# Alcoholism & Drug Abuse Weekly

News for policy and program decision-makers

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Our page 1 stories this week look at a policy instituted in the last days of the Trump administration to lift prescribing restrictions on buprenorphine, and at a failed trial for naloxone-bupropion to treat methamphetamine use disorder.
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## Trump's HHS eliminates x-waiver in last days of administration

The federal government's Jan. 14, 5 p.m. announcement that it would remove the eight-hour training requirement for buprenorphine prescribers in order to facilitate treatment for opioid use disorders (OUD) during the increasing overdose epidemic was met with approval by harm-reduction advocates and the American Medical Association (AMA). However, addiction treatment advocates, including the American Society of Addiction Medicine (ASAM), which appeared to be blindsided by the announcement; H. Westley Clark, M.D., J.D., former director of the Center for Substance Abuse Treatment at the Substance Abuse and Mental Health Services Administration (SAMHSA); David A. Fiellin, M.D., director of the Program in Addiction Medicine and Professor of Medicine, Emergency Medicine and Public Health at the Yale School of Medicine; and Elinore McCance-Katz, M.D., Ph.D., who abruptly resigned from her position as SAMHSA administrator because of her disgust at President

**Bottom Line...**
*The training requirement for buprenorphine prescribers was removed by outgoing federal officials days before they left office; the former official in charge, Elinore McCance-Katz, M.D., Ph.D., had fought to keep the requirement for years. She tells* ADAW *why.*

See **Buprenorphine** page 2

## Another trial falls short in search for stimulant use disorder treatment

Numerous challenges in identifying treatment targets have left the addiction treatment field without an approved medication option for treating stimulant use disorder, making the response to the growing stimulant crisis look markedly different from opioid crisis response. A great deal of hope has been directed toward identifying existing medications or medication combinations that can combat stimulant addiction, but a much-anticipated study released this month likely will dampen the enthusiasm.

Published in the Jan. 14 issue of the *New England Journal of Medicine*, the 12-week study found that a combination of naltrexone plus bupropion led to low response among patients with methamphetamine use disorder. Response was defined as at least three negative drug tests for methamphetamine out of four taken in one of the two six-week stages of the study.

Although the response rate for naltrexone-bupropion was higher than the response rate for placebo, the weighted average response across the two study stages was only 13.6% for the drug combination.

**Bottom Line...**
*About all that can be said for a newly published trial of naltrexone plus bupropion for methamphetamine use disorder is the low response rate was at least higher than the placebo response.*

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**Buprenorphine** from page 1

Trump's incitement of the Jan. 6 riots on Capitol Hill (see *ADAW*, Jan. 18), all expressed varying degrees of reservations about the policy.

If it works, it will be an experiment with human guinea pigs, succeeding in getting more patients into treatment. However, the human guinea pigs — patients as well as people in the community who use diverted buprenorphine as a result — could suffer.

The DATA waiver, also called the x-waiver, is actually a waiver from the 1914 Harrison Narcotics Act, which bans the use of narcotics (the word used at the time) to treat narcotic addiction. The only other drug allowed in the United States for the treatment of OUD is methadone, which can only be given in a strict setting — an opioid treatment program.

## Ethan Crislip: OD from buprenorphine

For example, 22-year-old Ethan Crislip passed from an overdose last May. His drugs of choice were cocaine and marijuana, but the toxicology reports found buprenorphine and Klonopin — a fatal mix, especially for the opioid-naïve youth — in his system. His father, Drew Crislip, a federal administrative law judge based in West Virginia who worked for the Department of Justice from 2010 to 2016 as Assistant General Counsel for the FBI, had never heard of buprenorphine before, although he had heard of the name brand, Suboxone. Crislip spoke to us about his son and his feelings about the new guidelines — which, despite everything, he tends to support — last week.

Taken alone in therapeutic doses, buprenorphine is not likely to cause overdose death. However, for opioid-naïve people like Ethan and for people who combine it with other central nervous system depressants, such as alcohol, benzodiazepines or other opioids, it can be lethal.

But the Crislips did not pursue anything with law enforcement. "I had no interest in reading the coroner's investigative report or autopsy report," Crislip told us last week. "The toxicology information was all I could do."

