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Addiction Medicine

ASAM Practice Pearls Transcript

GLP-1s in Addiction Medicine: *An Update Since Our Last Conversation*

Dr. Stephen Taylor: Hello, and welcome back to ASAM Practice Pearls, where we turn clinical expertise into everyday addiction care one conversation at a time. I'm your host, Dr. Stephen Taylor, and today's episode is special because we're coming back full circle to our very first Practice Pearls episode. That's right, we have an update on GLP-1 receptor agonists in addiction medicine.

In our inaugural episode at the beginning of season one, we discussed the science of GLP-1 receptor agonists and the current ongoing research behind GLP-1 receptor agonists as a treatment for alcohol use disorder. Today, we're going to revisit the topic to see where the research is now and how things have evolved. And to help us with that, we have Dr. Stephanie Weiss from the National Institute on Drug Abuse back with us, and we also have Dr. Anna Lembke, a prominent psychiatrist and professor of psychiatry at Stanford University, who has been prescribing GLP-1s in practice.

So today, get ready. Get your coffee, get your laptop or your AI tool, because you're going to need to take good notes, because we're going to hear insights from both research and clinical practice on this evolving treatment.

Dr. Weiss, Dr. Lembke, please say hello to our listeners. Thank you so much for joining us today.

Dr. Anna Lembke: Thank you. I'm delighted to be here.

Dr. Stephanie Weiss: Likewise. This is Stephanie Weiss, and super happy to be back on this podcast.

Dr. Stephen Taylor: It is great to have you back, Dr. Weiss, and to have you for the first time, at least for me, Dr. Lemke. And Dr. Weiss, I know you happen to have a case that you'd like to share with us that would be ideal for starting us off on our discussion today. So please, go right ahead.

Dr. Stephanie Weiss: Absolutely. So, I'm going to share this case with you with the caveat that our trial is still ongoing, and therefore it's still blinded.

And so, I'm not 100% sure who is on semaglutide and who is on placebo. But I did have a case that was pretty dramatic, of a gentleman in his late 30s who came in. We do not put patients who are treatment-seeking in this study. If they are interested in going on FDA-approved treatment, then we will refer them for treatment primarily with naltrexone. But this patient was pretty insistent he really did not want to be on naltrexone or otherwise

go into any kind of AUD treatment. He did recognize, though, that he had some issues. As he said to me, "I'm here because I need to get my drinking under better control." So, he did have some insight about that. And he had several comorbidities as well, besides just the AUD. He had severe obesity, hypertension. He had MetALD, so his transaminases were a little bit elevated. Had some depression that was in remission. So, we did go ahead and enroll him in this study because he was interested in doing the study even though he was not interested in being treated per se for AUD and really had very good success.

He basically lost about 50 pounds over the course of the study. His blood pressure normalized. His LFTs were not completely back to normal, but they were improved. He was able to report to me that his relationships were improved, so he was more present for his wife and children. He had two small kids. He was actually able to go and play with them.

He had enough energy now to exercise. He was doing better at work because he wasn't always recovering from hangovers and from drinking. So, I actually had him come back and talk to our colleagues about his experience because I thought everybody should hear about this, because people sometimes get this sense that addiction patients never get better.

And even if this gentleman was on placebo, we need to figure out how this worked because he really did benefit a lot from being in the trial, regardless of whether he got the real drug or not.

Dr. Stephen Taylor: That is awesome. What a fascinating case and what a great way to start us off. So, let's jump right into the questions. Dr. Weiss, a lot has happened since our first conversation.

What are the biggest developments in the research on GLP-1 receptor agonists and addiction medicine over the past year?

Dr. Stephanie Weiss: This has been an especially exciting year. We have now had two new clinical trials that have been published, not ours, actually, but two other trials of semaglutide for AUD.

One was published at the beginning of last year, that was Christian Hendershot's trial at UNC. The second one was just published a few months ago, and this was the Danish SEMALCO trial, both of which are positive, and they were in different patient populations, obviously different sites. And it does appear that there's a signal here.

There are two more studies that have been completed that will be getting published within the next year. And then our study, we literally just enrolled our last patient a couple of days ago, so we will hopefully be publishing, probably it'll be about a year. So,

for the AUD and semaglutide world, we are seeing a lot of progress. We're finally starting to get a lot of results from all these trials.

