#401: Updates in Addiction Medicine – SGIM 2023

Matt: Hey, Paul, I'm excited to tell you that we are launching a Curbsiders Patreon. Have you heard about this?

Paul: I did because I work with you, but tell me more about it.

Matt: [laughs] All right, Paul. Well, we want to be able to keep offering this great free content and we're doing things like upgrading our website, we offer transcripts now for episodes, recording new seasons of our miniseries, Teach and Addiction Medicine, the Digest is growing. And Paul, now we're on video. People could see us as we're talking right here.

Paul: What a treat for our listeners.

Matt: That's right. So, with Kashlak Admitting Privileges, they're going to get all episodes ad free, that's the whole back catalog, plus future episodes, and twice monthly, there're going to be bonus episodes where me and you recap a show and answer some listener questions. So, people should sign up today at *patreon.com/curbsiders,* and you get a whole lot of more of Paul, America's PCP.

Paul: [laughs]

[Disclaimer]

[The Curbsiders theme]

Matt: Here we are back with *The* Addiction Medicine crew again and a very special cohost. I should introduce myself first. I'm Dr. Matthew Watto, here with my great friend, Dr. Paul Nelson Williams, who must be sick of traveling with me at this point.

Paul: [laughs] It's been three straight weeks.

Matt: Yeah. And with us is Dr. Carolyn Chan. She is the host of our Addiction Medicine podcast, and a friend for many years now, and an Addiction Medicine physician herself. Carolyn, welcome back.

Carolyn: Really excited to be here.

Matt: So, you and Paul are going to walk us through this. I guess, we should probably let Paul tell people what it is that we do on Curbsiders before we get started. So, Paul, do you want to say your piece?

Paul: For sure. [laughs] Thanks for the chance. We are *the* Internal Medicine Podcast. We use expert interviews to bring you clinical pearls and practice-changing knowledge. And we have 4,000 experts with us right now?

Matt: Yes, and a lot to get through. So, I think we should just get to it. We will introduce all our wonderful experts. Well, you can look up their names in the show description, but also, we will introduce them as they come on mic.

Carolyn: You guys just gave amazing clinical updates in Addiction Medicine. I think my first question for you guys is we know that the X waiver, which was required to prescribe buprenorphine has been eliminated. So, I was wondering if folks could talk a little bit more about that and what this means for all the primary care docs listening.

Kenneth: All right. Well, thanks for that question, Carolyn. I'm Kenny Morford. I'm a General Internist and Addiction Medicine physician. Yeah, this is exciting news for us. So, in December of 2022, Congress passed the omnibus bill, and that included something called

the MAT Act, which is the Mainstreaming Addiction Treatment Act that announced the immediate elimination of the X waiver for prescribing buprenorphine for the treatment of opioid use disorder. So, what that means is that for any practitioner who has a DA registration that has Schedule III authority, they can now prescribe buprenorphine for OUD if permitted by state law. So, that's an important caveat to this is that, there are certain states where they still have training requirements. If those are in place, then that will take precedence over the federal law.

But with that said, some other things that are important about this MAT Act. So, anyone with a DEA registration can prescribe BUPE. It also means that these other federal requirements are out the window, so that includes discipline restrictions, patient limits. It used to be a 30-patient limit for how many prescriptions of buprenorphine you could write, as well as provision of counseling. So, that used to be a requirement to prescribe buprenorphine. You no longer have to have counseling services available to prescribe this medication.

Matt: We were asking you beforehand, do we have an idea of which states, is there anywhere we can point people of a handy list like, "Hey, your state is on this list, so you have to still do the training"?

Kenneth: So, I have yet to be able to find a list that just tells me which states these are. Actually, in the guidance we got from the DEA and SAMHSA about this announcement, they said for registrants to check with their state laws and see what they say. So, I've googled this. I just can't find it. I think part of it has to do with how dynamic the process is of which states may have laws in place that restrict buprenorphine prescribing. I think, Stefan, do you want to comment a bit on your experience?

Stefan: Most of the states can handle their decisions by entrusting them to a medical board which may not be in law. So, it may be wisest if you are an MD at least or an ODO to start with the medical board and say, "What do we know here?" Because those rules will not always be passed by the legislature.

Carolyn: I know too. Even when the X waiver was in place, we still had so many challenges getting folks to prescribe buprenorphine. What do you foresee or anticipate in next five years? Do we think we'll actually see a significant uptake in buprenorphine prescribing?

Kenneth: That's a great question. That is why this Act passed. The whole purpose is to get people to treat more opioid use disorder to relax these restrictions that really were unnecessary and a huge barrier to treating people with opioid use disorder. But we don't know right now. I think that there's a lot of stigma around substance use in general. Medical professionals are not adequately trained in how to treat people with substance use disorders. So, this is something we have to see, and I think it has to be paired with adequate training that happens at all levels, at the student level, residency and continuing medical education.

Stefan: I think it would help, if a number of celebrities came out and said that they had started buprenorphine recently and it was helping them, because just think about the people who are running to get a glutide like Ozempic now. As soon as everyone's talking about it, people start saying, "Okay, maybe this is for me.

Paul: So, the administrative burden has been reduced somewhat, so we no longer have to have a separate number. The patient tracking was a nightmare. I don't know if anyone was doing it particularly well. The counseling thing, I think it made some folks nervous. So, that's all great. From an individual prescriber standpoint, what is the education requirement going

to look like for them, and how might that--? I guess, so the administrative burden being taken care of, now what's the education component going to look like?

Kenneth: That's a great question, because it gets to the second part of the omnibus bill. So, same thing that was passed. There was actually another part of that bill called the MATE Act. So, not the MAT Act, but the MATE Act.

Paul: Perfect. [crosstalk] No, no.

Kenneth: Just to confuse all of us, right. It stands for The Medication Access and Training Expansion Act. I think what's important there is that it's pairing both medication access with training, which I think a lot of us were happy to see. So, there is a new training requirement that the DEA has now put out. It's a onetime eight-hour training requirement on the treatment of patients with opioid or other substance use disorders. And this is going to be required through basically a box that you checkoff when you either apply for your initial or renewal of your DEA registration.

Matt: I just did mine last week. Super easy. I just checked it off. In my case, it was true. I have been doing the work, but don't you have some concerns about this being a onetime thing?

