SCOPE of Pain

TRANSCRIPT

Part 1: Understanding Pain and Opioids	
SLIDE	**TEXT**
1	Thank you for participating in Boston University School of Medicine's Safer and Competent Opioid Prescribing Education: ***SCOPE of Pain*** program. I'm John Emery, your moderator.
2	This web-based program consists of two parts that follow the case of Kathy James to discuss management of acute and chronic pain. After each part, you'll be directed to a post-test. Further information about receiving credit is available on the information page, and will be provided at the end of the second part.
3	We'll discuss the case with Dr. Daniel Alford, Professor of Medicine, Associate Dean of Continuing Medical Education and Director of the Clinical Addiction Research and Education Unit at Boston University, and with Dr. Jessica Taylor, Assistant Professor of Medicine at Boston University and medical director of the Massachusetts Office Based Addiction Treatment ECHO tele-mentoring program. Both Drs. Alford and Taylor are general internists practicing primary care and addiction medicine at Boston Medical Center.
4	SCOPE of Pain was developed in collaboration with our national partners, the Council of Medical Specialty Societies and the Federation of State Medical Boards. This educational activity is supported by an independent educational grant from the Opioid Analgesic Risk Evaluation and Mitigation Strategy or REMS Program Companies.
5	Through the case presented in this program, you will learn how to ▪ Optimize safety when prescribing opioids for acute pain ▪ Determine when opioid analgesics are indicated for chronic pain ▪ Assess pain and prescription opioid misuse risk ▪ Educate patients about opioid risks and realistic benefits ▪ Monitor patients on opioid therapy for benefits and harms ▪ Assess and manage worrisome opioid-taking behaviors ▪ Safely taper long-term opioid therapy ▪ Identify and manage patients with an opioid use disorder
6	SCOPE of Pain covers strategies for the safer use of opioids for managing pain, by reviewing best practices and the CDC guideline recommendations, and sharing clinical pearls. This training does **NOT** cover palliative care or end of life pain management, due to the differences in overall treatment goals.
7	Let's begin Part 1: Understanding Pain and Opioids
8	Meet Kathy James. At 32, she was in a motor vehicle crash, resulting in a right hip fracture. On imaging she had a displaced femoral neck fracture. After successful surgery, her pain was managed with nerve blocks and intravenous hydromorphone. Dr. Alford, can you discuss acute pain assessment and what factors might predispose a patient to developing chronic pain?

9	**Assessing Acute Pain** In thinking about assessing acute pain, I think Dr. Oken got it right by saying many factors influence self-reported pain ratings, including gender, social support, provider characteristics, and trust. I think many clinicians are used to assessing acute pain by looking at: How intense is the pain? Where does it hurt? When did it start? How long has it been painful? Does it radiate? What makes it worse? And, what makes it better? And usually we're using numeric rating pain scales. On a zero to 10 scale, where usually the literature describes mild pain as 1 to 3 on a 10-point scale; moderate pain, 4 to 6; and severe pain, 7 to 10. But in certain instances, it's helpful to use visual analog scales with faces as demonstrated on this slide. So, we know that some individuals go from acute pain, which is a normal response to injury, such as surgery to develop chronic pain, which is really a maladaptive response to that injury, or surgery in this case.
10	**Risk Factors for Chronic Postsurgical Pain** And we don't completely understand why it happens, but we understand that there are some changes in the expression of neurotransmitters, receptors, and ion channels. There are actually changes to the nervous system, or plasticity in the structure, connectivity, and survival of neurons. There are multiple risk factors for developing persistent pain after surgery, and they include genetic, and patient-related disposition, being younger, or being female, certainly having mental illness prior to surgery, anxiety, depression. But there are surgical risk factors, as well, and we know that certain surgical procedures, like having an amputation, or mastectomy are higher risk for developing chronic pain. If the surgery involves nerve ligation, or injury, and certainly in the postoperative setting, if the person has high-intensity pain, or pain that lasts longer than expected, these are all risk factors for developing chronic pain. And chronic pain is really defined as pain that lasts more than three to six months, which really is longer than is expected for the surgical procedure.
11	**Progression to Chronic Pain** In terms of predicting who will develop chronic from an acute pain episode, here's one scale that's been validated specifically for acute back pain, and it's called the STarT Back Screening Tool. This is a patient self-administered questionnaire that helps identify modifiable risk factors, and they're really broken down into biomedical risk factors, psychological risk factors, and social risk factors for developing chronic pain disability. And by using this questionnaire, you're able to stratify patients into low, medium, and high risk for developing chronic back pain after the acute back pain.
12	After her surgery, Kathy was discharged, with visiting nurse and home-based physical therapy. On discharge, she received a prescription for oxycodone 5 mg; 1 to 2 tablets every 4 to 6 hours as needed. Her prescription was for 120 tablets. Dr. Alford, what is the correct amount of opioids to prescribe after surgery?

13	**Opioid Over-Prescribing After Surgery** Well, that's a very good question. We do know from recent studies that there's over-prescribing postoperatively. Looking at this slide, where there are different types of surgery – thoracic, C-section, and etc. – you can see when they followed up with patients to ask them, "How's your pain? The pain is resolved? Do you have any opioids leftover? How many of the opioids that were prescribed did you take?" You can see in the first three studies, over 70 percent took less than half their tablets that were prescribed. The next study showed that 84 percent, 86 percent had pills left over, and so forth. And so, clearly, we were prescribing too many opioids postoperatively.
14	**Source of Prescription Opioids Misused** The problem with this is that people have opioids left over. And from this survey, the National Survey on Drug Use and Health, where they asked individuals who had misused a prescription opioid in the past year where they obtained it, 53 percent said they got it from family or friend. You can see, also, on this graph that about a third got it from a single doctor, and only 1.4 percent got it from multiple doctors, or doctor shopping. But the vast majority got it from family or friend, because that family or friend had pills left over.
15	**Risk Factors for Acute to Chronic Opioid Use** Now, there are risk factors for developing chronic opioid use after getting opioids for an acute pain syndrome. And those risk factors include being male, being older than 50, but the biggest risk factor is having a history of a drug use disorder. You'll see the odds ratio there is 3.15, but also having an alcohol use disorder, benzodiazepine use, antidepressant use, and depression. And it turns out from multiple studies that about 3 to 5 percent of opioid-naïve patients were given an opioid in the acute pain setting, become long-term opioid users.