Dr. Stephen Taylor: That is awesome. Dr. Lemke, let me ask you, there are currently no clinical indications for GLP-1s in the treatment of SUD, but this may change in the future, which is why many clinical trials and research studies are currently underway.

You've already been integrating GLP-1 treatment into your practice, as have other clinicians. What prompted you to start prescribing GLP-1 medications, and what have you observed with your patients?

Dr. Anna Lembke: As you know, the evidence for the use of GLP-1s in addictive disorders, especially alcohol use disorder, consists of both anecdotal evidence, that is to say, what clinicians are seeing every day in practice, as well as an emerging body of evidence published in the peer-reviewed literature.

So, essentially it was my growing awareness of the anecdotal reports combined with what's being published in the literature that led me to decide to trial some of these GLP-1s in practice, not as first-line agents because of course they're not FDA-approved for any addictive disorder, but as second and third-line agents in people who have already tried the FDA-approved medications and are not full responders or are not non-responders.

Dr. Stephen Taylor: All right, you've started. What have been the hurdles? What have been the challenges that you've experienced so far, and how have you worked through them?

Dr. Anna Lembke: Probably the biggest challenge has been affordability. These medications are expensive. Insurance companies often will not pay for them off-label, which is to say they'll only pay for them if they're being prescribed for one of their FDA-approved indications, like diabetes or obesity.

We have managed to work around that challenge in many instances when prescribing to patients with diabetes or pre-diabetes and/or obesity or tending toward obesity by working together with their primary care doctors and having the primary care doctors prescribe the medication, sort of on our behalf. That's the way we've worked around it.

Other major hurdles are just that, like all psychiatric and psychotropic medications, they're very idiosyncratic. They work very well for a subset of patients, not at all for other patients, and in some instances, even when they work, they're poorly tolerated. So that's kind of the usual things that we have to deal with, and there's no exception with the GLP-1s.

Dr. Stephen Taylor: Given that last observation, which patients are you prescribing the GLP-1s for? And are there patients for whom you avoid the GLP-1s?

Dr. Anna Lembke: So, in general, we are prescribing GLP-1s in patients who have tried and failed FDA-approved treatments for alcohol use disorder primarily because that's where we've seen the largest signal both anecdotally and also in the peer-reviewed literature.

And I personally, because of my clinical experience, look out for patients who have alcohol use disorder and binge eating disorder or food addiction or are struggling with obesity, but as you know, people can have binge eating disorder and food addiction even when they're normal weight. And then interestingly, I have also been looking out for people with treatment-refractory depression and alcohol use disorder because in my clinical experience, I have seen the GLP-1s help people with depression, so that's been a bit of a surprise, but something else that I look out for in my practice.

People that I don't use them in are people who have already tried them, you know, often prescribed by other providers for diabetes or obesity, who don't tolerate them or for whom they just don't work. And I think that's a really important message that there can be a little bit of sort of media hype, the cart in front of the horse, thinking that this is a wonder drug. It's going to work for all of the people all the time, and that's never ever going to be true. And I've certainly seen in my patient population patients who I thought would be good candidates, and for whom the GLP-1s seem to do nothing at all.

Dr. Stephen Taylor: Wow, Dr. Lemke. That is quite a way to bust my bubble. You know, I was hoping that we now had the cure for addiction, obesity, and diabetes all in one set of drugs, and I guess you're telling me that's not the case.

Dr. Anna Lembke: I'm really excited about GLP-1s as a new tool. I'm just thrilled we have another tool in our toolbox, and I think this is going to help people for whom the existing tools aren't working, so I'm optimistic and excited. But yes, I think it's always good to proceed with caution and humility, that the holy grail of that wonder drug is probably never going to be found.

Dr. Stephen Taylor: Thank you for keeping it real for us. That said, I have spent a career teaching people that addiction is not a drug-specific disease. So, if GLP-1s can be helpful for alcohol use disorder, Dr. Weiss, could they be beneficial for different substances like opioids, tobacco, stimulants, or is it just alcohol?

