORDERS: DIFFERENTIAL EFFECTS BY PRIMARY SUBSTANCE.

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Aims: This secondary analysis of data from a large, multi-site effectiveness trial (NCT01104805) sought to determine whether effects of a web-based behavioral treatment (Therapeutic Education System [TES]) differed by participants' self-identified primary drug of abuse.

Methods: The all-comers sample of individuals entering outpatient psychosocial counseling treatment for substance abuse (N=497) cited cannabis (22.9%; n=114), stimulants (34.4%, n=171), opioids (21.7%, n=108), or alcohol (20.9%, n=104) as their primary substance of abuse. Participants were randomly assigned to receive treatment-as-usual (TAU) with or without TES substituted for approximately 2 hours of usual counseling. Multivariate analyses of abstinence outcomes examined interactions of treatment effects with primary substance.

Results: Adjusted odds ratios (AOR) demonstrated primary stimulant users receiving TES were more likely to be abstinent in the final four weeks of treatment compared to stimulant users receiving TAU (AOR=3.59, 95% CI=1.25-10.27). Adjusted odds ratios for alcohol (AOR=3.15, 95% CI=0.85–11.65) and cannabis (AOR=2.64, 95% CI=0.73-9.52) also were of similar magnitude to stimulants but did not reach significance. Abstinence among primary opioid users was not improved by the TES intervention (AOR= 0.35, 95%CI=0.09-1.47).

Conclusions: This study supports the TES web-delivered treatment as a viable intervention for the majority of substance users entering outpatient counseling treatment, with demonstrated effectiveness among stimulant users and promising effects in alcohol and cannabis users but little or no effect in primary opioid users. Web-delivered treatments hold promise for expanding availability of effective behavioral interventions for the majority of substance use disorders.

Financial Support: Supported by NIDA U10 DA13034 and T32 DA07209.

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A NOVEL ORAL OXYCODONE MAINTENANCE PROCEDURE FOR HUMAN LABORATORY STUDIES.

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Aims: The increased prevalence of prescription opioid use disorders necessitates development of safe, sensitive, and reliable methods to study potential treatments, drug interactions, and physical dependence. Here we describe findings for a novel maintenance regimen used to evaluate abuse deterrence and a putative pharmacotherapy.

Methods: Two parallel, double-blind, placebo-controlled, within-subject inpatient studies (n=10 & n=11) were conducted. Subjects physically dependent on short-acting opioids were stabilized and maintained on 30mg oxycodone (OC) p.o., q.i.d. (8A, 12P, 6P, & 10P) for up to 6 wks. After stabilization, subjects underwent pharmacological challenge sessions at regular intervals, where physiological and subjective data were collected. Placebo was substituted for maintenance doses under double-blind conditions to assess time course and severity of spontaneous withdrawal. In Study 2, pressure algometer and cold pressor pain were evaluated during stabilization and at Week 5.

Results: Withdrawal severity was positively related to time since last OC dose, with subjects rating greater withdrawal scores during placebo challenge sessions after omission of 3 versus 2 active doses. Subjects were sensitive to acute OC challenges of 30 and 60mg, evidenced by miosis, decreased respiratory rate, and increased drug "liking." Greater drug "liking" was observed after longer placebo-substitution periods. There were no significant differences in algesia under maintenance conditions between Weeks 1 vs. 5, nor did they vary systematically in response to 0, 30 & 60mg OC.

Conclusions: The dosing regimen was well tolerated by all participants and produced reliable and clinically relevant opioid withdrawal that varied in severity based on time since last active dose. Subjective and some physiological measures (but not pain response) were sensitive to agonist challenge. While pain tasks produced algesia, a lack of drug-induced analgesia suggests that more than twice the maintenance dose would be required to produce analgesia.

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CHARACTERISTICS AND PREDICTORS OF NALOXONE UTILIZATION IN A COMMUNITY-BASED OVERDOSE PREVENTION PROGRAM.

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Aims: Drug overdose is the leading cause of injury death among U.S. adults. Naloxone is being promoted nationwide to address overdose risk, often with limited resources, yet little is known regarding who should be prioritized to receive take-home naloxone. We sought to understand predictors of naloxone utilization.

Methods: We analyzed 2010-2013 data from a San Francisco naloxone distribution program that provides naloxone under a standing order to anyone at risk of experiencing or witnessing an opioid overdose. Participant (N=2500) and reversal (N=702) characteristics were assessed and predictors of refills and reversals were examined using multivariable logistic and zero-inflated Poisson regression.

Results: Naloxone recipients who had previously witnessed an overdose [AOR]=2.06(95%CI=1.58-2.68)] or used heroin [AOR=2.05(95%CI=1.63-2.57)], other opioids [AOR=1.30 (95%CI=1.03-1.64)] or methamphetamine [AOR=1.67(95%CI=1.35-2.07)] had higher odds of obtaining a naloxone refill, while African American [AOR=0.60(95%CI=0.44-0.83)] and Latino [AOR=0.65(95%CI=0.43-1.00)] participants had lower odds. Those who had witnessed an overdose [AOR=2.56(95%CI=1.68-3.92)] or used heroin [AOR=2.49(95%CI=1.81-3.42)] or methamphetamine [AOR=1.65(95%CI=1.23-2.23)] also had higher odds of reporting an overdose reversal with naloxone, while African American participants [AOR=0.52(95%CI=0.32-0.84)] had lower odds of reporting a reversal.

Conclusions: Naloxone recipients who have previously witnessed overdose and are active users of opioids or methamphetamine are the most likely to use naloxone to reverse a future overdose, suggesting that programs with limited resources should prioritize reaching active substance users.

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SMOKING AND MENTAL HEALTH FROM FIRST PRENATAL VISIT TO POSTPARTUM.

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Aims: The study aims to describe the trajectory of smoking and mental health from first prenatal visit through 3 months postpartum and compare postpartum outcomes based on intake smoking status.

Methods: The sample of 130 participants was drawn from pregnant women attending their first prenatal visit at a low-income obstetrics clinic. Intake and 3 month postpartum assessments were collected. Postpartum smoking status was based on self-report and urine cotinine validation. 'Current smokers' and 'recent quitters' were contrasted on demographic, smoking behaviors, and psychological variables.

Results: The sample was predominately African-American (80%), never married (74%), currently smoking (69%), with a mean age of 26. Intake and postpartum data were available for 97 (75% follow-up rate). At intake current smokers reported smoking 66 of the past 90 days and 11 times per day (TPD); women who recently quit reported smoking 13 of the past 90 days and 7 TPD (between-group difference at p<.01). Current smokers reported more depressive and stress symptoms at intake than recent quitters and less motivation to quit (p<.05). Postpartum current smokers reported smoking 64 of the past 90 days and 8 TPD; women who had quit at intake smoked 1 of the past 90 days and 0.2 TPD (all at p<.01). Depressive symptoms were not different between groups postpartum but stress symptoms were (p<.05). Motivation to quit declined for both groups postpartum (p<.05).The same women who had quit at intake remained quit postpartum (28%), though 65% reported having quit smoking for at least one week during their pregnancy.

Conclusions: Pregnant women who quit smoking prior to their first prenatal visit are more likely to be abstinent postpartum. Those who continued to smoke maintained a similar level of smoking postpartum, though a majority stopped smoking at least once during pregnancy, suggesting motivation to quit during pregnancy diminishes postpartum.

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SINGLE-CENTER, RANDOMIZED, DOUBLE-BLIND CROSSOVER STUDY EVALUATION OF THE ABUSE POTENTIAL, PK, AND SAFETY OF CRUSHED AND INTRANASALLY ADMINISTERED IMMEDIATE RELEASE OXYCODONE TABLETS IN RECREATIONAL OPIOID USERS.

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Aims: OCI is an IR oxycodone tablet (5 to 30 mg strengths) intended for the management of moderate to severe pain. OCI contains sodium lauryl sulfate intended to deter intranasal (IN) abuse by causing aversive effects when OCI is crushed and insufflated. OCI also includes xanthan gum and carbopol intended to deter IV abuse by producing a viscous solution when crushed OCI is dissolved in small volumes of aqueous media.

Methods: A double-blind, placebo- and active-controlled, randomized 4-way crossover study was conducted to evaluate the abuse potential, PD, PK, and safety profile of IN OCI compared to IN Roxicodone (ROX) and IN placebo (PBO) in recreational opioid users. Safety was assessed using AEs, clinical laboratory tests, vital signs, SpO_2, physical examinations, and ECGs. Assessments included IN tolerability.

Results: Mean oxycodone PK parameters for all treatments (IN ROX, IN OCI, and OCI intact oral [PO OCI]) were generally comparable. IN OCI showed statistically significantly less abuse potential than IN ROX, PO OCI, or PBO on the majority of endpoints, including the 3 primary (VAS) endpoints ("at this moment" Drug Liking, Overall Drug Liking, and Take Drug Again). The majority of subjects (63%) showed at least a 50% reduction in E_{max} of "at this moment" Drug Liking following IN OCI as compared to IN ROX (P<0.05). IN OCI had significantly higher E_{max} values compared to IN ROX and PBO on most observer-rated IN irritation assessments.

Conclusions: IN OCI demonstrated significantly lower ratings of drug liking and willingness to take again and significantly greater aversive effects compared to IN ROX. These observations demonstrate that IN OCI should be expected to reduce its IN abuse. PO OCI produced the expected positive reinforcing effects. There were no safety findings of concern for any of the treatments.

Financial Support: Financial Support: Purdue Pharma L.P.

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ALERRT™ VISUAL ANALOG SCALE: ASSESSING "WORK" REQUIREMENTS ASSOCIATED WITH TAMPERING OF ABUSE-DETERRENT OPIOID FORMULATIONS.

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Aims: Assess the amount of "work" (combination of time, effort, and resources) required to transform an abuse-deterrent (AD) opioid formulation into a form suitable for intranasal, oral, rectal, and/or smoked use or solutions that can be administered by various routes. The measure of work is based on visual analog scales (VASs) used for measuring behavioral effects in human abuse potential studies.

Methods: The authors developed a new tool for use in Category 1 (*in vitro* tampering) studies, as defined in FDA's 2013 Draft Guidance on AD opioids. The tool provides a quantitative estimate of the amount of work involved in physical manipulations of pharmaceuticals, including AD formulations (ADFs). The tool is referred to as the "Assessing Labor, Effort and Resources Required for Tampering" (ALERRT™) scale. It is comprised of VASs designed specifically to measure work across a continuum from very easily accomplished to extremely difficult. The scale evaluates physical manipulation practices used commonly with opioids (mortar/pestle, coffee grinder). Four experienced laboratory technicians (DrugScan, Horsham, PA) conducted independent assessments under standardized conditions with two ADF controlled-release opioids (A and B) and a non-ADF immediate-release (IR) opioid (C). The opioid formulations were assessed in random order. Each assessment was preceded by a calibration procedure. The primary analysis examined the difference in mean VAS scores between A and B and A and C. Results were interpreted descriptively and directionally.

Results: There was a trend across the 3 products indicative of the difficulty of tamperabilty such that A > B >> C. These data were consistent with subjective perceptions that product A exhibited higher resistance to tampering than product B and substantially greater resistance than product C.

Conclusions: The ALERRT scale provided a quantitative measure of work required for tampering with ADFs. Product A demonstrated the highest work requirement.

Financial Support: PinneyAssociates received no financial support.

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WOMEN CAN FORCE MEN TO HAVE SEX? FORCED SEX TACTIC AND SUBSTANCE USE AMONG SEXUALLY VICTIMIZED MEN.

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Aims: Sexual violence towards men by women has been grossly understudied in the literature. Moreover, the tactics used to force sex among men is virtually unknown. The aims were to investigate: (1) the tactics used to force men to have sex and (2) the role of substance use on forced sex and the tactics employed.
Methods: I used data from the National Survey for Family Growth (2006-2010) to investigate the association between forced sex and substance use among men who reported forced sex by a woman and the association between tactic used during the sexual attack and substance use in the last year. Six tactics were ranked according to force exhorted: given drugs/alcohol, bigger/older, threats to relationship, threaten physical harm, held down, physically hurt. The analytic sample was 8,108 and I used logistic regression to test the hypotheses.
Results: Five percent of men (N= 501) reported forced sex by a woman. The top 3 tactics endorsed were verbal pressure (69%), given drugs/alcohol (38%), and being held down (32%). Results indicate a difference in rates of marijuana use ($p=0.02$), crack use ($p<0.001$), crystal meth use ($p<0.001$) and a marginal difference for binge drinking ($p=0.058$) between men who reported forced sex and those who did not. Being given drugs or alcohol as a means of forced sex was associated with binge drinking (OR=1.76) and cocaine use (OR=3.04). Being held down was associated with marijuana (OR=2.04) and cocaine use (OR=2.89).
Conclusions: Men who reported forced sex had higher rates of substance use compared to men with no forced sex history. Although substance use was associated with force tactics at statistically significant levels, a clear trend of stronger tactics being associated with substance use was not observed. Longitudinal analysis of sexual practices should be conducted to better understand the role of alcohol/drug consumption preceding a forced sex event and to examine whether there is a cycle in which substance use increases risk of future sexual violence and thus violence increases risk of substance use among men.
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MARIJUANA USE AND UNDETECTABLE HIV VIRAL LOAD IN PERSONS LIVING WITH HIV IN FLORIDA.

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Aims: Helping PLWH to obtain an undetectable HIV viral load is part of the National HIV Strategy. Marijuana use is common among PLWH but little is known about its association viral load suppression. We sought to determine the association between marijuana use and undetectable viral load, and to assess the impact of antiretroviral (ART) medication adherence on this outcome.
Methods: We used data from the Florida Medical Monitoring Project (2009-2010), a CDC-sponsored study from a random sample of persons receiving HIV care in Florida. Marijuana use was characterized as any (past year) vs. none; undetectable viral load (≤ 200 copies/mL) was determined by chart abstraction. Multivariable logistic regression was used to determine the association between marijuana use and undetectable viral load while adjusting for demographic factors, depression, other substance use, and ART adherence (95% or more).
Results: Of the overall sample (n=803), 76% (n=528) had an undetectable viral load, 22% (n=173) reported any marijuana use in the past 12 months, including 7.7% (n=61) with daily use. Among those currently on ART (n=628), marijuana users were less likely to achieve an undetectable viral load (72% vs. 83%, $p=0.018$). In multivariable analysis, marijuana use was associated with a significantly decreased likelihood of having an undetectable viral load (OR: 0.57, 95% CI: 0.38 – 0.88). When adjusting for ART adherence, marijuana users remained less likely to have an undetectable viral load (OR: 0.65, 95% CI: 0.40 – 1.05), although the result was not statistically significant.
Conclusions: Marijuana use was relatively common in this sample of persons with HIV and was associated with a reduced likelihood of having an undetectable viral load. This relationship appeared to be partially, but not completely, related to non-adherence to ART.
Financial Support: Research was supported in part by NIH grant AAU2402002.

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IMPACT OF ADOLESCENT MARIJUANA USE ON EMOTION PROCESSING: AN FMRI STUDY.

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Aims: Marijuana is the most commonly used illicit drug in the U.S. Evidence exists for a potentially causal link between adolescent marijuana use and mood disorders later in life. Thus, the aim of this study was to examine associations among early marijuana use, emotion-related brain activity, and later emotional outcomes in young adults.
Methods: Participants were forty 17-22 year old males and females from an ongoing fMRI longitudinal study. They were classified as either heavy marijuana users (n=20) or controls with minimal marijuana use (n=20). An fMRI emotion-arousal word task was used to examine hemodynamic responses to positive, negative, and neutral stimuli. Resiliency (i.e., a flexible mechanism for coping with the environment) and negative emotionality were assessed at three times: marijuana use initiation, scan, and follow-up. We hypothesized that heavy marijuana users would show decreased resiliency and increased negative emotionality over time and that this would be mediated by neural responses to negative stimuli.
Results: Resiliency increased and negative emotionality decreased over time in controls but not in heavy marijuana users. Significant partial correlations were observed between marijuana use and resiliency at scan, controlling for resiliency at initiation ($r=-.51$, $p=.001$), and between marijuana use and negative emotionality at scan, controlling for negative emotionality at initiation ($r=.34$, $p=.033$). Activation of the middle frontal gyrus/dorsolateral prefrontal cortex to negative stimuli mediated the relationship between marijuana use and later negative emotionality. Activation of cuneus/lingual gyrus mediated the relationship between marijuana use and later resiliency.
Conclusions: These results support the mounting evidence that frequent early marijuana use affects emotional outcomes later in life. As marijuana use increases and perceptions of harm decrease nationwide, the importance of research on the cognitive and affective consequences of adolescent marijuana use will continue to grow.
Financial Support: R01 DA027261, R01 AA12217, R01 AA07065, K01 DA020088, T32 DA7268-22, T32 DA007267-20

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CANNABIS, LORD SHIVA AND HOLY MEN: CANNABIS USE AMONG SADHUS IN NEPAL.

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Aims: To explore the patterns of use and beliefs about cannabis use and its association with Lord Shiva and religious observance among sadhus attending the major Shiva festival at Pashupathinath temple complex in Kathmandu, Nepal.
Methods: A cross sectional face to face survey of 200 sadhus during the Shiva festival at Pashupathinath temple complex in Kathmandu, Nepal in February 2014.
Results: Most of the sadhus interviewed reported using cannabis daily. Around 1 in 4 believed cannabis and its use to be legal in Nepal, and a further ten percent were unsure. Around one in three believed cannabis should be used by Hindus, but only fourteen believed Lord Shiva promoted its use. Those less educated and from the Naga sect were more likely to hold such views, and to provide cannabis to devotees.
Conclusions: There is a need to provide religious leaders like Sadhus with more evidence-based information about cannabis. There should be greater knowledge of its potential harms and negative influence on engagement with other interventions such as OST. Sadhus can play an important cultural role in modifying cannabis use and supporting healthier choices. They should also not invoke Lord Shiva as an excuse for excessive cannabis use.
Financial Support: None outside the research team.

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CHANGES IN DIAGNOSED ADDICTION RATES IN PATIENTS PRESCRIBED OPIOIDS AFTER INTRODUCTION OF OXYCONTIN WITH ABUSE-DETERRENT PROPERTIES.

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Aims: The impact of opioids with abuse deterrent properties (ADPs) on addiction rates in patients prescribed opioids has not been assessed. We evaluated changes in diagnosed addiction among patients prescribed OxyContin® (extended-release (ER) oxycodone) after its reformulation with ADPs. Comparator opioids were used to distinguish OxyContin-specific changes from general opioid changes. Diagnoses of addiction have been shown to have high positive predictive value to detect addiction.
Methods: ICD-9 codes were used to identify addiction (304.0x and 304.7x) in a commercially insured US population (MarketScan). ICD-9 uses the term dependence for addiction. For OxyContin or 3 other opioids, changes in diagnosed addiction rates per 100 person-years of opioid use were calculated from 1 year before (August 2009- July 2010) to 1 year after (November 2010- October 2011) OxyContin reformulation, Changes were stratified by one or multiple opioid use since these have different addiction rates.
Results: Among 74 million insured individuals, 29,695 and 164,838 patients used OxyContin alone or with concomitant opioids, respectively. After reformulation, rates of diagnosed addiction decreased 27% among patients using OxyContin alone (95% CI: -37%, -16%, <0.0001) and 9% (95% CI: -15%, -3%, <0.0001) using OxyContin with other opioids.. For comparator opioids, rates of diagnosed addiction among patients prescribed immediate-release (IR) single-entity (SE) oxycodone increased 15% and 4% for single and multiple opioids, respectively; for ER oxymorphone changed +22% and -7%, and for ER morphine changed +1% and -11% for single and multiple opioids, respectively.
Conclusions: Rates of diagnosed addiction among patients prescribed OxyContin decreased significantly after its reformulation with abuse-deterrent properties; the decrease was greater for OxyContin used alone than used with other opioids; the decrease for OxyContin alone was greater than that for ER oxymorphone, ER morphine and IR SE oxycodone used alone.
Financial Support: Purdue Pharma L.P.

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MIRTAZAPINE PILOT TRIAL IN COMORBID MDD/SUD: LONG-TERM FOLLOW-UP RESULTS.

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Aims: To date, pharmacotherapy trials of comorbid major depressive disorder and substance use disorder (MDD/SUD) have focused on SSRI medications, with disappointing results, so effective treatments for that comorbid population are lacking. Results from our recent open label study suggest acute phase efficacy for mirtazapine for decreasing the depression and the drinking but not the cannabis use of that population. However, to date, no studies have evaluated the longer-term efficacy of mirtazapine in that population. We now report findings from a first long-term naturalistic follow-up evaluation involving subjects from the acute phase trial. We hypothesized that the improvements would persist at follow-up.
Methods: An eight-week open label study of mirtazapine and motivation therapy was conducted involving persons 18 to 55 years of age with DSM-IV diagnoses of comorbid MDD/AUD, most of whom had also used cannabis. Two years after entry into the acute phase study, a long-term evaluation was conducted to assess whether the improvements seen during the acute phase trial had persisted.
Results: Ten of the twelve patients who entered the acute phase study participated in the follow-up. The large magnitude improvements in depressive symptoms (BDI) and alcohol use (TLFB) persisted at the follow-up evaluation ($p<.01$), but no significant decrease in cannabis use was noted. Two of the subjects demonstrated MDD on structured interview at follow-up, while all ten had demonstrated MDD at baseline. Six of the ten subjects used antidepressants during the follow-up period.
Conclusions: These findings suggest long-term efficacy for mirtazapine for decreasing the depression and alcohol use of patients with comorbid MDD/SUD. Double-blind, placebo-controlled studies are warranted to clarify the efficacy of mirtazapine in patients with comorbid MDD/SUD.
Financial Support: K24-AA015320, R21 AA022123, R21 AA022863, RO1AA015173, RO1 DA09142

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MULTI-COMPONENT TOBACCO-FREE WORKPLACE PROGRAM IN COMMUNITY MENTAL HEALTH SETTINGS: THE ROLE OF PROVIDERS' TRAINING IN TOBACCO DEPENDENCE TREATMENT.

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Aims: Tobacco use and dependence is twice as high in people with mental and behavioral disorders compared to their counterparts. Due to a common misconception among practitioners that quitting tobacco may exacerbate or trigger psychiatric symptoms, evidenced-based cessation treatments are often not made available to smokers with mental disorders. Integrating tobacco cessation interventions into smokers' mental health care and implementing tobacco-free campus policies at mental health clinics can significantly reduce the smoking rates of people with mental disorders, their health care providers, and the communities in which they reside. Austin Travis County Integral Care's (ATCIC) Tobacco-Free Workplace Program is a multi-component tobacco-free (MCTF) campus intervention program that has reduced tobacco use among their patients and employees. The ongoing *Taking Texas Tobacco Free* (TTTF) Program aims to adapt and disseminate ATCIC's program to dozens of mental health clinics across Texas.
Methods: TTTF intervenes at four different levels: *clinic-level* for tobacco-free policy implementation and providers' training, *employee-level* to encourage and assist staff to quit smoking, *consumer-level* to provide brief tobacco cessation interventions among patients, and *community-level* to provide tobacco-related education to local communities.
Results: Providers and staff completed needs assessment surveys. Over 1,700 providers have been trained to treat tobacco dependence among psychiatric populations and in motivational interviewing.
Conclusions: Implementing a MCTF campus in community mental health clinics is generally well-received by the majority of the clinics. Provider training is a necessary component to successfully address tobacco dependence among persons with mental disorders and to attain the programs' sustainability.
Financial Support: The program is supported by Cancer Prevention Research Institute of Texas PP130032 and the abstract submission by NIDA R25DA030310 (VCF).

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EFFECTS OF CANNABIS USE ON OPIOID INJECTION FREQUENCY.

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Aims: Opioid abuse is a critical public health problem in the US, with 2.1 million people reporting past year pain reliever dependence in 2012. Opioid addiction may lead to criminality, injection drug use, HIV and mortality. The medical use of cannabis has been studied and therapeutic benefits observed. There is evidence that opioid users turn to cannabis to progress out of opioid use. Observational research has shown that cannabis users report using it as a substitute for alcohol, illicit and prescription drugs.
Methods: We conducted a longitudinal study of cannabis use and injection frequency among 357 opioid injectors recruited through street outreach in Denver from 2007-2012. To evaluate changes over time, we incorporated longitudinal negative binomial models of injection frequency, where the primary outcome of interest was the difference in injection frequency among cannabis groups over time while controlling for predictors of loss to follow-up. The interaction tested whether reductions over time were different between the three cannabis use groups.
Results: Reductions in injection frequency were seen across groups but notably at the twelve month period between the high cannabis use and low cannabis use groups. The significant interaction suggested a 47% decrease ($p=0.02$) in reported injection frequency in high cannabis-using individuals over individuals reporting low cannabis consumption at 12 months. We found significant decreases in injection frequency among individuals who used cannabis for 20 or more days per month over those who used less than 10 days per month.
Conclusions: The study findings suggest that further research should examine the relationship between cannabis and opioid use.
Financial Support: This study was supported by the National Institute on Drug Abuse, DA09832-15.

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SEX DIFFERENCES IN EFFECTS OF TRAIT IMPULSIVITY ON VULNERABILITY TO SUBSTANCE DEPENDENCE.

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Aims: Trait level impulsivity is a core feature of addictive processes. Research with non-clinical populations suggests that different components of impulsivity are most prominent among men (sensation seeking:SS) and women (negative urgency:NU). This study investigated potential sex differences in the relationship between sensation seeking, negative urgency and substance use among 271 participants with substance use disorders (SUDs).
Methods: 139 men and 132 women completed the UPPS-P Impulsive Behavior Scale as part of a larger study of sex differences in neurocognition and drug dependence. DSM-IV TR diagnoses were obtained using the SCID-Substance Abuse Module. All subjects were verified abstinent by toxicology screening.
Results: As predicted, men scored significantly higher on the SS ($p = .02$) (Cohen's $d = 0.50$) while NU scores were significantly higher for women ($p < .001$) (Cohen's $d = 0.3$). Among women, higher NU scores were significantly associated with past alcohol dependence, $p = .01$. By contrast, higher SS scores were significantly associated with cocaine dependence among men, $p = .004$. These results were unchanged when controlling for depression.
Conclusions: NU is an index of behavioral dyscontrol triggered by negative affect and SS is the tendency and openness to try new and exciting activities that vary in danger level. NU had a significant positive relationship with past alcohol dependence only for women and this effect could not be attributed to nonspecific effects of psychological distress, while SS was significantly associated with cocaine dependence, but only among men. These findings suggest that specific components of impulsivity interact with vulnerability to substance use disorders differently among men and women and that effective prevention and treatment strategies for alcohol and cocaine dependence may benefit from sex and substance specific tailoring.
Financial Support: Supported by the National Institute on Drug Abuse R01 DA12828

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INCREASED CORTICAL EXCITABILITY IN HUMAN MDMA USERS.

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Aims: MDMA produces serotonergic axon toxicity in animal models. Human recreational MDMA users have reduced serotonin in cortex. Serotonin is mainly inhibitory in cortex; therefore we posited that MDMA users would have increased cortical excitability. We measured cortical excitability using transcranial magnetic stimulation (TMS) in the primary visual and primary motor cortices of MDMA users and non-MDMA exposed control subjects.
Methods: We enrolled 16 MDMA users and 16 non-MDMA exposed control subjects (age was 22.3±2.3 years). All were free from drug use for 2 weeks, verified by repeated urine drug screening. A T1-weighted structural MRI scan was obtained and the TMS coil was stereotactically positioned using each subject's structural scan. We used a Magstim 2T Rapid stimulator (Magstim Company, UK) peak discharge = 1.8 kV; 70-mm figure-eight) to deliver cortical excitation. For visual cortex, we positioned the coil to allow evocation of the phosphene within 2° of the fovea; coil location was about 2 cm above the inion. Coil intensity was set at 90% intensity to yield a phosphene with eyes closed or motor twitch of the dorsal interosseous muscle of the right hand. TMS intensity was then reduced to 54% intensity and adjusted upward until the individual was able to detect the phosphene threshold or motor twitch generation on 75% of trials.
Results: MDMA users had increased cortical excitability (as indexed by lower TMS stimulation thresholds). Mean TMS threshold for visual system was 66.67±6.72% for MDMA users and 75.31±10.56% for controls ($p=0.012$). Mean TMS threshold for motor system was 63.43±7.90% for MDMA users and 73.75±8.06% for controls ($p=0.001$). Greater lifetime MDMA use was significantly associated with increased cortical excitability (reduced TMS threshold) for the visual system ($r_s=-0.82$; $p<0.001$) but not for motor threshold ($r_s=-0.15$; $p=0.575$).
Conclusions: MDMA users have increased cortical excitability.This finding is consistent with the predicted consequences of MDMA-induced serotonin neurotoxicity.
Financial Support: NIDA DA033341;Vanderbilt CTSA TR000445

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SHARED AND DISTINCT NEURAL MECHANISMS OF INHIBITORY CONTROL IN INDIVIDUALS WITH A HISTORY OF A SUBSTANCE USE DISORDER AND DEPRESSION.

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Aims: Substance Use Disorders (SUD) & Major Depressive Disorder (MDD) often co-occur, leading to poor functional & cognitive outcomes. However, little is known about the shared & distinct neural mechanisms of SUD & MDD. This study examined how a past history of SUD (hSUD) & active MDD impacts neural processing during inhibitory control (IC).
Methods: Six hSUD individuals, 14 hSUD+MDD, 22 MDD, & 37 healthy controls (HC), free of potential confounds, completed the Parametric Go/No-Go Task (PGNG) during fMRI. The PGNG is a measure of IC including commission trials.
Results: hSUD performed more poorly on IC than hSUD+MDD & HC, with no group differences in Go accuracy. MDD & hSUD+MDD had slower reaction time on the task than non-MDD. During commissions, hSUD had greater BOLD activation compared to all other groups in the right dorsolateral prefrontal cortex (rDLPFC). On the other hand, during commissions, hSUD had less BOLD activation compared to all other groups in the right insula/inferior frontal gyrus (rI/IFG). In addition, HC had greater activation in rostral anterior cingulate cortex (rACC) relative to all other groups during commissions.
Conclusions: Our results provide preliminary evidence that SUD & MDD have some distinct, as well as some shared neural mechanisms. hSUD individuals have poorer IC & differential activation in some areas important for Cognitive Control when successful in inhibiting prepotent responses (rDLPFC), as well as less activation in areas important for emotion & more implicit aspects of control (rI/IFG), suggesting differential mechanisms of dysregulation. On the other hand, HC had greater activation in areas implicated in error processing (rACC), indicating that this area may be underactive in both SUD & MDD. Future studies will further explore these distinct & shared neural profiles & include individuals with active SUD, to better understand state & trait neural mechanisms of SUD & MDD.
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GSK3B SILENCING IN THE NAC PRODUCES ADDICTION- AND DEPRESSION-LIKE PHENOTYPES OPPOSITE OF ENVIRONMENTAL ENRICHMENT AND ALTERS NEURONAL EXCITABILITY.

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Aims: Vast individual differences exist in the susceptibility and resilience to drug addiction. Understanding the molecular mechanisms may lead to better treatments for addicts. Our lab showed a decrease in mRNA levels of GSK3B in the nucleus accumbens (NAc) of environmentally enriched animals. Enrichment causes robust protective addiction and depression phenotypes and dysfunction of GSK3B is associated with other psychiatric disorders in addition to drug addiction. We hypothesized that knocking down GSK3B in the NAc would alter depression-, anxiety-like, and addiciton-related behavior and have an effect on neuronal excitability.
Methods: We created an shRNA vector targeting GSK3B, injected it in NAc and conducted behavioral tests to evaluate depression- and anxiety-like behaviors. We assessed cocaine- taking and -seeking behavior using IV cocaine self-administration. Finally, recordings from viral infected neurons were performed in NAc slices.
Results: Silencing GSK3B in the NAc reduces neophobia to an unfamiliar taste (sucrose), cold stress-induced defecation, preference for sucrose, and grooming of a conspecific. The vector also increased acquisition of cocaine self-administration (0.2mg/kg/inf), maintenance responding (0.5mg/kg/inf), and attenuated extinction responding. There was no change in spontaneous locomotor activity. NAc cells expressing the vector showed decreases in firing rates shown with loose-patch recordings.
Conclusions: Knocking down GSK3B in the NAc produces anxiolytic-like behavior while increasing depression-like and addiction-related behavior and alters the excitability of NAc neurons. These behavioral effects are opposite to the effects of environmental enrichment. The role of GSK3B in conferring the protective depression and addiction phenotypes of environmental enrichment is more complicated but these results provide additional evidence for the role of GSK3B in the susceptibility to affective disorders and addiction.
Financial Support: Funded by R01 DA029091, R01 MH095995, R01 NS081121, and T32 DA007287.

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USING FACEBOOK AD SAMPLING TO EFFICIENTLY SURVEY CANNABIS VAPORIZER USE.

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Aims: Vaporizer use appears to be rapidly increasing as a method for ingesting cannabis, although sparse data are available to verify this observation. In an attempt to efficiently obtain data to examine current trends in cannabis administration, we evaluate the use of Facebook Ads as a tool for recruiting cannabis users to complete surveys. We then examined demographic and substance using characteristics of respondents.
Methods: A 63-item survey was distributed using Facebook Ads in 10 24-hour campaigns, targeting 21,000,000 adults that were interested in pro-marijuana pages. Survey items addressed cannabis and nicotine use, and preferences for methods of ingestion.
Results: The Facebook ad was shown to N=79,336 people, with N=2,447 clicking the ad and N=1,036 completing the survey. Over 85% of respondents finished in less than 10 minutes. The average cost per participant was $0.27. Sixty-three percent of the sample reported vaporizer use. Age of first vaporizer use (M=21.9, SD=9.4) was 6.6 years later than age of first cannabis use (M=15.3, SD=9.4). Those that had used a vaporizer were 2.5 years older on average ($p < .01$) than those who had not. Males were more likely to use vaporizers than females (70.6% vs. 57.1%: $p < .01$). No race or ethnicity differences in vaporizer use were found. Most vaporizer users opt for inconspicuous pen-style devices (30.7%), followed by tabletop (20.8%) and portable (17.0%) devices. Those with increased levels of education were more likely to list vaporizers as their preferred method of cannabis use ($r = 0.13$, $p < .01$). Of note, 72.2% of people used a vaporizer to consume nicotine.
Conclusions: This study supports the utility of Facebook Ads as a cost-effective method of data collection. Future studies could improve targeting to increase efficiency. Vaporizer users were more likely to be male, older, more educated, with no clear racial and ethnic differences.
Financial Support: NIDA P30-DA029926, T32-DA037202, R01DA032243

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ABERRANT BRAIN FUNCTION AS AT-RISK CHILDREN MAKE RISKY DECISIONS.

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Aims: Childhood behavioral disinhibition (BD) predicts adolescent substance and conduct problems. Adolescents with such problems under-activate numerous decision-related brain regions when choosing between a risky or a cautious behavior. Is that abnormality a pre-existing contributor to the youths' excessive substance use or a toxic result of that use?
Methods: Subjects: 58 children (31 girls) 9-11 years old, recruited from the community or from families of patients in substance treatment. Assessments: Child Behavior Checklist Externalizing Scale for BD scores; Monitoring the Future questions for substance exposure. In 90 fMRI "decision trials" subjects decided between making a cautious response (win 1 cent) or a risky response (win 5 or lose 10 cents; loss odds increased as the game progressed). Hypothesis: during a 4-sec deliberation period before responses, the intensity of decision-related brain activation will associate negatively with BD scores.
Results: Substance exposure was minimal. BD scores ranged from low to very high. Before risky responses BD significantly, negatively associated with activation intensity (VTA-substantia nigra, dorsal/ventral striatum, insula, elsewhere). Before cautious responses the association was significantly positive (dl-prefrontal cortex, frontal pole, cuneus, precuneus, elsewhere).
Conclusions: Young children with minimal substance exposure but at risk for future substance problems had aberrant brain activation during risky decision-making. Adolescents with serious substance and conduct problems have similar abnormalities. Together, those observations suggest that such adolescents' brain abnormalities preceded, rather than resulted from, substance use. Neural abnormalities in risky decision-making may underlie some young children's later risky decisions to use substances excessively.
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MORPHINE AND FENTANYL CHRONIC EFFECTS ON LIPOPOLYSACCHARAIDE RESPONSE AND μ OPIOID RECEPTOR LOCALIZATION IN MAST CELLS.

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Aims: Fentanyl (Fen) is more potent than morphine (Mor) and induces less tolerance to its analgesic effects. Acute Mor inhibits the release of tumor necrosis factor (TNF) in response to bacterial LPS in peritoneal mast cells (MCs) in mice. To determine if Mor and Fen also differ in their immunological effects, the objectives of this work were: a) to compare the acute effects of Mor and Fen to inhibit TNF release produced by LPS; b) to analyze if repeated Mor and Fen administration induces tolerance to their immunosuppressive effects; and c) to analyze if opiate administration produces changes in TLR4 and μ opioid receptor localization in MCs.
Methods: Independent groups of mice (n=8, each) received one i.p. injection of Mor (0.1-10 mg/kg) or Fen (0.001-0.1 mg/kg) 10 min prior to LPS (1 mg/kg). Peritoneal TNF levels were determined 1 h later. Other groups were repeatedly injected with 10 mg/kg Mor or 0.1 mg/kg Fen (3x/day to complete 10 doses) and then challenged with LPS. MCs from animals with different treatments were isolated to analyze cell localization of TLR4 and μ opioid receptors.
Results: Fen was more potent than Mor to acutely inhibit LPS-induced TNF release. Repeated Mor administration produced tolerance to antinociception and LPS-induced TNF release. Repeated Fen injection did not induce significant antinociceptive tolerance but produced sensitization to LPS. Fen produced more μ opioid receptor internalization than Mor in MCs. Both opiates produced TLR4 receptor internalization.
Conclusions: Mor and Fen differ in their chronic effects on LPS-induced TNF release. As opposed to morphine, tolerance to immunosuppressive actions of Fen can be dissociated from antinociceptive tolerance. Similarly to what occurs in neurons, Mor and Fen differ in their capacity to induce μ opioid receptor internalization in MCs.
Financial Support: ANR-Conacyt 188565 to CGE and scholarship 219851 to LMMM.

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NEW EPIDEMIOLOGICAL EVIDENCE ON COCA LEAF CHEWING AND A DEPENDENCE SYNDROME IN 2008.

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Aims: Toxicological assays disclose cocaine-positive blood biomarkers five minutes after chewing coca leaf, and alcohol dependence (AD) history might increase likelihood of transitioning from coca leaf use toward a cocaine dependence syndrome (CD). Here, the aim is to estimate CD probability as a function of coca leaf and AD.
Methods: Data are from the Rural Peruvian Andean Highlands Mental Health Community Survey of 2008 (n=3,031 adults 18+ years). Standardized MINI neuropsychiatric interviews assessed CD and alcohol dependence (AD), with ICD-10 diagnostic guidelines. Contingency table, logistic regression for complex survey data, and weighted generalized linear model/generalized estimating equation analysis (GLM/GEE) produced the study estimates.
Results: CD was relatively rare among adults with coca leaf chewing histories (2.3%). Craving was the most prevalent clinical feature among among coca leaf chewers with AD (12.7%) and without AD (4.4%). GLM/GEE modeling showed an AD-excess of coca craving that was an estimated 3-4 times greater than expected ($p<0.05$). Even so, risk of having become a CD case was not elevated among AD-affected coca leaf consumers ($p>0.05$). In exploratory analyses, earlier age of coca leaf chewing was not predictive of CD, but older adults were more likely to have become CD cases.
Conclusions: Micro-doses of cocaine in coca leaf and slower absorption might help explain these findings, and larger samples might be needed to differentiate risks experienced by AD cases with and without coca leaf chewing histories. The polydrug combination of ethanol and coca leaf chewing deserves greater attention in the portfolio of research on cocaine effects if we are to understand population health impact of these behaviors in the Andean region of the Americas.
Financial Support: NIH/FIC/NIDA D43TW05819 (VC) & K05DA015799 (JCA).

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U.S. FEDERAL COCAINE ESSENTIAL ("PRECURSOR") CHEMICAL REGULATION IMPACTS ON US COCAINE AVAILABILITY: AN INTERVENTION TIME SERIES ANALYSIS WITH TEMPORAL REPLICATION.

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Aims: Research shows that essential/precursor chemical controls have had substantial impacts on US methamphetamine and heroin availability. This study examines whether US federal essential chemical regulations have impacted US cocaine seizure amount, price and purity—indicators of cocaine availability.
Methods: ARIMA-intervention time series analysis was used to assess the impacts of four US regulations targeting cocaine manufacturing chemicals: potassium permanganate/selected solvents—implemented 10/1989, sulfuric acid/hydrochloride acid—implemented 10/1992, methyl isobutyl ketone—implemented 05/1995, and sodium permanganate—implemented 12/2006: of these chemicals, potassium permanganate and sodium permanganate are the most critical to cocaine production. The setting was the conterminous United States (01/1987-04/2011). The measures were monthly time series: purity-adjusted cocaine seizure amount (in gross weight seizures < 6000 grams), purity-adjusted price (all available seizures), and purity (all available seizures). The data source was the Drug Enforcement Administration's System to Retrieve Information from Drug Evidence.
Results: The 1989 potassium permanganate/solvents regulation was associated with a seizure amount decrease (change in series level) of 28% ($P < .05$), a 36% increase in price ($P < .05$), and a 4% decrease in purity ($P < .05$). Availability recovered in 1-2 years. The 2006 potassium permanganate regulation was associated with a 22% seizure amount decrease ($P < .05$), 100% price increase ($P < .05$), and 35% purity decrease ($P < .05$). Following the 2006 regulation, essentially no recovery occurred through 04/2011. The other two chemical regulations were associated with statistically significant but lesser declines in indicated availability.
Conclusions: US essential chemical controls were associated with pronounced downturns in cocaine availability in the United States.
Financial Support: None

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CRIMINAL ARRESTS AMONG DRUG-USING ASSAULT-INJURED YOUTH SEEKING ED CARE: A PROSPECTIVE COHORT STUDY.

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Aims: Describe rates/characteristics of criminal arrest among assault-injured and non-assault injured drug-using youth during the 36-mos (12-mo. before/24-mo. after) surrounding an ED visit
Methods: 14-24 y/o youth screening positive for past 6-mo drug use and presenting for an assault (AIG) or as part of a proportionally-sampled comparison group (CG) of non-assaulted youth were enrolled (n=599) in a 2-year longitudinal study. Validated measures were administered at baseline and follow-up (6, 12, 18, 24-mo). Objective arrest data (for >18 y/o) was obtained from the Law Enforcement Information Network. Survival analysis was used to characterize arrest rates; parametric modeling identified baseline characteristics predictive of arrest.
Results: 599 youth (82% participation) completed the baseline survey; 97% (n=584) were ≥18 y/o during the study and were included in the analysis. At baseline, 59% were male, mean age 20, 65% African-American, 97% marijuana use, and 57% drug use disorder. Over 36-mo, the AIG had 30% greater risk of arrest than the CG (47%-vs.36%; RR 1.30, p<0.05), with 77% arrested during the 24-mo follow-up. The AIG had a higher mean # of arrests (2.23-vs.-1.72, p<0.01) with 50% of those arrested experiencing multiple arrests. 42% of arrests (n=509) involved a violent/weapon related crime; 28% property crime; and 22% drug-related crime. 63% of arrests resulted in no formal charges, 14% in jail/prison time, 11% in probation and 19% in judicial fines/restitution. Parametric modeling found that age (RR=1.04), male gender (RR=1.92), African-American race (RR=1.22) and a diagnosis of Drug Use Disorder (RR=1.25) and assault (RR=1.30) increased risk for criminal arrest.
Conclusions: Drug-using youth presenting to an Urban ED for assault have high rates of criminal arrest; Interventions at an index ED visit for assault addressing drug use and violence correlates may limit subsequent CJ outcomes and their associated long-term consequences.
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FAILURE TO GET INTO DRUG TREATMENT.

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Aims: Understanding why illicit drug users are not able to access drug treatment is an important health services research question.
Methods: 3561 individuals were recruited in Long Beach, CA and administered the Risk Behavior Assessment, and the Barratt Impulsivity Scale (BIS).
Results: Those who were not able to get into treatment were more likely to have: had previous treatment (OR=3.9), injected amphetamines (OR=2.7), be homeless (OR=1.7), ever used amphetamines (OR=1.6), traded sex for drugs (OR=1.6), had higher scores on the Nonplanning subscale of the BIS, and were less likely to have a paid job (OR=0.7). The major reasons for the failure to access treatment were: 1. Program did not have room, 2. Not enough money, 3. Did not qualify.
Conclusions: Findings highlight the importance of targeting treatment interventions for individuals at risk for rapid drop out of treatment, and increased opportunities for relapsed and chronic users.
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A RANDOMIZED CLINICAL TRIAL OF EMERGENCY DEPARTMENT INITIATED TREATMENT FOR OPIOID DEPENDENCE: TWO AND SIX MONTH OUTCOMES.

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Aims: Screening and Brief Intervention (SBIRT) followed by ED-initiated buprenorphine (Bup) with ongoing treatment in primary care (BupPC) is superior to referral to community-based treatment (RT) and SBIRT alone in engaging opioid dependent patients in treatment and decreasing drug use at 30-days. We evaluated the impact of these methods at 2 and 6 months.
Methods: We conducted a randomized clinical trial in 329 opioid dependent ED patients that compared RT, SBIRT, and BupPC. RT patients (n=104) received a referral to a substance use disorder (SUD) provider, SBIRT patients (n=111) received a Brief Negotiation Interview and a facilitated referral to a SUD provider, BupPC patients (n=114) received SBIRT and ED-initiated BUP with ongoing BUP in primary care for 10 weeks followed by transfer to ongoing SUD treatment or taper as per patient request. Primary outcomes were self-report of current engagement in SUD treatment and illicit opioid use at 2 and 6 months. Analyses were conducted using chi-square and analysis of variance.
Results: Patients in RT and SBIRT groups were less likely to be engaged in treatment compared with the BupPC group at 2 months, 53%, 47%, and 76%, respectively, p<0.001. There was no difference in treatment engagement between groups at 6 months, 56%, 57%, 55%; p >0.05. At 2 months, the mean number of days of illicit opioid use in the past week for RT, SBIRT and BupPC was 1.8, 2.0 and 1.1 days; p=0.04 for comparison between SBIRT and BupPC. There was no difference in illicit opioid use between treatment groups at 6 months: 1.5, 2.0, 1.6 days; p=0.54.
Conclusions: BupPC was superior to RT and SBIRT for engaging opioid dependent patients in treatment and reducing illicit drug use during the period that primary care-based BUP was provided. While all treatments engaged patients and decreased illicit opioid use, BupPC offers the greatest benefit to opioid dependent ED patients.
Financial Support: NIDA-5R01DA025991, 5K12DA033312

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"TIME FOR DABS": ANALYZING TWITTER DATA ON BUTANE HASH OIL USE.

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Aims: While media reports about the popularity of butane hash oil (dabs, budder) use in the U.S. have been increasing, data on the epidemiology of its use remain limited. The overall goal of the study is to explore Twitter data on hash oil use in the U.S. The study builds on mixed methods approach, and has the following aims: 1) examine differences in the volume of dabs-related tweets among states with varying cannabis legalization policies; 2) describe user attitudes towards dabs.
Methods: Tweets were collected over a 7-day period, November 3-9, 2014, using Twitter's streaming API. Twitter data filtering framework was available through eDrugTrends/Twitris system. SPSS was used to analyze differences among states with varying cannabis legalization policies. A sub-sample of tweets was manually coded using QDA to identify sentiments towards hash oil use.
Results: Over a 7-day period, we collected 18,333 tweets posted by 14,490 users. Over 20% (n=3,938) of tweets contained identifiable state-level geolocation information. Hash oil-related tweet volume for each state was adjusted to account for the number of tweets per state based on a randomly generated sample. Adjusted ratios of hash oil-related tweets were significanlty higher in the states that allowed recreational and medical use of cannabis. Qualitative analysis revealed that the majority of tweets conveyed positive views towards hash oil use.
Conclusions: Twitter data suggest highly positive attitudes towards "dabs" among users, and indicate greater popularity in the states that legalized recreational and/or medical use of cannabis. The study highlights the usefulness of Twitter data for drug abuse epidemiology research.
Financial Support: NIDA R01DA039454, Daniulaityte/Sheth, PIs

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NALOXONE DISTRIBUTION TO DRUG USERS IN CALIFORNIA AND OPIOID-RELATED OVERDOSE DEATH RATES.

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Aims: Opioid-related overdose is a leading cause of death in the United States. Since the 1990s, one response to increased overdose has been the distribution of naloxone, an opioid antagonist, to drug users and those in their immediate social circles. By 2010, at least 188 organizations were distributing naloxone to drug users in the United States, and collectively reported training at least 53,000 lay individuals to use naloxone, leading to at least 10,000 successful overdose reversals. In California, programs distributing naloxone exist in 14 of the state's 58 counties, allowing exploration of the impact of such programs on rates of overdose death.
Methods: To assess the impact of naloxone programs on accidental overdose deaths in California over an 11 year period, we fit four Poisson generalized linear mixed models, employing four different offset terms: all accidental poison deaths; all accidental deaths; all deaths; and population per county per year.
Results: The overall effect of naloxone distribution was statistically significant for accidental overdose deaths as a proportion of all deaths ($p = 0008$), with a significant effect for intervention x year ($p = 0002$), indicating that naloxone programs are associated with reductions in the rate at which overdose deaths grow as a proportion of all deaths. The overall effect of the intervention was also statistically significant for accidental overdose deaths as a proportion of county population ($p < 0001$), with a significant effect for intervention x year ($p < 0001$), indicating that naloxone programs are associated with reductions in the rate at which overdose deaths grow as a proportion of county population.
Conclusions: Our analysis provides support for the argument that distributing naloxone to active drug users and those around them reduces deaths.
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CONTINGENCY MANAGEMENT IN THE TREATMENT OF SUBSTANCE USE DISORDERS: TRENDS IN THE LITERATURE.

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Aims: The aim of the current review is to examine growth and change in research on Contingency Management (CM) treatments for substance use disorders (SUDs) over the past 5 years (November 2009 – November 2014) and to contrast these findings with those from two earlier reviews (1991-2004, 2004-2009) to examine how CM research is changing over time.
Methods: All studies in the current review were identified using PubMed and similar search methods and inclusion criteria as those used in the previous reviews.
Results: Fifty-five studies met the inclusion criteria. Consistent with the 2004-2009 review, these studies were categorized into six different trends: (a) extending CM to special populations (40% of articles), (b) extending CM to community clinics (14.5%), (c) improving longer-term outcomes (7.3%), (d) combining CM with pharmacotherapies (7.3%), (e) investigating parametric questions (27.3%), and (f) using CM interventions as a research tool (1.8%).
Conclusions: The mean number of studies identified in this 2009-2014 review is comparable to the 2004-2009 review and both are greater than the rate in the 1991-2004 review. A larger portion of CM research in the present review was focused on addressing parametric questions and extending CM to special populations than in the earlier reviews. There was also a substantial increase in the number of studies incorporating new technology, which holds promise for measuring target behaviors that were previously difficult to measure (e.g., alcohol intake).
Financial Support: This research was supported by National Institutes of Health Center of Biomedical Research Excellence award P20GM103644 from the National Institute of General Medical Sciences; research grants R01DA14028 and R01HD075669 from the National Institute on Drug Abuse and National Institute of Child Health and Human Development. The funding sources had no other role in this project other than financial support.

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HOSPITAL DISCHARGES FOR MARIJUANA DEPENDENCE OVER TIME IN COLORADO.

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Aims: This study aimed to examine public health impacts that may be related to medical marijuana legalization in Colorado, specifically hospital discharges. We utilized monthly hospital discharge data for marijuana dependence from 2009 through 2013, a unique time period preceding recreational legalization of sales but following the Odgen report, which transferred enforcement authority from the federal government to the states in July of 2009.
Methods: Monthly statewide hospital discharge counts of ICD9 coded marijuana dependence (ICD-9-CM 304.3), as well as applications for medical marijuana licenses, were obtained from the Colorado Department of Public Health and Environment. Due to relatively rare hospital counts, negative binomial regression with population as the offset was used to evaluate the changing rate of hospital discharges. Linear regression was used to evaluate applications for medical marijuana over time. The application analysis was followed with an analysis exploring population growth as a confounder. Autocorrelation was evaluated and an AR1 structure was used as necessary. Finally, the association between monthly medical marijuana applications and monthly discharges coded as dependence was tested with linear regression to explore an ecologic dose response relationship.
Results: From 2009 to 2013, both applications and discharges increased, where 4205 ($p<0.001$) additional applications were received per month, and a 0.9% ($p<0.001$) increase in population rate per month was detected in hospital discharges. This was not confounded by population growth. The association between applications and discharges was significant ($p<0.001$) but modest with only 1 discharge per 3159 applicants.
Conclusions: Although statistically significant increases were detected over time, the relation between applications and discharges was small in the time period preceding the legalization of recreational sales. Other states considering the legalization of medical marijuana can use this report to assist in the evaluation of public health related outcomes of policy change.
Financial Support: NIH/NIDA, 5R01DA031816-04, The Impact of Medical Marijuana in Metropolitan Denver

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MATERNAL AGE AND TRAJECTORIES OF MARIJUANA USE OVER 17 YEARS.

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Aims: Teen mothers engage in higher rates of marijuana use than adult mothers, including earlier use and delayed desistence (Carroll Chapman & Wu, 2013; De Genna et al., 2014; Gillmore et al., 2006). They may "age out" of substance use later, using marijuana while raising their children. However, no studies have examined the effect of maternal age on long-term patterns of marijuana use.
Methods: Pregnant women (ages 12-42) were recruited from an urban prenatal clinic and interviewed twice during pregnancy, providing data on marijuana use one year prior to pregnancy (N = 690). Mothers were re-assessed at delivery and during follow-up visits 6, 10, 14, and 16 years later. A growth mixture model (GMM) was applied (maternal use one year prior to pregnancy, first trimester, third trimester, and postnatal years 6, 10, 14 and 16) to examine variation in trajectories of use.
Results: GMM revealed a cubic growth curve with 5 patterns: low/non-use (53%), increased use after pregnancy (9%), chronic use including use during pregnancy (14%), pre-pregnancy use decreasing after pregnancy (22%), and chronic use with abstinence during pregnancy (3%). In a polytomous regression controlling for maternal race and educational attainment, the youngest mothers were significantly more likely to be in classes marked by increasing marijuana use after pregnancy and chronic marijuana users who abstained during pregnancy.
Conclusions: These results demonstrate that teen mothers are significantly more likely to use marijuana chronically before and after pregnancy. Importantly, a subset of them increase use for over a decade beyond the target pregnancy. These findings have implications for the next generation. Teen mothers should be screened for marijuana use up to 16 years post-pregnancy.
Financial Support: DA025734; DA037209 (PI: De Genna); AA08284, DA009275, AA022473 (PI: M. Cornelius); AA06390, HD36890, DA03874 (PI: N. Day)

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EXAMINING DSM AND ICD DEFINITIONS OF PHARMACEUTICAL OPIOID DEPENDENCE IN PEOPLE TAKING OPIOIDS FOR CHRONIC PAIN: FINDINGS FROM THE PAIN AND OPIOIDS IN TREATMENT STUDY.

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Aims: We compared definitions of pharmaceutical opioid use disorder/dependence in the World Health Organization's ICD-10 and ICD-11, and the American Psychiatric Association's DSM-IV and DSM-5 in a national, community-based sample of people living with chronic pain prescribed opioids for pain.
Methods: Pharmaceutical opioid use disorders (ICD-10, 11; DSM-IV, 5) were assessed using the Composite International Diagnostic Interview. Agreement between classification systems were examined, and confirmatory factor analyses tested fit of each definition to a unidimensional syndrome.
Results: In 1,422 people living with chronic pain prescribed strong opioids (for a median 4yrs, 56% female, mean 58yrs), similar proportions met lifetime criteria for dependence using DSM-IV (8.9%), ICD-10 (8.5%) and ICD-11 (9.9%); 9.1% were classified with moderate/severe DSM-5 use disorder. There was poor agreement between both ICD-10 and DSM-IV dependence diagnoses and DSM-5 use disorder (mild, moderate or severe). There was only fair agreement between DSM-5 moderate/severe use disorder and the other definitions. There was excellent agreement between ICD-10, ICD-11 and DSM-IV dependence (κ>0.90). The best model fit was for draft ICD-11 dependence; the worst for DSM-5.
Conclusions: Classification of problematic pharmaceutical opioid use varies across editions of ICD and DSM. Poor agreement between DSM-5 and other definitions was attributed to DSM-5 having more criteria, treating dependence and problematic use as a continuum. Despite the parsimony of ICD-11 dependence, it demonstrated both excellent model fit and agreement with previous classifications.
Financial Support: The Australian National Health and Medical Research Council

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PREVALENCE OF HEAVY FETAL ALCOHOL EXPOSURE DURING PREGNANCY IN CANADA: A POPULATION BASED MECONIUM STUDY.

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Aims: Alcohol consumption during pregnancy is associated with Fetal Alcohol Spectrum Disorder (FASD), which is a continuum of neurological disabilities. Meconium is the first stool passed by a neonate and allows for objective analysis of mainly third, and potentially second, trimester prenatal exposures. The established biomarker of in utero alcohol exposure, fatty acid ethyl esters (FAEEs), is used to objectively measure heavy maternal alcohol consumption during pregnancy. It is hypothesized that 3% of pregnancies in Canada involve heavy maternal alcohol consumption as the 1% prevalence of FASD in Canada is thought to only represent 40% of heavily exposed neonates.
Methods: In collaboration with the MIREC study, 2000 pregnant women were recruited from 10 cities across Canada, with 1537 consenting to meconium sample analysis. Meconium samples were analyzed for 4 FAEEs via GC-MS analysis. Any sample with a total [FAEE] greater than 2nmol/g is deemed positive for heavy fetal alcohol exposure. In addition to meconium sample collection, participating women completed questionnaires during pregnancy that included a section on alcohol consumption, which will serve as maternal self-report. Meconium sample analysis is currently ongoing at the Motherisk Laboratory.
Results: Thus far 782 samples have been processed with 696 eligible for analysis. After accounting for meconium sample collection time, the incidence rate of heavy fetal alcohol exposure in Canada is 2.17%. Fifty women reported above social level drinking and one reported binge drinking during pregnancy.
Conclusions: As these findings represent second and third trimester exposures when the pregnancy is known, the women who continue to consume alcohol are at risk of having alcohol dependence problems and their children of being impacted by FASD. This study is the first of its kind to objectively measure the rate of heavy fetal alcohol exposure in Canada.
Financial Support: Funding was provided by The Public Health Agency of Canada.

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THE GEOSPATIAL AND TEMPORAL CORRELATION OF OXYCODONE AND HEROIN DEATHS IN FLORIDA COUNTIES, 2011 TO 2013.

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Aims: There is growing concern that efforts to limit the availability of prescription opioids (e.g., oxycodone) has contributed to an emerging heroin epidemic. From 2010 to 2013, Florida reported a 66% decrease in the rate of oxycodone-caused deaths, consistent with a 24% reduction in oxycodone prescribing, but heroin-caused deaths increased by 293% over the same time period. The aim of this study is to test the hypothesis that, at the county-level, 1) death rates for both drugs are correlated, 2) death rates exhibit similar patterns of geographic clustering, and 3) heroin-caused mortality is correlated to a time lag in oxycodone-caused mortality.
Methods: We mapped county-level, mortality rates by quartile (determined from rates pooled over 3 years) for oxycodone and heroin in 2011 and 2013 using data from Florida's Medical Examiners Commission. We describe geographic clustering and used linear regression to test models for heroin-caused deaths as a function of a zero, one, or two-year lag of oxycodone-caused deaths at the county-level.
Results: For both oxycodone and heroin, we identified several persistently high rate mortality clusters. In 2013, counties with high rates of oxycodone-caused deaths did not appear to overlap with counties with high rates of death from heroin. Linear models for the zero and one-year lagged models had r2 of 0.01 and 0.03, respectively, whereas the two-year lagged model had r2=0.18. These models indicate that rates of oxycodone-caused deaths in 2011 were directly related to the rates heroin-related deaths in 2013 although several counties (e.g., Miami-Dade) had notable inverse relationships.
Conclusions: This work has county, state and national implications for monitoring persistent population-level problems with oxycodone and heroin abuse and the ability of health agencies to anticipate emerging trends in heroin abuse.
Financial Support: Internal funding only.

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CONTRASTING TRAJECTORIES OF INTERVENTION-RELATED SELF-MONITORING IN HIV PRIMARY CARE PATIENTS.

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Aims: Among HIV primary care patients, drug abuse is a common problem, for which brief, effective interventions are needed. Self-monitoring is an evidence-based element of brief intervention. In a randomized trial of "HealthCall," a technology-assisted self-monitoring intervention to reduce non-injection drug use, patients' engagement in self-monitoring varied. A better understanding of patient characteristics associated with the level and course of self-monitoring during intervention can assist counselors in improving personalized feedback and treatment outcomes.
Methods: In an on-going randomized trial, 79 patients in urban HIV primary care clinics who were abusers of non-injection drugs (stimulants, opioids) were randomized to receive MI + HealthCall. We applied growth mixture modeling analysis to identify groups with distinctive trajectory patterns across the 60 day intervention. We selected the best fit model based on AIC and BIC fit criteria. To investigate factors associated with trajectory patterns we conducted chi-square tests (for categorical variables), and Kruskal-Wallis one-way ANOVA (for continuous variables) to assess group differences.
Results: Growth mixture modeling identified three self monitoring trajectory groups: (1) high engagement, average 75% daily engagement (N = 28); medium engagement, average 58% daily engagement (N = 37), and low engagement, average 45.1% engagement (N=13). Patients with impaired cognitive functioning, Hispanic ethnicity and more years since HIV diagnosis were more likely to be in the high engagement (Impairment: p=0.02; Hispanic: p = 0.01; HIV Years: p = <0.01).
Conclusions: Our results indicate differential characteristics associated with engagement trajectory, thus suggesting the importance of a tailored intervention. The findings that cognitively impaired patients are more engaged in HealthCall suggest that this technology may be particularly suitable to enhance interventions for HIV-infected non-injection drug users, meriting further study.
Financial Support: R01DA024606; K05AA014223;R01AA014323

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A 6-MONTH FOLLOW-UP OF THE INTEGRATED TREATMENT FOR OPIATE ADDICTION AND HIV IN VIETNAM.

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Aims: To evaluate the implementation of an integrated drug treatment program within an HIV treatment setting in Ho Chi Minh City, Vietnam.
Methods: All the patients received opiate maintenance treatment (methadone or buprenorphine/naloxone), HIV and HCV testing and counseling sessions focused on substance use and HIV/ HCV risk-taking behaviors. Here we assess the impact of this program on treatment initiation, treatment adherence, and change in substance use at 6-month follow-up.
Results: 145 heroin injectors who met DSM-5 opiate use disorder diagnosis were enrolled, mainly males (96.4%), 32.4 y.o. (SD= 5.2), living with family (81%), reporting employment (50.4%). They reported using heroin for an average of 7.8 years (SD= 3.6, min-max= 1-20). The retention rate at 6-month was 96.6%, significantly higher than before the initiation of the integrated treatment program (86.3%). Treatment adherence was very high, 90.3% did not miss any methadone doses, 6 patients missed only one day of treatment. The methadone maintenance dose ranged from 30 mg to 220 mg per day. The counseling session attendance ranged from 83% to 100%, and none of the participants missed more than one counseling session. There was a significant decrease in opioid (heroin) use, 68% of the participants reported using heroin at 1 month, 13% at 2 months and none after 3 months of treatment. Fifty-one (35.2%) were HIV-positive, with four not previously known to be positive. All 51 HIV-positive participants received HIV treatment. Eighty-nine (68.0%) were HCV-positive, 42 (46.7%) were newly diagnosed. Only 2 participants (2.4%) had received HCV treatment.
Conclusions: At 6-month, the findings showed the added value of an integrated treatment program on drug use, HIV detection, and access to HIV care. Long-term follow-up is needed to confirm the impact of this program.
Financial Support: NIDA R01- DA033671-01

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MECHANISMS AND REVERSAL OF ADOLESCENT COCAINE-INDUCED HABITS.

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Aims: Adolescence is a period of vulnerability to the development of many psychiatric disorders, including substance dependence disorders. Incubation of certain biological factors associated with addiction may play a causal role. We explored this hypothesis in the context of cocaine-induced stimulus-response habits, which are considered a factor in the development and maintenance of addiction.
Methods: Adolescent or adult male C57BL6/J mice were exposed to cocaine (10 mg/kg i.p.), and decision-making strategies were characterized using response-outcome contingency degradation. Transgenic mice expressing *thy1*-derived YFP were utilized for dendrite and dendritic spine imaging. In separate experiments, STI-571, an Abl-family kinase inhibitor, was infused into the orbitofrontal prefrontal cortex (oPFC). Alternatively, fasudil, a Rho-kinase inhibitor, or ifenprodil, an NR2B-selective NMDA receptor antagonist, were administered systemically. All compounds were delivered immediately following response-outcome contingency degradation, but before a subsequent probe test.
Results: Mice with a history of subchronic cocaine exposure in adolescence developed stimulus-response habits at the expense of engaging in goal-directed decision-making strategies. In addition, oPFC dendritic spines were eliminated and dendrites were simplified. oPFC targeted infusion of STI-571 eliminated dendritic spines and biased responding towards stimulus-response habits, recapitulating the effects of adolescent cocaine. Conversely, fasudil and ifenprodil blocked cocaine-induced habits.
Conclusions: Together, these findings suggest that adolescent cocaine exposure confers behavioral vulnerabilities to stimulus-response habits in adulthood by altering cellular structure during development. Novel treatment strategies should aim to reverse the chronic effects of adolescent cocaine exposure, including behavioral, morphological, and neuroplastic consequences.
Financial Support: NIH DA034808, DA015040, the Emory Egleston Children's Research Center, Children's Healthcare of Atlanta, and P51OD11132.

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NON-ORAL ABUSE OF IMMEDIATE-RELEASE HYDROCODONE.

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Aims: Immediate-release (IR) hydrocodone combination products (eg, IR hydrocodone/acetaminophen) are the most frequently prescribed and most abused opioid analgesics. Most IR hydrocodone abuse occurs through oral routes; however, data on non-oral abuse is limited. Therefore, non-oral abuse of IR hydrocodone was examined in 2 pharmacoepidemiologic studies.
Methods: The study populations comprise substance abuse treatment-seeking individuals in the US (NAVIPPRO; 4Q11-1Q13) and opioid abusers in rural Kentucky (interviewed 12/10-09/11). Outcomes for the NAVIPPRO study include the number and proportion of individuals reporting intranasal or intravenous (IV) abuse of IR hydrocodone, and the opioid comparators IR oxycodone single-entity (SE) and extended-release (ER) morphine. Outcomes for the Kentucky study include the prevalence and frequency of intranasal and IV abuse among respondents.
Results: The absolute number of individuals reporting intranasal abuse of IR hydrocodone was 316-355 per quarter (21-25% of all individuals reporting IR hydrocodone abuse), compared to 43-63 per quarter for ER morphine, or 21-28% of individuals abusing ER morphine. IV abuse of IR hydrocodone was rare, with approximately 15 individuals reporting IV abuse per quarter (~1% of individuals reporting IR hydrocodone abuse), compared to 84-172 per quarter for ER morphine, or approximately 50-70% of ER morphine abusers. In the sample of rural Kentucky opioid abusers, 65% reported past 30-day intranasal IR hydrocodone abuse (mean days/month=14); no respondents reported IV abuse of IR hydrocodone.
Conclusions: Although the proportion of individuals entering substance abuse treatment who report snorting as a route of abuse for IR hydrocodone is relatively low, because IR hydrocodone is so widely abused the number of individuals snorting IR hydrocodone exceeds that of the comparator opioids. Within the sample of rural Kentucky opioid abusers, almost two-thirds reported snorting IR hydrocodone, with a relatively high frequency.
Financial Support: Funded by Purdue Pharma LP

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FACEBOOK AS A LOCATING AND TRACKING STRATEGY AMONG RURAL DRUG-USING WOMEN.

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Aims: The popularity of social media has exploded among the public in recent years, with Facebook (FB) leading the way. Individuals living in rural communities are just as likely as those living in urban areas to be FB users (71% vs. 75%; Duggan & Smith, 2013). Despite its popularity, FB has been underutilized in public health research to maintain contact with research participants. This study examines FB use among a sample of rural drug-using women transitioning to the community from jail. Specifically, the study 1) profiles rural drug-using women FB users and non-users and 2) examines predictors of utilizing FB as a successful locating and tracking strategy.
Methods: Face-to-face interviews were conducted with 267 randomly selected and screened women from rural jails in one Appalachian state. Analysis focused on bivariate differences between FB users and non-users, as well as a regression model to examine predictors of FB as a successful locating/tracking tool for follow-up.
Results: About half (56.2%) of participants were FB users. FB users were significantly younger than non-users, with women younger than 26 years old being significantly more likely to use FB ($p<.05$). FB users were also significantly more likely to be located for follow-up (72.0% vs. 25.6%; $p<.00$). Among FB users, 35.3% were successfully located for follow-up using a confidential study site. The only significant predictor for follow-up locating success using FB was number of previous incarcerations (OR = 1.159).
Conclusions: Study findings indicate that FB is a widely used and well-accepted mode of social networking among drug-using women in rural areas. While these study findings indicate that Facebook may strengthen study methodologies for long-term follow-up, it also suggests the possibility of social media platforms like FB for delivering effective interventions to rural drug-using women.
Financial Support: National Institutes of Health, Grants R01DA033866 and K02DA35116

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IMPAIRED COGNITIVE CONTROL IN LONGER-TERM ABSTINENT BUPRENORPHINE-ASSISTED TREATMENT OPIOID-DEPENDENT PATIENTS.

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Aims: Long-term abstinence is the goal of all treatment programs, but little is known about the underlying cognitive mechanisms that allow inhibition of response to drug cues. The purpose of this preliminary study was to test the ability of longer-term abstinent (> 3 months) buprenorphine-assisted opioid dependent patients to control their responses toward opioid and neutral cues. Here we report preliminary data of an ongoing study.
Methods: Six male (M=29.66 yrs. old) adult opioid dependent patients who were predominately Caucasians (83%), all high school graduates and all abstinent for at least 3 months and 12 undergraduate controls were tested on a Drug and Neutral Simon task. The Simon task is when participants categorize stimuli (Drug) with one hand (Left) for one response and the other hand (Right) for the other response (Neutral). Stimuli can appear on the screen on the left or right. Participants are slower and more error prone at responding when the stimulus appears on the side of the screen opposite the response.
Results: Patients showed a significant Simon effect ($p< .04$). In contrast to Controls, there was a strong trend for a bigger Simon effect for Drug than Neutral cues ($p= .09$) in the opioid dependent patients. Controls also showed a significant Simon effect ($p< .002$) but the effect was equivalent for Drug stimuli and Neutral Stimuli ($F< 1$).
Conclusions: These longer-term abstinent opioid dependent patients are still showing a significant slowing in cognitive control to Drug cues even after months of abstinence. These preliminary data suggest that drug cues are powerful stimuli that patients have difficulty in controlling responses to which persists even after longer-term abstinence is obtained.
Financial Support: College of the Holy Cross provided a Research Grant to GJD; NIDA Grant R01DA027138 provided funding to GG and GJD

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PPARγ AGONISM ATTENUATES COCAINE-SEEKING BEHAVIOR VIA ERK.

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Aims: A major hurdle in treating cocaine addiction is the high relapse rate even after prolonged abstinance periods. Rats lever press for cocaine-related cues following self-adminsitration (SA) as a function of forced abstinence (FA) period upon re-exposure to cocaine-related cues (incubation of cocaine craving). ERK activity (pERK) mediates some of the plasticity changes that drive drug-seeking behavior. We found a compelling interrelationship between pERK and PPARγ in learning and memory through pERK-PPARγ interaction. Here we tested if cocaine-induced pERK dysregulation and related behaviors would be attenuated by targeting PPARγ.
Methods: Sprague-Dawley rats (n=12/per group) were implanted with jugular vein canulae then randomized to sham or cocaine SA groups. 14 daily 3hr SA sessions with appropriate active lever presses delivering cocaine (.75 mg/kg/.1 mL) on a stepped fixed ratio schedule. Rats were assigned to FA treatment groups balanced for active lever presses and cocaine infusions. Pioglitazone was milled into standard rodent chow (30 mg/kg). After 30 days FA, lever pressing to cocaine-related cues was quantified; rats were immediately decapitated and brain regions dissected, stored frozen until immunoprecipitation/quantitative immunoblot.
Results: PPARγ agonism during prolonged FA significantly attenuated cocaine-seeking behavior upon re-exposure to cocaine-related cues without affecting motivation for natural reward or locomotor behavior. PPARγ agonism normalized pERK; pERK and PPARγ co-immunoprecipitation mirrored these effects in the medial prefrontal cortex and hippocampus. PPARγ antagonism with the specific and irreversible antagoinist, GW9662, reversed the behavioral and biochemical effects of PPARγ agonism.
Conclusions: PPARγ agonism attenuates cocoaine seeking behavior via a pERK-dependent mechanism within a subset of the mesocortico limbic circuitry, indicating that PPARγ represents a potential therapeutic target for the prevention of cocaine relapse.
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LOCOMOTOR DEPRESSION AND THC-LIKE DISCRIMINATIVE STIMULUS EFFECTS OF THREE NOVEL SYNTHETIC CANNABINOIDS: ADBICA, THJ-2201, AND ADB-PINACA.

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Aims: Synthetic cannabinoids have become increasingly popular as quasi-legal alternatives to marijuana in recent years. As is often the case with designer drugs, when one group of synthetic cannabinoids is scheduled, novel analogs are synthesized to replace them. Numerous adverse effects and incidences of overdose have been associated with newer synthetic cannabinoid analogs. The goal of the current study was to characterize the locomotor and discriminative stimulus effects of three novel synthetic cannabinoid compounds: ADBICA, THJ-2201, and ADB-PINACA.
Methods: The effects of these compounds on locomotor activity were tested in male Swiss-Webster (ND4) mice over an 8-hour period in an open field assay of locomotor activity (n=8 per dose). The discriminative stimulus effects of the compounds were tested in male Sprague-Dawley rats trained to discriminate 3 mg/kg Δ^9-THC from vehicle in a drug-discrimination assay (n=6 per drug).
Results: Δ^9-THC (ID_{50}= 13.2 mg/kg), ADBICA (ID_{50}= 1.0 mg/kg), THJ-2201 (ID_{50}= 0.8 mg/kg), and ADB-PINACA (ID_{50}= 0.28 mg/kg) produced significant depression of locomotor activity compared to vehicle. Locomotor depression induced by the test compounds was shorter acting (30-80 min) compared to Δ^9-THC (120-210 min). ADBICA (ED_{50}= 0.11 mg/kg), THJ-2201 (ED_{50}= 0.15), and ADB-PINACA (ED_{50}= 0.38) fully substituted for the discriminative stimulus effects of Δ^9-THC. ADBICA and ADB-PINACA significantly attenuated response rate at the doses tested.
Conclusions: Our results indicate that these novel synthetic cannabinoid compounds produce locomotor depression and discriminative stimulus effects similar to Δ^9-THC, and may have potential for abuse as alternatives to Δ^9-THC. The stimulus effects of each of the compounds were shorter acting and at least tenfold more potent than Δ^9-THC. Future studies on the reinforcing properties of these compounds are necessary to fully elucidate their abuse liability.
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EXPLORING THE FACTOR STRUCTURE OF A RECOVERY ASSESSMENT MEASURE AMONG SUBSTANCE-ABUSING YOUNG PEOPLE.

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Aims: To date, the measurement of recovery in the field of substance abuse is limited. Reliable and valid instruments are needed to adequately measure recovery among substance abusing youth populations. The Recovery Assessment Scale (RAS) has been validated with mental health client populations, however its measurement characteristics have not been examined for individuals undergoing substance abuse treatment. The current study explored the factor structure of an adapted version of the RAS with a substance abusing youth population.
Methods: The sample consisted of 80 substance abusing young people who completed the RAS at admission to an aftercare pilot program called Project ESQYIR (Educating & Supporting inQuisitive Youth in Recovery). Reliability analysis was examined to ensure the unidimensionality of the measure in item- and scale-level properties across the sample. Exploratory factor analysis (EFA) was performed to identify latent constructs of the adapted RAS with the substance abusing youth sample. To compensate for high variability in a small sample, Parallel analysis (PA) was run to confirm the number of factors.
Results: Results showed high reliability for the RAS measure among the substance abusing youth sample (α = .90). EFA identified four subscales (confirmed by the PA), including personal determination, skills for recovery, self-control in recovery, and social support/moving beyond recovery to have adequate psychometric properties for measuring recovery among substance abusing young people.
Conclusions: Reliability testing and EFA of the adapted RAS measure is important for the field of addiction since no current recovery measures exist, especially among youth populations. Results offer useful insight to the field on the initial factor structure of the RAS and associated domains for measuring recovery among substance abusing youth.
Financial Support: This study is supported by K01 DA027754 from the National Institute on Drug Abuse (NIDA).

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MORE THAN MEETS THE EYE: WHAT VISUAL CORTEX REACTIVITY TO CUES MAY TELL US ABOUT NEURAL PROCESSING IN ADDICTION.

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Aims: The visual cortex has not received a large amount of attention in fMRI drug-cue reactivity literature, despite its consistent and significant response in drug users who are exposed to substance cues. This literature review has two discrete sections – 1) results from a recent meta-analysis on visual cortex reactivity and 2) pilot data from a prospective study on visual cue reactivity.
Results: The meta-analysis revealed that 86% of drug-cue reactivity neuroimaging studies found significantly more activity in the visual cortex (BA 17 and 19) to drug cues versus neutral cues. This was consistent across diverse drug classes, including nicotine, cocaine, alcohol, and opiates. These findings were then directly tested in a prospective manner using multiband imaging in a cohort of nicotine smokers and non-smokers viewing cigarette images and neutral images.
Conclusions: Together these data demonstrate that the visual cortex, though often overlooked, in our discussions of the neural circuitry of addiction, consistently discriminates drug cues from neutral cues in substance dependent populations. Although it is unclear whether this is related to the rewarding properties of the drug or attentional mechanisms, these data suggest that this is a fruitful new area of exploration in addiction research.
Financial Support: This project was supported by NIH grant K01 DA027756(CAH)

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IMPLEMENTING ROUTINE EMERGENCY DEPARTMENT NALOXONE RESCUE KITS FOR PATIENTS AT RISK OF OPIOID OVERDOSE.

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Aims: In response to the opioid overdose epidemic, a safety net hospital implemented a policy to ensure emergency department (ED) patients at risk for opioid overdose are offered naloxone rescue kits (NRKs). Study aims are to: 1) determine the extent of implementation, 2) describe barriers and facilitators to adoption.
Methods: Mixed methods for formative evaluation: electronic medical record (EMR) query to identify patients at risk and rate of NRK provision, and qualitative interviews with diverse ED staff analyzed via grounded theory to identify barriers and facilitators.
Results: The policy supports 3 methods of NRK provision: 1) distribution by Licensed Alcohol and Drug Counselors (LADCs), 2) outpatient pharmacy prescriptions, 3) inpatient pharmacy distribution by ED staff (when LADCs unavailable). In the first 7 months, 1241 ED patients were at risk; of these 12% (n=150) received NRK (142 via LADCs, 5 outpatient prescriptions, 3 ED staff). Interview results indicate support for policy and implementation barriers. Patient barriers: population often not receptive to NRK, not accompanied to ED by a supportive other. Staff barriers: unfamiliarity with policy, lack of clarity regarding responsibility for distribution, lack of consensus on patients appropriate. Process barriers: method of obtaining kit unclear, confusion around standing verbal order, not integrated into EMR. Staff suggestions to improve uptake include: simplifying process, targeted training, role clarification, integration into EMR.
Conclusions: ED staff support provision of NRKs and many barriers are modifiable. Findings may have applications for integrating the intervention into other ED settings.
Financial Support: Boston University School of Public Health Pilot Grant Program

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A 3 YEAR FOLLOW-UP OF HCV INFECTION IN OPIOID USE DISORDER PATIENTS IN TREATMENT.

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Aims: In order to evaluate the changes in incidence of infection by HCV, drug use patterns and morbidity among opioid use disorder patients (OUDP), we conducted a 3 years prospective cohort study in an Addiction Treatment Center in Lille, France.
Methods: Intake and follow-up assessments included substance use patterns, viral evaluation, blood tests and fibroscan assessment.
Results: 488 participants were included, 251 (51.4%) underwent a final visit, of which 168 (34.4%) with final HCV serum test. 213 patients (84.9%) had medication assisted treatment (MAT): 47 (22.1%) buprenorphine-naloxone and 166 (77.9%) methadone. MAT were stopped for 16 (6.4%). Of the 35 patients that where neither injectors or sniffers at baseline, five were newly identified as sniffers and one as IVDUs (incidence = 4.7% and 0.9% by year, respectively). Of the 70 patients sniffers at baseline, 8 started IVDU (incidence = 3.8%/year). Two patients seroconverted for HCV during follow-up, and where all in the group of active sniffers (incidence = 3%/year). No HCV seroconversion or reinfection occured among the active IVDU. The global annual incidence of HCV among patients was 2 %. 22 deaths occurred (men = 81,1%, average age = 39 years, mortality rate 2.9%/year). Reported causes were overdose (27,3%), psychiatric (18.2%), cirrhosis (18.2%).
Conclusions: Interestingly, no HCV seroconversion was detected among IVUDs. However, sniffing appears as a major risk factor for HCV infection in this sample. Screening for sniffing and harm reduction focused on sniffing should be developed.
Financial Support: Laboratoire Roche (F. Hoffmann-La Roche, France)

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IDENTIFYING AND ADDRESSING UNMET MEDICAL NEEDS: A CALL TO BROADEN THE SCOPE OF DRUG COURTS.

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Aims: Drug courts are an effective approach to reducing drug use and crime. They offer substance abusing offenders the opportunity to avoid sentencing by engaging in court-supervised treatment. Although they address life issues like employment and housing, they do not generally address healthcare issues or provide linkages to medical care. This may represent a lost opportunity as these individuals may be susceptible to a host of illnesses due to their chronic substance use and maladaptive lifestyles. This study examines the prevalence of health-related issues in a drug court sample.
Methods: A total of 185 felony drug court clients completed an interview about their current health-related issues (e.g., health insurance status, last medical visit, chronic health conditions, treatment status) at entry into the program and 15-months post-entry. At the follow-up, clients were asked whether anyone from the drug court team talked to them about their chronic conditions or provided them with a referral to medical treatment.
Results: Significantly more clients had health insurance at follow-up than at baseline (74% vs. 59%, $X^2(1) = 11.83$, $p < .001$). At follow-up, 89% reported having visited a doctor and 74% having received a physical exam since they entered the program. Overall, 50% had at least one chronic medical condition with chronic respiratory problems (25%), high blood pressure (16%), diabetes (5%), and epilepsy (5%) reported most frequently. Among those with chronic conditions, 40% had conditions for which they were not receiving treatment. Members of the drug court team talked to 13% of these clients about their untreated conditions and 5% received a referral to medical treatment for them.
Conclusions: Findings suggest that drug courts should begin to widen their focus to address health-related issues. Individuals in this sample reported many chronic conditions that were going untreated and for which they did not receive a medical referral. These untreated medical issues may serve as a roadblock in clients' path to recovery.
Financial Support: NIDA grant #R01-DA-030257

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CAUTIOUS USE OF RACE IN ANALYSES TO PREDICT RETENTION IN SUBSTANCE ABUSE TREATMENT.

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Aims: This study examines differences in organizational characteristics and client retention in substance abuse treatment programs serving either predominantly African American or predominantly Non-African American clients.
Methods: Wilcoxon Exact Test or the Cochran Mantel-Haenszel Chi-Square was used to compare differences in organizational characteristics. Generalized Estimating Equation was used to consider client- and program-level independent effects and cross level interactions on retention in treatment.
Results: The findings show longer retention in predominantly African American programs ($\beta=2.36$, $p<0.01$); however, shorter retention among African American clients ($\beta=-0.24$, $p<0.01$), demonstrating the difficulty in making client level conclusions based on program level data, or vice versa. Mixed model analyses show program directors who had been at the facility for 10 years or less ($\beta=-0.45$, $p<0.05$), use of client/staff matching ($\beta=0.43$, $p<0.01$), and programs with low levels of legal coercion ($\beta=-1.03$, $p<0.05$) predict longer client retention.
Conclusions: The findings suggest organizational factors and race are important predictors of client retention in treatment and have important implications for behavioral health providers seeking to improve client retention. Knowledge of the interaction between racial composition and organizational characteristics can be helpful in improving program retention.
Financial Support: NIDA T32DA007292

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INDIVIDUAL DIFFERENCE IN OPIOID RESPONSE.

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Aims: Prescription opioids (POs) are the 2nd most commonly abused drug in the US and among the most frequently prescribed medications. Laboratory studies reveal pronounced between-person differences in opioid response, yet only 1 study has formally reported on these differences.
Methods: A placebo-controlled, double-blind, double-dummy, within-subject, dose-response evaluation of self-reported and physiological effects of heroin and hydromorphone, 3 active doses of each, each given both IV and SC, was conducted among 16 experienced opioid users. In a residential human laboratory Ss received randomized and blinded drug administrations, and effects were assessed for 3 hours.
Results: A composite of visual analog ratings (VAS) (drug effect, high, drug liking, rush, good effects) was derived and mean peak VAS, pupil diameter, and oxygen saturation (Sp02) were evaluated. In repeated measures ANOVAs each drug/route combination showed significant dose-response relationships, with significant dose effects on VAS ($p<.001$), pupil ($p<.001$), and Sp02 ($p<.001$) ratings, yet individual Ss varied widely on their dose responses., Nearly half (n=7) of participants reported almost no subjective response to either opioid, at any dose or route, whereas the remaining participants showed expected dose response curves. All participants showed some dose response relationship on pupil and Sp02 levels, though the 7 individuals with blunted subjective responses also had blunted physiological reactions, which suggests that differences observed were consistent within an individual.
Conclusions: These data demonstrate substantial and prevalent individual differences in several domains of opioid response, and also support the need to explore further the mechanisms underlying individual differences and to determine the degree to which these differences may impact opioid abuse potential and clinical response to analgesics.
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INCREASED RISK OF SUBSTANCE USE AND HEALTH-RELATED PROBLEMS AMONG MALE HOMELESS VETERANS.

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Aims: The present study sought to examine whether homeless veterans were more likely to report problems with addictions, mental health, and physical health compared to homeless non-veterans. Additionally, the study sought to compare emergency room utilization among veterans and non-veterans.
Methods: Secondary data analyses was conducted on male homeless veterans and non-veterans (N= 372) enrolled in the Alachua County Point in Time (PIT) study in Gainesville, FL. Participants were recruited at a homeless shelter and completed a questionnaire on demographics and health variables, including addictions, mental health, and physical health. Additional questions included recent emergency room visits and whether participants needed treatment services that they were not receiving. The use of this data was approved by the university institutional review board.
Results: Homeless veterans were more likely to report problems with addictions compared to homeless non-veterans (AOR=6.29, 95%CI: 3.43-11.53, $p<.001$). Veterans were also more likely to report mental health problems (AOR=4.12, 95%CI: 2.43-6.53, $p<.001$) and physical problems (AOR=1.83, 95%CI: 1.08-3.09, $p<.01$). Homeless veterans also had significantly greater odds than non-veterans of visiting a hospital emergency room in the past year (AOR = 1.73, 95% CI: 1.07 - 2.80, $p<.05$).
Conclusions: While much is known about the susceptibility of veterans for addiction and other health problems, our results reveal that over half of homeless veterans are presenting to hospital emergency rooms. This may be a missed opportunity for providing treatment and support.
Financial Support: No financial support was required for this study. Travel support sponsored by the University of Florida Substance Abuse Training Center in Public Health (NIDA-T32-035167).

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RELATIONSHIP BETWEEN CHANGES IN CANNABIS USE AND ANXIETY AMONG ADOLESCENTS.

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Aims: Adolescence is a critical period of neural development and is often associated with high levels of stress, anxiety, and initiation of cannabis use. Although cannabis users often cite acute anxiolytic effects, little is known on how levels of anxiety are affected, non-acutely, by changes in cannabis use. In this study, we examined how changes in cannabis use relate to changes in anxiety among adolescents.
Methods: We recruited high-risk adolescents (n=122) from South Florida via in-school presentations/informational fliers. Participants with significant mental health issues, neurological or developmental problems, and significant use of alcohol or drugs other than cannabis were excluded at baseline. All participants completed a baseline visit consisting of a structured clinical interview (SCID), drug use history questionnaire, and the depression, anxiety, and stress scale (DASS-21). A 6-month follow-up visit was conducted via phone survey, which included drug use history since the prior visit and a re-evaluation with the DASS-21. A participant was classified as "escalater" (n = 20) if their cannabis use increased significantly from baseline to follow-up. For example, someone who went from "weekend use" to "daily use;" otherwise, they were classified as "non-escalater" (n = 102).
Results: User status (escalater vs non-escalater) and baseline anxiety subscale scores from the DASS-21 were regressed on anxiety scores at follow-up using multiple linear regression. Being classified as an "escalater," was associated with greater increases in anxiety from baseline to follow-up (β = .17, p = .03) compared to the "non-escalater" group.
Conclusions: In contrast to the reported acute subjective effects of cannabis as an anxiolytic, our results suggest that increases in cannabis use over a 6-month period were associated with increases in anxiety among adolescents. Although causality could not be established, we speculate that CB1 receptor down regulation from increasing cannabis use could be a plausible mechanism for subjective ratings of increased anxiety among adolescents in our sample.
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INFLUENCE OF STEREOCHEMISTRY IN THE MACROCYCLIC TETRAPEPTIDE CJ-15,208 ON ANTINOCICEPTIVE EFFICACY AND OPIOID RECEPTOR SELECTIVITY.

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Aims: The macrocyclic peptide CJ-15,208 (*cyclo*[Phe-D-Pro-Phe-Trp]) and its D-Trp isomer exhibit different opioid activity profiles (mixed agonist/kappa opioid receptor (KOR) antagonist activity vs. only KOR antagonism, respectively). We hypothesized that the stereochemistry of the Phe residues would also influence opioid activity, and some stereoisomers may demonstrate analgesia with fewer liabilities of use.
Methods: CJ-15,208 and five stereoisomers were evaluated *in vivo* for opioid-mediated antinociceptive efficacy in C57BL/6J mice after oral administration with the 55°C warm water tail withdrawal assay. Analgesia against other types of nociception was screened in the acetic-acid stretching, inflammatory, and chronic nerve constriction injury models. Liabilities of use were evaluated with assays of locomotion, respiration and conditioned place preference (CPP).
Results: Following oral administration, both CJ-15,208 and the isomers exhibited naloxone-sensitive antinociception in the tail-withdrawal test, but the magnitude and opioid receptor selectivity depended on the stereochemical configuration. The isomers varied markedly when screened for potential liabilities, and one analog produced no change in respiration or locomotion and no conditioned place preference at a maximally antinociceptive dose (10 mg/kg, p.o.).
Conclusions: The stereoisomers retained antinociceptive activity, but the opioid-receptor selectivity was sensitive to changes in the aromatic residues. The identification of an analog demonstrating potent opioid-mediated antinociception without respiratory, locomotor or CPP effects at therapeutic doses in the initial screening is a promising development in the search for potential analgesics with improved liability profiles.
Financial Support: Research supported by NIDA grant R01 DA018832.

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PREVALENCE, CORRELATES, AND SUBSTANCE USE AND PSYCHIATRIC PREDICTORS OF REGULARLY DRINKING ALCOHOL BEFORE SEX AMONG ADULTS IN THE UNITED STATES.

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Aims: Drinking alcohol before sex increases the likelihood of engaging in sexual risk behaviors and risk for HIV infection. However, the prevalence, correlates, and predictors of this behavior have not been established in the United States. This study determined the prevalence, correlates, and substance use and psychiatric predictors of regularly drinking alcohol before sex in a nationally representative adult sample.
Methods: Participants were 17,491 sexually active adult drinkers from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Logistic regression models estimated the prevalence, correlates, and substance use and psychiatric predictors of regularly drinking alcohol before sex. Regularly drinking alcohol before sex was defined as drinking alcohol most or all of the time prior to sexual activity.
Results: Past year prevalence of regularly drinking before sex was 1.8% (approximately 4.3 million American adults). A variety of sociodemographic (i.e., age, gender, race, education, family income, marital status, employment status), substance use (i.e., alcohol, cannabis, nicotine, and other drug dependence; drinking frequency) and psychiatric (i.e., major depressive, dysthymic, generalized anxiety, and antisocial personality disorders) variables were associated with regularly drinking before sex at the bivariate level. After controlling for covariates, alcohol dependence (AOR=2.35; 95%CI=1.85-2.99) and generalized anxiety disorder (AOR=1.51; 95%CI=1.07-2.12) remained significant predictors of regularly drinking before sex.
Conclusions: This study can serve as a benchmark for future studies on substance use and psychiatric disorders as risk factors for regularly drinking alcohol prior to sexual activity. Substance abuse treatment should address co-occurring psychiatric disorders in efforts to reduce rates of regularly drinking before sex.
Financial Support: K23DA032323, U01AA018111, K05AA014223, NYSPI

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N-ACETYLCYSTEINE FOR COCAINE ADDICTION: A SYSTEMATIC REVIEW.

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Aims: Review the current available literature about N-acetylcysteine's (NAC) role in the treatment of cocaine dependence.
Methods: We screened all articles published before November 2014 that used NAC as a pharmacological intervention for cocaine dependence or discussed its potential as a therapeutic approach for cocaine dependence. Review papers were also analyzed. We described our results qualitatively as there was no quantitative information available to perform a meta-analysis.
Results: After poor-related papers exclusion, we found 22 studies that matched our search criteria; six of these studies were clinical trials and nine were animal studies. We also found seven review articles related to our investigation. Some clinical trials found interesting effects of NAC on reducing desire to use cocaine, time spent viewing slides containing cocaine's use stimulating material, self-reported use, craving, withdrawn and days spent using cocaine. Side-effects were mild. Review papers and preclinical studies further discuss NAC's mechanisms of action. NAC has been shown to reverse, at least partially, the disruption of glutamate homeostasis caused by long-term cocaine use. This disruption occurs by enhancing the function of the cystine-glutamate exchanger in glial cells and reversing downregulated GLT1 receptor function. Four studies also showed NAC's capacity to reduce craving, desire to use cocaine, cocaine cue viewing time and cocaine-related spending. NAC may be better suited for avoiding relapse in already abstinent subjects, as a double-blind placebo trial was mainly negative, except in the subgroup of patients who were already abstinent.
Conclusions: Although there is only preliminary clinical studies available, the current data suggests a promising view of NAC as a therapeutic agent, mainly as an anti-relapse agent.
Financial Support: No financial Support

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DO PRESCRIBED OPIOIDS IMPACT CD4 COUNT RESTORATION AMONG HIV+ PATIENTS INITIATING ANTIRETROVIRAL THERAPY?

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Aims: As some opioids are immunosuppressive, we aimed to determine whether prescribed opioids impact CD4 count restoration among HIV+ patients initiating antiretroviral therapy (ART).
Methods: We included HIV+ patients from the Veterans Aging Cohort Study initiating ART between 2002 and 2012 and followed them for two years. We excluded those who at ART initiation lacked a CD4 count or had an undetectable viral load. Using pharmacy data, prescribed opioid exposure was categorized as: none; short-term:<90 days; medium-term:≥90-364 days; and long-term:≥365 days. We examined CD4 trajectories. We then used a mixed model to assess the association between opioid exposure and CD4 count (square root transformation) over time, combining those with medium and long-term opioids.
Results: Opioid prescriptions were common among 4371 HIV+ participants: 36% short-term, 8% medium-term, and 4% long-term. Compared to those with none, those with short-term opioids had lower CD4 counts at baseline (228 vs. 213 cells/mm^3, p=.01) and 24 months (373 vs. 341 cells/mm^3, p=.04). Compared to those with none, those with medium/long-term opioids had similar CD4 counts at baseline (233 cells/mm^3, p=.48) and 24 months (372 cells/mm^3, p=.34). The overall improvement in CD4 count per year was 73 cells/mm^3 among those with none; 64 cells/mm^3 among those with short-term (p=.04); and 69 cells/mm^3 among those with medium/long-term opioids (p=.34).
Conclusions: While no effect was observed from medium and long-term opioids, short-term opioid exposure was associated with less CD4 restoration among HIV+ patients initiating ART. Potential mechanisms for this effect should be examined.
Financial Support: K12DA033312, U01AA13566, K23AG00826, VA HSR&D CDA08-276, F31DA035567

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EVALUATING THE EFFECTIVENESS OF TELEHEALTH-DELIVERED OPIOID AGONIST THERAPY ACROSS ONTARIO, CANADA.

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Aims: Opioid addiction is recognized as a critical health care issue across North America, and it has been declared a major health crisis in several rural communities across Canada. Opioid agonist therapy (OAT) is the standard of care for patients suffering from opiate dependence. Despite the increasing adoption of telemedicine as a delivery method for OAT, its efficacy has not been evaluated against traditional in-person treatment. Here we compare in-person versus telehealth-delivered OAT.
Methods: We conducted a retrospective cohort study using an administrative database for patients who commenced OAT between 2010 and 2012 across 48 clinics in the province of Ontario, Canada. Patients were stratified by primary treatment modality as being: face-to-face (<25% appointments by telehealth) or via telehealth (>75% appointments by telehealth). The primary outcome was continuous retention in treatment as defined by one year of uninterrupted therapy based on prescription refill data.
Results: A cohort of 5854 first-time OAT patients were identified. Patients being treated via telehealth demonstrated a retention rate of 59% (n=3689) whereas in-person patients were retained at a rate of 48% (p<0.001 at 365 days).
Conclusions: The results of our study demonstrate that telehealth is an effective method of delivering opioid agonist therapy, and this treatment is demonstrated to result in a clinically significant improvement of >10% in patient retention after one year in therapy.
Financial Support: Financial support was provided by the Northern Ontario Academic Medicine Association in the form of a Clinical Innovation Research Grant.

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EFFICACY OF ELECTRONIC CIGARETTES FOR SMOKING CESSATION IN VETERANS.

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Aims: To evaluate the efficacy of E-cigs vs. nicotine patch (NRT) on cigarette use and craving in veterans who meet DSM criteria for tobacco use disorder.
Methods: Veterans were randomized to either NRT (16mg patch; N=7) or E-cigs (16mg cartridge; N=4). Participants attended thrice-weekly visits during the first two weeks (week 1-"baseline" with participants smoking *ad libitum*) and attended five visits during the third week (week 3-"efficacy" with participants smoking as little as possible while using NRT or E-cigs). Self report of use, nicotine craving and withdrawal, and CO levels and salivary cotinine, were recorded during each visit.
Results: Participants were mostly African American (64%) males (82%), 52.6±1.9 (Mean±S.E.M) years of age, and smoked cigarettes for 35.0±1.9 years, 26.5±3.0 cigarettes/day, and FTND scores of 7.5±.5. NRT and E-cigs groups did not differ for any demographic or drugs use variables. Comparing week 3 versus week 1, the data reveal that NRT (t=3.4, *p*=.015) and E-cigs (t=5.3, *p*=.013) significantly reduced (~50%) self-reports of cigarettes smoked in last 24h, and this was confirmed by significant reductions of breath CO levels by NRT (t=3.7, *p*=.01) and E-Cigs (t=3.9, *p*=.03). E-cigs (t=5.3, *p*=.013), but not NRT (t=1.5, *p*=.18), significantly increased time since last cigarette. Also, E-cigs (t=3.8, *p*=.03), but not NRT (t=2.1, *p*=.08), significantly reduced QSU scores. Self-report E-cig use was robust (12.7±1.4 times/day and 6.1±.5 puffs/instance).
Conclusions: These preliminary data suggest that E-cigs reduce cigarette use, craving and withdrawal symptoms. Veterans randomized to E-cigs experienced reduced craving, used E-cigs with great frequency, perceived them as safe, and found them to be as rewarding as their own cigarettes. Further inquiry will illustrate the value of E-cigs in the context of tobacco cessation.
Financial Support: This work was conducted at and supported by resources at the MEDVAMC, including a MEDVAMC Research Enhancement Seed Grant to RD and DG.

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CARDIOVASCULAR TOXICITY OF SINGLE AND REPEATED INHALATION OF "KOLLA" – A LOCALLY ABUSED EGYPTIAN GLUE.

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Aims: This work aims at studying on the cardiovascular toxic effects of acute and chronic inhalation of "Kolla", a local glue widley abused by street children in Egypt. Effects of acute and chronic inhalation of "Kolla" on blood pressure of rats and their plasma electrolyte level was investigated using toluene as a standard solvent inhalant.
Methods: Two concentrations of "Kolla" (5000 & 10000 ppm) or toluene (28225 & 56450 ppm) were tested after single or 10 day repeated daily inhalation. Inhalation of glue or toluene vapors was performed in a sealed box designed to allow administration of adjusted and known concentrations of the vapors of each substance. Blood pressure was measured by the rat tail cuff method after 15 and 30 minutes following single inhalation and then hourly for 6 hours. For testing the effect of repeated inhalation of "Kolla" or toluene; rats were allowed to adapt for 15 minutes following the 10th inhalation and then the blood pressure was measured. In another group of animals; rats were decapitated after single or repeated daily inhalation and the blood was collected for determining effects on the plasma electrolyte levels of rats using a flame photometric method.
Results: Single inhalation of Kolla or toluene led to an initial brief phase of increase followed by prolonged decrease in rat's blood pressure. A 10 day repeated inhalation of Kolla or toluene led to a significant dose-dependent decrease in blood pressured when compared to the control group of animals. An increase in the plasma sodium was observed after repeated administration of "Kolla. No significant change in potassium or calcium was recorded.
Conclusions: Single inhalation of Kolla or toluene leads to an initial increase followed by prolonged decrease in rat's blood pressure. Repeated inhalation of either substance can lead to significant hypotension and hypernatremia.
Financial Support: NONE

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GENDER DIFFERENCES IN MORTALITY AMONG TREATED OPIOID-DEPENDENT PATIENTS.

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Aims: To assess gender differences in mortality rates, causes of death, and predictors of death among treated opioid-dependent patients**.**
Methods: Mortality data were obtained on all patients first enrolled in publicly-funded pharmacological treatment for opioid dependence in California from 2006 to 2010. Crude mortality rates (CMR) and standardized mortality ratios (SMR) were calculated by gender. Cox proportional hazards models with time-varying covariates were fitted to determine the effect of gender on the hazard of all-cause mortality, controlling for a range of covariates.
Results: Death occurred among 259 of 11,564 women (2.2%) and among 772 of 20,758 men (3.7%) over a median follow-up of 2.6 years (interquartile range: 1.4 - 3.7), corresponding to a CMR of 9.5 (95% CI: 8.4, 10.7) deaths per 1,000 person-years among women, and 15.7 among men (95% CI: 14.6, 16.8). Women had a greater increase of mortality risk compared to the general population (SMR 5.1 95% CI: 4.5, 5.7) than men (SMR 4.3 95% CI: 4.0, 4.6). The relative risk of death for women compared with men was 1.18 (95% CI: 1.02, 1.36). Similar percentages of women and men died of drug overdose (47.1%, 42.5%). As a main effect, women had a lower instantaneous hazard of all-cause mortality than men (HR 0.58, 95% CI 0.50, 0.68). A significant interaction effect indicated that concurrent opioid and methamphetamine/cocaine use increased mortality risk among women and decreased mortality risk among men.
Conclusions: Understanding factors that influence mortality risk differentially by gender has important implications for addressing gender-specific treatment needs, thereby aiding efforts to eliminate gender disparities in opioid-related morbidity and mortality.
Financial Support: NIDA R01DA031727 (PI: Nosyk) & P30DA016383 (PI: Hser).

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HETEROGENEITY OF ALCOHOL USE TREATMENT SERVICES: A LATENT CLASS ANALYSIS.

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Aims: Little is known about the types of treatment services used, how individuals may use these services in combination, and the degree to which there exists heterogeneity in the patterns of alcohol treatment services used.
Methods: Using data from the NESARC survey, latent class analysis was conducted to identify subgroups of alcohol treatment services used in a sample of individuals who had ever sought help for alcohol use (N=1910, 69.9% male). Nine indicators of types of treatment services were included: 12-step/Alcoholics Anonymous (AA), family/social services, inpatient, outpatient, halfway house, acute, employment assistance programs, religious, and medical professional services.
Results: Analyses indicate a model with 4 classes: 1) Primarily 12-step users (24.3%) characterized by high use of 12-step/AA, moderate use of medical professional services, and low use of other services; 2) Low service users (33.3%) characterized by moderate use of 12-step/AA, religious and medical professional services, and low use of other services; 3) Augmented 12-step/AA users (32.5%) characterized by high use of 12-step/AA and moderate use of acute and medical professional services; 4) High service users (9.9%), characterized by a high probability of almost all types of services, including 12-step/AA.
Conclusions: These findings demonstrate considerable heterogeneity in the types of alcohol treatment services used by adults. Three of the 4 classes showed very high use of 12-step/AA services (over 90% probability), with 12-step/AA services serving as the primary source of treatment for nearly 25% of adults. Conversely, only two classes showed moderate to high usage of more formalized treatment services, such as inpatient or outpatient services. Variability in services received may reflect differences in individual preference, need, and accessibility. Future research will examine the associations between individual characteristics and treatment class membership and explore whether certain combinations of services are associated with better treatment outcomes.
Financial Support: Funded by NIDA grants T32 DA017629 and P50 DA010075

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ASSOCIATION BETWEEN TOBACCO SMOKING AND DEATH BY SUICIDE: A COMPETING RISKS HAZARD ANALYSIS IN A LARGE TWIN COHORT WITH 35-YEAR FOLLOW UP.

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Aims: The aim of the study was to estimate the association between smoking and suicide, and the degree to which it is influenced by dose, cessation, psychiatric and somatic morbidity, genetic, and environmental factors.
Methods: 16,282 twin-pairs born before 1958 in Finland and alive in 1974 were queried with detailed health and smoking questionnaires in 1975 and 1981. Participants were followed for 35 years for psychiatric and medical treatment and vital status, including suicide determination by forensic autopsy.
Results: Current smokers had a higher cumulative suicide incidence than former or never smokers. Heavy current smokers had higher suicide risk (hazard ratio (HR)=3.47; 95% CI, 2.31-5.22) than current smokers who smoked less (HR=2.30; 95% CI, 1.61-3.23) (p=0.017). Compared to never smokers, current smokers had increased suicide risk (HR=2.84; 95% CI, 1.58-5.10) adjusting for depressive symptoms, alcohol and sedative-hypnotic use, and excluding those with serious somatic or psychiatric illness, while former smokers did not. In the 28 twin-pairs discordant for smoking and suicide, 24 of the suicides were in smokers and 4 in non-smokers (OR=6.0; 95% CI, 2.06-23.8).
Conclusions: Tobacco smoking is associated with completed suicide with a large, dose dependent effect, independent of demographic factors, depressive symptoms, heavy alcohol use, and major psychiatric and somatic illness. These results are consistent with an interpretation that genetic factors do not significantly modify the relationship between smoking and suicide and that tobacco smoking may have a causal role in relation to suicide.
Financial Support: Academy of Finland grants 141054, 265240, 263278 and 264146 (Dr. Kaprio); National Institute on Drug Abuse K24 DA030443 (Dr. Evins)

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THE KAPPA OPIOID RECEPTOR AGONIST 16-BROMOSALVINORIN A REDUCES COCAINE SEEKING IN RATS.

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Aims: Kappa opioid receptor (KOPr) agonists have known anti-cocaine effects but produce various side effects that limit therapeutic use. The aim of the current study was to determine if the novel salvinorin A analog 16-bromosalvinorin A (brSalA), could attenuate reinstatement of cocaine seeking preclinically with reduced side effects compared to traditional KOPr agonists.
Methods: Male Sprague-Dawley rats trained to self-administer cocaine in daily 2 hour sessions were subjected to extinction followed by administration of vehicle or brSalA (0.3 mg/kg, 1 mg/kg; n=6) and drug-prime reinstatement testing (20 mg/kg cocaine, i.p). Sedative effects were evaluated by determining locomotor activity in rats for 60 min following brSalA (1 mg/kg, i.p, n=6). To evaluate the effects of brSalA on natural reward pathways, drug naïve rats were trained to self-administer sucrose pellets and effects on responding after brSalA administration (1 mg/kg, i.p, n = 7) determined. Depressive effects were assessed by subjecting rats to forced swimming conditions for 5 min following an injection of brSal A (1mg/kg, i.p, n=8-9).
Results: BrSalA significantly decreased cocaine seeking but did not reduce locomotor activity and sucrose intake or increase immobility times in rats. This highlights a specific effect of brSal A on drug seeking not due to sedation or modulation of natural reward, and the minimal side effects of brSalA at the effective dose.
Conclusions: BrSalA reduces cocaine seeking with minimal side effects. These findings provide information for ongoing work in developing eective anti-addiction pharmacotherapies.
Financial Support: Neurological Foundation of New Zealand.

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CHARACTERISTICS AND CONSEQUENCES OF ADULTS WHO USE CANNABIS AS THEIR FIRST DRUG.

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Aims: The typical stages of drug initiation are tobacco and/or alcohol, followed by cannabis and other illegal drugs. African-American youths tend to initiate cannabis earlier and violate this typical sequence with unclear consequences. Research herein identifies characteristics of US adults who use cannabis as their first drug, and whether using cannabis first predicts current cannabis dependence (CD), heavy cannabis use, and illegal drug use.
Methods: Data are from the 2013 US National Survey on Drug Use and Health focused on a nationally representative subsample of cannabis-using adults (n=19,051). Self-reported age of onset for cannabis, cigarettes, alcohol, and other illegal drugs defined drug sequence. Logistic regression estimated relative odds (OR) of using cannabis first (vs. second or later) as predicted by sex, age, race/ethnicity, and age of cannabis onset. Using cannabis first was then modeled to predict CD, heavy cannabis use, and other illegal drug use outcomes.
Results: One-in-six (17%) cannabis-using adults used it as their first drug; the majority used cannabis as their second (36%) or third (42%) drug. Most who used cannabis first eventually used cigarettes (78%), alcohol (96%), and/or other illegal drugs (60%). African-Americans were three times (OR=3.5) more likely to use cannabis first than Whites, followed by Native American/Alaska Natives (OR=2.3), Asians, and Hispanics (both OR=1.9). Younger age and earlier age of cannabis onset predicted using cannabis first, but sex did not. Those using cannabis first were more likely to have CD (OR=1.4), less likely to use other illegal drugs (OR=0.8), but no more likely to use cannabis heavily.
Conclusions: Racial/ethnic minorities, particularly African-Americans, are more suseptible to using cannabis before tobacco, alcohol, and other drugs. A modest excess of cannabis problems may result, but offset by a possibly lower likelihood of progressing to other illegal drug use.
Financial Support: This research was supported in part (*or in its entirety*) by a grant from the National Institute on Drug Abuse (T-32DA007292, awarded to C. Debra M. Furr-Holden).

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E-CIGARETTES IN BALTIMORE ALCOHOL OUTLETS: GEOGRAPHIC AND DEMOGRAPHIC CORRELATES OF AVAILABILITY.

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Aims: The past decade has seen a rapid increase in the popularity and availability of e-cigarettes. Aside from understanding its pharmacokinetics, it is important to investigate obtainability. To date there is very limited research. This study looks at e-cigarette presence in licensed alcohol outlets in Baltimore, Maryland, with particular attention to possible disparities among varying sociodemographic neighborhood census tracts. Additionally, this study examines the relationship between e-cigarette availability and the selling of tobacco and drug products and paraphernalia within the outlets.
Methods: Data were obtained via field surveys of 667 licensed Baltimore alcohol outlets to determine if licensing requirements were adequately met. Protocol included assessments for food/drink consumption areas, tobacco and drug paraphernalia, youth and minority-oriented alcohol and tobacco advertising, adherence to anti-smoking ordinances, and business practices to prevent underage tobacco and alcohol purchases.
Results: Preliminary results show that of the 572 licensed alcohol outlets in Baltimore that were successfully surveyed, 107 outlets (18.7%) had e-cigarettes available for purchase at either above or below 3.5 feet from the floor. Of those 107 outlets, 5 (4.7%) had e-cigarettes available for purchase at both above and below 3.5 feet from the floor. Multiple logistic regression results showed statistically significantly higher odds ratios for e-cigarette availability when cigars (OR = 15.48, $p < 0.001$) or hookah (OR = 3.16, $p = 0.013$) were sold in an outlet.
Conclusions: E-cigarette availability is sparse among Baltimore's alcohol outlets, and very few have e-cigarettes available at heights physically accessible and visible for both adults and youth. Additionally, data suggest that e-cigarettes are sold as a complement to traditional tobacco products. Further analysis will investigate density of e-cigarette selling alcohol outlets in relation to neighborhood census tracts and their characteristics.
Financial Support: This study is supported by NIDA grant T32DA007292.

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ABUSE LIABILITY EVALUATION OF MEPHEDRONE IN HUMANS.

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Aims: Mephedrone is a synthetic cathinone included in the "Novel Psychoactive Substances". The objective of the present study was to evaluate the clinical abuse liability of mephedrone in comparison to 3,4-metylenedioxymethamphetamine (MDMA, ecstasy).
Methods: Twelve healthy male, recreational users of psychostimulants, participated as outpatients in three experimental sessions. They received a single oral dose of mephedrone (200 mg), MDMA (100 mg) and placebo. Design was double-blind, randomised and controlled. Study variables included: vital signs (blood pressure, heart rate, temperature, pupil diameter), subjective effects (visual analog scales-VAS, ARCI-49 item short form, VESSPA questionnaire). Blood and urine samples were obtained.
Results: Both mephedrone and MDMA produced similar increases in blood pressure, heart rate and temperature, but MDMA produced more mydriasis. Mephedone and MDMA induced pleasurable effects and euphoria. Mephedrone effects appeared earlier, were less intense and dissipate faster. Mephedrone elimination half-life was 2-3h.
Conclusions: Mephedrone presents an abuse liability similar to MDMA, but its shorter duration of effects can explain a more compulsive pattern of use.
Financial Support: Supported by grants from Instituto de Salud Carlos III (ISCIII, FIS-FEDER, FIS PI11/0196), ISCIII-Red de Trastornos Adictivos (RTA RD12/0028/0009). Clara Perez-Maña is a Rio Hortega fellowship (ISCIII, CM12/00085). Esther Papaseit is a Jordi Gras (PSMAR, 2013) and a Rio Hortega fellowship (ISCIII, CM13/00016, 2014).

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MEASURING "CRAVING" IN FOOD ADDICTION: TYPE, FREQUENCY, INTENSITY.

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Aims: Craving was included in the DSM-5 diagnostic criteria for substance use disorders (SUD). Some studies showed Food Addiction (FA) might be diagnosed using DSM-5 criteria adapted from SUD. The aim of this study was to assess craving for food in patients with SUD or other addictive disorders.
Methods: Consecutive subjects who sought treatment for at least one addiction (substance and non-substance) in outpatient addiction clinics in Bordeaux (France) were evaluated with the Mini International Neuropsychiatric Interview adapted for DSM-5 eating disorders, craving and FA adapted from DSM-5 SUD. Craving for sweet and fat was assed with a VAS.
Results: 80 patients were enrolled, mainly men (64%), mean age 41 years (SD=11), 43% overweight (BMI≥25), 11% met eating disorders diagnosis and 28% met FA diagnosis. Craving for food was reported by 33% of the entire sample (15% for sweet, 9% for fat and 9% for sweet and fat). In past 30 days, the median of days for which patients reported craving for fat was 8 and 5 for craving for sweet. The average intensity of craving for fat was 5.7 out of 10 (SD= 2.6), and 6 out of 10 (SD=2.9) for sweet. Patients with ED were more likely to report craving (100% vs 26%; p=.001) and presented more likely craving for both sweet and fat (p=.003 and p=.000, respectively). Similarly, patients with FA were more likely to report craving (65% vs 5.9%; p=.000) and presented more likely craving for both sweet and fat (p=.015 and p=.001, respectively). Severity of FA, was related to frequency of craving in past 30 days for sweet (Mild= None, Moderate= 5 d, Severe= 22 d) and for fat (Mild= 4 d, Moderate= 7 d, Severe= 12 d), but not with craving intensity.
Conclusions: Craving appeared to be a frequently endorsed criterion in FA like in other addictive disorders. These results provide further support for the plausibility of the existence of the construct of FA.
Financial Support: France: PHRC 2006, Brazil: CSF, CNPq, CAPES

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PREDICTING SEXUALLY TRANSMITTED INFECTIONS IN SEXUALLY TRANSMITTED DISEASE CLINICS IN U.S.: A MACHINE LEARNING APPROACH.

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Aims: Understanding how substance use and sexual risk behaviors are related to sexually transmitted infections (STIs) may help to target HIV risk reduction interventions for substance users. Random forests, a machine learning technique, provide a principled approach to explore a large number of effects including interactions to identify replicable sets of predictive factors.
Methods: We used data from Project Aware, a randomized clinical trial conducted among 5012 patients in 9 sexually transmitted disease clinics in the US. Predictive models for prevalence and incidence of sexually transmitted infections (STIs) were created. Substance use, sexual risk behaviors, characteristics of sexual networks were assessed and examined using a random forest machine learning approach.
Results: A total of 48 types of sexual acts and 36 types of substance use behaviors were included in the model. Overall, 30.6% of the participants reported weekly drug use, 6.1% were injection drug users, and 16.3% reported binge drinking in the last 6 months. 24.8% reported DAST-10 > 3. Results showed that large numbers of predictors (80-90) were useful in predicting STI with about 30% of predictors being sexual risk behaviors and 20% of predictors being substance use indicators. Interactions of these two classes of predictors were evident. High accuracy in predictions (70%) was achieved.
Conclusions: These results provide initial support for use of random forests to predict STI. A challenge with these methods is the lack of statistical test for significance of individual variables; nevertheless, these methods are useful for exploratory, model-building in substance abuse research.
Financial Support: RC2 DA028973 & R21 DA038641

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EFFECTIVENESS OF SUICIDE PREVENTION PROGRAMS WITH HIGH-RISK ADOLESCENT ALCOHOL USERS.

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Aims: Adolescents with high risk alcohol use are also at higher risk for suicidal ideation and attempts. But, are they benefiting from general suicide prevention programs? Or more specific interventions are necessary?
Methods: SEYLE study is a longitudinal cluster RCT to evaluate the efficacy of school-based preventive interventions of suicidal behaviors across Europe. In this case, 1029 adolescents (51.7% male; mean age: 14.52; SD: .70) from Oviedo (Spain) made up the sample. The RCT included three programs: QPR,YMHAP and SP, and a control group. Instruments: Beck Depression Inventory (BDI), WHO-5 Well-Being Index, Paykel Suicide Scale (PSS), specific questions about alcohol use. Adolescents were evaluated at baseline, and at 3 and 12 months. Two groups were created based on presence/absence of indicators of high risk alcohol use: high risk (HR) and low risk (LR). Differences in effectiveness of the preventive programs were evaluated.
Results: HR group presented at baseline with significantly higher scores in BDI, WHO-5 and PSS, and significantly higher prevalence of severe suicidal ideation ($p < .05$). For the whole sample, all programs achieved significant reductions in PSS scores at one or both follow-ups. More specifically, HR participants significantly reduced suicidal ideation at follow-ups under QPR and SP. Among those who had received interventions, no significant differences were found between HR and LR in severe suicidal ideation at follow-ups.
Conclusions: The aforementioned suicide prevention strategies showed to be effective for reducing suicidal ideation in HR and LR. Actually, at follow-ups HR and LR showed no significant differences in suicidal ideation. More studies are needed, but HR users appeared to benefit from this general prevention programs.
Financial Support: Coordination Theme 1 (Health). EU FP7. Grant No. HEALTH-F2-2009-223091

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DELIVERING HIV PREVENTION SERVICES TO DRUG COURT CLIENTS.

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Aims: The substantial burden of HIV infection and transmission among criminal justice clients is, in part, attributable to the large number of drug users under supervision and the close linkages between drug use and HIV transmission. Although a number of interventions have been developed and tested to reduce HIV risk among individuals while they are incarcerated and when they return to the community, few have been tested among the growing numbers of individuals who are diverted to community-based supervision and treatment. This study evaluates the efficacy of a computer-facilitated HIV prevention intervention for drug court clients.
Methods: A total of 78 felony drug court clients were randomly assigned to receive a 3-session computerized HIV prevention intervention or a 3-session attention control procedure with each session delivered approximately 6 weeks apart. The HIV prevention intervention addressed condom use, HIV testing, high risk behaviors, substance use and inhibition, and injection drug use. All sessions were approximately 30 minutes in length. Clients completed assessments at baseline and weeks 6, 12, 18, and 36. Outcomes assessed included HIV testing rates, engagement in high risk behaviors, and condom procurement.
Results: During the 36-week period, 59% of clients in the intervention condition obtained an HIV test compared with 32% of clients in the control condition, $p < .05$. In addition, clients in the intervention condition were more likely to procure condoms from a condom bowl in the assessment room than those in the control condition (60% vs. 41%, $p < .05$). No other differences were statistically significant.
Conclusions: These preliminary findings support the utility of using a computerized HIV-risk reduction intervention for drug court clients and highlight the importance of expanding the scope of drug court services to include HIV prevention. The computerized intervention developed in this study may provide an efficient and effective way to provide these much-needed services.
Financial Support: NIDA Grant #R01-DA-030257

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ALCOHOL AND TOBACCO USE AMONG BRAZILIAN HIGH SCHOOL STUDENTS: THE ROLE OF PSYCHIATRIC SYMPTOMATOLOGY.

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Aims: To investigate tobacco and alcohol use patterns of 15 to 18 year-old high school students in Brazil and to estimate associations with psychiatric symptoms.
Methods: A 2013 cross-sectional survey of 4034 high school students. The sample was drawn from 150 public and private schools in the São Paulo State in Brazil. All answered questions on substance use patterns and the Strengths and Difficulties Questionnaire (SDQ). Weighted data was analyzed through logistic regressions, stratified by gender and by socio-economic status.
Results: Almost forty-nine percent were male, most (81.3%) from public schools. There were no significant differences between males and females in past-year (64.4% vs. 66.7 %,), past month (37.6% vs. 38.5%), frequent (6.8% vs. 5.5%) or heavy alcohol use (3.7% and 2.8%). A positive SDQ total score (aOR = 1.33 [1.09, 1.62]) was significantly associated with past year alcohol use. Studying in a public vs. private school (aOR = 1.28 [1.00, 1.65) and having a positive SDQ total score (aOR = 1.41 [1.17, 1.71]) were significantly associated with past month alcohol use. There were no differences between males and females in past-year (13.9% vs. 14.7%), past month (9.5% vs. 8.6%), frequent (1.4% for both male and female) or heavy tobacco use (2.2% and 2.1%). Having a positive SDQ score was significantly associated with past year (aOR = 1.99[1.50, 2.64],) and past month (aOR = 1.70 [1.19, 2.42]) tobacco use. Studying in a public school (aOR = 6.36[1.41, 28.76]) was significantly associated with heavy tobacco use (aOR = 3,89 [1.35, 11.24]).
Conclusions: Psychiatric symptoms were associated with alcohol and tobacco use. Such findings might help prevention specialists, as they prompt the need for interventions focused on mental health care conditions.
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TESTING THE VACS INDEX AS A MEASURE OF HEALTH OUTCOMES ASSOCIATED WITH ABSTINENCE AMONG PATIENTS RECEIVING OPIOID AGONIST TREATMENT.

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Aims: Reductions in illicit drug use during opioid agonist treatment (OAT) can result in improved health. The Veterans Aging Cohort Index (VACS) is a validated prognostic measure of health in HIV research that includes assessments of liver, kidney, hematologic function, age, CD4 count and HIV viral load. In HIV-infected (HIV+) individuals the VACS Index reflects abstinence in patients entering OAT, including those with an undetectable viral load. We sought to evaluate its performance in HIV uninfected patients.
Methods: HIV uninfected patients initiating OAT between 2000 and 2011 were identified. Eligible patients had a VACS Index (with assumptions that CD4 count was > 500 cells/μL and viral load was < 20 copies/ml) within a year prior to initiating OAT, a VACS Index between 6 weeks and 1 year after OAT initiation, and at least 1 urine toxicology analysis in the 6 week interval prior to a VACS score. Abstinent intervals had no opioid positive urines in the 6 weeks preceding each VACS Index score. Non-abstinent intervals had ≥1 opioid positive urine during the 6 weeks preceding each VACS Index score. We assessed the association between non-abstinent/abstinent intervals and VACS Index scores with linear mixed models using a univariate model and a multivariate model that adjusted for pre-treatment VACS Index score, age, and race/ethnicity. Patient was specified as a random effect to account for multiple observations per patient.
Results: Among the 592 patients entering OAT, the mean age was 52 years, 99% were male, and 68% African-American. Sixteen percent initiated buprenorphine; 84% methadone. Mean VACS Index scores were 18.3 for abstinent intervals and 18.1 for non-abstinent intervals. Based on univariate and multivariate models, VACS Index scores did not differ between abstinent and non-abstinent intervals (p=.7, p=.4, respectively).
Conclusions: Despite responsiveness to abstinence in HIV+ individuals, the VACS Index does not appear to reflect the health benefits of efficacious OAT in those uninfected.
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POTENTIAL DETERMINANTS OF UNIQUE AND CO-OCCURING MAJOR DEPRESSION AND NONMEDICAL USE OF PRESCRIPTION OPIOIDS.

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Aims: Nonmedical use of prescription opioids (NMUPO) represents a substantial public health concern. Depression is the most prevalent psychiatric disorder in the US, and recent studies have documented an association between NMUPO and depression. There is a potential that depression has played a role in the rise of NMUPO, but this has not yet been fully investigated.
Methods: Data came from the 2011 and 2012 National Survey on Drug Use and Health (NSDUH). Adolescents and adults were examined independently because of differences in screening for major depression episodes (MDE). Weighted multinomial logistic regression models adjusted for sociodemographic and past-year drug use covariates investigated differences between persons with either past-year NMUPO or MDE compared to those with co-occurring NMUPO and MDE.
Results: Adolescent and adult females were more likely than their male counterparts to report MDE-alone (Adolescents: females [73%], males [27%]; Adults: females [66%], males [34%]) and co-occurring NMUPO and MDE (Adolescents: females [74%], males [26%]; Adults: females [60%], males [40%]). Adult males were marginally more likely than females to report NMUPO-alone (not significant among adolescents). Among adults, lower annual family income and being unemployed were associated with unique and co-occurring NMUPO and MDE. POs were more likely to be used nonmedically in combination with other drugs and alcohol than alone. Among adults, polydrug use was more pronounced among those with co-occurring NMUPO and MDE, compared to those with either NMUPO-alone or MDE-alone.
Conclusions: The differential population burden of MDE by sex remains consistent whether examining MDE-alone or co-occurring NMUPO and MDE. Sex may be a significant effect modifier in the relationship between MDE and NMUPO to be considered in future studies.
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TRICHOMONAS VAGINALIS INFECTION AND DRUG ABUSE RISK FOR WOMEN.