## The changes

The move was spearheaded by Adm. Brett P. Giroir, M.D., assistant secretary for health with the Department of Health and Human Services (HHS) until January 20, when President Biden was inaugurated. McCance-Katz, who was assistant secretary for mental health and substance use, was replaced by Capt. (U.S. Public Health Service) Meena Vythilingam on Jan. 13 (see *ADAW*, Jan. 18). Last week, Tom Coderre was made acting assistant secretary (see box, page 5).

But Giroir, who was no longer with HHS after President Biden was in charge of this new proposal. "The medical evidence is clear: access to medication-assisted treatment, including buprenorphine that can be prescribed in office-based settings, is the gold standard for treating individuals suffering from opioid use disorder," said Giroir in a Jan. 14 statement accompanying the announcement (which came just hours after *ADAW*'s deadline for the previous issue). "Removing some of the certification requirements for an X-waiver for physicians is a step toward providing more people struggling with this chronic disease access to medication assisted treatment."

Giroir, a Trump administration appointee, has chosen a very difficult path for the new Biden administration, picking up the pieces of this proposal.

Eliminating the x-waiver for prescribers for 30 patients at a time only is going to be difficult to enforce.

Below are the specific exemptions under the guidelines:

- The exemption only applies to physicians who may only treat patients who are located in the

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states in which they are authorized to practice medicine.
- Physicians utilizing this exemption will be limited to treating no more than 30 patients with buprenorphine for OUD at any one time (note: the 30-patient cap does not apply to hospital-based physicians, such as emergency department [ED] physicians).
- The exemption applies only to the prescription of drugs or formulations covered under the x-waiver of the Controlled Substances Act, such as buprenorphine, and does not apply to the prescription, dispensation or use of methadone for the treatment of OUD.
- Physicians utilizing this exemption shall place an "X" on the prescription and clearly identify that the prescription is being written for an OUD (along with the separate maintaining of charts for patients being treated for OUD).
- An interagency working group will be established to monitor the implementation and results of these practice guidelines, as well as the impact on diversion.

Fiellin, who led the research for the federal government that first allowed buprenorphine-naloxone to be approved, told *ADAW*, said McCance-Katz. he supports the expansion but does have concerns.

"The fentanyl epidemic and the COVID pandemic have dramatically increased fatal and nonfatal overdoses," Fiellin said in an email last week. "I think this is a reasonable incremental change given the current toll of addiction on our society."

However, he added that it "is important that we expand access to, and the quality of, the most effective medication-based treatments for opioid use disorder such as buprenorphine and methadone in addition to harm-reduction services." He noted that because "most prescribers in the U.S. have not received education or training on the treatment of opioid use disorder, prescriber education and support is key as efforts to expand access to buprenorphine are implemented." He added, "Many practicing clinicians need training on how to think about patients with addiction, how to speak about patients with addiction and how to treat patients with addiction."

Pill mills were mentioned as a concern by everyone. Cash-only practices that sell prescriptions for buprenorphine will not be helpful to patients or the public.

"We also need to monitor to make sure that this change does not lead to more cash-based detox episodes that will put our patients at risk," Fiellin told *ADAW*. "Patients with addiction are members of our society who have been marginalized for too long, and it is time the medical establishment develops, implements and monitors competencies throughout health care so we can treat with excellence and compassion. We can't let this need be forgotten or let the field of health care education, our federal partners or our health care infrastructure off the hook with this change."

Concluded Fiellin: "The bottom line is that patients with addiction in general and those with opioid use disorder deserved trained prescribers."

## Sabotaging Biden

"This is what happens when you give authority to people who have no experience in the field," McCance-Katz told *ADAW* in an interview early last week, when she had returned to her home in Rhode Island. "The people who made this decision don't treat opioid use disorder. They have never seen patients with OUD. I understand that they want to make decisions that they believe will be helpful and will actually reduce harm." But this decision will not, and she has made no secret of her opposition to elimination of the DATA waiver, even though SAMHSA was under pressure to remove it.

Treatment of OUD requires psychosocial support, she said. "Everyone with OUD and any other substance use disorder needs the benefit of a full evaluation and a broad-based treatment plan," she said.

SAMHSA has put millions of dollars into free training for physicians in order to obtain the waiver. "All of us have to keep up our licenses," she said, asking, as she has many times, why it's considered a burden to take a one-time eight-hour course on prescribing buprenorphine. All you need is your medical license and Drug Enforcement Administration [DEA] registration" to take the course, she said.

She added that Congress required the education component. "The secretary of HHS does not have the legal authority to eliminate the DATA waiver — only Congress has the authority to do that," she said.

