Welcome to the Biannual Bulletin from the Center for Addiction Research! The biannual bulletin contains news stories and summaries provided by CAR members about the great work they are doing. Thank you to those who shared stories for this edition! To have your work included in the next issue, coming in late July 2025, please send a brief summary/story accompanied by pictures or graphics (if available) to Jen Rowe (roweji@ucmail.uc.edu) any time prior to July 15th. Thank you!

CAR Biannual Bulletin

January 2025

Member Research Updates

2025 Next Bulletin Release Date: - Late July

2025 Next Deadline for Submitting Stories: - July 15th

Prenatal Cannabis Exposure Linked to Poor Executive Function, Aggression in Kids



Poor executive function and aggressive behavior at age 5 years was observed among children exposed to cannabis during pregnancy, a cohort study suggested.

Among 250 children, age-corrected standard scores for attention and inhibitory control on the NIH Toolbox Early Childhood Cognitive Composite were about 0.4 standard deviations lower for those exposed to cannabis compared with those who were unexposed (β = -6.1 points, 95% CI -10.8 to - 1.4) after propensity score weighting and adjustment for confounders, reported Sarah Keim, PhD, of the Abigail Wexner Research Institute at Nationwide Children's Hospital in Columbus, Ohio, and co-authors.

Exposed children were also more likely to show aggressive behavior, such as hitting in the face using a fist (β =0.17, 95% CI 0.02-0.31), they noted in JAMA Pediatrics.

"We embarked on this line of research because we noticed several years ago that there had been an uptick in the prevalence of cannabis use during pregnancy in the U.S.," Keim told MedPage Today. "We were familiar with research that had been done a couple of decades ago showing some of the harms of [cannabis exposure] to child development and behavior, but that research hadn't been updated with a more contemporary sample of children."

Keim added that cannabis use during pregnancy had more than doubled from 2003 to 2017, and the potency of cannabis has also increased dramatically -- some estimates show up to 13 times more potency -- in the past couple of decades.

Pointing to the association between cannabis exposure and worse attention and inhibitory control, she noted "that jumped out at us, in particular, because one, it was among the strongest associations we observed in the study, but also was so strikingly consistent with a couple of classic longitudinal studies that were done back in the 80s and 90s."

"These findings reinforce the existing clinical recommendations that are out there [from] the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists," Keim said. "Hopefully this evidence gives some renewed, fresh data for clinicians to use when they approach their patients." In an accompanying editorial, Ran Barzilay, MD, PhD, and Lauren White, PhD, both of the Perelman School of Medicine at the University of Pennsylvania in Philadelphia, noted that these findings "should be interpreted in the context of wider intergenerational influences on neurodevelopment."

"There is a critical need for more large-scale research that incorporates multiple environmental confounders and applies methods tailored to address causal effects of exposures in observational data," they wrote.

Until more research is available, Barzilay and White advised clinicians to consider cannabis exposure during pregnancy to be a broader risk factor for maternal health, as well as a child's neurodevelopment.

"It might suggest that women who use cannabis during pregnancy represent a high-risk group who may benefit from counseling and intervention beyond a recommendation for cannabis abstinence during pregnancy," they added.

For this cohort study, the authors collected data on 250 mother-child dyads who were patients at Ohio State University Wexner Medical Center from 2016 through 2020. All children were born between May 25, 2010, and February 7, 2016, and all assessments were conducted when the children were 5 years old.

Of the 250 children, 80 were exposed to cannabis (32%), 62% were Black or African American, 20% were white, and 4% were Hispanic. The authors noted that use of tobacco, other drugs, and alcohol during pregnancy were also common, and most families were living in poverty.

Cannabis exposure was measured prospectively by urine toxicology, maternal self-report, and obstetric record abstraction.

The study was limited by several factors, including the potential for the misclassification of cannabis exposure. The authors also did not have data on the dose or timing of cannabis exposure. Residual confounding factors were also possible.

Article from MEDPAGE Today: <u>Prenatal Cannabis Exposure Linked to Poor Executive Function, Aggression in Kids</u>

Read the study in JAMA Pediatrics: <u>Prenatal Cannabis Exposure and Executive Function and Aggressive Behavior at Age 5 Years</u>

UC researchers to study overdose hot spots in Cincinnati



A collaboration between the University of Cincinnati and the Hamilton County Office of Addiction Response — funded by a \$350,000 National Institute of Justice grant — is taking a new approach to help combat the growing overdose crisis in the region.