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Aims: Trichomoniasis is considered to be the "neglected" sexually transmitted disease (STD). We clarify the drug risk for this infection.
Methods: 2272 women were administered the Risk Behavior Assessment, and a subset had their blood tested for hepatitis A, B, and C, and HIV.
Results: Those who had Tvi were more likely to have ever used crack, powder cocaine, marijuana, heroin, speedball, and other opiates. They were also more likely to have been diagnosed with hepatitis B (HBV), gonorrhea (GC), syphilis, *Chlamydia* (CT), HPV, herpes, and yeast infection. For those who had been tested for other infections, there was a significant association with hepatitis B. The multivariate model included GC (*OR*=2.9), Black vs. Hispanic (*OR*=2.6), crack (*OR*=2.4), CT (*OR*=2.2), Syphilis (*OR*=1.8), and HPV (*OR*=1.6).
Conclusions: The associations of Tvi with drugs other than crack, and with HBV, herpes, HPV, and yeast infection in the US is a contribution to new knowledge and clarifies the risk profile for this infection.
Financial Support: The project described was supported in part by Award Numbers R01DA030234 from the National Institute on Drug Abuse, P20MD003942 from the National Institute of Minority Health and Health Disparities, and ID10-CSULB-008 from the California HIV Research Program. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse, the National Institute of Minority Health and Health Disparities, the National Institutes of Health, or the California HIV Research Program. NIDA, NIMHD, or CHRP had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

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A SMART DESIGN: RESPONSE TO REINFORCEMENT-BASED TREATMENT INTENSITY AMONG PREGNANT, DRUG-DEPENDENT WOMEN.

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Aims: Multiple randomized trials demonstrate that Reinforcement-Based Treatment (RBT) is an efficacious multi-component treatment. However, it is unclear whether some patients may respond to less intensive forms of RBT. Adaptive treatment designs may help to evaluate whether multi-component treatments can be tailored to patient response. The primary aim of the study was to evaluate different variants of RBT tailored to early treatment response.
Methods: 254 pregnant women enrolled in outpatient drug treatment provided informed consent to participate. In a sequential multiple assignment trial (SMART) 220 participants were randomized to receive treatment-as-usual RBT (n=109) or reduced-intensity RBT (n=111). After two weeks, participants were assessed for early treatment response based on drug use and treatment compliance. Early responders were randomized to receive the same (n=53) or *decreased* (n=52) RBT intensity; early non-responders were randomized to receive the same (n=56) or *increased* (n=59) RBT intensity. Primary outcomes assessed included maternal treatment utilization, drug use, and risk behaviors, infant birth outcomes, and infant hospitalization stay. **Statistical Analysis.** 7 planned comparisons were conducted to test 4 hypotheses related to tailoring treatment. Given the SMART design, the statistical model is an incomplete factorial with 8 cells on which the planned comparisons were conducted. Binary outcomes were analyzed with logistic regression, continuous outcomes with multiple regression, and repeated discrete outcomes with a GEE approach.
Results: None of the planned comparisons for any primary outcome was significant (all p-values>.05).
Conclusions: RBT treatment tailoring did not impact maternal or infant outcomes for pregnant women enrolled in outpatient substance abuse treatment.
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EFFECTS OF NORBINALTORPHIMINE PRETREATMENT ON THC-INDUCED PLACE AND TASTE AVOIDANCE IN SPRAGUE-DAWLEY RATS.

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Aims: Previous work assessing the aversive effects of Δ^9-tetrahydrocannabinol (THC) has argued that activity at the kappa opioid receptor (KOR) mediates such effects. Specifically, both genetic ablation and pharmacological antagonism of the KOR system blocks THC-induced place avoidance in CB57/BL mice. Given reported differences between mice and rats in other behavioral preparations involving cannabinoids, it is not known if this effect is evident in other species. To address this, the present experiment assessed the effects of the KOR antagonist, nobinaltorphimine (norBNI), on THC-induced place and taste avoidance in Sprague-Dawley rats.
Methods: Adult Sprague-Dawley rats were injected with 15 mg/kg of either norBNI or vehicle 24 h prior to the pairing of a distinct side of a place conditioning chamber (Experiment 1) or a novel taste (Experiment 2) with one of three doses of THC (0.56, 1.0, and 3.2 mg/kg) or vehicle. There were a total of for four conditioning trials followed by a final place or taste avoidance test, respectively.
Results: The place and taste avoidance designs are both considered valid assays of aversive drug effects, although research comparing the two demonstrates the taste avoidance design to have a lower dose threshold implying greater sensitivity. That norBNI was unable to affect THC-induced avoidance in either design suggests that the specific mediation of THC's aversive effects by KOR activity as assessed previously may be species dependent, i.e., evident in mice but not rats.
Conclusions: Previous work has implicated KOR activity as the primary mechanism mediating THC's aversive effects, norBNI had no discernable effect on place or taste avoidance assays of aversive drug effects demonstrates that KOR mediation of THC's aversive effects may be species specific.
Financial Support: Mellon Foundation Grant to ALR. Dean's Graduate Fellowship Grant to SMF.

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MEDICAL AND MENTAL HEALTH NEEDS OF LESBIAN, GAY, AND BISEXUAL CLIENTS IN SUBSTANCE ABUSE TREATMENT.

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Aims: This study identified the physical and mental health needs and service utilization of lesbian, gay, and bisexual (LGB) individuals relative to heterosexual counterparts in substance abuse treatment. Based on prior research and the minority stress model (Meyer, 2003), we hypothesized that LGB individuals would have higher rates of physical and mental health problems and service utilization relative to heterosexual individuals.
Methods: Physical and mental health problems and service utilization were examined within a database documenting 13,211 individuals who entered substance abuse treatment between 2007 and 2009 within San Francisco, CA. Differences between LGB (n=1,441) and heterosexual (n=11,770) individuals were identified using logistic regression, covarying race, ethnicity, and age, with separate models for males and females.
Results: Gay men ($_{adj}$OR:1.42, 99.9% CI:1.07,1.88) and bisexual women ($_{adj}$OR:1.70, 99.9% CI:1.06,2.74) were more likely than heterosexual counterparts to report recent physical health problems; this difference was not evident for bisexual men or lesbian women. Among men, gay ($_{adj}$OR:4.26, 99.9% CI:2.72,6.66) and bisexual ($_{adj}$OR:2.62, 99.9% CI:1.15,5.93) status predicted higher health care utilization; there were no differences among women. LGB status was predictive of higher rates of mental health diagnoses ($_{adj}$OR range across LGB groups 1.86-4.00) and current mental health prescription medications ($_{adj}$OR range 1.79-4.99) for LGB men and women. Both gay ($_{adj}$OR:3.38, 99.9% CI:2.22,5.16) and bisexual men ($_{adj}$OR:2.59, 99.9% CI:1.14,5.85), but not lesbian or bisexual women, were more likely to be receiving mental health treatment.
Conclusions: LGB individuals have greater physical and mental health needs, while lesbian and bisexual women do not have corresponding higher physical and mental health service utilization. These disparities could be addressed in substance abuse treatment settings.
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CONTINGENCY MANAGEMENT VS. NON-CONTINGENT REWARDS: INTERVENTION RESPONSE PATTERNS AMONG STIMULANT-USING MSM.

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Aims: Stimulant use has been associated with high-risk sex behaviors among MSM. Contingency management (CM) is an effective intervention for reducing stimulant use among MSM; to isolate the effects of contingent rewards, a yoked, non-contingent rewards condition was compared to a CM intervention to reduce stimulant use. It was hypothesized that CM would out-perform non-contingent rewards in promoting sustained stimulant abstinence.
Methods: From June 2010 thru June 2012, 140 stimulant-using MSM were randomized to either a CM intervention rewarding biomarker-confirmed stimulant abstinence (n=70) or a yoked, non-contingent control condition (n=70). Logistic group-based trajectory models (GTM) differentiated patterns of intervention response among participants.
Results: Best-fitting GTM models indicated four different intervention response patterns across participants: responders (i.e., predicted > 90% stimulant abstinence; 57.5% of sample); worsening intervention response (21.6%); treatment non-responders (11.3%); and, single-relapsers (9.6%); all estimated linear trajectory coefficients were significant at $p < 0.03$ (2-tailed). The CM intervention was not associated with increased probability of membership in any group.
Conclusions: CM did not outperform the application of yoked, non-contingent rewards in promoting improved intervention response (i.e., sustained stimulant abstinence) among this sample of MSM. The application of voucher rewards, regardless of contingency, promoted better-than-expected stimulant abstinence patterns in over half of all participants.
Financial Support: California HIV Research Program grant #MC08-LA-710

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PERPETRATOR VS. VICTIM SUBSTANCE USE ASSOCIATED ELDER ABUSE.

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Aims: The Institute of Medicine has projected significant increases in substance use (SU) among 65> and the WHO has identified SU as a significant risk factor for elder abuse (EA). This secondary data analysis of validated EA cases estimates the prevalence of SU related types of EA.
Methods: An exploratory descriptive analysis, of APS archived data with N=7580 EA cases substantiated between 2004-2008 in Texas was conducted. Demographics, EA type and SU data were collected.
Results: Mean age was 70 (SD=5.3). SU associated EA occurred in n=465 (6.1%) of the cases. SU rates differed among perpetrators (Perp) compared to victims (Vic) and varied among EA type. SU was substantiated in: C*aregiver Neglect (medical, physical, mental)* 85%Perp vs. 18%Vic, *Physical Abuse* 25.6%Perp vs. 7.4%Vic, *Emotional Abuse* 58.4%Perp vs. 2.6%Vic, *Financial Exploitation* 22.9%Perp vs. 9.5%Vic. Thirty two percent of SU were victims, 63% were perpetrators, and 5% were a combination. Most common types of EA among victims were *physical neglect(139), medical neglect(64),* and *mental health neglect(35).* Among perpetrators, *physical neglect(158), emotional/verbal abuse(148),* and *physical abuse(148)* were most common. Further exploratory results found that medical (OR = 4.2, 95% CI: 2.6-6.5), physical (OR = 13.0, 95% CI: 6.4-26.5) and mental-health neglect (OR = 8.7, 95% CI: 4.2-18.1) were highest among victim SU. Emotional abuse (OR = 75.6, 95% CI: 18.4-310.7) and physical abuse (OR = 12.8, 95% CI: 3.9-41.6) were most common among perpetrator SU.
Conclusions: This study found high rates of SU related EA. SU in EA substantiated cases is most commonly associated with perpetrators SU compared to victim SU. When perpetrators are abusing substances emotional/verbal, neglect and physical abuse were most common. Studies are needed to further understand these associations in order to determine appropriate prevention and intervention modalities in this vulnerable population
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EFFECTS OF REPEATED CUE EXPOSURE ON CANNABIS CRAVING.

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Aims: Craving is a key element of the cannabis withdrawal syndrome. While cue induced craving for cannabis has been established in single laboratory settings, procedures to sustain craving induction over multiple sessions are needed to support future intervention studies. The purpose of the present study was to determine if subjective and physiological cue-induced craving responses could be elicited in the same subjects across multiple sessions.
Methods: Eleven (5M, 6F) non-treatment-seeking daily cannabis users were enrolled. Five experimental sessions (1 neutral and 4 drug) included a 7-min cue exposure. Drug cue sessions involved handling cannabis paraphernalia, thinking about a recent enjoyable smoking experience, and viewing a video of young adults smoking. The neutral cue session involved handling school supplies, thinking about a relaxing time/place, and viewing a video of nature scenes. Responses on subjective (VAS/MCQ) and physiological (HR/BP) measures were assessed at baseline, immediately following cue exposure, and 30 and 60 minutes post-baseline. Peak effects were analyzed using one-factor, repeated-measures ANOVA.
Results: Cue exposure effects were found on VAS ratings of "Craving for Marijuana" and "Faster heartbeat." Ratings were increased during the first drug cue session relative to the neutral cue session, but no significant effects were found on subsequent drug cue sessions. No effects on heart rate or other measures were observed.
Conclusions: These data are in agreement with previous studies demonstrating increased subjective ratings of craving following drug cue exposure. Craving responses, however, were not maintained across sessions. In an ongoing study, cue exposure conditions have been modified in an attempt to sustain cue induced craving responses across multiple exposures.
Financial Support: T32 DA035200, R01 DA025605, UL1TR000117, Department of Behavioral Science Pilot Grant

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PHARMACOKINETICS OF BUPROPION SUSTAINED RELEASE IN PREGNANCY AND POSTPARTUM AT STEADY STATE.

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Aims: The use of bupropion sustained release (BUP SR) as an aid for smoking cessation during pregnancy is currently being evaluated at UTMB. The pregnancy-induced changes in maternal physiology may alter pharmacokinetics (PK) and pharmacodynamics (PD) of BUP, and consequently its effectiveness for smoking cessation during pregnancy.
Therefore, the objective of the current study is to determine the pharmacokinetics (PK) of bupropion SR in pregnant women at different gestational ages as well as during postpartum (with or without lactation) and postlactation periods.
Methods: Pregnant patients received an oral dose of BUP SR 150 mg twice per day. After reaching steady state, the PK of BUP SR was studied following a single oral dose. Blood samples were taken prior to dosing and at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, and 12 hours post-dosing. Urine samples were collected over the same 12-hour interval. The plasma and urine levels of BUP and its metabolites hydroxybupropion (OH-BUP), *threo-*, and *erythro*hydrobupropion (TB and EB) were determined by liquid chromatography-mass spectrometry (LC-MS). The PK parameters were calculated using noncompartmental analysis.
Results: Relative to the postpartum period, the average late-pregnancy clearance of BUP SR was greater (0.35 ± 0.13 vs. 0.21 ± 0.05 L/h) and the average $AUC_{0\text{-}12}$ values (491.5 ± 187.2 vs. 754.2 ± 180.5 hng/ml) were lower ($p<0.05$).
Conclusions: The higher ratio of AUCs for OH-BUP over BUP during late pregnancy (23.8 ± 9.9) as compared to postpartum period (16.2 ± 9.5) suggests that the observed increase in the clearance of BUP during late-pregnancy could be associated with a pregnancy-induced increase in its biotransformation to OH-BUP.
Financial Support: Supported by NIDA grant DA030998 to TN

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ORAL MIDAZOLAM CONSUMPTION USING A TWO-BOTTLE CHOICE PROCEDURE IN C57BL/6J MICE.

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Aims: Although there is concern regarding the abuse liability of benzodiazepines (BZs), the mechanisms underlying their abuse potential are not yet well understood. In recent years, both pharmacological and genetic approaches have shed considerable light on understanding the role of GABA-A receptors in the abuse-related effects of BZs. In order to use both approaches, we have initiated systematic studies on midazolam consumption with a "standard" two-bottle choice procedure with C57BL/6J mice (a commonly-used background strain for genetic studies).
Methods: Thirteen individually-housed mice were given 24-hour access to two bottles in their home cage: both containing 4% sucrose solution, with one bottle containing midazolam (0, 0.004, 0.008, 0.016, 0.032 mg/ml). The midazolam bottle side was switched daily, and subjects were exposed to each concentration for 14 days.
Results: Mice drank the 4% sucrose solution reliably across sessions, with overall consumption from both bottles averaged across 14 days increasing significantly as a function of MZ concentration. Based on the last 3 days of availability, average mg/kg/day of midazolam consumed increased significantly from 0.69 to 4.5 mg/kg, whereas percent midazolam choice tended to be an inverted U-shaped function, with choice above 50% at one concentration only (average= 66% at 0.008 mg/ml).
Conclusions: In the present study, oral midazolam consumption was robustly dose-dependent, with choice for midazolam+sucrose vs. sucrose alone being relatively modest. These findings demonstrate the feasibility of maintaining oral midazolam consumption in individually-housed C57BL/6 mice, providing a methodological platform for investigating the pharmacological and genetic basis of BZ taking.
Financial Support: Supported by grants DA033795 and DA011792.

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RETENTION IN A METHADONE MAINTENANCE TREATMENT: IMPACT OF COMORBIDITY.

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Aims: To describe medical and psychiatric comorbidity in patients admitted to a methadone maintenance treatment (MMT) program. To describe the impact of comorbidity in drop-outs.
Methods: Data on patients consecutively admitted in an out-patient community MMT program from January 2000 until December 2013. Demographics, clinical data (dual diagnosis, medical diagnosis) and reasons for drop out were assessed. Patients who voluntary dropped from treatment, were analyzed considering the last contact with the center: ≤ 3 months (early drop-out) and > 3 months (delayed drop-out).
Results: In the period analyzed, a total of 568 patients have been admitted to MMT (76% men, 38±9 years at admission). After 13 years, 424 patients (76% men, 37±9 years at admission) were not longer in the program. Reasons for discharge were: 33.3% moved to other centers/areas, 32.1% dropped out, 11.6% were transferred to other programs/medications in the same center (drug free program, slow-release morphine or buprenorphine), 7.8% died, 1.7% were transferred to therapeutic community and 0.4% for other reasons. Mean retention time in the same OST program was 83 months (95% CI: 72-93).<!—EndFragment—>
Conclusions: Methadone maintenance treatments are useful to maintain patients in treatment, even in patients with medical (HIV, HCV) and psychiatric comorbidity. Low doses of methadone have been observed in patients with early drop-outs; in those patients, other therapeutic strategies, with faster titration should be considered.
Financial Support: Fondo de Investigaciones Sanitarias, Instituto Carlos III (RD06/0001/1009) and AGAUR-Suport Grups de Recerca (2014 SGR790).

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FIDELITY MONITORING MODEL FOR AN MI BASED BRIEF INTERVENTION.

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Aims: Learning motivational interviewing (MI) is an ongoing process, involving much more than attendance at a single workshop. Once proficiency is achieved, therapists benefit from ongoing coaching with individual feedback based on observed practice to ensure continued fidelity. The aim of this study was to assess outcomes of the unique training and supervision model employed in a recent trial of MI.
Methods: The intervention tested in the six-site NIDA CTN 0047 trial was a 30-minute MI-based brief intervention delivered in the emergency department followed by two telephone booster calls delievered from a centralized call center. Thirty-one counselors and 3 booster counselors were trained in the intervention using a 2-stage process: local training in the MI process of engagement followed one month later by a 2-day training in MI. We employed a two-level model in which the formal coding was separated from the clinical supervision. One audio file per interventionist per week was coded using the MITI 3.1.1 coding system. This written feedback was available to clinical supervisors, who reviewed coding results during telephone supervision sessions.
Results: Eleven percent of sessions were coded on an ongoing basis during the trial, with a total of 380 initial sessions (90%) and 83 booster sessions (20%) coded upon completion of the trial. Mean global scores for initial sessions ranged from 4.25 to 4.67, and for the booster sessions from 4.64 to 4.86, well above the proficiency benchmark of 4.0. Inter-rater reliability assessed on a random sample of 124 tapes was excellent, with ICCs averaging 0.81 for global scores and 0.93 for behavior counts. On a therapist level, MITI scores tended to improve over time, demonstrating the strategies employed helped with adherence and continued learning in MI.
Conclusions: A comprehensive strategy for successfully learning and maintaining skills in MI emerged from the 0047 study, which employed a rigorous and novel plan for ensuring therapists adhered to the style of MI.
Financial Support: NIDA CTN

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PERINATAL ATTENTIONAL RETRAINING INTERVENTION FOR SMOKING - A PILOT STUDY.

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Aims: Almost half of women who smoke prior to pregnancy achieve abstinence during pregnancy, but nearly 50% relapse within 2 weeks of delivery. Despite considerable study, there are few strategies that effectively combat smoking relapse in this population. Thus, we tested a novel technique: the use of smartphones to administer attentional retraining (AR) as an ecological momentary assessment intervention for relapse prevention in postpartum women. We hypothesized that relative to control, women randomized to AR would show less attentional bias (AB) toward smoking-related stimuli, and a decrease in craving.
Methods: Women (N=11) were recruited during pregnancy and carried a smartphone as they went about their daily lives for 1-2 weeks in the last month of pregnancy and immediately postpartum. Participants were randomized to receive AR (N=6) or attentional control (N=5). The smartphone randomly alerted participants (4 times/day) to respond to questions assessing subjective states, followed by AR (or control) procedures utilizing a visual probe task. Outcome measures included attentional bias for smoking and craving.
Results: Participants carried a smartphone for a mean of 20.2 days, completed 444 assessments (60.14% pregnancy; 39.86% post-partum) and 2.92 assessments per day. Craving increased from pregnancy (M=1.40, SD=1.23) to postpartum (M=2.28, SD=2.27); postpartum participants reported having smoked since the last assessment on 12.64% of assessments, and 8 women reported smoking at least 1 cigarette during the study. AB was more negative in the AR group (n=35 assessments, M=-52.6 ms, SD=122) vs. controls (n=44 assessments, M=18.5 ms, SD=146) (p<0.05, using a linear mixed model).
Conclusions: Findings suggest that AR reduced AB to smoking cues and that women in the AR group attended ***away*** from smoking cues. This study demonstrates that AR can be administered on a mobile device, women experience craving postpartum, which is associated with AB, and AR can reduce AB to smoking cues in perinatal women.
Financial Support: This study was funded by NIDA, K12-DA-000167.

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SEROTONIN (5-HT) 5-HT$_{2C}$ RECEPTOR (5-HT$_{2C}$R) AGONIST LORCASERIN SUPPRESSES COCAINE OR OXYCODONE CUE REACTIVITY.

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Aims: Environmental stimuli associated with drug use lead to durable conditioned responses (cue reactivity). Investigational selective 5-HT$_{2C}$R agonists suppress cocaine intake and cue reactivity in self-administration assays. Lorcaserin is a first-in-class selective 5-HT$_{2C}$R agonist recently approved by the FDA for obesity. We tested the hypothesis that lorcaserin suppresses cue reactivity in rats trained to self-administer the psychostimulant cocaine or the opioid painkiller oxycodone.
Methods: Rats were trained to self-administer cocaine or oxycodone. Cue reactivity was assessed as lever presses for drug-associated cues (within subject; 1-2 tests/wk; min 3 intervening self-administration sessions). A subset of oxycodone-trained rats, extinction training preceded a single cue-induced reinstatement session. Lorcaserin (0, 0.25, 0.5, 1 mg/kg) was administered prior to each test session.
Results: Lorcaserin (1 mg/kg) significantly suppressed cue-reactivity vs vehicle (p<0.05) in both cocaine-trained and oxycodone-trained rats. Lorcaserin dose-dependently suppressed cue-induced reinstatement of oxycodone-seeking (p<0.05).
Conclusions: Lorcaserin suppressed cue reactivity in rats experienced in psychostimulant or opioid self-administration. Although the direct neural targets for psychostimulants and opioids to evoke their rewarding effects differ and the ability of lorcaserin to suppress drug-taking should be assessed, the present data suggest that the incentive saliency of psychostimulant- and opioid-paired cues involve shared 5-HT$_{2C}$R-mediated mechanisms. Further investigation is warranted, but the clinical availability of lorcaserin now allows treatment efficacy analyses in psychostimulant or opioid use disorders.
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NEURAL CORRELATES OF ATTENTIONAL BIAS FOR CANNABIS CUES: INFLUENCE OF SEX.

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Aims: Attentional biases (AB) interfere with decision making processes and AB to drug cues is a cardinal feature of addiction that may contribute to relapse. Thus it is critical to identify the neural correlates of AB for improving interventions. Cue responsivity and AB differ between males and females suggesting the neural correlates of AB to drug cues may also be sex-specific.
Methods: We explored associations between AB for cannabis cues (CCs) and neural responses to CCs among males (n=24) and females (n=14) seeking treatment for cannabis use disorder (CUD). CUDs were exposed to CCs and comparison cues (500 msec duration; 48 images of each cue type) presented in a quasi-random order in a BOLD fMRI fast event-related paradigm. Males and females did not differ in demographic or drug use characteristics. Male and female CUDs also completed a visual dot-probe AB task, which contained pictures of CCs and nondrug cues to examine whether sex influences AB and to investigate relationships between AB and neural responses to CCs.
Results: CUDs showed an AB to CCs (22.8 ± 4.7msec), which was not significantly different between males and females. Neural responses to CCs were strongest in the ventral striatum in females and the amygdala in males. Males showed positive correlations between AB and increased CC-induced brain activity in visual cortex and bilateral parahippocampus whereas females showed positive correlations (all bilateral) in the insula, lateral orbitofrontal cortex, dorsolateral prefrontal cortex and middle temporal cortex. (T values range from 3-6,p=0.01).
Conclusions: Results suggest that AB to CCs has different brain correlates for men and women. Thus, strategies to address AB may need to target sex-specific brain vulnerabilities for maximum impact on relapse.
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SEX DIFFERENCE IN BEHAVIORAL EFFECTS OF THE THC AGONIST CP55,940.

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Aims: Sexual dimorphism exists at different levels of the cannabinoid system and THC induced responses, including receptor distribution, metabolic processing of THC, and analgesic responses. Anxiety responses in both human and animal males are dose dependent: low acute doses of cannabinoids are anxiolytic while high and/or chronic doses are anxiogenic. In this study we aimed to examine if the biphasic behavioral effects of cannabinoids that have been demonstrated in males are also present in females.
Methods: Male and female Wistar rats (8 weeks old) received 0, 0.001, 0.01, 0.075 or 0.125 mg/kg i.p. of the THC agonist CP55,940—n=10-11 per group. Thirty minutes later, animals were placed in the elevated plus maze (EPM) for 10 minutes, and their behavior analyzed by Med Associates tracking software.
Results: A significant main effect of CP55,940 doses was observed [$F(4, 92) = 6.863$, $p < 0.01$]; 0.075 mg/kg showed a significant reduction in percent time in open arms compared to vehicle ($p = 0.05$). Furthermore, 0.001mg/kg showed significantly more time in open arms than: 0.01 ($p = 0.045$), 0.075 ($p < 0.01$) and 0.125 ($p < 0.01$).
Conclusions: Sex differences were observed in the effect of CP55,940 on anxiogenic and anxiolytic responses. Although males showed biphasic dose dependent responses to this THC agonist, female rats showed only an anxiogenic response to CP55,940. Our work is in agreement with previous studies suggesting sex-dependent behavioral effects of cannabinoids. Further research is needed to understand the underlying mechanisms responsible for these differences.
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ATTACKS ON PWIDS' DIGNITY: ASSOCIATIONS WITH BEHAVIORS.

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Aims: As with norms, stigma involves both internal & external processes. One important external process is having one's dignity attacked. We hypothesize: dignity attacks are associated with HIV risk behaviors.
Methods: We recruited 300 PWID by referral from a large New York City RDS study in 2012-13. Each was asked how often people had spoken or acted towards them in the last year in a way that felt like they were attacking their dignity or demeaning them. We tested associations of the frequency of such dignity attacks with the frequency of drug and sex behaviors in the last 30 days using Pearson correlations.
Results: Of 291 PWID with non-missing responses, 16% had not had their dignity attacked; 27% were attacked weekly or more frequently. The most common sources of dignity attacks on them were their mothers (41%), brothers (24%), sisters (29%), strangers (19%) and program staff or case managers (18%). 34% reported seeing others' dignity attacked daily or more frequently. The frequency of having one's dignity attacked was significantly ($p < 0.05$) correlated 0.22 with receptive syringe sharing, 0.19 with distributive syringe sharing, and 0.19 with crack use, but was not correlated with sexual risk behaviors. Frequency of witnessing attacks on others' dignity was significantly correlated with receptive syringe sharing ($r = 0.14$) and crack use ($r = 0.13$).
Conclusions: Attacks on both PWIDs' dignity and that of others in their vicinity are common. Such attacks on dignity are associated with injection risk behaviors and with crack use. Although these findings are cross-sectional, they suggest that relatives, strangers, and program staff are important sources of dignity attacks and that these attacks may be associated with more risk behavior. Research should develop efforts to reduce such attacks on the dignity of PWID and evaluate whether these reduce HIV risk and other harms.
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PATIENT SELECTION FOR EXTENDED-RELEASE NALTREXONE AMONG CRIMINAL JUSTICE-INVOLVED PERSONS WITH OPIOID USE DISORDER.

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Aims: One consideration in patient selection for XR-NTX is whether s/he can achieve a completely opioid-free state to avoid precipitated withdrawal. This secondary analysis examines predictors of this state among criminal-justice (CJ)-involved persons with opioid use disorder in the community.
Methods: In a 5-site XR-NTX effectiveness trial, potential subjects had to live in the community, volunteer, have DSM-IV opioid dependence and CJ involvement in the prior 12 months. Baseline bivariate predictors ($P<0.05$) of providing the opioid-free urine test required for randomization were entered into a stepwise logistic regression model.
Results: Of 435 potential subjects, 308 were completely opioid-free and randomized: mean age 44, 85% male, 48% Black, 87% lifetime heroin use and 73% on probation or parole. Bivariate predictors of achieving this opioid-free state versus not were taking buprenorphine (16% v 35%, respectively) or methadone (6% v 25%), attending AA/NA (52% v 37%), having health insurance (71% v 51%), non-white race (80% v 56%), past 30 day heroin use (25% v 72%), depression (mean BDI score, 10 v 13), sociopathy (mean CPI-So score, 21.2 v 19.7), and risky drug use (mean RAB Drug Score, 1.3 v 2.3). Independent predictors were using buprenorphine (OR .19; 95% CI .08 to .48) or methadone (OR .38; CI .18 to .80); recovery group meeting attendance (OR 2.3; CI 1.1 to 4.6) or being insured (OR 2.1; CI 1.1 to 4.1).
Conclusions: Recent use of buprenorphine or methadone among CJ-involved opioid users reduces their ability to achieve the duration of abstinence necessary to be completely opioid-free prior to XR-NTX injection. Attendance at recovery groups like AA/NA and having health insurance confer a greater likelihood of achieving the necessary opioid-free state.
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SUBSTANCE USE DISORDERS TREATMENT HISTORY AMONG HOSPITALIZED HIV-INFECTED SUBSTANCE USERS IN 11 U.S. CITIES.

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Aims: HIV-infected substance users (HIV-SUs) who are in substance use disorders treatment are more likely to receive HIV care than those not in treatment. Yet, substance use disorders treatment (tx) history of HIV-SUs not enrolled in HIV care is not well understood. We measured factors associated with tx history among HIV-SUs.
Methods: This analysis included 801 HIV-SUs from the baseline assessment of the NIDA Clinical Trials Network 0049 study, a RCT designed to help HIV-SUs recruited from hospital settings achieve viral suppression. We examined associations between substance use, health status and tx history.
Results: In the last year, 20% used opioids, 64% used stimulants, 18% injected drugs, and 49% were heavy alcohol users. Overall, 55% had ever participated in tx; of these, 36% participated in tx in the last year. Ever participated in tx was associated with likely depression and taking HIV medication. Likelihood of tx in the last year was higher among those with unstable housing or those who reported substance use-related discrimination.
Conclusions: Structural barriers (unstable housing) and possible motivators of tx participation (likely depression) were related to substance use disorder tx history. The association between discrimination and tx may promote the development of targeted strategies. Discrimination may lead to tx initiation or, alternatively tx experience may increase perceptions of discrimination. Similarly, taking HIV medication may prospectively be associated with better outcomes of intervention. The factors uncovered in the current analysis point to potential modifiers of Project Hope.
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CYTOTOXICITY OF SYNTHETIC CANNABINOIDS ON PRIMARY NEURONAL CELLS OF THE FOREBRAIN.

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Aims: The present study investigates the acute cytotoxicity of synthetic cannabinoids on mouse brain neuronal cells.
Methods: Synthetic cannabinoid (CP-55,940, CP-47,497, CP-47,497-C8, HU-210, JWH-018, JWH-210, AM-2201 and MAM-2201)-induced cytotoxicity was examined using forebrain neuronal cultures.
Results: These synthetic cannabinoids induced cytotoxicity in the forebrain cultures in a concentration-dependent manner. The cytotoxicity was suppressed by pretreatment with the selective CB1 receptor antagonist AM251, but not with the selective CB2 receptor antagonist AM630. Furthermore, Annexin-V-positive cells were found in the treated forebrain cells. Furthermore, we next examined whether the selective CB2 receptor agonist JWH-133 and CB-65 induced cytotoxicity in the forebrain cultures under similar conditions of the CP-55,940 treatment. Neither of the selective CB2 receptor agonists induced cytotoxicity. Synthetic cannabinoid treatment induced the activation of caspase-3 and pretreatment with a caspase-3 inhibitor significantly suppressed the cytotoxicity. The data show that these synthetic cannabinoids induce apoptosis through a caspase-3-dependent mechanism in the forebrain cultures.
Conclusions: Our results indicate that the cytotoxicity of synthetic cannabinoids towards primary neuronal cells is mediated by the CB1 receptor, but not by the CB2 receptor, and further suggests that caspase-cascades may play an important role in the apoptosis induced by these synthetic cannabinoids. In conclusion, excessive synthetic cannabinoid abuse may present a serious acute health concern due to neuronal damage or deficits in the brain.
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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FIELD EVIDENCE FOR STRESS-INDUCED DRUG USE.

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Aims: There is mounting evidence, from preclinical and clinical research, that stress plays a role in drug use. A weakness in the human data is that craving is often used as a surrogate for drug use. We used Ecological Momentary Assessment (EMA) in a novel way to examine discrete episodes of stress reported by drug users in real time in the hours and days preceding cocaine or opioid use.
Methods: For up to 16 weeks, outpatients in methadone (MTD) or buprenorphine (BUP) maintenance used smartphones to report each time they used a drug or felt more stressed than usual. Participants rated severity of stress events on a 10-point scale and as "a hassle," "something that could spoil the day" or "something that could do more than spoil the day." Stress reports made within 72 hrs before a cocaine-use report or an opioid-use report were binned into 24-hour periods (0-24, 25-48, 49-72 hours). Opioid- and cocaine-use reports were examined separately. When both drugs were reported simultaneously, we used that report in both sets of analyses.
Results: Participants (n=52, 36 MTD, 16 BUP) reported at least one stress event within 72 hr before drug use. In 41 participants who made stress entries before cocaine-use entries, the numerically rated severity of stress events linearly increased in the 72 hr prior to cocaine use (r_{effect}=.42, CL95 .17-.62, p=.00061). The % of stress entries rated as merely "a hassle" decreased linearly (r_{effect}=.39, CL95 .13-.60, p=.0105), and the % rated as "more than a day spoiler" increased linearly (r_{effect}=.34, CL95 .07-.56, p=.0292). No such patterns were seen in the stress entries made before opioid use (n=26 participants).
Conclusions: These EMA results show that stressful events were more strongly associated with cocaine use than with opioid use in our population. This finding supports the potential utility of stress-reducing interventions to reduce cocaine use among methadone- or buprenorphine-maintained outpatients.
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MARKERS OF INFLAMMATION AND MORTALITY IN A COHORT OF ALCOHOL-DEPENDENT PATIENTS.

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Aims: We aimed to assess the impact of three surrogate markers of inflammation (anaemia, fibrinogen and ferritin levels) on mortality of alcohol dependent patients.
Methods: Longitudinal study in a cohort of alcohol dependent patients admitted for hospital detoxification. Markers of inflammation and other clinical caharacteristics were assessed at admission.
Mortality was ascertained from clinical charts and mortality register. Mortality rates and Cox models were used to analyze the association between markers of inflammation and mortality.
Results: Between 2000 and 2010, 909 consecutive alcohol dependent patients were admitted. Patients were mostly male (80.3%), had a median age of 44 years (Interquartile range [IQR]: 38-50), and a median alcohol consumption of 192 g/day (IQR: 120-265) upon admission. At admission, anaemia (<12 g/dL in women and <13 g/dL in men) was present in 182 (20.5%) patients, 210 (25.9%) had fibrinogen levels >4.5 mg/dL and 365 (49.5%) had ferritin levels >200 ng/mL. At the end of follow-up (median 3.8 years [IQR: 1.8-6.5], accounting for total person-year of 3,861.07), 118 patients (12.9%) of the study population had died. Cox regression models showed that anaemia at baseline was associated with mortality [hazard ratio (HR) 1.67 (95% Confidence Interval (CI): 1.11-2.52), p <0.01], while high fibrinogen and high ferritin levels were not.
Conclusions: In alcohol dependent patients seeking treatment, only the presence of anaemia at admission was associated with an increased risk of death.
There is a need for more accurate markers of inflammation that could be used as prognostic factors for bad outcomes in this subset of patients.
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SMOKING AND CARDIAC REHABILITATION PROGRAM COMPLETION.

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Aims: Cardiac rehabilitation (CR), a program of structured exercise and educational sessions, is standard care following a heart attack, heart valve surgery or coronary bypass surgery and reduces morbidity, mortality and re-hospitalizations. Continued smoking following a cardiac diagnosis is strongly associated with increased morbidity and mortality and may be associated with non-compliance with secondary prevention strategies. Non-completion of the CR program by current smokers would be troubling. In this study we explored the association between smoking status and completion of a CR program.
Methods: A prospectively collected clinical database was analyzed to test the associations between self-reported smoking status at CR intake and number of CR sessions completed. Completion of the CR program was defined as attending ≥ 30 of 36 possible sessions. Age, sex, diagnosis (surgical vs. non-surgical) and depression scores (Geriatric Depression Scale) were also examined as potential covariates.
Results: Records with complete data on the variables of interest were extracted from the database and produced 1889 unique records for inclusion. The cohort had a median age of 64, was 28% female, and was 32% surgical patients. Current smoking was reported by 8% of patients, 54% were former smokers and 38% reported never smoking. Completion rates differed significantly by smoking status with 38.3% of never smokers, 37.8% of former smokers and only 14.2% of current smokers attending ≥ 30 sessions. Using generalized linear modeling, age above the median (OR 2.46, CI 2.01-3.01), surgical diagnosis (OR 1.30, CI 1.06-1.59) and current smoking (OR 0.35 CI 0.21-0.56) were independent predictors of program completion.
Conclusions: Self-reported current smoking is a robust predictor of non-completion of CR. Individuals who report smoking at CR intake may require additional support to complete the CR program.
Financial Support: This research was supported in part by NIH award P20GM103644 and NIDA/FDA award P50DA036114.

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THE SPATIAL-TEMPORAL RELATIONSHIP OF POLICING IN AREAS WITH HIGH DRUG ACTIVITY.

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Aims: In 2009, Mexico implemented a federal drug policy reform that de-emphasized drug law enforcement in favor of connecting drug-dependent persons with addiction treatment (narcomenudeo reform). It remains unclear to what extent the reform impacted drug arrests in areas with a history of drug-related violence, such as Tijuana, Mexico. This study examines the spatial-temporal trends of drug-related policing activity.
Methods: Location of self-reported arrests from 2011-2013 among a prospective sample of illicit drug users in Tijuana (n=564) was mapped across 9 districts corresponding to policing precincts. Official crime statistics detailing drug possession and sale arrests obtained from the Tijuana police department during the same period were layered onto the map. Moran's I statistic examined clustering and spatial dependencies of self-reported arrests and official drug possession arrest rates over the 3-year period using GeoDa software.
Results: Official drug possession arrest rates increased from 2011 to 2013 by 67.8% in Tijuana. There was significant clustering of self-reported arrests that persisted over time. We detected spatial dependencies between the location of self-reported and official arrests that remained stable over the 3 years; districts with a high number of self-reported arrests were also characterized by high rates of drug arrests.
Conclusions: Multiple sources of data suggest that individuals continue to be detained for drug-related offenses in Tijuana, despite the drug decriminalization reform, with highest concentrations of arrests in areas traditionally characterized by drug-related crime. We found no evidence that drug arrests are converted to referrals to drug treatment services, as contemplated by the narcomenudeo reform. Implications for additional steps to align policing with public health policy are discussed.
Financial Support: K01DA034523, R37DA019829, D43TW008633, Canadian Institutes of Health Research and the Trudeau Foundation

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MORTALITY AND GUIDELINE-CONCORDANT LONG-TERM OPIOID THERAPY FOR PAIN.

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Aims: To determine the association between guideline-concordant care and 1-year all-cause mortality among patients initiating long-term opioid therapy (LtOT) for chronic pain.
Methods: From the Veterans Aging Cohort Study, we identified patients initiating LtOT (≥ 90d) through the VA between 2000-2010. Patients were followed during the initial 6 months of LtOT to assess receipt of 6 quality indicators (QIs) derived from clinical practice guidelines. To control for confounding by indication, we used multivariable logistic regression to generate propensity scores and subsequently match patients (via a SAS greedy algorithm) on medical, psychiatric, and pain comorbidities for each QI. Time-updated Cox regression was used to examine the association between QI receipt and 1-year all-cause mortality.
Results: Of 17,044 patients initiating LtOT between 2000 and 2010, 1,048 patients (6%) died within 1year. Patients receiving psychotherapeutic co-interventions (hazard ratio [HR] 0.62; 95% confidence interval [CI] 0.51-0.75) or rehabilitative therapies (HR 0.81; 95% CI 0.67-0.98) had decreased all-cause mortality when compared to patients not engaged in such care, while patients prescribed benzodiazepines concurrent with opioids had a higher mortality risk (HR 1.39; 95% CI 1.12-1.66). Among patients with a current substance use disorder (SUD; n=3,006), those receiving SUD treatment had a lower mortality risk than untreated patients (HR 0.48; 95% CI 0.32-0.71). No association was found for urine drug testing (HR 0.91; 95% CI 0.74-1.12) or primary care visits (HR 0.99; 95% CI 0.79-1.25).
Conclusions: Initiatives are needed to limit LtOT initiation in conjunction with benzodiazepines and untreated SUDs. Patients are likely to benefit from multi-modal treatment models that address chronic pain and its associated comorbidities across multiple disciplines, including psychotherapeutic services and SUD treatment.
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GENDER DIFFERENCES IN ASSOCIATIONS BETWEEN CHILDHOOD SEXUAL ABUSE AND ILLICIT DRUG USE IN ADULTHOOD.

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Aims: We examined gender differences in the association between a history of childhood sexual abuse (CSA) and illicit drug use in adulthood in a nationally-representative sample of adults aged 24-32 years living in the United States.
Methods: We used data from the National Longitudinal Study of Adolescent to Adult Health to measure CSA by a parent or adult caregiver before the age of 18, which was assessed retrospectively at Waves III (emerging adulthood; ages 18-26 years) and IV (adulthood; ages 24-32 years). History of cocaine and crystal methamphetamine use and non-medical use of prescription drugs was reported during adulthood. Data from Waves I (ages 7^{th}-12^{th} grade), III, and IV were used to measure covariates, including age, race, education, emotional and physical abuse, and poverty. Using survey methods to obtain nationally-representative estimates, we used logistic regression to measure gender-specific associations between CSA and adulthood drug use.
Results: CSA was reported more commonly among females (11%) than males (7%) (p value= <0.0001). Among females, in unadjusted and adjusted analyses, CSA was associated with adulthood use of cocaine (adjusted odds ratio (AOR)= 1.46, 95% CI: 1.12-1.90), crystal methamphetamine (AOR=1.45, 95% CI: 1.03-2.04), and non-medical use of prescription drugs (AOR=1.55, 95% CI: 1.16-2.07). In contrast, CSA was not an independent correlate of use of these illicit drugs among males.
Conclusions: CSA appears to influence the risk of adulthood illicit drug use among females but not males. The findings suggest incorporation of trauma-informed approaches may improve drug use prevention interventions for females.
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EFFECTS OF THE 5-HT1B RECEPTOR AGONIST CP 94253 ON METHAMPHETAMINE SELF-ADMINISTRATION.

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Aims: We previously found that the selective 5-HT1B receptor (5-HT1BR) agonist, CP 94253 (CP), shifts the cocaine self-administration (SA) dose-response (DR) curve upward and left during training but produces a downward shift after 3 weeks of forced abstinence. This study examined whether CP has similar effects on methamphetamine (meth) SA.
Methods: Twenty male Sprague-Dawley rats were trained to self-administer meth (0.1 mg/kg) on a FR5 schedule. After drug intake stabilized, rats commenced within-session DR training wtih five doses (0.003, 0.01, 0.03, 0.1, & 0.3 mg/kg). Animals were then treated twice pre- and post-abstinence with CP (5.6 mg/kg, s.c.) or saline (1 mL/kg, s.c.) with order of treatment counterbalanced, to assess CP effects on meth SA. In addition, rats were tested on a progressive ratio (PR) schedule with 0.03 mg/kg meth available to evaluate CP effects on meth incentive motivation. PR testing occurred across two sessions for which rats received pretreatment with 5.6 and 10 mg/kg CP on the first and second sessions, respectively.
Results: Pre- and post-abstinence, rats exhibited the typical inverted U-shaped meth SA DR curve with the highest number of infusions obtained at the 0.01 mg/kg dose regardless of pretreatment. Prior to abstinence (n = 10), CP reduced total meth reinforcers obtained for the two highest doses. For post-abstinence (n = 12), CP had similar effects, reducing total reinforcers obtained for the last three highest doses. Paired sample t-tests for breakpoints on PR sessions indicated no significant effect of CP.
Conclusions: Unlike the abstinence-dependent modulatory role of 5-HT1BRs on cocaine SA, this study found similar effects of CP pre- and post-abstinence suggesting different mechanisms may regulate meth SA. These findings are important for understanding the clinical efficacy of 5-HT1BR agonists as treatments for psychostimulant disorders.
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LONG-TERM FOLLOW-UP OF PSILOCYBIN-FACILITATED SMOKING CESSATION: ABSTINENCE OUTCOMES AND QUALITATIVE ANALYSIS OF PARTICIPANT ACCOUNTS.

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Aims: We assessed long-term (>12 months) outcomes of psilocybin-facilitated smoking cessation, and qualitatively analyzed participants' accounts to inform potential psychological mechanisms of treatment efficacy.
Methods: 15 individuals who completed a pilot study of psilocybin-facilitated smoking cessation were invited for a long-term follow-up. Eleven (73%) returned and were interviewed about their current smoking and treatment experience (mean time since treatment=30 months, SD=17, Range=16-57). Exhaled carbon monoxide, and self-report measures of craving, temptation, and smoking abstinence self-efficacy were assessed.
Results: At 6 months, 10 of 11 (91%) participants were smoking abstinent. At long-term follow-up, 9 of 11 (82%) were still abstinent. Craving and temptation were not significantly different between 6-month and long-term follow-ups, and remained significantly lower than at baseline. Smoking abstinence self-efficacy showed significant persisting increases from baseline scores, and remained comparable to those at 6 months. Participants reported profound, insightful psilocybin experiences and good rapport with study staff as factors impacting treatment efficacy.
Conclusions: Psilocybin, administered under controlled conditions in a treatment context, is associated with ongoing smoking abstinence and persisting reductions in craving and temptation. Results were potentially related to personally meaningful experiences and rapport with study staff. Results showed lasting benefits in this sample consistent with prior research on long-term effects of psilocybin.
Financial Support: Heffter Research Institute, Beckley Foundation, NIDA T32DA07209 and R01DA003889.

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THE ROLE OF SMOKING-SPECIFIC EXPERIENTIAL AVOIDANCE IN THE RELATION BETWEEN PERCEIVED STRESS AND TOBACCO USE AMONG TREATMENT-SEEKING SMOKERS.

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Aims: The present study explored the role of smoking-specific experiential avoidance on the relation between perceived stress and clinically-relevant smoking behaviors among treatment-seeking smokers. It was hypothesized that smoking-specific experiential avoidance would have an indirect effect on relations, and that these effects would not be explained by gender, tobacco-related illnesses, presence of an Axis I psychiatric disorder, negative affectivity, alcohol use or cannabis use.
Methods: The sample consisted of 349 treatment-seeking adult daily smokers (45.3% female) who reported smoking at least 8 cigarettes per day during the past year and at least one serious lifetime quit attempt.
Participants responded to community advertisements to participate in a larger study examining the efficacy of two smoking cessation interventions. Data for this study came from the baseline assessment of this larger trial and before randomization. After providing written informed consent, participants were interviewed and completed an on-line survey.
Analyses were conducted using bootstrapping techniques through a conditional modeling program that utilizes an ordinary least squares-based path analytical framework to test for both direct and indirect effects of perceived stress, smoking-specific experiential avoidance, and criterion variables (i.e., severity of problematic symptoms during past quit attempts, latency to first cigarette of the day, nicotine dependence, and heaviness of smoking index).
Results: Smoking-specific experiential avoidance indirectly explained the relation between perceived stress and (a) severity of problems experienced while trying to quit, (b) latency to first cigarette of the day, (c) nicotine dependence, and (d) heaviness of smoking index after accounting for covariates.
Conclusions: The present findings underscore the importance of addressing smoking-specific experiential avoidance among smokers seeking smoking cessation treatment who report elevated perceived stress.
Financial Support: R01-MH076629-01A1

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COCAINE-CUE EXTINCTION LEARNING IN RATS: IMPACT OF COCAINE TRAINING DOSE AND MODULATION BY ENVIRONMENTAL ENRICHMENT.

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Aims: Environmental enrichment (EE) improves learning and memory across species. In this study, we determined the effects of brief periods of EE on extinction (EXT) learning in rats trained to self-administer different cocaine doses.
Methods: Rats were trained to self-administer either a moderate (0.3 mg/kg) or high (1.0 mg/kg) unit dose of cocaine under an FI2-min(FR5:S) second-order schedule. After ~ 45 sessions (1hr each), rats underwent weekly (3 for the moderate dose; 6 for the high dose) EXT sessions (cocaine unavailable, but cues contingently presented for 1hr) until reaching criterion (≤40% of baseline responses). To test for modulation of EXT learning by EE, rats (n=13 moderate dose; n=9 high dose) were exposed to EE for two 4hr blocks occurring 24hr before and immediately after each weekly EXT session. During EE, rats (3-4) were placed together in an arena that allowed for social interaction, cognitive stimulation and physical exercise. Controls (n=15 moderate dose; n=10 high dose) received EXT without EE. To test for extinction memory retention, reacquisition of cocaine self-administration was evaluated for 15 daily sessions.
Results: NoEE controls receiving the high vs. moderate training dose required more weekly sessions to reach the EXT criterion (5.3±0.4 vs. 1.9±0.3; $p<0.001$). After high dose training, EE reduced both number of sessions to the EXT criterion ($p<0.005$) and responses during EXT sessions 3 and 6 ($p<0.04$). After moderate dose training, EE reduced the number of responses during EXT session 3 ($p<0.01$). During reacquisition testing, EE/EXT deterred relapse to cocaine self-administration to a greater extent in rats trained with a moderate vs. high training dose.
Conclusions: EE facilitated EXT learning in both moderate- and high-dose trained rats. The smaller influence of the EE/EXT combination on relapse behavior after high dose cocaine self-administration training suggests a need to incorporate additional cognitive-enhancing strategies during EXT training to prevent cocaine relapse long-term.
Financial Support: DA024315

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6-MONTH FOLLOW-UP OF BACLOFEN TREATMENT IN PATIENTS WITH ALCOHOL USE DISORDER AND OTHER PSYCHIATRIC COMORBIDITIES.

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Aims: The efficacy of baclofen is still controversial in the literature and little is known on the impact of long-term baclofen treatment in naturalistic settings. The aim of this study was to evaluate the 6-month follow-up efficacy of baclofen treatment in alcohol use disorder patients in naturalistic settings.
Methods: In an open-label study, consecutive alcohol use disorder patients who have initiated a baclofen treatment in an outpatient addiction clinic in Bordeaux (France) were assessed at treatment initiation and at least once a month. Alcohol use, craving, side effects, treatment retention, over the first 6 months of treatment were analyzed.
Results: 89 patients were enrolled, 72% males, 42.6 y.o. (SD= 9.3), 89% exhibited another addictive comorbidity, 72% a mood disorder, and 65% an anxiety disorder. They reported 16.0 days (SD=11.0) of alcohol use past 30 days in average, 18.5 Alcohol Units (SD=14.6) per drinking day, and 23.9 days (SD= 9.9) of craving past 30 days in average. The mean baclofen dose was 132mg/day (SD= 78, range: 20-300). At 6 months, 22% had stopped baclofen because of side effects (72%), inefficacy (21%), or lack of treatment compliance (7%). At 6 months, 84% reported a significant decrease of craving, 40% reported a decrease of alcohol use. Although 40% did not report any change in alcohol use, the number of drinks per drinking day decreased and the severity of alcohol use significantly decreased ($p=.02$). Side effects were mild but reported by 60% of the patients, mainly sedation (36%), dizziness (8%), headache (6%), GI (6%), sexual disorder (6%).
Conclusions: These findings showed some benefits of baclofen treatment in alcohol use disorder patients with comorbid addictive and psychiatric disorders. Further studies are needed to identify the factors associated with efficacy of baclofen treatment in this realistic patient population.
Financial Support: PHRC 2006, MILDT 2010

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A TRIBAL COMMUNITY-WIDE INTERVENTION FOR ADDICTION.

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Aims: There is a paucity of research in the area of community based addiction treatment interventions implemented within tribal communities. Recently, Train for Change™, a national training company, joined with a tribal community in North Dakota to implement a community based intervention to address growing concerns of substance use and the impact on loved ones among the tribes. A self-directed combined behavioral intervention based on the Community Reinforcement and Family Training (CRAFT), Community Reinforcement Approach (CRA), and motivational interviewing (MI), delivered in an Interactive Journal format, will promote community wide change.
Methods: The team includes experts on the behavior change modalities employed, community stakeholders, and researchers familiar with strategies for adapting evidence-based treatments for an AI/AN population. Consistent with NIDA's mission to expand substance use interventions outside of specialty care settings, we developed two companion Interactive Journals intended for self-directed change by community members struggling with addiction or struggling with a loved one's addiction. Opportunities to intervene with people experiencing substance use problems will be enhanced by conducting several trainings in CRA, CRAFT and MI for both a clinical and lay audience. Finally, for identified "champions" of these behavior change approaches, ongoing coaching will be implemented to enhance and maintain skills. The collaborative approach will include efforts to incoporate community input throughout all stages of the process.
Conclusions: We describe our novel approach to implement a community-wide intervention designed to help family members and loved ones with substance use disorders in a North Dakota tribal community.This multi-pronged approach will increase accessibility of addiction services in the community to help decrease the disproportionate substance related health disparities among AI/ANs.
Financial Support: Train for Change

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NEURAL ACTIVATION TO SOCIAL INFLUENCE IN YOUNG ADULT CANNABIS USERS.

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Aims: To assess neural activation during a social influence task in young adults using marijuana and non-using controls in order to investigate how social influence may relate to substance use.
Methods: 16 marijuana-using young adults (MJ) and 16 controls (CON) completed a social decision-making task during functional magnetic resonance imaging scans. In this task, participants were presented with two lines and asked to judge which line was longer. They were then shown photographs of two ficticious 'peers', along with either fictitious responses from those peers, or a control condition during which peer responses were not revealed. Participants could either choose to follow or go against peer responses. Participants also completed a series of questionnaires including the Multidimensional Iowa Suggestibility Scale, a self-report scale of susceptibility to influence.
Results: MJ compared to CON demonstrated significantly greater bilateral activation in the putamen and the caudate, regions implicated in reward, during conditions in which social information was revealed (influence conditions). MJ scored greater than CON on the peer conformity subscale of the MISS ($p = .098$). Neural activation in the caudate and putamen in the influence compared to the no influence condition (i.e. when they were shown responses compared to no responses) positively correlated with peer conformity scores across groups (all $p < 0.05$).
Conclusions: This study suggests that receiving information from peers may be intrinsically rewarding to the MJ group, which may be a risk factor in the development of addiction. MJ but not CON showed activation bilaterally in the caudate, a structure involved in reward processing, suggesting that perhaps the MJ group found the social influence itself rewarding. Additionally, higher levels of peer conformity were associated with greater activation in the caudate as well as the putamen, suggesting that activation to social information may be a marker of susceptibility to influence.
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N-ACETYLCYSTEINE INHIBITS NICOTINE RELAPSE-ASSOCIATED SYNAPTIC PLASTICITY AND RESTORES GLIAL GLUTAMATE TRANSPORT IN NICOTINE-WITHDRAWN ANIMALS.

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Aims: Cigarette smoking is a leading cause of preventable death, and addiction to nicotine produces long-lasting, stable changes in brain synaptic physiology that might contribute to the vulnerability to relapse. Existing smoking cessation treatments are insufficient as relapse rates remain high. Thus, we examined the ability of N-Acetylcysteine (NAC), an antioxidant, to inhibit relapse, restore glial glutamate uptake, and inhibit relapse-associated synaptic plasticity in the nucleus accumbens core.
Methods: We examined the ability of NAC to reduce reinstatement of cue-induced nicotine seeking in a preclinical model nicotine relapse. NAC (30 mg/kg, i.p.) was given chronically for 5 days during withdrawal with extinction training from nicotine self-administration (0.02 mg/kg/infusion for 10 days). Following the last injection, animals were either sacrificed for sodium dependent (via the glial glutamate transporter, GLT-1) or independent (via the cystine-glutamate exchanger) glutamate uptake, or animals were given a 15 minute cue-induced reinstatement session and sacrificed for dendritic spine or electrophysiological analysis.
Results: NAC given chronically during withdrawal with extinction training from nicotine self-administration inhibited both cue-induced nicotine seeking and relapse-associated rapid, transient synaptic plasticity in the nucleus accumbens core measured via dendritic spine head diameter and AMPA/NMDA ratios in medium spiny neurons. In addition, we found reduced sodium-dependent glial glutamate uptake (via GLT-1) following withdrawal from nicotine self-administration, and NAC restored nucleus accumbens core glutamate uptake in nicotine-withdrawn rats compared to drug-naive controls.
Conclusions: These results show that NAC may be an important pharmacotherapeutic avenue in restoring glutamate homeostasis and in reducing nicotine relapse vulnerability.
Financial Support: NIH grants K99 DA036569 (CDG) and DA015369 (PWK)

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MINDFULNESS BASED RELAPSE PREVENTION IMPROVES STIMULANT USE AMONG ADULTS WITH MAJOR DEPRESSION AND GENERALIZED ANXIETY DISORDER.

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Aims: In a pilot randomized clinical trial, we evaluated the effects of an 8-week Mindfulness Based Relapse Prevention (MBRP) intervention, relative to a health education control condition among stimulant dependent adults receiving contingency management.
Methods: Stimulant dependent adults received a 12-week contingency management (CM) intervention; weeks 1 through 4 were a CM-only lead in phase. At week 5, participants were randomly assigned to one of two interventions: MBRP (n=31) or health education (n=32). The primary outcomes were stimulant use, measured by urine drug screens weekly and at 1 month post-treatment, and psychiatric severity, measured by the Addiction Severity Index and the Beck Depression Inventory at the same intervals.
Results: Medium effect sizes favoring MBRP were observed for negative affect and psychiatric severity. Depressive symptom severity changed differentially over time as a function of intervention condition, with MBRP participants reporting greater reductions through 1 month post-treatment (p=0.03; Effect Size=0.58). Likewise, the MBRP group evidenced greater declines in psychiatric severity (p=0.01; Effect Size=0.61 at post-treatment). Among those with Major Depression and Generalized Anxiety Disorder, stimulant use declined significantly in response to MBRP, relative to the control condition (stimulant-positive urines over time among those with depression and anxiety were less likely among those who received MBRP; Odds Ratio= 0.78, p=0.03 and OR=0.68, p=0.04).
Conclusions: MBRP has utility as an adjunct to behavioral interventions targeting stimulant use. This approach is particularly effective in reducing stimulant use among those with concomitant major depression and generalized anxiety disorder.
Financial Support: This reserach was supported by NIDA grants 1R21DA029255 and 1K23DA020085 awarded to S. Glasner-Edwards.

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FACTORS CONTRIBUTING TO TOBACCO USE AND CESSATION IN HISPANIC ADOLESCENTS.

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Aims: 12.5% of Hispanics in the United States smoke cigarettes. Hispanic adolescents participate fewer in tobacco cessation programs compared to other racial/ethnic groups. The difficulties engaging this minority group may be rooted in the different cultural components of this population such as nuances in language, historical contextual values related to tobacco use and tobacco products, degree and significance of parental involvement. There is a critical need to develop better interventions to reduce tobacco use among minority adolescents.
Methods: Eight focus groups will be conducted with a sample of 13-18 year old Hispanic and Non- Hispanic smokers attending one public high school in New Haven, CT (N=38-40). A standard focus group guide is being used to ask participants about their opinions about smoking use and smoking cessation. Group discussions are being recorded, transcribed, and examined using thematic analysis.
Results: Descriptive data obtained so far from 2 focus groups indicates that factors that are unique to Hispanic smokers may include stress over lack of resources and difficult family relations as possible predictors of tobacco use; while the use of self-called "Latino" cigarettes and jobs or other responsibilities makes it harder for Hispanic teens to participate in quit programs.
Conclusions: Targeting tobacco control efforts in the growing Hispanic population in the US is an important public health goal. Little is known about the most effective strategies to recruit Hispanic and Latino adolescents into smoking cessation programs. Understanding cultural factors affecting tobacco initiation and cessation among Hispanic adolescents will assist in efforts to build new, more effective tobacco cessation programs.
Financial Support: Supported by R25DA033221; P50DA009241; P50DA036151.

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RECOVERY 6 AND 9 MONTH RECOVERY TRAJECTORIES AMONG YOUTH WHO PARTICIPATED IN AN AFTERCARE PILOT STUDY.

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Aims: Substance use relapse among youth in recovery was examined after participation in a pilot aftercare study called Project ESQYIR (*Educating and Supporting inQuisitive Youth In Recovery*) that investigated the utility of a mobile texting intervention compared to a standard aftercare as usual control group. We hypothesized that youth exposed to mobile texting would have improved substance use, abstinence readiness, and aftercare adherence behaviors than those in the control.
Methods: Follow-up interviews were conducted at 6 and 9 months post-discharge from the pilot aftercare study with 80 youth, aged 14 to 26. Primary substance use relapse during the follow-ups by study conditions was analyzed. Secondary outcomes assessed at follow-up included recovery readiness and aftercare adherence measured by participation in 12-step and extracurricular recovery-related activities.
Results: Mobile texting participants were less likely to relapse to their primary drug at 6 and 9 month follow-ups ($p < .01$) compared to participants in standard aftercare as-usual. Youth with higher readiness to abstain were also less likely to relapse over the follow-up period ($p < .01$). Increased aftercare adherence behaviors we also observed mobile texting participants compared to aftercare as-usual at follow-ups. We found that mobile texting participants reported higher rates of 12-step participation than the control group at follow ups ($p < .05$) as well as reported engaging in more recovery related behaviors compared to the control group over the follow-up period ($p < .001$).
Conclusions: Findings highlight the utility of using novel aftercare methods, like texting to engage youth in recovery post-treatment. This study may serve to help clinicians improve their programs and services by incorporating mobile based solutions for recovery so that they can effectively treat young people with substance abuse issues.
Financial Support: This study is supported by K01 DA027754 from the National Institute on Drug Abuse (NIDA).

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CURBING THE RAISING HEROIN EPIDEMIC IN COLOMBIA: METHADONE-ASSISTED TREATMENT PROGRAMS.

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Aims: The aim is to assess the methadone protocols used in these new ambulatory programs, characterize the programs and participants, and document the barriers to access and remain in treatment.
Methods: 13 programs from priority regions were sent a questionnaire to collect information about the different programs, current participants, degree of development and implementation of standard methadone protocols, and potential barriers to access treatment. The aggregated summary of the programs are presented.
Results: 12 questionnaires were returned and included in the descriptive analysis. 538 patients were enrolled in methadone-assisted treatment programs. Most of these patients were male (85.5%) between the ages of 18 to 34 years (70%), and unemployed (47.7%). Among the patients enrolled in treatment, 40% were IVDUs, 25% admitted to sharing needles, and 21.8% had had an opioid overdose. Associated co-morbidities included mental illness (48%), hepatitis C (8.7%) and HIV (2%). Programs started methadone at 25.3 mg/day (SD = 8.9 mg/day), with maintenance doses between 41 to 80mg/day. Barriers to access include lack of alignment with primary care, problems with insurance coverage, and prejudice of methadone treatment by the community and the health providers. The lack of continuous availability of methadone in Colombia is identified as a modifiable cause of treatment interruption.
Conclusions: Most of the methadone assisted treatment programs in Colombia are developing standard protocols and implementing treatment programs that are addressing the epidemic of heroin use. There are some programs in early development stages that could benefit from additional consultation. Several barriers to access need to be addressed, including the responsible Colombian authorities guaranteeing the continuous availability of methadone for the treatment of opioid dependence in Colombia.
Financial Support: Supported by UNODC - Colombia Office

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MENTAL HEALTH AMONG SMOKERS IN THE U.S. FROM 2008 TO 2013: DIVERGING TRENDS BY SOCIOECONOMIC STATUS.

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Aims: To investigate the prevalence of depression and psychological distress among daily smokers in the US population from 2008 to 2013 annually and to examine whether trends in the prevalence of depression/psychological distress among smokers and non-smokers differ by socioeconomic status.
Methods: Data were drawn from the National Survey on Drug Use and Health (NSDUH), which includes cross-sectional data on cigarette smoking, depression and psychological distress among a nationally representative sample of adults in the US annually from 2008-2013.
Results: From 2008-2013, the prevalence of depression in the last year among smokers with family incomes of $75, 000 or more per year did not change significantly (from 6.5% to 7.1% (p=0.70)) nor did the prevalence of psychological distress (from 6.1% to 6.3%, p=0.90). Among smokers with family incomes below $20,000 per year, the prevalence of depression did not change (14.2% to 15.0%, p=0.64) while psychological distress increased (14.5% to 18.6%, p=0.06).
Conclusions: There appears to be a trend toward increasing psychological distress among smokers of lower socioeconomic status from 2008-2013. Our results demonstrate the importance of taking a more fine-grained approach to understanding the role of socioeconomic status in trends in mental health and smoking over time. Greater attention should be devoted to understanding the role of various mental health problems in the stagnation in smoking decline in the general population and particularly among low SES groups, and future research should focus on understanding the potentially differing role of mental health problems in smoking persistence among various SES groups in the population.
Financial Support: Work was supported by grant #DA20892-A1 from NIDA (Dr. Goodwin).

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AVERSIVE EFFECTS OF DRUGS: A COMPARISON OF CONDITIONED TASTE AND PLACE AVOIDANCE.

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Aims: The conditioned taste avoidance (CTA) and conditioned place avoidance (CPA) designs are both purported to index a drug's aversive effects, but it is unknown if they are comparable in this ability. From studies that have compared CTA and CPA designs, CTA appears to be a more sensitive index; however, these studies have procedural or measurement confounds that limit their conclusions. The present studies directly compared CTA and CPA procedures, minimizing previous confounds to establish the most sensitive index of a drug's aversive effects.
Methods: 84 male Sprague-Dawley rats (*n*= 42 per experiment) served as subjects. In the CTA assessment, rats were given one of two novel tastes followed by LiCl (0, 0.18, 0.32, 0.56 or 1 mEq/kg). They were then given access to an alternate novel taste followed by vehicle. This was repeated four times, followed by a final two-bottle test. In the CPA assessment, rats were given LiCl at the same doses and placed on one side of an unbiased two-chambered apparatus. They were then given a vehicle injection and placed on the other side. This was repeated four times followed by free access to both sides in an assessment of relative preference. Percent drug-paired taste consumed and time in the drug-paired chamber were compared.
Results: LiCl induced robust, dose-dependent taste avoidance with rats receiving 0.32 mEq/kg or greater consuming less of the drug-paired flavor than controls**.** LiCl did not induce place avoidance at any dose.
Conclusions: Given that drug use and abuse are thought to be a function of the balance of a drug's aversive and rewarding effects, using baselines that index such effects is important in predicting abuse liability. The present results suggest that the CTA design may be a more sensitive index of the aversive effects of drugs, suggesting that assessment of such effects should be evaluated in this baseline.
Financial Support: Supported by grants from the Mellon Foundation to ALR and JGL.

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COMBINED ENHANCEMENT OF ACETYLCHOLINE AND MONOAMINES CAUSES PERSISTENT REDUCTIONS IN COCAINE REWARD.

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Aims: Following pretreatment with certain cholinesterase inhibitors, some individual rats develop long-lasting reductions in cocaine-reinforced behavior, which can persist for weeks following treatment. In contrast, the cholinesterase inhibitor rivastigmine does not cause persistent effects on cocaine reward. To test the role of monoamines, this study combined rivastigmine with the nonselective monoamine oxidase inhibitor selegiline or the norepinephrine-dopamine reuptake inhibitor bupropion.
Methods: Rats were trained to self-administer intravenous cocaine under FR-5 (reinforcement after 5 lever-presses), at low, intermediate, or high doses (0.1, 0.2, or 0.4 mg/kg-injection). After a stable pattern of responding was established, they were then pretreated with test compounds delivered intravenously as a constant infusion for 21 hours preceding four consecutive self-administration sessions. Test compounds included 1.) Vehicle, 2.) Rivastigmine alone [10 mg/kg-day], 3.) Rivastigmine [10 mg/kg-day] and Bupropion [3.2 mg/kg-day], or 4.) Rivastigmine [10 mg/kg-day] and Bupropion [3.2 mg/kg-day].
Results: Cocaine self-administration was attenuated immediately after administration or rivastigmine with or without other agents. As previously reported, cocaine-reinforced responding returned to pretreatment levels with one day of pretreatment with rivastigmine alone. In contrast, combining rivastigmine with either bupropion or selegiline caused reductions in drug reinforced responding at later time points. For example, responding for intermediate-dose cocaine was attenuated 1 to 3 days after discontinuation of combined rivastigmine-bupropion pretreatment.
Conclusions: Persistent effects of cholinesterase inhibition on cocaine reward are most pronounced after pretreatment with tacrine, which inhibits monoamine oxidase A and B, as well as reuptake of dopamine, norepinephrine, and serotonin. Increased monoamines may contribute to therapeutic actions in Alzheimer disease. Findings by this study also implicate monoamines as a cause of persistent reductions in cocaine reward.
Financial Support: Supported by grants to KG from NIH and the Department of Veterans Affairs.

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PRAMIPEXOLE ALTERS GSK-3β SIGNALING AND AMPA RECEPTOR TRAFFICKING IN LIMBIC BRAIN STRUCTURES.

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Aims: Behavioral addictions are a side effect associated with pramipexole (PPX), a direct acting dopamine agonist used to treat Parkinson's disease and restless legs syndrome. The mesocorticolimbic system is involved in addictions, but the mechanisms that facilitate this development are poorly understood. The D3 receptor (D3R) is a key component in the addiction process, and PPX shows high affinity for this subtype. One D3R-mediated signaling cascade involves Akt/GSK-3β. Activation of D3R dephosphorylates Akt, blocking phosphorylation of GSK-3β and promotes strengthening of glutamatergic synapses *via* insertion of AMPA receptors (AMPAR) in cytosolic membranes; a phenomenon associated with addiction. We hypothesize that PPX administration will alter pGSK-3β and AMPAR trafficking in brain regions involved in addiction.
Methods: Rats were treated with saline or PPX one hr prior to tissue harvest. The nucleus accumbens (NAc), medial prefrontal cortex (mPFC) and ventral pallidum (VP) were dissected. A Western blot protocol was used to determine proteins that may link D3Rs to AMPAR trafficking (GSK-3β) and the surface/intracellular ratio (S/I) of the AMPAR subunits (GluA1, GluA2).
Results: PPX reduced the ratio of pGSK-3β (inactive)/GSK-3β (total) in the NAc and VP. Pretreatment with D3R-preferring antagonist PG01037 attenuated the PPX effects. This ratio did not change in the mPFC. The S/I ratio for GluA1 and GluA2 was increased in the NAc. Assessments of GluA1 and GluA2 S/I in the VP and mPFC are ongoing.
Conclusions: These studies indicate that PPX-mediated activation of D3R alters signaling through GSK-3β in the NAc and VP. At least in the NAc, PPX increased AMPAR trafficking to the cell surface, which can strengthen synapses. These maladaptive processes may link PPX with behavioral addictions.
Financial Support: USPHSG #NS087559; #DA033121.

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AN ONLINE NATIONAL SURVEY AND THE CRIME SURVEY FOR ENGLAND AND WALES: ARE THE DATA COMPARABLE?

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Aims: To compare data on the prevalence of illicit drug use collected in an online national survey of non-medical use of prescription medicine and the Crime Survey for England and Wales (CSEW).
Methods: The online national survey was undertaken in July 2014 using a market research company. Data included in this study were demographics and the prevalence of illicit drug use in those aged 16-59 years residing in England or Wales (n=1,594). CSEW is an annual household survey in England and Wales; the 2013/14 CSEW included 34,906 respondents aged 16-59 years. Lifetime and last year prevalence of illicit drug use was compared between the whole groups and in young adults (16-24 years).
Results: Prevalence of use of illicit drugs in the online national survey and CSEW were similar for the whole groups (lifetime use: online survey 32.6%, CSEW 35.6%. Last year use: online survey 8.6%, CSEW 8.8%) and young adults (lifetime use: online survey 31.4%, CSEW 36.3%. Last year use: online survey 15.0%, CSEW 18.9%). For lifetime use, cannabis was the most common drug in each data source (23.7% and 29.9%), amphetamines was the second (9.7% and 11.1%) and any cocaine was the third (8.2% and 9.5%).
Conclusions: The prevalence of use of illicit drugs was similar in the online national survey and the CSEW. The comparability of these findings demonstrates the feasibility of using an online survey administered with a market research company to obtain data comparable to the well-established household CSEW with a considerably smaller sample. This methodology could be used to further explore aspects of illicit drug use and non-medical use of prescription medicines.
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POLYSUBSTANCE COMBINATIONS INVOLVING PRESCRIPTION OPIOIDS AND RATIONALES FOR COMBINING AMONG PEOPLE WHO USE INTERNET DRUG DISCUSSION FORUMS.

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Aims: Prescription opioids alone or in combination with other substances are associated with a majority of unintentional drug overdose deaths. This study sought to explore prevalent combinations of prescription opioids with other drugs, and motivations for combining, according to opioid users frequenting an internet discussion forum.
Methods: Users of an online drug discussion forum were offered a survey in winter, 2013 about opioid use and motivations for combining medications. Chi square tests assessed differences by drug combination and gender.
Results: Among 695 respondents, 266 (38%) reported past year prescription opioid use, 154 of whom reported 252 combinations involving hydrocodone IR, oxycodone IR, oxycodone ER or oxymorphone ER plus additional substances. Immediate release opioids were more frequently combined than extended release opioids (81.3% vs 18.7%); benzodiazepines were the most commonly combined (50.4% of combinations). Females reported muscle relaxer-opioid combinations at higher rates than males (42.2% vs 26.2%) and males reported more cocaine-opioid combinations than females (20.6% vs. 2.2%). There were no gender differences for other combinations. Common combination rationales included attaining a desirable sensation (n=143) and boosting effects (n=112). A substantial minority took combinations as prescribed (n=52), reported inadequate pain relief from prescribed medications (n=46) or to self-treat mental (n=53) or physical (n=42) conditions.
Conclusions: A substantial proportion of respondents combine prescription opioids with other substances for medical and non-medical reasons. Interventions to reduce opioid overdose risk, including take-home naloxone, should ensure equal coverage of men and women. Prevalence of combining substances to self-treat health conditions indicates that efforts to engage substance users in health care may be an important initiative in advancing opioid safety.
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BEHAVIORAL ECONOMIC ANALYSIS OF MARIJUANA CONSUMPTION, DIVERSION, AND MEDICAL CERTIFICATION DEMAND IN HIV+ PATIENTS.

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Aims: Evaluate whether MJ consumption, diversion or medical certification demand relates to past 3-month drug use, psychiatric or medical factors in HIV+ patients.
Methods: MJ-using HIV+ patients (n=98, ongoing) complete an economic simulation to measure demand intensity (*L*) and elasticity (*a*) for MJ (# 0.1-oz units purchased/consumed on average day, income=$120) vs. MJ unit price (UP $2.50–20) and time to purchase one 0.1-oz (3–120 min). Survival analysis is used to measure MJ diversion (% willing to sell 0.1-oz MJ) vs. profit ($5-90), and demand for medical certification (% participation) vs. yearly certification cost ($10–150), # physicians visited to get certified (1–15), and delay until getting card (0.5–26 wk). All results reported are significant ($p<.05$).
Results: MJ demand intensity is higher for patients whose past 3-month MJ use is frequent (>270 times) vs. moderate (90-270) or infrequent (≤90), *L*= .62, .33, .32 oz/day). MJ demand intensity is higher for patients <41 than 42-49 and ≥50 yr (*L*= .55, .36, .29 oz/day). Certified patients have the lowest MJ demand intensity. Patients with slight or moderate pain severity have higher MJ demand intensity than patients with no pain or severe pain. Certification demand is higher for patients with severe pain (UP=card cost, delay until certification), opioid use (UP=card cost, #physicians), and frequent MJ use (UP=#physicians). MJ diversion is most likely among patients who report cocaine use. Psychiatric and other medical factors are not related to MJ use, certification, or diversion.
Conclusions: MJ use is price-elastic and modulated by MJ-use frequency, age and pain. Certified patients exhibit lower demand. Patients with severe pain, opioid use and frequent MJ use exhibit higher certification demand. MJ diversion potential is related to cocaine use. This knowledge may inform clinical and policy decisions.
Financial Support: NIH R01DA032678, Joe Young Sr./Helene Lycaki Funds (State of Michigan), Detroit Wayne Mental Health Authority.

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EFFECTS OF THE GLT-1 ACTIVATOR CEFTRIAXONE ON THE REWARDING AND LOCOMOTOR ACTIVATING EFFECTS OF 'BATH SALT' COMPOUND 3,4-METHYLENEDIOXYPYROVALERONE IN RATS.

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Aims: Synthetic cathinones are a group of amphetamine-like drugs that are gaining popularity worldwide. 3,4-methylenedioxypyrovalerone (MDPV) is the most commonly abused synthetic cathinone in the USA and remains popular. To date, all preclinical studies focusing on MDPV have focused on monoamines. The glutamate system has been extensively studied with the drugs of abuse and is an important mediator for controlling behavioral sensitization and relapse to drug seeking behavior. Ceftriaxone (CTX), a beta-lactam antibiotic, is an activator at the glutamate transporter subtype 1 (GLT-1), and attenuates the rewarding and locomotor activating properties of cocaine. We provide the first investigation of CTX effects on development of MDPV behavioral sensitization and reward.
Methods: MDPV or saline was administered to rats in a 7-day variable-dose paradigm (0.5 mg/kg IP on Day 1, followed by 1.0 mg/kg IP for 5 days, and 0.5 mg/kg IP on Day 7). Animals in the CTX group received CTX (200 mg/kg IP) for four days prior to MDPV treatment, and received CTX 30 minutes prior to each MDPV injection. Following 10 days of MDPV abstinence, a challenge dose (0.5 mg/kg IP) was administered and locomotor activity was recorded. MDPV's rewarding effects were evaluated using a 4-day conditioned place preference model.
Results: Sensitization of stereotypy was observed with repeated administration of MDPV compared to a single MDPV dose, and this sensitization was significantly attenuated in rats pretreated with CTX.MDPV (2.0 mg/kg IP) produced significant place preference compared to saline, and this effect was attenuated with pretreatment with CTX.
Conclusions: Taken together, these results indicate that glutamate levels mediated by GLT-1 plays a role in the locomotor activating and rewarding effects of MDPV, similar with what is observed with cocaine. This hypothesis warrants further study.
Financial Support: This research was supported by **DA013429 and DA032718**

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HOW DO GENDER AND RACE/ETHNICITY INFLUENCE PERCEIVED BARRIERS TO HELP-SEEKING FOR SUBSTANCE USE PROBLEMS?

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Aims: The goal of this study was to examine differences by gender and race/ethnicity in perceived barriers to seeking help for substance use problems.
Methods: Data are from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a general population survey conducted in 2001–02. The study sample includes African Americans, Latinos, and whites who had not sought help for problems related to their use of alcohol (N=1,012) or drugs (N=532). Reasons were categorized as: (a) financial, (b) stigma, (c) fear of treatment, (d) pessimism, (e) minimizing problem, (f) structural barriers, (g) natural recovery, and (h) continue to use. Logistic regression models for each reason were fit separately for alcohol and drugs and included covariates for background characteristics.
Results: The most frequently cited reasons for not seeking help for alcohol or drug problems referred to problem minimization (66%). Alcohol: males were less likely than females to cite financial, stigma, fear, and natural recovery, but more likely to refer to structural barriers (AOR=1.56). Compared with whites, African Americans were less likely to endorse financial, stigma, and fear; more likely to cite pessimism and natural recovery; and twice as likely to cite structural barriers. Latinos had lower odds of citing financial reasons, natural recovery, and continued use than whites, but were 30% more likely to cite pessimism. Drugs: males had lower odds of endorsing financial, fear, and natural recovery as reasons, but had higher odds of minimizing problems and structural barriers. African Americans were less likely than whites to cite financial problems and natural recovery, but more likely to minimize problems (AOR=1.72). Latinos were less likely than whites to cite financial, stigma, fear, natural recovery, and continued use, but were more likely to cite pessimism and structural barriers. [all: $p < .05$]
Conclusions: Strategies are needed to encourage help seeking that address health disparities by gender and race/ethnicity.
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REVERSAL LEARNING IS PREDICTIVE OF AND AFFECTED BY COCAINE SELF-ADMINISTRATION: DISSECTING DECISION-MAKING PROCESSES WITH COMPUTATIONAL MODELS.

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Aims: The compulsive drug-seeking and –taking, that is characteristic of addiction, may be a behavioral manifestation due to drug-induced disruptions in the brain circuits that allow behavior to remain flexible and goal directed. Substance-dependent individuals and animals chronically exposed to drugs are impaired in laboratory-based measures of adaptive decision-making, suggesting that chronic exposure to drugs of abuse may, in part, cause these behavioral impairments. However, recent evidence has suggested that pre-existing differences in decision-making processes may influence addiction liability.
Methods: To directly investigate this possibility, we used a novel three-choice probabilistic discrimination and reversal task (PDRL) to measure decision-making before and after rats (N=24) were trained to self-administer cocaine for 14 days.
Results: Performance in the reversal, but not the discrimination, phase of the PDRL predicted cocaine self-administration (R=-0.71; p=0.009) and was impaired following cocaine self-administration (p=0.002). Next, the choice behavior of rats in the PDRL was analyzed using a computational model to determine if different aspects of choice behavior were mediating the relationship between reversal performance and cocaine self-administration. We found that individual differences in the sensitivity of rats to positive, but not negative outcomes predicted cocaine self-administration (R=-0.78; p=0.003); in contrast, sensitivity to negative, but not positive outcomes was disrupted following cocaine self-administration (p=0.02).
Conclusions: These data indicate that dissociable aspects of adaptive decision-making processes are predictive of and affected by cocaine self-administration. Ongoing pharmacological experiments will identify the neurochemical processes underlying these behavioral processes to identify unique pharmacological targets for the prevention and treatment of addiction.
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U.S. ESTIMATES OF HOSPITALIZATION BY SUBSTANCE USE PROFILE.

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Aims: To characterize past-year hospitalization across substance use profiles in the US population.
Methods: Data from the 2009-2013 National Survey on Drug Use and Health (*N*= 281,411 individuals age 12 and older) was used to examine all-cause past-year hospitalizations by substance use profile [abstinent v. non-diagnostic use v. DSM-IV criteria for substance use disorder (SUD)]. Profiles were generated for alcohol, marijuana, and other substances (as a group, and specifically for heroin, opioid analgesics, cocaine, amphetamines, and sedatives/tranquilizers). 5-year annual average prevalence estimates were computed. Multivariate associations between hospitalization and substance use profiles were examined using logistic regression, adjusting for a range of potential confounds including demographics, economic characteristics, insurance, and health status.
Results: Unadjusted rates of past-year hospitalization for individuals with non-diagnostic use of alcohol, marijuana, and other substances were 8.9%, 8.0%, and 8.6%, respectively, while hospitalization rates for individuals with SUDs for these substances were 10.0%, 9.9%, and 19.6%, respectively. High prevalence of past-year hospitalization was found for individuals with SUDs for heroin (28.9%), sedatives/tranquilizers (26.6%), opioid analgesics (23.4%), cocaine (19.4%), and amphetamines (18.8%). In multivariate analyses, past-year hospitalization was weakly associated with alcohol use disorder (OR=1.15; p=.019), not associated with marijuana use disorder (OR=.93; p=.28), and strongly associated with SUD for other substances (OR=2.48; p<.001). Compared to abstainers, individuals with non-diagnostic marijuana use had slightly lower odds of hospitalization (OR=.88; p=.009), while non-diagnostic use of other substances was not significantly associated with hospitalization (ps>.05)
Conclusions: National estimates of all-cause hospitalizations for various substance use profiles were examined. Individuals with SUDs for substances other than alcohol and marijuana are especially likely to experience hospitalization.
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OPIOID USE TRAJECTORIES, INJECTION DRUG USE AND HCV RISK AMONG YOUNG ADULTS FROM THE FORMER SOVIET UNION IN NYC.

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Aims: Aim: To report findings of a mixed-methods study on opioid use and injection risk behavior among young immigrants from the former Soviet Union (FSU), a group among whom opioid use and IDU are thought to be common, but about whom there are limited data.
Methods: Methods: Structured interviews with 80 FSU immigrants (ages 18-29) who reported using opioids in the past month or being in treatment for opioid use assessed drug use trajectories, injection risk behavior, HCV testing and use of harm reduction services. A purposive sub-sample of 26 youth completed qualitative interviews probing similar topics.
Results: Results: Participants were 74% male (mean age=23.3 years); most immigrated to the U.S. during childhood from Ukraine (48%) or Russia (19%). Although 85% initiated opioid use with prescription opioids, most (64%) transitioned to heroin. Lifetime prevalence of IDU was 76%; 60% identified as current IDUs. Rates of injection risk behavior were high, with 1/3 of current IDUs reporting receptive syringe-sharing and 46% sharing secondary injection paraphernalia in the past year. Self-reported HCV+ status was 9%, but 24% had never been tested for HCV and only 40% of current IDUs reported using syringe exchange services in the past year. Qualitative data indicate that HCV knowledge was low, especially regarding risk associated with sharing secondary injection equipment, and that community stigma is a major barrier to the use of harm reduction services.
Conclusions: Conclusions: Although self-reported HCV rates are still fairly low among opioid-using FSU immigrant youth, given their high rates of IDU and injection risk, this group is vulnerable to transmission of HCV within injection networks. Harm reduction programs should make concerted efforts to reach young FSU immigrants, provide them with sterile injection equipment and educate them about the HCV risks associated with IDU.
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USE OF ELECTRONIC CIGARETTES AMONG SMOKERS IN ADDICTION TREATMENT.

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Aims: High rates of cigarette smoking and dependence have been reported in addiction treatment populations. As the prevalence of electronic cigarettes (E-cigs) continues to grow it is important to understand how and for what reasons a potentially vulnerable population is using these products.
Methods: A random sample of 737 clients from 16 addiction treatment centers in the NIDA Clinical Trials Network were surveyed. Cigarette and E-cig use, quitting history, readiness to quit, and reasons for using E-cigarettes were assessed. E-cig users (any E-cig use during the past month, n=225) were compared to combustible cigarette only smokers (n=387).
Results: 33.3% of all smokers had used an E-cig in the last 30 days with 85.7% of E-cig users reporting dual E-cig + combustible cigarette use over the past month. Overall E-cig users versus combustible cigarette users were younger (34.6±10.1 vs. 40.7±11.7), more likely to be female (56.1% vs. 47.7%), white (70.5% vs. 56.1%), and more educated (46.7% vs. 36.5% > HS). E-cig and cigarette only users did not differ in the percent seriously thinking of quitting smoking in the next 6 months (69.9% vs. 64.0%). However, 50.0% of E-cig users reported using E-cigs as a tool to reduce or quit cigarette smoking. Any E-cig use in the past 30 days was not associated with decreased cigarette smoking (cigarettes/ day, smoking days/ week), or dependence (time to first cigarette) compared to cigarette only smokers. However, a greater number of E-cig users versus cigarette only users reported voluntarily quitting smoking for at least 24 hr in the past year (56.0% vs. 42%, X^2=10.3, p<0.01); though there was no difference in number of quit attempts during the past year (5.3±7.5 vs. 5.8±8.1).
Conclusions: Dual use of combustible cigarettes and E-cigs was found to be very high in addiction treatment populations. E-cigs as a tool to quit or reduce cigarette smoking was a large reason for their use. More work is needed to evaluate the health implications of this dual use.
Financial Support: NIDA and FDA Center for Tobacco Products R01DA036066. Noah Gubner is a postdoctoral fellow supported through NCI Grant CA113710.

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NEGATIVE AFFECT MEDIATES RELATIONS BETWEEN ANXIETY SENSITIVITY AND SUBSTANCE USE PROBLEMS IN ADOLESCENTS.

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Aims: Anxiety sensitivity—fear of anxiety symptoms and their consequences—has been tied to substance use mostly in adults. Theoretically, anxiety sensitivity heightens negative affect, thereby increasing motivation to use substances for negative reinforcement, which is a risk pathway that may begin in adolescence. To the best of our knowledge, however, no prior study has tested the hypothesis that negative affect statistically mediates relations between anxiety sensitivity and substance use problems in adolescents.
Methods: In a cross-sectional design, we administered self-report measures of anxiety sensitivity, negative affect, tobacco dependence, and alcohol and other drug problems to 9th graders from 10 different schools in the Los Angeles area (N = 3126). Mixed regression models accounting for clustering by school examined mediational pathways predicting likelihood of endorsement of any substance use problem (vs. no problem) after adjusting for ethnicity, gender, and parental education.
Results: Anxiety sensitivity was associated with greater likelihood of endorsing tobacco dependence (b = .050, p < .001), alcohol problems (b = .020, p < .001), and other drug problems (b = .022, p = .002). Negative affect fully mediated anxiety sensitivity relations with tobacco dependence (b [95% CI] = .037 [.027 - .046]), alcohol problems (b [95% CI] = .016 [.012 - .021]), and other drug problems (b [95% CI] = .021 [.015 - .026]).
Conclusions: Although limited by a cross-sectional design, current findings suggest that adolescents high in anxiety sensitivity tend to experience negative affect, which in turn is related to substance use problems. Treatments that target anxiety sensitivity or negative affect may be helpful in preventing and reducing adolescent substance use problems.
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AMPHETAMINE EXPOSURE DURING ADOLESCENCE ALTERS BEHAVIOR, DOPAMINE RECEPTORS AND MEDIAL PREFRONTAL CORTEX FUNCTION IN ADULTHOOD.

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Aims: Amphetamine (AMPH) use typically begins in adolescence, with abuse during this time associated with cognitive dysfunction and a high lifetime rate of drug dependence. The mechanisms of adolescent vulnerability are not clear, but drug-induced changes in the normal development of mesocorticolimbic circuitry may play a key role. Here, we investigated the effects of repeated AMPH exposure early in life on psychomotor behavior and dopamine function in the medial prefrontal cortex (mPFC).
Methods: Male Sprague-Dawley rats (n = 67) were given 10 injections of saline or AMPH (3 mg/kg, i.p.) once every other day from postnatal day (P) 27-45. Rats were later tested at young adulthood (P70-P80). In Exp. 1, behavior was assessed in an open-field arena following challenges with dopamine D_1 or D_2 receptor-selective agonists (1 mg/kg SKF 82958 or 0.5 mg/kg quinpirole). In Exp. 2, rats were challenged with 3 mg/kg AMPH and were subsequently given a challenge with a D_1 or D_2 antagonist (30 μg/kg SKF 83566 or 30 μg/kg eticlopride). A subset of rats from Exp. 2 were implanted with microwire electrodes to allow for recordings of mPFC neurons.
Results: Adolescent AMPH exposure induced sensitization to the motor stimulant effects of AMPH and the dopamine agonists. In mPFC neurons, basal firing rate was similar between controls and AMPH pre-exposed rats. Following AMPH challenge, most cells decreased their firing and the proportion of inhibited cells was greater in pre-exposed rats (61%) compared to controls (47%). In addition, the magnitude of AMPH-induced changes in firing rate was greater in pre-exposed rats. Dopamine antagonists tended to reverse AMPH-induced changes in behavior and mPFC activity in both groups, but to a somewhat greater degree in pre-exposed rats.
Conclusions: These findings suggest that exposure to AMPH during adolescence leads to long-lasting plasticity in the mesocorticolimbic dopamine system that likely mediates changes in the response to the drug during adulthood and also might underlie heightened vulnerability in adolescent drug users.
Financial Support: NIH (R01 DA029815)

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REINSTATEMENT OF DRUG-SEEKING BEHAVIOR IN RATS TRAINED TO SELF-ADMINISTER INTRAVENOUS INJECTIONS OF MIDAZOLAM.

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Aims: Benzodiazepines (BZs) are positive allosteric modulators of the $GABA_A$ receptor and are commonly prescribed anxiolytics and anticonvulsants; yet their use is associated with side effects such as abuse and dependence. In the preclinical literature, there are few reports of self-administration of BZs in rodents and only with unlimited access to drug. In addition, to our knowledge, there are no reports of BZ-induced reinstatement of drug seeking, a phenomenon thought to model aspects of the relapse process. We sought to establish i.v. self-administration and reinstatement of the short-acting BZ midazolam in rats.
Methods: Ten Sprague-Dawley male rats with chronic i.v. catheters were trained to self-administer 0.3 mg/kg/injection of midazolam under a 2-response, fixed ratio (FR2) schedule of i.v. drug injection during daily 3-h sessions. Following three days of stable responding on the active lever (<25% of mean, no upward/downward trends, ≥ 10 injections/day) rats underwent extinction training. Active lever presses during extinction sessions had no programmed consequences. Once responding on the active lever decreased to ≤50% of active lever pressing during self-administration sessions, rats received a non-contingent i.v. priming injection of midazolam (0.01-1 mg/kg/injection) or vehicle along with restoration of the drug-paired stimuli (i.e., reinstatement test).
Results: Acquisition of self-administration at FR2 occurred within 21 days in 9/10 rats. Extinction criteria were met after an average of 7.7 days (±2.4 SEM). Midazolam induced dose-dependent reinstatement of drug seeking in 7/9 rats, engendering active lever presses significantly higher than observed during extinction.
Conclusions: These results show that a BZ can function as a positive reinforcer in rats under limited access conditions, and that reinstatement of BZ taking is robust and dose dependent. Furthermore, these results establish a new platform for systematic study of relapse to BZ-taking in a preclinical rat model.
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THE IMPACT OF E-CIGARETTE ADVERTISEMENTS ON E-CIGARETTE INITIATION AMONG MIDDLE AND HIGH SCHOOL STUDENTS.

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Aims: Little is known about the impact that e-cigarette ads have on adolescents' initiation of e-cigarettes. The present study examines whether exposure to e-cigarette ads predicts initiation of e-cigarettes in middle and high school students.
Methods: A total of 1750 participants (52% female, M_{age} = 14.16, SD = 1.94) who did not report e-cigarette use at baseline were included in this analysis. Data were drawn from a larger study examining attitudes about various tobacco products among middle and high school students. Baseline surveys were conducted in fall 2013 and follow-up surveys were conducted in spring 2014.
The following variables were included in a logistic regression analysis: age, gender, cigarette smoking history, exposure to e-cigarette ads on Facebook, Twitter, YouTube, Pinterest, Google Plus, television/radio, billboards, magazines, stores, mall kiosks, and tobacco shops (e.g., *Where have you recently seen advertisements or the following tobacco products being sold? Response options included "yes" or "no"*) where each site/location was entered as a separate predictor. The criterion was e-cigarette use at follow-up.
Results: Among never e-cigarette users in the fall 2013 sample, 9.7% reported e-cigarette initiation at follow-up. Analyses revealed that older age (p < .001), history of cigarette smoking (p < .001), and recent exposure to ads on Facebook (p = .016), Pinterest (p = .039), and stores (p = .008) significantly predicted initiation of e-cigarettes at follow-up.
Conclusions: Findings suggest that regulation of e-cigarette ads on social media and at convenience stores may reduce e-cigarette initiation among youth.
Financial Support: Supported by the following grants: P50DA009241 and P50DA03615.

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A TOBACCO CESSATION READINESS GROUP INCREASES INITIATION OF QUITTING IN RESIDENTIAL TREATMENT PATIENTS.

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Aims: To test the feasibility and efficacy of a novel 3-session Readiness Group (RG) to encourage smokers in addiction treatment to initiate tobacco cessation.
Methods: The study was conducted in two women-focused residential programs. RGs were conducted in 12 cohorts (2-12 participants per cohort), which incorporated the Prochange Expert Systems intervention in combination with a 24- hour practice quit attempt. Each cohort was randomly assigned to receive or not receive small incentives ($5 gift cards) for completing tobacco self-assessment tasks. Pre- and post-RG surveys included measures of smoking behavior, tobacco related risk perception, and smoking related attitudes and services received. 80 women enrolled in the RGs and 66 (82%) completed the post-RG survey.
Results: The rate of initiating tobacco cessation services, defined as attending at least one smoking cessation group, was 39% overall. The rates for incentive and control participants were, respectively, 33% and 45% ($p = 0.30$). Demographic characteristics, smoking behavior, and smoking attitudes and services pre-RG did not predict initiation of smoking cessation. Perceived risk of lung cancer (66% v 55%: $p < .05$) and mean number of RG sessions attended (2.5 v. 1.9: $p = .01$) were higher among those who initiated use of cessation services than those who did not. For the 66 women who completed post-RG surveys, a significant decrease was observed in self-reported smoking status (99% v. 80%, $p < .01$), and CPD (10.9 v. 7.3, $p < .001$), but not for mean expired CO (18.0 v. 16.1 ppm, $p = 0.14$). Significant pre-post increases were observed in quit attempts, use of nicotine replacement therapy, and use of tobacco cessation services, which were components of the RG.
Conclusions: A brief 3-session tobacco cessation readiness group promoted quit attempts and smoking cessation service use.
Financial Support: This work was supported by University of California Tobacco Related Disease Research Program (21XT-0088).

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CORRELATES OF PRESCRIPTION OPIOID LEGITIMACY ESTIMATIONS AMONG COMMUNITY PHARMACISTS IN TENNESSEE.

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Aims: Community pharmacists have a corresponding responsibility to evaluate and verify prescription legitimacy prior to dispensing. Yet, our previous research indicates pharmacists dispense prescriptions perceived to be illegitimate. We examined practice- and pharmacist-specific correlates of prescription opioid (PO) legitimacy estimations among Tennessee community pharmacists.
Methods: A cross-sectional study of 2000 Tennessee pharmacists was conducted to elicit pharmacists' self-reported attitudes, beliefs, and behaviors specific to PO dispensing and legitimacy. Pharmacist (e.g., gender, years in practice, hours worked per week) and practice (e.g., prescription volume, setting, geographic region) characteristics were obtained. PO legitimacy estimations were defined in tertiles as "low" (0-29%), "moderate" (30-79%), and "high" (80-100%) legitimacy. Multinomial logistic regression techniques were used to investigate correlates of low and moderate perceived legitimacy against the reference of high perceived legitimacy.
Results: Being female, practicing in a chain or independent practice setting, fear of employer disciplinary action if PO legitimacy is questioned, and self-confidence in one's ability to detect PO abuse increased the odds of low (vs. high) PO legitimacy estimation. Employment in chain and independent pharmacies, having POs as a greater percent of total prescriptions filled, and having the perception of PO abuse as a problem in the practice setting were significant positive correlates of moderate (vs high) PO legitimacy estimation.
Conclusions: Both modifiable and non-modifiable correlates were statistically significantly associated with PO legitimacy perceptions. Distinct correlates were noted across low and moderate as compared to high estimations of PO legitimacy.
Financial Support: ETSU RDC Major Grant #13-005M (NH)

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THE ANGIOTENSIN RECEPTOR BLOCKER CANDESARTAN ATTENUATES THE SUBJECTIVE EFFECTS OF METHAMPHETAMINE IN HUMANS.

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Aims: To examine in a laboratory-based interaction study the impact of candesartan (16 mg/day) vs. placebo on the subjective effects of methamphetamine (METH).
Methods: Nineteen METH volunteers with METH use disorder (79% male; 80% Caucasian,10% African American, 10% mixed race) were randomized in a double blind manner to receive candesartan or placebo over 8 days. Participants then received two different intravenous (IV) doses of METH (15mg and 30mg) and saline on days 6 or 8 of treatment. Following IV METH and saline, cardiovascular measures were documented using ECG and subjective effects of METH were assessed using visual analog scales over numerous time points within the test session (-15, 5, 10, 15, 20, 30, 45, 60, 90, 120 min).
Results: Treatment groups did not differ on baseline demographic characteristics and drug use ($p's > 0.05$). As expected, IV METH (15mg and 30mg) increased cardiovascular measures and subjective ratings compared to saline ($p's < 0.05$). Candesartan treatment did not significantly alter METH-induced increases in cardiovascular measures ($p's > 0.05$). In contrast, candesartan significantly attenuated METH's subjective effect ratings for "Good Drug Effects" ($p=0.019$), "Like Drug" ($p=0.016$) and "Anxious" ($p=0.008$). Candesartan was well tolerated with no significant adverse events recorded.
Conclusions: These preliminary results suggest that candesartan is well tolerated and attenuated some of METH's subjective effects. Results warrant further research assessing candesartan as a potential pharmacotherapy for METH use disorder.
Financial Support: Supported by NIDA grant P50 18197 and by the Michael E. DeBakey VAMC

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PATIENT ATTITUDES TOWARD TECHNOLOGY-ASSISTED TREATMENT DURING HOSPITAL-BASED DUAL-DIAGNOSIS TREATMENT.

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Aims: Technology-assisted treatment (TAT) using devices with Internet access has the potential to provide innovative and cost-effective treatment of substance use disorders (SUD) and other psychiatric disorders (PD). Many TAT studies occur in outpatient settings. The purpose of this study is to describe patient attitudes toward TAT during inpatient treatment.
Methods: 100 participants on two hospital-based dual-diagnosis psychiatric units voluntarily completed a 34-item online survey. This report is a descriptive analysis of data collected on demographics, access to technology, attitudes toward TAT, and preferences for content.
Results: Participants were 60% male, 64% single, 56% African American, 24% employed, and over 80% were at least high school graduates. All had a SUD and another Axis I PD. 87% had no TAT exposure prior to hospitalization. 76% of those with previous TAT exposure found it moderately or very helpful. 65% of participants thought technology-assisted SUD counseling would be moderately or very helpful. The preferred TAT session length was 15-30 minutes (45%). The most interest was in TAT that addressed drug use (68%) and other psychiatric (72%) or family problems (48%). 60% of participants would prefer a combination of TAT and face-to-face services for substance use counseling, while 37% preferred face-to-face only.
Conclusions: These data suggest that despite most patients having no previous TAT exposure, patients would welcome TAT during hospitalization and consider it helpful. Some patients preferred face-to face counseling alone, suggesting that TAT should not completely replace face-to-face counseling. Further research is needed on implementation of TAT during hospitalization and its portability from the hospital to the post-discharge setting.
Financial Support: NIDA grant K24DA023186

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CONTRACEPTIVE USE AND RISKY SEXUAL BEHAVIOR VARIES WITH FREQUENCY OF COCAINE, CRACK COCAINE, OR METHAMPHETAMINE USE.

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Aims: Illicit drug-using women use contraceptives less often than non-drug using women and those who do use contraceptives tend to rely on condoms and less effective methods. It is unclear how contraceptive use, method choice, and risky sexual behavior vary within drug-using women. We examined this by comparing contraceptive use and sexual behavior among women reporting different frequencies of illicit drug use.
Methods: Data from the 2006-2010 National Survey of Family Growth were analyzed. Women aged 15-44 reported demographics, sexual activity, contraceptive use and method choice at last heterosexual intercourse, and frequency of cocaine, crack cocaine, and methamphetamine use in the past year. Analyses were restricted to women who were not currently pregnant, not trying to become pregnant, and heterosexually active in the past year.
Results: Of 8538 respondents who provided complete data, 187 reported low rates of cocaine, crack cocaine, or methamphetamine use (1-2x/year), 79 reported moderate rates of use (several times/year), and 43 reported high rates of use (≥1x/month). Nearly half (43%) of the high-frequency drug users reported not using any contraceptive at their last intercourse vs. 13-14% of lower-frequency and non-drug users. Among those who used contraceptives, 21% of high-frequency drug users reported using a prescription method vs. 31-40% of lower-frequency and non-drug users. High-frequency drug users also had sex twice as often with three times as many partners as lower-frequency and non-drug users. Nearly all drug-using women also reported smoking cigarettes and marijuana and binge drinking.
Conclusions: Women who use cocaine, crack cocaine, or methamphetamine more often appear to be at risk of drug-exposed pregnancies due to nonuse of effective contraceptives and frequent engagement in risky sexual behavior. Risk of polydrug exposure may also be elevated in this population given high rates of cigarette smoking and binge drinking. Increasing effective contraceptive use in this population could prevent many unintended, polydrug-exposed pregnancies.
Financial Support: R01DA036670 & T32DA007242

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BEYOND PHARMACOTHERAPY: EMERGING DATA THAT NON-INVASIVE BRAIN STIMULATION MAY BE AN EFFICACIOUS STRATEGY FOR DECREASING DRUG CRAVING IN SUBSTANCE-DEPENDENT INDIVIDUALS.

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Aims: Non-invasive brain stimulation as a potential treatment tool for addiction has garnered significant attention in the past 5 years, such that there are now over 20 published investigations investigating the efficacy of repetitive TMS versus sham TMS as a tool to modulate craving in individuals with nicotine, alcohol, cocaine, and methamphetamine dependence. To date however nearly all rTMS studies in addiction have focused on amplifying activity in frontal-striatal circuits that govern cognitive control, rather than attenuating limbic circuitry. In this abstract we review recent work using TMS as a tool to decrease craving for multiple substances, provide a theoretical model for how clinical researchers might approach target and frequency selection for TMS of addiction, and present recent pilot data suggesting that attenuating MPFC activity through cTBS directly decreases craving and activity in the monosynaptic projection areas of the ventral striatum.
Conclusions: The pilot data from these single-blind, sham-controlled, crossover studies in 12 cocaine-dependent, 12 alcohol dependent individuals and 8 prescription opiate dependent individuals suggest that, while many TMS studies are focused on applying LTP-like stimulation to the DLPFC, the MPFC might be a new, efficacious, and treatable target for craving in cocaine dependent individuals.
Financial Support: This project was supported by R01DA036617 (CAH)

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IMPACT OF PRESCRIPTION MONITORING ON CARE OF OPIOID-DEPENDENT PATIENTS.

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Aims: This study examined NYC buprenorphine prescriber perspectives on the impact of DEA oversight of buprenorphine, and of a 2013 NY State Law mandating all physicians to participate in the state narcotics prescription monitoring program (PMP), on prescribers' interactions with patients. The study enhanced its focus on Staten Island, the NYC borough with four times the opioid overdose rate of any other borough.
Methods: Semi-structured interviews were conducted with 62 buprenorphine prescribers. All buprenorphine prescribers in public clinics of all five NYC boroughs listed on the SAMHSA buprenorphine prescriber list, as well as all SAMHSA listed private practitioners in Staten Island, were contacted. Transcripts were thematically coded using NVIVO 10 software with multiple coders and checks for interrater reliability.
Results: Prescriber assessments of the impact of DEA oversight were mixed; discouraging some from prescribing, but believed by others to reduce buprenorphine diversion. The PMP required burdensome recordkeeping, heightened their fears of sanctions, and reduced their willingness to treat narcotics dependent patients. Some had stopped treating opioid dependent patients, and patients could not get community based medical care as a result, turning to illicit sources of opioids. Exceptions were two prescribers who felt that the PMP enhanced patients' honesty.
Conclusions: State mandated narcotics prescription monitoring may reduce the availability of buprenorphine and of general medical care for opioid dependent people, and in some cases, paradoxically itself may contribute to illicit opioid use. Further research is needed to elucidate the aspects of presription monitoring that negatively influence on patient care, and to identify interventions such as physician education and support, that are needed in order to enhance access to clinical care for opioid dependent people.
Financial Support: Support for this study was provided by a NIDA K01 Award to H. Hansen

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GENDER DIFFERENCES IN THE DEVELOPMENT OF EMOTION CIRCUITRY IN YOUTH AT RISK FOR SUBSTANCE ABUSE: A LONGITUDINAL FMRI STUDY.

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Aims: Youth with a family history of substance use disorders (SUD) often have particular emotional and behavioral traits that are early predictors of later problem substance use. There is substantial evidence for a gender difference in risk trajectories such that females tend toward negative affectivity and males tend toward impulsivity. Gender differences in substance use are also evident during adolescence, concurrent with the appearance of gender-based developmental differences in the brain, indicating there may also be gender-specific neural predictors in those at-risk for developing SUD.
Methods: Longitudinal fMRI was conducted in males (n=18) and females (n=18) with a family history of SUD starting at ages 8–13yrs. Participants performed an emotional arousal word task during fMRI at 1- to 2-yr intervals (3–4 scans/participant), covering the age range of 8–17.5yrs. Emotional words were positive, negative, or neutral, and participants were required to press a button indicating they understood the word when it appeared on the screen. A voxel-by-voxel analysis was conducted in SPM8 using a multiple regression model, designed to represent mixed linear effects and identify age-related changes between groups.
Results: For performance measures, females demonstrated a significant reduction in reaction time to negative, positive, and neutral words across age, while males showed no change. Significant age-related differences were found between groups in the right premotor cortex (BA6) and right amygdala for the negative vs. neutral contrast, where males showed a significant decrease in activation with age (premotor: p=.006; amygdala: p=.001) and females non-significantly increased in activation (premotor: p=.111; amygdala: p=.351).
Conclusions: These results reveal developmental differences in brain functional responses in emotional arousal between males and females at-risk for SUD. These differences may underlie gender differences in behavioral risk trajectories for SUD.
Financial Support: R01 DA027261, R01 AA12217, R01 AA07065, T32 DA007267-19, and T32 DA7268-22

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DOPAMINERGIC GENETIC VARIATION MODERATES EFFECT OF NICOTINE ON CIGARETTE REWARD SELF-REPORT.

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Aims: Cigarette smoking is influenced by nicotine's effects on dopaminergic activity in the mesocorticolimbic pathway. Carriers of a long allele (L; 7+ repeats) of the 48-base repeat variable number tandem repeat (VNTR) polymorphism in the third exon of the dopamine receptor D4 (DRD4) gene demonstrate several effects suggesting reduced dopaminergic tone. These include reduced ligand binding, reduced cAMP formation when dopamine is receptor-bound, and greater smoking cue reactivity than those homozygous for the short allele (S). Here we examine whether these variants also impact subjective responses to cigarettes as a function of nicotine content over successive smoking bouts within a single session.
Methods: White, non-Hispanic smokers (n=96, cigarettes/day ≥ 15) attended two double-blind, counterbalanced experimental sessions, each preceded by overnight smoking abstinence. Participants smoked four nicotine (8.9 mg) cigarettes at one session and very low nicotine (1.0 mg) cigarettes at the other, with each cigarette followed by completion of the Modified Cigarette Evaluation Questionnaire (mCEQ). The 12 mCEQ items were separately examined using 2x2x4 ANOVAs with genotype (L versus S) as the between-subject factor and within-subject factors for nicotine content and smoking bout.
Results: Overall, smokers reported expected subjective reactions in response to nicotine cigarettes relative to placebo (e.g., reduced craving). In addition, smokers with the S genotype reported markedly reduced craving, increased satisfaction, and felt more calmed down in response to earlier smoked nicotine cigarettes, suggesting smokers with the L genotype displayed a blunted initial subjective response to nicotine relative to the S genotype.
Conclusions: These results provide a better understanding of how the DRD4 genotype may relate to risk for nicotine dependence, in terms of how smokers respond to initial and subsequent doses of nicotine following a period of abstinence. These data may also have implications for personalized smoking cessation treatment.
Financial Support: NIH grants R21 DA027001 and R21 DA02422

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THE MICROBIOTA-GUT-BRAIN AXIS AS A POTENTIAL THERAPEUTIC APPROACH FOR HIV-1+ COCAINE ABUSE.

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Aims: Dopamine transporter (DAT) proteins are significantly reduced in cognitively impaired HIV-1+ patients and DAT function is reduced further in HIV-1+ cocaine abusers. The HIV-1 Tg rat provides chronic exposure of the brain to HIV-1 viral proteins under the control of the natural promoter in disease appropriate cells; this resembles the aviremic state in HIV-1+ patients on combined antiretroviral therapy. The HIV-1 Tg rat was used to assess a therapeutic approach for the interactions of HIV-1 proteins with cocaine.
Methods: Adult female, ovariectomized Tg and F344 rats were randomly assigned to S-equol (TgE=10; F344E=11) and Control (TgC=9; F344C=10) groups. Rats were treated with S-equol (0.2mg or vehicle), a metabolite of daidzein, produced via the gut-microbiome. There were 3 cocaine self-administration phases: FR1 schedule, 0.2 mg/kg/inj for 5 days; PR schedule, 0.75mg/kg/inj for 14 days; and PR schedule (0.01-1.0 mg/kg/inj), for 12 days. We hypothesized that S-equol (phases 1 and 2) would resolve genotype differences in cocaine responding.
Results: S-equol treatment differentially affected cocaine responding in HIV-1 Tg vs. F344 rats. Phase 1: A significant day x genotype interaction ($p \leq .05$) confirmed HIV-1 Tg earned more infusions than F344 rats ($p < .01$), with no S-equol x genotype interaction. Phase 2: Overall, cocaine responding increased over the 14 day period ($p \leq .05$) with HIV-1 Tg earning more infusions than F344 ($p < .02$). S-equol was differentially effective in altering cocaine responding as a function of genotype (TgEp<.01 whereas F344E>F344C $p < .001$). Phase 3: After the end of S-equol treatment, HIV-1 Tg rats showed less sensitivity and response vigor than F344 and there was an increased sensitivity to cocaine regardless of genotype.
Conclusions: Chronic exposure of the brain to HIV-1 viral proteins altered responding to cocaine. Active S-equol treatment had beneficial effects on sensitivity to cocaine, but a prior history of S-equol per se did not maintain the therapeutic benefit.
Financial Support: DA013137, HD043680, DA031604, GM081740

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NOVEL BIVALENT SEROTONIN 5-HT_{2A} AND 5-HT_{2C} RECEPTOR LIGANDS DEMONSTRATE DISTINCT ACTIVITIES *IN VITRO* AND *IN VIVO.*

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Aims: The 5-HT_{2A}R and 5-HT_{2C}R are prominently expressed in the brain and play an important role in the pathogenesis of a number of psychiatric and neurological disorders. Co-administration of a 5-HT_{2A}R antagonist with a 5-HT_{2C}R agonist produces synergistic effects in animal models of impulsivity and cocaine use disorder. A ligand with dual action as a *selective* 5-HT_{2A}R antagonist/5-HT_{2C}R agonist presents a promising and novel pharmacotherapeutic strategy for treatment of brain disorders in which both receptors are implicated.
Methods: Ligands were composed of M100907 and WAY163909. Ligands were evaluated *in vitro* to affect Ca_i^{++} and $pERK_{1/2}$ in cells expressing the h5-HT_{2C}R, h5-HT_{2A}R or h5-HT_{2A}R and h5-HT_{2C}R. Select compounds were evaluated *in vivo* for their effect on basal and cocaine-evoked hyperactivity.
Results: The M100907:M100907 homobivalent molecules retained 5-HT_{2A}R antagonist properties *in vitro* and demonstrated *in vivo* efficacy, inducing dose-related (0.5-2 mg/kg, i.p.) suppression of cocaine-induced hyperactivity in rats. The M100907:WAY163909 heterobivalent molecules exhibited a novel profile *in vitro*, exhibiting agonism at low concentrations and antagonism at higher concentrations in dual expressing 5-HT_{2A}R- and 5-HT_{2C}R-CHO cells.
Conclusions: Novel M100907:M100907 homobivalent and M100907:WAY163909 heterobivalent molecules have distinct activities *in vitro* and *in vivo*. Extensive behavioral analyses are underway to evaluate our novel heterobivalent molecules in *in vivo* models of impulsivity and cue reactivity. The compounds present a promising and novel pharmacotherapeutic strategy for treatment of cocaine use disorder.
Financial Support: DA007287, DA020087, DA033374, DA033935

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GENDER DIFFERENCES IN CRAVING AND INTERNALIZING SYMPTOMS IN METHAMPHETAMINE DEPENDENCE.

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Aims: Methamphetamine (MA) users often have substantial psychiatric comorbidities, with nearly a third reporting lifetime mood disorders and over a quarter reporting anxiety disorders (Salo et al., 2011). Female MA users are more likely to endorse depression (Glasner-Edwards et al., 2009) and anxiety compared to men. Craving has received attention as a marker of substance disorders and has been shown to be related to psychiatric symptoms in MA users (Nakama et al., 2008); however, the impact of gender on this relationship is yet unknown. Therefore, the aim of this study is to examine the role of gender in the relationship between comorbid depression and anxiety symptomatology with craving.
Methods: Participants (n=126) were non-treatment seeking MA dependent users, recruited from the Los Angeles community for enrollment in a larger pharmacotherapy trial. At screening visit, participants completed the Methamphetamine Urge Questionnaire (MUQ), the Beck Depression Inventory (BDI-II), the Beck Anxiety Inventory (BAI), the Timeline Followback (TLFB), and a demographic questionnaire. Data was analyzed using Proc GLM in SAS 9.3.
Results: A significant gender x BDI interaction was observed ($F = 4.5$, $p = 0.036$), such that male participants with higher BDI scores reported greater craving as compared to males with lower BDI scores or females. Similarly, a significant gender x BAI interaction was observed ($F = 4.12$, $p = 0.044$) where males reporting greater BAI scores also reported greater craving.
Conclusions: These results suggest that men with greater affective symptomatology may be experience heightened craving compared to men with lower comorbid symptomatology or women. Given craving's propensity to predict relapse, these initial findings indicate the necessity of treating comorbid psychiatric problems in male MA users which may in turn assist in the attenuation of craving.
Financial Support: DA029831; T32 DA07272-21

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THE BRAIN MIND CONNECTION: EFFECT OF TRAIT MINDFULNESS ON RESPONSES TO REAL-TIME FMRI FEEDBACK IN NICOTINE-DEPENDENT SMOKERS.

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Aims: To examine the relationship between trait mindfulness and neural activity in the region of the medial prefrontal cortex between real-time fMRI (rtfMRI) neurofeedback vs. a no feedback control condition in nicotine dependent cigarette smokers.
Methods: Forty healthy nicotine-dependent cigarette smokers participated in a rtfMRI neurofeedback study investigating the efficacy of rtfMRI neurofeedback to strengthen self-regulation of cue-induced craving-related brain activation. Twenty participants received rtfMRI neurofeedback from an individualized craving-related region of interest, and 20 participants were randomized to a no-feedback control condition. Mindfulness was measured with the Mindfulness Attention Awareness Scale (MAAS). The interaction between mindfulness, condition and the ability to regulate craving-related activation was investigated with a regression analysis.
Results: A significant interaction was found between the neurofeedback condition and MAAS score, on percent signal change (PSC) in the craving-related ROI (b=2.28, t(36)=2.81, p=.008). In the control group, mindfulness significantly predicted PSC such that higher MAAS scores were associated with a greater reduction in craving-related brain activation (b=-.65, t(18)=-3.59, p=.002). However, among the neurofeedback group there was no relationship between MAAS scores and PSC (b=.32, t(18)=1.43, p=.171).
Conclusions: Trait mindfulness predicts the ability to decrease craving-related neural activation, but only in the control, no feedback condition. Realtime neurofeedback may be a means to facilitate self-regulation of craving regardless of self-reported levels of mindfulness.
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A COMPARISON OF THE BEHAVIORAL EFFECTS OF ELECTRONIC AND TOBACCO CIGARETTES FOLLOWING 24-HR TOBACCO DEPRIVATION.

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Aims: To examine electronic cigarettes as a potential smoking cessation tool, this study compared the behavioral effects of commercial electronic and tobacco cigarettes following 24-hours of tobacco deprivation.
Methods: Five of eight conventional cigarette smokers have completed an ongoing study on the self-reported effects of electronic and conventional cigarettes following 24-hour tobacco deprivation. During the first session on each of 4 two-session blocks, participants completed subjective measures after ad-lib smoking. On the second session following 24 hours of tobacco deprivation (verified with breath CO), participants completed subjective measures before and after paced smoking of a tobacco cigarette or an electronic cigarette yielding 0, 8, or 16 mg of nicotine.
Results: After 24 hours of tobacco deprivation, significant effects of tobacco deprivation were observed on multiple self-report variables. Smoking tobacco cigarettes significantly reduced the withdrawal symptoms “desire or craving to smoke” (-2.2 on a five-point scale) and “I have an urge for a cigarette right now” (-60.8 on a 100-point scale). Electronic cigarettes of 16 mg nicotine concentration significantly decreased the previous measures (-1.2 and 13.8, respectively), while electronic cigarettes of 0 and 8 mg nicotine concentration did not.
Conclusions: Interim analyses from this ongoing study demonstrate that commercial electronic cigarettes attenuate some of the behavioral effects of tobacco deprivation in a nicotine-dependent manner, but to a lesser magnitude than conventional cigarettes.
Financial Support: Supported by UL1TR000117

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ALCOHOL AND TOBACCO USE IN COCAINE-DEPENDENT PARTICIPANTS PROVIDED TREATMENT WITH BUPRENORPHINE/NALOXONE AND NALTREXONE.

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Aims: Many individuals with cocaine use disorders also use alcohol and tobacco. A recent study conducted by NIDA’s Clinical Trials Network investigated pharmacotherapy for treatment of cocaine use disorders and also assessed alcohol and tobacco use.
Methods: These secondary analyses address pre- and post-study use of alcohol and tobacco by those meeting DSM-IV criteria for cocaine use dependence with a history of opioid abuse/dependence. Participants were given extended release naltrexone (NX) and randomly assigned to 1 of 3 buprenorphine (BUP) conditions: 4mg BUP (BUP4), 16mg BUP (BUP16), or 0mg BUP (placebo; PLB). Smoking was assessed with the Fagerström Test for Nicotine Dependence (FTND) and alcohol use was assessed with the Addiction Severity Index (ASI), both administered at baseline and at the end of the 8 week medication phase.
Results: 76% of participants reported that they smoke, and 191 provided both FTND assessments. At baseline, a mean score of 3.91 (sd=2.44) was reported with a 3.70 score (sd=2.47) at week 8, indicating moderate dependence. Comparing the highly dependent group (FTND$\geq$ 6), a difference was found at week 8 between BUP16 and PLB (p=0.002), and between BUP4 and PLB (p = 0.016). Both ASI assessments were completed by 276 participants. No difference in alcohol use was found by condition at baseline with a median alcohol use of 6 days. At week 8, logistic analyses of those using above the median, adjusted for baseline alcohol use, shows a difference between BUP16 and PLB (p=0.04) and a trend between BUP4 and PLB (p=0.07). A significant reduction in alcohol use was found for the total sample from baseline to week 8 (p=0.0003).
Conclusions: Tobacco use was reduced in those with a high dependence FTND score who were given both NX and BUP compared to those given only NX. For those using alcohol above the median number of use days, use was reduced in those given NX and BUP compared to those given only NX. The use of this combination pharmacotherapy should be investigated further as treatment for both alcohol and tobacco use.
Financial Support: DA13045

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HOW LONG IS TOO LONG? THE CONTINUED MISUSE OF NON-ABUSE DETERRENT OXYCONTIN AFTER REMOVAL FROM THE MARKET IN A COHORT OF RURAL APPALACHIAN OPIOID ABUSERS.

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Aims: To examine the time from market removal (August 2010) to cessation of street use/availability for non-abuse deterrent OxyContin (NADO) in a cohort of rural prescription opioid abusers.
Methods: 503 rural Appalachian prescription opioid users have been followed longitudinally since 2008. Interviewer-administered questionnaires ascertained data on illicit and prescription drug use, demographics and sociometric networks at each follow-up visit. For the current analysis, six waves of data (concluding in August, 2014) were utilized. Multiple logistic regression was used to analyze trends in continued NADO use.
Results: Almost all (94.8%) participants reported NADO misuse at baseline. Significant declines in use were observed from baseline to 1- and 2-years post-market removal, as 39.3% and 3.4% still reported abusing NADO at those time points, respectively. The last participant to report use was interviewed in August, 2013. Those continuing to use NADO 1-year post market removal were more likely ($p<0.05$) to be under age 25, report recent (past 6-month) injection drug use, HCV-positive, and have greater levels of eigenvector centrality in the drug network. Those continuing to use NADO were significantly less likely to have been in substance abuse treatment (adjusted odds ratio: 0.44, 95% CI: 0.23, 0.85).
Conclusions: The majority of participants ceased NADO use within 2 years of market removal and only a handful (3.4%) continued to report use after that time. Not surprisingly, injection drug users (IDUs) and those who were more active in their drug networks were significantly more likely to be using 1-year post-market removal. While there are currently no participants reporting NADO use, there was still an active street market for NADO for more than two years post-market removal, which has important implications for policies surrounding prescription opioids.
Financial Support: R01DA024598 and R01DA033862 (both JRH).

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DISTRESS TOLERANCE MODERATES THE RELATIONSHIP BETWEEN TRAUMA SYMPTOMS AND DEPRESSION IN SUBSTANCE USERS.

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Aims: A considerable number of studies have reported an association between posttraumatic stress symptoms and depression. Much less is known about factors influencing the strength of this association. One factor worth considering is distress tolerance, defined as the ability to withstand negative emotional or physical states. The current study examined whether distress tolerance moderates the relationship between posttraumatic stress and depression in substance users. Specifically, we hypothesized that the association between posttraumatic stress and depression would be stronger in patients with low distress tolerance.
Methods: The sample included 353 substance users (74% male) presenting for treatment at an outpatient substance abuse research clinic. Depression scores were obtained from participant responses to the BDI-2. Distress tolerance scores were obtained from self-reported responses to the Distress Tolerance Scale (DTS) and trauma symptoms were measured through self-report using the Posttraumatic Stress Diagnostic Scale (PDS).
Results: Hierarchical multiple regression analysis was performed with PDS and DTS scores entered in Step 1 and the interaction term (PDS x DTS) added in Step 2. The interaction of PDS and DTS significantly improved the model, $\Delta R^2 = .008$, $\Delta F(1, 350) = 4.392$, $p < .05$. The entire model accounted for 37% of the variance in the depression score, $R^2 = .374$, $F(3, 353) = 69.815$, $p < .01$).
Conclusions: Findings of the study indicate that distress tolerance moderates the relationship between depression and posttraumatic stress symptoms in this sample of substance using adults. Posttraumatic stress symptomatology was a stronger predictor of depression in individuals with lower distress tolerance. The inclusion of distress tolerance skills in interventions for substance users with depression and posttraumatic stress symptoms may be beneficial.
Financial Support: None.

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EVALUATION OF REMIFENTANIL AND MORPHINE AS REINFORCERS IN A RAT INTRAVENOUS SELF ADMINISTRATION PROCEDURE.