Kenneth: I do. Oh, it's great that we now have a training requirement that's broader than just buprenorphine prescribing for opioid use disorder. This is for all substance use disorders. Before I get into my concerns about it to clarify what is this requirement, well, it's cumulative. So, it means you need to have a total of eight hours, which can include past trainings that people have done. So, if someone's been X waivered, they went through the DEA X waiver training in the past that counts. You can click that box. Similarly, if you're board-certified in Addiction Medicine or Addiction Psychiatry, you've satisfied the requirement, any other accredited trainings on substance use disorders will count towards this training requirement.

Matt: Does this include your podcast, Curbsiders, Addiction Medicine?

Kenneth: In fact, it does.

[laughter]

Matt: Shameless plug.

Kenneth: Yeah. But check it out, everybody. Also, the Addiction Episodes for Curbsiders Internal Medicine will count towards this as well. Oh, one other way to satisfy the requirement is that, if you've graduated from an accredited medical, dental, advanced practice nursing or PA school in the US in the past five years that has an eight-hour curriculum on substance use disorders, then those graduates will also be able to satisfy the requirement.

But to this question about, is this a satisfactory requirement? I think it's a start. But importantly, once you check off this box, it's never going to show up again on any of your subsequent DEA registration renewals. I'm concerned about that, because I think that we've seen so many changes with the drug landscape, with the field of addiction medicine, our available treatments, how we start buprenorphine, how we respond to fentanyl. Now we have xylazine, which I think we're going to talk about a bit later. Those have all happened in the past few years. We're saying that, if we do this one-time training, then you are good for life. It just seems inadequate. So, I would love to see something that incorporates--

Not trying to put more barriers on what we have to do to get a DEA license, but at least have more check ins or somehow ensure that people are up-to-date on how to treat people with substance use disorders.

Matt: All right. So, one more point we wanted to ask you about, I think. Carolyn, we have one last thing in this section on policy? Oh, yeah.

Kenneth: There's the baby.

Carolyn: Yeah, there is a baby in the background. Hot off the press that the baby is very excited about is that-

Paul: [laughs]

Carolyn: -naloxone now goes over the counter. So, I was wondering if you could talk us through a little bit more about the implications of this, when are we going to start to actually see this at the shelves, will our patients be able to access it?

Kenneth: Yeah. So, I think that this is exciting news. Pretty recent. So, March 29th, 2023, the FDA approved the first naloxone product for use without a prescription, and they did this to help reduce opioid overdose deaths. So, what does this mean? Well, this is specific to the brand name Narcan, that formulation. So, it's naloxone hydrochloride 4 mg nasal spray. That's what we're specifically talking about. It's going to require this change in labeling from prescription status to OTC status. The anticipated timeline is that this will probably be available in pharmacies in the late summer of 2023, but the manufacturer gets to determine the timeline for when it's available and how much it's going to cost.

Matt: So, what are the concerns about this?

Kenneth: Well, availability is one of those things where we'd love to see it as soon as possible. It'd be great to have it on the shelves. But I think we can wait a bit until it comes out. The big concern is the price. We don't know how much it's going to cost. I've heard some numbers floated around, like $50 for a Narcan kit. That will be cost prohibitive for a lot of people.

Matt: It's not a fun way to spend $50.

Kenneth: No, and who's going to walk into a pharmacy and be like, "Hey, let me drop $50 on Narcan?"

Matt: [chuckles]

Kenneth: I think if the point is really to make this more available for people, then is this the right way to do it? I'm not sure. Well, actually, I think if it's that expensive, it's not the way to do it. So, that is a concern that I know a lot of people in the Addiction Medicine world have been voicing. I will point out that during this changeover process, from prescription to OTC, you can still prescribe Narcan as that formulation and it will be available. But once it is completely changed over to OTC, it will no longer be available as a prescription medication. So, you can only purchase it from the pharmacy based on that price that's set.

Matt: Is the most preferred-- nasal 4 mg that's the most preferred formulation for overdose?

Kenneth: Yes. I think that there're benefits to that. So, one is that if someone only needs the 4 mg and they respond, great. There's no need to give them more naloxone. That can precipitate withdrawal and be very uncomfortable for somebody, which can lead to disengagement from subsequent medical care. So, we don't want to push people away,

make them not want to have medical interventions. I think having two 4 mg devices is beneficial. There is an 8 mg device that's out there, also a nasal spray. I think that there's a 3 mg that's soon to come out.

Matt: Well, Paul, this provides us a nice transition, because we're talking about overdose. And our next topic is overdose considerations? Am I jumping the gun here? Did you have more questions to ask?

Paul: [laughs] No, I was just thinking, hopefully, market forces would actually drive the cost down. I feel like this is an unusual over-the-counter medication in that, if people have access to it, it would keep them from dying, which is not true like intranasal fluticasone, say. So, I wonder if that wouldn't have some impact on cost, but I might be being overly optimistic.

Carolyn: I do hope that this means though that more community organizations will purchase it and carry it. I think that every single store should have it in their store. I think every school should have multiple vials or nasal sprays everywhere. So, I do think in terms of hopefully disseminating it, maybe not directly to unfortunately the patients who need it most, but having it more available just broadly. I'm hoping and I'm optimistic, hopefully, that we will see more people start to carry it in case of emergencies.

Paul: Terrific point. Yes, to overdose, Matt.

Matt: So, Stefan Kertesz. Am I saying your last name right? Kertesz. Kertesz.

Stefan: I think [crosstalk] Kertesz.

Matt: Kertesz.

Stefan: I've used a lot of pronunciations of [crosstalk]

Matt: Okay. Introduce yourself, pronounce your name correctly-

Stefan: Sure.

Paul: [laughs]

Matt: -and plug your own podcast.

Stefan: Yeah, sure. I'm Stefan Kertesz from University of Alabama at Birmingham, Heersink School of Medicine. Actually. I'm a co-podcaster with Dr. Saul Weiner, a show called On Becoming a Healer, which really focuses on the deficiencies in how we relate to patients, but usually through a topical lens, such as judgmentalism, genetic testing, mistreatment of medical trainees. But all of it is based on trying to correct the way in which we form relationships to be more helpful to the patients and rewardings to us as clinicians.

Matt: Yeah. And his book also fantastic, book of the same name.

Stefan: *On Becoming a Healer.*

Matt and Stefan: Yeah.

Matt: All right. Carolyn or Paul, where are we starting here?

Paul: You teased tranq, which is not a sentence I should probably say,-

[laughter]

Paul: -but we mentioned tranq or xylazine already earlier in this episode. So, why don't we start there and talk about broad trends that we've seen in terms of the impact on xylazine and on opioid overdoses?

