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**Kendal Williams (Host):** Welcome everyone to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams. So, over the last several years, we have had two epidemics in the United States. One of them is thankfully receding, the COVID epidemic. But another one is still very much with us and that is the opiate use epidemic. If you do any inpatient time at all, you know that this is still a very common problem. I see much more opiate use problems in hospitalized patients than I do COVID nowadays. Probably, it's the most common thing I see when I do my inpatient time. And there have been significant changes in how we manage opiate abuse. And now, we're trying to do it within primary care.

**Host:** So, to talk about all those changes, I asked two of our Penn colleagues to come on. Dr. Jeff Jaeger is a Professor of Clinical Medicine at Penn. He's been intimately involved in the Penn Internal Medicine Residency Program for much of his career, but then went back and got board-certified in Addiction Medicine and is one of the leaders at Penn in that area. Jeff, thank you.

**Jeffrey Jaeger, MD:** It's a pleasure to be here. Thank you, Kendal.

**Host:** Maggie Lowenstein is an Assistant Professor of Medicine at Penn. She went to med school at Penn, trained at UCSF, and then came back as faculty. She does research focusing on implementing strategies to reduce harm related to opiate use. She serves several roles in Addiction Medicine at Penn. Also, sees patients at Prevention Point, which is a historic nonprofit organization devoted to folks involved in the opiate use epidemic. So, Maggie, thanks so much for coming.

**Margaret Lowenstein, MD:** Thank you.

**Host:** So, you know, I wanted to bring you on to talk about this because there's been these changes. We are very much still in the midst of this. It's very striking when you're on your inpatient blocks of how many young people you see with opiate use. So, let me just lay the land a little bit. Since we've really seen a spike since 2013, the numbers of deaths really started to go up in 2014, 2015 time period. And there's been a tenfold increase over five years. In 2021, we had 106,000 deaths, from opiate use in this country. To give you a sense, this was a recent thing I saw on CNN, in all of the armed conflicts all around the world in 2022, we had 237,000 deaths. So, we're talking about something that is taking the lives of a similar age group to armed conflict. And, you know, it's half as

much in the US as compared to all the armed conflicts worldwide. Largely, that's due to synthetic opioids, which we're going to talk about. Remarkably, life expectancy in the US is actually reduced by about a half a year, largely because of the opioid epidemic. So Maggie, I mean, you do this all the time and feel the breadth of this epidemic. Can you comment on it?

**Margaret Lowenstein, MD:** Yeah. I mean, I think zooming out is really helpful or really important because this is really like a generational challenge. The numbers that you're quoting, the over a hundred thousand deaths in a year over the last several years are actually just overdosed deaths, not including many of the other complications that we know exist that we see in the hospital, or they see in primary care like infections, accidents, things like that. This is a really, really striking problem nationally. And in Philadelphia, we are unfortunately one of the urban epicenters in the US of overdose crisis. We've had more than 1200 deaths in the city of Philadelphia annually over the last couple of years and overdose deaths. And I think we're feeling it in a lot of different clinical settings and, you know, really I think need to take this on as a profession.

**Host:** When this became recognized as a reality several years ago, it was recognized we really needed to change the way we treat opiate use disorder, decentralize it to a large degree. Most of it was done in addiction centers by psychiatrists who could prescribe methadone. And then, recently, they actually got rid of the waiver, which was put in place in order to prescribe Suboxone. Jeff, you have a great way of explaining this whole waiver thing and what it meant in the past and what it means now. Can you explain that for us?

**Jeffrey Jaeger, MD:** Sure, Kendal. So most of us, if not all of us, have trained and practiced in an era when there were significant limitations on who could prescribe medications for opioid use disorder. And you mentioned Suboxone, which is a brand name for a combination of buprenorphine and Naloxone, but there are other formulations of buprenorphine that can be prescribed as well. The waiver refers back to a law that was passed in the early 20th Century that outlawed the prescription of opioids to treat opioid use disorder. So, it used to be well known that if you had someone who was a heroin addict in your practice, you could treat them with morphine or heroin and keep them off the streets. It clearly was not an effective means of treatment and the law was passed, I think, in the 1910s or 1920s to make that practice illegal. When buprenorphine was introduced as a drug with all its potential for treatment, the FDA was skeptical about approving another opioid. And the manufacturer said, "Well, how about we make it so you can only prescribe it if you've gone

through a certain amount of training? And then, we, the manufacturer, plus the FDA will issue a waiver from that law." So, that's what the waiver referred to.

What that led to, unfortunately, was not only a marked decrease in the number of people prescribing this medication, but a sense of stigma associated with the medication that made it seem much more complicated than it actually is. For me, prior to my getting my waiver, it always felt like chemotherapy or some other drug that only experts or people with a special kind of expertise could prescribe. And it wasn't until I did my training that I realized it was a very easy-to-prescribe lifesaving drug. Thankfully, in the last two presidential administrations, both the Trump administration and the Biden administration, the executive branch has pushed to have the waiver removed, and recently it was in fact removed completely.

So, all those restrictions on prescribing buprenorphine, physicians with a DEA no longer have restrictions. Any physician with a DEA can write a prescription for any formulation of buprenorphine, not only to treat opioid use disorder, but to treat pain as well. But that's the background behind the waiver and, thankfully, physicians training now will know nothing of that unusual restriction.

**Host:** We should say that one of the explicit purposes of our podcast today is to try and increase the number of providers in the Philadelphia region, Penn and otherwise, who are inspired to become comfortable treating this with Suboxone. We'll talk about methadone, but that still remains under a restricted environment. But that's part of the reason we're all here, is to talk about what you need to do as a primary care physician if you want to start treating this within your primary care practice. I mentioned methadone and I think it's worth talking about, because that's the historic thing that we all know as a tool to treat opiate addiction. So Maggie, let's talk about methadone and how it's being used nowadays.