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Aims: Intravenous self-administration (IVSA) in rats is an established test to predict whether CNS-active compounds have abuse liability potential in humans. We reported the relative reinforcing effect of stimulants can be determined by comparing break-points after PR testing (Heal et al, 2014, CPDD Meeting, Abst 89). We investigated morphine and remifentanil (RFL) to see whether this approach can be extended to asess the relative reinforcing effects of sedative euphoriants.
Methods: Male, Sprague-Dawley rats trained to selfadminister morphine (75 μg/kg/injection, iv) on a FR2 schedule were used. After saline extinction, morphine (7.5, 22.5, 75, and 225 μg/kg/inj) and RFL (3.0 μg/kg/inj) were evaluated. All drugs were dosed as base. When positive reinforcement was stable, breakpoints for responding were determined using a PR schedule in 4.0h sessions.
Results: Compared with saline, RFL and 2 doses of morphine served as positive reinforcers (>8.0 infusions/session) (mean total infusions/session ± SEM: RFL = 19.4 ± 0.5 [n = 7], p<0.001; Morphine [22.5 μg/kg/inj] = 10.3 ± 1.6 [n = 10], p<0.01; 75 μg/kg/inj = 12.0 ± 1.0 [n = 10], p<0.001). Total infusions of RFL were significantly (P<0.001) greater than all doses of morphine. On a PR schedule, the break-point of operant responding (mean lever-presses ± SEM) for RFL (38.3 ± 7.3 [n = 7]) was significantly higher (p<0.01) than the most reinforcing dose of morphine ([75 μg/kg/inj] = 14.6 ± 2.5 [n = 10]). Compared with previous results, the break-point of RFL was not significantly different from the most reinforcing doses of cocaine (0.29 μg/kg/inj = 42.3 ± 4.0 [n = 7]) or methylphenidate (0.1 μg/kg/inj = 41.3 ± 9.4 [n = 6]), but the morphine break-point was significantly (p<0.001) lower.
Conclusions: RFL and various doses of morphine served as positive reinforcers in rats. However, as indicated by break-point analysis, the relative reinforcing effect of morphine was lower than RFL, methylphenidate or cocaine. Thus, RFL is a better opioid reference comparator in rat IVSA tests.
Financial Support: Part funded by Alkermes, Inc.

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CORRESPONDENCE BETWEEN SELF-REPORTED AND BIOCHEMICAL MEASURES OF CIGARETTE SMOKING IN PREGNANT WOMEN.

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Aims: The majority of female smokers are unable to quit on their own when they find out they are pregnant, but report reducing their cigarettes per day (CPD) by ~50% before entering prenatal care, typically ~6 weeks gestation. Without intervention, the majority will continue to smoke for the remainder of the pregnancy, but it is unclear whether they make additional reductions in smoking over the remaining ~34 weeks of the pregnancy and if so, whether the decreases are paralleled by changes in biochemical measures of smoking. To answer these questions, this study examined self-reported smoking rate and biochemical measures of smoking in pregnant women participating in clinical trials for smoking cessation.
Methods: Self-reported CPD, breath CO, and urine cotinine were collected at the intake assessment (~10 weeks gestation), at a second assessment 1 month later (Early Pregnancy Assessment), and again at the end of pregnancy (≥ 28 weeks gestation; Late Pregnancy Assessment).
Results: Of 289 total trial participants, 156 (54%) reported smoking at each of these assessments and were included in the analysis. Self-reported CPD decreased from 10.6 to 7.0 and 7.6 at Intake and Early and Late Pregnancy Assessments, respectively ($p < .001$). Mean CO was 11.8, 10.7, and 11.3 ppm ($p = .13$) and mean urine cotinine was 1112.3, 971.7 and 1044.3 ng/ml ($p = .004$), respectively.
Conclusions: Overall, self-reported CPD decreased ~31% while CO and cotinine declined only ~8%. Potential explanations for discrepancies between self-report and biochemical measures include misrepresentation of smoking or actual reductions in cigarettes per day offset by changes in smoking topography (i.e., compensatory smoking). Either way, these data suggest that the many female smokers not only continue to smoke throughout pregnancy, but are exposing themselves and their offspring to a similar level of toxicants despite reports of reducing their smoking rate.
Financial Support: R01 DA14028, R01 HD07566, & P50 DA036114

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ASSOCIATION OF GENDER AND GENETIC ANCESTRY WITH FREQUENCY OF METHAMPHETAMINE USE AMONG METHAMPHETAMINE- DEPENDENT HISPANIC AND NON-HISPANIC WHITES.

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Aims: Higher pre-treatment methamphetamine use frequency is associated with poor treatment outcomes for methamphetamine use disorders. We examined potential influences of gender and genetic ancestry on methamphetamine use frequency.
Methods: 263 Hispanic and Non-Hispanic White methamphetamine dependent volunteers self-reported number of days with methamphetamine use in the past 30 days prior to entering one of several clinical trials in Los Angeles. Genetic ancestry was assessed via genotyping a panel of ancestry informative markers. Logistic regression was used to examine potential effects of gender and proportion Native American ancestry on frequency of methamphetamine use.
Results: Male gender ($B = -5.9$, $S.E. = 1.3$, $p = 1.2 \times 10^{-5}$) and greater proportion of Native American ancestry ($B = -9.4$, $S.E. = 2.9$, $p = 0.001$) were significantly associated with lower mean number of days with methamphetamine use in the past 30 days after controlling for age and use of alcohol, tobacco, and marijuana.
Conclusions: Future studies should investigate the contribution of biological versus social factors underlying observed differences in methamphetamine use by gender and genetic ancestry.
Financial Support: K23 DA023558, UL1 TR000124

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EVALUATION OF ELECTRONIC NICOTINE DELIVERY SYSTEMS: REGULATORY PRECEDENTS FROM THE FDA 2013 DRAFT GUIDANCE FOR ABUSE-DETERRENT OPIOIDS.

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Aims: In 2013, FDA issued a draft guidance on abuse-deterrent (AD) opioids that discusses potential test methods and labeling implications for new formulations. Some of FDA's approach is applicable to rapidly evolving electronic nicotine delivery systems (ENDS). While ENDS enable cigarette smokers to eliminate exposure to tobacco smoke, some products allow manipulations that may alter their emissions, and lend themselves to the administration of cannabinoid extracts, cocaine, and opioids. The AD guidance provides a framework for evaluating drug products for resistance to modifications that increase the amount and speed of drug delivery in its Category 1 *in vitro* laboratory assessments. Similar to Category 1 assessments of opioid products, tampering studies of ENDS products should be conducted that evaluate the potential for individuals to increase the dose and speed of delivery of nicotine and the substitution of other abusable drugs. These assessments would identify product vulnerabilities and lead to development of more tamper-resistant ENDS technologies.
Conclusions: Without addressing the degree to which flexible dosing designs by ENDS should be allowed, this presentation will demonstrate how the 2013 AD guidance might be adapted to quantify product flexibility and potential vulnerability to uses that are not in the interests of public health.
Financial Support: PinneyAssociates provides consulting services to NJOY, Inc., on electronic nicotine delivery systems (ENDS); this work was undertaken without the support or involvement of NJOY. JEH, EJC, JGG and JMP also own an interest in intellectual property covering a novel nicotine medication that has not yet been commercialized.

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GENDER DIFFERENCES IN CANNABIS WITHDRAWAL SYMPTOMS AMONG TREATMENT-SEEKING CANNABIS USERS.

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Aims: Over 300,000 individuals enter treatment for cannabis use disorders (CUDs) in the U.S. annually, and treatment outcomes are generally poor. Cannabis withdrawal has been associated with functional impairment and relapse, but few studies have examined gender differences in withdrawal. The aim of this study is to examine gender differences in cannabis withdrawal symptoms among treatment-seeking cannabis users.
Methods: Treatment-seeking cannabis users (62 women/120 men) completed a demographics/substance use questionnaire and a Marijuana Withdrawal Checklist (MWC; Budney et al., 2003) to retrospectively characterize withdrawal experienced during their most recent quit attempt. Questionnaire data, MWC sum scores, and scores on individual MWC items were compared between women and men (significance determined by $p<0.05$).
Results: Women and men did not significantly differ on current use of cannabis (2.5 vs. 3.2 grams/day) alcohol (3.9 vs. 3.5 drinks/week) or cigarettes (4.3 vs. 4.1 cigarettes/day). Women first used cannabis at a later age than men (16.0 vs. 14.2 years old), but women and men did not differ on years of regular cannabis use (17.0 vs. 15.9). MWC sum scores were significantly higher among women than men (13.6 vs. 11.0). Women had significantly higher scores than men on five individual items, which clustered in two areas, gastrointestinal symptoms (decreased appetite, nausea) and mood symptoms (violent outbursts, irritability, restlessness).
Conclusions: Women seeking treatment for CUDs reported experiencing more severe gastrointestinal and mood symptoms of cannabis withdrawal than men during their most recent quit attempt. Prospective studies of gender differences in cannabis withdrawal are warranted, and inform the development of gender-specific pharmacotherapies for CUDs.
Financial Support: This project was supported by U01 DA031784 and T32 DA07209 from the National Institute on Drug Abuse.

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OPIOID USE SEVERITY AND TREATMENT OUTCOMES IN COCAINE-DEPENDENT PARTICIPANTS WITH A HISTORY OF OPIOID ABUSE/DEPENDENCE.

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Aims: Secondary analyses examine opioid use and treatment outcomes in a NIDA Clinical Trials Network sponsored study of treatment for cocaine dependent participants with a history of opioid abuse or dependence.
Methods: The parent study investigated buprenorphine/naloxone treatment in 302 cocaine-dependent participants with a history of opioid abuse/ dependence. Participants were given long-acting naltrexone and randomized to daily sublingual buprenorphine (4mg, 16mg, 0mg). Baseline markers of opioid severity include injection opioid use, type of opioid used (heroin, prescription opioid [PO]), DSM-IV opioid diagnosis, and frequency of opioid use. Measures include the DSM-IV, ASI, and urine drug screens (UDS).
Results: 69% met criteria for past-year opioid dependence. Results by injection and type of opioid show injection heroin use (29%), non-injection heroin use (25%), injection PO use (4%), and non-injection PO use (43%). No difference was found in UDS during the last 4 study weeks by injection or drug use, but a difference in UDS by DSM-IV diagnosis was found (p=0.001). A difference in retention was found between heroin injectors and non-injectors (52 vs.46 days, p=0.010). Other outcomes are presented.
Conclusions: Some differences in outcomes were found based on markers of opioid use severity in cocaine-dependent participants. Because severity of drug use has been found to predict outcome in some recent studies, these results suggest that severity of all drug use should be assessed when developing a treatment plan.
Financial Support: DA13045

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DRUG-FREE PERIOD FROM NON-OPIOIDS BEFORE START OF THE TREATMENT WITH METHADONE OR BUPRENORPHINE FOR HEROIN-DEPENDENCE IMPROVES EFFICACY.

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Aims: To investigate if the length of the drug-free period from non-opioids before start of the treatment with methadone or buprenorphine influences the treatment efficacy
Methods: All patients who started treatment with methadone or buprenorphine for heroin dependency in Sörmland County 2006-2011 were included in the study. During this period there were different physicians/psychiatrists running the programs and they had different demands on the patients. We considered this a form of randomization, since the length of the drug-free period depended on the physicians/psychiatrists and not on the patient. Data were collected from the files for fourteen months, two months before treatment and twelve month after start of the treatment. The data collected were: gender, age at the start, duration of heroin dependency, the result of the urine samples during the observation period. The patients were divided into three groups depending on the drug-free period from non-opioid drugs before start of the treatment.
< 1 month before start
1-2 months before start
> 2 month before start
Results: There were 51 initiated in treatment (12 female and 39 male) during this period of which 34 received buprenorphine and 14 who received methadone. Three patients switched from buprenorphine to methadone under the observation period. Successful treatment was defined as 12 months retention and less than 3 % positive urine samples for illicit drugs. The statistical analysis showed significant better outcome for those patients who were free from non-opioids longer before treatment start (p< 0,05) but no difference concerning gender, age and length of opiate dependence.
Conclusions: Illicit non-opioid drug abuse before treatment start is a risk factor for poor treatment outcome. The demand for a longer drug-free period from non-opioids before treatment improves outcome.
Financial Support: Sörmland County Council

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MODELING THE OPIOID SYSTEM'S EFFECTS ON COCAINE REINFORCEMENT IN ENVIRONMENTALLY ENRICHED AND IMPOVERISHED RATS USING AN ECONOMIC DEMAND FUNCTION.

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Aims: The endogenous opioid system has been implicated in motivational processes but its precise role in reward remains undetermined. Environmentally enriched (EC) and impoverished (IC) rats were pretreated with the opioid receptor ligands naltrexone and morphine before undergoing cocaine self-administration using a within session demand procedure. It was hypothesized that naltrexone would increase the essential value (α) of cocaine in both EC and IC rats. Additionally, because of their proposed higher opioid tone, EC rats were hypothesized to show greater increases in essential value after naltrexone pretreatment compared to IC rats.
Methods: Eleven male Sprague-Dawley rats were placed in EC or IC immediately after weaning. Upon reaching adulthood, all rats were trained on a within session demand procedure that measured cocaine consumption under changing cocaine price by decreasing the dose of cocaine earned throughout a 60 min session. Rats were able to self-administer cocaine on a FR1; every 10 mins the cocaine dose was systematically decreased (0.75 - 0.003 mg/kg/infusion cocaine). After 10 days of training on this procedure, rats were randomly pretreated with 0, 0.3, and 3 mg/kg morphine once every 3 days, followed by random pretreatments of 0, 1, and 3 mg/kg naltrexone once every 3 days. Economic demand functions were fit to each rat's cocaine consumption from each pretreatment, and best-fitting α and Q(o) parameters were analyzed using separate 2 (environment) x 3 (pretreatment dose) mixed ANOVAs for morphine and naltrexone.
Results: Morphine significantly increased α for both EC and IC rats. Additionally, EC rats had a significantly greater α compared to IC rats after morphine pretreatment. Naltrexone tended to increase α for EC but not IC rats, but this result was not significant.
Conclusions: This study sheds light on the opioid system's contribution to reward value attribution and provides new insights into endogenous opioid functioning in EC and IC rats.
Financial Support: DA016176, DA035200, DA012964

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DYSREGULATION IN THE CHOLINERGIC SYSTEM AFTER ADOLESCENT NICOTINE IS REVERSED BY DIETARY CHOLINE.

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Aims: Adolescent nicotine abuse is problematic because earlier ages of initiation are correlated with nicotine dependence later in life and increases the risk for cognitive impairments. Chronic administration of nicotine during adolescence leads to persistent deficits in hippocampus-dependent contextual fear learning in adulthood. Since the hippocampus has a high concentration of nicotinic acetylcholinergic receptors, it is possible that adolescent nicotine disrupts normal cholinergic functioning within the hippocampus. This study tested whether prior nicotine exposure in adolescence leads to a hypo- or hyper-responsive nicotinic acetylcholinergic system.
Methods: Animals were chronically treated with nicotine (12.6mg/kg/day) starting at post-natal day 38 (p38) for 12 days after which they underwent a 30 day washout after which animals were trained and tested in fear conditioning. Acute nicotine or saline was administered at the time of testing and training at varying doses (0.045mg/kg, 0.18mg/kg, and 0.36mg/kg/day).
Results: While the medium dose (0.18mg/kg) enhanced learning in mice pretreated with saline the higher dose of nicotine reversed the learning deficit caused by adolescent nicotine exposure. Thus, the adult cholinergic system is hypo-responsive following adolescent nicotine as a larger dose of nicotine was needed to enhance learning. Further, alteration of the cholinergic system by choline in the diet (9g/kg) following the cessation of chronic adolescent nicotine treatment and continuing through training and testing of fear conditioning in adults reversed deficits in adult hippocampus-dependent learning associated with adolescent nicotine exposure.
Conclusions: Taken together, these findings suggest that adolescent nicotine exposure creates a hypo-responsive cholinergic system resulting in learning deficits that emerge in adulthood and these deficits are reversed with choline in the diet. The results from this study could help explain why adolescent nicotine abuse leads to more severe dependence later in life.
Financial Support: NIDA (T.J.G. DA017949)

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THE EFFECTS OF MIRTAZAPINE ON PRAMIPEXOLE-INDUCED RISKINESS IN A RAT MODEL OF PARKINSON'S DISEASE.

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Aims: Riskiness is a common feature of many impulse control disorders (ICDs), such as pathological gambling. It can be measured using probability discounting tasks in which an individual can choose between a small, certain reinforcer, and a larger, uncertain reinforcer. Riskiness is defined as a preference for selecting the large reinforcer when its probability is low. Patients with Parkinson's disease (PD) who are treated with dopamine agonist therapies (e.g., pramipexole; PPX) to alleviate motor deficits are more likely to express the riskiness associated with ICDs than PD patients prior to PPX therapy or normal controls. The present study used a probability discounting procedure to assess whether mirtazapine (MIRT), an antagonist at the 5-$HT_{2/3}$ and $\alpha_2$norepinephrine receptors, would reduce PPX-induced riskiness in PD-like rats while still maintaining the therapeutic benefits of PPX.
Methods: Rats were implanted with a stimulating electrode in the medial forebrain bundle, and lesioned in the dorsolateral striatum with 6-OHDA to induce PD-like motor deficits. They were then assessed in a probability discounting task in which they could choose between small, certain rewarding brain stimulation and a large brain stimulation delivered at various probabilities (i.e., 0.8, 0.5, 0.2, 0.1). Following stability, rats were implanted with subcutaneous osmotic minipumps that infused PPX (1.2 mg/kg/day) for 4 weeks, and behavior was assessed daily. At the start of week 3, rats were implanted with a second minipump that co-infused MIRT (0.5 mg/kg/day) or vehicle with PPX for 2 weeks.
Results: PPX increased preference for the larger reinforcer at the 0.2 and 0.1 probabilities compared to baseline, and reversed motor deficits caused by the lesion. MIRT (vs. vehicle) reduced PPX-induced riskiness and did not interfere with the motor enhancing effects of PPX.
Conclusions: MIRT may be an effective adjunct treatment in PD patients with ICDs.
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PERCEIVED APPROVAL OF SUBSTANCE USE IN SOLDIERS VS. CIVILIANS.

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Aims: The prevalence of substance use in the military tends to differ greatly compared to civilians. One potential reason for this may be different expectations or perceived approval (i.e., norms) about substance use in military members compared to civilians. Further, previous work has suggested that, among civilians, a partner's expectations about substance use was directly related to one's own substance use. The objective of this work was to examine norms about substance use (alcohol, tobacco, illicit drugs and nonmedical use of prescription drugs) among a sample of US Army Reserve Soldiers and their partners.
Methods: Data are from the baseline assessment of Operation: SAFETY (Soldiers and Families Excelling Through the Years), an ongoing longitudinal study of Reserve Soldiers and partners. For each substance, participants were asked if people who were important to them would approve of their use of the substance and if those same people would want them to use the substance.
Results: Among female soldiers, there was less approval of the use of tobacco compared to civilian women ($p < .05$). However, regardless of perceived approval, both civilians and soldiers reported that their social network would not want them to use tobacco. There was also some evidence that female soldiers, compared to civilian women, reported lower approval of the use of illicit drugs ($p=.08$). Similarly, regardless of perceived approval, both civilians and soldiers reported that their network would not want them to use illicit drugs. Among women, partner's military status did not impact one's own approval of substances. For men, there were no differences in perceived approval of substance use between soldiers and civilians.
Conclusions: Despite the differences in prevalence rate for various substance use among soldiers vs. civilians, there does not appear to be large differences in the perceived approval/disapproval of substance use among social network members of military vs. civilian populations.
Financial Support: R01-DA034072 (GGH)

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REDEFINING THE RECREATIONAL DRUG USER POPULATION IN HUMAN ABUSE POTENTIAL STUDIES.

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Aims: Human abuse potential (HAP) studies are essential to the drug development of all CNS active drugs to elucidate the relative abuse potential of new drugs. HAP studies are conducted in subjects with a current history of non-dependent recreational drug use. HAP studies to date have been conducted using The Diagnostic and Statistical Manual of Mental Health Disorders Fourth Revision (DSM-IV) for excluding subjects with substance dependence. Despite the release of the DSM 5 in May 2013, HAP studies continue to use DSM-IV criteria. DSM 5 has redefined substance use disorder. Substance dependence and abuse are no longer classified as different disorders. The DSM 5 has combined criteria from both the substance dependence and abuse disorders on a continuum with mild, moderate and severe substance use disorder. The introduction of the DSM 5 has altered the way we think about substance use disorder. This is particularly relevant for HAP studies as exclusion criteria has been based on DSM-IV which clearly differentiated between dependence and abuse. Now that the DSM 5 has redefined diagnostic criteria, this poses a significant problem in defining the "non-dependent" recreation drug user population in HAP studies.
Conclusions: Given the vast changes to the DSM 5 substance use disorder criteria, an active working task force has been created and is tasked with redefining the recreational drug user population. In order to accomplish this task, we are running a retrospective data analysis investigating the endorsement of DSM-IV-TR criteria from subjects with non-dependent recreational drug use history in various HAP studies. This will begin to elucidate and define the recreation drug user population based on the number of criteria as well as the nature of the criteria endorsed on the DSM-IV-TR.
In the interim, we caution against adopting DSM 5 criteria as exclusionary criteria for substance use disorders in HAP studies as additional research will be needed to develop valid criteria utilizing DSM 5 criteria to define this population.
Financial Support: No

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HOW ARE PRIVATE HEALTH PLANS PROVIDING DRUG AND ALCOHOL SERVICES IN AN AGE OF PARITY AND HEALTH REFORM?

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Aims: Rapid changes in the U.S. healthcare system, most recently the federal parity law and national healthcare reform legislation, require significant changes to health insurance for alcohol, drug and mental health services, which can directly influence patients' access to care, as well as cost and quality. We explore key decisions that health plans have made including benefit design, alternative payment models, provider network design, integration of behavioral and medical care, and access to specialty treatment.
Methods: Data are from the most recent rounds of an in-depth survey on the provision of alcohol, drug and mental health services in private health plans in 60 market areas. The 2010 survey preceded full implementation of parity and health reform and the 2014 survey followed full implementation. Each plan was asked about its top three commercial products, and in 2014, the top silver plan available on the new insurance exchanges. The 2010 survey had an 89% response rate (351 plans reporting on 939 products). Data are weighted for national estimates.
Results: Coverage of drug and alcohol treatment services was very high in 2010. Following initial parity implementation, only 5% of health plan products required prior authorization for outpatient treatment of substance use disorders, down from 14% in 2009. Plans reduced prior authorization for specialty medical care, while required re-authorization for continuing treatment increased. Very few reported that any purchasers dropped coverage for behavioral health services. The new exchange products were very similar to the commercial products. Health plans in 2014 are open to adopting new payment models for the delivery of behavioral health services.
Conclusions: As parity and health reform are implemented it is critical to examine and understand changes health plans are making. These findings provide an important window into the delivery and management of drug and alcohol services before and after passage of parity legislation and at the beginning of federal health reform implementation.
Financial Support: NIDA R01 DA029316, NIAAA R01 AA010869

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CASEIN KINASE-1 INHIBITORS AS A NOVEL TREATMENT FOR SUBSTANCE USE DISORDERS.

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Aims: Casein Kinase 1 (CK1) is a protein kinase that phosphorylates multiple proteins with significant physiological functions, most notably circadian clock timing. Additionally, CK1 modulates Period (PER1-3) gene expression and phosphorylates dopamine cAMP-regulated neuronal phosphoprotein-32 (DARPP-32) which play important roles in drug addiction. PF-5006739 is a dual inhibitor of CK1d and CK1e that dose-dependently induces significant circadian phase delays in both rodents and monkeys, suggesting potential efficacy in circadian rhythm disorders. Given the link between CK1 and substance use disorders, the purpose of the current work was to evaluate the effects of PF-5006739 on reinstatement of fentanyl-seeking behavior as a non-clinical model of relapse to opioid seeking.
Methods: Male Sprague Dawley rats were initially trained to self-administer intravenous fentanyl under a fixed ratio schedule of reinforcement using a standard 2-lever choice design with each drug infusion paired with auditory and visual cues. Following acquisition of this behavior, access to fentanyl was removed, and responding consequently extinguished. Once a stable extinction baseline was achieved, the effect of PF-5006739 on reinstatement of fentanyl seeking behavior was determined. Reinstatement of fentanyl seeking was induced by either a combination of drug-associated cues and a fentanyl prime, presentation of drug-associated cues alone or a combination of drug-associated cues and a yohimbine prime.
Results: Results showed that PF-5006739 robustly inhibited combined cue and fentanyl prime-induced reinstatement in a dose-dependent manner. PF-5006739 did not inhibit cue-induced reinstatement; however, a trend was observed for inhibition of combined cue and yohimbine prime-induced reinstatement.
Conclusions: These data support further investigation of CK1 inhibitors for the treatment of substance use disorders.
Financial Support: N/A

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CONSTRAINED CHOICES:THE CARE-DECISION-MAKING EXPERIENCE FOR PREGNANT OPIOID-DEPENDENT WOMEN.

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Aims: The aim of the study was to understand the role of pregnant opioid dependent women participating in medical decision making regarding their prenatal care and the postpartum period while addressing thier addiction.
Methods: Qualitative health research was utlized to gain information about pregnant opioid dependent women's perspectives on their process of seeking health care. The data analysis was an interpretative phenomenological analysis which focused on the women's attempts to make meaning out of their experience.
Results: The sample consisted of N=20 post partum women who were opioid dependent from the Eastern New England region. The age range of the participans was 20-38 years with an average age of 28 years. All of the women in the study reported their race and ethnicity as White, all indicated they held Medicaid insurance, and 80 % stated they were unemployed. The majority of the women had a polysubstance use history. Results were analyzed with the use of NVIVO 10 and the theoretical lens of self-determination and stigma theories. The women in the study whared the many perceptions and feelings they had about their addiction and fears related to having a child while receiving Opioid Replacement Therapy (ORT), as well as their experiences of internal and external stigma that impacted their prenatal and postpartum experience.
Conclusions: Given the following factors, there are a range of implications that would suggest further research, possible clinical practices that might be evaluated, and potential policy changes that could be implemented: shared decision making (SDM) is being promoted in health care, The participants recommended increasing awareness about the potential for prescription opioid addiction and improved collaboration between providers and patients. Due to the complexity and multifaceted issues surrounding opioid addiction and pregnancy it is recommended to add Decision Aid Tools to routine obstetrical care in assisting the pregnant opioid dependent women.
Financial Support: There was no financial support in this disseration research required for the Degree of Doctor of Philosophy at the Simmons College School of Social Work.

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SMOKING STATUS ON DAY 3 OF A QUIT ATTEMPT PREDICTS FUTURE SMOKING OUTCOMES.

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Aims: Aim: Smoking abstinence achieved during the first two weeks of a quit attempt has been shown to predict subsequent outcomes. However, of interest is how early one's longer-term smoking cessation success can be accurately predicted. Indeed, being able to forecast a smokers' future outcomes in the early days of a quit attempt could aid efforts to identify those at risk of relapse and intervene with additional resources. We examined this question in opioid-dependent smokers receiving a uniform, empirically-supported behavioral intervention for smoking cessation.
Methods: Methods: Participants were 119 methadone- and buprenorphine-maintained patients who smoked 18.2±8.6 cigarettes/day. They visited the clinic daily for 14 days, provided breath carbon monoxide (CO) and urine cotinine samples, and received financial incentives contingent upon biochemically-verified abstinence. We examined whether abstinence (breath CO ≤ 6 ppm) at Day 1, 2, or 3 predicted patients' smoking status during the remainder of the study.
Results: Results: Smoking status on Day 3 was the best predictor of later abstinence. Participants meeting the CO abstinence criterion on Day 3 had lower cotinine levels at that visit than those who did not (197.9 vs. 843.9 ng/ml, respectively; $p<0.05$). Their cotinine levels remained lower at every subsequent visit, with an overall mean cotinine value of 258.4 vs. 1177.7ng/ml ($p<0.05$). By the final day of the study, 60.7% of participants who met the Day 3 criterion were still smoking abstinent compared to 0% of those who had not ($p < 0.001$).
Conclusions: Conclusion: Smoking status on Day 3 of a quit attempt may help identify individuals most likely to succeed. Alternatively, failing to meet this criterion may warrant an infusion of additional resources (e.g., higher magnitude incentives, psychosocial support, pharmacotherapies). Overall, pairing smokers with a treatment approach that maximizes outcomes may reduce relapse rates, thereby reducing the public health costs and consequences associated with continued tobacco use.
Financial Support: Support: R01 DA019550, T32 DA007242, P20 GM103644

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THE BRAIN STRUCTURAL CHANGES ASSOCIATED WITH STAGES OF COCAINE ABSTINENCE.

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Aims: Structural brain changes have been associated with chronic cocaine addiction, but less is known regarding the impact of years of abstinence on brain structures involved in addictive behaviors. This study used structural Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI) to compare structural brain differences among men with varying years of abstinence.
Methods: Data were obtained from 40 adult men (M=56.5 ± 5.4 years) using a Siemens 3T MRI scanner. Participants were categorized into 4 groups based on date of last use: 10 were current users (within past year), 5 with1-5 years abstinent, 6 with 6-10 years, and 12 with over 10 years without cocaine use. An additional 7 age-matched controls also completed the protocol.
Results: Regional gray matter volume (GMV) was examined using FSL-VBM. Results revealed that increasing years of abstinence was associated with increased GMV in the dorso-lateral prefrontal cortex, posterior cingulate cortex, and superior parietal lobe, suggesting that participants with increased abstinence have more GMV in regions important for inhibition control. However, results also revealed that increased years of abstinence was associated with decreased GMV in the ventral striatum; thus suggesting that increased abstinence may be associated with less GMV in regions important for habitual reward processing. DTI results showed increased inter-hemisphere communications between left and right ventro-medial prefrontal cortex, an area vital for risky decision making, among those with more years of abstinence.
Conclusions: Although preliminary, these results suggest that years of abstinence may influence important structural brain changes. Specifically, variations in GMV and increased inter-hemisphere communications, areas involved in inhibition control, risky decision making, and habitual reward processing, were impacted by length of abstinence. Larger studies such as this can contribute to our understanding of processes involved in sustained cocaine abstinence.
Financial Support: NIDA R03DA032542-01A1 P30DA016383 (PI: Hser)

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RECENT TREND OF DRUG-ARRESTED CHARGES AND HOSPITAL VISITS IN TAIWAN: 2009-2013.

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Aims: We sought to examine the recent trend in main illegal drugs involved in drug-arrested charges in Taiwan from 2009 to 2013 and to identify potential changes in socioedemographic characteristics.
Methods: Data were derived from two national datasets in Taiwan: drug-arrested suspects records (n=3,629) and the Surveillance System of Drug Abuse and Addiction Treatment (SSDAAT, n=113,350) from 2009 through 2013. Drugs of abuse were confirmed by urine test for suspects and physicians' diagnosis for hospital visitors.χ^2 test were used for comparison.
Results: Evidence from both drug-arrested suspects and hospital visit records suggested that ketamine appeared to become more common in the past 5 years (drug arrest records: n=118 to 286; hospital visits: n=203 to 1,421). The majority of occupation in both the drug-arrested suspects and hospital visits was unemployment and labor. Meanwhile, new psychoactive substances (e.g., bk-MDMA, mephedrone and synthetic cannabinoids) was noted to gradually emerge in arrested drug-involved suspects. For drug-involved suspects, the average ages were lowered from 34 to 32 (p=0.059), and the proportion of higher educational attainment was increased from 48% to 60% (p<0.001); however, such change did not appear in hospital visitors.
Conclusions: National statistics suggested that a sharp increase in cases involving ketamine, MDMA, and emerging psychoactive substances in community in Taiwan. The results may give government critical information for and policy formulation and resource allocation to reduce illegal drug problems in certain subpoulations.
Financial Support: Food and Drug Administration, Ministry of Health and Welfare, Taiwan

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A PROSPECTIVE STUDY OF ALCOHOL ADVERTISEMENT ON ALCOHOL EXPERIENCES AMONG ADOLESCENTS IN TAIWAN.

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Aims: Alcohol advertisement has been indicated as an important factor shaping youngster's decision to drink. This study aims to investigate the association between alcohol ads with drinking intention and behaviors among adolescents in Taiwan.
Methods: The data were derived from the Alcohol-Related Experiences among Children II. The baseline sample comprised 1926 7th-8th graders from 11 public middle schools in Taipei by multi-stage sampling; follow-up was conducted in 9th grade (follow-up rate=97%). Data concerning sociodemographic and family characteristics, exposure to alcohol ads on eight marketing channels, and drinking experiences were collected by web-based self-administrated questionnnaires. Complex survey analyses were used to evaluate the predictors for drinking behaviors in 9th grade, with stratification by prior drinking experiences in childhood.
Results: Approximately 45% students had tried alcoholic beverages at least once in 7th grade. Annual incidence of alcohol initiation was estimated 18%. 90% of adolescents were exposed to alcohol ads on television in 7th grade, and the estimates for pamphlets and website was 27% and 68%, respectively. After statistical adjustment for potential confounders at baseline, exposure to alcohol ads on pamphlets, television, website, and stores was significantly linked with subsequent alcohol initiation (aOR=1.3 ~3.4); continued drinking was only linked with pamphlet ads (aOR=1.2). Website alcohol ads exposure may increase future drinking intention in noncurrent drinkers by 46%~50%.
Conclusions: Our results demonstrate that alcohol advertisement on marketing channels may have differential effects on youngsters' involvement of drinking behaviors and intention through early adolescence. Preventive strategies targeting underage drinking should consider restrain marketing channels from certain advertising content (e.g., website).
Financial Support: This work was supported by the Ministry of Science and Technology to Chen, C..

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EVIDENCE FOR ANHEDONIA IN EARLY RECOVERY FROM PRESCRIPTION OPIATE ADDICTION: AFFECT MODULATED STARTLE RESPONSE SUGGESTS BLUNTED HEDONIC RESPONSES TO NATURAL REWARD CUES.

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Aims: Aims: Addiction to opioids is associated with subjective anhedonia, and, in animal models, a decreased preference for natural rewards and elevated thresholds in a self-stimulation paradigm. These findings have been used to support the hypothesis that changes in the brain reward system, as a consequence of addiction to opioid drugs, contribute strongly to risk of relapse. The period directly following opiate withdrawal is marked by diminished pleasure from natural rewards and continued focus on drug related stimuli. This study used a well-established psychophysiological paradigm (affect modulated acoustic startle response; AMSR) to objectively evaluate hedonic responses in recently withdrawn prescription opiate dependent patients (RWP) in a clinical setting.
Methods: Methods: RWP (abstinent from opiates 10-14 days; n=9) and healthy controls (HC; n=4) were evaluated using AMSR as they viewed hedonically positive (rewarding), neutral, negative (threatening/disgusting), and drug related stimuli. Standardized electromyographic (EMG) and startle response data were collected. EMGs were averaged by stimulus category, and T-tests were used to compare AMSR amplitude across groups.
Results: Results: As predicted, RWP showed a lack of startle inhibition while viewing naturally rewarding stimuli relative to HC ($p<.05$), whereas HC showed the typical startle inhibition associated with positive hedonic evaluation.
Conclusions: Conclusion: RWPs failed to respond to naturally rewarding visual stimuli as hedonically positive. Their lack of positive response to natural rewards is consistent with the hypothesis that recovering opiate addicts experience anhedonia, likely as a result of dysregulated brain reward systems. The results demonstrate the feasibility of obtaining objective data on patients in a clinical setting that comport with findings in behavioral neuroscience-an important step in translational research.
Financial Support: Funding Source: R01DA035240-01

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ADHD AND SUBSTANCE USE DISORDERS: SUBTYPE AND GENDER DIFFERENCES.

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Aims: Attention deficit hyperactivity disorder (ADHD) and substance use disorders (SUD) are highly comorbid. However there is a lack of knowledge regarding the impact of gender and ADHD subtype on addiction severity and psychiatric comorbidity. This study aims to describe sociodemographic, addiction and psychiatric characteristics in a population of SUD treatment-seeking patients with ADHD and to highlight differences according to gender and ADHD subtype.
Methods: Newly admitted patients to an outpatient addiction clinic were interviewed with the Addiction Severity Index (ASI) for substance use history and addiction severity, the Mini International Neuropsychiatric Interview for DSM-IV Axis I psychiatric disorders and antisocial personality disorder (ASPD), and Conners' Adult ADHD Diagnostic Interview for DSM-IV (CAADID) for the diagnosis of lifetime ADHD.
Results:
58 patients with ADHD and current SUD were included between March 2011 and October 2014 (mean age: 31.1 y.o. (±8.8); 82.2% male). Interviewer ASI severity rates did not differ between gender, however the combined ADHD subtype (C subtype) was associated with higher rate for ASI Legal ($p=.013$). Regarding psychiatric comorbidities, borderline personality disorder was more prevalent in female (62.5% vs. 21.3%; $p=.02$), polyaddiction was more prevalent in the C subtype (84.6% vs. 39.1% in hyperactivity/impulsivity (HI) and 52.4% in inattentive (IN) subtype) and ASPD tended to be more prevalent in the C and HI subtype groups. We observed that the prevalence of the HI subtype was higher in women than in men (60.0% vs. 35.4%), however this difference was not statistically significant.
Conclusions: Results suggest the existence of differences in psychiatric comorbidities according to gender and differences in psychiatric comorbidities and addiction severity according to ADHD subtype. This highlights the needs of further studies with a larger sample to better define these patterns and to confirm the unusual ADHD subtype distribution in women.
Financial Support: PHRC 2006, MILDT 2010

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UNPREDICTABLE AVAILABILITY AS A DETERMINANT OF COCAINE CHOICE.

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Aims: Changing the responses required and reinforcer magnitude for drug and non-drug reinforcers can alter drug choice. These effects have been demonstrated primarily with fixed schedules and magnitudes of reinforcement. However, among humans and relative to non-drug reinforcers, illicit drugs may be less predictable in terms of availability, quality, location, time, and price. Thus, predictability may be an important aspect of reinforcement that differs for illicit drugs relative to other alternatives. We hypothesized that cocaine would be a more potent reinforcer in rhesus monkeys when the responses required and magnitude of each dose were made unpredictable.
Methods: Four male rhesus monkeys chose between doses of cocaine. In control conditions, both schedule and magnitude (i.e., cocaine dose) were fixed. In other conditions, the schedule, magnitude, or both were made variable (i.e., unpredictable) on one lever while all aspects on the other lever remained fixed. Sessions consisted of 6 sample and 12 choice trials. Each trial was separated by a 20-min timeout.
Results: Three of four subjects chose the variable over the fixed schedule, two of four subjects chose the variable over the fixed magnitude, and all subjects chose the variable option when both schedule and magnitude were made variable.
Conclusions: Not all subjects reliably chose the unpredictable schedule or magnitude alone. However, the combination of variability in schedule and magnitude reliably shifted choice toward the variable alternative. These findings suggest that unpredictable cocaine availability may serve to increase its potency and value as a reinforcer. Furthermore, unpredictability may be an important aspect of drug choice, especially for illicit drug abusers.
Financial Support: This research was supported by NIH grants DA076919 to SLH, DA027666 to KBF, DA033795 and DA011792 to JKR.

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FOOD INSECURITY AND HIV DRUG AND SEX RISK BEHAVIORS AMONG RUSSIANS LIVING WITH HIV.

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Aims: Food insecurity (FI), the limited availability or inadequate procurement of nutritionally sufficient food, has been shown to be associated with HIV transmission, with few studies in drug-using populations. We hypothesized that FI is associated with HIV risk behaviors among Russians living with HIV, many with recent substance use.
Methods: We analyzed baseline data from the Russia ARCH Cohort, a study of ART-naive people living with HIV (n=264) to assess the association between FI and HIV transmission risk. Primary outcomes were recent needle sharing and number of unprotected sexual contacts (USC). The Household Food Insecurity Access Scale was used to assess FI (any vs. none). Analyses used negative binomial and logistic regression models.
Results: FI was common in this cohort 146 (55%) with 96 (36%) current injection drug and 163 (62%) recent heavy alcohol users. Risk behavior characteristics were as follows: 26 (10%) reported 30-day needle sharing, and mean number of past 90-day USC was 15 (interquartile range 0-17). In analyses adjusted for age, gender, BMI, and employment, FI was associated with needle sharing (OR=4.10; $p=0.02$). There was no significant association between FI and number of USC (IRR=0.79; $p=0.46$) in analyses controlling for demographics, substance use, and number of sex partners.
Conclusions: Food insecurity occurred in a majority of HIV-infected Russians and was significantly associated with needle sharing but not sex risk. In a drug-related HIV epidemic, establishing and maintaining food security among key populations may be important to achieve effective HIV prevention and reduce drug risk behaviors.
Financial Support: U01AA020780;U01AA020779

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PRESCRIPTION OPIOID DEATH RATES ARE GREATER FOR FEMALES THAN MALES.

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Aims: In July 2013, the CDC showed prescription opioid deaths increased 400% for females compared to 265% for males from 1999-2010. We examined data from the RADARS® System Poison Center Program for similar trends.
Methods: We included data from the RADARS System Poison Center Program (49 poison centers) for adult deaths from January 2006-June 2014 mentioning oxycodone, hydrocodone, fentanyl, hydromorphone, morphine, oxymorphone, tapentadol, or tramadol. Death rates were analyzed using Poisson regression adjusting for gender-specific population and prescriptions dispensed. Covariates included gender, linear and quadratic terms for year-quarter, and linear and quadratic year-quarter by gender interactions. The trend in number of prescriptions per population was examined by gender using polynomial regression. Average quarterly changes in prescriptions per population were compared between genders.
Results: Prescriptions per population increased for both genders from 2006-2011, then leveled out. On average, females were dispensed 31.5% more opioid prescriptions per population ($p<0.001$). Population adjusted death rates increased for both genders until July 2010 then declined. Prescription adjusted death rates increased until October 2009 then declined. The death rates were higher for women than men in any given quarter, with the population adjusted death rate 45.2% higher for females than males ($p<0.001$), and the prescription adjusted death rate 10.5% higher for females ($p=0.069$). Quadratic models were significant for population and prescriptions rates and a cubic model was significant for prescriptions per population.
Conclusions: While trends in prescription opioid deaths are similar between genders, population and prescription adjusted rates of prescription opioid deaths were higher for females than males. The higher death rates in females may be due to greater drug availability.
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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THE GENDERED RISK ENVIRONMENT FOR INJECTION DRUG USE: AN EVENT SPECIFIC ANALYSIS OF INJECTION RISK BEHVAIOR.

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Aims: Previous research on injection risk behavior has largely focused on who is most likely to engage in these behaviors rather than examining when, where, and with whom individuals may be at heightened risk. The current study uses event specific data on injection drug use episodes to examine dyadic, network, and situational characteristics associated with injection risk behavior.
Methods: Data on multiple observations of injection episodes nested within participants (participant n = 784, episodes n = 1778) were used to examine both within and between person variation in injection risk behavior via multilevel structural equation modeling. Injection risk behavior was measured using a single latent variable with the following observed indicators: receptive sharing, distributive sharing, dividing drugs, non-syringe related sharing. Random slopes were estimated for the effect of gender concordance and sexual partnership on injection risk behavior to examine the variability of these associations across male and female injection drug users (IDUs).
Results: Results indicate that gender concordance was a significant predictor of injection risk behavior for females ($\gamma = 1.10$, $p = 0.001$) but not males ($\gamma = -0.51$, $p = 0.060$) and sexual partnership was a significant predictor of injection risk behavior for both males ($\gamma = 1.07$, $p < 0.001$) and females ($\gamma = 1.07$, $p < 0.001$). However, sexual partnership was more positively associated with injection risk behavior for females as compared to males.
Conclusions: The current study provides further evidence that IDUs injecting with sexual partners tend to be at higher levels of injection risk behavior. Furthermore, the effect of sexual partnership and gender concordance on injection risk behavior varied across male and female IDUs suggesting these dyadic characteristics may be more detrimental to female IDUs. However, future studies are required to further explore situational and dyadic predictors of injection risk behavior given that substantial within-person variability remained after including all predictors in the final model.
Financial Support: T32DA021129-07

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TREND IN SUBSTANCE USE ADMISSIONS AMONG OLDER ADULTS.

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Aims: To analyze the trend in substance use admissions among older adults (aged 55 and older) between 2000 and 2012.
Methods: Treatment Episode Data Set - Admissions (TEDS-A) for the period between 2000 and 2012 was used. We analyzed the trend in substance use admissions for older adults over the period between 2000 and 2012. Substance use admissions for older adults as a proportion of total substance use admissions were compared. Also, trend was analyzed for admission where the reason for admission was one of the following primary substances: cocaine/crack, marijuana/hashish, heroin, non-prescription methadone, other opiates and synthetics, methamphetamine, and benzodiazepines.
Results: Of the total admissions for substance use in 2000, 3.4 percent of admissions were for older adults. There was a gradual increase of this proportion over time, and in 2012, 7.0 percent of all substance use admissions were attributable to older adults. The older adults group also showed steep increase in proportion of admissions between 2000-2012 where primary substance that led to the treatment episode was cocaine/crack (63% increase), marijuana/hashish (150% increase), heroin (26% increase), non-prescription methadone (200% increase), other opiates and synthetics (221% increase), methamphetamine (275% increase), and benzodiazepines (67% increase).
Conclusions: While the total number of substance use admissions between 2000 and 2012 increased only marginally, the proportion of admissions attributable to older adults increased substantially. Substance use is an important psychosocial co-morbidity in older persons and episodes of admissions for substance use treatment appear to be on the rise for certain types of substances. Presence of substance use translates into treatment need, may affect health outcomes and complicate treatment of other co-morbid conditions. Thus a rise in substance use in older persons coupled with the aging of the US population has strong implications for the health system. The stage is set for development of appropriate preventive and treatment polices targeted towards older adults.
Financial Support: None

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CHANGES IN P300 EVENT-RELATED POTENTIALS VARY WITH CHANGES IN CRAVING AMONG METHAMPHETAMINE-DEPENDENT PATIENTS FOLLOWED AT 3 AND 6 MONTHS AFTER CESSATION.

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Aims: The study measured changes in P300 event-related potentials elicited by MA-related words in MA-dependent individuals at baseline and after 3 and 6 months of abstinence, examining the relationship of ERP changes to craving.
Methods: 26 MA-dependent patients newly enrolled in compulsory treatment centers in China and 29 healthy controls were included in this study. At baseline (2-3 weeks in treatment) and after 3 and 6 months of abstinence from MA use, we obtained ERP data during a MA Addiction Stroop task. Self-reported craving was measured by Visual Analog Scale (VAS). We hypothesized that the objective ERP data would correlate with subjective data on craving for MA.
Results: Increased P300 amplitudes elicited by MA-related words were observed over left-anterior electrode sites. Abnormal P300 amplitudes declined to the normal levels of healthy controls at the end of 3 months of abstinence, and the decrease was maintained to the end of 6 months of abstinence (GEE analysis: F GROUP*TIME =28.986, p0.001; Post hoc tests: baseline vs. end of 3 months: MD: 0.99399, $p=0.003$; end of 3 months vs. end of 6 months: MD: 0.01216, $p=0.973$). The behavioral data from both groups in the MA Addiction Stroop task did not show similar changes. The relationship between the changes of VAS scores for MA craving and the changes of P300 amplitudes over left-anterior electrode sites elicited by MA-related words within the first 3 months was significant ($r=0.181$, $p=0.034$).
Conclusions: These findings support the association between attentional bias for MA-related cues measured by the MA Addiction Stroop Task and drug craving, and also highlight the potential use of ERP as an objective index to track changes in subjective MA craving among MA-dependent patients.
Financial Support: This work was supported by the Shanghai Narcotics Control Fund (Grant number: 2012003), Ministry of Science and technology project (2012BAI01B07), and Shanghai Jiao Tong University School of Medicine Doctoral Innovation Fund (Grant number: BXJ201239).

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COMPARING ATTITUDES TOWARD ADDRESSING PATIENT DRUG USE AMONG HEALTH PROFESSIONALS IN TRAINING.

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Aims: The Substance Abuse and Mental Health Services Administration recently funded grants to train health professionals to conduct alcohol and drug use screening and brief intervention (SBI). Prior to training advanced practice nursing students (APRNs) in SBI, baseline survey data were collected and results compared to identical measures from first year medical residents.
Methods: APRNs (N=291) and first year medical residents (N=182) at 6 nursing schools and 6 residency programs completed a survey measuring attitudes and beliefs about addressing alcohol and/or drug misuse and current SBI practices.
Results: Respondents ranked the level of importance and their level of confidence in performing 9 components of drug SBI. APRNs rated 8 of 9 importance items significantly higher than residents. Only 1 confidence item differed: residents reported higher confidence than APRNs in advising at-risk patients to stop or reduce drug use. Respondents also ranked the level of importance placed on reasons for and barriers to addressing drug use in patients. APRNs scored significantly higher on all 8 items related to positive outcomes associated with drug SBI (e.g. improving family relationships, reducing healthcare costs). APRNs also scored higher on 4 of 9 items measuring barriers to performing SBI (e.g. inadequate training, uneasiness discussing drug use). Residents scored higher on only 1 barrier item related to preferring to diagnose and treat primary health issues rather than give preventive advice such as drug SBI.
Conclusions: Compared to residents, APRNs placed more importance on addressing patient's drug use and potential positive outcomes associated with SBI. While SBI training efforts may be more readily accepted among APRNs, perceived barriers could limit SBI implementation. Future studies should assess the ability of training programs to translate positive attitudes into increased SBI behavior.
Financial Support: SAMHSA

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COMPREHENSIVE WOMEN-CENTERED TREATMENT FOR SUBSTANCE USE DISORDERS IN GEORGIA: INITIAL EXAMINATION OF SEX RISK.

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Aims: Aims: Evaluate a comprehensive women-centered intervention to reduce illicit substance use and HIV risk among women in Georgia.
Methods: Study Design: Two-group randomized controlled trial compared an adapted comprehensive women-centered intervention Reinforcement Based Treatment and Women's Co-Op (RBT+WC) to usual care (UC).
Participants: 128 women met eligibility criteria: sexually active and injection of illicit drugs in the past 30 days.
Procedures: RBT+WC participants received a structured 12-session intervention focusing on reducing substance use and risky sex, and improving mental and physical health. UC participants received 12 sessions of case management and informational pamphlets focused on the same topics noted above. Assessments were conducted at baseline, treatment completion, and 3-month follow-up.
Hypotheses: Relative to UC participants, RBT+WC participants will, on average, show significant decreases in unprotected sex acts and increases in self-efficacy beliefs regarding abilities, proper condom use behaviors and negotiating safe sex encounters after treatment.
Results: Results. GEE models with a between-groups Treatment factor (RBT+WC v. UC) and a within-groups Time factor (baseline v. treatment completion v. 3-month follow-up) revealed only a significant decrease over Time for past 30-day number of unprotected sex acts ($p<.05$). Likelihood of unprotected sex at the most recent encounter, condom self-efficacy, or safe-sex self-efficacy were nonsignificant ($ps>.1$ for all effects).
Conclusions: Conclusions: Further evaluation of comprehensive women-centered interventions for reducing sex risk for substance-using women in Georgia is needed.
Financial Support: Financial Support: NIDA R01 DA029880 (Hendrée Jones, PI)

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A COMPARISON OF MECONIUM SCREENING OUTCOMES AS AN INDICATOR OF THE IMPACT OF STATE-LEVEL RELAXATION OF MARIJUANA POLICY.

Joseph T Jones, Aileen Baldwin, I Shu; Lab, United States Drug Testing Laboratories, Des Plaines, IL

Aims: A November 2012 ballot initiative allowing full commercialization which included large-scale production and statewide distribution went into effect in January of 2014. This study addresses the impact of relaxed marijuana policy on maternal marijuana use. The objectives of this study were two-fold. First, has there been an increase in the proportion of THCA positive meconium specimens? Second, has there been an increase in the concentrations observed for THCA in marijuana positive meconium originating from Colorado hospitals?
Methods: Meconium from high-risk newborns were collected and forwarded to USDTL. The specimens were homogenized, subjected to solid phase extraction, and the extracts were analyzed for cannabinoids using immunoassay. Presumptive positives were confirmed for THCA using GC/MS. The database query was limited to specimens originating from hospitals within Colorado and the first 9 months of the years 2012 and 2014. The data were analyzed for changes in the proportion of positive outcomes and the mean concentrations of THCA, the primary metabolite of marijuana, for each time period.
Results: The THCA positivity rate for all specimens in our database originating in Colorado increased from 10.6% to 11.7%, representing a 10.4% increase of positive specimens. The means of the determined concentrations of THCA in the meconium increased 69% with means of 213 ng/g ± 230.9 ng/g and 361 ng/g ± 420.3 ng/g for 2012 and 2014, respectively.
Conclusions: The data presented here showed that there was an increase of maternal marijuana users between the years 2012 and 2014. Also, it appeared that exposed neonates experienced substantially more exposure to marijuana *in utero*. The effects of prenatal marijuana exposure and the impact of state-wide marijuana policy on maternal marijuana use are largely unknown. This study demonstrated the need for more research to describe the effects of prenatal marijuana exposure and the need for policy makers to be aware of the unintended consequences of state-level marijuana policy.
Financial Support: USDTL

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ADOLESCENT D-AMPHETAMINE TREATMENT IN A RODENT MODEL OF ADHD: PRO-COGNITIVE EFFECTS DURING ADOLESCENCE AND COCAINE ABUSE RISK DURING ADULTHOOD.

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Aims: Despite high comorbidity of ADHD and cocaine abuse, the consequences of ADHD medications on cocaine abuse risk remain controversial, especially in teenagers. Preclinical work suggests that adolescent methylphenidate (MPH) treatment increases adult cocaine self-administration in the well-validated Spontaneously Hypertensive Rat (SHR) model of ADHD, emphasizing the need to identify less risky stimulant medications. We hypothesized that adolescent d-amphetamine (AMP), a stimulant with a different mechanism of action than MPH, would improve ADHD-related cognitive deficits without increasing later cocaine abuse risk in the SHR model.
Methods: Male SHR, Wistar-Kyoto (inbred control) and Wistar (outbred control) rats (n=8-12/strain and treatment) were treated throughout adolescence (P28-55) with a low therapeutic dose of AMP (0.5 mg/kg, i.p.) or saline (VEH). Cognitive function was assessed in adolescence by a strategy set shifting task, and cocaine abuse risk was assessed in adulthood by self-administration and cue-reinstatement procedures under a second-order schedule.
Results: During adolescence, VEH-treated SHR showed multiple deficits in set shifting performance compared to controls ($ps \leq 0.04$). Adolescent AMP treatment improved set shifting performance in SHR but not in controls ($ps \leq 0.04$). In adulthood, cocaine seeking and cocaine intake were higher in SHR than controls following adolescent VEH treatment ($ps \leq 0.03$). Adolescent AMP treatment did not further modify cocaine seeking or cocaine intake in adult SHR.
Conclusions: These findings highlight the utility of the SHR model in evaluating medication effects on ADHD-related cognitive deficits and cocaine abuse risk. Unlike MPH, AMP improved behavioral flexibility in adolescent SHR and did not increase cocaine abuse risk in adult SHR after treatment was discontinued. AMP may therefore be a safer stimulant medication than MPH for teenagers beginning ADHD treatment for the first time.
Financial Support: DA011716

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DEVELOPING A MULTIDIMENSIONAL MEASURE OF MARIJUANA-SPECIFIC COMMUNICATION WITH FRIENDS.

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Aims: Past peer-influence research has predicted adolescent drug use by assessing whether peers use drugs or how often peers communicate in general. Further research is needed to uncover the complexity of peer influence, paying particular attention to the content of conversations about drugs. This study aims to: (a) develop a multidimensional measure of communication, focusing on friends and marijuana use, and (b) determine how each message uniquely directly or indirectly relates to pro-marijuana beliefs.
Methods: Cross-sectional survey data were collected from 259 9th-12th grade students (M = 16.3 years, SD = 1.1; ages 14-18; 89% non-Latino White; 47% female). Confirmatory factor analyses (CFA) determined whether marijuana-specific communication with friends is multidimensional. Structural equation modeling (SEM) was used to examine anti- and pro-marijuana messages' direct and indirect associations with pro-marijuana beliefs.
Results: CFA results supported 11 different messages (e.g., conversations about disapproval of marijuana use or where to buy marijuana). SEM results did not support indirect associations but revealed significant direct associations. Conversations referring to negative attitudes toward marijuana, disapproval of marijuana use, and different types of marijuana were negatively related to pro-marijuana beliefs. Conversations referring to stereotypes about marijuana users, positive consequences of marijuana use, intentions to use marijuana, and the prevalence of peer marijuana use were positively related to pro-marijuana beliefs.
Conclusions: The content of conversations matters; peer influence occurs through a variety of verbal messages in addition to nonverbal ones (e.g., observing marijuana use). Certain messages may discourage pro-marijuana beliefs, whereas others may encourage them. Marijuana-specific communication with friends is nuanced, which is essential to capture to increase the efficacy of adolescent-focused drug prevention interventions and campaigns.
Financial Support: The Campus Research Board Award, University of Illinois at Urbana-Champaign

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A PILOT TRIAL OF VIGABATRIN FOR THE TREATMENT OF COCAINE AND ALCOHOL DEPENDENCE.

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Aims: Vigabatrin is an irreversible inhibitor of GABA transaminase and thus elevates brain GABA concentrations. It is approved for use as an anticonvulsant. In preclinical trials vigabatrin has been shown to reduce self-administration of both cocaine and alcohol. In three previous clinical trials it was shown to reduce cocaine use in cocaine dependent patients. It has not been previously evaluated in patients with comorbid alcohol and cocaine dependence.
Methods: This was an 8-week double blind, placebo controlled parallel group clinical trial involving 29 DSM IV cocaine dependent subjects with concurrent alcohol dependence. Subjects received 3 grams of vigabatrin or identical placebo each day along with weekly individual cognitive behavioral relapse prevention psychotherapy. Primary outcome measures included cocaine use measured by self-report, confirmed by twice weekly urine drug screens. And alcohol use measured by self-report. Additional outcome measures included cocaine craving measured by the Brief Substance Craving Scale (BSCS), alcohol craving measured by the Penn Alcohol Craving Scales, cocaine withdrawal symptoms measured by the Cocaine Selective Severity Assessment (CSSA), and adverse events.
Results: Twenty-one subjects (72%) completed the trial, with no significant between-group difference in treatment retention. Vigabatrin was not superior to placebo in promoting abstinence from cocaine or alcohol. There were no medication associated serious adverse events. Adverse events in this trial were generally mild and were evenly distributed between the two groups.
Conclusions: Vigabatrin is not a promising medication for the treatment of comorbid cocaine and alcohol dependence.
Financial Support: NIDA P50-DA-012756

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AMPHETAMINE EXPOSURE DURING ADOLESCENCE ALTERS ANXIETY- AND DEPRESSION-LIKE BEHAVIORS AND PREFRONTAL CORTEX DOPAMINE RECEPTOR EXPRESSION IN ADULTHOOD.

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Aims: We have previously demonstrated in male rats that repeated exposure to amphetamine (AMPH) from early- to mid-adolescence [postnatal day (P) 27 to 45] persistently alters the function of dopamine D_1 receptors in the medial prefrontal cortex (mPFC). Here, we determined if this functional change was associated with altered D_1 expression in the mPFC and nucleus accumbens (NAc), whether the timing of drug exposure (early- vs. late-adolescence) influenced drug-induced plasticity, and whether adolescent AMPH exposure altered anxiety- and depression-like behavior
Methods: Male and female Sprague-Dawley rats (n=78) were treated with saline or 3 mg/kg AMPH (i.p.) every other day (10 injections total) during early (P27 to 45) or late adolescence (P37 to 55). Sucrose preference (SP) tests were then performed after 1, 7, and 21 days of withdrawal. For each test, the consumption of water and 1% sucrose was measured for 48 h. Before the last SP test, anxiety-like behavior was assessed by measuring activity in an open-field arena and an elevated plus maze (EPM). Rats were sacrificed after finishing the last SP test, the mPFC and NAc were collected, and D_1 protein levels were measured using Western blot analysis.
Results: AMPH exposure induced a decrease of SP during the first test. In the EPM, early, but not late, AMPH treatment increased time spent in open arms. Lastly, we found decreased D_1 levels in the mPFC following early AMPH exposure.
Conclusions: Our preliminary findings suggest that adolescent AMPH exposure induces lasting changes in mPFC D_1 expression, which may play a role in the anhedonia and "risk taking" behavior we observed. Importantly, these drug-induced changes are more robust following early- compared to late-adolescent exposure, suggesting a heightened vulnerability to AMPH in early adolescence.
Financial Support: This study is supported by NIH (DA 029815)

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A NOVEL NEUROPEPTIDE REGULATOR OF BEHAVIORAL SENSITIZATION TO COCAINE.

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Aims: Neuromedin U (NMU) is a neuropeptide expressed in the mesolimbic pathway. NMU receptor 2 (NMUR2) is a GPCR and found in addiction associated areas of the brain including the nucleus accumbens shell (NAcSh). NMU signaling has been shown to regulate food reward, but has not been studied in the context of drugs of abuse. Therefore, we evaluated the effects of NMU on behavioral sensitization to cocaine and explored the underlying circuitry.
Methods: NMU's effect on the expression and development of cocaine sensitization was assessed by locomotor activity after microinjecting NMU directly to the NAcSh of sensitized or non-sensitized male Sprague-Dawley rats (n=10/group) before a cocaine challenge or during sensitization, respectively. The synaptic localization of NMUR2 was investigated using immunohistochemistry (n=3) and electron microscopy (n=3). Presynaptic function of NMUR2 was evaluated using retrograde knockdown of NMUR2 in the NAcSh followed by cocaine sensitization (n=10). Locomotor data was analyzed using one-way ANOVA.
Results: NMU decreased acute, but not sensitized, cocaine-evoked locomotion ($p<0.05$). NMU blocked cocaine-evoked locomotion when administered throughout the development of sensitization ($p<0.05$). NMUR2 was expressed presynaptically and colocalizes with an anterograde tracer from the dorsal raphe. Presynaptic knockdown of NMUR2 in the NAcSh potentiates cocaine-evoked locomotion after sensitization ($p<0.05$).
Conclusions: NMU in the NAcSh modulates the development, but not expression of behavioral sensitization to cocaine. The likely site of action for this behavioral effect is presynaptically expressed NMUR2 in the NAcSh. This work suggests a novel pathway in which NMUR2 is trafficked from the dorsal raphe to NAcSh synapses and regulates behavioral responses to cocaine.
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NEUROIMAGING AND COGNITIVE ABNORMALITIES IN ANABOLIC ANDROGENIC STEROID ABUSERS.

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Aims: In vitro studies suggest that supraphysiologic levels of testosterone and other anabolic-androgenic steroids (AAS) are neurotoxic, and one study has now found cognitive deficits in human AAS abusers. However, to our knowledge, no systematic brain imaging studies of AAS abusers exist. In a pilot study, we performed magnetic resonance imaging (MRI) and spectroscopy (MRS) in AAS abusers and controls.
Methods: We recruited male weightlifters age 35-55 reporting ≥ 2 years of cumulative lifetime AAS use (N = 10) or no AAS use (N = 10) for a psychiatric interview, cognitive testing including the CANTAB Paired Associates Learning (PAL) visuospatial function task, and a Siemens 3T MRI exam. Dorsal anterior cingulate cortex (dACC) J-resolved PRESS MRS scans were acquired from 8 AAS and 10 control subjects. MRI scans were reviewed by radiologists and analyzed with Freesurfer to detect volume differences. MRS spectra were analyzed using LCModel and a GAMMA-simulated J-resolved basis set.
Results: AAS users made more PAL errors (6 shapes) than controls (mean [SD]: 6.8 [5.4] vs 2.9 [2.5]; P = .036). We found no sigificant differences between groups in brain structural measures, but AAS abusers showed markedly decreased dACC scyllo-inositol (sI) levels vs. controls (.019 [.005] vs .031 [.010]; P = .003) – representing a very large effect size (Cohen's d = 1.6). Moreover, within the AAS users, lifetime AAS dose was negatively associated with sI levels at the trend level (ρ = -.63; P = .097).
Conclusions: Our findings of visuospatial cognitive deficits and sI depletion in AAS users appear consistent with prior findings suggesting AAS-induced neurotoxicity. Since sI is known to inhibit neurotoxicity induced by β-amyloid and other neurotoxic proteins, an AAS-induced dose-related sI depletion might represent a mechanism by which cognitive deficits may arise in long-term AAS abusers. Given that 2.9-4.0 million Americans have abused AAS, these findings should be pursued in a larger study.
Financial Support: NIDA grants R01DA029141 (HP, GK, JH) & K01DA029645 (AJ)

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THE RELATIONSHIP BETWEEN RISKY SUBSTANCE USE AND FRIENDS' USE OF NICOTINE, ALCOHOL, AND OTHER DRUGS IN AN ADOLESCENT SAMPLE.

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Aims: To examine the relationship between adolescents' use and their friends' use of nicotine, alcohol, and other drugs in a sample of primary care patients.
Methods: 525 adolescents 12-17 years old awaiting primary care appointments in Baltimore were recruited for a study evaluating a substance use screening tool. Participants were administered the Brief Screener for Tobacco, Alcohol, and Drugs (BSTAD), which is NIAAA's alcohol screening tool for youth expanded to include tobacco and drug use. The screening tool asks patients to report their substance use in the past year as well as their friends' use (friends questions are asked first for younger patients as a less threatening topic entree). The current study used contingency tables and joint frequency distributions for each substance to examine friends' use (no, yes) against patients' personal use risk level (low, high) based on previously-validated BSTAD cutpoints.
Results: Of the 37 adolescents with high risk nicotine use, 36 (97%) reported having friends who used nicotine in the past year. Similarly, 83 of 98 (85%) adolescents with high risk alcohol use and 73 of 77 (95%) adolescents with high risk use of other drugs had friends who used these substances. Conversely, 239 of 487 (49%) adolescents with lower risk for nicotine, 169 of 427 (40%) adolescents with lower risk for alcohol, and 156 of 445 (35%) adolescents with lower risk for other drugs had friends who used these substances in the past year.
Conclusions: Adolescents with high risk use of nicotine, alcohol, and other drugs are likely to report having friends who also use these substances. However, many adolescents who are not currently at risk based on personal use also have friends who use substances. Future research should evaluate the ability of the questions about friends' substance use delivered in pediatric settings to identify youth at risk of future problems, as well as its utility in guiding preventive interventions.
Financial Support: NIDA: R01 DA026003-S1

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POSITIVE ASSOCIATION BETWEEN CINGULATE BRAIN VOLUME AND SENSATION SEEKING IN YOUNG ADULTS.

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Aims: The impulsivity dimensions of Sensation Seeking (SS) and Disinhibition (DIS) are factors associated with drug use. Identifying neural correlates of these constructs during critical phases of brain development can inform clinical neuroscience-based efforts to understand and prevent transitions to substance abuse.
Methods: We used voxel-based morphometry to examine relationships between SS, DIS, and grey matter volume (GMV) in 87 young adults (45f, 42m; average age: 22.7 years). Non-correlated measures of SS and DIS, along with age and sex, were regressed in general linear models against modulated and smoothed brain maps representing tissue volume. Probability-based cluster corrections were performed.
Results: Based on well-established gender differences in brain development, analyses of correlations between SS, DIS and GMV were conducted separately for males and females. Analyses revealed a significant positive correlation between SS and GMV in clusters in the anterior and mid cingulate in males. A similar association was observed in females but did not reach statistical significance.
Conclusions: These data demonstrate that increased GMV in the cingulate cortex is associated with increased sensation seeking in young adults. Ongoing analyses are examining the relationship between GMV and functional measures of impulsivity. These results clearly identify the anterior and mid cingulate as a developmentally critical region associated with the biological expression of impulsivity – a well-established risk factor for drug abuse.
Financial Support: P50 DA005312 and UL1TR000117

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CONFLICT, SUBSTANCE USE AND HIV.

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Aims: This study developed and tested a longitudinal explanatory model of the relationship between conflict (between 2002-2008) and HIV disability-adjusted life years (DALYs) in 2010. This model differentiated between pre-existing background susceptibility factors and vulnerability factors reflecting conflict-induced changes that serve as moderating and mediating processes, respectively, through which conflict indirectly affects HIV morbidity/mortality. Special emphasis was given to alcohol and illicit drug use as a critical susceptibility construct.
Methods: Data on conflict (number of deaths from civil war, terrorism and one-sided violence), 2010 HIV attributable DALYs and susceptibility and vulnerability factors consisted of country-level data for each WHO Member State assembled from multiple sources. Partial least squares structural equation modeling was used to test the model.
Results: The first susceptibility construct (per capita alcohol consumption, injection drug use prevalence and illicit drug use prevalence indicators) served as a moderator of the conflict-HIV association ($t = 1.74$, $p < 0.05$) while the second susceptibility construct (ethnic heterogeneity, baseline HIV prevalence and number affected by natural disaster indicators) did not moderate the conflict-HIV association, but rather directly served to increase HIV DALYs ($t = 6.52$, $p < 0.05$). The vulnerability construct consisting of the number of people on ART, total spending on HIV and number of refugees, was shown to mediate the conflict-HIV association (conflict → vulnerability construct; $t = 6.62$, $p < 0.05$; vulnerability construct → HIV DALYs, $t = 8.65$, $p < 0.05$).
Conclusions: This study suggested that HIV interventions for conflict prone states include programs to reduce rates of alcohol use/illicit drug use, to reduce impact of natural disasters on the populace, and to foster political will to mitigate issues arising from ethnic heterogeneity. Among conflict-affected countries this paper suggests rapid scale up of ART, treatment for acute/chronic substance abuse, and consideration of influx of refugees on HIV morbidity/mortality.
Financial Support: NIDA (F32DA0364431: Dr. Kerridge); NIAAA (K05AA014223: Dr. Hasin)

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INSPECTION TIME AS A GENERAL MEASURE OF COGNITIVE IMPAIRMENT FOLLOWING ACUTE OPIOID EXPOSURE.

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Aims: Inspection Time (IT) is used to assess speed of information processing in a manner that, unlike other cognitive tests, is independent of motor components and reaction time. IT has been utilised to assess a range of disruptions in brain activity and is affected by drugs such as alcohol, but there is no information on the effect of acute opioid administration. We hypothesised that acute opioid administration would produce a concentration-related increase in IT comparable to that produced by moderate doses of alcohol.
Methods: Healthy volunteers were administered a single oral dose of immediate release oxycodone hydrochloride (20mg, n=37) or assigned to a control condition (n= 37). At 0, 1, 2, 4 and 6 hours post-administration, IT scores, blood samples and self-reported drug effects on validated scales were collected.
Results: IT scores were significantly higher compared to the control condition at 1hr (p=0.04), 2hr (p=0.02) and 6hr (p=0.03) post-administration oxycodone time points (ANOVA, post hoc). IT scores positively correlated to plasma oxycodone concentration (p=0.0009) and self-reported fatigue/inertia scores (p=0.03). Effect sizes (d) for oxycodone were 0.71, 0.59, 0.56 and 0.60 for 1, 2, 4 and 6 hours respectively. These effects are similar to those we previously reported for alcohol at a concentration of 0.045% (d=0.65) and greater than the peak effects of chronic methadone administration (d=0.40).
Conclusions: The results demonstrate that a conventional analgesic dose of oxycodone produces a long lasting slowing of information processing and that the magnitude of effect is comparable to the slowing produced by alcohol at a concentration prohibited for driving in many places. IT has significant potential as an objective measure of sedation/general performance impairment caused by a range of drugs.
Financial Support: Supported by an NHMRC Grant and an Australian Postgraduate Award

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ASSOCIATION BETWEEN MORNINGNESS/EVENINGNESS, ADDICTION SEVERITY AND PSYCHIATRIC DISORDERS AMONG INDIVIDUALS WITH ADDICTIONS.

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Aims: Chronotype, or morningness-eveningness preference, is defined as a "continuum" between two extremes; Morning-type (MT) and Evening-type (ET). Several studies have shown that Evening-Type (ET) subjects used more stimulating and sedative substances, and presented more psychiatric disorders than Morning-Type (MT) subjects. However, there is a lack of data on the chronotype of patients with addiction. The aim of our study was to describe chronotype and associated factors in a sample of outpatients beginning treatment for addiction.
Methods: Subjects were recruited in an outpatient addiction treatment center. Chronotype was assessed with the morningness-eveningness questionnaire (MEQ) of Hörne & Ostberg. Associated factors (addiction severity, socio-demographic characteristics and psychiatric co-morbidities) were evaluated with the Addiction Severity Index (ASI) and the Mini International Neuropsychiatric Interview (MINI).
Results: 333 substance use disorder subjects were included in this study (mean age= 40, SD=11; Men =63%). Evening-type (32%) was more prevalent than morning-type (20%). When comparing ET to MT (n=172), multivariate analysis showed that ET was significantly associated with poly-substances addiction (p=.01), non-substance addictions (p=.02), cannabis addiction (p=.01) compared to tobacco addiction (reference group), and mood disorders (p=.02), but not with severity of addiction. MT was associated with antisocial personality disorder (p=.02).
Conclusions: Results suggested that chronotype was associated with specific addiction pattern and psychiatric disorders, but not with addiction severity. Nevertheless, our study highlights an association between the ET and poly-substances addiction, non-substance addictions, cannabis dependence and depression.
Financial Support: PHRC 2006, MILDT 2010

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THE POINT OF A JOINT: A MULTIVARIATE CLASSIFICATION OF MARIJUANA USE MOTIVES.

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Aims: The marijuana-using population is highly heterogeneous, and understanding the factors that lead individuals to use marijuana (MJ) is the first step in preventing and treating cannabis use disorders (CUDs). We hypothesized that motives for MJ use would classify populations of MJ users, across demographic and cannabis use factors, personality, psychopathology and problems related to MJ use.
Methods: To that end, we used multiple correspondence analysis to identify relationships between MJ use motives (Marijuana Motives Measure) and age, age of onset of MJ use, frequency of MJ use, personality traits (NEO Five Factor Inventory), depression (Beck Depression Inventory), anxiety (Beck Anxiety Inventory), stress (Perceived Stress Scale), and, indicators of problematic MJ use (Marijuana Problem Scale) in 90 current, heavy MJ users (mean age = 26.25, 62 males, mean duration of use = 11.86 years). Bootstrap confidence intervals were calculated to determine significance.
Results: The results indicated five significant components. Component 1 differentiated older (> 30 years old), casual users from younger users with CUDs and who use MJ to cope with stress. Component 2 differentiated introverted users who use MJ to be social from those who use MJ to expand their creativity and awareness. Component 3 differentiated educated, introverted females who have social problems associated with MJ use from social, less educated males who use MJ to conform. Component 4 differentiated social users who have trouble fulfilling responsibilities from those with MJ withdrawal symptoms and who use MJ to cope with depression and anxiety. Component 5 differentiated older, educated women who started using MJ in their late teens from casual male users who started before the age of 13.
Conclusions: These results demonstrate clear distinctions between various factors that promote MJ use and the effects that result from MJ use. In conclusion, effective treatment strategies should take into account individual factors that surround MJ use, including MJ use motives, age, age of onset, gender, personality, education, and mood.
Financial Support: NIDA K01 DA021632, awarded to Dr. Filbey

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ONE FOR THE ROAD: THE ROLE OF SUBSTANCE MISUSE ON OUTCOMES FROM TRAUMATIC BRAIN INJURY.

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Aims: The relationship between substance use and TBI has been well established. Substance use is often implicated as a causal factor of TBI, with rates of intoxication at hospital admission ranging from 33-50% (Chen et al, 2012). Although much attention has focused on the relationship between TBI and comorbid substance misuse, fewer studies have examined the relationship between pre-existing substance misuse and outcomes. The present study seeks to futher elucidate this relationship.
Methods: Data for the present sample were abstracted from a trauma registry of individuals admitted to an urban, university based, Level I trauma center ED (N=2686). Inclusion criteria consisted of: ICD-9 diagnosis of TBI, between 18 and 65 years, and available alcohol and drug toxicology information (N=1872). Binary logistic regression and Poisson regression analyses, adjusting for age, gender, race, and general medical trauma severity, were run to compare TBI subjects with positive (TBIPOS) to TBI subjects with negative drug toxicology (TBINEG) on TBI outcome measures.
Results: Individuals with TBI who screened positive for illicit drugs or alcohol on ED admission (TBIPOS, n=762), and those with negative screens (TBINEG, n=1110) were compared. The majority were male (67%), Caucasian (56%), and mild TBI (86%). Results of the regression analyses noted significant differences between groups on proportion of ICU admissions (p= 0.0024), and TBI severity (p=0.0011), with TBIPOS subjects exhibiting worse outcomes. Further, results of the Poisson regression analyses revealed TBIPOS subjects had greater ICU lengths of stay (p=.009). No significant differences were noted between groups regarding hospital length of stay.
Conclusions: Study findings demonstrate the negative impact of pre-existing substance misuse on TBI outcomes. The low number of treatment referrals supports the need for a standardized system of screening and referral for this high-risk group.
Financial Support: Supported by VCU IDAS, U54DA038999

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CHILDHOOD PARENTAL INCARCERATION AND HIV-RELATED DRUG AND SEX RISK OVER THE YOUNG ADULT LIFE COURSE.

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Aims: To evaluate the association between childhood parental incarceration and marijuana use, sex risk behavior, and sexually transmitted infection (STI) from adolescence into adulthood.
Methods: We used Waves I (grades 7-12; adolescence), III (18-26 years; emerging adulthood) and IV (24-32 years; adulthood) of the National Longitudinal Study of Adolescent to Adult Health to measure associations between parental incarceration prior to age 18 years and marijuana use (adolescence: any prior use, emerging adulthood/adulthood: past year use); multiple (≥2) sexual partnerships (adolescence: any history, emerging adulthood/adulthood: past year history); and chlamydia, gonorrhea or trichomoniasis (adolescence/adulthood: self-reported STI, emerging adulthood: biologically-confirmed STI). We adjusted for age, race, gender, poverty and eight other childhood traumas (e.g., neglect; physical, emotional or sexual abuse; exposure to violence).
Results: Approximately 18% of respondents reported childhood parental incarceration; 28% of African Americans *versus* 16% of whites. In adjusted analyses, parental incarceration was significantly associated with marijuana use in adolescence (odds ratio (OR)=1.87, 95% confidence interval (CI): 1.59-2.19), emerging adulthood (OR=1.31, 95% CI: 1.09-1.56), and adulthood (OR=1.52, 95% CI: 1.27-1.81); multiple sex partners in adolescence (OR=1.40, 95% CI: 1.14-1.71) and adulthood (OR=1.20, 95% CI: 1.02-1.40); and STI in emerging adulthood (OR=1.42, 95% CI: 1.09-1.86) and adulthood (OR=1.76, 95% CI: 1.22-2.52).
Conclusions: Findings highlight the need for trauma-informed programming for those affected by the incarceration of a parent and for alternatives to incarceration, particularly for low level offenders with children.
Financial Support: NIDA R01DA036414

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RISK OF SEXUAL ABUSE AMONG ECSTASY USERS DIFFERS BY GENDER AND OTHER DRUG USE.

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Aims: Ecstasy users espouse PLUR (peace, love, unity, and respect) and may have lower risk for sexual abuse than other drug users. We hypothesized that among ecstasy and marijuana users, those who use other illicit drugs have a higher likelihood of experiencing lifetime sexual abuse, especially females.
Methods: Data come from the Tri-City study which recruited 644 recent ecstasy users, 16 to 59 years of age, from three sites in Florida, Missouri and Australia. Self-reported lifetime alcohol, marijuana, and other drug use (cocaine, heroin, sedatives, stimulants, opium, PCP, inhalants, hallucinogens, and steroids), lifetime sexual abuse, sex with a same sex partner, exchanging club drugs for sex, and number of sex partners were among the variables assessed. Analysis was restricted to 18 to 35 year olds (n=608) to reduce variance in years at risk.
Results: Overall, 38% endorsed ecstasy and marijuana use only, of which 12% reported lifetime sexual abuse. Among 62% who endorsed additional illicit drug use, 20% reported lifetime sexual abuse. Multivariate analysis showed an increased risk of lifetime sexual abuse for females, those having more sex partners, and same sex partners, and for those who used additional drugs. Separate logistic regression analyses showed that among women, having 3 or more sex partners versus less than 3 increased the odds of reporting sexual abuse (OR=3.0). Among men, additional drug use (OR=4.1) and exchanging club drugs for sex (OR=3.2) increased the risk of sexual abuse compared to their counterparts.
Conclusions: The risk of lifetime sexual abuse is higher among ecstasy and marijuana users who use additional illicit drugs than ecstasy and marijuana users alone. Gender differences in lifetime sexual abuse indicate a possible need for gender-specific interventions to reduce the risk of sexual abuse among ecstasy users. Further studies are needed to assess temporality.
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THE ACQUISITION OF COPING SKILLS FROM COMPUTERIZED COGNITIVE BEHAVIORAL THERAPY FOR SUBSTANCE USE DISORDERS: IT'S ALL WHERE YOU START.

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Aims: This study examined the acquisition of coping skills as a mediator of computerized cognitive behavioral therapy (CBT4CBT) at reducing cocaine use, attempting to replicate findings from a prior study.
Methods: Participants were drawn from an 8-week randomized trial comparing CBT4CBT to treatment as usual (TAU) among 101 cocaine-dependent individuals enrolled in a methadone maintenance program. An audio-taped role-play assessment, the Drug Risk Response Test (DRRT), was used to measure coping skills, with participant responses to high-risk situations rated by independent evaluators blind to treatment condition. Cocaine use was measured by self-report and urine screens during treatment and through a 6-month follow-up.
Results: 65 participants (TAU=33; CBT4CBT=32) completed the DRRT at pre- (week 0) and post-treatment (week 8). Repeated measures ANOVA revealed a significant effect of time [$F(1,64)=86.00, p<.001$) and treatment group [$F(1,64)=4.67, p<.01$], but no time x group interaction on the change in quality of coping skills. When level of coping skill quality at pre-treatment was categorized (low, medium, high), MANOVA revealed a significant time x group x level interaction [$F(2,59)=4.68, p<.01$] indicating those with lower quality skills at baseline showed greater improvement from CBT4CBT than TAU. Although the quality of coping skills was significantly associated with cocaine abstinence during treatment ($r=.36, p<.01$) and during a 6-month follow-up period ($r=.42, p<.01$), additional analyses did not support a mediation model.
Conclusions: Although this study did not replicate the quality of coping skills as a mediator of CBT4CBT, quality of skills acquired were related to cocaine abstinence, and those who started treatment with poorer quality skills showed greater improvement following CBT4CBT rather than standard outpatient drug treatment. This may have implications for tailoring drug treatment based on individuals' baseline coping skills set.
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CHEMOKINES AND CXCR4: ROLE IN COCAINE DEPENDENCE AND RELAPSE.

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Aims: Chemokines are best known for their neuromodulatory and chemotactic functions, but recent evidence suggests a role in cocaine addiction. The chemokine, CXCL12, is elevated in the plasma of cocaine abusers and activation of its receptor target and CXCR4 activation can enhance dopamine and glutamate transmission in reward circuits. Our study characterized the effect of CXCR4 receptor inhibition by AMD3100 on cocaine taking and relapse. Cellular and regional expression of CXCR4 at different stages of chronic cocaine exposure was also examined.
Methods: To assess AMD3100's effect on cocaine taking, rats were allowed to self-administer cocaine (0.375 mg/kg/inf) under a daily 2 hr FR-1 schedule. To investigate AMD3100's effect on relapse to cocaine, rats that successfully acquired self-administration under FR-1, were subjected to daily 2-h extinction sessions until extinction criteria were met and a one-time cue-induced reinstatement session. CXCR4 expression was examined by immunostaining prefrontal cortex (PFC), nucleus accumbens(Acb) and ventral tegmental area(VTA) of rats withdrawn from cocaine for 2 h and 2, 10 and 30 days.
Results: Cocaine intake was significantly decreased in rats treated with AMD3100. CXCR4 was differentially expressed in PFC, Acb and VTA and by dopaminergic neurons and astrocytes.
Conclusions: We provide the first evidence that the chemokines, specifically the CXCL12/CXCR4 system, can influence cocaine's addictive effects. The ability of AMD3100 to disrupt the cocaine acquisition and identification of CXCR4 in mesolimbic and corticolimbic substrates points toward studying the CXCR4 as an endogenous target for developing strategies to treat cocaine dependence and relapse.
Financial Support: RC1DA028153,T32 DA 07237

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CIGARETTE SMOKING AND FOOD INSECURITY IN SOCIOECONOMICALLY DISADVANTAGED YOUNG ADULTS.

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Aims: Tobacco use remains disproportionately high in certain groups, such as young adults and individuals with low socioeconomic status (SES). Prior research has shown that among low-income families, those with food insecurity (inability to afford enough food) have higher smoking prevalence than those without food insecurity. We examined associations between food insecurity and cigarette smoking among young adults with low SES.
Methods: We conducted a secondary analysis of the 2011/2012 California Health Interview Survey, a state-wide population-based telephone survey. Inclusion criteria for analysis included individuals who were (1) young adults (aged 18-30) and (2) considered low SES, defined as (a) having no more than a high school education and (b) being below 200% of the federal poverty level. Multinomial logistic regression analyses were conducted to identify correlates of smoking status (current, former, never) including demographics, health care source and utilization, alcohol use, distress, and food insecurity.
Results: Analyses included 1,511 young adults with low SES (21.8% non-Hispanic Whites; 53.1% female; 33.3% foreign born; 19.8% current smoker; 8.0% former smoker). Adjusted multinomial logistic regression analyses showed that current smoking was associated with past year food insecurity (p<.01), not having a usual source of health care (p<.05), past year binge drinking (p<.05), and past year psychological distress (p<.01). Former smoking was associated with past year binge drinking (p<.01) and past year experience with food insecurity (p<.01).
Conclusions: In a diverse young adult sample with low SES, experience of past year food insecurity was associated with both current and former cigarette use. This association persisted after controlling for demographic, behavioral, and psychological correlates of smoking. The association between food insecurity and cigarette smoking among socioeconomically disadvantaged young adults warrants greater attention given the disproportionately high rates of smoking in this group.
Financial Support: NIDA T32 DA007250, P50 DA09253

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MEDICAL MARIJUANA LAWS AND ANNUAL OPIOID ANALGESIC SALES IN THE UNITED STATES.

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Aims: To date, twenty-three states have enacted some type of medical marijuana legislation (MML), and more states may soon pass similar legislation. Concurrently, the epidemic of prescription opiate overdoses has recently shown signs of decline. It has been hypothesized that the increased availability of medical marijuana has provided a viable substitute for opioids in the treatment of chronic pain, resulting in fewer overdose deaths. This study assesses whether state MMLs are associated with actual opiate use, as measured by annual state opioid sales for the years 1999-2001.
Methods: Annual opioid sales for 1999-2011 were culled from the Automation of Reports and Consolidated Orders System (ARCOS), compiled by the Drug Enforcement Administration (DEA). This data includes annual sales of oxycodone, hydromorphone, hydrocodone, meperdine, and morphine to pharmacies, hospitals and practitioners by state. Morphine equivalent doses (MED) per 100,000 residents were calculated for each state-year observation. States were classified as having a MML based on the date the law became effective. Mixed models with a fixed effect for year and a random effect for state were used to estimate differences in the (natural log) average MED rate for states with and without MML by year and across years, while also taking into account state and year specific prescription opioid policies/regulations and unemployment rates.
Results: For both states with and without MML, the mean MED increased from 1999 to 2011 (25267 mgs vs. 23067.5 mgs and 89114.3 mgs vs. 89956.1 mgs, respectively). After controlling for this statistically increasing annual trend in MED (β=0.12, t-value=60.5, p-value<0.0001), a one percent reduction in annual opiate sales was observed for each additional year a MML was in effect (β=-0.01, t-value=-3.17, p-value=0.0016).
Conclusions: These findings suggest that medical marijuana laws are significantly associated with reduced prescription opioid sales at the state level. Further research is warranted.
Financial Support: NIDA grants T32DA031099 and R01DA037866

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CAN PERSONS WITH A HISTORY OF MULTIPLE ADDICTION TREATMENT EPISODES AND CHRONIC RELAPSE BENEFIT FROM TECHNOLOGY-DELIVERED BEHAVIOR THERAPY?

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Aims: A growing line of research has shown positive treatment outcomes from technology-delivered (e.g., web) behavior therapy for substance use disorders (SUDs). It is yet unknown if technology-based interventions can be effective with persons who have a history of multiple SUD treatment episodes and relapse. We examined the effectiveness of the Therapeutic Education System (TES), a web-based behavioral intervention grounded in the Community Reinforcement Approach to behavior therapy compared to traditional SUD treatment, for persons with varying SUD treatment histories.
Methods: We conducted a 12-month randomized controlled trial (n=160) with patients entering methadone maintenance treatment for opioid dependence, comparing standard treatment vs. a model where standard counseling was reduced in half and replaced with TES (the standard + TES). Urine results for opioids and cocaine abstinence were analyzed. Number of lifetime SUD treatment episodes, detoxification episodes, and inpatient/outpatient treatment episodes, which were categorized into three levels based on their one third quartiles, were treated as moderating factors.
Results: The standard + TES condition produced significantly better opioid abstinence than standard treatment for those with 1) a moderate or high frequency of lifetime SUD treatment episodes, 2) those with all levels (low, moderate and high) of detoxification, inpatient, and outpatient treatment episodes, p < .01. The standard + TES condition significantly enhanced cocaine abstinence compared to standard treatment among people with 1) a moderate or high frequency of lifetime SUD treatment episodes, 2) those with a high level of detoxification episodes, and 3) those with a moderate or high level of inpatient treatment history, p < .01.
Conclusions: Technology-assisted SUD therapy can be more effective than standard treatment, even among persons with a history of multiple SUD treatment episodes and chronic relapse.
Financial Support: NIH/NIDA R01 DA021818 and NIH/NIDA P30DA029926

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DOES SCREENING AND BRIEF INTERVENTION FOR DRUG USE IN PRIMARY CARE INCREASE RECEIPT OF SUBSTANCE USE DISORDER TREATMENT?

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Aims: Little is known about the efficacy of "RT" (referral to treatment) for increasing receipt of substance use disorder (SUD) treatment by patients with unhealthy drug use identified by screening. We compared receipt of SUD treatment between baseline and 6 months across three randomized groups: no intervention and two types of brief interventions.
Methods: Adults presenting to a hospital-based primary care clinic with recent drug use (Alcohol, Smoking and Substance Involvement Screening Test [ASSIST] drug specific score ≥4) were enrolled in a randomized clinical trial comparing: 1) 10-15 minute structured interview conducted by health educators (BNI), 2) 30-45 minute intervention based on motivational interviewing by Masters-level counselors (MOTIV) or 3) no brief intervention. All received information on treatment resources. We assessed receipt of any SUD treatment in a statewide database. Logistic regression analyses adjusted for main drug (self-identified), drug dependence and past SUD treatment.
Results: Among 528 participants the main drug was marijuana (63%), cocaine (19%), and opioids (17%); 46% met 12-month drug dependence criteria (Composite International Diagnostic Interview Short Form); 18% had ASSIST scores (≥27) consistent with dependence (past 3-months). At 6 months, 14% (73/528) received any SUD treatment. There were no significant differences in SUD treatment receipt: BNI vs control (adusted odds ratio [AOR] 1.16, 95%Confidence Interval [CI] 0.59, 2.30, Hochberg adjusted p-value=0.66); MOTIV vs control (AOR 0.45, 95%CI: 0.21, 0.97, Hochberg adjusted p-value=0.08). There were no significant interactions between intervention and main drug, severity (ASSIST), or prior SUD treatment.
Conclusions: Brief intervention did not increase receipt of SUD treatment in primary care patients. Future research should address how to make referral to treatment successful among screen-identified patients who could benefit from it.
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AN ASSESSMENT OF MDPV-INDUCED PLACE PREFERENCE IN ADULT SPRAGUE-DAWLEY RATS.

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Aims: Drugs of abuse have both aversive and rewarding effects, and the use and abuse potential of such drugs is thought to be a function of a balance of these affective properties. Characterizing these effects and their relative balance may provide insight into abuse vulnerability. One drug that has received recent attention is methylenedioxypyrovalerone (MDPV), a monoamine transport inhibitor similar to, but significantly more potent than, cocaine. MDPV is self-administered and produces aversive and rewarding effects in adult rats. The present study extended this characterization of the affective properties of MDPV by examining its ability to support place conditioning at a range of doses known to produce taste avoidance (Merluzzi et al., *Developmental Psychobiology*, 2014, *56*, 943-954).
Methods: Male Sprague-Dawley rats were injected with MDPV (1, 1.8 or 3.2 mg/kg) or saline and placed on the non-preferred side of a place conditioning apparatus for 30 min. On the next day, they were given an injection of saline and placed on the preferred side. This was repeated three times for a total of four conditioning cycles, and side preference was assessed on a final test.
Results: All doses of MDPV produced significant increases in time spent in the drug-paired chamber, an effect not seen in vehicle-treated animals. There were no significant differences in the degree of place preference conditioned by the three doses of MDPV.
Conclusions: At doses previously reported to produce conditioned taste avoidance in rats, MDPV induced place preferences, suggesting that like a variety of other drugs of abuse it has both aversive and rewarding effects. Given that such affective properties are important in drug use and abuse, understanding the various factors that impact each of these effects will be important in predicting vulnerability to MDPV.
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RANDOMIZED, CONTROLLED TRIAL OF CRAFT FOR PARENTS OF TREATMENT-RESISTANT ADOLESCENTS AND YOUNG ADULTS: INTERIM RESULTS.

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Aims: Little research has examined methods for helping parents with treatment-resistant adolescents (12-17 yrs) and young adults (18-25 yrs). We adapted the Community Reinforcement and Family Training (CRAFT) program for treatment-resistant adults for use by parents dealing with treatment resistant youth (12-25 yrs) and evaluated the revised program on efficacy in facilitating treatment entry, reducing drug use, and reducing behavior problems.
Methods: Parents (N=56) were randomly assigned to receive 12 individual sessions of either CRAFT (n = 32) or Alanon/NarAnon Facilitation Training (AFT; n = 24) delivered at our Family Training Program (FTP). Youth treatment entry was monitored weekly and at 3- and 6- month follow-up assessments. Substance use and behavior problems were monitored through parent report at 3- and 6-month follow-up assessments.
Results: Large differences were seen in the number of youth receiving a treatment referral with 75% of the CRAFT parents getting their child to FTP for a referral compared to 33% in the ANF group (X^2= 9.722, p=.002). Rates of transfer for youth from FTP to specialty treatment in the community were lower: 41% vs 29% in CRAFT and ANF, respectively. Although not statistically significant, there were small to moderate effect sizes for a group by time interaction for drug use (d=.38) and for problem reduction (d=.36 for adolescents; d=.62 for young adults) favoring greater reductions in CRAFT.
Conclusions: Preliminary results suggest that the modified CRAFT program is more efficacious than ANF in getting youth into treatment. Effects on drug use and problem behavior are not yet clear.
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A TEST OF THE AVERSIVE VERSUS THE REWARDING EFFECTS OF NICOTINE IN RATS NEONATALLY TREATED WITH QUINPIROLE.

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Aims: Neonatal quinpirole (a dopamine D2-like agonist) treatment to rats has been shown to increase dopamine D2 receptor sensitivity throughout the animal's lifetime, and increased dopamine D2 sensitivity is a hallmark of schizophrenia. Schizophrenics are 3 to 4 times more likely to smoke than the normal population, but there is no delineating mechanism.
Aim 1: Behaviorally test a rewarding versus averisve dose of nicotine in adolescent rats neonatally treated with quinpirole tested in a place preference paradigm;
Aim 2: Analyze phosphorylated cylic AMP response element bidning protein (CREB) in brain areas that mediate drug reward.
Methods: Rats were neonatally treated with quinpirole from postnatal days (P)1-21. After two drug free preferene tests were given in a place preference shuttle box at P41-42, animals were conditioned with saline, a 0.6 or a 1.8 mg/kg free base dose of nicotine for eight consecutive days. A post-conditioning test was given 24 h after conditioning. Time in the paired and unpaired context were measured. Approximately 24 h after the post-condioning test, brain tissue was harvested, flash frozen, and later analyzed for pCREB in the dorsal and nucleus accumbens.
Results: Results revealed that neonatal quinpirole enhanced the rewarding associative effects of the lower dose of nicotine compared to animals neonatally treated with saline and conditioned with the same dose of nicotine, which showed a slight place preference. Interestingly, although neonatal saline animals conditioned with the higher dose of nicotine demonstrated conditioned place aversion, neonatal quinpirole treated animals demonstrated no aversion to this same dose. Analyses for p-CREB will be presented.
Conclusions: Rats neonatally treated with quinpirole demonstrate an enhancement of the rewarding properties of nicotine, but do not demonstrate an aversion to higher doses of nicotine. These data are congruent with recent self-administration data in our lab, and suggest that increases of dopamine D2 sensitivity may blunt aversive aspects of nicotine.
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EMOTIONAL TRAITS PREDICT INDIVIDUAL DIFFERENCES IN AMPHETAMINE-INDUCED POSITIVE MOOD.

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Aims: Previous research on emotional correlates of individual differences in subjective responses to *d*-amphetamine (AMPH) has focused on relatively broad personality traits. Yet, emotional functioning is best characterized by many narrow intermediate phenotypes, each of which contribute to AMPH response. Here, we examine several subdomains of emotional functioning in relation to acute AMPH response.
Methods: Stimulant-naïve volunteers (N=97) completed baseline measures of seven subdomains of baseline emotional functioning: anhedonia, depressive and anxious distress, anticipatory and consummatory pleasure, and positive and negative affect. Then participants completed two 4-hour sessions during which they received a single dose of 20-mg oral AMPH or placebo in counterbalanced order. Subjective drug response measures were completed before and repeatedly after drug administration. Drug response data were reduced using principal component analysis (AMPH – placebo) into three higher-order factors: "positive mood," "arousal," "drug high." Separate regression analyses were conducted for these drug effects, in relation to the seven emotional functioning scales, controlling for sex, age and ethnicity.
Results: The combined set of emotional functioning indicators accounted for approximately 22% of the variance in AMPH-induced positive mood controlling for demographics. Greater anticipatory pleasure, lower trait negative affect, greater anhedonia, and greater anxious distress each uniquely predicted greater AMPH-induced positive mood. Emotional functioning did not significantly predict AMPH-induced changes in arousal or drug high.
Conclusions: These results suggest that: 1) emotional traits moderate positive mood, but not other dimensions of AMPH effects; and 2) different expressions of emotional functioning may differentially modulate AMPH's subjective effect profile. Several domains of emotional functioning may predict both acute responses to stimulants and perhaps also addiction risk.
Financial Support: Supported by NIDA K08-DA025041 (Leventhal).

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COMPREHENSIVE WOMEN-CENTERED TREATMENT FOR SUBSTANCE USE IN GEORGIA: INITIAL EXAMINATION OF DRUG USE AND HIV RISK.

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Aims: The aim of the study is to develop a comprehensive women-centered intervention to reduce illicit substance use and the rate of HIV infection among women.
Methods: Randomized controlled trial compared a Reinforcement Based Treatment and Women's CoOp (RBT+WC), to usual care (UC). Treatment and Women's CoOp (RBT+WC), to usual care (UC). 128 sexually active women who injected illicit drugs in the past 30 days. The RBT+WC condition provided a structured 12-session intervention designed to reduce HIV/HCV risk and drug and alcohol use, and improve mental and physical health, while the UC condition provided information booklets on a same topics as in the RBT+WC condition and case management for 12 sessions. Urine drug screening was conducted at each session and at 3-month follow-up. Assessments were conducted at baseline, treatment completion and 3-month follow up.
Results: Hypotheses: Compared to participants in the UC condition, participants in the RBT+WC condition will, on average, show significant decreases in frequency of sharing syringes and other injection paraphernalia, frequency of use of opioids, stimulants and alcohol.
Sharing of needles and injection paraphernalia rarely occurred in the sample, precluding inferential analyses. The decrease in past 30-day opioid use days from baseline to treatment completion to 3-month follow-up was larger in the RBT+WC (Means = 9.6 to 2.7 to 0.6) than in the UC condition (12.2 to 6.1 to 3.0), p=.047.
Conclusions: RBT+WC represents a promising comprehensive women-centered intervention for reducing drug use and HIV risks for substance-using women in Georgia.
Financial Support: NIDA R01 DA029880 (Hendrée Jones, PI)

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PROBLEMS OF TREATMENT DEMANDS RELATED TO SUBSTANCE DEPENDENCY.

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Aims: To study developments in substance-related treatment demands based on Federal statistical data in the Russian Federation, which is a part of medical monitoring.
Methods: Data on total registered prevalence and incidence from patients with substance abuse to state-supported narcological (addiction treatment) outpatient facilities in the Russian Federation during 2009-2013 was used. Analysis of indicator time series and their rates of change was conducted.
Results: Reduction in the total prevalence indicators was observed: alcohol -15%, all drug addictions -9%, other substance substances of abuse -24%. Exceptions were increase among some conditions, such as psychostimulant dependency, poly-drug dependency (+47%) and hazardous drug use without dependency.
The number of IDUs seeking treatment decreased, prevalence of HIV infection among registered IDUs has increased accordingly from 13% to 17%. The most alarming tendencies were observed for registered incidence indicator for psychostimulants which increased 8-fold, and for other drugs including poly-drug use which increased 2-fold in the last four years.
Conclusions: During 2009-2013 there was an overall downward trend in outpatient narcological treatment indicators. Along with this, a marked increase in treatment demands from patients with cannabinoid dependency, psychostimulant dependency, and other drugs including poly-drug dependency was observed. These trends in registered prevalence and incidence in the Russian Federation emphasize the need for further epidemiological studies in this field in order to investigate new trends in drug use prevalence, as well as the reasons behind narcological treatment demands' decrease. There is an urgent need for measures to encourage substance-related treatment demands from the population
Financial Support: 5K05DA17009-10

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KAPPA OPIOID AGONIST MESYL SAL B ATTENUATES BEHAVIORAL SENSITIZATION TO COCAINE WITH FEW SIDE-EFFECTS.

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Aims: Aims Acute activation of kappa opioid receptors is known to suppress the effects of cocaine. However, side-effects such as aversion, sedation, anxiety and depression limit their clinical use. Mesyl Sal B, is a potent and selective analogue of salvinorin A with improved pharmacokinetics. Recently Mesyl Sal B been shown to attenuate cocaine-prime induced drug seeking in rats. We aim to evaluate the anti-cocaine effects of Mesyl Sal B utilizing locomotor tests and screen for side effects.
Methods: Methods: The effects of Mesyl Sal B (0.3 mg/kg) were evaluated preclinically in male Sprague Dawley rats. The effects of Mesyl Sal B pretreatment on cocaine-induced hyperactivity (20 mg/kg; i.p) and behavioural sensitization to cocaine were determined (20 mg/kg; i.p daily, days 1-5, testing day 10). Sucrose self-administration was used to evaluate anhedonia and conditioned taste and place aversion paradigms were used to test for aversion. The elevated plus maze was used to measure anxiety and the forced swim test was used to evaluate depression.
Results: Results: Mesyl Sal B pretreated rats show reduced cocaine-induced hyperactivity and a significant reduction in locomotor activity following behavioural sensitization. Mesyl Sal B had no effect on oral sucrose reinforced responding or taste aversion. Mesyl Sal B had no significant effects on time spent in the open arm in the elevated plus maze. In contrast, salvinorin A, significantly decreased the time spent in the open arm of the elevated plus maze. However, increased immobility was observed in the forced swim test indicating pro-depressive effects.
Conclusions: Conclusions: Mesly Sal B is a longer acting analogue of salvinorin A with improved side effects. It attenuates the locomotor effects of cocaine without inducing aversion, modulating sucrose reward or inducing anxiety in rats. However pro-depressive effects remain.
Financial Support: Neurological Foundation of New Zealand

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TREATMENT EXPECTATIONS PREDICT QUIT ATTEMPTS, REDUCTION IN CIGARETTES PER DAY, AND READINESS TO QUIT IN SMOKERS WHO WERE NOT READY TO QUIT.

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Aims: Treatment expectations predict outcomes for many interventions and could be especially important for the majority of smokers who are not motivated or not able to quit in the near future. The current study examines expectations for three non-pharmacological telephone based brief interventions to increase quit attempts (QA) in smokers who are not ready to quit. We hypothesized that greater expectations for treatment will predict increased 1) number of QA, 2) reduction in cigarettes per day (CPD), and 3) readiness to quit.
Methods: 410 participants who smoked ≥10 CPD and were not ready to quit in the next month were randomized to receive usual care, a reduction-based intervention, or a motivation-based intervention. Expectation for treatment was measured using a modified version of the Credibility/Expectancy Questionnaire (CEQ). The CEQ is a self-report measure of the extent to which participants believe that the intervention is logical and will lead to changes in their smoking. QA (defined as 24 hours of abstinence), readiness to quit, and CPD were measured via self-report at the end of treatment (four weeks after participants' initial counseling call).
Results: CEQ scores significantly predicted QA (β=0.20, p<.01), reduction in CPD (β=0.16, p<.01), and readiness to quit (β=0.23, p<.001). Participants with a CEQ score above the sample's median made a mean of 0.45 QA while those below made a mean of 0.27 QA. Further, those above the median CEQ reduced by a mean of 4.17 CPD while those below reduced by a mean of 2.79 CPD. There was not a significant interaction between CEQ and condition. Six month abstinence data will be reported.
Conclusions: Smokers' expectations for treatment predict subsequent QA, reduction in CPD, and readiness to quit. Implications from these findings and analyses examining other constructs will be discussed.
Financial Support: This work was supported by NIDA 5 T32 DA 7242-23 and NCI CA163176.

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ALCOHOL SCREENING AND BRIEF INTERVENTION AMONG OPIOID AGONIST PATIENTS IN A PRIMARY CARE AND OPIOID TREATMENT PROGRAM.

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Aims: Problem alcohol use is associated with adverse health and economic outcomes, especially among people in opioid agonist treatment. Screening, brief intervention and referral to treatment (SBIRT) are effective in reducing alcohol use; however, SBIRT implementation among opioid agonist patients is unknown.
Methods: To assess identification and treatment of alcohol use disorders, we reviewed clinical records of opioid dependent agonist patients screened for an alcohol use disorder in a federally qualified health centerprimary care clinic (n =208) and in an opioid treatment program (n = 204) over a two year period.
Results: In the primary care clinic, 193 (93%) buprenorphine patients completed an annual alcohol screening and six (3%) had elevated AUDIT scores. Among the patients treated in the opioid treatment program, an alcohol abuse or dependence diagnosis was recorded for 54 (27%) methadone patients. Practitioner focus groups were completed in the primary care (n = 4 physicians) and methadone clinicsopioid treatment program (n = 11 counsellors) to assess experience with and attitudes towards screening opioid agonist patients for alcohol use disorders. Focus groups suggested organizational, structural, provider, patient and community variables hindered or fostered alcohol screening.
Conclusions: Alcohol screening is feasible among opioid agonist patients. Effective implementation, however, requires physician training and systematic changes in workflow.
Financial Support: National Institute of Drug Abuse (NIDA) financed this research via INVEST Fellowship award (2013). Additional support was provided through the Western States Node of the National Drug Abuse Treatment Clinical Trial Network (U10 DA015815) and an award from the Substance Abuse and Mental Health Services Administration for SBIRT Oregon (TI020272).

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ACCESS TO BUPRENORPHINE TREATMENT: IS THE PATIENT LIMIT A BARRIER?

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Aims: Physicians in the US who are waivered to prescribe buprenorphine for opioid dependence are limited to 30 patients at any one time in the first year, after which they may submit a notification to treat up to 100 patients concurrently. Some contend these patient limits are a barrier to treatment. This study aims to address whether the 100-patient limit should be raised.
Methods: The percentages of physicians holding the 30-patient and 100-patient waivers were extracted from the DEA's Controlled Substance Act Registrants Database. Data on current caseloads and perceptions of the 100-patient limit were obtained via mailed surveys of current prescribers (n=193) from June-November 2014.
Results: In November 2014, 25,738 physicians were waivered to prescribe buprenorphine; only 31.0% held the 100-patient waiver. The average caseload was greater for 100-patient prescribers (mean=63.3, SD=34.6) than 30-patient prescribers (mean=19.6, SD=21.0; t=-10.2, p<.001), but both averages represent just two-thirds of current treatment capacity. When rating the statement, "I could provide quality care to more than 100 patients if there was a higher patient limit" on a scale ranging from 1 (strongly disagree) to 5 (strongly agree), the average response was 3.2 (SD=1.4). Although 100-patient prescribers more strongly endorsed this statement (mean=3.6, SD=1.3) than 30-patient prescribers (mean=2.6, SD=1.2; t=-5.4, p<.001), the mean for the 100-patient prescribers was between "neither" and "agree."
Conclusions: Current prescribers of buprenorphine report ambivalence about providing high quality care to more than 100 patients. Furthermore, prescribers are only treating about two-thirds of the patients allowed by their waivers. These data, coupled with the limited number of prescribers with the 100-patient waiver, suggest that raising the patient limits may have a limited impact on treatment access while potentially eroding the quality of care.
Financial Support: Supported by the National Institute on Drug Abuse (R33DA035641).

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ASSESSMENT OF HUMAN ABUSE POTENTIAL OF DASOTRALINE COMPARED TO METHYLPHENIDATE AND PLACEBO IN RECREATIONAL STIMULANT USERS.

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Aims: Dasotraline is a novel dopamine norepinephrine reuptake inhibitor currently being investigated in clinical studies for the treatment of ADHD at doses up to 8 mg/d. It was hypothesized that dasotraline would be characterized by minimal subjective reinforcing effects based on potent inhibition of norepinephrine reuptake and its pharmacokinetics of slow absorption/elimination in humans. This study evaluated the abuse potential of dasotraline compared to placebo and methylphenidate.
Methods: Recreational stimulant users (N=48) who had specific experience with cocaine, and who were able to distinguish methylphenidate (60mg) versus placebo in a qualification session, were randomized to a 6-period, double-blind, crossover treatment phase. Treatment phase consisted of placebo, methylphenidate (40mg, 80mg), and dasotraline (8mg, 16mg, 36mg). Subjective measures were evaluated over 72h postdose. The primary endpoint was Emax on the Drug Liking Visual Analog Scale (VAS).
Results: All 3 doses of dasotraline were not significantly different when compared to placebo on the primary (Drug Liking VAS) and most secondary endpoints. Methylphenidate significantly increased Drug Liking (VAS Emax, p<0.001), supporting the validity of the study and sensitivity of the measures for detecting abuse-related effects. The 8mg and 16mg doses of dasotraline were associated with a similar incidence of adverse events (AEs) as placebo. A greater number of AEs and negative subjective effects (VAS Emin, p<0.004 vs. placebo) were observed at 36mg dasotraline. Among potentially abuse-related AEs, incidence with dasotraline was lower than with methylphenidate.
Conclusions: These results suggest that dasotraline has minimal abuse potential and is unlikely to be recreationally abused. Dasotraline is an investigational agent being evaluated for the treatment of ADHD which presents a novel pharmacologic and pharmacokinetic profile.
Financial Support: Supported by Sunovion Pharmaceuticals Inc.

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A BEHAVIORAL ECONOMIC DEMAND MODEL MODIFICATION TO IMPROVE VERSATILITY.

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Aims: Behavioral economic demand curves quantify the relationship between the price of a commodity and the consumption of that commodity and are often used to measure how an individual or group values a commodity, including drugs of abuse. The exponential model of demand proposed by Hursh and Silberberg (2008) quantifies this relationship and provides indices of demand elasticity (sensitivity to price) and demand intensity (amount of consumption unrestricted by price). One limitation of this model, however, is that it relies on consumption measured in logarithmic units, which prevents consumption values of zero units from being incorporated into analyses. Replacing zeros with nonzero values also presents problems, with the specific value chosen often affecting the statistical conclusions.
Methods: Here, we present a modification of this formula that allows the valid inclusion of unaltered consumption values of zero units. We compared the two functions on a large dataset of hypothetical drug purchase task data (n = 1215) collected online.
Results: Our model modification provides measures of demand intensity and elasticity that are highly correlated with and directly comparable to the measures produced by the Hursh and Silberberg (2008) equation, but was able to fit 100% of the individual subject data series instead of just 69%.
Conclusions: Our model provides a more flexible approach to analyzing demand data that can accommodate more datasets and provides estimates of demand intensity and elasticity that are backward compatible with the popular Hursh and Silberberg (2008) model. Details of the model modification, curve fit comparisons, and discussion of advantages and disadvantages will be presented.
Financial Support: NIH/NCI grant U19 CA157345 and institutional funds to WKB.

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EFFECTS OF L-METHAMPHETAMINE ON THE DISCRIMINATIVE STIMULUS AND REINFORCING EFFECTS OF COCAINE.

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Aims: Monoamine releasers such as methamphetamine (MA) have been shown to significantly reduce cocaine use and craving in human subjects, supporting their use in the management of cocaine dependence. However, high abuse potential limits the clinical utility of d-MA and similar monoaminergic drugs. Interestingly, the MA molecule consists of a chiral center containing two isomers; d- and l-MA. The d-isomer is a potent stimulant with high abuse liability while l-MA is not, possibly due to its lower potency as a dopamine releaser. The present study investigated the ability of l-MA to substitute for the discriminative stimulus effects of cocaine and its ability to decrease cocaine self-administration.
Methods: Adult rhesus monkeys (N=5) were trained to discriminate cocaine (0.4 mg/kg, IM) from saline using food-maintained performance in standard drug discrimination procedures. The discriminative-stimulus effects of l-MA were then studied in time-course and interaction studies. Another group of monkeys (N=4) responded under a second order FR2(VR16:S) schedule of food or IV cocaine (0.032 mg/kg/inj) reinforcement. The effects of chronic treatment (5-10 days) with l-MA (0.032-0.32 mg/kg/hr, IV) on food- and cocaine-maintained responding were then assessed.
Results: In cocaine-discrimination studies, l-methamphetamine dose-dependently increased responding on the cocaine-associated key in a time-dependent manner. Acute pretreatment with l-MA did not significantly alter the cocaine discrimination dose-effect curve. In self-administration studies, chronic treatment with l-MA dose-dependently decreased cocaine-maintained responding with complete suppression of cocaine intake at the highest dosage tested. Food-maintained responding was not appreciably affected by l-MA treatment.
Conclusions: These results suggest that l-MA shares discriminative stimulus effects with cocaine and reduces cocaine self-administration. Further evaluation of l-MA as a candidate agonist replacement therapy for cocaine dependence is warranted.
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INFORMING THE REGULATION OF E-CIGARETTES TO RESTRICT YOUTH ACCESS.

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Aims: The FDA proposes to regulate e-cigarettes, with a focus on protecting youth. To better inform the FDA, we evaluated how adolescents obtain e-cigarettes, where they use e-cigarettes, and how they view e-cigarettes.
Methods: We conducted surveys in 5 high schools and 2 middle schools in CT (N=5152) in Spring 2014 to assess these important issues. The sample was 51% female and 15.3 (SD=1.9) years old.
Results: Among lifetime-e-cigarette users (23%), 37% reported obtaining e-cigarettes from friends, 13% from tobacco shops, 9% from gas stations, and 7% from online stores. Among adolescents <18 years old who tried to purchase an e-cigarette from a store (n=429) or an online store (n=367), 77% and 89%, respectively, reported that they were not denied purchase. Lifetime e-cigarette users reported using e-cigarettes in their home (51%), school (25%) and public places where smoking is not allowed (24%). Among the total sample, the availability of different flavors (17%), ability to do smoke tricks (14%), and the ability to customize flavors (9%) were the top appealing components of e-cigarettes. Logistic regression analyses showed that lifetime e-cigarette users were more likely than never-users to view the availability of different flavors (OR=94.07), the ability to do smoke tricks (OR=218.74), and the availability of odorless vapors (OR=4.25) as appealing; whereas, non-users were more likely than lifetime users to view external features of e-cigarettes, such as its shape (OR=5.11) and the ability to "light up" (OR=4.38) as appealing.
Conclusions: The findings underscore the need to regulate e-cigarette sales to minors, including online purchases, and prohibit e-cigarette use indoors where cigarette smoking is prohibited. Furthermore, restricting various flavors, eliminating visible vapors, and reducing the appeal of the e-cigarette design may lessen youth interest.
Financial Support: P50DA009241, P50DA036151, UL1 TR000142, KL2 TR000140

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ORAL HUMAN ABUSE POTENTIAL OF OXYCODONE DETERX: AN ABUSE-DETERRENT, EXTENDED-RELEASE FORMULATION IN RECREATIONAL OPIOID USERS.

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Aims: Oxycodone DETERx(DETERx) is a multiparticulate, extended-release, abuse-deterrent analgesic. The oral abuse potential of chewed and intact DETERx was compared with crushed immediate-release(IR) oxycodone.
Methods: Subjects with a history of recreational opioid use who were nondependent, nontolerant to opioids were enrolled. After passing the Drug Discrimination Test, subjects entered into a double-blind, randomized, triple-dummy Treatment Phase: intact DETERx(fed), chewed DETERx(fed), crushed IR oxycodone(fasted), and placebo(fed). Endpoints: Drug Liking (primary: bipolar visual analogue scale[VAS]), Drug Effects Questionnaire, Overall (Global) Drug Liking, Addiction Research Center Inventory-Morphine Benzedrine Group, Take Drug Again, Price Value Assessment, Pupillometry. Plasma samples were collected to determine standard pharmacokinetic(PK) parameters. Safety was assessed.
Results: 38 subjects completed the study. Primary pharmacodynamic measurements for crushed IR oxycodone v. placebo confirmed study validity ($p < 0.0001$). LS Mean E_{max} for Drug Liking was significantly lower for chewed and intact DETERx than crushed IR oxycodone($p<0.0001$). TE_{max} was significantly longer for chewed and intact DETERx than for crushed IR oxycodone($p<0.0001$). Chewed and intact DETERx demonstrated less liking than crushed IR oxycodone for Any Drug Effects, High, Good Drug Effects, Sick, Sleepy, Dizzy, ARCI-MBG, Overall(Global) Liking($p \leq 0.0319$). Results of all other end point assessments supported the results of Drug Liking. DETERx chewed did not change the PK profile compared with intact DETERx. IR oxycodone crushed fasted resulted in higher C_{max} and shorter T_{max}(greater AQ), than after all methods of administration of DETERx. Study treatments were well tolerated.
Conclusions: These study results demonstrate lower abuse potential of chewed and intact Oxycodone DETERx in the fed state than crushed IR oxycodone when taken orally.
Financial Support: Collegium Pharmaceutical, Inc.

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GENDER DIFFERENCES IN HISTORY OF SEXUAL AND PHYSICAL ABUSE IN RELATION TO ADDICTION SEVERITY.

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Aims: Many individuals with substance use disorders (SUD) have a history of sexual and/or physical abuse. We hypothesized a stronger association between abuse and addiction severity in women versus men.
Methods: Using baseline data from six SUD treatment studies in the National Drug Abuse Treatment Clinical Trials Network (CTN 01, 02, 04, 05, 06, and 07; total 589 women and 810 men), t-tests and regression modeling were used to examine gender differences in the association between lifetime report of sexual and physical abuse in relation to subscale composite scores of the Addiction Severity Index (ASI).
Results: Women had higher scores than men on severity ratings for the drug ($p=0.002$), employment ($p=<0.0001$), family/social ($p<0001$), medical ($p<0.0001$), and psychiatric ($p<0.0001$) composites of the ASI. For men and women, sexual and physical abuse were associated with higher severity on medical, family/social, and psychiatric composites. In women only, abuse was associated with higher severity on the legal composite (0.16 vs. 0.10 for sexual abuse, $p=0.0008$; and 0.14 vs. 0.11 for physical abuse, $p=0.03$); however, in regression models, the gender interaction terms were not significant. Women with no history of abuse had significantly better scores on the legal composite (range 0.10-0.11) than both genders with abuse history and men without reported abuse (range 0.14-0.16).
Conclusions: While abuse history was associated with higher ASI severity in many domains, only the legal composite subscale demonstrated a stronger association for women between history of abuse and greater addiction severity. This composite is based partially on illegal activities for profit, suggesting that the constellation of experiences associated with a history of abuse in women are related to increased engagement in illegal activity for profit to the level seen in men. More research is warranted to more closely investigate the specific illegal activities (e.g. drug dealing, prostitution), as these may differ significantly between men and women.
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RISKY DECISION-MAKING IN HIV-INFECTED AND NON-INFECTED METHAMPHETAMINE USERS.

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Aims: To assess impulsive decision-making in persons with methamphetamine use disorder. We hypothesized that a novel sexual delay discounting task would correlate with other impulsivity measures in subjects with and without HIV infection.
Methods: Eligible subjects were age 18-55, sexually active, with methamphetamine dependence, and excluded for past 30 day opioid use or serious illness. In the sexual probability discounting task (SexPD), participants made a list of 10 people in order of sexual appeal (10=most appealing) and then chose between having sex with a "10" with varying chance of sexually transmitted infection (STI) (0%-15%) vs. sex with a less attractive partner with 0% chance of STI. Choices repeated varying sexual appeal and STI risk to calculate indifference curves. Subjects completed standard delay discounting (SDD), probability delay discounting (PDD), and Barrett Impulsivity Scale (BIS). Risk Assessment Battery (RAB) assessed risk behaviors. We assessed correlations between tasks and associations using Pearson correlation coefficients and linear regression.
Results: Of 48 subjects, 67% were male, 31% HIV-infected and mean age was 37 (SD 9.7) years. 58% reported unprotected sex and 23% reported injection drug use in past 30 days. The SexPD task was correlated with BIS (0.494, p=.002) and no other measures. Mean SexPD AUC was greater in HIV-infected vs. non-infected subjects (0.63 vs. 0.31, p<.001). In HIV-infected subjects, SDD was associated with increased injection drug use (β=0.46, 95% CI 0.15, 0.76) and RAB drug risk score (β=0.15, 95% CI 0.04, 0.26), and a trend between SexPD and RAB sex risk score was identified (β=0.02, 95% CI -0.02, 0.06).
Conclusions: HIV-infected subjects with methamphetamine use disorder demonstrate increased risky decision-making regarding sexual decision using a novel sexual delay discounting task. Further research is needed to assess correlates with risky behaviors.
Financial Support: NIH (R21DA033182, P50 DA018165, UL1 RR024140 01, UL1TR000128)

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REDUCING THE COST OF FREE TIME: TREATMENT SUCCESS IN A RANDOMIZED TRIAL OF CLONIDINE AS ADJUNCT TO BUPRENORPHINE MAINTENANCE IS ASSOCIATED WITH MORE LEISURE ACTIVITIES IN THE CLONIDINE CONDITION.

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Aims: In an RCT examining regular clonidine for prevention of stress-induced lapses to opioid use during buprenorphine maintenance, we found clonidine increased time to lapse and longest duration of abstinence. In Ecological Momentary Assessment (EMA) data from the trial, clonidine decoupled stress from craving. Here we specifically examine clonidine's effects on daily-life activities.
Methods: Outpatients (N=118) received clonidine (0.3 mg/day) or placebo during buprenorphine maintenance. A split half on longest opioid abstinence created two treatment success levels. Using SAS PROC GLIMMIX models, we assessed the likelihoods of different types of daily activity (assessed 4x/day by EMA) as a function of clonidine vs. placebo, treatment success category, and their interaction.
Results: In the clonidine group, treatment success was associated with higher frequency of leisure activities with the effects being reversed or not present for the placebo group (interaction effects: TV, F=108, P<.0001; music, F=124, P<.0001; socializing, F=73, P<.0001; reading, F=48, P<.0001; thinking, F=164, P<.0001; waiting, F=20, P<.0001). In the placebo group, treatment success was associated with higher frequency of activities associated with responsibilities, such as working (F=17, P<.0001) and child or elder care (F=20, P<.0001).
Conclusions: The protective effect of time spent at work for our standard-care group is consistent with previous EMA findings showing that participants are less stressed at work than at home or elsewhere. Our new results suggest clonidine's decoupling of stress from craving helped participants engage in free-time activities with less risk of using opiates.
Financial Support: *NIDA, IRP*

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IS MARIJUANA USE ASSOCIATED WITH LESS OPIOID USE AMONG PEOPLE WHO INJECT DRUGS?

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Aims: Research has shown various therapeutic uses of marijuana. With increasing opioid use in the U.S. and States starting to legalize marijuana, there is a large population of people who use both opioids and marijuana. Ethnographic and experimental research is suggesting that people use marijuana to moderate their opioid use. We seek to learn if there is an association between marijuana use and the frequency of opioid use among people who inject opioids.
Methods: People who inject drugs were recruited using targeted sampling methods in Los Angeles and San Francisco, California, 2011-2013. We limited analysis to people who report having used opioids in past 30 days (N=652). Outcome variable: self-reported number of times used any opioids by any route of administration (including heroin, speedballs, goofballs, and opiate pills) in past 30 days. Explanatory variable: any marijuana use past 30 days. Statistics: multivariable linear regression with a log-transformed outcome variable.
Results: About one third (34%) reported marijuana use in past 30 days. The mean and median number of times used opioids in past 30 days were significantly lower for people who used marijuana than those who did not use marijuana in the past 30 days (mean: 58.3 vs. 76.4 times; median: 30 vs 60 times, respectively; p<0.003). After controlling for age, age at first injection, ethnicity, city, health insurance, and methadone treatment in past month, people who used marijuana used opioids less often (in a log transformed variable) than those who did not use marijuana (Beta: -0.116; 95% confidence interval: -0.575, -0.116; p<0.003).
Conclusions: There is a statistical association between recent marijuana use and lower number of recent times used opioids among people who inject opioids. This suggests the need for a prospective longitudinal study of this association.
Financial Support: NIDA grants R01DA027689 and R01DA030427

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DISRUPTION OF CORTICAL N-METHYL-D-ASPARTATE RECEPTOR TONE GOVERNS IMPULSIVE ACTION.

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Aims: Impulsivity is a complex, multifaceted trait broadly defined as action without sufficient foresight; high inherent impulsive action may increase the likelihood that drug use escalates into dependence and relapse. Glutamate neurotransmission within the medial prefrontal cortex (mPFC) may critically regulate the cognitive and/or behavioral dimensions underlying impulsive action. We tested the hypothesis that disruption in NMDAR expression within the mPFC drives inherent impulsive action, and that pharmacological potentiation of NMDAR attenuates high inherent impulsive action.
Methods: A one-choice serial reaction time (1-CSRT) task was used to identify outbred male Sprague Dawley rats with high (HI) or low (LI) inherent impulsive action. Rats nose-poked for food pellets. Premature responses indexed impulsivity; the upper and lower 25% of rats were identified as HI or LI rats, respectively. Rats from one cohort were sacrificed and mPFC synaptosomal protein extracted; western blots were used to assess NMDAR subunit expression. Effects of saline (1 ml/kg, ip) or D-cycloserine (DCS, agonist at strychnine-insensitive glycine site of NMDAR; 20 mg/kg, ip) on impulsive action were assessed in a separate cohort of HI and LI rats.
Results: Performance on the 1-CSRT task was rapidly acquired and allowed stable identification of HI and LI rats across 70 training days (p<0.001). HI rats had lower mPFC GluN1 and GluN2A synaptosomal protein expression compared to LI rats (p<0.05). Differences in GluN2B expression between HI and LI rats were not detected. DCS decreased impulsive action in HI, but not LI, rats (p=0.05).
Conclusions: Diminished mPFC GluN1/GluN2A signaling may drive high inherent impulsive action, which can be rescued by selective potentiation of NMDAR function. Increased understanding of the neurobiology underlying inherent differences in impulsive action may aid development of pharmacotherapies targeting drug dependence, relapse, and other disorders characterized by aberrant impulsivity.
Financial Support: NIH K99 DA033374

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THE COST-EFFECTIVENESS OF OPIOID AGONIST TREATMENT IN CALIFORNIA'S PUBLICLY-FUNDED DRUG TREATMENT FACILITIES.