Finally, she is very concerned that "doctors are going to go out and start practicing without a DATA waiver, and will get into trouble," she said. "They may engage in activities that are not helpful, such as cash-only practices."

In addition, this is sabotaging the next administration with extra work. "It's unfair to the incoming administration, but I hope they'll be able to take a look at this early on and determine the right course," said McCance-Katz. "The Biden administration has so much work to do to get their programs and policies into place, and to do something like this at the 11th hour that could get doctors into trouble — it's heinous."

McCance-Katz had tried to put forward another proposal: that there would be a much higher patient cap for addiction experts. But that proposal didn't get traction.

She did get a call from HHS saying that by law, they had to ask her for her consultation on the proposed change. "I expressed my concerns and said that it shouldn't happen," she said. But the "consultation" was just pro forma. There was

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no thought of taking her seriously, she said.

A survey of prescribers by SAMHSA found that the reason many physicians were prescribing far below their cap — 30 or 100 — was because they felt they needed more education. Some worked for organizations that didn't allow the treatment of OUD. "This is about workforce needs," she said. "I read those results and put together the alternative of eliminating the cap for experts." Legal counsel had said a notice of proposed rulemaking was needed in order to do that.

"This was done without the input of major stakeholders," said McCance-Katz. "SAMHSA was not consulted until very close to the time that the secretary (of HHS, Azar) would sign the document."

Fiellin was not consulted, either.

"We already know from the NSDUH [National Survey on Drug Use and Health] that buprenorphine is the most diverted medication," she said.

The guidelines also eliminate the 30-patient limit, as well as the waiver, for emergency departments. "But who's going to treat these patients? Are the emergency departments expected to become OTPs? They put someone on buprenorphine for a very short period of time," said McCance-Katz. When the buprenorphine wears off and craving takes over, where will the patients get opioids? she asked. "To have not thought that through is unethical," she said.

What could fix the problem? State boards of medicine could certify DATA waiver training, she said. "I would urge states to take a look at this," she said.

## Devil is in the details

The approach HHS is taking appears laudable on its face, but there are some key problems, said Clark, whose comments frequently cite "the devil is in the details."

First, physicians need to know eliminating the training doesn't eliminate them from DEA scrutiny. Another question is what happens when the physician writes the "x" on the prescription, as is required (this is instead of actually have the x number assigned by the DEA). This x alerts the pharmacist, the prescription drug monitoring program (PDMP) and the DEA.

Another issue is that while the ED physicians can have more than 30 patients, if the patients can't find an office-based physician, the patients will have to go back to the ED. "So, instead of ED visits just for initiating medical withdrawal, the ED will become the primary access point for buprenorphine management, something that the ED may question, especially during the time of a pandemic," said Clark.

The guidance only applies to physicians; it doesn't apply to advance practice nurses and physician assistants.

The DEA will still be able to identify and scrutinize the practices of those who use buprenorphine for the treatment of OUD.

Furthermore, it enhances the risk of buprenorphine "pill mills," as all a deviant doctor needs to do is a cursory physical exam one time and then write a script.

"From SAMHSA's perspective, this new approach might torpedo SAMHSA/HHS's ability to track what's going on with buprenorphine and buprenorphine prescribers," noted Clark. "You could have 100,000 physicians prescribing buprenorphine without a formal waiver. Since this group of physicians would have no formal waiver, SAMHSA could not include them in the buprenorphine treatment locator. The quasi-waivered physicians would use their DEA numbers and would report patients to the PDMP. This diminishes the utility of the buprenorphine treatment locator. In addition, some pharmacies check the SAMHSA database to verify the credentials of buprenorphine prescribers — the new guidance will prevent them from being able to do this. Thus, it may not enhance access."

Furthermore, how will the 30-patient cap be monitored? If you don't need a formal waiver for 30 patients, why would you get a waiver for 31 patients or 35 patients or 50 patients? "You wouldn't," said Clark, who calls the "x" required to be scribbled on the prescription by the new policy a "quasi-x." "SAMHSA would have to get data from the DEA, state PDMPs or IQVIA in order to assess the impact of the new policy. It could then match up those with formal x-waivers with those with the quasi-x-waiver. This would require resources (funding)."

So on the one hand, the new guidelines may liberalize access to buprenorphine, but they may also create more problems.

