# SCOPE of PAIN: Safer/Effective Opioid Prescribing Education

Podcast - October 1, 2023

## Episode 3

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**Ilana Hardesty:** Thanks for listening to Boston University Chobanian & Avedisian School of Medicine's Safer and Competent Opioid Prescribing Education: *SCOPE of Pain* Podcast Series. I'm Ilana Hardesty.

This series has eight episodes. If at any point you want more information on receiving credit, please visit our website, scopeofpain.org. There are also resources that accompany this series. All of it can be found at scopeofpain.org.

In this episode, we'll speak again with Dr. Daniel Alford and Dr. Erica Bial, along with Kristin Wason, a primary care nurse. And we'll bring in Patrick Kelly, a senior lecturer in the Department of Pharmacy practice at the University of Rhode Island with a primary focus on the integrated pharmacy practice laboratories.

In the last episode, we reviewed the wide range of available therapies to manage chronic pain: treatments that include non-medications, non-opioids and opioids.

Let's start with the elephant in the room. Our case study patient Michelle is taking chronic opioids, 60 morphine milligram equivalents, for her chronic musculoskeletal and neuropathic pain. But do opioids really work for chronic pain?

**Dr. Daniel Alford:** Well, there have been some meta analyses that have shown that opioids versus placebo, looking just at high quality studies, that opioids actually have a statistically significant, however small, improvement in pain and physical functioning. What about opioids versus non-opioids? Well, those are really low to moderate quality studies that show there's similar benefits between the two. What's really key to understand here is that these studies, the follow up ends at six months. Most of them are around three months. So what happens after six months in terms of efficacy? We don't know. It hasn't been studied. There was a randomized controlled trial (RCT) that looked over 12 months, looking at musculoskeletal pain-related function, comparing opioids versus non-opioids and found that they were similar. Okay. Whenever you look at an RCT, you should think about does this study generalize to the patient sitting across from me? And there are some limitations to generalizability. When you look at the methods, they excluded any individual who was already on long term opioids. So our patient here, Michelle, would not have qualified for this study. And of those that were eligible, 89% said, No, thank you. I don't want to be enrolled in this study. So of the 11% who were not already on long term opioids who were eligible, there's no difference between opioids and non-opioids. So again, think about the generalizability.

There were two longer term follow up studies that were observational studies with an outcome of at least 50% pain relief, and they found that 44.3% of individuals on chronic opioids had at least 50% pain relief. So it's not 0%, it's not 100%. So that's what we know about efficacy. Erica, what do we know about safety and risks?

**Dr. Erica Bial:** You know, there are two sides to every coin and they do carry safety challenges and important risks. I think the first risk you always want to think about with any substance that you're going to expose a patient to is allergy. True opioid allergies are quite rare. But there are other important risks that we don't think about much, things like immunosuppression. So in fact, in animal models, opioid-induced immunosuppression does exist. And we do know that humans who are on chronic opioids, especially at high doses, do seem to have an increased risk of pneumococcal disease, as well as community-acquired pneumonias. There are direct and indirect organ toxicities related to opioid exposures, especially endocrinopathies, so adrenal suppression as well as gonadal suppression, can in fact be problems. And particularly at high doses, so greater than 50 MMEs, these doses are associated with a two-fold increase in fracture risk, and it's not clear whether that's directly related to changes in bone metabolism or if they're related to endocrinopathies or another factor. There are also direct adverse effects of the opioids. Nausea, sedation, urinary retention, and sweating are all frequently seen, especially in institution of or with changing of dose therapy. Constipation, which sometimes really does not tolerate, hypodynamic bowel and quite dry stool. Pruritus occurs for many patients. And the most important one, the one that's the key takeaway here, is the risk of respiratory depression and death.

So how might we want to manage those adverse effects? I made it sound terrible. Well, you know, when we do make the choice to use an opioid, nausea and vomiting will actually usually resolve in a few days; just exposure to the substance, and that kind of acclimatizes. You could certainly use antiemetics, or just switching agent for many patients is adequate to resolve that symptom.

We need to always, always recognize the risk of sedation. So if a patient is experiencing sedation, especially when you're instituting opioid therapy or when you've had a dose increase, the treatment is decrease the dose because sedation is a preamble to respiratory depression and death.

