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 2023, 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 2023

Member Research Updates

2023 Next Bulletin Release Date:
- Late July

2023 Next Deadline for Submitting Stories:
- July 15th

WHAS: UC professor expresses concerns about Kentucky's medical marijuana executive order

On Jan. 1, an executive order from Kentucky Gov. Andy Beshear's desk went into effect, allowing Kentuckians to purchase medical marijuana in states where it is legal and then bring it back.

Kentucky residents with no more than 8 ounces of medical marijuana will be pardoned from possession charges, and to be eligible, a doctor must diagnose and certify the patient with one of 21 conditions.

WHAS, Louisville's ABC affiliate, featured University of Cincinnati cannabis researcher LaTrice Montgomery, PhD, in its coverage leading up to the executive order going into effect.

"I'm like, wow, there's no sort of tracking," Montgomery told WHAS after reviewing the executive order's language. "That's what I'm a huge advocate of, is just tracking everything because I think it would help for us to know first. How many people are actually being affected by this?"

Montgomery said she is also concerned that there is no requirement for patients to follow up with physicians after receiving a diagnosis, which could lead to people mixing marijuana with prescription medications.

"We don't know drug-drug interactions, we still have so many unanswered questions," said Montgomery, research associate professor in the Addiction Sciences Division of the Department of Psychiatry and Behavioral Neuroscience in the UC College of Medicine.

UC News story by Tim Tedeschi:
WHAS: UC professor expresses concerns about Kentucky's medical marijuana executive order

Watch or read the WHAS report:
Cincinnati doctor expresses concerns about Kentucky's medical marijuana executive order

CNN: More adolescent e-cigarette users report vaping within five minutes of waking up

UC's Ashley Merianos, an associate professor of human services, is cited as an expert for national media in a review of new tobacco and vaping research on adolescents and vaping.

The research, which CNN covered and appears in JAMA OPEN Network, found that among adolescents who only use e-cigarettes, the percentage who used the products within the first five minutes of waking up in a day was less than 1% between the years 2014 and 2017, but that shifted to 10.3% from 2017 through 2021.

This study's findings suggest that e-cigarettes may be putting a new generation of adolescents at risk for nicotine addiction, and research has shown that many adolescents are unaware that most e-cigarettes contain nicotine, said Merianos.

Merianos, who was not involved in the study, stated: "It is encouraging that the prevalence of e-cigarette use has declined among U.S. adolescents from 2019 to 2021. However, the addiction and intensity of use trends reported in this study are concerning, especially since tobacco use is typically established during adolescence."

In addition to being on faculty at UC, Merianos is also a research affiliate member of Cincinnati Children's Hospital Medical Center and the Thirdhand Smoke Research Consortium. She is a prolific researcher and has extensive training and experience in the epidemiology and prevention of substance use with an emphasis on tobacco, quantitative statistical methods, and clinical and translational research in the pediatric healthcare setting.

UC News story by Angela Koenig:
CNN: More adolescent e-cigarette users report vaping within five minutes of waking up

Read the CNN article:
More adolescent e-cigarette users report vaping within five minutes of waking up, new study finds

NIH grant funds HIV research
UC team studying how alcohol, fentanyl affect medications

The United States has set a goal of reducing the number of new HIV infections by 75% by 2025 and by at least 90% by 2030, mirroring the United Nations' initiative to end the AIDS epidemic as a global health threat by 2030.

Part of reaching these goals is ensuring the safety and efficacy of HIV medications in different situations, and researchers at the University of Cincinnati have recently been awarded a $3.5 million National Institutes of Health grant that will examine how current medications are affected by alcohol use alone or in combination with fentanyl.

Study background

Bingfang Yan, PhD, DVM, contact principal investigator of the research, said there is no clear data showing how alcohol with or without fentanyl affects HIV medications, including pre-exposure prophylaxis (PrEP) medication taken to reduce the chance of contracting HIV.

"It is well accepted that unhealthy alcohol use has been associated with poor adherence of PrEP, skipping medication," said Yan, professor and associate dean for research and innovation at UC's James L. Winkle College of Pharmacy. "However, it is not clear whether and how alcohol with or without fentanyl directly affects the efficacy and safety of HIV medicines."

A research team from differing backgrounds was formed to learn more, including co-principal investigators Jason Blackard, PhD, professor of internal medicine at UC's College of Medicine, and Jennifer Brown, PhD, associate professor at Purdue University and a former faculty member in UC's College of Arts and Sciences. Yan brings research experience in medication metabolism, Blackard's lab studies virus interactions, and Brown has a research focus on alcohol and substance use.

"This is a collaborative effort and represents an excellent example of bringing complementary expertise together to resolve important health issues," said Yan.

Study details

Yan said this project will analyze cell cultures as well as blood, hair, urine and white blood cell samples from patients who enroll in the study.