**Margaret Lowenstein, MD:** Yeah. So, I think it's important even though we're not actually going to be prescribing it typically or ever currently in primary care to just have a general kind of understanding as internists about methadone and so that we can talk to our patients about treatment options for opioid use disorder. Methadone, as you said, has been around for a while. The first studies of it for opioid use disorder treatment were in the '60s. It is highly effective. You know, the studies actually, it's a little bit more effective in terms of retention than buprenorphine partly because of the environment that it's delivered in likely.

But like buprenorphine, it reduces overdose and all-cause mortality by more than 50%. So, these are incredibly effective medicines compared to most things we use in primary care. So, methadone is a long-acting full opioid agonist. And currently for opioid use disorder treatment in the US, it can only be administered in licensed opioid treatment programs, which are sort of what we colloquially call methadone clinics. These are facilities where people go and take the medicine and sort of under supervision initially. That's a little bit siloed from the rest of the treatment system, so often we're not necessarily educated in that. They will go through a process of up-titrating the medication where patients are assessed and treated typically daily for a time period. And then, as they become more stable, there are certain criteria that they need to meet. They can get take-homes, which means they can not have to attend to the clinic every day, but they can take doses at home.

I think, you know, methadone is still pretty stigmatized and gets a bad rap for many reasons. But I think it's important to just recognize it's a really effective treatment. For some patients, buprenorphine is not as effective. And for others, you know, it is. And, you know, people have different individual preferences. Some of those are clinical and some of those are structural, right? Because going to a methadone clinic every day or very frequently may be more or less appealing to people.

So, the major thing that we should all be able to talk about, I think, is that both are highly effective medications for opioid use disorder treatment. Talk a little bit about sort of the pros and cons in terms of how methadone is delivered in these methadone clinic settings. And then, sort of know where to point people if they're interested in initiating methadone in the community. So, either kind of locating an opioid treatment program that's convenient for the patients, where they live or work and helping them sort of connect there.

**Host:** Maggie, the question I would have if I were to explain this to a patient is how often they actually have to go to the methadone clinic. And you had mentioned there are take-homes. What is the practice currently?

**Margaret Lowenstein, MD:** So, it's highly variable, I will say. And some of that's because like buprenorphine, there's been some policy changes during COVID that have permitted much more flexibility and kind of clinician discretion around how quickly and how many take-homes someone is allowed. I think traditionally really, it was hard to get take-home doses prior to being enrolled for 90 days. So, some clinics, a lot of clinics are closed on Sundays, so you'd maybe get one take-home on Sunday. But in COVID, that was relaxed a bit to allow some discretion and, you know, sort of quicker and more initial

take-homes. But adoption has been sort of variable across clinics. So, it's hard to say exactly, and many are doing take-homes, but maybe only a couple days earlier on. So, it's still going to involve pretty intensive visits and travel and things like that, which has been a big barrier too in otherwise really effective medication.

**Host:** I don't know exactly where all the methadone clinics are, but I would imagine that somebody might have to travel 10, 15 miles to get their dose every day in some circumstances.

**Margaret Lowenstein, MD:** Certainly, I mean, in urban environments, it's a pain, but it's more feasible. I think Wyoming does not have a single methadone clinic. So rural areas in particular, this is really burdensome and you can imagine you could spend hours of your day trying to get to a methadone clinic. So, it's a big issue in a sort of very active policy space. Probably, a little beyond where we're going to go today, but there's lots out there if people are interested.

**Host:** So, suboxone is what we're going to spend most of our time talking about because that is what primary care physicians can prescribe within the context of their practices, can initiate a patient today. If they come in, you can start them right away and there's no limitations and so forth. So, Jeff, let's talk about Suboxone. What's the advantage I suppose?

**Jeffrey Jaeger, MD:** Great. So, Suboxone again is a brand name for a combination drug that includes buprenorphine and naloxone. The naloxone is in the drug not for therapeutic purposes, but as an abuse deterrent. So, you cannot grind up, cook, do, snort Suboxone because the naloxone in the product will counteract the buprenorphine in the product. So, it's important to know that you're not really getting any medical benefit from the naloxone in the product. It's a medication that is taken by a patient either once, twice or three times a day. It is absorbed through the mucosa, so it is taken as a sublingual tablet or as a strip that the patient affixes to their lower lip or their gum and it dissolves and enters the bloodstream that way.

The main advantage to buprenorphine, Suboxone, is that it can be prescribed through your doctor's office. It can be dispensed by a pharmacy like any other medication, and you can come to the physician's office or the provider's office at whatever interval you and the provider decide is appropriate based on where you are in your recovery. That's the main advantage. It mainstreams the treatment of addiction and of opioid use disorder and puts it into the normal path of primary care in much the same way we might initiate semaglutide or another complex medication that we have to counsel patients about that has side

effects, that we're going to see them weekly for a while until they get up to speed and we're making sure they're taking it correctly. And of course, it has side effects and there's some difficulties with it. But that's the main advantage.

The main principles that make it work so well is that it is a mixed agonist antagonist for the opioid receptors. What that effects in real life or what that leads to in practice is you get some opioid effect, you have some of the feeling that you would have by taking the opioid, but there's a ceiling effect on it. So, you get to a certain point and there's no increase in the opioid effect. You don't get an increase in sedation. You don't get the high or the euphoria that comes from taking excessive amounts of opioids. You don't get respiratory depression, which is key. But it suppresses your cravings, it makes you feel like you've taken an opioid that day, and you can go on with your day without that constant craving that consumes the life of someone who's suffering from addiction.

