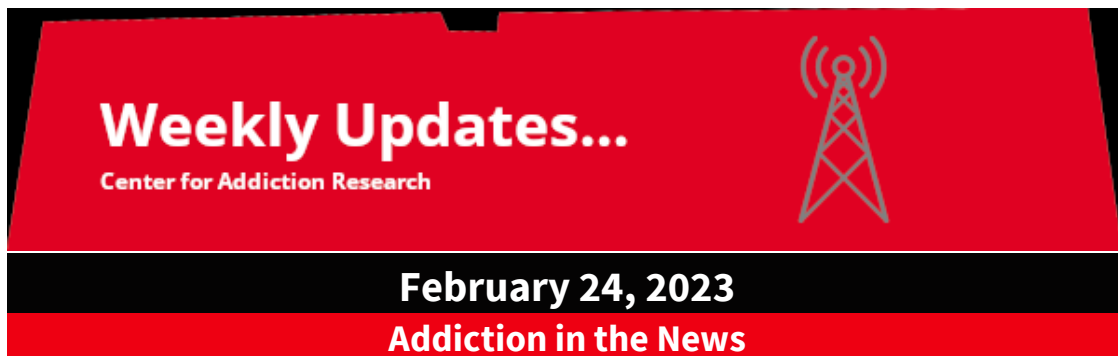


Welcome to the weekly newsletter from the Center for Addiction Research! Each newsletter includes highlights from addiction in the news topics, active funding opportunities offered by NIDA/NIAAA, and information about any new publications from CAR members. Please email Jen Rowe ([roweji@ucmail.uc.edu](mailto:roweji@ucmail.uc.edu)) to change your communication preferences. Thank you.

Thank you for your interest in the Center for Addiction Research - our mission is to accelerate scientific progress in the prevention and treatment of substance use disorders and their consequences by fostering research collaborations across: 1) UC departments, colleges, and centers including Cincinnati Children's Hospital Medical Center; 2) Local, regional, and state community and governmental partners; and 3) Other academic institutions and industry."



### **UC/ Regional News**

#### **New study reveals ketamine could be effective treatment for cocaine-use disorders (related publication below)**

As cocaine use continues to climb across the United States, scientists have struggled to develop an effective pharmacological approach to treat the devastating disorder. But by seamlessly combining artificial intelligence (AI), human intelligence, clinical testing and computer analysis, researchers at Case Western Reserve University have unearthed an existing option that appears to hold promise. "Ketamine, a small synthetic organic molecule used clinically as an anesthetic and a depression treatment, was found to be associated with significant improvement in remission among people with cocaine-use disorders," said the study's corresponding author Rong Xu, professor... **(second author, Dr. T. John Winhusen, CAR Director, and Principal Investigator of the Ohio Valley Node of the National Drug Abuse Treatment Clinical Trials Network where the study was funded.)**

#### **Free Naloxone access cabinets coming to Ohio colleges, universities**

COLUMBUS, Ohio — The Ohio Department of Higher Education, the Ohio Department of Health and RecoveryOhio, an initiative from Ohio Governor Mike DeWine, have announced a collaboration to provide emergency naloxone access cabinets on public college and university campuses around the state. Naloxone, known by the brand name Narcan, is a medication that can reverse an opioid-caused overdose. When administered, naloxone blocks the effects of opioids on the brain and quickly restores breathing. Officials say the wall-mounted emergency

access cabinet, which will be similar to an AED machine, will be an effective and easy way to provide the public with...

## **National News**

### **Pill for skin disease also curbs excessive drinking, new study shows**

Researchers from Oregon Health & Science University and institutions across the country have identified a pill used to treat a common skin disease as an "incredibly promising" treatment for alcohol use disorder. Their study was recently published in the Journal of Clinical Investigation. On average, the people who received the medication, called apremilast, reduced their alcohol intake by more than half—from five drinks per day to two. "I've never seen anything like that before," said co-senior author Angela Ozburn, Ph.D., associate professor of behavioral neuroscience in the...

### **Study finds computer-based intervention is cost-effective at reducing binge drinking among adolescents**

A computer-based intervention associated with reduced binge drinking episodes among high school students could yield a cost savings of eight thousand euros, according to a Spanish study published in Alcohol: Clinical and Experimental Research. The study found the computer-based intervention cost-effective, resulting in societal savings of €8,000 for each binge drinking episode averted. Computer and web-based interventions can potentially reach a far larger number of students than face-to-face screening and intervention. The study analyzed the cost-effectiveness of Alerta Alcohol, a...

