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 January 2024, please send a brief summary/story accompanied by pictures or graphics (if available) to Jen Rowe (roweji@ucmail.uc.edu) any time prior to January 15th. Thank you!

CAR Biannual Bulletin

July 2023

Member Research Updates

2024 Next Bulletin Release Date:
- Late January

2024 Next Deadline for Submitting Stories:
- January 15th

Register Now! Center for Addiction Research Summer Speaker Series, final session, Wednesday, August 9, 2023 at 12:00 PM, featuring Dr. Nichole Nidey and Tara Cain, "Examining Substance Use Around the Timing of Pregnancy from a Health Equity and Patient-Centered Perspective". Sponsored by: Center for Clinical & Translational Science & Training

UC research examines the role of genetics in opioid use disorder

New research out of the University of Cincinnati examines the association between genetics and the presence of opioid use disorder (OUD). The study identified six single nucleotide polymorphisms (SNPs) or genetic variants that are linked to OUD.

“We are trying to identify some of the genetic variants that might play into OUD,” says Caroline Freiermuth, MD, associate professor in the Department of Emergency Medicine at the UC College of Medicine and principal investigator for the study. “Patients received an oral swab that gets put inside their cheek, and those swabs were sent off for genetic testing looking for 180 single nucleotide polymorphisms.”

According to the Centers for Disease Control and Protection, more than 107,000 people in the U.S. died in 2021 from drug overdose, with overdose deaths involving synthetic opioids increasing 23% from the year before. The economic cost of OUD and opioid-related overdose mortality exceeds $1 trillion annually in the United States.

The study enrolled about 1,300 patients within three large urban emergency departments in Ohio, which has ranked in the top five for opioid overdose deaths since 2014.

“We wanted to determine for any random person who comes to the emergency department what their genetic link might be and do they now or did they ever have opioid use disorder in their life, and do we think their genetics have played a role in that,” says Freiermuth. “We found that there were quite a few single nucleotide polymorphisms that seem to be associated with opioid use disorder.”

The study found that although genetics play a role in disease, there is also significant interaction from the environment. Freiermuth says further study is needed to highlight the true impact of the genetic variants and how external factors contribute to the development of OUD. Further exploration of biogeographical genetic ancestry groups and their association with OUD is warranted, the study concluded, “I think this is really exciting because it

should help us try to figure out who is truly at risk when they are exposed to opioids and that could make it easier for us to decide who we can and can't prescribe opioids to," Freiermuth says. "This could help determine who might need further monitoring in the future instead of just blanket saying 'nobody should ever get more than a certain amount.'"

UC News story by Bill Bangert:
https://www.uc.edu/news/articles/2023/04/university-of-cincinnati-research-examines-the-role-of-genetics-in-opioid-use-disorder

Read the study published in the journal Clinical Pharmacology & Therapeutics.

Eat, Sleep, Console' Approach Slashes ICU Stays for Opioid-Exposed Newborns

The "Eat, Sleep, Console" care approach (ESC) is more effective than usual care approaches for treating opioid-exposed infants, according to multi-center study results announced April 30, 2023, at the Pediatric Academic Societies annual meeting.

In fact, treating opioid-exposed newborns in neonatal intensive care units (NICUs) with this approach reduced their hospital lengths of stay from an average of 14.9 days to an average of 8.2 days. In addition, only 19.5% in the ESC group needed medications to treat opioid withdrawal compared to 52% among infants treated according to guidelines set by the more-commonly used Finnegan Neonatal Abstinence Scoring Tool (FNAST).

The findings, published concurrently in *The New England Journal of Medicine*, included Cincinnati Children's neonatologist Stephanie Merhar, MD, MS, among the leading co-authors, as well as three Cincinnati Children's Perinatal Institute partner hospitals: the University of Cincinnati Medical Center NICU, TriHealth's Good Samaritan Hospital NICU, and the St. Elizabeth Healthcare NICU.

Combined, these hospitals contributed the largest number of subjects to the study, which was funded by the National Institutes of Health and coordinated by the ACT NOW Collaborative. Cincinnati Children's world-class neonatologists provide medical care at all Level III NICUs in the Cincinnati/Northern Kentucky region.

"Ohio and Kentucky have been hit hard by the opioid epidemic," says Merhar, who oversaw the regional participation in the study.

"Understanding ways to improve the outcomes of babies and families affected by opioids is of particular importance to us, and ESC will help many babies in our region."

Opioid-exposed newborns can develop symptoms of neonatal opioid withdrawal syndrome (NOWS), which includes tremors, excessive crying and irritability, and problems with sleeping and feeding.

Hospitals have widely different approaches for caring for these babies. They often use the Finnegan Neonatal Abstinence Scoring Tool (FNAST) to assess newborns with NOWS. The FNAST is an extensive scoring system that assesses signs of withdrawal in more than 20 areas. Concerns have been raised about its subjectivity and overestimation of the need for opioid medication.