UC criminal justice researchers will conduct a study of data from emergency medical calls, overdose response teams and local coroner records to pinpoint areas or hot spots to determine where in Cincinnati overdoses are occurring most frequently.

With this information, a research team will then implement and study interventions aimed at reducing overdose incidents in these hot spots.

According to the most recent data, Cincinnati has experienced between 270 to 500 overdose deaths each year since 2020.

"The overdose epidemic has hit certain areas harder than others, and this project is focusing on identifying specific areas where overdoses are most concentrated," says the study's lead investigator Ben Feldmeyer, professor and criminal justice researcher in UC's College of Education, Criminal Justice, and Human Services.

Study methods

A randomized trial that will test the effectiveness of several harmreduction strategies is key to the project, Feldmeyer says. The team will place free, publicly accessible kits with the drug naloxone, a medicine that rapidly reverses an opioid overdose, as well as placing fentanyl test strips in strategic locations, giving people tools to prevent overdose deaths. In some areas, additional resources like educational materials and information about drug treatment programs will also be provided.

The project will focus on 36 hot spots, with half receiving the intervention and the other half serving as control groups. Researchers will track overdose incidents and gather feedback from the community to understand the impact of these efforts.

Research team

"Data collection will help us better understand where resources are most needed and how we can make a real difference," says **study coinvestigator Sarah Manchak, a UC associate professor of criminal justice**.

The research team includes co-investigator Cory Haberman, associate professor and director of the Institute of Crime Science.

The study will help assess whether these interventions can reduce overdose deaths and improve access to life-saving resources, especially in underserved communities, say the investigators.

Partnership and potential

In addition to the local impact, the project's results could inform similar initiatives across the country as such harm-reduction strategies become more common in U.S. communities. The researchers will share their findings through reports, academic publications and public outreach efforts like community talks and policy briefs.

"We're excited to work together with local partners to find innovative ways to reduce overdose deaths and support those in need," says Meagan Guthrie, director of the Hamilton County Office of Addiction Response.

This project, all say, aims to make a real difference in the fight against overdoses in Cincinnati, providing both immediate relief and long-term strategies to help people affected by substance abuse

UC News story by Angela Koenig: <u>UC researchers to study overdose hot spots in Cincinnati</u>

Campaign leads to a 37% drop in overdose deaths from drugs mixed with opioids, including fentanyl



Ohio Healing Communities Study



Expanded treatment options, increased naloxone distribution and targeted education campaigns likely led to a 37% reduction in overdose deaths from opioids combined with stimulant drugs other than cocaine, according to the results of a large study.

The finding came from a planned study of secondary outcomes of the HEALing (Helping to End Addiction Long-Term) Communities Study (HCS), which tested an intervention encompassing data-driven adoption of evidence-based practices for reducing overdose deaths in Kentucky, Massachusetts, New York and Ohio.

Death rates from specific combinations of opioids with stimulants other than cocaine, most commonly fentanyl mixed with methamphetamine, were 8.9 per 100,000 adults in intervention communities compared to 14.1 per 100,000 adults in comparison to communities that did not receive the intervention—a statistically significant difference.

The findings were published Oct. 21, 2024 in JAMA Network Open.

With the prescription medications that started the opioid crisis harder to obtain by the time the trial began, fentanyl was rapidly entering the illicit drug market in combination with methamphetamine, cocaine, counterfeit pills and other stimulants, said Bridget Freisthler, lead author of the new study and a professor at The Ohio State University.

"Now we have a whole new group of people developing addiction to opioids," said Freisthler, Ohio's principal investigator for the HEALing Communities Study.

"It was nice to see that we were able to achieve reductions in overdose deaths involving this combination of opioids, primarily fentanyl and psychostimulants, not including cocaine, because that's the most recent wave in the epidemic that we're seeing."

Analysis of other drug combinations showed that intervention communities had lower rates of overdose deaths from an opioid mixed with cocaine (6%) and an opioid mixed with benzodiazepine (1%), but that these differences did not reach statistical significance.

The National Institutes of Health (NIH) launched the HEALing Communities Study in 2019. Participating community coalitions implemented 615 strategies to address opioid-related overdose deaths across health care, justice and behavioral health settings.

Based on data indicating which interventions were best suited to areas they served, agencies selected from three "menus" of evidence-based practices focused on overdose education and naloxone distribution, increasing exposure to medication for opioid use disorder, and safer opioid prescribing. Researchers reported in June on the main outcome of HCS - that the intervention did not result in a statistically significant reduction in opioid overdose death rates during the evaluation period.