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Aims: California treats the largest population of opioid dependent individuals in the USA. We assessed the cost-effectiveness of the current standard of OAT in California, compared to a scenario in which all entrants access non-time-limited (or maintenance-oriented) OAT.
Methods: We adapted a previously-published semi-Markov cohort model to capture the chronic, recurrent nature of opioid dependence. We used linked state-wide administrative data on drug treatment and incarceration, supplemented with other published data, to populate our model, which distinguishes between prescription opioid (PO) and heroin users. We compared an 'actual practice' scenario based on the observed distribution of PO and heroin users across detoxification and maintenance at first treatment to the hypothetical scenario of all treatment entrants initiating maintenance. Calculations were done over 1, 5, 10-year and lifetime horizons.
Results: Allowing all treatment entrants to have access to maintenance treatment at first treatment episode was found to be a dominant strategy in each of the time horizons, resulting in lower total costs and higher quality-adjusted life-year (QALY) gains. Over a lifetime horizon, our model showed that people who initiated maintenance upon first treatment entry gained 13.0 discounted QALYs on average (vs 12.1 for those receiving the standard of care) and generated a societal cost of $0.74 million (vs $1.02 million). Cost savings were realized primarily because of treatment retention and the lower costs of criminality associated with the reduced time spent out-of-treatment.
Conclusions: Synthesizing population-level data on OAT in publicly-funded drug treatment facilities in California, we found that immediate access to maintenance treatment may be more effective and less costly than the current standard of care for people with chronic opioid dependence.
Financial Support: NIDA R01DA031727 (PI:Nosyk) R01 DA032551 (PI:Nosyk) P30DA016383 (PI:Hser)

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PREDICTORS OF E-CIGARETTE USE AMONG ADOLESCENTS.

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Aims: To develop an understanding of perceptions, use patterns and predictors of e-cigarette use among adolescents.
Methods: Surveys conducted in CT middle schools (MS) and high schools (HS) in November 2013 (Time 1; n=4780) and June 2014 (Time 2; n=5012).
Results: Cross-sectional analyses at Time 1 indicated high rates of lifetime use (3.5% MS, 25.4 % HS) and current (past month) use (1.5% MS, 12% HS) of e-cigarettes and these rates increased further at Time 2 (lifetime use: 7.4% MS, 28% HS; past month use: 3.7% MS, 12% HS). At Time 1, males (OR=1.70, p<0.01), older students (OR=1.39, p<0.05), Caucasians (OR=2.01, p<0.001), students who had tried cigarettes but were not current cigarette smokers (ever smokers; OR= 13.04, p<0.001), and current cigarette smokers (OR= 65.11, p<0.001) were more likely to be lifetime e-cigarette users, and report greater susceptibility to future e-cigarette use (Males: OR=1.30; Caucasians: OR=1.14; ever cigarette smokers; OR=3.85; current cigarette smokers; OR=9.81; p's<0.01). Longitudinal examinations with students surveyed at both time-points (n=2090) observed that among those who were never e-cigarette users (n=1750) at Time 1, adolescents who were older (OR=1.24, p<.0001) and lifetime cigarettes users (OR=2.93, p=0.009), and who did not think that e-cigarettes were harmful (OR=0.47p<.0001) and thought that e-cigarettes were safer than regular cigarettes (OR=2.11, p=0.0003), and who were susceptible to future e-cigarette use (OR=3.37, p<.0001), were more likely to try e-cigarettes at Time 2.
Conclusions: While most e-cigarette use appears to be associated with anticipated predictors like cigarette use, there is increased use among adolescents who are not cigarette smokers
Financial Support: P50DA009241 & P50DA036151

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INFLUENCE OF REPRODUCTIVE HORMONES ON SOCIAL RANK AND VULNERABILITY TO COCAINE REINFORCEMENT IN FEMALE CYNOMOLGUS MONKEYS.

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Aims: The present study utilized female cynomolgus monkeys and examined whether estrogen (E2), progesterone (P4) and total testosterone (T) predicted eventual social rank, changed following hierarchy establishment, or was associated with susceptibility to cocaine self-administration.
Methods: Blood serum was collected for three months prior to social housing, then for one month once hierarchies were stable. Following stable hierarchy formation, monkeys were trained to respond for food under a fixed-ratio 30 schedule of reinfocement and then given access to ascending doses of cocaine (0.0003-0.1 mg/kg/inj).
Results: Prior to social housing, E2 exposure across the menstrual cycle was greater in eventual subordinate compared to eventual dominant monkeys, while there were no differences in P4 concentrations. After stable hierarchies formed (4 monkeys/pen), E2 in subordinates decreased and differences between groups were no longer observed. Furthermore, dominant animals had decreases in P4 after hierarchies stabilized, whereas subordinate animals showed increases in P4 following stable social group formation. T concentrations did not predict or differ between ranks; decreases in T concentrations were observed across all ranks following stable hierarchy formation. Subordinate monkeys acquired cocaine self-administration at lower doses than dominant monkeys. This effect could be driven by higher circulating E2 since there was an inverse relationship between E2 concentrations and dose of cocaine at which acquisition occured.
Conclusions: These results enhance our understanding of an individual's response to environmental manipulations, such as attainment and occupation of social ranks and between-rank variation in hormone dysregulation as well as their relationship to cocaine self-administration. Such information will aid in the development of pharmacological treatment strategies for drug addiction.
Financial Support: DA017763, DA036973

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ANHEDONIA, DEPRESSION, ANXIETY, AND CRAVING FOR OPIATES IN OPIATE ADDICTS STABILIZED ON ORAL NALTREXONE AND LONG ACTING NALTREXONE IMPLANT.

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Aims: Naltrexone is a μ-opioid receptor antagonist that blocks the analgesic and euphoric effects of heroin and other opioids. Opioid craving, depression, anxiety, and anhedonia are triggers for relapse, and concerns have been raised that naltrexone increases them due to its blockade of endogenous opioids.
Methods: Patients with opioid dependence (N=306) were enrolled into a three cell (102ss/cell) randomized, double blind, double dummy, placebo-controlled 6-month trial comparing implantable naltrexone, oral naltrexone (50 mg/day), and placebo (oral and implant).
Results: The percentage of patients that completed six months of treatment without relapse was 52.9% in the naltrexone-implant group, 15.7% in oral naltrexone, and 10.8% in the placebo group (survival analysis, Log Rank Mantel-Cox c^2=68,4; p<0.001 to naltrexone implant group). There was a significant decrease of craving over the course of treatment from 3-3.5 on a 10-point scale at baseline to 0.5-1.1 at six months among those who were retained in treatment and did not relapse (F5, 1095= 21.2; p < 0.001). Depression, anxiety, and anhedonia were moderately elevated at baseline and decreased to normal levels within the first 1-2 months for patients who remained in treatment and did not relapse with no significant difference between groups.
Conclusions: The improvements in opioid craving, depression, anxiety, and anhedonia among those who remained in treatment and did not relapse are most likely an effect of treatment success and not specifically related to naltrexone since they occurred regardless of medication group. Long-term blockade of opiate receptors with naltrexone did not induce anhedonia or depression.
Financial Support: 1-RO1-DA 017317

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THE EFFECTS OF ESTROUS CYCLING ON COCAINE SELF-ADMINISTRATION IN SOCIALLY HOUSED MALE-FEMALE DYADS.

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Aims: Previous studies have reported that cocaine self-administration in female rats varies across the estrous cycle, with cocaine intake increasing during estrus. One limitation of these studies is that they have only examined cocaine self-administration in females housed and tested in isolation. Consequently, we do not know if the presence of a male partner influences cocaine self-administration in females, or whether estrous cycling in females influences cocaine self-administration in a male partner. The purpose of the present study was to examine cocaine self-administration in socially housed male-female dyads.
Methods: Male and female rats were housed and tested in pairs using custom-built operant conditioning chambers that separated the two rats using a wire screen. The wire screen allowed visual, auditory, olfactory, and limited tactile contact between the two rats 24 hours/day, but prevented the two rats from mating. After acclimation to housing, rats were implanted with intravenous catheters and trained to self-administer cocaine on a progressive ratio schedule of reinforcement. Estrous cycle was monitored daily for the duration of the study.
Results: Cocaine self-administration varied across the estrous cycle in females, peaking on the night of estrus as previous studies have reported. In contrast, cocaine self-administration in males was stable and did not vary according to the estrous cycle of their female partners.
Conclusions: These data indicate that the presence of a male partner does not influence the effects of estrous cycling on cocaine self-administration in females, and that estrous cycling of females does not influence cocaine self-administration in their male partners.
Financial Support: Supported by NIDA grants R01DA031725 (MAS) and R01DA0274855 (MAS).

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ADAPTIVE REWARD LEARNING IS INTACT IN YOUNG ADULTS WITH REMITTED SUBSTANCE USE AND DEPRESSIVE DISORDERS.

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Aims: There is increasing awareness that adolescent and young adult Substance Use and Major Depressive Disorders (SUD & MDD) often co-occur, and that they can disrupt attainment of educational, social and vocational milestones. Diminished reward processing (RP) may be a stable trait that mediates poor outcome in these substance and mood disorders. Individuals completed the modified, individually titrated Monetary Incentive Delay (MID) task to examine RP. This task is designed to equalize chances of success in all groups by individually equating response time. Despite this titration, those with MDD tend to underperform relative to HC. We expected the same underperformance in those with remitted MDD (rMDD) and a history of SUD (hSUD).
Methods: Ten hSUD + rMDD individuals, 18 rMDD, & 17 healthy controls (HC), free of current symptoms/drug use (mean age 21.2, SD = 1.8) completed the MID task in the quiescent state of illness.
Results: rMDD participants earned less money than the HC group ($F(1,35) = 7.12$, $p = .01$). In contrast, and opposite of expectation, rMDD+hSUD did not earn less money than HC, and actually earned more money than rMDD ($F(1,27) = 6.94$, $p = .01$). In addition, the rMDD+hSUD group had greater additive and sustained reward learning than rMDD ($F(3,81) = 2.71$, $p = .05$).
Conclusions: Apart from expectation, these initial results suggest that the presence of hSUD and rMDD in a young adult group may substantially change the way that individuals approach and learn reward tasks. These effects suggest that RP is intact and no different than HC in rMDD+hSUD. Study of those with hSUD and no MDD may exhibit differences in reward and those potential effects will be studied in the future.
Financial Support: RO1 MH 081911 (SAL), F31DA038388 (NAC), NARSAD Young Investigator Award (SAL).

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EFFECTS OF AN ANATABINE AND YERBA MATé LOZENGE ON CRAVING IN SMOKELESS TOBACCO USERS AND HEAVY SMOKERS.

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Aims: New non-addictive, non-nicotine treatments for tobacco dependence are needed. Anatabine is a *Solanaceae* plant family alkaloid that is a nicotinic acetylcholine receptor agonist. It has no discernable abuse potential and attenuates nicotine's reinforcing effects in animals. Yerba maté is a plant which is brewed into a beverage commonly consumed in South America. Maté contains several active ingredients including xanthines, polyphenols, minerals, and vitamins. We evaluated the effects of an oral lozenge containing anatabine and yerba maté extract (YME) on acute craving in studies of smokeless tobacco (ST) users and heavy smokers (HS).
Methods: Adult daily ST users (≥3 cans per week for ≥1 year) and HS (≥1 pack per day for ≥5 years) completed double-blind, crossover studies to evaluate the effects of two lozenge formulations of anatabine and YME. The large lozenge (LL) contained 0.4 mg anatabine and 75 mg YME; the small lozenge (SL) contained 0.3 mg anatabine and 18 mg YME. Outcome measures included safety, the Questionnaire on Smoking Urges (QSU), the Minnesota Withdrawal Behavior Rating Scale (MBRS), and the Product Rating Questionnaire (PRQ).
Results: ST and HS subjects reported significant ($p<0.0001$) reductions from baseline in QSU and MBRS scores following administration of each lozenge. HS reported greater ($p<0.05$) reductions in QSU scores following the SL versus the LL. ST users rated the size and other attributes of the LL as more favorable than the SL on 64% of the PRQ questions, whereas HS rated the SL as more favorable on 71% of PRQ items. Both formulations were safe and well tolerated.
Conclusions: Anatabine alone and anatabine/YME combination products reduce acute tobacco craving and represent novel approaches to treating tobacco dependence. ST users and smokers may require variations in product characteristics, such as dose or lozenge size, to satisfy their cravings. Further study is warranted to determine how effective these products are for cessation of ST use and smoking.
Financial Support: This work was funded by Rock Creek Pharmaceuticals, Inc., Sarasota, FL.

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SEX DIFFERENCES IN ALCOHOL USE DISORDERS AND RISKY DRINKING AMONG CHRONIC NON-CANCER PAIN PATIENTS RECEIVING OPIOID THERAPY.

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Aims: Chronic non-cancer pain (CNCP) patients receiving opioid therapy may be at increased risk of alcohol-related harm. This study aimed to examine (i) the prevalence of lifetime alcohol use disorders (AUD), (ii) current patterns of drinking, and (iii) sex differences.
Methods: Baseline data from the Australian POINT cohort study of 1,423 persons prescribed strong opioids for CNCP were utilized. ICD-10 lifetime AUD were assessed using the CIDI. The sample was grouped according to past 12 month drinking patterns: 'Non-drinkers' (n=593), 'Non-risky drinkers' (n=488), 'Occasional risky drinkers' (n=233) and 'Regular risky drinkers' (n=110).
Results: 33% of the sample reported lifetime AUD (20% harmful use and 13% dependence). Lifetime AUD were more frequently reported by males (49%; 95% CI: 45-53) than females (19%; 95% CI: 17-22), although females were more likely to report past 12 month symptoms (6% vs. 2%). Males (17%: 95% CI: 14-20) were more likely to report onset of chronic pain prior to onset of AUD compared to females (11%; 95% CI: 9-13). Males (14%) were more likely than females (8%) to be in the 'Regular risky drinkers' group (OR 5.3, 95% CI: 3.3-8.5).
Conclusions: There is a high prevalence of lifetime AUD among CNCP patients and males typically report riskier patterns of alcohol consumption.
Financial Support: This study received funding from the Australian National Health and Medical Research Council (NHMRC, #1022522).LD, BL, SN, WH and RPM are supported by NHMRC research fellowships (#1041472, #1073858, #1013803, #569738 and #1045318).

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DIAGNOSIS OF HEPATITIS C VIRUS INFECTION AFTER ENTRY TO OPIOID SUBSTITUTION THERAPY.

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Aims: Hepatitis C virus (HCV) infection is highly prevalent among people who inject drugs (PWID). With the advent of effective short-course HCV therapies, elimination of this disease among PWID may be possible. Strategies are needed to enhance diagnosis of HCV infection among people who inject drugs to improve engagement in antiviral therapy, and stem the growing burden of HCV-related morbidity and mortality.
Methods: This was a retrospective observational cohort study using linked administrative data in New South Wales (NSW), Australia. In NSW, all entries to opioid substitution therapy (OST) are recorded in the Pharmaceutical Drugs of Addiction System, and positive HCV test results must be notified to the Notifiable Conditions Information Management System. We linked these two databases, and calculated rates of incident HCV notifications among people entering OST, and compared HCV notification rates in and out of OST.
Results: Following adjustment for sex, age and year, rates of incident HCV diagnosis were significantly higher during periods of OST, compared to periods out of OST (adjusted incident rate ratio: 1.70; 95% confidence interval: 1.63, 1.77). This effect was seen across multiple treatment periods. HCV notifications were highest among women and people aged under 25 years.
Conclusions: Routine HCV testing within OST settings increases diagnosis of HCV infection in the high-risk population of PWID.
Financial Support: This work was supported by the National Health and Medical Research Council. The National Drug and Alcohol Research Centre at the University of NSW is supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvements Grant Fund. The Kirby Institute is funded by the Australian Government Department of Health and Ageing.

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ROLE OF GENDER IN AGE OF INITIATION OF NONMEDICAL USE OF PRESCRIPTION DRUGS AMONG YOUTH 10 TO 18 YEARS.

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Aims: Early onset of substance use is linked to later dependence and poorer health outcomes. This association may vary by gender. Identification of factors associated with age of nonmedical use of prescription medication (NMU) initiation will be critical in ascertaining pathways to prevent or delay use. The study aims to examine gender specific factors associated with initiation age of NMU of stimulants, benzodiazepines or opioids using a hazards model.
Methods: Youth aged 10 to 18 years (N=11,048) from 10 US cities were surveyed in the National Monitoring of Prescription Stimulants Study using an entertainment venue intercept method. Age of NMU initiation was determined by self-report of NMU of stimulants, benzodiazepines or opioids. NMU was defined as medication use more than prescribed, that belonged to someone else, by non-oral routes, or to get high. Assessments included socio-demographic characteristics and age of initiation of smoking and alcohol. The hazard of NMU initiation stratified by gender was estimated. Cox proportional hazards models were used to assess factors associated with NMU initiation.
Results: Overall, 5.6% of youth reported past 30 day NMU; 52% of the sample were female. The hazard of NMU initiation differed by gender; females had 1.15 increased hazards of initiating NMU compared to males. Females with ADHD and early alcohol use initiated NMU 1.3 and 2.8 times earlier than their counterparts. Males who had initiated alcohol use earlier were more likely to initiate NMU than later alcohol users (Hazard Ratio 2.1).
Conclusions: It is important to understand more about early onset of NMU. This national sample of over 11,000 youth helps us understand gender differences in vulnerability to NMU initiation. Findings have implications for targeted programs to prevent or delay NMU onset.
Financial Support: Fogarty International Centre Indo-US Training Program in Non-Communicable Diseases (D43-TW009120; Lasopa, Fellow; PI: Cottler). N-MAPSS was conducted under contract with Pinney Associates, with provided funding by Shire Pharmaceuticals and Noven Pharmaceuticals.

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THE ISRAELI CLUB DRUG CULTURE: A QUALITATIVE EXAMINATION OF GENDER DIFFERENCES IN SUBSTANCE USE AND SEXUAL RISK BEHAVIORS.

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Aims: This preliminary study examines gender differences in substance use and sexual risk behavior among men and women participants in Israeli club drug culture. Data include in depth qualitative interviews with men and women who were over age 18 and reported recent (past 90 days) and regular use of club drugs (e.g., cocaine, ecstasy, LSD, GHB, ketamine, or methamphetamine) and attendance at large Israeli nightclubs.
Methods: In depth qualitative interview respondents were between the ages of 22-35 and both genders reported binge drug and alcohol use and the trendiness of cocaine, MDMA (ecstasy), and other hallucinogens. Most were students and also part-time employed in clubs, bars and/or restaurants.
Results: Women described common cultural practices, such as trading sex for drugs inside club restrooms, and being in control of "being out of control." Straight men described paying substantial amounts of money for drugs, and consequently for sex with female club-goers. Men who self identified as either gay or bi-sexual described that is common practice in the gay-scene to use GHB with potential partners before engaging in sexual activity. Women, on the other hand, described GHB as a drug they would never knowingly take. However, they also describe a milieu in which they take various drugs from men they do not know, without knowing exactly what they are being given. Additional themes were identified and will be presented.
Conclusions: The interviews suggest that, both in groups and alone, women are particularly vulnerable to negative consequences of drug use, including victimization, substance use disorders, and transmission of HIV or other sexually transmitted infections. Prevention efforts must address multiple social ecological factors to increase safety and decrease risk exposure for young adults in the Israeli club drug scene.
Financial Support: None

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ASSIST IN HIV/AIDS SERVICE SETTINGS: COMPARISON OF SELF-SCREENING AND PEER-SUPPORT SCREENING METHOD.

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Aims: In Vietnamese context, the HIV epidemic has been driven largely by injection drug use and it is common for people to continue using illicit drugs and alcohol during their HIV treatment. A reliable and easy-to-use screening method is particularly important since no routine testing for substance use among patients attending HIV services is conducted. This study compared the effectiveness of two different methods of substance use screening: patient doing self-screening with a tablet versus peer educator-assisted screening with a tablet.
Methods: This was a cross-sectional study, using The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) integrated onto a PC tablet to conduct screening for patients aged 18 and above in 2 outpatient HIV treatment clinics and 1 HIV testing center. Patients were randomized into two groups. The prevalence of each substance use and the risk of dependence on that substance were compared between self-administered (SA) group (n = 297) and peer educator-assisted (PA) group (n = 296).
Results: The prevalence of self-reported substance use in the SA group was significantly higher than the PA group for Cocaine (p=0.03), Inhalants (p=0.00) and Alcohol (p=0.01). The risk of dependence was significantly higher in the SA group than the PA group for Tobacco (p=0.01), Alcohol (p=0.05), Inhalants (p=0.00) and Sedatives/sleeping pills (p=0.05).
Conclusions: This first ever study using the ASSIST for screening substance use among patients attending HIV services in Vietnam showed that self-administered screening has higher percentage reporting use and dependence as compared to peer educator-assisted screening. It is important to provide opportunities for patients of HIV services to report and discuss their continued drug use in order to improve treatment outcomes.
Financial Support: The study was funded by a supplement to NIDA Grant DA032733

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REACTIONS TO THE FDA PROPOSED GRAPHIC WARNING LABELS AMONG SMOKERS IN ADDICTION TREATMENT CENTERS.

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Aims: We evaluate knowledge & attitudes of cigarette health risks and smoking behaviors with respect to the FDA proposed graphic warning labels (GWLs) among smokers in the addiction treatment centers where smoking prevalence is 3-4 times higher than in the general population

Methods: 376 clients from 8 addiction treatment centers in New York were surveyed from May to September 2013. Participants were asked about cigarette use harms and attitudes about quitting smoking after exposing to current warning labels. The GWLs were introduced to participants and the same set of questions was repeated. Participants were also asked questions related to smoking behaviors, intention to quit and attitudes towards cessation program.

Signed tests were used to compare how participants responded to the same set of questions for current warning labels and the GWLs. The association between levels of perceiving health risk from the GWLs and smoking behaviors were examined by t tests and chi-square tests.

Results: 67% of participants (n = 252) were current smokers. The GWLs consistently have the higher impact than the current warning labels on: knowledge of cigarette use harms (55.8% vs 35.9%, p<0.001), positive attitudes about quitting smoking (53.7% vs 34.6%, p<0.001), staying quitting (50.0% vs 34.2%, p<0.001), and stopping from having a cigarette (34.6% vs 6.5%, p<0.001)

Among smokers who thought "somewhat/a lot" about the health risks of smoking after exposing to the GWLs, they were more likely to attempt quitting (66.7% vs 48.6%, p=0.019), have intention to quit in the next 6 months (68.2% vs 46.1%, p<0.001), and also have positive attitudes towards smoking cessation programs (3.29 vs 3.00, p=0.002).

Conclusions: The GWLs have greater impacts than the current warning labels in term of conveying health risks of smoking and promoting quitting among this high prevalence smoking population. Perceiving greater health risks from smoking are also more likely to increase the quit attempts, intention to quit and positive attitudes towards smoking cessation.

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PARALLEL DEVELOPMENT OF LONGITUDINAL TOBACCO SMOKING AND ALCOHOL CONSUMPTION: THE AMSTERDAM GROWTH AND HEALTH LONGITUDINAL STUDY.

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Aims: The primary aim of this investigation was to examine the longitudinal, parallel change in alcohol consumption and tobacco use among a young adult population, from the ages of 21 to 32 years old.

Methods: Data for this investigation came from participants (n=484) enrolled in the Amsterdam Growth and Health Longitudinal Study. Individuals in this sample were community-dwelling adults in an epidemiologic investigation examining disease across the lifespan. We utilized parallel latent growth modeling in order to assess the potential time-varying relationship between alcohol (grams/week) use and tobacco (grams/week) use across more than 11 years.

Results: The linear change for alcohol use was significantly related to linear change in tobacco use over time (β=11.33, p<0.05). In addition, initial smoking status at age 21 was predictive of alcohol use over time (β=-131.45, p<0.05) and alcohol use at age 21 was predictive of smoking over time (β=-131.45, p<0.05). There were also significant sex differences observed such that females exhibited significantly more decline in alcohol use over time (β=3.94, p<0.05) and females also exhibited significantly less alcohol use at initial status (β=-64.13, p<0.05). There were no sex differences found in linear change in tobacco use over time or for initial smoking status.

Conclusions: Change in tobacco use and change in alcohol use over time (age 21 to age 32) were significantly related to one another in a community sample of young adults. This relationship bolsters recent calls for a better understanding of the relationship between alcohol and nicotine use over time. This data will inform interventions for the effective treatment of alcohol and nicotine co-addiction.

Financial Support: Life Science Discovery Fund, Department of Justice, Bureau of Justice Affairs (Roll, PI), Seed Grant Program at Washington State University, Spokane (McPherson, PI).

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PRIZE CONTINGENCY MANAGEMENT FOR SMOKING CESSATION AMONG PEOPLE LIVING WITH HIV/AIDS: PRELIMINARY ANALYSIS.

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Aims: PLWHA are more likely to smoke cigarettes and experience smoking-related health problems than the general population. Few studies have examined the efficacy of behavioral treatments for smoking cessation among PLWHA.

Methods: An ongoing, adaptive sequential multiple assignment randomized trial (SMART) is examining the efficacy of adding prize-based CM treatment to standard smoking cessation care that includes sustained release bupropion and counseling. This presentation addresses initial treatment response in phase 1 of the study. To date, 11 PLWHA have been randomly assigned to receive standard treatment with CM that involves weekly prize draws for reduced urine cotinine scores, and 9 PLWHA have been randomized to receive standard care alone, during the first four weeks (phase 1) of the 12-week trial.

Results: Preliminary findings reveal that 5 (45.5%) participants receiving prize CM have exhibited reduced cotinine scores during the first four weeks of treatment compared with 1 (11.1%) participant receiving only standard care. Average urine cotinine score (on a 0-6 point semi-quantitative scale) at final phase 1 treatment contact is 4.5 (SD = 1.9) for participants in CM and 5.7 (SD = 1.0) for participants in standard care, which is indicative of a large effect size (d = .82).

Conclusions: These data reveal that adding CM to standard smoking cessation treatment may result in greater reduction of smoking in the early phase of treatment compared with standard care alone.

Financial Support: NIH R01 DA034537, Joe Young, Sr./Helene Lycaki Funds (State of Michigan), and Detroit Wayne Mental Health Authority.

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CHARACTERIZING VAPORIZER USE AMONG CANNABIS USERS.

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Aims: Electronic devices for vaporizing tobacco and cannabis are rapidly emerging and becoming popular among tobacco and cannabis users. The overarching aim of this project is to increase knowledge of the prevalence and phenomenology of vaping cannabis. Understanding the function of vaping (e.g., Is it substituting for smoking cannabis? Is it being combined with nicotine?) across subsets of cannabis users can inform prevention, treatment and policy development.

Methods: A 63-item anonymous survey hosted on Qualtrics was distributed through Facebook ads targeting pages focused on interests related to cannabis use. 1,036 volunteers completed the survey and provided valid data. Sample characteristics were as follows: 81% male, 86% Caucasian, mean age 27.3 (SD 11.5) years, 87% and 55% reported over 100 and 1000 days of lifetime cannabis use respectively.

Results: Lifetime prevalence of vaping was 72% with 15% reporting vaping as their preferred method of use. Among those that endorsed ever vaping, smoking remained the most common method of current (past 30 days) use for 79%. Only 13% of vaporizer users reported that their rate of smoking cannabis decreased since initiating vaping, suggesting that vaping was not substituting for smoking for the majority of users. Daily smokers were more likely than occasional smokers to report vaping in the past 30 days [43% vs 20%, p<.01]. Those who vaped cannabis were more likely than non-vaporizers to report e-cig use [78% vs 59% p<.01], but few participants (9%) reported ever mixing nicotine and cannabis in a vaporizer.

Conclusions: Data from this select sample of cannabis users suggest that although most cannabis users have tried vaping, only a small subset prefer it over smoking and few have replaced smoking with vaping. At this time, vaporizer use appears associated with heavier patterns of cannabis use and greater e-cig use, although few appear to simultaneously vaporize nicotine and cannabis.

Financial Support: NIDA P30DA029926, T32DA037202, R01DA032243

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EXTENDED-RELEASE NALTREXONE FOR OPIOID RELAPSE PREVENTION AMONG OPIOID-DEPENDENT, CRIMINAL JUSTICE-INVOLVED ADULTS.

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Aims: XR-NTX is increasingly considered as a therapeutic option for opioid use disorders in criminal justice settings despite limited evidence for its effectiveness. This 5-site open-label randomized effectiveness trial examined whether XR-NTX reduced relapse compared with treatment as usual (TAU) among opioid dependent CJS participants.
Methods: Eligibility: DSM-IV criteria for opioid dependence, criminal justice involvement last 12 months, baseline urine test negative for all opioids. The XR-NTX group received 6 monthly injections of 380 mg and a Medical Management visit; the TAU group received referral to available community treatment options. Assessments occurred every 2 weeks over a 24-week treatment phase and at 12- and 18-month follow-ups. The primary outcome was an opioid relapse event, defined as either self-report or urine toxicology evidence of ≥10 days of opioid misuse in a 28-day (4 week) period; positive or missing samples counted as 5 days of misuse.
Results: The 153 subjects randomized to XR-NTX and 155 to TAU did not differ at baseline: 87% reported lifetime heroin use, 73% on probation or parole. Rates of retention on XR-NTX were 61% at 6 months. The relapse event was less common in the XR-NTX arm (43% vs. 64%, p<0.0001; Hazard Ratio 0.48 [95% CI 0.35-0.66]), the median time-to-relapse longer (10.5 vs. 5.0 weeks, p<0.0001), and overall rates of urine samples negative for opioids higher (74% vs. 56%, p<0.0002 [Odds Ratio 2.3 [1.49-3.56]). 5 overdose events (2 fatal) occurred in the TAU arm; none were observed among XR-NTX participants.
Conclusions: Six months of XR-NTX opioid relapse prevention therapy among CJS-involved outpatient participants was associated with lower rates of opioid relapse and overall opioid misuse versus treatment-as-usual. ClinicalTrials.gov: NCT00781898
Financial Support: NIDA (R01DA024549-55). Study medication provided in-kind by Alkermes, Inc.

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EFFECTS OF PRENATAL COCAINE AND NICOTINE ON MATERNAL WHITE MATTER INTEGRITY IN EARLY POSTPARTUM.

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Aims: Cocaine exposure (CE) in pregnancy disrupts postnatal nurturing critical for offspring development, and is linked to child neglect/abuse, maternal hostility and depression. CE interrupts birth-induced changes in mid-brain that are thought to encode maternal neural circuitry underlying optimal maternal behavior. Our aim is to assess CE effects on maternal brain white matter (WM) tract integrity assessed with diffusion tensor imaging (DTI).
Methods: Since prenatal cigarette smoking occurs in >90% of CE mothers, we compared 19 CE to 33 drug-free mothers (CTL) and 15 with prenatal nicotine without CE (NIC). Subjects were scanned at 3 months postpartum (3T Siemens Allegra; 42-direction diffusion-weighted images; b=1000). We used FSL's TBSS for hypothesis generation; UNC-Utah NA-MIC fiber analysis toolkit for detailed analysis. TBSS yielded regions of potential group differences in fractional anisotropy (FA) maps. A high-quality, unbiased study-specific DTI atlas was built; fibers associated with significant regions were tracked on this atlas; subject-specific FA tract profiles were extracted and statistically analyzed with fiber statistic tool FADTTS. Results are corrected for multiple comparisons ($p < 0.05$).
Results: FA was significantly lower in right lateral posterior corticospinal tract (CST) and left posterior inferior fronto occipital fasciculus (IFOF) in CE compared with NIC or CTL mothers. Both CE and NIC had significantly lower FA in central left fornix, inferior right medial CST and cerebral peduncle compared with CTL.
Conclusions: We found CE-specific deficits in WM integrity/organization in visual and auditory integration and motor tracts which may contribute to aberrant responses to infant cries and cues that are reported in CE mothers. We observed lower FA in fornix in NIC and CE. This may impair hippocampal connection to hypothalamus, thalamus, nucleus accumbens and cingulate, thus contributing to altered reward value or memory of infant stimuli involved in encoding salience of infant contact.
Financial Support: K01DA019949-01A1, P01DA02246 (KG); R01MH091645, U54HD079124, U54EB005149, HD003110 (MS)

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SUBSTANCE USE AND OFFENSES AMONG JUVENILE OFFENDERS.

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Aims: Substance use is common among juvenile offenders. However, limited research has examined how urban, suburban and rural residence relate to substance use and juvenile offenses. The current study 1) profiles substance use and offenses among Kentucky juvenile offenders in urban, suburban, and rural areas and 2) identifies independent correlates of substance use severity.
Methods: This study examines 2013 data from the Kentucky Department of Juvenile Justice (DJJ) as part of the JJ-TRIALS cooperative agreement. DJJ records for 713 juvenile offenders are included. CRAFFT screener severity score and juvenile offenses for: urban, suburban, and rural are profiled and compared. Bivariate analyses determined differences on demographics, CRAFFT score, and juvenile offenses. Regression analysis identified CRAFFTpredictors.
Results: The average age was about 15 and more than 85% were male. Rural youth were more likely to be white (89.6% vs. 75.1% urban and 78.1% suburban). Urban youth had significantly higher CRAFFT scores (2.11) as well as a positive score (49.9%), used more substances, and were more likely to have been detained for a weapons or court-related offense. Regression analysis revealed that suburban youth had a significantly lower CRAFFT score than urban youth (p=<.007), but there were no differences between urban and rural youth. Overall, age and being detained were positively related to a higher CRAFFT score (p=<.001).
Conclusions: Findings indicate that urban youth were more substance-involved and more likely to engage in juvenile offenses. However, there were unique trends among rural and suburban youth, consistent with existing research, which suggests that rurality is not a protective factor for substance use. Implications for treatment and prevention will be discussed.
Financial Support: JJ-TRIALS is funded by NIDA grant UO1 DA036158 in collaboration with SAMHSA and DOJ.

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COPING STRATEGIES AS A MEDIATOR OF INTERNET-DELIVERED PSYCHOSOCIAL TREATMENT: SECONDARY ANALYSIS FROM A NIDA CTN MULTISITE EFFECTIVENESS TRIAL.

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Aims: Coping skills are a predictor of abstinence among patients with substance use disorders. However, little is known regarding the role of coping skills in the effectiveness of the Community Reinforcement Approach (CRA). Using data from a 12 week randomized control trial assessing the effectiveness of the Therapeutic Education System (TES), a web-delivered version of the CRA combined with contingency management, we tested the hypothesis that increased coping skills act as a mediator of treatment effectiveness.
Methods: 507 participants entering 10 outpatient addiction treatment programs received either treatment-as-usual (TAU), a counselor-delivered treatment (Arm 1), or reduced TAU plus TES wherein 2 hours of TAU per week were replaced by TES (Arm 2). Abstinence from drugs and heavy drinking was evaluated using urine toxicology and self-report. Coping skills were measured using the Coping Strategies Scale-Brief Version. Mediation analyses were done following Baron and Kenny's approach.
Results: The average baseline coping strategies scores were not significantly different between the two treatment arms. TES intervention was associated with better coping strategies scores (Mean=19.3, SD=4.3) compared to TAU (Mean=17.9, SD=4.7) (P=.0007), and higher coping strategies scores were associated with an increased likelihood of abstinence at the end of treatment. The effect of TES on abstinence was no longer significant after controlling for coping strategies scores.
Conclusions: Our results support the importance of improved coping skills as at least a partial mediator of the effectiveness of a web-version of the CRA combined with contingency management.
Financial Support: This work was supported by a grant from the National Drug Abuse Treatment Clinical trial network, NIDA U10 DA013035 (EV Nunes, J Rotrosen) and by NIDA K24 DA022412 (EV Nunes).

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EXAMINING THE RELATIONSHIP BETWEEN SOCIAL CONTEXT AND PRESCRIPTION OPIOID INITIATION ROUTES AMONG YOUNG ADULTS ENTERING DETOXIFICATION.

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Aims: Prescription opioids (PO) remain the second most popular drug among young adult substance use initiates, and PO treatment admissions continue to rise for this group. Few studies have explored the influence of social context in the process of drug initiation and transitions to alternate routes of administration among PO abusers. This study examines the social context surrounding PO initiation and its relationship to route of administration among young adults entering medical detoxification in South Florida.
Methods: In-depth, semi-structured interviews were conducted with young adults (n=20) entering detoxification for opioid dependence to explore PO misuse, initiation, characteristics associated with alternate routes of administration, and related health and social risks. Interviews were transcribed from digital recordings; grounded theory was used for analysis.
Results: PO use was initiated either orally (n=10) or via alternate routes (n=10), with the majority transitioning to injecting (n=16). Over half (n=12) transitioned to heroin. Four categories of initiation emerged: with peers in social or school settings; with fellow employees at work; with family; or alone. Most (n=15) initiated a social setting; nearly all initiating with alternative routes did so within a social context (n=9) and described how peers taught them to abuse POs.
Conclusions: Results suggest that the social context of initiation among young adult PO abusers influences the use of alternate routes of administration. Prevention efforts should focus on educating youth about the increased likelihood of dependence resulting from utilizing alternate routes of administration.
Financial Support: Research was supported by the Center for Applied Research on Substance Use and Health Disparities.

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ACCEPTABILITY OF A MOBILE PHONE BASED HEPATITIS C INTERVENTION.

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Aims: Injection drug users have high rates of sexual risk behavior and high rates of hepatitis C virus (HCV) infection. Sexually transmitted disease (STD) clinics are important locations for HCV testing. HCV infection rates among STD clinic patients have been reported as high as 42%, with higher rates among injection drug users. Mobile phones are emerging as a tool to address individual and structural-level barriers in the prevention and management of infectious diseases, including for HIV and other STDs. However, it is unclear if patients attending urban STD clinics possess the devices and access to take advantage of interventions delivered via mobile phones. This study assessed mobile phone ownership, use, and acceptability of text messaging to promote linkage to HCV evaluation and treatment among patients seeking STD diagnostic and treatment services in an urban STD clinic.
Methods: An interviewer-administered survey was conducted with 100 patients in a STD clinic to assess: a) mobile phone ownership and use; b) acceptability of text messaging to encourage HCV testing, engagement in HCV risk behavior screening, and notification of appointments for HCV evaluation and treatments ; and c) concerns about privacy.
Results: Survey participants averaged 33.15 years of age, with 74% male, 37% White, 29% Hispanic, and 24% African American. Ninety-five percent owned a mobile phone and all mobile phone owners reported sending and receiving text messages; 84% of participants reported having an unlimited text messaging plan. Ninety-six percent indicated they felt comfortable receiving text messages encouraging them to get tested for HCV, to participate in an HCV risk behavior screening, or to notify them about scheduled HCV clinic appointments.
Conclusions: High acceptability of receiving HCV text messages, coupled with high rates of mobile phone ownership and text messaging plans, suggests that text messaging may be an effective delivery method for a mobile phone-based HCV intervention to STD clinic patients.
Financial Support: P50-DA009253.

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CHARACTERISTICS OF GAMBLERS CHOOSING SELF-EXCLUSION FROM CASINOS: A PROSPECTIVE STUDY IN A FRENCH OVERSEAS TERRITORY.

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Aims: To analyze the characteristics and gambling practices of subjects making a request for voluntary self-exclusion from casinos in Reunion Island, France (overseas territory).
Methods: From July 2013 to September 2014, all subjects requesting voluntary self-exclusion from gambling places were interviewed with the Addiction Severity Index modified to include gambling and other non-substance additions and the Mini International Neuropsychiatric Interview (MINI). A follow-up interview was proposed in the following 4-14 months.
Results: 33 subjects were included (20 women, average age=52 y.o. (SD=11)). 27 (81%) met DSM-5 gambling disorder (GD) diagnosis. 15 subjects (45%) had at least one mood and/or anxiety disorder, 1 subject had an eating disorder, 2 subjects met criteria for videogame addiction. No subject had gambling treatment history. Although 29 subjects exhibited a need for gambling treatment (ASI severity score ≥4), the majority of them did not report major concern or need for help. At follow-up, 2 out of 17 subjects were still engaged in gambling activities. The majority (53%) of those meeting DSM-5 GD diagnosis at baseline reported current gambling-related concerns at follow-up. Only one subject was in treatment for GD at follow-up.
Conclusions: A majority of subjects who use self-exclusion from casinos meet DSM-5 criteria for GD and would deserve specific care for GD. Improvement of coordination between gambling places, regulatory authorities and addiction clinics is needed to increase access to treatment.
Financial Support: Internal funds and MILDT 2010

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EFFECTS OF THE TRACE AMINE ASSOCIATED RECEPTOR 1 AGONIST RO5263397 ON BEHAVIORAL INDICES OF METHAMPHETAMINE IN RATS.

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Aims: Methamphetamine is a major drug of abuse with no effective pharmacotherapy available. Trace amine associated receptor 1 (TAAR 1) is implicated in cocaine addiction and represents a potential therapeutic target. However, the effects of TAAR 1 agonists on addiction-related behavioral effects of methamphetamine is unknown.
Methods: This study examined the effects of a TAAR 1 agonist RO5263397 on methamphetamine-induced behavioral sensitization, methamphetamine self-administration, cue- and methamphetamine-induced reinstatement of drug-seeking and cue-induced reinstatement of sucrose-seeking behaviors in rats. Male Sprague-Dawley rats were used to examine the effects of methamphetamine alone and in combination with the TAAR 1 agonist RO5263397 (3.2-10 mg/kg).
Results: RO5263397 dose-dependently attenuated the expression of behavioral sensitization to methamphetamine, reduced methamphetamine self-administration, and decreased both cue- and a priming dose of methamphetamine-induced reinstatement of drug-seeking behaviors. However, RO5263397 did not alter cue-induced reinstatement of sucrose-seeking behavior.
Conclusions: Taken together, TAAR 1 agonists attenuate some abuse-related behavioral effects of methamphetamine, strongly suggesting that drugs activating TAAR 1 may be potentially useful for the treatment of methamphetamine addiction and warrant further studies.
Financial Support: NIH R21DA033426

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HEALTH STATE TRANSITIONS AMONG PRESCRIBED OPIATE PATIENTS ACCESSING PHARMACOLOGICAL TREATMENT FOR OPIOID DEPENDENCE IN CALIFORNIA, 2006 - 2010.

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Aims: Among patients accessing pharmacological treatment for opioid dependence, we (1) characterize patterns of transitions between periods in and out of treatment and incarceration and (2) assess the effect of prescribed opiate (PO) on these health state transitions.
Methods: We examined 94,021 health state episodes among all patients (n=30,524 individuals) first admitted to public agonist treatment for opioid dependence in California from 2006 to 2010 and for whom information was obtainable on mortality and incarceration. We used a Cox proportional-hazard model for all-cause risks and a proportional subdistribution hazards model for competing risks to assess the effect of (a) PO use (vs. heroin) on the probability of transitioning among 4 states: (1) detoxification treatment, (2) maintenance treatment, (3) incarceration, and (4) out-of-treatment. Models were estimated under a competing risk of mortality and controlling for demographics and addiction severity.
Results: Both PO and heroin users were mostly in an out-of-treatment state over the median 2.5 years of observation. PO vs. heroin use (1) decreased the hazard of becoming incarcerated no matter the initial health state (ORs were 0.19 to 0.53); (2) increased the hazard of transitioning from detoxification to maintenance treatment (OR: 1.63; 95% CI 1.52, 1.75); and (3) decreased the hazard of transitioning from out-of-treatment to detoxification (0.74; 0.69, 0.80) or to maintenance (0.84; 0.79, 0.90).
Conclusions: The course and consequences of addiction are less severe among PO users than among heroin users, however more effective treatment-engagement strategies are needed for both types of disorders.
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DECREASED THALAMOCORTICAL CONNECTIVITY IN CHRONIC KETAMINE USERS.

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Aims: Previous studies have revealed thalamic abnormalities in schizophrenia. Ketamine, a potent N-methyl-D-aspartate glutamate receptor antagonist, can mimic schizophrenia-like symptoms. In this study, we aimed to address whether the thalamus as a whole shows altered functional connectivity to the cerebral cortex in chronic ketamine users compared to healthy controls.
Methods: 130 subjects (41 ketamine users and 89 control subjects) underwent resting-state functional MRI. To investigate the specific functional relationships between the cortex and the thalamus, the cortex was partitioned into nonoverlapping six regions of interest (the prefrontal cortex, motor cortex/supplementary motor area, somatosensory cortex, temporal cortex, posterior parietal cortex, and occipital cortex). Mean BOLD time series were extracted for each region of interest and entered into a seed-based functional connectivity analysis.
Results: We found that the ketamine use group showed significantly less connectivity between the thalamus and the cortical regions of interest, including the prefrontal cortex, the motor cortex /supplementary motor area, and the posterior parietal cortex. However, no increased thalamic connectivity was observed for the ketamine users compared with control subjects. The functional connectivity between the posterior parietal area and the right lateral dorsal nucleus was significantly correlated to individual ketamine craving score ($p<0.05$, corrected).
Conclusions: This study provides first evidence for abnormal thalamocortical connectivity of resting state brain activity in chronic ketamine users. Our data further support a disruption model of the thalamocortical network and are consistent with a disconnection hypothesis of schizophrenia, and emphasize the functional importance of the thalamus in the pathophysiology of schizophrenia. Further understanding of glutamatergic mechanisms in schizophrenia may facilitate the evaluation of much-needed novel pharmacological agents for improved therapy of this complex disease.
Financial Support: Natural Science Foundation of China (Grant No. 81100996) and Sheng Hua “Lie Ying” Program of Central South University

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A PRE–POST COMPARISON IN HEALTHCARE SERVICE UTILIZATION AMONG HEROIN USING WOMEN IN THE METHADONE MAINTENANCE TREATMENT IN TAIWAN.

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Aims: The present study aims to (i) investigate the differences in healthcare service utilization between women in the Methadone Maintenance Treatment (MMT) and general population, and (ii) examine potential pre-post MMT enrollment differences and explanatory predictors among female heroin users.
Methods: Building on the National MMT database in Taiwan, we identified 3482 heroin-dependent women who received the first methadone treatment during the calendar years of 2006- 2008. For comparison, a total of 34820 age-, income-, and residence-matched women were randomly drawn from the National Health Insurance Research Database (NHIRD). Through encrypted identification number, healthcare utilization records for both groups were obtained from the NHIRD.
Results: An estimated 29% and 16% of women in MMT have utilized emergency and inpatient cares in the year preceding MMT enrollment, significantly higher than the estimates of their matched counterparts (15% and 8%, $p<0.001$); however their rate of outpatient care was significantly lower (71% vs. 78%, $p<0.001$). After the MMT enrollment, a slight elevation was noted in both healthcare visit and hospital stay. Having no treatment history in heroin-related problems (e.g., substance use disorder, alcohol use disorder, mental disorders, and hepatitis C) before enrollment was associated with an increased change (e.g., outpatient department: 2.07-4.75 visits, $p<0.01$).
Conclusions: Heroin-using women had excess utilization of emergency room and inpatient care, regardless of MMT enrollment status. History of medical care prior to the MMT enrollment prominently affected the change in health care utilization. Reducing barriers in accessing integrated healthcare to address unmet health needs due to substance use problems should warrant further attention when designing and delivering methadone treatment.
Financial Support: Funding for this study was provided by the National Health Research Institutes (NHRI) grant to Dr. Chen (02A1-NPSP02-021).

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COORDINATED AND HOMOLOGOUS INTRAVENOUS COCAINE SELF-ADMINISTRATION PROCEDURES IN MONKEYS AND HUMANS: A TRANSLATIONAL APPROACH TO MEDICATIONS DEVELOPMENT.

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Aims: The goal of this research is to establish a translational platform to screen medications for cocaine-use disorders using self-administration choice procedures in humans and non-human primates.
Methods: Initial study design was based on dosing parameters and schedules of reinforcement used in previous clinical studies and adapted for use in monkeys. Under these procedures, i.v cocaine (0, 0.043, 0.14 or 0.43 mg/kg/inj in monkeys, corresponding to 0, 3, 10 and 30 mg/70 kg in humans) and a species-specific alternative reinforcer (0, 1, 3 or 10 food pellets in monkeys; $0.01, 1.00 and 3.00 in humans) are made available on independent, concurrent progressive-ratio schedules. During each session, subjects complete a sampling trial in which they receive the dose of cocaine and the alternative reinforcer available that day, followed by nine choice trials.
Results: In these ongoing studies, 2-3 male rhesus monkeys have completed each of the cocaine dose and food magnitude combinations. Six human subjects who met criteria for cocaine-use disorder and reported current use of smoked cocaine have completed the protocol. In both species, i.v. cocaine is maintaining dose-dependent increases in the number of drug trials completed, and the alternative reinforcer is producing magnitude-dependent downward shifts in the cocaine-dose response curves. In addition, in the human subjects, the cardiovascular and subjective responses to i.v. cocaine have increased an orderly, dose-dependent fashion. Additional human and non-human primate subjects will be enrolled until the target number have completed; data will be analyzed by ANOVA.
Conclusions: The concordance in self-administration results across species supports the use of these translational procedures to more efficiently screen medications for cocaine-use disorders.
Financial Support: R01 DA033364, K02 DA031766 and UL1TR000117.

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A GENDER STRATIFIED ANALYSIS OF ADOLESCENT SUBSTANCE USE ON VIOLENCE TRAJECTORIES.

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Aims: This study examines the effect of substance use in adolescence on longitudinal patterns of violence from adolescence through adulthood. It considers how this process differs by gender.
Methods: Using data from Waves 1-4 of the Add Health study, group trajectory analyses were conducted to identify violence trajectories separately for males (n=5,077) and females (n=6,086). These trajectory groups were then used as outcome variables in gender stratified multinomial logistic regression models to determine whether and the extent to which adolescent (Wave 1) substance use affects the probability of membership in these trajectory groups. Adolescent substance use measures were: regularly drinking alcohol, smoking marijuana, and smoking cigarettes.
Results: Four trajectories were identified for males and females: early desister, late desister, chronic perpetrator, and adult escalator. Although the names of the trajectories are the same, the shapes and distributions differ by gender. The early desister group for each gender was the reference group in the respective stratified analyses because it is the largest and least violent one. Gender differences in the relationship between substance use and violence trajectories were found. Drinking alcohol, smoking marijuana, and smoking cigarettes increased the risk of membership in the female late desister than the early desister group ($p<.05$), however only drinking and smoking marijuana increased this risk in the male late desister group ($p<.05$). Similarly, all three behaviors increased the risk of being in the male chronic perpetrator group than the early desister group ($p<.05$) whereas smoking marijuana was not significant in the respective female group. None of the behaviors increased the risk of being in the male adult escalator group whereas all three were significant in the female adult escalator group ($p<.05$).
Conclusions: Adolescent substance use is associated with higher adolescent violence, adult onset violence, and persistent violence from adolescence into adulthood. The effects of the specific substances on violent patterns vary for males and females.
Financial Support: 5T32DA07272-22

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EXPOSURE TO ETHANOL IN BRAZILIAN GASOLINE STATION ATTENDANTS.

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Aims: This study aimed to assess the potential exposure to inhalant ethanol of gasoline station attendants to this harmful drug, using breathalyzer and oral fluid (OF) analysis by headspace gas chromatography/mass spectrometry (HS-GC/MS).
Methods: Cross-sectional study with a target sample of 162 GSA which were invited to respond a questionnaire covering the socio demographic profile of the study population and the pattern of drinking and driving behavior, followed by a breath test and OF collection. Categorical variables were described by absolute and relative frequency, and compared between groups of gender using Fisher's exact test.
Results: Ethanol was found in all samples, and 72.83% was positive by HS-GC/MS (above quantification limit of 0.00125 g/dL), while only one sample (0.62%) had a positive result (0.03 mg/L) in the breath tests.
Conclusions: The results presented here demonstrate the ethanol occupational exposure of the GSA and the importance of confirmatory analysis for the breathalyzer by HS-GC/MS. Moreover, the study suggests that may be relevant to develop psycho educative strategies in order to prevent brain and other clinical injuries caused by chronic exposure to ethanol in this vulnerable population.
Financial Support: CNPq for financial support and scholarships, State Traffic Department of Rio Grande do Sul by lending the breathalyzer, and Immunalysis Corporation for donation of Quantisal™ OF collection devices. Brazilian Secretariat of Drug Policies (SENAD).

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TRAJECTORIES OF NONMEDICAL USE OF PRESCRIPTION OPIOIDS IN ADOLESCENTS IN PRIMARY CARE.

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Aims: The rise in non-medical use of prescription opioids (NMUPO) is an escalating public health problem in adolescents. To improve clinical practice, it is vital to examine this issue in the primary care setting. In order to better understand different risk factors for NMUPO and different patterns of use, this study examined different trajectories of non-prescription opioid use among a sample of adolescents who presented to primary care clinics over one year follow-up.
Methods: Data were from a sample of primarily African-American (62.6%) youths ages 12-18, presenting to community health clinics in the United States (n=1076) that were enrolled in a prevention and early intervention study of substance use and completed assessments at baseline, three, six, and 12 months. Group based trajectory modeling was used to empirically identify distinctive trajectory patterns of NMUPO over the one-year follow-up. Further analyses examined baseline markers associated with the different trajectories of NMUPO.
Results: Trajectory analysis identified three groups: non-users (n = 969), decreasing users (n=63), and persistent high users (n=44) over the 1-year follow-up. Substance use (including heroin and cocaine use and sedative and stimulant misuse), delinquency, parental and friend drug use, and depressive symptoms were associated with the NMUPO trajectories (both decreasing and persistent NMUPO trajectories).
Conclusions: Adolescents with NMUPO have higher rates psychosocial risk factors and those who continue to misuse prescription opioids over time may constitute a distinctive subgroup that may be at higher risk for developing future problems. Further studies should examine the efficacy of primary care interventions that account for the heterogeneity of use patterns.
Financial Support: National Institute on Drug Abuse #DA020075 and NIDA-AACAP Resident Research Award in Substance Abuse and Addiction

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UTILIZATION OF AN ELECTRONIC INFORMATION SYSTEM TO EVALUATE AND ENHANCE PRACTICE AT A MEDICATION-ASSISTED OPIOID TREATMENT PROGRAM.

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Aims: START Treatment & Recovery Centers (formerly Addiction Research and Treatment Corporation) is an outpatient medication-assisted opioid treatment program that also provides primary medical care, including HIV/AIDS care to approximately 3,000 predominantly minority adults in New York City. Several years ago, we received NIDA funding to evaluate the implementation of an electronic health information system. We now utilize the capabilities of the electronic system for performance measurement in order to improve patient care.
Methods: We measured and evaluated Outcomes; Regulatory and Contractual Compliance; and Productivity monthly. This was particularly timely, given that the NYS Office of Alcoholism and Substance Abuse Services instituted fee-for-service payment methodology to replace capitation; and the Affordable Care Act mandated meaningful use of electronic systems.
Results: The ability to provide monthly reports of Outcomes (opiate and cocaine-free status; HIV viral load suppression; < 7 for diabetes mellitus; and BP < 140/90 for hypertension); Regulatory and Contractual Compliance (timely completion of behavioral and medical assessments); and Productivity (all clinical/administrative disciplines) resulted in improved performance over time. Specifically, we found that Outcomes targets for opiates/cocaine were met (negative toxicology for >80% of patients); and targets for HIV viral load suppression; HgbA1c < 7 for diabetes mellitus; and <140/90 (> 75% of patients) were approached. For Regulatory and Contractual Compliance, 100% target was attained or approached; and Productivity improved over time.
Conclusions: Electronic systems are critical to measure outcomes with precision; meet challenges presented by changes in reimbursement and documentation; and navigate changes resulting from the Affordable Care Act.
Financial Support: National Institute on Drug Abuse (R01 DA022030) for the original research

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GENDER DIFFERENCES AMONG MST SURVIVORS ON CHRONIC OPIOID THERAPY.

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Aims: Military sexual trauma (MST) recognition is increasing among US veterans. Survivors of MST (MST-S) are at greater risk of lifelong sequelae, affecting physical and mental health. In addition, patients receiving chronic opioid therapy (COT) has increased. However, prescription opioid use among MST-S has not been completely described. The purpose of this project is to further define possible associations between gender and COT among MST-S.
Methods: After IRB approval, we identified patients who received at least 3 consecutive, monthly opioid prescriptions during a 90 day period at the Cincinnati VAMC and defined them as COT patients. For each subject, we also obtained patient demographic data and all ICD-9 codes. We then calculated the average daily opioid dose in morphine equivalents (ME) for every subject. Categorical variables were compared using Fisher's exact testing and continuous data were compared using either ANOVA or Kruskal-Wallis testing.
Results: Complete dosing data was available for 815 subjects, of which 37 subjects (4.6%) were MST-S. In the entire COT cohort, 66 (8.2%) were females. Of the female COT subjects, 22 (33.3%) were MST-S, while 15 (2.0%) of the male COT subject were MST-S. Female MST-S were significantly over-represented in the COT population (p=0.000). The median daily opioid dose for female MST-S was 31.4 (IQR 21, 59)mg ME/day. For males, the median dose was 21.5 (IQR 11.8, 36)mg ME/day (p=0.147). In terms of age, male COT MST-S had a mean age of 56.7 (SD=7.4) while female COT MST-S had a mean age of 49.2 (SD=8.3) (p=0.008). For chronic health of MST COT subjects, 54.5% of females versus 13.3% of males had a Charlson score of 0-1 (p=0.044).
Conclusions: Female COT subjects were more likely to be MST-S versus male COT subjects. Although females trended towards a higher dose, the difference was not statistically different. However, the female COT MST subjects were significantly younger and had lower Charlson index scores. Therefore, their cumulative exposure to risks of COT may be greater. This work supports the need for increased recognition allowing risk reduction in MST-S.
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CHRONIC PAIN, CRAVING AND RECENT OPIOID USE AMONG PATIENTS TREATED FOR OPIOID USE DISORDERS.

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Aims: Chronic pain is common among persons with opioid use disorders and has the potential to worsen addiction treatment outcomes. In a sample of patients receiving opioid agonist therapy, we evaluated whether having chronic pain was associated with a) opioid craving and b) illicit opioid use.
Methods: In a cross-sectional study of adults on buprenorphine or methadone maintenance, we assessed past week craving for opioids (primary dependent variable) and recent illicit opioid use (secondary dependent variable). Opioid craving was measured using a numeric scale (0-10); any response >0 was considered positive. Recent illicit opioid use defined as a urine drug test positive for opioids. The main independent variable was chronic pain, defined as self-reported bodily pain that had been present for at least 3 months. Multivariable logistic regression models were fit for each outcome, adjusting for age, sex and non-white race.
Results: The sample included 106 adults on methadone or buprenorphine maintenance. Mean age was 43.8 (SD±9.4) years, 48% were female, 32% non-white. Chronic pain was present in 68% of the sample, 51% reported craving opioids in the past week, and 16% had urine drug test positive for opioids. Chronic pain was associated with a 3-fold higher odds of reporting opioid craving in the past week (aOR=3.10; 95% CI: 1.28-7.50, p-value=0.01). The relative odds for having a positive urine drug test was also higher for participants who had chronic pain versus those who did not, however, results were not statistically significant (aOR=2.52; 95% CI: 0.64-9.90, p=0.18).
Conclusions: In this sample of patients treated with buprenorphine or methadone for their opioid use disorders, individuals with chronic pain had higher odds of reporting craving for opioids. Chronic pain with its associated increased craving among patients with treated opioid use disorders potentially places this population at risk for relapse to opioid use.
Financial Support: NIH/NIDA grant K23DA027367.

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PERSONALITY AND GAMBLING CHARACTERISTICS OF PROBLEM GAMBLERS WITH AND WITHOUT ALCOHOL DEPENDENCE.

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Aims: A large proportion of individuals with gambling disorder also present with a history of alcohol dependence, but few studies have directly examined the relationship between these two conditions. This study examined the relationship of personality traits, psychiatric disorders and gambling characteristics to co-occurring lifetime (current/past) alcohol dependence status among community-recruited problem/pathological gamblers (PPGs).
Methods: Problem/pathological gamblers (N = 150) were clinically interviewed for co-occurring psychiatric disorders, and completed measures of personality and gambling characteristics (e.g., gambling severity, gambling involvement, delayed discounting of monetary rewards).
Results: A co-occurring lifetime diagnosis of alcohol dependence (n = 61, 40.7%) was associated with lower personality scores for Control, Well-Being, Achievement, Traditionalism, and Harm Avoidance, as well as higher Alienation scores in bivariate analyses. PPGs with lifetime alcohol dependence were more likely to report current and lifetime substance dependence, lifetime antisocial personality disorder, current mood disorder, greater lifetime gambling severity, greater past-year gambling involvement, and steeper delayed discounting. Multivariate analyses indicated that lower Well-Being, Control, and Traditionalism and a co-occurring lifetime substance dependence diagnosis best accounted for a co-occurring lifetime alcohol dependence diagnosis.
Conclusions: PPGs with co-occurring lifetime alcohol dependence demonstrate addictive behavior across multiple domains and report a personality style characterized by hopelessness, impaired control, and resistance to externally-motivated treatment approaches. Implications for the treatment of these complex cases are discussed.
Financial Support: The Ontario Problem Gambling Research Centre, Joe Young Sr./Helene Lycaki Funds (State of Michigan), Detroit Wayne Mental Health Authority, and a postdoctoral research fellowship from the Wayne State University Office of the Vice President supported this research.

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SECOND HAND SMOKE EXPOSURE DURING PREGNANCY AND ANXIETY DISORDER IN CHILDREN AT AGE 11-13.

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Aims: While the impact of active maternal smoking during pregnancy on child health has been well investigated, the effect of maternal passive smoking, AKA, environmental tobacco smoke (ETS), or second-hand smoke, is less clear. Particularly, few studied the association between ETS and specific types of child emotion and behavior disorder. This study addresses this gap by examining the association between maternal ETS exposure during pregnancy and children anxiety disorder.
Methods: A sample of 591 mother-child pairs from Jintan China Cohort Study were used in the analysis. Mother's self-reported exposure to tobacco smoking at home, the workplace, and other places during pregnancy (as a measure of ETS, 65.57% of mothers reported some exposure during pregnancy) was assessed when children were 5 years old, and Screen for Child Anxiety Related Disorders(SCARED) were reported by mothers when the children were 11-13 years old. Logistic regression models were constructed to examine the adjusted association between maternal exposure to ETS during pregnancy and SCARED scales, adjusting children's age and gender.
Results: After adjusting age and gender of the children, ETS exposure was associated with higher risk of total anxiety disorder (OR=1.55, 95% Confidence interval[CI] 1.02-2.35), panic disorder(OR=1.50, 95% CI 1.01-2.22), and generalized anxiety disorder(OR=1.54, 95% CI 1.05-2.26) in the exposed mothers. However, EST exposure was not significantly associated with separation anxiety disorder, social anxiety disorder, and significant school avoidance
Conclusions: This study suggests that maternal ETS exposure during pregnancy is associated with overall child anxiety disorder as well as some specific subtypes of anxiety disorders but not others. Results have important implications to the identification of risk factors for specific types of anxiety disorders and the development of preventive intervention strategies tailored to individual needs.
Financial Support: None

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INDIVIDUAL CHARACTERISTICS AND SOCIAL PROCESS IN INFLUENCING MATERNAL SMOKING BEHAVIOR: A LONGITUDINAL ANALYSIS OF A NATIONAL BIRTH COHORT.

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Aims: The purpose of this study is to a) describe longitudinal patterns of maternal smoking before, during, and after pregnancy through the early childhood parenting years, as well as heterogeneity in these patterns; and b) relate baseline individual characteristics and social process predictors to these patterns.
Methods: Among 9,050 mothers of a national birth cohort, we estimated trajectories of maternal smoking with general growth mixture model (GGMM), and examined how baseline predictors are associated with these patterns over a 5 to 6 year period beginning three months prior to pregnancy. Social process is measured by social support and connectedness experienced by mothers, and their involvement in community activities, and individual characteristics include social demographic variables as well as behavioral variables such as breastfeeding and postpartum depression.
Results: A 5-class solution identified trajectories of nonsmokers (70.5%), temporary quitters (9.4%), pregnancy-inspired quitters (3.3%), delayed initiators (5.1%), and persistent smokers (11.7%). Modifiable risk factors included postpartum alcohol consumption and co-resident smokers, while breastfeeding beyond six months and religious service attendance were protective characteristics.
Conclusions: While individual characteristics are the strongest predictors of maternal longitudinal patterns of smoking during the critical perinatal period, expanding the identifying characteristics of such patterns beyond individual characteristics may serve to enhance identification of those at risk as well as inform program design for both prevention and cessation.
Financial Support: This study was funded by the National Institute on Drug Abuse (1R01DA030496).

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ATTENUATING EFFECT OF ENVIRONMENTAL ENRICHMENT AND ABSTINENCE ON CARDIAC AND RENAL TOXICITY INDUCED BY KETAMINE AND METHAMPHETAMINE SELF-ADMINISTRATION IN RATS.

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Aims: The current study was designed to investigate the effect of abstinence in combination with environmental enrichment (EE) on cardiac, liver and renal toxicity induced by ketamine and methamphetamine self-administration (SA).
Methods: In Experiment 1, rats underwent 14 days of drug SA. In Experiment 2, the animals completed 2 weeks of drug SA followed by 2 and 4 weeks of abstinence. In Experiment 3, animals underwent 14 days of drug SA and 4 weeks of abstinence in which isolated environment (IE) and environmental enrichment (EE) was introduced. In Experiment 4, heart,liver and kidney changes were compared between sham (SA surgery without drug access) and control animals.
Results: Two weeks of drug SA caused significant increases in organ weight, FAS/Kidney Injury Molecule-1, and apoptotic level of heart, liver and kidney. Cardiac and renal impairment induced by drug SA was significantly attenuated by abstinence. Although 4 weeks of abstinence produced better attenuating effects, but still resulted in partial recovery. Finally, introduction of EE during the period of abstinence greatly promoted the protective effect of abstinence on drug-induced cardiac and renal toxicity. Reduced oxidative stress level was also evident in the animals housed in the environmental enrichment condition, in constrast to those in isolated environment.
Conclusions: The interactive effect of EE and abstinence was promising to promote the recovery of cardiac and renal toxicity of ketamine and methamphetamine.
Financial Support: This work was supported in part by the National Natural Science Foundation of China (U1132602), the National Key Technology R&D Program in the 12th Five-Year Plan of China (2012BAI01B07), K.C.Wong Magna Fund in Ningbo University, Zhejiang Provincial Key Laboratory of Pathophysiology (Ningbo University School of Medicine), and the Program for Innovative Research Team in Ningbo City (2009B21002).

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ASSOCIATIONS BETWEEN BUPRENORPHINE TREATMENT TRAJECTORIES AND CLINICAL OUTCOMES IN A LARGE MEDICAID PROGRAM.

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Aims: Buprenorphine (BUP) is an effective treatment for opioid use disorder; however, there is little evidence on the optimal duration of BUP treatment. Uncertainty about treatment duration may produce substantial variation in treatment patterns and patient outcomes. Using a large Medicaid dataset, we estimated BUP trajectories based on prescription refills, and examined clinical outcomes associated with these trajectories. We hypothesized that longer duration would be associated with better outcomes.
Methods: We analyzed a retrospective cohort data of 10,945 Pennsylvania Medicaid enrollees (18-64 years) who initiated a new episode of BUP treatment between 2007-2012. We used group-based trajectory models to identify BUP trajectories in the 12 months following initiation. Multivariate Cox proportional hazard models were used to examine the associations between trajectories and all-cause hospitalizations and emergency department (ED) visits in the year after the index treatment year.
Results: Six trajectories of BUP treatment were identified: 4 groups discontinued BUP (24.9% discontinued <3 months, 18.7% at 3-5 months, 12.4% at 5-8 months, 13.3% >8 months); 9.5% refilled intermittently; 21.2% refilled persistently. Factors associated with discontinuation were minority race, history of frequent ED visits and hospitalizations, and comorbid psychoses. After adjusting for sociodemographics, health status, and provider-level covariates, patients who refilled persistently had a 20% lower risk of all-cause hospitalizations (hazard ratio [HR]= 0.80, 95% CI, 0.68-0.94) and 15% lower risk of an ED visit (HR=0.85, 95% CI, 0.77-0.94), compared to those discontinuing BUP at 3-5 months.
Conclusions: BUP treatment durations were highly variable in this large Medicaid cohort, with 6 distinct patterns over the first year. Patients who used BUP persistently had lower risk of all-cause hospitalizations and ED visits than those experiencing early discontinuation.
Financial Support: The University of Pittsburgh and the Commonwealth of Pennsylvania.

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CAN DRONABINOL, A CB1 AGONIST, SUPPRESS OPIOID WITHDRAWAL IN HUMANS?

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Aims: Prevalence of opioid use disorders and demand for treatment in the U.S. have increased. Preclinical data show that the cannabinoid (CB) and opioid systems exhibit functional neuropharmacological cross-talk, with reports that CB1 agonists can attenuate opioid withdrawal signs. This proof-of-concept study examined the efficacy of dronabinol (DB), a CB1 agonist, to suppress withdrawal in opioid-dependent humans.
Methods: This double-blind, randomized, inpatient, crossover study enrolled opioid-dependent subjects (n=8) who were stablized on 30mg p.o. oxycodone (OC) qid for ~5 weeks. Seven 6.5 hr test sessions (72 hr apart) assessed the following oral conditions: 0mg, OC (30, 60mg), DB (5, 10 & 20mg [30 excluded here; see abstract by Nuzzo et al.]) for their ability to suppress withdrawal after blinded placebo substitution for OC (test at 22 hrs after last active OC). A broad array of physiological, subject and observer ratings were collected.
Results: Significant main effects of dose and dose x time interactions ($p<.05$) were found for several opioid withdrawal measures, including subject-rated visual analog ratings of "withdrawal", SOWS and the observer-rated OOWS scales. OC produced dose-related reductions in opioid withdrawal ratings and reversed mydriasis. Planned comparisons revealed that DB 20mg also significantly ($p<.05$) reduced some withdrawal measures but, overall, the magnitude of withdrawal suppression produced by DB 20mg was less than by OC.
Conclusions: Consistent with our study hypothesis, DB suppressed signs and symptoms of opioid withdrawal during spontaneous withdrawal in humans. However, the magnitude of suppression was fairly modest, less robust than that produced by OC, and accompanied by significant tachycardia (see Nuzzo et al., abstract). Overall, these data suggest that the CB1 receptor system is a rational target for opioid withdrawal suppression but safety concerns and tolerability will limit the utility of DB.
Financial Support: Funding by NIDA DA033932 (Walsh), T32-DA035200 & NCATS ULTR000117.

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NEUROPSYCHOLOGICAL EFFECTS OF PLACEBO STIMULANTS IN COLLEGE STUDENTS.

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Aims: To examine whether ingestion of a placebo stimulant improves neuropsychological functioning across four tasks.
Methods: Participants (*N*=166; *M* age=18.78; 48.8% male) were recruited via an online research participation website. Participants initially completed an online survey regarding ADHD symptoms, nonmedical prescription stimulant (NPS) use and expectancies, and medical exclusionary criteria. If inclusion criteria were met, participants were invited for an in-person study where they completed four neuropsychological tasks (d2 Test of Attention, Digit Span, PASAT, Passage Comprehension). They were randomized to control or experimental groups and provided water and/or placebo stimulant followed by a 30-minute absorption period and a second round of the tasks. Positive physiological symptoms rating scales were completed three times across the absorption period.
Results: Preliminary data analysis revealed no demographic differences between conditions. Performance improved at significant levels for d2, Digit Span and Passage Comprehension, across participants regardless of condition. The experimental condition improved significantly more on the PASAT ($F(1,164)=6.412$, $p=.012$). Additional analyses will be conducted to understand the role expectancies and self-reported physiological symptoms play in change across time as expectancies may enhance susceptibility to self-reported physiological changes.
Conclusions: Findings demonstrate improvements on the PASAT, a task requiring information processing utilizing sustained and divided attention. The experimental group did not demonstrate improvements beyond practice effects measured in controls on the other tasks. The PASAT is a difficult task that may be less susceptible to practice effects, yielding no overall significant change until participants believed there was another factor, stimulant medication, enhancing their abilities. Future research should continue to study what drives changes in neuropsychological task performance beyond the placebo effect in regards to NPS.
Financial Support: No financial support.

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ECIG-INDUCED SUPPRESSION OF NICOTINE/TOBACCO ABSTINENCE SYMPTOMS.

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Aims: Electronic cigarettes (ECIGs) produce an aerosol by heating a nicotine-containing liquid. The extent to which different concentrations of nicotine in the liquid produce differences in abstinence symptom suppression has not been explored systematically. The purpose of this clinical lab study is to examine the relationship between liquid nicotine concentration and abstinence symptom suppression in ECIG-naïve tobacco smokers and ECIG-experienced users after short-term ECIG use.
Methods: Thirteen cigarette smokers (mean 16.4 cigs/day) and 11 ECIG users (mean 2.2 ml liquid nicotine/day) used an "eGo" ECIG battery (3.3 V; 1000 mAh) attached to a dual-coil, 510-cartridge during 4 independent, double-blind sessions that differed by liquid nicotine concentration (0, 8, 18, or 36 mg/ml). In each session participants used the ECIG in 2 bouts (10 puffs; 30 sec interpuff interval). Abstinence symptom severity was assessed before and after each bout using standard scales (modified for ECIG users).
Results: Data were analyzed using mixed ANOVA, with liquid nicotine concentration and time **as** within-subject factors and group as the between-subject factor. Significant interactions of concentration and time were observed on "intention to smoke/vape", "craving", and "urge" [Fs (27,594)>2.2, ps<.05], with higher nicotine concentrations associated with lower scores on these measures. There was a significant main effect of group for the measures "anticipation of withdrawal relief" and "anxious", with smokers scoring significantly higher than ECIG users overall [Fs (1,22)>5.8, ps<.05].
Conclusions: Short-term ECIG use suppresses abstinence symptoms in ECIG-naïve cigarette smokers and ECIG-experienced users. Abstinence suppression may depend on liquid nicotine concentration and ECIG experience. Understanding the extent to which liquid nicotine concentration and ECIG experience is related to withdrawal suppression and other effects is critical to empirically-based regulation of these products that have uncertain individual and public health implications.
Financial Support: P50DA036105

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DELAY DISCOUNTING AND ALCOHOL ABUSE AMONG EARLY ADOLESCENTS.

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Aims: Delay discounting is a behavioral measure of impulsivity that describes how a reinforcer loses value as the delay to its receipt increases. Early adolescence appears to be the time of greatest increases in delay discounting, and alcohol use begins during this period. The aim of this study was to assess the relationship between delay discounting rates and alcohol abuse among early adolescents.
Methods: The sample was made up of 494 adolescents (55.7% male) who were randomly recruited from ten secondary schools in the Principality of Asturias (northern Spain). Mean age was 13.97 years (SD = 0.526). Participants completed a computerized version of a delay discounting task using hypothetical monetary rewards. They also reported whether or not they did binge drinking within the last month and completed a Spanish version of the Rutgers Alcohol Problem Index (RAPI) in order to assess problems related to alcohol use. Mann-Withney U tests were conducted to determine whether delay discounting rates (using the area under the curve, AUC) differ as a function of both binge drinking within the last month and RAPI scores.
Results: Results: Participants who engaged in binge drinking in the last month discounted significantly more by delay (Md = 0.06, n = 34) than those who did not (Md = 0.19, n = 460), U = 5081, p < .01, = .32. Also, participants who reported problems related to alcohol use had significantly higher delay discounting rates (Md = 0.05, n = 22) compared to those who did not (Md = 0.18, n = 472), U = 3839, p = .039, = .37.
Conclusions: This study adds evidence about the association between impulsivity and alcohol abuse and related problems among early adolescents. Thus, a delay discounting task could be a suitable screening tool when designing early intervention programs and strategies for preventing alcohol use among early adolescents.
Financial Support: This work was supported by one grant of the Government Delegation for the Spanish National Drug Plan MSSSI-12-2013/131 and by a predoctoral Grant BP11-031 from FICYT.

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INCREMENTAL COST-EFFECTIVENESS OF A VOUCHER-BASED CM PROTOCOL ADDED TO A CBT FOR SMOKING CESSATION.

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Aims: Contingency management (CM) is a behavioral intervention that has demonstrated its efficacy in reducing smoking consumption. However, CM has been criticized for its costs. This study analyzed the incremental cost-effectiveness of using a voucher-based CM protocol in combination with a cognitive behavioral treatment (CBT) for smoking cessation among treatment-seeking patients in a community setting.
Methods: Incremental cost-effectiveness analysis (ICEA) is based on a randomized clinical trial conducted at the Addictive Behaviors Clinic (University of Oviedo, Spain). A total of 92 patients were randomly assigned to CBT (n=49) or CBT+CM (n=43). CM included a voucher program through which nicotine abstinence was reinforced on a schedule of escalating magnitude with a reset contingency. Primary patient outcomes were both continuous abstinence and the longest duration of confirmed abstinence (LDA). A secondary patient outcome included the total number of nicotine-negative urine cotinine tests submitted during the treatment.
Results: The average cost per participant was $173.54 (95% CI=103.07-210.01) in the CBT condition and $514.88 (95% CI=148.77-566.18) in the CBT plus CM condition (p<.01). The incremental cost of using voucher-based CM to lengthen maintained abstinence at a 6-month follow-up by 1% was $26.24, and to lengthen the LDA by 1 week was $67.46. Based on the ICERs, an extra nicotine-negative result cost $227.56.
Conclusions: Adding a voucher-based CM protocol to a CBT required additional costs but also achieved better outcomes at a 6-month follow-up assessment. CM could increase long-term benefits and futures studies should address this issue in order to implement CM for smoking cessation in the broader community.
Financial Support: Spanish Ministry of Science and Innovation Grant (PSI2001-22804) and Predoctoral Grant BP12-037 from the Foundation for the Promotion of Applied Scientific Research and Technology in Asturias (FICYT).

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BORN IN THE USA: ESTIMATED ANNUAL INCIDENCE RATES FOR USE OF CANNABIS IN THE 21ST CENTURY UNITED STATES.

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Aims: Aims: Cannabis smoking trends in the United States (USA) apparently do not affect all population subgroups equally. As part of our NIDA "Born in the USA" enviromics research program, we aim to estimate the degree to which US-born young people might be more likely to start using internationally regulated drugs (IRD), versus peers born abroad in 18 diverse self-ethnic identified subgroups in the US. Here, the focus is newly incident use of cannabis.
Methods: Methods: The US National Surveys on Drug Use & Health (NSDUH) drew large nationally representative probability samples of 12-17 year olds, 2002-11 (n= 148,200), all assessed via computer-assisted self-interviews, with data entered into the RDAS online analysis system. We constructed these RDAS estimates as ratios of newly incident users among those at risk for first onset of cannabis, stratified by age, family origin, and place of birth, with due attention to analysis weights and Taylor series variance estimation.
Results: Results: For every 1000 12-17 year olds at risk, an estimated 58 start using cannabis each year (95% CI = 56 to 59). Overall, annual incidence estimates for the US-born (5.9%/year) exceed estimates for those born abroad (3.7%/year; $p<0.05$). Risk differences are seen with special clarity among Hispanics, and to a lesser extent, among Native Americans.
Conclusions: Conclusions: Notwithstanding limitations, we are prompted to ask about social environments of young adults, including country of origin and length of USA residence, that might explain observed risk variations. Development of ethnically-informed preventive intervention approaches might be needed in programs that seek reduced cannabis smoking prevalence in the multi-ethnic USA population.
Financial Support: Financial Support: NIDA T32DA021129 (CLQ); MSU (RB); K05DA015799 (JCA)

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MARIJUANA USE, HEAVY DRINKING, AND COGNITIVE DYSFUNCTION IN PEOPLE WITH HIV-INFECTION AND SUBSTANCE DEPENDENCE.

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Aims: To test the hypotheses that heavy drinking and marijuana use are associated with cognitive dysfunction in HIV-infected people.
Methods: Boston ARCH cohort participants were HIV-infected adults with substance dependence or current or past injection drug use (n=230). In cross-sectional regression analyses we tested the association between number of heavy drinking days (HDDs) in the past 30 (≥4 drinks for women, ≥ 5 for men in 24 hours), days of marijuana use in the past 30, and 3 measures of cognitive dysfunction: i) memory and ii) attention domains of the Montreal Cognitive Assessment (MOCA), and iii) 4 item cognitive function scale from the Medical Outcomes Study HIV Health Survey (MOS-HIV, range 0-100). Analyses were adjusted for demographics, primary language, comorbidities, depressive symptoms, anxiety, antiretroviral therapy (ART), HIV symptoms, opioid prescription, illicit sedative or opioid, or cocaine use, CD4 count, and hepatitis C.
Results: Participant characteristics: Mean age 49 years; 36% female; 51% Black, 25% Hispanic; 85% English primary language; 66% ≥12 years education; 88% on ART; 39% with current opioid prescription; 26% illicit sedative or opioid use; 31% cocaine use; 60% hepatitis C; CD4 cell count/mm^3 <200 (10%), 200-<500 (33%); 71% with HIV viral load <200 copies/mL; 47% no alcohol use, 25% 1-4 HDDs, 28% ≥5 HDDs; 55% no marijuana use, 16% 1-4 days, 19% 5-29 days, and 10% 30 days. HDDs, marijuana use, and their interaction were not significantly associated with either MOCA score. HDDs and the HDD-marijuana use interaction were not associated with MOS-HIV score. However, days of marijuana use was associated with lower MOS-HIV score (β -0.22, p=0.04).
Conclusions: Marijuana use may be associated with cognitive dysfunction in HIV-infected people. Further research should explore the direction of association and the role of long term alcohol and marijuana use.
Financial Support: U01AA020784, U24AA020779, U24AA020778

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GENDER DIFFERENCES IN METHAMPHETAMINE USE IN A MEXICO-U.S. BORDER CITY.

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Aims: Identify ways, forms, and paraphernalia (works) for methamphetamine (meth) use and how these differ by gender in Cd. Juarez, a Mexican city in the Mexico-U.S. border.
Methods: A cross-sectional study assessed socio-demographic characteristics and measures for meth use including ways (ingested, smoked, inhaled, snorted, injected, anally), forms (tablet/pill, liquid, powder, rock, smoke), and works (pipe, light bulb, syringe, straw, foil). Sample includes Mexican adults (age >21) who used meth in the past three months, recruited through convenience and snowball sampling. Descriptive statistics of the first 88 participants (target N=150) and bivariate analysis by gender are provided.
Results:
Median age of participants is 28; 64.8% are men and 35.2% are women and transgender women; 87.5% were born in Mexico; 28.4% crossed the border to the U.S. in last 12 mo. In their lifetime, 67% had been in jail and 27.6% had acquired meth or money in exchange for sex.
Median age of first use was 18 and days since last meth use was 5. Most had also used alcohol (97%), cocaine/crack (94%), marihuana (93%), or tobacco (93%). Most common use forms were tablet/pill (69%) and powder (60%); works were light bulb (58%) then pipe (49%); and meth was smoked (68%) and ingested (67%).
Conclusions: There were significant gender differences for rock and power use, and snorting by nose ($p<0.05$), and high rates of poly-drug use. These findings have implications for future interventions and harm reduction efforts among meth users, which would need to be tailored by gender, particularly the type of paraphernalia used. These findings may also be indicative of meth using behaviors among Hispanic populations living in cities on the U.S.-Mexico border region.
Financial Support: <span style="font-family:avenir book; font-size:12.0pt; mso-ansi-language:EN-US; mso-bidi-font-family:" times="" new="" roman";="" mso-bidi-language:ar-sa;="" mso-fareast-font-family:"times="" mso-fareast-language:en-us"="">Supported by NIDA funded UTEP Vulnerability Issues in Drug Abuse (VIDA) Project (1R24DA029989-01)

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A NON-PARAMETRIC METHOD FINDS GENETIC ETIOLOGY OF NICOTINE DEPENDENCE DIFFERS IN MALES AND FEMALES.

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Aims: To study the genetic heterogeneity of complex diseases, we develop a non-parametric method for association analysis of high-dimensional genetic data, and use it to study the genetic heterogeneity of Nicotine Dependence (ND).
Methods: In this work, we propose a heterogeneity weighted U (HWU) method for association analyses specifically taking into account genetic heterogeneity. HWU can be applied to various types of phenotypes and is computationally efficient for high-dimensional genetic data. Through simulations and a genome-wide association study (GWAS) of ND, we compared HWU with a non-heterogeneity weighted U (NHWU) method and the conventional generalized linear model (GLM).
Results: The results showed that HWU attained higher power than NHWU and GLM when the underlying genetic etiology of a disease was heterogeneous. In the absence of this heterogeneity, HWU attained similar performance to NHWU and GLM. Using HWU, we conducted a genome-wide analysis of ND. The genome-wide analysis of the Study of Addiction: Genetics and Environments dataset took 7 hours, identifying heterogeneous effects of two new genes on nicotine dependence.
Conclusions: Converging evidence from previous study suggests that complex diseases undergo substantial genetic heterogeneity. The development of new statistical methods with the ability to model genetic heterogeneity could facilitate the gene discovery process, as well as improve our knowledge of the complex mechanisms underlying human diseases. By applying the new method to a large-scale GWAS dataset, we found no evidence of genetic heterogeneity due to ethnic or genetic background. However, our results suggested that the genetic causes of nicotine dependence might differ in males and females.
Financial Support: NIDA K01DA033346 (QL), T32DA021129 (OV), and K05DA015799 (JCA).

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MAGNITUDE AND DURATION OF CUE-INDUCED CRAVING FOR MARIJUANA IN VOLUNTEERS WITH CANNABIS USE DISORDER.

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Aims: Evaluate whether subjective and physiologic response magnitude to neutral and marijuana (MJ)–related cues vary by gender, and duration of these cue-induced responses.
Methods: 33 volunteers (16 F) who met DSM-IV criteria for Cannabis Abuse or Dependence were exposed to neutral (first) then MJ-related visual, auditory, olfactory and tactile cues. Changes in mood, drug craving and physiology were assessed as a function of gender and cue type. Data were collected at baseline, post-neutral, post-MJ and 15-min post MJ cue exposure. For a subset of participants (n=16; 8 F), measures of craving and physiology were collected at 30-, 90-, and 150-min post-MJ cue to examine duration of cue-effects.
Results: Main effects for cue type were observed for visual analog scale (VAS) items craving for, urge to use, and desire to use MJ, Total and Compulsivity subscales of the Marijuana Craving Questionnaire (MCQ), self-rated anxiety, and diastolic blood pressure (BP). Posthoc analysis indicated these indices were significantly elevated following MJ cue vs. neutral cue exposure, and remained elevated 15 min post-MJ cue exposure. Estimates of observed power were large (range .68 – 1.00). Subset analyses indicated that MJ-cue induced elevations in desire and urge to use MJ remained significantly elevated at 30-, 90- and 150-min post cue exposure, relative to baseline and neutral cue exposure. For example, mean urge to use MJ was 75.2 during MJ cue, and 71.9, 69.0 and 69.9 at 30-, 90- and 150-min post-MJ cue exposure. There were no gender differences.
Conclusions: Presentation of poly-sensory marijuana cues increased self-reported MJ craving, anxiety and diastolic BP relative to baseline and neutral cues. MJ craving remained elevated up to 150-min after MJ cue presentation. This finding confirms that carry-over effects from drug cue presentation must be considered in cue reactivity studies.
Financial Support: NIH R21 DA019236, and Joe Young Sr./Helene Lycaki Funds (State of Michigan).

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IMPLEMENTATION OF CASE MANAGEMENT TO LINK HIV-INFECTED RUSSIAN ADDICTION PATIENTS TO HIV SERVICE.

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Aims: Access to HIV services for HIV-infected addiction patients is challenging in Russia due to separate addiction and HIV care systems. This qualitative study aimed to investigate experiences with a peer delivered *strengths-based case management* (CM) program to link addiction patients to HIV services in St. Petersburg, Russia.
Methods: We recruited 38 HIV-infected addiction patients from LINC (Linking Infectious and Narcology Care), a randomized trial (n=350) testing a CM program. Using a semi-structured questionnaire, we conducted 6 focus groups (5 to 8 patients post-CM) in the Russian language. Discussions were audiorecorded, translated and transcribed into English. Two investigators coded transcriptions and analyzed data thematically using Nvivo.
Results: Participants were 84% male, median age 36 years, 37% employed, median 14 years of drug use and 7 years since HIV diagnosis. Post-intervention linkage to HIV care was reported by 68%. Those who linked to HIV services embraced the concept of CM, preferably from a peer in recovery, as facilitating their navigation of HIV services in Russia's fragmented health system. Some felt CM empowered their coping with health system challenges and stigma. Among participants not connecting to HIV services, themes such as "lack of motivation", "no need for HIV care" and "active drug use" emerged as major barriers both to engage with CM and to seek HIV care.
Conclusions: Russian addiction patients who linked to HIV care credit CM for facilitating linkage, while those not linking attribute it to personal (rather than external) issues. Implementation of CM in Russia should focus on empowerment and support in addressing both personal and system factors such as stigmatization. Programs need to consider strategies to overcome barriers such as poor motivation.
Financial Support: Funded by NIDA, R01DA032082, R01DA032082-03S1.

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INTRINSIC CLUSTERING OF TREATMENT OUTCOME IN RECOVERY FROM OPIOID USE DISORDER: RESULTS FROM STARTING TREATMENT WITH AGONIST REPLACEMENT THERAPIES.

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Aims: Treatment success and failure in recovery from opioid use are generally defined by clinical intuition and consensus. Clustering patterns in patient's urine toxicology screens and genotypes may define subtypes of clinical outcomes.
Methods: We analyzed a subset of individuals from a multicenter trial, Starting Treatment with Agonist Replacement Therapies (START) who have genetic data available (n=663). The trial compared buprenorphine/naloxone and methadone over 24-weeks. Urine toxicology screen and clinic attendance records were clustered using principal component analysis and k-means. Associations with genotype of the rs678849 locus in OPRD1 (δ-opioid receptor gene) and treatment group assignment were analyzed using linear regression.
Results: Methadone treatment was associated with cluster 1 placement, which corresponds to a behavioral subtype of patients who attended clinic consistently, with or without negative urine toxicology (p<1E-5). C/C Genotype of the rs678849 locus in OPRD1 is also associated with cluster 1 placement (p<1E-3). Stratifying for ethnicity, rs678849 genotype is significantly correlated to cluster 1 placement for both African Americans (p<1E-3) and European Americans (p=0.01), and treatment by genotype interaction is observed in African Americans (p=0.03).
Conclusions: It may be possible to define opioid treatment outcome through clustering of urine toxicology screens and associations with genotypes. Both treatment group assignment and δ-opioid receptor genotype influenced cluster placement. This analytical strategy may be applied to other clinical trial data that use urine toxicology screen as an outcome metric.
Financial Support: This work is partially supported by NIH (5T32DA007294, SXL).

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INHIBITORY CONTROL: A BRAIN CONNECTIVITY STUDY COMPARING COCAINE-DEPENDENT SUBJECTS AND CONTROLS.

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Aims: We used the SPM12 module, dynamic causal modeling (DCM), to test if the effective connectivity underlying inhibitory control is altered in cocaine dependent subjects (CDs). Functional magnetic resonance imaging (fMRI) based effective (directional) connectivity in DCM is modeled at the neuronal level rather than the blood oxygen level dependent level, suggesting that DCM is less confounded by disruption by disease or drugs on neurovascular coupling and/or hemodynamic response.
Methods: The DCM analysis was conducted based on fMRI data acquired from 13 CDs and 10 healthy controls (CTLs) while they performed a Go/NoGo task with two levels of difficulty (Easy and Hard) in the NoGo condition. DCM Network Discovery, was used to search for the optimal model in each group.
Results: The performance on the Go/NoGo task was similar between CDs and CTLs. The prefrontal-striatal connections were modulated (influenced) by the NoGo conditions for both groups. The connectivity from left (L) anterior cingulate cortex (ACC) to to L caudate was the only connectivity modulated by the Easy NoGo condition for both groups. There was no group difference in this modulation effect. The connectivities from right (R) dorsolateral prefrontal cortex to L caudate and from R inferior frontal cortex to L caudate were modulated by the Hard NoGo condition in the CTLs, but the connectivity from L ACC to L caudate was the only connectivity modulated by the Hard NoGo condition in the CDs.
Conclusions: These results indicated that during Hard NoGo trials, CDs showed a different pattern of prefrontal-striatal connectivity while achieving behavioral performance similar to CTLs.
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DRUG SCHEDULING OF STIMULANTS: DOPAMINE TRANSPORTER EFFECTS, BRAIN OCCUPANCY AND ABUSE LIABILITY.

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Aims: Newly emerging designer psychostimulants target the dopamine transporter (DAT). Some with scant in vivo pharmacological data have been consigned to Schedule I on the basis of chemical analogy and receptor/transporter activities in vitro. DAT occupancy in living brain conceivably is a rapid, accurate predictor of abuse liability.
Methods: DAT occupancies of compounds with in vitro DAT affinities were monitored by PET, using the DAT probe [11C]CFT. Baseline DAT density (binding potential, BP) was measured in rhesus monkeys, the test compound (1 mg/kg or higher, i.v.) was administered and PET scans were repeated 1 hour later after a second [11C]CFT injection. Occupancy was calculated as reduced BP, and for some compounds, data was compared with locomotor stimulant and drug discrimination effects in rodents.
Results: DAT substrates were potent inhibitors of [3H]dopamine transport but far less potent at [3H]CFT binding sites on the DAT. Potencies of DAT blockers for [3H]CFT binding and [3H]dopamine transport were similar. Some compounds with high DAT affinity *in vitro* occupied DAT sites in living primate brain. Several potent inhibitors of DAT transport and [3H]CFT binding sites *in vitro* occupied few or no DAT sites in living brain, suggesting limited or no abuse liability.
Conclusions: (1) High potencies using radioligand binding or transporter assays are not necessarily predictive of DAT occupancy in vivo. (2) PET imaging in living brain rapidly measures DAT occupancy. (3) Compounds with high potency in vitro that do not occupy the DAT in living brain may not cross the blood brain barrier, or undergo rapid metabolism, or storage in lipid sites. (4) DAT occupancy in living brain conceivably is a better predictor of the psychostimulant effects and abuse liability of DAT inhibitors.
Financial Support:
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THE USE OF A PARALLEL LATENT GROWTH MODEL IN UNDERSTANDING SMOKING AS A COMORBID DISORDER.

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Aims: The aim of this paper is to demonstrate the usefulness of using a parallel latent growth curve model (LGCM) when studying two comorbid disorders. Secondary data analyses will be applied to two randomized clinical trials in order to outline the effectiveness of such a methodological approach; the first evaluates the relationship between smoking cessation and ADHD (Study A), while the second involves smoking cessation and stimulant use (Study B). The use of a parallel LGCM will allow for the simultaneous evaluation of two disorders with the intent to answer these several questions about the relationship between the two disorders: (1) Are the initial levels of the two disorders related?; (2) Are the growth trajectories of the two disorders related?; (3) Does the initial status of one disorder predict change in the other disorder over time?; and (4) Does treatment influence change in either of the disorders over time?
Methods: Disorders will first be estimated separately in order to establish a reliable and accurate latent growth model for each. A series of analyses will allow us to focus on the form and strength of change for each, the average baseline value (i.e., intercept), change over time (i.e., slope), and whether the intercept and slope *within* each disorder is correlated. Once a good fitting model for both disorders is established (for Study A and Study B), a parallel LGCM will be estimated in order to answer the previously stated questions.
Conclusions: The association between smoking and ADHD, as well as smoking with stimulant use is strong enough where the application of a parallel LGCM seems appropriate. As stated previously, the purpose of this study is to demonstrate the effectiveness of a parallel LGCM when working with two comorbid disorders. By doing so, researchers are able to answer many more questions than analyzing disorders separately, which may yield advancement to clinical practices.
Financial Support: N/A

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EFFICACY AND TOLERABILITY OF DOXAZOSIN IN PSYCHOSTIMULANT-DEPENDENT PATIENTS.

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Aims: Examine safety and efficacy of doxazosin (DOX) extended release (ER) (8mg/d) vs placebo (PLA) to reduce methamphetamine (METH) and cocaine (COC) use in METH and COC dependent (dep) volunteers over 10-wk pilot outpatient trial.
Methods: 14 COC (50% M; 71% AA) and 8 METH (62.5% M; 12.5% AA) dep participants (PTS) were randomized by sex, race and withdrawal severity to DOX ER (8 mg/d) or PLA in a 10-wk, double blind, placebo-controlled outpatient trial. PTS were inducted onto DOX or PLA (wks 1-2), and continued DOX or PLA wks 3-8. Subjects participated in wkly individual CBT. Study adherence was facilitated by CM procedures (fixed monetary incentives and fishbowl pulls to attend appointments and return blister packs). Supervised urines and vitals were obtained 2X wkly. After 8 wks, PTS were tapered off study medication over 1-wk, monitored for 1 wk, then referred for treatment.
Results: Treatment groups did not differ on baseline characteristics, though COC dependent PTS were more likely than METH dependent PTS to be AA (Fisher p=0.02). COC users were older (44.3±7.6) than METH users (34.5±6.2; p=0.006). COC and METH + urines significantly increased over time in DOX relative to PLA (OR=1.05, z=2.20, p<0.03). Supine, seated and standing systolic and diastolic BP did not differ significantly over time between groups, nor was there significant interaction effect between time and primary drug of choice for BP. COC dependent PTS had significantly lower mean sitting HR (t=-2.15, p=0.04) and supine HR (t=-3.21, p<0.005) compared to METH dependent PTS. Adverse events were mild and those occuring at a frequency > than placebo included palpitations (N=1), shortness of breath (N=1), heartburn (N=1) and fatigue (N=1).
Conclusions: These results suggest that DOX seems to be well tolerated from a cardiovascular standpoint, but the current dose may be inadequate for reducing psychostimulant use.
Financial Support: NIDA grant DA018197-06

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PREDICTORS OF INDUCTION ONTO XR-NTX IN PATIENTS WITH OPIOID USE DISORDER.

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Aims: Naltrexone induction of patients with opioid use disorder (OUD) is often limited by high rates of drop out, and a better understanding of factors that may contribute to treatment failure is in order. We therefore examined characteristics of patients with OUD as predictors of naltrexone induction in a series of patients entering a clinical trial of extended release naltrexone (XR-NTX) treatment.
Methods: Treatment-seeking individuals with moderate to severe OUD were given decreasing doses of buprenorphine with increasing doses of naltrexone (LNTX-BUP) during a 7-day outpatient XR-NTX induction procedure. Withdrawal discomfort, craving, and drug use were assessed daily until the XR-NTX injection. Logistic regression was used to identify participant characteristics that may predict successful administration of XR-NTX after induction.
Results: No significant differences in socio-demographic or clinical characteristics, and in-treatment measures of withdrawal intensity and drug use were found between patients who received XR-NTX (N=24), and those who did not complete treatment (N=8). In a stepwise logistic regression model, higher intensity of opioid withdrawal at baseline was significantly associated with the likelihood of XR-NTX administration [Beta= 0.263 (0.114), Wald 5.35 (1), p= 0.02, 95% CI 1.020-1.570], explaining 35% of outcome variance.
Conclusions: Baseline conditions, including the degree of withdrawal discomfort at admission, may affect outpatient LNTX-BUP induction to NTX among OUD individuals. Further studies will contribute to identify specific characteristics of patients who respond positively to different methods of XR-NTX treatment induction.
Financial Support: Financial support and XR-NTX injections were provided through an Investigator-Initiated Trial Grant from Alkermes, Inc

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PATTERNS OF OPIOID USE AND CO-MORBIDITY IN NON-TREATMENT-SEEKING INDIVIDUALS WITH OPIOID USE DISORDER.

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Aims: Most individuals with opioid use disorder (OUD) do not seek treatment, and little is known about risk factors for overdose. Thus, we analyzed screening data from non-treatment-seeking individuals with OUD, hypothesizing higher rates of medical and psychiatric co-morbidity, and polysubstance use.
Methods: During screening visits for research studies, data from self-report, clinical interviews, and urine toxicology findings were analyzed.
Results:
There were 205 screens: 83% Male, 42% Black, 29% Caucasian, and 25% Hispanic. The average age was 44 (±8.5 (SD)) years. Most used heroin exclusively (47%); 16% used prescription opioids, and 37% reported using both. Among heroin users, IV, IN, IV/IN use was respectively 41%, 48%, and 7%. Average amount of heroin use was 6 bags per day (±4.6) for 12.7 years (±11.0). The average duration of prescription opioid use was 2.3 years (±5.6). Medical co-morbidities included chronic pain, primarily low back pain (25%/12%), hepatitis C (24%), hypertension (4%), asthma (3%), and HIV (1%). Psychiatric co-morbidity included: depression (11%), anxiety (4%), and bipolar disorder (2%). About 13% reported a history of opioid overdose, and 79% had past legal problems. Sixty-one percent had prior methadone use, with 34% having attended a methadone program. About 58% reported past buprenorphine use; of which, only 31% was prescribed. Reported current other drug use was cocaine 39%, marijuana 31%, and benzodiazepines 27%, whereas urine toxicology results were opiates 79%, cocaine 43%, oxycodone 36%, methadone 36%, buprenorphine 36%, benzodiazepines 26%, and marijuana 20%.
Conclusions: Our sample showed high rates of hepatitis C, chronic pain, and polysubstance abuse, especially cocaine, benzodiazepines, and mixed opioid use. A significant minority of non-treatment-seeking individuals with OUD have previously received agonist therapy, suggesting potential to be engaged in treatment. Moreover, overdose prevention strategies targeting this population are needed.
Financial Support: NIDA DA 31022,9236,16759

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SLEEP QUALITY DOES NOT PREDICT FRONTOLIMBIC WHITE MATTER INTEGRITY IN YOUNG MARIJUANA USERS.

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Aims: Marijuana (MJ) is the most commonly used illicit drug in the United States, with 31% of young adults (age 19-28) endorsing use during 2012 (Johnston et al., 2012). Acute THC administration leads to disrupted sleep, such as decreased REM, and MJ users report reduced sleep quality (Freemon, 1974; Maple et al., in prep). Greater MJ use predicts decreased white matter integrity in young adults (Baker et al., 2013) and white matter integrity has been related to sleep (Piantoni et al., 2013). Thus, we hypothesized that decreased sleep quality would be related to reduced frontolimbic white matter integrity within a sample of MJ users.
Methods: Data were collected from 42 MJ users ages 18-25 (26M/16F). Individuals were excluded for psychiatric, major medical, and neurologic disorders. Quantity of past year alcohol, nicotine, MJ, and other drug use was assessed (Sobell & Sobell, 1992) and participants completed the Pittsburgh Sleep Quality Index (PSQI). White matter integrity was measured using fractional anisotropy (FA) and mean diffusivity (MD) with FreeSurfer's tractography software (Yendiki et al., 2011). Multiple regressions tested whether sleep quality predicted white matter integrity of frontolimbic tracts (corpus callosum forceps minor, right/left uncinate fasciculus, and right/left anterior thalamic radiations) after controlling for demographics.
Results: After controlling for age, gender, verbal intelligence, alcohol use, cotinin levels and past year MJ use, sleep quality did not predict white matter integrity in any frontolimbic tracts ($p > 0.10$) in a group of young adult MJ users.
Conclusions: These findings suggest that comorbid sleep problems do not explain differences in white matter integrity between MJ users and controls found in this sample (Shollenbarger et al., under review). Future studies should include larger sample sizes and comparison to a non-using control group. Clinical implications will be discussed.
Financial Support: 3R01DA030354 (PI: Lisdahl); 1R03DA027457 (PI: Lisdahl)

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LABORATORY DRUG ADMINISTRATION DOES NOT INCREASE USE IN THE NATURAL ECOLOGY IMMEDIATELY FOLLOWING STUDY DISCHARGE.

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Aims: The experimental administration of drugs is critical for the identification of safe and effective pharmacotherapies to treat substance-use disorders. However, ethical codes dictate that drugs administered in research settings should not (1) exacerbate current drug use or (2) precipitate new drug use outside the laboratory. Laboratory drug administration does not increase drug use at one to six months following study completion. Drug use immediately following discharge has not been assessed. We hypothesized that experimental drug administration would not change naturalistic drug use in the first three weeks following completion of an inpatient research protocol.
Methods: Data from four inpatient studies in which cocaine or methamphetamine was administered alone and in combination with a candidate putative pharmacotherapy were included in this retrospective analysis. Participants were non-treatment-seeking, current stimulant users (N=19). Drug urine specimens and self-reported drug use three weeks prior to admission and following discharge were compared using Wilcoxon sign-ranked tests.
Results: Urine specimens and self-reported drug use were not significantly different in the three weeks following discharge relative to the three weeks prior to admission (p's > 0.05).
Conclusions: Experimental administration of stimulants did not exacerbate subsequent drug use or precipitate new use outside the laboratory in this sample. This analysis is the first to report that drug use is not altered in the first three weeks following discharge, when perceived risk for increased use is highest. The impact of drug administration on drug use in natural settings should be verified empirically to self-monitor research protocols.
Financial Support: NIDA R01 DA025032; R01 DA 032254; R21 DA035481; T32 DA035200 (CRR); R01 DA033364 (JAL); NCATS TL1 TR000115 (KRM)

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VERBAL MEMORY IS IMPAIRED AMONG HIV+ FEMALE, BUT NOT HIV+ MALE COCAINE USERS.

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Aims: Use of crack cocaine by HIV+ women uniquely predicts accelerated disease progression and cognitive impairment, but a parallel association has not been investigated among HIV+ men. We addressed this question by comparing verbal memory among 213 HIV+ and HIV- men and women with a history of cocaine dependence.
Methods: The sample consisted of 84 HIV+ and 129 HIV- adults, including 114 men and 109 women, enrolled in a larger study of neurocognitive effects of sex and HIV status among crack users. All subjects met DSM-IV criteria for cocaine dependence but were verified abstinent by toxicology screening. Subjects completed measures of addiction severity and psychiatric comorbidity, as well as a neurocognitive battery that included the Hopkins Verbal Learning Test, a standardized memory task requiring subjects to learn a 12-item word list over 3 learning trials.
Results: The four groups were comparable in racial composition, estimated verbal IQ, prevalence of alcohol and cannabis history, and comorbid psychiatric disorders. We analyzed total words recalled using a Sex x HIV Serostatus x Trial mixed-model analysis of variance. We found a significant interaction of sex and HIV serostatus, $p < .05$. HIV+ women recalled significantly fewer words compared with HIV+ men and both HIV- groups, $p < .05$. consistent with expectation HIV- women significantly outperformed HIV- men.
Conclusions: Among HIV+ and HIV- crack cocaine users, HIV+ women showed a verbal memory deficit compared with HIV+ men and both HIV- groups. This finding suggests that HIV's neurotoxic effects are more deleterious among female compared with male crack cocaine users; however, similar studies of alcohol or opioid dependence and additional neurocognitive functions are needed to determine the extent that neuroAIDS appears to manifest itself differently among men and women and investigate if this pattern is specific to stimulant addiction.
Financial Support: Supported by the National Institute on Drug Abuse R01DA12828 to EM Martin.

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TREATING SMOKERS IN SUBSTANCE TREATMENT WITH CONTINGENT VOUCHERS, NICOTINE REPLACEMENT AND BRIEF ADVICE ADAPTED FOR SOBRIETY SETTINGS.

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Aims: Smokers with substance use disorders (SUD) have difficulty quitting smoking yet SUD treatment provides an opportunity to intervene. Adding nicotine replacement (NRT) to voucher-based treatment with motivational counseling may improve outcomes observed with vouchers without NRT. The aim was to investigate effects of vouchers contingent on smoking abstinence (CV) versus noncontingent vouchers (NV), both combined with NRT and brief advice adapted for sobriety concerns

Methods: Smokers who had not sought smoking treatment (n = 340) in residential SUD treatment were provided 14 days of vouchers for complete smoking abstinence after a 5-day smoking reduction period, or received vouchers not contingent on smoking, plus 4 sessions of brief motivational advice and access to NRT. Smoking was assessed during the 14 days of vouchers for abstinence (carbon monoxide [CO] confirmation) and at 1, 3, 6 and 12 months after treatment start using self-report and cotinine confirmation of past 7 days point-prevalence abstinence.

Results: Within treatment, 20% had complete abstinence with CV, 5% with NV ($p < .001$). In CV, 57% of CO readings indicated abstinence compared to 32% in NV ($p < .001$). In GEE analyses, CV resulted in fewer cigarettes per day (2.0 fewer) at 1, 3 and 6 months ($p < .01$) and fewer percent days smoking (8% fewer, $p < .03$) across 1, 3, and 6 months after CV started. Only 2% more had point-prevalence abstinence in CV versus NV from 1 to 12 months (ns). No differences in substance use were seen.

Conclusions: Within-treatment effects are stronger than in a prior study using with CV without NRT but effects are minimal after vouchers end. Implications for voucher treatment include investigating effects when combined with stronger smoking medications. Smoking treatment did not harm SUD recovery.

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ARE MEDICAL MARIJUANA USERS DIFFERENT THAN RECREATIONAL MARIJUANA USERS?

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Aims: To describe the profiles of recreational versus medical marijuana users.

Methods: Data came from the 2013 U.S. National Survey on Drug Use and Health 54,981 respondents aged 12 and older. Respondents were asked about past-year marijuana use (MU) recreationally and/or as prescribed by a doctor. Using weighted multinomial logistic regression, we compared respondents who were non-MU, recreational MU, medical MU, and recreational+medical MU on demographic characteristics, living in a state with or without medical marijuana laws (MMLs), psychiatric disorders, substance use, and perceived risk of drug use.

Results: Of the US population 12 years and older, 11.5% were past-year recreational MU, 0.7% were past-year medical MU, and 0.4% were medical/recreational MU. States with MMLs versus those without such laws had higher prevalence of recreational MU (13.1% vs. 10.8%, $p<0.001$), medical MU (1.7% vs. 0.2%, $p<0.001$) and recreational+medical MU (0.7% vs. 0.3%, $p<0.001$). Compared to recreational MU, medical users, and recreational+medical MU were more likely to be 18 and older vs. 12-17, to have past-year anxiety disorder and to be past-month alcohol abstainers, and less likely to be Asian vs. non-Hispanic White, adjusted for all other covariates. Past-year major depressive episodes were significantly associated with medical/recreational use vs. recreational-only MU in states without MMLs. Recreational, medical and recreational+medical MU were less likely than non-users to perceive great risk in using marijuana weekly. Recreational users were less likely than non-users to perceive great risk in daily heavy drinking. Similar associations were found in analyses stratified by state MML.

Conclusions: Medical MU users report more psychiatric comorbidity and lower levels of alcohol use compared to those of recreational users. All MU subgroups have lower levels of perceived risk of MU compared to non-users.

Financial Support: NIDA grant R01DA037866 (PI: Martins).

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AGE OF CIGARETTE SMOKING ONSET IS ASSOCIATED WITH IMPULSIVE RESPONDING ON A SMOKING GO/NOGO TASK.

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Aims: Initiation of cigarette smoking during adolescence coincides with structural and cognitive neuromaturation. Thus, early onset smokers (EOS; <16 yrs) may be at unique risk of altered normal executive function development relative to late onset smokers (LOS; >16 yrs). This study investigated differential effects of age of smoking onset on response impulsivity and inhibitory control using a novel smoking Go/NoGo task (Luijten et al., 2011).

Methods: Adult EOS (n=6) and LOS (n=10) in acute nicotine withdrawal and adult non-smokers (NS;n=10) were shown Smoking or Non-Smoking images with either a blue (Go) or yellow (NoGo) frame. Participants were instructed to respond to blue-framed Go trials quickly and accurately, and withhold responding for yellow-framed NoGo trials. Each Smoking and Non-Smoking image was shown 3 times as a Go stimulus and once as a NoGo stimulus.

Results: EOS and LOS exhibited more Go errors ($p<0.01$) and a greater false alarm rate ($p<0.01$) than NS. EOS and LOS showed lower overall Go response accuracy ($p<0.01$), and EOS also exhibited lower Smoking Go accuracy ($p<0.03$), than NS. EOS and LOS exhibited lower Smoking NoGo accuracy ($p<0.02$), and LOS also showed lower Non-Smoking NoGo accuracy ($p<0.02$), than NS. Smoking Go accuracy and Non-Smoking NoGo accuracy were each correlated with age of smoking onset ($p<0.01$) and daily cigarettes smoked ($p<0.02$).

Conclusions: EOS had difficulty responding accurately to Smoking Go stimuli, suggesting that these distracting images disrupted attention to task demands. In contrast, LOS had difficulty withholding responses to both Smoking and Non-Smoking NoGo stimuli, indicating greater impulsivity and deficits in inhibitory control, regardless of category. Collectively, preliminary findings suggest age of smoking onset differentially impacts task-related attention and response inhibition, thus individualized cognitive approaches may improve executive function in smokers in treatment programs.

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RISKS ASSOCIATED WITH NONMEDICAL PRESCRIPTION OPIOID USE: TRANSITION TO HEROIN USE AND DRUG INJECTION, OVERDOSE AND HEPATITIS C.

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Aims: To elucidate drug use trajectories among young nonmedical prescription opioid (PO) users and the risks associated with such trajectories (heroin use, overdose, drug injection and Hepatitis C infection).

Methods: New York City young adults (N=109) were recruited via respondent-driven sampling for an ongoing epidemiological survey to assess drug use patterns and overdose experiences. Eligible participants were ages 18-29 and had used POs nonmedically and/or heroin in the past 30 days. Participants were also tested on-site for HCV antibodies.

Results: Participants were 31% female, 16% Latino, 82% White and 14% other races (mean age=23.3 years). Regarding education, 23% did not complete high school, 35% received a high school diploma/GED and 42% attended or graduated college. Most participants (86%) initiated PO use in their teens (mean age=16.2 years). For 88 % of participants, PO initiation led to regular (1 or more times/week) PO use by 18 years old on average, and 62% experimented with PO injection (mean age at first PO injection=18.5 years). Ninety-seven percent of participants also used heroin (mean age at heroin initiation=18.4 years) and 90% injected heroin (mean age at first heroin injection=19.8 years). Thirty one participants (29%) tested positive for HCV antibodies. Most participants (56%) had experienced overdose (3.7 overdoses per participant on average); about two thirds of these required emergency personnel response and/or hospitalization.

Conclusions: For many youth, early PO initiation led to long-term opioid use, heroin use, drug injection and repeated overdose. Drug injection carries a serious risk of HCV infection. There is a pressing need to develop innovative prevention programs to help younger teens avoid initiating nonmedical PO use and to assist current PO users in preventing escalation of opioid use, drug injection and HCV infection.

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EARLY PARENTAL SUPPLY OF ALCOHOL AND ALCOHOL CONSUMPTION IN MID-ADOLESCENCE: A LONGITUDINAL STUDY.

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Aims: The strength of the association between early parental supply of alcohol and teenage drinking remains unclear. Research is largely cross-sectional, with limited samples, short follow-ups, and important confounders are unmeasured. We aimed to provide a comprehensive analysis of the associations between parental provision of alcohol and mid-teen alcohol consumption, adjusting for known child, parental, familial, and peer covariates.
Methods: A cohort of 1927 adolescents was assessed in four school years (Grades 7-10) for parental supply of alcohol, and a wide range of adolescent demographics and behaviours (externalising, internalising, social problems), parental/familial characteristics, peer characteristics, and alcohol use. The associations between these variables and drinking at Year 10 were assessed using logistic regression.
Results: After covariate adjustment, adolescents exposed to parental supply of alcohol had higher rates of drinking whole beverages (OR=3.00, 95% CI, 1.50-6.01) than adolescents not exposed. Dose-response relationships between frequency of parental supply and odds of drinking whole beverages were observed. Other predictors after adjustment included past drinking, age, sex, and peer influences.
Conclusions: Parental supply of alcohol in early teen years increases the odds of drinking whole beverages in mid teen years after controlling for a range of other variables.
Financial Support: Australian Research Council Discovery Project grant DP:1096668.

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NON-MEDICAL PRESCRIPTION OPIOID USE AND COMMERCIAL SEX WORK AMONG ADULTS IN RESIDENTIAL SUBSTANCE USE TREATMENT.

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Aims: High rates of substance use have been documented among individuals involved in commercial sex work (CSW) and a significant proportion of adults seeking substance use treatment report prior CSW. Little is known about the relationship between CSW and non-medical prescription opioid use (NMPOU), as research in this area was conducted before the escalation NMPOU in the US. The aims of this study were to describe the prevalence of recent CSW in a large residential substance use treatment center; and examine the association between NMPO use and CSW after controlling for demographic and clinical risk factors.
Methods: Participants were 504 adults recruited from a residential treatment center between 2009-2013. Participants completed self-report measures of CSW, NMPOU, substance use and psychiatric symptoms. Bivariate and multivariate logistic regressions were used to examine the relationship between CSW and NMPOU, before and after adjusting for demographic and clinical correlates of CSW.
Results: Results indicated that 14% (n = 71) of participants engaged in CSW in the previous month. NMPOU use was more common in those with a history of CSW (84% of sex workers vs. 54% of non-sex workers; OR = 4.48, p <.05). In the multivariate model, CSW was associated with female gender, ethnic minority status, global psychiatric symptom severity and cocaine use. After controlling for these factors, NMPOU remained significantly more common in those who engaged in CSW (OR = 2.39, p <.05).
Conclusions: Individuals engaged in sex work reported extremely high rates of NMPOU, and NMPOU was associated with sex work after adjusting for psychiatric symptoms and other substance use. Residential treatment provides a unique opportunity to address the complex psychosocial and psychiatric needs of substance users involved in CSW, but continued work is needed to develop interventions for this vulnerable group.
Financial Support: This research was a supported by DA029587 (MAI),DA03531 (ASBB) and DA036008 (EEB).

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CHALLENGES TO OPIOID TREATMENT PROGRAMS AFTER HURRICANE SANDY: IMPACT, PREPAREDNESS, AND RECOVERY.

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Aims: To describe how Hurricane Sandy impacted opioid treatment programs (OTPs) and present recovery and disaster planning policy recommendations.
Methods: Staff (via surveys), clients (via focus groups) and directors (via interviews) at nine OTPs in the NYC metro area shared their perspectives on how preparation for, and recovery from Hurricane Sandy was handled at their site.
Results: Patients reported treatment disruptions such as transportation and communication problems, methadone dose reduction, suspenstion of psychiatric medication, and increased "pick-up" schedule. Some patients reported resumption of illicit opioid use due to difficulties obtaining methadone. Staff reported challenges in arranging guest-dosing, protocol for providing take home doses, responding to unanticipated problems with electricity and heat, and guests from other sites and states. Directors reported how local, state, and federal regulations helped or hampered continuity of care, administrative and fiscal challenges associated with changing caseloads, and long term effects of service disruption. There were also several occurrences of how stigma toward methadone maintenance (especially reported by patients) appeared to contribute to treatment disruption. Despite these multiple disruptions, there was also evidence that treatment continuity was sustained for most patients during this period.
Conclusions: The consequences of Hurricane Sandy varied greatly based on program location and storm preparations. Data collected to date suggest that factors to assure treatment continuity during and after a catastrophic event should include better communication among OTPs and government authorities (e.g., DEA), transportation resources, and comprehensive and consistent emergency preparedness/recovery plans among OTPs.
Financial Support: Dept. of Health and Human Services, ASPR HITEP140014-01-00

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HAPTEN SELECTION FOR HEROIN VACCINES.

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Aims: The aim of this study is to select a heroin hapten for a heroin vaccine. Heroin rapidly degrades to 6-acetylmophine and morphine after injection. We hypothesize that a heroin hapten can be designed that is chemically stable and can induce antibodies that bind to heroin and its metabolites.
Methods: Seven different opioid haptens were synthesized. A mercaptopropanamide group was attached as the linker at the C3, C6 or the bridge nitrogen. The acetyl groups of heroin were replaced with acetamide or 2-oxypropyl groups. The haptens were attached to tetanus toxoid and mixed with liposomal lipid A. Mice were immunized with 3 doses every 3 weeks. The sera were assayed for hapten antibodies. The mice were challenged by the subcutaneous route with heroin (0.75-1 mg/kg) and efficacy was assessed by nociception assays.
Results: Anti-hapten titers ranged from 100,000 to 6,000,000. Mice immunized with haptens coupled at the bridge nitrogen were only partially protected with a % maximal potential effect (%MPE) ≥50. Animals immunized with C3 position haptens were not challenged due to low antibody titers. Mice immunized with a C6 linked morphine hapten (MorHap) had a %MPE of 35. After optimization of the MorHap conjugation procedure, the %MPE was <10 and was maintained 9 weeks after the last vaccination.
Conclusions: The best hapten was MorHap, which induced high antibody titers that protected the mice from heroin challenge. MorHap was coupled at the C6 position, whereas bridge nitrogen linked haptens induced high titer antibodies, but only had moderate efficacy.
Financial Support: This work was supported by a Cooperative Agreement (W81XWH-07-2-067) between the Henry M. Jackson Foundation and the US Army Medical Research and Materiel Command; an Avant Garde award from NIDA (1DP1DA034787-01); and the NIH Intramural Research Programs of NIDA and NIAAA.

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PATTERNS OF BEHAVIORAL HEALTH SERVICES PROVIDED IN A 2012 NATIONAL SAMPLE OF U.S. OUTPATIENT SUBSTANCE USE DISORDER TREATMENT FACILITIES: IMPLICATIONS FOR THE TREATMENT OF CO-OCCURRING DISORDERS.

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Aims: According to the 2012 National Survey on Drug Use and Health, of the 20.7 million adults meeting substance use disorder (SUD) criteria, 8.4 million (40.7%) had co-occurring mental illness; only 12.2% received specialty treatment for SUD. Facilities often identify their main treatment focus, but the categories may not fully describe clusters of services. To address this potential discrepancy, we empirically derived classes of specialty SUD outpatient treatment facilities using patterns of behavioral health services provided in the United States.
Methods: Data were obtained from the 2012 National Survey of Substance Abuse Treatment Services (N-SSATS). The current study included community-based facilities offering outpatient treatment in the 50 states and the District of Columbia. Latent class analysis (LCA) was used to identify unobserved classes of facilities based on patterns of observed behavioral health services offered.
Results: Of the 14,995 facilities participating in the 2012 N-SSATS, 11,488 (76.6%) met inclusion criteria. Facility-identified primary treatment focus included SUD treatment (52.0%), mental health (7.5%), SUD and mental health (36.4%), and general health/other (4.1%). Over a third (38.9%) of facilities had special programs or groups for people with co-occurring disorders. Preliminary analyses indicated an 8-class structure distinguishing facilities beyond their primary treatment focus. These findings will be discussed, along with the relationship between empirically-derived classes and treatment foci.
Conclusions: Behavioral health comorbidities are highly prevalent in SUD treatment samples. Given the evolving healthcare environment, understanding the degree to which facilities nationwide provide treatment for co-occurring disorders has clinical and policy implications.
Financial Support: Ms. Mauro and Dr. Furr-Holden receive funding from NIDA T32DA007292.

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CHANGES IN THE PAIN ANALGESIC AND HEROIN EPIDEMIOLOGY.

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Aims: The abuse of analgesic pain relievers and/or heroin is a significant public health concern. The hypothesis is that the patterns of use of opioid pain pills and heroin have changed and the treatment need is greater than available services.
Methods: Data from following national dataset were analyzed: National Household survey on Drug Use and Health (2002-2012), Monitoring the Future (1999-2014), American Association of Poison Center Cases of human exposures (2004-2012), SAMHSA Drug Abuse Warning Network emergency department cases (2004-2011), SAMHSA Treatment Episode Data Set admissions (1992-2012), National Center on Vital Statistics drug poisoning deaths (1999-2013), grams of opiate drugs distributed to pharmacies and hospitals as reported in DEA's Automated Reports and Consolidated Orders System (1997-2013), and number of seized items identified in reports to DEA's National Forensic Laboratory Information System (2005-2013).
Results: Findings include shifting from narcotic analgesics to heroin. The age distributions are changing: heroin users are becoming younger while the age distribution for analgesic pain pills is bimodal, with increasing rates of younger users seeking treatment and increasing rates for older decedents reported in the mortality data.
Conclusions: Since 2010, the datasets examined show decreases in the numbers of other opiates, hydrocodone, and oxycodone, with increases in heroin. According to NSDUH, the number of those currently dependent on or new users of analgesic pain medications or heroin totals nearly 5.2 million, while less than 1.5 million opioid dependent patients are receiving methadone or buprenorphine or naltrexone according to SAMHDA's National Survey of Substance Abuse Treatment Services (N-SSATS) and IMS Health.
Financial Support: Funding by the University of Texas at Austin, Center for Social Work Research

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ALTERNATIVE ENDPOINTS BASED ON HEALTH OUTCOMES IN STIMULANT USERS TRIALS.

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Aims: Identifying patterns of drug use that are consistent with health outcome changes is essential to defining a surrogate measure to evaluate treatment effectiveness and broaden the concept of recovery. The goal is to identify alternative endpoints other than drug use for future trials.
Methods: Health outcomes based on the Addiction Severity Index (ASI) and World Health Organization quality of life (WHO-QoL) assessments are explored. ASI composite scores were calculated for seven domains (medical, employment, alcohol use, drug use, legal, family/social, psychiatric) from five randomized controlled trials from the NIDA Clinical Trials Network of stimulant users (N=1665). Four WHO-QoL domains (physical health, psychological, social relationships, environment) and two questions were assessed in two of the trials (N=364). Associations between the baseline health outcomes and baseline stimulant use and between the changes in stimulant use and changes in health outcomes were assessed.
Results: The drug use ASI composite score is associated with stimulant use. No other associations were found between changes in stimulant use and either ASI-lite composite or the WHO-QoL domain scores. The WHO-QoL question: "How would you rate your quality of life?" showed a potential association with baseline stimulant use. In one study, the average number of baseline stimulant use days for those responding very poor was 12 of the past 30, and for those responding very good, the average was 6 of the past 30.
Conclusions: Based on the stimulant user trials evaluated, no measure was identified as related to reduction in drug use outcomes over a short follow-up period. Further investigation of other health outcomes or the development of new metrics related to a meaningful reduction in use is needed.
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IN VIVO EVALUATION OF NOVEL SEROTONIN 5-HT$_{2C}$ RECEPTOR POSITIVE ALLOSTERIC MODULATOR CYD-1-79.