The other key piece of buprenorphine, and this is what makes it more complicated than some other drugs, is that it has highly competitive binding at the receptor site and will knock off any opioid that's currently attached to that receptor site. It will also prevent those opioids from working. So, someone who is religiously taking their Suboxone, if they slip up, if they relapse, if they go to get high, they will not have the same effect from that drug. Now, it's simplistic to say they won't feel anything, and my patients have told me that's a myth. You will feel something if you use Fentanyl, for example, while using Suboxone, but the effect will be marketedly limited. And that's one of the main ways it prevents overdose, is through the competitive binding.

Now, as I mentioned, the dosing formulations, it can be taken sublingually, it can be taken buccally or on the gum or the lip. There's also an injectable form that lasts for about a month, that suits some patients. And again, just as Maggie was saying, just as the daily dosing of methadone is actually helpful for some patients, the idea of having to check in once a day as part of their recovery. For some patients, the idea of taking something daily just feels like taking their opioid back in the bad old days when they were abusing the drug. And that monthly injection is really a godsend. Other patients, they don't like the monthly injection. They'd really rather that daily reminder that the medicine is getting into their system. So, there are a lot of options. I would say that for someone new to the practice of prescribing this, prescribing the injectable formulation, which is called Sublocade, is a little bit more advanced and should probably be reserved until you've gotten your sea legs under you taking care of patients with addiction somewhat.

One of the complexities and part of what the four hours of training used to focus on is the starting of the medication, the initiation of buprenorphine. Because of the competitive binding, there is a phenomenon that occurs when you initiate buprenorphine. If you are taking opioids currently, it will very rapidly bring you into a state of opioid withdrawal. And for patients who have been through this, they will tell you it's the most uncomfortable thing in the world and they will do anything to avoid ever going through that again. We call it precipitated withdrawal. It basically brings about a very severe opioid withdrawal that will knock all the fence nail off your receptors and bring you down to what we think of as an acceptable level of opioid stimulus. Because of that, the traditional teaching has been that the patient has to be completely free of opioids until they are in a pretty uncomfortable state of withdrawal. At which point, taking the Suboxone or the Buprenorphine will make them feel much better. I will say that that traditional teaching in the era of fentanyl and the pharmacodynamics and pharmacokinetics of fentanyl has somewhat gone out the window. Because Fentanyl, while it's a short-acting drug, there are fat stores and that can lead to a sustained level of opioids receptor stimulation by fentanyl. That will make the traditional induction with Suboxone of waiting until withdrawal and starting the drug very problematic. I think, Maggie, you've probably got some more experience with what we call the microdosing or microdose initiation.

**Host:** Before we do that, I want to ask two questions. The first just kind of goes back to the earlier part of what you were saying. We obviously use opiates for pain control. Does Suboxone have any pain benefit?

**Margaret Lowenstein, MD:** So, suboxone does, or buprenorphine in general does have good analgesic properties. You know, it's approved in a buprenorphine-only product actually for pain treatment. And typically, those are at lower doses. Even though buprenorphine formulations common doses of 2, 4, 8 milligrams, those are actually equivalent probably to hundreds of morphine milligram equivalents. It's a very potent drug. So, the pain dosing is often like an order of magnitude less, so like micrograms. But it does have good analgesic properties for many people. When I first started doing this, there was discussion of buprenorphine doesn't really provide good analgesia. And the teaching now is really that it can be used for that. I think a couple of key things to know is that the analgesic properties of buprenorphine typically last only about six to eight hours. And many people take it for opioid use disorder maintenance treatment just once a day. So for patients who have chronic pain or acute pain, you would want to split the dosing to somewhere, you know, three or four times a day. The thought is that there's not a ceiling effect on the pain treatment. But I think because of the partial agonist nature of it, people definitely experience that differently. And so, when folks have acute pain, we'll often actually use short-acting opioids on top of buprenorphine. So, for example, like a surgery or a

fracture or something like that, or in the hospital, we will sort of use both. But I think what Jeff said is really important that you need to kind of have the buprenorphine there first because if you sort of layer on short-acting opioids or other opioids on top of it, the effect may be diminished but will be there. But if you just start with opioid, full agonist opioids and then you put buprenorphine on, it's going to create that very unpleasant precipitated withdrawal phenomenon that we don't want, and patients definitely don't want.

So for patients where you might be thinking about that, you need to talk to them about it. But I think again, the main takeaway is that buprenorphine is effective for pain management. And that's really helpful because a lot of the patients, pain is part of the driver of their ongoing use. And so if you can reassure them that they're going to get some relief, that can be a big way to build rapport and buy-in.

**Host:** So, several years ago, I went through the waiver training and what I learned is that patients do have to stop their existing opiates. You let them get into a withdrawal state. We would measure that by a scale. When they reached a certain level, we would start to dose it. I remember that 16 micrograms I think was in general the average amount that people were going to be on. But you would start with-- I don't remember-- two or four. So as you can see, I haven't done this. So, practically, how would I do this? Let's talk about the classical approach, because we want to start with that. And by the way, this classical approach that Jeff refers to and I just referred to, is it still out there? Is this still what some people do?

**Margaret Lowenstein, MD:** For sure.

**Host:** Okay. So, let's be very practical about the dosing. Maggie, somebody comes in to see you, they're ready to start today. What do you do?

**Margaret Lowenstein, MD:** So, we advise patients to wait to be in mild to moderate withdrawal, which may be a little hard for patients to know exactly what that means. So typically, we think of like three objective signs or symptoms of withdrawal. So, things like sniffly nose, rumbly stomach, like tearing or like a little bit of nausea, things like that, a little bit of goosebumps. So, you want a couple of those typically, and patients are going to know this better than you are. But we wait for those symptoms to appear. And then, there are different induction protocols out there. But I think the one that we have in the Penn Pathways and I personally use is starting with a two-milligram dose. And then, about two hours later, we do an additional two milligrams and sort of take the first eight milligrams in that small dose. So two milligrams, two

milligrams, two milligrams, two milligrams. And then once they're tolerating that, I tell people to take an additional pill. That's a little bit different than an additional eight-milligram pill for a total of 16 milligrams.

