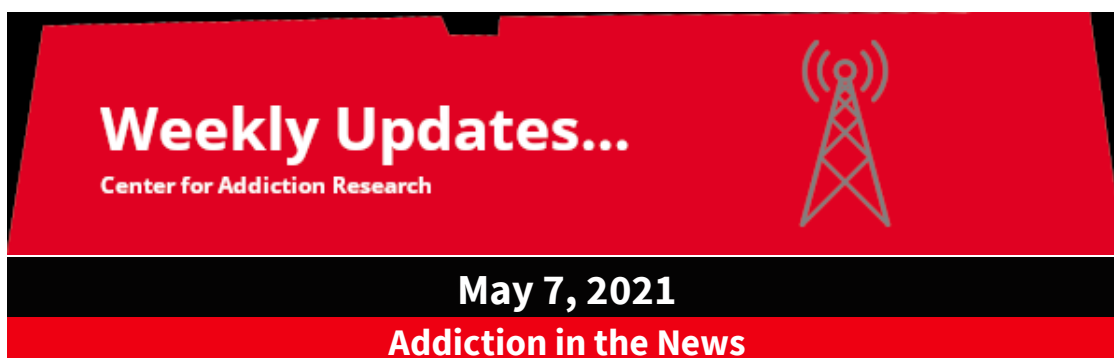


UC CAR Weekly Newsletter 5.7.2021

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

COVID-19 brought easier access to methadone but Ohio's ending it. Expert is asking 'why?'

Go get your medication, bring it home and take it once daily. It's what a lot of people in America do. But not with methadone for opioid use disorder. At least, not until the novel coronavirus pandemic emerged. In March 2020, federal officials relaxed methadone dosing restrictions, letting more people take home their methadone to prevent the spread of COVID-19. Ohio was among the first to come up with a plan. On April 15, the Department ...

Kentucky sharing in \$300 million drug settlement

FRANKFORT, Ky. (KT) – Kentucky is sharing in a \$300 million multistate settlement with Indivior to resolve allegations of improperly marketing and selling opioid addiction recovery medication. Under the terms of the settlement, Indivior agreed to pay over \$203 million to Medicaid and more than \$90 million to the states, the District of Columbia, and Puerto Rico. Attorney General Daniel Cameron says Kentucky will receive \$10,311,150.98 in

National News

FDA Unveils Plan To Ban Menthol In Cigarettes, Small Cigars.

The [Washington Post](#) (4/29, Bernstein, 10.52M) reports on Thursday, the FDA vowed “to issue new rules within a year that would ban menthol in cigarettes and small cigars – a longtime goal of civil rights and anti-tobacco groups, who say aggressive marketing of the products has disproportionately harmed Black communities.” It will probably take the FDA years to implement the ban. Mitch Zeller, director of FDA’s Center for Tobacco Products, said, “There are ‘very important considerations, starting with legal considerations, about getting this right as we move forward in the rulemaking. ... It’s really impossible to predict how long it would take to complete the rulemaking.’” The article adds, “Zeller and acting FDA commissioner Janet Woodcock said the menthol ban would reduce health disparities between White and Black smokers.”

The [Los Angeles Times](#) (4/29, Logan, 3.37M) reports studies indicate “7 out of 10 Black youths who smoke use menthol. More than 90% of Black adults who smoke began by using menthol cigarettes in comparison to less than 45% of white adults, according to another study.” The agency “said it is working to propose regulations banning menthol flavor within the next year, a move that could lead more than 900,000 smokers to quit within the first year and a half of a ban, including more than 200,000 Black Americans, its statement said.”

[ABC News](#) (4/29, Ebbs, 2.44M) reports Zeller “said the agency does not plan to pursue action against individuals for possessing menthol cigarettes or flavored cigars if the ban is enacted. He said FDA’s authority would apply to entities that manufacture, import, distribute, or sell the products and that the FDA would work to make sure other federal and local law enforcement agencies understand it doesn’t criminalize possession.” Zeller told reporters, “Given all of the ongoing, and very understandable concerns about what’s going on with policing, we would make sure that law enforcement agencies at all levels understand that when it comes to the enforcing of such a rule were it to go final, that, our jurisdiction ends with manufacture, distribution, sale, imports, retailers, and that we do not enforce against possession.”