16	**Oral Analgesics for Postoperative Pain** So, now if we compare oral analgesics for postoperative pain, this was cognitive review that looked at all of the various studies that compared agents in the postoperative setting, and most of these were in dental procedures, dental extractions, where individuals had moderate to severe pain. And the outcome was the number needed to treat versus placebo. And the number needed to treat was to achieve greater than, or equal to 50 percent maximal pain relief over 4 to 6 hours. That is what number of patients, or individuals needed to be treated to achieve that outcome. So, the smaller number is better. And so you can see that Ibuprofen, it took about two and a half individuals to achieve that outcome, the same for other NSAIDs. Acetaminophen, it took about three and a half individuals to achieve that outcome, and then, oxycodone, codeine, gabapentin were worse than those agents. The best results were when they combined agents, and the best result was Ibuprofen and Acetaminophen, where it only took one and a half individuals to achieve that outcome of greater than, or equal to 50 percent maximal pain relief over 4 to 6 hours. And you can see that these studies in combination included over 50,000 participants in about 460 high-quality studies.
17	**Post-Op Pain Management Clinical Practice Guideline** This is consistent with national guidelines around postoperative pain management, where the recommendations are to offer multimodal analgesia, which is a strong recommendation with high-quality evidence, and that most severe postoperative pain diminishes rapidly within the first few days, but you need to remember to individualize your approach, based on the patient that you're treating. Yet there's insufficient evidence to guide how quickly to taper an opioid. However, the general recommendation is that you can decrease by 20 to 25 percent every one to two days, if the pain is improving, and that minor surgeries, it's totally appropriate to discharge the patient on non-opioids, like Acetaminophen, or NSAIDs, or a combination of the two, and that if you do prescribe an opioid in the postoperative setting, it really should be with a limited supply, realizing that the acute pain is going to resolve. This is consistent with the CDC guideline recommendation; that is, if you're going to prescribe opioids for acute pain, it should be a short duration, such as less than three days is often sufficient; rarely would you need more than seven days.

18	We next see Kathy James 8 years later, when she presents for an initial appointment with a new primary care provider. **Dr. Alford:** Good Morning Ms. James, I'm Dr. Alford. It's nice to meet you. Let's see, what brings you here today? **Kathy:** Hi Dr. Alford. It took forever to get an appointment with you. You must be a very busy doctor… I made an appointment with you because Dr. Robertson, my old doctor, retired. Basically, I'm here because of my diabetes and the pain in my feet and hip. Here: I brought my medical records for you… **Dr. Alford:** *PAUSE*…OK, thanks…so let's see. Looks like you've had diabetes for a few years, and that's likely the cause of your foot pain, and your hip pain started after your accident and surgery…and your weight… **Kathy:** …oh I know you're going to tell me I need to lose weight. That's what Dr. Robertson always said too. And while we're at it I know I should quit smoking too.
19	**Dr. Alford:** Well it's good that your diabetes is controlled, and I see you're on a couple of different pain medications too. **Kathy:** Yeah, and I've tried EVERYTHING else! All the other things either didn't work, or they gave me bad side effects.
20	**Dr. Alford:** OK…tell me about yourself…How about work and home? **Kathy:** Well, I'm married, and we have three kids. Once the littlest went to first grade I went back to work, but only part time, so I could be home when the kids get home from school. **Dr. Alford:** OK…how much do you smoke and when did you start? **Kathy:** I smoke about a pack a day…Although I don't smoke the entire cigarette and I used to smoke over a pack per day…I've been smoking since I was in college. **Dr. Alford:** Do you sometimes drink beer, wine or other alcoholic drinks? **Kathy:** Not too often. I'll have a one or two glasses of wine during the holidays, or occasionally on weekends, when we're celebrating someone's birthday or something. I don't do anything worse than that though. My mom was alcoholic, and I saw what it can do to you AND your family!

21	**Dr. Alford:** So tell me what's going on with your pain medications at this point. **Kathy:** Well… honestly, because it took so long to get an appointment with you, for the past couple of weeks I've been trying to ration out my pain pills. Just taking it twice a day instead of 4 times. But I'm in awful pain! I'm taking half my dose, and I'm in more than twice as much pain! I just took my very last pill this morning, so I definitely need another prescription today. Dr. Alford, How will you assess her chronic pain? What are the issues around chronic pain and opioids?
22	**Acute versus Chronic Pain** Well, let's start thinking about the difference between acute versus chronic pain. Acute pain is a life-sustaining symptom. It's adaptive, and it really elicits motivation to minimize harm, or to allow for healing. But let's move on to chronic pain, which is – which really can be a disease in itself. It's maladaptive. It's pathological. And it's really a disorder of the somatosensory pain signaling pathway, influenced by genetic, and epigenetic factors. We usually think about chronic pain as nociceptive, that is pain that's somatic, or visceral, cause by some noxious stimuli, or neuropathic pain, which usually involves nerve injury, or nerve impairment. It's also important to note that chronic pain has been associated with higher risks of fatal and non-fatal suicide attempts.
23	**Barriers to Adequate Pain Care** There are also lots of barriers to adequate pain care, and they include negative attitudes, and disparities in pain care, inadequate training in managing patients with chronic pain, lack of decision support for chronic pain management. And I think a really major issue is the financial misalignment favoring the use of medications. It's a whole lot easier to prescribe a medication, than it is to refer someone to non-pharmacotherapies. There's also lack of access to pain specialists, and comprehensive pain care, and finally, an overburdened primary care system, where we have lots of competing priorities.
24	**Opioid Prescribing Declining Since 2010** What's interesting to note is looking at opioid prescribing over time, and really starting in the 1990s, we saw a dramatic increase in opioid prescribing. And there's a lot of reasons for this. However, you can see that around 2010-2011, we saw a leveling off, and those are the green bars, to the point now where we're seeing a gradual decrease, both in opioid prescribing, as well as the red line, which shows a decrease in morphine milligram equivalents. That is, we're prescribing less opioids, and we're prescribing less high-dose opioids. Now, the reason for this is, is it more judicious prescribing, or is it more fearful prescribing? It's unclear. The bottom line is we are prescribing less opioids. However, you can notice that we're still not even close to where we were in the 1990s.

25	**Opioid Trends** So, in terms of opioid overdose deaths, we can see that there have been three waves since the 1990s. The first wave is the purple line, which shows an increase in overdose deaths associated with prescription opioids. But that over time started to level off, probably due to decreased opioid prescribing, as we've previously talked about. But that was taken over by the orange line, which are overdose deaths driven by heroin use, because heroin was flooding the market, and was available and cheap. And in the third wave, which is what we're currently in is overdose deaths that are driven, or attributable to synthetic opioids, namely illicit fentanyl that's being sold on the streets.
26	**Opioids and Chronic Pain in Perspective** But let's put opioids and chronic pain in perspective. We all know, from multiple systematic reviews, that the long-term efficacy of opioid therapy for chronic pain, has been inadequately studied, and that opioid prescribing should be more judicious, and that opioid misuse could be fatal, including overdose, and use disorders, and that opioids for chronic pain are only indicated after alternative safer options are inadequate, and only one tool for a multimodal approach for managing severe, chronic pain. And these are really consistent with the CDC guideline recommendation, which states clearly, "Do not use opioids as first-line therapy, and if they are used, combine with other therapies."
27	**Dr. Alford:** Ms. James, can you tell me a bit about your pain right now? **Kathy:** So, even now, even eight years after my car crash, my hip still hurts, especially when I try to move a lot. Also, it's really bad when I try to stand up after sitting. And my feet are terrible, I always have burning and tingling…and they get numb sometimes. There are days when I can't put on my shoes because of the pain. **Dr. Alford:** It sounds like you are really uncomfortable. Can you tell me on a scale of 0 to 10 – with 0 being no pain, and 10 being the worst pain imaginable, where would you rate your overall pain right now? **Kathy:** Oh jeez. Right now? It's a 20! Dr. Alford, what does it mean when a patient reports their pain beyond the scale like in this case?
28	**Building Trust: Patient Issues** The first thing I think about is trust, and certainly during those first visit, or visits, patients may assume that you don't believe the severity of their pain complaints, or how much it's disabling them. And that's expressed by, or demonstrated by exaggerating pain scores, and exaggerating functional limitations, such as, "Ms. James, what are you able to do?" And if she said, "I can't do anything," I would think that would be an exaggerated functional limitation, since she clearly is working, and taking care of her family. Again, I think it has to do with mistrust.

