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) 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

## Ohio Veterans Battle America's Opioid Epidemic in New Documentary 'Small Town Strong'

Sarah Wilson is telling her story on a sunny summer day in 2022, during a break in a CrossFit competition in downtown Portsmouth, Ohio. She has just dragged a massive tractor tire back and forth across a parking lot before carrying a boat three blocks away to the Ohio River. Before arriving at the lot, Wilson did enough weightlifting, pull-ups and other exercises to make even an Ironman competitor flinch. But it wasn't too long before our meeting that she was a homeless addict, sleeping under bridges and in hospitals, on felony probation for writing fake prescriptions. That was her life for at least 13 years. "After I graduated, I was an adult, so I had to pretty much figure out how to live on my...

# Defunct Ohio drug distributor to settle opioid cases with remaining insurance funds

Aug 9 (Reuters) - A now-defunct Ohio drug distributor has agreed to pay no more than about \$4 million to settle lawsuits by cities and counties that it contributed to the U.S. opioid epidemic, after the state's top court ruled that one of its insurers did not have to cover costs stemming from the cases. The settlement is limited by the funds available from Masters Pharmaceutical Inc's only available insurance policy, through Chubb, according to a Wednesday order by U.S. District Judge Dan Polster in Cleveland halting litigation against the company. Both sides agreed to halt the litigation in light of the potential settlement, which is not yet final, in order to avoid further depleting the available funds...

## 'FEND off Fentanyl Act' could provide reprieve amid overdose epidemic, Cuyahoga County officials say

U.S. Sen. Sherrod Brown was in Cleveland Wednesday to promote his Fentanyl Eradication and Narcotics Deterrence (FEND) off Fentanyl Act, following its passage by the Senate as part of the national defense bill last Thursday. The act would sanction international fentanyl traffickers, cut off their flow of money and disrupt the supply chains which funnel the drug into Northeast Ohio, according to Brown's office. The legislation would also allow federal agencies to prosecute those involved in the manufacturing, distribution and smuggling of the drug. Cuyahoga County is currently experiencing a surge in overdose deaths linked to fentanyl. On July 27, Cleveland officials reported six suspected...

### Anthem Blue Cross and Blue Shield Foundation Provides Mental Health Grant at Indiana State Fair

INDIANAPOLIS – Mental Health America of Indiana (MHAI) announced a 3-year, \$900,000 grant from Anthem Blue Cross and Blue Shield Foundation during "Mental Health Matters Day" at the Indiana State Fair. Representatives from Anthem Blue Cross and Blue Shield Foundation presented the grant alongside Lt. Gov. Suzanne Crouch and Douglas Huntsinger, Executive Director for Drug Prevention, Treatment, & Enforcement for the State of Indiana and Chairman of the Indiana Commission to Combat Substance Use Disorder, to MHAI's Indiana Recovery Network for their Regional Recovery Hub – Emergency Department Program. "With bi-partisan efforts in the general assembly and collaboration with...

## National News

### Drinking alcohol not likely to increase risk of a breast cancer recurrence

A Kaiser Permanente study provides new information that may help oncologists answer one of the most common questions they hear from breast cancer survivors: Is it safe to drink alcohol? The new study, published August 9 in Cancer, is the largest prospective study to look at short-term alcohol use after breast cancer. The findings suggest drinking alcohol is not associated with an increased risk of breast cancer recurrence or dying from the disease. "We know that women who drink alcohol are at increased risk of developing breast cancer and that the risk increases as alcohol use increases," said lead...

# Study suggests cannabis use during pregnancy could cause lifelong cognitive deficits for offspring

While previous research has shown that prenatal cannabis exposure can obstruct the normal growth of a fetus, the long-term impacts on brain development are still unknown. Western researchers are now providing fresh insight into this area, while also identifying a possible direction to treat the adverse effects. Led by Addictions Research Group member Mohammed H. Sarikahya and Schulich Medicine & Dentistry professor Steven Laviolette, a new study, published in the journal Molecular Psychiatry has shown that prenatal exposure to cannabis in rodents led to lasting, substantial effects on cognitive and...