Commentary: Easier Access To Fentanyl Test Strips Will Help The US Address Growing Substance Use Disorder Problem.

Regina LaBelle, acting director of the Office of National Drug Control Policy, Tom Coderre, acting assistant secretary for mental health and substance use in the federal Substance Abuse and Mental Health Services Administration, and CDC Director Dr. Rochelle P. Walensky write in a [STAT](#) (5/4, 262K) op-ed that the COVID-19 pandemic “has frayed societal connections. For Americans with substance use disorder, connections that were already fragile are at a serious breaking point.” The authors say, “Over the long term, the U.S. must take the necessary steps to build an addiction infrastructure that can prevent addiction, link people to and provide

quality treatment for people with substance use disorders, and support long-term recovery.” In the meantime, the US must address the issue by “scaling up syringe services programs...to provide a connection to services and care,” and providing easier access to fentanyl test strips. The authors point out that in April, the Biden Administration removed restrictions which prevented recipients of federal grants from using those funds to purchase fentanyl test strips.

Opioids For COVID-19 ‘Long Haulers’ Raise Addiction Concerns.

The [Washington Times](#) (4/29, Tan, 626K) reports “health experts are raising concerns over physicians prescribing opioids to COVID-19 ‘long haulers,’ saying it could lead to an increased risk of addiction among those who experience coronavirus symptoms long after having been infected.” Physicians “wrote nine more prescriptions for opioids for every 1,000 long COVID patients who were treated at a Veterans Affairs facility than they normally would have and wrote 22 additional prescriptions for potentially addictive sedatives such as Xanax [alprazolam] to treat anxiety, according to a [study](#) published last week in *Nature*.” NIDA Deputy Director Wilson Compton said, “As we’ve seen during the opioid crisis, opioid analgesic medications come with risks that include the possibility of developing addiction or experiencing an overdose.”

Senate Passes Temporary Extension Of Opioid Enforcement Tool.

The [AP](#) (4/29, Balsamo) reports the US Senate on Thursday temporarily extended “a sweeping tool that has helped federal agents crack down on drugs chemically similar to fentanyl,” approving “legislation extending until October an order that allows the federal government to classify so-called fentanyl analogues as Schedule I controlled substances.” According to the article, “The legislation headed to President Joe Biden’s desk temporarily classifies the synthetic opioids as a Schedule I drug under the federal Controlled Substances Act, making it easier for prosecutors to build cases against traffickers.”

Opinion: New Buprenorphine Prescription Guidelines Are “Step In Right Direction.”

In a [STAT](#) (4/29, 262K) op-ed, Groups Recover Together Chief Medical Officer Jacob Crothers and Treatment Research Institute founder Thomas McLellan call recent DEA-related guidelines from HHS that are intended to make it easier to prescribe the opioid use disorder treatment drug buprenorphine “a step in the right direction.” However, the op-ed authors, who claim the DEA “has increased surveillance activities that discourage potential” buprenorphine prescribers, argue that more is needed if the US hopes to reduce fatal drug overdoses. The authors urge the Administration to “prioritize a bold, coordinated agenda against opioids, which have been killing Americans by the thousands for decades – most of them in the primes of their lives.”

DIA:**Transdermal Amphetamine Therapy Effective At Treating Pediatric AD/HD In Small Phase II Trial, Researchers Say**

[MedPage Today](#) (5/3, Monaco) reports, “A transdermal amphetamine therapy was effective at treating pediatric” attention-deficit/hyperactivity disorder (AD/HD), investigators concluded in a two-part, phase II, 110-patient trial. The findings were presented at the American Psychiatric Association virtual annual meeting.

FDA Approves High-Dose Naloxone Nasal Spray.

The [AP](#) (4/30, Johnson) reported the Food and Drug Administration on Friday “approved Hikma Pharmaceuticals’ Kloxxado [naloxone hydrochloride], a spray containing 8 milligrams of naloxone – double the highest dose currently available.”

According to the article, “Experts and patient advocates say the more potent medicine is needed because low-dose naloxone sprays and injections sometimes must be given multiple times to keep someone alive until medical help arrives.”