Constipation is the most common problem that we see with chronic opioid therapies. And really it should be anticipated and planned for. So anytime you're instituting therapy, you should be talking to patients about a bowel regimen. So a range of options: stool softeners, osmotic stimulants, peripherally-acting opioid antagonists, or you could try switching opioids, which sometimes works. But we want to remind patients to avoid bulking agents, so things like fiber supplementation, they are not useful and can actually cause harm in this circumstance.

When patients experience pruritis with an opioid, that also usually only exists at the institution of therapy, but you could rotate or switch agents, or you could apply an antihistamine, either systemically or topically.

When you see urinary retention, you could rotate opioids, so switch agent, or you could try decreasing the dose.

**Dr. Daniel Alford:** I think in addition to just knowing general adverse effects, we should also think about our patient. Do they have specific risks because of who they are? For instance, as our patients age, there is a decline in therapeutic index and there is a predisposition to adverse drug effects and there's an increased risk of falls and worsening cognitive function when we prescribe opioids in some of our patients who are aging.

Also, some of our patients will have liver disease or kidney disease, and there are certain considerations for those patients. For liver disease, we know there's a decrease in opioid clearance. Specifically, morphine, oxycodone, and hydromorphone need to have their doses reduced or we need to prolong the dosing interval.

For patients with kidney disease, there is a decrease in opioid excretion. The preferred opioids would be hydromorphone or fentanyl or buprenorphine or methadone. Oxycodone would be considered a second line opioid due to the active metabolites, and we should probably avoid morphine and codeine because of their active metabolites.

Now, I also know that there are specific drug-drug interactions (DDIs) and I'm going to turn it over to our pharmacist, Pat, to talk to us about how should we think about opioids and other drugs?

**Patrick Kelly:** Really, what I would recommend when you're prescribing is to kind of do a holistic view, which you're doing already, which would be a best practice. What other medicines is this individual on? As a pharmacist, what I go through is, is there anything here that would be a contraindication, and then I start looking, is there any issue where we're worried about additive effects? Are other CNS depressants that may not be opioids, may not be used for pain, may not be controlled substances, but still have a sedating effect because all of these things can be additive and could make someone experience respiratory depression or something along those lines.

**Dr. Daniel Alford:** So how do you generally communicate those concerns with prescribers and then with patients?

**Patrick Kelly:** Well, it depends. Ideally that would be an actual conversation and most of the time that's going to be over the phone unless you're in some kind of clinic where the pharmacist and the provider are sharing space, you know, you could grab someone and you know, between exam rooms. But most of the time it's going to be over the phone, ideally, and you want to talk to the prescriber directly, especially if it's something that's serious enough to rise to the level of, Hey, as a pharmacist, we need to do something about this drug-drug interaction. That would probably be the main course of action and that would be the first line of communication. And then there would always be that follow up with the patient as well. So the pharmacists are really communicating with both and sometimes acting as a mediator between the two, trying to get bits of information, as possible, from both parties to kind of form some kind of opinion.

**Ilana Hardesty:** What about addiction? Aren't we all at risk for developing an addiction?

**Dr. Daniel Alford:** Well, that's what some people think. And I'm going to dispel that myth, based on probably the best study that I'm aware of, which was a systematic review of 38 studies. About a quarter took place in primary care and about half in pain clinic settings, and the other quarter were in other specialty clinics treating patients with pain. What did they find? Well, they found that opioid misuse rates were somewhere between 21 and 29%. So misuse means that the patient took the opioid contrary to the way it was prescribed or the reason it was prescribed. For instance, you're prescribing it for their neuropathic pain and they took it for their headache, or you're prescribing it for their back pain, and they took it because it helped them sleep. That would be considered misuse. So about a quarter of your patients might do that. But what about addiction, which was really your question? And it's somewhere between eight and 12% in this study. Addiction was defined as a pattern of continued opioid use, despite negative consequences, despite harm. And so, again, that was about 8 to 12%.

**Dr. Erica Bial:** Dan, I'm really glad you brought that up because, of course, the risk here is not only to the patient, but also there are collateral risks in the community. Right? Just having those medications around presents risks to others. So there are risks to young children and inadvertent ingestion and overdose. Adolescent experimentation can lead to overdose as well as to addiction. And, of course, other family household contacts: family, visitors, others. How do we mitigate some of those risks? We need to talk to our patients, particularly about safe storage, like a lockbox; safe disposal, and we can provide some resources for ways to dispose of opioids safely in one's community; as well as opioid overdose education and naloxone distribution. I think this one cannot be stressed enough. We want to use a number of different risk mitigation strategies, including naloxone co-prescribing every time that we're prescribing a chronic opioid.