Stefan: Yeah. So, over the last few years, in some communities, but now an increasing number of them, there's been a rise in the percentage of opioid overdoses, where in those people who die, a veterinary sedative is also found, and that is xylazine. Xylazine is a centrally acting alpha-2 agonist. So, I guess, we could say, it's a super powerful clonidine. Would that be correct? I bet. It is used in veterinary medicine. That's what it's approved for. The paper that we reviewed actually looked at, both local history of people's understandings of how xylazine emerged in the drug market, specifically in Philadelphia, and then it looked at 25 communities around the country to see what percentage of overdose deaths included xylazine.

As a local matter, it looks like xylazine probably got its biggest move forward in Puerto Rico and then moved into some East Coast cities including Philadelphia. And folks working on the streets there over time, speaking to harm reduction activists, patients. Cops were saying, there's this new drug where it doesn't reverse as easily if you give naloxone. Sometimes, a person has it mixed with fentanyl and that might be called tranq dope. There are also people who wind up with these necrotic skin wounds and low blood pressure at the time of their overdose. And so, they got an impression.

At the same time, the people who did this paper found that there was a steep rise in the percentage of overdoses in some communities where those deaths actually were included. In my community, I think it had gone from 0% to about 5% to 10% of overdose deaths between 2019 and 2021. And in other communities, sometimes it was more than 15%, also included xylazine. It's still relatively uncommon, at least as of the time of this publication on the West Coast. But these things did seem to be moving from East to West.

Matt: Yeah. We talked about this. I don't know, Carolyn, what have you heard about why people are doing this? I feel like that's part of the question that-- I've heard different things. I don't know if you have.

Carolyn: I have heard different things as well. I think where I practice, it's definitely not as common. I think as what folks are seeing in Philadelphia, but I've heard a variety of things. In the paper that you guys actually mentioned, there's some ethnographic data that people are stating that maybe it extended the effect of fentanyl and also, there are patients though, who absolutely are not looking for this at all. So, I think it's a mix. There's a lot of heterogeneity in the substances right now, so I think we'll probably see a lot more, unfortunately, in the next year.

Stefan: The local understanding in Philly at least was that fentanyl tended to wear off quickly in terms of the euphoric effect that "has short legs." Tranq which had no really euphorigenic effect seemed to somehow prolong the overall effect. But this is being packaged in a packaged deal that people don't always know what they're getting.

Matt: Yeah, we've anecdotally have heard like, the cheaper bags have more tranq and the more expensive bags are more fentanyl. Some of the patients at least tell us that they're trying to avoid the tranq.

Paul: Yeah, it's tricky. The patients that I see are, by and large, patients who are receiving medications for opioid use disorders. I recognize that my sample might be different than a lot, but I will say that those patients that I talk to fuse xylazine with horror and are hoping to avoid it, and it's not something they're actually actively pursuing. They're scared of the idea

of it actually being in whatever the supply is. But that's a very narrow population that I'm talking to.

Kenneth: So, I work primarily in an opioid treatment program, and there's a primary care clinic embedded in it where I take care of patients, also start methadone for patients. I've had a similar experience to Paul. Most of my patients, when they find out that they may have been exposed to xylazine, don't want it. I've seen it a lot with these skin and soft tissue wounds at injection sites. I've seen it primarily at injection sites. But the history that we've taken is to ask patients, "How long have you been injecting?" And sometimes people say like, "Oh, well, 10 years." "When did you start seeing this?" "These wounds only started a couple of years ago." That's when we started to think, what's going on here?

The other clinical signal that we got were people having overdoses and ending up in the hospital and not responding to naloxone, and then being put on these naloxone infusions for three days. And it's like, "Listen, at this point, it's not going to reverse anything."

[laughter]

Paul: The ship has sailed.

Kenneth: "But something else is going on here." We knew we were missing something and I think now we figured out what that was.

Carolyn: I know that we're all huge proponents of harm reduction, right? So, I'm curious, with this evolving supply, have you developed any patient strategies or things you're counseling individuals on in particular to help minimize the risk of overdose deaths from xylazine?

Kenneth: Well, so, we recently got our hands on just a sample of these rapid xylazine tests similar to fentanyl testing strips, but they're xylazine testing strips. We're excited about them that they exist in terms of sensitivity, specificity. I don't know how good they are, [chuckles] but they're something that we're looking at as a potential tool that we can use to help people detect what's in their drug supply. And then I think the other thing we're doing is just, it's really awareness. It's letting people know that this is out there and it can cause these things like excessive sedation if they're injecting or now it turns out that I think that other routes of administration can be associated with these unique wounds, so just letting people know that this is in the drug supply now.

Paul: We can omit this from the show, if you want. I don't think I ever told you, Matt. I just received a package. It was like three weeks ago that showed up in the mail, no return address. That was just a kit. It was a harm reduction. It's amazing, by the way. It had xylazine test strips, it had clean water, it had condoms, it had Band Aids. I don't know why it came to me, what the point was, but it's nice that's out there in the world and the ether.

Matt: Wow. Maybe someone New Year-- [crosstalk]

Paul: So, someone's putting together care packages. I just have to figure out where it came from. So, I just need to [crosstalk]

Matt: Yes. You can plug whoever's doing that. Maybe they somehow found your address, I don't know.

Kenneth: So, it's possible that was NEXT Distro, which is an online service that provides harm reduction materials to people all over the country? You can go on to the website and you can receive naloxone, safer injection, safer smoking supplies, and they deliver it to you in an unmarked box. So, it's a great tool for people who either want to-- They don't want to

go seek out harm reduction supplies or they're in a state that doesn't allow them to pick it up easily, this might be an option for them.

Matt: All right. What do we have next, Carolyn?

Carolyn: I think we should talk a little bit about telehealth, because I have to say, I started my Addiction Medicine fellowship when telehealth started, because I started becoming a fellow in the midst of a pandemic. So, actually, I don't know how to fully practice Addiction Medicine without the use of telehealth. I know you guys brought up a really interesting study about the role of telehealth management, specifically in patients who have opioid use disorder, and how it can help with opioid overdose prevention. Do you mind walking us through their findings?

Stefan: Sure. Yeah. So, at the beginning of our horrific pandemic in March of 2020, certain rule changes were offered by the DEA to allow the initiation of buprenorphine for care of opioid use disorder, and actually to allow other forms of controlled substance prescribing in the context of not being able to see people face to face. I think that at the time it was just understood that we need to continue access to treatment. It likely also allowed more people to consider ways to access treatment when there's nobody nearby who can prescribe buprenorphine. Even we saw the emergence of telehealth companies that might do practice across states. There has been some real uncertainty as to what the rules should be going forward. The DEA is still considering that issue.