In this study, the authors found that intervention communities had an 8% lower rate of all drug overdoses compared to control communities, which was estimated to represent 525 fewer drug overdose deaths.

In the new paper, researchers reported that more than 40% of overdose deaths in the study involved the combination of at least one opioid and a stimulant.

The evidence of higher prevalence of fentanyl in the illicit drug market led coalition agencies to adjust communication efforts accordingly, said Freisthler, also the Cooper-Herron Professor in Mental Health at the University of Tennessee, Knoxville.

"We were already shifting to where psychostimulants had fentanyl in them and messages weren't reaching the right folks because people who use psychostimulants think of themselves as using meth or cocaine, not opioids," she said.

"So we had to make it clear that fentanyl could be in every drug and that nobody was really immune from the possibility of an overdose. Communities emphasized that this is a multiple-drug issue, not just a fentanyl issue or an opioid issue.

"In many ways, the fact we're looking at this particular outcome is because communities were so invested in it and so concerned, and wanted it to be a focus of the study."

The potential for naloxone to prevent overdose deaths in people who use multiple drugs was also incorporated into communication campaigns implemented by all intervention communities, which may have helped prevent deaths, researchers said.

Participating agencies were very good at advocating for themselves, Freisthler said, and the front-end work ideally will leave communities even better prepared to address overdoses going forward.

"The HCS was beneficial to Brown County in numerous ways," said Deanna Vietze, executive director of the Brown County Board of Mental Health and Addiction Services in southwest Ohio.

"It affirmed the work already underway, allowed for expansion of best practices, helped engage new partners, strengthened existing partnerships, and allowed innovative purchases that forged outreach opportunities that will continue to positively impact Brown County citizens for years to come." Ohio study leaders are intent on making sure lessons and success stories from the study are widely available through a website providing a range of materials, and are meeting with groups interested in implementing the evidence-based practices in their own communities.

"The drug overdose crisis is pervasive in our communities, and we've got multigenerational and intergenerational trauma affecting families. That's not going to change overnight," Freisthler said. "That means we need to continue to improve understanding of this crisis, and reduce overdose deaths so we don't have another generation experiencing the same sort of trauma."

Article from Medical Xpress: <u>Campaign leads to a 37% drop in overdose deaths from drugs mixed with opioids, including fentanyl</u>

Read the study in JAMA Network Open: <u>Communities That HEAL Intervention and Mortality Including Polysubstance Overdose Deaths</u>

Clonidine Comparable to Morphine for Infants With Opioid Withdrawal



Length of treatment and neurobehavioral scores did not significantly differ between infants with prenatal opioid exposure randomized to either clonidine or morphine, researchers found.

Among infants with neonatal opioid withdrawal syndrome (NOWS), median length of treatment was 15 days for infants who received morphine and 17 days for those who received clonidine (P=0.48), reported Henrietta Bada, MD, MPH, of the University of Kentucky in Lexington, and colleagues.

At the end of treatment, neurobehavioral performance, a predictor of childhood outcomes, also did not differ between groups, Bada and colleagues noted in Pediatrics.

However, more of the clonidine-treated infants needed adjunct therapy compared with those in the morphine group (45% vs 10%; adjusted odds ratio 8.85, 95% CI 2.87-27.31, P<.001).

"Future studies are needed to investigate the optimal dose and frequency of clonidine administration for improved efficacy and the decreased need for adjunctive therapy in NOWS," Bada and colleagues noted.

Increased use of prescribed and illicit opioids among women of childbearing age in the U.S. has contributed to an uptick in NOWS, with diagnosed infants at higher risk of hospital readmission after birth.

The researchers noted that smaller studies have suggested that clonidine -- a non-opioid alpha-2 adrenergic agonist -- can work in NOWS, as a single-drug therapy and as an adjunct therapy. Preclinical work has shown that it "has advantages over morphine" including the fact that it "stabilizes breathing and temperature control that is disrupted by morphine" and "downregulates opioid receptor expression in neonatal mononuclear cells."

In their earlier pilot study, clonidine was associated with shorter length of treatment and improved neurobehavioral performance compared with morphine for neonatal abstinence syndrome, which "supported evaluating a non-opioid drug as an alternative to treat NOWS," they wrote.