#### Dr. Sanjay Gupta: Cannabis is having a senior moment

(CNN) — Prior to filming our first documentary on cannabis a decade ago, I was highly skeptical about its use as a medicine. I had even written a story for Time magazine a few years earlier to make the case that the evidence simply wasn't there. But, as so often happens when we start to dig into things, a different picture started to emerge. I traveled the world, visited tiny labs and, most important, spent time with patients — even young children — who changed my mind. I came to the realization that in some cases, not only did cannabis provide relief, it was the only thing that did so. Yes, there are real risks, as...

### Doctors Sound Alarm About Child Nicotine Poisoning as Vapes Flood the US Market

Hospital toxicologist Ryan Marino has seen up close the violent reactions of children poisoned by liquid nicotine from electronic cigarettes. One young boy who came to his emergency room experienced intense nausea, diarrhea, and vomiting, and needed intravenous fluids to treat his dehydration. Kids can also become dizzy, lose consciousness, and suffer dangerous drops in blood pressure. In the most severe case he's seen, doctors put another boy on a ventilator in the intensive care unit because he couldn't breathe, said Marino, of Case Western Reserve University School of...

#### Team develops effective cigar warning signage

A new study published by UNC Family Medicine's Sarah Kowitt, Ph.D., MPH, and colleagues looked at the impact of different types of warning signs for large and premium cigars sold individually at the point of sale. The team's newly developed graphic and text warnings were more effective than the FDA's proposed text-only warnings and could potentially increase the effectiveness of warning signs for large and premium cigars. Cigars are linked to increased risk of cancer, cardiovascular disease, lung disease and other negative health effects such as gum disease and tooth loss, just like cigarettes. Most cigars come in...

#### Awareness of vaping risks key to reducing e-cigarette use among young people

The 15- to 30-year-olds in the U.K. who perceived e-cigarettes as harmful were 40% less likely to use them compared to those who do not consider them harmful. Yet only 53% of those using e-cigarettes at least monthly said they had seen warning labels on packaging, finds research from The George Institute for Global Health. The findings, published today in the Journal of Public Health, are based on a survey of more than 1,000 individuals that was designed to better understand the attitudes, behaviors, and beliefs around e-cigarettes (electronic cigarettes, also known as "vapes") among this age...

#### Just 1 in 5 Americans Struggling With Opioid Misuse Gets Meds That Can Help

MONDAY, Aug. 7, 2023 (HealthDay News) -- The U.S. opioid abuse epidemic wages on, and overdose deaths continue to rise, yet just 1 in 5 people receives potentially lifesaving medication such as methadone, buprenorphine or naltrexone to treat their addiction, a new study finds. "These medications are effective for prescription opioids like hydrocodone [Vicodin] and oxycodone [OxyContin] and all those medications we rely on for pain, or street opioids such as fentanyl, heroin and a handful of others," said study author Dr. Wilson Compton. "Despite the availability of medication, the vast...

#### **Buprenorphine Cost a Potential Barrier for Opioid-Addicted Youth, Adults**

For young people with opioid use disorder (OUD), buprenorphine costs have declined overall but with drastic variation by payer type, researchers found. Examining buprenorphine prescriptions dispensed for U.S. youth ages 12 to 19, mean daily out-of-pocket costs declined 57.6% from 2015 through 2020 (from \$4.03 to \$1.71), with an increasing percentage of prescriptions paid by Medicaid, Andrew Terranella, MD, MPH, of the CDC, and colleagues reported in JAMA Pediatrics. However, those costs were approximately 24 times higher with commercial payers and 119 times higher for self-pay than with...