But in the middle of this, the centers for disease control and prevention, people there did some analyses of the overall rates of opioid use disorder treatment and death from overdose in people who had received telehealth services for opioid use disorder, and separately, people who had received medications for opioid use disorder very often in association with telehealth. And so, the CDC took two big giant Medicare databases and created two big cohorts, one which is pre-pandemic and one which is during two years of the pandemic, and essentially identified everybody who had an opioid use disorder diagnosis, and counted up how many got telehealth services, how many got methadone potentially from a methadone program, which was also allowed to use telehealth, and how many got buprenorphine, which is typically from a regular outpatient doctor for their OUD. They just computed death rates, both pre-pandemic and then in the other cohort post-pandemic.

What they found is that, overall, in the country death rates went up during the pandemic from all causes, not just COVID. Drug overdose mortality went up. We can have a conversation about why we've had a rise in drug overdose. The percentage of deaths due to overdose in the two cohorts though, between the pre-pandemic and pandemic wasn't different. Then looking at that pandemic group, they found that receiving telehealth services for opioid use disorder, receiving medications from methadone program, and receiving buprenorphine were all associated with substantial reductions in the likelihood of death from overdose compared to not receiving those things.

I can tell you that the magnitude of the relative risk reduction in death is pretty similar to what we've seen in all studies of medication for opioid use disorder. So, broad strokes, the general inferences looks like telehealth and these medications worked fine during the pandemic when they were mainly by telehealth. This isn't truly a comparative trial, of course, but if you had to make a best guess at this point, we would say that telehealth administered medications for opioid use disorder are as effective as non-telehealth administered medications for opioid use disorder. That's the main finding of the study, and it's probably going to weigh into how the DEA formulates its next rules.

Paul: In terms of how they define telehealth, because I feel like there's a lot of hand-wringing about what it's going to look like and whether we have to have a video component and the quality of the telehealth, I will say that some of the telehealth that I did during COVID was-- It was a phone call mostly and who knows where the patient was. They are concerned about confidentiality. So, I guess, what I'm asking is, how do they define telehealth and are there concerns about the quality of the telehealth that's being done if this would continue?

Stefan: So, the telehealth definition in this study was a broad range of CPT codes. I think many of us relied on telephone-only telehealth a good deal of the time, as well as audiovisual telehealth. The first draft of new rules for the post-pandemic era put forth by the DEA, and I said first draft because they're not final, proposed that we're going to need to make more of this audiovisual. I think they might still allow initiation by initial telephone if you can document that you couldn't do real time audiovisual connections. All of that's on hold right now because there's discussion of what should be done. No one wants to lose access to a service.

I think there's implicit in what you said or what you asked. Is there a real loss of quality of care for some reason when it allows telephone only as opposed to audiovisual? I think the answer is, we really don't know. I don't think that we know that looking at someone-- I think I know as a human being, looking at someone helps me feel more comfortable with what's going on and I sometimes draw inferences from that. But we don't know if you take 100,000 people who can only do telephone only calls and might have difficulty with audiovisual, would they better served by all being given training and access to a smartphone, or just continuing with telephone for the care of their opioid disorder? We don't know the answer to that to you, because I figured you have something really smart to say.

Matt: [laughs]

Paul: Right. But I will say, not to monopolize the conversation, I'll put my microphone down after this. In primary care, where you have these older multimorbid patients where you're just doing a phone call, you're like, "This doesn't feel good." But I think a lot of the telehealth where you're giving medications for opioid use disorder, those patients are otherwise really healthy for the most part and don't have a lot going on. I agree with you. Seeing them in the room with me, it feels nice because I'm a social person as everyone knows. But I also don't know that I gave any different quality of care if it was just a phone call. So, I'd be curious to see if that gets studied and what the outcomes look like.

Stefan: There's clearly an equity concern here too, because-

Paul: Yeah, you are right.

Stefan: -as you get to populations that are older, potentially subject to cognitive limitation from prior addiction or prior medical history, they may or may not have the smartphone, but they may or not even know how to operate all of the functions on it. We certainly won't want to exclude those folks from care.

Carolyn: A lot of folks are using their phone cameras. I have to say, I may get a quarter of a face like-

Paul: [laughs]

Carolyn: -just a nose. "Hey, can we move this back a little?"

Paul: I invariably with opioid use disorder telemedicine, get the *Blair Witch* effect. Patients are just walking around with me, they're smoking a cigarette, I'm like, "Could you just pretend

you respect me for five minutes and just not smoke in front of me? That's all I'm asking." But usually, they take me for a walk when the phone cameras used.

Stefan: I once did have a patient who I related to for quite a while who told me that they had just used cocaine. I caught them on the phone. I actually felt like this was one level disturbing, because I was trying to treat cocaine addiction, but at another level really encouraging, because I was thinking, "Okay, they trust me enough to say that that's what they just did."

Paul: For sure.

Matt: That's definitely a glass half full-

Paul: [laughs]

Matt: -view of that situation. Okay. If we go for half hour, I want to make sure we have a lot to get to, so let's keep going through. Are we moving on to alcohol use disorder? Do we have more--?

Carolyn: I think we should touch briefly about the trajectory of overdose deaths in our adolescent population. So, I know we have some new data out on that. Yeah.

Stefan: So, we know that from now, according to the CDC and the National Center for Vital Statistics, overdose tests involving individuals aged 10 to 19 rose by roughly 100% from the first six months of 2019 to the last six months of 2021. It was actually a curve. Meaning, it rose and peaked in June of 2021 and seemed to go down a little bit by the end of 2021. These overdose deaths are 85% or so illicitly manufactured fentanyls. They are not all related to getting a pill that looks like Percocet from a friend. In fact, that was a minority of the deaths. They were all different formulations, but fentanyls that were in other products that youth accessed, many of whom did not have a known history of opioid use to the people who knew them.

The other thing that is tragic about these deaths is that many are 60% happened at home, 67% happened with someone nearby, meaning that there was potentially a real chance to reverse these deaths at the time that they were happening, if only somebody was aware and had access to naloxone.

Matt: So, the idea is that these young people were maybe taking, they thought it was a pill of Xanax or something like that. I know that's a brand name, but that's what they would probably [crosstalk] by.

Stefan: That's a percentage. It seems to be 20% to 25%, where there seems to be evidence of some sort of pill that they took that, may be an undercount, because medical examiners don't always see all pills that were taken. But it looks like that story, which is very much part of what's going on, isn't the full story.

Matt: That's not the full story.

