

Dr. Selby: Hello and welcome back. This is ASAM Practice Pearls, a podcast series from the American Society of Addiction Medicine. I'm your host, Dr. Peter Selby, and I'm thrilled to be joined by a knowledgeable expert and chair of the multidisciplinary group that developed ASAM's guidelines on benzodiazepine tapering. Welcome to our show, Dr. Emily Brunner.

Dr. Brunner: Thanks so much for having me. I'm delighted to be here and to get to talk about this issue.

Dr. Selby: Thank you. So, in the next half an hour, we're going to get a run-through, and you're going to leave with information about how to taper benzos. But let's go back. You know, although we prescribe benzodiazepines for the management of alcohol withdrawal, chronic use in anxiety, insomnia, for some seizure disorders, benzodiazepine prescription is under some scrutiny because of the harms seem to outweigh the benefits if used chronically. At the time, when they were introduced in the early 60s, they were a safer option than barbiturates, which had a narrow therapeutic index, and people were overdosing and dying, but benzos were less likely to kill people. However, it did become one of the best-selling drugs of all time in the 70s.

Now, why did that happen? A little story. Before OxyContin, there was diazepam. Did you know that Arthur Sackler of Purdue fame made their first hundred million dollars in peddling diazepam through doctors for a relatively made-up condition called psychic tension to differentiate it from chlordiazepoxide, which is used for anxiety?

And interestingly, those same marketing tactics were later used after his death to create the OxyContin epidemic. Diazepam was nicknamed "Mother's Little Helper" after the Rolling Stones song by the same name. And continues in modern-day shows, although under lorazepam in, for example, if you've seen the third season of *White Lotus*, you can see that it's still being used as a way for women to manage their existential issues or stresses. And it gets pushed as such.

Having said that, we need to think about, we as physicians, whether you're in primary care or addiction medicine, we either have patients who are on relatively high doses of diazepam equivalents and are getting it regularly, or you've inherited a patient from somebody who's retired, and now you have this issue of this person who is really taking a large dose of benzodiazepines, and what are we going to do?

With that in mind, I'm going to turn it over to Dr. Brunner and ask her what are some of the other ways in which we come across patients who have chronic doses of benzodiazepine and what seems to be the problem of people being on these high doses for long periods of time?

Dr. Brunner: Thanks so much for that question. I think that the prototypical situation that I like folks to keep in mind, that we're all really familiar with, is that there's a physician in your area or practice who has a lot of patients who are on higher dose benzodiazepines and has been on them for years, maybe someone trained during those past decades that you spoke of, and they're retiring.

And then, all those patients are needing to transfer to another doctor. And the folks they're transferring to don't want to be continuing those benzodiazepines, but they also don't have a great strategy for how to safely stop them or provide alternatives. So, really, that common clinical scenario is one we were trying to really keep in our head, as something a lot of docs face, and it can be really stressful and high-pressure and feel really scary.

Dr. Selby: Yeah, so, this *Joint Clinical Practice Guideline on Benzodiazepine Tapering* considerations when the risks outweigh the benefits was released at the beginning of March. What are your hopes for our listeners to know about this guideline?

Dr. Brunner: Number one, that really, really focuses into individualizing care, and I think that was our most important focus. I know that the temptation is to really want a recipe to be able to use on all patients. But we just weren't able to find the data that would make a safe case for how to do that.

And so, I think the other major thing is just that the vast majority of these patients have a physical dependence issue, which is separate from an addiction issue. So, in the majority of cases, there has been a tolerance developing, but that has occurred because of iatrogenically being given the medication over time.

And it is not indicative of an addiction issue. And so, by far, the most common way that we would focus on doing this doesn't take very much extra learning at all. It would just be focusing in on listening to the patient and individually working with them to slowly go down over a long period of time, and this could even be over years, you know, generally, [if] these people didn't get into this issue in a couple weeks, then it's not going to be something that you can get out of in a couple weeks either.

Dr. Selby: That's fantastic. That really makes sense. It's coming in a very humane way and approaching people. And again, we're trying to prevent what happened with the de-prescribing of opioids, which found people just suddenly cut off, and really, you're trying to prevent that happening with benzos because if people get suddenly cut off, really bad things happen to them. And so, what

were those considerations during the drafting of the guideline? What thoughts did y'all give to that particular issue, of what physicians should not do?