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Aims: Minimizing lapses to drug use is an attractive target to improve treatment success in cocaine use disorder. Our recent findings suggest that dampened 5-HT$_{2C}$R signaling capacity is an important component of vulnerability to relapse. A novel drug design strategy to ameliorate 5-HT$_{2C}$R hypofunctionality is to develop 5-HT$_{2C}$R PAMs. Here, we synthesized new chemical entities to develop 5-HT$_{2C}$R PAMs and evaluated their ability to augment 5-HT$_{2C}$R signaling *in vivo*.
Methods: Based on the structure of synthetic 5-HT$_{2C}$R PAM PNU-69176E, we synthesized 35 compounds and evaluated them in a Ca_i^{++} release assay. We evaluated lead compound CYD-1-79 in rat *in vivo* DMPK assays and the drug discrimination (DD) assay. Rats were trained to discriminate WAY163909 (0.75 mg/kg, IP) from saline (n=12). After establishing the WAY163909 dose-response (0.125-1 mg/kg), we assessed CYD-1-79 (0.125-1 mg/kg) in substitution and combination tests.
Results: Lead compound CYD-1-79 potentiated 5-HT$_{2C}$R- and WAY163909-induced Ca_i^{++} release in stably-transfected h5-HT$_{2C}$R-CHO cells (p<0.05), but alone did not alter Ca_i^{++} release. After administration of CYD-1-79 (50 mg/kg), 555 ng/g was recovered from rat brains. In the DD assay, 1 mg/kg of CYD-1-79 evoked a partial substitution. A combination of low doses of CYD-1-79 *plus* WAY163909 fully substituted for the training dose (90% WAY163909-lever responding).
Conclusions: We have synthesized new chemical entities with the profile of 5-HT$_{2C}$R PAMs; CYD-1-79 crosses the blood-brain barrier and evokes behavioral effects consistent with a 5-HT$_{2C}$R PAM. Optimization of our newly-identified 5-HT$_{2C}$R PAMs and further evaluation in preclinical models will allow us to develop novel pharmacotherapies for cocaine use disorder.
Financial Support: MH093844, DA020087, DA033374, DA007287

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WHAT IS THE IMPACT OF "PROFESSIONAL SUBJECTS" ON MEDICATION EFFICACY TRIALS?

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Aims: Professional subjects, defined here as subjects who enroll in clinical trials only for financial gain, have an unknown impact on medication efficacy trials. The current studies were conducted to model their impact.

Methods: Two types of professional subjects were considered: those who are "destined to succeed" (DS) and those who are "destined to fail" (DF). An example of a DS subject is someone who feigns depression to enroll in an antidepressant trial and then answers questions truthfully after randomization (no longer appearing to be depressed). An example of a DF subject is a smoker who enrolls in a smoking cessation trail with no intension of trying to quit. After setting success rates in legitimate subjects at 5% for placebo and 15% for active treatment, modeling studies evaluated the impact of DS and DF subjects on apparent success rates, the number of subjects required for 80% power (α 0.05, two-sided chi squared test), and apparent effect size (odds ratio).

Results: With no professional subjects, 141 subjects per group yielded 80% power, and the odds ratio was 3.35. With 10% DS subjects, apparent success rates rose to 14.5% and 23.5%, 298 subjects per group were required for 80% power, and the apparent odds ratio fell to 1.81. With 20% DS subjects, apparent success rates rose to 24% and 32%, 494 subjects per group were required for 80% power, and the apparent odds ratio fell to 1.49. In contrast, the impact of DF subjects was modest. With 20% DF subjects in the study population, apparent success rates were 4% and 12%, 180 subjects per group yielded 80% power, and the apparent effect size was 3.27.

Conclusions: While all professional subjects negatively impact efficacy trials, DS subjects are especially problematic. A small percentage of DS subjects in a study population can greatly reduce apparent effect size, a phenomenon that cannot be overcome by increased sample size.

Financial Support: The author was an employee of NIH/NIDA while conducting the current studies.

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SCALING UP SBIRT: STATEWIDE IMPLEMENTATION IN THE OREGON HEALTH PLAN.

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Aims: Oregon approved 16 Coordinated Care Organizations (CCOs) to manage and provide primary care and care for mental health and substance use disorders for Medicaid recipients. To monitor quality of care CCOs report on performance measures including the percentage of adults 18 years and older who completed a validated structured screen for alcohol or drug abuse. The analysis examines change in the use of screening and brief intervention and describes the challenges and solutions supporting statewide and regional implementation.

Methods: A mixed methods analysis describes Oregon's statewide implementation of screening and brief intervention. Medicaid utilization data assessed change in the percent of adults screened and variation among CCOs. Procedure codes (i.e., 99408, 99409, 99420 plus V79.1 or V82.9, V79.1, G0442, G0396, or G0397) tracked the number of patients who completed a standardized and validated instrument for assessing at risk alcohol and drug use. Qualitative interviews with CCO leadership and other stakeholders identified implementation challenges and processes.

Results: Medicaid utilization data reflected minimal implementation of screening and brief intervention during baseline (2010 and 2011) (1% screen rate)and through the second half of 2012 (2%). Change accelerated in the first half of 2013 (3 to 4%); CCOs varied between 1% and 8%. Qualitative analysis noted the challenges of training staff, changing workflow in primary care settings, and using the approved procedure codes.

Conclusions: Screening for alcohol and drug use disorders may facilitate integration by alerting practitioners to the presence of alcohol and drug use and its contribution to medical problems. Scaling up SBIRT procedures has been a substantial challenge for primary care centers and CCOs. Rates remain low but are increasing. The Oregon Health Authofity anticipates that statewide screening will contribute to their efforts to stabilize the costs of care.

Financial Support: Awards from NIDA (R33 DA035640) and NIMH (R01 MH1000001) supported the investigation.

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OPIOID PRESCRIBING PRACTICES OF MEMBERS OF THE NATIONAL DENTAL PRACTICE BASED RESEARCH NETWORK.

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Aims: To examine dental prescribers' perceptions of prescription opioid misuse among their patients, as well as their familiarity with and use of recommended opioid prescribing risk mitigation strategies.

Methods: Participants (N=537) were recruited between October 15 and November 3, 2014, to participate in a five-question 'Quick Poll' via an email disseminated to the membership of the National Dental Practice Based Research Network (www.NationalDentalPBRN.org). Questions assessed frequency of: (1) opioid prescribing; (2) concern regarding potential patient misuse of prescribed opioids; (3) patient education; (4) use of their state's prescription drug monitoring program (PDMP); and (5) interest in continuing education opportunities germane to prescription opioid risk mitigation strategies.

Results: The majority of respondents (80%) reported at least monthly opioid prescribing. Among prescribing respondents (n=429), concerns of patient misuse of opioids were prevalent (75%); however, regular provision of patient education and PDMP use were not common. One-quarter of respondents were not aware of their state's PDMP program. Interest in continuing education was high (83%).

Conclusions: Results indicate that although many dentists reported prescribing opioids for pain management, knowledge and implementation of risk mitigation strategies was not common among this group of practitioners. Future research should apply more rigorous methodologies to examine current dental prescribing practices and the relative contribution of dental opioid prescriptions to misuse, abuse, and diversion. Efforts should be made to extend educational opportunities to dentists regarding use of PDMPs, as well as other risk mitigation strategies.

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REMOTELY MONITORING SMOKING AND RELAPSE IN ADOLESCENTS AND EMERGING ADULTS.

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Aims: Adolescent and emerging adult smokers are highly likely to continue smoking into adulthood, resulting almost inevitably in smoking-related illnesses. Understanding the process of relapse to smoking during a quit attempt is critical for the development of highly efficacious treatment interventions, yet very little is known about the natural history of relapse in this group. A comprehensive technology-based monitoring system would allow for the detailed analysis of smoking and relapse and is a highly fruitful avenue to explore.

Methods: With this goal in mind, a remote monitoring system to detect smoking was developed that utilizes biochemical verification of smoking through breath carbon monoxide (CO) with ecological momentary assessment (EMA), delivered via a smartphone platform (Android and iOS). The process of developing this application (app) was iterative and decision-making was based on preliminary acceptability ratings from representative participants.

Results: The smartphone app consists of several novel features including facial recognition to ensure identity, character recognition of CO values, dynamic programming based on user input, and immediate data transfer to secure servers to monitor and encourage compliance. These features, among others, contribute substantially to reduced burden for research staff and participants.

Conclusions: The use of remote monitoring to detect smoking represents a significant step forward in the improvement of treatment strategies to promote cessation. The development of these systems, however, requires iterative steps and sufficient piloting with the target population prior to implementation. Remotely monitoring smoking allows for the fine-grained characterization of behavioral processes, rather than outcomes that may not capture the complex process of relapse. This knowledge can then inform maximally effective, just-in-time interventions delivered at critical moments to promote long-term abstinence.

Financial Support: NIDA grants K01DA036739, K12DA031794, ACS IRG 97-2919-14.

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PREVALANCE AND PREDICTORS OF ANTENATAL ALCOHOL USE PRIOR TO AWARENESS OF PREGNANCY.

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Aims: Adverse effects of heavy alcohol exposure to the fetus are well established, including cognitive, behavioural and physical deficits. Despite public health guidelines advising abstinence, many women consume alcohol during pregnancy. Contributing to this is the high rate of pregnancies that are unplanned, and high levels of alcohol use amongst women of childbearing age.
The purpose of this study was to examine prevalence and predictors of alcohol use by women prior to awareness of their pregnancy.
Methods: 1200 women and their partners from antenatal clinics completed detailed interviews about alcohol and drug use in each trimester. Alcohol consumption before and after awareness of pregnancy was recorded separately.
Results: Between conception and awareness of pregnancy, 59.7% of women consumed alcohol. At least one occasion of binge drinking in this period was reported by 13% of the sample. Following awareness of pregnancy to the end of the first trimester, the rate of consumption decreased to 21.4% of women. Factors associated with alcohol use included income, age, education, smoking, partner alcohol consumption and IQ.
Conclusions: Most women reduce or cease consumption after becoming aware of the pregnancy. Strategies to reduce drinking in early stages of pregnancy may be needed. Demographic and social factors are related to alcohol use during this period.
Financial Support: NHMRC project Grant #GNT630517

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THE EFFECT OF CHRONIC CONCURRENT INTAKE OF ALCOHOL AND COCAINE ON NEURAL STEM CELL SURVIVAL AND DIFFERENTIATION.

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Aims: Aim 1: Evaluate neural stem cell survival in a transgenic mouse model following chronic concurent treatment with alcohol and cocaine.
Aim 2: Evaluate changes in neural stem cell differentiation in this same mouse model.
Aim 3: Correlate behavioral changes with changes observed in neural stem cell survival and differentiation.
Methods: This study utilizes a novel model of concurent alcohol and cocaine intake. The mouse line is a transgenic fate tracing mouse which enalbes lineage tracing of endogenous neural stem cells. Mice are treated with alcohol and cocaine daily for 6 weeks. Behavioral experiments are performed at the six week mark. Follwing behavior experiments, brains are analyzed using immunohistochemistry for markers of stem cell survival and differentiation.
Results: A significant change in context discrimination behavior was observed in the concurrent drug intake mice compared to mice given cocaine or alcohol alone. Changes in both neural stem cell survival and differentiation were also observed upon immunohistochemical analysis.
Conclusions: Concurrent use of alcohol and cocaine significantly decreases hippocampal learning as shown by context discrimination trials. Additionally, concurrent use also results in exacerbated changes in neural stem cell survival compared to singular drug use.
Financial Support: NIDA T32 Adminstrative Supplement and The John S. Dunn Foundation

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DISTRESS INTOLERANCE AND PRESCRIPTION OPIOID ABUSE IN CHRONIC PAIN PATIENTS.

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Aims: A substantial portion (30-50%) of individuals with chronic pain receiving long-term opioid therapy will misuse their medications. The identification of risk factors for prescription opioid abuse in this population would provide potential therapeutic targets for the prevention and treatment of opioid abuse. Distress intolerance is the perceived inability to tolerate negative physical and emotional states and is a motivator of harmful avoidance behaviors that provide strong and immediate relief from distressing states, such as substance use. In chronic pain, the inability to tolerate pain and emotional responses to pain may lead to the misuse of opioids to avoid these states. The aim of this study was to examine differences in distress intolerance between chronic pain patients with and without prescription opioid abuse.
Methods: Patients receiving opioid medication from a pain management clinic with chronic back or neck pain (N=47, 47% female) were recruited for this study. Participants completed self-report and behavioral measures of distress intolerance, a battery of pain reactivity tests, and measures of opioid abuse.
Results: Results from a logistic regression with presence of opioid abuse as the dependent variable found that distress intolerance was a strong predictor of the presence of opioid abuse (B=0.17, SE_B=0.05, $p < .01$) controlling for age, gender, and severity of pain. For each one-point increase in distress intolerance (on a scale of 10-50), the odds of opioid abuse increased 18%. Participants with opioid abuse had a mean distress intolerance score almost twice that of those without ($t = -4.15$, $p < .001$).
Conclusions: These results suggest that distress intolerance is substantially higher in chronic pain patients who abuse their medications relative to those who do not. Given that distress intolerance is modifiable with treatment, future studies aimed to examine this association prospectively may inform novel therapeutic interventions in this population.
Financial Support: This study was supported by NIDA grants DA034102 and DA035297 (PI: Dr. McHugh).

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EXPOSURE TO HIV-1 TAT PROTEIN POTENTIATES THE REWARDING EFFECTS OF MORPHINE AND REINSTATES EXTINGUISHED CONDITIONED PLACE PREFERENCE.

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Aims: While exposure to the HIV-1-accessory protein Tat is known to increase striatal dopamine levels, the functional consequences of Tat protein on the behavioral response to abused drugs are little known. We hypothesized that HIV-1 Tat expression in brain would modulate the rewarding effects of morphine.
Methods: Using the GT-tg bigenic mouse model, where brain-selective Tat expression is controlled by activation of a doxycycline (Dox) promotor, we tested the effects of Tat protein on morphine-conditioned place preference (CPP). Microdialysis was performed with additional mice expressing Tat protein and repeatedly administered heroin.
Results: Although GT-tg bigenic mice expressing Tat demonstrated saline-conditioned place preferences similar to uninduced littermates and saline- or Dox-treated C57BL/6J mice, Tat expression for 7 days significantly doubled morphine-CPP. The potentiation of CPP for morphine was dependent on the magnitude of exposure to Tat protein. Consistent with this observation, exposure to Tat protein increased the levels of dopamine released in response to heroin in GT-tg mice. Of interest, among GT-tg bigenic mice demonstrating extinction of morphine-CPP, subsequent expression of Tat protein for 7 days resulted in the reinstatement of the extinguished place preference response in previously uninduced mice.
Conclusions: Overall, these data suggest that expression of HIV-1 Tat protein in mouse brain potentiated heroin-induced dopamine release and the rewarding effects of morphine in a dose- and duration-dependent matter. Moreover, the Tat-induced reinstatement of an extinguished place preference for morphine suggests a biological means by which HIV infection may increase the vulnerability to substance abuse and relapse in abstinent subjects.
Financial Support: Funded by R01-MH085607 from NIMH and funds from the State of Florida, Executive Office of the Governor's Office of Tourism, Trade, and Economic Development.

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A COMPARISON OF ATTEMPTED SUICIDE RATES BY METHYLPHENIDATE EXPOSURE IN ADULT AND ADOLESCENT POPULATIONS.

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Aims: Adolescent and adult suicide rates in the U.S. increased during 2009-2012[1]. We compared attempted suicide rates by intentional exposure to methylphenidate in adolescents and adults. Methylphenidate is a prescription stimulant drug used to treat the symptoms of attention-deficit/hyperactivity disorder.
[1] Centers for Disease Control and Prevention Data & Statistics Fatal Injury Report for 2012
Methods: Data from the RADARS® System Poison Center Program from first quarter 2009 to second quarter 2014 were used. The Poison Center Program obtains data from calls to participating poison centers in the U.S. from the general population and healthcare providers about potentially toxic exposures. The number of suspected suicide cases involving methylphenidate was summed for each quarter over the time period. Suspected suicide cases are intentional exposures to a drug for self-destructive reasons. These totals were divided by the total number of methylphenidate prescriptions dispensed in covered 3-digit ZIP codes each quarter to calculate prescription adjusted rates. Adolescent rates (13-19 years) were compared to adult rates (20 and older). Poisson regression was used to compare changes in rates over time.
Results: There were 3695 adolescent and 2853 adult suspected suicide cases in this time period. Prescription adjusted rates show a significant increase of 0.8% per quarter in suspected suicide cases involving methylphenidate for the adolescent population ($p=0.017$) and a significant decrease of 1.5% per quarter for the adult population ($p<0.001$).
Conclusions: Findings suggest a steadily increasing trend of prescription adjusted rates among adolescents attempting suicide by exposure to prescription methylphenidates. In contrast, there was a decrease in adults attempting suicide by exposure to prescription methylphenidates. These trends suggest that adolescent groups may be a high risk group for intentional exposure to methylphenidates motivated by suicidal intent.
Financial Support: The RADARS® System is funded by subscriptions from pharmaceutical manufacturers.

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A COMPUTERIZED SYSTEM FOR ENTERING AND SUMMARIZING TIMELINE FOLLOWBACK INFORMATION ON MULTIPLE SUBSTANCES.

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Aims: Timeline Followback (TLFB) is a widely used method for collecting daily substance use information. Existing computerized systems for entering TLFB data: 1) collect only one drug 2) collect limited quantity information, and 3) provide limited summary information. These limitations are especially problematic for assessing adolescents, who are commonly polysubstance users. **Aims:** Via our grant (R01 DA034604) we are developing a user-friendly, flexible, calendar-based system for collection of use on multiple substances that has utility in various clinical and research settings, provides useful summary information, and stores data in a format conducive for trajectory analyses.
Methods: In 2013, we began tailoring and refining our TLFB system. Earlier versions were used in school-based and clinical programs and revised to the current version. An outpatient clinic for adolescents (STEP) began using the current version in September 2014 and we are collecting feedback from those using the system, as well as TLFB data on STEP patients.
Results: The current TLFB system includes pull down menus to avoid entry errors, tracks up to 8 drug categories, tracks daily use prior to treatment and for up to 6 months of treatment, provides equivalent quantity conversions for different routes of use of commonly used substances (cannabis, alcohol, tobacco), and provides monthly substance-specific summaries of use. To date, data are being collected on 14 patients at STEP who have completed 6 weeks of treatment on average and use 2 drug categories on average (range 1-5), including cannabis, alcohol, cocaine, heroin, cigarettes, and sedatives. By May 2015, we anticiapte that 20-30 patients will have completed treatment and provided their data, including summary information on use of each substance.
Conclusions: This TLFB system is unique in tracking daily use of multiple substances. It will potentially facilitate the collection of real-world, clinical data that can be used for research purposes. We seek input from others that will be incorporated before the final system is made publicly available.
Financial Support: DA034604

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PREVALENCE AND CORRELATES OF SIMULTANEOUS HEROIN AND METHAMPHETAMINE INJECTION IN TWO PARALLEL COHORTS OF PWID IN SAN DIEGO, CA, AND TIJUANA, BC, MEXICO.

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Aims: Although persons who inject drugs (PWID) in the western U.S.-Mexico border region inject both heroin and meth, less is known about the prevalence and risks associated with simultaneous injection of this depressant-stimulant combination. Baseline data from two cohort studies of PWID conducted concurrently in San Diego and Tijuana were used to measure the prevalence and identify correlates of simultaneous injection of heroin and meth.
Methods: PWID age ≥18 years who reported injecting illicit drugs in the past month were recruited using street outreach and targeted advertising in San Diego (n=574) and Tijuana (n=735). Participants completed interviewer-administered questionnaires that included socio-demographics and past 6 month drug use, overdose history, and engagement in HIV-associated drug and sexual risk behaviors. Bivariate and multivariable logistic regression analyses were used to identify correlates of simultaneous heroin and meth injection.
Results: The prevalence of simultaneous injection was 39.9% overall and was higher in Tijuana (55.8%) than in San Diego (19.8%). In multivariable analyses adjusting for study site, distributive syringe sharing [AOR: 1.80], using a prefilled syringe [AOR: 1.49], finding it hard to get new syringes [AOR: 1.51], reporting great or urgent need for treatment [AOR: 1.41], and younger age [AOR: .99] were independently associated with simultaneous injection. A significant interaction between overdose and study site showed that simultaneous injection was associated with a higher odds of past 6 month overdose in San Diego [AOR: 3.08] than in Tijuana [AOR: 1.29].
Conclusions: These findings indicate that simultaneous heroin and meth injection is more common in Tijuana than in San Diego, yet this practice had a stronger association with overdose in San Diego than in Tijuana. Simultaneous heroin and meth injection was also independently associated with HIV injection risk behaviors.
Financial Support: T32DA023356

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EXPANDED BRIEF INTERVENTION IN PRIMARY CARE RESULTS IN REDUCED SELF-REPORTED SUBSTANCE USE AT SIX-MONTH FOLLOW-UP: PRELIMINARY RESULTS.

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Aims: Brief intervention in primary care settings for substance use has a mixed track record in reducing alcohol and drug use; trials with booster sessions and expanded treatment appear to provide more robust results. We conducted a randomized clinical trial of a 1-session brief intervention (SBIRT) against a 2-6 session intervention that combined motivational enhancement and CBT (SBIRT+) in the context of three urban federally-qualified healthcare centers (FQHCs).
Methods: Primary care patients at FQHCs were screened for risky substance use. Consenting patients were randomized to receive: 1) 1 session of SBIRT with a 10-15 minute follow-up within one month, or 2) 2-6 sessions of SBIRT+ with monthly brief recovery check-ups. We collected self-report of substance use and urine samples at baseline and every 90 days for 12 months.
Results: A total of 10,935 primary care patients were prescreened. Enrolled patients (N=600) self-reported primary problems with alcohol (35%), marijuana (38%) or other illicit drugs (27%). Preliminary analyses on patients with complete data at 6-month follow-up (N=245) indicate that participants in the SBIRT+ condition reported greater reduction in self-reported days of alcohol use compared to participants in the SBIRT condition ($F=3.20$, $p=.046$), but not on days of illicit drug use. Participants receiving SBIRT+ attended more treatment sessions in the community at both 3 and 6-months ($F=4.14$, $p=.043$).
Conclusions: Preliminary results indicate that SBIRT+ is effective but may not significantly improve illicit drug use outcomes. Final analyses will examine severity and problem type as moderators and extend the analyses to a 12-month follow-up.
Financial Support: PA DOH SAP No.4100055578

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POSTPARTUM CONTRACEPTIVE BEHAVIOR OF OPIOID-MAINTAINED PREGNANT WOMEN.

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Aims: Unintended pregnancies are associated with greater risk of adverse maternal and child outcomes and result in over $12 billion in added costs each year. Approximately 80% of opioid-dependent pregnant women report unintended pregnancies, yet their contraceptive behavior remains understudied. The aims of this study are to characterize how pregnant women who received agonist treatment for opioid dependence utilized postpartum reproductive health care services and identify the prevalence rate and contraceptive methods of this population.
Methods: Data on contraceptive use were collected around the time of the postpartum OB visit for participants in the MOTHER (Maternal Opioid Treatment: Human Experimental Research) study for this secondary analysis.
Results: Among the 175 MOTHER participants, data about contraceptive method were only available for 43% (n=76) of the sample and many reported not attending their postpartum OB visit. Among those with data, 45% of participants (n=34) reported not using any contraception. Among those reporting contraceptive use, methods included Depo-Provera shots (13%; n=10), oral contraceptives (12%; n=9), IUDs (12%; n=9), tubal ligations (9%; n=7), condom use (8%; n=6), and natural family planning (1%; n=1).
Conclusions: These results suggest opioid-maintained pregnant women frequently utilize postpartum reproductive health services inadequately and indicate current strategies to address their reproductive health needs may not be the most efficacious. Predictors of contraceptive use postpartum need to be identified and treatment strategies revised to support prompt initiation of effective contraception. Due to regulations around opioid maintenance treatment, opioid-maintained women attend their treatment clinic on a regular basis, even early in the postpartum period. This situation may present a unique opportunity to engage opioid-dependent pregnant women about their reproductive health needs, optimize postpartum contraceptive use, and integrate their health care services.
Financial Support: NIDA T32 DA007242

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SCIENTIFIC EVALUATION ON SUBSTANCE ABUSE RESEARCH THROUGH WEB OF SCIENCE OVER THE 2008-2012 PERIOD.

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Aims: Identify and analyze scientific production and studied drugs on specific and not specific substance abuse journals.
Methods: Design of search strategy, treat the bibliographic information, classification of articles regard to drugs studied, bibliometric analysis, identify research groups altogether and by each drug studied was the method used.
Results: 44,822 articles have been evaluated, the 26.88% have been published in journals (1.08%) of Web of Science (WoS) Category Susbtance Abuse (CSA), while the rest of works were published in 3,382 journals belonging to 95 WoS categories of Health Sciences and Social Sciences. The 67.02% of the articles only study 1 drug; while that alcohol, tobacco and cannabis, and on the other hand cocaine and amphetamines are the drugs most studied jointly. The 27% of the authors (n=35,223) have published more than 1 paper. Collaborations between 2 or more authors made up 95.18% of documents, with a collaboration index of 5.24.
Conclusions: A growth in productivity of scientific research on substance abuse has been identified. The most productive journals that do not belong to WoS CSA accumulate a 0.42% more of papers that these. The multidisciplinary character of this research field is reflected in the wide range of journals as well as the collaboration index and index of transient authors, as has been noted in other studies of Biomedicine and Social Sciences. Although USA, UK, Canada and Australia great producers dominate the consolidated research groups, main producers of not English speaking countries of European Union have the highest international collaboration indexes.
Financial Support: Plan Municipal de Drogodependencias, Ayuntamiento de Valencia, Spain.

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SCREENING AND BRIEF INTERVENTION FOR LOW RISK DRUG USE IN PRIMARY CARE: A PILOT RANDOMIZED TRIAL.

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Aims: Universal screening and brief intervention (SBI) for drug use among primary care (PC) patients lacks efficacy but the efficacy of SBI for low risk drug use is unknown. This 3-arm pilot study tested the efficacy of two brief interventions (BIs) for drug use compared to no BI in PC patients with low risk drug use identified by screening.
Methods: We randomly assigned participants identified by screening with Alcohol Smoking and Substance Involvement Screening Test (ASSIST) drug specific scores of 2 or 3 (consistent with low risk drug use) to: no BI, a brief negotiated interview (BNI), or an adaptation of motivational interviewing (MOTIV). BNI was a 10-15 minute structured interview conducted by health educators. MOTIV was ≤45 minutes with an optional booster conducted by trained master's-level counselors. Primary outcome was number of days use of self-identified main drug in the past 30 as determined by validated calendar method at 6 months. Analyses were performed using negative binomial regression adjusted for baseline use and main drug.
Results: Of 142 eligible adults, 61(43%) consented and were randomized. Participant characteristics were: mean age 41; 54% male; 77% black. Main drug was marijuana 70%, prescription opioid 10%, cocaine 15%; 7% reported injection drug use and mean days use of main drug (of 30) was 3.4. At 6 months, 93% completed follow-up and adjusted mean days use of main drug were 6.4 (no BI) vs 2.1 (BNI) (incidence rate ratio (IRR 0.33, 95% CI 0.15-0.74) and 2.3 (MOTIV) (IRR 0.36, 95% CI 0.15-0.85).
Conclusions: Brief intervention (both a brief negotiated interview and an adaptation of motivational interviewing) appears to have efficacy for preventing an increase in drug use in patients with low risk use identified by screening. These findings raise the possibility that low risk drug use in primary care may be uniquely amenable to brief intervention and warrant replication in a larger trial.
Financial Support: R01DA025068, UL1TR000157

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UNDERAGE DRINKING DIVERSION: CHARACTERIZING RISK WITH LATENT CLASS ANALYSIS.

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Aims: Background: Alcohol and drug use of youths in late adolescence (YLA) is associated with serious safety and risk factors that can lead to numerous harmful consequences throughout the life cycle. Little is known about the heterogeneity among YLAs entering diversion programs and the impact of client characteristics on clinical decision making and program completion. This study utilized latent class analysis (LCA) and non-parametric tests to characterize program participants. **Aims** of the study were to: 1) identify subgroups of YLAs in the Southwest based on demographics and substance use characteristics and 2) examine the differences among groups based on clinical decision making, treatment type, and program completion.
Methods: Methods: The current study is a secondary analysis of an Underage Drinking and Alcohol Possession Diversion Program in the Southwest. Available data included 1,260 court-referred YLAs (2009-2011). Data related to alcohol and drug problems were collected via Substance Abuse Subtle Screening Inventory.
Results: Results: LCA demonstrated a three-class solution (AIC= 15729.37, BIC= 15909.23, entropy = .92). Bootstrapped likelihood ratio and LMR tests were significant. The high risk group (5%; n=66) and the moderate risk group (35%; n=446) were characterized by higher use of alcohol and marijuana, being over the legal limit at arrest, and being male (compared to the low risk group). The moderate risk group was more likely to be white and have less education than the higher risk group. The low risk group (59%; n=748) was more likely to have attended college and be female. For the low risk group, chi-square tests demonstrated lower instances of referral to treatment decisions and higher program completion compared to moderate and high risk groups.
Conclusions: Conclusion: Findings highlight heterogeneity of YLAs based on demographics and these group differences may have implications for clinical decision making, treatment type, and completion. Results underscore the need to adapt diversion programs to meet the needs of substantially different YLAs.
Financial Support: City of Phoenix Prosecutors Office.

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MULTIDIMENSIONAL ASSESSMENT OF CUE-ELICITED INCREASES IN INCENTIVE SALIENCE FOR MARIJUANA.

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Aims: Incentive salience is a multidimensional construct that includes craving, drug value, and implicit motivation such as attentional bias to drug cues. Laboratory-cue reactivity (CR) paradigms have been used to evaluate marijuana incentive salience with measures of subjective craving or arousal, but not with behavioral economic measures of relative marijuana value or implicit attentional processing. This study used multidimensional assessment of acute increases in marijuana incentive salience during a CR procedure.
Methods: Marijuana users (*N*=93, 34% female) underwent exposure to neutral cues followed by exposure to actual marijuana cigarettes with repeated assessments of subjective craving and a state behavioral economic demand for marijuana, via a Marijuana Purchase Task (MPT), after each cue set. A modified Stroop task with cannabis and control words was completed after the marijuana cues.
Results: GEE analyses indicated that marijuana vs. neutral cues significantly increased subjective craving, B = .48, 95% *CI* = .37, .59, $p < .001$, and MPT indices of demand, including consumption at zero cost (intensity), B = .02, $p < .01$, and maximum expenditure on marijuana (Omax), B = .03, $p < .01$. Craving was significantly correlated with MPT indices (*r*'s: 0.23–0.33). Marijuana users displayed significant attentional bias for cannabis by slower color-naming marijuana vs. neutral words, B = 31.01,$p < .001$. Cue-elicited changes in intensity predicted greater attentional bias for marijuana words, B = 415.41, $p < .05$, but subjective craving did not.
Conclusions: These findings validate the CR paradigm with actual marijuana cigarettes, as greater incentive salience indexed by subjective, behavioral economic, and implicit measures was observed after marijuana vs. neutral cues. Findings support the utility of a behavioral economic approach in detecting cue-elicited changes in marijuana demand and attentional bias for marijuana stimuli.
Financial Support: R03DA027484 (Metrik, Knopik)

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EFFECTS OF IBUDILAST ON THE REINFORCING, SUBJECTIVE AND ANALGESIC EFFECTS OF OXYCODONE – PRELIMINARY RESULTS.

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Aims: Preclinical studies have shown that glial cell attenuators, such as ibudilast (ibu), decrease the rewarding effects of opioids while increasing opioid-induced analgesia. The aim of this randomized, placebo(pbo)-controlled, double-blind, 6-week-inpatient study is to investigate the ability of ibu to alter the reinforcing, subjective, and analgesic effects of oxycodone (oxy) in humans.
Methods: Seven opioid-dependent male volunteers were detoxified from opioids before randomization to active (50mg BID) or pbo ibu. They completed 6 laboratory sessions with varying doses of oxy (0,15,30mg/70kg PO); 3 sample sessions, assessing subjective and analgesic effects of oxy, were each followed by a drug vs. money choice session. They then switched over to the other medication condition (pbo or active ibu), and again completed 6 sessions. Mixed-model ANOVAs were applied.
Results: In the pbo condition, oxy produced significant dose-related increases in self-administration (p=0.002, 0mg vs. 30mg), whereas no significant differences in self-administration were found in the active ibu condition. Peak oxy-induced ratings of "I feel high" were significantly reduced by active compared to pbo ibu ($p<0.05$), as were "I liked the dose" and "I would pay" when 15mg oxy was given ($p<0.05$). Craving for heroin was significantly lower ($p<0.05$) under active ibu compared to pbo, as for tobacco and cocaine in the 15mg oxy condition. Consistent with the preclinical data, oxy-induced analgesia was enhanced in the active ibu condition.
Conclusions: Ibu demontrates promising results in regard to the rewarding effects of oxy, opioid-induced analgesia and drug craving in a recently detoxed opioid-dependent population. Further studies are warranted to determine whether ibu is a useful treatment option for opioid use disorders.
Financial Support: NIDA
Medicinova

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FINANCIAL INCENTIVES PROMOTE SMOKING ABSTINENCE AMONG PATIENTS WITH PULMONARY DISEASE.

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Aims: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality, with an estimated 90% of all COPD deaths in the U.S. attributable to smoking. While smoking cessation is identified as the most effective intervention to reduce COPD-related consequences, patients with COPD show poorer outcomes across a range of smoking-cessation interventions. In this randomized pilot study, we are examining the efficacy of a behavioral economic intervention for promoting initial smoking abstinence in patients diagnosed with COPD.
Methods: Daily smokers (N=30) diagnosed with COPD ($FEV_1/FVC<70\%$) will be randomized to an Incentive or Control experimental group. Participants visit the clinic daily for 14 days and provide breath and urine samples for biochemical verification of smoking status. Incentive participants earn financial incentives delivered contingent upon smoking abstinence. Controls receive vouchers of the same value but independent of smoking status. Abstinence is defined as a breath CO level $\leq$6ppm during Study Days 1-5 and a urinary cotinine level $\leq$80ng/ml on Days 6-14.
Results: Thus far, 23 participants have been randomly assigned to the Incentive (n=11) or Control (n=12) experimental groups. Participants are 57 years old, 48% male, and diagnosed with moderate COPD (FEV_1=59% of normal). At intake, participants report smoking 24 cigs/day, have smoked regularly for 38 years, and present with moderate nicotine dependence (FTND=6.1). Preliminary analyses show significant group by visit interactions for breath CO (p=0.006) and urinary cotinine (p=0.03), with lower CO and cotinine levels in the Incentive vs. Control group. Final biochemical and abstinence data will be available for presentation at the June 2015 meeting, as will additional measures of nicotine withdrawal, craving, and respiratory symptomatology.
Conclusions: These results suggest that an incentive-based intervention may be feasible and effective in producing initial smoking abstinence in this hard-to-treat sample of smokers.
Financial Support: T32 DA007242, P20 GM103644

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WITHDRAWN

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TRAUMA EXACERBATES THE EFFECT OF GENETIC VARIANTS IN THE DOPAMINE SYSTEM ON CANNABIS USE.

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Aims: Although cannabis use is heritable, few studies have examined genetic risk for cannabis use alone, and of the studies that have been published, few genetic risk variants have been identified. In addition, the evidence for gene-environment interactions (GxE) in substance use behaviors is growing, with several GxE studies indicating that the effects of specific genetic variants are exacerbated by traumatic experiences. However, there have been no published GxE studies for cannabis involvement to date. Several biological systems that potentially incur risk for cannabis involvement have been identified via neurobiological studies, including variation in the *dopamineric system. For example, Volkow and colleagues investigated the effects of chronic cannabis use on the human brain using PET imaging, and found that cannabis abusers showed markedly blunted responses when challenged with methylphenidate, a drug that elevates dopamine.*
Methods: *In this study, we provide evidence of association between sets of genetic variants in the dopamine system (96 single nucleotide polymorphisms across DRD1-DRD4)* and frequency of cannabis use (days/month, within the past 30 days) in two independent majority African-American population based samples (Detroit Neighborhood Health Study, n=788; Grady Trauma Project, n=3752; p<0.01).
Results: Importantly, we also found that the experience of trauma (measured via the Traumatic Life Events checklist) in both samples exacerbated the influence of the dopaminergic system on frequency of cannabis use. However, the effect sizes are quite modest (β=0.23-0.89, p<0.01-0.03).
Conclusions: These data provide additional evidence that variation in the dopaminergic system impacts risk for cannabis involvement, and that these effects are increased for individuals who have experienced trauma in their lifetime. These results also highlight the subtly of genetic and GxE effects for complex behavioral traits such as cannabis involvement.
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DO PRIVATE PRACTITIONERS PROVIDE QUALITY CARE TO ADOLESCENTS WITH SUBSTANCE ABUSE DISORDERS?

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Aims: Of the 1.7 million adolescents with an SUD, only 10% actually receive treatment and less than 50% of them receive it in a *specialty* SUD treatment program. Instead, many receive treatment in PPs' offices. While there is progress in understanding the quality of care in specialty programs*, we know virtually nothing about the approaches PPs use*.
Methods: We surveyed a national sample of 433 psychologists, clinical social workers, and family therapists to assess under what conditions they treat adolescent SUD (e.g., substance type, problem severity) and what features of SUD Evidence Based Practices and Treatments (EBPs/EBTs) they offer. The internet survey contained ~70 questions and differed for PPs who did/did not treat adolescents with SUDs in the past year.
Results: Eighty percent (n=340) had treated adolescents with SUD in the past year. Sizable portions of these PPs treated SUD *regardless of type of drug or SUD severity* with ~25% treating cocaine, prescription opiates, hallucinogens, inhalants, and designer drugs, >33% treating prescription stimulants and prescription depressants, and ~50% treating alcohol and marijuana. Over 50% referred youth to specialty care if use included heroin or methamphetamine. The use of standardized assessments was rare and only ~33% reported use of motivational interventions. Cognitive behavioral therapy was the predominate treatment delivered in individual youth sessions (85%); 75% provided family sessions but <20% were familiar with family-based EBTs. Less than 33% endorsed trauma-informed care as a therapeutic approach. Only 33% monitored substance use progress through urine testing. Referral to recovery-oriented services was uncommon.
Conclusions: These data suggest that many youth with SUDs are treated by PPs who do not use SUD-focused EBPs/EBTs and do not address the related problems of these youth. Given that SUD begins in adolescence in >90% of cases, it is critical that PPs be included in our effort to improve adolescent treatment quality.
Financial Support: P50-DA027841

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TRENDS IN USE OF AND ATTITUDES TOWARD MARIJUANA AMONG YOUTH BEFORE AND AFTER DECRIMINALIZATION: THE CASE OF CALIFORNIA 2007-2013.

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Aims: This analysis examines decriminalization as a risk factor for future increases in youth marijuana acceptance and use. Specifically, we examine marijuana-related behaviors and attitudes of 8th, 10th, and 12th graders in California as compared to other U.S. states during the years before and after California passed legislation in 2010 to decriminalize marijuana.
Methods: *Data*
Data come from the annual Monitoring the Future study, which since 1975 has used questionnaires administered in classrooms to survey nationally representative samples of American students. This analysis uses the annual samples of American 8th, 10th, and 12th graders between 2007 and 2013 (n=~15,000 per grade per year). The time span includes three years before and three years after the 2010 California legislation.
Results: In 2012 and afterwards California 12th graders as compared to their peers in other states became (a) 25% more likely to have used marijuana in the past 30 days, (b) 20% less likely to perceive regular marijuana use as a great health risk, (c) 20% less likely to strongly disapprove of regular marijuana use, and (d) about 60% more likely to expect to be using marijuana five years in the future. Analysis of 10th graders raises the possibility that the findings among 12th graders may reflect a cohort effect that was set into place two years earlier.
Conclusions: These results provide empirical evidence to support concerns that decriminalization may be a risk factor for future increases in youth marijuana use and acceptance.
Financial Support: The study was funded by grants from the National Institute on Drug Abuse (R01 DA 001411).

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METHODS FOR ASSOCIATING TRAJECTORIES OF COMORBIDITIES: ADHD AND SUBSTANCE USE.

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Aims: Does marijuana abate symptoms of ADHD as some suggest or induce attention problems as other data suggest? Does cigarette smoking decrease as an indirect result of treatment for marijuana use or increase in compensation for reduced marijuana use? Trajectories of comorbidities over time are often nonlinear or based on outcomes with different distributions. Our R01 is developing methods to evaluate associations among them to address hypotheses in adolescents with ADHD and substance use: (1) Changes in ADHD and marijuana use are interrelated and their association differs between those who respond to ADHD treatment (RESP) and non-responders (non-RESP). (2) Associations between rates of cigarette and marijuana use differ between RESP and non-RESP.
Methods: Using data from the Clinical Trials Network study of ADHD and substance use in adolescents (CTN28), we estimated latent stochastic trajectory parameters (e.g. slopes) in RESP and non-RESP by joint models of weekly ADHD score (continuous) and daily marijuana use (count) and by joint models of marijuana and cigarette use (counts). We estimated correlations (r) and partial correlations (r_a) and compared them between RESP and non-RESP with various methods: Wald-type t-tests, likelihood ratio tests, Fisher's Z transformation.
Results: Change in ADHD scores and in rate of joints smoked are associated (r=0.38; p< 0.001) but not different between groups, unless adjusted for baseline: RESP n= 28, r_a=0.68 vs. non-RESP n=64, r_a=0.11; p<.005 . In regular users of both, correlation between rates of joints and cigarettes smoked is greater in RESP (n=21, r=0.57) than non-RESP (n=44, r=0.04); the difference is amplified by adjusting for baseline (RESP r_a=.83; non-RESP r_a=.03; p<0.001). Modelling issues (e.g. restrictions on random effects, which test to use) will be discussed.
Conclusions: Trajectories of comorbidity outcomes can be associated and compared as latent stochastic parameters within multivariate generalized linear mixed models. Different modelling and testing methods mostly converge and show stronger positive associations among those whose ADHD responds to treatment.
Financial Support: DA034604

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GENDER DIFFERENCES IN STROOP PERFORMANCE FOLLOWING GUANFACINE VERSUS PLACEBO IN EARLY ABSTINENT COCAINE- DEPENDENT MEN AND WOMEN.

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Aims: No FDA-approved medications currently exist for cocaine dependence (CD). Moreover, gender-specific treatments may be of value as women are more vulnerable to the development and the detrimental effects of CD. While "agonist therapies" and anxiolytics have shown some success, there are concerns regarding abuse potential and sedation-induced cognitive decrement, respectively. Alpha-2 agonism may demonstrate low stimulant and sedative properties as well as enhance inhibitory cognitive processes in the face of stress. Notably, based on prior findings, we also suggest that gender may moderate these effects.
Methods: Forty inpatient treatment-seeking CD individuals (13F/27M) were randomly assigned to receive either placebo (PLA) or up to 3mgs of guanfacine (GUAN) in a double-blind manner over four weeks. Three laboratory sessions were conducted in week 4, where patients were exposed to three 5-min personalized guided imagery conditions (stress -S, alcohol cue -C, neutral/relaxing -N), one per day, on consecutive days in a random, counterbalanced order. Cocaine craving, anxiety, negative mood and the Stroop task were administered at baseline and immediately following imagery exposure. Subjective measures were also administered at regular recovery timepoints.
Results: The GUAN women reported significantly reduced cocaine craving immediately following exposure to stress imagery compared with PLA women (p=.003). This effect was not observed in the GUAN men. GUAN also attenuated anxiety (p<.0001) and negative mood (p<.05) in women, but not men. Similarly, GUAN women also improved their performance on the Stroop task following exposure to all 3 imagery conditions compared with PLA women (p=.05). Again, this improvement in cognitive inhibitory performance was not observed in the GUAN males.
Conclusions: Attenuating anxiety and enhancing the ability to cognitively regulate in the face of stress, may be key targets for medications development in CD women.
Financial Support: This study was supported by NIH-NIDA grants K01DA029040 (Fox) and R01-DA027130 (Sinha).

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ONLINE FEASIBILITY STUDY ABOUT HIV-NEGATIVE MALE COUPLES SUBSTANCE USE WITH WEEKLY ECOLOGICAL MOMENTARY DIARY ASSESSMENTS.

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Aims: To date, little is known about male couples' use of substances despite the role that substance use plays in HIV seroconversion among gay men. The aims of the present study were twofold: 1) to assess whether panel dyadic data could be collected from HIV-negative male couples about their substance use using online weekly ecological momentary diary assessments; 2) to examine couples' rates of substance use and contexts of their usage.
Methods: A longitudinal study design using ecological momentary weekly electronic diaries was used to examine male couples substance use with/out sex, and the contexts of their usage over a 6-week period. Targeted facebook ads were used to recruit the sample along with a partner referral system to invite eligible participants' main partners. 531 men took the screener; of these, 97 were eligible, consented and enrolled in the study.
Results: Although 97 partnered men enrolled, only 13 male couples with both partners and 15 male couples with one partner participated in the study. Over the 6-week period, men's engagement in UAS with their main partner, alcohol consumption, and use of erectile dysfunction medication, prescription pain medication (PPM), and/or illicit drug(s) varied. Men frequently used marijuana and/or alcohol in a variety of contexts including sex. Among the 13 male couples, both partner's use of illicit drugs including marijuana (ICC 0.97, P <.05) and PPM (ICC 0.98, P <.05) were highly similar to one another whereas more variability between partners existed for lite (ICC 0.61, P <.05) and heavy alcohol use (ICC 0.59, P <.05).
Conclusions: Our findings suggest dyadic data collection about male couples substance use is feasible, but additional resources are needed to bolster enrollment. Results highlight the need for further inquiry with a larger sample size to develop HIV and substance use prevention interventions for at-risk male couples, of which, few currently exist.
Financial Support: N/A

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DOPAMINE, TIME PERCEPTION, AND FUTURE TIME PERSPECTIVE.

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Aims: Aims: Impulsivity is a known risk factor for substance use disorders. Impulsivity itself is thought to be comprised of at least 3 different component processes: prospection, time perception, and true behavioral impulsivity. We have previously demonstrated that the catechol-O-methyltransferase (COMT) inhibitor tolcapone, which is hypothesized to increase cortical dopamine tone, reduces impulsive decision making in a delay discounting paradigm. Moreover, this tolcapone-induced change covaries with connectivity between the pregenual cingulate and ventral putamen. Consistent with the hypothesized role of dopamine in these component processes, we now show that tolcapone also affects time perception.
Methods: Methods: In a randomized, double-blind, within-subject crossover study, tolcapone and placebo were administered orally to 42 healthy control subjects in a laboratory setting to examine whether single dose tolcapone alters time perception, and whether a relationship exists between these effects and basal measures of time horizon.
Results: Results: Subjects typically showed a compressed time perspective at baseline. Tolcapone extended time perception, improving the accuracy of subjects' estimates for short time intervals ranging from 5 to 60 seconds (F = 5.65, p = 0.02; N = 42). Importantly, variability in baseline time perception at 5 seconds correlated with performance on the Stanford Time Perception Inventory (STPI) "Future" subscale (R = .41, p = .007, n= 42), suggesting that the effects reported here for short time intervals may extend to the longer time scales captured by the STPI.
Conclusions: Conclusions: Together these data suggest that the type of impulsivity associated with compressed time perception may be ameliorated by administration of the COMT inhibitor tolcapone. Additional studies are necessary to determine whether tolcapone administration could concomitantly attenuate addictive behaviors, including drug/alcohol abuse and pathological gambling.
Financial Support: Financial Support: National Center for Responsible Gaming and the Department of Defense.

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"SMOKING POT HELPS ME FOCUS": A QUALITATIVE ANALYSIS OF INTERNET FORUM DISCUSSIONS OF ADHD AND CANNABIS USE.

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Aims: ADHD is a risk factor for cannabis use. Despite that cannabis use is associated with disruptions in attention in the general population and attention processes are already disrupted in ADHD independent of cannabis use, there appears to be a perception among ADHD patients that cannabis is therapeutic. However, such perceptions have not been examined. We performed a qualitative analysis of web-forums involving cannabis use and ADHD. We hypothesized that internet discussion forum participants would emphasize the therapeutic benefits of cannabis for ADHD. We explored additional themes to generate novel hypotheses to guide future quantitative studies.
Methods: A web search using a combination of various terms (e.g., ADHD and marijuana) was conducted and yielded a total of 269 internet discussion threads discussing some aspect of ADHD and cannabis use. We randomly selected 15% of threads with >5 posts for analysis.
Results: Qualitative analysis of individual posts indicated that internet discussion participants emphasized the therapeutic effects of cannabis for ADHD—fewer endorsed either a null or harmful impact. Exploratory analysis also indicated that participants perceived fewer concerns about cannabis due to it being "natural," that cannabis is perceived to improve impairment in ADHD (e.g., driving), distrust of the medical community regarding stimulant medication efficacy, and a preference for particular cannabis strains.
Conclusions: Cannabis use in the US is changing and there is a need for further research of how cannabis impacts at-risk groups, such as those with ADHD. This qualitative study provides new insight into currently held perceptions about cannabis use in ADHD. We propose a number of novel hypotheses guided by qualitative analysis of web-forum content, which can guide future quantitative studies. This study also illustrates the potential use of web-based data to study substance use.
Financial Support: NIDA (K23 DA032577)

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SEX DIFFERENCES IN INTRINSIC CONNECTIVITY DURING FMRI STROOP IN COCAINE-DEPENDENT AND HEALTHY COMPARISON SUBJECTS.

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Aims: Previously we found cocaine-dependent (CD) versus control subjects (HC) showed greater mean-adjusted connectivity in the ventral striatum, putamen, inferior frontal gyrus, anterior insula, thalamus and substantia nigra. However, the extent to which women and men showed differences in functional connectivity was not previously examined. This study investigated sex differences in intrinsic connectivity distribution (ICD) in CD subjects during fMRI Stroop performance.
Methods: 38 current CD (19 female) and 38 matched HC subjects (19 female) completed an fMRI Stroop task. Mean-adjusted ICD analyses were conducted to identify sex differences.
Results: Both increases and decreases in connectivity were observed in all four comparisons (Females CD-HC; Males CD-HC; CD Males-Females; HC Males-Females), and an interaction between gender and diagnostic group implicated connectivity differences in the orbitofrontal cortex (OFC), ventral striatum, precuneus/cuneus, cingulate gyrus, and occipital lobe. Out-of-scanner behavioral Stroop data did not reveal differences between males and females between diagnostic groups, but did show sex differences within the CD group but not the HC group.
Conclusions: Differences in intrinsic connectivity involved the OFC, cingulate, and striatum, areas implicated in cocaine dependence and cognitive processes including decision-making and inhibitory control. Differences in regions associated with language and visual processing were also observed. The extent to which these patterns of connectivity relate to clinically relevant measures of cocaine dependence warrants additional investigation.
Financial Support: ORWH, OD, NIDA (K12-DA031050, R01-DA020908, R01-DA035058, P50-DA09241, R01-DA019039, P20-DA027844)

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COUNSELORS' VIEWS OF PROVIDING PATIENT-CENTERED METHADONE TREATMENT IN A CLINICAL TRIAL.

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Aims: To examine the views of methadone program counseling staff regarding the impact of providing a patient-centered treatment approach on their clinical roles and treatment processes.
Methods: In-depth, semi-structured interviews were conducted in a clinical trial comparing methadone treatment-as-usual to patient-centered methadone (PCM) treatment in which the counselor's supervisor enforced clinic rules and counseling services were designed to be flexible in frequency and duration. The eight participants included counselors and clinical supervisors with the sample predominantly female (75%) and African American (63%). Participants were interviewed at baseline and 12-month follow-up. Data were analyzed in Atlas.ti using an iterative process to capture and code emergent and anticipated themes.
Results: Counselors reported being most affected during PCM by removal of their role as the program rule enforcer. In some cases, it permitted them to spend more time building a therapeutic alliance with patients because they were not dealing with non-adherence to program rules including missed counseling sessions. However, some counselors were frustrated by not being able to "hold" the patients' dose to require counseling attendance and some began to use more pro-active and innovative strategies for engaging patients. Sessions in PCM tended to include a broader range of counseling topics that were individually pertinent to each patient than were covered in TAU.
Conclusions: PCM treatment changed the relationship between the counselor and patient providing more freedom for the patient to control the type and number of sessions. Adjusting to the new counselor role was challenging and required counselors to shift tactics to try to engage some patients in counseling voluntarily. It also frustrated some of the counselors who were used to "holding" methadone doses to encourage counseling attendance.
Financial Support: This study was supported by the National Institute on Drug Abuse grant number 2R01DA015842.

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NICOTINE SHOWS A THERAPEUTIC EFFECT ON IMPULSIVITY THROUGH A DIFFERENT MECHANISM FROM THAT OF PAROXETINE.

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Aims: Nicotine (NCT) has been reported to show positive effects on psychopharmacological function. Therefore, NCT could be hypothesized to show beneficial effects on impulsivity. For that purpose, a new animal model was developed to estimate the effects of NCT on impulsivity by using rats.
Methods: Rats implanted with an electrode into the medial forebrain bundle were trained to hold a lever for 4 seconds to obtain an intracranial self-stimulation (ICSS) reward, and to release the lever immediately after they had obtained a reward. As for estimating impulsivity, a number of reward gain per min (RGR) through 4 seconds lever-holding behavior is regarded to reflect impulsivity related to "action restraint", whereas a time for releasing the lever (TFR) after the rats had obtained a reward is regarded to reflect impulsivity related to "action cancellation".
Results: Acute subcutaneous administration of NCT at 0.4 mg/kg decreased TFR, whereas mecamylamine-precipitated NCT-withdrawal increased TFR, which may indicate that NCT withdrawal increased impulsivity related to "action cancellation". A D3/D3 receptor agonist pramipexole (PPX), which has been reported to cause impulse-control disorders, decreased RGR and increased TFR, indicating that PPX increased both types of impulsivity. Subcutaneous administration of NCT at 0.4 and 0.8 mg/kg decreased TFR, whereas intragastric administration of paroxetine (SSRI) at 10 and 30 mg/kg increased RGR in the PPX-treated rats.
Conclusions: These results indicated that NCT improved impulsivity related to "action cancellation", whereas paroxetine improved impulsivity related to "action restraint". Therefore, NCT is suggested to have a potential to show therapeutic effect on impulsivity through a different mechanism from that of paroxetine.
Financial Support: The Ministry of Education, Culture, Sports, Science and Technology of Japan (No. 23591682), the Smoking Research Foundation.

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SOCIAL RANK AND COCAINE DEPENDENCE: ESTIMATES FOR THE UNITED STATES, 2005-2013.

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Aims: Past research indicates downward social rank shift of cocaine use, with odds of cocaine use becoming greater at lower social rank levels. Here, we seek estimates of cocaine dependence transition probabilities (CDTP) in relation to indicators of social rank, beginning with poverty level gradients.
Methods: Data are from United States National Surveys on Drug Use and Health, 2005-2013, with nationally representative samples and standardized computer-assisted assessment modules and n>50,000 persons each year (US; NSDUH; SDA samples). US Census Bureau poverty rank is based on participant age, total family income, family size, and number of children in the household. Estimates are produced for each year, with meta-analysis used to create a summary estimate.
Results: In meta-analysis, no statistically robust variation in CDTP estimates can be seen in relation to this social rank gradient. For those in poverty, CDTP is an estimated 4.7% (95% CI = 2.3, 7.2). Estimated middle-income CDTP is 4.6% (95% CI = 2.4, 6.9). Estimated higher income CDTP is 6.7% (95% CI = 4.2, 9.2).
Conclusions: Whereas there now might be an inverse social rank gradient in incidence or prevalence of cocaine use, this gradient cannot be seen in estimates for the probability of making a rapid transition from onset of cocaine use to onset of cocaine dependence. These epidemiological estimates underscore the importance of drawing distinctions between cocaine use per se and cocaine dependence per se. Epidemiological patterns in the occurrence of cocaine use might well differ from epidemiological patterns of cocaine dependence.
Financial Support: NIDA T32DA021129 (AMM); K05DA015799 (JCA)

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A HIGHER HILL TO CLIMB! OLDER COCAINE-ADDICTED PATIENTS VIEWING 500 MSEC COCAINE CUES HAVE REDUCED ACTIVATION OF MODULATORY CIRCUITS AND INCREASED ACTIVATION OF MOTIVATIONAL CIRCUITS.

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Aims: Chronic cocaine use may exacerbate the effects of aging on the brain (e.g., prefrontal cortex atrophy). Here, we examined the association between age and the early brain response to cocaine cues in a sample of cocaine-dependent patients. We hypothesized that older participants viewing 500 msec cocaine cues would have **either,** decreased activation of prefrontal modulatory ("STOP!") regions, **or** increased activation of mesolimbic dopamine ("GO!") regions, **or** both.
Methods: Cocaine-dependent patients (n=38) were scanned with event-related BOLD fMRI during exposure to brief (500 msec) evocative (cocaine, sexual, aversive) vs. neutral cues. The age of the participants (range: 34-60 years) was then used as a single regressor in a pre-planned (cocaine-neutral) cue contrast examining the first and second halves of the task separately. In order to examine if the age-brain correlations were due to the older participants using cocaine for more years than the younger participants, age was correlated with years of cocaine use.
Results: For the first half of the task, age correlated *positively* with the brain response to the cocaine cues in several reward-relevant nodes: bilateral insula, right amygdala, and medial orbitofrontal cortex (OFC; $2 \leq t \leq 6$). For the second half of the task, age correlated *negatively* with several prefrontal modulatory regions: bilateral superior & middle frontal gyri, frontal pole, lateral OFC, subgenual cingulate cortex, and paracingulate gyrus ($2 \leq t \leq 6$). Furthermore, age did **not** correlate with years of cocaine use (r=0.05, p=0.8).
Conclusions: Here, we demonstrated that older cocaine-dependent patients may be **both** more sensitive to the motivational "pull" of reward cues and less able to modulate this "pull" – giving them a "higher hill" to climb towards recovery.
Financial Support: Commonwealth of Pennsylvania CURE Addiction Center of Excellence; NIH/NIDA (P5012756; T32DA028874); VA VISN 4 MIRECC

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PHYSICIAN INTEGRATION IN FORMERLY "DRUG-FREE" OUTPATIENT PROGRAMS PROVIDING BUPRENORPHINE.

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Aims: To examine issues associated with the delivery of buprenorphine treatment within three formerly "drug-free" outpatient treatment programs.
Methods: In-depth, semi-structured interviews (n=15) were conducted with behavioral health and medical staff in three outpatient buprenorphine programs. Respondents were predominantly African American (n=11) and female (n=12). The research team used an iterative coding process using Atlas.ti.
Results: The implementation of buprenorphine within these previously "drug free" outpatient programs required the integration of medical and behavioral health services, which were co-located in two clinics and fully integrated in the third. Having co-located but not fully integrated physicians created a conflict resulting from the differing perspectives and training backgrounds of medical and counseling staffs and led to the marginalization of the physicians, despite their central role of prescribing buprenorphine. Although both medical and behavioral health staff agreed on the centrality of counseling, they disagreed on the best ways to combine the use of medication and counseling. Counseling staff reported giving medical advice and medical staff reported giving counseling advice.
Conclusions: The implementation of buprenorphine treatment in an outpatient counseling program created opportunities for each type of staff to provide conflicting advice to patients in ways that extended beyond their professional training when the physicians were not fully integrated into the treatment process. These findings suggest the need for attention to team building and the benefits of fully integrating physicians when providing medications, such as buprenorphine, into previously "drug free" outpatient treatment clinics.
Financial Support: NIDA R01DA028407

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THE TRUTH ABOUT MARIJUANA IS ALL ROLLED UP IN A BLUNT: PREVALENCE AND PREDICTORS OF BLUNT USE AMONG YOUNG AFRICAN-AMERICAN ADULTS.

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Aims: The present study was designed to examine the prevalence rates and predictors of blunt (i.e., hollowed-out cigars filled with marijuana) use among African American young adults.
Methods: A secondary analysis of data from the 2012 National Survey on Drug Use and Health was conducted to examine prevalence rates and demographic and psychosocial predictors of blunt use among African American women (n = 246) and men (n = 312) between the ages of 18-25.
Results: Among participants who reported using marijuana in the past month, 74.4% of women and 82.7% of men used a blunt to smoke their marijuana in the past 30 days (current blunt smokers). Logistic regression analyses revealed that current blunt smokers, both men and women, were approximately 5 times more likely to drive under the influence of illicit drugs in the past year than former and non-blunt smokers.
Conclusions: Future marijuana research should examine the dual use of marijuana and tobacco rather than focusing solely on marijuana use, especially among young African American men and women.
Financial Support: None.

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FDA GUIDANCE ASSESSMENT OF ABUSE POTENTIAL OF DRUGS.

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Aims: To provide an overview of the Food and Drug Administration (FDA) current thinking on the assessment of abuse potential of drugs.
Methods: Sponsors and researchers have indicated on numerous occasions their uncertainty on how to proceed with assessing abuse potential. The Agency has also experienced many challenges when reviewing INDs and NDAs for drugs that may have abuse potential. To that end, the Center for Drug Evaluation and Research at FDA has developed guidance regarding the assessment of abuse potential of drugs (first drafted January 2010). Several meetings, workshops, or seminars were held between the FDA and academicians, researchers, and industry to get input in this very challenging area.
Results: The involvement of the stakeholders and the input gathered from the stakeholders at the various meetings, seminars and workshops are invaluable. FDA considered the feedback and input which helped with FDA's current thinking for assessing the abuse potential of drugs. Although all suggestions or recommendations from the various stakeholders could not be implemented by the FDA; the interactions afforded the opportunity for clarity and a better understanding of what the Agency needs in order to make decisions regarding the INDs and NDAs involving drugs which may have abuse potential. The interactions and feedback will also provide clearer answers to the numerous questions the Agency received from academicians, researchers, and industry regarding their responsibilities in assessing the abuse potential of drugs.
Conclusions: In order for the Agency to receive applications that include what is needed for the Agency to evaluate submitted data, the sponsors must know what is to be included in the applications and when to submit an abuse potential assessment to the Agency. The finalization of the 2010 draft guidance should aid the industry in the submission of applications that are more appropriate for the review by the Agency of drugs which may have abuse potential, thus meeting Agency requirements and acceptance by the Agency without further revisions.
Financial Support: N/A

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SYMMETRICAL DISCOUNTING OF THE FUTURE AND THE PAST IN HEAVY SMOKERS AND ALCOHOL DRINKERS.

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Aims: Within the field of addiction, overvaluation of the present day is a hallmark of substance dependence. Extensive work has been conducted to characterize discounting of future rewards in substance users; however, few have focused on the bidirectional feature of the discounting both into the future and into the past. Here, we assess the rate of temporal discounting both when looking forward and backwards in time.
Methods: We compared the rate of discounting hypothetical monetary rewards up to one year in the future and one year in the past using Amazon's Mechanical Turk to recruit participants that were between the ages of 18-65. We collected Fagerstrom Test for Nicotine Dependence (FTND) to assess for cigarette smoking and Alcohol Use Disorders Identification Test (AUDIT) to assess for alcohol use. Our sample included 65 non-smokers, 28 heavy smokers, 47 light or non-drinkers, and 27 heavy drinkers.
Results: Across all groups, discounting of past and future rewards were highly linearly correlated (R= 0.69). Heavy smokers discounted future and past rewards significantly more than non-smokers ($p<0.01$ and $P<0.001$, respectively). Similarly, heavy drinkers discounted future rewards significantly more than light drinkers ($p<0.05$); however, heavy drinkers did not discount the past significantly more than light drinkers ($p=0.103$). Additionally, a small subset of the sample (n=10) were both heavy smokers and drinkers, this group evidenced significantly greater discounting of future and past rewards ($p<0.01$ for both).
Conclusions: Our results indicate that discounting of the future and the past is symmetrical across substance using and non-using groups. Furthermore, discounting of the future and past is broadly consistent in heavy smokers, drinkers, and combined heavy smoker/drinkers. The observed results indicate that discounting may be a bidirectional phenomena. Importantly, treatments that target improvement of excessive discounting may consider if both directions of discounting are improved and clinical implications for unidirectional improvement.
Financial Support: NIDA R01DA034755

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SUBSTANCE USE AMONG HIGHLY SEXUALLY ACTIVE GAY AND BISEXUAL MEN: EXAMINING SEXUAL COMPULSIVITY, HYPERSEXUALITY, AND SUBSTANCE USE.

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Aims: Research has suggested the need to differentiate those with symptoms of sexual compulsivity (SC) vs. hypersexual disorder (HD). Little is known about differences in substance abuse disorders in gay and bisexual men (GBM) across the SC/HD severity continuum. We examined this among three groups of highly sexually active GBM: men with SC, men with HD, and men with neither.
Methods: A diverse sample of 337 highly sexually active (≥9 partners in previous 90 days) GBM, aged 18-73 (*M* age=37.13), completed a survey including measures of SC/HD, a timeline follow-back interview of substance use behavior, and the Computerized Diagnostic Interview Schedule (CDIS) on substance abuse and dependence. Nearly half (48.9%) the sample was classified as neither SC nor HD, 30.0% were classified as SC, and 21.1% were classified as HD.
Results: Overall, half of the sample met criteria for substance abuse (52.3%) and dependence (48.1%). Chi-square analyses indicated that men with HD were significantly more likely than men with SC or men with neither to report lifetime substance abuse ($p<.01$), lifetime substance dependence ($p<.01$), and current substance dependence ($p<.05$). There were few significant differences in days of various substances used, but HD men reported significantly more days of club drug use than men without SC or HD.
Conclusions: Despite group similarities in the types of substances being used and some similarities in the frequency of recent use, HD men were at increased risk for abuse and dependency over their lifetime. Substance abuse/dependency is a key factor in addressing out of control sexual behaviors. These findings demonstrate the utility of examining distinctions in the severity of HD and SC and could help to target substance use treatment/therapy to those at greatest risk for developing a problem.
Financial Support: R01-MH087714, PI: Parsons

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PSYCHIATRIC SYMPTOMS AND TREATMENT OUTCOMES IN COCAINE-DEPENDENT ADULTS TREATED WITH BUPRENORPHINE AND LONG-ACTING NALTREXONE.

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Aims: This study examines the prevalence of psychiatric symptoms and their association with treatment outcomes in cocaine dependent adults with a history of opioid abuse or dependence.
Methods: This secondary analysis utilizes data collected in a double-blind, placebo-controlled study of 302 participants, sponsored by the NIDA Clinical Trials Network. Participants were provided with sustained-release naltrexone and randomly assigned to 1 of 3 buprenorphine/naloxone (BUP) conditions: 16mg/day (BUP16), 4mg/day (BUP4), placebo (PLB). Medication was provided for 8 weeks in combination with weekly cognitive behavioral therapy (CBT). Self-reported psychiatric symptoms were assessed with the Addiction Severity Index (ASI) administered at baseline. Urine drug screens (UDS) were collected 3 times weekly during the last 4 weeks of the study.
Results: Self-reported psychiatric problems included lifetime depression (61.2%), past-month (28.5%), anxiety (35.7%), hallucinations (6.3%), concentration problems (28.2%), violence (9.9%), and suicidal thoughts (1.7%). There was no difference in outcomes between those with (n=163) and without (n=139) a psychiatric problem as measured by cocaine-negative UDS ($p=0.44$), retention ($p=0.41$), or CBT attendance ($p=0.13$). Those reporting suicidal thoughts were less likely to attend CBT ($p=0.048$) and to drop out of the study earlier than those not reporting suicidal thoughts (37.0 vs. 48.4 days; $p=0.032$).
Conclusions: Participants reported a relatively high prevalence of psychiatric symptoms. Although no relationships were found between psychiatric problems and treatment outcomes for the total sample, some conditions may be more likely to manifest problems during treatment participation suggesting the need for attention to screening and treatment needs in dually diagnosed populations.
Financial Support: NIDA CTN Grants U10DA013045, U10DA01714; and NIDA Contracts N01DA92217 and N01DA102221

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ADOLESCENT INPUT ON A WEB-BASED PRESCRIPTION OPIOID ABUSE PREVENTION TOOL.

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Aims: Although abuse of prescription opioids (PO) has increased dramatically among many age groups in the US in recent years, the rate of abuse in teens is more than 2.6 times the rate in adults. Although science-based, interactive, drug-abuse prevention programs exist focused on preventing use of non-prescription drugs in youth, no science-based, interactive program for the prevention of PO abuse among youth exists. The aims of this project were to: (1) develop 3 modules (i.e. Introduction, What are PO?, Misconception that PO are safe and non-addictive) of a web-based PO abuse prevention program for high school-aged youth; and (2) conduct feedback sessions with youth to obtain reactions to beta versions of modules.
Methods: To achieve aim 1, we conducted 2 focus groups and 1 interview (audiotaped: ~ 90 minutes) with high school-aged youth (n=12) along a continuum of exposure to opioids to determine how to best present program information to this age group. To achieve aim 2, thirty youth participated in feedback sessions to assess program acceptability and utility.
Results: Focus group results reveal that youth have some accurate information about PO, but also highlight misconceptions and lack of knowledge about PO. Feedback session results demonstrate that participant knowledge about PO increased significantly following exposure to the program (66% to 100%) and misconceptions were corrected (68% to 95%), measured by pre-post knowledge tests. Participants also rated the program highly. We are currently developing six additional web-based modules (development data collected will be reported at the 2015 conference) and will conduct a randomized, controlled trial to evaluate the effectiveness of the tool.
Conclusions: Results reveal the utility of including potential program users in program development, and highlight the potential effectiveness of the tool to increase knowledge about PO.
Financial Support: NIDA Grant #2R42DA023731

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IMPACT OF YOHIMBINE AND COCAINE-CUES ON EXECUTIVE FUNCTION IN COCAINE-DEPENDENT MEN AND WOMEN.

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Aims: Noradrenergic activity plays an important role in behavioral inhibition and attention. Data from previous studies suggest that noradrenergic dysregulation plays an important role in craving and relapse in cocaine-dependent women. The aim of this study was to examine the impact of yohimbine and cocaine cues on executive function in cocaine-dependent men and women.
Methods: In a double-blind placebo controlled cross-over study, cocaine-dependent men (n=11), cocaine-dependent women (n=25), control men (n=31) and control women (n=25) received either yohimbine or placebo prior to two cocaine cue exposure sessions. Executive function was assessed using the Connors Continuous Performance Task.
Results: Yohimbine decreased omission errors as compared to placebo ($p=0.04$). Cocaine-dependent women exhibited more omission errors ($p<0.001$) and greater reaction times ($p<0.05$) than cocaine-dependent men. Control men exhibited greater omission errors than control women ($p<0.05$).
Conclusions: These data suggest that cocaine-dependent women exhibit greater deficits in sustained attention compared to cocaine-dependent men. These data add to a growing literature demonstrating gender differences among cocaine-dependent individuals.
Financial Support: *(Funding K12 HD055885; P50 DA016511)*

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ALEXITHYMIA LEVEL AND RESPONSE TO COMPUTER-BASED TRAINING IN COGNITIVE BEHAVIORAL THERAPY AMONG COCAINE-DEPENDENT METHADONE-MAINTAINED INDIVIDUALS.

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Aims: Aims: Computerized cognitive behavioral therapy (CBT4CBT) has been shown to be an effective adjunct to treatment, but little is known regarding the types of individuals who achieve the most benefit. Alexithymia, a characteristic marked by poor ability to identify, define and communicate emotions, has been shown to be associated with treatment outcome, including traditional clinician delivered CBT. We set out to determine the effectiveness of computerized CBT in drug using individuals with alexithymia.
Methods: Methods: Seventy-three methadone maintained, cocaine dependent individuals participating in an 8-week randomized clinical trial comparing standard methadone maintenance to methadone maintenance plus CBT4CBT completed the Toronto Alexithymia Scale (TAS) at pretreatment, end of treatment and a 6-month follow-up.
Results: Results: At baseline, individuals with higher alexithymia (TAS score > 61) did not significantly differ from those with lower alexithymia on multiple demographic and substance use variables, with somewhat higher scores on some indicators of psychological distress. Indicators of treatment process, including retention in treatment, adherence to treatment, and therapeutic alliance, did not differ by alexithymia level. There was a significant interaction of alexithymia level and outcome, such that individuals with higher levels of alexithymia submitted a significantly higher percentage of cocaine-negative urine specimens and were significantly more likely to reach 21 days of abstinence within treatment when assigned to CBT4CBT compared with treatment as usual.
Conclusions: Conclusions: These findings suggest that alexithymia may differentially impact within-treatment outcomes based on type of therapy received for cocaine dependence, and that individuals with high alexithymia especially benefit from computerized CBT.
Financial Support: The primary source of funding was the National Institute on Drug Abuse grants R37-DA 015969 and P50-DA09241. Clinicaltrials.gov ID number NCT00350610.

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MEETING THE HIV AND HEPATITIS C NEEDS OF FEMALE DRUG COURT PARTICIPANTS IN THE CONTEXT OF THEIR TRAUMA.

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Aims: Examine intervention sessions to better understand needs and impact of this health services research project.
Methods: Staff recruited women from drug treatment court (DTC) and screened them for HIV and Hep C. The first 9 positive for either condition underwent the 6-session manualized intervention. Team members reviewed 45 taped sessions and conducted a consensus-based framework qualitative analysis. Themes were mapped onto a theoretical model integrating self-determination motivational theory (SDT) and the socioecological model (SEM).
Results: Among 52 women screened for HIV and HCV, 2 were HIV positive and 15 were Hep C positive. All had child and/or adult abuse histories, drug dependence, and unmet medical needs. SDT-related need support included: 1) autonomy: sobriety enhanced desire to address broad healthcare issues including HIV or Hep C; 2) competence: success in sobriety empowered women to address HIV or Hep C; 3) relatedness: relationships with partners, family, children, healthcare providers, and court staff combined could be overwhelming but enhanced motivation and support for treatment. Socioecological-related themes included: 1) intrapersonal: recent sobriety, structure of DTC, and supportive living situations contributed to stability that engendered self-care which trauma experiences undermined; 2) interpersonal: stability provided at times overwhelming options to assist oneself balanced against needs of children, partners, and family; 3) institutional: DTC increased sobriety but intermittent incarceration made women miss needed medical appointments; 4) community: women in supportive, trauma informed recovery oriented transitional housing had enhanced sobriety.
Conclusions: The SDT and SEM frameworks illuminate interpersonal, community, and court strategies which mobilize women to access needed healthcare.
Financial Support: NIDA1K23DA031612-01A1, PI-Morse

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PREVALENCE OF OPIOID MISUSE IN CANCER SURVIVORS IN PALLIATIVE MEDICINE CLINIC AT A TERTIARY CANCER CENTER.

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Aims: Estimate the prevalence of opioid misuse in cancer survivors in Palliative Medicine clinic at a tertiary cancer center.
Methods: We conducted an audit of a tertiary cancer center outpatient Palliative Medicine (PalMed) specialty clinic to examine the risk of opioid misuse and abuse among our cancer survivors on chronic opioids seen in our PalMed clinic over a one year period.
Results: 1. Among our clinic patients, 90 distinct patients who completed at least first line treatment and were determined to have no evidence of disease were considered to be cancer survivors.
2. Over the period of one year, out of the 90 cancer survivors on opioids, 9 patients (10%) were diagnosed with recurrence and 6 (7%) with a second malignancy.
3. Fifteen patients (17%) were noted to misuse/ abuse opioids with it interfering with pain assessment and pain treatment. Of these, five patients were discharged to local addiction specialists for significant non-compliance. Two patients were started on Suboxone in our program: one patient is being treated successfully and the second patient was discharged to a local MMP due to significant non-compliance.
4. Out of 15 patients with opioid misuse/ abuse, 7 had previous history of substance abuse and 7 had no previous history of substance abuse. Of those patients with no history of aberrant drug taking, 7 were younger than 30 years old, 2 were survivors of breast cancer, 2 of liquid tumor, 2 of sarcoma and 1 of testicular cancer.
Conclusions: Chronic opioid therapy in cancer survivors is associated with increased prevalence of opioid misuse/abuse. Age younger than 30 years is associated with a greater risk of aberrant drug-related behaviors. These trends are similar to the trends seen in the general population and trends recently reported in cancer patients. Increased awareness of the risk of opioid addiction among younger cancer survivors should prompt more close monitoring of analgesia and compliance and when appropriate, opioid taper and discontinuation. Such decisions should not be made unless a recurrence or secondary malignancy have been considered and ruled out.
Financial Support: none

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PREDICTORS OF EARLY RELAPSE IN ADOLESCENT CRACK USERS AFTER HOSPITAL DISCHARGE.

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Aims: To identify predictors of early relapse among adolescent crack users.
Methods: Eighty-nine youths aged 12 to 17 meeting criteria for crack abuse or dependence were selected among psychiatric inpatients of two different hospitals in Porto Alegre, Brazil. They were followed for one and three months after hospitalization and urine tests and self and/or family reports were collected to investigate relapse. K-SADS-PL and T-ASI were used to investigate substance use disorders and other psychiatric comorbidities and severity of substance use, respectively. Crack consumption profile was analyzed with a 27 questions questionnaire developed by the group of researchers. The association between demographic data, consumption profile, severity of use, comorbidities and early relapse were analyzed.
Results: The relapse rates in the first and third month were respectively 65.2% and 85.4%. The median age of those adolescents who relapsed at month one was significantly higher than those who remained drug free (15.81 x 15.07, p=0,02). Statistical significance was also found among the association between Length of Use (36 months x 18 months, p< 0,01) and Binge Use (64.3% x 36.7%, p=0,02) and the outcome Early Relapse. Other variables, including Comorbidity, were not significant.
Conclusions: Severity of crack use may predict early relapse, while comorbidity is not an important predictor, at least in the first three months after discharge. Intensive treatment strategies should be developed and implemented for severe crack users during hospitalization to avoid quick relapse after detoxification.
Financial Support: Brazilian Secretariat of Drug Policies of the Brazilian Ministry of Justice.

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DO THEY REALLY INJECT HEROIN? A STUDY ON THE POSSIBLE CHANGES IN OPIOID CONTENT DURING HEROIN PREPARATION FOR INTRAVENOUS INJECTION.

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Aims: Studies in our lab showed that metabolism of heroin outside the brain can be crucial for the distribution of the main active metabolites, 6-monoacetylmorphine (6MAM) and morphine, and thus for heroin effects. The administration of heroin base requires preparation steps (addition of an acid, warming) to make it soluble and ready for intravenous injection, which can affect the content of heroin and metabolites. The present study examined if this procedure changes the opioid composition of the solution to be injected, and therefore the relation between heroin and active metabolites.
Methods: Heroin samples from twenty different seizures (heroin content ranging from 0.5 to 32.1%) from the Norwegian police were used. From the samples, 237±10 mg were weighted, placed on a metallic spoon, and 40±2 mg ascorbic acid and 750 µl tap water were added. The spoon was warmed up with a lighter for 40 seconds. The resulting solution, without the residues, was collected and analyzed for heroin, 6-MAM, and morphine by LC-MS/MS.
Results: Heroin content decreased by 18%, whereas 6MAM increased 40%, and morphine more than 2000%. Despite the statistic significant (p<0.05) changes in heroin and its metabolites, the composition remained quite constant in the final solution, with 6MAM representing about 15% (11.3% at start) and morphine 4.7% (0.25% at start) of total heroin opioids. Heroin was still the prominent opioid with an 80.4% (88.5% at start) after the procedure.
Conclusions: Preparation of base heroin for intravenous injection produce a change in the composition of heroin and its active metabolites, with a decrease in the former and an increase of the metabolites. However, this increase in the metabolites does not change the final proportion of active metabolites (from 11.5 to near 20% together) in an extent which might have significant effects on heroin physiological and behavioral outcome.
Financial Support: NIPH

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ASSESSING THE COST-EFFECTIVENESS OF A CONTINGENCY-MANAGEMENT INTERVENTION FOR STIMULANT USE AMONG COMMUNITY MENTAL HEALTH PATIENTS WITH SERIOUS MENTAL ILLNESS.

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Aims: To examine the cost-effectiveness of contingency-management (CM) for stimulant dependence among community mental health patients with serious mental illness (SMI).
Methods: Economic evaluation of a 12-week randomized controlled trial investigating the efficacy of CM added to treatment-as-usual (TAU), relative to TAU without CM, for treating stimulant dependence among patients with a SMI. The trial included 176 participants diagnosed with SMI and stimulant dependency who were receiving community mental health and addiction treatment at one community mental health center in Seattle, Washington. Participants were also assessed during a 12-week follow-up period. Positive and negative syndrome scale (PANSS) scores were used to calculate quality-adjusted life-years (QALYs) for the primary economic outcome. Previously analyzed clinical outcomes included days of stimulant and alcohol use, and injection drug use.
Results: Neither the 12-week, nor the 24-week total treatment cost differentials for CM relative to TAU were significantly different at the 5% level ($8,213.27, p=0.56; $12,648.55, p=0.53). This was also true of QALYs gained (0.009 = 3.29 days, p=0.24; .005 = 1.83 days, p=0.71). Prior analyses of the clinical outcomes found CM to be associated with significantly fewer days of stimulant use (-3.76, p<0.05) and alcohol use (-2.48, P<0.05), and a significantly lower rate of injection drug use engagement (37% vs. 66%, p<0.05), during the treatment period. Days-of-stimulant-use was also significantly lower for CM relative to TAU during the follow-up period (-1.82, p<0.05).
Conclusions: Contingency management added to TAU is cost-effective relative to TAU from a third-party payer perspective.
Financial Support: Supported by National Institute on Drug Abuse grant R01 DA022476-01 (Ries, PI).

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PREVALENCE AND CORRELATES OF SPOUSAL SEXUAL VIOLENCE AGAINST MARRIED WOMEN IN INDIA.

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Aims: This study examined the prevalence and correlates of spousal sexual violence against married women in India.
Methods: We used a nationally representative sample of 65,502 married women of childbearing age from the 2005-2006 National Family Health Survey (NFHS-3) data.
Results: About 9% of the women had experienced sexual violence by their husbands. The risk of sexual abuse increased by over four and a half times for women whose spouses humiliated them (OR:4.52; CI: 4.24-4.82). Also, the risk of sexual abuse increased by two times for women whose spouses controlled them (e.g., suspected of infidelity) (OR: 2.38; CI: 2.23-2.54). Women whose husbands consumed excessive alcohol were more likely to be sexually abused (OR=1.40; CI=1.31-1.49). Women who were married before the legal age of 18 were 23% more likely to be sexually abused that their counterparts were married at age 18 or later (OR:1.23; CI: 1.15-1.32).
Conclusions: Preventing underage marriage will reduce the risk of sexual violence against women within marriage. Intervention programs should target women and their families across the life-span: teenage brides, women whose husbands control and humiliate them, and women whose husbands consume excessive alcohol.
Financial Support: No financial support.

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SCREENING, BRIEF INTERVENTIONS AND REFERRAL TO TREATMENT FOR SUBSTANCE USE DISORDERS IN SOUTH AFRICAN HEALTH SERVICES: OPPORTUNITIES AND CHALLENGES.

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Aims: Traditionally, substance use services have not been provided at South African health services, limiting access to treatment. A lack of mental health workers has slowed plans to integrate these services into the health system. This has prompted calls for the task-shifting of some treatment responsibilities to non-specialty health workers. This paper aims to review evidence for the feasibility and acceptability of implementing screening, brief interventions and referral to treatment (SBIRT) for substance use disorders within South African health services, explore evidence in support of the efficacy of BI, and describe challenges and opportunities to implementing these services.
Methods: We present findings from three projects that used a task-shifting approach to integrate BI into primary care. The first involved using community health workers to deliver BI services in a hospital setting. In our 3 month evaluation, we found significant reductions in substance use ($p<0.001$). The second involved a community health worker-delivered BI within emergency services. In a randomised controlled trial, participants were assigned to a session of motivational interviewing (MI), a 5-session blended MI and problem-solving therapy (PST) intervention, or a control group. At 3 months, ASSIST scores were significantly lower in the MI-PST group than in the other groups ($p<0.001$). Third, we integrated a nurse-delivered BI intervention into an antenatal clinic. There was low detection of alcohol use, however tobacco use decreased significantly following the intervention ($p<0.001$).
Conclusions: SBIRT is a promising approach to addressing substance use among patients presenting for primary health care services in a low resourced setting, with evidence of the feasibility, acceptability topatients and providers, and promising substance use outcomes. However, more work is required to improve screening detection rates and referral to care.
Financial Support: Funding provided by the Western Cape Provincial Department of Health

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SUPPRESSION OF ACUTE UP-REGULATION OF PHOSPHORYLATED-EXTRACELLULAR REGULATED KINASE BY MU-OPIOID RECEPTOR AGONIST IN VENTRAL TEGMENTAL AREA RELATED TO RESISTANCE OF REWARDING EFFECT UNDER BONE CANCER MODEL MICE.

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Aims: When opioids were used appropriately for cancer patients, psychological dependence is not a major problem. However this mechanism is not well understood. The present study was to investigate the mechanism underlining the suppression of the rewarding effect by opioids in mice femur bone cancer (FBC) model.
Methods: Rewarding effects and antinociceptive effect of subcutaneously administered morphine and oxycodone were assessed using conditioned place preference test and von-Frey test in sham and FBC model mice. Phosphorylated-extracellular regulated kinase (p-ERK) level was detected by western-blotting.
Results: In FBC model, antinociceptive doses of morphine (30 mg/kg) and oxycodone (5 mg/kg) did not show the rewarding effects, but excessive dose of morphine (300 mg/kg) and oxycodone (100 mg/kg) produced rewarding effects. Using western-blotting, a transient and statistically significant increase in p-ERK level was observed in ventral tegmental area (VTA) 5 min after morphine (10 mg/kg) administration in sham-group. Interestingly, in FBC model, although morphine (10 mg/kg) did not increase p-ERK level, high dose morphine (300 mg/kg) showed the increase in p-ERK level at that time schedule. Consistent with this, rewarding effects of morphine (10 mg/kg) in sham-operation and high dose morphine (300 mg/kg) in the FBC model were significantly inhibited by MEK inhibitor U0126 (10 nmol, i.c.v.).
Conclusions: These findings suggest that acute up-regulation of p-ERK by opioid in VTA is important role for opioid reward, and suppression of ERK pathway might result in resistance of rewarding effect in bone cancer condition.
Financial Support: A. Nakamura is employee of SHIONOGI Co., Ltd, the manufacture of oxycodone and morphine.

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HIGH RATE OF ED PRESENTATIONS IN A COHORT OF PEOPLE WHO INJECT DRUGS: 2008-2013.

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Aims: To examine trends in emergency department (ED) use between January 2008 and June 2013 in a cohort of people who inject drugs (PWID).
Methods: Unique identifiers from 678 PWID in the Melbourne Injecting Drug User Cohort Study (MIX) were deterministically linked to state-level routine ED data collection records. We examined trends in annual ED presentations using Poisson regression. We defined annual frequent use as three or more presentations per year and analysed correlates of frequent presentation using logistic regression.
Results: Over a third (36%) of the cohort presented to the ED at least once over the study period at a rate of 24.3 presentations per 100 person-years (95%confidence interval(CI)=23.0–26.3). This represented 918 presentations among 244 PWID. The mean annual increase in ED presentations was 24%, although the increase was not statistically significant across the follow-up period. The most common diagnoses were mental and behavioural disorders (17%) and poisoning and other externalities (13%). A quarter (26%) of PWID who presented were classified as a frequent ED user in at least one calendar year, contributing to over half (56.9%) of all presentations. Frequent presentation was correlated with self-referral to ED (adjusted odds ratio (AOR)=2.4, 95% (CI)=1.4–4.0), non-injury related presentations (AOR=2.0, 95%CI=1.1–3.8), homelessness (AOR=1.9, 95%CI=1.3–2.8), younger age: 15-24 compared to ≥30 years (AOR=1.6, 95%CI1.1–2.3), 25-29 compared to ≥30 years (AOR=1.7, 95%CI=1.2–2.3), and season: spring compared to autumn (AOR=1.8, 95%CI=1.2–2.7).
Conclusions: The presentation rate is high considering the relatively young age of the cohort. Primary or specialist care management of chronic medical conditions, particularly those relating to mental health, may reduce ED presentations rates.
Financial Support: The work is supported by the Victorian Operational Infrastructure Support Program.

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THE ROLE OF CARBONYL REDUCTASES IN BIOTRANSFORMATION OF BUPROPION AND 4-METHYLNITROZAMINO-1-(3-PYRIDYL)-1-BUTANONE BY HUMAN PLACENTA.

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Aims: Bupropion sustained release (BUP SR) is being evaluated as an aid for smoking cessation during pregnancy. The predominant metabolic pathway of BUP in placenta is reduction to *erythro-* (EB) and *threo*hydrobupropion (TB), the major placental metabolite of BUP; the reaction is catalyzed primarily by 11β-hydroxisteroid dehydrogenase (11βHSD) and aldoketoreductases.
Maternal cigarette smoking has been associated with prenatal exposure to NNK, which is the most abundant and potent carcinogen of cigarette smoke. One of the metabolic pathways of NNK is carbonyl reduction to 4-methylnitrosamino-1-(3-pyridyl)-1-butanol (NNAL) that initiates NNK detoxification.
The goal of the current investigation is to determine placental metabolism of NNK and to identify placental enzymes responsible for its reduction.
Methods: Term placentas were collected from women who smoked during pregnancy and from non-smokers. NNK metabolism was determined *in vitro* using placental microsomal and cytosolic subcellular fractions; the formation of NNAL was quantified by HPLC-UV.
Results: The apparent K_m and V_{max} values for the reaction in placental subcellular fractions were determined. The formation of NNAL in placentas of heavy smokers was lower than in placentas of non-smokers: 12.1 ± 3.5 vs. 17 ± 6.3 nmol.mgP^{-1} for cytosolic fraction ($p<0.05$) and 21 ± 2.7 vs. 23.6 ± 4.6 nmol.mgP^{-1} for microsomes. By contrast, the formation of TB in placentas of smokers, 447.9 ± 260 pmol.mgP^{-1}, was higher than in placentas of non-smokers (300.6 ± 102.3 pmol.mgP^{-1}), $p<0.05$.
Conclusions: These data suggest that reductive metabolisms of NNK and BUP in placenta are catalyzed by different carbonyl reductases. The identification of placental enzymes catalyzing NNK reduction is currently under investigation.
Financial Support: Supported by NIDA grant DA030998 to TN

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SELF-ADMINISTRATION OF SECOND-GENERATION SYNTHETIC CATHINONES IN RATS.

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Aims: The commercial distribution and abuse of synthetic cathinone compounds, commonly referred to as 'bath salts', has increased at an alarming rate in recent years. New structural variants of these compounds, referred to as second-generation synthetic cathinones, have been reported in confiscated samples. The DEA has temporarily scheduled ten of these compounds into schedule I. The current study characterized three second-generation cathinones as reinforcers and compared them to the prototypical stimulant methamphetamine.
Methods: Male, Sprague-Dawley rats (n=6-8/group) were implanted with intravenous jugular catheters and trained to self-administer methamphetamine (0.05 mg/kg/inj) under a 5-response, fixed-ratio schedule of i.v. drug injection. Once self-administration was stable, synthetic cathinone compounds, alpha-pyrrolidinopentiophenone (alpha-PVP), 4-methyl-alpha -pyrrolidinopropiophenone (4-MePPP), and (4-methyl-N-ethylcathinone) 4-MEC were made available for self-administration in separate groups of animals.
Results: All three synthetic cathinones functioned as reinforcers. There was individual-subject variability in the doses that maintained behavior above saline levels. At least one dose within the following dose ranges functioned as a reinforcer: methamphetamine (0.012-0.1 mg/kg/inj), alpha-PVP (0.003-0.1 mg/kg/inj), 4-MEC (0.4-3.2 mg/kg/inj), and 4-MePPP (0.2-3.2 mg/kg/inj). Rank order of potency the drugs' reinforcing effects was alpha-PVP>methamphetamine>4-MePPP>4-MEC.
Conclusions: The current findings demonstrated that three second-generation synthetic cathinones functioned as reinforcers in rats, providing some justification for permanent scheduling of these drugs by regulatory agencies. Future research in our laboratory will assess the reinforcing effectiveness of these three compounds with a behavioral economics approach.
Financial Support: This research was supported by the UMMC Drug Abuse Development Fund and R01 DA12970 to BB.

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SEROTONIN 5-HT$_{2C}$ RECEPTORS IN THE VENTRAL SUBICULUM REGULATE COCAINE-EVOKED HYPERACTIVITY IN RATS.

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Aims: The ventral subiculum (vSUB) interconnects with limbic-corticostriatal circuit which regulates the behavioral effects of cocaine. Serotonin neurons innervate the vSUB, however, little is known about its role or the 5-HT receptors that are functionally relevant in this region. We investigated the vSUB localization of the 5-HT$_{2C}$ receptor (5-HT$_{2C}$R) and its role in the control of cocaine-evoked hyperactivity.
Methods: The expression of the 5-HT$_{2C}$R and co-localization with GAD 67 (marker for GABA) in the vSUB were evaluated using immunohistochemical analyses in rats (n=3). We employed virally-mediated genetic knockdown strategy to test the hypothesis that knockdown of the 5-HT$_{2C}$R in the vSUB of rats (n=5) will modulate cocaine-evoked hyperactivity. Motor activity was assessed after saline or cocaine (10-20 mg/kg) in modified open-field chambers and analyzed using repeated measures two-way ANOVA.
Results: Dense immunoreactivity (IR) for 5-HT$_{2C}$R was observed throughout the vSUB. Only a small proportion of 5-HT$_{2C}$R-IR was co-localized with GAD 67-IR that was restricted to the distal end of the vSUB. Rats with the viral-mediated knockdown of the 5-HT$_{2C}$R in the vSUB exhibited reduced cocaine-evoked hyperactivity compared to control rats ($p<0.05$). No significant differences were observed in the basal locomotor activity between groups.
Conclusions: The co-localization of 5-HT$_{2C}$R- and GAD 67-IR was observed in only a small number of vSUB cells and we are currently analyzing colocalization in glutamate neurons. The reduction in cocaine-evoked hyperactivity after knockdown of vSUB 5-HT$_{2C}$R may reflect changes in output of the vSUB to other regions in the limbic-corticostriatal circuit known to mediate cocaine-evoked hyperactivity.
Financial Support: P50DA033935 (KAC), K05DA022087 (KAC)

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THE DRUG USE PATTERNS OF LATINO DAY LABORERS IN BALTIMORE.

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Aims: Studies suggest that Latino immigrant day laborers, many of whom are undocumented, are at heightened risk of drug abuse given their distinct social, situational and contextual circumstances. With Latinos having some of the lowest rates of access and utilization of drug treatment and related health services, research on the social epidemiology of drug use and related HIV risk behaviors is needed to reduce existing health disparities among this population.
Methods: Utilizing a rapid assessment methodology, qualitative interviews were conducted with 77 Latino male immigrant day laborers in Baltimore. Participants were recruited from day labor sites, were male 18 years of age or older; self-identified as being from a Latin American country, and currently residing in Baltimore and work as a day laborer. Analysis of the qualitative data consisted of defining the broad dimensions and specific variations distinguishing the patterns of drug use.
Results: During the month prior to the interview, participants reported the use of alcohol (94.8%), marijuana (63.6%), cocaine (46.3), crack (17.5%) and heroin (10.4%). Of particular interest are the high rates of heroin use. Of those who reported any drug use in the past month, 15.4% reported heroin use, previously found by other studies to be very low, among this population.
Conclusions: The emergence of heroin use and other drugs among this subgroup of Latino immigrant day laborers is particularly problematic from a public health perspective as this population tends to lack access to preventative and health care services. Implications include this immigrant population's potential to act as a ''bridge for infection'' in the spread of HIV and other blood borne pathogens.
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INTERNALIZING AND EXTERNALIZING DISORDERS AS RISK FACTORS FOR THE INCREASE OF CANNABIS USE AND THE ONSET AND STABILITY OF CANNABIS USE DISORDERS: A SYSTEMATIC REVIEW OF COHORT STUDIES FROM THE GENERAL POPULATION.

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Aims: In the last decades, longitudinal cohort studies have examined internalizing and externalizing disorders as risk factors of cannabis use (CU) and cannabis use disorders (CUD). We aimed to systematically review the evidence of these studies considering the stages of CU increase, stability and cessation and CUD onset, stability, remission and relapse.
Methods: A systematic review was conducted with Web of Knowledge, Scirus, PubMed and PsyIndex using cohort studies of predictors of CU and CUD. 18 of 1461 screened articles published between 06/94 and 06/14, examining one or more of the above mentioned risk factors were selected.
Results: Results from longitudinal studies on anxiety - (N=7) and mood disorders (N=8) as predictors of CU and CUD stages were inconsistent. Five studies found no evidence, while in single studies (each N=1) severe depressive symptoms predicted continued CU, major depression and mania/hypomania predicted CUD onset, social anxiety disorder predicted cannabis dependence and a new onset of any anxiety or mood disorder after CUD remission predicted relapse. In contrast, externalizing behaviors predicted CU increase in four and CUD onset and stability in five studies. Externalizing disorders did not predict the transition from regular use to CUD in one study.
Conclusions: The risk of CU and CUD by externalizing behaviors and disorders appears evident and consistent, whilst the risk stemming from internalizing disorders may be restricted to specific conditions and more evident in later CU stages. Externalizing behaviors might indicate the need for preventive measures related to CU and CUD.
Financial Support: Sponsored by Martin Iguchi

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SUBJECTIVE RESPONSES TO ACUTE COCAINE ARE MODERATED BY VARIANTS OF THE SEROTONERGIC SYSTEM.

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Aims: To test whether subjects with specific serotonergic genetic variants are associated with subjective responses to cocaine.
Methods: Cocaine-dependent non-treatment seeking participants (N=66) received randomized infusions of saline and cocaine (0 and 40 mg, IV) over a two minute period. Fifteen minutes prior to and at five minute intervals (5, 10, 15, and 20 min) post-infusion subjective effects were recorded. Scores were subtracted from -15 minute baseline value and then saline values subtracted from cocaine values to yield subjective effect score. Participants were genotyped for the *SLC6A4* (serotonin transporter) *5-HTTLPR*, *TPH1* rs1799913, and *TPH2* rs4290270 variants. Repeated measures ANOVA corrected for population structure was used to analyze the data.
Results: Participants had a mean age of 43 years, were 80% male and 73% black, and smoked 2.3 g cocaine per day. Self-report of "Desire" and "Access" were found to be in association with the triallelic *5-HTTLPR* (p=3x10^{-5}, p=2x10^{-4}, respectively). Self-report of "Stimulated" and "Access" were found to be in association with the *TPH1* rs1799913 (p=3x10^{-4}, p=4x10^{-5}, respectively). Self-report of "Good effect" was found to be in association with the *TPH2* rs4290270 (p=4 x10^{-4}).
Conclusions: The serotonergic system may contribute to the subjective effects produced by acute cocaine exposure, which has relevance to models of drug-induced relapse. The role that these serotonergic genes and variants moderate these effects may aid in the development of specific pharmacotherapies tailored to those with specific genetic backgrounds.
Financial Support: Supported in part by NIH/NIDA P50 DA018197 (TK), for DN through MD Anderson's Cancer Center Support Grant NIH/NIDA DA026120, 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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CHANGING PATTERNS OF TREATMENT SEEKING FOR PHARMACEUTICAL OPIOIDS IN AUSTRALIA (2002-2011).

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Aims: Despite well-documented increase in use and harms with pharmaceutical opioids (PO), few detailed studies have examined treatment delivery, particularly for interventions other than opioid substitution treatment. We aimed to explore changes in opioid treatment for PO over time using national treatment data.
Methods: Data from closed drug and alcohol treatment episodes from the Alcohol and Other Drug Treatment Services National Minimum Data Set (AODTS-NMDS), representing non-opioid substitution treatment) in Australia for 2002–03 to 2010–11 were examined. In the four jurisdictions where detailed data was available, episodes where heroin was the principal drug of concern were compared to episodes where the four most frequently reported opioids (morphine, codeine, fentanyl and oxycodone) were recorded as the principal drug of concern.
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Results: In 2002-3, most (93%) opioid treatment was related to heroin with seven percent of all opioid treatment episodes reporting a PO as the principal drug of concern. In 2010-11 20% of all opioid treatment episodes were attributed to pharmaceutical opioids. Distinct changes over time were observed for different opioids: an increase in the average age at the start of the episode was seen for heroin and oxycodone; and a reduction in the proportion of females in codeine episodes, with 67% in 2002-3 compared with 44% in 2010-11. Codeine and oxycodone users had the lowest current or past injection.
Conclusions: Clear differences were observed over time and between different opioids. Monitoring these emerging patterns will be important to inform treatment needs, particularly in light of different patterns of poly drug use, different routes of administration and changing demographic characteristics.
Financial Support: NHMRC Reserach Fellowships (#1013803, #1041472).

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SUBSTANCE DEPENDENCE CRITERIA, NOT SUBSTANCE USE, ASSOCIATED WITH HIV VIROLOGIC CONTROL.

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Aims: This study aims to a) describe a cohort of HIV-infected people on antiretroviral therapy (ART) who use substances and b) explore which substance use-related factors are associated with lack of virologic control.
Methods: Participants were selected from the Boston ARCH cohort (i.e. HIV-infected adults with 12-month DSM-IV substance dependence or ever injection drug use) who were currently taking ART. Substance use predictors of interest included number of DSM-IV alcohol and drug dependence criteria and past 30 day substance specific use. Associations with HIV virologic control (HIV viral load [HVL] <200 vs ≥200 copies/mL) were tested using logistic regression models. Multivariable analyses were adjusted for age, gender, homelessness and anxiety or depression.
Results: Participants (n=200) were median age 50 years, 67% male, 51% African American, 76% self-reported ≥90% ART adherence, and 80% HVL <200 copies/mL. In the past 30 days, 52% reported the use of alcohol in heavy amounts, 77% cigarettes, 45% marijuana, 27% cocaine, 16% heroin, and 14% illicit prescription opioids. In unadjusted analyses, both number of DSM-IV alcohol dependence criteria (past 12 months)(odds ratio [OR]=1.18 for each additional criterion, 95% confidence interval [CI]: 1.03-1.34) and number of DSM-IV drug dependence criteria (OR=1.27, 95% CI: 1.09-1.48), but not alcohol, tobacco, marijuana, cocaine, heroin, or illicit opioid use, were associated with a detectable HVL. After adjusting for covariates, only number of drug dependence criteria remained significant (adjusted OR=1.21, 95% CI: 1.03-1.42).
Conclusions: More than 3/4 of an addiction HIV cohort had HIV virologic control and ≥90% ART adherence. Substance dependence criteria (drug dependence in particular), and not substance specific use, were associated with a lack of virologic control. This suggests that substance dependence criteria warrant particular clinical attention by HIV care providers.
Financial Support: U01AA020784, U24AA020778, U24AA020779, R25DA033211

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THE EFFECTS OF OPIOID SUBSTITUTION TREATMENT AND HIGHLY ACTIVE ANTIRETROVIRAL THERAPY ON THE CAUSE-SPECIFIC RISK OF MORTALITY AMONG OPIOID-DEPENDENT INDIVIDUALS WITH HIV/AIDS.

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Aims: Opioid-dependent individuals are known to be at drastically elevated risk of mortality; this risk is further elevated amongst people living with HIV/AIDS (PLHIV). The objective of this study is thus to determine the independent and joint effects of OST and highly active antiretroviral therapy (HAART) on mortality, by cause, within a population of injection drug using (IDU) PLHIV initiating HAART.
Methods: We employed a range of time-to-event analytic methods, including competing risks, Cox proportional hazards models with time-varying covariates, and marginal structural models, to identify the independent and joint effects of OST and HAART on all-cause, as well as drug-related and HIV-related mortality, controlling for a range of covariates.
Results: Among 1,727 IDU-PLHIV, 493(28.5%) died during a median 5.1 years(interquartile range: 2.1-9.1) of follow-up: 18.7% due to drug-related causes, 55.8% due to HIV-related causes, and 25.6% due to other causes. Standardized mortality ratios were 12.2(95%CI:9.8,15.0) during OST, and 30.0(27.1,33.1) during periods out of OST. Both OST (adjusted hazard 0.34; 95%CI:(0.23,0.49)) and HAART(0.39(0.31,0.48)) independently decreased the hazard of all-cause mortality, however individuals were at lowest risk of death when these medications were used jointly (0.16(0.10,0.26)). Both OST and HAART independently protected against not only HIV-related death, but also drug-related death and death due to other causes.
Conclusions: While both OST and HAART are life-saving treatments, there is an urgency to provide access to OST to opioid-dependent PLHIV to protect against mortality due to drug overdose, as well as HIV-related causes.
Financial Support: NIDA R01DA031727(PI: Nosyk), R01DA032551(PI: Nosyk), P30DA016383(PI: Hser)

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MIXED-AMPHETAMINE SALTS INCREASE ABSTINENCE FROM MARIJUANA IN PATIENTS WITH CO-OCCURRING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COCAINE DEPENDENCE.

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Aims: To test the hypothesis that stimulant treatment would decrease marijuana use in a randomized controlled trial of extended release mixed amphetamine salts (MAS-XR) for treatment of co-occurring ADHD and cocaine use disorders over the course of the study.
Methods: The original trial utilized a 3-arm randomized design with one-week placebo lead-in, comparing placebo, MAS-XR 60mg and MAS-XR 80mg. Marijuana users were defined as participants with reported marijuana use in the 30 days before study initiation. Marijuana use data was collected with timeline follow-back. For this analysis, both MAS-XR groups were combined to maximize statistical power, leaving n=20 in the placebo group and n=37 in the MAS-XR group. The primary outcome was proportion of subjects reporting any marijuana use per study week. Comparisons between groups were made using a logistic mixed effects model incorporating multiple predictors and modeling time-by-treatment interactions.
Results: There was a significantly lower proportion of participants using marijuana per week in the MAS-XR group compared to placebo. There was no baseline difference in marijuana use frequency or quantity between the groups.
Conclusions: Treatment of ADHD and comorbid cocaine use disorders with extended release mixed amphetamine salts is associated with increased abstinence from marijuana in those who use marijuana.
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NOVEL PSYCHOACTIVE SUBSTANCE USE IN THE EUROPEAN UNION.

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Aims: Novel psychoactive substances (e.g., bath salts, Krokodil, synthetic marijuana) are synthetic, semi-synthetic or natural compounds, often advertised and sold as 'legal' alternatives to illicit drugs. The current study is among the first population-based studies in the EU to identify their prevalence and characteristics.
Methods: General population surveys, modelled after the United States' National Survey of Drug Use and Health, were conducted by RTI International in seven European countries (29 metropolitan strata, sample n=22,057) in 2014. Self-report (in English or native language) surveys among persons aged 12 or older were collected and weighted to achieve country-specific representative estimates.
Results: The lifetime estimates for NPS ranged from 0.7% (Denmark) to 2.2% (Great Britain), with a mean of 1.8% and a population estimate of 5.5 million. An estimated 500,000 (0.5%) persons reported past-year NPS. Controlling for country, latent class models indicated 6 classes of past-year illicit drug use, with NPS present in a homogenous class characterized by males (AOR=2.5, p<.001), whites at higher risk relative to black/African descent (AOR=1.6, p<.05), and Asian (AOR=3.3, p<.001). Youth (ages 18-24) were at higher risk for NPS relative to those ages 12-17 (AOR=1.5, p<.001) and 35+ (AOR=1.6, p<.001). Mood/anxiety disorders conferred higher risk of NPS compared to those with no disorder (AOR=2.5, P<.001), or subthreshold symptom levels (AOR=1.6, p<.001). NPS users also reported a greater use of social media.
Conclusions: With the increasing erosion of geographic boundaries and increased increased communication, studies are desperately needed to identify the international landscape of drug use. Additional waves are planned to identify trends in transmission patterns between countries and population sub-groups.
Financial Support: Shire, NIH, RTI International, the European Drug Union.

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EFFECTS OF WITHDRAWAL FROM CHRONIC NICOTINE ON EMOTIONAL AND COGNITIVE BEHAVIORS IN ADULT AND ADOLESCENT MICE.

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Aims: Aims: Nicotine dependence correlates with increased risk for emotional, cognitive, and neurological impairments later in life. This study investigated the long-term effects of nicotine on measures of depression, drug reward, anxiety, and learning in adolescent and adult mice.
Methods: Methods: Male C57BL6/J mice received saline or nicotine (12.6 mg/kg/day) for 12 days via osmotic pumps implanted on postnatal day 32 (adolescent) or 54 (adults). 24 hours or thirty days after cessation of nicotine/saline, mice were tested for the conditioned rewarding effects of cocaine and morphine, depression-like behaviors using the forced swim test, anxiety-like effects with the elevated plus maze, or learning effects using contextual fear conditioning.
Results: Results: Increased depression-like responses were seen in both adolescent and adult mice when tested during acute (24 hr) nicotine withdrawal (2-way ANOVA, p<0.01). Heightened depression-like behaviors persisted when tested 30 days later in mice exposed as adolescents (p<0.01, N=15-16/group), but not those exposed as adults. No differences in the conditioned rewarding effects of cocaine (10mg/kg) or morphine (5mg/kg) between age or nicotine exposure were found. Adolescent mice, but not adults, exposed to nicotine showed a non-significant increase in anxiety (lower open arm time) when tested after 30 days of abstinence. Nicotine exposure during adolescence caused deficits in contextual fear learning indicated by lower levels of freezing to the context as compared to saline controls.
Conclusions: Conclusions: These results demonstrate that nicotine exposure and withdrawal can have long-term effects on emotional and cognitive functioning, particularly when nicotine exposure occurs during the critical period of adolescence. Potential mechanisms underlying this age-specific response are under investigation.
Financial Support: Financial Support: Supported in part by PA Department of Health

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PHYSIOLOGIC EFFECTS OF DRONABINOL DURING OPIOID WITHDRAWAL IN HUMANS.

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Aims: Dronabinol, a CB1 agonist, is currently being evaluated for its efficacy in relieving opioid withdrawal (see abstract by Gill et al.). This abstract reports on safety outcomes from that proof-of-concept study.
Methods: Ten healthy non-treatment seeking adult volunteers with opioid dependence completed this within-subject, randomized, double-blind study. Participants were inpatients maintained on oral oxycodone (OC) 30 mg at 8am, and 12, 6 & 10pm daily. Placebo (P) was substituted for three OC doses preceding each experimental session (sessions ≥ 72 hours apart) to ensure that opioid withdrawal was present. Initial test doses (one/session) included P, OC (30 and 60mg), and dronabinol (DB: 5, 10, 20, and 40mg). DB 40mg was replaced with 30mg due to safety concerns. Physiologic parameters [e.g., systolic and diastolic blood pressure (SBP, DBP), heart rate (HR)] were measured before and for 6 hrs after drug administration. Analyses excluded DB 40mg data; n=10 for all doses except n=7 for DB 30mg.
Results: Only two volunteers received DB 40 mg; both experienced sustained sinus tachycardia (i.e.,HR > 100 bpm) for ~2.5 hrs accompanied by feelings of panic/anxiety. Maximum HR was 144 bpm in one participant (baseline HR=79) and 126 bpm (baseline HR=61) in the other. SBP also increased for both volunteers. Of the remaining eight subjects, one had increased HR, BP and anxiety after receiving DB 20mg so DB 30 mg was not given. There were significant effects of dose on mean peak max HR (p<0.0001), but not on SBP or DBP. Max HR (mean bpm) for DB 20 (112) and DB 30 (114) was higher than for P (84), OC 30 (77), and OC 60 (81).
Conclusions: The therapeutic potential of DB is limited due to tachycardia, which emerged in the context of early opioid withdrawal, a state characterized by increased noradrenergic outflow.
Financial Support: This study was supported by NIDA DA033932 (Walsh), T32 DA035200, and NCATS ULTR000117.

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AN *M*HEALTH APPLICATION FOR INCREASING HIV AND HEPATITIS KNOWLEDGE IN WAITLISTED OPIOID ABUSERS.

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Aims: Opioid-dependent patients can remain on waitlists for months before a treatment slot becomes available, during which they are at significant risk for contracting and transmitting HIV and hepatitis (HCV). Our team has developed a single-visit, in-person intervention shown to improve HIV and HCV knowledge in illicit drug abusers (Dunn et al., 2013; Heil et al., 2005; Herrmann et al., 2013). We sought to adapt this intervention for delivery via a mobile health (*m*Health) platform more compatible with the resource-constrained settings. We report here on the initial piloting of our HIV+HCV iPad application in opioid-dependent adults awaiting treatment.
Methods: Participants were 11 adults (54.5% male, 35±9.1yrs old) participating in a randomized trial evaluating the efficacy of interim buprenorphine treatment. Most (82%) endorsed prescription opioids as their primary drug, and 45% reported a lifetime history of IV use. They completed a baseline HIV and HCV knowledge assessment and then received corrective feedback via the application. Participants then completed an educational module including an interactive HIV flipbook and animated HCV video, followed by a repeat of the HIV+HCV assessment. Finally, they repeated the assessments at 4 and 12 months following intake.
Results: The *m*Health application was associated with significant improvements in HIV and HCV knowledge. Percentage of correct HIV items increased from 73% to 87%, representing a 19% increase in accuracy (p=.003). HCV scores increased from 57% to 86%, representing a 51% increase in accuracy (p=.005). Preliminary data also suggest that these improvements are sustained though the 4-month assessment.
Conclusions: Preliminary data suggest that this *m*Health intervention, delivered via an automated iPad application, enhances HIV and HCV knowledge in opioid abusers awaiting treatment. Data from a much larger sample will be available for the June 2015 meeting, as will data from the 4- and 12-month follow-up timepoints evaluating whether these improvements persist.
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ADHD AND THE RISK OF INITIATION OF MARIJUANA USE AMONG A NATIONAL SAMPLE OF YOUTH 10 TO 18 YEARS OF AGE.

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Aims: To examine the effect of self-reported Attention Deficit Hyperactivity Disorder (ADHD) on risk of initiation of marijuana use
Methods: Data from the National Monitoring of Adolescent Prescription Stimulants Study (N-MAPSS), which included 11,048 10 to 18 year olds, were analyzed. The primary predictor, history of self-reported ADHD, was a participant's response to the question: "*has a doctor ever told you or your parents that you have ADHD*? *(Yes/no)*.The primary outcome, age of initiation of marijuana use, was defined as the age a participant reported that they first used marijuana. A cox-proportional hazard model was used to estimate hazards of initiation of marijuana use as a function of ADHD status. Model was adjusted for socio-demographics, academic performance, tobacco use, peer and environmental influence.
Results: Among participants in this sample, 47.8% were male, 13.8% self-reported a history of ADHD and 29.3% reported having ever used marijuana. Participants who reported a history of ADHD were significantly more likely to be male (59%) and white (55%). The hazard of initiation of marijuana use peaked at age 18 years for both groups; however the hazard rate at 18 years was 25% vs. 16% for those with and without a history of ADHD, respectively. In adjusted analysis, participants with a history of ADHD, as compared to those without, had increased hazards of initiation of marijuana use [hazard ratio (HR) =1.15, 95% confidence interval (CI) =1.05 – 1.27].
Conclusions: In this national sample of youth, those with self-reported ADHD had an increased hazard of initiating marijuana use.
Financial Support: N-MAPSS was conducted under contract with Pinney Associates, Inc., with funding provided by Shire Development LLC and Noven Pharmaceuticals. NIDA T32DA035167-01A1 (Okafor, Fellow; PI: Cottler), Fogarty International Centre Indo-US Training Program in Non-Communicable Diseases (Grant No D 43-TW009120; Sonam O Lasopa, Fellow; PI: Cottler), NIAAA U2402002 (PI: Cook).

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IMPACT OF CYP2D6 PHENOTYPE ON RESPONSE TO METHAMPHETAMINE IN HEALTHY VOLUNTEERS.

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Aims: Genetically mediated metabolic factors have been shown to impact vulnerability for drug dependence. Methamphetamine (MA) is initially metabolized via the cytochrome P450 2D6 (CYP2D6) enzyme system, which has several clinically relevant genetic variants. The purpose of this study was to determine whether genetically mediated metabolic factors modify response to MA.
Methods: Healthy volunteers (18–50 yrs), stratified by CYP2D6 phenotype (extensive (EMs) vs poor (PMs) metabolizers) after an 8-hr debrisoquine urinary recovery ratio test, underwent 5 sessions in which MA (10 and 15 mg), caffeine (500 mg), codeine (120 mg) or placebo was administered in random order. Subjective and cardiovascular measures were obtained pre- and at 30, 60, 90, 120, 180, 240, 300 and 360 min post-drug. For each measure, AUC was generated within each session. Data were entered separately for placebo and each drug into mixed models ANOVA with CYP2D6 phenotype and dose (e.g., placebo, MA10, MA15; placebo, caffeine; placebo, codeine) as factors.
Results: Thus far, 5 EMs and 2 PMs at CYP2D6 have completed all sessions and 2 PM are actively participating. Preliminary AUC change from placebo data showed several main effects for MA, such that MA at 15 mg increased ratings of arousal ($t=2.71$, $p<0.03$) and vigor ($t=2.33$, $p<0.05$) on the POMS and systolic ($t=2.30$, $p<0.05$) and diastolic ($t=2.86$, $p<0.02$) blood pressure relative to placebo regardless of metabolizer status. MA-induced ratings of on the MBG subscale of the ARCI relative to placebo were significantly greater for EMs than PMs ($t=2.92$, $p<0.02$). No significant main effects or interactions have occurred with caffeine or codeine.
Conclusions: These preliminary results suggest that MA-induced euphoric-like effects may differ depending on CYP2D6 phenotype. The lack of caffeine- or codeine-induced main effects or interactions may be due to the doses not being high enough.
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THE RELATIONSHIP BETWEEN AFRICAN-AMERICAN WOMEN'S HEALTH DISCUSSION NETWORKS & HIV RISK BEHAVIORS.

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Aims: HIV is an epidemic in the African American community, where personal relationships are salient and can influence health behaviors. Yet, there is limited research examining egocentric social networks and African American women's HIV risk behaviors. This study examines the relationship between African American women's health discussion networks (size, composition, strength, and function) and HIV risk behaviors.
Methods: Using data from the Black Women in the Study of Epidemics (B-WISE, n=344), multivariate models investigated associations between characteristics of health discussion networks and two risk behaviors: a positive drug screen and unprotected vaginal sex.
Results: The average participant was single, 35 years old, and the number of health discussion network members ranged from 0 to 5, with 22% having no one to talk to about their health (mean=1.39, S.D.=1.10). African American women were less likely to use drugs when they reported larger (AOR=.71; 95% CI: .55-.92) or closer (AOR=.79; 95% CI: .68-.92) networks, as well as those comprised of people who provided a variety of support functions including instrumental (AOR=.52; 95% CI: .31-.88) or financial (AOR=.59; 95% CI: .34-.99) support, health information (AOR=.44; 95% CI: .25-.78), and discussing health (AOR=.51; 95% CI: .28-.90). In contrast, health discussion network variables were not associated with unprotected sex.
Conclusions: It is concerning that almost one-quarter of women had no one to talk to about their health considering that larger, closer-knit, and more supportive networks are protective against drug use for African American women. Risky sexual behaviors are challenging to change, which is problematic as most new HIV infections among African American women are acquired via heterosexual contact. Future research should examine the characteristics of African American women's health discussion networks as predictors of drug treatment and include health discussion networks in HIV interventions.
Financial Support: This research is funded by NIDA (R01-DA022967 & K02-DA35116, PI: Oser).

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DRUG USE AND INJECTION PRACTICES IN TAJIKISTAN: QUALITATIVE STUDY IN KULOB AND KHOROG.

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Aims: To understand drug use practices and related behaviors in two Tajik cities – Kulob and Khorog.
Methods: 12 focus group discussions (6 per city) with 100 injection drug users recruited through needle and syringe program (NSP) outreach. Topics were related to drugs injected, drug prices and purity, access to sterile equipment, safe injection practices and types of syringes and needles used. Qualitative thematic analysis was done using NVivo 10 software.
Results: The participants were all male, of mean age 42.4 (range 20-78). Thematic analysis showed that cheap Afghan heroin, often adulterated by dealers with other admixtures, was the only drug injected. Drug injectors often added Dimedrol (Diphenhydramine) to increase the potency of "low quality" heroin. NSPs were a major source of sterile equipment. Prevalence of direct sharing was low. However, joint preparation of drugs using a common cooker, a common syringe and frontloading was a common practice. Withdrawal was a major reason for sharing syringes, preparing and injecting drugs in an unsafe place, using non-sterile water, not boiling and not filtering the drug solution.
Conclusions: Results provide useful information for defining further research questions and planning risk reduction interventions in Tajikistan.
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DUAL BLOCKADE OF ENDOCANNABINOID HYDROLYZING ENZYMES REVEAL A CB_1 RECEPTOR-MEDIATED INTEROCEPTIVE STIMULUS.

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Aims: The observation that dual blockade of endogenous cannabinoid degradative enzymes monoacylglycerol (MAGL) and fatty acid amide hydrolase (FAAH) elicits THC-like psychotropic effects suggest FAAH & MAGL function as dual brakes in curtailing the pharmacological effects of endogenous cannabinoids. To test this hypothesis, we examined whether blockade of FAAH and MAGL would produce an interoceptive stimulus in mice, using the drug discrimination paradigm. Drug discrimination is an assay used to infer the subjective effects of drugs. Here we tested whether elevating levels of the naturally occurring endogenous cannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) via inhibition of both degradative enzymes would serve as an interoceptive stimulus in mice, N = 7-8. Towards this end, we employed the dual FAAH & MAGL inhibitor SA-57 as the training drug.
Methods: Mice were trained using a double alternation between SA-57 and vehicle (DDVVDD) and acquired the task over 40 days.
Results: The discriminative stimulus effects of 10 mg/kg SA-57 were dose-related (ED_{50} (95% CI) = 4.49 (3.77 – 5.35) mg/kg) and were antagonized by the CB_1 receptor antagonist rimonabant (3 mg/kg), but not the CB_2 receptor antagonist SR144528 (3 mg/kg). CP55, 940 as well as the dual FAAH/MAGL inhibitor JZL195 substituted for SA-57, and rimonabant blocked the substitution of both. Low doses of SA-57 (<3 mg/kg), which completely inhibit FAAH, but not MAGL, did not substitute for SA-57.
Conclusions: These findings suggest that inhibition of FAAH alone is not sufficient to elicit SA-57-like subjective effects. Taken together, this study represents the first example that elevating levels of naturally occurring endogenous cannabinoids serves as a discriminative stimulus. Thus, MAGL and possibly FAAH serve as brakes in curtailing the psychotropic effects of endogenous cannabinoids.
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USING CELLPHONE TECHNOLOGY TO MONITOR AND INCREASE DOSING ADHERENCE.

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Aims: Cellphone technology has become ubiquitous in substance abuse research over the last few years. Cellphone text reminders and status assessments allow a virtual 24-hour assessment window; previous research used cellphones to remind participants to take their study medication and to take photos when dosing.
Methods: A current study conducted under the auspices of the NIDA Clinical Trials Network, the Accelerated Development of Additive Pharmacotherapy (ADAPT) trial, extends the usefulness of cellphone technology. Participants are provided with smartphones to capture medication dosing in video format, and reimbursement is given for each valid video submitted.
Results: Cellphones were provided to 49 study participants at 3 study sites. Smartphone use in this study addresses several concerns typically in research on participants with substance use disorders: 1) provides a method of contact with participants outside the clinic visit; 2) serves as a reminder to take study medication; 3) encourages adherence by incentivizing submission of valid dosing videos; 4) allows participant to enter clinic appointments in cellphone calendar and set reminders; 5) confirms self-reported medication adherence; and 6) may increase retention as participants keep smartphones at study completion. Including cellphones in the study design has also introduced some challenges: 1) ensuring privacy and confidentiality of study data; 2) difficulties in teaching participants how to use the device; and 3) navigating new ground in terms of regulatory approvals.
Conclusions: Cellphone technology as used in the treatment studies may improve treatment or medication adherence, participant engagement and retention, serving to improve collection and validation of study data.
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THE IMPACT OF NICOTINE DOSE ASSIGNMENT ON AFFECT AND DEPRESSION DURING EXTENDED EXPOSURE TO EXPERIMENTAL SPECTRUM CIGARETTES: FINDINGS FROM CENIC PROJECT 1 STUDY 1.

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Aims: To explore how nicotine dose assignment impacts affect and depression status during 6-week exposure to experimental cigarettes.
Methods: Data came from the Center for Evaluation of Nicotine in Cigarettes (CENIC) Project 1 Study, a randomized clinical trial among general population current cigarette smokers in the U.S. (2013-2014). Descriptive statistics were used to describe the sample, and logistic regression and linear mixed models were used to explore the association between nicotine dose assignment (usual brand, 0.8 mg, 0.26 mg, 0.12 mg, 0.07 mg, 0.04 mg high tar, 0.03 mg yield) and affect, measured by the Positive and Negative Affect Scale (PANAS) and depression, measured by the Centers for Epidemiologic Studies Depression scale, outcomes.
Results: Compared to those randomized to smoke their usual brand of cigarettes, participants who were randomized to smoke 0.8 mg, 0.12 mg, 0.07 mg, and 0.03 mg nicotine yield Spectrum cigarettes reported significantly less positive affect. Conversely, nicotine dose assignment did not impact negative affect experienced by participants. Nicotine dose assignment did not have an impact on depression during the study, either.
Conclusions: Assignment to experimental cigarettes was associated with decreased positive affect compared to those who were assigned to smoke their usual brand cigarette. Nicotine dose assignment was not associated with differences in positive affect or depression.
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CRACK USERS WITH CONDUCT DISORDER HAVE MORE ASSOCIATION WITH VIOLENCE, TRAUMA AND PSYCHIATRIC COMORBIDITIES.

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Aims: To compare in and outpatient crack users with and without symptoms of Conduct Disorder.

Methods: A cross-sectional sample of 720 current adult crack users from outpatient and inpatient Brazilian clinics. Participants were evaluated with ASI-6 and MINI. Data were analyzed using SPSS v.21. Participants were divided into two groups - individuals who presented Conduct Disorder (n=354) and other crack users (n=366). Data were compared by Chi-square test. A Poisson Regression was performed later.

Results: Crack users with symptoms of Conduct Disorder (CD) showed a higher prevalence of Social Anxiety (22.9%, p=0.001), PTSD (20.2 %, p=0.003), Alcohol Abuse (12.8%, p = 0.002), Lifetime Psychotic Symptoms (36% p<0.001). Medians of age of first use of substance were lower for patients with CD than of those with no CD symptoms (marijuana - 13 and 15 years old, respectively; cocaine = 16 and 18 years old; crack = 21 and 23 years old; inhalants = 15 and 17 years old). Individuals with CD symptoms showed a higher association with violence, crime and trauma (intake before 18 years old – *PR* 1.3, p=0.004; physically injured by someone known – *PR* 1.2 p=0.011; victim of a violent crime – *PR* 1.1, p=0.044; have been in a treat life situation – *PR* 1.2, p=0.011).

Conclusions: This study corroborates literature pointing that CD is a serious condition that can bring a wide range of harm, not only to the individuals, but also to the community. Hence, it is relevant to emphasize that crack users with CD are at risk of committing violent actions and be exposed to traumatic situations, worsening their condition. These results may guide therapeutic strategies in Brazil's public health.

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DIFFERENT PATTERNS OF DRUG USE AMONG CRACK AND POWDER COCAINE USERS IN BRAZIL.

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Aims: Multiple substance use is receiving increasing recognition as an important topic for research and may involve either concurrent or sequential use of different substances. In Brazil, people who seek treatment for substance use often report crack or powder cocaine use. However, in the scientific literature, little is known about differences between these two populations. The purpose of this study is to compare drug use patterns among crack and cocaine patients who seek treatment in public addiction settings.