At initial testing, clonidine-treated infants scored worse on arousal, hypertonicity, and stress abstinence. But between initial and final assessments, this group showed significant improvement (less handing, excitability, and stress abstinence, and improved arousal and regulation), ultimately faring as well as their morphine-treated counterparts.

At final measure, median neurobehavioral scores based on the NICU Network Neurobehavioral Scale were not significantly different between groups.

There was also no significant difference in median length of hospital stay between clonidine and morphine groups (22 days vs 19 days; P=0.30).

The current study by Bada and colleagues "is a robust new clinical trial in the field of NOWS demonstrating efficacy of clonidine as a primary pharmacologic agent with comparative hospitalization outcomes to morphine, with the exception of higher secondary agent use," wrote Elisha Wachman, MD, of Boston University Chobanian & Avedisian School of Medicine, and Hayley Friedman, MD, of Washington University School of Medicine in St. Louis, in a commentary accompanying the study.

"Future studies should incorporate multicentered designs, examine longerterm neurodevelopmental outcomes, emphasize the importance of standardized nonpharmacologic care bundles as primary medical management, compare clonidine to methadone and buprenorphine, and incorporate symptom-triggered dosing and the [Eat, Sleep, Console] care approach for broadest generalizability into clinical practice," they added.

For this randomized clinical trial, enrollment criteria included gestational age of at least 35 weeks, ≤7 days postnatal age, prenatal opioid exposure, and no other medical condition. Infants were enrolled from December 2017 to February 2022 at a single children's hospital in the U.S.

There were 120 infants randomized to oral clonidine at a dose of $1 \mu g/kg$ or morphine at a dose of 0.06 mg/kg, every 3 hours. Those showing no improvement had their doses increased by 25% of the initial dose every 12 to 24 hours. Those without improvement by the fourth dose received adjunct therapy. All infants had non-pharmacological intervention, such as swaddling, low noise and lighting environment, rooming in, and infant massage.

Initiation and monitoring of treatment were guided by Finnegan Neonatal Abstinence Scoring System scores (FSs), which are used to monitor withdrawal symptoms. Clonidine or morphine started when an infant had three consecutive FSs ≥8 or two consecutive FSs ≥12. The aim was FSs consistently <8.

Prior to treatment, the median of maximum FSs was similar in infants who received clonidine (14.5, 95% Cl 14.1-15.6) and those who received morphine (14, 95% Cl 13.9-15.5). By the third day of treatment, the maximum FS was significantly lower in the morphine-treated group, with a median of 8 (95% Cl 7.3-8.6) versus 11.5 (95% Cl 11.0-12.5) in the clonidine-treated group (P<0.001).

Over time, though, similar patterns of mean FS emerged. After 6 days, mean daily scores for the clonidine group trended lower than the morphine group; however, CIs overlapped.

Limitations of the study included that it was not powered to show equivalence or non-inferiority, and that the pandemic affected plans to enroll a larger sample at an additional site.

Article from MEDPAGE Today: <u>Clonidine Comparable to Morphine for Infants With Opioid Withdrawal</u>

Read the study in the *Pediatrics Journal*: <u>Clonidine as Monotherapy for Neonatal Opioid Withdrawal Syndrome: A Randomized Trial</u>

Researchers report effects of intervention on overdose education and naloxone distribution



New research shows that the HEALing (Helping to End Addiction Long-term) Communities Study (HCS) significantly increased community access to naloxone, a lifesaving medication that quickly reverses the effects of opioids and helps restore breathing in someone who is experiencing an overdose.

The paper, published in the American Journal of Public Health on Oct. 10, analyzed results from the HEALing Communities Study (HCS), which included the University of Kentucky as a research site.

Launched in 2019, the landmark study was aimed at reducing overdose deaths in 67 communities across four states highly impacted by the opioid crisis: Kentucky, Massachusetts, New York and Ohio.

Kentucky communities achieved the greatest increase in naloxone distribution among the four participating states. The eight Kentucky

Ohio Healing Communities Study



counties participating in the study's first wave implemented 104 different strategies to distribute nearly 6,400 units of naloxone. These intervention communities tripled their naloxone distribution compared to control communities—an increase more than twice that of any other state in the study.

The new study results showed that across all four states, communities implementing the intervention distributed 79% more naloxone units compared to control communities. The increase was driven by several different strategies including providing naloxone at addiction treatment centers, community outreach programs and increasing availability at local pharmacies.