#### An Rx for a Better Government Response to the Opioid Crisis

The federal government spends billions of dollars each year to address the overdose crisis, but challenges remain when it comes to directing funding where it's needed most, even as disparities in care persist. Fortunately, federal and state policymakers have an opportunity to address the current addiction epidemic more effectively and help turn the tide in this decades-long fight. Traditionally, policymakers have looked at the issue through a narrow lens, focusing solely on pieces of the continuum of care in silos, but to make true progress in the fight, the federal government must develop a holistic strategy...

#### **Teens With Addiction Are Often Left to Detox Without Medication**

DENVER — When Denver Health wanted to open an inpatient opioid detox unit specifically for teens, doctors there searched high and low for a model to copy. They didn't find one. Teens who land in emergency rooms with an opioid overdose generally receive naloxone to reverse the effects of dangerous drugs in their system and are sent home with a list of places they can go for follow-up care. But too often, those teens never seek additional help. They are left to suffer through the agony of withdrawal with no medications to ease their cravings. As a result, many, seeking relief, go back to opioids, often with tragic...

## New study shows drug manufacturers actually increased opioid marketing after Kentucky's Purdue pharma lawsuit

Kentucky's 2007 lawsuit against Purdue Pharma marked a major turn in the opioid crisis. It was the first time a member of the Sackler family, who owned Purdue, was

deposed about the company's role in the opioid epidemic. Because the judge unsealed the court documents, public outrage soared, and other potential plaintiffs against Purdue across the country gained access to the case's evidence. But a new study in the Strategic Management Journal finds that the case dissuaded only Purdue's opioid marketing. Promotion of opioids by competing drug companies actually increased. "Despite growing...

## Risk of overdose higher when opioid agonists are prescribed with other medicines

Patients prescribed medicines to replace illicit drugs are at higher risk of overdose resulting in hospital admission when taking other medicines which treat mental health conditions or pain, University of Manchester researchers have found. The authors of the study, published in the journal Addiction on August 3, say doctors should avoid co-prescription of opioid agonists, with benzodiazepines, gabapentinoids, antipsychotics or Z-drugs if harm is greater than the benefit to patients. Opioid agonists, medicines which include methadone or buprenorphine, are used as a substitute for illicit drugs when...

#### The landscape of opioid prescribing has changed, but is it for the better?

Globally, opioid prescribing has increased significantly over the past three decades. In 2019, Australia had the eighth highest level of opioid use in the world. Although opioids play an important role in managing pain, increases in prescription opioid use has led to more opioid related deaths. In the 10 years from 2007 to 2016, opioidrelated mortality doubled from 591 to 1119 in Australia, with most deaths attributed to prescription opioids. Prescription opioids are used for medical treatment (e.g., for pain or opioid dependence treatment), and for nonmedical reasons (e.g., for their euphoric effects). Harms can...

# Human antibody that targets carfentanil, fentanyl and related opioids reverses overdose effects in preclinical study

An antibody in single-chain fragment variable (scFv) format that binds to the powerful opioid carfentanil was shown to reverse signs of carfentanil overdose in preclinical tests conducted by scientists at Scripps Research. Carfentanil is a variant of the synthetic opioid fentanyl, and about 100 times as potent as its chemical cousin. Along with fentanyl and other fentanyl variants, it is commonly mixed with illegal drugs such as heroin and cocaine to enhance their euphoric effects, resulting in many fatal overdoses. In the study, published in ACS Chemical Neuroscience on August 3, 2023, the researchers developed a...

#### Study finds health care workers face increased risk for fatal drug overdoses

A study of health care workers (HCWs) found that registered nurses, social or behavioral health workers, and health care support workers were at increased risk for drug overdose death, suggesting the need to identify and intervene on those at high risk. The findings are published in Annals of Internal Medicine. The increasing number of drug overdose deaths in the United States, mostly involving opioids, has prompted efforts to identify high-risk populations and offer preventive interventions. Drug overdose risk among certain occupational groups is unknown. HCWs regularly prescribe or...