Methods: A cross-sectional study with a target sample of subjects recruited from hospitals and specialized clinics for substance abuse treatment in four Brazilian state capitals. Participants who had reported as primary problem the use of powder cocaine or crack were included in the study. The Sixth version of the ASI6 was applied by trained psychologists. We recruited a total of 419 drug abusers – 293 crack abusers (CA) and 126 powder cocaine abusers (PCA). The pattern of use taken into consideration was the number of days of drugs used in the 30 days prior to admission. A comparison between the two groups was performed through the Mann-Whitney Test for asymmetric variables.

Results: Crack and powder cocaine users showed a different pattern of drug use related to the consumption of alcohol (median of 5 and 7.5 days, respectively p<0.045), marijuana (median of 4 and 0 days, p<0.001) and crack or cocaine (median of 10 and 5 days, respectively p<0.001).

Conclusions: The pattern of use may interfere in the treatment prognoses and may require specific therapeutic approaches in each case. In addition, these results may lead to a better comprehension of polydrug use and its implication on these individuals' health.

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A QUALITATIVE INVESTIGATION COMPARING SEXUAL EFFECTS OF ALCOHOL AND MARIJUANA AMONG ADULTS.

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Aims: Alcohol and marijuana (cannabis) are the two most commonly used psychoactive drugs and each appears to have its own unique sexual effects on users. With marijuana use increasing in the United States, along with more liberal state-level policies, it is important to examine and compare sexual effects and sexual risk behavior associated with these drugs in order to inform prevention of HIV, other sexually transmitted infections and unplanned pregnancy.

Methods: We conducted semi-structured interviews with 24 racially and ethnically diverse adults in New York City (mean age=27.4, SD=5.8). To be eligible, subjects must have 1) been between ages 18-35, 2) had sex while high on marijuana in the last 12 months, 3) had sex while not high on marijuana in the last 12 months; and 4) must not have used any other illicit drug in the last 12 months. All subjects self-identified as heterosexual and HIV-negative, and 50% were female.

Results: Thematic analysis yielded various themes. Many subjects described differences between the two drugs with regard to interactions and contexts in use before sex, partner choice, perceived attractiveness of self and others, disinhibition, adverse sexual effects and sexual dysfunction, and dose effects. Differences were also commonly described regarding libido, length and intensity of sex and orgasm, specific sexual behaviors (including risk behavior), and feelings such as regret after sex. Compared to marijuana, alcohol was more likely to be associated with atypical partner choice and lead to regret. Illegality of marijuana sometimes facilitated intimate encounters.

Conclusions: Results can inform prevention efforts regarding specific sexual risks and allow us to design more realistic prevention programs and interventions to guide potential users to make safer choices.

Financial Support: This pilot study was funded by the Center for Drug Use and HIV Research (P30DA011041)

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MODERATORS OF ELECTRONIC SCREENING AND BRIEF INTERVENTION FOR MARIJUANA AMONG STUDENTS IN A HEALTH CENTER: ECHECKUP TO GO BOLSTERS EFFORTS OF THOSE WHO ARE ALREADY TRYING TO CHANGE.

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Aims: Electronic screening and brief intervention has been identified as a potentially low cost strategy to address marijuana use among students presenting to health services, however, there is little known about who will be most responsive to this intervention approach. This secondary analysis examined whether indices of readiness-to-change moderated the influence of a web-based intervention (eCHECKUP TO GO-marijuana) on 3-month outcomes.

Methods: Eligible students were those who reported at least monthly marijuana use on a web-based screening instrument completed in student health and scored < 27 on a subsequent Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) completed at baseline. Participants were randomly assigned to either eCHECKUPTO GO-marijuana or a health information control condition after completing 90-day marijuana frequency and readiness-to-change measures. Negative binomial regression analyses were conducted to examine whether the effect of the intervention on marijuana use at 3-months was moderated by the Action or Problem Recognition subscales, adjusting for baseline frequency of use.

Results: Of 1,080 students screened, 206 reported monthly marijuana use, 133 completed the baseline ASSIST measure which resulted in a final sample of 123 eligible students. Analyses showed a significant Intervention x Action interaction effect. Probing of interaction effects at different levels of the Action subscale indicated that those in the intervention group reported significantly fewer days of use than those in the control condition among those with high scores on the Action subscale only. The Problem Recognition subscale did not moderate the influence of the intervention on outcomes.

Conclusions: These results suggest that eSBI may be effective for bolstering change efforts among students who already have taken steps toward changing their marijuana use.

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PRELIMINARY REPORT ON THE RESIDUAL EFFECTS OF CANNABIS ON YOUNG DRIVERS' PERFORMANCE OF DRIVING-RELATED SKILLS.

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Aims: The effects of cannabis on driving abilities may not be limited to the time period immediately after use. This current study examines the residual effects of cannabis on driving-related skills in young drivers using a high-fidelity driving simulator. We hypothesize that impairment on psychomotor functions and driving abilities will be observed at 24 and 48 hrs following a single dose of cannabis.
Methods: The study is a randomized, double-blind, placebo-controlled mixed design trial, including regular cannabis-using drivers, between the ages of 19-25, who smoke cannabis 1-4 times per week. Eligible participants undergo a practice session followed by 3 testing days (drug administration and 24 and 48 hrs post-drug) consecutively. Measures of simulated driving performance, cognitive and psychomotor functions, and subjective drug effects are collected concurrently with levels of cannabinoids in biological fluids before and after a one-time cannabis administration (approximately 12.5% (active) or <0.01% (placebo) THC). Data analyses conducted focus on comparison of baseline to 24 and 48 hrs post-drug.
Results: 40 participants (60% male, age=22 ± 2) of the target sample of 114 were included in this analysis. Preliminary data suggest that, in the driving only condition, following distance behind a slow moving vehicle increased in the active group 48 hrs after smoking ($p<0.05$). Although not statistically significant, trends were observed in reduction of verbal recall memory, increase in omission and commission errors of a sustained attention task, and increase in total collisions in the driving only scenario at both 24 and 48 hrs post-dose.
Conclusions: Preliminary data suggest that there may be some residual effects of cannabis on driving but findings are not conclusive. An increase in the sample size will help to yield more definitive results.
Financial Support: Funded by the Canadian Institutes of Health Research.

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A NEW REPEATED MEASURES APPROACH OF SEXUAL AND SUBSTANCE USE RISK BEHAVIORS AMONG PATIENTS IN TRANSMITTED DISEASE CLINICS.

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Aims: Although extensive studies have examined sexual and substance use behaviors that put people at risk for sexually transmitted infections (STI) including HIV, most focus on an overall measure of aggregate risk or a few simple and particular sub-types of sexual acts. We explored creating a more sensitive measure to assess how the relative characteristics of the sex acts determine the level of risk in which an individual choses to engage. There were two aims: 1) describe a new approach to examine the count of sexual acts using a fully disaggregated repeated measure design, 2) show how this new measures could be used to evaluate interactions between substance use, STI and other health outcomes.
Methods: We analyzed data from Project Aware, a randomized clinical trial conducted among 5012 patients in 9 STD clinics in the US. Profiles of 16 different types of sexual acts were assessed using the repeated measures approach. Potential interactions of the sex acts—having a primary/non-primary sex partner; partner's HIV status; vaginal/anal; involvement of substance use with sex act; and patterns of substance use were examined. Generalized Estimating Equations (GEE) with negative binomial models were used.
Results: Overall, participants had 2.1 partners and 23.3 condomless sex acts in the last 6 months. 56% reported ever using drugs, 6% were injection drug users, and 16% reported binge drinking in the last 6 months. Participants with problematic drug use (IRR=3.24, $p<0.0001$) and STI (IRR=1.38, $p=0.02$) were more likely to report an increased count of sex acts. Significant interactions were found for substance use with sex and problematic drug use ($p<0.0001$), partner status with STI prevalence ($p=0.04$) and incidence ($p=0.01$).
Conclusions: This approach extends our understanding of how people make choices among sexual risk behaviors. The repeated measures approach may be useful in future research on disaggregated characteristics of sex acts.
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AGE AND GENDER EFFECTS ON SUBJECTIVE DRUG EFFECT OF D-AMPHETAMINE.

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Aims: Prior studies suggest that sex differences in d-amphetamine response are related to hormonal fluctuations that occur during the luteal phase. Thus, studies control for sex differences by running females during the follicular phase when hormones are relatively low. However, studies showing no sex differences under these conditions have relatively small sample sizes. Thus, it is still unclear if there are sex differences – unrelated to luteal phase hormonal fluctuations– in d-amphetamine response. Age may also be an important predictor of subjective drug response, as illicit drug use varies by age. Few experimental studies have investigated the effect of age on drug response. The present study assessed gender and age as predictors of subjective drug response.
Methods: Healthy stimulant-naïve volunteers (n=75 normally cycling women in the follicular phase; n = 29 men) aged 18-35 completed this two-session, double-blind, within-subjects study during which they received a single dose of 20-mg oral *d*-amphetamine or placebo in counterbalanced order. Subjective measures of drug response were completed at repeated intervals before and after drug administration over a 4-hr period and under the curve drug response difference scores (e.g. d-amphetamine – placebo) computed. Partial correlations were run to evaluate relationships between sex, age, and subjective drug response.
Results: After controlling for age, males reported greater subjective responses on the Drug Effects Questionnaire (DEQ) 'Feel Drug', 'Like Drug' and 'Want More' (rs = .20 - .21, ps = .01-.04). After controlling for gender, younger individuals reported greater scores on the DEQ 'Want More' (r = -.26, p = .007).
Conclusions: These results might suggest age and gender differences in abuse liability for young adults who may be prescribed d-amphetamine for clinical conditions (e.g., ADHD or narcolepsy) or start experiment with d-amphetamine recreationally.
Financial Support: TRDRP grant 22FT-0062, NIDA grants R21-DA034768 and K08-DA025041.

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SCHOOL CONTEXT AND MARIJUANA USE AMONG MARYLAND HIGH SCHOOL STUDENTS.

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Aims: We examined: (1) whether the prevalence of marijuana use among high school students varied across schools, and (2) whether school-level risk factors were associated with student marijuana use, after accounting for individual-level covariates.
Methods: Multilevel modeling was used to analyze data from 27,874 high school students participating in the 2013 Maryland Safe and Supportive Schools Climate Survey. Individual-level factors included gender, age, race/ethnicity, alcohol use, tobacco use, fighting, and perceptions of school safety and support. School-level factors included alcohol use prevalence, tobacco use prevalence, urbancity, suspensions, racial composition, fighting prevalence, student/teacher ratio, proportion receiving special education services and free/reduced price meals, and student mobility rate.
Results: 21% of youth reported marijuana use. Variance was greater at the classroom level (σ=0.15, SD=0.39) vs. the school level (σ=0.02, SD=0.13). Students at schools with a higher proportion of racial/ethnic minorities (AOR = 1.01, 95% CI: 1.00, 1.01), mobility rate (AOR = 1.02, 95% CI: 1.00, 1.04), and alcohol use prevalence (AOR = 1.03, 95% CI: 1.01, 1.04) were slightly more likely to report marijuana use. Individual-level factors were more strongly associated with marijuana use than school-level factors, including older age, Black race/ethnicity, alcohol use, tobacco use, and fighting.
Conclusions: Marijuana use is common among high school students, despite differences in school-level factors. Given the continued loosening of marijuana policies, it is likely that adolescent marijuana use will increase. Schools may need to reconsider approaches to drug use prevention education.
Financial Support: This work was supported by the U.S. Department of Education's Safe and Supportive Schools Initiative and a NIDA T32 Training Grant (3T32DA007292-21).

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CANNABIS SMOKING CLUSTERS WITHIN SECONDARY SCHOOLS: RESULTS FROM THE UNITED STATES MONITORING THE FUTURE STUDY 1976-2013.

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Aims: To estimate the degree of clustering, within schools, of cannabis smoking. Clustering within schools should be expected, to the degree that there is social sharing of cannabis experience among student peers, perhaps with 'contagion' processes previously described by the late Richard De Alarcon in his classic epidemiological research on person-to-person spread of heroin injection practices in Great Britain 50 years ago.
Methods: Each year between 1976 and 2013, roughly 16,000 12-graders in ~135 schools completed questionnaires for the Monitoring the Future study (MTF). This project uses Generalized Estimating Equations to derive pairwise odds ratio estimates (PWOR) for evidence of cannabis smoking clusters each year, with PWOR>1 providing evidence of clusters. (Note: Unlike margin-sensitive alternatives, the PWOR does not depend upon prevalence of cannabis smoking.)
Results: Meta-analysis summary estimates and 95% confidence intervals for pre-specified time intervals were as follows: 1976-1986, an interval with >50% cannabis smoking prevalence (PWOR=1.22; 95%CI=1.19,1.24); 1987-1992, an interval when prevalence dropped to the 35% level (PWOR=1.18; 95%CI=1.16,1.21); 1993-2000, an interval when prevalence increased toward 50% (PWOR=1.16; 95%CI=1.13,1.18); 2001-2013, an interval with prevalence ~45% (PWOR=1.16; 95%CI=1.14,1.18).
Conclusions: Tangible within-school clustering of cannabis smoking is seen during all intervals, consistent with models for social sharing of cannabis experience among students. Nonetheless, this study's estimates are more modest than corresponding published PWOR estimates for cannabis and cocaine clusters in US communities, which are on par with PWOR estimates for within-village clustering of childhood diarrheal illness in low-income countries. We now seek more definitive evidence on regional variations and school characteristics that might account for school-level variation in degree of clustering.
Financial Support: Supported by NIDA T32DA021129 (MAP); K05DA015799 (JCA).

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TESTING DIFFERENTIAL IMPLEMENTATION FEASIBILITY AND INITIAL EFFICACY IN A CULTURALLY ADAPTED PARENTING INTERVENTION FOR LATINO/A IMMIGRANTS.

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Aims: The purpose of this presentation is to describe feasibility and initial efficacy findings from a program of cultural adaptation prevention research with Latino immigrants in the U.S.
Methods: This NIMH-funded investigation consisted of an RCT aimed at contrasting the impact of two differentially culturally adapted versions of an efficacious parenting intervention (i.e., PMTO^{R}). Participants were randomly allocated to: (a) culturally adapted PMTO (CA), (b) culturally-enhanced PMTO (CE), or (c) a wait-list control. Measurements were completed at baseline (T1), treatment completion (T2) and 6-month follow up (T3). It was hypothesized that both interventions would be associated with enhanced parenting skills and lower levels of child internalizing and externalizing behaviors.
Results: Data from 169 individual parents confirmed that the hypotheses were partially supported. HLM analyses indicate statistically significant improvements on parenting skills for fathers and mothers at 6-month follow-up in both adapted interventions, when compared to the control condition (e.g., fathers' scores were .0.33 higher than control in the CA and 0.53 higher in the CE intervention ($p<.001$). Mothers in the CE intervention reported lower child withdrawn symptoms (-1.31, $p<.05$) when compared to control. Fathers' reports of child symptomatology were lower than the control on internalizing behaviors (-4.03 for the CA and -6.54 for the CE intervention, $p<.05$) and externalizing behaviors (-5.23 for the CE intervention, $p<.01$).
Conclusions: Present findings highlight the importance of adhering to the core components of evidence-based interventions in order to ensure efficacy. The CE intervention also had an added effect compared to the CA intervention. However, there was a significant gender effect. These findings indicate the importance of considering cultural and gender variables in intervention design.
Financial Support: NIMH R34MH087678, NIDA 1K01DA036747-01, & NIDA R25DA030310 (RPC), K05DA015799 (J.C. Anthony)

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BINGE DRINKERS HAVE GREATER VULNERABILITY TO ENGAGE IN RISKY BEHAVIORS IN TRAFFIC AND DRUG USE.

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Aims: To compare the differences between three groups of drivers: a) those who binge drank in the last year, b) those who drank but did not binge drink in the last year, and c) those drivers who did not drink in the last year - in relation to risky driving behaviors and other drug use.
Methods: A knowledge, attitude and practices (KAP) survey was conducted among drivers from five Brasilian capital cities. Between October 2013 and September 2014, 8,101 face-to-face interviews were conducted (24.4% binge-drinking [BD], 34.2% no binge-drinking [NBD] and 41.4% no drinking [ND]); sampling was done by quotas, according to driver's sex and age. Variables were analyzed through Pearson chi-square test and Mann-Whitney test.
Results: Binge drinkers comprised a greater proportion of drivers who used a cell phone while driving (BD:42.4%; NBD:36.3%; ND:26.6%, $p<0.001$), driving over the posted speed limit (BD:71.5%; NBD:62%; ND:52.4%, $p<0.001$) and were involved in a road traffic crash after drinking in their lifetime (BD: 12.6%; NBD: 5.5% and ND: 4%, $p<0.001$). Regarding use of drugs other than alcohol, binge drinkers comprised a greater proportion of drivers that used cocaine (BD:7.6%; NBD:1.8%; ND:1.5%, $p<0.001$), cannabis (BD:30.3%; NBD:15.8%; ND:6%, $p<0.001$), ecstasy/lsd (BD:3.3%; NBD:0,9%; ND:0.5%, $p<0.001$) and multiple drugs (BD:11.8%; NBD:7.7%; ND:6.5%, $p<0.001$).
Conclusions: Similar to global patterns, we found a greater proportion of binge drinkers engaging in other risky behaviors, which could translate to greater vulnerability to road traffic injury. We suggest additional research be done to understand motives behind drinking and driving behaviors, particularly among binge drinkers, and also evaluate the use of other drugs associated with driving.
Financial Support: Bloomberg Philanthropies.

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INHIBITORY PROCESSING IN RELATION TO AGE OF FIRST SUBSTANCE USE AND AGE OF FIRST REGULAR SUBSTANCE USE.

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Aims: The current project aims to identify that age of first regular substance use (AFRU), compared to age of first substance use (AFU), will significantly predict poor performance on three inhibitory processing subcomponents.
Methods: Analysis consisted of preliminary baseline data of a 6-month longitudinal research study investigating the relationship between inhibitory processing and substance use. 186 young adults (109 females), ranging from 18-25 years old 20.94±1.88), were recruited from three undergraduate universities in South Florida, USA. Participant's inhibition (via Stop Signal, Go-No Go, and Simon task) and drug use history (e.g., alcohol and illicit drugs) were assessed at baseline.
Results: AFRU significantly differed from AFU for the following substances: alcohol consumption [$t(167)= -14.32$, $p<.001$], binge drinking [$t(117)= -6.41$, $p<.001$], marijuana [$t(72)= -7.99$, $p<.001$], and cigarettes [$t(277)= -4.80$, $p<.001$]. Among male users, AFRU for binge drinking significantly predicted poor performance on the Simon task, measured as the number of incongruent response errors, $b= -.426$, $t(81)= -3.26$, $p<.001$. Similar results were found with AFRU for marijuana, $b= -.480$, $t(25)= -2.68$, $p<.01$. Among female users, an opposite effect was found, albeit through the Simon effect. AFRU for alcohol consumption significantly predicted better performance on the Simon task, measured by the Simon effect (i.e., incongruent reaction time minus congruent reaction time), $b= .204$, $t(98)= 2.06$, $p<.05$. Similar results were found with AFRU for binge drinking, $b= .277$, $t(69)= 2.36$, $p<.05$.
Conclusions: In conclusion, AFRU significantly predicted poorer inhibitory performance among male binge drinkers and marijuana users, while AFU did not. These findings, in combination with the significant differences found between AFRU and AFU, suggest that initiation of regular drug use is a better predictor of future inhibitory functioning among males than the age in which the substance was used for the first time.
Financial Support: Gift donation by the Ricardo Puente Family Foundation Inc.

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OPIOID THERAPY FOR CHRONIC NON-CANCER PAIN: DOES TYPOLOGY OF RISK PREDICT ABERRANT BEHAVIOUR?

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Aims: Guidelines have been developed to reduce risk of aberrant opioid medication-related behaviors and iatrogenic dependence when prescribing opioid analgesics for chronic non-cancer pain (CNCP). However, these tools often: 1) rely on cross-sectional/retrospective data, and 2) consider risk factors in isolation. The aims of this study were to identify subgroups of people with CNCP prescribed opioids based on their risk factors for aberrance and determine whether group membership predicts aberrance.
Methods: The Pain and Opioids IN Treatment (POINT) prospective cohort comprises 1,514 people prescribed pharmaceutical opioids for CNCP interviewed at baseline and 3 months. Using baseline data, latent class analysis was run using risk factors for aberrance identified in identified in prescribing guidelines and screening tools.
Results: A 4-class model was selected: 1) *Poor Physical Functioning Group* (27%); 2) *Poor Coping/Physical Functioning Group* (35%); 3) *Younger and Substance Use Problems group* (14%); and 4) *Physical, Coping, Substance Use and Mental Health Problems group* (25%). The latter three groups recorded higher rates of aberrance compared to the *Poor Physical Functioning Group*. After controlling for duration of opioid use and baseline aberrance, the latter two groups were more likely to report dose-escalation, early script renewal, using diverted medication, stock-piling, and unsanctioned dose alteration at 3 months.
Conclusions: Distinctive clusters of people with CNCP were identified based on risk factors for aberrance, with varying associated risk suggesting the type of risk factor and complex interplay between factors may differentially predict medication-related behaviors. These results indicate that potential risk factors should not be equally weighted in the decision to prescribe, with greater emphasis on the interaction of certain risk factors.
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HAND FUNCTION IS ALTERED IN INDIVIDUALS WITH A HISTORY OF ILLICIT STIMULANT USE.

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Aims: Clinical reports of chorea and dystonic reactions in individuals with a history of illicit stimulant use suggest that abnormal movement may be an under-recognized consequence of stimulant use. The aim of this study was to investigate hand movement in adults with a history of illicit stimulant use. We hypothesized that prior use of illicit stimulant drugs is associated with abnormal manipulation of objects.
Methods: The study involved 22 adults (29±8 yrs) with a history of methamphetamine, ecstasy and/or cocaine use and a negative and positive control group comprising 27 non-drug users (25±8 yrs) and 17 cannabis users with no history of stimulant use (22±5 yrs), respectively. Each subject completed screening tests prior to gripping and lifting a light-weight object with their dominant hand. Grip force, lift force, acceleration and EMG activity in the first dorsal interosseus muscle were recorded during three trials.
Results: In trial one, peak grip force was significantly greater in the stimulant group (12.8±3.9 N) than in the control groups (non-drug: 10.3±4.6 N; cannabis: 9.4±2.9 N, $P<0.022$). However, peak grip force did not differ between groups in trials two and three. Peak lift force, peak acceleration and time to peak force did not differ between groups.
Conclusions: The results suggest that individuals with a history of illicit stimulant use overestimate the grip force required to manipulate a novel object but, are able to adapt their grip force in subsequent trials.
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COMPARISON OF DWI PREVALENCES AMONG FATAL, NON-FATAL AND ROADSIDE SAMPLES OF BRAZILIAN DRIVERS.

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Aims: To compare DUI prevalences of fatal and non-fatal victims from traffic accidents, as well as from drivers stopped at roadside checkpoints.
Methods: Sample 1: 609 non-fatal victims from traffic accidents had samples collected in the two emergency hospitals (EH) of Porto Alegre, Brazil. BAC was measured through breathalyzer, and substance use through urine. Sample 2: an electronic database record (ER) of fatal crashes who were autopsied between July 2008 and June 2009 (n= 348). Blood, urine and liver fragments were used to ascertain the level of alcohol and other drugs of abuse. Sample 3): 267 drivers at a roadside checkpoint (RSCP) had their saliva (drugs) and breath (alcohol) collected. Prevalences between samples were compared utilizing the chi-square test.
Results: Mean ages were 32.8 to 42.1. Alcohol had the stronger association with fatal crashes, being significantly more prevalent in the autopsy sample when compared to EH and RSCP (37.1% (31.1-43.5); 8.3% (6.1-11); 3.4% (1.6-6.3) respectively, $p<0.001$). Cocaine prevalence was higher in the HR when compared to RSCP (6.7% (4.5-9.5), 1% (0.1-3.7) respectively, $p=0.006$). THC rates were higher among the HR than RSCP (9.5% (7,0-12,7); 2.6% (0,8-5,9), respectively, $p=0.003$). Screening for benzodiazepines was not different among the three samples.
Conclusions: Alcohol was most involved in traffic accidents with death. Nevertheless, cocaine and THC had high prevalences among fatal victims of traffic accidents. Therefore, EH and RSCP should be appropriate locations for identification and prevention programs for drivers who are involved in accidents because of DUI, considering the high prevalence of reoccurrences of DUI accidents, as well as the high prevalence of cocaine and cannabis use among the sample recruited in EH. Also – ideally databases from these sources should be integrated.
Financial Support: National Secretariat for Drug and Alcohol Policies, Brazil

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PERSONALITY RISK FOR CRACK COCAINE INITIATION.

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Aims: Initiating crack use is associated with other delinquent behaviors. Personality factors, specifically impulsivity and trait displaced aggression, may be important predictors of early crack use.
Methods: 1188 individuals were recruited in Long Beach, CA and administered the Risk Behavior Assessment, the Displaced Aggression Questionnaire (DAQ), and the Barratt Impulsivity Scale.
Results: Those who ever used crack were: Black, have traded sex for drugs, have lower education, lower income, less likely to be in jail recently, had a history of drug treatmen, had ever used powder cocaine and other drugs. In contrast, the model for age of first use of crack (lower age, $R^2 = .1914$)) included sex trading for both drugs and money, history of gonorrhea and Chlamydia, use of powder cocaine, speedball, other opiates, other drugs, lower education, and importantly both motor and attentional impulsivity, and the Angry-Rumination and Displaced Aggression subscales of the DAQ.
Conclusions: Personality characteristics such as impulsivity and trait displaced aggression are important predictors of early crack cocaine use, but not of ever using crack in lifetime.
Financial Support: The project described was supported in part by Award Numbers R01DA030234 from the National Institute on Drug Abuse, P20MD003942 from the National Institute of Minority Health and Health Disparities, and ID10-CSULB-008 from the California HIV Research Program. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse, the National Institute of Minority Health and Health Disparities, the National Institutes of Health, or the California HIV Research Program. NIDA, NIMHD, or CHRP had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

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CIGARETTE CRAVING IS ASSOCIATED WITH BLUNTED REWARD PROCESSING IN NICOTINE-DEPENDENT SMOKERS.

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Aims: Reward processing plays a role in the development and maintenance of addictive disorders. It is well established that chronic drug users simultaneously overvalue drugs of abuse and undervalue natural rewards. However, it remains unclear if there is a link between the desire to use a drug and blunted responsivity to other reinforcers.
Methods: To test this relationship, 30 smokers (Sm) and 25 non-smokers (NS) completed the study. Sm met DSM-IV criteria for current nicotine dependence, reported smoking > 10 cigarettes daily, and had an expired air carbon monoxide of > 10ppm. NS reported smoking <5 cigarettes in their lifetime. Study measures included the probabilistic reward task (PRT) to assess responsivity to monetary reward and the Questionnaire of Smoking Urges-brief (QSU) to measure cigarette craving. Measures were completed 4 hours after the Sm smoked a cigarette. Independent samples t-tests were used to compare PRT performance between groups and correlations between PRT performance and QSU scores were examined within the Sm group.
Results: There were no differences between Sm and NS on reward responsivity during the PRT, indicating that sated Sm and NS have equivalent sensitivity to monetary rewards. Within Sm, reward responsivity was negatively correlated with craving (r= -.397, p= .03, two tailed). There were no relationships between reward responsivity or craving and variables associated with smoking history.
Conclusions: Collectively, these results confirm a relationship between heightened craving and blunted responsivity to a non-drug reinforcer. Further, we have supported the hypothesis that the desire for drugs occurs at the expense of other rewards. Thus, drug cessation treatments may benefit from attending to these processes simultaneously.
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INCENTIVIZING ATTENDANCE TO PROLONGED EXPOSURE IN METHADONE MAINTENANCE.

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Aims: Determine whether voucher incentives increase methadone maintenance treatment patients' attendance to Prolonged Exposure (PE) therapy and are associated with greater improvement in posttraumatic stress disorder (PTSD) severity, treatment retention, and drug use.
Methods: Patients with PTSD were randomized to receive PE therapy alone (PE) or receive voucher incentives (PE+I) to attend the sessions ($30 escalating to $60; max $480). Assessed at baseline, week 6, and week 12; methadone maintenance treatment retention was continuously monitored. Results are presented for the first 41 participants with data through week 12 (PE+I n=20, PE n= 21).
Results: Participants were mostly women (85%) and Caucasian (66%), with a mean age of 35. PE+I participants attended a mean (SD) of 7.4 (4.1) sessions compared to 1.4 (1.6) for PE participants (p<.001). The higher rate of attendance corresponded to more exposure sessions [4.8 (3.4) vs. 0.2 (0.6); p < .001]. PE+I participants showed a trend toward greater improvement on the Clinician-Administered PTSD Scale between Baseline and Week 12 as [26 (21) points vs. 15 (21); p = .14], and were more likely to be retained in methadone maintenance treatment at 6 weeks (95% vs. 71%; p = .09) and 12 weeks (75% vs. 52%; p = .13). PE+I participants also reported no change in drug use while PE participants reported a small increase, although the difference was not significant [-0.1 (6.0) vs. 0.8 (12.9) ; p = .79].
Conclusions: Voucher incentives increase attendance to an otherwise poorly-attended PTSD treatment, including attendance to exposure. In this partial sample, incentives were associated with nonsignificant but greater improvement in PTSD symptoms and better methadone maintenance treatment retention. Drug use did not appear to differ between groups. We expect to present data on the full sample at the meeting.
Financial Support: Research supported by NIH R34DA032689.

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DOES CUE EXPOSURE TREATMENT IMPROVE OUTCOMES IN SMOKING CESSATION TREATMENT? A CONTROLLED TRIAL.

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Aims: Cue exposure techniques (CET) consist of controlled and repeated exposure to cues that provoke craving in order to extinguish the urge to smoke. Previous studies showed that cigarette craving can be reduced through CET. However, very few studies have explored the efficacy of CET for smoking cessation.
This randomized clinical trial explored the effectiveness of a CET procedure when added to a Cognitive Behavioral Treatment (CBT) for smoking cessation among treatment-seeking smokers.
Methods: The sample was made up of 102 treatment-seeking smokers with current DSM-IV nicotine dependence. Participants were randomly assigned to one of two treatment conditions: CBT or CBT+CET. The CBT intervention involved group-based sessions during 6 weeks. In addition to CBT, participants in CBT+CET condition received 5 individual sessions of CET through virtual reality.
Results: Of the patients in the CBT+CET group, 78% attended all treatment sessions compared to 73.1% in the CBT group (p = .56). At the end of the treatment, 56% of the patients in the CBT+CET condition achieved abstinence, versus 51.9% in the CBT condition (p = .68). At one month follow-up, 38% in the CBT+CET condition were abstinent compared to 38.5% in the CBT condition (p = .87). Lastly, 24% of patients treated with CBT+ CET were abstinent at six-month follow-up compared to 25% who received CBT alone (p = .90).
Conclusions: Results showed that neither abstinence levels nor treatment retention rates were better in the CET+CBT compared to CBT alone. The CET procedure does not appear to improve outcomes in a smoking cessation program. Results from this randomized clinical trial suggest that CET is not an effective strategy for smoking cessation.
Financial Support: This work was supported by the Spanish Ministry of Science and Innovation (MICIIN) (Ref. PSI2008-05938/PSIC) and the predoctoral grant from the Spanish Ministry of Economy and Competitiveness (Ref. BES-2012-053988).

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THE ROLE OF THE α7 AND α4β2 NICOTINIC RECEPTORS IN NICOTINE SENSITIZATION AND NEURAL PLASTICITY OF ADOLESCENT RATS NEONATALLY TREATED WITH QUINPIROLE.

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Aims: We have established that neonatal treatment with quinpirole, a dopamine D2/D3 agonist, results in increases of dopamine D2 receptor sensitivity throughout the animal's lifetime and has a number of consistencies with schizophrenia.
Aim 1: Analyze the roles of α7 and α4β2 nicotinic receptors in nicotine sensitization in adolescent male and female rats neonatally treated with quinpirole.
Aim 2: The roles of the α7 and α4β2 nicotinic receptors were analyzed in their effects on Brain-Derived Neurotrophic Factor (BDNF) and mammalian target of rapamycin (mTOR) in rats neonatally treated with quinpirole and sensitized to nicotine.
Methods: Animals were neonatally treated with quinpirole or saline from postnatal days (P)1-21. Beginning on P33, animals were ip injected with nicotine (0.5 mg/kg free base) or saline and tested every second day from P33-49. Approximately 15-30 min before the nicotine or saline injection, animals were ip injected with either the α7 nicotinic receptor (nAChR) antagonist methllycacontine (MLA; 2 or 4 mgkg) or the α4β2 nAChR antagonist dihyro-β (DhβE; 1 or 2.5 mg/kg) erythrodine. Brain tissue was taken 24 h after the last day of testing.
Results: Neonatal quinpirole enhanced nicotine sensitization and DhβE blocked nicotine sensitization regardless of neonatal treatment and was more effective in blocking sensitization in males versus females. MLA failed to block nicotine sensitization. Howeer, MLA blocked the acute hypoactive response to nicotine in males, and the higher dose of MLA reduced sensitization in males. Neonatal quinpirole sensitized the accumbal BDNF response to nicotine, but neonatal quinpirole resulted in a decrease of mTOR in both brain areas.
Conclusions: The α4β2 receptor plays a critical role in adolescent nicotine sensitization. Interstingly, the α7 nAChR appears to be important in the acute response to nicotine and is more important in nicotine sensitization in males. Both nAChRs appear to be important in accumbal BDNF and their roles will be analyzed in the mTOR response.
Financial Support: NIH grant ID 1R15DA034912-01A1

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GENDER DIFFERENCES IN THE LONGITUDINAL DEVELOPMENT OF NORMATIVE BELIEFS FOR TOBACCO, ALCOHOL AND MARIJUANA USE AMONG MIDDLE AND HIGH SCHOOL STUDENTS.

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Aims: Gender specific sequential General Growth Mixture Models for ordinal outcomes will be estimated to characterize developmental patterns in normative beliefs as well as developmental transitions between middle and high school.
Methods: Data comes from the Adolescent Substance Abuse Prevention Study (Sloboda et al., 2009). The focus is on control students who were 12-13 years of age. Of the 4411 students, 43.8% were male and 32.2% had used at least one of the three substances (alcohol, nicotine, marijuana) at baseline. Data were collected using self-administered surveys completed by study participants over the five-year study period at seven time points.
Results: For both genders, three developmental profiles during middle and high school were supported by the data, i.e., lower-, medium- and high levels of normative beliefs about tobacco use (Results for alcohol and marijuana will be presented at the conference). During middle school, females were more likely than males to perceive cigarette use as medium to highly normative (68.7% versus 58.6%). During high school these differences were less pronounced (Female: 74.4%; Male: 79.8%). With respect to transitions, females were more likely than males to remain in the high (82.9% versus 70.7%) and the low profile (72.5% versus 64.2%). In comparison, males were more likely than females to remain in the medium group (80.6% versus 71.5%).
Conclusions: Heterogeneity in normative beliefs might moderate the receptivity to substance use prevention programming and standard evaluations using mediation analysis might have to be augmented by moderated mediation analyses acknowledging the existence of subgroups in longitudinal profiles.
Financial Support: No financial support.

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THE NORTH-SOUTH DIVIDE: SUBSTANCE USE RISK, CARE ENGAGEMENT, AND VIRAL SUPPRESSION AMONG HOSPITALIZED HIV-INFECTED PATIENTS IN 11 U.S. CITIES.

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Aims: To examine differences among hospitalized HIV-infected patients in 11 Southern vs. Non-Southern U.S. cities for substance use risk and HIV treatment, care retention and viral load.
Methods: The study analyzes screening data from the NIDA Clinical Trials Network 0049 study. From July 2012–January 2014, 2291 HIV-infected patients from 11 U.S. hospitals were screened for study inclusion. We used Chi-square tests and multiple logistic models to evaluate differences in substance use and HIV outcomes between participants in 4 Southern (N=1204) vs. 7 Non-Southern (N=1087) sites.
Results: Participants were predominantly Black (74%), male (77%), and earned <$20,000 per year (66%); median age was 44.7. Southern patients were less likely to have used drugs in the last year (p<.001), ever injected drugs (p<.001) or shared needles (p=.013). In adjusted models Southern vs. Non-Southern patients were less likely to report drug or alcohol use (aOR=0.68, 95% CI=0.57-0.82), ever been in HIV care (aOR=0.55, 95% CI=0.43-0.70), ever taken antiretrovirals (aOR=0.72, 95% CI=0.58-0.90) or currently take antiretrovirals (aOR=0.56, 95% CI=0.45-0.69). Southern vs. Non-Southern patients had a median viral load of 61,200 (vs. 9,519; p<.001) and were more likely to be virally unsuppressed (>200 copies/ml; aOR=3.10, 95% CI=2.34-4.11).
Conclusions: There were substantial geographical differences in HIV treatment, care retention and viral suppression despite fewer substance use risks among Southern patients. This suggests that social and structural interventions focused on care linkage and retention are needed to address these disparities. None of the study's Southern States have expanded Medicaid, a decision that will disproportionately affect the poor and uninsured and prevent the full benefits of the Affordable Care Act.
Financial Support: NIDA CTN U10DA013720

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TRAIT, STATE, AND PLACE: THE ROLE OF PERSONALITY AND ENVIRONMENT IN DRUG USE.

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Aims: Addiction is complex with both environmental and inherited causation factors. The environment, particularly neighborhood, and personality traits may contribute to drug use. We sought to determine the influence of trait, state, and place on drug use.
Methods: Participants were administered the NEO Five Factor Inventory to assess 5 personality factors – neuroticism, extraversion, openness, agreeableness, and conscientiousness, and the Addiction Severity Index to assess personal and family drug use history. Environment was assessed with the Neighborhood Inventory for Environmental Typology (NIfETy) a standardized inventory assessing the incidence and prevalence of environmental indicators of physical, social, and drug-related disorder (1 lowest to 8 highest disorder). Analysis was done with Stata 10 and included *t* tests, Pearson X^2, Fisher's exact and multivariate logistic regression.
Results: Participants included 104 current opioid/stimulant users (CDUs) and 88 non drug users (NDUs). The groups differed in age (p<0.001) and gender (p<0.001) but not race (p=0.109). Neuroticism percentiles were higher in the CDUs (p<0.001); and extraversion, openness, agreeableness, and conscientiousness percentiles were lower (all p<0.001). NIfETy scores were higher for CDUs (mean(SD) 5.1(1.5) vs. 3.9(1.8), p<0.001). In the multivariate model predicting drug use status, age (OR 1.10, CI(1.05,1.17), p<0.001), gender (OR 0.22, CI(0.07,0.66), p=0.007), years of cannabis use (OR 1.26, CI(1.12,1.42, p<0.001), nuclear family history of addiction (OR 4.34, CI(1.49,12.6), p=0.007), openness (OR 0.97, CI(0.95, 0.99), p=0.007), agreeableness (OR 0.98, CI(0.96, 1.00), p=0.03), and NIfETy scores (OR 1.53, CI(1.08, 2.16), p=0.017) were significant.
Conclusions: While state, trait, and place determined drug use status, a nuclear family history of addiction and neighborhood physical, social, and drug-related disorder were stronger predictors than personality.
Financial Support: This research was supported by the NIDA-IRP

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TRANSITION FROM FIRST SUBSTANCE USE TO CRACK-COCAINE: PREDICTORS OF FASTER ADDICTION PROGRESSION, AND CLINICAL CHARACTERISTICS IN CRACK-COCAINE ADOLESCENTS USERS.

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Aims: To evaluate predictors to earlier transition from any substance experimentation to crack-cocaine addiction and to describe clinical characteristics of adolescent inpatients who are crack-cocaine addicts.
Methods: Cross-sectional study, with a consecutive sample of 90 adolescents under crack-cocaine detoxification on psychiatric wards. Comorbidities were assessed using K-SADS-PL, and drug use with T-ASI. Comorbidities were compared with a community sample of non-drug addicts (n=77).
Results: Mean age was 15.6, (85.55% boys; 14.44% girls). All of them used another drug before crack-cocaine: 61.4% tobacco [mean age at first use (AFU) = 11.61), 44.3% alcohol (AFU=12.43) and 54.5% cannabis (AFU=12.15). Patients used crack-cocaine 23.2 days in the last month and AFU for crack-cocaine was 13.38 years. The most common comorbidity was Conduct Disorder (81.8%), followed by Oppositional Defiant Disorder (52.3%) and Attention-Deficit/Hyperactivity Disorder (44.3%), all those more prevalent than in controls (for p < 0.005). The T-ASI questionnaire showed severe consequences on most areas. Mean crack-cocaine initiation was at 13.3 years. Using Cox Regression Models, predictors of faster progression of use to crack-cocaine were AFU, for any drug, [HR=1.54 (1.321-1.179; p<.001] and age at admission [HR=.734 (.610-.882; p=.001].
Conclusions: Patients, despite the young age, had problems according do T-ASI in multiple life areas, supporting the idea of treatment by a multidisciplinary heath team for their complete recovery. AFU plays a major role in the progression to crack-cocaine abuse. Prevention programs aimed at delaying any substance initiation could delay progression to harder drug use.
Financial Support: This study was funded by SENAD/BRAZIL.

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COCAINE IMAGES AND ALCOHOL ADMINISTRATION IMPAIR INHIBITORY CONTROL.

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Aims: Cocaine users who relapse after treatment are more likely to report drinking alcohol on the day of relapse than those who remain abstinent. Cocaine users display impaired inhibitory control after viewing cocaine, relative to neutral, images. This study investigated inhibitory control after alcohol administration paired with simultaneous presentation of cocaine images. We hypothesized: 1) cocaine images and alcohol would impair inhibitory control to a greater degree than neutral images and placebo, respectively; 2) impairment following alcohol paired with the presentation of cocaine images would be greater than with neutral images.
Methods: Cocaine users completed the Attentional Bias-Behavioral Activation task with cocaine (n = 25) or neutral (n = 25) images as the go cue. Subjects completed the task during a baseline practice session and following two doses of alcohol (0 and 0.65 g/kg).
Results: At baseline, subjects in the cocaine go condition displayed 13% inhibitory failures, which increased to 16% inhibitory failures following placebo and 19% inhibitory failures following alcohol. At baseline, subjects in the neutral go condition displayed 7% inhibitory failures, which increased to 9% inhibitory failures following both placebo and alcohol.
Conclusions: These results replicate findings showing impaired inhibitory control following cocaine images. The increase in inhibitory failures following alcohol relative to placebo in the cocaine, but not the neutral go condition suggests that alcohol further impairs the ability to inhibit prepotent responses in the presence of cocaine images. Impaired inhibitory control may contribute to increased risk of relapse following alcohol consumption. Thus, cocaine users in treatment, particularly in the early stages, should be advised to avoid use of alcohol. Inhibitory control training could be added to current treatment approaches to improve outcomes and reduce the risk of relapse.
Financial Support: NIDA R01 DA025032, NIDA R01 DA025591 (CRR); NCATS TL1 TR000115 (KRM).

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IMMEDIATE AND PERSISTENT EFFECTS OF SALVINORIN A ON THE KAPPA OPIOID RECEPTOR IN RODENTS, MONITORED *IN VIVO* WITH PET.

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Aims: To investigate opioid receptor function *in vivo* with PET following opioid agonist administration.
Methods: A total of 21 male Sprague-Dawley rats were anesthetized with isoflurane and treated at 1 min or 3 h with either vehicle or the kappa opioid receptor (KOR) agonist Salvinorin A (0.032 – 1.8 mg/kg, i.v.) prior to administration of the KOR selective radiotracer [^{11}C]GR103545. Rats underwent 60 min dynamic PET brain scans following injection of the radiotracer. Images were co-registered to a rat brain atlas and regional binding potential values (BP_{ND}) were calculated using the Logan graphical analysis.
Results: We observed specific binding in regions of highest kappa opioid receptor density in striatum, nucleus accumbens, amygdala, hypothalamus, midbrain, and periaqueductal gray. When Salvinorin A was administered 1 min prior to injection of the radiotracer, [^{11}C]GR103545 BP_{ND} decreased dose-dependently, indicating receptor binding competition. The unique pharmacokinetics of Salvinorin A (half-life ~8 min in nonhuman primates) allowed us to study the drug's residual impact on KOR after the drug was eliminated from the brain. When rats were treated with low doses of Salvinorin A (0.032 mg/kg) at 3 h prior to [^{11}C]GR103545, BP_{ND} was consistent with vehicle treated animals. Elevated doses of Salvinorin A (0.600 mg/kg) administered 3 h prior to the radiotracer resulted in a persistent reduction of [11C]GR103545 BP_{ND} comparable to the 1 min pretreatment at equal dose.
Conclusions: Our results indicate that at low doses, Salvinorin A temporarily decreases BP_{ND} of [^{11}C]GR103545, but at elevated doses causes a persistent reduction in KOR function well after Salvinorin A has been eliminated from the brain.
Financial Support: This research was supported by the NIH (S10RR015728, S10RR026666) and NIH-NIDA postdoctoral fellowship (2T32DA015036).

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PREDICTORS FOR HIGH DOSE CHRONIC OPIOID THERAPY.

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Aims: Chronic opioid therapy (COT) and associated complications are a major health problem. Practitioners must balance treating chronic pain with mitigating risks. Risk mitigation strategies appear to be underutilized. Prior studies have shown COT patient characteristics that categorize individuals at risk for misuse. One identified risk factor for misuse is high dose COT. Therefore, we hypothesize that clinical features exist that separate high dose from low dose COT subjects. The purpose of this study is to identify characteristics that differentiate these cohorts.
Methods: After IRB approval, we identified patients who received at least 3 consecutive, monthly opioid prescriptions during a 90 day period at the Cincinnati VAMC and defined them as COT patients. For each subject, we obtained patient demographic data and all ICD-9 codes. After obtaining the average daily opioid dose in morphine equivalents (ME), subjects were stratified into high dose (>100mg ME/day) and low dose (<100mg ME/day) COT cohorts. We then utilized logistic regression to identify characteristics that differentiated the 2 cohorts.
Results: Complete dosing data was available for 815 subjects. The range of opioid dosing was 0.45 to 983.5 mg ME/day, median dose (IQR) was 28.13 (13.35, 63.33)mg ME/day, and mean dose (SD) was 61.32 (96.57)mg ME/day. Variables assessed in univariate analysis: age, race, sex, tobacco use, BMI, MST, Charlson score, and psychiatric diagnoses. Age 30 to 60yo (OR=1.85; 95%CI 1.27, 2.70; p=0.001) and tobacco use (OR=1.77; 95%CI 1.20, 2.61; p=0.004) were significantly associated with high dose COT. The final multivariate model met adequacy criteria. Predictors significantly associated with high dose COT were female gender (OR=0.45; 95%CI 0.21, 0.98; p=0.045), tobacco use (OR=1.57; 95%CI 1.05, 2.32; p=0.027) and age 30 to 60yo (OR=1.83; 95%CI 1.24, 2.71; p=0.002).
Conclusions: Potential predictors for high dose COT include male gender, tobacco use, and age 30 to 60. Identification of those at risk for dose escalation may allow early referral for primary prevention and harm reduction. This data supports the need for further studies on this important topic.
Financial Support: Research in Addiction Medicine Scholars Program, R25DA033211.

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REPORTING ERRORS ON COMBINED USE OF CAFFEINE AND ALCOHOL QUESTIONS IN A QUALITATIVE QUESTIONNAIRE.

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Aims: The increasing prevalence of combined caffeine and alcohol drink (CAD) consumption is concerning. Those using CADs are more likely to report alcohol dependence, marijuana use, and risk-taking behavior compared to those who report comparable alcohol consumption without caffeine (Arria et al., 2010; Arria et al., 2011). The present exploratory study investigated the extent to which reports of CAD use are accurate.
Methods: Participants (*N*=111) were undergraduate students in a Biology 101 class attending a central Virginia university. Students completed a paper-and-pencil survey with questions examining CAD use and side effects of caffeine. Qualitative responses were coded based on a grounded approach. The present study focused on the three survey items addressing CAD use.
Results: From the total number of responses (excluding N/A), 51.00% included reporting errors. Out of the entire sample, 15.32% of participants reported CADs that listed a non-caffeinated mixer in their response to at least one of the questions. Out of the participants that responded to at least one of the three questions (excluding N/A), 17.89% responded with a non-caffeinated mixer. From the total number of responses, 8.03% contained non-caffeinated mixer errors.
Conclusions: Findings show a high rate of reporting errors, which is a potential barrier to the accurate assessment of CAD use. The high rate of misreporting non-caffeinated mixers could suggest there is a general lack of knowledge about what contains caffeine. Further study is warranted to investigate if these errors significantly impact survey reporting.
Financial Support: Not applicable.

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PREDICTORS OF HIV RISK AMONG EX-OFFENDERS ENTERING SOBER LIVING RECOVERY RESIDENCES FOR DRUG PROBLEMS.

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Aims: 1. Describe demographic characteristics, HIV risk factors, and past 12-month drug and alcohol dependence among probationers and parolees entering sober living houses (SLHs).
2. Assess the extent to which unstable housing prior to entering the SLH and other factors predicts HIV risk.
3. Assess rates of HIV testing over the past 6 months.
Methods: Using data from an ongoing study of SLHs for parolees and probationers in Los Angeles, we examined HIV risk among 108 participants within the first month of entering a SLH. Study instruments included a measure of demographic characteristics, the DSM-IV checklist for alcohol and drug dependence, and the Risk Assessment Battery for HIV. Logistic regression was used to predict HIV risk.
Results: Sample characteristics included 76% male, 39% white, 28% African-American, and 19% Hispanic. Twenty percent self-identified as LGBT. The most common drug dependencies were methamphetamine (58%) and alcohol (37%). HIV risk behaviors during the 6 months prior to the interview were high: 23% reported injection drug use, 17% shared needles, 32% had sex with 2 or more partners and 47% of those having sex never used condoms. However, only 61% had been tested for HIV during the past 6 months. Unstable housing prior to entering the SLH was a significant predictor of injection drug use (OR=3.2, CI=1.3 – 8.1, p<.05), number of sexual partners (OR=2.8, CI= 1.3 – 5.9, p<.01) and trading or buying sex for drugs (OR=2.9, CI= 1.1 – 7.9, p<.05). Other predictors of risk included 6-month measures of alcohol and drug use.
Conclusions: Results highlight the need for increased HIV testing for parolees and probationers entering sober living recovery houses. Findings also document the important role of stable housing for preventing HIV risk among this population. Expanding the availability of SLHs for ex-offenders could play an important role in meeting thee housing needs. Future analyses will examine changes in risk behaviors and HIV testing over 12 months.
Financial Support: DA034973.

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PREDICTORS OF CAFFEINE-WITHDRAWAL HEADACHE IN COLLEGE STUDENTS.

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Aims: The purpose of this study was to examine whether reports of caffeine-withdrawal headache varied by gender, daily caffeine use, alcohol use, and nicotine use in a sample of college freshmen. We hypothesized that gender, daily caffeine use, current alcohol use, and current cigarette use would predict caffeine-withdrawal headache.
Methods: Participants were N=1958 freshmen (age 18 and older) who completed an on-line research survey (Spit for Science*) and reported recent caffeine use. The present study focused on survey demographic items, type(s) of caffeinated beverages consumed (coffee, tea, sodas, energy drinks (e-drinks) and occurrence of caffeine withdrawal symptoms (e.g., headache, fatigue, anxiety, depression, and/or nausea after stopping all caffeine for a day or more). Descriptive statistics were used to characterize caffeine use and occurrence of caffeine withdrawal. Logistic regression analysis was used to assess whether gender, daily caffeine use, and current alcohol and nicotine use predicted participant report of caffeine-withdrawal headache.
Results: One-fifth (20.6%) of current caffeine users reported 1+ symptoms of withdrawal, with headaches most prevalent (15.6%). A test of the full model against a constant-only model was significant, $c^2(4, N=423) = 17.24$, p = .002, indicating that as a set, the predictors reliably distinguished between those with and without caffeine-withdrawal headache. According to Wald tests, only gender ($c^2(1) = 9.21$, p = .002) and nicotine use ($c^2(1) = 7.80$, p = .005) reliably predicted caffeine-withdrawal headache.
Conclusions: Not as predicted, gender and current nicotine use significantly predicted caffeine-withdrawal headache, while current alcohol use and daily caffeine use did not.
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PERCEPTIONS AMONG HEALTHCARE PROFESSIONALS OF PRESCRIPTION DRUG MISUSE.

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Aims: Prescription drug misuse (PDM) is a leading public health and safety concern in North America. Healthcare professionals play a critical role in addressing this issue; however, few studies have examined their part in identifying, preventing or inadvertently enabling PDM among patients. A clearer understanding of healthcare professionals' perceptions of PDM can help to inform the development of educational and prevention initiatives and to improve the capacity to address this public health and safety crisis.
Methods: This study investigated perceptions among 1,063 Canadian healthcare professionals, including physicians, registered nurses and nurse practitioners, pharmacists, and dentists through an anonymous online survey.
Results: Findings revealed that the misuse of prescription opioids and sedatives/tranquilizers was suspected to be more frequent among patients with chronic pain, a substance abuse history or a mental health diagnosis. Healthcare professionals did not feel overly effective in preventing or addressing PDM in patients; they cited a lack of training and lack of access to chronic pain or addiction specialists as barriers to identifying PDM. Communication issues were reported between pharmacists and physicians.
Conclusions: This study raises the concern that Canadian healthcare professionals do not believe they are optimally effective in preventing and addressing PDM and most do not feel supported to do so. Professional colleges and associations are well placed to provide or promote continuing education that addresses the identification of PDM and the potential for screening, brief intervention and referral, as well as guidelines, policies and regulations for risk-management and prescribing practices. Additionally, to enhance the safety of prescribing and dispensing practices and overall patient outcomes, improvements in interdisciplinary communication are needed.
Financial Support: This research was supported by a financial contribution from Alberta Health.

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PRELIMINARY RELIABILITY AND VALIDITY OF AN OPIOID OVERDOSE RISK BEHAVIOR SCALE IN A COMMUNITY-BASED SAMPLE OF RECENT VETERANS.

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Aims: To better understand opioid overdose risks there is a need for a more complete assessment of relevant drug use behaviors. As part of an ongoing cohort study of opioid misuse among recent veterans, we developed an Opioid Risk Behavior Scale (ORBS), based on existing scales for prescription opioid (PO) misuse and other known overdose risks.
Methods: We recruited veterans who reported opioid use in the past month using venue-based and chain referral recruitment. We modified initial items using in-depth interviews with 50 veteran overdose survivors, and 15 pilot assessments. The ORBS consisted of 20 items that elicited the number of days in the past 30 in which the participant engaged in each specified behavior, grouped into 4 subscales. We assessed reliability using Cronbach's alpha. We assessed validity of the total ORBS and that of its four subscales using Pearson's correlations with items from an existing scale for opioid misuse (COMM), and with a scale we developed to assess recent experiences of overdose (EOD).
Results: Data for 169 primarily minority and low-income opioid-using veterans were available for analysis. The 4 subscales: 1) PO Use Not As Prescribed, 2) Using Alternate Methods of PO Ingestion, 3) Mixing Opioids With Other Drugs, and 4) Solitary Opioid Use showed good reliability (alphas ranged from 0.66 to 0.84) and validity (correlations with the COMM and EOD ranged from 0.40 to 0.65). A Cronbach's analysis of the mean subscale scores showed an alpha of 0.87; this total ORBS score was correlated 0.54 with COMM and 0.61 with EOD scores.
Conclusions: The ORBS preliminarily shows strong evidence of reliability and validity. It can be used to better understand behavioral risks associated with overdose in order to better target risk reduction efforts. We plan to study associations of these behaviors and overdose events with changes in physiological, psychological and social/structural factors over the 2-year course of the study.
Financial Support: R01DA036754

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AMBULATORY FIELD MEASUREMENT OF HEART RATE IN OPIOID/COCAINE USERS.

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Aims: Monitoring physiological changes in the field could improve our understanding of the antecedents, patterns, and consequences of drug use and become the basis for a mobile intervention that detects and intervenes in behaviorally risky situations.
Methods: Polydrug users (N=40) in opioid agonist maintenance wore AutoSense, a suite of biosensors that wirelessly transmits data to a smartphone, for up to 4 weeks during waking hours. Participants self-reported craving, stress, mood, and activities on electronic diaries at 3 randomly prompted (RP) times/day as they went about their daily lives. We compared ambulatory heart rate (HR) across types of self-report using multilevel modeling (SAS Proc Mixed).
Results: Usable ECG data were obtained for 11.3 (SD 0.9) hrs/d out of the mean 13.2 hrs/day that sensors were worn. HR (mean bpm; SEM) was significantly higher when participants reported craving heroin (85.0; 0.2) compared when they reported not craving (82.0; 0.1) ($F(1,16)=230.9$, $p<.0001$). HR was also significantly higher when participants reported craving cocaine (86.4; 0.3) compared when they reported not craving (82.2; 0.1) ($F(1,14)=157.2$, $p<.0001$). HR was significantly ($p<.05$) lower around RPs in which participants reported feeling relaxed, feeling happy, or doing sedentary activities such as watching TV. HR was significantly higher around RPs in which participants reported feeling stressed, being hassled and physical activity, e.g. walking.
Conclusions: Our study shows that high-yield, high-quality heart rate data can be obtained from heroin and cocaine users in their natural environment as they go about their daily lives, and that the resultant data robustly reflect mental and behavioral events of interest.
Financial Support: Supported by NIDA Intramural Research Program, NSF grants CNS-0910878, CNS-1212901, IIS-1231754, and NIH Grants U01DA023812 and R01DA035502.

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DYNAMIC CAUSAL MODELING IN HUMANS OFFERS A NOVEL APPROACH TO DELINEATE PREFRONTAL-STRIATAL SEROTONERGIC DRIVERS OF IMPULSIVITY IN RATS.

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Aims: The prefrontal-striatal network is a major driver of impulsivity and altered neurotransmission in this circuit may underlie heightened impulsivity in cocaine use disorder (CUD). Serotonin transmission through 5-HT_{2A} receptors (5-HT_{2A}R) and 5-HT_{2C}R governs prefrontal-striatal networks. This study employed fMRI based DCM to investigate prefrontal-striatal effective connectivity underlying impulsivity in CUD. We also aim to translate our human findings to rodent models to analyze the modulatory role of the 5-HT system within the prefrontal-striatal network that drives impulsivity.
Methods: Ten control and 13 CUD subjects underwent fMRI while performing Go/NoGo tasks with Easy and Hard NoGo difficulty. Connectivity was determined via DCM analyses.
Results: There were no differences in overall performance ($p=0.9$) or modulation effects on Easy NoGo ($p=0.4$) between groups. Hard NoGo influenced right dorso- and ventrolateral prefrontal connectivity to left caudate in controls but left anterior cingulate connectivity to left caudate in CUD subjects ($p<0.05$).
Conclusions: CUD subjects utilize different connectivity during impulsive responding to perform similarly to controls. Altered top-down control may be mediated by impaired 5-HT transmission at 5-HT_{2A}R and 5-HT_{2C}R. Ongoing studies are testing if 5-HT_{2A}R:5-HT_{2C}R imbalance in the prefrontal-striatal circuit shifts effective connectivity governing impulsivity in CUD.
Financial Support: DA020087, DA033935, DA034131, DA033374

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BRAIN DEFAULT MODE NETWORK FUNCTIONAL CONNECTIVITY IN POLYSUBSTANCE USING EMERGING ADULTS DURING OPIOID DEPENDENCE TREATMENT.

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Aims: The default mode network (DMN) is an interconnected set of brain regions typically active at rest and during low cognitive demand conditions. Heroin-dependent adults show DMN connectivity abnormalities correlated with lifetime heroin use. Functional organization abnormalities are especially pertinent to younger substance-using persons who have ongoing neurodevelopment, higher risk of relapse and lower treatment completion rates. This study examined brain connectivity indices and associations with acute drug use in ten emerging adult patients (ages 18-27) in partial relapse prevention treatment for opioid dependence.
Methods: Patients who met DSM-IV criteria for current opioid dependence and used opiates in the past month received resting-state functional magnetic resonance imaging (fMRI) scans within 24 hours of admission. Potential participants were not excluded for other drug use or dependence; in most cases this included marihuana, sedatives and/or nicotine. Seven participants also met dependence criteria for at least one other substance. Imaging data were analyzed using an independent components analysis followed by dual regression to identify subject-specific spatial maps of the DMN. A non-parametric permutation testing method was used to correlate DMN with total days of any substance use in the past 30 days.
Results: Increased drug use over the past 30 days was correlated with *less* connectivity between the DMN and insula, dorsal striatum and post central gyrus (cluster corrected $Z = 2.3$, $p < 0.05$, 5,000 permutations).
Conclusions: These findings provide evidence that polysubstance use is associated with functional adaptations in the DMN of emerging adults seeking treatment for opiate dependence. Further research is needed to delineate if these connectivity changes are related to recent detoxification.
Financial Support: T32 DA015036, K23 DA027045, K01 DA029645

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CURRENT DRUG SCHEDULING REVIEWS OF SYNTHETIC CATHINONES BY THE U.S. DRUG ENFORCEMENT ADMINISTRATION.

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Aims: In accordance with the Controlled Substances Act (CSA), DEA collects and reviews scientific, medical and other data for substances with abuse potential to evaluate them for possible control under the CSA. Numerous synthetic cathinones have become popular among drug abusers in recent years. The administrative process for scheduling is currently ongoing for 10 synthetic cathinones.
Results: On March 7, 2014, DEA emergency scheduled 10 synthetic cathinones into schedule I under the CSA to avoid an imminent hazard to the public safety (79 FR 12938). The 10 synthetic cathinones include(1) 4-methyl-N-ethylcathinone ("4-MEC"); (2) 4-methyl-alpha-pyrrolidinopropiophenone ("4-MePPP"); (3) alpha-pyrrolidinopentiophenone ("α-PVP"); (4) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one ("butylone"); (5) 2-(methylamino)-1-phenylpentan-1-one ("pentedrone"); (6) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one ("pentylone"); (7) 4-fluoro-N-methylcathinone ("4-FMC"); (8) 3-fluoro-N-methylcathinone ("3-FMC"); (9) 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one ("naphyrone"); and (10) alpha-pyrrolidinobutiophenone ("α-PBP"). These synthetic cathinones have been identified in products that have been falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," "plant food or fertilizer," "insect repellants," or "bath salts" and are being abused for their psychoactive properties.
Conclusions: DEA continues to monitor and gather information on these 10 synthetic cathinones and other synthetic cathinones for possible scheduling under the CSA. To do this, DEA collects information on the pharmacology, toxicology, and abuse of these substances and evaluates these substances for possible federal control action.
Financial Support: Drug Enforcement Administration

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MODELING ANHEDONIA IN SERINE RACEMASE KNOCKOUT MICE: IMPLICATIONS FOR CO-MORBID SUBSTANCE ABUSE AND SCHIZOPHRENIA.

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Aims: Substance abuse shares substantial co-morbidity with schizophrenia, possibly due to a shared neural substrate, N-methyl-D-aspartate receptor (NMDAR) dysfunction. A common symptom in these disorders is anhedonia, an impaired capacity to experience pleasure. Our laboratory has developed a transgenic mouse line lacking the synthetic enzyme serine racemase (SR), which produces D-serine, an obligatory NMDAR co-agonist in the forebrain. Null mutants (SR-/-) exhibit NMDAR hypofunction. An intracranial self-stimulation (ICSS) paradigm was implemented to investigate the effect of NMDAR hypofunction on reward processing.
Methods: Monopolar electrodes were implanted into the brains of SR-/- and wildtype (WT) mice in the right medial forebrain bundle (MFB) at the level of the lateral hypothalamus. Following recovery, mice began training in operant chambers where responses were rewarded with electrical pulses. Current was adjusted until responding reached a rate of 1 reward per second. Then, stimulation threshold and maximum response rate were calculated for each animal from responses made across 15 descending frequencies. The ability of cocaine to facilitate responding for brain stimulation was tested using a within-subject design. Each animal was tested with 3 doses of cocaine (3, 6, and 12 mg/kg i.p.) and saline.
Results: As expected, WT mice exhibited a dose-dependent leftward shift in stimulation threshold in response to cocaine (i.e., cocaine facilitated responding for brain stimulation at frequencies that were previously too low to maintain responding). However, cocaine treatment had no effect on maximum response rate. Interestingly, in SR-/- mice cocaine had no effect on stimulation threshold. Maximum response rate also was not affected.
Conclusions: These results suggest that glutamatergic dysfunction, specifically, NMDAR hypofunction, may be a common neural substrate underlying substance abuse and schizophrenia, and highlight NMDAR modulation as a possible avenue of treatment for these co-morbid disorders.
Financial Support: This research was supported by DA015036, DA035427, and MH51290.

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STRENGTH FROM RECOVERY: FORMER DRUG-DEPENDENT INDIVIDUALS DISCOUNT THE FUTURE LESS THAN CURRENT USERS AND CONTROLS.

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Aims: Delay discounting is a measure of future valuation previously implicated as a behavioral marker of addiction. This behavioral marker can identify current from former drug-dependent individuals, where former drug-dependent individuals are likely to discount the future less than current drug-dependent people. The addiction literature suggests that ex-smokers have similar discounting rates as controls and lower discounting rates than current smokers. The aim of the current study was to evaluate differences in delay discounting between current poly-drug dependent individuals, former poly-dependent individuals, and controls to ascertain evidence that delay discounting can function as a behavioral marker distinguishing former drug-dependent individuals from community controls.
Methods: 84 participants completed a monetary delay discounting task as part of a larger study. Of those participants, 56 were dependent on alcohol, stimulants, or both and 28 were controls. 52 participants in recovery from alcohol, stimulants, or both completed an online delay discounting task as part of quitandrecovery.org, an international website devoted to understanding addiction recovery.
Results: A one-way ANOVA revealed a significant main effect of group F (2, 133) = 157.6, $p < 0.0001$. Tukey post-hoc comparisons showed statistically significant differences between all groups where former poly-drug dependent participants (mean=-9.14, SD=1.937) discounted the future less than community controls (mean=-5.100, SD=2.051) and current poly-dependent individuals (mean=-2.63, SD=1.814).
Conclusions: This is the first report using a psychophysical titration delay discounting task indicating that former poly-drug dependent individuals discount less than controls and suggests that delay discounting may be sensitive enough to identify former drug-dependent individuals from controls.
Financial Support: R01DA034755

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ABUSE LIABILITY OF CONTROLLED-RELEASE OXYCODONE FORMULATIONS.

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Aims: Controlled-release opioid formulations may have differential abuse liability profiles related to rates of drug delivery. The aim of this study was to examine the abuse liability of a single 40mg intact oral dose of 3 controlled release oxycodone formulations (Apo-Oxycodone CR®, OxyNEO®, and the original OxyContin®) by performing pharmacodynamic and pharmacokinetic analyses.
Methods: This was a single-dose, double-blind, placebo-controlled, randomized, crossover, abuse liability study conducted in healthy, non-dependent, recreational opioid users. Participants received 40mg single doses of the oxycodone formulations and placebo. Assessments were conducted at baseline, and 11 times over 8 hours post drug intake. Assessments included the primary outcomes of 'drug high' and 'drug liking' VAS, as well as additional VAS measures, the Addiction Research Centre Inventory, the Profile of Mood States, the Digit Symbol Substitution Test, pupillometry and plasma oxycodone concentrations. Group differences were evaluated with one-way ANOVAs, with differences examined with Bonferroni adjustment for multiple comparisons.
Results: Eleven subjects participated (8 male/3 female; mean age 38.3±7.9 years). OxyContin® was not available for 6 subjects due to product expiry. Preliminary analysis indicates significant overall differences for mean peak 'drug high' ($p<0.001$), 'drug liking' ($p=0.006$), 'drug good effect' ($p=0.001$), and pupil constriction ($p<0.001$). Post-hoc analysis primarily demonstrated differences between placebo and the oxycodone controlled-release products, with no significant differences within the active formulations.
Conclusions: Further analyses are pending, including pharmacokinetic outcomes. Preliminary results suggest that the 3 different controlled-released oxycodone formulations evaluated have similar abuse liability profiles when taken intact orally.
Financial Support: Internal funding.

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GEOGRAPHIC DISTANCE TO NATIONWIDE PROFESSIONAL TREATMENT FOR ALCOHOL USE DISORDER IN MEXICO.

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Aims: Compared to other countries, Mexico presents a high burden of disease attributed to alcohol use. Approximately 75% of people with AUD in Mexico never receive treatment. To appropriately allocate the limited resources available for AUD, it is important to identify the distribution of AUD burden across the country. The aim is to determine distance to formal treatment (i.e. public and private hospitals and addiction centers) for people with alcohol use disorders (AUD) across Mexico.
Methods: A geospatial euclidean distance analysis of the 2008 National Addictions Survey state-level prevalence of AUD, 2010 census state-level population density, and 2010 census geographic location of all registered professional AUD treatment (i.e. public and private hospitals, clinics, and rehabilitation centers) was performed to determine the distance to any professional treatment for AUD.
Results: Assuming normal distribution of AUD by state, there were 8,635 people (1.0%) in need of treatment at a 10 km distance from any professional AUD treatment, 23,536 (2.7%) between 10-20 km, 93,698 (10.7%) between 20-50 km, 236,917 (26.9%) 50-100 km, 344,365 (39.2%) 100-200 km, and 170,754 (19.5%) >200 km. People closest to treatment are located in the central part of the country.
Conclusions: Most people with AUD (58.7%) would be required to travel a distance >100 km to get treatment. To travel this distance, people will not only need to be determined to reach treatment, but may need considerably more social and financial support than others at a closer distance to services. Primary care clinics distributed throughout the country may be an opportunity to reach that population.
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ADOLESCENT C57BL/6J MICE SELF-ADMINISTER MORE OXYCODONE THAN ADULT MICE IN AN EXTENDED-ACCESS PARADIGM (4HRS).

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Aims: Prescription opioid abuse among adolescents is a major public health issue in the United States. The goal of this study is to compare the behavior of adolescent with adult C57BL/6J mice during extended access self-administration of oxycodone.
Methods: Surgeries were performed on groups of adolescent (4 weeks old, n=6) and adult (11 weeks old, n=6) mice to implant catheters into their jugular veins. After recovering from their surgeries, mice were placed in self-administration chambers for 4 hrs/day for 14 consecutive days. The mice were either allowed to self-administer oxycodone (0.25mg/kg/infusion) or served as yoked-saline controls.
Results: Over the course of the 14 daily sessions, adolescent mice showed a greater increase in responses at the active hole and a more robust escalation in the amount of oxycodone self-administered than did adult mice. From the 6th through the 14th self-administration session, adolescent mice self-administered significantly more oxycodone than adult mice did.
Conclusions: This study shows the feasibility of using an extended access oxycodone self-administration paradigm in adolescent as well as adult mice. Moreover, it demonstrates that adolescent mice, when given longer access to oxycodone, self-administer more oxycodone than adult mice do. This may result in specific and greater neurobiological adaptation in the adolescents.
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BEHAVIORAL LABORATORY MEASURES OF IMPULSIVITY AND DECISION-MAKING IN CIGARETTE SMOKERS.

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Aims: Impulsivity and decision-making are known to be impaired in different substance using populations. However, few studies have examined measures of impulsivity and decision-making in cigarette smokers. The purpose of this study was to compare cigarette smokers and control subjects on a measure of decision-making (the Iowa Gambling Task/ IGT), a measure of response inhibition (the immediate memory task/ IMT), and a measure of self-report impulsivity (the Barratt Impulsiveness Scale/ BIS-11) and to examine the interrelationship among these measures.
Methods: Regular cigarette smokers (n=10) and non-smoking control subjects (n=27) were recruited from a similar demographic setting. Information on participants' smoking, drug use history and demographics was collected at intake. Both groups completed the computerized behavioral tasks IGT, IMT and the BIS -11 and were compared on their performance.
Results: Cigarette smokers displayed higher commission errors, indicative of poor impulse control on the IMT, and lower total scores on the IGT compared to controls. However they did not differ from controls on the BIS-11 total scores or sub-scales. Furthermore, among the cigarette smokers, IMT commission errors correlated with net scores on IGT during the second, third, fourth and fifth blocks and between IGT total net score.
Conclusions: Consistent with previous studies, these preliminary results suggest that cigarette smokers are more impulsive. In addition, this study found that smokers make poor decisions in laboratory behavioral tasks. Furthermore, there was a correlation between decision making as measured by the IGT and impulsivity measured on the IMT. However, given the small sample size of the cigarette smokers these data should be interpreted cautiously.
Financial Support: Supported by NIDA Grants P50DA009262, R01 DA034131, U54 DA038999 and P50 DA033935

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CONTENT ANALYSIS OF CANNABIS SMARTPHONE APPLICATIONS.

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Aims: With a global audience expected to total 1.75 billion in 2014, Smartphone technology is pervasive and widely used to obtain information about drugs such as cannabis. Previous reviews of Smartphone applications ("apps") about health behavior highlight the wide variety of resources available to users without clear scientific or theoretical basis. There is a need to understand more about the available resources for those searching for Smartphone cannabis apps. We investigated 60 cannabis apps for iPhone and Android phones as of November 26, 2014.
Methods: iTunes and GooglePlay app stores were searched using the terms "cannabis" and "marijuana." Two trained coders classified the top 20 apps for each term and each store, using a coding guide. Apps were examined for presence of 8 categories, 18 subcategories, and features.
Results: Total apps available for each search term were 124 (cannabis) and 218 (marijuana) in iTunes, and 250 of each cannabis and marijuana in GooglePlay. The Top 20 apps in each category were coded for a total of 60 independent apps (31 iTunes, 29 GooglePlay). On iTunes, the most popular apps provided cannabis strain classifications (52%), street names for cannabis (39%), or general facts about cannabis (39%). Only one app (3%) provided any information or resources related to cannabis abuse. Most apps were free (74%), all were rated "17+," and average rating was 4.0/5. On GooglePlay, the most popular app types offered games (28%), phone utilities (e.g., wallpaper, clock; 21%) and cannabis recipes (21%); one app (3%) addressed addiction. Most apps were free (93%), rated "high maturity" (79%), and average rating was 4.1/5.
Conclusions: The top cannabis apps for iPhone tend to provide information or education, while top Android apps tend to be primarily entertaining. Apps addressing addiction or cessation were underrepresented in the most popular cannabis Smartphone applications.
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DOES ELECTRONIC CIGARETTE LIQUID NICOTINE CONCENTRATION AND USER EXPERIENCE INFLUENCE PLASMA NICOTINE CONCENTRATION?

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Aims: Electronic cigarettes (ECIGs) heat a nicotine-containing liquid and the resulting aerosol is inhaled by the user. The nicotine concentration of the liquid and experience of the user may influence plasma nicotine concentration. The purposes of this clinical lab study were to examine the relationship of ECIG liquid nicotine concentration on user nicotine exposure following ECIG use and to compare the plasma nicotine concentration and ECIG use behavior (puff topography) of ECIG-experienced users and ECIG-naïve cigarette smokers.
Methods: Eleven ECIG-experienced and 13 ECIG-naïve cigarette smokers used an "eGO" ECIG battery (3.3 V;1000 mAh) attached to a dual-coil (1.5 ohm), 510-cartridge during 4 independent, double-blind sessions that differed by liquid nicotine concentration (0, 8, 18, or 36 mg/ml). Within each session, puff topography was recorded in 2, 10-puff ECIG-use bouts (30 sec interpuff interval). Blood was sampled periodically for later analysis.
Results: Plasma nicotine concentration depended on liquid nicotine content [concentration*time F (27,513)=6.2; p<0.01]. *Post hoc* testing revealed that plasma nicotine concentration increased significantly after each bout with 8, 18, or 36 mg/ml liquid and also differed by user experience at the 8 and 36 mg/ml concentrations. ECIG-experienced users took longer and larger puffs [Fs (1,22)>6.6; ps<0.05].
Conclusions: ECIGs can deliver nicotine reliably and that delivery is in part dependent on liquid nicotine concentration. Also, ECIG-experienced users are exposed to more nicotine in some cases, perhaps because they take longer and larger puffs. A comprehensive understanding of that factors that influence ECIG nicotine delivery (device characteristics, liquid nicotine concentration, user behavior) is vital to future, empirically-based, ECIG regulation.
Financial Support: P50DA036105

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ASSESSING POTENTIAL ABUSE AND MISUSE OF TESTOSTERONE AND OTHER ANABOLIC STEROIDS AMONG MIDDLE-AGED AND OLDER MEN PRESCRIBED STEROIDS.

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Aims: Products containing testosterone and its esters are classified as Schedule III (CIII) drugs under the Controlled Substances Act (CSA). Anabolic steroids, however, have an abuse profile that is different than other drug groups, such as opioids and stimulants. Studies show that anabolic steroids are abused mainly for their ability to increase muscle mass and strength and decrease fatigue, more for their physiological effects, as opposed to behavioral effects. Opioids and stimulants typically are abused for their psychoactive effects such as for euphoria and stimulation. Still, the abuse of steroids, including testosterone is reported by athletes as well as non-athletic users. With the recent increase in reported use of testosterone by middle aged and older men for low energy and sexual interest, the risk of abuse and misuse of testosterone is a heightened safety concern for this population. From an abuse prospective, dose and duration of testosterone use may be factors that should be considered in relation to potential risk of dependence development.
Conclusions: The dose and the duration of testosterone use may be associated with adverse effects related to testosterone abuse or misuse in different populations. These include possible increased risk of cardiovascular-related events and include possible withdrawal symptoms once testosterone use is discontinued. These factors and others are considered and presented.
Financial Support: N/A

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USE PATTERNS, PERCEPTIONS OF RELATIVE HARM, AND GENDER EFFECTS IN DUAL USERS OF ELECTRONIC AND TOBACCO CIGARETTES.

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Aims: Awareness and use of e-cigarettes is increasing. Concerns regarding potential positive (e.g., smoking reduction/cessation) and negative (e.g., delay of cessation) public health consequences may be informed by studying dual users of e-cigarettes and tobacco cigarettes.
Methods: An online survey assessed demographics, product use patterns, and beliefs about product benefits and harms among male (n=184) and female (n=166) dual users. Descriptive statistics described survey results; *t-tests*/*chi-square* analyses evaluated gender effects.
Results: Females used tobacco cigarettes for more years and more frequently than males, however both groups showed similar use patterns and harm perceptions of tobacco cigarettes and e-cigarettes. Participants reported a 30% reduction in tobacco cigarette smoking since using e-cigarettes. Compared to tobacco cigarettes, e-cigarettes were used less often and associated with lower dependence. Reported primary reasons for e-cigarette use were harm reduction and smoking cessation. E-cigarette use was reported as more likely in settings with smoking restrictions and when others' health could be adversely affected. Participants reported using tobacco cigarettes more often than e-cigarettes in hedonic situations, outdoors, or when stressed. Participants were twice as likely to report wanting to quit tobacco cigarettes than e-cigarettes and intended to quit tobacco cigarettes sooner. Tobacco cigarettes were described as more harmful and addictive, but also more enjoyable, than e-cigarettes.
Conclusions: Participants provided evidence consistent with both positive and negative public health consequences of e-cigarettes, highlighting the need for experimental laboratory research and clinical trials. E-cigarettes were associated with a major reduction in smoking. Use patterns and reasons were generally insensitive to gender. Policies should consider potential public health benefits of e-cigarettes, in addition to potential harms.
Financial Support: T32DA07209 R01DA032363

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IMPACT OF AN EXERCISE INTERVENTION ON METHAMPHETAMINE USE OUTCOMES POST RESIDENTIAL TREATMENT CARE.

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Aims: We examined the efficacy of an 8-week exercise intervention on post-discharge substance use outcomes among methamphetamine (MA) dependent individuals enrolled in residential treatment. We hypothesized that MA dependent clients exposed to a structured exercise program would have improved MA use outcomes than those in a health education control and that there would be subgroup differences in outcomes by select characteristics.
Methods: A total of 135 MA-dependent individuals newly enrolled in residential care were randomly assigned to an 8-week thrice weekly exercise intervention or to an 8-week thrice weekly health education control condition. Interview, self-reported data and urine samples were collected at 1-month and 3-months post-residential care.
Results: While fewer exercise group participants returned to MA use at 1-month (25% vs 17%) and 3-month follow-ups (36% vs 29%), respectively, these differences were not statistically significant. We also found subgroup differences in MA use outcomes at follow-ups by MA use severity at treatment admission, session attendance, and continued exercise post-treatment.
Conclusions: Results support the utility of incorporating a structured exercise program for various sub-groups of MA-dependent individuals, including those who use MA for less than 18 days at treatment admission, those who have better treatment compliance (session adherence), and those who continue to exercise post-treatment.
Financial Support: This study is supported by R01 DA027633 from the National Institute on Drug Abuse (NIDA).

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THEORY-BASED TEXT-MESSAGING TO REDUCE METH AND SEX RISKS AMONG MSM.

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Aims: Meth use among MSM is deeply integrated into socio-sexual networks and digital spaces such as cell phone apps, websites, and digital chat rooms. In the West Coast, meth use has been identified as a major force in the transmission of HIV among MSM. A text-messaging intervention was designed to capitalize on the use of digital spaces and to intervene when meth-using MSM are most likely to engage in high-risk behaviors. It was hypothesized that text messages transmitted by Peer Health Educators (PHEs; rather than by automation or a control condition) would produce significantly greater reductions in meth use and sex risks.
Methods: 285 out-of-treatment, meth-using MSM will be enrolled in an 8-week, gay-specific, theory-based text-messaging intervention designed to decrease meth use and HIV sex risks. Participants are randomized into 1 of 3 conditions: (1) 5 gay-specific, theory-based text messages sent by automation each day and unlimited messages interactively transmitted by PHEs plus a weekly text-message assessment; (2) 5 automated text messages but no interaction with PHEs plus a weekly text-message assessment; (3) a weekly text assessment-only control. 616 pre-written gay-specific text messages were developed according to the theoretical principles of Social Support Theory, Social Cognitive Theory, or Health Belief Model. Enrollment began in March 2014 and, as of November 2014, 124 participants had enrolled and 84 had completed an 8-week follow-up assessment at intervention completion.
Results: Most participants identified as gay (82%), Black (30%) or Hispanic (30%), and half (52%) were HIV positive; mean age was 41.4 (SD = 10.5). From baseline to 8-week follow-up, participants reported reductions in average days of meth use (10.1 vs. 8.0), number of sex partners (11.1 vs. 6.1), episodes of meth use with sex (6.2 vs. 4.1), and unprotected anal intercourse (15.5 vs. 6.4) in the past 30 days.
Conclusions: Preliminary results are promising; full enrollment and distal follow-up will determine differential and sustained effects and cost effectiveness, by condition.
Financial Support: NIDA #R01DA035092

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EVALUATING THE DOCUMENTATION OF RISKY SUBSTANCE USE IN FEDERALLY QUALIFIED HEALTH CENTERS.

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Aims: To evaluate the presence and reliability of documentation of substance use among risky drug using primary care patients in community health center medical records and ascertain whether Quit Using Drugs Intervention Trial (QUIT) affected reporting in the medical record of screening, diagnosis, counseling, clinician treatment, or health educator counseling for risky substance use among primary care patients.
Methods: Single-blind randomized controlled trial of primary care clinic patients of five FQHCs in Los Angeles with 3-month follow-up. Eligible adult patients who screened positive for risky drug use were invited to participate in the QUIT trial. Based on clinic chart availability and participant consent, 484 (94.5%) charts were eligible for review. A retrospective chart review of 447 participants from the QUIT was performed using a standardized abstraction form to assess for documentation of substance use six months prior to enrollment. The primary measures were documentation in the medical record of substance use screening, diagnosis, or treatment.
Results: Review of participants' charts revealed: 10.3% of visits included no mention of alcohol screening. Per documentation, 5% of those with documented use of alcohol received counseling and recommendations to reduce use. Although all patients had risky drug use, 20.6% of visit notes included no mention of drug use or drug use screening. Of charts that documented drug use, 13.9% recorded any counseling or recommendations to reduce/quit usage.
Conclusions: FQHC rates of documentation regarding substance use screening and counseling are not ideal among risky drug using patients. Via further data collection and analysis, we hope to evaluate the effect of race, gender, number of health conditions, patient's clinician, study clinic, and enrollment in QUIT on documentation and provision of substance use care.
Financial Support: NIDA DA 022445, NIDA 3P30DA027828-02S1 and -02S2

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MEDIATIONAL PATHWAYS AMONG ATTENTIONAL IMPULSIVITY, HEROIN USE CONSEQUENCES, MOOD, AND STRESS LEVEL.

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Aims: This study aimed to examine whether lifetime heroin-use consequences mediate the relationship between trait impulsiveness and 1) current depression symptoms, 2) current stress levels, and 3) current negative perception of stressors.
Methods: Three mediation tests were conducted to assess the causal influence of lifetime consequences of heroin use (Drug History and Use Questionnaire) on the relationship between trait impulsiveness (Barratt Impulsiveness Scale-11) and the outcomes of depression (Beck Depression Inventory-II), stress (Depression Anxiety Stress scale - Stress subscale), and perception of daily stressors (Hassles and Uplifts scale) among regular heroin users (*N*=126). Each model included attentional impulsiveness as the predictor variable, heroin use consequences as the mediating variable, and depression, stress levels, and perception of stressors as three separate outcome variables (Baron & Kenny, 1986).
Results: Attentional impulsivity was positively associated with lifetime number of heroin use consequences (r=.21), depression symptoms (r=.51), experienced stress level (r=.52), and perceived negative impact of stressors (r=.25), all Ps<.01. Non-planning and motor impulsivity subscales were not significantly related to lifetime heroin use consequences and were excluded from analyses. As hypothesized, lifetime adverse heroin-use consequences partially mediated relationships between attentional impulsivity and (1) current depression symptoms (R^2=.28), (2) levels of stress (R^2=.30), and (3) perceived negative impact of stressors (R^2=.10).
Conclusions: Heroin-related consequences function as a pathway between trait impulsiveness and current depression symptoms, levels of stress, and how negatively this stress is perceived.
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INCENTIVES IN PUBLIC ADDICTION TREATMENT SYSTEMS: CONTEXT AND EFFECTS ON ACCESS, RETENTION, SELECTION AND OUTCOMES.

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Aims: Value-based purchasing (VBP) aims to align program incentives and purchaser goals, often to improve quality of care, yet is uncommon in addiction treatment systems. Maine is the only state currently using an incentivized contract (IC) in its public addiction treatment system. We aim to understand the context in which the IC was implemented and determine whether rewarded measures (access and retention), client selection, and outcomes changed under the IC.
Methods: We use state administrative data (N=37,470 admissions) and multivariate multilevel modeling with a difference-in-difference approach and a non-IC comparison group. Propensity score techniques adjusted for pre-period differences in IC and non-IC admissions. Program director interviews collected information on activities implemented in response to the IC and more broadly to understand the context for any potential changes.
Results: The probability of receiving 4 or more outpatient treatment sessions did not change significantly between the 2005-07 pre-period and the 2008-11 post-period and was not significantly different in IC agencies and non-IC agencies (p=.43). Neither waiting time nor probability of remaining in treatment for over 90 days was significant. Admission rates of people with diagnosed mental disorders did not indicate selection effects. Early substance use and criminal justice outcomes showed little difference across IC and non-IC groups over time. While most program directors acknowledged making changes to respond to the IC system, they quickly became acclimatized to the IC, with incentives not a large driver in changing how they approach care or do business. Non-IC programs are less likely to think of quality and outcomes measurement in a precise way.
Conclusions: Introduction of an IC is a significant change in payment design that may affect addiction treatment service delivery, thus increasing our understanding of its effects is critical. We find the overall net effect of incentivized contract is very small and not significant.
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THE VALIDITY OF DSM-5 CRITERIA FOR SUBSTANCE-RELATED AND ADDICTIVE DISORDERS ADAPTED FOR "FOOD ADDICTION"

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Aims: Several research groups are developing the "Food Addiction" (FA) construct using as a base the concept of DSM substance-related and addictive disorders. The aim of this study was to describe the psychometric properties of the DSM-5 criteria for substance-related and addictive disorders adapted for FA.
Methods: Cross-sectional study, conducted, in 2014, with a large target sample of 3,822 undergraduate students (i.e., business, law, health science, engineering, etc.) recruited by invitation from a Federal University in Southeast of Brazil (65% female; mean age 26 ±7.6 yrs; 67% normal weight, 26% overweight (BMI≥25 kg/m^2). Food Addiction was assessed by an adapted questionnaire which includes the 11 DSM-5 criteria. Factor analysis and Rasch Model analysis were used to check the psychometric properties (i.e. scale unidimensionality and item severity) of the FA instrument.
Results: A unidimensional model provided an adequate and parsimonious interpretation for the 11 DSM-5 criteria for FA (CFI=.973; TLI=.967; RMSEA=.050). This model showed a good reliability (Cronbach's Alpha=.79). All 11 criteria fit a Rasch model well, with infit values ranging from 0.91 to 1.14. Criteria covered a broad range of severity ranging from -3.34 to 3.28. "Larger amounts", "Craving" and "Psychological and physical problems" were the least severe symptoms. However, "Give up activities" was the most severe symptom for the diagnosis of FA (3.28).
Conclusions: Findings showed that this FA diagnostic instrument have good psychometric properties. This study suggests that the DSM-5 criteria for substance-related and addictive disorders are valid for FA and can be used as screening instrument. In addition, these evidences may help to develop prevention and treatment strategies for FA.
Financial Support: CNPq, CAPES

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CORRELATES BETWEEN BRAZILIAN CLUB DRUG USERS MEN WHO HAVE SEX WITH MEN, PSYCHIATRIC VULNERABILITIES AND MULTIPLE SEXUAL PARTNERS.

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Aims: Studies demonstrate an association between MDMA use, sexual behaviors and psychiatric problems. Since these substances are linked to HIV infection and transmission, this represents a potential public health problem. The study explores the differences in psychiatric symptoms, substance use and sexual risk behaviors between men who reported sex with another man (MSM) and men who reported sex with only women (MSWO) young club drug users.
Methods: Cross-sectional study conducted using targeted sampling and ethnographic mapping. Standardized questionnaire was used with 240 participants between 18 and 39 years, who used MDMA and/or LSD in the last 90 days, and who were not in treatment for drug problems.
Results: Male participants were divided into two groups - those who had sex with another male (MSM) (18%, n=30) and those who did not (82%, n=109). Average age of the participants was 22 years (DP 4.59); MSM were more likely than MSWO to report several past year sexual risk behaviors, including: having 2 + sex partners (Prevalence Ratio (PR 3.112), having sex involving anal intercourse (PR 2.91) and trading sex (PR 3.112). 55.6% of MSM participants reported inconsistent use of condom with recent anal sex. Relevant symptoms of depression (p=0.006), anxiety (p=0.002) and moderate traumatic stress (p=0.017) were more likely to be reported by MSM compared to MSWO.
Conclusions: These data demonstrate differences in risk behaviors beteween MSM and MSWO. Interventions are justified in the areas of sexual risk reduction, prevention and treatment for substance abuse and mental health. Public health programs prioritizing the different populations are necessary.
Financial Support: Financial Support: Fogarty International Center; Grant 1R03TW007612;
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CRACK, POWDERED COCAINE, BOTH OR NEITHER: A GENERALIZED LOGIT ANALYSIS OF A COMMUNITY-BASED SAMPLE.

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Aims: To understand factors associated with use of both crack cocaine and non-injected powered cocaine.
Methods: The Risk Behavior Assessment (RBA; 1993) was used to elicit information on past month, past 48-hours and drugs used before/during sex drug use in a sample of out-of-treatment drug users (N = 8538). Past 30 day, past 48 hour, and before/during sex drug use were coded into 1) use of crack (smokable cocaine) only, 2) powdered cocaine use only, 3) both drugs used during the timeframe and 4) neither drug used. Generalized logit analysis was used to develop models for each timeframe (48-hour and 30-day). For all models the reference group was using neither drug.
Results: Respondents who reported use of both crack and powdered cocaine (N=306) included both men (n=207) and women (n=99). The 48-hour, 30-day, and before/during sex models were almost identical. Those who reported using both crack and cocaine were more likely to: be Black (OR=1.65, CI 1.27, 2.14); bisexual (OR=1.85, CI 1.39, 2.47); trade sex for drugs (OR=4.88 CI 3.73, 6.39); to be homeless (OR=3.50, CI 2.66, 4.62), have higher number of days used alcohol in the past month (OR=1.09, CI 1.08, 1.10); and to have had gonorrhea (OR=1.42, CI 1.07, 1.88).
Conclusions: The general logit model highlights factors associated with use of both crack and powdered cocaine within the same timeframe, including homelessness, and being a member of an ethic or sexual minority, and sex trading.
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LIABILITY FOR VIOLENCE IN YOUNG WOMEN.

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Aims: Substance use and violence are often intertwined. Previous work with male subjects indicated that transmissible liability for substance use disorders was also an indicator of future commission of violent offenses. Currently, we have developed an index of transmissible liability for female adolescents (F-TLI) by harmonizing data from CEDAR's female sample (N=228) with two other longitudinal NIDA-funded projects at the University of Pittsburgh. The F-TLI scores predicted future cannabis use disorder (CUD) in the CEDAR group. The current analyses are being conducted to examine the ability of the F-TLI to predict future perpetration of violence in young adulthood (ages 19-25) among females.
Methods: Methods: Violence data were compiled for N=228 female subjects from several instruments which contained questions regarding perpetration of violence across up to 3 timepoints, ages 19, 22 and 25. Summary variables were created to indicate the following categories of perpetration of violent acts: child abuse or neglect (8 items), intimate partner violence (33 items), sexual assault (9 items), other acts of violence (e.g. fighting, assaults, use of a weapon) (32 items).
Results: Preliminary Results: 1.8% admitted to perpetrating child abuse or neglect, 18.1% IPV, 29.1% sexual abuse, and 42.3% perpetrated other acts of violence. Bivariate correlations indicate that F-TLI is significantly correlated with perpetration of IPV (r=.244, p<.001) and of other types of violence (r=.234, p<.001). Regression analyses indicated that F-TLI predicted future IPV perpetration, and other types of violent acts, and neither relationship was mediated by affiliation with violent peers at age 16. Further analyses are to be conducted.
Conclusions: Conclusions: Transmissible liability measured at age 12 previously shown to predict CUD in females by age 22 is also predictive of perpetration of violent acts in young adulthood, regardless of affiliation with violent peers in adolescence. Intervention with these identifiable high risk girls may prevent future criminality.
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CANNABIS USERS SHOW INCREASED SUSCEPTIBILITY TO FALSE MEMORIES.

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Aims: Previous studies on the neurocognitive impact of cannabis use have found working and declarative memory deficits that tend to normalize with abstinence. An unexplored aspect of cognitive function in chronic cannabis users is the ability to distinguish between veridical and illusory events; a crucial aspect of reality monitoring that relies on adequate memory function and cognitive control.
Methods: Sixteen heavy cannabis users not seeking treatment for their cannabis consumption were matched to a group of healthy controls taking into account sex, age, years of education, verbal intelligence and fluid intelligence. All participants performed a modified version of the Deese-Roediger-McDermott paradigm in an MRI scanner. Following a study phase, subjects were presented with 75 old words, 40 semantically unrelated new words and 40 semantically related new words or lures. They were required to judge whether a word had been presented in the study phase and make an old vs. new decision by button press.
Results: Cannabis users showed an increased susceptibility to false memories, failing to identify lure stimuli as events that never occurred. In addition to impaired performance, they displayed reduced activation in areas associated with memory processing within the medial temporal lobe (MTL), and in parietal and frontal brain regions involved in attention and performance monitoring. Reduced activity in the MTL was associated with greater cannabis consumption.
Conclusions: These findings indicate that cannabis users have an increased susceptibility to memory distortions even when abstinent and drug-free, suggesting a long-lasting compromise of memory and cognitive control mechanisms involved in reality monitoring.
Financial Support: This research was supported by the "Plan Nacional Sobre Drogas" of the Spanish Government

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CAMKII INHIBITION AFFECTS COCAINE-CUE MEMORY PROCESSES TO ATTENUATE REINSTATEMENT.

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Aims: We have identified a novel phosphorylation site on CaMKIIα (Ser331) that is increased in the BLA after drug-cue memory extinction and decreased after memory reactivation. Here, we assessed whether CaMKII inhibition in the BLA could enhance extinction or inhibit reconsolidation of cocaine-associated memories to reduce relapse-like behavior in an animal-model of addiction. Ongoing studies are testing the mechanism for the observed behavioral change by mutating CaMKIIa-Ser331 and measuring kinase activity.
Methods: Rats trained to self-administer cocaine paired with an audiovisual cue were subjected to cue-reactivation to induce memory reconsolidation or were exposed to cue-extinction. KN-62 or KN-93 was infused into the BLA immediately following memory reactivation or extinction to inhibit CaMKII. The behavioral effect of this inhibition was measured in a cue-induced reinstatement session. Next, HEK-293 cells were transfected with either wildtype or mutated (Ser331Ala) forms of CaMKIIα. Whole cell lysates were collected and specific kinase activity was assessed.
Results: Intra-BLA infusions of CaMKII inhibitors decreased responding during cue-induced reinstatement relative to vehicle-controls. Thus, CaMKII activity plays a role in drug-cue memory reconsolidation and that inhibiting this process can reduce drug-seeking behavior. CaMKII inhibition after cue-extinction also resulted in decreased lever pressing during reinstatement, suggesting that CaMKII activity interferes with the ability of cue-extinction to reduce drug-seeking behavior.
Conclusions: Drug-cue memory extinction and reconsolidation may differentially effect CaMKII kinase activity through phosphorylation at Ser331. Additionally, blocking the activity of CaMKII in the BLA can enhance extinction and weaken reconsolidation to mediate drug-seeking behavior. Therefore, CaMKII activity may be required for drug-memory reconsolidation and CaMKII inhibitors may be useful adjuncts to extinction training in addiction therapy.
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COCAINE IMPAIRS SERIAL FEATURE NEGATIVE LEARNING: IMPLICATIONS FOR COCAINE ABUSE.

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Aims: Exposure to high energy (Western) diets compromise blood-brain-barrier (BBB) integrity which in turn affects hippocampal function. Consequently, the rat's ability to use satiety signals to terminate bouts of eating is impaired, contributing to obesity in these animals. Bolus injections of cocaine also compromise BBB integrity, suggesting that a similar process may be involved in escalated drug intake, i.e., cocaine may impact the BBB and damage hippocampal functioning, impairing the use of drug signals to terminate drug intake. If so, tasks involving the hippocampus, e.g., sFN learning, which is thought to mediate control by satiety signals, should be impaired by cocaine exposure (as in high energy diet exposed rats).
Methods: Male Sprague-Dawley rats were trained on a sFN discrimination in which a cue alone signaled the presence of food, but the same cue signaled the absence of food when preceded by a second stimulus. The same animals were also trained on a simple discrimination where one cue signaled food and a second cue signaled its absence. Following acquisition of both discriminations, they were injected IP with cocaine (20 mg/kg) or saline for 20 days during which they were exposed to both discriminations.
Results: Initially, all rats performed comparably on both discriminations. By the 18th day of injections, the sFN problem was impaired for rats receiving cocaine relative to those receiving saline. No significant differences between the groups were observed on the simple discrimination.
Conclusions: Cocaine impaired performance on the sFN task. That no deficits were seen with the simple discrimination suggests that there was no general learning deficit associated with drug exposure. These data suggest that hippocampal damage associated with cocaine exposure may contribute to an inability to use drug satiety cues and thus escalated intake.
Financial Support: Supported by a Mellon Foundation grant to ALR and NIH Grant R01 HD29792 to TLD.

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THE LONGITUDINAL INFLUENCE OF MULTIPLE DEPRESSANT USE ON NONFATAL OVERDOSE AMONG YOUNG PEOPLE WHO INJECT DRUGS.

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Aims: Overdose is the most common cause of death yet few studies have considered age-restricted longitudinal predictors of overdose. With the understanding that nonfatal overdose is among the strongest predictors of fatal overdose, our aim was to determine predictors of non-fatal overdose in a cohort of young people who inject drugs (PWID).
Methods: In the ongoing "UFO" cohort study, 235 young (< age 30) PWID were interviewed and assessed quarterly between April 2010 and February 2014. Generalized Estimating Equations were used to estimate the population-level effects of demographic and drug use factors on non-fatal overdose during the 3.8 year study period.
Results: The rate of non-fatal overdose during the first 12 months of follow-up was 0.14. Adjusted longitudinal analysis showed that overdose increased as the number of heroin injection-days increased (AOR=1.37; 95% CI=1.19-1.57), benzodiazepine pill-taking days increased (AOR=1.25; 95% CI=1.07-1.47), and when alcohol consumption exceeded 10 drinks/day compared to 0 drinks/day (AOR=3.73; 95% CI=1.55-9.02).
Conclusions: Even after accounting for heroin use, benzodiazepine and alcohol use independently predict overdose among young PWID. Similar findings have been recognized in settings outside of individuals known to be at higher risk. However, perceptions of health risks from drugs like benzodiazepines in the general public are still reportedly low and risks from multiple CNS depressant use are not routinely discussed in primary or emergency medicine settings. Broadening simple messages regarding the risks of multiple CNS depressant use beyond individuals known to be at high risk, and including health services, public programs and popular press campaigns for the general population, may increase awareness more broadly and reduce overdose among young PWID.
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EARLY MORTALITY AFTER ENTERING A METHADONE TREATMENT PROGRAM IN BADALONA, SPAIN.

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Aims: Methadone is effective for the treatment of heroin dependence and it also improves survival. However, it has been reported an increased risk of death during the first weeks of treatment. We aimed to analyze early mortality and causes of death in the only community-based methadone treatment program in Badalona, Spain
Methods: Longitudinal study in heroin users enrolled in the MTP since its introduction in January 1992 through December 2010.
Socio-demographic, drug use characteristics, serology for HIV, Hepatitis B, Hepatitis C and psychiatric co-morbidity were assessed at entry. In all cases information on date and cause of death was obtained from clinical charts and the Catalonian mortality register. Causes of death were established according to the International Classification of Diseases (ICD-9 and ICD-10).
Results: Between 1992 and 2010, 798 patients (83% men) started treatment with methadone; median age at admission was 29 years (IQR: 25-34 years), age at first heroin use was 19 years (IQR:16-23 years) and 75% were injection drug users. Regarding other characteristics, 56% had at least 8 years of education. Prevalence of HIV, HCV and HBV (HBcAb) infections was 50%, 67% and 58%, respectively. At the end of study in Dec. 2010, 220 (27.6%) patients had died; 10/220 (4.5%) died during the first month of methadone treatment; all of them were men and 50% of deaths occurred in the first period of admission (1992-96). Among the deceased patients, 6 were HIV-positive and 4 had history of psychiatric disorders. Causes of death included: drug-related in 3 cases, cardio-respiratory in 3 cases, liver-related (2), non-natural (1) and unknown (1).
Conclusions: We observe an increased risk of death at the beginning of treatment with methadone in a low threshold program. Mortality is not only drug-related but also attributable to the impact of HIV/Aids before the introduction of HAART.
Financial Support: The Ministry of Science and Innovation.The Municipal Institute for Personal Services Badalona

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GENDER EFFECTS ON ZOLPIDEM EFFICACY AND SAFETY.

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Aims: Gender-related PK differences in zolpidem have been reported. In May 2013 the FDA issued an advisory for reducing zolpidem doses in women (5 mg). Few studies have assessed gender-related PD differences. In post hoc analysis of data assessing 12 months nightly 10 mg zolpidem in insomnia, we evaluated gender effects.
Methods: Insomniacs (N=89) meeting DSM-IV-TR criteria and sleep efficiency (SE) of ≤85%, ages 23-70 yrs, without psychiatric disease or drug dependency were randomly assigned to receive 10mg zolpidem or placebo, double-blind, nightly for 12 months. In months 1 & 8, efficacy and safety was assessed with a 8hr nocturnal polysomnogram (NPSG) and Multiple Sleep Latency Test (MSLT). Also dose escalation and rebound insomnia were assessed at months 1, 4, and 12. Three efficacy measures (SE, sleep latency, wake during sleep) and 3 safety measures (MSLT for residual effects, # capsules self-administered (SA) for dose escalation, SE < screening SE for rebound) were analyzed by gender [male (n=33), female (n=56)] and zolpidem (n=47) versus placebo (n=42).
Results: Zolpidem improved SE (p=0.001), sleep latency (p=0.001) and wake during sleep (p=0.002) in months 1 and 8 with no gender x drug interactions. No main effects of zolpidem or gender on MSLT were found. In months 8 and 12 there was a gender by zolpidem interaction (p=0.05), with zolpidem reducing MSLT in men, but not in women. More zolpidem was SA than placebo (p=0.04), but there was no dose escalation and no gender differences in SA. Zolpidem discontinuation did not induce rebound insomnia and there were no gender differences in rebound.
Conclusions: Gender-related PK differences do not translate into gender-related zolpidem efficacy and safety differences.
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VARENICLINE VERSUS NICOTINE PATCH PLUS BRIEF ADVICE FOR SOBER SMOKERS IN SUBSTANCE TREATMENT.

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Aims: Smokers with substance use disorders (SUD) have great difficulty quitting smoking during their first year of sobriety. Varenicline (VAR) is the most effective medication for smoking cessation, has few contraindications, targets nicotine receptors selectively, and reduces alcohol use, so may be best in this population. The aim was to investigate effects of treatment with varenicline versus nicotine replacement (NRT), both combined with brief advice adapted for sobriety concerns, for smokers in treatment for SUD.
Methods: Smokers abstinent < 12 months in any SUD treatment (n = 137) from the community were randomized to 12 wks varenicline vs. nicotine patch, double-placebo, plus 8 sessions brief advice adapted to address sobriety concerns. Randomization was stratified by depression diagnosis and gender. Smoking point-prevalence (7-day) abstinence was assessed during the 12 weeks and at 3, 6 and 12 months after treatment start using self-report and cotinine confirmation of past 7 days point-prevalence abstinence.
Results: Within treatment, 12% had complete abstinence at 8 weeks in each condition (ns). At 3 months, 13% with VAR and 3% with NRT had point-prevalence abstinence ($p < .05$) and at 6 months 9% with VAR and 3% with NRT had point-prevalence abstinence ($p = .18$). At 6 months, heavy drinking was reported by 29% in VAR and 16% in placebo, and drug use by 29% in VAR and 32% in placebo (all non-significant).
Conclusions: Varenicline with brief advice greatly increased the odds of smoking abstinence at 3 months and did not harm SUD recovery. While varenicline resulted in 3 times as much abstinence as placebo at 6 months, the results were no longer significant. Thus, varenicline has utility in this population.
Financial Support: This research was supported by a grant from the National Institute on Drug Abuse (R01DA024652), and a Senior Research Career Scientist Award from the Department of Veterans Affairs

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GENDER INFLUENCE ON COMORBIDITY AND CLINICAL FEATURES OF COCAINE-DEPENDENT PATIENTS.

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Aims: Cocaine dependence disorder is certainly well-documented, though differences due to gender have not been studied as broadly.
Methods: We performed a cross-sectional, observational study in 1014 patients (35.8 yo, 20.7% women) with a cocaine dependence according DSM-IV criteria, seeking treatment between 2005 and 2014. Socio-demographic and clinical variables were collected. The SCID-I, SCID-II, EuropASI and a structured interview about cocaine-induced psychosis were performed. Descriptive statistics were carried out for demographic and clinical data, a bivariate analysis was made to compare the main variables by sex and, finally, logistic regression was performed.
Results: In the bivariate (but not the multivariate) analysis, women were found to be less severe in the legal subscale and more so in the psychological area (p= .0001), as well as having used less cocaine in the month prior to the study (p= .009) greater history of sedative use (p= .002), and more affective(p= .009), anxiety(p= .019) and dependent-personality disorders (p= .004).
In the bivariate (as well as the multivariate) analysis, women tended to be married or with a couple (p= .011) and to have made more suicide attempts(p= .0001), as well as having more employment problems(p= .0001), food and eating disorders(p= .0001), histrionic (p= .017) and borderline (p= .0001) personality disorders, and less antisocial personality disorders(p= .004) .
Conclusions: Gender significantly determines the clinical features of cocaine-dependent patients. Female addicts often present more social and emotional troubles and display less antisocial behaviour. Sedative dependence and anxiety/affective disorders should be investigated in cocaine-dependent women in order to treat these conditions.
Financial Support: None for this research

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A SMARTPHONE APPLICATION FOR MANAGING CANNABIS USE.

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Aims: With increasing frequency of cannabis use, especially amongst young people, the ready availability of free and appealing intervention materials is even more urgent. This study aims to assess the feasibility and impact of a consultatively developed smartphone app on levels of cannabis use and related problems.
Methods: A single group repeated measures study of n=111 past month cannabis users assessed at baseline for patterns of cannabis use, dependence and cannabis-related problems; exposed to the smartphone app for one month; assessed again immediately following removal of app availability; and then assessed again one month later.
Results: Of the n=111 participants 64% were male with a mean age of 26.7 years (SD7.8). The majority were employed full time (76%) and had completed secondary education (89%). They had a mean of 2.3 (SD 2.1) previous quit attempts and 11% had previously attended treatment for cannabis use disorder. Compared to baseline measurement there were significant reductions in number of days of cannabis use, levels of cannabis-related problems post app exposure and self-efficacy to resist cannabis (p<.001) and 1 month follow-up (p<.001); significant reduction in level of dependence at 1 month follow-up; and significant improvement in DASS scores of anxiety and depression (p<.002).
Conclusions: This smartphone app is acceptable to young, male cannabis users and has been found to be associated with reduce levels of cannabis use, dependence, cannabis-related problems and dysphoria following use and in the short term thereafter. This warrants testing in a large randomised, controlled trial to assess efficacy.
Financial Support: NCPIC is funded by the Australian Government's Department of Health

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OVERLAP BETWEEN FOOD ADDICTION AND DSM-5 EATING DISORDERS IN A TREATMENT SEEKING SAMPLE.

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Aims: Although the diagnosis of Food Addiction (FA) is not formally recognized, some studies showed that DSM-5 criteria for substance use disorder (SUD) might be transferable to FA. We aimed to verify possible overlap between DSM-5 eating disorders (Anorexia, Bulimia and Binge Eating Disorder) **and FA.**

Methods:

In 2014, consecutive patients enrolled in an addiction treatment program in Bordeaux, France were assessed with the ASI modified to include eating behaviors, the Mini International Neuropsychiatric Interview **for psychiatric disorders including DSM-5 criteria for SUD, gambling, eating disorders (ED) and FA criteria based on DSM-5 criteria for SUD.**

Results: 80 patients were enrolled, **64% males, mean age 41years (SD=11), 43% overweight (BMI≥25), 90% with SUDs, 10% with gambling, 64% with other psychiatric comorbidities. 11% met a DSM-5 eating disorder diagnosis.** FA diagnosis was met by 28% of the entire sample (10% mild, 7% moderate, 11% severe). Those patients met an average of 5.2 criteria out of 11 (SD=2.8) and the most endorsed were "larger amounts than intended" (54%), "craving/strong desire" (39%) and "unsuccessful efforts to cut down" (35%). Patients with DSM-5 Eating disorders were more likely to meet FA diagnosis (78% vs 21%, p=.001) and individuals with ED met more FA (32% vs 3%, p=.001). No association between FA diagnosis and the others psychiatric comorbidities was found except for ADHD. Patients with FA diagnosis exhibited higher ASI severity score in medical, family/social and eating domains.

Conclusions: FA diagnosis is highly associated with DSM-5 eating disorders and might overlap with some diagnoses. Patients with FA exhibited impairment comparable to SUD patients. Further studies are needed to address the validity of FA diagnosis using the DSM-5 SUD criteria.

Financial Support: France: PHRC 2006, Brazil: CSF, CNPq, CAPES

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RISKY SEXUAL BEHAVIOR AMONG OEF/OIF VETERANS WITH AND WITHOUT RECENT SUBSTANCE USE.

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Aims: Between Veterans with/without recent substance use:

1. Compare self-reported sexual risk behavior
2. Compare biological risk indicators (2:4 digit ratio, CAGn)
3. Compare behavioral measures of impulsivity and risk-taking

Methods: Study Procedures:

OEF/OIF Veterans will provide written informed consent. Data collection will include saliva sample, 2:4 digit ratio calculation, Sexual History questionnaire, HIV Risk Behavior Scale, Immediate and Delayed Memory Task (IMT/DMT), Risk and Ambiguity Task, 28-day substance use TLFB

Behavioral tasks will be performed in a counterbalanced sequence.

Parametric and non-parametric tests will compare groups with and without recent substance use on risk outcomes.

Results: Substance use and sexual risk-taking data were summarized for the first 57 Veteran participants. Participants were 23-59 years old (Mean=33); 38 (67%) reported illicit drug use or alcohol use to intoxication in the past 28 days. Participants' mean age at first sex was 16; mean lifetime sexual partners was 27 (range 1-150). Number of partners in the past 12 months ranged from 0 - 20 (Mean = 2.2). Twenty-two percent of participants reported a lifetime STI. Veterans with and without substance use did not differ on lifetime sexual behavior variables, but the former were significantly more likely to report recent sex under the influence of drugs or alcohol (p=.034) and were less likely to have used a condom with a casual sexual partner in the past 28 days (p=.033). Other measures to be compared include performance on two behavioral tasks: the IMT/DMT (Dougherty) and the Risk and Ambiguity Task (Levy), and biological indicators of risk propensity: 2:4 digit ratio and CAGn.

Conclusions: Veterans reporting recent illicit substance use or risky alcohol use reported greater likelihood of engaging in recent high-risk sexual behavior. Analyses comparing these groups on biological propensity to take risks and performance on behavioral risk-related tasks are underway and will be reported.

Financial Support: This study is funded by the MIRECC; Department of Veterans Affairs

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REDUCTION IN PRESCRIPTION OPIOID MISUSE AMONG ENROLLEES INTO OPIOID TREATMENT PROGRAMS.

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Aims: To examine 6-year trends of prescription opioid (PO) non-medical use among opioid-dependent patients enrolling in opioid treatment programs (OTPs).

Methods: Newly admitted patients to OTPs, in a nationwide prevalence study, completed a one-page self-administered survey of past month heroin and non-medical PO use. Data were collected from 42,502 patients in 96 OTPs across 34 states from January 2008 to March 2014.

Results: Respondents' average age was 34, 55% male, 81% white ethnicity; 38% reported employment as the major source of income. Over the six years, 77% reported non-medical use of at least one type of PO and 55% reported heroin use. Heroin use declined from 57% in 2008.Q1 (1st quarter of 2008) to 49% in 2010.Q3 and then increased to 61% in 2014.Q1. PO use increased from 79% in 2008.Q1 to 84% in 2010.Q3, and then decreased to 66% in 2014.Q1. Misuse of extended-release oxycodone (Oxy-ER) increased from 39% in 2008. Q1 to 47% in 2010.Q2 and then showed a steep decline to 16% by 2014.Q1. Except for buprenorphine, non-medical use for other POs also decreased, but not at as steep as Oxy-ER, with methadone misuse showing the greatest decline from 44% in 2008.Q1 to 24% in 2014.Q1.

Conclusions: This study documents a modest increase in PO misuse from 2008 to 2010 followed by steep declines in the misuse of ER-Oxy as well as other prescription opioids extending to 2014. During this latter period several systemic changes associated with POs occurred such as introduction of tamper proof/abuse deterrent medications and establishment of drug monitoring programs in several states. The findings underscore the importance of ongoing surveillance of illicit use of POs and suggest that changes in opioid prescribing practices and formulations may have influenced declines in PO misuse.

Financial Support: Financial Support: Denver Health is part of the Researched Abuse Diversion and Addiction-Related Surveillance (RADARS®) System.

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MODERATING EFFECTS OF DECISION-MAKING ON CANNABIS USE AND BODY MASS INDEX AMONG ADOLESCENTS.

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Aims: One side effect of cannabis use is increased appetite; however, the research on the association between cannabis use and body mass index (BMI) has produced contrary findings. Research has found that cannabis use is associated with a higher BMI among adolescents, but lower BMI with adults. These contradictory findings may be explained, in part, by differences in decision-making (DM), as DM deficits are often reported among individuals with cannabis addiction, as well as those with higher BMI scores, and are also better developed among adults compared to adolescents. The current study evaluated if DM moderated the relationship between lifetime amount of cannabis use and BMI among adolescents. We hypothesized that more cannabis use would be associated with greater BMI but only among those with poor DM (as assessed by the Iowa Gabling Task [IGT]).

Methods: Participants were 127 adolescents, ages 14-17, recruited from South Florida middle and high schools, a majority who are at risk for escalating cannabis use. Exclusion criteria included a history of neurological, developmental or psychiatric disorders.

Results: Multiple linear regressions revealed that the interaction between cannabis use and DM performance predicted BMI (p = .04). Simple slope difference tests concluded that among those with below average DM, more cannabis use was associated with a higher BMI, β = .42, $t(120)$ = 2.88, p < .01. Those with average DM performance also showed a positive relationship between more cannabis use and a higher BMI, but of a smaller magnitude, β = .18, $t(120)$ = 2.12, p = .04. In contrast, there was no association between cannabis use and BMI among those with above average DM (p = .72).

Conclusions: Our results support previous findings of greater amounts of cannabis use being associated with higher BMI among adolescents. However, above average DM performance appeared to mitigate these effects.

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NICOTINE DEPENDENCE, NICOTINE METABOLISM, AND THE EXTENT OF COMPENSATION IN RESPONSE TO REDUCED NICOTINE CONTENT CIGARETTES.

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Aims: Reducing the nicotine content in cigarettes may lead to lower levels of addiction. Smokers however may compensate by smoking more cigarettes and/or smoking more intensely. The objective of this study was to test whether individual differences in the level of nicotine dependence and/or the rate of nicotine metabolism influence smoking behavior and exposure to tobacco toxicants when smokers are switched to reduced nicotine content cigarettes (RNC).
Methods: Data from 51 participants from a previously published clinical trial of RNC were analyzed. Nicotine content of cigarettes was progressively reduced over six months and measures of smoking behavior, as well as nicotine metabolites and tobacco smoke toxicant exposure, *CYP2A6* and nicotinic *CHRNA5-A3-B4* (rs1051730) genotype were measured.
Results: Higher baseline FTND predicted smoking more cigarettes per day (CPD), higher cotinine and smoke toxicant levels while smoking RNC throughout the study, with no interaction by RNC level. Time to first cigarette (TFC) was associated with differences in compensation. TFC within 10 min was associated with a greater increase in CPD compared to TFC greater than 10 min. Neither rate of nicotine metabolism, nor *CYP2A6* or nicotinic receptor genotype, had an effect on the outcome variables of interest.
Conclusions: FTND is associated with overall exposure to nicotine and other constituents of tobacco smoke, while a short TFC is associated with an increased compensatory response after switching to RNC.
Financial Support: The clinical trial was funded by NCI (R01CA078603, NLB). FCB and KCR were funded as postdoctoral scholars at the University of California, San Francisco (NCI grant 5R25CA113710-08). RFT was supported by a University Endowed Chair in Addictions for the Department of Psychiatry, by the PGRN PNAT (U01DA020830 to RFT and NLB), the Canadian Institutes of Health Research (TMH109787), and the Centre for Addiction and Mental Health and the CAMH foundation.

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IDENTIFICATION OF NOVEL ALLOSTERIC DOPAMINE TRANSPORTER LIGANDS WITH NANOMOLAR POTENCY.

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Aims: Published studies have described novel allosteric modulators of the dopamine transporter (DAT). *N*-(diphenylmethyl)-2-phenyl-4-quinazolinamine (SRI-9804), *N*-(2,2-diphenylethyl)-2-phenyl-4-quinazolinamine (SRI-20040), and *N*-(3,3-Diphenylpropyl)-2-phenyl-4-quinazolinamine (SRI-20041) partially inhibited [^{125}I]RTI-55 binding and [^{3}H]dopamine uptake, and allosterically modulated *d*-amphetamine-induced dopamine (DA) release. New analogs of these ligands were synthesized and evaluated for activity at DAT.
Methods: Using synaptosomes prepared from rat caudate, we conducted [^{3}H]DA uptake inhibition assays, DAT binding assays with [^{3}H]WIN35428, and DAT-mediated release assays with [^{3}H]MPP$^+$ or [^{3}H]DA.
Results: The initial set of compounds binned into 3 groups of [^{3}H]DA uptake inhibitors: 1) full efficacy agents with a one-site fit, 2) full efficacy agents with a two-site fit and 3) partial efficacy agents with a one-site fit. We focused further studies on the partial efficacy inhibitors. These agents were partial inhibitors of uptake at DAT, SERT, and NET, but much less potent at inhibiting [^{3}H]WIN35428 binding. For example, SRI-29574 partially inhibited DAT uptake with an IC_{50}=2.3±0.4 nM, without affecting DAT binding. At concentrations less than 1 μM, these agents did not alter DAT-mediated [^{3}H]MPP$^+$ release in the absence or presence of 100 nM *d*-amphetamine. At a dose 25-times greater than its IC_{50} for DAT uptake inhibition, SRI-29574 had no significant effect on the *d*-amphetamine EC_{50} or Emax for DAT-mediated release of [^{3}H]MPP$^+$. The full data set will be presented at the meeting.
Conclusions: These studies demonstrate the existence of potent DAT ligands that partially block DA uptake, without affecting DAT binding or *d*-amphetamine-induced [^{3}H]MPP$^+$ release. These compounds may be useful probes of transporter function as well as leads for novel therapeutics.
Financial Support: This work was supported by the NIDA/IRP and grant DA029962 from NIDA, NIH, DHHS.

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PATTERNS OF PERFORMANCE AND IMAGE ENHANCING DRUG USE AMONG MEN ACCESSING NEEDLE AND SYRINGE PROGRAMS IN SYDNEY, AUSTRALIA.

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Aims: To describe drug use, associated physical and mental health issues, and blood borne virus transmission risks among men who inject PIEDs.
Methods: This was a voluntary, anonymous, self-complete cross-sectional survey conducted across 5 districts in Sydney, NSW. The 9 recruitment sites together provided free injecting equipment to approximately 75% of men who last injected PIEDs and accessed a NSP in the state of NSW in 2013 (Kirby Institute 2013). The current analysis examines a preliminary sample involving 50 men over 18 years old (*M*=27.8) who inject PIEDs and attended an NSP during the study period. In this sample, 1 man identified as gay and 49 as straight. The majority of participants were from culturally diverse backgrounds (*n*=38, 79.2%). Analyses used were descriptive statistics, chi-squared, and ANOVA.
Results: Participants reported injecting anabolic steroids (*n*=28, 56%), peptides (*n*=5, 10%), and growth hormone (*n*=4, 8%); 15 (30%) participants were not specific about which PIEDs they inject. The majority (*n*=32, 65.3%) of participants had been injecting for at least 12 months (*M*=30.8), yet a large minority (*n*=11, 22.4%) had been injecting for 4 weeks or less. Age was positively correlated with length of time injecting PIEDs (*r*=.589, *p*<.001). Number PIED-use cycles previously completed positively correlated with participants' intentions to do a greater number of cycles in the future (*r*=.477, *p*<.001). Based on 41 responses, most frequently reported side effects were shrinking testicles (*n*=8, 19.5%), anger (*n*=8, 19.5%) and rage (*n*=7, 17.1%). Length of time injecting PIEDs was not associated with more side effects reported (*p*>0.05). Although reporting risky injecting practices was generally low, 20 (40%) participants reported being injected by another person in the last 12 months.
Conclusions: The study makes a timely contribution to an improved understanding of the prevalence of health and social factors associated with PIED use in Sydney.
Financial Support: Drug and Alcohol Multicultural Education Centre, Network of Drug and Alcohol Agencies

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EVIDENCE FOR SEDATIVE EFFECTS OF BENZODIAZEPINES INVOLVING UNEXPECTED $GABA_A$ RECEPTOR SUBTYPES.

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Aims: A disconnect exists between preclinical non-human animal models and clinical human studies regarding the presence or absence of sedative properties of benzodiazepine (BZ)-type compounds acting at specific $GABA_A$ receptor subtypes.
Methods: We examined the preclinical effects of alprazolam (non-selective BZ), zolpidem (preferential binding to alpha1 subunit-containing $GABA_A$ receptors), and 8-ethynyl-6-(2'-pyridine)-4*H*-2,5,10b-triaza-benzo[*e*]azulene 3-carboylic acid ethyl ester; HZ-166 (functional selectivity for alpha2 and alpha3 subunit-containing receptors) using quantitative behavioral observation techniques in rhesus monkeys. To examine further the role of alpha1 subunit-containing $GABA_A$ receptors in BZ-induced sedative effects, doses of alprazolam, zolpidem, and HZ-166 were re-assessed in the presence of the alpha1 subunit-preferring BZ antagonist beta-carboline-3-carboxylate-*t*-butyl ester (BCCT).
Results: Increasing doses of alprazolam resulted in the emergence of effects associated with sedative-motor properties of classical BZs, including observable ataxia, rest/sleep posture, moderate and deep sedation. In contrast, zolpidem engendered dose-dependent observable ataxia and deep sedation only, while HZ-166 induced primarily rest/sleep posture. The sedative-motor effects engendered by alprazolam and zolpidem generally were attenuated by BCCT pretreatments, whereas rest/sleep posture was insensitive to BCCT administration.
Conclusions: Taken together, these data suggest that different levels of observable sedation may be mediated by different $GABA_A$ receptor subtypes, and suggest specifically that alpha1 subunit-containing $GABA_A$ receptors may play a role in moderate and deep sedation, but not rest/sleep posture.
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SIMULTANEOUS DETERMINATION OF THE EFFECTS OF METHAMPHETAMINE ON GABA, GLUTAMATE AND MONOAMINES BY MICRODIALYSIS IN THE PREFRONTAL CORTEX AND HIPPOCAMPUS OF RATS.

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Aims: Methamphetamine is a highly abused drug with complex pharmacological actions in the brain. Intracerebral microdialysis in freely-moving rats provides valuable insights in such cases, but is often limited by the number of neurotransmitters that can be measure in each sample. We have used this technique to investigate methamphetamine's effects simultaneously on GABA, glutamate (GLU), dopamine (DA), noradrenaline (NA) and 5HT in the prefrontal cortex (PFC) and hippocampus (HIP).
Methods: Under gaseous anaesthesia, 4.0 mm microdialysis probes were stereotaxically implanted into PFC (relative to bregma: AP +3.4mm; ML +/-0.8 mm; DV 5.0mm relative to dura) and HIP (AP -5.3mm; ML +/-4.8mm; DV -7.5mm) of male, Wistar rats (250-350g; n=5). Dialysate samples were collected at 15min intervals for 2h. GABA, GLU were analysed by UHPLC-ECD and DA, NA, 5HT by HPLCECD using Antec ALEXYS™ systems. Methamphetamine (3.0 mg/kg) was dosed IP.
Results: Compared with pre-intervention baseline values, methamphetamine produced rapid neurotransmitter changes that peaked 30-45min after dosing. In PFC, there were increases in DA (533%, p<0.001), NA (408%, p<0.001), 5HT (1500%, p<0.001), GABA (452%, p<0.05) and a decrease in GLU (-56%, p<0.001). In HIP the same pattern of effects was observed, but the changes in monoamines were much greater with increases in DA (1781%, p<0.001), NA (765%, p<0.001), 5HT (11,058%, p<0.001), GABA (451%, p<0.01) and a decrease in GLU (31%, p<0.01).
Conclusions: Methamphetamine produced large increases in DA and NA in PFC and HIP, but surprisingly its greatest effect was to potentiate 5HT efflux. The increases in extracellular monoamines were accompanied by concomitant reductions in GLU and increases in GABA in both regions. It is probable that decreased excitatory and enhanced inhibitory amino acid neurotransmission in PFC and HIP were homeostatic responses to attenuate the pharmacological effects of methamphetamine. The increases in 5HT may also have been part of this response.
Financial Support: None

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THE CHANGING NATURE OF OPIOID-RELATED MORTALITY IN AUSTRALIA.