Dr. Stephanie Weiss: Yeah, it's a great question. And of course, everybody is really interested on the research side in this question as well as on the clinical side. So, especially for SUDs like stimulant use disorder and cannabis use disorder, where we

really don't have much in the way of good treatments. Obviously, for opioid use disorder and for nicotine use disorder, we do have some other drugs available.

So, the answer to your question is people are exploring this and testing in all these different areas. I suspect we may find this useful even as an adjunct potentially in the case of SUDs, for example, like nicotine, where one of the fears patients sometimes have and one of the reasons that potentially can drive their relapse is that they are concerned about gaining a lot of weight.

And so, potentially, this could be something that would be helpful for those types of patients. In terms of for opioid use disorder and cannabis use disorder, I think the jury is still out. We're really early on. We don't have a lot of data, but people are doing trials. And so, I'm excited to see what happens

Dr. Stephen Taylor: Dr. Weiss, I'm going to stay with you for a second because I happen to know that you aren't just looking at this from the research side. You've also started using it in a clinical setting as well. Can you share what side effects, tolerability concerns, or adherence challenges that you're observing in the patients that you've been treating, and what are we most likely to expect as we go forward? And then I'm going to ask Dr. Lembke to address the same question.

Dr. Stephanie Weiss: Yeah. It's a great question, and I do want to say this with the caveat that our study is still blinded, and so half of my patients are actually on placebo, and so I don't know for sure what any patient is on yet until we are complete with the whole study, which it takes seven months start to finish. So, in seven months we'll be able to close the study and break the blind. But in terms of what's the most common side effect that we see, actually in everybody, right? Because very few people, and particularly AUD patients, very few people go seven months of their life without having an occasional symptom of some kind.

We do see quite a number of GI symptoms, which is, I think, the most commonly reported symptom that even people who know they're on GLP-1s are reporting. So, you can get some nausea, some constipation. You can get some diarrhea, some abdominal discomfort, increased gas, increased belching. So, we are seeing that as well, and that is the most common thing.

People do not necessarily have to come out of the study if the symptoms are relatively mild. And if people develop symptoms, we coach them. For the most part, we have not had to withdraw patients or had people withdraw themselves due to having symptoms that are so severe. And so, this was really important because unsurprisingly, many of our patients also have baseline GERD, and particularly associated with their AUD, as well as potentially if they're obese with their obesity. And so, we do sometimes have some folks

who might have some worsening of their GERD symptoms, but we have not, for the most part, had people have to withdraw from the study because of that.

And then the more serious symptoms that we look out for, we have so far not seen either. And I would say pancreatitis is probably one of the big things we worry about because obviously AUD patients are already at risk of pancreatitis.

And just from the drinking, if they're obese and potentially have gallstones that we don't know about, then that could also be a risk factor. And then the drug itself is potentially a risk factor. We do see some asymptomatic bumps in lipase sometimes, which again, could just be the AUD. But we are not thus far seeing any severe surgical emergencies, pancreatitis, anything like that.

Dr. Stephen Taylor: That's good news. Dr. Lemke, from the clinical practice side, what have you been seeing?

Dr. Anna Lembke: Well, I think Dr. Weiss did a good job covering many of the most common medical side effects. I might throw out there a more subtle psychiatric phenomenon that we sometimes observe, which is a kind of general loss of desire. So, not just decreased appetite for alcohol, but let's say if we're treating someone with alcohol use disorder for a GLP-1, they might then also describe a general loss of appetite or desire for foods that normally give them a lot of pleasure, or even, in some cases, activities that they really enjoy.

Now, this is not entirely unexpected when you think about the mechanism of action, the fact that GLP-1s are probably working directly on the brain to decrease dopamine release in the nucleus accumbens, dopamine being our appetitive, reinforcing, rewarding neurotransmitter. This is also not an entirely novel phenomenon. We see this sometimes with naltrexone, the opioid receptor blocker to treat opioid use disorder or alcohol use disorder. We will occasionally, in that context, also get a patient who says, "Well, yeah, I'm not craving alcohol, but I'm also not enjoying, you know, my favorite hot dog or even getting that kick from my morning run."