29	**Building Trust: Provider Issues** In terms of building trust, I think providers, after you've taken a complete and thorough pain history, and focused physical exam, and appropriate diagnostic testing, I think we need to show empathy for the patient's experience. It's obviously causing them a great amount of distress. Then we should validate that we believe their pain is real, and I would argue that we can validate and believe their pain 100 percent of the time with zero percent risk. The reason why I can say that is because just because you believe a patient's pain complaint, does not mean that opioids are indicated. It doesn't mean that any specific treatment is indicated. That's where our clinical judgment comes in. That is, based on the patient's pain complaint, and what their risk profile is, we decide on what the best treatment modalities are for that person's pain complaint.
30	**Chronic Pain Assessment** Now, there are lots of ways to assess chronic pain. One would be using a pain scale, a unidimensional pain scale, similar to what we use in the acute pain setting. However, it's really just focused on pain, obviously, and I think we'd prefer to use something more multidimensional that asks about pain, and function, and quality of life. And there are some validated instruments, like the McGill Pain Questionnaire, the Graded Chronic Pain Scale, and the Brief Pain Inventory. Unfortunately, these scales are pretty impractical for routine use in most primary care settings. Thankfully, we do have a scale called the PEG Scale, Pain, Enjoyment and General Activity Scale, which is only three questions, which asks about pain, function, and quality of life. Let's apply this to our patient, Kathy James.
31	**Dr. Alford:** Ms. James, I absolutely believe you have terrible pain but I really need you to tell me where your pain is within the scale. So, let's try a different measurement: What number best describes your pain on average in the past week, where 0 is no pain and 10 is Pain as bad as you can imagine? **Kathy:** Ugh. It's – it's pretty bad. I'd have to say it's the worst. It's a 10. **Dr. Alford:** Okay. Well, what number best describes how during the past week pain has interfered with your enjoyment of life? Zero, it doesn't interfere at all; 10 it completely interferes with your enjoyment of life. **Kathy:** It's ruining my life right now. I'd have to say it's a 9. **Dr. Alford:** Okay. And how about interfering with your general activity? Zero, it doesn't interfere at all; 10 it completely interferes with your general activity. **Kathy:** That's also a 9. I really can't do anything.

32	Kathy's physical shows no acute distress and normal vitals, cardiopulmonary function, and musculoskeletal exam, except for her right hip which has decreased range of motion and pain on internal rotation. Her neurologic exam is consistent with her diabetic neuropathy, as is her foot exam including loss of protective sensation by vibration and monofilament testing. Dr. Alford, how would you think about coming up with a pain treatment plan for this patient? How effective and how safe are opioids for chronic pain?
33	**Multidimensional Care for Chronic Pain** I think it's important to take a multidimensional care approach. And as you can see on this slide, it really starts in the middle with self-care, teaching patients to pace themselves, and care for themselves. And there are lots of apps, and online programs that patients can interact with to learn about self-care, and that our goals include restoring function, reducing pain, improving quality of life, and cultivate well-being. And how do we do that? Well, we can use physical modalities: Exercise, manual therapies, certainly cycle behavior therapies, CBT, cognitive behavioral therapy, meditation, and so forth; procedures like acupuncture, and nerve blocks, steroid injections, and then medications. And there are lots of medications we can choose from, including NSAIDs, anticonvulsants, topical agents, and opioids. And we're going to talk more about those in a while. It's important to note, however, that studies on all pharmacologic, and non-pharmacological treatments for chronic pain, are generally assessed for less than 12 months, and the vast majority are less than 12 weeks. So, we really don't have any long-term studies on any treatment for chronic pain. We do know from systematic reviews that multimodal approaches are more cost-effective than single modality options.
34	**Non-Opioid Pharmacotherapies** But talking about non-opioid pharmacotherapies first, let's start with nonsteroidal anti-inflammatory drugs, and these include the COX-1 and COX-2 agents, as well as the COX-2-specific agents, but aspirin, salicylates, and these are anti-inflammatory, analgesic, and antipyretic. Acetaminophen doesn't have an anti-inflammatory property, but it is analgesic, and antipyretic. And in general, these agents have a ceiling analgesic effect. There's no known analgesic tolerance. There is an additive role, that is to add Acetaminophen and an NSAID is better than having one alone, and side effects are common, especially with high doses, and certainly with certain patient populations, those with chronic kidney disease, or liver disease, or heart disease. And we'll talk more about that later.

35	**Non-Opioid Pharmacotherapies: Adjuvant** Some other non-opioid pharmacotherapies include the adjuvant analgesics, or co-analgesics, and these are medications that the primary indication is for something other than pain. And they include antidepressants, anticonvulsants, antispasmodics, and local anesthetics. Please keep in mind, however, that these agents could also be misused, and there's an addiction potential, specifically with the gabapentinoids, including gabapentin, and pregabalin. But there's also misuse and addiction related to the muscle relaxant carisoprodol, which metabolizes into a barbiturate-like substance, so we need to be careful. But also, cyclobenzaprine has also been shown to be misused. So, we just need to prescribe these medications more carefully, and when we talk about the principles around safe opioid prescribing, it will apply these medications, as well.
36	**Opioids** So, let's move on to opioid pharmacotherapy. And that really starts with opiates, the natural compounds codeine, and morphine. And you can take these natural compounds, and bring them to the lab, and alter them, and create semisynthetic opioids, like diacetylmorphine, which is heroin, or hydrocodone, hydromorphone, oxycodone. And the important thing to remember here is that these semisynthetic opioids came from codeine and morphine, and they can convert back to morphine and codeine in the body and show up in the urine as an opiate. We're going to talk more about urine drug testing later on, but it's important to remember that when you send a urine in that says opiate positive, the person is either taking codeine or morphine, or they're taking a semisynthetic opioid that converted back to an opiate. But that's different than the synthetic opioids, like methadone, meperidine, and fentanyl. They never came from an opiate, and they will never turn your urine positive for an opiate.
37	**Opioid Analgesics** So, what do opiate analgesics do? They turn on the descending inhibitory pathway, which is in the periaqueductal grey, which is a norepinephrine serotonin system. They also prevent the ascending transmission of the pain signal. They inhibit the terminals of the pain or C fibers in the spinal cord in the dorsal horn. They inhibit activation of the peripheral nociceptors, and we also know that opioid analgesics result in variable responses, depending on the patient, that not all patients respond to the same opioid in the same way. And we now know that there are greater than 3,000 polymorphisms in the human mu opiate receptor gene, and that there are SNPS, or single nucleotide polymorphisms that have been identified that affect opiate metabolism, transport of opioids across the blood-brain barrier, activity of target receptors, and ion channels. We also need to keep in mind that opioids act at the reward pathway in the midbrain, which is a dopaminergic system, and that opioids can be very reinforcing, and very rewarding, which can lead some people down the path of misuse, and overuse.