So of course, I would be concerned that these risks might also increase with higher dose opioids. Dan, how do you deal with that, especially in primary care?

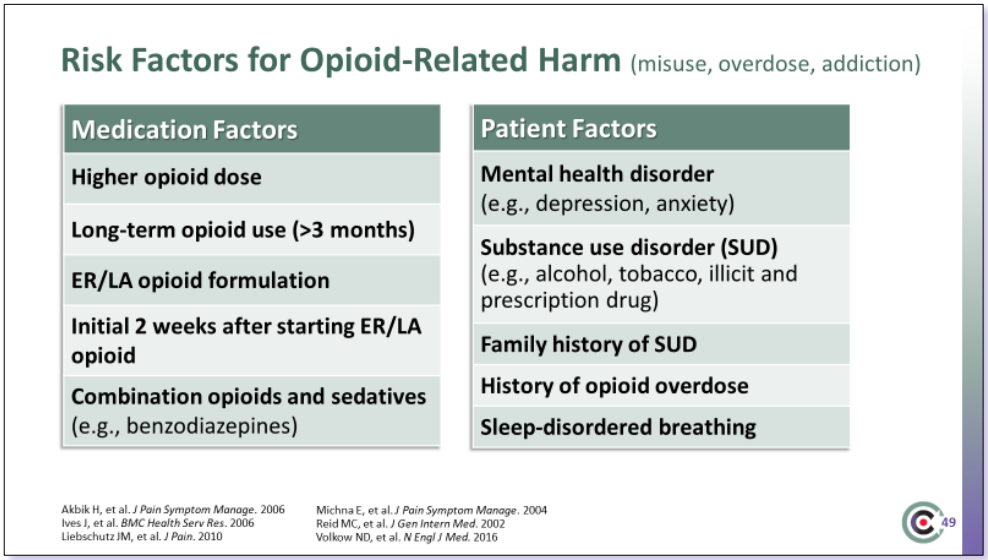
**Dr. Daniel Alford:** Yes, that's a good question. And higher doses are absolutely associated with risk, such as developing hyperalgesia, which is increase in pain sensitivity; a risk of decreased function; immunosuppression, which you had talked about; and overdose. And there have been a number of population-based studies that have looked at dose compared to overdose risk. All of the studies show a gradual increase that's dose-dependent. And some studies have shown that the overdose risk actually is two-fold once you get above 20 morphine milligram equivalents and it actually jumps up to nine-fold when you get above 100 morphine milligram equivalents. So we need to be aware that increasing the dose of opioids carries increased risk.

And the CDC guideline addresses this issue of high dose opioids by saying when starting opioids prescribe the lowest effective dose, use caution with any dose, make sure you talk to patients about the risks when considering increasing the dose, and really try to avoid increasing doses above levels with diminishing benefit relative to risk.

Now, what about patients who are already on high dose opioids? What do you do about those? And we should manage them as higher risk. How do we do that? Well, you're going to increase the amount of monitoring and support that you offer them. And again, the CDC addresses this specific issue. And that is, for patients who are already on high dose opioids, carefully kind of measure and weigh the benefits and risks. If the benefits outweigh the risks, continue the opioids, but optimize other therapies as well. However, if you think the risks are greater than the benefits, optimize other therapies and gradually taper opioids to lower doses. Very importantly, they say, and I agree, unless there's some life-threatening issue, that is, an impending overdose, do not discontinue opioids abruptly or rapidly reduce opioids from higher doses. So we need to be really careful here when we decide that opioids need to be tapered, we should do it in a controlled and evidence-based way.

**Ilana Hardesty:** For our case study Michelle, or any patient on opioids, is there a way to determine the risk for opioid misuse and harm?