I would say that's my practice and you will hear actually a lot of variability among clinicians in their practice. I think the original studies for home induction were starting with a four-milligram dose and then going up to 12 milligrams on day one and up to 16 on day two. And I think what we've learned is that we know that probably 12 to 16 milligrams is the minimum dose that people are going to feel therapeutic on. Those are sort of older data. So, I think in Philadelphia, someone who's using fentanyl, probably 16 milligrams is a minimum dose that want to aim for, and getting them there quicker is okay. Many people end up on three films a day or three eight-milligram films a day, so that's a 24-milligram dose. And because there's a ceiling effect on some of the side effects like respiratory depression, we can be very aggressive in up-titrating Suboxone quickly. So, I think that's another advantage of it. I don't know if this is just making people more sort of confused, but I think there are a lot of protocols out there that you can look at. They all essentially work the same way where you want to sort of clear the opioid receptors and you know that those are cleared by the symptoms that somebody is experiencing of withdrawal. And then, you put the buprenorphine onto the receptors and that relieves those symptoms that people should feel better.

**Host:** When you're starting somebody, Maggie, do you talk to them the next day? I mean, are you seeing them daily for a period of time?

**Margaret Lowenstein, MD:** No, not necessarily. I think, you know, there's a lot of good data at this point supporting the safety of doing an offsite or unobserved induction. So, I feel very comfortable with that. It depends a lot on the patient. For many patients, this is not their first time trying buprenorphine. A lot of people try non-prescribed buprenorphine before getting it in a therapeutic setting or have used it sort of to treat withdrawal here and there, or have tried it before. So, it's actually fairly common that people have tried it before and have some sense of what they're getting into. I will go by the patient. I definitely don't need to see them every day, but I'm happy to check in or sort of just walk them through it if this is their first time or they're feeling nervous. The starting period's really important because you want people to get on it, you want them to feel good and that's a time where we often lose people. So, the handholding is helpful from that perspective, especially if it's the patient is interested.

**Host:** So Jeff, I want to ask you if this is what you do, in terms of how you start, because Maggie mentioned there may be some variability. And then, I'm just

going to ask some really practical questions about prescribing films, how much they cost, where do you get them, that kind of thing.

**Jeffrey Jaeger, MD:** I would say that I've been blessed to be on the receiving end of-- most of my patients are already on buprenorphine. So, the referral pathway in primary care at the downtown campus is generally through the emergency room where patients are initiated on buprenorphine or they're coming out of inpatient or they're coming from a treatment program. We've done for better, for worse, precious few inductions out of our practice. The ones we have done, we've been using what's called a microdosing protocol. And again, similar to what Maggie said about the classical dosing, there's scores of different microdosing protocols out of there. But the general principle around microdosing is you use extremely small doses and you give them to a patient while they're still using opioids. And you ramp it up over several days to the point where their receptors are completely blocked and they don't have to go through precipitated withdrawal. So, you're using sometimes half-milligram doses. You take the two-milligram strips and you have the patient cut it into quarters and they'll take a half milligram on one day, a half milligram the next day, then go up to half milligram twice a day. And again, we have these regimens written out in our smart phrases. I don't have them memorized, but the general gist of it is that the patient doesn't have to go through withdrawal in order to get onto buprenorphine. And this is becoming more and more accepted. So, that's the protocol that I've used having had a number of patients try and fail at the classical induction over the years.

**Margaret Lowenstein, MD:** I think one of the challenging parts, I use microdosing a lot as well, or we sometimes we hear it called like low-dose induction or ultra-low-dose induction. I think as providers, currently we're not allowed to prescribe opioid agonists like outside for treatment of OUD. So, you're basically relying on the patient to continue to use whatever they're using on the street, as they're sort of agonists, while you up-titrate the buprenorphine. And as Jeff said, I think this is becoming a more accepted practice. It's sort of a practical, you know, it works well and it's obviously harm reduction. We want people to get onto treatment, but I think it does rely on the patient continuing to take their street drug supply typically. And so, I think that's worth mentioning, that often the biggest challenge in the low-dose induction is people sort of pull back on their street drugs and then don't feel so hot and you're trying to figure out is it the buprenorphine or is it just regular old withdrawal, which often it's usually the latter.

So, there's some great protocols that are out there. There's also, I think, on Penn Pathways and on the Penn Center for Addiction Medicine and Policy website,

we have some patient handouts that we've created to give to people. But that's where I do tend to follow patients more closely, because sometimes you need to do a little tweaking and coaching. So if you're thinking about that approach and you're a novice, it might be a good idea to call a friend. But I've pretty much always been able to get it to work. It just takes some doing sometimes.

**Host:** So if somebody slips into withdrawal, because they don't have access to their native drug, if you will, I mean, you just switch them over to the classical pathway and just go through it that way, right? I mean, you could potentially just do it that way.

**Margaret Lowenstein, MD:** Yeah, I think one of the challenges is just fentanyl is a little bit different. Because it's stored in the fat, we know that people often will sort of have detectable fentanyl levels for days or even sometimes weeks out. And in terms of the half-life practically in the body for someone who uses chronic high-dose fentanyl, it's almost like methadone, like it lasts very long time. And it's also incredibly potent and people use it very frequently. So, people may start to feel some withdrawal or not feel so great, but they'll still have fentanyl in their body. And those are the folks where I think they've often tell us that they've struggled with a classic induction or they're nervous about precept, they'll call it. So, those are the patients I definitely think of offering the low-dose induction to.