The first aim of the study is to determine metabolite signatures and pharmacological biomarkers of PrEP in HIV-negative populations using alcohol with or without fentanyl versus those who do not.

"Altered metabolite signatures and pharmacological biomarkers will suggest that alcohol consumption alone or in combination with fentanyl would make PrEP less effective," Yan said.

The second aim is similar, comparing the efficacy and safety as well as adherence of HIV therapy in HIV-positive populations who use alcohol alone or in combination with fentanyl versus those who do not.

"Aim 1 focuses on prevention and Aim 2 on therapy," Yan said. "It's very comprehensive, so information gained will be really meaningful."

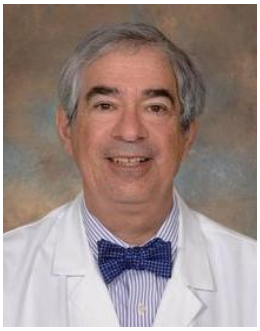
UC News story by Tim Tedeschi:
NIH grant funds HIV research

Recent publication highlights the impact of morphine during pregnancy on brain development using a mouse model

Rates of opioid use during pregnancy have increased in parallel with the opioid epidemic and children exposed to opioids during the prenatal period (before birth) are at an increased risk of developing behavioral disorders. Smith et al. use a mouse model to study the behavioral effects of prenatal opioid exposure in both male and female offspring. Male exposed offspring have deficits in learning, motivation, and attention, while females are much less affected. Both sexes show an increase in sociability after morphine exposure. Finally, the brain's immune system may play a role in shaping brain development after prenatal opioid exposure. This work was led by Dr. Brittany Smith, a K99-funded postdoctoral fellow in the lab of Dr. Teresa Reyes.

Perinatal morphine exposure leads to sex-dependent executive function deficits and microglial changes in mice
Brittany L. Smith, Tess A. Guzman, Alexander H. Brendle, Collin J. Laaker, Alexis Ford, Adam R. Hiltz, Junfang Zhao, Kenneth D.R. Setchell, Teresa M. Reyes.
https://www.eneuro.org/content/9/5/ENEURO.0238-22.2022

UC research could change vaccine practices
Study finds three-dose hepatitis B vaccine regimen protects people living with HIV



New research out of the University of Cincinnati shows that a course of a hepatitis B vaccine provides complete protection for people with HIV.

The UC research shows that a three-dose course of the hepatitis B vaccine HEPLISAV-B provides complete protection for people living with HIV who have never been vaccinated against or exposed to the hepatitis B virus (HBV).

The study findings were presented at the IDWeek conference in Washington, D.C., in October. IDWeek is a joint annual meeting of various groups focused on diseases, including the Infectious Diseases Society of America, Society for Healthcare Epidemiology of America, the HIV Medicine Association, the Pediatric Infectious Diseases Society and the Society of Infectious Diseases Pharmacists.

“Hepatitis B is highly ranked among liver-disease-related causes of death among people living with HIV,” says Kenneth Sherman, MD, PhD, Gould Professor of Medicine and director, Division of Digestive Diseases in the Department of Internal Medicine at the UC College of Medicine and study chair and senior author of the research. “This finding may well change routine vaccine practices among persons living with HIV.”

HBV, which is spread mostly through sexual contact and the sharing of contaminated needles, causes the hepatitis B liver infection. People living with HIV are at greater risk of liver-related illness and death when co-infected with HBV. The HEPLISAV-B vaccine was approved by the Food and Drug Administration in 2017 as a two-dose vaccine regimen for adults, but little was known at that time about its ability to protect people living with HIV.

“The difference in HEPLISAV-B from other vaccines is that it contains a product called CPG, which is a type of immune booster that could improve response to the vaccine by the body’s immune cells,” says Sherman. “In the pivotal clinical trials that were done leading to that vaccine’s licensure, it was shown that the vaccine with just two doses rather than the usual three-dose series required for prior vaccines actually achieved equivalent or greater levels of response. However, persons with HIV do not have high rates of response to the older vaccine preparations. That is why it was suspected that a three-dose regimen with the new vaccine might lead to better overall response rates.”

The analysis included 68 adults living with HIV at 38 sites in the United States, South Africa and Thailand. None of the people enrolled in the study group had received HBV vaccination previously or had evidence of being exposed to HBV and all were on antiretroviral therapy. The levels of antibody produced were higher than what has been observed following older vaccine

preparations. “Higher antibody levels often translate to better vaccine durability,” according to Sherman.

“While this will not cure those who already have hepatitis B, it will keep others from getting the disease,” says Sherman.

The multicenter, multinational study is ongoing and will also provide data regarding those who failed prior vaccination for hepatitis B.