"These findings show that engaging communities to implement evidencebased strategies can make a real difference in getting this lifesaving medication to those who need it most," said the study's lead author Trish Freeman, Ph.D., a professor in the UK College of Pharmacy who led the HEAL Prevention Team and coordinated HEAL's naloxone education and distribution efforts in Kentucky.

HCS used the "Communities that HEAL" intervention, a process in which communities work with researchers to establish and expand proven practices for preventing overdose deaths—including increasing access to naloxone. In Kentucky, a team of more than 25 researchers from across UK's campuses led implementation efforts in partnership with community members, state and local leaders, and public and private agencies.

"Kentucky's high level of engagement reflects the strong partnerships we've built between community members, state and local leaders, and public and private agencies—and our shared commitment to developing sustainable solutions for the opioid crisis," said Freeman.

Increasing access to naloxone is one of the three primary evidence-based strategies implemented in the HCS intervention, which also focuses on effective delivery of medication for opioid use disorder and improved prescription opioid safety practices.

An analysis of the HEALing Communities Study published earlier this year showed promising results in reducing opioid-related deaths. Communities implementing the intervention experienced a 9% lower rate of opioid overdose deaths compared to control communities.

Researchers are continuing to examine the study's impact on overall overdose deaths, deaths with specific drug combinations like opioids and stimulants, and nonfatal overdoses. The UK's HCS team also continues to analyze outcomes specific to the Commonwealth, as well as key lessons from implementing the study during the unprecedented challenges of COVID-19 and fentanyl.

Their goal is to use these findings to shape more effective strategies for tackling opioid addiction and preventing overdose deaths, both in Kentucky and across the nation.

Article from Medical Xpress:

Researchers report effects of intervention on overdose education and naloxone distribution

Read the study in the American Journal of Public Health: <u>Effect of the Communities That HEAL Intervention on Overdose Education and Naloxone Distribution: A</u> <u>Cluster-Randomized, Wait-List Controlled Trial</u>

Are teen 'just say no' campaigns effective? UC expert joins WVXU's Cincinnati Edition roundtable discussion



The Kentucky Opioid Abatement Advisory Commission recently announced a new three-year drug prevention initiative, funded by grants from the state's opioid settlement fund for prevention, enforcement, treatment and recovery efforts.

The University of Cincinnati's LaTrice Montgomery joined WVXU's Cincinnati Edition to discuss youth drug prevention programs and what research says about the most effective approaches.

The popular DARE (Drug Abuse Resistance Education) program that began in the 1980s originally featured a uniformed officer speaking to kids in a lecture style on how to "just say no" to drugs.

"As we now know, that lecture style doesn't always resonate with youth," said Montgomery, PhD, adjunct associate professor in the Department of Psychiatry and Behavioral Neuroscience in UC's College of Medicine and a licensed clinical psychologist. "So we've learned it needs to be much more interactive and include not only drug resistance skills but social and emotional skills."

As research has progressed, Montgomery said DARE is still around but features a different approach that includes the REAL (Refuse, Explain, Avoid and Leave) method.

Chris Evans, executive director of the Kentucky Opioid Abatement Advisory Commission, told WVXU their team is using a research-based approach to tailor their programs to what will be most effective.

"It's really designed to encourage young people to make positive life choices and help build up their resilience," he said. "What this program does is really shine a light again on those strengths of kids and finding a way for them to identify and strengthen what's going on with them. And we've seen the studies have indicated that is a better approach to dealing with kids nowadays in terms of getting them to be educated and to listen and to make positive choices in this space."

UC News story by Tim Tedeschi: <u>Are teen 'just say no' campaigns effective?</u>

Read and listen to WVXU's Cincinnati Edition here: <u>Are teen 'just say no' campaigns effective?</u>

Health effects of secondhand marijuana smoke Local 12 turns to UC marijuana researcher



As more states, including Ohio, legalize recreational marijuana, there is still little research into its health effects. This includes a lack of research around secondhand marijuana smoke, according to University of Cincinnati researcher LaTrice Montgomery, PhD.

"A lot of the studies that are out now sort of draw from the tobacco industry," Montgomery, adjunct associate professor in the Department of Psychiatry and Behavioral Neuroscience in UC's College of Medicine and a licensed clinical psychologist, told Local 12.

The problem, Montgomery said, is that since marijuana and tobacco are different it is not known if it has the same risks on the heart and lungs that secondhand tobacco smoke does.

Montgomery said one National Institutes of Health study tested security workers for an outdoor concert venue who were exposed to secondhand cannabis smoke for several hours. There was detectible THC, the psychoactive component in cannabis, in blood and urine samples, even at an outdoor event with circulating air.

