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# A new study found a big problem with a popular opioid addiction medication

A long-awaited study compared two opioid addiction treatments. There's good and bad news.

Updated by German Lopez | @germanrlopez | [german.lopez@vox.com](mailto:german.lopez@vox.com) | Nov 15, 2017, 12:30pm EST

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An advertisement for Vivitrol, an opioid addiction medication. | Andrew Lichtenstein/Corbis News via Getty Images

With the death toll of America's opioid epidemic now in the tens of thousands every year, one of the most pressing public health questions facing the nation today is how to treat the addiction that leads people to misuse and overdose on these drugs.

That's why a lot of experts have been keeping a close eye on the new research on extended-release naltrexone (also known as Vivitrol), a promising, relatively new medication for opioid addiction. Although we already have proven medications in methadone and buprenorphine (also known as Suboxone), the hope is that naltrexone will also prove effective



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and provide more choice for people with opioid addictions who don't do as well on the older medications.

These medications deter people from using opioids — buprenorphine and methadone by reducing cravings and withdrawal, and naltrexone by primarily blocking the effects of opioids. The question is whether either of these approaches is better.

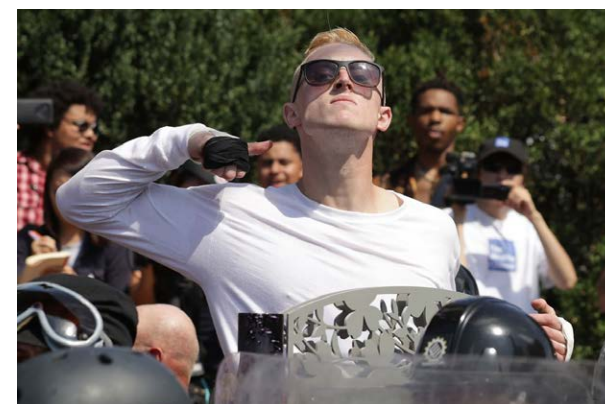
For the first time, a new study in *The Lancet*, sponsored by the National Institute on Drug Abuse (NIDA), compared the effectiveness of naltrexone with buprenorphine in the US. The results were both promising and disappointing. While naltrexone is as effective as buprenorphine once treatment begins, it is also significantly more difficult to actually start naltrexone because it requires an extensive detox period — which can span more than a week — that buprenorphine does not.

This is important. Drug overdoses killed more than 64,000 Americans in 2016, with most of those overdoses linked to opioids like OxyContin, heroin, and especially **fentanyl**. Not getting on treatment, because a particular medication requires a full detox period or some other barrier, can heighten the chances someone will use drugs once again and overdose.

Medication-assisted treatment, which uses drugs like buprenorphine and naltrexone, is considered the gold standard of care for opioid addiction. Various studies, including systematic reviews of the research, have found



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that medication-assisted treatment can cut the all-cause mortality rate among addiction patients by **half or more**. That's why it's recommended by various public health groups, including the Centers for Disease Control and Prevention, the National Institute on Drug Abuse, and the World Health Organization.

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But since the drugs work differently and none of them is a perfect cure (with relapse rates still above 50 percent with either), it's expected that different medications will work better for different patients.


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Much of this research, however, has focused on methadone and buprenorphine, which have been used for opioid addiction for longer. So the question now is how, exactly, naltrexone compares. The new study gives us some promising answers — but it also gives us some reasons to be cautious about naltrexone compared to the older drugs.

## What the study found

The study was sponsored by NIDA, a federal agency. Four of the researchers reported conflicts of interest, previously receiving free drugs, research support, or consulting fees from the pharmaceutical company Alkermes, which manufactures extended-release naltrexone. The other 19 authors reported no conflicts of interest related to Alkermes.

The study was a randomized controlled trial — the top standard in research — at eight US community-based inpatient services conducted between 2014 and 2016. It placed about half of its 570 participants into naltrexone treatment, and the other half into buprenorphine treatment. Then it tracked their relapse rates over 24 weeks.