The National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, sponsors the ongoing Phase 3 ACTG A5379 clinical study.

UC News story by Tim Tedeschi:
UC research could change vaccine practices

Center for Addiction Research 2022 Summer Speaker Series Impact

To view the recordings and presentation slides, please visit the 2022 Summer Speaker Series webpage. The 2021 Summer Speaker Series recordings and presentation slides are also available.

Increased overall attendance 34% TY/LY
Increased community attendance 104% TY/LY
152 overall unique attendees (113 LY)
92 community members (45 LY)
37 UC Staff (26 LY)
20 UC Faculty (24 LY)
3 UC Students (18 LY)

CAR website	# Users Visited
April 15 – 30, 2022	122
May 2022	197
June 2022	263
July 2022	360
August 2022	287
Total	1229

Increased CAR awareness and drove another 1200 new users to the CAR website.

The success of the SSS has driven, 3200 new users to the CAR website since March 31, 2021.

Increased the number of individuals receiving the CAR newsletter by 69% with 99 additions.

News from the Ohio Valley Node

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

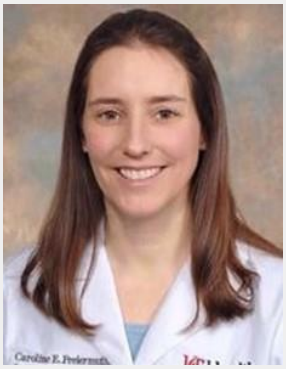
CTN-0129 - The Great Plains Initiative
Tribal communities in the Great Plains are diverse, and each has concerns and priorities to address addiction and recovery focused on local needs. There has been increasing concern about the use of opioids and methamphetamine, and data indicates that tribes in the Great Plains region (North/South Dakota, Nebraska, Iowa) suffer from many health and socioeconomic disparities at rates even greater than the other US tribal regions. Further, treatment resources in this region are geographically dispersed, adding to the already- long list of general barriers to substance use disorder (SUD) treatment.

CTN-0129 will build collaborations with reservation-based treatment centers and urban clinics serving AIs in the Great Plains to define treatment needs and to determine research priorities *with* tribal communities and not *for* them. **Read about the study's 2 objectives in the full update here**.

The Great Plains Initiative is a collaboration between CTN Ohio Valley Node researchers at the University of Cincinnati, the University of North Dakota, and Johns Hopkins University (LI: Donald Warne, MD, MPH). The team has received the support of the Great Plains Behavioral Health Directors, as well as from one tribal entity. Data collection at the two participating urban sites has begun, and data collection at the approved reservation-based program is scheduled to begin in the spring. Work continues to obtain all necessary approvals for the remaining five reservation-based programs who have expressed interest in study participation, as well as for a tribally owned urban program.

CAR Member Recognition

CoM Office of Research recognizes Gallery of Awardees for faculty awarded external grants of $100,000/yr. Congratulations to the included two members of the CAR below!



Congratulations to **Caroline Freiermuth, MD**, Associate Professor, Department of Emergency Medicine, Center for Addiction Research Population Health and Health Services Core Co-Leader.

- Award: Centers for Disease Control and Prevention Award
- Project Title: Emergency Department Comprehensive Care (EC23)
- Project Period: 9/1/2022-8/31/2023
- Summary: This research will improve ED processes to identify people at risk of opioid use disorder (OUD) while minimizing false positives and ensure there is a process for further screening to determine if they have the disease. This work will leverage community partnerships and expand hours of linkage counselors and peer recovery specialists to improve pathways to longer-term care and supportive services, with means to identify populations of focus such as pregnant patients, those that reside in rural communities or are of Appalachian descent, and those that may be at risk for human trafficking. Also, this project will implement protocols to deliver medication for OUD and harm reduction services at Bethesda North Hospital and Bethesda Butler Hospital.

Congratulations to **Jason Blackard, PhD**, Professor, Department of Internal Medicine, Division of Infectious Diseases.

- Award: National Institute on Alcohol Abuse and Alcoholism R01
- Project Title: Therapeutic and Mechanistic Significance of Altered Metabolism of HIV Medicines by Alcohol- or Alcohol/Synthetic Opioid Combination
- Project Period: 9/10/2022-7/31/2027
- Summary: Excessive alcohol use has been linked directly to increased HIV viral load, high risk HIV behaviors, and poor adherence to anti- HIV medications including both pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP) Tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide fumarate (TAF) are listed in ~75% of HIV regimens used for both PrEP and TasP. This research will evaluate the metabolism-based interactions of tenofovir drugs with alcohol +/- fentanyl using a combination of patient-based studies and ex vivo experiments to provide

mechanistic details on how these contributing factors interplay, validate biomarkers for efficacy/safety and adherence monitoring, and build strong foundations for developing mitigation strategies.

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