**Host:** So, you're just having them take the half a milligram, and they're adjusting it as they go and as they start to feel like their Suboxone dose is high enough, then they stop using their native drug, right?

**Jeffrey Jaeger, MD:** Yeah. Ideally, that's the way it should work. I mean, there's always bumps in the road. The patient has to be committed to recovery, committed to abstinence at some point as a goal. So, there's challenges, there's very rarely a straight linear path towards this. But when it works, it works great. It works very well in the hospital. You know, we've got microinduction pathways in the hospital. And the hospital's great because you've got supportive nurses, supportive staff. You've got someone to make sure they get the medication that they're taking it correctly. So, it works a little better there. When you've got someone who knows that, as my patient has once told me, it's easier to get fentanyl around here than to find a good electrician. You know, when they know it's right outside their door, it's more of a challenge to get someone to suffer through those first few days.

**Margaret Lowenstein, MD:** I will say though, I think it's important for people who might be listening to this and feeling a little intimidated or like, "Ooh," you

know, buprenorphine is very effective with or without perfect adherence and with or without perfect abstinence. Like it's a long-acting drug, it reduces overdoses substantially, even if people continue to use opioids and definitely also if they continue to use other substances.

So, I think when I first started doing this in residency, like it was a little iffy to continue to prescribe buprenorphine if someone was using other substances and definitely if someone was using opiates. But at this point, I think we really recognize that there's a lot of benefit to the medication, even for folks who aren't sort of ready, I'm using air quotes, you can't see or hear that, but people who are sort of ready in the traditional sense. If they're taking their buprenorphine, like they're going to likely see a benefit and a mortality reduction and reduction of a lot of other really serious outcomes. So, I think for folks new to this, it can be a little intimidating to think about, "Oh, my patient's going to keep using drugs, or could keep using drugs" and, you know, "Am I going to get in trouble or am I harming the patient?" And the answer is no, you are not. Like if they're taking their buprenorphine, they're very likely seeing a benefit. And it's okay even if folks have bumps in the road or continue to use.

**Jeffrey Jaeger, MD:** That's really a key point. And I would emphasize, that when I first started doing this, I was working on a model of strict adherence to opioid treatment plans for my patients who had been on oxycodone for years or Dilaudid or MS Contin with finger-wagging at abnormal urine tests and not showing up for appointments. And I've really moved over to a model of, if you showed up this week, it's a good week. You know, there are people like you who never come back to a doctor or who, god forbid, end up dead from their opioid use. So, maybe you didn't take it right this week, maybe you relapsed once or twice in the week or the month, you know, however off we're seeing them. But you're back here again, and we can high five and say, "This was a successful month." And we're moving towards a future where you can resume life, resume work, resume care of your family. And there's going to be bumps in the road. And like Maggie said, it's almost impossible to do harm with this drug. It's a really easy-to-use medication that is a life-saving drug and pretty remarkably safe compared to a lot of the other medications we prescribe.

**Margaret Lowenstein, MD:** What Jeff described I think is very akin to what we do a lot in primary care, whether it's diabetes or other chronic disease management where people may not have perfect adherence or do all the behavior changes we counsel them on. So, I actually think as primary care doctors, we're pretty well positioned to do this kind of harm reduction in meeting patients where they are. And this particular skill may feel new, but it's something we do all the time. And when I'm stuck on a tough case, I will sort of

switch out in my mind and say like, "Okay. If this were diabetes and the patient wasn't doing the thing I wanted them to do, or they were doing X, Y, or Z, like, how would I handle it?" And I find that really helpful because we're all like trained to do this as primary care doctors.

**Host:** So, I'm going to ask some very practical questions. So, a film is new to us, right? So Jeff, you had mentioned comes in films, comes in sublingual tablets, and then the depot injection, that's basically a month's worth, right? But then, when you guys started talking, you didn't talk at all about the sublingual. Is that because it's expensive or not available or...?

**Jeffrey Jaeger, MD:** You know, if you swallow the medication, it doesn't work. It doesn't get absorbed through the gastric mucosa. So, the way you are supposed to use the sublingual tablet, if you read about how to take the medication, it's almost comical about how challenging it is. You put the drug under your tongue, you try not to swallow your saliva. You shouldn't be talking too much because you naturally swallow while you're talking. You have to lean forward so the saliva doesn't run down your throat. It's the cheaper version of the medication. And many insurance companies used to require us to use the sublingual first before they'd let us prescribe the film. So, everybody had to go through this. You'd had to prescribe this and have the patient come back and say, "It was gross. I don't like the taste. It burned under my tongue." So, I think I only have one or two patients still using the sublingual.

Now, I think most insurers are willing to cover the film because they know adherence is so much better, and the film is so easy. I mean, I've had patients take it in front of me. They open the film. They love showing me, "I'm here. I'm taking my drug. I'm saving my life. We're doing this together." And they'll just pull down their lip, put it on there, and then they just keep talking and having a conversation. So, it's a much easier drug to take as the film. It looks like a little Band-Aid. It's a tiny little Band-Aid that sticks to the gum.

**Margaret Lowenstein, MD:** But both are sublingually absorbed though. It's just that the film is much more palatable than the tablet.

**Host:** I don't think I've ever eaten a Lifesaver in my life and actually gotten through the whole thing just in my mouth without chewing it or swallowing it or something. I mean, that thing never makes it to the full dissolved state. Okay. So, I got a patient in front of me. I'm going to order this and I'm going to order films. Now, Maggie, you said two milligrams. Let's say there's a half a milligram. The films come in two, four, and eight, you said?