38	**Opioid Tolerance & Physical Dependence** When talking about opioid pharmacology, we also need to remember what opioid tolerance and physical dependence are. Tolerance and physical dependence are physiologic adaptations to being chronically exposed to opioids. Tolerance means you need an increased dose to achieve a certain effect, or over time, the effect starts to diminish, and you need a higher dose. We know that tolerance develops readily for CNS and respiratory depression, less so for constipation, and in terms of developing analgesic tolerance, it's somewhat controversial. It seems that some patients do develop analgesic tolerance, but others don't. And physical dependence means that you have signs and symptoms of withdrawal by abrupt opioid cessation, or rapid dose discontinuation, or by giving somebody an antagonist like naloxone, or naltrexone.
39	**Opioid Efficacy for Chronic Pain** How good are opioids for chronic pain? What is the efficacy for chronic pain? Now, this is different than acute pain, and I would argue that the efficacy for acute pain is probably 100 percent effective. For someone who comes in with a femur fracture, we would never withhold an opioid, because we assume that they'll be some efficacy. There may be variability in terms of how much relief somebody gets, but we wouldn't withhold it from someone with severe pain like that. For chronic pain, it's completely different. We've already talked about it as being more like a chronic disease. Well, lately, in the past year, we've had a couple of meta-analyses that have looked at opioids versus placebo for chronic pain. Unfortunately, these studies only evaluate for up to three to six months, and follow-up. So, we don't have long-term studies, but in these short-term studies for chronic pain, they show that opioids were statistically significantly better, but with a small improvement in pain, and function, versus placebo. And when they compared opioids versus non-opioids, unfortunately, these studies were low to moderate quality, they showed that both were similar in terms of benefits. There was a study that looked comparatively between opioids, and non-opioids. It was a randomized clinical trial that found that opioids were not superior to non-opioids for improving musculoskeletal pain-related function over 12 months, so a long-term outcome. However, an important limitation is that only 5 percent of those that were randomized actually entered into the study. So, what that tells me is that someone who's willing to enter into a study where they could be randomized to an opioid or non-opioid that they seem to do equally well on either one. What happens to that 95 percent who said, "I don't want to be entered into the study?" It's unclear. Two longer-term follow-up studies, up to about a year, found that 44.3 percent of individuals on chronic opioids for chronic pain had at least 50 percent pain relief. So, it's not zero percent; it's not 100 percent. So, it's around 50 percent of individuals on opioids for chronic pain will get adequate pain relief.

40	**Opioid Safety and Risks** What about safety and risks? Well, we know that allergies are rare. We're learning more and more about immunosuppression. We knew from animal models that opioids do induce some immunosuppression, and more recently from human studies that showed an increased risk of invasive pneumococcal disease in individuals on chronic opioids, and even more recently, an increase in community-acquired pneumonia in individuals on chronic opioid therapy. We also know that organ toxicities can be significant, such as suppression of the hypothalamic pituitary gonadal axis, which in one study found that individuals on greater than 50 milligrams of morphine equivalents had a twofold increase in fracture risk. But adverse effects are common, including nausea, sedation, constipation, urinary retention, and sweating. Individuals can develop itching, or pruritis, and this is not an allergy, but it really is a histamine release. And for some reason, we have mu receptors on our mast cells, which causes histamine release. And the one we worry about the most is respiratory depression, because this is the adverse effect that can be lethal, especially in our patients with sleep apnea, whether it be obstructive, or central sleep apnea.
41	**Rates of Problematic Opioid Use in Chronic Pain** So, what are the rates of problematic opioid use in chronic pain? Well, in my mind, the best study was a systematic review of 38 studies where about a quarter were taking place in primary care settings, half in pain clinic settings, and the rest in other subspecialty settings. And what they found was the misuse rates were about a quarter of those individuals. Misuse was defined by opioid use, contrary to the directed, or prescribed pattern of use. So, for instance, if you had a patient who you were prescribing chronic opioids for their back pain, but they took it for their headache, that would be considered misuse. So, about a quarter of patients in these studies did that, as opposed to addiction rates, which were around 10 percent, 8 to 12 percent. And addiction was defined as a pattern of continued use with experience of or demonstrated potential for harm.

42	**High Dose Opioids** We also need to worry about high-dose opioids, and high-dose opioids is defined differently by different authors in the literature, and most would say that greater 100 milligrams of morphine equivalents is considered high-dose. What does that mean? Well, higher doses have been associated with analgesic tolerance, hyperalgesia, which is worsening pain, which we'll talk more about later, reduced function, overdose, and immunosuppression. So, if a patient is on high-dose opioids, we need to manage them as higher risk, and that means increasing the monitoring and support that we give that patient. So, the CDC guideline discusses high-dose opioids. They say to use caution with any dose, and if possible, avoid doses greater than 90 morphine milligram equivalents. And for patients already on greater than 90 morphine milligram equivalents, to explain the overdose risk, and offer to work with the patient to taper opioids to safer dosages if the patient agrees. Nowhere does it say in the guideline to involuntarily taper people down to less than 90 milligrams. However, we need to talk to patients about the new known risks, and work with them if they're willing and able to taper. Dr. Taylor, Can you determine the risk for opioid misuse and harm?
43	**Medication-related Risk Factors** Thanks, John. So, you've asked a very difficult question, and I think providers who might be listening in can all relate to the challenge of sitting with a patient and trying to predict if they are someone who could come to harm from an opioid medication. But we do know that there are both patient-related, and medication-related factors that increase the risk of overdose and addiction. And we'll review those now. So, beginning with medication-related risk factors, we know as was mentioned before, that high-dose opioids, and by that we mean greater than 100 morphine milligram equivalents, are associated with both overdose, as well as the development of a use disorder in the future, or an addiction. We also know that long-term opioid use, meaning greater than three months, is likewise associated with both overdose, and addiction. And there are several other opioid-specific factors that are associated with overdose. So, use of an extended release, or a long-acting formulation, the combination of opioids and benzodiazepines, and also the transition period to extended release, or long-acting opioids, specifically those first two weeks after starting an extended release formulation does carry an increased risk of overdose. Consistent with what we've just described, the CDC recommendations include advice to avoid prescribing opioid pain medication, and benzos, concurrently, wherever possible.