Stefan: They're also getting access to other drugs which do not seem to involve consuming a pill where they're caught by surprise. The pill stories actually made the media in a very big way. So, I want people to be aware that a good number of these deaths, it looks like the majority are still not, "I got a pill and then died." But actually, something else. Maybe they were procuring what they thought was heroin or fentanyl. Maybe they thought it was cocaine. Who knows what they thought it was. But it's not always a pill.

Matt: Okay, thank you. Thank you for clarifying. Ximena-- All right, so would you like to introduce yourself, say where you work if you'd like, you can say Kashlak, just if you want to feel cool?

Ximena: Yeah, sure. So, I'm Ximena Levander. I'm an Assistant Professor at Oregon Health & Science University in Portland, Oregon. I do Addiction Medicine in different clinical settings. I do inpatient addiction, consult service, outpatient addiction care, and I also work at a telehealth low barrier buprenorphine clinic, and I also do research.

Matt: All the things.

Ximena: All the things. Yes.

Matt: Paul, I think you had some questions about this.

Paul: We'll introduce the topic first. So, you spoke about a couple of papers on alcohol use disorder treatment in primary care. I think the first one that you referenced was actually talking about screening initially. So, I wonder if you would just talk about the broad strokes of that and then we can ask specific questions.

Ximena: Yeah, sure. So, this paper was published this past year, and it was looking at alcohol screening during US primary care visits. And the idea is that, when we asked patients, did clinicians or someone in the healthcare setting ask you about your alcohol use, they, at pretty high rates, say that they were asked about 80%, whether it's NSDUH or CDC studies. But when we look then at the electronic health record, are clinicians actually using an evidence-based screening tool to ask about alcohol use and screen for unhealthy alcohol use and alcohol use disorder? Are they using a recommended screening tool and putting it in the EHR?

So, this paper wanted to look at EHR level data that they abstracted, looking at the individual visits to see which proportion of visits the alcohol screening was completed using AUDIT-C, MAST, CAGE, [unintelligible [00:34:12] and then they wanted to look at which were some factors that would have increased the odds of alcohol screening or alcohol-related counseling happening during that visit. They wanted to see, because we may be doing things that aren't being documented in the electronic health record. If it's not in electronic health record, did it really happen?

Matt: That's a good question. That's an existential question. [chuckles] Do you have a favorite alcohol screening question? Do you believe in a single screening questionnaire or something else that you would recommend the audience to use?

Ximena: Yeah, the AUDIT-C, which is three questions is the one that I usually recommend that people use. It has high correlation with being a positive screen that person needs to be further evaluated and provide brief intervention and then screen for alcohol use disorder.

Paul: I think even the inclusion of CAGE, which I don't think is well validated in the outpatient settings. It seems like even if we grade on a curve, only 3% of patients actually had alcohol screening documented in the EHR, which seems remarkably low.

Carolyn: If you had to give us a grade in terms of how we're doing as a whole, what would you give us?

Ximena: Pretty poor, maybe a D.

[laughter]

Katherine: Yeah. And this is Kat. I haven't spoken yet, but I just wanted to mention since you brought up CAGE also. The sensitivity is pretty low, because the questions are really geared more toward detecting dependence rather than just unhealthy use for instance. So, I don't know that it's necessarily a great screening tool on that level.

Paul: I did want to ask you that you'd actually mentioned some of the factors that even I think specifically I'd like to hear about the ones that decreased the likelihood of someone being screened. I thought those were actually interesting and also/alarming.

Ximena: Yeah. So, they looked at patient and visit characteristics that were associated with increased odds of having screening with an evidence-based tool in the EHR. And the ones that had a lower likelihood were patients coming in with a new problem. So, new cough or new rash, which I think I can understand why maybe that person isn't screened for alcohol use disorder during that visit. So, that sort of patient reason for visit made sense.

The one that was concerning for me was around pre and post surgery. So, I work on our inpatient addiction consult service, and have seen patients where we get consulted day one and a half to two of admission post surgery where the patient is now in severe alcohol withdrawal and having pretty poor outcomes from that hospitalization, because now we're having to try and catch up when if we had appropriately screened and been on it from the beginning, we could have potentially avoided that withdrawal from happening. So, I think that correlation was particularly concerning for me.

Matt: Right. It's like probably that person had a MICA or RCRI score, even if they were had zero risk factors, but no one asked them if they drank alcohol when that was maybe just as big a danger for them. So, it should be one of those things. It should be on a checklist that you go through when you're doing your review of systems, like, what comorbidities does this person have that could cause problems after the surgery. It's a good point. I like to think that I know my patients that I'm pre-oping, but it's a good point to ask about.

Carolyn: Even clinically, I see much more often that the surgeons will find some very old urine toxicology screen that has one positive substance and they'll be like, "Surgery canceled." And we'll be like, "Wait, hold up." But we aren't even doing this basic thing." Well, it sounds like in our pre-op patients for screening for alcohol use.

Matt: We're talking about alcohol use disorder and we're going to keep talking about it, Paul, but we're going to delve a little bit into the treatment here by talking about hallucinogens, which I-

Paul: [laughs]

Matt: -said right the second time. All right, so, Kat, introduce yourself and tell us about this. We're going to talk about psychedelics or psilocybin?

Katherine: Yes, or hallucinogens. So, this was actually a pretty confusing distinction. I'll just say first. I'm Kat Mullins. So, I work at NYU Langone-

Matt: Yes, thank you.

Katherine: -in Brooklyn. Yeah. So, the internet has a lot of different opinions about what actually falls into the category of hallucinogens versus psychedelics. But really hallucinogens is a broad category of compounds that includes both psychedelics and dissociatives. So, the classic psychedelics that we think about are things more like psilocybin, LSD, and then the dissociatives, which have a slightly different mechanism of action include ketamine and PCP.

Matt: Okay, that is more clear. I did not make that distinction. We talked about a study on our hotcakes. Paul, I believe you presented this, right? This was the psilocybin. So, do you want to talk us through this study a little bit, maybe any limitations that you see or if you want to speak about the implementation of this maybe, that would be interesting?

Katherine: Absolutely, yes. So, the article was called Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder. And I will say this was the number one addiction article of the year, so it received a lot of media attention. But essentially, the authors included 1995 people, they randomized people into either a psilocybin group or the placebo which they use diphenhydramine. They offered people both therapy sessions and then the study drug. So, people got four therapy sessions and then the study drug. I think it's interesting when people-- So, the day people got it, they had to stay in the room with the therapist for eight hours, and they were not allowed to leave. So, intense intervention there. Then after study drug, four more sessions and then study drug and then four more therapy sessions.