**Margaret Lowenstein, MD:** Yup.

**Host:** So if you're doing microinduction, let's start with that. You give them two-milligram ones, you tell them to cut it in four, right?

**Margaret Lowenstein, MD:** That honestly is sometimes the hardest part of the microinduction is getting people to cut the films correctly. But I'll usually provide lower dose films and tell them to cut it. And then, you'll start with 0.5 milligrams and then go to one milligram, so half a strip and then two milligrams. And we have on our website that I mentioned, and I'll plug again at Penn Center for Addiction Medicine and Policy, we have these patient handouts that actually show pictures of how to cut the films, because numeracy can be challenging with this. And then for more traditional inductions, I'll prescribe eight milligrams and I'll instruct them to cut their first film into four pieces and start with the twos. And honestly, that's part of why I use that approach is just it's easier to explain to patients than trying to like do multiple cuts and multiple doses. So, some of this is guided by practicality.

**Host:** So if you're doing classic, you're going to do eight milligrams. You're going to cut it up and dose it that way. If you're doing microinduction, you're going to give two milligrams, but you're going to cut it up the same way and you're going to dose it like that. That sounds pretty, I can do that. If I can prescribe ozempic, which actually Wegovy is harder, I think, still I usually try Ozempic and I tell patients that I want you to start on the lower dose, but the reality is that I just don't prescribe Wegovy very well, and I just want to do this. In any case, that's another subject. So, you send two milligrams to the pharmacy, they go pick it up, and maybe you've shown them on a handout exactly how to do it. Okay. It's great. And the Penn Pathway site is good.

Now, let's talk about fentanyl a little bit because this whole thing is about fentanyl. The reason we're in this situation is largely because of the use of synthetic opioids. You mentioned that it does produce a ceiling effect. And one of the most important things you said in this whole podcast, I think, is that when you're on Suboxone, even if you're using, you're less likely to overdose, right? But fentanyl's a very powerful agent, right? And it's highly addictive and it lives in the fat. So, that's creating a lot more challenges. Is there anything more to say about the fentanyl aspect of this whole process?

**Margaret Lowenstein, MD:** Okay. I would say fentanyl, I mean, part of it is it's still an opiate. There's nothing sort of magical or, you know, totally wildly different about it. I do think that the long-lasting nature of it can present challenges that we've sort of gone over. But the other challenges I think are just

that we find that folks have very high tolerances and the sort of euphoric effects of fentanyl are fairly short-lasting. And so, what anecdotally and sort of some of the research has shown is that people tend to use more frequently. The olden days, people would use heroin maybe three, four times a day. Now, people often are injecting fentanyl like 10 or more times a day, is not totally uncommon. So every time you have an injection, you're more prone to complications or various risks, overdose, infection, things like that. So, I just think it's sort of amplified a lot of the preexisting risks and complications that we've seen. And people often need more higher doses to manage craving and withdrawal.

**Jeffrey Jaeger, MD:** And I do think it's not only do they need higher doses of the narcotic, it's whopping numbers in terms of morphine milligram equivalents. So when patients with fentanyl addiction come into the hospital, the amount of opioids they will need to get pain relief and to avoid withdrawal is in the range of numbers we've never, ever used. And I can't believe I've gotten accustomed to this. But since I've started doing addiction medicine, I'm recommending doses, you know, for patients in the hospital just to keep them in the hospital of 60, 80, 100 milligrams of oxycodone every four hours just to keep them in the hospital, keep them from going into withdrawal. So, it's just mind-blowing to see what happens the more and more fentanyl you use. And I think early on, some of us were disbelieving about just how much fentanyl people could be using and still be alive. But it's the nature of the opioid, it's the nature of any addictive substance that you get tolerance and you need more and more to gain the same effect.

I think one important principle that's come up in the Fentanyl era, but it's true of addiction no matter what, is that once you're on a drug and you've been using it for a long time, you're not using it to feel good, you're using it to feel normal. And the absence of the drug makes you feel awful. So, a lot of the stigma around drugs is that these people don't want to live in reality, they want to escape. And the reality is whether it's nicotine or benzodiazepines, alcohol or opioids, once you're in the throes of the use disorder, you're just using it to not feel horrible. And the nature of fentanyl, unfortunately, and a lot of the adulterants that are in it, is that it can cause this awful respiratory depression. The people we see slumped over on the subway sometimes and half asleep on the street. But as that element of it wears off, they may feel normal first before they start to go into withdrawal. So, it's just an important part of finding empathy for these patients and welcoming them into our practice and finding ways to communicate with them that says you understand the nature of this horrible disease.

**Host:** So, the other drug that we've all come to know very well in all of this opiate use epidemic is Narcan. And so, Maggie, how does Suboxone and street drugs, how does it all feed into Narcan? How do we understand Narcan?

**Margaret Lowenstein, MD:** So, Narcan is the brand for naloxone, and it's the opioid reversal agent. So, it's a strong opioid antagonist and is used to reverse opioid overdoses. At this point, Narcan is an incredibly important public health intervention and we really should be doing as much as we can to get it in the hands of patients either likely or at risk of overdose themselves or at risk of sort of witnessing or, you know, coming into contact with an overdose. I carry Narcan myself, I've used it in the community. I mean, we live in a city where overdose is prevalent. So, it's really important to empower people to use it. And I think sometimes it's guideline-based for anybody who either has opioid use disorder, whether they're in treatment or not, to prescribe Narcan, similarly for like high dose chronic opioids or opioids plus benzos.