### **Improved accuracy of screening tools for fetal alcohol spectrum disorder may lead to faster diagnosis**

A new screening instrument has the potential to more accurately identify fetal alcohol spectrum disorder (FASD), reducing missed and erroneous diagnoses in affected children and facilitating treatment and support, a new study suggests. Prenatal alcohol exposure (PAE) is a known cause of birth and growth defects and neurobehavioral issues. Children with more obvious physical differences may be appropriately diagnosed with fetal alcohol syndrome (FAS). The majority of children affected by PAE, however, present largely with neurobehavioral issues that align with the diagnostic...

### **Medication targeting brain stress response may help cardiovascular symptoms of alcohol withdrawal**

Prazosin, a medication FDA-approved for hypertension and used off-label for alcohol use disorder, may help prevent drinking relapse in people with cardiovascular or behavioral symptoms of alcohol withdrawal, according to a new study involving active-duty soldiers. Alcohol use disorder (AUD) is highly prevalent among soldiers. Prazosin reduces the noradrenergic signaling that is key to regulating the brain stress response. Overactivity of the noradrenergic system

produces irritability, anxiety, "fight or flight" responses, and sleep disturbance. Noradrenergic activity can increase during...

### **Correspondence shows troubling interactions between US officials and the alcohol industry**

There is growing evidence that the alcohol industry uses a variety of strategies to influence public policy in a way that is advantageous to its own corporate interests, rather than the interest of public health. Recent communication between employees of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and alcohol industry groups shows extensive interaction on policy-relevant scientific issues, according to a new study in the Journal of Studies on Alcohol and Drugs. Researchers at the University of York in the United Kingdom conducted a thematic content analysis on 4,784 pages...

### **Long-term alcohol use is a potential risk factor for COVID-19 complications**

Studies from animal models suggest that frequent alcohol consumption may lead to an increased risk of COVID-19 infection and present a potential for complications in disease progression. The COVID-19 pandemic has been a major challenge for many people. As a result, rates of mental illness have steadily increased and alcohol has become a commonly used means of escaping the worries of everyday life. Many risk factors, such as age and obesity, that contribute to infection and an unfavorable course of COVID-19 disease are known. However, the extent to which alcohol consumption...

### **Cannabis may alleviate opioid withdrawal but appears to have a narrow therapeutic window**

Cannabis shows some preliminary promise in the treatment of opioid withdrawal, according to new research published in Drug and Alcohol Dependence. But more controlled studies are needed to better understand the proper dose range that provides safe and effective therapy with minimal adverse effects. When someone stops taking opioids after regular use, their body goes through a period of withdrawal, which can be characterized by a range of symptoms, including nausea, vomiting, diarrhea, anxiety, insomnia, and muscle aches. Cannabis interacts with the endocannabinoid system in...

### **Cannabidiol could help curb the urge for smoking cigarettes**

Cannabidiol or CBD, a non-psychoactive component of cannabis, inhibits the metabolism of nicotine, new research has found, meaning it could help tobacco users curb the urge for that next cigarette. A team led by Washington State University researchers tested the effects of CBD and its major metabolite on human liver tissue and cell samples, showing that it inhibited a key enzyme for nicotine metabolism. For the nicotine-addicted, slowing metabolism of the drug could allow them to wait before feeling the need to inhale more of it along with all the other harmful things found in cigarette...

## **Researchers: Rethink e-cigarettes' role in treating cigarette smokers' nicotine addiction**

Should electronic cigarettes, or vapes, be accepted more widely as an effective and respected tool for treating adult smokers' nicotine addiction? Kenneth Warner, dean emeritus and the Avedis Donabedian Distinguished University Professor Emeritus at the University of Michigan's School of Public Health, says there is enough evidence to support e-cigarettes' use as a first-line aid for smoking cessation in adults. "Far too many adults who want to quit smoking are unable to do so," Warner said. "E-cigarettes constitute the first new tool to help them in decades. Yet relatively few smokers and indeed...