So, primarily, they looked at percent heavy drinking days and also evaluated percent drinking days overall as well as number of drinks per day, and they followed people for 32 weeks. They actually had pretty impressive results in favor of the psilocybins. So, for people in the psilocybin arm, the number of heavy drinking days was much lower than the placebo group. Same with the number of drinking days overall and the number of drinks per day, and that was consistent over the study period. I'll say retention was also quite impressive.

You mentioned limitation. So, I think a common theme in a lot of the psychedelic research right now is that the participants were primarily white. I think that inclusion and access has been a real problem for these and may continue to be. So, I think that's a really important note as we're talking about how to develop the research from the beginning onward, and then how are we actually going to get this intervention to people when it becomes therapeutic. It was a small study. And everybody who got the study drug knew that they got the study drug. So, I think the blinding is really challenging in these studies and there's something with placebo effect there too.

Paul: The comment I might make about this and I would love to hear your thoughts on this is something we talked about a little bit before we started recording. I guess, my only concern is, you mentioned how much excitement there is and there was so much talk about this and it made it into the popular media. I just worry a little bit that it might be a distraction from the medications that we already have that can be prescribed by primary care doctors who have great numbers needed to treat for alcohol use disorder. So, specifically things like naltrexone and acamprosate, which we know from even the study that we just talked about are widely underprescribed. So, is there any concern that this might be a distraction from the modalities that we already have that work pretty well already?

Katherine: Yeah, completely. I think that's a great point. We know that the number needed to treat for naltrexone, depending on what you look at, is somewhere between 7 and 13. And then for acamprosate, we also have good data, disulfiram, probably a little bit lower, and we're not prescribing those frequently enough from primary care settings. So, I think it's really important to continue to educate around that. I would hope that having a new therapy available would not detract from the fact that we're not treating it sufficiently with the tools that we already have.

Matt: Can I ask for you or Carolyn as the Addiction Medicine doctors currently holding microphones? I prescribed a lot of naltrexone since I learned to do that on this show with variable success, but I don't think I've caused harm by it, and some patients have said it

helped them. But what about acamprosate? Have you found that useful? It's hard, right? It's like, either one pill three times a day or two pills three times a day if they have kidney disease or not. Most patients that I'm prescribing, it's two pills three times a day.

Katherine: Yeah, I actually have a few patients who have done quite well with it, but that pill burden is significant for anyone. The times that I've considered it really are when naltrexone is not an option due to liver function or concurrent opioid use. So then, yeah, there actually is good data for acamprosate. I think disulfiram is interesting because the best data is actually in monitored settings. So, if somebody has someone to ensure that they're actually taking the medication or if it's coming from a methadone clinic as an entrusting model, for instance, but there the data is really a little bit lower.

Carolyn: Just add to just in my expert opinion, the pill burden is really high. Yet, I've also had some patients do pretty well and say, "Doc, honestly, I'm taking this twice a day." And I say, "Well, it's helping and you're taking it twice a day and that's okay."

Matt: Yeah.

Carolyn: So, I think being really patient centered and using your judgment in that context. And again, it's most helpful for people who want to be abstinent. I have a lot of patients who more so want to just decrease their heavy alcohol use than be abstinent per se. It can't, per se, the best data is really for folks who are interested in abstinence.

Matt: Right.

Ximena: I think I'll also add that before we start jumping to non-FDA-approved medication like psilocybin and ketamine, which aren't really approved for many things, there are also other medications that are not FDA approved that do have a lot of evidence of efficacy for alcohol use disorder. So, like baclofen, topiramate, gabapentin also do have pretty strong evidence for both abstinence and reduction in heavy drinking. So, I would probably turn towards those before I turn towards something that there's still not sufficient evidence for.

Carolyn: You got a bunch of Addiction Medicine-- [crosstalk]

Paul: That's the best thing always.

Kenneth: A quick note about acamprosate, because similar to Kat, I have had some luck with it. It's usually for patients who are concurrently treated with methadone or buprenorphine. So, they can't take naltrexone, but they do have alcohol use disorder as well. One funny thing I see is that, when gabapentin started to be used off label for alcohol use disorder, people felt really comfortable doing it, because I think we just prescribe gabapentin for everything. It became this catch all for something that's not an opioid. The pill burden of gabapentin is also high and sometimes higher than acamprosate. But I see this a lot where people say like, "Oh, well, you know, two pills three times a day is too much." So, instead I'm going to give this person gabapentin, I'm thinking-

Paul: Three pills three times a day.

Kenneth: -you're getting three pills three times a day.

Paul: [laughs]

Matt: And it's going to give you the side effects of dizziness, weight gain, edema, [crosstalk] blah, blah, blah. Yeah.

Kenneth: So, it's just something that, for me, it was helpful because I also have used gabapentin for this indication, but it was a check for my own bias around it.

Matt: Yeah. So, use acamprosate before you reach for gabapentin-

Kenneth: Exactly.

Matt: -unless you have a really good reason.

Kenneth: Exactly.

Matt: I love that point. Thank you.

Paul: All right. I have much less experience than our experts, but I will say, I've heard some anecdotal evidence about helping issues with sleep and insomnia as well, which is very common, especially in the early stages of recovery. So, I've had success with the acamprosate in those patients as well.

Katherine: It might also help just to frame where psilocybin actually stands right now, because it's not a legal medication that anyone can just provide in clinic to their patient. So, I will say, it's federally legal, so it's a Schedule I drug. It has been decriminalized in a number of states and cities. And Oregon in 2020 passed a measure legalizing psilocybin for therapeutic use. Actually, just in the past few weeks, Oregon approved the first license in the country for a psilocybin service center. So, I think there's not a lot of information about what that's going to look like. I think it's an interesting change, but I think access is going to continue to be a challenge here.

Ximena: Yeah, I'm from the state of Oregon, so we're the state that legalized, also caveat is that the psilocybin that was legalized is psilocybin derived from mushrooms. So, the psilocybin that's used in a lot of these trials is pharmaceutical grade psilocybin or LSD. So, that's one point to keep in mind. And yes, the first clinic opened and if you go to their website, you can see their prices. But one session is in the like $2,000 range.

Matt: Super affordable for everyone. I feel like people are just going to be getting shrooms from their friend. That's what I think this is going to be, because it's such a hot topic in the news. There's like Michael Pollan's book. There's no shortage of people talking about this in the media. So, I think people are going to take matters into their own hands, which hopefully that won't cause a lot of harm.