Dr. Brunner: We had some really specific outreach to patient groups, and we got a lot of patient comments that we responded to during our process of posting the guidelines for comment, and we really took those seriously. We heard loudly and clearly from the patients that they often felt belittled and stigmatized during this process and that, by far, the most helpful thing for them was to have a long, slow taper, not to be prescribed, for example, a lot of other adjunctive medications.

Dr. Selby: Yeah, and cutting people off benzodiazepines, especially alprazolam, can cause them to have seizures suddenly. So, we don't want to be causing more harm just because we, I, want to help somebody come off. And speaking about patients, I know there's the benzoinfo.com website that has promoted the Ashton Method for many years.

And so, can you talk a little bit about how your committee looked at that resource that is quite common—many physicians use it, many clinicians use it, many patients use it—how the committee either aligned or had a difference with what the Ashton Method suggests?

Dr. Brunner: We found it to be still a really valuable resource. I think what can be confusing about the Ashton is that it can give the impression that things are really objective and that you can really scientifically calculate, for example, equivalent dosage of a different type of benzodiazepine, and a lot of that basic scientific stuff is based on some pretty nebulous and not very scientific ways of creating those equivalencies. So, we really wanted to focus on the importance of listening to patients and being really careful because patients have such different ways of metabolizing. And then, of course, different health conditions, different situations that they're in stress-wise; all that stuff has to be taken into account.

Dr. Selby: Exactly. I mean, if anything, [they] were done based on, you know, diazepam equivalence, on sedation, not on long-term use of chronic tolerance or for other reasons. And so are the anxiolytic properties. So, exactly, as you say, we have all this variety of different metabolic pathways, and the rates of metabolism vary.

So, one really has to individualize it. That's what I'm hearing coming through this. So, when they start tapering or decide to taper, are benzos all bad? And what are some of the risks and benefits that physicians should consider when engaging patients in the conversation about tapering?

Dr. Brunner: Well, I think that you already alluded to one of the real main concerns, which is that benzodiazepines, like alcohol, are one of the few substances that can kill you, both during intoxication and during withdrawal. So, it's incredibly important to take this seriously and to treat it with respect and a focus on reacting to how patients respond as opposed to tagging them with being quote "liars" end quote.

And I think that throughout the addiction field, there can be this tendency, especially in primary care, to feel like patients don't want to be telling us the truth. Their data that they're giving us isn't accurate, and we see very much the opposite when we do objective studies of those things.

One really important piece of data that recently had come out that we kept in mind was the paper by Dr. Donovan Maust, who looked at patients being discontinued, for any reason, from their benzodiazepines and found an increased mortality rate in those patients.

Dr. Selby: Yeah, so basically, don't enter into this lightly. Really look at what are the reasons, and let's maybe talk about what are the benefits of coming off benzodiazepines. We've heard about the association with falls and hip fractures, and other cognitive issues. So, is this primarily because we're getting a much more aging population, or is there something else going on?

Dr. Brunner: Yeah, I think that we have a lot of opportunity to do a lot more research to get better characterization, but benzodiazepines are on the Beers Criteria, meaning that they're generally something that's not recommended to be prescribed in adults who are elderly at all. And so, certainly, that doesn't mean we have to overreact and immediately stop them by any means. The devil is always in the details.

Dr. Selby: Yeah. And are the Z-drugs any safer?

Dr. Brunner: We did not specifically scope this to include the Z-drugs just because of the paucity of data on how to make good decisions. But generally, those drugs have many of the same risks and dangers and can be associated with increased mortality over time.

Dr. Selby: So, I know we are talking more about ambulatory management. Are there other settings in which you could taper people off benzodiazepines or help discontinue benzodiazepines? Did your committee talk a little bit about that?

Dr. Brunner: Certainly, and I think that, in any patient who's had a severe side effect, like repeated car accidents, repeated falls, anyone with an identified

addiction issue or a benzo use disorder, it would be worth considering, potentially, doing a residential or medically managed program to help get them off the medication safely, and maybe use some different, more long-acting, drugs like phenobarbital.