### White House ONDCP Statement on New Sanctions Against Sinaloa Cartel Fentanyl Suppliers

Washington, D.C. – Today, in support of President Biden's Unity Agenda effort to beat the overdose epidemic, White House Office of National Drug Control Policy (ONDCP) Director Dr. Rahul Gupta released the following statement on new United States sanctions against three Sinaloa cartel fentanyl suppliers in cooperation with Mexico: "As part of President Biden's Unity Agenda, we have now sanctioned more than 170 drug traffickers," said Dr. Gupta. "A key driver of the overdose epidemic is drug traffickers and their profits. President Biden has made clear: we will crack down on the illicit drug supply chain at every...

#### Nonprofit naloxone maker celebrates FDA approval by donating 200,000 doses

A nonprofit naloxone manufacturer is celebrating its recent market approval by giving away 200,000 doses of its over-the-counter nasal spray. Harm Reduction Therapeutics said in a statement that it will donate nearly a quarter-million doses of its new product to the Remedy Alliance, an organization devoted to affordable naloxone access. The announcement comes on the heels of the Food and Drug Administration's approval of Harm Reduction Therapeutics' product RiVive, a new nasal naloxone spray used to reverse opioid overdose. The 200,000-dose donation represents roughly 10% of Harm...

#### As States Dole Out Billions for Opioid Relief, Educators Rarely Get a Say

Educators won't have much of a direct role in influencing how states will spend billions of dollars in legal settlement funds for addressing the opioid addiction crisis. Most states have formed commissions or councils to oversee or directly control the flow of funding. But only three states—Arkansas, Illinois, and Nevada have included a school district representative on their commission, according to an Education Week analysis of a database of state opioid council members published by Kaiser Health News. Another three—Hawaii, Idaho, and Oklahoma—included someone from the state department...

### As clinics pivot post-Roe, battle rages over syringe service in opioid-ravaged West Virginia

CHARLESTON, W.Va. -- Staff at Women's Health Center of West Virginia know what it's like to provide controversial health services that government officials have sought to ban or restrict. The Charleston clinic was the state's only abortion provider for years until the state Legislature passed a near-total ban on the procedure last year. The clinic remained open, providing other reproductive care. Now it's trying to open a syringe service program for drug users, which is another contentious health service that has been regulated by Republican lawmakers in the deep red state. The proposal, which is scheduled...

### Changes in gut microbiome alters rewarding effects of cocaine and cravings

According to the 2021 National Survey on Drug Use and Health, 4.8 million people (ages 12 and up) reported using cocaine within the previous 12 months, and 24,486 people died from an overdose involving cocaine. Because there are no FDAapproved medications for cocaine use disorder, there is an urgent need to develop therapeutic interventions. In a new preclinical study from Wake Forest University School of Medicine, scientists provide the first evidence that changes in the gut microbiome have significant effects on cocaine use and cravings after withdrawal. The study has been published in the...

### Peer Support Helps St. Louis Construction Workers Battling Addiction

Construction workers are more likely to die by suicide or of a drug overdose than workers in almost any other field, and a St. Louis-based peer support system and hotline wants to change it. According to the American Addiction Centers, those who work in construction have nearly twice the rate of substance use disorders as the national average. Don Willey, pension chairman and Trustee for Laborers Local 110, helped initiate "LEAN-STL," which stands for Laborers Escaping Addiction Now-St. Louis. He said the program's peer support specialists have lived experience, which is effective in helping others in...

# 60% of Americans battling drug or alcohol addictions also have jobs. Here are the professions with the highest rates of substance-use disorder

Of the 46 million Americans who struggle with at least one substance-use disorder, most—some 60% of those over the age of 12—have a job, according to the National Survey on Drug Use and Health. That's an uncomfortable and largely unacknowledged reality in American business, where talking about addiction to alcohol or drugs has traditionally been taboo. Even though substance-use disorder is a protected status under the Americans With Disabilities Act (so long as an individual is not currently engaged in the illegal use of drugs) studies show that many avoid acknowledging it for fear of...