## **Viewpoint: E-cigarettes should be in plain packaging—just like cigarettes**

Vaping is a rapidly growing habit in Great Britain, particularly among younger people. Research by the anti-smoking charity Action on Smoking and Health found that in 2022 7% of 11- to 17-year-olds in Great Britain used e-cigarettes, up from 3.3% the year before. Plain packaging needs to be brought in to protect young people's health. This would undermine efforts to hook a new generation on nicotine. Without logos, colors or images to draw on, vape products will be less able to communicate with potential customers. Vapes are aggressively marketed to young adults. Packaging...

## **FDA Files Civil Money Penalty Complaints Against Four E-Cigarette Product Manufacturers**

Today, the U.S. Food and Drug Administration announced it has filed civil money penalty (CMP) complaints against four tobacco product manufacturers for manufacturing and selling e-liquids without marketing authorization. This is the first time the FDA has filed CMP complaints against tobacco product manufacturers to enforce the Federal Food, Drug, and Cosmetic (FD&C) Act's premarket review requirements for new tobacco products. It is illegal to manufacture, sell, or distribute e-liquids that the FDA has not authorized. The FDA previously warned each of the companies that, by making...

## **Addiction researchers denounce Australia's NHMRC statement on e-cigarettes**

Eleven top international addiction scientists argue that the 2022 statement on e-cigarettes issued by Australia's peak health and medical body, the National Health and Medical Research Council (NHMRC), fails to meet the high scientific standard expected of a leading national scientific body. The NHMRC statement, published in June 2022, aims to provide "public health advice on the safety and impacts of electronic cigarettes (e-cigarettes) based on review of the current evidence." This critique of the NHMRC statement, published in the journal *Addiction*, argues that the statement does not...

### **Researchers identify brain circuit involved in fentanyl abuse and relapse**

The ongoing opioid epidemic continues to take a heavy toll on American communities, with more than 80,000 opioid-related deaths reported in 2021, according to the National Institutes of Health. Despite the severity of this issue, the neurological mechanisms underlying opioid addiction, withdrawal and relapse are not fully understood. A study recently published in Cell Reports sheds light on the subject. Jun Wang, associate professor in the Department of Neuroscience and Experimental Therapeutics at the Texas A&M University School of Medicine, and members of his laboratory have...

### **How AI can help design drugs to treat opioid addiction**

Approximately three million Americans suffer from opioid use disorder, and every year more than 80,000 Americans die from overdoses. Opioid drugs, such as heroin, fentanyl, oxycodone and morphine, activate opioid receptors. Activating mu-opioid receptors leads to pain relief and euphoria, but also physical dependence and decreased breathing, the latter leading to death in the case of drug overdose. Preclinical studies have shown that blocking kappa-opioid receptors may offer a promising pharmacological approach to treating opioid dependence. By discovering drugs that inhibit the...

### **Study one of first to compare pain relief options for chronic low back pain patients already on opioids**

To help patients manage chronic, often debilitating pain, physicians frequently prescribe medications as first line therapy, although treatment guidelines often call for non-pharmacologic approaches. One of the first studies to compare the effectiveness of the two approaches in low back pain patients already on long-term opioids has found that pain improvement was somewhat greater with nurse-delivered medication management than with psychologist-delivered cognitive behavioral therapy. Although the difference in pain relief was perceived as significant by patients, it was...

### **New Jersey regulation not associated with curbed opioid prescriptions or shortened usage**

Regulation designed to reduce prescription opioid pain medications in New Jersey may not have had the intended effect: A Rutgers analysis of Medicaid records found that progression from short-term to long-term opioid use did not decline following new legislation capping initial prescriptions for acute pain to five days. Total new prescriptions fell at a monthly rate of 0.76 per 10,000 after the rule took effect, but they had been declining at a monthly rate of 1.62 per 10,000 before policy implementation. (It's unclear whether this change somehow stemmed from the regulations or from the fact that...

## **Study finds 'staggering increase' in methamphetamine deaths tied to opioid co-use**

The U.S. methamphetamine mortality rate increased fiftyfold between 1999 and 2021, with most of the added deaths also involving heroin or fentanyl, researchers report in the American Journal of Public Health. "We looked at trends from 1999 to 2021 and we saw this staggering increase in methamphetamine mortality accompanied by a proportional increase in those deaths that also involved heroin or fentanyl," said Rachel Hoopsick, a University of Illinois Urbana-Champaign professor of kinesiology and community health who led the research. According to data collected by the U.S. Centers...

