Seven-day buprenorphine is safe for those with minimal opioid withdrawal, study shows

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Credit: Michael S. Helfenbein, Yale University

A seven-day, extended-release version of buprenorphine—a treatment for opioid use disorder (OUD) that can reduce opioid use and overdose deaths—is safe and effective for people with OUD experiencing minimal symptoms of withdrawal, a new Yale study finds.

Individuals with minimal opioid withdrawal are often not prescribed the more common under-the-tongue, or sublingual, version of buprenorphine, in part because the treatment itself can induce sudden withdrawal. Withdrawal is measured through the Clinical Opioid Withdrawal Scale, which ranges from 0 to 48, and individuals were invited to participate in the study if they had a score of 7 or less, indicating minimal to mild withdrawal.

In the new study, only 7% of participants overall, and 3% of those at the higher end of the minimal withdrawal scale, experienced induced withdrawal with the extended-release version.

The findings—reported July 8 in *JAMA Network Open*—indicate that extended-release buprenorphine can be used before moderate to severe withdrawal develops, which, researchers say, means more people can receive treatment and more lives can be saved.

"This is a gamechanger," said Gail D'Onofrio, the Albert E. Kent Professor of Emergency Medicine at Yale School of Medicine and lead author of the study. "The emergency department is a huge access point for opioid use treatment, but around 50% of patients with opioid use disorder who come to the emergency department are not at sufficient levels of withdrawal to use sublingual buprenorphine."

In those cases, physicians currently may prescribe buprenorphine—which patients would have to pick up at a pharmacy—and instruct them how to self-start it later when their withdrawal symptoms increase. Some emergency departments may turn patients away without any medication.

Extended-release buprenorphine is administered by injection and remains in a person's system—and protects them from overdose—for seven days. Sublingual buprenorphine, on the other hand, has a smaller

protective window and is often administered daily.

"With this extended-release version, we can not only initiate treatment in patients with minimal withdrawal immediately during their emergency department visit, but we can protect them from overdosing for seven days, not just for 24 hours," said D'Onofrio, who is also a professor of epidemiology (chronic diseases) at Yale School of Public Health. "That extra time can give people a chance to find a long-term treatment provider or treatment program."

Four emergency departments located in the Northeast, mid-Atlantic, and Pacific regions of the United States conducted the study, which involved 100 patients. Participants were adults with moderate to severe opioid use disorder who tested positive for opioids after arriving at one of the emergency departments, but who were experiencing minimal to mild withdrawal.

The participants received one injection of the extended-release buprenorphine—also known as Brixadi—which was approved for use by the U.S. Food and Drug Administration in May 2023. They were observed for four hours post-injection for signs of induced withdrawal.

Of the seven participants who experienced induced withdrawal, five had initially scored between 0 and 3 on the withdrawal scale, while two had scores between 4 and 7.

The extended-release formula increases the blood concentration of buprenorphine more gradually than the sublingual version, which could explain why fewer people experience induced withdrawal.

"Based on these findings, we recommend extended-release buprenorphine as safe to use for patients with OUD and withdrawal scores of 4 or greater that include at least one sign of objective

withdrawal, such as enlarged pupils, yawning, or high resting heart rate," said D'Onofrio.

Withdrawal scores decreased for most patients following treatment. In the seven days following the injection, participants received surveys via text message that assessed their craving and use of nonprescribed opioids; between 72 and 88 participants completed an assessment on any given day. Of those who responded, 33% to 43% reported no cravings and between 78% and 85% reported no use of opioids.

Previous research has shown that administering buprenorphine can increase the likelihood people will seek addiction treatment. In the new study, 73% of participants went on to receive medication-based treatment at the end of the seven-day dose.

"The physicians conducting this study were all very experienced with administering buprenorphine and all partnered with clinics they could direct patients to for longer-term treatment. So this percentage may be higher than it would be elsewhere," said D'Onofrio. "But it's still great to see."

Further, the majority of participants said they found the treatment to be effective, with the extended-release version offering clear benefits. Those benefits include not requiring daily medication, reducing visits to the pharmacy, improving privacy and ease of traveling, and reducing the likelihood of missing treatment doses.

"The goal now is to get hospitals to approve use of this treatment in their emergency departments, inpatient services, and outpatient clinics," said D'Onofrio. "We're still in the midst of the opioid epidemic and we're still seeing a lot of deaths. We struggle with getting people to initiate and remain in treatment. But this is a really important new option. It's an opportunity to save a life."

Other Yale authors include Kathryn Hawk, Patricia Owens, Shara Martel, James Dziura, and David Fiellin.

More information: Gail D'Onofrio et al, Extended-Release 7-Day Injectable Buprenorphine for Patients With Minimal to Mild Opioid Withdrawal, *JAMA Network Open* (2024). DOI: 10.1001/jamanetworkopen.2024.20702

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