Clark also wondered if buprenorphine manufacturers will be happy with the new approach, even though it does stand to profit them. In the future, state attorneys general may hold them liable, as they are holding manufacturers of opioid analgesics liable, for failing to act if buprenorphine "becomes the new OxyContin."

As for the AMA, it stands to reason that it would favor a move to reduce regulations on its members. There are many reports that the prescribers who obtained DATA waivers did so to be able to treat their few current patients, and not to add new patients with addiction, a population they do not necessarily want to solicit. This move would eliminate the waiver requirement.

## The AMA

As Marilyn Heine, M.D., of the AMA notes, there are several important considerations to keep in mind:

- Use of buprenorphine by a person who has OUD but is not in withdrawal can precipitate withdrawal. This is a significant adverse experience. It dissuades patients from adherence to treatment.
- Meaningful treatment of OUD involves more than medication

 

alone. Counseling is an important component to help provide patients with the opportunity to develop effective coping skills. To attain and maintain recovery, it is essential to identify and manage underlying mental illness — a major driver of substance use disorder (SUD).

- To optimally benefit ED patients, initiation of buprenorphine in the ED should be coupled with a bridge to designated meaningful treatment for OUD.
- The effectiveness of buprenorphine at managing the cravings felt by a person who has OUD depends on the potency of the opioid the person is using. It is generally not adequate in the care of a person who uses fentanyl. Methadone is often necessary for these persons.
- Elimination of the x-waiver requirement for buprenorphine prescribing does not address the stigma of OUD where the NSDUH showed persons with SUD were deterred from seeking care due to fear of exposure and associated known risk of losing job, housing, custody and insurance. Further measures are necessary to resolve these issues.

"I believe the guidelines were hastily conceived and hastily presented to the community," concluded Clark. "Critical details that would permit monitoring and evaluation were omitted. In short, this will be someone else's responsibility."

## More about Ethan

Crislip said diversion is "almost certainly" how his son got buprenorphine. But he still approves of the decision to make buprenorphine more widely available, though not without concern for diversion, understandably. "I've tried to think like a lawyer, rather than a father, and consider both sides," he said. "I know there will be negatives, but I hope many people will be helped due to greater access."

Crislip is grateful that he and his wife, Annette, said Ethan could come home. They hadn't seen him for three months. He had been vulgar and stolen from them, and was violent sometimes. "I told him, 'I know you; you aren't like this,'" said Crislip. "It's an insidious disease. My brother and sister and I somehow escaped it." He and his wife worried about their son for the last five years, constantly. "I don't worry about him anymore, but worry has been replaced by grief."

Ethan was nine years younger than the youngest of the five children, "an unexpected surprise, and much loved," Crislip said. There are genetic factors of addiction in the family, said Crislip. His father was an alcoholic, his mother was addicted to prescription drugs. Depression is also in the family. When at the age of 14 Ethan started smoking marijuana, his father told him, "You don't have the genetics for weed."

That said, Crislip supports marijuana legalization, because he believes regulation will make the drug safer.

Just over a year ago, after many stints in treatment centers, Ethan started using cocaine. "But he always said he was afraid of opioids, and I believe that he had never used them based on being around him and him not having any withdrawal symptoms, based on talking to friends whom I believe, and based on information from his physicians," Crislip said.

Just before the fatal overdose last May, Ethan called his parents from the West Coast, where he had just left a treatment program and was staying with a friend, and said he wanted to come home. Ethan had given his psychiatrist, Adina Elise Bowe, M.D., clearance to talk to his

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## New acting leadership at SAMHSA and ONDCP under Biden

Last week, the Substance Abuse and Mental Health Services Administration (SAMHSA) got a new acting head — Tom Coderre, who was chief of staff at the agency during the Obama administration. He was then senior advisor to Rhode Island Governor Gina Raimondo, a strong proponent of substance use disorder treatment who President Biden nominated to be commerce secretary. Coderre is beloved in the recovery community, and SAMHSA staff will be relieved to have him in charge while waiting for an official nomination for permanent assistant secretary for mental health and substance use with the Department of Health and Human Services.

Regina LaBelle is now acting deputy director of the Office of National Drug Control Policy (ONDCP). She was chief of staff of the agency during the Obama administration and led the Biden transition team for the agency. She is also a distinguished scholar and program director of the Addiction and Public Policy Initiative at the O'Neill Institute for National and Global Health Law at Georgetown University, but last week announced a leave of absence from that position. She is a consummate professional who will help lead the agency while waiting for an official nomination for a permanent director.