## **Funding Opportunities**



PAR-23-251 Alcohol Health Services Research (R01 Clinical Trial Optional) <u>PAR-23-252</u> <u>Alcohol Health Services Research (R34 Clinical Trial Optional)</u>

### PAR-23-250

<u>Alcohol Treatment, Pharmacotherapy, and Recovery Research (R01 Clinical Trial</u> <u>Required)</u>

### PAR-23-249

<u>Alcohol Treatment, Pharmacotherapy, and Recovery Research (R34 Clinical Trial</u> <u>required)</u>

## NOT-DA-23-032

Notice of Change to Application Due Date and Instruction in Section IV in RFA-DA-24-007, "Avenir Award Program for Chemistry and Pharmacology of Substance Use Disorders (DP1- Clinical Trial Not Allowed)"

## **CAR Member New Publications**

## Eat, Sleep, Console Approach or Usual Care for Neonatal Opioid Withdrawal

Leslie W. Young, M.D., Songthip T. Ounpraseuth, Ph.D., Stephanie L. Merhar, M.D., Zhuopei Hu, M.S., Alan E. Simon, M.D., Andrew A. Bremer, M.D., Ph.D., Jeannette Y. Lee, Ph.D., Abhik Das, Ph.D., Margaret M. Crawford, B.S., Rachel G. Greenberg, M.D., P. Brian Smith, M.D., Brenda B. Poindexter, M.D., et al., for the ACT NOW Collaborative

*The New England Journal of Medicine* DOI: <u>10.1056/NEJMoa2214470</u>

## ABSTRACT

**Background:** Although clinicians have traditionally used the Finnegan Neonatal Abstinence Scoring Tool to assess the severity of neonatal opioid withdrawal, a newer function-based approach — the Eat, Sleep, Console care approach — is increasing in use. Whether the new approach can safely reduce the time until infants are medically ready for discharge when it is applied broadly across diverse sites is unknown.

**Methods:** In this cluster-randomized, controlled trial at 26 U.S. hospitals, we enrolled infants with neonatal opioid withdrawal syndrome who had been born at 36 weeks' gestation or more. At a randomly assigned time, hospitals transitioned from usual care that used the Finnegan tool to the Eat, Sleep, Console approach. During a 3-month transition period, staff members at each hospital were trained to use the new approach. The primary outcome was the time from birth until medical readiness for discharge as defined by the trial. Composite safety outcomes that were assessed during the first 3 months of postnatal age included in-hospital safety, unscheduled health care visits, and nonaccidental trauma or death.

**Results:** A total of 1305 infants were enrolled. In an intention-to-treat analysis that included 837 infants who met the trial definition for medical readiness for discharge, the number of days from birth until readiness for hospital discharge was 8.2 in the Eat, Sleep, Console group and 14.9 in the usual-care group (adjusted mean difference, 6.7 days; 95% confidence interval [CI], 4.7 to 8.8), for a rate ratio of 0.55 (95% CI, 0.46 to 0.65; P<0.001). The incidence of adverse outcomes was similar in the two groups.

**Conclusions:** As compared with usual care, use of the Eat, Sleep, Console care approach significantly decreased the number of days until infants with neonatal opioid withdrawal syndrome were medically ready for discharge, without increasing specified adverse outcomes. (Funded by the Helping End Addiction Long-term (HEAL) Initiative of the National Institutes of Health; ESC-NOW ClinicalTrials.gov number, NCT04057820. opens in new tab.)