44	**Patient-related Risk Factors** We also know that there are several patient-specific factors that increase the risk of overdose, as well as addiction. So, having a co-occurring mental health disorder, such as depression, or anxiety is a risk factor for overdose, and addiction; having a co-occurring substance use disorder, for example, an alcohol use disorder, an illicit drug use disorder, but even a nicotine use disorder increases the risk of overdose and addiction, as does a family history, which increases the risk of future opiate misuse. We know that age can be a risk factor to take into consideration, so in our younger patients, we think about the risk of both addiction, as well as misuse, and in our older patients we think about the risk of side effects of opioid medications, and particularly overdose. We also think about overdose in our patients with a history of sleep disorder breathing, such as sleep apnea. And we should be cautious about the potential for misuse in our patients who have a history of criminal justice involvement, a history of sexual abuse, or trauma. And then, finally, and most importantly, a history of overdose really needs to be taken into consideration. As we'll discuss, having a history of overdose is a very potent risk factor for a subsequent overdose, and this is even in the case of accidental overdose in patients who don't have a substance use disorder. So, any history of overdose should prompt you to really consider carefully the patient's risk of a future overdose.
45	**Psychiatric Co-Morbidities** And so, taking a closer look at how psychiatric comorbidities interact with chronic pain, we know that psychiatric conditions, including mood disorders, personality disorders are very prevalent among our patients who have chronic pain. A variety of trials have shown us that mood disorders, such as depression and anxiety may be seen in up to half of our patients with chronic pain. Likewise, personality disorders, post-traumatic stress disorders, and substance use disorders, are also very – very commonly co-occurring in our patients who have pain. And for all of these reasons, it's important that we screen carefully for these co-occurring mood and psychiatric disorders in our clinics. Now, we all know that we're often dealing with competing priorities and limited time, when we're making these assessments.

46	**Screening for Depression** So, it's important to use tools that are effective, as well as brief and manageable in the clinic setting. And one that we'd like to suggest for screening for depression is called the PHQ-2. It is a two-question instrument that asks about two symptoms over the last two weeks. First, little interest or pleasure in doing things. And second, feeling down, depressed, or hopeless. And patients are asked if they've had those symptoms not at all, several days, more than half the days, or nearly every day. A score of greater than, or equal to 3 points is considered positive, and using this cutoff as both sensitive and specific for diagnosing depression, and the need to do further – further questioning. So, if a patient scores less than 3 points, you're done. You don't have to ask further questions or do a longer instrument. But if the patient does screen in or score positive with greater than or equal to 3 points, it's recommended to go on, and administer the entire PHQ-9 questionnaire, so that you get a better sense of the burden of their symptoms of depression.
47	**Screening for Anxiety** Similarly, the GAD-2 is a brief screening instrument that can be used to assess for the presence of anxiety. It asks about feeling nervous, anxious, or on edge, and then not being to stop or control worrying over the past two weeks. Likewise, this instrument uses a cutoff of greater than or equal to 3 points, and this, like the PHQ-2 has been validated in primary care populations. There are, of course, other screening instruments that you could work into your clinical setting, including screenings for PTSD, suicidal ideation, and thoughts of self-harm, and I think the key is, as we mentioned before, using instruments that are brief, easy to use, and allow you to complete a full assessment.

48	**Screening for Substance Use** Finally, it's also very important to screen for substance use, and substance use disorders. And by this we mean both substance use disorders, but also risky use, because we know just looking at the pyramid here that substance use disorders are the top of the pyramid, but screening only for substance use disorders does not account for a large proportion of patients that may have unhealthy use, or risky use that puts them at risk. And the way we screen for both of these things is to ask patients, for example, for alcohol, "Do you sometimes drink beer, wine, or other alcoholic beverages?" If the patient says, "No," that's actually a good opportunity to pause and say, "Why not?" Because we know that in the United States, drinking alcohol on occasion is fairly normative, and so, if a patient does not drink alcohol it's important to know why that is. They might share, for example, that they've had a family history of a substance use disorder, or a personal history of difficulty with alcohol, and that's important information for you to know. If patients do use alcohol, even on occasion, go on to ask how many times in the past year they have had five or more drinks in a day for men, or four or more drinks in a day for women? And here, a positive answer is anything other than, "Never." Anything greater than zero is considered a positive response, and that's a sign that you should go on to – to ask follow-up questions to assess for risk use, as well as a substance use disorder. But the single question screening is an effective way of identifying patients who need further follow-up. Likewise, when asking about drug use, it's effective to say, "How many times in the past year have you used an illegal drug, or used a prescription drug for a non-medical reason?" And here, again, a positive answer is anything other than, "Never," anything greater than zero, and that should lead you to go on to ask further follow-up questions to determine if your patient falls into the risky use, the unhealthy use category, or if perhaps, they meet criteria for a substance use disorder. And we'll go through those criteria in detail later on in this presentation. I want to just make one more comment, which is that the way that you ask these questions really matters. So, the way these questions are phrased normalizes a positive response. You'll not that we didn't say, "You don't use any illegal drugs, do you?" Because that really doesn't create a safe space for patients to share what their experiences are, and give you a candid, and honest answer, so that you have all the information you need to make good recommendations.
49	As we know, Kathy has a tobacco use disorder. She screened negative for other unhealthy substance use, depression, and anxiety. Dr. Alford, How do you decide when opioids are indicated and if indicated, how do you assess for opioid misuse risk?