I think the other really important group that we often overlook with Narcan are people using other substances that are not opioids. We know, and that's something that we've seen more in this fentanyl era as well, is contamination of other drugs. So, people purchasing stimulants, buying things that they think are pills but are actually sort of pressed tablets that may contain fentanyl. You know, many street drugs actually have fentanyl in them at this point in Philadelphia and many places in the country. And the real danger there is that many folks using some of those drugs may be opioid-naive. I think this is a really important opportunity. You know, folks who are using actually a wide variety of substances really would benefit from Narcan and a discussion about that. There's also fentanyl test strips, which can be used for drug checking and are primarily useful for non-opioid drugs because we know most street opioids in Philadelphia are fentanyl, but people using pills or powdered substances like stimulants.

So, again, this is a little bit like outside our comfort zone, I think, often as primary care doctors. But it's probably one of the most valuable preventative interventions we can do for folks using a wide variety of drugs. Narcan is prescribed and covered with no copay by all the Pennsylvania Medicaid plans. Some of the commercial plans have a little bit higher of a copay, but there are free resources out there where patients can get copay assistance or free mailed Narcan. And it was recently FDA approved to be over-the-counter. And so, we're still sort of seeing how that's going to play out in terms of cost and access. But it was obviously deemed to be safe enough to be over-the-counter. It doesn't cause harm if you administer Narcan to someone who's not overdosing. So,

there's really like very little downside and huge upside. It can save somebody's life with just a little spritz in the nose, like a Flonase dose.

**Host:** If I wanted to get it for myself to carry, how do I get it? I don't even know the answer to this.

**Jeffrey Jaeger, MD:** You can just walk into a pharmacy and say, "I'd like my Narcan." In the state of Pennsylvania, we all have a prescription for it on file signed by the state. I forget her name, but the head physician in the state basically signed a blanket prescription for anyone in the state. You walk in, they process it like any other prescription, it goes through your insurance. They will bill your insurance company, charge you whatever copay your insurance says that you need to pay and you'll walk out with your Narcan. Like Maggie, I keep one in each car. My kids know that there's one in each car. If you come up on someone who's unresponsive, you know, give Narcan, call 911. We keep track of the expiration dates. We replace them when they need to be replaced. And it's just important to normalize it. If you're taking chronic opioids or your patients are taking chronic opioids, there should be Narcan in the house and a caregiver should know how to use the medication.

And I think for many of my patients, that's made them aware of just how high risk a medication their high dose oxy is. When I say you need this drug in your house, because you're at higher than average or higher than acceptable risk of doing your self-harm unintentionally with this medication. So, I totally agree with Maggie that we need to normalize having it everywhere these days.

**Host:** So, I want to bring you back to talk about specific scenarios and I just want to put it out there to the Penn primary Care community, if you have specific questions for Maggie and Jeff, please email me within the email system and we'll do another podcast and bring those back. And there are some specific scenarios that I want to get to, but we're not going to be able to do that today.

What I do want to ask is another scenario that may be common and that as a patient shows up as a new patient in your office, they're on suboxone, their previous primary care provider in, I don't know, Ohio, prescribed it for them and now they need a prescription from you because you're their new doc. I assume it's just a matter of continuing the same dose and writing the prescription and that should be it. I mean, if they're at their dose that's effective for them, there shouldn't need to be some dose titration in that scenario, right?

**Jeffrey Jaeger, MD:** Right. So, we see this scenario a lot of the time. So, we treat it like any other opioid. We have the patient sign an opioid agreement in

the practice that stipulates what their rights are, what their responsibilities are, and what the responsibilities of the practice are in prescribing this medication, including that we will do periodic urine testing to assure you're taking the medication correctly and that it's getting into your system, and that you're not taking medications that might make this a more complicated drug, that you'll show up for appointments, that you will attend to any specialist appointments we ask you to attend to, including, if necessary, mental healthcare. So, that's our standard opioid use agreement. And anybody taking Suboxone signs off on that.

We do monthly visits for nearly everyone. In part because you can't write for more than a month of opioids and it's a natural time to check in with someone. And in part, it's just nice to make sure the drug's still working. When you're talking about overdose prevention, it's great to see everybody once a month and just make sure, "How's your recovery going? Is this controlling your cravings?" I do have several patients who are so stable in their recovery and they're working full-time and they say, "Can't we space this out to two months?" And I've done that a couple of times and we treat it like any other opioid. But as of yet, I'm not on the quarterly basis with any of my patients.

Urine testing is pretty straightforward. We send off a urine drug screen in the Penn system. If there's any opiates, they will check to make sure the opiates are there and you're looking for buprenorphine as well as the buprenorphine metabolites. Norbuprenorphine is the metabolite you want to look for. And I think I can speak for Maggie and say any of us with addiction expertise will help guide you through interpretation of a urine drug screen. It's a little complex the first time you see it, but it's not that complicated and it's an easy skill to learn as to how to interpret the drug screens.

Other than that, it's a pretty straightforward drug to use. Patients take it, they know they need it. When they start to run out, they call for refills. Probably, the hardest thing is just making space for the patient on the schedule once a month because we all have access issues. But frankly, these visits have gotten pretty quick for some of my more stable patients.

**Host:** Do you do telemedicine?

**Jeffrey Jaeger, MD:** We have a number of patients we're doing telemedicine for standing, you know, who have been on it for a while. During the pandemic, we were allowed to do initiations over telemedicine. Maggie, I'm not sure, is that still the case that you can do initiations?

**Margaret Lowenstein, MD:** That is correct. There's still some flux about how long you can keep a patient solely telehealth. The DEA has a proposed rule out that got a lot of pushback. And so, that's kind of still under discussion. But yes, you can still initiate buprenorphine via telehealth now.

**Jeffrey Jaeger, MD:** Certainly during the pandemic, everybody was getting telehealth. And many of the patients found that it worked great for them if they don't live close to Penn. We do insist on coming in to drop off a urine at least quarterly for our patients who are on telehealth.