"What they found is they did find a small, detectible level of THC within their blood levels, very small so they wouldn't fail a drug test, but there were still levels there nonetheless," said Montgomery. "They also found that the law enforcement officers were more likely to report itchy eyes, the burning red eyes, headaches, higher levels of anxiety, things we associate with cannabis use."

UC News story by Tim Tedeschi: <u>Health effects of secondhand marijuana smoke</u>

Read the story from Local 12: Weeding into new ground: Health effects of secondhand marijuana smoke

AI Identifies Ketamine as a Potential Treatment for Amphetamine-Type Stimulant Use Disorder



What's the Question?

Stimulant use in the United States is on the rise, and amphetamine-type stimulants are the second most-used illicit drugs in the world. Along with this rise in stimulant use has been a corresponding increase in overdose deaths related to stimulants, as well as increases in serious and lasting health effects for stimulant users.

All of this has highlighted the need to find effective treatments for stimulant use disorder. To date, there have been no medications approved for treating stimulant use disorder, but finding a medication that would work could make a significant difference not just in treatment outcomes but also in encouraging people to engage in treatment to begin with.

"Drug repurposing," which identifies new uses for previously approved drugs with established safety profiles, offers a faster and more efficient way to find new treatments for diseases compared to traditional drug development or discovery. But this process can be complex and timeconsuming... for humans. Artificial intelligence (AI), on the other hand, can process and analyze vast amounts of biomedical data quickly, speeding this process up dramatically. This study, part of the NIDA Clinical Trials Network study CTN-0114, aimed to put an AI-driven drug discovery framework to work on finding a medication that is already FDA-approved and might work as a treatment for amphetamine-type stimulant use disorder (ATSUD). In a previous study, this same AI-driven framework had discovered that ketamine appeared to improve outcomes for patients with cocaine use disorder – would the AI model also identify ketamine as an effective treatment for ATSUD?

How Was This Study Conducted?

The first step was exploring potential drug candidates for ATSUD. The AI model constructed a knowledge graph, a visualization of relationships between different entities, by integrating multiple biomedical databases and identifying FDA-approved drugs with potential for ATSUD treatment through a systematic analysis of interactions within the knowledge graph.

From there, researchers selected the top 10 ranked drugs as potential candidates. They then reviewed results from clinical trials to see how well these drugs had worked at treating ATSUD. Based on these results, they selected ketamine as their target drug for the rest of the study.

Researchers then analyzed 100 million patient electronic health records (EHR) to look at the association between ketamine and ATSUD remission in clinical cases. Finally, they analyzed the potential mechanisms of action of ketamine in the context of ATSUD, looking at both genetic and molecular factors.

What Did Researchers Find Out?

Patients included in the analyses all had diagnosed ATSUD and had either received anesthesia (n=3663) or been diagnosed with depression (n=4328) (two common reasons patients might be given ketamine). Researchers looked at how many patients who had received ketamine had achieved ATSUD remission within a year.

Ketamine for anesthesia in ATSUD patients was associated with greater ATSUD remission compared with other anesthetics. Similar results were found for ATSUD patients with depression when comparing ketamine with antidepressants, including bupropion/mirtazapine (two medications that have previously shown limited efficacy in treating ATSUD).

Analysis of how ketamine might work to treat ATSUD found that it targets several ATSUD-associated pathways. Ketamine's interaction with certain genes also highlights its potential to modulate critical neurotransmitter systems, like dopamine and serotonin, which are involved in the reward pathways that contribute to addiction.

In conclusion, the researchers' AI-driven drug discovery framework identified clinician-prescribed ketamine as a promising treatment for ATSUD.

Future work, including randomized controlled trials, is needed to confirm this finding and to better understand the underlying mechanisms and potential adverse effects.

What Are the Implications for the Workforce? Stimulant use disorder remains a significant challenge for clinicians, as there are very few evidence-based behavioral interventions and no approved medications. In the U.S., fewer than 20% of people using publicly funded programs for substance use disorders are receiving treatment specifically for stimulant use disorders, even though we know the prevalence of stimulant use disorders is increasing. There are many barriers to receiving behavioral-type interventions for ATSUD, however, including stigma, lack of awareness that these options exist, insufficient treatment resources in a community, and personal barriers like fear of legal consequences or loss of employment. Effective medication treatments, however, could remove a lot of these barriers and potentially attract more people to seek care for their ATSUD.