50	**When are opioids indicated?** So, when I think about opioids, and when are they indicated, well, the pain needs to be severe; it should have a significant impact on their function, and quality of life, but it should also be a pain type that's potentially opioid-responsive. And we know that things like fibromyalgia, and migraine headaches are less opioid-responsive than musculoskeletal, and neuropathic pain. I'd also like to see some evidence of inadequate benefit from non-opioid treatment modalities, and if the person is already on opioids, like our case, is there documented benefit?
51	**Getting Help from a Pain Specialist** There are times, also, to consider getting help from a pain specialist, when they're available. So, when do I use a pain specialist? Well, one, if I'm unsure of the pain diagnosis. What's generating this person's chronic pain? Am I missing something? But also, if I'm unsure about other treatment options. So, I've tried non-opioids. I've tried some non-pharmacological treatments. Are there other treatment modalities that I should be considering? Or, if you just want a second opinion on opioids for this individual patient, but you really need to know what services your pain specialist offers. If your pain specialist an anesthesiologist that does interventional treatments? Or, is your pain specialist someone who works within a comprehensive, multimodal pain program? You really need to know that before you send your patient to that specialist. So, when you don't have a pain specialist available to you, I think you can always get a second opinion from your colleague. And I find it incredibly helpful to ask a colleague to look at a chart, or even meet the patient, and just give me their impressions as to how they think the patient is doing in the therapy that they're currently on.
52	**Assess for Opioid Misuse Risk** Now, if you're going to consider prescribing an opioid for chronic pain, you really want to assess for opioid misuse risk prior to prescribing. And this would include urine drug testing to confirm substance use history that you obtained, and adherence with the prescribed medication if they're already on an opioid. You want to check the state prescription drug monitoring program to confirm the medication the person is on, the prescriber history, as well as absence of multiple prescribers. You want to review old medical records. You want to try to talk to the previous provider. And then there are some validated questionnaires you can use, including the Opioid Risk Tool, the DIRE, which is the Diagnosis Intractability Risk Efficacy tool, and the SOAPP, and the STAR, and there are others. And these questionnaires all have pros and cons.

53	As we return to our clinical case, keep in mind that Ms. James came in asking for an opioid prescription today. **Dr. Alford:** Before you came in, I checked, as I do with all my patients, the state database of prescriptions written and filled, and I verified that you've been getting the same medications over the last year from Dr. Robertson. While I wouldn't normally prescribe an opioid pain medication to a new patient on the first visit, I'm going to give you a prescription for enough pills for two weeks, which will give me a chance to review your medical records and come up with a treatment plan. I'm going to give you a prescription for a pill that also includes Acetaminophen in combination with the oxycodone to try to improve your pain control, since as you know, there's lots of concerns about the risks of opioid pain medications, we require all patients on opioids to agree to urine drug testing to confirm that you're taking your medication safely. The medical assistant will help you with that. And then, before you come back, I'll look over these records. **Kathy:** Oh, it sounds like you really don't trust me, but I get it. I keep reading about people overdosing, and people with pain being shut off from their medications. It really is a terrible situation. I'll see you in a couple of weeks. Kathy's problem and medication lists are reconciled, and Dr. Alford reviews the radiology reports. He also thoroughly reviews her records from her previous PCP. There is inadequate documentation about benefits and no record of monitoring including urine drug testing, but there's no evidence of misuse of her prescription opioid.
54	Before Kathy's next visit, Dr. Alford is concerned about a number of things: • Should Kathy's dose be changed? • If so, should she be switched to an extended-release/long-acting opioid? (Remember, he prescribed oxycodone with acetaminophen to be taken every 6 hours.) • What other adjuvant medications or therapies (or both) should be considered? • What sort of treatment plan should be developed for Kathy James? As we begin the next section, keep those questions in mind. As we conclude Part 1, Dr. Alford, could you please summarize what we've learned so far?
55	**Summary: Part 1** So, in summary, opioids should never be the first-line treatment option, as they're just one tool in a multimodal approach that includes self-care. And side effects are common, but they could be managed, but that they carry significant risks, including addiction, overdose, and death, but that misused risk could be assessed using a systematic approach, which includes screening for comorbidities, and using validated risk assessment questionnaires.
Part 2: Safer Opioid Prescribing	
56	Welcome back, to Part 2 of SCOPE of Pain, Safer Opioid Prescribing. Now let's return to Kathy James, and her second appointment with Dr. Alford.

57	**Dr. Alford:** Good to see you again, Ms. James. I normally try to speak with referring doctors, but unfortunately I was unable to reach Dr. Robertson. But your old records and your urine results from the last visit were completely helpful for me. Thank you. **Kathy:** Yes, I think Dr. Robertson moved away when he retired. **Dr. Alford:** OK Let's review how you're doing now… **Kathy:** Well, I'd say that my pain is pretty much a 6 out of 10 most of the time, except right before I'm scheduled to take my next pill when it's definitely a 10 out of 10. But I've been taking my pills just as you told me to, and they haven't made me tired or anything. Dr. Alford, would you continue or change Kathy's opioid prescription?
58	**Opioids 1** Well, first I like to think about opioids in terms of immediate release versus extended release, and I put them side by side on this slide to show you that they are really essentially the same molecules. It's just the way they're formulated. The long-acting opioids are short-acting opioids but just in a long-acting formulation. And the important thing to remember is that if somebody disrupts that formulation, that is they break it or crush it or take it in other ways that were not intended you'll get a whole lot of short-acting all at once and we learned that lesson from extended release long-acting Oxycodone.

69	**Opioids 2** So, when do I decide between a short acting versus a long acting? Well, I certainly would use a short acting when someone is opioid naïve. That is, they have no opioid tolerance because the long-acting opioids come at high dosages, which really would require someone to already have some level of tolerance, or if the patient has intermittent or occasional pain. There would be no reason to put them on a medication that's going to last all day. I would consider a long-acting opioid if they had opioid tolerance, if they had constant, severe, around-the-clock pain similar to our patient that we've been discussing to stabilize pain relief when a patient's taking multiple doses of short-acting opioids. Note that there really aren't any adequate studies looking at long-acting opioid safety during pregnancy. But remember, if you're going to use a long-acting opioid you need to remind the patient of the dangers of disrupting that formulation. That is, the pill should not be broken, chewed or crushed. Now, this is all consistent with the CDC guideline recommendations stating when starting opioids use immediate release opioids, again, in opioid-naïve patients. Another very important principle is to always start low and go slow. Now we know the patient may be in severe pain and feeling very desperate and may want us to go fast. But we really need to sort out can this patient benefit from this treatment and can they take it safely and that's going to take some time to sort out. And I really don't feel bad about that because if they're benefitting, even at this lowest dose, then they're better off today than they were yesterday when they weren't on any medication. And so really, start low and go slow, and I wouldn't make those changes for weeks, if not months, until you sort out how the patient is doing.
60	**IR/SA vs ER/LA Uncertainties** Now there are some uncertainties if you look at the literature around short acting versus long acting in terms of benefit or harm. There's insufficient evidence to determine whether long-acting opioids are more effective or safer than short acting, and there's debate, whether bolus dosing of short-acting or continuous exposure of long acting is more likely to result in analgesic tolerance, hyperalgesia or addiction. So, what do I do clinically? I individualize the treatment. That is, I choose the option that best meets my patient's needs.
61	**Transdermal Preparations** Now I'm going to talk about some specific opioids and opioid formulations that are unique, the transdermal preparation for example. Well, there's a Fentanyl product and a Buprenorphine product that comes as a patch, Fentanyl every 72 hours, Buprenorphine every seven days. These are incredibly convenient in terms of dosing, but they do have a slow peak onset. They can take a day or more to actually achieve peak onset. There's also delayed offset. So, if you overshoot and the person is sedated, they may remain sedated for a prolonged period of time. It also requires a predictable blood flow and adequate subcutaneous fat in order to get that sustained release mechanism and that the absorption is increased if the person is febrile or has broken skin and it will be decreased if they have edema or anasarca. Also keep in mind that some patches have a metal foil backing which may not be compatible with an MRI scan.