So, that's something that we do see. I will say that even in those cases, patients usually want to continue their GLP-1, and I'll just quote Kate Moss here, that "No food tastes as good as skinny feels."

Dr. Stephen Taylor: That's great. So, I'm going to stay with you for a second, Dr. Lembke, because there is understandable excitement around GLP-1s, right?

But we already have FDA-approved medications for AUD, and those medications remain underutilized. So, how should clinicians think about GLP-1s with all this understandable excitement in relation to the existing treatments and where they might ultimately fit in in

the treatment toolbox? You touched on this a little bit earlier, but I'd like for you to expound on that, if you would, please.

Dr. Anna Lembke: Yeah, I mean, I would encourage clinicians to do what they're probably already doing in their decision algorithm when it comes to prescribing. That is to say, start with on-label FDA-approved medications for a given indication. For alcohol use disorder, that means starting with things like naltrexone, acamprosate, disulfiram. These are our FDA-approved medications for alcohol use disorder.

And then if patients are not responding, then you go to your second-order medications. These are ones that are not FDA-approved but for which the evidence base is robust, meaning that there are at least two to three placebo-controlled trials showing efficacy, and only then going to sort of these off-label third-order with less evidence. And then I would say this is where the GLP-1s might come in.

Dr. Stephen Taylor: Thank you for that. Dr. Weiss, you researchers are particularly good at answering this next question I'm going to ask you. So please tell us what don't we know that we should know or that we need to know? What questions remain unanswered regarding GLP-1 treatment, and what research is still underway?

Dr. Stephanie Weiss: In all seriousness, we could talk for hours about all the things we don't know, but I'm going to give you one specific thing that I think is a question that comes up quite a bit dealing not only with when I speak to patients but also when I speak to other clinicians, which is a question of are these forever drugs? Meaning, like, do people have to go on them and stay on them? Can they be on them for a while and then come off them? Patients, of course, do not typically want to stay on medications indefinitely, and as Dr. Lemke pointed out, these are, at this point, still for the most part on patent, although some of them, the older ones, are starting to come off patent. Actually, semaglutide is coming off patent in Canada already, and it will come off patent in this country in the next few years as well.

So, from that sense, the situation will improve. But we really don't have a lot of data yet about folks taking these medications over the long term. So sometimes people say to me, "Well, what happens 20, 30, 40 years from now? If somebody starts taking this medication in their 20s, what kinds of potential long-term effects might they have in their 50s or 60s?" And we just don't know the answer to that. And I always have a discussion with both patients and clinicians I think completely get this. Nothing is without risk, and you basically have to sit and talk about or think about the risks versus the benefits. And it's not going to matter what happens in 50 years from the semaglutide if the person dies in five years from their addiction. From that standpoint, it may make sense to take the risk, but we don't honestly know.

And then we've already touched on the fact that, of course, for other substance use disorders besides AUD, we really don't know how useful these medications will be. Alcohol's a little bit unique because if you think about it, it's really the only drug that has caloric value in and of itself, right? Because a lot of our placebo patients lose weight, too. Sometimes people ask me, "Well, how do you not know who's on placebo? They don't lose any weight." But actually, a lot of them do. A lot of people do lose weight because if they cut down their drinking and they don't replace that with other sources of calories, then many of them do lose some weight just based on that. So, I think alcohol is a little unique compared to a lot of other drugs or really any other drugs.

That's part of, I think, the question, too, is just is it unique to the sense that it's the only one that's really going to show a lot of benefit or is this more something that's affecting reward pathways and not so much related to satiety and calories, and so maybe then it will be more useful for other SUDs as well. And I think the answer to that is we don't honestly know. But I'm really looking forward to finding out as some of these trials start getting done.

Dr. Stephen Taylor: As you point out, there's so much more that we don't know than there is that we know, and that's kind of the fun of doing the research, isn't it? So, Dr. Lembke, I'm going to get you and Dr. Weiss talking to each other for a second. Do you have any questions for Dr. Weiss from her perspective as a researcher about GLP-1s, especially given that you are actively using them for some of your patients?

Dr. Anna Lembke: Yeah. You know, I have seen a systematic review looking at the impact of GLP-1s on depression, and that has shown that overall, it appears to have a positive impact on mood.