Katherine: I think because of that, we also need to remember that there are risks and we need to be able to discuss those with people. These studies really had very stringent inclusion criteria.

Matt: Eight hours in a therapist office, right? [laughs]

Katherine: That's one of them. Yeah. So, think about the therapy requirement. Think about how therapy is reimbursed in this country. That is not going to be cheap in itself. But also, nobody who is taking antidepressant, nobody who's in treatment right now for alcohol use disorder, this is a really limited cohort. This is not the average person who's coming and seeking treatment.

Matt: I will say, my comments, I am very enthusiastic about the fact that we're having new medications being tried and everything. I don't mean to say that I'm totally against all this, in case I'm going to get angry emails about this, Paul. I can see it-- [crosstalk]

Paul: You will get anyway.

Matt: I can see it now. Yeah. Anyway, I said enough about that. All right, Paul, what's next? Move us forward.

Paul: Let's move on to the ketamine article that you discussed in the presentation. I would love to, as we're talking about novel treatments for alcohol use disorder. Talk us through what we're doing with ketamine, and then we'll talk about the robots at the end.

Matt: [laughs] I love the headline you have written there. All right, we'll save that.

Katherine: Great. Yeah, and I'll just mention first what ketamine actually is, because again, it's one of those dissociatives. The mechanism of action is a little bit different than it was for psilocybin. So, this acts on the glutamate system. It is antagonist to the N-methyl-D-aspartate or NMDA receptor. So, it's a dissociative anesthetic and it does have some hallucinogenic effects. We know that people who are in early treatment for alcohol use disorder have high rates of comorbid depression and ketamine, at least esketamine is approved for depression and ketamine has some antidepressant effects. So, that may be one reason that this is a potential treatment.

Another thing is that it does alter neurogenesis and synaptogenesis in ways that may create this window period for people to be more receptive to therapy when they're actually on the study drug. So, I think that's an interesting reason that often therapy is incorporated here. So, this was a double-blind placebo-controlled phase 2 trial. They included 96 patients with severe AUD, and they randomized them to four conditions. So, two of the conditions were given ketamine infusions and two were given a placebo saline infusion. And then they further broke those two groups down into patients who received psychotherapy or patients who received psychoeducation. That was a no therapy involvement at all, just strictly information while people were getting the study drug. So, the primary outcomes here, so they looked at self-reported percentage of days abstinent and confirmed alcohol relapse at six months. Relapse, they defined as heavy drinking. So, five or more drinks for men in a day, four or more drinks for women in a day.

So, for the results here, so when they looked just at the ketamine group versus the placebo group, they did see a higher mean percentage of days abstinent in the ketamine group. There really was a significant difference there. When they incorporated the therapy versus education aspect, there really was not a significantly different outcome, but there was a signal. So, it seems like therapy group may have fared a little bit better in terms of percentage days abstinent compared to the psychoeducation group, and they also did not see any difference in relapse. So, the heavy drinking, there wasn't a difference between the ketamine or the placebo group, or therapy, or the psychoeducation group.

Paul: These were all self-reported returns to use. Like, was there any biochemical testing or any confirmation of either abstinence or usage?

Katherine: Interestingly, they also had people wearing a bracelet that could assess alcohol use. The main thing was this timeline follow back, that was at the end of the day, somebody would report their use, but they also had these bracelets that were biochemical.

Matt: Okay, we should check that.

[laughter]

Matt: That sounds pretty cool, that sounds pretty cool.

Carolyn: I'm just curious too if you could comment a little bit about some of the risks associated with ketamine use. Because I do think that there are risks associated with it. If you could just discuss that, that would be great.

Katherine: Yeah, one of the big things they were monitoring was the heart rate and blood pressure. So, there are cardiovascular effects. At higher doses, it's dissociative. People can have really negative psychologic experiences. Again, the cohort here was very restrictive. So, there was nobody with severe psychiatric illness. There was nobody with severe medical comorbidities. Yeah, so how generalizable, again, is this to our populations.

Carolyn: I know too. I have not seen this much in my practice, but I've heard from West Coast colleagues where ketamine is more accessible that there are patients who probably are developing ketamine use disorder where they're just using it a lot to a point where it's really unhealthy and becoming more out of control and a compulsive use, which I think is something to be mindful about too for some of these therapies.

Katherine: Yeah. People with the psilocybin and LSD, people develop a tolerance very quickly. So, partially for that reason the likelihood of developing a use disorder is probably lower and that's not the case for ketamine.

Matt: So, I guess, the last thing we wanted to talk about, Paul, I think, let you set this up?

Paul: Yeah. [laughs]

Matt: What are you calling this section, Paul?

Paul: Yeah, just for the listeners, our loose outline of things to talk about, I titled this Robot [unintelligible [00:52:56] ketamine-infused cocaine, which was just shorthand to give you a chance to talk about this fascinating study about incorporation of AI with expert opinion and maybe developing novel ways to treat cocaine use disorders specifically. So, if you could talk us through this since AI is going to replace us, it sounds like next year, and you can just let me know how that's going to look like for Addiction Medicine, that'd be great.

Katherine: Yeah, so moving along that trajectory. Yeah. So, the authors of this study used artificial intelligence in a prediction model. They looked at major data phenome wide, genome wide, that's all publicly available. Basically, the AI based on all of that identified 35 drugs that might be candidates that could be repurposed to treat cocaine use disorder. What was interesting is that they also needed the expert panel. So, the AI didn't totally replace the humans in this case. But when the expert panel looked at the 35 candidates, they identified ketamine as the top ranked candidate to be repurposed to treat cocaine use disorder.

Matt: Well, we got the robots we have to listen to them-- [crosstalk]

Paul: [laughs]

Carolyn: I was going to say, so my lesson is the robots can't get us without our permission. Is that--?

Katherine: Yeah, I think that's an optimistic outtake. The other thing they did after that was to look at 90 million electronic health records, and they found people who had cocaine use disorder, and then received ketamine either for anesthesia or for depression, and they propensity matched those people to people who did not receive ketamine. Basically, the people who received ketamine had higher rates of cocaine use disorder remission compared to the people who were propensity matched who did not receive ketamine. So, that was also another big data interesting finding.

Stefan: Matching people through electronic health records is not necessarily really matching, particularly when the thing we're discussing is an outcome in life that depends on decisions people are making about where they are in life, none of which is recorded in the medical records. So, we should take it as purely as a signal of something worth studying rather than as the next great wave of addiction treatment.