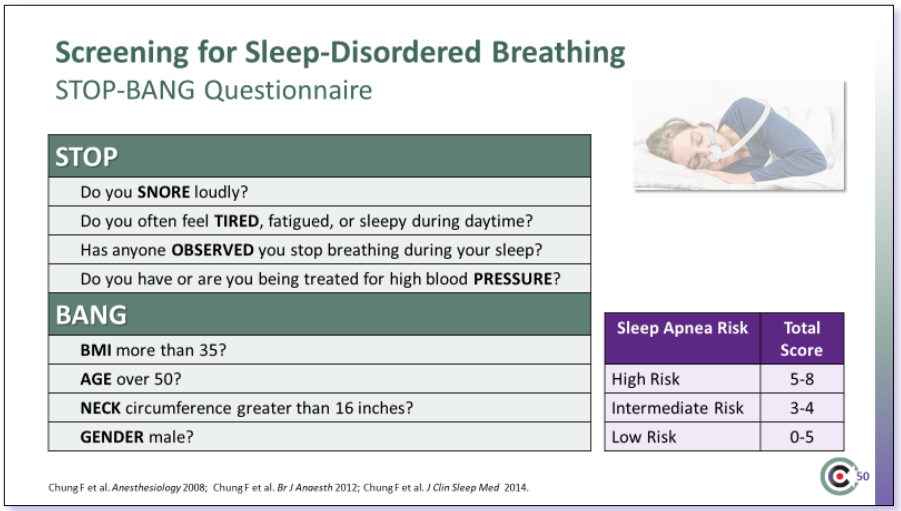
**Dr. Erica Bial:** It's a great question. It's impossible to 100% predict the risks of opioid misuse and harm, but certainly there are risk factors that the clinician can be aware of to help us side. To find those patients that might need to be monitored a bit more closely. So there are factors related to the medication choice: so higher opioid doses; if the patient is taking these medications long term, which I would define as more than about three months; patients who are on long acting formulations; and any time that there is the institution of therapy or any time that you are starting to rotate the patient from short acting to long acting therapy, those first two weeks are a critical period. And any time that the patient is taking medications that have a synergistic increased risk. So particularly combinations of opioids and benzodiazepines which carry that black box warning.




In addition, there are patient factors that we should be aware of and thoughtful about. So co- presentation with mental health disorders, including depression and anxiety. If a patient has a known preexisting substance use disorder, whether that is opioid as the substance or another substance, so things like alcohol, tobacco, as well as illicit and prescription drug use. If there's a family history of substance use disorder, certainly if the patient has a history of prior opioid overdose and if the patient has sleep disordered breathing. So a challenge in recognizing all of this is that that's an awful lot of risk to be assessing and monitoring and screening for. Dan, how do you do it in a primary care environment?

**Dr. Daniel Alford:** Great question. You know, in primary care, we have lots of competing priorities. So how do we actually screen for these patient-related factors? So I'm going to talk a little bit about it, but then I'm going to hand it over to Kristin, because, to be quite frank with you, a lot of these screenings are done before I even see the patient. So I'm going to have her talk about how that gets done.

But let me just talk about one in particular, and that is screening for sleep-disordered breathing, because it's so critical that we know whether our patients have sleep apnea because of the risk of overdose. What I use is one that I can remember quite easily, and




that's called the STOP-BANG Questionnaire. So **STOP** stands for Does the patients **snore** loudly? Does the patient feel **tired**? That's the T. The O is, has anyone **observed** the patient stop breathing during sleep? And then the P is, is the patient being treated or do they have high blood **pressure**? P for pressure. So snore, tired, observed, stopping breathing and pressure. The BANG part is: is the patient's **BMI** more than 35? A is **age** over 50. N is **neck** circumference greater than 16 inches. And G is **gender** for male. And based on the number of these items that are positive, you can classify your patient as being low, intermediate and high risk for sleep apnea.

Okay. So what about psychiatric comorbidities, which are really important in terms of risk stratifying our patient for opioid misuse. And they're common in our patients with chronic pain, whether we look at sleep disorders, depression, anxiety, personality disorders, PTSD, and substance use disorders. Not only are they common in patients with chronic pain, but there is a bi-directional relationship. These psychiatric co-morbidities make pain worse and harder to treat, and chronic pain makes these psychiatric co-morbidities worse and harder to treat, and we should be looking for them and co-managing them. So these psychiatric co-morbidities are common. We heard from Erica that they can predict risk to opioid misuse if patients have them. And the question is, in primary care, how do you screen for them? So, Kristin, can you talk to us about how you screen for sleep disorders, depression, anxiety?