62	**Methadone is Different** What about Methadone? Well, Methadone is really a different opioid and the problem is it's potentially the most dangerous opioid because it has a long variable and unpredictable half-life. Its analgesic half-life is six to eight hours, but it's soon half-life can last for days. We also know there's a risk for QTc prolongation and the risk of torsades. There are some possible advantages to Methadone such as, along with activating the mu-opioid receptor, it also is an NMDA receptor antagonist, which potentially results in less analgesic tolerance and better efficacy for neuropathic-type pains. There are also no active metabolites, it's incredibly inexpensive and it also comes in small dosage units, 5mg tablets that could be broken in half. So, this is an example of a long-acting opioid, long acting because of its pharmacology, not its formulation. So, in this case someone could break their tablet in half and take 2.5mg three times a day, for example.
63	**Dual Mechanism Opioids** And then there are the dual-mechanism opioids. The examples are Tramadol and Tapentadol and they're mu-opioid receptor agonists, but they also act on the descending inhibitory pathway with norepinephrine and serotonin reuptake inhibition. For these medications there is a seizure risk. People absolutely become physically depending on them and they're controlled substances because there's an addiction potential for both of these substances.
64	**Abuse Deterrent/Resistant Formulations** Now the pharmaceutical industry is spending a lot of time and money trying to develop safer or abuse-deterrent, abuse-resistant formulations and this includes creating physical barriers so that the tablet or the formulation cannot be disrupted. That is, it can't be crushed, or putting an antagonist with the agonist. That is if the person breaks the tablet, they don't get the actual agonist. They don't get the opioid. They get an antagonist which would put them in withdrawal, putting in components that cause side effects like if someone takes too much they get flushing or creating pro-drugs. That is, if they don't take it as prescribed, they don't actually get the active drug. When these products are developed and, on the market, there seems to be less misuse than the formulations that are not abuse-deterrent. However, I will say that currently there are no proven 100 percent abuse-resistant opioids or opioid formulations and probably there never will be. And the reason why I say that is because if the body can figure out a way to extract the opioid, which it needs to be able to do, there's probably some chemist out there that can do it as well. Dr. Taylor, are there special considerations when prescribing opioids for pain?

65	**Opioid Choice and Dosing: Considerations** There are. So, a number of considerations that come up include the duration and onset of action of the medication. We've already heard from Dr. Alford about short and long-acting formulations and when thinking about which one to choose it's important to consider whether a patient's pain is intermittent compared to continuous. We also have heard that it's important to consider patients' prior experience with opioid medications both in terms of different effects related to the differences at the mu-opioid receptor and differences in side effects. We know that patients do metabolize opioids differently and this can play a role in which medications we choose. We, of course, also want to consider patients' level of opioid tolerance, whether they've been on medications before and in the immediate past, and that can help with decision making around starting an immediate release opiate compared to an extended release formulation. Additionally, thinking about the route of administration is important. So, we've heard that we have oral formulations as well as transdermal formulations. Those will be the two that we use most commonly in the outpatient setting but there are others. And then of course we want to consider access, so cost and insurance issues that could make a specific medication more or less accessible to our patients.
66	**Rational Polypharmacy** Treating chronic pain is also a situation where we want to think about rational polypharmacy, and for many of us this is actually the opposite of what we were trained to do in our training. We often learn that polypharmacy is bad, and we should try to minimize medications and use the most streamlined regimen possible. But in the case of chronic pain we really want to use a multimodal approach that explores the different mechanisms that many of our pain control modalities tend to target. So, for example, we might choose medications from a variety of classes targeting peripheral sensitization, targeting descending inhibition and targeting the spinal cord to really optimize pain control and we know that using synergy is a very effective strategy.
67	**Exploit Synergism (e.g., treating neuropathic pain)** So, we want to share a couple of examples from populations dealing with neuropathic pain that looked at patients prescribed Morphine as well as a second agent. In this first trial that's here on the left patients were prescribed Morphine as well as Gabapentin and they found that pain control was the best when those were used in combination and lower dosing was actually able to be used. This has also been shown for the combination of Morphine and Nortriptyline. And the principle is that synergy will potentially improve pain control and let you use lower dosing of both medications, but I say this with a word of caution because we do know, as was mentioned earlier, that Gabapentinoids are associated with an increased risk of misuse. We know that they do have street value and some very recent data from 2018 suggested that there is a dose-dependent increased risk for overdose death when Gabapentinoids are combined with opioids.

68	**Drug-Drug Interactions** It's important to consider drug/drug interactions, and opioid medications have a number of interactions. Most importantly we worry about interactions with other CNS depressants, which can cause over-sedation and inadvertent, unintentional overdose. So, specifically benzodiazepines, alcohol, other sedatives, tricyclic antidepressants, any other sedating medications. We do worry about alcohol specifically both because of its interaction but also because of a phenomenon called dose dumping. We know that when certain long acting extended release formulation opioids are combined with alcohol it can cause the medication to release its entire dose immediately. This is called a dose dump, and that can cause a sudden and very unexpected increase in opioid-related side effects including sedation and respiratory depression. We also know that even when this dose-dumping phenomenon doesn't happen alcohol can increase circulating concentrations of certain opioid medications. There has also been a concern about the interaction between opioids and certain diuretics. I would say this is more of a theoretical risk. It's not one that I've seen commonly in my clinical practice, but opioids can reduce the efficacy of diuretics by inducing the release of ADH, antidiuretic hormone, and additionally as we heard from Dr. Alford, we know that some opioids, specifically Methadone and Buprenorphine, can prolong the QTc interval. In these cases, it's very important to avoid other medications that prolong the QTc interval and also to be mindful of medications that interact with these opioids and potentially increase their own QTc prolonging effect. When prescribing an opioid that you might be less familiar with side effects can come up that you may not have come across before. And so, one resource that may be helpful is DailyMed. This is an NIH sponsored resource that provides the packaging insert for specific opioid medications in a more concise digestible form that can make it easier to just get a quick rundown of what the interactions and concerns are that you should be aware of if you're prescribing an opioid that you haven't used very much in the past or if a patient has specific conditions or concerns.