Addiction Technology Transfer Center (ATTC) Network article by Meg Brunner: <u>Al Identifies Ketamine as a Potential Treatment for Amphetamine-Type Stimulant Use Disorder</u>

Read the publication in *Addiction*: <u>Artificial intelligence-based drug repurposing with electronic health record clinical corroboration: A case</u> <u>for ketamine as a potential treatment for amphetamine-type stimulant use disorder</u>

CAR Member Recognition



Congratulations to **Dr. Jayme McReynolds, recipient of an Early-Stage Investigator Merit award from the National Institute on Drug Abuse (NIDA)**. This is a 7-year award that reflects Dr. McReynolds' outstanding priority score on her R01 application, as well as the esteem with which she is held by NIDA leadership. Congratulations Dr. McReynolds on your welldeserved award!

Research Rising Star Awardee

The College of Medicine celebrates Research Rising Stars who demonstrate an outstanding commitment to health-related research. A Research Rising Star is in the top tier of career benchmarks among peers. Congratulations to Dr. Jayme McReynolds, Assistant Professor, Department of Pharmacology, Physiology, and Neurobiology, chosen as a Research Rising Star recipient. Dr. McReynolds received her PhD in Neuroscience from the University of Texas at Dallas before completing a postdoctoral fellowship at Marguette University in the Biomedical Sciences Department. She was awarded a NIDA K01 fellowship and joined the Pharmacology, Physiology, and Neurobiology department at the University of Cincinnati in November 2019 as a tenure-track Assistant Professor. She has been highly productive in her career with 23 peer-reviewed primary research papers and reviews and an H-index of 20 and serves as a Section Editor at the journal Physiology & Behavior. She has established her research program at UC investigating the neurobiological mechanisms that underlie the impact of stress on addiction-related behavior using a combination of innovative behavioral, molecular, and physiological techniques. She was awarded a R37 Early-Stage Investigator MERIT Award from NIDA in 2024 as recognition of her standing and potential as a researcher in her field.



CoM Office of Research recognizes Gallery of Awardees for faculty who have been awarded external grants of \$100,000/yr. Congratulations to **Jason Blackard, PhD**, Walter A. and George McDonald Foundation Professor of Medicine, Department of Internal Medicine, Division of Digestive Diseases.

- National Institute of Diabetes and Digestive and Kidney Disease T35; "Short-term Institutional Research Training Grant".
- National Heart, Lung, and Blood Institute R01; "Initiators of Thrombotic Microangiopathy".



Silver Apple awarded

Medical Sciences undergraduate students have named the 2024 recipients of Gold and Silver Apple Awards for the best courses this past academic year in the Medical Sciences Baccalaureate Program. The students selected their most impactful courses to recognize the excellent teaching by instructors. Congratulations to **Terry, Kirley, PhD**, Class of 1982, professor, Department of Pharmacology and Systems Physiology, who was the recipient of the Silver Apple in 4000 Level Courses for "Fundamentals of Medical Pharmacology".

Center for Addiction Research 2024 Summer Speaker Series Impact

To view the recordings and presentation slides, please visit the <u>2024 Summer Speaker Series</u> webpage. Links for previous years recordings and presentation slides are also available on the <u>2024 Summer Speaker Series</u> webpage.



Highest rated SSS sessions and topics on post-event evaluations, of any year, with a 100% rating of Excellent or Very Good.

Highest rated SSS speakers on post-event evaluations, of any year, with a 98% rating of Excellent or Very Good.

CAR website	# Users Visited
April 5 – 30, 2024	164
May 2024	146
June 2024	296
July 2024	394
August 2024	363
Total	1363

Increased CAR awareness and drove another 1363 new users to the CAR website.

The success of the SSS has driven 7600 new users to the CAR website since March 31, 2021.

		1

Increased the number of individuals receiving the CAR newsletter by 29 additions.

News from the Ohio Valley Node



The CTN-OVN has successfully completed the <u>CTN-0150</u> (TOME; LI – Winhusen) study activities and is now heading into data analysis. This study was part of the supplemental IMPROVE funds from NIDA and the NICHD awarded to the OVN to utilize the <u>CTN-0080</u> study as a platform to collect additional data regarding Opioid Use Disorder in pregnant/postpartum populations. TOME included two objectives: 1) to evaluate the ability of the Personally Tailored Opioid-overdose and Medication for opioid use disorder (MOUD) Education (TOME) intervention to increase MOUD and opioidoverdose knowledge in pregnant and postpartum (PP) persons (Primary), and 2) to evaluate the ability of TOME to decrease MOUD-related internalized stigma and expected difficulty in avoiding drug use (Secondary). Six of the 13 MOMs sites participated and enrolled 131 participants (goal: 120). Congratulations and thank you to the TOME sites!