And I've seen that, as I mentioned, in my own clinical work, specifically a patient with an alcohol use disorder who we had first on naltrexone. It helped to some degree with her alcohol use, but then she developed some binge eating. We put her on topiramate, which, as you know, is off-label for binge eating disorder. It helped somewhat, but through all of that, we were also struggling with a co-occurring treatment-refractory depressive disorder and cycling through a number of different antidepressants. And then at one point, I just sort of thought to myself, you know, "Let's give a GLP-1 a try and see what happens." And in her case, what happened was it had a remarkably positive impact on her alcohol use.

She was able to abstain from alcohol, but it also had an even more remarkable impact on her mood. She became undepressed for the first time in many years. We were able to taper her off of the naltrexone, off of the topiramate, and off of the many different antidepressants we had trialed so that we also massively reduced the polypharmacy that we'd been struggling with.

So, I'm curious, what are you seeing in your clinical trial in terms of impact on mood? Are you studying that? How long do you think it will be before people are actually conducting placebo-controlled trials looking at GLP-1's impact on mood? How do you reconcile this emerging evidence for a positive impact with the original black box warning that was issued with GLP-1s, cautioning against it potentially increasing the risk of suicide?

I know that the black box warning has now been removed, but curious about your thoughts on that.

Dr. Stephanie Weiss: With the caveat that our study is still blinded, and so half of my folks are actually on placebo, and also the fact that, of course, this is an artificial setting because in our trial, the patients are coming in on a weekly basis for 20 weeks. So, most of them do have a history of other comorbid mental health conditions. We have quite a number of folks with depression, anxiety, some PTSD, even a couple with OCD, and we do monitor them more carefully in that case. So, that is not the purpose that our trial was designed for, but we are actually going to have some data because we are monitoring that.

We screen them for suicidal ideation each week and depressive symptoms, so both clinically, and then some of them are even doing extra questionnaires for it, too, again, like I said, if we're monitoring them more closely because of their history. So, they do not have to be in complete remission from depression to be in the study. We can monitor them.

And actually, what we have found is that, overall, people tend to do better over the 20 weeks that they're coming in weekly. That's during the dosing phase. I did have one young lady who chose to withdraw. She was one of my OCD patients, actually, and she felt like her symptoms were getting worse, her mental health symptoms.

She is really the one exception I can think of. Overall, we've even had other OCD patients since then. I actually just had a gentleman with OCD who just finished the full study, the full 27 weeks, and wants to know when he can come back and do another study. So yeah, I think it's hard to tease apart right now because we're still blinded and because no question, we're not doing nothing even for the patients that are in the placebo group. But I do not see anything that makes me alarmed that we are systematically worsening people's other mental health conditions. And if anything, what we're seeing is more along the lines of what you're describing, maybe not quite that dramatic, but that, if anything, people's mood improves over the course of the study.

In terms of do we need to worry about giving these medications in patients that have those conditions, there's no evidence to my knowledge that that's an issue. Again, as you

said, there was some concern about it, not only our FDA, but the European EMA, which is their equivalent, were concerned about it and did a bunch of investigatory work before concluding that it doesn't appear to be an issue.

Dr. Anna Lembke: That's great to hear that you're also generally seeing as a trend improvements in mood and no huge signal for worsening other co-occurring mental health disorders. Because you're a researcher, I'm going to put out a plug for the study that I would love to see. I would love to see a controlled trial where you have two cohorts. You have folks who have depression and alcohol use disorder, folks who just have depression, and treat them with GLP-1s versus placebo.

Because when I think about the mechanism of action and what might be contributing to improved mood, I'm really curious about whether it's an actual pharmacologic mechanism in the brain or whether what's really happening is that in people with addiction, when they're no longer struggling with the cognitive load and cognitive lift of having to deal with constant craving, that alone is enough to relieve their depression symptoms, not to mention that they're not using their drug of choice as they were before because especially with alcohol and other drugs, we know that can act as a depressant over the long term.

I'd be really curious about, you know, what the mechanism of action is, and I'm thinking that might be one way to get to it.

Dr. Stephanie Weiss: I love that idea. Lorenzo Leggio is my boss. Lorenzo, if you're listening, this is our next trial.