**Kristin Wason:** Yeah. And so I'll say this is a great way to utilize other members of your care team because patients a lot of times are like seeing the nurse first or a lot of times we can have more casual conversations with patients sometimes. And so I think with that, like we get a lot of face-to-face time with folks and nurses are trained on chronic disease management. And so chronic pain is like right in our wheelhouse. We really are also trained in having this whole-person approach and really trying to understand, you know, someone's sort of mental health, their physical health, and their social wellbeing. And so again, like

pain and mental health conditions play right into here. And so in our practice we do this a few ways. When patients are coming in for primary care visits, a lot of times as they go and check in at the front desk, they're handed like a one-page form that has a few different screening tools on it. I work in a large academic urban medical center, so we have this form available in many, many languages, and typically the patients will fill it out as they're being roomed and the medical assistant or the nurse will actually go in and check on the patient and then enter and all that information into the electronic medical record. And any positive screen is then brought to the provider so that the provider can then go in and sort of address this in more detail during their visit.

So we have a number of like abridged tools. First one that I'll mention is our tool that we use for screening for sleep disorder, and what we use is an Insomnia severity Index or something called an ISI-3. And what this is, it's a short screening tool that's used to identify clinically significant insomnia. And so it's a shorter version of our longer seven item ISI screen. It's three quick questions that ask patients to rate the severity of their insomnia problem over the last two weeks from a scale of 0 to 4. And so a zero would be that you are very satisfied with this particular component of your sleep. And a four would be that you're very dissatisfied. And so those three questions have to do with the satisfaction with your sleep. How is sleep interfering with your daily functioning, and are you worried or stressed about your sleep? Anyone that screens less than a seven would be a negative screen and then you're basically done. But if it's a seven or more, then that would be a positive screen. And so that person really would need to have more of a discussion and maybe a diagnosis about like the type of insomnia that they have and how we should pursue treatment.

**Dr. Daniel Alford:** And what about depression and anxiety?

**Kristin Wason:** The tool that we use is the two-question PHQ-2. And what this PHQ-2 screening tool is, is it ask patients over the last two weeks, how often have you been bothered by having little interest or pleasure in doing things or two, feeling down, depressed or hopeless? And patients will answer basically as a zero, it's not an issue at all up to a three, which would be this is occurring to me like every day or nearly every day. And so what we'll do is we'll add up these scores of 0 to 3, depending on the severity of their symptom. And anyone that screens 3 or more is, again, a positive screen. And then that person would buy themselves a PHQ-9, where we ask more questions about their depression, where we can sort of help lead us to if this is a true diagnosis or not.

For anxiety, we use a GAD-2, which again looks at symptoms over the past two weeks, how often have you been bothered by any of the following: one, feeling nervous, anxious or on edge, or two, not being able to stop or control your worrying? And so again, we're rating these as like a zero, it's not an issue to a three, this is something that is really affecting my day to day life. And a score of 3 or more is where we would then move on to the more thorough GAD-7 screener.

**Dr. Daniel Alford:** Kristin, I should also mention that there are short screeners available for screening your patients for PTSD and suicidality. And these are really important issues that need to be looked for in our patients with chronic pain.

I also want to talk about screening for substance use. And again, in primary care, we're looking for the briefest way to do that. The tool that I would like to use is TAPS. T-A-P-S. T is for **tobacco**, A is for **alcohol**, P is for **prescription** medications, and S is for other **substance** use. And it's all about in the past 12 months, we ask how often have you used tobacco or any other nicotine? And that includes e-cigarettes and vaping. Had five or more drinks (for men) or four or more drinks (for women) containing alcohol in one day? Used any prescription medication just for the feeling, more than prescribed, or they were not prescribed to you? And then finally, used any drugs, including marijuana, cocaine, crack, heroin, methamphetamine? It's really critical that if you have others asking these questions in your practice, that they ask it the way it was validated. They don't say, "do you use drugs?" or "you don't use drugs, do you?" It's important to say in the past 12 months, **how often have you**…? Because even if somebody's under reports the amount of times they had four or more or five or more drinks, anything other than never for any of these questions is considered positive.

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**Ilana Hardesty:** Thank you. Doctor Alford, Doctor Beal, Patrick Kelly and Kristen Wason.

Michelle screened negative for sleep disordered breathing and negative for insomnia, depression, anxiety and substance use. Join us for episode four when we need to respond to our patient's request for opioids to be prescribed at this first visit. Remember, she just ran out.

Should the new PCP prescribe opioids or not? We will discuss how to determine when and if opioids are the appropriate choice for the treatment of chronic pain.

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I'm Ilana Hardesty. Thanks for listening.