## **Documenting the experience of police, paramedics responding to people affected by methamphetamines**

Researcher and nurse Dr. Rikki Jones, from the University of New England's School of Health, has documented the experiences of both police and paramedics responding to people affected by methamphetamines in the first study of its kind in Australia. The revealing findings, published in the journal Nursing & Health Sciences and International Journal of Mental Health Nursing, highlight the complex safety issues they face in the fraught hours before hospital admission. Dr. Jones, who has spent the past five years investigating the impact of crystal methamphetamine (or ICE) use, is now...

## **US plans to allow Medicaid for drug treatment in prisons**

CAMDEN, N.J. (AP) — The federal government is planning to allow states to use Medicaid funds to provide drugs to combat addiction and other medical services for people at state jails and prisons in an effort to help some of those most at risk of dying in the nation's overdose epidemic. Dr. Rahul Gupta, director of the White House Office of National Drug Control Policy, announced Tuesday that states would be encouraged to submit proposals for how to use money from the joint federal-state low-income health insurance program for incarcerated people. Those that do would be required...

## **FDA Advances Additional Activities to Prevent Drug Overdoses and Reduce Death**

Addressing the drug overdose crisis and substance use disorder (SUD) is an issue of great concern for our nation and remains a top public health priority for the U.S. Food and Drug Administration. Upon returning to the FDA as Commissioner, I expressed my commitment to respond to all aspects of this ongoing crisis. As an agency focused on protecting public health, combatting this evolving emergency is an issue of particular urgency for us. Of note, a public health emergency, as a consequence of the opioid crisis, was declared by the U.S. Department of Health and Human Services in October...

## **Study: Trauma causes high levels of intergenerational substance use among Black women**

Government data show that approximately 7.2 million women in the United States have substance use disorders (SUDs) and almost 20 million reported illicit substance use in the past year. New research suggests that trauma leads to high levels of intergenerational substance use among Black women, and race and gender may play a role, according to researchers from Penn State and the University of Kentucky. "More attention is needed to better understand the needs among Black women as the relationship between trauma and SUDs may be more pronounced because of their race and gender," noted Abenaa Jones, assistant professor of human development and family studies and Ann Atherton Hertzler Early Career Professor in Health and Human Development.

## **Decriminalizing hard drugs in BC could help reduce the stigma of substance abuse**

Substance use disorder is a chronic but treatable medical condition. Unlike other physical and mental health conditions, however, substance use disorder—or addiction—has historically been seen as a moral failing and was for many years relegated to the fringes of the medical community. Instead of receiving treatment in an accessible medical setting, many individuals went untreated or turned to a largely unregulated system of public and private treatment options. Drug use was criminalized and because many still believe that people who use drugs are engaging in deliberately deviant behavior, we...

### **Funding Opportunities**



[RFA-NS-24-018](#)

[HEAL Initiative: Discovery of Biomarkers and Biomarker Signatures to Facilitate Clinical Trials for Pain Therapeutics \(UG3/UH3 Clinical Trial Optional\)](#)

### **CAR Member New Publications**

#### **Repurposing ketamine to treat cocaine use disorder: Integration of artificial intelligence-based prediction, expert evaluation, clinical corroboration, and mechanism of action analyses**

Zhenxiang Gao, T. John Winhusen, Maria Gorenflo, Udi E. Ghitza, Pamela B. Davis, David C. Kaelber, Rong Xu

*Addiction*

DOI: <https://doi.org/10.1111/add.16168>

## ABSTRACT

**Background and Aims:** Cocaine Use Disorder (CUD) is a significant public health issue for which there is no Food and Drug Administration (FDA) approved medication. Drug repurposing looks for new cost-effective uses of approved drugs. This study presents an integrated strategy to identify repurposed FDA-approved drugs for CUD treatment.

**Design:** Our drug repurposing strategy combines artificial intelligence (AI)-based drug prediction, expert panel review, clinical corroboration, and mechanisms of action analysis being implemented in the National Drug Abuse Treatment Clinical Trials Network (CTN). Based on AI-based prediction and expert knowledge, ketamine was ranked as the top candidate for clinical corroboration via electronic health record (EHR) evaluation of CUD patient cohorts prescribed ketamine for anesthesia or depression compared with matched controls who received non-ketamine anesthesia or antidepressants/midazolam. Genetic and pathway enrichment analyses were performed to understand ketamine's potential mechanisms of action in the context of CUD.

