

Buprenorphine initiation in the ER found safe and effective for individuals with opioid use disorder who use fentanyl

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Results from a multi-site clinical trial supported by the National Institutes of Health showed that less than 1% of people with opioid use

disorder whose drug use includes fentanyl experienced withdrawal when starting buprenorphine in the emergency department. The findings, which appeared today in *JAMA Network Open*, are strong evidence that buprenorphine, a medication approved by the U.S. Food and Drug Administration to treat opioid use disorder, can be safely started in the emergency department without triggering withdrawal, even for people who use stronger opioids. Clinician concern over this type of withdrawal can be a barrier to using this treatment.

Withdrawal induced by medications to treat [opioid use disorder](#)—called [precipitated withdrawal](#)—is a debilitating experience marked by rapid onset of symptoms such as aches, nausea and vomiting, diarrhea, and abdominal cramps that can occur within two hours after the first dose of [buprenorphine](#). Although instances of buprenorphine-precipitated [withdrawal](#) have only been reported in relatively small case studies and anecdotal evidence, some clinicians and patients worry that the risk of experiencing precipitated withdrawal from buprenorphine might be increased among people who use fentanyl.

This has led some clinicians to prescribe buprenorphine at lower doses, especially for people using extremely potent illicit opioids such as fentanyl. Because initiating low-dose buprenorphine following initial cessation of illicit opioids can be less effective in relieving these symptoms, individuals may be more likely to resume use of illicit opioids.

The study, supported by the National Institute on Drug Abuse (NIDA) through NIH's Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative, should help assuage concerns over precipitated withdrawal following buprenorphine treatment in the [emergency department](#).

"We are in an overdose crisis, and we need to deploy every tool we have

to help address it," said Nora D. Volkow, M.D., director of NIDA. "The emergency department is a crucial care setting for people with [substance use disorders](#). This study provides further evidence that all emergency department physicians can and should be using buprenorphine to help individuals take the first steps into treatment and toward recovery."

There has been an urgent need to better understand how the [prevalence of fentanyl in the drug supply](#) affects the process of addiction treatment for people with [opioid](#) use disorder. The study addressed this question prospectively by analyzing data from 1,200 individuals at 28 U.S. emergency departments participating in an [ongoing clinical trial](#). The trial is comparing the relative impact of a weekly extended-release buprenorphine injection at a dose of 24 milligrams versus daily administration of 8 to 16 mg buprenorphine as a tablet or film.

The trial recruited [adult patients](#) with untreated moderate to severe opioid use disorder, opioid-positive and methadone-negative urine tests, and a [Clinical Opiate Withdrawal Scale](#) score greater than or equal to 4. In this study, precipitated withdrawal was defined as when a patient demonstrated marked escalation by five points or more on the Clinical Opiate Withdrawal Scale within two hours of starting buprenorphine. Researchers found that despite high fentanyl use prevalence—about 76%—among 1,200 people with opioid use disorder, precipitated withdrawal occurred in nine out of the total 1,200 people, or 0.76%, and only 0.98% of those who had used fentanyl. The rate of precipitated withdrawal was similar to that reported in people using heroin or prescription opioids without fentanyl.

"Clinicians should encourage patients with opioid use disorder to take buprenorphine if they need it," said lead author Gail D'Onofrio, M.D., professor of emergency medicine at Yale University, New Haven, Connecticut. "We know that less than 23% of people with opioid use disorder are getting treated for it, and we only have a few medications

for opioid use disorder that have been found to be very effective for opioid withdrawal to date. If we take away one of these, we're going to have an even bigger gap between need and treatment. We hope that both clinicians and patients understand that buprenorphine is a safe and effective option."

These findings build upon existing evidence that administering buprenorphine in emergency departments helps people begin addiction treatment and that higher-dose buprenorphine (more than the standard upper limit of 16 mg) is [safe and well tolerated](#) in people with opioid use disorder experiencing withdrawal symptoms. They also bolster support for expanding access to buprenorphine. Recent legislation removed barriers to access, including the [elimination of the X-Waiver in December 2022](#), and policy efforts have been initiated that maintain COVID-19 era-initiated flexibilities related to [prescribing buprenorphine via telehealth evaluations](#).

"The emergency department is an important touchpoint for providing life-saving medication and resources for people at risk for overdose," said Rebecca G. Baker, Ph.D., director of the NIH HEAL Initiative. "We need to meet people where they are amid an increasingly deadly overdose crisis."

More information: Incidence of Precipitated Withdrawal during a Multi-site Emergency Department-Initiated Buprenorphine Clinical Trial in the Era of Fentanyl, *JAMA Network Open* (2023). [DOI: 10.1001/jamanetworkopen.2023.6108](https://doi.org/10.1001/jamanetworkopen.2023.6108)

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