[Axios](#) (5/1, Gonzalez, 1.26M) reported FDA Center for Evaluation and Research Director Dr. Patrizia Cavazzoni stated, “Today’s action meets another critical need in combatting opioid overdose. ... Addressing the opioid crisis is a top priority for the FDA, and we will continue our efforts to increase access to naloxone and place this important medicine in the hands of those who need it most.”

Minnesota Saw 27% Increase In Overdose Deaths Last Year, Data Show.

The [Minneapolis Star Tribune](#) (5/3, Howatt, 855K) reports drug overdose deaths rose 27% in Minnesota last year, “with the first large increase coming in March as the state saw its first coronavirus cases and deaths, according to the Minnesota Department of Health.” In response to rising overdose deaths nationwide, federal officials last week “eliminated a rule that required doctors and other health care professionals to receive more training in order to prescribe buprenorphine, a medication for opioid use disorder.” Since the pandemic began, “the number of buprenorphine prescribers has increased 12% in Minnesota” according to the Substance Abuse and Mental Health Services Administration, but 31 Minnesota counties still have no prescriber listed.

Behavioral Health Conditions Increase Amid Pandemic, Yet Access To Care Decreases, GAO Report Indicates.

[Fierce Healthcare](#) (5/4, Minemyer, 150K) reports, “Data suggests that the prevalence of behavioral health conditions has increased under the pandemic, but in-person access to needed services has decreased in tandem, a new GAO report finds.”

According to the article, “Two-thirds of behavioral health providers surveyed by the National Council for Behavioral Health said demand for their services was higher due to COVID, GAO found,” but “27% of NCBH member organizations reported that they laid off employees, and 45% reported closing some programs.” Meanwhile,

CDC data show “the number of adults reporting symptoms of anxiety or depression averaged 38% between April 2020 and February 2021.”

Reduction In Mental Healthcare Access During Pandemic Has Led To More Drug Overdoses, GAO Report Says.

[Kaiser Health News](#) (4/30, Huetteman) reported, “Therapists and other behavioral healthcare providers cut hours, reduced staffs and turned away patients during the pandemic as more Americans experienced depression symptoms and drug overdoses, according to a new report from the Government Accountability Office.” The GAO’s report details “the tip of the iceberg” in how people “with mental, emotional and substance use disorders are treated differently than those with physical conditions, said JoAnn Volk, a research professor at Georgetown University’s Center on Health Insurance Reforms who studies mental health coverage.” The findings paint “a picture of an already strained behavioral health system struggling after the pandemic struck to meet the treatment needs of millions of Americans with conditions like alcohol use disorder and post-traumatic stress disorder.”

Researchers Say MDMA Aided People With Severe PTSD Undergoing Therapy.

The [New York Times](#) (5/3, Nuwer, 20.6M) reports researchers found in a 90-person phase 3 trial that people with severe PTSD “who received MDMA during therapy experienced a significantly greater reduction in the severity of their symptoms compared with those who received therapy and an inactive placebo.” In the trial, “two months after treatment, 67 percent of participants in the MDMA group no longer qualified for a diagnosis of PTSD, compared with 32 percent in the placebo group.” The study “is expected to be published later this month in *Nature Medicine*.”

At-Home, Remotely Supervised Brain Stimulation Offers Pain Relief.

[Medscape](#) (4/30, Lowry, Subscription Publication, 219K) reported, “Transcranial direct-current stimulation (tDCS), performed at home but supervised remotely, is feasible and effective in managing osteoarthritis (OA) pain in older adults, new research shows.” In a “small, open-label study of 20 patients with knee OA, 2 weeks of at-home treatment with tDCS significantly reduced pain scores by more than 50%.” The findings “were presented at the virtual American Academy of Pain Medicine (AAPM) 2021 Annual Meeting.” On the “basis of the positive findings from this pilot study,” study investigator Hyochol Brian Ahn of the University of Texas Health Science Center “has been awarded a 3-year grant by the National Institutes of Health (NIH) to continue his research.”

Opinion: Coronavirus-Level Response To The US Drug Crisis Is Needed.