Dr. Stephen Taylor: Lorenzo, I really hope you're listening because I also would love to see that trial done.

Dr. Weiss, turnabout is fair play. It's your turn. Do you have any questions for Dr. Lemke from a clinician's perspective?

Dr. Stephanie Weiss: Yeah. I'm super curious because of course, as I said, we're blinded, and even though sometimes I have a pretty good idea about what the patients are on, sometimes I don't. And so sometimes I really don't have a good sense, and I have definitely been surprised in other studies when we've unblinded and people that I thought got one condition were actually on the other, and vice versa.

Since you do have the ability to know exactly what people are on, I would really like to know how you're using the GLP-1. So, in our trial, everybody starts out at the 0.25 starting dose, which is thought to be subtherapeutic, although we don't actually know what the right dose is. Even if this medication works for AUD, we don't actually know what the right dose of it is to give people, which is why we're going all the way up to the 2.4 milligrams.

But I'm curious, how are you doing this exactly?

Dr. Anna Lembke: Yeah. Well, because, you know, this is off-label, and it's new, and we don't exactly know how it's working; we proceed very cautiously. We start at the lowest starting dose, and we really titrate to either intolerable side effect or efficacy, and we do that very slowly over time.

So yeah, we proceed very cautiously, and as I said before, we're working in close concert with the primary care doctor who often is the actual prescriber, primarily for insurance reasons.

Dr. Stephanie Weiss: That makes total sense. So, I'm curious what dose you're finding works for the patients that you've been able to use it in successfully.

Dr. Anna Lembke: You know, I'm not really finding that it's a one-size-fits-all. Some people seem to respond at very low doses; others need much higher doses, and we're really just titrating to tolerance and efficacy. And also importantly, I want to say that, you know, we're not using these medications in a vacuum. We're combining with individual and group psychotherapy, participation in 12-step.

So, all of our usual interventions, we are doing. But yeah, it's not really a one-size-fits-all, and that's in general my experience also with all the other psychotropics we prescribe, that it really varies person to person. I do want to, though, go back a little bit to something that Steve asked you about earlier or that you had mentioned earlier in terms of what we still don't know, and namely, what do you do after GLP-1s?

The data that I've seen shows that the people who lose the most weight on GLP-1s are also the most likely to gain that weight back when they stop them and then some, which is obviously very concerning. In response to that phenomenology, which we are also seeing in our patients when they stop their GLP-1s, either a return to drinking or a return to binge eating or just feeling appetitive out-of-controlness, people are using GLP-1s in novel ways, sometimes referred to as chipping, which is to say that they're not using the full dose every time they use.

They're reducing the dose, and they're also spreading out the injections. So, using in a way that is very much personalized for their needs when they notice that cravings return, or in the case of eating and food addiction and obesity, when their tendency to overeat returns. I mean, it's already happening. It's not a matter of any doctor necessarily prescribing or recommending that. We don't prescribe or recommend that. It is what patients are doing and finding it useful. So, I'm curious of your thoughts about that.

Dr. Stephanie Weiss: Yeah, and this is kind of relating to some of the things we mentioned a little bit before, which is in terms of what happens in the long term.

We were concerned about potentially rebound drinking happening, or even people maybe drinking more than they did before they started. So, there was a monkey study that was actually done with a different drug, liraglutide, but one of the other GLPs, that suggested that there could be some rebound increase in drinking after the drug was stopped, which is why we have such a long follow-up period.

We follow up the patients for almost two months, and I say long, it's long in the sense of for acute we can see, but obviously it's not going to help us if, you know, now a year has gone by and, or maybe two years, and the person then comes to you and says, "Doc, can I discontinue this drug? Am I going to relapse and start drinking again?"

We definitely do not have a good answer to that question, and I think unfortunately, this is the kind of thing we're going to really just not going to be able to answer anytime soon because none of the trials are long enough, you know, multi-year trials like that where we can follow people over the long term and then discontinue the drugs and see what happens. So, it's going to be a while till we know, unfortunately

Dr. Stephen Taylor: Dr. Weiss, I have one more question I just have to ask you. What has surprised you most since you first began studying GLP-1s and addiction?