The latest study involved more than 1,300 newborns treated at 26 hospitals across the US. The study found that the ESC care approach substantially decreased the time until infants were medically ready for discharge.

Newborns cared for with ESC were medically ready for discharge approximately 6.7 days earlier and were 63% less likely to receive drug therapy, compared to newborns cared for under the FNAST approach. Safety outcomes at three months of age were similar between both groups.

The ESC care approach was developed about eight years ago but before this trial it hadn't been rigorously evaluated in a large and diverse population of infants with NOWS.

ESC provides a function-based assessment of withdrawal severity centered around how well an infant can eat, sleep, and be consoled. The method prioritizes nonpharmacologic care, including increased family presence, holding, swaddling and rocking in low-stimulus environments, as first-line treatment.

A two-year follow-up study of a subset of the infants is ongoing.

Merhar and Jennifer Vannest, PhD, CCC-SLP, at Cincinnati Children's also have received an $8 million research grant to further study the longer-term impacts of preterm opioid exposure.

About the Eat, Sleep, Console Study
The trial is a collaborative effort between the NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the NIH Environmental influences on Child Health Outcomes (ECHO) Program.

Cincinnati Children's is part of the NICHD Neonatal Research Network (NRN), which partnered with the IDEA States Pediatric Clinical Trials Network to conduct this large study. Merhar was the NRN representative for this study and one of the lead investigators, along with Young and Devlin representing the ISPCTN.

The trial is funded by the Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative®—a trans-agency effort to speed scientific solutions to stem the national opioid crisis.

Read the study published in *The New England Journal of Medicine*:
Eat, Sleep, Console Approach or Usual Care for Neonatal Opioid Withdrawal

The Synthetic Opioid Fentanyl Increases HIV Replication and Chemokine Co-Receptor Expression in Lymphocyte Cell Lines

The number of opioid overdose deaths in the United States has increased dramatically in recent years, and synthetic opioids such as fentanyl are a common cause. Although fentanyl, fentanyl analogs, and fentanyl metabolites are frequently detected in persons experiencing overdoses, their effects on viral replication are poorly characterized. Thus, the Blackard laboratory evaluated the effects of fentanyl on HIV-susceptible/infected cell types and chemokine receptor expression.

Fentanyl enhanced expression of two HIV entry factors - CCR5 and CXCR4 chemokine co-receptors - in a dose- dependent manner in HIV-susceptible and infected cell lines. Similarly, fentanyl induced viral protein synthesis and proviral DNA expression in multiple lymphocyte cell lines and peripheral blood-derived CD4+ T cells. Multiple genes associated with apoptosis, antiviral/interferon response, chemokine signaling, and NFκB signaling were differentially regulated in the presence of fentanyl. Increased virus levels suggest that opioid use may increase the likelihood of transmission and accelerate disease progression.

Read the entire article published in *Viruses* as part of the Special Issue HIV and Drugs of Abuse 2.0:
The Synthetic Opioid Fentanyl Increases HIV Replication and Chemokine Co-Receptor Expression in Lymphocyte Cell Lines

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

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 conducted.)**

Read an article in Medical Express about this study:
New study reveals ketamine could be effective treatment for cocaine-use disorders

Read the study published in *Addiction Journal*:
Repurposing ketamine to treat cocaine use disorder: integration of artificial intelligence-based prediction, expert evaluation, clinical corroboration and mechanism of action analyses

Updates from the Ohio Valley Node - CTN-0080
"Medication treatment for Opioid use disorder in expectant Mothers (MOMs)"

CTN–OVN
The National Drug Abuse Treatment Clinical Trials Network–Ohio Valley Node

In response to the complex issues that pregnant and postpartum individuals (PPI) with Opioid Use Disorder (OUD) experience, the Substance Abuse and Mental Health Services Administration (SAMHSA), American College of Obstetricians and Gynecologists (ACOG), American Society of Addiction Medicine (ASAM), and World Health Organization (WHO) have established recommendations for a comprehensive approach to treatment that brings together providers and services from multiple disciplines. However, we know little about the settings, services delivered, and staff/providers who are implementing this integration of multidisciplinary care for PPI with OUD and to what extent the expert recommendations are being followed. Winhusen, et al. are leading the NIDA Clinical Trials Network study "Medication treatment for Opioid use disorder in expectant Mothers (MOMs): a pragmatic randomized trial comparing extended-release and daily buprenorphine formulations (CTN0080) in study sites that were selected in part because of the comprehensive array of services provided to pregnant individuals with OUD. To characterize the organizational factors associated with MOMs sites, the investigative team developed and administered the Pregnancy and Addiction Services Assessment (PAASA). Although all sites offered many services recommended by expert consensus groups, they varied in how they coordinated these services. Even these exemplary sites were unable to integrate the full range of recommended services within their programs, instead collaborating for some services with other providers within their organization while providing the remaining services via linkage/referral to external providers. This article by Kropp, et al. provides some preliminary information about types of providers, services offered, and population served within the group of academic

health centers and large community-based organizations providing treatment for PPI with OUD.