## Neurocognitive predictors of adherence to an online pain self-management program adjunct to long-term opioid therapy

David E Fleck, Marian Wilson, Daniel Lewis, Jeffrey A Welge, Grace Arya, Anoop Sathyan, Kelly Cohen, T John Winhusen

Journal of Clinical and Experimental Neuropsychology DOI: <u>10.1080/13803395.2023.2221396</u>

### ABSTRACT

**Introduction:** While pain self-management programs can significantly improve patient outcomes, poor adherence is common and the need for research on predictors of adherence has been noted. A potential, but commonly overlooked, predictor is cognitive function. Our aim, then, was to examine the relative influence of various cognitive functional domains on engagement with an online pain self-management program.

**Method:** A secondary analysis of a randomized controlled trial testing the impact of Ehealth (a 4-month subscription to the online Goalistics Chronic Pain Management Program) plus treatment as usual, relative to treatment as usual alone, on pain and opioid dose outcomes in adults receiving long-term opioid therapy of morphine equivalence dose ≥20 mg; 165 E-health participants who completed an on-line neurocognitive battery were included in this sub-analysis. A variety of demographic, clinical, and symptom rating scales were also examined. We hypothesized that better processing speed and executive functions at baseline would predict engagement with the 4-month E-health subscription.

**Results:** Ten functional cognitive domains were identified using exploratory factor analysis and the resultant factor scores applied for hypothesis testing. The strongest predictors of E-health engagement were selective attention, and response inhibition and speed domains. An explainable machine learning algorithm improved classification accuracy, sensitivity, and specificity.

**Conclusions:** The results suggest that cognition, especially selective attention, inhibitory control, and processing speed, is predictive of online chronic pain self-management

program engagement. Future research to replicate and extend these findings seems warranted.

ClinicalTrials.gov Registration Number: NCT03309188.

# Outcomes of Babies with Opioid Exposure (OBOE): protocol of a prospective longitudinal cohort study

Carla M Bann, Jamie E Newman, Brenda Poindexter, Katherine Okoniewski, Sara DeMauro, Scott A Lorch, Deanne Wilson-Costello, Namasivayam Ambalavanan, Myriam Peralta-Carcelen, Catherine Limperopoulos, Kushal Kapse, Jonathan M Davis, Michele Walsh, Stephanie Merhar

Pediatric Research DOI: <u>10.1038/s41390-023-02662-7</u>

### ABSTRACT

**Background:** While the health, social, and economic impacts of opioid addiction on adults and their communities are well known, the impact of maternal opioid use on the fetus exposed in utero is less well understood.

**Methods:** This paper presents the protocol of the ACT NOW Outcomes of Babies with Opioid Exposure (OBOE) Study, a multi-site prospective longitudinal cohort study of infants with antenatal opioid exposure and unexposed controls. Study objectives are to determine the impact of antenatal opioid exposure on brain development and neurodevelopmental outcomes over the first 2 years of life and explore whether family, home, and community factors modify developmental trajectories during this critical time period.

**Results:** Primary outcomes related to brain development include cortical volumes, deep cerebral gray matter volumes, resting-state functional connectivity measures, and structural connectivity measures using diffusion tensor imaging. Primary neurodevelopmental outcomes include visual abnormalities, cognitive, language, and motor skills measured using the Bayley Scales of Infant Development and social–emotional and behavioral problems and competence measured by the Brief Infant-Toddler Social and Emotional Assessment.

**Conclusions:** The OBOE study has been designed to overcome challenges of previous studies and will help further understanding of the effects of antenatal opioid exposure on early infant development.

#### Impact:

• This study will integrate MRI findings and comprehensive neurodevelopmental assessments to provide early insights into the functional topography of the brain in this high-risk population and assess MRI as a potential biomarker.

- Rather than conducting neuroimaging at a single time point, the study will include serial MRI assessments from birth to 2 years, allowing for the examination of trajectories throughout this period of rapid brain development.
- While previous studies often have had limited information on exposures, this study will use umbilical cord assays to accurately measure amounts of opioids and other substances from 20 weeks of gestation to birth.

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