The CTN-0080-A3 project (LI – Kropp) has completed development of a large suite of dissemination and training projects aimed at underserved populations of pregnant and postpartum individuals with Opioid Use Disorder. NIDA has approved these materials for dissemination to the public, and the <u>Prenatal Action for Taking Healthy Steps (PATHS) Toolkit</u> is now available; culturally and linguistically appropriate versions are also available for American Indians/Alaska Natives and Spanish speakers. Two new studies in development! The CTN-OVN has recently been approved to move forward with two new studies, both of which will be funded by the NIH HEAL Initiative:

<u>CTN-0152</u>: Evaluation of Tirzepatide as an Adjunct to Buprenorphine for the treatment of opioid use disorder: A pragmatic, multi-site, double-blind, Randomized, placebo-controlled, trial (TAB; LI – Winhusen) will test tirzepatide, which is a GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) agonist, as an adjunct to buprenorphine for the treatment of opioid use disorder. Following an intensive site selection process, 10 sites were selected to recruit approximately 310 participants into this 30-week study with a goal of starting recruitment in September 2025. The study is currently engaged in the initial study start-up tasks, including regulatory reviews, documentation development, and training development.

<u>CTN-0153</u>: Effects of Semaglutide and Tirzepatide on Incidence and Outcomes of Stimulant Use Disorders (StUD) and Opioid Use Disorder (OUD) in Real-world Populations: Target Trial Emulation Using Patient Electronic Health Records (GLP-SUD; Co-LIS Xu and Winhusen) will entail conducting emulation target trials utilizing a nationwide electronic health records (EHR) database of over 118 million US patients including 945,000 patients with OUD, and 842,000 with StUDs including 470,000 with methamphetamine use disorder. By emulating clinical trials using a large EHR database, this study will provide clinical evidence gathered from real-world patient populations to support prospective randomized-controlled trials in testing the effectiveness of semaglutide and tirzepatide for treating StUD and OUD. The study is currently in protocol development.

Original story from the Clinical Trials Network (CTN): <u>News from the Ohio Valley Node</u>

Adaptation and Implementation of a Community Pharmacy-Based Prescription Drug Monitoring Program Opioid Risk Assessment Tool



A prescription drug monitoring program-based clinical decision support platform, with clinically actionable opioid risk information, is not widely available in the field of community pharmacy. This project will: (1) integrate risky opioid use thresholds established in CTN-0093 into a nationally scalable prescription drug monitoring platform; (2) adapt the platform to direct pharmacy staff in performing confirmatory opioid misuse screening, opioid medication misuse intervention, naloxone dispensation, and warm handoff; and (3) evaluate patient outcomes. To evaluate patient outcomes, our interdisciplinary team will conduct a type-1 implementation mixed methods study using a two-arm parallel group clustered randomized trial to test the platform in a large retail pharmacy chain. This study will also examine facilitators and barriers of platform adoption and continued utilization from corporate partners. Results of this study will facilitate critical advancements for protecting patient health and addressing the national opioid epidemic by leveraging community pharmacy.

CTN-0138 from the Clinical Trials Network (CTN)

Read more in Addiction Science & Clinical Practice: <u>CTN-0138: adaptation, implementation, and cluster randomized trial of a Community Pharmacy-Based</u> <u>Prescription Drug Monitoring Program Opioid Risk Assessment Tool—a protocol paper</u>

Center for Addiction Research (CAR)

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Changing outcomes, saving lives through work on opioid, stimulant, cannabis, and alcohol use disorders



CAR Mission

To accelerate scientific progress in the prevention and treatment of substance use disorders and their consequences by fostering research collaborations across:

- UC departments, colleges, and centers including Cincinnati Children's Hospital Medical Center
- Local, regional, and state community and governmental partners
- Other academic institutions and industry

The CAR includes three research concentrations (cores):

- Addiction Treatment Development and Testing (ATT)
- Perinatal Addiction/Developmental-consequences (PAD)
- Population Health and Health Services (PHHS)

Find out more about the CAR using the website link below: <u>https://med.uc.edu/institutes/CAR/home</u>

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