Q&A: Methadone is effective for opioid use disorder, so why aren't more patients using it?

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Credit: AI-generated image (disclaimer)

Since the 1970s, methadone has been used to treat opioid use disorder (OUD) with great success—reducing the likelihood of dying from an opioid overdose by 50% or more. Yet for patients and prescribers alike, choosing the drug for OUD treatment is complicated.

That's because methadone is subject to strict prescriber regulations that other FDA-approved OUD medicines, like buprenorphine, aren't—regulations that have been unchanged for half a century. Under these guidelines, methadone may be dispensed only by specially certified providers in particular facilities—meaning your primary care provider can't write you a prescription—and initial dosages are fixed, not personalized for each patient.

Caleb Alexander, MD, MS, a professor in Epidemiology and founding co-director of the Center for Drug Safety and Effectiveness, and Michael Fingerhood, MD, director of Addiction Medicine at the School of Medicine and professor in Mental Health, say these antiquated regulations, along with restrictive monitoring programs and social stigma, are keeping patients from accessing and health care providers from providing this lifesaving medication.

What do we know about the effectiveness of methadone as a treatment for opioid use disorder?

CA: One of the ironies of the opioid epidemic is how much harm has occurred while we have had effective treatments on standby. Methadone, like other FDA-approved treatments for opioid use disorder (OUD), is safe and effective and can reduce the likelihood of dying from an overdose by up to 50%.

Not only do we have well-designed, rigorous randomized clinical studies, we have systematic reviews at the top of the evidence pyramid that synthesize all of the information from these individual studies. And they concur.

MF: Depending on the population, the reduction in mortality rate may even be better than that. If you look at patients who are at the highest

risk of overdose death, like someone who has been released from incarceration, for the first two weeks after release, the impact is likely more than 50%.

The evidence for [the effectiveness of methadone] is overwhelming. All studies point to the fact that methadone has a dramatic impact on saving lives through preventing opioid overdose.

How does it compare to other medications used to treat opioid use disorder?

MF: We have three medications that are approved for treating opioid use disorder: methadone, buprenorphine, and naltrexone. Naltrexone is a pure opioid antagonist—a medication that blocks the activation of opioid receptors in your central or peripheral nervous system—[that is administered by an] injection that lasts 30 days. The patient acceptance rate for naltrexone is not very high. It's very difficult to get people past their first injections to stay on it.

Then we're left with methadone and buprenorphine—and both are very effective. Generally, we have a discussion with patients about how each of [the medications] could fit into their life. Methadone is very regulated in terms of specific treatment programs that provide and dispense the drug. Buprenorphine we've had since 2002, and until then, there was little we could do in an office setting aside from methadone to alleviate opioid withdrawal and treat opioid use disorder.

How does methadone work?

MF: In the late 1960s, researchers showed that if a patient has a long-acting oral opioid on their opioid receptor, they don't go into withdrawal. They don't wake up the next day sick. In fact, what most people with

opioid withdrawal do is try to prevent themselves from being sick. They're not actually high. Methadone on that receptor prevents the big swings between the effects of opioid medication and going into withdrawal.

What are the outcomes for people who receive methadone treatment vs. those who don't?

CA: Addiction is a disease of isolation characterized by chaos. People who are in the throes of active addiction—their lives are dominated by the addiction. The cravings and compulsions and urges to use can be ever-present, and they're incredibly disruptive to any semblance of a healthy and ordered life.

People who are in methadone treatment and entering recovery have increased opportunities and likelihood of maintaining employment, of reconciling with friends and family members, of maintaining stable housing, of reducing other high-risk behaviors that may be injurious to improved health, wellness, and management of other chronic conditions they may have.

It's not just about not dying, it's about living. Methadone allows people to reintegrate with society and live healthy and rewarding lives.

How is it regulated? Why are these regulations so strict?

CA: The regulations require that methadone be dispensed only by specially certified providers in particular settings and limit people's ability to take home methadone. Historically, pre-pandemic, it was all what we call DOT, directly observed therapy, where you would go in [to a facility], get your methadone dose, and be observed taking it. Some of

those policies relaxed during the pandemic.

Other drugs aren't regulated this way, and I think to some degree, methadone has been subject to a bit of exceptionalism. After all, it's not as if other opioids that have been prescribed so heavily are risk-free. And, the opioid epidemic is not an epidemic of methadone overdose. It's an epidemic of overdose of other opioids.