In an opinion for [The Hill](#) (4/29, 5.69M), contributor [Dr. Mitchell S. Rosenthal](#) writes that President Biden “has so far done remarkably little to address a national drug crisis and surge in overdoses that last year killed an estimated 90,000 Americans.” He adds, “Even with the number of drug deaths spiraling out of control during his first months in office, Biden has delivered only a \$1.5 billion allocation through the American Rescue Plan for the prevention and treatment of substance use disorders.” Rosenthal argues that the Administration “must propose and win congressional passage of legislation and funding at the level Biden promised as a candidate” and “it must help raise public awareness of what equated to roughly 250 Americans dying per day from overdose in 2020.”

Critics Accuse Study Researchers Of Exploiting Black Patients In Colonoscopy Study.

[STAT](#) (5/4, St. Fleur, 262K) reports, “At a time when medical researchers are under pressure to increase diversity in clinical trials, a Johns Hopkins study is sparking outrage among some physicians because of its large number of Black patients.” The research, published last fall, “caused a stir on social media in recent weeks” because in the “retrospective study analyzing the abilities of three specially trained nurse practitioners to perform colonoscopies,” almost 75% of the more than “1,000 patients who received screening colonoscopies from the nurse practitioners between 2010 and 2016” were Black. Fred Hutchinson Cancer Research Center gastroenterologist Rachel Issaka said, “When I saw the paper, my immediate concerns were around informed patient consent.” **(It’s important to raise awareness of these issues for future trials.)**

Funding Opportunities



GRANTS & FUNDING

NIH Central Resource for Grants and Funding Information

[RFA-DA-22-019](#)

[Leveraging Artificial Intelligence \(AI\) tools for Substance Use Disorders \(SUD\) drug discovery and development \(R43/R44 - Clinical Trial Not Allowed\)](#)

[RFA-DA-22-021](#)

[Leveraging Artificial Intelligence \(AI\) tools for Substance Use Disorders \(SUD\) drug discovery and development \(R41/R42 - Clinical Trial Not Allowed\)](#)

CAR Member New Publications

“The synthetic opioid fentanyl enhances viral replication *in vitro*” Ling Kong, Rebekah Karns, Mohamed Tarek M. Shata, Jennifer L. Brown, Michael S. Lyons, Kenneth E. Sherman, Jason T. Blackard

Journal PLOS ONE,

DOI: <https://doi.org/10.1371/journal.pone.0249581>

ABSTRACT

The US is in the midst of a major drug epidemic fueled in large part by the widespread recreational use of synthetic opioids such as fentanyl. Persons with opioid use disorder are at significant risk for transmission of injection-associated infections such as hepatitis B virus (HBV) and hepatitis C virus (HCV). Commonly abused substances may antagonize immune responses and promote viral replication. However, the impact of synthetic opioids on virus replication has not been well explored. Thus, we evaluated the impact of fentanyl and carfentanil using *in vitro* systems that replicate infectious viruses. Fentanyl was used in cell lines replicating HBV or HCV at concentrations of 1 ng, 100 ng, and 10 ug. Viral protein synthesis was quantified by ELISA, while apoptosis and cell death were measured by M30 or MTT assays, respectively. HCV replicative fitness was evaluated in a luciferase-based system. RNAseq was performed to evaluate cellular gene regulation in the presence of fentanyl. Low dose fentanyl had no impact on HCV replication in Huh7.5JFH1 hepatocytes; however, higher doses significantly enhanced HCV replication. Similarly, a dose-dependent increase in HCV replicative fitness was observed in the presence of fentanyl. In the HepG2.2.15 hepatocyte cell line, fentanyl caused a dose-dependent increase in HBV replication, although only a higher doses than for HCV. Addition of fentanyl resulted in significant apoptosis in both hepatocyte cell lines. Cell death was minimal at low drug concentrations. RNAseq identified a number of hepatocyte genes that were differentially regulated by fentanyl, including those related to apoptosis, the antiviral / interferon response, chemokine signaling, and NFκB signaling. Collectively, these data suggest that synthetic opioids promote viral replication but may have distinct effects depending on the drug dose and the viral target. As higher viral loads are associated with pathogenesis and virus transmission, additional research is essential to an enhanced understanding of opioid-virus pathogenesis and for the development of new and optimized treatment strategies.

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