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Aims: To investigate trends in all opioid-related mortality in Australia over time (2000 to 2013), as well as analyse differences in characteristics between heroin and pharmaceutical opioid (PO) deaths.
Methods: Data extracted from the National Coronial Information System (an online Australia-wide database that comprises all deaths reported to a coroner) on deaths where opioid toxicity was considered to have caused or contributed to the death.
Results: Prior to the disruption of heroin availability in Australia in 2001, heroin-related deaths comprised approximately 70% of all opioid-related deaths. From 2001 onwards, heroin deaths have comprised between 30 to 44% of these deaths. More recently PO (including morphine, codeine, oxycodone, methadone and fentanyl) have comprised the majority (70%) of opioid deaths. Heroin decedents were significantly younger, and more likely to be male compared to PO decedents. Preliminary analysis shows the majority (83%) of heroin decedents had a recorded history of injecting drug use (IDU). This figure was also high (63%) among fentanyl deaths. High proportions of oxycodone deaths had a recorded history of chronic pain (49%) and mental health problems (54%).
Conclusions: What distinguished heroin from PO deaths was that decedents were younger and more likely to be male. What distinguished PO deaths from heroin deaths was a history of chronic pain and mental health problems. Different clinical responses are clearly required in reducing both heroin and PO related mortality. While PO deaths are of increasing concern in Australia, heroin deaths are on the rise again after a sharp decline in 2001.
Financial Support: The National Illicit Drug Indicators Project (part of the Drug Trends program at the National Drug and Alcohol Research Centre) is funded by the Australian Government under the Substance Misuse Prevention and Service Improvement Grants.

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INFORMED CONSENT PRACTICES AMONG NIH-FUNDED RESEARCHERS.

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Aims: Participation in a study must be intelligent, knowing, and voluntary. The extent to which investigators utilize effective strategies to protect study participants is unclear. In this study, we surveyed researchers funded by NIH agencies including NIDA and NIAAA to determine what procedures they use to help ensure informed consent.
Methods: We invited principal investigators who received NIH R01 grant funding in 2012 (identified through NIH RePORTER) to complete a web-based survey. The 26-item survey took approximately 10 minutes to complete. A total of 673 investigators agreed to take part in the survey. Of these, 384 (57%) conducted research that required consent and were eligible for participation.
Results: Fifty-nine percent (N=220) conducted research with vulnerable populations. The majority (89%) relied on observation to determine capacity of subjects. Only 18% used a consent quiz to evaluate understanding of consent information. These quizzes utilized open-ended (67%) and true/false (34%) response formats. Almost all (97%) researchers provided participants with copies of the consent and 55% reminded them about their rights throughout the study. To ensure autonomy, researchers told potential participants that the decision to enroll was voluntary (99%), it would not affect their treatment (88%), delayed consent for further consideration (40%), and lowered compensation rates (37%). Most researchers (92%) indicated it was very important to remember consent information over the course of a study but less than half felt that this actually occurred.
Conclusions: Results from this study suggest that researchers generally do not employ standard procedures to determine whether consent is intelligent, knowing, and voluntary. It is necessary to identify ways to promote the widespread use of effective consent strategies. This is particularly true for research that is conducted with vulnerable populations including substance abusers, prisoners, and adolescents.
Financial Support: NIDA R01-DA-025687

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ASSOCIATION OF ALCOHOL USE WITH DRUG USE AND WEAPON CARRYING AMONG THAI ADOLESCENTS.

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Aims: Alcohol, drug use, and weapon carrying are a public health concern especially among students because they can have deleterious effects on physical and mental health. This study determined the prevalence of and gender specific factors associated with these behaviors among Thai adolescent students.
Methods: A cross-sectional study in high school and vocational school in Bangkok, Thailand was conducted in 2014. Self-administrated questionnaires assessed past 30 day behaviors among students between 11 and 18 years of age (2,561 students from 26 schools).
Results: Overall, one fourth (24.4%) of students reported past 30 day alcohol use, 2.5% reported drug use, and 7.8% reported weapon carrying. Older youth were more likely to report drinking than those younger (p<.0001). Multivariate logistic regression analyses showed that alcohol use was almost four times higher among drug users than nondrug users (OR 3.93). Students who carried a weapon had nearly three times the risk of drinking than their counterparts (OR 2.74). Overall, females who used drugs or who carried a weapon were 7.94 and 3.15 times respectively to report drinking compared to males. All other factors adjusted for were also more strongly associated with drinking among females than males; factors include number of friends who smoke (OR 2.66 vs OR 1.77), weight issues (OR 2.10), smoking (OR 5.36 vs OR 4.59), and energy drink use (OR 3.41 vs OR 2.04).
Conclusions: An increased association of drug use and weapon carrying with alcohol use was found for adolescent females in Thailand. Findings indicate gender specific interventions are needed for adolescents for these behaviors.
Financial Support: Financial support from the Thailand Research Fund through the Royal Golden Jubilee Ph.D. Program (Grant No. PHD/0184/2553) to On-anong Saiphoklang and Professor Kua Woongboonsin, PhD is acknowledged. And University of Florida Substance Abuse Training Center in Public Health (DA-T32-035167).

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REGIONAL GREY MATTER VOLUME AND EXTERNALIZING SCORE: NOT YET RELATED IN MIDDLE CHILDHOOD.

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Aims: Adolescents (ages 14-18 years) in treatment for substance use disorder (SUD) have less brain grey matter volume (GMV) than controls, a finding replicated for SUD and related phenotypes. Such results might either pre-exist and predict SUD, or could result from adolescent substance exposure.
Methods: We recruited 9-11 year old subjects (n=66, 32 female) about equally from control families and patient families (i.e., at least one first degree relative in SUD treatment). Subjects had no or minimal lifetime substance exposure. Brain structural scans were obtained using a 3T GE MRI scanner. Voxel-based morphometry analyses regressed regional brain volume against a predictor of future substance problems (Child Behavior Checklist externalizing behavior scores), while controlling for exact age and sex.
Results: No regions of GMV were significantly (positively or negatively) related to externalizing behavior scores.
Conclusions: We find that GMV, reduced in adolescents with SUD, is not reduced in younger children who are unexposed but at risk for SUD. Thus, GMV differences in adolescents with SUD may be related to substance exposure or developmental changes, which occur in adolescence. Although our sample size is similar to those in our prior studies, we may lack power to detect small differences, and large, longitudinal imaging studies are needed to confirm these findings. FreeSurfer analyses of cortical thickness in this sample will also be presented.
Financial Support: NIDA DA 09842, 11015 and 031761, The Kane Family and Hewit Family Foundations.

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TAURINE EFFECTIVELY INHIBITS COCAINE PREFERENCE IN MALE AND FEMALE RATS: CANDIDATE FOR SUD TREATMENT.

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Aims: Cocaine (COC) is a commonly abused psychostimulant that causes alterations to the mesocorticolimbic circuitry and addiction-related behaviors characterized by loss of inhibition to use. Females have been shown to be more vulnerable to the effects of COC when compared to males, requiring lower doses and less time of exposure before the onset of addiction. Taurine (TAU) is an organic acid with neuroprotective and neuromodulatory roles.Thi study aimed to determine if taurine could reduce cocaine preference in male and female subjects.
Methods: Male and female rats were pretreated with TAU (pre-tau; 100mg/kg) for two weeks before undergoing a conditioned place preference protocol. They were randomly divided into four groups (n=9/group): (1) TAU pretreatment (pre-TAU) and TAU + COC co-administration during conditioning, (1) pre-TAU and COC during conditioning, (3) pre-TAU and TAU during conditioning, and (4) COC during conditioning.
Results: Males and females that were not pre-treated with COC showed a significant preference to the COC-paired chamber. Neither male nor female subjects showed a preference to the TAU-paired chamber. Taurine was effective in inhibiting cocaine preference in both male and female subjects after the pre-TAU; however, females show a significant preference towards the cocaine-paired chamber when TAU and COC are co-administered.
Conclusions: Coc-induced behaviors often persist for years after abstinence and the best form of treatment is yet to be determined. This study provides evidence that taurine might deserve study as a treatment for cocaine addiction; however, sex may influence its efficacy. Further studies will be performed to assess possible mechanisms by which taurine inhibits cocaine preference, its relationship to gonadal hormones.
Financial Support: Supported by NIDA R25DA030310 (KSR); NCRR 5G12RR003060-26, NIMHHD 8G12MD7603-27 (EF, KSR); NIH MARC U*STAR 5T34 GM007639-32 (KU) ; K05DA015799 (J.C. Anthony, sponsor).

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HIV-RELATED STIGMA AND SUBSTANCE USE IN A RUSSIAN COHORT OF HIV+ RISKY DRINKERS.

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Aims: To determine whether HIV-related stigma contributes to substance use and dependence among HIV+ Russian individuals with risky alcohol use.
Methods: We used data from HERMITAGE, a randomized controlled trial of 700 HIV+ individuals with past 6-month risky sex and risky alcohol use in St. Petersburg, Russia (2007 to 2011). Demographics, clinical and behavioral characteristics were collected by survey at baseline, 6 and 12 months. We measured HIV-related stigma using the abbreviated Berger HIV-related stigma scale. We assessed past 30 day drug use (modified Risk Behavior Scale), risky alcohol use (Timeline Followback), and substance dependence (CIDI short form). Generalized estimating equations were constructed to examine the association between high HIV-related stigma (score $\geq 75^{th}$ percentile) and substance use over time (any prior 30 days heroin or stimulant or risky alcohol use [per NIAAA criteria]). Secondary outcomes were 1) any prior 30 days heroin or stimulant use; 2) prior 30 days risky alcohol use; and 3) past year alcohol or drug dependence. We adjusted for demographics, education, marital status, intervention group, time since HIV diagnosis, depressive symptoms, antiretroviral therapy use, CD4 count, and social support.
Results: At baseline, the mean age was 30 (SD 5) years, with 41% women. Twenty-eight percent reported high HIV-related stigma; 87% reported substance use in the prior 30 days. In adjusted models, high HIV-related stigma (AOR=0.86 [95% CI 0.51, 1.45]) was not significantly associated with substance use. These findings were similar for the secondary outcomes.
Conclusions: HIV-related stigma does not appear to be associated with substance use among risky drinkers. Future efforts to identify modifiable factors which contribute to substance use among HIV+ individuals with risky alcohol use are needed.
Financial Support: R01AA016059; K12DA033312; R25DA013582

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IMPACT OF TELEHEALTH IN-HOME-MESSAGING DEVICES ON ALCOHOL USE IN DUALLY DIAGNOSED VETERANS.

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Aims: The telehealth In-Home-Messaging Device (IHMD) is an electronic message-delivering and monitoring device that provides assessment and self-management education to patients in their home. We conducted an RCT that investigated the efficacy of IHMD's programmed with a substance abuse intervention, Substance Use Disorder Tele-Health Management Program ('IHMD-SUD'), compared to a treatment-control condition (TCC) for reducing alcohol consumption among dually diagnosed Veterans.
Methods: Veterans (n = 121) with alcohol use disorders were randomized to IHMD-SUD or TCC through the Charleston VAMC substance abuse outpatient program. IHMD-SUD (n = 62) consisted of two daily components spanning 27 days (~8 mins per day): 1) alcohol or drug use and risk assessment; and 2) self-management skills development dialogues designed to provide motivational, coping skills, and support-building. TCC (n = 59) consisted of four 1 hr. therapist-led group sessions consisting of standardized educational presentations on addiction. Data analyses utilized zero-hurdle Poisson models with random intercept to account for correlation between repeated measurements of the responses within subjects. Using the Time Line Follow Back, we assessed number of alcohol consumption and binge drinking days at 1 and 3-month follow-up.
Results: At 1-month follow-up, participants in IHMD-SUD *drank alcohol on significantly fewer days* (Est = -0.22, t = -2.45; p = .02) and demonstrated *fewer binge drinking days* (Est = -0.56, t = -4.73; p <.0001) compared to TCC. Differences at 3-month follow-up were N.S. on *number of alcohol consumption days*, although differences on *binge drinking days* between groups continued, favoring IHMD (Est = -0.43, t = -3.79; p < .001) compared to TCC.
Conclusions: IHMDs offering substance abuse treatment dialogues may offer a practical, accessible, and effective intervention for patients with substance use disorders, particularly for patients facing treatment barriers.
Financial Support: This study was supported by VA CSR&D (DA-2-016-08S) to PI: Dr. E. Santa Ana

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ESTIMATED RAPID TRANSITION FROM FIRST STIMULANT USE UNTIL ONSET OF STIMULANT DEPENDENCE: LARGER FOR METHAMPHETAMINE USERS?

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Aims: We expected newly incident methamphetamine users (NIMU) to show stimulant dependence transition probabilities (SDTP) resembling those seen for newly incident cocaine users (NICU; i.e., with 5%-6% becoming dependent within 12 months of 1st use), and with lower SDTP estimates seen for newly incident extra-medical users of stimulants (NIEMSU) when METH has not been used.
Methods: Data are from 2002-2011 US National Surveys on Drug Use and Health (RDAS), yielding nationally representative samples of more than 4,000 NIEMSU and NIMU, all assessed via confidential computer-assisted self-interviews. Estimates from five independent year-pair replications with analysis-weights and Taylor series variance estimation are summarized using meta-analysis.
Results: For NIEMSU, the meta-analytic SDTP estimate is 4.1% (95% CI=3.1, 5.0). For NIMU, the corresponding STDP estimate is 3.3% (95% CI= 1.5, 5.0).
Conclusions: Our presentation will extend this line of stimulant dependence research with subgroup analyses intended to help us understand lower STDP estimates for NIMU as compared to NICU and the NIEMSU with no METH use, which contradicted our expectations. Strata of interest involve METH injection versus other routes of administration, onset-age, which stimulant product is used by NIEMSU, and whether there is concurrent or past cocaine use.
Financial Support: NIDA OSR (T32DA021129); JCA (K05DA015799)

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CURRENT CHALLENGES IN IMPLEMENTING PRESCRIPTION MONITORING PROGRAMS.

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Aims: Prescription monitoring programs (PMPs) are electronic databases to track the dispensing of controlled substances, e.g., opioid analgesics. PMPs are important surveillance tools for monitoring the use/abuse trends of opioids. However, implementation barriers may limit their use and effectiveness. In support of a study evaluating the feasibility of implementing a PMP in the Department of Defense Military Health System, our aim was to conduct a literature review on PMPs including factors associated with their effectiveness.
Methods: An electronic search of PubMed for papers published from 1996 to 2014 using the key words 'Prescription monitoring programs' and 'Opioid abuse' yielded 85 articles.
Results: Emerging evidence supports the implementation of PMPs to reduce opioid misuse. Numerous barriers were identified. For example, sources identified the inability to link PMP data to electronic medical records, limitations on individuals ability to access PMPs (i.e., physicians but not their staff), passive versus active reporting systems, and participation in interstate prescription drug usage data sharing (i.e., to circumvent obtaining drugs from another state). A number of facilitators of successful PMP implementation were reported. These included physician training, active reporting system, and leveraging health information technology (HIT).
Conclusions: PMPs are potentially powerful tools for opioid risk mitigation. Effectiveness is limited by a variety of issues. Implementation is optimized by understanding how PMPs are used by health care providers.
Financial Support: None

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CHILDHOOD TRAUMATIC EXPERIENCE AND ILLICIT DRUG USE IN ADOLESCENCE, EMERGING ADULTHOOD, AND ADULTHOOD.

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Aims: We assessed associations between childhood traumatic experience and illicit drug use in adolescence, emerging adulthood, and adulthood in a nationally-representative sample.
Methods: Using data from Wave I (adolescence; respondent age: 7th-12th grade), III (emerging adulthood; age: 18-26 years) and IV (adulthood; age: 24-32 years) of the National Longitudinal Study of Adolescent to Adult Health (n=12,288 with sample weights), we measured nine types of childhood trauma: neglect; emotional, physical, or sexual abuse; parental incarceration; parental binge drinking; and witnessing, being threatened with, or experiencing violence. Indicators of ever having experienced each trauma were summed to create a score indicating cumulative traumatic dose. We measured associations between childhood trauma exposure and illicit drug use (marijuana, cocaine) at each wave.
Results: Approximately 56% experienced childhood trauma: 28% one trauma, 14% two traumas, 8% three traumas, 3% four traumas, 1% five traumas, and 0.6% ≥6 traumas. In adjusted analyses, we observed dose-response relationships between cumulative traumatic dose and adolescent marijuana use (odds ratio (OR) for one trauma *vs.* no trauma=1.66, 95% confidence interval (CI): 1.42-1.95; two traumas= 2.71, 95% CI: 2.24-3.28; ≥6 traumas=16.56, 95 % CI: 7.25-37.82) and cocaine use (OR for one trauma *vs.* no trauma=2.17, 95% CI: 1.38-3.41; two traumas= 2.78, 95% CI: 1.66-4.65; ≥6 traumas=4.01, 95% CI: 1.34-12.09). The cumulative traumatic dose likewise demonstrated a dose-response relationship with illicit drug use in emerging adulthood and adulthood. In models adjusting for covariates and all other traumas, each individual trauma was independently associated with either marijuana or cocaine use in adolescence, emerging adulthood, and/or adulthood.
Conclusions: Trauma-informed practice is needed to address substance use over the life course.
Financial Support: NIDA R01DA036414

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DRUG-SEEKING FOLLOWING EXTINCTION OF MDMA SELF-ADMINISTRATION: ROLE OF DOPAMINE AND SEROTONIN.

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Aims: The present study was designed to determine the role of dopamine and serotonin in cue- and MDMA-produced drug seeking.
Methods: Rats self-administered MDMA during daily 2 hr sessions until a total of 350 mg/kg had been self-administered (25-40 days). Sessions then increased to 6 hr and continued until responding was stable (7-14 days). Thereafter, daily extinction trials were conducted during which MDMA was replaced with vehicle solution and the light stimulus was omitted. When responding decreased to 20% or less of baseline, drug-seeking tests were conducted during which rats were injected with a range of dopamine or serotonin ligands either alone or prior to MDMA. Responding on the previously active MDMA lever was reinforced with reintroduction of the light stimulus that had been paired with self-administered infusions but only saline infusions were delivered.
Results: Reintroduction of the light stimulus reinstated extinguished MDMA responding. This effect was potentiated by MDMA (2.5-10.0 mg/kg), amphetamine (1.0 mg/kg), GBR12909 (1.0-10.0 mg/kg) and quinpirole (0.5-1.0 mg/kg), but not by apomorphine (2.0-4.0 mg/kg), SKF81297 (1.0 - 4.0 mg/kg), DOI (1.0 mg/kg), mCPP (0.6-2.5 mg/kg), clomipramine (10.0 mg/kg), or 8-OHDPAT (0.003 - 1.0 mg/kg). The MDMA potentiation of drug-seeking was decreased by the dopamine antagonists, SCH23390 (0.02-0.04 mg/kg) and eticlopride (0.0125-0.05 mg/kg) but not by serotonin antagonists, WAY 100635 (0.03 - 1.0 mg/kg) or GR127935 (1.0-3.0 mg/kg). A marginal attenuation of MDMA-produced drug seeking was observed following pretreatment with ketanserin (1.0-10.0 mg/kg) or ritanserin (5.0.- 10.0 mg/kg)
Conclusions: The data support the idea that drug-seeking following extinction of MDMA self-administration is mediated by dopaminergic mechanisms and that serotoninergic mechanisms play little, if any, role in this response. These findings are consistent with the idea that following MDMA self-administration sensitized dopamine responses underlie the continued self-administration of this drug.
Financial Support: Supported by funds from Victoria University of Wellington.

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HIGHER LEVELS OF BDNF ARE ASSOCIATED WITH INPATIENT TREATMENT ADHERENCE OF CRACK-COCAINE USERS.

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Aims: To evaluate the association between BDNF levels in crack users during inpatient treatment and its association with treatment adherence**.**
Methods: 66 male inpatient crack users (mean age = 33.89 ± 8.65, average number of rocks/month = 300) were recruited in a treatment unit, and blood samples were collected at intake and discharge, in order to measure BDNF serum levels. Average length of stay for the whole sample was 26 days. Subjects were divided into treatment completers (n=32) and treatment non-completers (n=34). Drug use pattern and sociedemographic data were assessed using the ASI-6.
Results: When comparing BDNF levels between intake and discharge, we observed a trend of increase only in the subjects who completed the whole program (completers: mean difference average of 1.672 [-0.39 - 3.73], p=0.108 – non-completers: -0.097 [-2.17 - 1.97], p=0.924). Treatment completers had significantly higher levels of BDNF (17.76 ± 5,03) when compared to non-completers at discharge (14.78 ± 5.36) (p=0.025).
Conclusions: Our findings suggest an association between higher levels of BDNF and inpatient treatment completion in crack users. We hypothesize that these individuals may have less impulsivity due to brain injuries caused by drug use, especially in executive functions, which will be tested in future studies. These results related to changes in BDNF levels during the course of treatment may help identify important biological markers that can determine prognosis and perhaps develop tailored treatments according to patient characteristics.
Financial Support: National Secretariat of Drug Policies - SENAD**.**

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BODY TEMPERATURE AND CARDIOVASCULAR EFFECTS OF SOME SYNTHETIC CANNABINOIDS FOUND IN "SPICE" PRODUCTS.

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Aims: Products containing synthetic cannabinoids have seen increased use recently. These drugs produce subjective effects similar to THC. However, because of their unique chemical structures and high potency, we sought to compare the physiological effects of these drugs with those of THC.
Methods: Separate groups of male rats were implanted with telemetry transmitters for either the measurement of body temperature or blood pressure (BP). In addition to THC (0.3–1.0 mg/kg), we tested: CP55940 (0.01–0.3 mg/kg), JWH018 (0.1–3.0 mg/kg), AM2201 (0.03–0.3 mg/kg), XLR11 (0.3–3.0 mg/kg) and UR144 (0.3–3.0 mg/kg). Rats were injected s.c. prior to being placed in an isolation cubicle on top of the telemetry receiver. Rats were monitored for 3 h. Rimonabant (1 mg/kg) and AM630 (5 mg/kg) were given prior to selected drugs.
Results: All of the cannabinoids produced clear decreases in body temperature of up to 3°C during the last 2 h of the session. The order of potency was CP55940 > AM2201 = JWH018 > THC = XLR11 = UR144. The hypothermic effects were reversed by pretreatment with the CB1 antagonist rimonabant. None of the drugs had a significant effect on heart rate. Rats injected with the synthetic cannabinoids, except UR144, showed elevated BP in the first h following the injection when compared to vehicle. The order of potency was CP55940 > AM2201 > JWH018 = XLR11. Rimonabant had a similar effect on BP, while the combination of rimonabant plus CP55940 had effects intermediate to the drugs alone. The CB2 antagonist AM630 did not alter the BP effect of CP55940.
Conclusions: On body temperature the synthetic cannabinoids mimicked the effects of THC. Rats treated with the synthetic cannabinoids were more likely to show higher BP following treatment, an effect not seen with THC. Although the hypertensive effect was modest, our results illustrate that there may be differences from THC in the effects of the synthetic cannabinoids.
Financial Support: Intramural Research Program of NIDA, NIH, DHHS.

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EVALUATION OF RELATIVE INTRANASAL ABUSE POTENTIAL OF A HYDROCODONE EXTENDED-RELEASE TABLET FORMULATED WITH ABUSE-DETERRENCE TECHNOLOGY IN NONDEPENDENT, RECREATIONAL OPIOID USERS.

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Aims: Misuse and abuse of opioids is a serious public health concern. A hydrocodone bitartrate extended-release (ER) tablet, made with CIMA® Abuse-Deterrence Technology, resists rapid release of hydrocodone when tablets are crushed or taken with alcohol. This study examined the relative abuse potential of finely milled intranasal hydrocodone ER in healthy nondependent adults with a history of recreational, intranasal opioid use.
Methods: Subjects able to tolerate a 45-mg intranasal dose of hydrocodone active pharmaceutical ingredient (API) powder and discriminate effects of hydrocodone from placebo were randomized into a double-blind, 5-period crossover, treatment phase. Subjects received each of the following: intranasal finely milled hydrocodone ER 45 mg, intranasal hydrocodone API 45 mg, intact oral hydrocodone ER 45 mg, intranasal finely milled Zohydro 45 mg, and matching placebo.
Results: In total, 34 subjects were evaluable for pharmacodynamics assessed through 48 hours after administration of drug. Maximum effect (E_{max}) of "at this moment" drug liking based on a bipolar Visual Analog Scale (VAS; primary endpoint) was significantly (P=0.004) lower for hydrocodone ER (72.8) vs. hydrocodone API (80.2) and Zohydro (83.2) and significantly (P<0.001) higher vs. oral hydrocodone ER (57.3) and placebo (58.6). E_{max} of end-of-day/next-day Overall Drug Liking VAS (co-primary endpoint) was also significantly (P=0.004) lower for hydrocodone ER (68.5) vs. hydrocodone API (77.1) and Zohydro (79.8) and significantly (P≤0.001) higher vs. oral hydrocodone ER (57.8) and placebo (57.7). No new safety signals were seen.
Conclusions: Abuse potential via the intranasal route, a common route of abuse, was significantly lower with hydrocodone ER vs. non–abuse-deterrent opioid products, including Zohydro. When administered intact orally, liking scores for hydrocodone ER were similar to placebo.
Financial Support: Study sponsored by Teva Pharmaceuticals (Frazer, PA).

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PILOT STUDY OF ATOMOXETINE FOR BUP/NX-MAINTAINED PATIENTS WITH CO-OCCURRING OPIOID AND ATS USE DISORDER.

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Aims: To evaluate the tolerability, acceptability, and potential efficacy of the selective norepinephrine transporter inhibitor atomoxetine for treating amphetamine-type stimulant (ATS) use disorder in patients receiving buprenorphine/naloxone (BUP/NX).
Methods: Patients with opioid and ATS use disorder with ≥ 2 days per week ATS use (N=66) were inducted on BUP/NX (16-24 mg daily) and withdrawn from ATS during 10-14 days as inpatients, randomized to daily atomoxetine 80 mg (n=33) or placebo (n=33) administered double blind, and continued medications for 16 weeks following hospitalization. All patients received manual-guided counseling. Urine toxicology testing and self-reported drug use were assessed at baseline and weekly. Mixed models procedures were used to compare proportions of ATS-negative urine tests and the number of days abstinent from ATS in 4 successive 4-week intervals. Results were analyzed for the intention-to-treat (ITT) sample and for patients with high adherence (≥60 days of atomoxetine (n=12) or placebo (n=16)).
Results: Baseline demographic and drug use characteristics and treatment retention did not differ significantly between treatment groups. In the ITT sample, atomoxetine was associated with significantly fewer days per week of ATS use (p=0.038) and a higher proportion of ATS-negative urine tests (p=0.14). Among high adherence patients, days per week ATS was significantly lower (p=0.005) and the proportion of ATS-negative urine tests was significantly higher (p=0.017) with atomoxetine. One placebo-treated patient died at week 14 of liver failure; there were no other serious adverse events.
Conclusions: The findings of this pilot study of high retention, no serious adverse effects, and greater reductions in ATS use associated with atomoxetine support the tolerability, safety and potential efficacy of atomoxetine for treating ATS use disorder in this population.
Financial Support: DA014718; State of CT; USM

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DOES DRUG OF CHOICE MATTER IN MHEALTH DELIVERY? COMPARISON OF METHAMPHETAMINE AND HEROIN DEPENDENT PATIENTS.

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Aims: mHealth tools can be an effective way to provide motivation and coping strategies in real-time in substance abuse treatment. While there is growing evidence that individualized feedback is key ("clean counter" for days abstinent, graphs of craving and use), less is known regarding how drug of choice impacts desired features of phone apps aimed at promoting recovery. This study investigates the perspectives of patients receiving methadone maintenance treatment (MMT) for heroin dependence versus those in treatment for methamphetamine (MA) dependence.
Methods: 40 MMT and 10 MA out-patients participated in separate focus groups aimed at gathering information on how best to design a phone app for enhancing coping skills when faced with high risk situations. All focus groups were audio taped and transcribed. Atlas.ti7 was used to analyze data.
Results: Overall, MA patients were younger in age, had less time in treatment, and more likely to be in treatment due to external factors (e.g., drug court). Patients agreed that a phone app recovery tool would be helpful for finding AA/NA meetings, providing coping messages, and giving general health information. MMT patients wanted more medical messages, specifically those related to foods and medications that affect the liver, coping strategies for chronic pain, and health tips for HCV; conversely, MA patients were less interested in physical health but thought that some tips on sleep and weight gain would be helpful. MA patients were interested in having the app connect them to "felon friendly" jobs, daycare, and educational opportunities. MA patients also noted that the app would be most beneficial at the very start of treatment and again upon moving into aftercare.
Conclusions: Design and implementation of a phone app as an adjunct to treatment should consider the needs associated with different drug-using populations. Variations in age, lifestyle, and motivation should be taken into account in order to optimize utilization of mHealth tools.
Financial Support: NIDA R21DA033285-01A1, P30DA016383 (PI: Hser)

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A RANDOMIZED DELAYED IMPLEMENTATION TRIAL OF COMPUTERIZED BRIEF INTERVENTION FOR DRUG MISUSE.

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Aims: Our prior randomized trial found that computerized brief intervention (CBI) was as effective as in-person brief intervention (IBI) delivered by a behavioral health counselor in two primary care clinics in New Mexico. However, that study lacked an assessment only control condition. The present study examined the effectiveness of CBI relative to assessment only using a randomized delayed implementation design.
Methods: Patients at a community health center in New Mexico with moderate-risk drug use (N=80) were randomly assigned to receive CBI immediately, or after a 3-month delay. Follow-up interviews were conducted at 3- and 6-months post-baseline. Measures included the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) and hair testing for marijuana, cocaine, amphetamines, and opiates. Data were analyzed using generalized linear mixed models and logistic regression.
Results: Most participants reported moderate-risk marijuana use at baseline (90%). There were decreases in Global (p=.009) and Marijuana-specific ASSIST scores (p<.001) in both the immediate and delayed conditions. Analyses revealed no significant differential between-group decreases for global drug risks (p=.06), marijuana-specific risks (p=.89), drug-positive hair tests for any drug (p=.35) or marijuana specifically (p=.14).
Conclusions: This trial, while small and potentially underpowered, was unable to establish the effectiveness of CBI compared to an assessment only control condition in reducing drug use or drug risks. Decreases in ASSIST scores can be attributed to regression to the mean or assessment reactivity.
Financial Support: NIDA Grant Number 1 R01DA026003

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A COMPARISON OF MALE AND FEMALE CAREGIVERS: CAREGIVER DEPRESSION AS A MEDIATOR IN THE PATHWAY FROM CAREGIVER PROBLEMATIC DRUG USE TO CHILD INTERNALIZING BEHAVIORS.

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Aims: Among families reported to child protective services (CPS), caregiver PDU is a common concern that has been associated with negative outcomes for children, including CIB. Comparing female to male caregivers, this paper tests the role of caregiver depression as a mediator in the relationship from caregiver PDU to CIB.
Methods: Using data from the National Survey of Child and Adolescent Well-Being II (NSCAW II), path analysis models were conducted utilizing a subset of the NSCAW II in which the children remained in the home following a CPS investigation. A random half sample was drawn (n=1087) to conduct two separate models for female and male caregivers. Results were confirmed on the second half of the sample. PDU was measured continuously with the 20-item Drug Abuse Screening Test. Caregiver depression was measured with the Composite International Diagnostic Interview-Short Form. CIB was measured continuously with the internalizing subscale of the Child Behavior Checklist. Control variables were child age, child gender, and family poverty. Analyses accounting for stratification, clustering, and weighting were conducted with Mplus 7.0. Standardized estimates and asymmetrical confidence intervals are reported.
Results: Female caregivers' depression was found to fully mediate the relationship from PDU to CIB (μ=.048, σ=.015, 95% CI .021-.081). Among male caregivers, depression was not a significant mediator in the relationship from PDU to CIB (μ=.007, σ=.039, 95% CI - .068-.099). Fit for the female caregiver model was strong (RMSEA=.000, p=.99; CFI=1.00).
Conclusions: Among families reported to CPS where a female caregiver is engaged in PDU, the presence of comorbid depression is an important indicator of need for intervention. Addressing these comorbid disorders may lead to decreases in CIB. Unavailable in this dataset, future research should examine anxiety as another potential mediator.
Financial Support: F31DA034442; T32DA015035; Doris Duke Fellow; Fahs-Beck Scholar

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PATIENT PRE-TREATMENT EXPECTATIONS AND SUBSTANCE USE TREATMENT OUTCOMES.

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Aims: To determine if expectations at pre-treatment are associated with substance use treatment outcomes.
Methods: Treatment expectations were examined in two randomized controlled trials (RCTs) utilizing Motivational Enhancement Therapy (MET) for the treatment of substance use conducted in the CTN. One RCT was delivered in English (MET-E) and one was delivered in Spanish (MET-S). There were 461 participants MET-E sample and 405 participants MET-S. Participants responded to the following item at pre-treatment: "Do you think you will reduce or stop your use of drugs or alcohol as a result of this treatment?" ANOVAs and chi-square tests were used to examine the relationship between treatment expectations and treatment outcomes in the two samples.
Results: Treatment expectations were not associated with any of the treatment outcomes in MET-E. However, in MET-S, expectations were significantly associated with most of the post-treatment outcomes. Among these, treatment expectations were significantly associated with the percentage of drug positive urines within the treatment period, F (1, 1,163) = 18.83, p = .000, and the percentage of days abstinent from primary drug use while in treatment and through follow-up, F (1, 1,364) = 23.78, p = .000.
Conclusions: There are several possible interpretations to the divergent findings between samples. The first is that the MET-S sample had fewer previous treatments, and that when a treatment is novel, expectations may have more of an influence. The second interpretation is that there may be cultural components that may affect how an individual relates to the treatment process. These findings are preliminary and future research should examine treatment expectations across cultures.
Financial Support: This research was supported in part through a National Institute on Drug Abuse (NIDA) T-32 grant, 5T32DA007238-23 (Petrakis), and used data from studies that were funded by the Clinical Trials Network.

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DOES CRAVING INTENSITY INFLUENCE CUE EXPOSURE REPORTS? AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY IN PATIENTS WITH ALCOHOL, TOBACCO, CANNABIS AND HEROIN USE DISORDER.

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Aims: Although it is now well established that exposure to substance-related cues could induce craving, less studies have examined if individuals experiencing higher levels of craving are more likely to report exposure to cues. Here, we aimed to examine the influence of craving intensity in the prediction of cue exposure reported in daily life.
Methods: A total of 132 participants were recruited from an outpatient addiction clinic and completed 2 weeks of computerized ambulatory 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 craving intensity and exposure to cues. Data were analyzed using hierarchical linear models (HLM) to examine the influence of craving intensity (T0) on later reports of cues (T1: 4 hours later).
Results: Craving intensity at T0 strongly predicted number of cues (γ = 0.104, p<0.001) reported at T1. As craving intensity also predicted later substance use and as substance use was associated with same time cue reports, we ran an additional model controlling for substance use at T1. Craving intensity remained a good predictor of later reports of cues (γ = 0.072, p<0.01).
Conclusions: In this study individuals who are experiencing higher levels of craving were more likely to report exposure to cues at the next assessment, even after controlling on substance use at T1. We hypothesize that craving increases the consciousness of cues and that individuals who are experiencing higher levels of craving are more likely to notice cues. Further studies are needed to explore this hypothesis.
Financial Support: PHRC 2006, MILDT 2010, CRA 2009, PRA-CNRS-CHU 2008, CNRS ATIP

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ASSESSING ABERRANT BEHAVIORS RELATED TO PRESCRIPTION DRUGS IN THE PATIENT POPULATION: RECENT STUDIES, METHODOLOGIES AND FINDINGS.

Beatrice Setnik[3], Cynthia Kornegay[4], Marta Sokolowska[2], Carl L Roland[1], Pierre Geoffroy[3]; [1]Pfizer Inc, Cary, NC, [2]Grunenthal, Bedminster, NJ, [3]INC Research, Toronto, ON, Canada, [4]CDER/OSE/OPE, FDA, Silver Spring, MD

Aims: Aberrant behaviors related to prescription drug use in the patient population remains to be an understudied phenomenon. Whilst there are several tools that may help to predict risk or estimate a patient's predisposition to drug abuse, limited tools are available that can assess and quantify events related to prescription abuse, misuse, and diversion that occur in the patient setting. Some studies suggest that up to 80.5% of the patient population evaluated may have exhibited one or more aberrant behaviors related to prescription drugs such as opioids [1-4]1. Passik SD, Pain Med. 2014 Aug;15(8):1365-72, 2. Passik SD, J Pain Symptom Manage. 2011 Jan;41(1):116-25, 3. Fleming MF, Pain Med. 2008. 9(8):1098-1064, 4. Setnik B., American Pain Society Meeting. May 2013. Since prescription drugs are primarily intended for the patient, assessing and understanding the complexity of this issue in this vulnerable population is critical. Various newer methods and findings from clinical and database studies that have assessed aberrant behaviors in the patient population will be reviewed and summarized. Clinical perspectives from high risk patients with substance use disorder will be discussed and methodological approaches will be covered. Also, the regulatory perspective will be provided with relevant updates from a recent study in progress assessing prescription opioid abuse, misuse, overdose, and addiction, in a population of pain patients receiving long-acting opioids[5].5. http://www.fda.gov/Drugs/NewsEvents/ucm384489.htm
Results: Based on review of available data, aberrant prescription opioid drug taking behaviors related to abuse and misuse are prevalent in the patient population. Furthermore, this population is infrequently studied for such risks. It is integral to refine methodologies and tools to better assess the prevalence of presence of abuse and misuse in the patient population and to mitigate such risks.
Conclusions: Based on review of available data.
Financial Support: Submission fee supported by INC Research.

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REDUCED ACC RESPONSE TO PRESENTATION OF NEGATIVE FEEDBACK DIFFERENTIATES STIMULANT ABUSERS FROM NON-ABUSERS AND PREDICTS ABSTINENCE AT 12-MONTHS.

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Aims: Several studies suggest substance abuse is characterized by deficient error-monitoring; however, the precise nature and clinical importance of this deficit remain largely uncharacterized.
Methods: Forty-nine stimulant abusers and 26 non-abusers performed a time-estimation task specially designed to isolate neural responses associated with the expectation and presentation of contingent negative feedback. On each trial, participants received feedback regarding their attempts to estimate a one-second duration. On *Informed trials,* feedback consisted of a plus or minus sign (indicating accuracy or inaccuracy). On *Uninformed trials*, feedback consisted of a question mark (thus providing no indication of accuracy). Whereas participant's performance necessarily differed on *Accurate* versus *Inaccurate* trials, the $Inaccurate_{INFORMED}$>$Inaccurate_{UNINFORMED}$ contrast differed only in the nature of the presented feedback. Thus, the task afforded a careful parsing of participants' neural reactivity to the presentation of contingent feedback, unconfounded by any differences in performance or expectation.
Results: Stimulant abusers showed reduced ACC response following negative feedback in the $Inaccurate_{INFORMED}$>$Inaccurate_{UNINFORMED}$ contrast (with expectancies controlled; *FWE-corrected*, that disappeared in the $Inaccurate_{INFORMED}$>$Accurate_{INFORMED}$ contrast (with expectancies uncontrolled; *p>.30).* Additional analyses indicated that only expectation-controlled ACC activity a) predicted magnitude of post-feedback behavioral adjustments, b) correlated with years of stimulant use, and c) predicted abstinence 12-month later.
Conclusions: This is the first study to demonstrate reduced neural response to the presentation of negative feedback in stimulant abusers, despite seemingly intact formation of error expectancies. Evidence that this deficit predicts severity of use history, as well as future abstinence success, suggests that it may hold considerable clinical significance.
Financial Support: NIH support to MSS (5R01DA026932)

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SELF-REPORTED DRUG USE PATTERNS FOR DRUG USERS PRESENTING IN EMERGENCY DEPARTMENT.

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Aims: To understand the patterns of daily self-reported drug use among participants enrolled in the National Drug Abuse Treatment Clinical Trials Network (NIDA CTN)-sponsored Screening, Motivational Assessment, Referral and Treatment in the Emergency Department (SMART-ED) clinical trial.
Methods: In the SMART-ED study, daily self-reported drug use data were collected via Time-line Follow Back (TLFB) at baseline to assess the 30-day baseline measure of substance use and for 90-day periods during follow-up prior to the 3, 6 and 12 month follow-up visits. Patterns of daily drug use (self-reported drug use percent on a given day) using line plots over the one-year period were investigated to describe short-term temporal variations over 7 day periods to describe impact of day of the week, as well as temporal variations over longer periods of time.
Results: There was a reduction in self-reported drug use days over the one-year period. For cocaine, baseline self-reported drug use reduced from 12% for the 30 days prior to baseline to 8% for the 90 days preceding the Month 3 visit, 6.4% for the 90 days preceding the Month 6 visit, and 5.4% for the 90 days preceding the Month 12 visit. Although there was higher self-reported use for cannabis and any drug, similar trends were observed over the one-year period. For the weekly temporal patterns, self-reported drug use percent was always higher on Friday and Saturday (Any drug = 46%-47%, Cannabis = 30%-31% and Cocaine = 9.1%-9.5%) compared with other days of the week (Any drug = 40%, Cannabis = 25%-26% and Cocaine = 6%-6.4%). Moreover, the weekly self-reported drug use pattern was similar throughout the assessment period for a given visit.
Conclusions: This study helps understand the pattern of the self-reported drug use in patients presenting in an emergency department. Overall, the percent of drug use days continues to decrease over time, suggesting attending a follow-up visit as part of the research study may have impacted self-reported drug use. Higher drug use on Fridays and Saturdays shows weekend effect on the self-reported drug use.
Financial Support: NIDA-HHSN271201400028C/N01DA-14-2237.

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PREVALENCE AND PATTERNS OF THE USE OF NOVEL PSYCHOACTIVE SUBSTANCES, "*KIKEN* DRUGS", AMONG YOUNGER ADULTS AT DANCE PARTIES IN JAPAN.

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Aims: The abuse of *kiken* drugs, including synthetic cannabinoids, is a growing health problem in Japan. "*Kiken* drugs" is a general term for novel psychoactive substances (NPSs) that have not been legislated as illegal under Japanese law. The aim of this study was to examine the prevalence of NPS use and their using patterns in younger adults at dance parties in Japan.
Methods: An anonymous field-based survey was conducted using laptop computers between Aug 2012 and Nov 2013 at four dance parties at three different venues in Tokyo. Participants were asked about their lifetime use of NPSs by type (herbs, powders, liquids) and their using patterns.
Results: The questionnaires were completed by 307 (44% female, median age 30 years) partygoers. Among the participants, 24.4% reported NPS use (herbs 22.8%, powders 7.2%, and liquids 3.3%) in their lifetime. The primary reasons for NPS use were peer pressure (37.3%), and curiosity (37.3%). In addition, 61.3% reported obtaining NPSs from close friends. Compared with non-liquid users, liquid users were significantly more likely to use as a couple ($p = 0.048$). Moreover, liquid users were significantly likely to use at hotels ($p = 0.001$) and in vehicles ($p = 0.002$).
Conclusions: Our results clearly suggest that younger adults at dance parties have a higher lifetime prevalence of NPS use than the Japanese general population (0.4% reported in 2013). As the social stigma associated with drug use is extremely high in Japan, law evaded, easily available *kiken* drugs may be more acceptable among partygoers. The present study also indicates that liquid-type products may be used as "sex drugs". Some basic studies have reported that synthetic cathinone was detected in liquid-products; such products may enhance sexual pleasure.
Financial Support: This study was supported by HLSRG from the Ministry of Health, Labour and Welfare of Japan.

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CHILDHOOD MALTREATMENT AND ALCOHOL USE IN YOUNG ADULTHOOD: THE ROLE OF SELF-REGULATION.

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Aims: Exposure to childhood maltreatment (CM) has been linked to alcohol use and dependence in young adulthood. However, few studies have examined the pathways linking CM to alcohol use in young adulthood. We examined if individual differences in self-regulation processes are a critical factor that mediates the association between exposure to CM and risk for alcohol use and dependence.
Methods: Young adults (N=339; 52% females; mean age=21.7) were recruited from the community, and participated in an hour-long structured interview. A battery of assessments completed by the participants included the Childhood Trauma Questionnaire, Wills Self-Control Scale, Brief Symptom Inventory, Rutgers Alcohol Problem Index, and Structured Clinical Interview for DSM-IV. We performed two separate analyses of structural equation modeling (SEM) to specify the roles of two related, but different self-regulations (i.e., behavioral self-regulation and emotional self-regulation) in linking CM to later alcohol use. We also examined the effects of CM subtypes (e.g., physical abuse, neglect) on four types of alcohol use including drinking frequency, binge drinking, alcohol-related problems, and alcohol dependence.
Results: The final models fit the data well (CFI > .95; RMSEA ≤ .04). Structural modeling analyses indicated indirect effects for CM primarily through pathways to both poor behavioral and emotional self-regulation. In a SEM analysis for emotional self-regulation, the paths from CM to poor emotional self-regulation to level of alcohol use were greater for pathological drinking behaviors such as binge drinking and alcohol-related problems than frequency of alcohol use.
Conclusions: We found that both behavioral and emotional self-regulations play a significant role in linking CM to problematic alcohol use in young adulthood. The results of this research suggest that self-regulation processes would be potentially useful targets to prevent problematic alcohol use among young people who have exposure to CM.
Financial Support: This research was supported by NIDA (DA030884) and the AMBRF/The Foundation for Alcohol Research to Dr. Shin.

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STATE-LEVEL TOBACCO-RELATED NORMS AND POLICIES SHOW DIFFERENTIAL EFFECTS ON CIGARETTE SMOKING IN POPULATION SUBGROUPS.

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Aims: Determining how the potentially modifiable group-level tobacco-related norms and policies work together with individual-level risk factors to influence cigarette use is important to more fully understand the impact of these group-level norms and policies, and inform efforts to change them to benefit public health.
Methods: With data from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions (N=34,638), a nationally representative sample of US adults, we investigated the associations between past-year cigarettes per day (CPD), individual-level risk factors (childhood maltreatment, parental substance problems) and state-level norms and policies (perception of risk due to smoking, average price per pack of cigarettes, smoke-free air laws). Using additive interaction, we determined if the state-level variables showed different effects in subgroups defined by the individual-level risk factors.
Results: All individual risk factors and state-level policies/norms were significantly related to CPD. Significant interactions showed that each state-level factor showed significantly greater effects among respondents with each individual risk factor than those without. For example, among respondents with parental substance problems, respondents in states with lower cigarette price smoked 1.5 more CPD than respondents in states with higher cigarette price. Among respondents without parental substance problems, respondents in states with lower cigarette price smoked 0.2 more CPD than respondents with higher cigarette price (interaction p-value=0.003).
Conclusions: Tobacco-related state-level variables have stronger effects in higher risk subgroups. A more complete understanding of these state-level effects can inform the design of improved public health prevention and intervention strategies, including tobacco control policies.
Financial Support: Supported by U01AA018111-01, K05AA014223, K01AA021511, T32DA031099, New York State Psychiatric Institute.

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CORRELATION BETWEEN PFC GYRIFICATION AND WHITE MATTER INTEGRITY IN YOUNG CANNABIS USERS.

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Aims: Our lab previously found reduced gyrification in prefrontal (PFC) regions and reduced frontolimbic white matter (WM) integrity among young adult cannabis users compared to controls. Here, we examined the relationship between PFC gyrification and underlying WM microstructure in cannabis users and non-using controls. Based on others' findings, we hypothesized that lower PFC gyrification would be correlated with reduced WM integrity in both groups.
Methods: Participants were 33 emerging adult cannabis users and 34 controls without major neurological, psychiatric disorders or heavy other drug use. Participants underwent a MRI and drug use interview. Variables included anterior, medial (mPFC), and ventral (vmPFC) gyrification indices, and mean diffusivity (MD) and fractional anisotropy (FA) of frontolimbic tracts (Uncinate fasciculi, UNC; corpus callosum forceps minor, fMinor). Pearson R correlations determined the association between indices.
Results: Among cannabis users, there were positive correlations between fMinor MD and mPFC and frontal poles, and left UNC MD and left vmPFC. Negative correlations were found between fMinor FA and left mPFC and left frontal pole, and bilateral UNC FA and left vmPFC (*p's*=.003-.03). No significant associations were found in controls.
Conclusions: These findings suggest that frequent cannabis use in youth may impact the association between PFC gyrification and underlying WM cohesion. While users in this sample demonstrated reduced gyrification compared to controls, those with the lowest gyrification had better WM integrity, suggesting possible compensation. Due to a lack of significant associations in controls, this may also represent a disrupted relationship between WM integrity and gyrification in chronic cannabis using youth. Future studies should characterize the association between brain indices in a longitudinal design.
Financial Support: 1R03DA027457 PI Lisdahl; AOP fellow Shollenbarger; T32 DA015036 Price

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AN EXPLORATORY HUMAN ABUSE POTENTIAL ASSESSMENT OF CENTANAFADINE, A NOVEL TRIPLE REUPTAKE INHIBITOR.

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Aims: Centanafadine (CTN) is a triple reuptake inhibitor (TRI) under development for treatment of attention-deficit hyperactivity disorder (ADHD), as it inhibits reuptake of norepinephrine and dopamine (DA), both known to mediate symptoms of inattention, impulsivity and hyperactivity in ADHD. Since TRIs inhibit DA reuptake, the potential for misuse and abuse should be considered. This exploratory study assessed CTN's abuse potential in recreational stimulant users.
Methods: In this double-blind, randomized 5-way crossover study, 36 recreational stimulant users received single oral doses of CTN (400 and 800 mg), damphetamine (d-AMP 40 mg), lisdexamfetamine (LDX 150 mg) and placebo. Eligible subjects passed a qualification session to ensure they could discriminate and like the effects of dAMP. In the treatment phase, subjective effects (visual analog scales [VAS], Addiction Research Center Inventory [ARCI] scales) and safety measures were assessed up to 24 hours after each dose.
Results: Maximum Drug Liking VAS (DL E_{max}) was significantly higher for d-AMP and LDX vs. placebo ($p<0.05$), confirming study validity. DL E_{max} for CTN was higher than placebo and numerically, but not statistically lower than dAMP and LDX. Minimum DL (E_{min}) for CTN was significantly lower compared to placebo, dAMP and LDX, indicating significant disliking. Bad Effects and Nausea VAS scores revealed distinct aversive effects of CTN compared with d-AMP, LDX and placebo. CTN had significantly lower E_{max} scores on ARCI Amphetamine and ARCI Benzedrine Group scales compared with d-AMP and LDX. CTN was associated with a higher incidence of nausea (eg, 56.3% at 800 mg) and emesis (59.4%) vs. d-AMP, LDX and placebo (0-3%).
Conclusions: These exploratory results indicate that CTN's subjective effects profile is distinct from that of dAMP and LDX, and suggest a lower abuse potential compared with these typical stimulants.
Financial Support: Neurovance, Inc.

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GENDER DIFFERENCES IN ASSOCIATIONS BETWEEN NEUROCOGNITIVE IMPAIRMENT AND COCAINE USE AMONG HIGH-RISK COCAINE-DEPENDENT METHADONE-MAINTAINED PATIENTS.

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Aims: Previous research suggests possible gender-related interactions between cognitive-deficits and cocaine use; however, no studies specifically explain gender-based differences in neurocognitive impairment (NCI) among cocaine-users receiving clinical-care. Knowledge about this association can aid in the development of targeted prevention strategies to reduce adverse health outcomes. This study was designed to examine the role of gender in the relationship between NCI and cocaine-use among cocaine-users receiving substance-abuse treatment.
Methods: The Neuropsychological Impairment Scale (NIS) was administered to 199 cocaine-dependent methadone-maintained patients (98 males; 101 females) to assess NCI by identifying patients' awareness of neuropsychological symptoms. T-test comparison was done to find neurocognitive differences between males and females and multiple regression analysis was used to explore the relative contribution of gender to NCI.
Results: Consistent with prior work, high NCI was evident within this sample, as indicated by high scores on most of the NIS subscales. Females reported greater impairment than did males as evidenced by significantly higher scores on several NIS subscales, after controlling for age and years of cocaine-use. Interestingly, cocaine craving significantly predicted NCI among males but not among females, as suggested by significant association between cocaine craving and all except one of the NIS subscales.
Conclusions: These findings suggest that cocaine-users enter into treatment with a range of NCI – with women having significantly more neurocognitive deficits than men - that may contribute to differential treatment outcomes. This highlights the need to include additional services, such as neuropsychological screening and gender-specific treatment programs, to optimally reduce adverse health outcomes in these high-risk cognitively impaired patients.
Financial Support: NIDA Grants (R01-DA022122; K02DA033139) to Michael M. Copenhaver

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INTERIM BUPRENORPHINE TREATMENT: LEVERAGING TECHNOLOGY TO BRIDGE WAITLIST DELAYS.

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Aims: Despite the undisputed effectiveness of agonist maintenance for opioid dependence, opioid-dependent individuals can remain on waitlists for months before treatment becomes available. One highly efficacious effort to mitigate the risks associated with these delays is interim methadone treatment (daily medication + emergency counseling only). However, restrictive federal regulations on methadone may limit the widespread use of this approach. We aim to develop a novel Interim Buprenorphine Treatment (IBT) for waitlisted patients that includes buprenorphine dispensed via a computerized device (Med-O-Wheel Secure, Finland), daily patient monitoring via an Interactive Voice Response (IVR) phone system, IVR-issued random call-backs for urinalysis and pill counts, and HIV+Hepatitis education via iPad.
Methods: Following initial piloting with 10 opioid-dependent adults, we will evaluate the efficacy of IBT in 70 participants randomized to IBT (n=35) or a Waitlist Control (WLC; n=35). IBT participants will visit the clinic bimonthly while receiving the above components; WLC participants will remain on their waitlists but complete the same follow-up assessments as IBT.
Results: We recently completed piloting with 10 participants (35.7±9.4 yrs old, 50% female). Most (90%) reported a prescription opioid as their primary drug, 40% had a history of IV use, and the mean waitlist duration was 3.4±4.2 months. IBT produced robust decreases in illicit opioid use, with 100% positive urines at intake decreasing to 20% during the 12-week study. Adherence was also high, with participants completing 98% of daily IVR calls and satisfying 87% of random call-backs.
Conclusions: Current treatment capacity is inadequate in many areas of the country, and opioid abusers are at high risk for morbidity and mortality during delays to treatment. IBT may reduce illicit drug use and associated risks during this time. In addition to these pilot study outcomes, our June 2015 presentation will also include data from the randomized trial.
Financial Support: NIDA R34DA037385, NIGMS P20GM103644

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ADOLESCENT SUBSTANCE USE AND SPECIFICITY OF ASSOCIATION WITH EDUCATIONAL ATTAINMENT IN YOUNG ADULTHOOD.

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Aims: Concerns have been raised about the extent to which adolescent alcohol and cannabis use may have specific and non-specific effects on psychosocial outcomes. We examined the association between adolescent alcohol use and educational under-achievement in young adulthood, comparing the findings with those for adolescent cannabis use.
Methods: We integrated participant-level data from 3 longitudinal studies: the Australian Temperament Project, the Christchurch Health and Development Study, and the Victorian Adolescent Health Cohort Study. We investigated the association between the maximum frequency of alcohol/cannabis use before age 17 (never, less than weekly, weekly or more) and failure to complete high-school, failure to enrol in university, and failure to obtain a degree by age 25. The number of participants varied by analysis (N= 2037 to N=3678).
Results: There was a lack of a robust association between adolescent alcohol use and educational attainment. After adjustment, adolescent alcohol use (weekly+) was weakly associated with only high-school non-completion (OR=1.51, 95%CI=1.04, 2.22); whereas adolescent cannabis use (weekly+) was strongly associated with all educational outcomes (high-school non-completion, OR=1.84, 95%CI=1.25, 2.72; university non-enrolment, OR=1.54, 95%CI=1.08, 2.22; degree non-attainment, OR=2.22, 95%CI=1.54, 3.20).
Conclusions: Individual, parental and peer factors explain much of the association between early alcohol use and later educational under-achievement. Findings provide evidence of the specificity of the relationship between early cannabis use and subsequent educational attainment, strengthening the case for the drug's harmful effects on adolescent development.
Financial Support: The study was supported by an NHMRC Project Grant. NDARC at UNSW is supported by funding from the Australian Government.

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SOCIOECONOMIC DISPARITIES IN ELECTRONIC CIGARETTE USE AMONG ADOLESCENTS.

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Aims: Low socioeconomic status (SES) is associated with engagement in health-risk behaviors such as cigarette smoking. However, the association between SES and electronic cigarette (e-cigarette) use among adolescents is unknown. Thus, we examined the relationship between SES and cigarette and e-cigarette use among adolescents.

Methods: Participants (n = 1,888; 51.3% female; 85.6% White; M age = 16.0 years), drawn from a larger study of smoking, completed school-wide surveys in spring 2014. We assessed SES with the Family Affluence Scale (Boyce & Dallago, 2004), which provides composite scores corresponding to low, medium or high SES. We combined low and medium SES groups into one category, as only 2.1% of participants were low SES. We used logistic regression to examine whether dichotomized SES (low/medium SES = 1; high SES = 0) was associated with lifetime cigarette and e-cigarette use. We used multinomial regression to examine whether SES was associated with preference for cigarette, e-cigarette or neither.

Results: Altogether, 23% of participants reported cigarette use, 34% reported e-cigarette use and 41% reported low/medium SES. Controlling for race, age and gender, low/medium SES, relative to high SES, was associated with increased odds of cigarette (OR 1.8; 95% CI 1.3, 2.3) and e-cigarette (OR 1.8; 95% CI 1.4, 2.3) use. Low SES, relative to high SES, was not associated with odds of preferring e-cigarettes relative to cigarettes (OR .7; 95% CI .4, 1.3).

Conclusions: Lower SES, relative to higher SES, is a risk factor for adolescent smoking regardless of cigarette delivery method (i.e. conventional or electronic).

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WEAVING EVIDENCED-INFORMED, CULTURE-BASED INTERVENTIONS INTO TREATMENT IN NATIVE AMERICAN AND ALASKA NATIVE COMMUNITIES.

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Aims: In the current climate of increasing mandates on the use of Evidenced Based Practices (EPB), it is becoming increasingly evident that in Indian Country, these mandates need to be tempered with a respect and appreciation for Native culture, knowledge, healing practice and a sensitivity of cultural context in order to be effective with the American Indian and Alaska Native communities.

There are Native Americans (NA) holding traditional spiritual beliefs being diagnosed with psychosis and OCD while operating appropriately within the context of their traditional spiritual beliefs. EBP were not developed nor validated within NA communities and are not necessarily a good fit for NAs given their traditional beliefs. Additionally, the concept of a mandate is in conflict with the concept of tribal sovereignty.

Methods: In our project, we invited spiritual leaders and identified medicine men and women from Canada, Alaska, the Southwest, Southeast, and Upper Midwest United States to come together for a discussion on spirituality, cultural issues and treatment of behavioral disorders with non-Native behavioral health providers. This forum raised awareness by providing education and a dialogue between NA spiritual leaders and providers. This approach leads to dissemination of knowledge within the behavioral health workforce.

Results: Through the education of providers, we can help them provide more culturally informed care to their NA clients and, subsequently help NA achieve better health.

Conclusions: Appropriate diagnosis and treatment must occur with respect and as much understanding of the cultural context (and the clients' level of assimilation) as is possible in order to be effective.

Financial Support: This project is funded by SAMHSA.

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TREATING IMPULSIVITY FOR COCAINE AND FOOD IN FEMALE AND MALE RATS BY REPURPOSING THERAPEUTICS.

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Aims: The ability to engage in recreation drug use requires one to forgo drug use until an appropriate time and place. For instance, many problem users are prone to consume drugs throughout the day, including at work. Treating such compulsions is an important component in treating individuals with drug abuse problems.

Methods: The present research modeled impulsive choice for cocaine and food in rats. Specifically female and male rats were given a choice between a larger-later and smaller-sooner alternative. In some conditions, choices were between amounts of food (1 or 3 food pellets) and in others, doses of cocaine (.3 mg/kg or .9 mg/kg infusions of cocaine). In both conditions, once preference for the large alternative was established, delays to the large alternative were introduced and increased each session in ascending order (7.5, 15, 30, 60 sec). Following establishment of a delay gradient (large preference decreased across delay), rats were treated with Progesterone (.05 mg/kg), Atomoxetine (1.5 mg/kg) or together as a combination treatment to determine how they altered impulsivity for food and cocaine.

Results: Rats' preference for the large alternative decreased with increases in large-alternative delay to form a delay gradient. When choosing between doses of cocaine, treatment with Atomoxetine and Progesterone decreased impulsivity (increased large alternative preference relative to baseline) compared to vehicle control in female rats. However, when choosing between amounts of food, neither treatment altered impulsive choice compared to baseline.

Conclusions: The initial findings suggest that both Progesterone and Atomoxetine reduce impulsivity for cocaine, but not impulsivity for food. A mechanism thought to the effect is that these treatments reduce the reinforcing efficacy of cocaine; follow-up studies employing a progressive ratio schedule were conducted to examine this possibility. These findings suggest the treatments employed could serve as an effect component in the treatment of cocaine addiction.

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THE EFFECTS OF STRENGTH TRAINING ON HEROIN 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 heroin self-administration in rats responding on a fixed ratio (FR1) schedule of reinforcement.

Methods: Female, Long-Evans rats were obtained as young adults and assigned to exercising or sedentary conditions. Exercising rats climbed a vertical ladder wearing a weighted vest and were trained 6 days/week for the duration of the study. Training in this group used a three-set "pyramid" in which the number of repetitions and amount of resistance varied across three sets: 8 climbs carrying 70% body weight (BW), 6 climbs carrying 85% BW, and 4 climbs carrying 100% BW. Sedentary control rats were placed repeatedly on the ladder turned horizontally on its side to equate handling and exposure to the apparatus. After 3 weeks, rats were implanted with intravenous catheters and heroin self-administration was examined on an FR1 schedule of reinforcement.

Results: Heroin self-administration was significantly lower in exercising rats than sedentary rats when responding was maintained by low and moderate doses of heroin. These effects were not due to nonspecific differences in operant responding because no differences were observed in responding during a saline substitution test.

Conclusions: These data indicate that resistance exercise decreases the positive reinforcing effects of heroin and suggest that strength training may be an effective intervention for opioid use disorders.

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CHILDHOOD ADVERSITY, STRESS-SENSITIZATION, AND LOWER LIKELIHOOD OF CIGARETTE SMOKING CESSATION IN A U.S. NATIONALLY REPRESENTATIVE SAMPLE: A STUDY OF SEX DIFFERENCES.

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Aims: Research has documented important sex differences in relation to early stress, stress-sensitization, and psychiatric outcomes. The current study was the first to investigate whether sex differences in stress-sensitization extended to cigarette smoking cessation.
Methods: Data were analyzed from the National Epidemiologic Survey on Alcohol and Related Conditions (waves 1 and 2), selecting for current smokers at wave 1 (n = 3,751 men; n = 4,155 women). The primary statistical tests of interest were three-way interactions between sex, childhood adversity, and stressful life events in the prediction of smoking cessation.
Results: Among women, stressful life events (financial stress, interpersonal violence/crim victimization, and moving/having someone come live with you) were more strongly related to smoking cessation among those with childhood adversity than those without. This interaction was not found among men.
Conclusions: The interaction between childhood adversity and stressful life events (i.e., stress-sensitization) may be more saliently related to smoking cessation among women than men.
Financial Support: Funding for this study was provided by Grant Number P50 DA033945 from the National Institute on Drug Abuse (NIDA), the Food and Drug Administration (FDA), and the Office of Research on Women's Health (ORWH), OD, awarded to S.A.M. Funding was also provided by the Yale B.I.R.C.W.H. Scholar Program on Women's Health and Addictive Behaviors (NIDA, NIAAA; K12 DA031050; PI: Carolyn Mazure).

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DIVERTED BUPRENORPHINE USE AMONG APPALACHIAN PEOPLE WHO USE DRUGS.

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Aims: This study examined illicit buprenorphine use among a cohort of people who use drugs (PWUD) in rural Appalachia.
Methods: Rural Appalachian PWUD (n=503) were recruited to participate in an ongoing longitudinal study to assess HIV risk and social network characteristics through interviewer-administered questionnaires; the present study was a cross-sectional analysis of the sixth wave (n=415). Participants were asked about frequency of and motivation for use, route of administration, source, and cost of diverted buprenorphine. Desire for and barriers to buprenorphine treatment were also assessed, as well as other illicit drug use. Mann-Whitney tests were used to compare continuous variables and Fisher's exact tests were used to compare categorical variables.
Results: Of those completing the sixth follow-up interview, 36.4% (n=151) reported using illicit buprenorphine (tablets and/or film) in the previous six months; 86.1% (n=130) reported only using buprenorphine film. The primary sources of buprenorphine were dealers (63.5%) and family members or friends (24.6%). The primary motivation behind using illicit buprenorphine was self-detox (34.4%) and most used buprenorphine orally (86.9%). There was a significant association between the route of administration and motivation for use of buprenorphine film; oral administration was associated with self-detox, while injection use was associated with wanting to get high (p=0.04). Nearly half of the respondents (46.0%, n=58) indicated they were interested in receiving buprenorphine treatment, but noted cost as the primary barrier (81.0%).
Conclusions: Given that the majority of subjects who use illicit buprenorphine (film or tablets) are using it correctly (i.e., orally) and many are using it to self-treat, the need for increasing availability of and access to office-based opioid dependence treatment using buprenorphine is clear.
Financial Support: Grants awarded to Dr. Jennifer Havens by NIDA (R01DA024598 and R01DA033862).

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EFFECTS OF WORKING MEMORY TRAINING REGIMEN ON LEARNING ACQUISITION AND SCORE ASYMPTOTE IN ALCOHOL DEPENDENTS.

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Aims: The competing neurobehavioral decision system theory states that a regulatory imbalance between the impulsive and executive decision systems is present in addicts. Previous literature shows that training working memory (WM) restores balance by strengthening executive system function and, as a result, decreases impulsive decision-making in stimulant addicts and reduces alcohol consumption in problem drinkers. Clinical translation of this approach would benefit from identifying the WM training dose that leads to sustained improvement.
Methods: In the present study, alcohol-dependent participants were allocated to one of three WM training dose groups. Using the Cogmed© adaptive visual-spatial and verbal WM training program, high, medium, and no dose participants underwent 20, 10, and 0 active training sessions, respectively. Prior to active training, participants completed control sessions where exercises were performed at the lowest level of training (non-adaptive training). The number of control plus active sessions equaled 22 for all groups. Curve fits for acquisition learning of the WM training were compared between the high- and medium-dose groups.
Results: In all 6 WM training modules, learning curves for the high dose group reached higher max score plateau values over medium dose, of which 3 reached significance ($p<0.05$). Further, significant differences were obtained in the rate of acquisition.
Conclusions: While these data show that WM can be trained in alcohol dependent participants using Cogmed© WM regimens, it also suggests that control sessions may constrain the achieved asymptote. Collectively, the data from this on-going study support the trainability of alcohol dependent individuals and may suggest some detrimental aspects of a control condition.
Financial Support: Research supported by NIH R01 AA021529.

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SCIENTIFIC WRITING SEMINAR TO HELP EARLY-STAGE INVESTIGATORS PUBLISH RESEARCH.

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Aims: In the addictions field there is insufficient information on how to increase the writing productivity of early-stage investigators. Possible ways to increase productivity range from brief "check ins" (Edwards, 2002) to classes and formal writing groups (Gianaros, 2006). We found no published studies addressing this issue; thus we aimed to fill a knowledge gap by reporting outcomes of a scientific writing seminar for postdoctoral fellows offered over 14 years.
Methods: 113 postdoctoral trainees participated in 14 cohorts of the writing workshop conducted from 1999-2012. Ongoing records of submission and publication rates were analyzed. The writing seminar, called the Writers' Task Force, occurred annually in 10 sessions over five months. Offered through NIDA training and center grants, the focus was on drug abuse treatment and services research. The initial meeting framed expectations, modeled the review process used in the seminar, and had fellows commit to writing and reviewing their work in future sessions. Remaining meetings focused on fellows' manuscripts, with copies distributed a week before, author presentation of issues, three critiques by colleagues, and discussion. The seminar sometimes included presentations on writing/publishing topics but emphasized the active processes of writing and review.
Results: Of the 113 participants, 98 (87%) submitted a manuscript for publication, and 88 participants (78%) published their manuscript. Mean time to publication after the end of the writing seminar was 2.68 years (SD = 1.49), and the median time to publication was 2 years.
Conclusions: In this evaluation there was no control group, and the submission and publication rates of these papers without the seminar is unknown. A scientific writing seminar may benefit writing productivity; more research is needed to compare this training model to other approaches.
Financial Support: NIH P50DA09253, T32DA07250, U10DA015815, P50DA09253, R25DA035163

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DISRUPTION OF SEROTONIN 5-HT_{2C} RECEPTOR (5-HT_{2C}R) INTERACTION WITH PROTEIN PHOSPHATASE AND TENSIN HOMOLOGUE (PTEN) RESULTS IN DISTINCT PATTERNS OF CORTICAL PHOSPHORYLATED EXTRACELLULAR-SIGNAL REGULATED KINASE$_{1/2}$ ($PERK_{1/2}$).

Claudia Soto[1], Noelle C Anastasio[1], Sarah E Swinford-Jackson[1], Robert G Fox[1], Huang C Du[2], Scott Gilbertson[2], Kathryn A Cunningham[1]; [1]Ctr Addiction Res, University of Texas Medical Branch, Galveston, TX, [2]Dep Chem, University of Houston, Houston, TX

Aims: The 5-HT_{2C}R in the medial prefrontal cortex (mPFC) mediates relapse vulnerability in preclinical studies of cocaine use disorder. The mechanisms through which the 5-HT_{2C}R modulates mPFC signaling are understudied. The 5-HT_{2C}R interacts with $Ga_{q/11}$ leading to nuclear $pERK_{1/2}$ translocation and also directly associates with β-$arrestin_2$ resulting in cytoplasmic $pERK_{1/2}$ sequestration. $pERK_{1/2}$ subcellular localization dictates its functional impact on signal transduction. Protein:protein interactions emerge as a mechanism to shift 5-HT_{2C}R signal transduction towards a given pathway and thereby regulate $pERK_{1/2}$ subcellular distribution. Disruption of 5-HT_{2C}R:PTEN by TAT-3L4F potentiates 5-HT_{2C}R agonist-induced $pERK_{1/2}$ *in vitro*. We tested the hypothesis that 5-HT_{2C}R stimulation and/or disruption of 5-HT_{2C}R:PTEN results in distinct mPFC $pERK_{1/2}$ subcellular distribution.
Methods: Male Sprague-Dawley rats received saline, 5-HT_{2C}R agonist WAY163909 (1 mg/kg), TAT-3L4F (10 μmol/kg), or the combination of WAY163909 *plus* TAT-3L4F. The mPFC tissue was harvested (20 min post-treatment) and nuclear and cytoplasmic $pERK_{1/2}$ levels evaluated by immunoblotting.
Results: WAY163909 increased nuclear and cytoplasmic $pERK_{1/2}$ vs saline ($p<0.05$). TAT-3L4F increased cytoplasmic ($p<0.05$), but not nuclear $pERK_{1/2}$. WAY163909 *plus* TAT-3L4F increased cytoplasmic ($p<0.05$), but not nuclear, $pERK_{1/2}$.
Conclusions: TAT-3L4F may sequester $pERK_{1/2}$ in the cytoplasm through a β $arrestin_2$-dependent mechanism while WAY163909 induces a distinct mPFC $pERK_{1/2}$subcellular distribution. These data also suggest that disruption of 5-HT_{2C}R:PTEN may alter WAY163909-induced intracellular signaling pathways (i.e., shift in $pERK_{1/2}$ from the nuclear to soluble fraction). Taken together, these data provide novel insight into the mechanisms through which 5-HT_{2C}R modulates signaling in the mPFC.
Financial Support: DA030977, DA020087, DA033374, DA07287

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CIGARETTE SMOKING TRAJECTORIES AMONG COMORBID COCAINE-DEPENDENT AND ATTENTION DEFICIT/ HYPERACTIVITY-DISORDER INDIVIDUALS TREATED WITH EXTENDED-RELEASE MIXED AMPHETAMINE SALTS.

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Aims: To determine whether cocaine use correlates with nicotine use in ADHD/ cocaine dependent individuals, and to examine the effects of MAS-XR on smoking in this population.
Methods: The original randomized, double-blind, 14-week placebo controlled trial was conducted at Columbia University and at the University of Minnesota. This secondary analysis targeted treatment seeking adults who met DSM-IV criteria for ADHD, used cocaine ≥4 times in the past month at consent, and were cigarette smokers (≥1 cigarette per day; ≥4 days per week). Participants were randomly assigned to MAS-XR (80mg), MAS-XR (60mg), or placebo (n=37). This analysis combined the two active treatment arms (n=61). Cigarette smoking was assessed via self-report. Linear mixed effects models were used to model cigarette smoking as a function of cocaine use and treatment interaction.
Results: The correlation between cocaine use and smoking was significant for both the MAS-XR group and the placebo group ($p<0.0001$). Patients smoked 1.3 more cigarettes on cocaine-using days when compared to non-cocaine using days. There was a significant interaction between treatment and placebo groups for the amount spent on cocaine as a predictor of smoking ($p=0.01$). Specifically, patients receiving MAS-XR spent $43 more on cocaine to increase their smoking by 1 cigarette, while patients receiving placebo spent $56 more on cocaine for the same result.
Conclusions: Cocaine use correlates with smoking habits in both MAS-XR and placebo treated patients. For those who continue to use cocaine, MAS-XR with concurrent cocaine use may trigger greater smoking among ADHD/cocaine dependent smokers when compared to the placebo group.
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BRAZILIAN CRACK/COCAINE INPATIENTS SHOW MORE LEGAL AND FAMILY SOCIAL PROBLEMS THAN OUTPATIENTS.

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Aims: There is lack of information about crack/cocaine users characteristics and what kind of treatment they seek in puclic health. To compare drug use and psychosocial characteristics of crack/cocaine users of inpatient and outpatient in public health.
Methods: 768 male and female drug users were recruited in two Addiction Psychiatric Inpatient Unit and six Psychosocial Care Centers/CAPS from six Brazilian state capitals. Subjects were divided into two groups: A)inpatients (n=219, mean age=29.43 ± 8.06; 64.4% caucasian, 47.9% never married; 39.3% completed high school) and B)outpatients (n=549, mean age=32,45 ± 8,57; 32,2% non-white; 38,8% never married; 48,5% completed elementary school). ASI-6 was applied by trained psychologists. Normal and asymmetric variables were compared through t-student test and Mann-Whitney test, respectively.
Results: ASI-6 showed significant differences between the two groups: Alcohol Use (A: median of 52.5; B: 58, $p<0.001$), Medical Problems (A: mean=46.01 ± 7.82; B: 50.20 ± 9.66, $p=0.005$), Legal Problems (A: median of 59; B: 46, $p<0.001$), Employment (A: median of 35; B: 42, $p<0.001$) and Family Social Problem (A: median of 58; B 54, $p<0.001$). Regarding Psychiatric Problems, Drug Use, Social Family Support and Child Problems, there were no significant differences between groups.
Conclusions: This is one of the first multicenter studies that evaluate characteristics of crack users in Brazil. Our findings suggest that inpatients show more Legal and Family Social Problems than outpatients. Adversely, outpatients show more problems related to Alcohol Use, Medical Problems and Employment. These results indicate that approaches need to be developed according to specific profiles.
Financial Support: Brazilian National Secretariat on Drug Policies #005/2009

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MODULATION OF REINSTATED POLYDRUG (COCAINE/ HEROIN) SEEKING BY NORADRENERGIC α_2 AGONISTS.

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Aims: Noradrenergic α_2 agonists can alleviate opioid withdrawal and have been proposed for prevention of relapse to stimulant abuse. We investigated the potential of these drugs for attenuating relapse to polydrug (cocaine/heroin) abuse using a nonhuman primate model of reinstated drug seeking.
Methods: Squirrel monkeys were trained to respond under concurrent second-order FR10 (FR5:S) schedules of i.v. cocaine/heroin (10:1) self-administration and milk delivery. Responding on the drug-associated lever subsequently was reduced to ~10% of baseline by discontinuing drug injections and presentations of the drug-paired stimulus, while keeping the concurrent schedule of milk delivery intact. We next determined the degree to which drug seeking could be reinstated by: 1) restoring the drug-paired stimulus, 2) priming with a 10:1 cocaine/heroin mixture, or 3) priming + restoration of the drug-paired stimulus. Each condition was studied after pretreatment with vehicle or doses of α_2 agonists that had no significant effects on an inventory of unconditioned behaviors: 0.1 mg/kg clonidine, 0.1 mg/kg lofexidine, 1.0 mg/kg guanfacine, and 0.03 mg/kg brimonidine.
Results: Pretreatment with each α_2 agonist attenuated reinstatement of drug-seeking induced by cocaine/heroin priming and had less effect on reinstatement induced by the drug-paired stimulus. Clonidine, lofexidine, and guanfacine also attenuated the more pronounced reinstatement induced by priming + restoration of the drug-paired stimulus. Additionally, clonidine and lofexidine reduced % responding on the drug-associated lever when reinstatement was induced by priming alone and/or priming + restoration of the drug-paired stimulus.
Conclusions: The profile of effects seen with clonidine and lofexidine (attenuation of reinstated responding with a reduction in % responding on drug lever) suggests a selective effect of these α_2 agonists on reinstated drug seeking and encourages further evaluation of their potential for polydrug relapse prevention.
Financial Support: NIH grants DA031299, RR00168 and OD011103.

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APPLYING SBIRT TO NEW SETTINGS: PRELIMINARY FINDINGS OF SUBSTANCE USE DISORDER RISK IN COMMUNITY MENTAL HEALTH SETTINGS.

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Aims: Aims: Screening, Brief Intervention, and Referral to Treatment (SBIRT) has not yet been tested in community mental health treatment settings despite the elevated risk of substance use disorders (SUD) among individuals with mental health disorders. This presentation reports on preliminary findings of SUD risk among 334 adult participants treated in community mental health clinics in Southern California. SUD risk was calculated from the AUDIT and DAST-10 screening tools.

Methods: Methods: All participants are currently enrolled in a randomized controlled trial of SBIRT. Participants were recruited from four outpatient clinics and one inpatient clinic. High risk for SUDs was defined by scores on the AUDIT (≥13 for women and ≥15 for men) and the DAST-10 (≥3 for women and men). Associations between SUD risk and presence of mood disorders, anxiety disorders, and psychotic disorders were examined using chi-square tests.

Results: Results: Results showed that 37% of participants were at high risk for alcohol disorders and 66% of participants were at high risk for illicit drug use disorders. Alcohol disorder risk was significantly associated with mood disorders (X^2=13.25, p<.01) and anxiety disorders (X^2=8.6, p<.05). Illicit drug use disorder risk was significantly associated with anxiety disorders (X^2=25.96, p<.001). Presence of psychotic disorders was not associated with SUD risk.

Conclusions: Conclusions: High rates of SUD risk in this community mental health sample were found. Participants with mood and/or anxiety disorders were found to be at high risk of SUDs. Subsequent research will test the efficacy of SBIRT for reducing SUD risk and linking participants with possible SUDs to treatment.

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PRESCRIPTION MONITORING PROGRAMS: BEST PRACTICE AND CANADIAN PROGRAM REVIEW.

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Aims: Prescription monitoring programs (PMPs) are one important component of an overall strategy in addressing prescription drug abuse. The objectives of this review were to examine research evidence to support best practices in PMPs and to review PMPs in Canada.

Methods: As an update to a previous review, a search from 2012 to May 2014 was conducted using PubMed, PsycINFO, Project Cork and Google Scholar to identify articles about the effectiveness of PMPs. Search terms included: prescription drug monitoring, prescription monitoring, doctor shopping, multiple prescribers, unsolicited reporting, proactive reporting and controlled substance monitoring. Grey literature sources included individual PMP websites, PMP organization websites and Google. Information on the features and practices of the PMPs in Canada was obtained by reviewing program websites and telephone interviews conducted with key contacts from each program.

Results: PMPs have varied features and practices, including models of administrative oversight, drugs targeted for monitoring, methods of data collection, types of interventions and degree of information sharing. There are very few research studies evaluating the effectiveness of PMP features or overall performance; primarily observational studies are available. Several best practice recommendations have been suggested based on opinion and experience. In Canada, there are currently seven provinces operating some form of a PMP and two provinces with programs in development; all have different histories and features and are not linked.

Conclusions: There is limited supporting research evidence for most aspects of PMPs at this time, although there is growing research attention in the area, and the number of research reports is increasing each year. As programs across Canada continue to be developed and expanded, further work is needed to evaluate the various features of PMPs to determine their impact, and to establish the overall value of PMPs in promoting the safe and effective use of prescription products that are associated with significant harms.

Financial Support: Alberta Health

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HEALTH RELATED ISSUES AMONG PEOPLE WHO INJECT DRUGS IN AUSTRALIA.

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Aims: The Illicit Drug Reporting System (IDRS) monitors the price, purity and 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 other issues related to drug use including injection-related problems and mental health. This presentation provides a closer look at health-related issues among people who inject drugs interviewed in the 2014 IDRS.

Methods: The IDRS involves the collection and analysis of three data sources: (1) interviews with people who inject drugs (IDRS), (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: Nationally, around 900 people who inject drugs were interviewed for the IDRS in 2014. Less than one-fifth of people who injected drugs reported lending a needle or using a needle after somebody else. Around one-quarter reported sharing injecting equipment (not including needles), around half re-used their own needle and over half re-used injecting equipment. Over half reported an injection-related issue in the last month, mainly scarring/bruising. Self-reported mental health problems in the last six months were reported by around half of the national sample. The most common mental health problem reported was depression followed by anxiety. IDRS participants reported higher levels of distress on the Kessler Psychological Distress Scale 10 compared to the Australian general population.

Conclusions: A greater understanding of the health-related issues among people who inject drugs regularly is required to better inform policy decisions and treatment delivery.

Financial Support: The IDRS Project is supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvement Grants Fund

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DOES URBAN SIZE AND REGION PREDICT OUTPATIENT SUBSTANCE ABUSE TREATMENT COMPLETION?

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Aims: This study examines the influence of urban size and region on the likelihood of treatment completion for outpatient settings using the 2011 SAMHSA TEDS-D dataset.

Methods: Logistic regression was employed using treatment completion as the dependent variable (N=897,888). Two geographic variables served as independent variables. 'City size' is a five-class ordinal variable representing the population of the U.S. Census metropolitan or micropolitan region in which the subject resides, ranging from areas with a population of less than 50,000 to greater than 750,000. 'Geographic division' distinguishes among the ten U.S. Census-defined regional divisions of the U.S. (e.g. Mid-Atlantic, New England). The Mid-Atlantic division (New York, Pennsylvania, and New Jersey), which is the division with the highest number of subjects in the data set, served as the reference category. We also controlled for the subject's age, race, sex, primary substance use problem, and severity of use.

Results: The resulting model had an overall percentage correct=60.4%, and a Receiver Operating Curve (ROC) analysis resulted in an Area Under the Curve=0.63, p<0.005). Results indicate that larger city size is associated with a greater likelihood of treatment completion, and while the city size odds ratio is relatively small (OR=1.05, p<0.005), it is of greater magnitude than the odds ratio for sex (where males are significantly more likely to complete treatment). Geographic division was also highly significant, with certain divisions such as the Mountain division (e.g. Colorado, Utah) showing a particularly higher likelihood of treatment completion (OR=2.07, p<0.005) compared to the Mid-Atlantic division. Other divisions, such as the East North Central division (eg. Ohio and Michigan) showed a significantly lower likelihood (OR= 0.73, p<0.005).

Conclusions: Treatment effectiveness at a system level may be improved by examining these geographic variations in outpatient outcomes. Further research needs to identify the reasons for these locational differences in treatment completion.

Financial Support: None.

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EFFECTS OF VARENICLINE AND GZ-793A ON METHAMPHETAMINE AND FOOD SELF-ADMINISTRATION UNDER A MULTIPLE SCHEDULE OF REINFORCEMENT IN RATS.

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Aims: Currently there is no FDA pharmacological treatment for methamphetamine (METH) addiction. A widely accepted preclinical model used to develop and test potential pharmacotherapies is the rodent intravenous (i.v.) self-administration paradigm. The aim of the current study was establish rodent i.v. self-administration under a multiple schedule with alternating components of METH and food reinforcement. Once behavior stabilized on this schedule we tested two potential pharmacotherapies for METH addiction: GZ-793A, a vesicular monoamine transporter 2 (VMAT2) inhibitor and varenicline, a partial agonist at a4b2 nicotinic acetylcholine receptors (nAChR).
Methods: Following catheterization surgery, male Sprague-Dawley rats acquired both i.v. METH (0.3 mg/kg/infusion) and food self-administration under a multiple schedule of reinforcement. Following stable responding pretreatments of GZ-793A (0, 10, 15, or 30 mg/kg, s.c.) and varenicline (0, 0.3, 1, or 2 mg/kg, s.c.) were administered in a Latin Square design with half of the animals receiving GZ-793A first while the other half received varenicline first.
Results: Both GZ-793A and varenicline decreased METH self-administration. However, GZ-793A was more selective at decreasing METH intake without altering food-maintained responding. More specifically, the 20 mg/kg of GZ-793A significantly decreased METH intake compared to saline without effecting food-maintained responding. Also, the lowest dose of GZ-793A significantly decreased METH intake compared to the lowest dose of varenicline, again without disrupting food-maintained responding. No dose of varenicline significantly lowered METH intake compared to a saline control.
Conclusions: Cumulatively, this suggests that VMAT2 inhibition, rather than nAChR partial agonism, is a more promising avenue to pursue for a potential pharmacotherapy for METH addiction
Financial Support: This project was funded by the Ferlic Summer Research Fund to MMK.

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WOMEN'S INTERVENTION TO STOP HIV/HCV (WISH).

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Aims: *Background*: The Appalachian region has been the focus of national media highlighting the serious problems arising from prescription opiate abuse. Rural drug users report that injection is the primary method of drug administration in this area. Injection drug use creates significant public health concern among an understudied and vulnerable group of high-risk rural women and their risks associated with HIV and HCV. Thus, there is significant need to implement evidence-based practices focused on rural HIV/HCV risks. *Aim*: The overall aim is to describe the implementation of an evidence-based intervention (*Motivational Interviewing for HIV Risk Reduction*) with high-risk incarcerated rural women. *Program description*: The program uses rural jails to outreach to drug-using rural women at high-risk for HIV/HCV. Participants are randomly selected, screened for substance use using the NIDA-modified ASSIST, and randomly assigned to four brief jail intervention sessions using MI-HIV or to the NIDA education comparison group. MI-HIV includes four private individual sessions in the jail. Sessions are recorded and reviewed to ensure intervention fidelity. The therapist follows a basic structure to guide each session. This presentation will highlight session content, describe fidelity approaches, and review adaptations for this culturally unique population of high-risk women in the jail context
Conclusions: *Conclusion:* Little is known about implementing evidence-based practices in non-therapeutic environments such as jails. This program is promising as an approach to high-risk drug use behavior in Appalachia among vulnerable women. Considering service limitations in the area, this program utilizes a real-world setting to identify and intervene with high-risk women drug users.
Financial Support: Research was supported by the National Institute on Drug Abuse of the National Institutes of Health under Awards R01DA033866 and K02DA35116.

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SUBJECTIVE AND OBJECTIVE EVIDENCE OF LOW ABUSE POTENTIAL OF THE PERIPHERALLY-ACTING KAPPA OPIOID, CR845, COMPARED WITH PENTAZOCINE.

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Aims: CR845, a potent, peripherally-acting, selective kappa opioid, is being developed for the treatment of acute and chronic pain. The primary objective of the trial was to measure the relative abuse potential of 2 doses of CR845 compared to an intravenous (iv) dose of pentazocine, a Schedule IV opioid analgesic with mixed mu and kappa opioid activity.
Methods: Recreational polydrug users with opioid and hallucinogenic drug experience were enrolled in this single-center, randomized, double-blind, active- and placebo-controlled study. Subjects (N=39) received a single bolus iv dose of the following 4 treatments in a balanced Williams crossover design, with 48-hour washout periods: CR845 5 mcg/kg (therapeutic dose), CR845 15 mcg/kg (supra-therapeutic dose), placebo, and pentazocine 0.5 mg/kg. In addition to subjective measures of drug abuse liability, changes in pupillary diameter were measured.
Results: The primary measure of "drug liking" Emax on a visual analog scale (VAS) for CR845 was significantly lower than pentazocine (p <.0001). Similarly, the VAS scores for "drug liking" and drug effect "high" for CR845 were lower than those for pentazocine over the entire 8-hour observation period. In addition, "overall drug liking" and "take drug again" VAS scores were lower for CR845 compared to pentazocine (p <.0001) and were equivalent to placebo. Pentazocine produced a decrease in the mean pupillary diameter compared with no change with either dose of CR845 or placebo (p <.0001).
Conclusions: This study provides evidence that CR845 exhibits substantially less abuse potential than pentazocine. The lack of effect of CR845 on pupillary diameter is consistent with preclinical studies demonstrating an absence of CNS mu opioid activity, which further supports a low abuse potential compared with mu opioids.
Financial Support: The study was funded by Cara Therapeutics, Inc.

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EPISODIC FUTURE THINKING REDUCES DELAY DISCOUNTING IN CIGARETTE SMOKERS.

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Aims: Episodic future thinking (i.e., mental simulation of future life events) has been shown to reduce delay discounting in healthy and obese populations. In the present study, we sought to determine whether episodic future thinking would reduce delay discounting in cigarette smokers and whether this effect would differ between nicotine-deprived and -sated states.
Methods: Cigarette smokers (N = 12) completed a guided interview designed to generate vivid future events to occur following each of five delays used in a hypothetical delay-discounting task (i.e., one day to one year). In a within-subjects design, participants completed the discounting task in both nicotine-deprived and -sated states while we presented textual cues associated with future events (active sessions) and recent past events (control sessions).
Results: Episodic future thinking significantly reduced discounting when participants were both nicotine-deprived and –sated (in both cases, $p < .05$). However, Cohen's d effect sizes indicated relatively stronger effects of episodic future thinking in the nicotine-deprived (d = 0.55) vs. -sated (d = 0.41) state.
Conclusions: The present study extends prior research by demonstrating that episodic future thinking reduces delay discounting in cigarette smokers. The longevity and clinical impact of acute reductions in discounting with the use of episodic future thinking has yet to be determined.
Financial Support: Institutional funds (WKB)

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PRESCRIPTION DRUG ABUSE, HEROIN, & IV DRUG USE AMONG INCARCERATED BLACK MEN.

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Aims: Incarcerated Black males are not included in national household surveys. Abuse of prescription opiates and sedatives increase risk for intravenous heroin use. Compared to other groups, Black men in the South have been least likely to report injection drug use. However, this may be shifting. The purpose of this study is descriptive by examining the self-reported prescription drug abuse, heroin use, and intravenous drug use among adult incarcerated Black males.
Methods: Black males (N = 4017; age M = 36.02) incarcerated in Kentucky state prisons enrolled in substance abuse treatment from 2011-2014 were interviewed. Respondents were asked 'In the past 12 months prior to this incarceration, have you used non-prescription opiates, stimulants, sedatives, or have you ever injected any drug?' Chi-square tests of were conducted. It was hypothesized that between 2011 and 2014 there would be a significant increase in non-prescription drug abuse, heroin and intravenous drug use.
Results: Between 2012 (n = 174) and 2013 (n= 229) there was a significant increase in non-prescription opiate abuse (χ^2 = 7.51, p < .001). Between 2013 and 2014 there was a significant decrease in non-prescription stimulant abuse (χ^2 = 11.77, p < .001). Lastly, across all four years of cohorts (2011-2014) there was a significant increase in heroin use (χ^2 = 8.96, p = 0.002).
Conclusions: Although results are preliminary, the significant increase in non-prescription opiate abuse and heroin use among Black males is a public health concern. Black men in the South are contracting HIV infection at alarming rates. It is critical to better understand the recent increase these patterns of drug abuse in order to understand cultural needs regarding drug abuse treatment and reduce the risk of HIV infection within the Black community.
Financial Support: Commonwealth of Kentucky: PON2-527-14000019121; NIDA K08-DA32296; NIDA T32-DA035200

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CLINICAL CHARACTERISTICS AND GENOTYPE FREQUENCIES OF THE DOPAMINE TRANSPORTER GENE (*DAT1/SLC6A3*) 3'UTR VARIABLE NUMBER OF TANDEM REPEATS IN CRACK-COCAINE USERS.

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Aims: To compare the prevalence of genotype frequencies created by the 3'UTR VNTR at *DAT1* gene between adult CCU with different clinical characteristics. Due to its mechanism of action on drug addiction, this gene can be a good candidate for molecular studies.
Methods: Cross-sectional study with a target sample of 360 current adult crack abusers or dependents (DSM-IV TR criteria) from public in- and outpatient clinics was conducted in Brazil. Subjects were evaluated with ASRS, ASI6 and MINI-Short. DNA samples extracted from whole blood or saliva were genotyped for the *DAT1* 3'VNTR. The hypothesis of association was investigated using Logistic regression tests.
Results: CCU were divided in two subgroups for each test using five ASI6 questions: number of previous treatments, being in prison anytime, physical abuse, living with another drug abuser 30 days prior to treatment and having someone else to help in treatment except families and close friends. All analyses were adjusted by sex, age, ethnic group, educational level, ADHD, depressive and anxiety symptoms and suicide risk. The putative 10.10 risk genotype did not differ significantly between CCU groups in any test (p values ranging from 0.05 to 0.92).
Conclusions: The putative risk genotype suggested in crack-cocaine dependence, namely the *DAT1* 3' VNTR 10.10, does not appear to be a good isolated genetic biomarker for these specific characteristics. However, more analyses must be performed with this and other dopaminergic variants and other aspects related to drug use, in order to identify a possible molecular component for crack-cocaine severity models.
Financial Support: SENAD, FAPERGS, CNPq, CAPES, PRODAH

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TEMPORALLY RAPID, PHARMACOLOGICAL STATE-DEPENDENT HEROIN DELAY DISCOUNTING MODULATED BY DRUG-USE IMPULSIVITY.

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Aims: Examine whether drug-use impulsivity and education modulate heroin behavioral-economic valuation at ecologically-relevant time intervals under two hypothetical pharmacological states.
Methods: Intensive heroin users (N=181; $M\pm SD$=42.7+9.9 yr old; 51% African-American; 67% male; 12.4±1.5 yr education) completed a temporal discounting task under two imagined states: heroin satiation and withdrawal. Delays were 3, 6, 12, 24, 48, 72 and 96 hr; maximum heroin amount was thirty $10 bags. Drug-use impulsivity was assessed with subscales from the Impulsive Relapse Questionnaire (IRQ; 30 items, each on a 5-point Likert scale that reflects drug relapse potential).
Results: Repeated measures analysis using square-root transformed AUC data revealed a significant (p<.05) state-dependent effect, $F_{(1,180)}$=369.67: heroin discounting was steeper (smaller AUC) during withdrawal compared to satiation. IRQ subscales and education were first entered separately as covariates in repeated-measures models. Condition significantly interacted with IRQ Capacity for Delay, $F_{(1,179)}$=7.95 (e.g. 'I think a lot about using drugs before I start using again', higher delay capacity = less discounting); and marginally for IRQ Speed, $F_{(1,179)}$=3.85, p=.051 (e.g. 'I crave for less than a few minutes before I start using again', faster to use = more discounting); but not education (p=.155). A final model with all 3 individual difference covariates revealed a significant interaction of condition and IRQ Capacity for Delay, $F_{(1,177)}$=5.87, but not Speed (p=.097) or education (p=.305).
Conclusions: Heroin delay discounting varied across pharmacological state (satiation vs. withdrawal) and was modulated by drug-use impulsivity but not educational level.
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ABUSE POTENTIAL OF ORAL PHENDIMETRAZINE IN COCAINE-DEPENDENT INDIVIDUALS.

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Aims: Phendimetrazine is a prodrug for the monoamine releaser phenmetrazine, a drug with known abuse potential. Preclinical studies suggest that phendimetrazine has limited abuse potential and may have promise as an agonist-like replacement therapy for cocaine dependence. No clinical studies have evaluated the abuse potential of phendimetrazine. The hypothesis of this study was that phendimetrazine would have reduced abuse potential relative to d-amphetamine in cocaine-using humans.
Methods: Nine cocaine-dependent volunteers (N = 9) completed this double blind, placebo-controlled, within-subjects study. The cardiovascular and subjective effects of oral phendimetrazine (35, 70, and 105 mg), d-amphetamine (10, 20, and 30 mg) and placebo were assessed at regular intervals for 6 h after drug administration. Data were analyzed as peak effect using repeated-measures analysis of variance with Fisher's least significant difference post hoc tests to compare between means.
Results: The highest dose of phendimetrazine significantly increased heart rate compared to placebo, but did not systematically alter blood pressure. d-Amphetamine dose-dependently increased blood pressure and heart rate. Neither phendimetrazine nor d-amphetamine significantly increased ratings of positive or negative subjective effects relative to placebo.
Conclusions: These preliminary findings suggest that phendimetrazine and d-amphetamine have limited abuse potential in cocaine-dependent individuals, a clinically relevant sample that could receive these medications to help manage cocaine use disorder. Future studies are needed to further elucidate the potential utility of phendimetrazine as an agonist-like replacement therapy for cocaine dependence.
Financial Support: Grants R01DA025032 and T32DA035200.

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COMPULSIVE SEXUAL BEHAVIOR, SUBSTANCE ABUSE, AND SEXUAL RISK-TAKING AMONG EMERGING ADULT GAY AND BISEXUAL MEN IN NEW YORK CITY: THE P18 COHORT STUDY.

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Aims: Previous behavioral research has shown that young gay, bisexual and other men who have sex with men (YMSM) are at increased risk for substance abuse, mental health burden, and the Human Immunodeficiency Virus (HIV). As informed by syndemic theory, this analysis sought to further delineate the impact of compulsivity in sexual risk-taking behavior among a new generation of YMSM ages 18-19.
Methods: The current analysis administered the Compulsive Sexual Behavior Inventory (CSBI) as well as additional psychological, psychosocial, alcohol/drug use, and sexual behavior measures to 509 racially and economically diverse, confirmed HIV-negative, YMSM sampled from the New York City metropolitan area. A multivariable model was tested to determine whether the use of alcohol and drugs mediated the relation between compulsive sexual behavior and sexual risk-taking.
Results: Alcohol and drug use were shown to significantly and completely mediate the relation between compulsive sexual behavior and condomless anal sex (b = .069, $t(507)$ = 1.54, p =.125). A Sobel test was conducted and found full mediation in the model (z = 2.75, p = .01). In addition, depression was shown to moderate the relation between compulsive sexual behavior and sexual risk-taking (ΔR^2 = .008, $\Delta F(1, 505)$ = 4.004, p < .05), where higher rates of depression were associated with significantly more condomless anal sex among those YMSM who scored high in sexual compulsivity.
Conclusions: Findings suggest that compulsive sexual behavior in concert with depressive symptoms and substance use exacerbate risk for sexual risk-taking among YMSM. Clinicians must take a holistic approach when providing care and need to address the underlying psychological symptoms that exacerbate risk behaviors in order to reduce HIV-risk among this new generation of YMSM.
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CHARACTERIZING NICOTINE WITHDRAWAL IN OPIOID-MAINTAINED SMOKERS.

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Aims: Withdrawal is a central tenet of nicotine dependence and its severity is associated with relapse risk. Withdrawal typically peaks in the first two days of a quit attempt then gradually diminishes, though less is known about its pattern in opioid-dependent smokers, who have notoriously high smoking rates. We have developed a behavioral intervention, wherein smokers receive financial incentives contingent upon biochemically-verified abstinence, which produces robust initial abstinence (Dunn et al., 2008, 2010; Sigmon et al., in prep). Here we characterize nicotine withdrawal in smoking-abstinent opioid-dependent participants and contrast it with that seen previously in non-substance abusing, healthy smokers (Bradstreet et al., 2014; Yoon et al., 2009).
Methods: 52 methadone- and buprenorphine-maintained smokers (33.3±10.4 yrs old, 17.7±6.6 cigs/day) received incentives contingent on abstinence and provided >85% smoking-negative specimens during the 2-week study. Historical controls were 25 healthy smokers (27.3±9.1 yrs old, 18.2±6.0 cigs/day) under similar experimental conditions. Withdrawal was assessed daily using the Minnesota Nicotine Withdrawal Subscale (Hughes & Hatsukami, 1998).
Results: Mean baseline MNWS score for opioid-dependent smokers was 1.8±0.1, which decreased over time to 0.7±0.1 on Day 14. Healthy controls presented with lower baseline scores of 0.7±0.2 which increased upon quitting, peaked on Day 1 (1.5±0.2) and then decreased to 0.8 ±0.2 on Day 14. While both groups' withdrawal trajectories were consistent with a cubic function, they did differ significantly (F(1, 832)=15.76, p<.0001), largely due to the differences in scores at the beginning of the 2-week period.
Conclusions: The pattern of nicotine withdrawal in opioid-dependent smokers may depart from that typically seen in the general population. The mechanism underlying these differences, including possible pharmacological interactions whereby opioids may attenuate withdrawal, warrants further study and may have implications for quitting.
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THE RELATIONSHIP BETWEEN METHAMPHETAMINE SELF-ADMINISTRATION AND SUBJECT-RATED EFFECTS.

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Aims: Drug self-administration and subject-rated measures are two of the most commonly used human laboratory methods to evaluate the abuse potential of drugs and to screen putative interventions. The purpose of the present retrospective analysis was to examine the relationship between intranasal methamphetamine self-administration and subject-rated effects to determine which factors best predict methamphetamine-use behaviors.
Methods: Data were combined from five studies (n = 18 subjects) in which the reinforcing and subject-rated effects of intranasal methamphetamine (0, 10, and 30 mg) were assessed using identical procedures. Analysis of variance, Pearson correlation coefficients, and model selection using multilevel modeling and Bayesian information criterion were used to examine the relationship between peak subject-rated effects and methamphetamine breakpoints.
Results: Methamphetamine produced dose-dependent increases on prototypic subject-rated effects. Nine of these ratings were positively correlated with methamphetamine breakpoints. Model selection using multilevel models controlling for inter-subject and inter-dose variability found that the combination of two ratings (i.e., Good Effect and High) best predicted breakpoints. Fixed effect coefficients indicated that ratings of Good Effect were positively associated, whereas ratings of High were negatively associated, with breakpoints.
Conclusions: Methamphetamine produced dose-dependent increases in ratings of stimulant-like subject-rated effects that were also positively associated with methamphetamine breakpoints. Model selection revealed that the combination of ratings for Good Effect and High best predicted future self-administration behavior, which is concordant with previous findings with cocaine. These findings identify potential primary human laboratory outcomes for the assessment of interventions targeting methamphetamine.
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INELIGIBLE FOR MOST PROTOCOLS: WHAT DIFFERENTIATES DRUG USERS?

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Aims: Drug users are are routinely excluded from research participation, but drug use is common and non-medical exclusions unnecessarily bias research results. A NIDA ambassador intervention to increase enrollment of drug users in relevant research and change the research enterprise gave us the opportunity to study differences in the lives of drug users and non-drug users that may be linked to advances in research and treatment access.
Methods: Data came from the Transformative Approach to Reduce Research Disparities Towards Drug Users study that randomized drug users and non-drug users to an ambassador (individual attention and transportation) or a standard navigator intervention (individualized study matching) to increase access to medical care and opportunities to participate in research. Final 60 day assessment of intervention effectiveness will conclude this month. For this analysis, we consider whether the lives of drug users and nonusers differ in ways that are more relevant and less discriminatory than drug use.
Results: The sample is 285 community recruited adults, 18 to 80, who endorsed no drug use, and 280 who endorsed current drug use. Drug users were significantly more likely to consider themselves homeless (22% vs. 15%), be food insecure (43% vs. 35%), have unpredictable daily activities (51% vs. 39%), feel unsettled (40% vs. 31%), have more days of the month where they felt unable to control important things [8.25 (95% CI 6.91,9.51) vs. 5.88 (4.74,7.03)] and have more overall life chaos [4.98 (95%CI 4.61,5.34) vs. 3.97(95%CI 3.65,4.3)]. Evictions, jail time, having a child removed, and social support, were not different by drug use.
Conclusions: Biased attitudes towards drug users, especially given the legalization of marijuana in many states, are untenable. Understanding and measuring daily life challenges among potential participants is important to decrease prejudicial enrollment practices, and to improve the ability to fully participate in research and attend relevant services for those who use drugs.
Financial Support: R01DA027951 Transformative Approach to Reduce Disparities Towards Drug Users, Cottler LB, PI.

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THE PERCEIVED STIGMA OF SUBSTANCE ABUSE SCALE: RELIABILITY AND VALIDITY WITH SUBSTANCE USING PEOPLE LIVING WITH HIV.

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Aims: Substance use (SU) stigma may be especially deleterious for people living with HIV (PLHIV), impacting both SU and HIV treatment. To date, tools to assess SU stigma are limited to use with people in treatment programs, & no tool has been validated for use in PLHIV. This study examines the reliability & validity of the PSAS for use with PLHIV who are current users.
Methods: The PSAS was administered to154 PLHIV who are current substance users and who attend a University outpatient HIV clinic for care. Data was examined for internal & reliabilty.
Results: The mean of the PSAS was 20.89 (SD=4.24) (range: 08-32, higher scores equals greater levels of perceived stigma). Confirmatory analysis indicate that a one-factor solution fits, with an eigenvalue of 3.06, explaining 38.27% of the variance. Reliability coefficients, including Cronbach's alpha (α=0.734), Guttman split-half (0.706), and item–total correlations indicate adequate internal reliability. Convergent validity was demonstrated through correlations with the fear of enacted SU stigma scale (r = .399, p < .000), the SU Stigma Avoidance Scale (r= .328, p < .000), & the internalized HIV-related stigma scale (r=.195, p < .05). To assess divergent validity, perceived SA stigma was not significantly correlated with measures of the number of close friends a person reports having (r=.-.055] or close relatives a person reports having (r=-.055).
Conclusions: The PSAS scale is a reliable and valid instrument for use with current users living with HIV.
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THE ROLE OF SEROTONIN 2A (5-HT_{2A}) AND 2C (5-HT_{2C}) RECEPTORS IN THE ASSOCIATION BETWEEN BINGE EATING AND IMPULSIVE ACTION.

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Aims: Binge eating disorder (BED) is the most prevalent eating disorder in the U.S., and is linked to severe obesity and psychological and medical morbidity. Impulsive action is a key factor underlying the etiology and evolving pathogenesis of BED. We hypothesize that impulsive action and binge eating are mechanistically-linked to disrupted serotonin (5-HT) signaling through 5-HT_{2A}R and 5-HT_{2C}R in brain regions, particularly the medial prefrontal cortex (mPFC), that drive the incentive-motivational salience of food and cues that predict food.
Methods: Rats were identified as high (HI) or low (LI) impulsive action phenotypes in the 1-choice serial reaction time (1-CSRT) task. Binge eating in HI vs. LI (n=12/group) was assessed upon 2-hr access to high-fat chow. HI and LI were subjected to a self-administration/forced abstinence paradigm to assess the reinforcing and motivational efficacy of high-fat pellets and associated cues. The mPFC 5-HT_{2A}R and 5-HT_{2C}R protein expression profiles were identified in HI vs. LI rats.
Results: HI consumed significantly more kcal during the 2-hr binge vs. LI (p<0.05). The reinforcing efficacy of high-fat pellets was identical in HI and LI. HI exhibited a higher breakpoint for high-fat pellets and higher cue reactivity vs. LI (p<0.05). A positive correlation between premature responses and the ratio of 5-HT_{2A}R:5-HT_{2C}R protein expression in the mPFC (r=0.558, p<0.01) was observed.
Conclusions: These data suggest that the level of inherent impulsive action is a determinant of the magnitude of binge eating high-fat chow. We propose that high-fat food is more "wanted" by HI vs. LI, making impulsive responding and binge intake more difficult to withhold in HI. Further, these data support the hypothesis that inherent impulsive action and binge eating coalesce at the level of imbalanced 5-HT_{2A}R:5-HT_{2C}R homeostasis within the mPFC.
Financial Support: Klarman Family Foundation for Eating Disorders, K99 DA033374 (NCA), K05 DA020087 (KAC)

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COMORBIDITY AND FUNCTIONING OF SUBSTANCE-DEPENDENT WOMEN WITH SEXUAL ABUSE HISTORY IN THE STAGE II WOMEN'S RECOVERY GROUP THERAPY TRIAL.

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Aims: The Women's Recovery Group (WRG) Study is a Stage 2, RCT comparing single-gender group therapy (WRG) to mixed-gender group therapy (Group Drug Counseling; GDC) for substance use disorders (SUD). Women were randomized to the WRG (n = 52) or Group Drug Counseling (GDC; n = 48), and men were assigned to GDC (n = 58). Characteristics of women with a history of sexual abuse were examined in these post-hoc analyses.
Methods: Participants ≥18 years with SUDs were included if they used substances in past 60 days. Sexual abuse (SA) history was assessed using the Life Experiences Questionnaire; functioning with the Global Assessment of Functioning (GAF) scale; and the CIDI was used to determine psychiatric diagnoses.
Results: Of the 100 women in the trial, 39% reported a history of SA. Compared to women without a history of SA, those with a SA history had lower GAF scores (t=2.7, df=98, p<.01) and higher rates of major depressive disorder (85% vs. 64%; χ2(1)=5.05, p<.05), PTSD (39% vs. 13%; χ2(1)=8.63, p<.01), and panic disorder (26% vs. 8%; χ2(1)=5.68, p<.05). We divided women into 3 groups: (1) no history of SA, (2) SA either before OR after age 16, and (3) SA before AND after age 16. Women with abuse before and after had the lowest GAF scores (M=56, SD=4.7), followed by those with one type of abuse (M=59, SD=5.7); women with no history had the highest GAF scores (M=61, SD=5.3). Women assigned to the GDC group who had a history of SA rated the helpfulness of having men and women in the group as significantly lower than those without a history of SA (t=-2.4, df=40, p<.05); women in the WRG rated the helpfulness of the all-women group composition as high regardless of SA history.
Conclusions: Women with SA history had lower functioning and greater psychiatric comorbidity. Single-gender SUD group composition was endorsed as helpful by those with and without SA history but may be especially important for those who have experienced sexual abuse.
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DIFFERENTIAL BRAIN RESPONSE TO SUCCESSFUL AND FAILED RESPONSE INHIBITION: COCAINE-DEPENDENT VS. HEALTHY SUBJECTS.

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Aims: Our laboratory previously introduced an affectively congruent Go/NoGo task (GNG) using affective stimli with inherent ecological validity (Go="positive" stimuli; NoGo="negative" stimuli) and showed adequate task validity and reliability. In the current investigation, we compare the prepotent response inhibition performance and associated brain response using our GNG task between COC and HC.
Methods: COC (n= 32) and HC (n= 19) underwent GNG in an fMRI setting. We used event-related BOLD fMRI at 3T to measure brain responses during GNG performance. Data were analyzed within SPM8. Pre-planned analyses focused on the brain response during trials in which inhibition was successful (STOPS) and trials in which inhibition failed (ERROR) for COC and HC. Prior to task administrations, COC subjects spent approximately 4-7 days in a controlled therapeutic setting to ensure stable, cocaine-free state.
Results: HC and COC performed at a comparable rate and were not significantly different (p=0.11). In COC, STOP, as compared with ERROR, was associated with activation of DLPFC, DMPFC and the amygdala (p<0.001), whereas significantly less activation was observed in HC (p<0.001). Further analyses showed that COC and HC did not differ in their response to STOP (p<0.001). During ERROR trials, HC demonstrated significantly higher activation in OFC, DLPFC and VMPFC than in COC (p<0.001).
Conclusions: COC and HC performed comparably when they attempted to inhibit a prepotent response. STOP was associated with activation of modulatory circuitry and the regions critical for evaluating incoming stimuli. Interestingly, failed attempts elicited a lower activation in medial OFC and DLPFC for COC (vs. HC), suggesting attenuated brain response during ERROR. Prepotent response inhibition marker (success and failure) may represent important phenotypic indicator of chronic cocaine use.
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DECREASED BRAIN CREATINE KINASE ACTIVITY IN METHAMPHETAMINE ABUSERS: PRELIMINARY RESULTS.

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Aims: Methamphetamine (MA) causes oxidative stress and mitochondrial dysfunction in rat brain. MA also inhibits enzymatic activity in the Krebs cycle and the mitochondrial respiratory chain. Among the enzymes involved in brain energy metabolism, creatine kinase (CK) plays a significant role in energy homeostasis since CK replenishes adenosine triphosphate levels in a phosphocreatine-CK-creatine circuit. Because MA toxicity may be associated with altered creatine kinase kinetics, we investigated brain CK activity in subjects with MA use disorders as a potential biomarker of mitochondrial toxicity.
Methods: Phosphorus (P-31) magnetization transfer (MT) spectroscopy (MRS) evaluated MA abusers (n=9) and age-matched healthy controls (n=3). A two-dimensional MT chemical shift imaging pulse sequence was used to calculate apparent intrinsic relaxation rate ($1/T_1'$) of phosphocreatine with different saturation times at -2.7 ppm as well as steady state (M_{ss}) and thermal equilibrium (M_0) magnetization. CK activity was computed using $(1-(M_{ss}/M_0))/T_1'$. Average *in vivo* CK forward rate constants in the whole brain was compared between the two groups.
Results: MA abusers tended to have decreased (-13.1%) CK activity compared to values observed in controls (t=-1.848, p=0.09), despite the small number (n=3) of the healthy subjects. The statistical power of our data was estimated to be approximately 0.8 with a target sample size of n=18 and 9.
Conclusions: Our preliminary results provide evidence that MA toxicity may be associated with compromised CK activity, consistent with oxidative stress and mitochondrial dysfunction, which are two interdependent and reinforcing damage mechanisms that play a role in several mental disorders such as schizophrenia, and mood disorders (Clay, 2011; Jou, 2009). In humans, CK forward rate constants are tightly correlated with brain activity levels (Du, 2008). Thus, decreased CK activity might contribute to the hypo-metabolism and neurocognitive dysfunction known to be present in MA users.
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THE USE OF NEW PSYCHOACTIVE SUBSTANCES AMONGST A SAMPLE OF REGULAR PSYCHOSTIMULANT USERS, 2010-2014.

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Aims: Over the past decade, Australia has witnessed the rapid emergence of an alternative drug market which contains substances collectively referred to as 'new psychoactive substances' (NPS). Although the prevalence of NPS use remains low amongst the general Australian population, rates of use have been found to be particularly high amongst sub-samples of illicit drug users. This paper aims to examine the prevalence and correlates of NPS use amongst a sample of regular psychostimulant users (RPU), from 2010-2014.
Methods: This paper uses data from the Ecstasy & Related Drugs Reporting System; a national monitoring study which is aimed at detecting emerging trends in illicit drug markets. Participants were selected on the basis of at least monthly use of psychostimulants in the six months preceding interview. Across 2010-2014, 3,360 participant surveys were completed.
Results: In 2010, 32% of RPU reported using an NPS in the six months preceding interview. The prevalence of NPS use increased significantly in 2011 (41%; $p<0.01$; 95% CI: 0.037-0.14), and has remained relatively stable since. In regards to the use of specific NPS, the use of 2CB and DMT have steadily increased across 2010-2014, whilst there has been an inverse downturn in the use of mephedrone, 'herbal highs' and synthetic cannabinoids. In 2014, participants who had used recently NPS were more than seven times more likely to have purchased a drug online in the past year (OR 7.4 95% CI: 2.03-26.94) and more than four times more likely to have recently used magic mushrooms (AOR 4.28 95% CI: 1.31-13.97).
Conclusions: The NPS market has established itself as an ongoing and significant part of Australia's recreational drug scene. However it remains a highly dynamic market, with the popularity of specific NPS changing considerably over time. Given the potential for access of these substances via the internet, research should be undertaken to develop an effective school based prevention campaign targeting NPS.
Financial Support: Funded by the Australian Government under the Substance Misuse Prevention and Service Improvement Grants Fund.

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SEX DIFFERENCES IN REINSTATEMENT OF COCAINE-SEEKING IN RATS AFTER ACUTE TREATMENT OF PROGESTERONE AND ATOMOXETINE.

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Aims: Male and female rats show differences in cocaine-seeking behavior that are influenced by hormonal fluctuations. Progesterone (PRO) decreases cocaine self-administration and reinstatement in female rats, but the effects of progesterone on male rats were inconsistent in initial studies. In addition, progesterone and atomoxetine have never been studied in combination to determine if there is an additive or synergistic effect between therapeutics. The purpose of this study was to determine sex differences in treatment effects of progesterone, atomoxetine (ATO) and a combination treatment on reinstatement of cocaine-seeking behavior.
Methods: Adult male and female Wistar rats (n=6-11 per group) were trained to lever-press on a FR1 schedule for cocaine infusions (0.4 mg/k/ inf, 20-second timeout following infusion). After 14 days of stable responding in daily 2-hour sessions, rats were placed on extinction for 21 days. Rats were then separated into four groups based on the treatments given on reinstatement days (PRO+vehicle [VEH], PRO+ATO, VEH+ATO, VEH+VEH). Progesterone, atomoxetine and the corresponding vehicle injections were given 30 min prior to reinstatement sessions. Reinstatement to cocaine, caffeine, and cues as well as the combination of drugs and cue were tested after extinction.
Results: Male and female rats showed differential responsiveness to treatment with progesterone and atomoxetine, specifically when presented in a combination treatment. Sex and group differences depended on the type of reinstatement, with caffeine and cocaine producing disparate results between males and females.
Conclusions: The effectiveness of progesterone and a progesterone/atomoxetine combination treatment is dependent on sex and the stimulus used to induce reinstatement; however, progesterone shows potential as a therapy for relapse for both males and females.
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DEVELOPMENT OF A PROSPECTIVE MEMORY TRAINING PROGRAM FOR SUBSTANCE USE TREATMENT.

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Aims: Substance misusing populations show poorer prospective memory (i.e., the ability to implement an intention in the future) and working memory (i.e., the ability to hold in mind and manipulate information over short periods of time), thus improvement of these cognitive processes is a good target for intervention. To our knowledge, no intervention has been designed to train prospective memory. Therefore, our objective is to develop a prospective memory and working memory training program that is a feasible adjunct to substance use disorder treatment.
Methods: We designed and programmed a computerized prospective training program that uses an immersive interface to simulate real life prospective memory challenges that occur in the context of ongoing working memory demands. Participants perform working memory tasks via commercially available working memory training program, framed as a "work-at-home" job. Participants must also complete prospective memory tasks by interacting with objects in the immersive environment (e.g., When Al calls, ask about babysitting; at 10:00 AM wash the laundry). Our ongoing study (N=15) is determining the optimal number of prospective memory tasks for training (i.e., between .70 and .90 proportion correct) in a community substance use treatment population.
Results: Program development is complete. Using modular training parameters, initial results suggest that training six prospective memory tasks is within an appropriate range of difficulty.
Conclusions: We successfully developed a training program that integrates aspects of prospective memory and working memory. Future work will determine the optimal number of training sessions required for prospective memory improvement and ultimately whether repeated memory training sessions improve drug use outcomes.
Financial Support: NIDA R01DA035277, T32DA007209.

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DIFFERENTIAL MODULATION OF COCAINE-RELATED BEHAVIORS CONSEQUENT TO KNOCKDOWN OF SEROTONIN 5-HT$_{2C}$ RECEPTOR IN THE NUCLEUS ACCUMBENS SHELL VS. VENTRAL TEGMENTAL AREA.

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Aims: The mesoaccumbens pathway mediates the hyperlocomotive and reinforcing effects of cocaine and cue-evoked cocaine-seeking. The 5-HT$_{2C}$R in this pathway is poised to regulate dopamine transmission and cocaine-related behaviors. Intra-NAcSh 5-HT$_{2C}$R agonist administration augments cocaine-evoked hyperactivity. Intra-VTA 5-HT$_{2C}$R agonist administration attenuates cocaine-evoked hyperactivity and cocaine-taking. We hypothesize that 5-HT$_{2C}$R knockdown in the NAcSh vs. VTA will differentially modulate cocaine-related behaviors.
Methods: Rats were tested for cocaine-evoked hyperactivity (10 mg/kg) following intra-NAcSh or -VTA 5-HT$_{2C}$R knockdown or control virus. Rats were trained to self-administer cocaine (0.25 mg/kg/inf); the cocaine dose-response (0.05, 0.125, 0.25, 0.75 mg/kg/inf) was established. Cocaine-taking was stabilized and cue reactivity was measured 24 hr later.
Results: Rats with 5-HT$_{2C}$R knockdown in NAcSh, but not VTA, displayed enhanced cocaine-evoked hyperactivity ($p<0.05$) vs control rats. Cocaine infusions received were lower at 0.05 and 0.125 mg/kg/inf cocaine after 5-HT$_{2C}$R knockdown in NAcSh ($p<0.05$), but not VTA. Cue reactivity was higher after 5-HT$_{2C}$R knockdown in NAcSh ($p<0.05$), but not VTA.
Conclusions: These data suggest lower 5-HT$_{2C}$R tone in NAcSh, but not VTA, confers enhanced sensitivity to the hyperlocomotive and reinforcing effects of cocaine and cue reactivity. A neuroanatomically distinct role for the 5-HT$_{2C}$R to regulate cocaine-related behaviors is indicated. Future studies will explore region-dependent 5-HT$_{2C}$R-mediated shifts in dopamine transmission in relation to cocaine-related behaviors.
Financial Support: DA035620 DA024157 DA033935 DA033374

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DEVELOPMENT AND VALIDATION OF A DEVICE FOR THE INTRAPULMONARY DELIVERY OF Δ^9-TETRAHYDROCANNABINOL TO RATS.

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Aims: Popularization of non-combustible methods for intrapulmonary delivery of psychoactive drugs to humans (Volcano, e-cigarette, etc) has stimulated interest in intrapulmonary administration models for rodent studies. Intravenous self-administration of Δ^9-tetrahydrocannabinol (THC) in rats has never been convincingly established and e-cigarette technology provides multiple methodological advantages. This study developed a sealed rodent chamber, with a well regulated air flow, suitable for controlled exposure to psychoactive substances.
Methods: An e-cigarette type delivery system was found to afford excellent dosing control for this purpose. Validation studies were conducted in male rats to verify the in vivo efficacy of THC delivery using implantable radiotelemetry to assess body temperature and locomotor responses.
Results: It was found that hypothermic responses to inhaled THC are time and concentration dependent and may be attenuated with the CB_1 antagonist SR141716 (Rimonabant). The temperature nadir was reached within 40 min of exposure, was of comparable magnitude (~3 °Celsius) to that found after 30 mg/kg THC, i.p. and had resolved within 3 hours (compared with a 6 hour time course following i.p. THC). Studies also demonstrated that rats will nosepoke for 2 min deliveries of THC vapor.
Conclusions: These studies show that an electronic cigarette delivery system can be successfully used to model intrapulmonary drug delivery in rats and has the potential to support operant reinforcement studies. These techniques will be of increasing utility as recreational users continue to adopt "vaping" for the administration of cannabis extracts
Financial Support: Supported by USPHS Grants DA024105 and DA035482

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THE IMPACTS OF GRAPHIC WARNING LABELS IN AN ADDICTION TREATMENT POPULATION.

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Aims: To investigate the impacts of FDA-approved cigarette graphic health warning labels (GWL) on behavioral and communication outcomes of men in a residential treatment program. We hypothesize that participants exposed to GWLs for 30 days are more likely to initiate smoking cessation compared to non-exposed controls.
Methods: Successive cohorts of men in an residential addiction treatment cohort have stickers placed on their cigarette packs 3 x per week for a period of 30 days. Experimental cohorts receive stickers with FDA GWLs, while control cohorts receive blank transparent stickers. At baseline, each participant completes a computerized survey measuring behavioral and communication outcomes in relationship to tobacco product use. Following the baseline visit, each participant is asked to report to a research assistant 3 times a week for 4 weeks to have their cigarette and rolling tobacco packs labeled. On completion of the intervention, each participant completes a follow up survey and has the opportunity to attend an on-site, 4 week smoking cessation group.
Results: For 118 participants to date, 30% of GWL participants and 22% of controls initiated smoking cessation (defined as attending at least one cessation group). However, this difference is not statistically significant ($p = 0.327$). A regression analysis of follow up survey data controlled for baseline values showed no significant difference in cigarettes per day, risk perception, attitudes, or readiness to quit between the two groups.
Conclusions: While the preliminary difference in Smoking Cessation Group initiation is not statistically significant, an 8% difference in initiating smoking cessation, if supported through further research, may be meaningful at a population level.
Financial Support: This work was supported by grant number P30 CA082103_S1 from the NCI and the FDA Center for Tobacco Products (CTP), and by the University of California Tobacco Related Disease Research Program (TRDRP: 22XT 0049). The content is the responsibility of the authors and does not necessarily represent the official views of the NIH, FDA, or TRDRP.

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PROTEOMICS ANALYSES: PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA AGONIST FOR CHRONIC COCAINE ADMINISTRATION IN RODENTS.

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Aims: Preclinical studies show that PPARγ agonists reduce cue reactivity in cocaine self-administering rodents. There is also some evidence that PPARγ agonists (e.g., pioglitazone) have neuro-protective ability in animal studies. The current study hypothesizes that pioglitazone will be neuro-protective in rodent model of chronic cocaine administration.
Methods: The proteomics study compared control rodents (n= 3) with those exposed to neurotoxic doses of cocaine (osmotic mini pump; n= 3), cocaine plus pioglitazone (oral; n= 3), and pioglitazone (n= 3). In this study, we used iTRAQ coupled to tandem mass spectrometry, to elucidate some of the complex proteome changes that occur in nucleus accumbens after pioglitazone treatment in chronic cocaine administered rodents.
Results: Pioglitazone was able to revert the change in the expression profile of RabGDI-α, however, not of Syntaxin-binding protein 1 and Synaptosomal-associated protein beta. The proteins involved in metabolism and maintenance of neuronal structure which replicated the findings of cocaine self-administration (CSA) non-human primate model showed a favorable response to pioglitazone, including α-enolase and neurofilament- L/M/H.
Conclusions: Pioglitazone reverts proteins involved in synaptic plasticity, neuronal neurotransmitter secretion/signaling, metabolism and structure- similar to the expression profiles seen in the CSA model of non- human primates and cocaine overdose human victims.
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ADOLESCENT SUBSTANCE USE: LATENT CLASS AND TRANSITION ANALYSIS.