But we really wanted to focus on the crux of this, which is that, in 90+ percent of patients, the best way to do this is outpatient management with a long, slow taper that is guided by frequent visits with their provider.

Dr. Selby: Yeah, and speaking about that, so that, you know, tapering slowly, making it long, maybe pausing for certain periods of time. You brought in the concept that the bulk of these people are physically dependent. They won't meet criteria for a use disorder. And we've seen this similarly with people being tapered off opioids, who have chronic pain. It's the same kind of issue. So, with benzos, what happens, or how should the clinician approach, if the person is coming back with re-emergence of anxiety? How do they sort that out, as what is withdrawal? What is a re-emergence of an underlying anxiety disorder? And how should they pay attention to this re-emergence of symptoms?

Dr. Brunner: Yeah, I think, great question. I think always looking at the time course is really important because you definitely would want to make sure that the time course made sense. So that it was happening with the step downs. And also, then determining, is it something as self-limited that goes away in a couple weeks? Which would then indicate that's more likely to be related to the taper, as opposed to something that's persistent, and may indicate emergence of the underlying issue.

Certainly, things like considering other types of adjunctive medications that might deal with the underlying issue are very important to think about. But just because we really wanted to focus on the scope of how do you safely manage benzodiazepine tapering—without presuming to think we could dictate management for anxiety, PTSD, insomnia—some of the most difficult things we treat in primary care. We want it to stay in that lane.

Dr. Selby: So, as part of the monitoring, what recommendations were made around urine drug screens, or what could the physician do to make sure that the tapering is actually proceeding? [That] They're following through, and it's working?

Dr. Brunner: Urine toxicology is certainly one tool we can use to determine what the exact benzodiazepines are. It's a pretty imperfect tool at best, especially with benzodiazepines, because many of them don't show up on dipstick testing that's used in ambulatory care clinics. It also is not the criteria for having an addiction issue.

And I think it often gets weaponized against patients without having the results discussed with them. So, I think it's just important to keep in context—how is it being used? Why is it being used? I would be much more likely to see a patient back frequently or to see about bringing in their family member to help be part of the process of the taper, as opposed to punitively using your intoxicologies, sort of, to catch them.

Dr. Selby: Yeah. So, very consistent with how we should be providing patient-centered addiction medicine. We wouldn't change that. We wouldn't use urine toxicology, and we should probably make sure we have more confirmatory tests so that we know exactly what people are using, as opposed to not. But use it as a guide, but not as a way to punish people.

And I think that's really an important point to bring forth here because we saw what happened when people were trying to get people off opioids for their pain disorder. The patients reported it being quite punitive and stigmatizing. So, we don't want to have that recur, and I'm really glad that the committee thought to put that in.

Did your committee have an opportunity to look at the scourge of synthetic and illicit designer benzodiazepines, especially as they might be contaminating some of the street fentanyl, or other things like that, or just basically Xanax bars, that are sold illicitly, which have a variety of benzodiazepines that are causing that?

Dr. Brunner: We did really think about that. There is not a lot of scientific evidence to give guideposts, but certainly, what we wanted to highlight was that, in patients who have an opioid use disorder, who are being prescribed evidence-based medication like buprenorphine or methadone, you would still want to continue that prescription, during this process.

You wouldn't want to stop the buprenorphine, you know, take that out of the equation, which I've seen happen to folks. And I did want to jump back to what you were saying regarding the use of the urine toxicology.

One story I tell my detox nurses every time I'm training them is that when I was in residency, we had a patient come in and say they were regularly using Ativan for years. The lorazepam was not something that got picked up by our test, that we did in our hospital, and that patient had their lorazepam abruptly stopped. Ended up having, like, an intractable seizure and passing away. And that whole time, right embedded within the record, it said, this does not pick up lorazepam.

Dr. Selby: No, exactly. I mean, you're right. We should not use point-of-care drug testing as a diagnostic test. It's a screener. It has high false negative rates when it comes to benzodiazepines. And wow, that's really a shocking outcome, just because people were not able to pick up [that] the person was on Ativan. And I'm sorry for that happening. That's really an unfortunate thing.