**Setting:** The study utilized TriNetX to access EHRs from over 90 million patients worldwide. Genetic and functional level analysis used DisGeNet, Search Tool for Interactions of Chemicals, and Kyoto Encyclopedia of Genes and Genomes databases.

**Participants:** 7,742 CUD patients who received anesthesia (3,871 ketamine-exposed and 3,871 anesthetic-controlled) and 7,910 CUD patients with depression (3,955 ketamine-exposed and 3,955 antidepressant-controlled) were identified after propensity score-matching.

**Measurements:** EHR analysis outcome was a CUD remission diagnosis within 1 year of drug prescription.

**Findings:** Patients with CUD prescribed ketamine for anesthesia displayed a significantly higher rate of CUD remission compared with matched individuals prescribed other anesthetics (Hazard Ratio (HR): 1.98, 95% confidence interval [CI]: 1.42-2.78). Similarly, CUD patients prescribed ketamine for depression evidenced a significantly higher CUD remission ratio compared with matched patients prescribed antidepressants or midazolam (HR: 4.39, 95% CI: 2.89-6.68). The mechanism of action analysis revealed that ketamine directly targets multiple CUD-associated genes (BDNF, CNR1, DRD2, GABRA2, GABRB3, GAD1, OPRK1, OPRM1, SLC6A3, SLC6A4) and pathways implicated in neuroactive ligand-receptor interaction, cAMP signaling, and cocaine abuse/dependence.

**Conclusions:** Ketamine appears to be a potential repurposed drug for treatment of cocaine use disorder.



## **Community selected strategies to reduce opioid-related overdose deaths in the HEALing (Helping to End Addiction Long-term SM) communities study**

Redonna Chandler, Edward V Nunes, Sylvia Tan, Patricia R Freeman, Alexander Y Walley, Michelle Lofwall, Emmanuel Oga, LaShawn Glasgow, Jennifer L Brown, Laura Fanucchi, Donna Beers, Timothy Hunt, Rachel Bowers-Sword, Carter Roeber, Trevor Baker, T John Winhusen

*Journal Drug and Alcohol Dependence*

DOI: <https://doi.org/10.1016/j.drugalcdep.2023.109804>

### **ABSTRACT**

The Helping End Addictions Long Term (HEALing) Communities Study (HCS) seeks to significantly reduce overdose deaths in 67 highly impacted communities in Kentucky (KY), Massachusetts (MA), New York (NY), and Ohio (OH) by implementing evidence-based practices (EBPs) to reduce overdose deaths. The Opioid-overdose Reduction Continuum of Care Approach (ORCCA) organizes EBP strategies under three menus: Overdose Education and Naloxone Distribution (OEND), Medication Treatment for Opioid Use Disorder (MOUD), and Safer Prescribing and Dispensing Practices (SPDP). The ORCCA sets requirements for strategy selection but allows flexibility to address community needs. This paper describes and compiles strategy selection and examines two hypotheses: 1) OEND selections will differ significantly between communities with higher versus lower opioid-involved overdose deaths; 2) MOUD selections will differ significantly between urban versus rural settings.

**Methods:** Wave 1 communities (n = 33) provided data on EBP strategy selections. Selections were recorded as a combination of EBP menu, sector (behavioral health, criminal justice, and healthcare), and venue (e.g., jail, drug court, etc.); target medication(s) were recorded for MOUD strategies. Strategy counts and proportions were calculated overall and by site (KY, MA, NY, OH), setting (rural/urban), and opioid-involved overdose deaths (high/low).

**Results:** Strategy selection exceeded ORCCA requirements across all 33 communities, with OEND strategies accounting for more (40.8%) than MOUD (35.1%), or SPDP (24.1%) strategies. Site-adjusted differences were not significant for either hypothesis related to OEND or MOUD strategy selection.

**Conclusions:** HCS communities selected strategies from the ORCCA menu well beyond minimum requirements using a flexible approach to address unique needs.

**Keywords:** HEALing Communities Study; Medication for opioid use disorder (MOUD); Naloxone; Opioid prescribing; Opioid-overdose Reduction Continuum of Care Approach (ORCCA).