Speculation about who will be nominated for these two positions continues, with H. Westley Clark, M.D., J.D., formerly director of SAMHSA's Center for Substance Abuse Treatment and currently Dean's Executive Professor at Santa Clara University, favored by the treatment field for any high level position. ONDCP would be a natural fit as Clark is both a physician and an attorney with broad experience in substance use treatment, recovery, public health and the interface with the criminal justice system.

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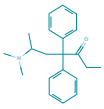
parents, and they made a plan, were prepared to buy plane tickets and were hopeful. However, two days before the planned flight, Ethan said he had changed his mind.

In addition to the buprenorphine, Ethan had Klonipin, for which he had a prescription, in his system when he overdosed. "We think it was the buprenorphine-Klonipin mix that did it," Crislip told *ADAW*. He also had his other prescribed drugs, Trileptal and Effexor, in his system. The only other drug in his system was marijuana. "He had wanted cocaine, but unfortunately he got buprenorphine," Crislip said. "And he was completely naïve to opioids."

Some other details about Ethan's life:

- Ethan, in 2011, was both nationally and internationally ranked in speed cubing (Rubik's Cube). His fastest time in competition was under 8 seconds. Along with his parents, he attended the World Speedcubing Championships in Bangkok, Thailand.
- When he was 18, he realized girls liked guitar better than cubing, so he took up guitar.
- His beloved dog, Jack, 14, had a large benign tumor on his leg which in December became septic; however, the veterinarian did not want to operate because she believed he would not survive the surgery. She gently urged euthanasia. The Crislips told her of their loss and explained Jack had been a great comfort to them, and she agreed to operate. "Against all odds, Jack survived, and remains a sweet reminder of our son for us, our four other kids, and our eight grandchildren." •

For the practice guidelines, go to https://www.hhs.gov/sites/default/files/mat-physician-practice-guidelines.pdf.



OPIOID TREATMENT PROGRAMS

# Patients with anxiety and depression likely to have cravings

Researchers have found that delay discounting (future versus immediate rewards) and cue-induced craving were increased in patients in methadone maintenance treatment (MMT) compared to controls. The delay discounting and craving scores were unrelated to methadone dosage, duration on methadone, withdrawal symptoms or nicotine dependence. Elevated delay discounting is of course present with opioid use disorder (OUD) as it is with all substance use disorders, but whether it continues with treatment was unclear.

These patients still, compared to controls, do have this elevated measure of impulsivity. It means it can still be difficult for some methadone patients, at least, to fight the cue-induced craving to use drugs for an immediate payback, ignoring the worse effects in the future. This doesn't mean they don't fight it successfully — they do. But it does mean treatment can do something to help them. The study, "Impulsivity and craving in subjects with opioid use disorder on methadone maintenance treatment," by Jun Li and colleagues and published in the current issue of *Drug and Alcohol Dependence*, found that anxiety and depression, not associated with methadone but as co-existing with OUD, were predictors of this elevated delay discounting and should be addressed in treatment.

According to the researchers, from China and the United Kingdom, there is a role for trait effects (anxiety and depression) in delay discounting. In addition, this study found that in contrast to earlier, small studies, there were no impairments of executive function (which did exist prior to the methadone), and only impaired learning related to depressive and anxiety symptoms. The research also did not find any continuing increased impulsivity in patients maintained on methadone, although of course these patients had increased impulsivity prior to treatment.

## Details

Delay discounting, reflection impulsivity, risk-taking and motoric impulsivity are four types of impulsivity that were measured by the researchers. They also looked at executive functions (spatial working memory, paired associate learning and strategic planning) and cue-induced craving in a cohort of patients on MMT, and compared them with healthy controls. The researchers also looked at whether the abnormal impulsivity levels observed in the patients were related to MMT-related variables or psychological variables.

The 115 MMT outpatients were from three MMT clinics in Shanghai, matched to healthy volunteers.

## Implications

The researchers showed that MMT patients had greater delay discounting and cue-induced craving compared to healthy volunteers. However, no significant difference was found with risk-taking and motor response inhibition. In addition, the impulsivity findings were not related to associative learning, craving measures, methadone use severity or nicotine dependence.

There were impairments in associative learning but not when the results were controlled for depression and anxiety, which suggests "an important role for comorbid symptoms in influencing cognitive function in MMT patients," the researchers wrote.

Methadone has been used for treating OUD since the 1960s, and