Read the study published in *Journal of Substance Use and Addiction Treatment*:
Collaborative care programs for pregnant and postpartum individuals with opioid use disorder: Organizational characteristics of sites participating in the NIDA CTN0080 MOMs study

Center for Addiction Research 2023 Summer Speaker Series

To view the completed sessions recordings and presentation slides, or to register for the final virtual August session, please visit the 2023 Summer Speaker Series webpage.

Addressing Substance Use Among Youth in Foster Care: Implementation and Evaluation of Screening, Brief Intervention, and Referral to Treatment (SBIRT) in a Foster Care Clinic

Wednesday, June 14, 2023
12:00–1:00 p.m.


Shauna P. Acquavita, PhD, MSW, LISW-S
University of Cincinnati


Mary Greiner, MD, MS
University of Cincinnati


Sarah Beal, PhD
University of Cincinnati

Participants ≈≈ 53

Survey Rating:

88% rated the session as being very good or excellent

The Perfect Storm: Examining the Associations Among Alcohol Use and Intimate Partner Violence in the Age of COVID-19

Wednesday, July 12, 2023
12:00–1:00 p.m.


Joel Sprunger, PhD,
University of Cincinnati

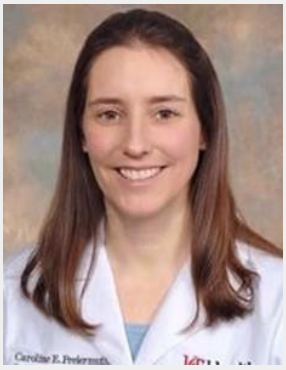

Rev. Etta Caver, MSW, PhD Student,
Miami University

Participants ≈≈ 56

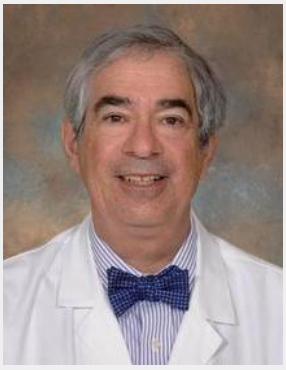
Survey Rating:

90% rated the session as being very good or excellent

CAR Member Recognition



Congratulations to **Caroline Freiermuth, MD**, associate professor, Center for Addiction Research Population Health and Health Services Core Co-Leader, on receiving the SAEM Academy for Women in Academic Emergency Medicine (AWAEM) Social Medicine Advocacy Award, which honors a female faculty who has made significant contributions toward social justice and advocacy on behalf of patients or the community within emergency medicine.



At its June 27 meeting, the UC Board of Trustees officially approved **Kenneth Sherman, MD, PhD**, professor emeritus, Department of Internal Medicine, effective July 1, 2023. Congratulations!

UC Addiction Sciences Division featured in the College of Medicine May 2023 Indispensable ad

For people suffering with addiction, recovery can sometimes seem like an impossible dream. But through cutting edge research, education, and the most holistic treatment options available in the area, UC Physicians and UC College of Medicine faculty offer healing and hope. Using a multidisciplinary approach that relies on a full spectrum of professionals—from nurses and social workers to peer specialists, psychologists, and addiction physicians—UC Addiction Sciences is helping people from all walks of life reclaim their dignity, their purpose, and their lives. To obtain an appointment with the Addiction Sciences Division, call 513-585-8227. **(Dr. T. John Winhusen is Director, Center for Addiction Research and Vice Chair of Addiction Sciences, also pictured are Dr. Christine Wilder, CAR member and Addiction Sciences Medical Director & Co-Chair, CAR member Dr. LaTrice Montgomery, and CAR Associate member, Dr. Joel Sprunger)**

Congratulations to UC's Research Rainmakers, and members of the CAR, FY2022 Outstanding Sponsored Research Awardees!

Earlier this year the Office of Research celebrated the outstanding sponsored award recipients for fiscal year 2022 who received $225,000 or more in the arts, humanities, or social sciences or $400,000 or more in science, technology, engineering, mathematics, or medicine. Below is the list of researchers, who are CAR members, their colleges, and the number of times they have been recognized for this accomplishment.

COLLEGE OF MEDICINE
T. John Winhusen, 7
Jason Blackard, 6
Andrew Norman, 6
Kenneth E. Sherman, 6
Teresa Reyes, 4
Caroline Freiermuth, 3

COLLEGE OF ALLIED HEALTH SCIENCES
Jennifer Jean Vannest, 2

COLLEGE OF EDUCATION, CRIMINAL JUSTICE & HUMAN SERVICES
Ashley Merianos, 4

Center for Addiction Research (CAR)

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CAR Director:
Dr. T. John Winhusen

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

University of CINCINNATI
CENTER FOR ADDICTION RESEARCH

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: https://med.uc.edu/institutes/CAR/home