Dr. Stephanie Weiss: So, there have been several things that have been surprising, but I think one of the things that most surprised me, you know, you tend to think in terms of a dose response that if you take a higher dose of a medication, you should have a larger response. And pharmacologically, that makes sense. In terms of the side effects that people have, we're actually not seeing that, and not all the patients have side effects. Of course, some of them are on placebo, but even the ones that I think are maybe or probably on the real drug, if they have side effects, it tends to be worse in the first month or two, and then they tend to do better.

So, sometimes people will be concerned they have a lot of symptoms at the 0.25 milligram dose, and they say, "What's going to happen to me by the time I get up to the 2.4?" And I tell them, "You actually probably have less symptoms." And I think part of it is because people pharmacologically do obviously get used to the drug, but also because of behaviorally, people get used to it.

People learn by trial and error, and that's what I tell patients. You will figure out by trial and error what you can and cannot do, and if it makes you feel bad or makes you sick or hurts, then don't do it.

Dr. Stephen Taylor: That's so true. Dr. Lemke, I've got to ask you this one too. So, one lesson that you learned from prescribing that you would offer to other addiction medicine specialists who are thinking about prescribing GLP-1s. What would that one lesson be?

Dr. Anna Lembke: I guess I would say to folks, take a chance. I think in general, these medications are pretty well-tolerated, and in some cases, they really can radically alter the course of someone's disease process. If you've got a patient and you've tried most everything and they're still not doing well, give the GLP-1s a try.

As all clinicians know, when you've struggled to help a patient, and then you find a remedy for them, and it's transformative, I mean, there's almost nothing more satisfying than that.

Dr. Stephanie Weiss: Yeah, I agree with that. And I think the monitoring should be individualized too, and even in the trial, we do that. I don't monitor every patient as closely for depressive symptoms, but if they have a history of it, and particularly if they're still active, then of course we monitor them more closely.

Same with the OCD patients, and I don't do an OCD questionnaire on every patient, but if they have active OCD, then we do monitor it and whatnot.

Dr. Anna Lembke: I would agree with that, and in terms of the monitoring, you don't need to go it alone, right? You can do that in conjunction with their GI specialist or their primary care doctor, right? It can be a team effort.

Dr. Stephen Taylor: Awesome. Thank you. Let's go ahead and get both of you on record talking about what the main Practice Pearls are, or action items are, that you want them to remember from this episode.

Dr. Anna Lembke: Yeah, I would say number one, if you're treating a patient with refractory alcohol use disorder who's on a lot of polypharmacy and not making much headway and potentially also struggling with depression and/or binge eating or obesity, you might consider a trial off-label of the GLP-1s, certainly giving informed consent to the patient that it is off-label and all the risks that that entails. But you might discover the GLP-1s in some patients are extremely effective, where other agents have not been.

Dr. Stephanie Weiss: The biggest thing I would want people to remember is don't forget that for AUD at least, we are fortunate enough to have three FDA-approved medications. Granted, those also don't work for everyone, and the effect size is not as large as we would like it to be for any of them. But for patients who do not have an FDA indication for a GLP-1, which currently is obesity or diabetes, to definitely consider initiating naltrexone or acamprosate. If you haven't tried them yet, don't forget about them.

I agree particularly for folks who do have a comorbid FDA indication, so for example, if they do have diabetes and alcohol use disorder, or if they do have obesity with significant medical issues relating to it and alcohol use disorder, it's kind of a no-brainer that those are people that you would consider initiating a drug like semaglutide in.

Dr. Stephen Taylor: Thank you both so very much. We are out of time, and I'm very saddened by that because we could go for another hour, I'm sure. But for more information on GLP-1 receptor agonists in addiction medicine, I want to invite our listeners to check out the list of resources that we're going to have on our website.

Don't forget to visit ASAM's e-Learning Center to claim your CE credits for this episode. I know you learned a whole lot because I did. Make sure to subscribe and share this episode with colleagues who may find this information helpful. I want to thank Dr. Anna Lembke, Dr. Stephanie Weiss for being fabulous experts on this episode.

Thanks for listening. We'll see you next time on ASAM Practice Pearls, where we turn clinical expertise into everyday addiction care one conversation at a time.