Clearly, you know, when I look at this, as we said, we have these iatrogenic issues, but when we are trying to fix iatrogenic benzodiazepine dependence, we should not cause more harm because we're in a rush to get people off something that they've been on for so long because we have to do that carefully, thoughtfully.

And if we are going to use tests like urine drug screens, we should make sure that we have the right one, we know what we're doing with them, and not just simply rely on immunoassay point-of-care testing that doesn't tell us the whole story, especially when it comes to benzodiazepines. So, yeah, I think that's really important for our listeners as well, to understand this really nuanced aspect of things.

Now, can we just switch a little bit to the side effects when people are tapering off? And what are some of them, and what can we do to help them manage those discontinuation side effects?

Dr. Brunner: So, certainly, patients describe re-emergence of insomnia, anxiety, feelings of tremulousness, sort of, general, not feeling well often, and so, I think that's where it comes down to a really slow taper. Like, we recommended no more than 5 to 10% every two to four weeks, which is significantly slower than some other guidelines, but still, was something we got patient feedback was a little bit too fast.

I think, of course, the devil, again, it's always in the details. If it's a patient who's only been on a benzodiazepine at a relatively medium dose for a month, that's going to be a really different situation from someone who's been on a high dose for a decade.

Dr. Selby: You know, and clinically, we tend to switch people to longer-acting benzodiazepines, so, either to clordiazepoxide or diazepam—diazepam preferred because it's highly orally bioavailable, has a long-acting metabolite, and it comes in lower doses. As you're tapering those 10%, you can really bring it down to two and one-milligram doses. I find it much harder with lorazepam. And, of course, we tend not to use or switch alprazolam patients onto diazepam because of the risk of these suddenly idiosyncratic seizures that might emerge. What kind of evidence did the committee discover about this?

I know we do this clinically, but was there any evidence to support what we're doing clinically, right now?

Dr. Brunner: You know, that was one of the amazing things to me is—there really wasn't high-quality evidence. And I think there's a real opportunity to do some studies and get some because it is a common way that we're trained, especially within addiction medicine, to transfer over. And we have all these calculators that make it seem very much like you're getting the exact diazepam equivalent they need, and to find out many of those equivalencies were based on people just subjectively saying that they felt about the same level of sedation was startling, and really helped explain why patients have such a hard time with those types of treatments.

Dr. Selby: My recommendation was, at least clinically, to switch over. You're roughly hitting about 50% replacement, and then you have to actually go up till they are comfortable before you go down because, otherwise, you're going to get immediate reemergence of symptoms. And so, we are beginning to see that we have these cultural practices of addiction medicine, but the evidence really needs to be built further. So, we're going to put that as, right now, with incomplete information, be safe, do it slowly. But there are these cultural practices of switching, but the evidence is pretty weak, other than just, you know, what we've done to practice our knowledge.

Now, one of the barriers that we often come across is patients are not ready. They're afraid. And why do you think that is, and what can we do to help them reduce these fears, and help them navigate the tapering process?

Dr. Brunner: I think that often that fear relates to having experienced maybe a couple days of running out of the medicine, having had really wicked withdrawal symptoms during that time, or having read some horror stories, or heard from other patients how awful the experience can be. And it truly can be very uncomfortable for folks, and so we want to honor and take that into account.

As I mentioned before, you know, it can even be lethal, but I think that when patients feel like you're on their side, that you authentically want to help them, that you will be there with them, and that they can call you and return to clinic, and that they're being given support. I think that can be a really different experience.

I was taught by a fantastic mentor to always think about, what is the menu of things I can safely offer to a patient? And over time, that menu might get smaller if they have a couple of benzo car-related accidents. Obviously, that is not a safe path anymore, for example, but what are the paths forward that you

can go to? And so, I think keeping that just long, slow focus in mind is always helpful.

Dr. Selby: That is very helpful. There are other cultural practices that have come into addiction medicine, such as giving weekly prescriptions or daily prescriptions, depending on how people are. And, of course, people can have both: a need for benzodiazepines but also develop benzodiazepine use disorder. And were there any tips or guidance to clinicians of how to do a differential diagnosis when you're not really sure what's going on?