**Margaret Lowenstein, MD:** Yeah. I use telehealth a lot too often, even for my less stable patients where I want to be checking in with them more regularly and not necessarily send them off with a month of prescription and sort of hope for the best, but it is burdensome for them to come in. So, you were actually always allowed to do telehealth for followup, but it really only became a more normalized practice during COVID. And I think it's a really great tool to have when you're asking patients to see you very often. It can, you know, kind of reduce the burden but still allow you to check in and use it and interspersed with in-person visits pretty frequently.

**Host:** I want to ask about the urine drug screen. So, you're testing, the vibe I got from you both earlier, is that if another drug shows up, you're like, "Hey, that's what it is." And you have that kind of communication with your patients such that, you know, it used to be that people get kicked out of clinics and all this stuff, but that's not happening anymore, but you also are monitoring their use of other agents. Even though some of them may not work very well, like oxycodone, I don't think works very well if you're already on Suboxone. But nevertheless, you're monitoring that.

**Jeffrey Jaeger, MD:** Well, the common scenarios are patients taking other illicits or non-prescribed drugs along with their buprenorphine. And it is dangerous to take benzodiazepines with an opioid, even if it's buprenorphine. If I have a patient regularly taking benzodiazepines, again, we won't kick them out of the practice, we do often suggest that this is not the right setting for them, that they should maybe be in an addiction treatment program that we will aim to get them off their benzos. Sometimes a methadone program is better for them because it gets them in front of an addiction specialist on a daily basis who can help them in their recovery and help them avoid dangerous drug combinations. So, that's a common scenario that we see patients abusing benzodiazepines while they're in their recovery and taking buprenorphine, and that's a challenging one.

The other scenario that we see less often is patients simply not taking their buprenorphine. And when that's the case, most of us will after a while say, "Okay. I can't continue to prescribe this medicine. For whatever reason, it's not getting in your system." I don't accuse the patient of selling it or diverting it. I'll just say, "I don't know why this isn't working, but it's not in your body. So, I can't in good conscience continue to prescribe a medication that is not getting into your bloodstream and then into your urine. So, we've got to come up with a different solution for your use disorder."

**Margaret Lowenstein, MD:** And when that happens, which it does occasionally happen, I think that's often a reason that people are like very hesitant to prescribe. But we know that buprenorphine that gets diverted or sold or given away is usually used for the same reasons that we use it for treatment. So, I'm not a proponent of diverted buprenorphine. But I think from a safety perspective, there's a little different story than someone selling their month supply of oxycodone. I do a similar thing to Jeff in terms of how I talk about it with patients, but I will say like, "Here are a couple of other options. Maybe methadone, maybe this, maybe that." And I'll also sort of invite them to come back and continue to be my primary care patient. And I've definitely had patients where I've stopped prescribing buprenorphine, but we've maintained some relationship. And down the line, they're like, "You know what, I'm ready for it again." And it's been successful.

So, I do think that's another advantage of doing this in primary care is that we have reasons to see people besides addiction. So like maybe someone's not doing well from an addiction perspective, maybe they stop coming for a little while, but they'll come back and we can treat their hep C and we can do other things and then we can restart them on buprenorphine. So, I really do try to treat each sort of engagement as a fresh start and really try to let people know that the door's open. Because we're primary care, we can see them for whatever they need. That has varying levels of success, but I think philosophically that's a real advantage to doing it in our setting.

And, you know, we know that buprenorphine treatment or all medications for opioid use disorder only treat opioid use disorder. So, we shouldn't expect that someone struggling with other substance use disorder is going to just immediately stop. And, you know, I agree with Jeff, sometimes a little bit of a higher level of care is important. But really, you know, if someone's taking their buprenorphine, It's almost always advantageous to continue to prescribe it to them, because the alternative of abusing fentanyl is going to be far more dangerous. So, we think about ways to increased structure, increased support. But I really am loathed to stop buprenorphine in someone who's taking it, even

if they're using other substances because, you know, it really is a lifesaving drug.

I think for novices though, really the easiest way to get started is sort of the scenario you started this question with, Kendal, which is like a patient who's stable on buprenorphine. I think it's going to be like the easiest visit you've ever had. Are they taking their medicine? Are they having withdrawal? Are they having craving? Are they using anything? No. Great. See you in a month. And you can see just like how effective this medication is. And it's just so gratifying you hear people's stories and sort of hear where they've come from and where they are now. It's a real like antidote to I think some of the day-to-day struggles or burnout that sometimes we feel in primary care. So, I think like the complicated questions like Jeff said, many of us are really happy to help answer those things, but I think getting your feet wet and just sort of trying one patient who's already on buprenorphine, just kind of try out maintenance treatment like, I think you'll be surprised how easy it is and it can be really gratifying.

**Host:** Maggie, I was going to ask you for something to say to the primary care community to end this podcast, and I think that was actually a very nice way to phrase it. Jeff, do you have any thoughts to finish off of what people should know?

**Jeffrey Jaeger, MD:** No, I'll just echo what Maggie said. It's been truly my burnout prevention tool is doing this work. And it was rare that I would have a day with tears and hugs in primary care where people really felt like I had saved their lives. And there's not a week that goes by at our buprenorphine clinic where I don't have someone show me pictures of their kids, show me their certificate at completing, you know, the union certification for being a pipe fitter, or just tell me once again how surprised their family is that they're still alive. And there's tears, there's true gratitude. And it's been really a very rewarding shift in my career. So, I strongly encourage people to ask us questions, ask people who've prescribed it before and add it to your toolbox.

**Host:** Well, that's terrific. I'm just going to end by saying again that if you have specific questions that you'd like us to review in a part two of this podcast coming up sometime in the future, please email me. And thanks again for joining the Penn Primary Care Podcast. Thanks to Jeff and Maggie for being here. Come back again next time.