Right out of the gate, naltrexone hit a big hurdle: Patients had a tougher time getting on it than buprenorphine. While 6 percent of the buprenorphine group failed to start on the treatment, 28 percent of the naltrexone group — more than four times — initially dropped out.

This is because of a key difference in how the drugs work. Buprenorphine is an opioid, and it works by activating the same opioid receptors that other opioids do — albeit at lower levels, not producing a high when taken as a prescribed — to stave off cravings and withdrawal. Naltrexone, on the other

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hand, is *not* an opioid; what it does, instead, is block opioid receptors from activating — so even if someone does use heroin while taking naltrexone, it will block them from feeling high. But because naltrexone is not an opioid, it won't stave off withdrawal.

In fact, naltrexone *requires* going through withdrawal, because it only works once opioids are washed out of a person's system. So while buprenorphine only requires a partial detoxification process (usually 12 hours to two days), naltrexone requires full detoxification to use (usually three to 10 days of no opioid use).

This full detox period creates a significant barrier. The *Lancet* study shows just how big: Buprenorphine proved to be the much more accessible drug.

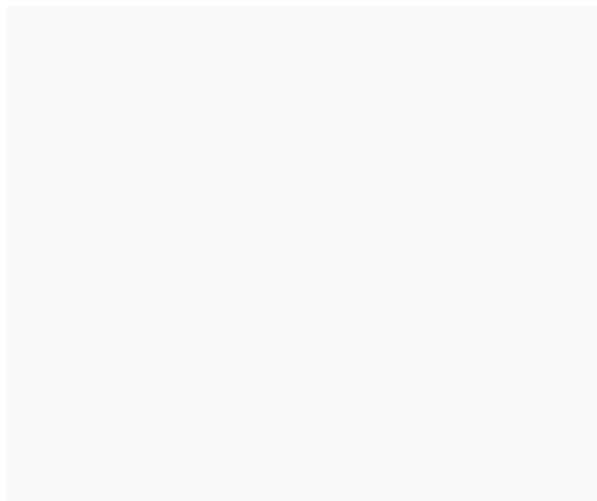
The good news, though, is that buprenorphine and naltrexone were similarly effective once patients got over the initial hurdle. For naltrexone, the opioid relapse rate was about 52 percent. For buprenorphine, it was 56 percent. These were statistically similar, with no difference between men and women. Other measures, such as opioid-negative urine samples, opioid-abstinent days, and overdoses, did not differ between naltrexone and buprenorphine.

Keith Humphreys, a drug policy expert at Stanford who was involved in the *Lancet* study, summarized the findings: "If you get on the medication, both are equally effective, but it's harder to get on naltrexone because you need the detoxification first."

The outcomes matched [a previous study](#) conducted in Norway comparing naltrexone and buprenorphine. Unlike the *Lancet* study, however, the Norway study only took in people who had already detoxified — eliminating

one of the key hurdles to naltrexone. The *Lancet* study avoids that limitation, providing a fuller comparison between both of the drugs.

Anna Lembke, a Stanford psychiatrist who was not involved in either study, said the findings matched what she's seen in the real world: Naltrexone is "a useful medication when people get on it, stay on it, and are motivated to abstain. The problem is that in the real world, which seldom resembles the clinical study world, patients are much less interested in this option."



One limitation in the *Lancet* study is it only looked at an inpatient population, which Lembke characterized as "a captive audience." As the researchers acknowledged, this likely made it easier to initiate people on naltrexone. In an outpatient population, naltrexone may fail to retain even more patients — and have even worse outcomes compared to buprenorphine.

### **This is all really important as doctors tackle the opioid crisis**

For the opioid epidemic, the study presents good and bad news.

First, the bad news: Naltrexone is not a wonder drug. It comes with a big downside in that it's much more difficult to start using than buprenorphine.

This accessibility problem is particularly important in addiction medicine. One

of the key hurdles to getting people into treatment is lack of access. As the surgeon general [reported](#) in 2016, only about 10 percent of people with a substance use disorder get specialty treatment. The report attributed that low rate in part to severe shortages in the supply of care — which can lead to waiting periods of weeks or even months.