Dr. Brunner: I think that in those situations, it's just really important to have a sense of the landscape of specialists and support tools that you can use for when those situations arise. Because I think that while 95% of this can be done excellently by primary care docs—docs of all types—I do think there is that 5 to 10% of times where you really need that, sort of, specialty lens and ability to take a more detailed look.

Dr. Selby: Exactly. So, when their specialty lens—typically, some of the things we do is switch them to less potent benzodiazepines, get that dose up to the dose that keeps them comfortable, give them a monitored prescription that gets picked up regularly from the pharmacist.

And then one of the things that we've also done is if you're not sure, and people are trying to meet criteria, is to give them maybe 10 days' worth of medication and have them come back in seven days, making sure that they are demonstrating control over the medication. It's good for their self-esteem that they can actually do it. And if they don't do it, then you know that maybe they, themselves, are having a problem with the medication and overusing it.

So, those are several strategies that specialists like us would do to help tease that apart, much like how we try to figure out the pain and addiction when somebody's on an opioid, similarly to kind of separate it out, to see, and of course, never diminish the experience that people are having, you know, they're having symptoms of addiction. We still want to be empathic towards that.

Dr. Brunner: Yeah, I think nurse visits can be a nice way to do that, too. Like having those be weekly. That can be, kind of, a nice space, and then that builds out some expertise within your team as well about feeling comfortable having those conversations.

Dr. Selby: Oh, that's a great idea. You could use the multidisciplinary team in primary care that can divide some of the work. So, the physician does some of that prescribing, but then the weekly follow-up, and then brief counseling, and

how things—checking in with the nurse creates that sort of safety, around the patient. Sounds like a great thing.

I know we're coming close to the end, and I wanted to ask you if there are any other tips that you want our audience to know about the new guideline, or is there anything else that you'd like to add before we go into the key takeaways from today's talk?

Dr. Brunner: Maybe just that it is quite long. So, if anyone who's interested in a more detailed dive, there are going to be some ASAM webinars that should focus on different aspects. But then, just the other [thing] is, just keep in mind the scientific limits of what we're doing in this area because another just fascinating thing, we had docs of all different disciplines, from all over the country, and there was just such a dramatically different way of treating based on how we were trained because of the paucity of data.

So, whenever there's variable practice like that, I think it makes it really clear that we need better data.

Dr. Selby: Absolutely. So, thank you so much for that. And if you don't mind just summarizing the key takeaways for listeners?

Dr. Brunner: I would focus on going low and slow. Really being careful about distinguishing physical dependence versus an addiction issue. And then always paying attention to how the patient feels and creating a plan for them for next steps if things aren't going well during any step-down.

Dr. Selby: I heard your compassion coming through is that we need to take a compassionate, patient-oriented, patient-centered approach to this, and believe our patients' experience, and listen to them as they're going through this process. And sometimes, that means we may need to stop the tapering for a moment.

In fact, sometimes I've noticed I have to go up for a bit because somebody is having a really bad time. Life issues are happening. We pause the taper. We go up for a bit and then come back down again.

Dr. Brunner: Yeah, I think that, definitely, using the same level of humane compassion and love that we lean into treating other diseases with is so important in this particular disease as well. And then, also, recognizing that it doesn't need to happen immediately and there's no, at all, recommendation in this to put large quantities of patients immediately on some forced taper. I think that the way that was sort of extrapolated out of the CDC pain guidelines, they

were never meant to be used that way. But it does make me feel fear to think about these being used in that way.

Dr. Selby: Absolutely. Thank you so much, Dr. Brunner, for sharing your valuable insights on benzodiazepine tapering and the new joint clinical practice guideline. A link to the guidelines can be found in today's show notes.

Make sure you download your copy today and review it. For additional information on tapering benzodiazepines, don't miss ASAM's free webinar series that Dr. Brunner alluded to. They will explore the considerations in greater depth on when you're considering tapering of benzodiazepines, especially tapering for older adults, tapering in primary care, and addressing some of the challenges we highlighted today.

Don't forget to subscribe and share this episode with colleagues who might find this information helpful. We'd also love to hear your thoughts, what challenges you have encountered when it comes to benzodiazepine, and what solutions have worked for you.

Be sure to check out our social media posts and join the conversation. Thanks for listening, and we'll see you next time on ASAM Practice Pearls.