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Aims: Rates and consequences of adolescent substance use remains a serious public health concern. A better understanding of when adolescents move from one substance to another will aid in intervention. While longitudinal research has addressed the rate of alcohol, marijuana, and other drug use over time, less is known about the development of prescription drugs, and few studies have examined patterns of drug use simultaneously. Thus, we explore: 1) whether there are distinct subgroups based on past-year substance use; and 2) whether adolescents change substance use classes over time.
Methods: 1,042 ethnically diverse adolescents participated (57% female; M age=16). Past-year alcohol, cigarette, marijuana, synthetic marijuana, rx, and other drugs (cocaine, amphetamines) were measured at baseline and follow-up, when students were primarily Sophomores and Juniors, respectively. Latent Transition Analysis (LTA) with measurement invariance was used to examine transition probability of an individual's latent status at follow-up given their latent status at baseline.
Results: Three substance use classes were identified: 1) low users (LU, 58% baseline, 56% follow-up); 2) alcohol-marijuana users (AMU, 30%; 31%); and 3) heavy multi-substance users (HMSU, 12%; 13%). Most adolescents stayed in the same class over time (probability to stay in the same LU class the following year: .89; same AMU class: .88; same HMSU class: .85). If an adolescent in the LU class changed, they were more likely to move to the AMU class (11%); if adolescents in the AMU class changed, they were more likely to move to the HMSU class (9%); youth in HMSU class who changed were most likely to move to AMU class (14%).
Conclusions: Findings suggest that 1) pattern of substance use is fairly well established by mid-adolescence; and 2) when a transition does occur, it is typically to a more dangerous/illegal class of substances.
Financial Support: Grant award #2012WGBX0005 from the National Institue of Justice (Temple)

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TREATMENT SATISFACTION IN THE CTN COCAINE USE REDUCTION WITH BUPRENORPHINE STUDY.

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Aims: Treatment satisfaction in research may be associated with treatment retention, engagement, and outcomes. Including a satisfaction measure not only collects data on participants' attitudes about the treatment provided, but provides an unspoken message that participants' opinions are valued. The current study examines results of a treatment satisfaction survey administered to participants enrolled in the multi-center NIDA CTN Cocaine Use Reduction with Buprenorphine (CURB) trial to assess opinions about study participation.
Methods: This secondary analysis utilizes a 9-item satisfaction survey self-administered by cocaine-dependent participants at the end of the 8-week study. All participants received extended-release injectable naltrexone and were randomly assigned to 1 of 3 daily sublingual buprenorphine/naloxone (BUP) conditions: 16mg BUP (BUP16), 4mg BUP (BUP4), 0mg BUP (placebo, PLB), plus weekly CBT. Satisfaction ratings were based on a 5-point Likert Scale.
Results: 278 surveys were collected for a 92% completion rate. Most participants (93.5%) reported being satisfied or very satisfied with their overall experience in the study, and 84.9% reported that they would definitely participate again if given the opportunity. No difference in overall satisfaction was found between the BUP groups and the PLB group (BUP4 vs PLB, p=0.08; BUP16 vs PLB, p=0.43). Satisfaction was not associated with retention, CBT attendance, or cocaine use outcomes. Participants were also asked to what medication group they thought they were assigned, and 56.8% had an opinion whereas 43.2% were unsure. Of those with an opinion, 26.3% correctly guessed their group assignment. Additional analyses of items addressing participant opinion of the study medication and counseling will be presented.
Conclusions: Given the high rates of treatment satisfaction reported by study participants, it is not surprising that satisfaction is not related to treatment performance and outcome. Interestingly, participant guesses about assigned treatment were no better than chance. This seems to demonstrate the effectiveness of the study blinding process.
Financial Support: DA013045

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BORDERLINE PERSONALITY DISORDER DIAGNOSIS, DIAGNOSTIC CRITERIA, AND CRITERION COUNT AS PREDICTORS OF REGULARLY DRINKING ALCOHOL BEFORE SEX AMONG ADULTS IN THE UNITED STATES.

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Aims: Borderline personality disorder (BPD) is a complex psychiatric disorder characterized by pervasive instability in regulation of emotion, self-image, interpersonal relationships, and impulse control, often demonstrated by substance abuse and sexual risk behaviors. Drinking alcohol before sex increases the likelihood of engaging in sexual risk behaviors and risk for HIV infection. However, no study has examined the relationship between BPD and drinking alcohol before sex in the United States. This study examined whether BPD increased the likelihood of regularly drinking alcohol before sex in a nationally representative adult sample.
Methods: Participants were 17,491 sexually active adult drinkers from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Logistic regression models estimated the effects of BPD diagnosis, individual diagnostic criterion, and diagnostic criterion count on the likelihood of regularly (most or all of time) drinking alcohol before sex.
Results: Adjusted for demographics (race, age, gender, education), drinking frequency, relationship status, any Axis I mood, anxiety, or psychotic disorder, and antisocial personality disorder (ASPD): (1) a diagnosis of BPD more than doubled the risk of regularly drinking before sex (AOR=2.26; CI=1.63-3.14); (2) the diagnostic criterion of impulsivity in areas that are self-damaging (AOR=1.82; CI=1.42-2.35) was the only of 9 diagnostic criteria to remain a significant predictor of regularly drinking before sex; and (3) risk for regularly drinking before sex increased by 20% for each endorsed diagnostic criterion (AOR=1.20; CI=1.14-1.27).
Conclusions: This is the first study to examine the relationship between BPD and regularly drinking alcohol before sex in national data. Substance abuse treatment should assess regularly drinking before sex, particularly among patients with BPD.
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AN IN-DEPTH ANALYSIS OF COCAINE-INDUCED NEGATIVE SUBJECTIVE EFFECTS IN HUMANS.

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Aims: To determine the magnitude, time-course, and predictive factors and of cocaine-induced negative subjective effects.
Methods: Non-treatment-seeking individuals diagnosed with cocaine-use disorder (N=65) received randomized infusions of saline or cocaine (0 and 40 mg, IV). Heart rate (HR) and subjective effects (using visual analog scales) were measured at baseline and at 7 time-points post-infusion.
Results: Participants were mostly African American (77%) and male (82%), 43.0±0.8 (Mean±S.E.M) years of age, and reported using cocaine for 17.1±1.0 years and 18.1±1.0 of the last 30 days, and used on average 1.9±0.2 grams of cocaine per day. As expected, in comparison to saline, cocaine significantly increased several positive subjective effects ("Good Effects", "High", "Like") and HR (all p's<0.001). Of interest, cocaine also significantly increased all negative subjective effects (i.e., "Depressed", "Bad Effects", "Anxious")(all p's <0.001) and these occurred along the identical time-course. Males and females exhibited similar increases in negative subjective effects. There were no positive correlations between any negative subjective effect and increases in HR or any cocaine use variable. Race may be important since Caucasians were more likely than African Americans to report cocaine-induced "Depressed" (p=0.13) and "Bad Effects" (p=0.17). There were significant positive correlations between peak cocaine-induced "Anxious" and Profile of Mood States sub-scores for Tension-Anxiety (p=0.0003) and Total Mood Disorder (p=0.008).
Conclusions: To our knowledge, this is the first study to specifically focus on the negative subjective effects produced by acute IV cocaine exposure in the laboratory. While clearly smaller in magnitude (25-40%) than positive subjective effects, the presence of cocaine-induced negative subjective effects may have important treatment implications. Specifically, negative subjective responses to cocaine, especially "Anxious", may predict increased cue-reactivity which may increase likelihood of relapse.
Financial Support: Funding: NIDA

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A LONGITUDINAL MEDIATIONAL STUDY OF THE STABILITY OF ALEXITHYMIA AMONG ALCOHOL TREATMENT SEEKERS.

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Aims: Up to 67% of alcohol-dependent patients have alexithymia, a trait associated with emotion regulation difficulties. Although alexithymia may have a negative impact on treatment outcomes, research investigating sex differences in its stability as well as underlying mechanisms are scarce. Such research is essential to explore whether alexithymia may be amenable to change. As social learning processes contribute to and maintain alcohol problems, the reinforcement of alcohol expectancies (AE) is a plausible mechanism that links the emotional difficulties related to alexithymia and alcohol use. The objective of the present study, therefore, was to evaluate this association, to examine whether AE mediate the stability of alexithymia, and to test for sex differences in the findings.
Methods: 92 consecutively enrolled patients (72% male), 18-66 years of age in 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) and the Drinking Expectancy Profile (DEP).
Results: TAS total score, Difficulties Identifying Feelings (DIF) and Difficulties Describing Feelings (DDF) decreased significantly over time with a larger decrease in alexithymia scores for females. Path analyses showed that the stability of TAS total score, DIF and DDF were mediated through assertion AE.
Conclusions: These findings highlight the importance of AE as a longitudinal mediator of the stability of alexithymia in those with alcohol-dependence. Additional research is needed to determine the most appropriate model of care for alcohol treatment seekers with alexithymia.
Financial Support: Innlandet Hosp Trust.

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SMOKING CESSATION INTERVENTION ON FACEBOOK: WHICH CONTENT GENERATES THE BEST ENGAGEMENT?

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Aims: Social media offer great opportunity to deliver smoking cessation treatment to young adults; and data allow for unprecedented investigations of how intervention content is linked to participant engagement. We examined engagement generated by content based on Motivational Interviewing (MI) and stage-matching strategies of the Transtheoretical Model of Behavior Change (TTM) in a motivationally tailored smoking cessation intervention on Facebook.
Methods: Participants (N=79, 20% female, Mean age = 20.8) were assessed for readiness to quit smoking (precontemplation, contemplation, preparation) and assigned to a total of 7 secret Facebook groups tailored to their stage of change. Daily postings were made over 3 months, and content was coded for strategy: MI, one of ten TTM processes of change, or TTM Decisional Balance (DB). Engagement was operationalized as the number of comments to each post. A total of 514 posts generated 640 individual comments. Predictors of number of comments were analyzed using negative binomial regression analyses controlling for group, day of week, and time the post was made.
Results: In precontemplation groups, DB and MI themed posts generated high engagement (both $p<.05$). In contemplation groups, DB posts also resulted in high engagement and Dramatic Relief posts resulted in low engagement (both $p<.001$). In preparation groups, Consciousness Raising ($p<.001$) and Helping Relationships posts ($p<.01$) generated high engagement. Participant engagement was independent of day of the week and time of day the content was posted to the groups.
Conclusions: Participants not ready to quit in the next 30 days engaged most when prompted to think about the pros and cons of behavior change, while those in the preparation stage engaged most when posts increased awareness about smoking and social support. Participants' readiness to change a particular substance use behavior should be considered when tailoring social media interventions meant to produce engagement.
Financial Support: NIDA DA032578 and DA09253, NCI CA-113710

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SMOKING TOPOGRAPHY IN MEN AND WOMEN WITH AND WITHOUT CURRENT DEPRESSION: FINDINGS FROM A 10-SITE CLINICAL TRIAL.

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Aims: Depression is associated with heightened risk of nicotine dependence and smoking persistence. Women have higher rates of depression than men, and have greater difficulty quitting smoking. Little is known about mechanisms that underlie these associations. One basic question is whether men and women with and without depression differ on smoking topography, i.e., patterns of puffing behavior. We used data collected during a clinical trial conducted at 10 sites across the US to examine the separate and combined effects of gender and depression symptom severity on smoking topography.
Methods: The trial enrolled 839 smokers who smoked at least 5 cigarettes per day (CPD). At a baseline session, depression symptoms were assessed using the CESD scale, on which a score ≥ 16 indicates high current depression severity. Topography data were collected from a subset of participants (n = 762; 42% women) who smoked a usual-brand cigarette through a handheld topography device. ANOVAs were used to investigate the effects of gender and current depression on topography.
Results: Analyses indicated: (1) a gender x depression interaction ($p < .05$) on CPD indicating that high-depression women smoked more CPD than low-depression women, whereas high- vs. low-depression men did not differ on CPD; (2) effects of gender on several variables (all p's < .01): total puff number (higher in women), average puff volume and puff duration (both lower in women); (3) a trend for a gender x depression interaction on total puff volume ($p = .13$) indicating that high-depression women tended to have greater total puff volume than low-depression women, whereas high- vs. low-depression men did not differ on this variable.
Conclusions: These findings suggest that, among women, current depression symptoms are associated with experiencing stronger reinforcing effects of smoking, a mechanism that may contribute to their low cessation rates.
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LEARNING OF FINE MOTOR SKILLS IS NOT IMPAIRED IN INDIVIDUALS WITH A HISTORY OF ILLICIT STIMULANT USE.

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Aims: Use of illicit stimulant drugs is associated with long-lasting changes in movement-related brain regions. The aim of the current study was to investigate the long-lasting effect of stimulant use on motor skill learning in humans. We hypothesised that history of illicit stimulant use is associated with impaired learning of fine motor skills.
Methods: Motor skill learning was assessed in abstinent stimulant users (n=21; 27±6 yrs) and in two gender-matched control groups comprising non-drug users (n=16; 22±4 yrs) and cannabis users (n=16; 23±5 yrs). Motor learning was assessed with the grooved pegboard test (3 trials) and a 3 min visuomotor tracking task. The visuomotor task involved following a moving target with the index finger. Pattern matching was assessed by cross-correlation of metacarpophalangeal joint angle and target traces. Distance from the target (tracking error) was also calculated.
Results: Motor learning was evident in the visuomotor task. Pattern matching improved over time (cross-correlation coefficient; $P<0.001$) and tracking error decreased ($P<0.001$). Motor learning also occurred in the grooved pegboard test with performance time decreasing across trials ($P<0.001$). However, performance of both tasks did not differ between groups and there was no significant group-by-time interaction on the visuomotor task.
Conclusions: The ability to learn new fine motor skills is not impaired in individuals with a history of illicit stimulant use. This is surprising given that individuals with a history of illicit stimulant use exhibit long-lasting changes in excitability of the motor cortex, a brain region that plays a key role in motor learning.
Financial Support: Ramaciotti Foundation, National Health and Medical Research Council, University of South Australia, Australian Government

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THE ABUSE LIABILITY OF BUPRENORPHINE IS BLOCKED BY SAMIDORPHAN, A NOVEL OPIOID MODULATOR, IN RATS TESTED IN THE INTRACRANIAL SELF-STIMULATION PARADIGM.

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Aims: Buprenorphine, a partial opioid agonist, has been recently examined in clinical studies and has demonstrated antidepressant effects, particularly in patients with treatment-resistant depression. The use of buprenorphine in the treatment of depression is hampered by its risk of abuse and addiction. Currently buprenorphine in combination with samidorphan, an opioid antagonist, is in clinical trials for treatment of major depressive disorder. Previously it has been demonstrated that a combination of buprenorphine (0.1 mg/kg, SC) and samidorphan (0.3 mg/kg, SC) attenuates the neurochemical effects of buprenorphine, and also has antidepressant-like effects as demonstrated by a decrease in immobility in the forced swim test in rats.
Methods: Rats were surgically implanted with monopolar stainless steel electrodes implanted in the medial forebrain bundle and then trained to respond (FR1) for rewarding brain stimulation utilizing a rate-frequency curve shift paradigm. Once response behavior was stable, the effects on brain reward systems of both buprenorphine and samidorphan alone, and then in combination were tested.
Results: Buprenorphine (0.1 mg/kg) enhanced brain stimulation reward similar to other known drugs of abuse. Samidorphan (0.1 – 1.0 mg/kg, SC) when administered alone did not affect brain stimulation reward, indicating that it has little or no rewarding or anhedonic properties. When rats were pre-treated with samidorphan (0.1, 0.3 or 1.0 mg/kg, SC) and then tested in the intracranial self-stimulation paradigm after buprenorphine (0.1 mg/kg) administration, the rewarding effects of buprenorphine were fully blocked at the two higher doses of samidorphan, but not at the lower dose.
Conclusions: This combination blocks the addictive potential of buprenorphine when tested in the intracranial self-stimulation paradigm, while maintaining the antidepressant-like properties of buprenorphine in rats.
Financial Support: This study was funded by Alkermes, Inc

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INTEGRATING TEXT MESSAGING IN A SAFETY-NET OFFICE-BASED BUPRENORPHINE PROGRAM: A FEASIBILITY STUDY.

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Aims: 1) Assess feasibility of a text message appointment reminder (TMR) intervention
2) Determine the clinical impact of the TMR on appointment adherence
Methods: A 52-item survey was administered to 100 patients in an urban, public sector, office-based buprenorphine program between June 2013 and March 2014. Survey domains included: demographic characteristics, communication patterns, and content preferences for supportive, informational, and relapse prevention TM interventions. A TMR was then sent 7, 4, 1 day prior to the patients' upcoming appointment followed by a 16 item survey that assessed satisfaction and feedback for the TM reminders (n=72).
Results: Respondents were predominately African-American (42%), unemployed or reliant on public assistance (68%), and lacked permanent housing (52%). MP ownership was common (93%) with the caveat of a high turnover of phones (2) and phone numbers (2) in the past year. Most reported TM use (93%) and comfort with sending TM (79%).
The feasibility survey demonstrated satisfaction with the TMR (100%) and most preferred receiving text reminders (88%) in place of telephone reminders at 6 months. There was no significant difference between participants receiving the TMR compared to patients that did not receive the reminders.
Conclusions: TM based interventions are an acceptable and feasible strategy for enhancing the delivery of care in a safety net, office-based buprenorphine program.
Financial Support: Babak Tofighi was supported by a NRSA T32: Postdoctoral Primary Care Research Training Program (HRSA T32HP22238-01-00) and the Research in Addiction Medicine Scholars Program (R25DA03211). None of the authors have any financial disclosures or conflicts of interest.

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OPIOID SUBSTITUTION TREATMENT IN SPAIN: 20 YEARS OF EXPERIENCE IN HARM REDUCTION PROGRAMS.

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Aims: To describe the impact of the implementation of opioid substitution treatment (OST) during 20 years in terms of HIV infection incidence in patients dependent on heroin, in Spain.
Methods: In Spain, heroin epidemics reached its peak during the 80s, when there was a poor coverage of methadone maintenance treatments (MMT): only 1000 patients were in MMT in 1987. In parallel, HIV infection rates related to intravenous injection grew up until 33146 new cases.
The great spread of HIV infection needed a response and OST were progressively expanded in public health settings, including prisons. MMT treatments were followed a harm reduction approach. The main characteristics of them are: public funding, no restrictions in dose and no restrictions in the length of treatment. Also harm reduction centers, as supervised injection facilities have progressively been implemented.
Results: There was an increase of patients enrolled in OST, with a peak in 2002 (90488 patients), decreasing progressively, until 2012 (66945 in MMT and 2166 in buprenorphine). Also, a significant increase in the availability of MMT in prisons was observed: In 1992, 90 prisoners were enrolled in MMT, while in 2001, they were 24304 patients. Since then, the number has decreased..
Harm reduction resources have increased; in 2012, 12 supervised injection rooms were available in Spain, and 5915 subjects have been attended.
Opioid dependent patients general health improved, with a reduction in mortality. A decrease in the number of new drug injection related HIV cases have been observed: from 15836 in 1992 to 151 cases in 2012.
Conclusions: OST should be integrated in harm reduction programs, highly available, in public facilities and in prisons. Adequate coverage of health needs will help to improve the health of drug users.
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FACTORS ASSOCIATED WITH PARTICIPATION IN HIV CASE MANAGEMENT INTERVENTION AMONG RUSSIAN DRUG USERS.

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Aims: Linking HIV-infected people with a history of drug use to HIV care can be challenging. In the Russian LINC study (n=349), patients in an addiction treatment hospital were randomized to strengths-based case management (CM) to facilitate HIV care initiation. We sought to determine if individual characteristics were associated with engagement in CM .
Methods: In exploratory analyses we examined whether gender, the main independent variable, and other baseline factors (age, education, employment, relationship status, drug dependence, depressive symptoms, anxiety, impulsivity, CD4 cell count) were associated with participation in CM. Completing multiple sessions (2-5 vs 0-1) was the primary outcome and number of completed intervention sessions (0-5) was the secondary outcome. Separate multiple logistic and proportional odds models were fit including each potential predictor and adjusting for age, gender, education, and employment
Results: 174 participants were randomized to the intervention: mean age 34 years (range 22-50); 75% males; 7.5% with university education; 36% currently employed, and 35% with a partner. Completed CM sessions were 11% for 0 sessions, 14% for 1, 11% for 2, 9% for 3, 6% for 4 and 49% for 5. Age was associated with participation in a greater number of sessions (AOR=2.47 per 10 year increase, 95% CI: 1.35 – 4.52, p-value <0.01). Gender was not associated with intervention participation.
Conclusions: Older individuals had higher odds of participating in multiple CM sessions to link HIV-infected people who use drugs to HIV care. Extra efforts may be necessary to engage younger subjects in such activities.
Financial Support: Supported by R01DA032082

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COMPARISON OF COCAINE REINFORCEMENT IN LEAN AND OBESE ZUCKER RATS: DOSE-SENSITIVITY AND REINSTATEMENT OF EXTINGUISHED OPERANT RESPONDING.

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Aims: Over 35% of American adults meet criteria for obesity, and indications are that the trend is rising. Clinical observations suggest obese individuals are less likely to abuse drugs, including cocaine. However, we have recently determined that the reinforcing effectiveness (i.e., value) of cocaine is equivalent in lean and obese Zucker rats. Given that this was the first investigation of cocaine reinforcement in an animal model of obesity, more work is needed to characterize drugs as reinforcers in lean and obese subjects.
Methods: The current study investigated cocaine's relative potency as a reinforcer in lean and obese Zucker rats self-administering i.v. cocaine (0.06-1.0 mg/kg/inf), and subsequently tested these subjects in cue- (light) and drug-primed (i.p. cocaine; 10mg/kg) reinstatement of extinguished operant responding.
Results: Cocaine functioned as a reinforcer in a dose-dependent manner in all rats, and, following extinction of responding, the cue- and drug-primes reinstated extinguished lever-pressing. No significant differences in cocaine reinforcement or reinstatement were observed as a function of obesity.
Conclusions: These results, combined with our previous observations, demonstrate that cocaine's reinforcing effects are comparable in lean and obese Zucker rats and do not support evidence that obesity is associated with a decreased reinforcing effect of cocaine.
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EFFECTS OF FIXED OR SELF-TITRATED DOSAGES OF SATIVEX ON CANNABIS USERS.

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Aims: To assess the feasibility of the use of Sativex® (Δ^9-tetrahydrocannabinol/cannabidiol) on cannabis withdrawal and craving among cannabis-dependent subjects
Methods: Cannabis-dependent users (n=9) underwent an 8-condition double-blind trial (an ABACADAE study design lasting 5 weekdays each); four smoke as usual conditions (SAU) and four cannabis abstinence conditions. Abstinence conditions (B, C, D, E) included self-titration and fixed doses of placebo, self-titration or fixed doses of Sativex (up to a max of 40 sprays/day ≈ 108 mg THC). Each medication phase was followed by a washout period when was permitted to smoke cannabis as usual (A condition)
Results: Scores on Cannabis Withdrawal Checklist (CWC) were significantly lower during the fixed Sativex condition (as compared with withdrawal scores during baseline) ($F(1,8)= 14.4$ $p<.01$). Withdrawal scores using the Cannabis Withdrawal Scale (CWS), were also decreased during the fixed Sativex and self-titrated dose conditions ($p<.05$). None of the placebo conditions reduced withdrawal. No changes in craving were observed in this study. Significant differences ($F(3,24)= 5.09$ $p<.01$) in the change in body weight between Sativex and placebo fixed conditions (+1.36 vs -1.96 lb, respectively) were observed. No SAEs were associated with the study medication (Sativex)
Conclusions: This pilot study demonstrates the feasibility of our approach and seems to indicate promising effects of Sativex on cannabis withdrawal, even in a small sample of subjects, which justify the implementation of larger studies investigating the potential benefits of Sativex as a replacement therapy for cannabis dependence
Financial Support: This study was funded by the Canadian Institutes of Health Research. Medication was provided by GW pharmaceuticals

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EXPLORING SUBSTANCE GROUP DIFFERENCES ON THE SIMULTANEOUS ALCOHOL AND TOBACCO EXPECTANCY QUESTIONNAIRE IN A YOUNG ADULT COMMUNITY.

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Aims: The aim of the current study was to evaluate group differences of a novel measure of motives and expectancies specific to simultaneous alcohol and tobacco use (SATU) in a community sample of young adults with varying levels of alcohol and tobacco consumption.
Methods: Participants were 744 young adults (age 18-25) with at least one SATU episode in the past month. Participants were recruited through local and online advertisement from January 2013 to March 2014. *SATU expectancies* were assessed with the Simultaneous Alcohol & Tobacco Expectancy Questionnaire (SAT-EQ). This scale contains 18 items that load onto four distinct factors described as: affect regulation (AR), social enhancement (SE), craving/automaticity (CA), and social avoidance (SA). *Alcohol and tobacco use* were assessed via the Timeline Follow-Back on which participants reported the quantity and frequency of alcohol and tobacco use in the past 30 days. *Hazardous drinking was* measured with the AUDIT-PC which is a 5-item version of the original AUDIT.
Results: Respondents were stratified according to both presence of hazardous drinking (A+/A-) based on AUDIT-PC and daily smoking (T+/T-) as follows: A+T+ (15% of sample); A+T- (32%); A-T+ (21%); and A-T- (32%). Those with hazadous drinking had the highest levels of engaging in SATU for AR; non-daily smokers had the highest rates of SATU for SE; daily smokers endorsed the highest rates of SATU due to CA; and hazardous drinkers who did not smoke daily had the highest rate of SATU for SA.
Conclusions: The current study highlights how expectations and motives for co-use of alcohol and tobacco varies as a function of smoking and drinking status. Future research will explore more of the mechanisms of this dynamic relations among high-risk substance use behaviors to help identify potential targets for intervention.
Financial Support: Supported by the UCSD Academic Senate and the National Institute on Alcohol Abuse and Alcoholism grant R21 AA021822 (Co-PIs: Doran & Trim).

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INFLAMMATORY CYTOKINES AND PAIN IN PATIENTS WITH OPIOID USE DISORDERS.

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Aims: It is unknown whether biomarkers of inflammation are associated with hyperalgesia or chronic pain among persons receiving opioid therapy. The primary aim is to explore whether inflammatory biomarkers, specifically, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-10 (IL-10), are associated with impaired cold pain tolerance (i.e. hyperalgesia). A secondary aim is to assess whether these biomarkers are associated with chronic pain.
Methods: We conducted a cross-sectional study of adults on buprenorphine or methadone using the cold-pressor test. The primary dependent variable was cold pain tolerance (seconds). The secondary dependent variable was chronic pain. Independent variables were serum levels of IL-6, TNF-α and IL-10, each dichotomized at the highest quartile. Multivariable linear and logistic regression models adjusted for age, sex, non-white race and HCV/HIV infection status.
Results: In the sample (n=106), the mean age was 43.8 (SD±9.4) years, 51 (48%) were female, 34 (32%) non-white and 71 (68%) had chronic pain. There were no significant differences in the adjusted means for pain tolerance among participants with high (i.e. ≥75th percentile) versus low (<75th percentile) levels of IL-6 (23.3 v. 25.4, p=0.54), TNF-α (22.6 v. 25.5, p=0.38) or IL-10 (24.8 v. 24.7, p=0.96). Likewise, there were no differences in the odds for chronic pain among participants with high versus low levels of IL-6 (OR=1.00; 95% CI: 0.36-2.76, p=0.99) or TNF-α (OR=1.05; 95% CI: 0.39-2.87, p=0.92). Participants with higher levels of IL-10, which is considered "anti-inflammatory", appeared to have lower odds of having chronic pain, although results were not statistically significant (OR=0.42; 95%CI: 0.15-1.17, p=0.10).
Conclusions: In this exploratory study of adults on buprenorphine or methadone for treatment of opioid use disorders, biomarkers of inflammation did not appear to be associated with pain tolerance or chronic pain.
Financial Support: NIH/NIDA grant K23DA027367

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FACTORS ASSOCIATED WITH ILLICIT METHADONE INJECTING IN A CANADIAN SETTING.

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Aims: We examine the prevalence of and risk factors associated with injection of methadone in an urban population.
Methods: Between December 2005 and November 2013, data were derived from two open prospective studies of persons who inject drugs (PWID) in Vancouver, Canada. Generalized estimating equations (GEE) logistic regression was used to determine factors independently associated with illicit methadone injecting.
Results: Over the study period, 1911 individuals were recruited, including 34% women. Of these, 134 (7%) participants reported methadone injecting at least once. In the multivariable analysis, Caucasian ethnicity [adjusted odds ratio (AOR) = 1.90, 95% confidence interval (CI) = 1.21 – 3.00]; homelessness (AOR = 1.50, 95% CI = 1.12 – 1.99); drug dealing (AOR = 2.13, 95% CI = 1.53 – 2.98); ≥ daily heroin injection (AOR = 1.59, 95% CI = 1.10 – 2.29); ≥ daily crack smoking (AOR = 2.06, 95% CI = 1.44 – 2.94); and being a victim of violence (AOR = 1.54, 95% CI = 1.08 – 2.20) were independently and positively associated with methadone injection. Conversely, female gender (AOR = 0.48, 95% CI = 0.30 – 0.77) was negatively associated with methadone injecting.
Conclusions: Diversion of methadone for illicit injection was prevalent in this urban setting and was associated with several markers of addiction severity and other health and social vulnerabilities. These findings underscore the need to ensure methadone accessibility while limiting diversion-related risk.
Financial Support: The study was supported by the US National Institutes of Health (R01DA011591, R01DA021525). This research was undertaken, in part, thanks to funding from the Canada Research Chairs program through a Tier 1 Canada Research Chair in Inner City Medicine which supports Dr. Evan Wood. Dr. Milloy is supported in part by the United States National Institutes of Health.

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MODULATION OF BUPRENORPHINE PARTIAL AGONISM BY THE OPIOID ANTAGONIST SAMIDORPHAN: A MECHANISTIC PK/PD MODEL.

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Aims: Buprenorphine (BUP) is a μ opioid receptor partial agonist; administration may result in euphoria and pupil constriction. Samidorphan (SAM) is a novel antagonist that, in combination with BUP, is in development for the treatment of depression. A mechanistic PK/PD model was developed to elucidate the ability of SAM to modulate the PD response of BUP.
Methods: PK data were obtained in 12 subjects administered BUP (8 mg) coadministered with SAM (0-16 mg). PD response was assessed by pupillometry. PK/PD model development and analysis were conducted in WinNonlin v5.2. A mechanistic, time-independent, receptor-occupancy mediated PD model was linked to a multi-compartment PK model; linear and nonlinear signal transduction and effect site concentration models were evaluated. SAM data 1-4 mg and 8-16 mg were utilized for model development and verification, respectively. Assumptions: linear PK; all PD activity due solely to BUP/SAM.
Results: One- and two-compartment models best described SAM and BUP PK, respectively. SAM has a short half-life (4 hr) vs. BUP (49 hr). A competitive μ occupancy PK/PD model well characterized the SAM blockade of BUP pupil constriction with sigmoidal SAM PK input. The effect site association (k_{on}) and disassociation (k_{off}) rate constants for SAM were 0.88 ml/ng-hr and 0.020 hr^{-1}, respectively, and for BUP (alone) were 0.41 ml/ng-hr and 0.74 hr^{-1}, respectively. SAM has a longer receptor dissociation half-life (34 hr) vs. BUP (0.94 hr). SAM has a lower receptor k_d (0.063 nM) vs. BUP (3.6 nM), which suggests that SAM has much stronger mu receptor binding affinity than BUP. These data explain the durability of SAM blockade of BUP PD effect, independent of the shorter half-life of SAM. The model well predicted the blockade of BUP-induced pupil constriction at 8 mg and 16 mg SAM doses.
Conclusions: A PK/PD model was developed and verified to estimate the level of SAM blockade of BUP induced objective PD effect. This model may be useful in describing the pharmacologic activity of SAM blockade on BUP PD across a wide dose and/or exposure range.
Financial Support: Alkermes, Inc., NIDA N01DA-6-8867, NIDA N01DA-7-8870

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DRUG AND ALCOHOL EXPOSED PREGNANCIES: MATERNAL AND INFANT OUTCOMES.

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Aims: The primary aim of this study was to describe the maternal treatment and infant birth outcomes for pregnancies exposed to alcohol and drugs (ADE: n=91) versus those exposed to drugs only (DE: N=566).
Methods: N=657 pregnant women enrolled in substance abuse treatment in Baltimore between 2007 and 2013. Data included psychosocial variables, urinalysis results, and maternal and infant outcomes. Chi-square was used for dichotomous variables and ANOVA was used for continuous variables. ANCOVA was used to control for pre-treatment differences.
Results: The ADE group was more likely to be African American, older, and to enter treatment earlier in gestation than the DE group (p values <.05). The ADE and DE groups did not differ on daily number of cigarettes smoked. However, the ADE group reported more problematic use of cocaine and marijuana compared to the DE group (p values <.05). The ADE women were more likely to report a history of domestic violence, and to have a diagnosis of major depression (p values <.05). The two groups did not differ on rates of within-treatment drug use. On obstetrical measures, the ADE women were more likely to deliver preterm and to remain in the hospital longer post-delivery (p values <.05). Infant outcomes for the ADE group were significantly compromised. There were more fetal deaths in the ADE group compared to the DE group (0.9% vs 5.7%, p=.009). ADE group infants had lower birth weight, lower Apgar scores, and spent more days in the neonatal intensive care unit than DE infants (p values <.05). There were no differences between groups on rates of neonatal abstinence syndrome.
Conclusions: Alcohol is commonly abused by pregnant women enrolled in substance abuse treatment, and results in adverse maternal and infant birth outcomes. The extent of adverse outcomes cannot be determined at birth, indicating a need for long term follow up for alcohol exposed infants
Financial Support: None.

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A NOVEL DATA-DRIVEN RESTING STATE CONNECTIVITY ANALYSIS REVEALS DISTINCT NETWORKS ASSOCIATED WITH DELAY DISCOUNTING BETWEEN CONTROLS AND SMOKERS.

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Aims: Imaging studies has focused on prefrontal and striatal regions in studying delay discounting (DD). However, it remains unknown what networks are associated with DD in a resting brain. Using a novel data-driven approach that is not restricted to current hypothesis, the current study explored resting networks involved in DD between controls and smokers.
Methods: Thirty-four smokers and 34 age- and gender-matched controls completed a six-minute resting-state scan in a 3T Siemens Trio scanner and a hypothetical DD task on the bench. BOLD echoplanar images with TR of 2000ms were analyzed in AFNI and SPM. Using voxel-wise whole brain analysis, degree of each voxel, a connectivity strength of one voxel to other voxels in the brain, was correlated with DD to identify associated brain regions. Then, using the identified regions as seeds, we performed seed-based analysis to identify brain networks related to DD.
Results: DD did not differ between controls and smokers (p = .08). The voxel-wise correlation revealed that bilateral thalamus and left cerebellum is significantly correlated with DD (p = .01). The seed-based connectivity analysis for each of the three seeds correlating to DD revealed that a resting network of controls involves cerebellum (p = .01), whereas that of smokers involves prefrontal and striatal regions (p = .01). While all other networks showed decreased strength with an increase in DD, a right thalamus – left OFC network in smokers showed increased strength with an increase in DD.
Conclusions: Despite no group difference in DD, distinct resting networks related to DD were identified. The controls use cerebellum-centered networks while the smokers use prefrontal and striatal-centered networks. Of particular note is the role of a right thalamus – left OFC network in smokers, which suggests that smokers utilize OFC to compute value when they discount.
Financial Support: This research was supported by the Intramural Research Program of the NIDA/NIH.

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TOPIRAMATE EFFECT ON WEIGHT GAIN DURING METHADONE MAINTENANCE.

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Aims: Methadone maintenance [MM] is associated with weight gain. Topiramate [Top] combined with other agents has been approved for obesity treatment. A randomized controlled trial of Top vs placebo [P] during MM for opioid and cocaine dependence found Top ineffective for decreasing cocaine use. We now report on weight change of 114 individuals (46% Top) retained in the 20-week study.
Methods: Participants (34% AA, 48% F, 42 ± 7 ys old, 11.3 ± 1.7 ys education) were inducted onto MM (100 mg daily) over 3-weeks. Top (or P) was inducted weeks 6–12, with Top steady at 300 mg daily weeks 12–20. Weight was measured at weeks 0, 4, 8, 12, 16, 20 and 24. Change from baseline was calculated for weight (kg) and Body Mass Index (BMI; kg/m^2). Repeated measures ANOVAs evaluated the effects of Top and time on weight change from baseline. Gender and cocaine use severity (high use: ≥ 40% cocaine positive urine samples) were entered in the model.
Results: Over 20 weeks, P participants (n=62) experienced more weight gain (6.2±7.8 kg, p<0.0001), compared to Top participants (n=52; 1.9±6.5 kg, p=0.045). The effects of Top ($F_{1,596}$ = 20.4, p<0.0001), Time ($F_{1,596}$ = 29.0, p<0.0001) and Top x Time interaction ($F_{1,596}$ =12.2, p=0.0.0005) on weight change were statistically significant. One way ANOVA at each time point showed statistically significant Top effect at week 16 (4.7±6.6 vs 1.2±5.1 kg; $F_{1,106}$=9.18; p=0.0031) and 20 (6.2±7.8 vs 1.9±6.5 kg; $F_{1,112}$=10.1, p=0.002), i.e. during steady Top 300 mg daily dosing. Adding gender and cocaine use severity did not change the significance of Top and Time. Cocaine use (high/low) had a significant effect on weight. Gender had no effect on weight change.
Conclusions: Topiramate minimized weight gain during methadone maintenance.
Financial Support: NIDA R01 DA 021808; T32 DA07209; K24 DA023186.

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MAKING THE MOST OF MINDFULNESS: WHICH SPECIFIC MINDFULNESS DEFICITS MIGHT BE TARGETED TO OPTIMIZE ADDICTION TREATMENT?

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Aims: Mindfulness is a multidimensional capacity thought to include observing on a moment-to-basis, describing one's experience with facility, acting with awareness, suspending judgment, and maintaining non-reactivity. Recently, mindfulness-based therapies have been used to treat substance use disorders (SUDs), but it is unknown which dimensions of mindfulness are most relevant to addiction. Previous studies have shown mindfulness may be correlated with impulsivity and stress sensitivity, two established targets of treatment for SUDs. We hypothesized that deficits in acting with awareness and non-reactivity would correlate with impulsivity, and that deficits in non-reactivity and non-judgment would correlate with stress sensitivity.
Methods: We investigated mindfulness using the Five Facet Mindfulness Questionnaire (FFMQ) in 55 cocaine dependent individuals. Two step-wise multivariate linear regressions evaluated correlations between each of the 5 dimensions of mindfulness and 1) impulsivity (Barratt Impulsiveness Scale: BIS) and 2) stress sensitivity (Perceived Stress Scale: PSS).
Results: FFMQ scores were inversely correlated with both impulsivity (β = -0.293, $p < 0.05$) and stress sensitivity (β = -0.292 $p < 0.05$). The acting with awareness (β = -0.576 $p < 0.0001$) and non-reactivity (β = -0.298 $p < 0.01$) facets of mindfulness were significantly and inversely correlated with impulsivity, and the non-judgment (β = -0.520 $p < 0.0001$) and non-reactivity (β = -0.282 $p < 0.05$) facets were significantly and inversely correlated with stress sensitivity.
Conclusions: These results suggest that the non-judgment, non-reactivity, and acting with awareness facets of mindfulness may be suitable targets of mindfulness-based treatment for SUDs. Because it was highly correlated with both impulsivity and stress sensitivity, non-reactivity may be a particularly important target of mindfulness-based treatment. Future research is needed to give insight into the clinical relevance of these findings.
Financial Support: The authors thank NIDA for funding this research through grants DA009236, DA009236, and DA031771.

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PARTICIPATION IN THE BINATIONAL QUIT TRIAL FOR REDUCING PROBLEM DRUG USE AMONG PATIENTS OF COMMUNITY HEALTH CENTERS IN EAST LOS ANGELES AND TIJUANA: THE ROLE OF CROSS-BORDER MIGRATION.

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Aims: To estimate trial participation rates and characteristics of participants and non-participants in Tijuana and LA that may identify disparities in SBIRT trial participation.
Methods: Adult patients of 2 CHCs in LA and 6 CHCs in Tijuana who screened positive for risky drug use were asked to participate in QUIT. Participation rates include: 1) rates of trial eligibility among problem drug users; 2) rate of enrollment among eligible patients; 3) rate of receipt of the intervention (at least one HE session) among enrolled intervention group patients; 4) rate of completion of 3 month follow-up assessment among enrolled patients.
Results: Nearly all patients were Latino and 2/3s were male. Problem drug users in the past 3 months were 128 in LA and 68 in Tijuana. Participation rates were (LA vs. Tijuana): eligibility rate 88% vs. 87%); enrollment rate 89% vs. 56%; intervention rate 76% vs. 17%; completion rate 80% vs. 27%. Cross-border migration affected all study stages: willingness to be screened for study eligibility (LA), willingness to enroll in this trial of a stigmatized health behavior (LA), and reduced intervention rates and trial completion rates because of being lost to follow-up when crossing the border (Tijuana > LA).
Conclusions: Binational-QUIT had high eligibility rates, however we found lower enrollment, intervention and completion trial rates in Tijuana. Stigma and confidentiality may have affected enrollment rates and cross-border migration may have affected intervention and completion rates. Future research should test the feasibility/acceptability for study patients to contact study teams on the other side of the border when they migrate.
Financial Support: NIDA DA 022445, NIDA 3P30DA027828-02S1 and -02S2

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UNDERREPORTING OF RISKY DRUG USE AMONG PRIME CARE PATIENTS IN FEDERALLY QUALIFIED HEALTH CENTERS.

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Aims: To estimate, and identify correlates of, drug use underreporting among risky drug users of FQHCs.
Methods: Eligible adult patients with moderate ("risky") drug use (ASSIST score 4-26) on the self-administered WHO ASSIST who participated in the "Quit Using Drugs Intervention Trial (QUIT)" were asked to submit a urine sample (4/5 study clinics assented to urine drug testing). Under-reporters were defined as individuals who stated they did not use a specific drug category in the past 30 days in their baseline questionnaire but the urine drug test was positive for recent use of that drug. Individuals with negative or indeterminate urine drug tests were excluded from the analysis.
Results: 189/196 (96%) patients in the QUIT study agreed to provide urine samples. Of those, 54 urine studies were negative or indeterminate which resulted in 135 participants for this data analysis. The mean age of participants was 40 years (range 18 to 67). Positive urine drug testing results were: 18 tested positive for opiates, 6 amphetamines, 21 cocaine, 97 marijuana, and 36 tested positive for more than one drug. Thirty patients (22%) underreported drug use and 105 (78%) reported their drug use accurately. Underreporting by specific substances was as follows: underreporting was highest for the least commonly used drugs (amphetamines 66% and opiates 45%), but underreporting was lowest for the most commonly used drugs (cocaine 14%, and marijuana 7%). Logistic regression revealed that underreporting of any drug was associated with: being older than 45 years old (OR 4.3), poly-drug use (OR 8.9) (all p<.05).
Conclusions: Overall underreporting of risky drug use was low among adult FQHC patients at 22%. This varied considerably based on the substance used from 7% among marijuana users to 45% and 66% among opiate and amphetamine users. Clinicians should consider screening their patients for drug use using urine drug testing in populations most likely to underreport.
Financial Support: NIDA DA 022445, NIDA 3P30DA027828-02S1 and -02S2

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CANNABIDIOL ATTENUATES THE INCREASED SUSCEPTIBILITY TO FALSE MEMORIES PRODUCED BY TETRAHYDROCANNABINOL.

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Aims: We studied the acute effects of cannabidiol (CBD), tetrahydrocannabinol (THC), and their combination on true and false memory recollection and recognition in healthy subjects.
Methods: Twenty-four none cannabis users, healthy male volunteers participated in a randomized, double-blind, placebo-controlled, cross-over trial. Volunteers participated in four experimental sessions 7 days apart . At each session, they received sublingual doses of: 7.5mg THC, 7.5mg CBD, the combination of 7.5mg THC and 7.5mg CBD, or placebo. Ninety min after administration, participants performed a modified version of the Deese/Roediger-McDermott (DRM) semantic memory task. Two min after the initial word presentation, participants listed all the words they could remember (memory recall), and 20 min later they identified the words from a list of the previously presented words (true recognition), and new semantically-related and semantically-unrelated words (false recognition).
Results: True memory was not modified during recall or recognition phases by either drug or their combination with respect to placebo. However, THC significantly increased false memories compared to placebo during the recognition phase. CBD did not induce any effects when administered alone, but decreased the deleterious effect of THC on false recognition when the two drugs were combined.
Conclusions: Our results indicate that acute administration of THC impairs reality monitoring evidenced by an increased susceptibility to experience false memories. These effects can be attenuated by CBD.
Financial Support: This work was supported by the Spanish Health Department (PI 08/0741) and by "La Marató de TV3" (TV3 070710). Dr. M. V. is supported by FIS (CP04/00121 from the Spanish Health Department in collaboration with Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau)

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FUNCTIONAL AND BEHAVIORAL CONSEQUENCES OF DRD4 GENETIC VARIATION IN MACAQUES.

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Aims: The dopamine D4 receptor (DRD4) associates with addiction-related phenotypes, including novelty seeking, risk taking, and stress resilience. This study aimed to investigate the consequences of genetic variation in DRD4 in macaques, model species often utilized in substance abuse research. We sought to identify genetic variation and characterize haplotypes across the genus, then test the functional effects of this variation on cAMP signaling and initiate studies on the behavioral impact of these polymorphisms in rhesus macaques.
Methods: The DRD4 receptor was resequenced in 64 rhesus, 32 cynomolgus, and 32 Japanese macaques. HEK293 and AV12 cells with CRE-responsive firefly luciferase reporters were transfected with macaque and human *DRD4* alleles. Cells were treated with forskolin and variable concentration of DRD4 agonist (A-412997). Luciferase fluorescence was measured and quantified. Genotyped rhesus macaques were presented with novel and familiar fruit stimuli. Latency to physical contact and ingestion served as a measure of novelty seeking.
Results: 15 nonsynonymous SNPs were identified in multiple individual macaques; 11 localized to the third intracellular loop. C749T, (MAF > 20%) showed an EC_{50} shift following agonist treatment (HEK293: 1.7 nM vs. 2.6 nM; AV12: 9.6 nM vs. 3.1 nM) comparable to that observed in humans comparing the 7-repeat and 4-repeat alleles (HEK293: 7.6 nM vs. 3.2 nM; AV12: 3.3 nM vs. 5.0 nM). In behavioral assays, animals harboring the T749 allele have a longer latency to both touch (1.5 seconds) and eat (6 seconds, n=9) the novel fruit.
Conclusions: In macaques, a polymorphism (C749T) is observed that parallels the human repeat variation in both signaling and behavioral assays. This commonality may offer insights into both the natural history of the species and the genetics of novelty-seeking behavior associated with substance abuse.
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PREDICTORS OF AGREEMENT BETWEEN HAIR ANALYSIS AND SELF-REPORT OF DRUG USE.

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Aims: To examine predictors of agreement between hair analyses and self-report of drug use.
Methods: This is a secondary analysis from the National Drug Abuse Treatment Clinical Trials Network (NIDA CTN) randomized trial "Screening, Motivational Assessment, Referral, and Treatment in Emergency Departments (CTN-0047; SMART-ED)". Self-reported drug use during follow-up over a 90-day recall period on the Timeline Follow Back Instrument was compared to drug use from hair analysis for Cannabis, Cocaine, Prescribed Opioids [PO] and Street Opioids[SO]. Measures of agreement/disagreement, including under-reporting (self report negative when hair indicates drug use) and over-reporting (self-report positive when hair does not indicate drug use) were calculated. The following variables were examined as predictors of disagreement: source of hair (head vs. body), drug of choice, site, AUDIT-C score, DAST-10 score, visit, treatment arm, sex, race, ethnicity and age. Of the 1,285 randomized participants, 1120 (87%), 875 (68%), 893 (69%) and 832 (65%) provided hair samples at baseline, 3-, 6-, 12-month visits, respectively.
Results: The agreement between the hair sample results and TLFB was high for cannabis (cohen's κ = 0.49-0.54) and SO (κ = 0.73-0.81), but lower for cocaine (κ = 0.31-0.35) and PO (κ = 0.18-0.30). Drug of choice, irrespective of being cannabis, cocaine, SO or PO, had statistically significantly lower under-reporting of drug use compared with other self-reported drug use (all p-values < .01). Of note, females (p=.0085; F vs M; OR = 1.33) and older age (p=.0076; 45-<55 vs 18-<25; OR = 2.02) were associated with under-reporting of cannabis use. Few predictors of over-reporting were identified.
Conclusions: Hair collection can be an important biological measure to assess drug use, and can be used to assist in corroborating self-report. From these analyses, there are a number of factors that impact agreement between drug use as measured by hair and drug use through self-report.
Financial Support: NIDA-HHSN271201400028C/N01DA-14-2237

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EXPLORING THE FEASIBILITY TO QUANTIFY PRESCRIPTION DRUG MISUSE AND ABUSE: FOCUS GROUP FINDINGS.

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Aims: The epidemic of prescription drug misuse and addiction is increasing in the United States and researchers need to accurately quantify drug intake to categorize users and develop effective prevention interventions. This paper presents the findings on accurate quantification of prescription pill misuse from a series of focus groups (FGs) as part of a NIDA funded Prescription Drug Misuse and Abuse study in St. Louis.
Methods: Fourteen FGs, seven each with older (aged 50-65 years) and younger adults (aged 18-25 years) were conducted using a semi-structured interview guide. All 38 participants were asked to estimate the total number of pills they misused in their lifetime. Sessions were audio taped, transcribed, and analyzed using the Atlas ti™.
Results: Though participants in all FGs reported misusing prescription drugs, only one older group participant and three younger group participants mentioned that they could calculate the approximate number of lifetime prescription drugs they had misused or abused. Among older adults, barriers to calculating the number of pills misused included a very long duration of use, the use of pills for both prescribed and non-prescribed motivations, and infrequent mixing of pills with alcohol and other illegal substances. Among the younger group, those who had childhood prescriptions for a specific condition such as ADHD, and those who reported misusing pain pills, reported that they would be able to provide a rough estimate of the number of lifetime pills consumed. All others felt it would be a task to estimate the number of pills on the spot, citing the same reasons as the older adults.
Conclusions: The study findings highlight the need for pill cards and other methods to enhance recall of the number of lifetime prescription pills misused. Understanding the barriers to quantifying this information among two most vulnerable populations, older and younger adults, is necessary to emphasize on need for prevention interventions.
Financial Support: This study was funded by NIDA R01-DA20791 (PI: Cottler)

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THE PROTECTIVE EFFECT OF ENRICHMENT ON DRUG ABUSE VULNERABILITY MAY REFLECT A DECREASE IN MOOD-BASED IMPULSIVITY USING A RAT MODEL OF NEGATIVE URGENCY.

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Aims: Explored the effects of enriched and isolated housing in a behavioral rat model of negative urgency

Methods: ***Subjects***: 24 Male Sprague-Dawley rats were used***. Housing:*** Enriched condition (EC): 8 rats were housed in cage with 14 novel objects. Social condition (SC) 2 rats were rearing in NIH standard housing conditions. Isolated condition (IC): rats were placed singly housed. ***Behavioural Task:*** Rats were trained in an operant conditioning to expect a non-contingent food reward (US) upon presentation of a light (CS). They then received response-contingent operant training for food reward on an FR10 sheduele. After acquisition, the Pavlovian (PV) and operant (OP) components were alternated and the number of responses in the OP were measured. Randomly, the expected food reward in the PV was omitted and responding in the OP was measured. *Negative urgency was defined by the increase in responding observed following reward omission compared to responding following reward presentation.*

Results: To address differences in response rates a 2x3 (trial type x environment) ANOVA was conducted. A significant main effect for trial type [$F(1, 42)=13.15$, $p<0.0001$]. environment [$F(1,42)=19.59$, $p<0.0001$] and interaction effect [$F(1, 42) = 8.49$, $p <0 .0001$] was found. Tukey's HSD test revealed that IC rats increased their operant response rates following unexpected reward omission ($p<0.01$). In contrast, neither EC nor SC rats modified their response rate after the omission trials.

Conclusions: The current results indicate that IC rats, but not EC nor SC rats, developed negative urgency as modeled by a reward omission task. This results are important within the context of previous work showing that enrichment protects against drug abuse in preclinical models. We are performing immunofluorescence analysis in order to identify the possible neurobiological mechanisms involve in the expression of the environment-dependent negative urgency phenotype.

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SUBSTANCE USE AMONG SEXUAL MINORITY COLLEGIATE ATHLETES: A NATIONAL STUDY.

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Aims: Examine different types of substance use during the past 30 days, and diagnosis/treatment of substance use disorders during the past 12 months, among sexual minority collegiate athletes.

Methods: This study uses data from college students for the fall semester between 2008 and 2012 from the American College Health Association-National College Health Assessment. The sample for this study uses data from 123,735 college students from 157 different U.S. universities. Sexual minority athletes made up .5% of the sample (Male:n=148; Female:n=442), heterosexual athletes made up 7.6% of the sample, sexual minority non-athletes made up 7.6% of the sample, and heterosexual non-athletes made up 84.3% of the sample.

Results: The analysis revealed that sexual minority athletes have higher odds of engaging in alcohol use during the past 30 days when compared heterosexual athletes (AOR=1.33,95%CI=1.08,1.64), sexual minority non-athletes (AOR=1.22,95%CI=1.01,1.47), and heterosexual non-athletes (AOR=1.55,95%CI=1.26,1.91). Moreover, sexual minority athletes have higher odds of being diagnosed/treated for a substance use disorder when compared to heterosexual athletes (AOR=4.55,95%CI=2.71,7.63), sexual minority non-athletes (AOR=1.96,95%CI=1.26,3.06), and heterosexual non-athletes (AOR=4.29,95%CI=2.71,6.77). Additional analyses indicated that male sexual minority athletes are at the greatest risk of being diagnosed/treated for a substance use disorder.

Conclusions: Possible explanations as to why sexual minority athletes may be at a greater risk of substance use disorders could be related to social stressors including the difficulty of trying to maintain a legitimate athletic identity within a social environment that is traditionally homophobic. Alternatively, sexual minority athletes may be in a better position to receive treatment for substance use disorders given greater access to mental health resources for athletes.

Financial Support: None.

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COMBINED AND INDEPENDENT RELATIONSHIPS BETWEEN CURRENT MARIJUANA AND CIGARETTE USE AND CARDIOMETABOLIC DISEASE RISK AMONG UNITED STATES EMERGING ADULTS: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEYS 2007-2012.

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Aims: Emerging adults ($\leq$ 25 years old) have the highest prevalence of current marijuana use and cigarette use compared to other age groups in the United States (US). Rates of obesity/related diseases also remain high among this age group. The relationships between current marijuana, current cigarette, and current combined use and cardiometabolic disease risk factors in US emerging adults are unclear. Our aim was to examine these independent and combined relationships in a nationally representative sample.

Methods: A cross-sectional analysis of 20-to-25 year olds (N=1,942) from the 2007-2012 National Health and Nutrition Examination Surveys was conducted. Self-report substance use was categorized into four groups: no lifetime use (reference group), past 30-days use of marijuana only (CMU), past 30-days use of cigarettes only (CCU), and past 30-day combined-use (CMU+CCU). Logistic regression analyses assessed each category and a cluster of $\geq$ 3 cardiometabolic disease risk factors (CMDR) (fasting blood glucose, serum triglycerides, total, high- and low-density lipoprotein cholesterol, systolic/diastolic blood pressure, and waist circumference).

Results: About 34%, 67%, and 5% reported CMU, CCU, and CMU+CCU, respectively. Over 12% presented with CMDR. After controlling for age, gender, ethnicity, and poverty-to-income ratio, the odds of having CMDR was highest among CMU + CCU (AOR: 4.3, 95% CI: 1.1-16.1). There were no significant relationships between CMU nor CCU with CMDR.

Conclusions: The combination of CMU+CCU presents a significant risk for CMDR in emerging adults. Findings have important implications since the prevalence of substance use is the highest in emerging adults. Future studies should examine the impact of frequency of combined-use on CMDR.

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THE INTERRELATIONSHIP OF CULTURE AND DEPRESSION IN THE BARRIO.

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Aims: Latinos in the barrio face multiple risks for drug use. Cultural values are known determinants of Latino behavior. Less is known on the association between depression, drug use and cultural values. This study aimed to test the following hypotheses: 1) Familismo would be inversely related to depression; 2) Personalismo would be inversely related to depression; 3) Fatalismo would have a direct relationship with depression; and 4) Machismo would have a direct relationship with depression.

Methods: The study sample consisted of Mexican-American injection heroin using men. A cross-sectional research design, field intensive outreach and key informants endemic to the barrio were utilized. Analysis involved dividing the sample (n=227) into "depressed" and "non-depressed" groups using their scores on the CESD. Chi-squares and logistic regression were used to investigate relationships. Baseline correlation analysis revealed influential covariates that were entered into a logistic regression.

Results: Familismo and fatalismo were both protective of depression (β = -0.754, AOR = 0.471 and, β = -1.372, AOR = 0.254 respectively). In addition as age increased for the sample, the likelihood of depression decreased (β = -0.086, AOR = 0.918). Neither personalismo nor machismo had a significant effect on depression.

Conclusions: Findings from the study revealed 43% of the sample scored as having depression. Given the tremendous risk for depression that these individuals are confronted with on a daily basis it is surprising that 57% tested negative for depression. Results from the logistic regression revealed the buffering effects of familismo and fatalism on depression. Clinicians should be aware that depression is associated with high risk drug use behaviors and a better understanding of the relationship between cultural values and depression can help guide practice.

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ACCEPTANCE AS A RELEVANT MINDFULNESS FACET FOR CIGARETTE SMOKERS.

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Aims: Mindfulness is one dispositional factor related to smoking (e.g., lower nicotine dependence, greater likelihood of cessation; Heppner et al., under review; Vidrine et al., 2009), and mindfulness-based interventions have demonstrated initial efficacy for enhancing smoking cessation (Brewer et al., 2011; Davis et al., 2014). Given mindfulness is a multifaceted construct, understanding which components of mindfulness are most associated with smoking behavior is an important next step to better inform treatment development and outcome. The current study hypothesized that mindfulness (specifically the acceptance component) would predict less smoking behavior and less strong positive smoking expectancies.
Methods: Participants completed the following self-report measures: Smoking Consequences Questionnaire (SCQ), Center for Epidemiologic Studies Depression Scale (CESD), and the Kentucky Inventory of Mindfulness Skills (KIMS); data on cigarettes smoked per day (CPD) were also gathered.
Results: Participants included 72 daily college smokers (75% female; 94.4% Caucasian); average age was 21.44 (*SD*=4.87). Five hierarchical linear regression analyses were conducted, with the criterion variables being CPD and the four subscales of the SCQ. For Step 1 of each model, gender and age were entered as covariates (CPD was also entered for the SCQ models), CESD was entered at Step 2, and Step 3 included the four subscales of the KIMS (observe, describe, acting with awareness, accepting without judgment). Results indicated that only accepting without judgment was negatively predictive of CPD, $F(7,61)=2.90$, $p=.01$ ($\beta=-.41$) and the SCQ negative reinforcement subscale $F(8,57)=9.94$, $p=.001$ ($\beta=-.43$), accounting for 16% and 52% of the variance, respectively.
Conclusions: Findings support recent research (Adams et al., under review) indicating that the acceptance component of mindfulness may be particularly relevant to smoking behavior. Increasing the ability to accept without judgment within the context of smoking cessation may be a relevant treatment target.
Financial Support: N/A

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WORKING MEMORY PREDICTS OUTCOME FOR YOUTH OPIOID ADDICTION TREATMENT.

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Aims: Better understanding of factors that impact outcome is important for treatment. Working Memory (WM) impairment has been linked to poorer performance in SUD treatment. The current pilot aims to describe the profile of WM capacity among youth seeking treatment for opioid addiction and evaluate the impact on treatment outcome.
Methods: Participants are a convenience sample of 58 youths (age M=19.1, range=17-21; SD=1.5) admitted to inpatient opioid detoxification between Feb 2013 and Oct 2014. WM was assessed using subscales on the WAIS-IV (Digit Span and Letter-Number Sequencing). Rates of initiation and attendance at subsequent outpatient treatment, and urine test results were collected from treatment charts for 12 weeks.
Results: Patients were 41% female, 95% Caucasian, 70% injection users, with average 11 years of education. Of the total sample, 40% (n=23) were referred to continuing outpatient care at the center following inpatient discharge because of geographic proximity. Of these, the linkage rate within 30 days (M=3.8d; range 0 – 24) from residential to outpatient initiation was 65% (N=15). 9 patients were treated with buprenorphine and 6 with extended release naltrexone. WM mean score was 36%ile (range 4-93%ile) compared to aged matched norms. Average outpatient attendance was 4.9 weeks (range 1-11). Mean # of weeks with urine test negative for opioids was 4.1 (range 0-8) weeks. WM correlated highly with number of weeks attended (R=.64, p<.05) and moderately with number of opioid negative urines (R=.41, p<.05). At week 12, 33% were retained in treatment (any attendance within past 2 weeks) and13% had returned to inpatient for treatment of relapse.
Conclusions: In this small pilot, while rates of continuing care linkage and retention were relatively modest, WM in opioid addicted youth was related to treatment attendance and rates of opioid negative urines. Additional research on WM and interactions with other patient and treatment characteristics is warranted to improve intervention and outcomes for this critical population.
Financial Support: MMTC

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CHALLENGES ENCOUNTERED WHILE RECRUITING FREQUENT MARIJUANA SMOKERS FOR AN OUTPATIENT LABORATORY STUDY.

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Aims: A multi-site outpatient study sought to enroll marijuana (MJ) users. Recruitment was unexpectedly difficult given MJ use prevalence. This abstract describes the challenges encountered at one site.
Methods: Study inclusion criteria were: past month MJ use ≥4x/week, literate, good health, and age 18-50 years old. Exclusion criteria were: abnormal labs/ECG, history of seizure/head trauma, pregnancy, BMI>30, current prescriptions, medical or psychiatric diagnoses, recent violent behavior, and seeking treatment. Advertisements were distributed regionally for 14 months. Respondents completed phone screens and those qualified were invited for in-person screening over two visits.
Results: Only 29% of the 710 individuals completing phone interviews qualified; 66% were disqualified and 5% could not be reached for additional questions. Of the 205 qualified, 33% could not be reached. 134 were scheduled for Screen 1: 52 did not show; 6 arrived, but were disqualified before consent (medical issues); 76 individuals completed Screen 1. Of those completing Screen 1, 42% were disqualified (medical>mental health>behavioral issues) and contact was lost with 24%. Of the 28 scheduled for a second screen, 2 did not show, 8 were disqualified, 1 could not be contacted. Overall, 17 participants were enrolled, 9 dropped out, 1 was discharged, 7 completed.
Conclusions: Of those completing phone screens, only 1% completed the study, indicating that a population of frequent MJ smokers is surprisingly unhealthy and difficult to recruit and retain as outpatients. However, recent changes in MJ policy will increase the need to study this population. For future studies, we suggest establishing several means of contact with participants, scheduling multiple screening visits, and completing cognitive and medical assessments during initial appointments.
Financial Support: U10DA013732

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ESTIMATED PROBABILITY OF BECOMING A CASE OF DRUG DEPENDENCE IN RELATION TO DURATION OF DRUG-TAKING EXPERIENCE: A FUNCTIONAL APPROACH.

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Aims: At CPDD 2014, we applied functional analysis to estimate probability of drug dependence as a function of users' days of drug use, observed soon after onset of use. Here, we aim to apply functional analysis to estimating development of dependence in relation to newly incident users' elapsed time from first to last use of the drug (ETFL), with cocaine and cannabis as exemplars.
Methods: Data are from the 2004-2013 National Survey on Drug Use and Health (NSDUH), with focus on newly incident users (cocaine: n=3186; cannabis: n=103263). Standardized modules identify cocaine and cannabis dependence cases with onset within 12 months of first use, and measure ETFL. Nonlinear functional regression based on the Hill equation was implemented with attention to sampling weights and clustered sampling via the R "survey" library.
Results: Hill function estimates suggest 2% of cocaine users become cocaine dependent with ETFL~<=2 months (95% CI=2%,4%), after which risk shifts upward (slope, k = 6.6) toward pmax of 14% (95% CI=12%,17%) at ETFL>~3 months. For cannabis, few become cannabis dependent with ETFL~<2.5 months, estimated slope k = 2.2 (95% CI=1.4,3.5), and pmax=13% (95% CI=10%,23%) when ETFL~>7 months.
Conclusions: Limitations are present, including ETFL and 'becoming dependent' as interdependent response variables, so that plotting one vs the other is somewhat artificial. Nonetheless, doing so, we gain four possible insights in 'comparative epidemiology' of drug dependence: (1) Hill function estimates may aid assessment of 'dependence liability' in community contexts; (2) dependence observed at short ETFL might be studied as a distinctive phenotype; (3) absence of dependence observed at long ETFL might give clues for resilience research; (4) to the extent that drug availability fosters longer ETFL and does not alter these estimates, one result of increased availability might be upturning numbers of dependence cases perhaps observable as soon as ~7.5 months after regime change.
Financial Support: Supported by NIDA T32DA021129 (OAV); K05DA015799 (JCA).

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FEASIBILITY OF WEB-BASED TREATMENT DELIVERY FOR COCAINE USE DISORDER: PROFILE OF INTERNET ACCESS BY ACTIVE COCAINE USERS.

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Aims: Web-based interventions have received recent attention for the treatment of substance abuse disorders. This study sought to determine the availability of Internet access in cocaine users undergoing screening to participate in human behavioral pharmacology studies as a means for assessing feasibility of such interventions.

Methods: Internet-use data were examined for 66 (27 female) subjects aged 19-55, screened during a one-year period (09/01/2013-08/31/2014) to participate in studies based at the University of Kentucky. All subjects were current cocaine users verified by a cocaine-positive urine. The relationship between Internet access and subject profiles were analyzed using descriptive statistics, independent samples *t*-tests, and Fisher's exact tests.

Results: Over 2/3 of subjects (~69%) reported regular Internet access. These subjects most typically used library services (~59%) and reported accessing the web approximately 17 days per month. Younger individuals were more likely to report Internet access than older subjects (M = 38.8 & 44 years). Internet access did not differ as a function of other demographic variables (e.g., gender, education). The proportion of other drug positive urine screens was generally higher in Internet users than non-users. Likewise, self-reported cigarette and other drug use was significantly higher in Internet users.

Conclusions: Overall, a majority of cocaine using individuals screened for participation reported regular Internet use. Demographic profiles generally did not impact Internet usage patterns, but younger individuals were more likely to report Internet access. Internet users were more likely to report other drug use. These data suggest that Internet-based interventions will likely be feasible in cocaine-using populations, especially younger cocaine users.

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INTRANASAL BUPRENORPHINE ALONE AND IN COMBINATION WITH NALOXONE: REINFORCING EFFICACY AND ABUSE LIABILITY IN PHYSICALLY DEPENDENT OPIOID ABUSERS.

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Aims: Buprenorphine/naloxone (BUP/NX) was designed to prevent misuse by the intravenous (IV) route, as high naloxone IV bioavailability may precipitate withdrawal. We previously demonstrated that intranasal (IN) administration of BUP/NX results in appreciable absorption of naloxone. The present study explored whether IN BUP/NX has lower abuse potential and reinforcing efficacy compared to IN BUP alone in opioid dependent individuals.

Methods: Eleven opioid dependent volunteers were enrolled as inpatients for 6 weeks, stabilized and maintained on oxycodone (30 mg, p.o., qid) throughout the study. Eight sets of paired sessions (Sample followed 24 hr later by Progressive Ratio self-administration) were conducted with ≥48 hr between sets. Placebo was substituted for two consecutive oxycodone doses before each session (i.e., test doses given 14.5 hr after last active oxycodone dose); test doses included placebo, oxycodone 60, BUP [2, 8 & 16] and BUP/NX [2/.5, 8/2 & 16/4] mg, IN in a quasi-randomized order.

Results: All active drug conditions produced prototypic mu opioid agonist effects (i.e., miosis, decreased respiration, increased ratings of drug liking). With BUP and BUP/NX, positive subjective effects often peaked at the 8 or 8/2 mg dose. Only modest signals of opioid withdrawal were detected that were greater than those produced by the placebo substitution. Oxycodone and BUP 8 mg were self-administered significantly more than placebo ($p<.05$). For all doses, BUP was self-administered to a greater extent than BUP/NX for matched doses (e.g., 8 vs. 8/2).

Conclusions: These data suggest that, while IN BUP/NX did not produce robust precipitated withdrawal, it appears to have lower reinforcing efficacy compared to BUP alone and may offer some deterrence benefit against misuse by the IN route.

Financial Support: Supported by NIDA R01 DA016718 (SLW) and NCCR/NCATS UL1TR000117.

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THE COCAINE USE REDUCTION WITH BUPRENORPHINE STUDY: COCAINE USE FINDINGS.

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Aims: The Cocaine Use Reduction with Buprenorphine (CURB) study, conducted under the National Drug Abuse Treatment Clinical Trials Network, investigated the safety and effectiveness of buprenorphine/naloxone (BUP, as Suboxone®) provided on a platform of extended-release injectable naltrexone (XR-NTX, as Vivitrol®) for reducing cocaine use in participants who met DSM-IV criteria for cocaine dependence and past or current opioid dependence or abuse.

Methods: This multi-centered, double-blind, placebo-controlled study provided XR-NTX to 302 participants before random assignment to 1 of 3 daily sublingual BUP conditions: 4mg BUP (BUP4, n=100), 16mg BUP (BUP16, n=100), and 0 mg BUP (PLB, n=102). Participants received pharmacotherapy for 8 weeks, with thrice-weekly clinic visits for observed dosing, provision of take-home medication, urine drug screening (UDS), and assessments. Cognitive Behavioral Therapy was provided weekly. Follow-up assessments occurred at 1 and 3 months post-intervention.

Results: Planned primary analyses of self-reported cocaine use corrected by UDS found no difference in cocaine use during the last four weeks of medication (weeks 4-8) between placebo and each BUP group (BUP4 vs PLB, p=0.143, BUP16 vs PLB, p=0.165). Secondary longitudinal analysis of UDS found a significant difference between BUP16 and PLB (p=0.030), but no difference between BUP4 and PLB (p=0.529). No differences across groups were found for adherence, retention, or adverse events.

Conclusions: Although the primary outcome analysis did not find a treatment effect, other analyses suggest that treatment with buprenorphine/naloxone, used in combination with naltrexone, may be beneficial in reducing cocaine use for some individuals. Future studies to evaluate this medication combination pharmacotherapy for cocaine use disorder appear warranted.

Financial Support: DA13045

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OPIOID ANTAGONIST TREATMENT MODULATES THE BRAIN RESPONSES TO BABY SCHEMA IN OPIOID-DEPENDENT PATIENTS.

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Aims: Caring for the young is fundamental to species' survival. Prior studies show that in healthy participants, caretaking is triggered by a set of infantile facial features described as the "baby schema" (BS), and that it is associated with activation of the mesocorticolimbic system. Addiction has been reported to adversely affect caretaking behaviors through mechanisms that are not well understood. We explored how opioid antagonist treatment modulates the brain responses to BS in opioid dependent (OD) patients.

Methods: 47 OD patients (29±7 years old, 22 F) were studied. Following detoxification, subjects received monthly injections of extended release naltrexone (XR-NXT) for up to 3 months. Subjects underwent functional magnetic resonance imaging (fMRI) immediately before and 1-2 weeks after the first injection, while viewing a sequence of infant faces that have been parametrically manipulated for their BS content, resulting in portraits at 3 levels: High, Unmanipulated and Low BS.

Results: Brain response to infant faces across BS levels in the Precuneus, Nucleus Accumbens (NAcc), Thalamus and Medial Frontal Gyrus was greater before than during XR-NXT treatment ($z\geq2.3$ $p<0.05$). A whole-brain voxel-wise test of linear increase in BOLD fMRI signal with increased BS revealed that women showed greater activation in the right NAcc, left Middle Frontal Gyrus and Precuneus, while men showed greater activation in the right Lateral Frontal Gyrus and Temporal Pole (p=0.05 uncorrected).

Conclusions: Our findings provide preliminary characterization of the pattern of brain response to a correlate of caretaking in OD patients. Future work will determine the clinical relevance of these findings, including the degree to which they are modified by treatment and abstinence.

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ARIPIPRAZOLE AND RISPERIDONE IN TREATMENT OF METHAMPHETAMINE ASSOCIATED PSYCHOSIS IN CHINA: A PILOT RANDOMIZED STUDY.

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Aims: We evaluated tolerability and efficacy of aripiprazole and risperidone for treatment of methamphetamine associated psychotic symptoms in China.
Methods: Patients hospitalized with acute psychotic symptoms and methamphetamine use (N=42), with Positive and Negative Syndrome Scale total score (PANSS) between 60 and 120 were randomized to aripiprazole (initial dose 5-10 mg/day followed by flexible doses 5-15mg/day) or risperidone (initial dose 2-4 mg/day followed by flexible doses 4-6mg/day) from day 3 to 25. Outcome measures included PANSS, Clinical Global Impressions-Severity of Illness scale (CGI-S) and Clinical Global Impressions-Efficacy Index (CGI-EI), Brief Substance Craving Scale, Abnormal Involuntary Movement Scale, Barnes Assessments Akathasia Scale, Simpson Angus Scale, and self-reported adverse effects evaluated at baseline, during treatment, and at treatment end point. Retention was evaluated using Kaplan-Maier survival analysis, we used repeated measures ANOVA for continuous variables, and chi-square tests for categorical variables.
Results: Overall, 71% of patients completed the entire study, but aripiprazole group had a significantly lower retention than risperidone group (p=0.007), primarily due to medication related adverse effects: aripiprazole-treated patients had significantly more akathisia (p=0.03), agitation (p=0.02), and anxiety (p=0.06) than risperidone-treated patients. In the sample of treatment completers (n=30), both groups showed significant improvements from baseline in PANSS total scores and CGI-S scores at day 25 (all p<0.001). The CGI-EI scores at day 25 were also significantly higher for respiridone group (p=0.005).
Conclusions: Aripiprazole was associated with more adverse effects and higher discontinuation rates. Patients in both groups who tolerated their medications and completed the entire study protocol achieved comparable reductions of psychotic symptoms.
Financial Support: National Science and Technology Support Program in China 2012BAI01B07

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STAFF ACCEPTABILITY OF CONTINGENCY MANAGEMENT TO PROMOTE LONGER BREASTFEEDING DURATION AT WIC.

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Aims: The current study conducted a qualitative feasibility interview with staff at the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) in a mid-Atlantic region to apply contingency management (CM) for health behavior such as breastfeeding.
Methods: We surveyed 10 WIC staff at the two WIC offices that are part of the ongoing pilot study to increase breastfeeding duration among Puerto Rican mothers. The survey asked whether they would support the weekly peer support group meetings and CM, whether they think these programs might be helpful to Puerto Rican mothers to breastfeed, and whether perceived barriers and pro-CM beliefs influence their decision making to implement CM.
Results: More than half the participants answered that they would be willing to help weekly peer support group meetings (i.e., seven out of 10 participants) and CM program (i.e., eight out of 10 participants) to increase breastfeeding among Puerto Rican mothers, and all thought that these programs would be helpful (Scale 3-5). Except for one participant, all other participants rated a higher percentage of survey items in the category of pro-CM beliefs than that for perceived barriers as strong influence or very strong influence to make a decision to implement CM.
Conclusions: This study demonstrated that the CM program in conjunction with weekly peer support meetings to increase breastfeeding duration among Puerto Rican mothers at a WIC setting was acceptable to WIC staff, increasing the potential to implement and sustain such programs within WIC programs that are available nation-wide.
Financial Support: This study was supported by an NIH grant, 1R03HD077057.

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A VERY BRIEF INTERVENTION FOR CANNABIS USERS IN AN EMERGENCY DEPARTMENT SETTING.

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Aims: To explore the feasibility and acceptability of a very brief intervention for cannabis use in an ED setting and to test the hypothesis that cannabis and related problems will be significantly reduced at one month follow-up compared with ED baseline.
Methods: A pre-post design feasibility testing pilot study of a BI (5-10 minutes) delivered opportunistically to cannabis users (n=70) presenting to a hospital emergency department. The BI consists of 3 components: screening, assessment, and brief personalised feedback delivered by a trained researcher within the ED at Prince of Wales Hospital, Sydney. Follow-up data was collected one-month following presentation to the ED.
Results: The intervention was feasible and acceptable to participants. Compared with baseline, participants reported significantly fewer days of cannabis use (p <0.02); fewer cannabis-related problems (p < 0.03) and levels of dependence (p < 0.04) at one month follow-up.
Conclusions: Establishing the efficacy of such BIs has implications for those at-risk of developing cannabis related harms and dependence, by bridging the gap between primary prevention activities and more intensive treatment for those diagnosed with cannabis use disorders.
Financial Support: NCPIC is supported by the Australian Government Department of Health.

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THE DIFFERENTIAL ROLE OF DA AND 5-HT IN THE DISCRIMINATIVE STIMULUS PROPERTIES OF HIGH VS. LOW DOSES OF ±3,4-METHYLENEDIOXYMETHAMPHETAMINE.

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Aims: ±3,4-methylenedioxymethamphetamine (MDMA) produces discriminative stimulus effects that can be measured in humans and animals using the drug discrimination paradigm. Previous research has suggested that MDMA has a complex discriminative stimulus profile that is primarily mediated by serotonin (5-HT). However at some doses, MDMA produces dopamine mediated behaviours such as hyperlocomotion and conditioned place preference. The current experiment examines the roles of dopamine (DA) and serotonin (5-HT) in the discriminative stimulus effects of MDMA.
Methods: Subjects were male Sprague-Dawley rats weighing approximately 300g at the beginning of testing. Two groups of rats were trained to discriminate between MDMA (1.5mg/kg or 3.0mg/kg) and vehicle in a typical 2-lever drug discrimination paradigm. Rats were trained to make one response in the presence of the MDMA stimulus, and another response in the presence of the vehicle stimulus. The ability of DA (d-amphetamine, apomorphine) and 5-HT (mCPP, DOI, Fluoxetine) agonists to produce MDMA-appropriate responding (substitution) was then tested.
Results: Serotonin agonists substituted more readily in rats trained with a low dose of MDMA (1.5mg/kg) compared to those trained with a higher dose (3.0mg/kg). Conversely, DA agonists partially substituted in the high dose group but not in the low dose group.
Conclusions: Our results suggest that the discriminative stimulus effects produced by high vs. low doses of MDMA are qualitatively distinct. The relative contributions of 5-HT and DA at these doses may underlie this observed difference. These findings have implications for the characterisation of MDMA as a potential drug of abuse.
Financial Support: Victoria University of Wellington

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ABUSE QUOTIENT: AN ESSENTIAL MEASURE OF OPIOID ANALGESIC HUMAN ABUSE POTENTIAL (HAP).

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Aims: Increases in abuse of opioid analgesics have occurred in conjunction with expanded prescribing of these drugs and are augmented by the inherently high Human Abuse Potential (HAP) of many formulations. These concerns, along with regulatory-authority directives, have led to the development of opioid formulations expected to have abuse-deterrent properties. The attractiveness of opioids for abuse have been quantified using validated measures of subjective pharmacodynamic (PD) effects (e.g., Drug Liking, Drug High), as well as select pharmacokinetic (PK) characteristics of opioids, such as peak plasma concentration (C_{max}) and time to achieve C_{max} expressed as t_{max}.
For example, tampering with opioid formulations (e.g., altering the mode of administration) may increase PD effects by increasing C_{max} and/or shortening t_{max}. Given this PK relationship, which may foster a drug's attractiveness for abuse, the C_{max}/t_{max} ratio has been called the abuse quotient (AQ). This investigation examined the putative validity of using AQ as a surrogate clinical measure to characterize the HAP of opioid analgesic formulations.
Methods: PK and PD data were retrospectively gathered from a series of randomized, double-blind, controlled clinical trials (RCTs) exploring the HAP of proposed abuse-deterrent extended-release opioid formulations in comparison with control opioid formulations with high abuse potential and, in some cases, placebo. Correlations of AQ, C_{max}, and t_{max} with subjective PD effects influencing drug abuse were assessed within and between RCTs.
Results: In all instances, there were statistically significant and high correlations of AQ and PD effects, with higher AQ denoting greater abuse potential. Overall, these associations were stronger for AQ than for C_{max} or t_{max} individually.
Conclusions: The AQ appears to be an essential parameter of HAP when developing abuse-deterrent opioid formulations. Further analyses using real-world surveillance data for comparison are recommended.
Financial Support: Funded internally by PRA Health Sciences, Salt Lake City, UT, USA.

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CIGARETTE SMOKING AND RISK OF SUBSTANCE USE AND SUBSTANCE USE DISORDER RELAPSE AMONG ADULTS IN RECOVERY.

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Aims: Little is known about the relationship between smoking and long-term substance use disorder (SUD) treatment outcomes. The purpose of the current study was to examine the association between cigarette smoking (versus no smoking) and the risk of SUD relapse among adults with remitted SUDs.
Methods: Data were drawn from Wave 1 (2001-2002) and Wave 2 (2004-2005) of the National Epidemiologic Survey on Alcohol and Related Conditions. Analyses included the subsample of respondents who completed both waves of data collection and reported a history of any substance abuse and/or dependence prior to Wave 1 (n=1,890). Relationships between Wave 1 cigarette smoking status (smoker, non-smoker) and Wave 2 substance use and SUD relapse (i.e., met criteria for abuse and/or dependence) were examined using logistic regression analyses. Analyses were adjusted for demographics; mood, anxiety, and alcohol use disorders; and nicotine dependence.
Results: The odds of reporting substance use (odds ratio [OR]=1.62, 95% confidence interval [CI]=1.44-1.81) and SUD relapse (OR=1.95, 95% CI=1.68-2.27) were significantly higher for Wave 1 smokers than Wave 1 non-smokers. These relationships persisted after adjusting for significant covariates.
Conclusions: Cigarette smoking is associated with significantly increased risk of relapse to substance use and SUD, compared with those who do not smoke, among adults in recovery from SUDs. Cigarette use may have a harmful impact on long term SUD treatment outcomes through increasing vulnerability to relapse to SUDs. Incorporating smoking cessation treatment into substance abuse treatment may be one way to improve long-term substance use outcomes for adult smokers with SUDs.
Financial Support: Work on this study was supported in part by NIH grant 2R01-DA20892 (Dr. Goodwin).

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LONG-TERM OUTCOMES FROM THE NATIONAL DRUG ABUSE TREATMENT CLINICAL TRIALS NETWORK PRESCRIPTION OPIOID ADDICTION TREATMENT STUDY.

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Aims: Despite the growing prevalence of prescription opioid dependence, no longitudinal studies to date have examined long-term response to treatment in this population. The current study thus examined outcomes over a 42-month follow-up period among participants from the Prescription Opioid Addiction Treatment Study (POATS), conducted through the NIDA Clinical Trials Network.
Methods: POATS was a multi-site randomized clinical trial of buprenorphine-naloxone and counseling for prescription opioid dependence. A subset of participants (N=375 of 653) enrolled in a follow-up study. Measures of opioid and other substance use and treatment utilization were administered by telephone interviews approximately 18, 30, and 42 months after enrollment in the main trial.
Results: The majority of follow-up participants were no longer opioid-dependent at Month 18; less than 10% met criteria for current opioid dependence at Month 42. Participants who reported a lifetime history of heroin use at study entry were more likely to be opioid-dependent at Month 42 (OR=4.56, 95% CI=1.29-16.04, p<.05). 61% percent reported past-month abstinence from opioids at Month 42. Approximately one-third of the sample received opioid agonist treatment during follow-up; engagement in agonist treatment was associated with a greater likelihood of abstinence at Month 42. Eight percent (n=27/338) used heroin for the first time during follow-up; 10.1% reported first-time injection heroin use.
Conclusions: Long-term outcomes for those dependent on prescription opioids demonstrated clear improvement from baseline. However, a small subgroup of participants exhibited a worsening course, characterized by the initiation of heroin use and/or injection opioid use.
Financial Support: NIDA grants U10 DA15831, K24 DA022288, U10 DA020024, K23 DA02297, and K23 DA035297

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SEX DIFFERENCES IN DOPAMINE AND SEROTONIN ACTIVATION OF BRAIN PATHWAYS IN ADOLESCENT RATS EXPOSED TO SOCIAL PARTNERS OR AMPHETAMINE.

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Aims: Adolescent male rats show socially-induced conditioned place preference (CPP). When rats were allowed a choice between a social and drug paired compartment concurrently, males preferred the social paired compartment, whereas females showed no preference for either compartment. The current experiment determined if these behavioral differences relate to sex-dependent differences in activation of monoamine brain systems.
Methods: *Experiment 1* Adolescent male and female rats were habituated to a CPP chamber for 30 min. The next day, half of the subjects were placed into a chamber alone for 30 min, and the other half were paired with a sex-matched conspecific for 30 min. Immediately following the session, brains were dissected into medial prefrontal cortex (mPFC), nucleus accumbens (NAcc), midbrain, and hypothalamus; brain levels of the metabolites DOPAC and 5-HIAA were quantified by HPLC-EC.
Experiment 2 Procedure was similar to Experiment 1, except instead of social interaction, rats were given either amphetamine (1 mg/kg s.c.) or saline before being placed into a chamber for 30 min.
Results: Using a 2x2 ANOVA (treatment x sex), results showed that social interaction increased 5-HIAA in the mPFC ($p=0.038$) and hypothalamus ($p=0.01$) and females had greater 5-HIAA and DOPAC levels than males in NAcc ($p<0.01$; $p<0.01$) and hypothalamus ($p=0.036$; $p<0.01$). Following amphetamine, there was a main effect of sex for 5-HIAA ($p=0.023$), with females having greater levels than males.
Conclusions: These results show that adolescent females show higher metabolism of 5-HT during social interaction and following amphetamine administration than adolescent males, particularly in regions associated with reward. These data suggest that the ability of social interaction to decrease amphetamine preference in males, but not females, may be due to reduced amphetamine-induced activation of reward systems in males.
Financial Support: NIH grants P50 DA05312 and T32 DA016176

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BLACK-WHITE DISPARITIES IN RISK FOR CANNABIS USE AND PROBLEMS IN WOMEN: THE ROLE OF EARLY TOBACCO USE, TRAUMA TYPE AND PSYCHIATRIC PATHOLOGY.

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Aims: To examine racial disparities in the risk of cannabis use and time to first cannabis use disorder (CUD) symptom by considering the contribution of early tobacco use, trauma exposure type, posttraumatic stress disorder (PTSD), and major depressive disorder (MDD).
Methods: Data are from wave 4 of the Missouri adolescent female twins study (N = 3787) where 14.6% identified as African American (AA) and 85.4% as European American (EA); mean age = 21.7 (range 18 – 29). Early tobacco use (before age 16), trauma type, PTSD, and MDD were modeled as time-varying predictors of first cannabis use and transition from first use to first CUD symptom onset using Cox proportional hazards regression analysis. Violations of proportional-hazards assumptions were assessed.
Results: AAs were more likely to use cannabis (X^2=4.57, p = .03), and experience a CUD symptom (X^2=8.27, p = .004). Early tobacco use increased risk of using cannabis regardless of race [AA: HR=3.68 (2.03-6.70); EA: HR=2.79 (1.92-4.06)]. Only in the EAs, experiencing a sexual assault, physical assault, natural disaster, or witnessing an assault before age 17 increased risk for cannabis use. Of those who ever used cannabis, MDD was associated with progression to a CUD symptom both in EA [HR=1.65 (1.20-2.67)] and AA [HR=2.76 (1.53-4.96)] females. However, PTSD [HR=1.9 (1.21-3.09)], but not trauma without PTSD, significantly increased the hazard of CUD symptoms only in the EA sample.
Conclusions: Our results indicate delaying initiation of tobacco use could reduce the risk of cannabis initiation in both AA and EA participants. MDD did not predict initiation of cannabis use, but did increase the hazard to CUD symptoms in both EA and AA females above early onset cannabis. Screening for cannabis use in females with MDD and EA females with PTSD could be useful in identifying those at increased risk for cannabis symptoms.
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CLASSIFICATION OF DRUG AND PLACEBO WITH FUNCTIONAL MAGNETIC RESONANCE IMAGING.

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Aims: The substance abuse field will benefit from using imaging technology to identify brain states associated with the presence of pharmacological agents that treat clinical conditions, but are also abused. To compliment mass univariate approaches to achieving this goal (e.g., statistical parametric mapping), machine-learning methods offer a multivariate approach for identification and prediction.
Methods: We applied support vector machine (SVM) classification to fMRI data from six individuals who received *d*-Amphetamine (AMP) and placebo (PLB). BOLD signals were recorded in four 15 min blocks (i.e., Pre, Post1, Post2 and Post3) as subjective experiences were reported. SVM models were constructed for each block with whole-brain and striatal masks in a 6-fold, leave one subject out cross-validation scheme. Significance values were obtained from 100 repetitions of a permutation test. Vector weights were projected in brain space to reveal patterns contributing to classifications.
Results: Whole-brain data significantly predicted classes in all blocks (each p<0.01). Vectors contributing most to AMP were observed throughout the prefrontal cortex in the Pre block, while vectors contributing most to Post blocks were in movement, visual, cingulate and insular cortices. Striatal data alone failed to distinguish AMP from PLB in the Pre block. However, they significantly predicted class association in all Post blocks (Post1=91.7%, Post2=75%, and Post3=83.3%; all p<0.04).
Conclusions: These data highlight a benefit of multivariate classification, which considers joint and connected features in an attempt to classify brain states. Furthermore, they demonstrate that drug-specific information processed in the striatum is sufficient for discrimination of the presence of a monoaminergic agonist.
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SIMULTANEOUS PET/MRI OF NEUROVASCULAR COUPLING TO THE μ-OPIOID RECEPTOR OCCUPANCY.

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Aims: The interaction between the brain's opioid and dopamine systems has been highlighted as potentially pivotal in opioid addiction. Simultaneous PET/MRI is a novel imaging technology and could be used to investigate receptor system interactions and to dissect complex fMRI signals into neurochemical constituents.
Methods: Simultaneous PET/MRI were acquired on two male macaques on a 3T Siemens PET/MRI. CBV-fMRI data were obtained following iron oxide injection. [^{11}C]Carfentanil (~8mCi) was given as a bolus-infusion. An opioid antagonist, naloxone (0.005, 0.01, 0.03, and 0.05 mg/kg), and a μ-opioid agonist, remifentanil (10 μg/kg), were given i.v. in separate scans. PET data was analyzed for receptor binding potentials (BP_{ND}). A gamma function was used to model the temporal response to a drug challenge.
Results: At baseline, PET BP_{ND} maps showed a high-level of binding in the thalamus, caudate, putamen, frontal cortex, which corresponded well to known μ-opioid receptors distribution. μ-Opioid receptor BP_{ND} and %CBV were reduced after naloxone challenges in a dose-dependent manner. A dose of 0.05 mg/kg naloxone achieved >90% receptor occupancy. The largest BP_{ND} reductions were observed in the thalamus and caudate, while the largest CBV changes were observed in the putamen. Regional analyses of the BP_{ND} and CBV data revealed a linear coupling relationship. Naloxone induced a negative CBV response, which could be due to activating the inhibitory neurotransmitter, GABA, and/or its downstream effects (i.e., GABA depletes basal dopamine in the basal ganglia). A μ-opioid agonist (remifentanil) evoked robust bi-directional CBV responses in the basal ganglia. Drug-evoked dopamine release may be responsible for the initial negative CBV.
Conclusions: Future pharmacological studies modulating the GABA and dopamine systems can be used to confirm the opioid direct vs. indirect modulations on the fMRI signals.
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REINFORCING EFFECTS OF VERY LOW NICOTINE CONTENT CIGARETTES: A REVIEW.

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Aims: The US Food and Drug Administration has the authority to reduce the nicotine content of cigarettes to very low (potentially sub-addictive) levels. Effective implementation of such a plan would benefit from careful analysis of the relative effects of very low-nicotine (VLNC) and high-content (HC) cigarettes.
Methods: Experimental laboratory studies comparing VLNC and HC cigarettes were reviewed.
Results: VLNC and HC both reduce self-reported craving and withdrawal, both are sensitive to price increases, and both how similar measures of relative reinforcing efficacy when tested alone (e.g., no differences in Progressive Ratio breakpoint). When presented concurrently, HC are preferred over VLNC cigarettes (i.e., they differ in relative reinforcing effects).
Conclusions: Laboratory studies indicate that VLNC and HC cigarettes are both effective in suppressing withdrawal and craving, suggesting VLNC cigarettes could be effective substitutes for HC cigarettes on that dimension. However, when concurrently available there is a clear preference for HC cigarettes, suggesting that VLNC cigarettes would not compete effectively with HC cigarettes in the market where both were available unless they were less expensive or supplemented in some manner. Research parametrically comparing concurrently available VLNC and HC cigarettes at varying prices would be helpful in identifying a price differential that can reliably promote preference for VLNC over HC cigarettes.
Financial Support: This research was supported in part by National Institutes of Health Center of Biomedical Research Excellence award P20GM103644 from the National Institute of General Medical Sciences, Tobacco Centers of Regulatory Science award P50DA036114 from the National Institute on Drug Abuse and U.S. Food and Drug Administration, and an Institutional Training grant T32DA07242 from the National Institute on Drug Abuse. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the Food and Drug Administration.

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STABLE HOUSING, STABLE SUBSTANCE USE? EVALUATION OF TWO 'HOUSING FIRST' PROGRAMS FOR HOMELESS INDIVIDUALS.

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Aims: Australian and international evidence highlights the heightened prevalence of substance use disorders in homeless populations. In recent years, adaptations of the Housing First initiative, whereby chronically homeless individuals are provided long-term housing with support, have been implemented across Australia. Two such adaptions include scatter-site (private rental apartments; SS) and congregate site (apartments in the one building; CS) models. There is currently limited Australian evidence on the effect that these variations of Housing First programs have on client outcomes. The primary aim of this study was to undertake a longitudinal evaluation of two adaptations of the Housing First model (one SS and one CS) in relation to clients' housing and health outcomes, specifically substance use patterns and service utilisation.
Methods: Longitudinal mixed-methods design comparing process and outcome measures at baseline and 12 months post-baseline.
Results: A recruitment rate of 67% was achieved at baseline for both programs, of which 78% were successfully followed-up at 12 months post-baseline. Clients in both models did not differ significantly on demographics, homelessness history or proportion with a substance use disorder. However, at baseline a significantly higher proportion of clients in the CS model had an anxiety disorder (67% vs. 34%) and had recently injected (42% vs. 19%). Findings over time showed that whilst injecting behaviour reduced in the SS model (19% to 11%), it remained unchanged in the CS model. Whereas deceasing trends were observed for all justice system outcomes in the SS model, overall increases were found for the CS model.
Conclusions: A number of factors distinguished outcomes in the two Housing First models. Clients entering the CS model appeared to be less well and were injecting drugs more often, suggesting high rates of illicit drug dependence.
Financial Support: New South Wales Department of Housing

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ORAL JPC-077 AND JPC-141, VESICULAR MONOAMINE TRANSPORTER-2 INHIBITORS, REDUCE METHAMPHETAMINE SELF-ADMINISTRATION AND METHAMPHETAMINE-INDUCED REINSTATEMENT IN RATS.

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Aims: Rcently, we synthesized a series of compounds that may aid in reducing methamphetamine (METH) abuse and relapse. These compounds, 1,4-diphenethyl analogs of lobelane (a defunctionalized derivative of lobeline), are potent and selective vesicular monoamine transporter-2 (VMAT-2) inhibitors. Here, we report the effects of oral administration of two analogs from this series (JPC-077 and JPC-141) on METH self-administration and reinstatement in rats.
Methods: After surgical implantation of a jugular catheter, rats learned that METH infusions (0.05 mg/kg) could be earned via responding. To assess the effect of JPC-077 and JPC-141 on METH self-administration, rats (n =6/compound) earned infusions 15 min after gavage with compound. To assess METH-induced reinstatement, a separate group of rats (n =5/compound) experienced similar training then underwent 10 extinction sessions. During three test sessions, subjects were gavaged with two doses of compound or vehicle alone while receiving a METH (0.5 mg/kg) i.p. injection to induce METH-seeking.
Results: JPC-077 (100,170 and 300 mg/kg) reduced METH self-administration. Further, JPC-077 at 100 and 300 mg/kg blocked METH-induced reinstatement. JPC-141(130 and 170 mg/kg) reduced METH self-administration. Likewise, JPC-141 (130 and 170 mg/kg) blocked METH-induced reinstatement.
Conclusions: JPC-077 and JPC-141 reduced both METH self-administration and reinstatement. Importantly, doses of JPC-077 that blocked METH self-administration and reinstatement were approximately three-times lower than those required to significantly reduce locomotor activity (previous work from our laboratory), indicating that current results were not due to nonspecific suppressant effects. Thus, JPC-077 and JPC-141 represent novel orally bioavailable leads for treating METH abuse.
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SYSTEMIC AND INTRAACCUMBENS MGLUR2/3 AGONISM ATTENUATE ETHANOL-REINFORCED APPETITIVE RESPONDING.

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Aims: Previous studies suggest that group II metabotropic glutamate receptors (mGluR2/3) are involved in regulating ethanol (EtOH) drinking and seeking following extinction. The sipper tube model, which allows for procedural separation of seeking and intake, was used to further clarify the role of mGluR2/3 in EtOH-seeking and consumption. A microinjection study was also performed to examine the role of nucleus accumbens (NAc) core mGluR2/3 in EtOH-seeking using the mGluR2/3 antagonist LY341495 (LY34).
Methods: For the systemic agonist experiments, male Wistar rats [n=8-9 group; LY379268 (LY37) (0-2.0 mg/kg)] were trained to complete a response requirement (RR) of 10 lever presses that resulted in access to 10% EtOH or 2% sucrose (in separate groups) for a 20-minute drinking period. For drinking testing, weekly drug injections preceded a RR1. The RR was then increased over sessions to a RR20. For seeking testing, weekly drug injections preceded a non-reinforced extinction session. To determine effects of blockade of NAc core mGluR2/3 on agonist-induced suppression of EtOH-seeking, a separate group of rats (n=15) was trained to complete a RR10 for access to 10% EtOH. Animals were implanted with bilateral NAc core cannulae and then received four sets of injections in a balanced design (Systemic + core: vehicle + vehicle, LY37 + vehicle, LY37 + LY34, and vehicle + LY34) and a final non-balanced LY37 microinjection.
Results: Systemic administration of the mGluR2/3 agonist LY37 significantly reduced EtOH- and sucrose- seeking with no systematic effect on locomotion. Systemic LY37 also significantly reduced sucrose consumption. NAc core LY34 did not block the effects of LY37, but LY37 in the core also significantly reduced EtOH-seeking.
Conclusions: These findings suggest that modulation of glutamatergic neurotransmission by systemic LY37 significantly reduces general reinforcer seeking. Suppression of EtOH-seeking following NAc core LY37 suggests that NAc core mGluR2/3 are involved in modulating EtOH-seeking during maintenance drinking.
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PILOT EVALUATION OF THE "TAILORED TELEPHONE INTERVENTION DELIVERED BY PEERS TO PREVENT RECURRING OPIOID- OVERDOSES"

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Aims: Individuals experiencing non-fatal opioid-overdose (OOD) are at heightened risk for future OODs. To date, there are no validated interventions targeting these patients. We created and piloted TTIP-PRO, a computer-facilitated, peer-delivered, individually-tailored intervention designed to 1) increase patient knowledge about OOD, and 2) encourage patients to initiate medication assisted treatment (MAT).
Methods: Two peer interventionists, individuals who have been abstinent from illicit opioids for at least a year, enrolled in MAT, and have personal experience with OOD, were recruited from the institution's MAT clinic by word of mouth; the outcomes of interest were their ability to complete training and certification and their feedback on implementing TTIP-PRO. Recruitment letters were sent to patients treated for OOD in the UC emergency department within the prior 8 months. Eight patients received the TTIP-PRO intervention combined with assessment before and after. Outcomes of interest were participant satisfaction with TTIP-PRO and pre-post change in 1) knowledge about OOD (risk factors for OOD, signs of OOD, appropriate response to OOD, and MAT), and 2) interest in initiating MAT.
Results: Both peer interventionists completed training and certification within the designated 4 hour time-frame and rated their satisfaction with providing TTIP-PRO as 4 on a 4-point scale (4.0, SD=0.0). Participants' OOD knowledge increased significantly, with 69.9% (SD=12.5%) correct responses pre- TTIP-PRO and 93.6% (SD=2.5%) correct responses post-TTIP-PRO (W=8, p=.0078). Participant interest in receiving MAT, measured on a 10-point scale, increased from 8.1 (SD=3.2) pre- TTIP-PRO to 9.5 (SD=1.1) post-TTIP-PRO, but this was not statistically significant (W=3, p=.25), likely reflecting a ceiling effect (5 of the 8 participants had a pre-rating of 10). All participants rated the helpfulness of TTIP-PRO at the maximum on a 4-point scale (4.0, SD=0.0).
Conclusions: A larger study of TTIP-PRO may be warranted.
Financial Support: University of Cincinnati

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PARENTS AS INTERVENTIONISTS TO ADDRESS ADOLESCENT DRUG ABUSE.

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Aims: The importance of parents as "interventionists" is supported by reviews of the treatment literature as well as the emerging science that home-based initiatives by parents can contribute to desired health changes in adolescents. The aim of this study is to investigate the efficacy of an indicated preventive intervention in which parents were taught skills in motivational interviewing and psycho-educational counseling, and with assistance from a coach, they delivered the program in the home to their drug abusing teenager. This paper will report the 6-month outcome data.
Methods: A detailed manual for parents was developed. Consisting of four sessions, the program's content stressed strengthening parental communication skills; improving parental monitoring of the adolescent's compliance with family drug-free expectations; and strengthening commitment to assist the child to cope with drug triggers. Delivery of the program in the home was to occur across 4 weeks. Families were randomly assigned to this target condition (n = 82) or to a control group (n = 68) (manual adjusted to be education-based and no coaching was included). Assessments occurred at baseline, and 6- and 12-months post intervention.
Results: Based on 6-month outcome data, adolescents in the target condition showed significant improvement on all drug involvement variables (marijuana and alcohol use frequency; rates of marijuana and alcohol abstinence; count of drug problems and SUD symptoms) compared to adolescents in the control condition.The exception was that the groups did not differ in terms of changes in psychological distress variables (equal reduction in both groups).A significant mediator of intervention effects was parent-child relations; improvement in family solidary was associated with reduced drug use involvement.
Conclusions: These findings offer provisional support for the view that parents can engage their drug-using teenager in an interventionist role, and this engagement may contribute to reduced drug involvement by their teenage son or daughter.
Financial Support: NIDA grants P50-DA027841 and K24-DA035882.

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USING BEHAVIORAL ECONOMICS TO PREDICT OPIOID USE DURING PRESCRIPTION OPIOID DDEPENDENCE TREATMENT.

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Aims: Research using behavioral economics has previously linked addictive behavior to disrupted decision-making, reward-processing, and drug reinforcement value. These principles have not been examined in prescription opioid addiction, which is currently a major public health problem. This study examined whether pre-treatment drug reinforcement value predicted opioid use during outpatient treatment of prescription opioid addiction.
Methods: Secondary analyses of a multi-site clinical trial (NIDA CTN-0030) for adults with prescription opioid dependence who received 12 weeks of buprenorphine-naloxone and counseling (N = 353). Analyses covaried for opioid dependence severity and opioid source. Predictors were naturalistic indices of drug reinforcement value including the total amount and proportion of income spent on drugs. Outcome was opioid use during treatment assessed by weekly urine drug screens.
Results: Obtaining opioids from doctors was associated with lower pre-treatment drug spending, while obtaining opioids from dealers/patients was associated with greater spending. Controlling for demographics, opioid dependence severity, and opioid source frequency, patients who spent a greater total amount (OR = 1.30, p < .001) and a greater proportion of their income on drugs (OR = 1.31, p < .001) were more likely to use opioids during treatment.
Conclusions: As indicated by pre-treatment allocation of economic resources to drugs, individual differences in drug reinforcement value reflect propensity for continued opioid use during treatment among individuals with prescription opioid addiction. Future studies should examine disrupted decision-making and reward-processing in prescription opioid users more directly and test whether reinforcer pathology can be remediated in this increasingly prevalent population.
Financial Support: NIDA 5T32DA026400 and the NIDA Clinical Trials Network.

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MIGRATION AND TIME TO FIRST TOBACCO CIGARETTE AFTER WAKING.

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Aims: At CPDD2014, we reported on suspected effects of migration on tobacco smoking. Here, studying 12-24 year old active smokers, we aim to estimate possible migration effects on time to first cigarette (TTFC) after waking up, which is one of the most robust indicators of tobacco dependence. For many immigrants, migration into the United States (US) includes major environmental shifts. Accordingly, with increasing elapsed time since in-migration (ETSI), one might expect convergence of immigrant TTFC estimates with TTFC estimates for the US-born.
Methods: Data are from active tobacco smokers (n~98,357 12-24 yr olds) identified via the United States National Surveys on Drug Use and Health Restricted-use Data Analysis System (NSDUH, R-DAS) 2002 – 2011, which use stratified multistage area probability sampling and IRB-approved computer-assisted standardized assessments. Estimates are based on analysis weights and Taylor series variances.
Results: Just over one in three of 12-24 year old US-born active smokers have short TTFC (36.1%; 95% CI = 35.7, 36.3). The corresponding estimate for the most recent immigrants (ETSI<5 years) is just under one in five (17.2%; 95% CI = 15.0, 19.7), and is just over one in five for immigrants with ETSI ≥ 10 years (21.8%; 95% CI = 19.7, 24.0). In an exploratory subset analysis focused on newly incident smokers, the TTFC estimates are 15.9% for the US-born and 4.7% for long-residence immigrants (ETSI ≥ 10 years).
Conclusions: Our expectations are contradicted by these novel epidemiological estimates. By the time of presentation at CPDD2015, we will have some additional evidence on protection against TTFC apparently enjoyed by immigrant smokers relative to US-born smokers (e.g., greater presence of smoke-free home rules; constraints on disposable income).
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INFLUENCE OF DORSOLATERAL PREFRONTAL CORTEX AND VENTRAL STRIATUM ON RISK AVOIDANCE IN ADDICTION: A MEDIATION ANALYSIS.

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Aims: Alterations in frontal and striatal function are hypothesized to underlie risky decision-making in drug users, but how these regions interact to affect behavior is incompletely understood. We used mediation analysis to model the contributions of prefrontal cortex and ventral striatal activity to risk avoidance in drug users.
Methods: Thirty-seven abstinent substance-dependent individuals (SDI) and 43 controls underwent fMRI while performing a decision-making task involving risk and reward. We tested whether activity in dorsolateral prefrontal cortex (DLPFC) and ventral striatum (VST) explained group differences in risk avoidance behavior. Next, we conducted a whole-brain mediation analysis to explore other brain regions that may influence the relationship between VST activity and risk avoidance.
Results: Right DLPFC (RDLPFC) positively mediated group differences in risk avoidance (p < 0.05). RDLPFC activity was higher in SDI and predicted greater risk avoidance across groups, controlling for SDI vs. controls. Conversely, VST activity negatively influenced risk avoidance (p < 0.05). VST activity was higher in SDI and predicted lower risk avoidance. Whole-brain analysis revealed that RDLPFC and left temporal-parietal junction positively (p ≤ 0.001), while right thalamus and left middle frontal gyrus negatively (p < 0.005), mediated the VST activity-risk avoidance relationship.
Conclusions: RDLPFC activity mediated less risky decision-making while VST activity mediated greater risky decision-making across SDI and controls. These results suggest that an imbalance in prefrontal and striatal function may adversely influence choices involving risk in drug users. Modeling the contributions of multiple brain systems to behavior through mediation analysis could lead to a better understanding of mechanisms of behavior and suggest future targets for addiction treatment.
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THE MODERATING ROLE OF NEGATIVE URGENCY IN THE RELATION BETWEEN DISTRESS INTOLERANCE AND ALCOHOL DRINKING MOTIVES.

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Aims: Both distress intolerance (DI) and negative urgency (NU) have been linked to negative-reinforcement oriented drinking motives. The aim of the study was to investigate the moderating role of NU in the relation between DI and drinking motives. We hypothesized that low NU would reduce the relation between DI and negative reinforcement oriented drinking motives (e.g., coping and conformity).
Methods: One hundred and forty three undergraduate students (M_{age} =18.9, SD=1.1; 78.3% female; 73.4% Caucasian) who reported having at least 1 drink/past week, completed a questionnaire battery online via Qualtrics. The battery included indices of DI, NU, mood and anxiety symptoms, as well as coping and conformity drinking motives. For the moderation analysis, we utilized PROCESS while controlling for gender, depression, and anxiety symptoms.
Results: NU significantly moderated the relation between DI and coping (ΔR^2=.03, F(6, 136)=5.34, p<.01) and conformity (ΔR^2=.05, F(6, 136)=2.63, p<.05) motives to drink. In both models, individuals low in DI and low in NU evidenced lower coping and conformity motives. However, individuals high, not low, in NU and low in DI evidenced higher coping motive. Individuals high in DI and low in NU evidenced higher conformity motive.
Conclusions: Low NU did not appear to affect the relation between high DI and coping motive, instead, the combination of low DI and high NU resulted in greater coping motive. Also, low, rather than high, NU strengthened the relation between DI and conformity motive. Despite the cross-sectional nature of this relation, these unexpected findings suggest unique relations between DI and NU and coping and conformity motives to drink among college-aged students and may be used to develop targeted interventions based on differential risks.
Financial Support: None

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UNITED STATES NATIONAL ESTIMATES OF PARENTING LEVEL AND RISK OF NEWLY INCIDENT DRUG USE: 2002-2013.

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Aims: It is rare to see nation-level estimates of the degree to which parenting might have positive outcomes such as prevention of tobacco, alcohol, and other drug use. Our aim is to produce initial estimates on a nation-level scale across multiple community samples that include school dropouts as well as attenders, first for 12-17 year olds as a group, and eventually with a 'mutoscope' look at individual birth cohorts traversing adolescence, in preparation for new prevention research focused on the 'limit time with friends' facet of parenting, with parenting level held constant.
Methods: Data are from confidential computer-assisted self-interviews for the US National Surveys of Drug Use and Health (NSDUH, 2002-2013; SDA). Within a structural equations/measurement model framework, a 'newly incident drug use' construct (NIDU: tobacco, alcohol, and cannabis) is regressed on parenting level, as tapped by 4 standardized items on parenting (homework supervision, support, chores, limiting TV time). Estimates are from analysis-weighted Taylor series procedures in MPlus.
Results: In these multiple national adolescent samples, higher parenting levels signal lower incidence levels (p<0.05). The possibility that NIDU has influenced parenting level exists, but analyses stratified by elapsed time between NIDU and assessment suggest that this is not the case (p>0.05).
Conclusions: This work is a step toward testing our primary hypothesis that the 'limit time with friends' facet of parenting has special importance in prevention of newly incident adolescent drug use. Limitations exist, such as shared methods co-variation in adolescent self-reports of these constructs. Even so, this initial work should help in planning of more definitive longitudinal research for which cross-sectional estimates of this type are needed to specify sample size and to project statistical power.
Financial Support: NIDA K05DA015799 (HHY, RBS, JCA)

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DIFFERENT PATTERNS OF NEURAL ACTIVITY AMONG COCAINE-DEPENDENT INDIVIDUALS WITH AND WITHOUT CURRENT METHADONE TREATMENT: RELATIONSHIP TO TREATMENT OUTCOMES.

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Aims: Cocaine abuse is common among individuals receiving methadone-maintenance treatment for opiate-dependence and is associated with measures of negative functioning and poorer treatment responses. In non-methadone-maintained populations, research suggests that individual variability in response to treatments for cocaine dependence may be related to individual differences in neural functional responses (as assessed using functional magnetic resonance imaging; fMRI). However, the relationship between neural function and treatment outcomes has not been assessed among individuals maintained on methadone. Elucidation of the functional neurobiology of this challenging-to-treat population may aid in the improvement of existing treatments.
Methods: fMRI data (acquired during performance of a monetary incentive delay task) from methadone-maintained individuals with cocaine dependence (n=24), non-methadone-maintained individuals with cocaine dependence (n=20) and healthy comparison participants (n=21) was compared using whole-brain ANOVAs in SPM8 (pFWE<.05).
Results: In comparison to both healthy comparison and non-methadone-maintained cocaine-dependent participants, methadone-maintained cocaine-dependent participants had reduced activity within fronto-parietal regions (e.g., inferior frontal gyrus, posterior cingulate). Among methadone-maintained, cocaine-dependent individuals, pretreatment neural responses within the left and right caudate were negatively associated with days of consecutive abstinence during treatment and positively associated with reductions in negative affect during treatment.
Conclusions: These data suggest neurofunctional differences related to treatment outcomes between individuals with cocaine dependence with and without methadone treatment, which may relate to differences in the efficacies of existing treatments.
Financial Support: This research was supported by NIH grants from NIDA (P50 DA009241, R01 DA030058). SWY receives support from DA007238-23 (PI: Petrakis).

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EYE TRACKING MEASURES OF ATTENTIONAL BIAS TO INDIVIDUALLY-CALIBRATED MARIJUANA CUES.

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Aims: The aim of this ongoing study is to examine eye-tracking based measurement of AB in individuals with cannabis use disorder (CUD) using cues calibrated to indiivudal subject reactivity, and examine correlations among AB, stress, and CUD-severity.
Methods: Twenty-five subjects (12 female) who met DSM-5 criteria for CUD were first exposed to MJ and matched neutral pictures. Measures of pupillary, cardiovascular, respiratory, and subjective reactivity were acquired and scored as a composite. For each subject, 6 high-reactivity MJ pictures and 6 low-reactivity neutral pictures were then used in AB testing. AB testing utilized eye-tracking methodology in a pro-saccade (look at) and anti-saccade (look away from) test paradigm. AB was defined as the number of anti-saccade errors (MJ vs. neutral).
Results: The reactivity score for MJ pictures was greater than for neutral pictures (p < .001). Subjects made more anti-saccade errors on MJ vs. neutral trials (p = .001). There were no differences in errors on pro-saccade trials (p = .687), and no significant associations among AB and measures of CUD severity or stress.
Conclusions: Eye tracking-based measurement of reactivity to MJ cues, using individually-calibrated stimuli, provides a sensitive index of AB to MJ stimuli. AB is not related currently to stress or CUD severity. The measurement system is amenable to repeated measures and pharmacological interventions for drug-cue reactivity.
Financial Support: NIH/NIDA grants R21 034825 and P50 09262

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A RAPIDLY CHANGING RECREATIONAL DRUG MARKET: FINDINGS FROM THE CANADIAN COMMUNITY EPIDEMIOLOGY NETWORK ON DRUG USE.

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Aims: Since 2000, the recreational psychoactive drug market has undergone unprecedented changes. Abuse of prescription drugs and the introduction of many new synthetic drugs, has blurred the line between illicit and non-illicit drug use. These changes have made monitoring emerging drug use trends challenging. In response, the Canadian Centre on Substance Abuse developped the Canadian Community Epidemiology Network on Drug Use (CCENDU), a sentinel surveillence, early warning system. We will present information on the new and emerging drug-patterns and trends in Canada using data from the network.
Methods: Between June 2012 and September 2014, a variety of leading-edge indicators were collected from CCENDU sites across Canada. Information was analyzed in real-time and CCENDU notifications were issued on drug-related topics of significance to public health. Information was also analysed to identify overarching themes/trends.
Results: Ongoing surveillence and analysis of data led to eight CCENDU notifications being issued on the following: an amphetamine type stimulant colloquially referred to as "bath-salts", the misuse of opioids in Canadian communities; non-pharmaceutical fentanyl, unconfirmed reports of desomorphine ("Krocodil"), recreational use of bupropion, abuse of counterfeit oxycodone tablets containing fentanyl, synthetic cannabinoids, and drug overdoses at music festivals. In addition, analysis revealed three overall trends/themes in the data: 1) the emergence of new psychoactive substances, 2) adulteration of heroin, 3) abuse of pharmaceutical agents.
Conclusions: Themes identified support the assertion that the Canadian illicit drug market is rapidly changing. Unlike The United States and Europe, Canada has no national early warning system designed to detect new drugs and new drug use trends. The results suggest that the CCENDU surveillance system can reliably function to detect drug-related adverse events and alert stakeholders to new trends in drug use, however there is a need to strengthen and expand its capabilities.
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DO ALCOHOL-FOCUSED INTERVENTIONS REDUCE MARIJUANA USE IN MANDATED COLLEGE STUDENTS?

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Aims: Marijuana use among college students is highly prevalent and associated with poorer academic outcomes. Although brief motivational interventions (BMIs) have been shown to be efficacious with reducing alcohol use in college students, little is known about the utility of alcohol BMIs in reducing other addictive behaviors, such as marijuana use, that often co-occur with drinking. The purpose of the current study was to examine the impact of alcohol-focused BMIs implemented within a stepped care approach in reducing marijuana use.
Methods: Participants were 530 college students who violated campus alcohol policy and were mandated to receive an alcohol-focused brief advice (BA) session. Of the 530 participants, 39% (N = 208) reported baseline marijuana use and were included in the current analyses. Participants who reported continued risky alcohol use (4 or more heavy drinking episodes and/or 5 or more alcohol-related problems in the past month) six weeks following the BA session were randomized to BMI (n = 92) or assessment only (n = 90). Follow-up assessments were conducted 3, 6, and 9 months post-intervention.
Results: Repeated measures ANOVA revealed that students did not reduce their frequency of marijuana use following a BA session, nor did the BMI significantly reduce marijuana use compared to the assessment-only group.
Conclusions: Despite reductions in alcohol use, marijuana use did not change following alcohol-focused intervention efforts. This suggests that marijuana users can still benefit from alcohol-related interventions yet may need a more intense and targeted marijuana focused intervention to induce changes in marijuana use.
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PROBLEMATIC PREGABALIN AND GABAPENTIN USE: RESULTS FROM THE CANADA VIGILANCE ADVERSE REACTION ONLINE DATABASE.

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Aims: Pregabalin and gabapentin are increasingly used gamma-aminobutyric acid (GABA) analogues indicated for the treatment of anxiety, seizures, and neuropathic pain. Both are being investigated as treatments for opioid, alcohol, and benzodiazepine withdrawal and dependence. Analyses of adverse drug reaction registries in Germany and Sweden have demonstrated problematic pregabalin use since 2008. The aim of this study was to evaluate trends and characteristics of reports of problematic pregabalin or gabapentin use in Canada.
Methods: A search for adverse effects suspected to have been caused by pregabalin and gabapentin was completed using the Canada Vigilance Adverse Reaction Online Database (1965 to 30 June 2014). Adverse effects are classified by the Medical Dictionary for Regulatory Activities (MedDRA) v.17.0. Reports listing terms suggesting problematic gabapentinoid use (i.e., *Drug abuse, Euphoric mood, Drug dependence, Intentional drug misuse*) or possible problematic use [i.e., (*Drug) withdrawal syndrome, Drug tolerance (increased*)] were evaluated. Cases of *Intentional drug overdose* were reviewed separately.
Results: The total number of unique cases suggesting problematic use of pregabalin was 48 (earliest 2006), and for gabapentin was 18 (earliest 2003). Where data was available, results showed that problematic users of pregabalin were predominantly female (65.1%), mean age 52±15 years, with mean daily doses interpreted as 552 mg/day (range 25 to 3750mg/day), and concurrent use of other psychoactive substances in 56% of cases (opioids in 41% of cases). Problematic users of gabapentin also tended to be female (78%), mean age 54±16 years, with mean daily doses interpreted as 1650mg/day (range 300 to 4200mg/day), and concurrent use of psychoactive substances in 78% of cases (opioids in 67% of cases). Intentional drug overdose was reported in 4 cases with pregabalin and 6 cases with gabapentin.
Conclusions: Problematic use of pregabalin and gabapentin has been reported in Canada since 2003 and 2006, respectively.
Financial Support: None

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RETINOIC ACID SIGNALING IN THE NUCLEUS ACCUMBENS: A NOVEL MECHANISM CONTROLLING ADDICTION-RELATED BEHAVIOR.

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Aims: Previous research has shown that environmental enrichment produces a protective addiction phenotype. A next generation RNA sequencing study in our lab revealed that retinoic acid (RA) signaling pathway was significantly regulated in the nucleus accumbens (NAc) of rats by environmental enrichment. It is known that RA signaling pathway plays an important role in brain development and homeostasis. However, the role of RA pathway in addiction is not clear. CYP26b1 is an essential enzyme responsible for RA degradation, the lack of which leads to increased RA signal in brain. Therefore, the purpose of this project is to investigate the behavioral response of rats with CYP26b1 knocked down in the NAc shell in cocaine self-administration.
Methods: Twenty-four Sprague Dawley rats were injected with either an adeno-associated virus (AAV) expressing CYP26b1 shRNA or AAV expressing a non-targeted hairpin in the NAc shell. After three weeks, spontaneous locomotor activity was tested in a 2 hour session. Before the cocaine self-administration study rats were first placed in a two-lever operant chamber and allowed to respond for sucrose pellets. Following sucrose responding, rats self-administered cocaine in acquisition, maintenance responding (dose-response), extinction and reinstatement.
Results: Our results demonstrate that rats with CYP26b1 knockdown in the NAc shell exhibited higher spontaneous locomotor activity. In cocaine self-administration, knocking down CYP26b1 enhanced acquisition of low dose of cocaine and increased extinction responding. In addition, CYP26b1 knockdown showed leftward and an upward shift in dose response curve compared to control rats. Ongoing experiments are testing cocaine induced reinstatement.
Conclusions: Increasing RA signaling in the NAc shell produces a susceptible addiction phenotype. Thus, decreased retinoic acid signaling may underlie the protective phenotype of environmental enrichment.
Financial Support: These experiments were funded by NIDA and supported by DA 029091.

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THE EFFECT OF 1-SUBSTITUTION ON TETRAHYDROISOQUINOLINES AS SELECTIVE ANTAGONISTS FOR THE OREXIN-1 RECEPTOR.

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Aims: Selective blockade of the Orexin-1 receptor has been suggested as a potential approach to drug addiction therapy because of its role in modulating the brain's reward system. We have recently reported a series of OX_1 selective antagonists 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. Aimed at elucidating SAR requirements in other regions of the molecule and further enhancing OX_1 potency and selectivity, we have designed and synthesized a series of analogs bearing a variety of substituents at the 1-position of the tetrahydroisoquinoline.
Methods: All target 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.
Results: The results show that an optimally substituted benzyl group is required for activity at the OX_1 receptor. Several compounds with improved potency and/or selectivity have been identified. When combined with structural modifications that were previously found to improve selectivity, we have identified compounds with apparent dissociation constants (Ke) less than 20 nM at the OX_1 receptor and >500-fold selectivity over the OX_2 receptor. In vivo, select compounds blocked the development of locomotor sensitization to cocaine in rats.
Conclusions: These finding will expedite the development of potent and selective OX1 antagonists as medications for the treatment of OX1-mediated disorders such as drug addiction.
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EFFECTS OF ENVIRONMENTAL ENRICHMENT ON MICRORNA-221 EXPRESSION AND ERK PHOSPHORYLATION IN THE RAT PREFRONTAL CORTEX FOLLOWING NICOTINE-INDUCED SENSITIZATION OR NICOTINE SELF-ADMINISTRATION.

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Aims: The purpose of the current study was to determine the underlying mechanism(s) by which environmental enrichment results in neuroprotective effects in repeated nicotine administration.
Methods: Rats were raised in either an enriched condition (EC) or an impoverished condition (IC) during postnatal days 21-53. Rats underwent nicotine sensitization for 15 days or nicotine self-administration for 21 days. After the final behavioral test sessions, we profiled microRNA (miR) expression using microarrays and examined the phosphorylation levels of ERK1/2 (pERK1/2) in the prefrontal cortex (PFC).
Results: Repeated nicotine (0.35 mg/kg) injections induced pERK1/2 to similar levels in IC rats; however, the induction of pERK1/2 in EC rats by nicotine was not significantly different from saline controls, owing to their high baseline. Similarly, following nicotine self-administration, compared to saline controls, IC rats exhibited increased pERK1 and pERK2, whereas the levels of pERK1/2 were not altered in EC rats. In addition, miR-221 expression was region-selectively upregulated in the PFC of EC rats relative to IC rats after repeated nicotine administration or nicotine self-administration. Overexpression of miR-221 via lentiviral (LV) techniques attenuated nicotine-induced increase in pERK1/2 in PC12 cells. Moreover, LV-miR-221 overexpression in the medial PFC potentiated nicotine-mediated locomotor activity in IC but not in EC rats in response to 15-day repeated nicotine (0.35 mg/kg) injections.
Conclusions: Collectively, these findings suggest that environmental enrichment, via upregulation of prefrontal miR-221 expression, modulates the nicotine-induced ERK activation in the mPFC, which forms a potential mechanism to enhance sensitivity to nicotine
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PSYCHIATRIC SYMPTOMS AMONG PREGNANT AND NEWLY POSTPARTUM WOMEN RECEIVING FINANCIAL INCENTIVES FOR SMOKING CESSATION.

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Aims: Financial incentives for smoking cessation increase smoking abstinence and decrease Beck Depression Inventory (BDI) ratings among depression-prone pregnant and newly postpartum women. The aim of the present study was to use the Brief Symptom Inventory (BSI) to investigate whether this treatment effect impacts a broader array of psychiatric symptoms than BDI ratings.
Methods: Participants (N = 289) were smokers at the start of prenatal care who participated in four controlled clinical trials on the efficacy of financial incentives for smoking cessation. Women were assigned to either an intervention wherein they earned vouchers exchangeable for retail items contingent on abstaining from smoking or a control condition wherein they received vouchers of comparable value independent of smoking status. BSI ratings were examined across 8 antepartum/postpartum assessments. Women who reported a history of prior depression or had BDI scores $\geq$ 17 at the start of prenatal care were categorized as Depression-Prone (Dep+) while those meeting neither criterion were categorized as Depression-Negative (Dep-). Treatment effects on BSI ratings were analyzed in a three-way repeated measures ANCOVA.
Results: There was a significant three-way interaction of treatment, depression status, and time ($p < .0001$) on BSI Total scores, with the contingent incentives intervention decreasing Total scores below scores in the control condition from late-antepartum through 12-weeks postpartum among Dep+ but not Dep- women. Peak effects occurred at 8-weeks postpartum and included significant reductions across the BSI Depression, Anxiety, Phobic Anxiety, Somatization, Interpersonal Sensitivity, and Psychoticism subscales.
Conclusions: This incentives-based intervention reduces the severity of a broad array of psychiatric symptoms among depression-prone women.
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