But access is a problem even in states with plenty of supply. Vermont, for example, has [spent the past few years](#) building up addiction treatment and integrating it into the rest of its health care system through its “hub and spoke” model. As a result, it has managed to cut waiting periods for care, and estimates it has about half of people with an opioid use disorder on medications — much better than the national average. Yet it has struggled to get the other half of potential patients into the system, in large part because hurdles, such as lack of transportation and stigma, remain.

In this context, that naltrexone creates yet another potential barrier by requiring full detox is a big problem. Access is already an issue; anything that makes it even more of one is far from ideal.

Still, there’s good news: Once people are initiated into naltrexone, it fares as well as buprenorphine. That means it can be another option for opioid use disorder patients.

Different options are needed. As Humphreys told me, “In the rest of medicine, we accept that there are multiple treatment paths and that patient preference matters.” The same should be true for addiction. After all, even though buprenorphine is still considered the gold standard for addiction care, the *Lancet* study found it still had an average relapse rate above 50 percent. It’s clear that buprenorphine doesn’t serve all patients and that other options

are needed.

For example, some patients believe that taking buprenorphine or methadone is simply replacing one opioid with another, making them feel like they aren't truly recovering from their addiction. This is a common knock on the drug, but experts argue that it's the wrong way to look at buprenorphine — since it stabilizes addiction and seriously cuts mortality rates, it is simply not the same as using street drugs like heroin and fentanyl. But for patients who sincerely hold this view, having a non-opioid alternative like naltrexone could encourage them to seek treatment.

Naltrexone also only requires one shot a month, while buprenorphine is typically taken daily as a pill. That could make naltrexone much easier for some patients, given that a common problem with medicine is getting people to actually follow their prescriptions.

At the same time, naltrexone is also two to three times as expensive as buprenorphine.

All of these factors and more will need to be considered by health care providers and patients as they decide what treatment to use.

Still, outside of clinical trials, patients often have only one or neither of these options available to them. Alkermes, for one, has [lobbied policymakers](#) to make naltrexone the medication of choice in the criminal justice system. And many counties, particularly in rural areas, have no doctors that can prescribe buprenorphine and no opioid treatment programs that provide medications, according to the [White House's opioid epidemic commission](#).

For now, then, much of the study's findings are largely theoretical. Yes,

buprenorphine seems to have a key advantage. Yes, naltrexone can be an alternative if someone is willing to go through full detox. But until patients actually have access to both drugs, genuine choice will remain illusory — and many people will continue to overdose and die.

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**Correction:** Due to a typo, this article originally misstated the percent of patients who initially dropped out of buprenorphine treatment in the *Lancet* study.