MF: The regulations [on methadone] are 50 years old, and they've never been changed. They say that only specific places can dispense methadone. For the first 90 days of treatment, every patient must show up every day, and their initial dose must be 30 milligrams. In this age of fentanyl, that dose is miniscule and really has little impact.

There are also regulations that a physical exam must be done before the patient can initiate treatment. There can't be initiation of methadone via telemedicine; everything has to be in person. And physicians, nurse practitioners, and physician's assistants can prescribe oxycodone or morphine, yet there are rules that they can't prescribe medication for opioid use disorder without further specialized training.

There was some slight policy relaxation during COVID. SAMHSA [Substance Abuse and Mental Health Services Administration], in coordination with the DEA, announced that there could be take-home doses for the first time within those first 90 days of treatment.

How do we change these regulations?

CA: I think we have to recognize the safety and clinical value of these medicines and their important role in managing opioid use disorder. There are many conditions where we don't have safe and effective treatments. This isn't one of them. Methadone is safe and effective.

Yes, it's prone to diversion. So too is every other opioid. Yes, one can overdose from it. So too can one overdose from many other opioids. We've treated it as if it's a black swan. It's an opioid, and it has some unique features that require care and caution. But I think clinicians are up to the task. Policies that make it easier for clinicians to prescribe methadone are important.

MF: I think people are realizing that there's no evidence that diversion of methadone happened at a greater level during COVID, when a lot of these rules were relaxed. There's no evidence that there were overdoses related to diversion of methadone. COVID taught us that for methadone, relaxing the strict 90-day rule of showing up every day had no negative impact.

Are there other obstacles to prescribing methadone—bias, or insurance restrictions for example?

CA: Fortunately, in 2023, we're at a point where it's going to be pretty hard to find an insurer imposing draconian restrictions on treatments for opioid use disorder. I think insurers have come around and typically will reimburse such treatments as they should be.

I would not be surprised if there's some preference toward [prescribing] buprenorphine. You can prescribe it in primary care, you can give someone a 30-day supply of pills, etc. For methadone, you have to go to a special clinic and come in each day for therapy and be observed swallowing the pill. It introduces this sense that methadone is somehow more problematic.

MF: I treat patients with buprenorphine for opioid use disorder in the primary care setting, where I mix in treatments of hypertension,

diabetes, and their other health problems at the same time. There are people with opioid use disorder who don't want to show up at a place that they sometimes view negatively, and perhaps self-stigmatize going to a program rather than being able to receive medication for opioid use disorder in a "regular" medical center.

Another challenge has been the punitive nature of some outpatient methadone treatment programs. Rather than reward, they work through a punishing model. There's also a strict rule related to attending groups and having regular meetings with counselors. That isn't of benefit for every patient, and some programs are understaffed—they don't have enough counselors. The treatment of opioid use disorder is very pharmacologic. Not to say there are no patients who benefit from counseling, but it's 90% medication and 10% other things.

If it were up to you, how would methadone be prescribed and administered?

MF: As a physician, I should be able to prescribe methadone for opioid use disorder the same way I prescribe buprenorphine, and then a patient should be able to fill it at a pharmacy. That's already happened in Canada and European countries.

The reason it hasn't happened [in the U.S.] is because the majority of methadone treatment programs are for-profit. They try to perpetuate the current rules with a fear that we're going to lose our for-profit methadone treatment programs if we allow any change in the rules of how methadone is used.

CA: There are more than 20,000 products approved by the FDA, and many of them have toxicities equal to or greater than that of methadone.

There's one main question, one elephant in the room, which is, should this just be prescribed and dispensed like other medicines in clinical practice? There are some additional restrictions you could put in place. One middle ground might be a setting that requires prescriber certification, and the FDA has a program for that. That might be the most politically expedient approach that appeases those who are concerned about freeing up access to this medicine.

But if you look at the enormity of harms that continue to occur from overdose in the U.S., and weigh that against the incredible benefits and effectiveness of these medicines, it's hard not to conclude that we need to make changes that make methadone more accessible, easier to prescribe, and easier for patients to take.

What's the biggest misperception you encounter about methadone?

MF: Probably the largest misperception for both buprenorphine and methadone is that you're just substituting one drug for another. That's just stigmatizing and demonstrates a lack of understanding of addiction as a brain disorder. We wouldn't say to somebody who's diabetic, who we are prescribing medication for, that if they could just stop eating and lose weight and exercise, they wouldn't need medication. You also frequently hear people say, "I don't believe in methadone or buprenorphine." If someone goes to a 12 Step meeting, participants might say, "You're not in recovery if you're on medication." That's really unfortunate.

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