Ximena: I was going to say the same point like, our electronic health records aren't research tools. They're used for billing purposes and for clinical documentation. And so, we then try and use them for research, we have to take them with a grain of salt. That how cocaine use disorder is diagnosed or cocaine use documented in electronic health record. But that's what these large language models could be helpful for is trying to parse through these large, massive data sets that are unusable, really for humans to comprehend, to try and look at trends. So, I think it's not like, we're not saying we should be treating cocaine use disorder with ketamine. We're saying this is the next drug that we should study, because these large clinical trials are very expensive and we currently have no FDA-approved treatments for cocaine use disorder.

Matt: If you all have time for one last question, we were talking about this topic a little bit beforehand. I wanted to ask, if there's-- I know this wasn't included in the updates talk, but this is kind of an update, I guess. We've talked a lot about buprenorphine on our show, on your show, and I was asking you ahead of time like, is there any common mistake that you're seeing made right now? Carolyn, do you want to start us off and maybe we can pull if other people are thinking the same thing about the dose of buprenorphine that needs to be given?

Carolyn: I think that fentanyl has changed the landscape of the treatment of opioid use disorder, just because it is so potent. I'm finding that patients generally need higher doses of buprenorphine, often somewhere between 24 mg to 32 mg to adequately, truly manage their withdrawal and cravings. And of course, there can be restrictions on the maximum dose of buprenorphine depending on States insurance companies. [crosstalk]

Matt: I think the package label says 16 mg a day, right? Isn't it really wimpy compared to what we know patients might need? It says like, the first day you can give 8 mg or up to 16 mg or something like that.

Carolyn: Yeah, totally. The standard inductions, probably when they first started prescribing [crosstalk] buprenorphine, they were giving like--

Matt: Yes, this is in the heroin era.

Carolyn: Right. They were giving 4 mg right at the first dose and now we think that you probably need to-- You can still consider a standard induction, but you may also need to consider a high dose induction and consider just giving 8 mg, 16 mg, 24 mg depending on the context or sometimes patients opt for a low-dose induction. So, I think we're seeing a lot more in terms of how do we start buprenorphine and fentanyl as well as making sure we're adequately treating patients. Because I think in medicine too, sometimes we have this paradigm that lowest is best, you know, be on the lowest possible dose of medication.

But I think that we can't really think about that with buprenorphine, because oftentimes, my patients who opt to choose buprenorphine more from a [unintelligible [00:57:48] induction perspective, they choose the lower doses, because it doesn't block fentanyl. They can still use on top. So, they're going to say, "I'm going to use 8 mg to 12 mg and that's because I just want to use every so often, and still function, and it'll manage most of my withdrawal," while we need much higher doses, honestly, truly, to block some of the euphoric effects of fentanyl.

Matt: So, you're finding that most of your patients on buprenorphine maintenance are on 24 mg to 32 mg a day is the take home-- [crosstalk]

Carolyn: Yes, if they're predominantly using fentanyl.

Matt: Yeah.

Carolyn: I will say, my patients who are maybe just transitioning from oxycodone, those patients tend to not need 32 mg of buprenorphine. I'm still seeing those patients probably closer too.

Matt: Yeah, because a bundle of fentanyl has, at least in Philadelphia, the milligrams morphine equivalent is through the roof, if you compare it to anything else.

Carolyn: Totally.

Matt: Any other comments? Is this similar to what other people are seeing--?

Kenneth: Yeah, I'm seeing that as well. I've been increasing the doses of buprenorphine for people who use fentanyl. I do have a lot of luck with extended-release injectable buprenorphine. I think it's an important option for people and we should be thinking about it. So, typically, the way that it would work is that if you've received at least 8 mg of sublingual buprenorphine a day for seven days, then you can start the injectable formulation. The first two doses are loading doses of 300 mg, and then after that it's subsequently 100 mg, and that's given each month. But in some cases, if patients don't feel like they're getting adequate symptom control, meaning their cravings or withdrawal symptoms aren't adequately controlled on the 100 mg, so we could just keep them on 300 mg.

So, I want to just put that out there that this is an option for people who have a hard time taking the films or the tablets, this is something that could be useful for them. In terms of an overdose prevention standpoint, I know that I feel a lot better when one of my patients is receiving injectable buprenorphine, even if they're still using other substances on top of it.

Carolyn: You can achieve quite high plasma levels using the long-acting injectable buprenorphine compared to the sublingual, just because you think about the absorption process, there's incomplete absorption sometimes when folks are using the sublingual products.

Matt: Now, if someone wanted to hear you two talk about this kind of thing for hours and hours, would there be another season of your show? Actually, this is going to come out, I think, the week before your seasons, the Monday before. So, next Monday, I think. Is there a new season of your show starting?

Carolyn: So glad you asked that, Matt, [Matthew laughs] because yes, indeed. July 6th, the Curbsiders Addiction Medicine Season 2 is going to kick off and we have some great guests and great cohosts such as Kenny and Kat who are here with us today. Actually, we have an episode specifically on that actually long-acting injectable buprenorphine and some of the advantages and how to dose it and it's going to be a great season.

Matt: All right, so, look out for that. Look out for that. It will be on our channel, but then you'll have to go over to their channel to get all the episodes as they come out. I wanted to thank all our wonderful guests for being on the show.

Paul: This has been another episode of the Curbsiders, bringing you a little knowledge food for your brain hole.

Chris: Yummy.

[laughter]

Matt: That was Chris Chiu.

Paul: The yummy from the back. Still hungry for more? Join our Patreon and get all of our episodes ad free, plus twice monthly bonus episodes at *patreon.com/curbsiders*. You can find our show notes at *thecurbsiders.com,* and sign up for our mailing list while you're there to get our weekly show notes in your inbox. This includes our Curbsiders Digest recapping th latest practice-changing articles, guidelines, and news in Internal Medicine.

Matt: And we're committed to high value practice changing knowledge, and we want your feedback. You can find the show on YouTube, Spotify, or Apple Podcasts. You can also email us at *askcurbsiders@gmail.com*. A reminder that this in most episodes are available for CME through VCU Health at *curbsiders.vcuhealth.org.* I wanted to give a special thanks to everyone at this table for helping to write and produce this episode and to our whole Curbsiders team. Our technical production is done by Pod Paste. Elizabeth Proto runs our social media, Chris “The Chiu Man" Chiu is the moderator on our Discord, and Stuart Brigham composed our theme music. With all that, Paul, until next time, I've been Dr. Matthew Frank Watto.

Carolyn: And I've been Dr. Carolyn Chan.

Paul: And as always, I remain, Dr. Paul Nelson Williams. Thank you and goodbye.

[music]