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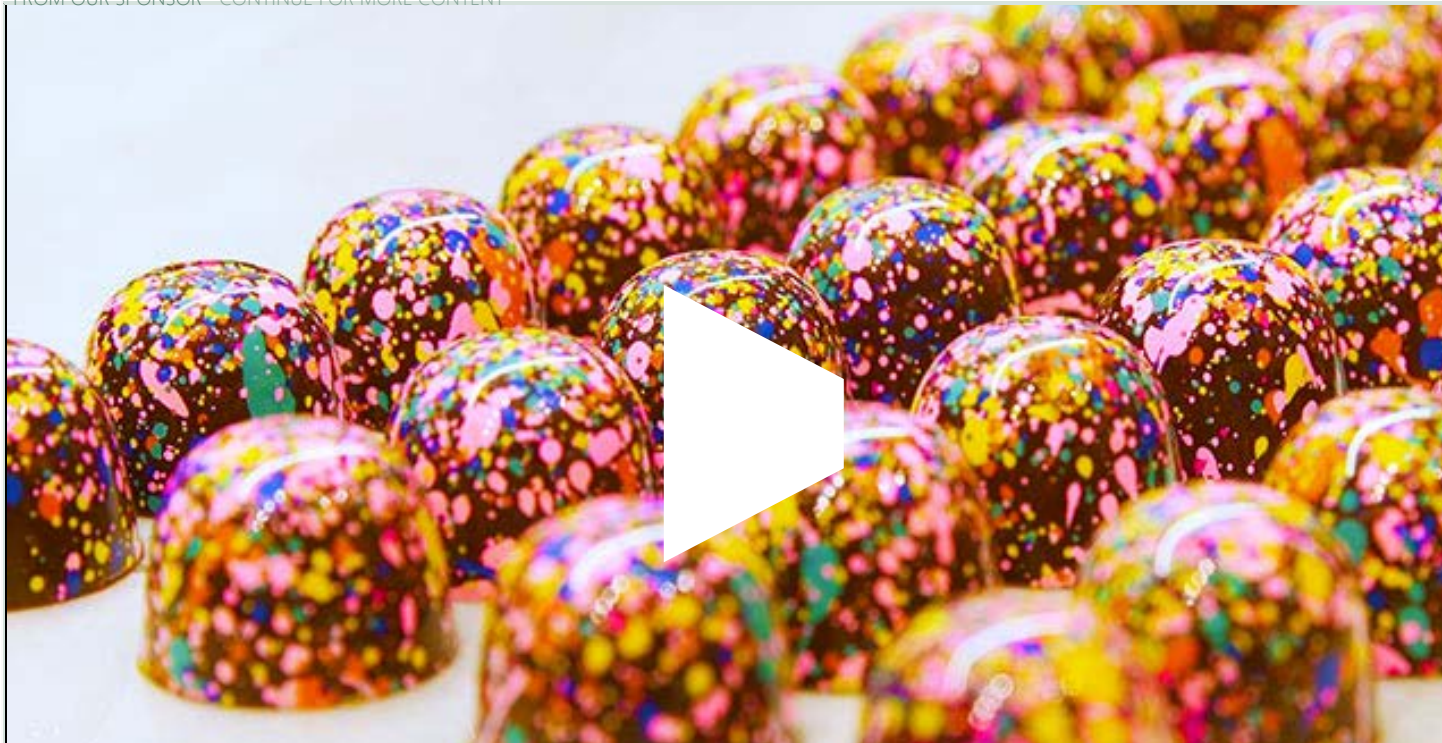
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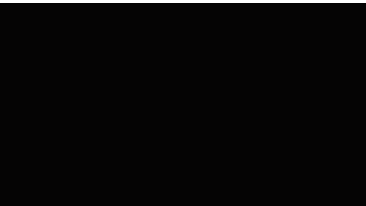
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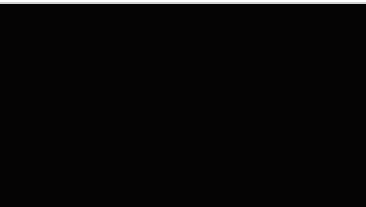
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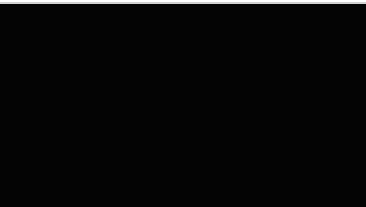


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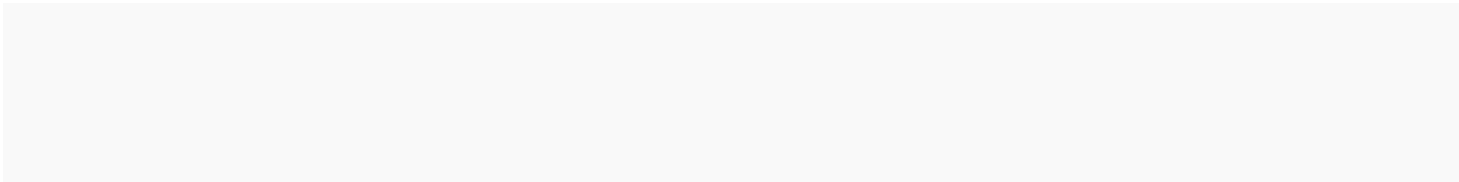
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