69	**Age Considerations** Additionally, we've alluded to earlier the fact that age does play a big role in the risk of opioid medications and in the side effects that patients can experience. So, in the elderly, which is the population that has a high burden of polypharmacy, we do want to use a lot of caution around polypharmacy and drug/drug interactions. We also want to think about some specific drug/disease interactions. Certain chronic conditions are very prevalent in the elderly including liver and renal disease. We'll talk about those in more detail a bit later as well as changes in mental status such as dementia. And opioids in this population become tricky because we find that there is actually a very narrowing therapeutic index and a much higher rate of opioid side effects including things like changes in mental status and falls. We want to do very cautious shared decision-making with our elderly patients and really make sure you've discussed these risks in detail and that we're using the lowest possible doses that are effective when necessary. And additionally, in the pediatric population we have only two extended release long-acting opioid formulations approved based on safety studies. These are long-acting formulations of Oxycodone as well as Fentanyl.
70	**Special Populations – Liver Disease** I mentioned a moment ago that both liver and kidney disease are important considerations when you're thinking about opioids for pain control. And just zooming in for a moment on the issues that we think about in patients with chronic liver disease, we do know that opioid clearance is impacted by hepatic insufficiency. This is a population where we need to use a very high level of caution because there is a risk of side effects in patients with severe advanced liver disease such as cirrhosis. We also know that there are high rates of hepatic encephalopathy when opioid medications are used. This is a little bit different depending on which opioid you select, so some opioids including Fentanyl may be a bit safer in patients that have modest hepatic dysfunction. But we know that other opioids, including ones that we very commonly use, Morphine, Oxycodone, Hydromorphone, do require substantially reduced doses, prolonged dosing intervals, meaning more time between doses, and many of these other meds just haven't been studied in detail. The challenge in this population is that non-opioid medications also pose concerns. So, Acetaminophen for example, should be limited 2g per day in patients with chronic liver disease and NSAIDs may carry a risk of increased bleeding. And this is specifically true in patients with advanced liver disease or cirrhosis where we worry about variceal bleeding. We worry about the impact of NSAIDs on renal function and we worry about other complications, including severe ascites that's diuretic resistant. And then furthermore, some of our other adjunct medications, Gabapentinoids as well as tricyclic antidepressants can be used. But again, here we would want to use lower doses and monitor carefully.

71	**Special Populations – Renal Disease** In renal disease we also want to approach opioids with caution, and this is partly because this is, in many cases, a data-free zone. Many of our opioid medications have not been studied in end stage renal disease patients and we know that the pharmacokinetics and pharmacodynamics can really be unpredictable in patients with low GFRs. The preferred opioids, if they do need to be used, are Hydromorphone, Methadone, Fentanyl and Buprenorphine and there are a few that we want to specifically avoid. Oxycodone and Morphine both, in renal disease, have the buildup of metabolites that can have toxic side effects. So, these two opioids should be avoided in advanced renal disease. Non-opioids also require some consideration in this population. Of course, NSAIDs as we mentioned before should be avoided in patients with advanced renal disease, but we have a few options. So, Acetaminophen and the Gabapentinoids can generally be used.
72	**Dr. Alford:** OK, Ms. James, here's what I suggest that we do moving forward. Since you have severe pain all day and tolerate the Oxycodone four times per day, but you told me you experience pain right before your next dose, I'm going to switch you to a long-acting version of the same medication, which you'll only have to take two tabs per day. And that should stabilize your blood levels and should prevent that end-of-dose failure or the worsening of pain right before your next dose. With the longer acting medication and more stable blood levels, I'm going to decrease your overall daily dose and see how that works. And I want to remind you, please, don't break or crush the tablet because that could be very dangerous. I'm also going to increase your Gabapentin because that's going to help the Oxycodone work better. I'm also going to refer you to physical therapy to help work on that hip of yours. **Kathy:** I don't understand how getting a lower amount of pain med is going to help my pain. Dr. Robertson never recommended these changes. **Dr. Alford:** I hope you can trust that I'm really trying to improve your pain control and at the same time keep you safe. And also, because we know that opioids carry serious risks, I'm going to walk you through our office policies around how we'll monitor you, again, to keep you safe. Let's go over the agreement, which outlines my responsibilities and yours, and then if you agree we'll both sign it and then I'll have the nurse out front get you that appointment with physical therapy. **Kathy:** Wow. Okay. That's a lot of stuff to do, and I'm really worried that this isn't going to work. Note here that Dr. Alford **did not** assume that Kathy would need medication for breakthrough pain when he switched her to long acting opioids. And before ending the appointment, they discuss Kathy's weight loss and smoking cessation strategies. Dr. Taylor, can you give us some detail about the monitoring strategies you put into place in order to try to keep your patients on chronic opioid therapy safe?

73	**Universal Precautions** Sure. When we think about how to prescribe opioid medications safely in an office-based practice, we really want to apply universal precautions, and by that, I mean using the same standard policies for all patients that these are important both to keep patients safe but also to ensure that policies are fair and unbiased. And the reason these are important is that, as we said before, it's really tough to predict who at the individual patient level is at risk of opioid misuse or the subsequent development of a use disorder. We want to make sure that we're not introducing bias into our decision-making. We also know that using the same policies in a standardized way reduces stigma. We want to normalize this type of mentoring so that it doesn't feel stigmatizing or personal, and using universal precautions are also consistent with expert guidelines from a wide variety of groups including the American Pain Society, the American Academy of Neurology and a number of other organizations.
74	**Common Universal Precautions 1** And so, what do universal precautions entail? First and foremost, they include a comprehensive pain assessment. That includes not only evaluating the patient's history of pain, their functional limitations, their quality of life, but also helping them to arrive at a specific pain diagnosis. We want to know what is causing their pain. We should not be charting on the diagnosis of chronic pain that is not more specific. We, of course, also want to evaluate the risk for opioid misuse and we spoke earlier about how that can be accomplished. And we want to set the stage with patients that opioid prescriptions, like any medical intervention, should be considered a test or a trial meaning that it will be re-evaluated to determine if the benefits outweigh the risks over time, and usually every one to three months is a reasonable interval to re-evaluate the pros and cons and risks and benefits of opioid medication. When we write prescriptions, we should include the maximum number of tablets per day so that it's clear to everyone involved what the maximum dose per day is, and we should see our patients regularly face-to-face to continue these conversations. Of course, because of the increased overdose death rate, even with prescribed opioid medications we should consider co-prescribing Naloxone, which is the intranasal medication that can be used to reduce opioid overdose death. And then, finally, in our documentation we want to be very clear in how we're outlining our thought process around the opioid medication, specifically around the risks and benefits and the plan for next steps with the opioid medications so that it's clear to all members of the care team and anyone who might be reviewing the chart in the future.

75	**Common Universal Precautions 2** Common universal precautions are also carried out through a variety of strategies in the clinic. First and foremost, patient-prescriber agreements. These are sometimes also called contracts. But what these are, are just a way to help providers do informed consent with patients. They are typically signed by both the patient and the prescriber, but it's an opportunity to sit down with your patient and outline your responsibilities as the provider and the patients' responsibilities for keeping themselves and the community safe with these medications. We want to make sure that these are written at a reading level that is accessible to our patient population. We don't have strong data supporting the use of patient-prescriber agreements and reducing overdose, reducing misuse but we do know that there's no evidence that they cause harm and it can be a tool to facilitate appropriate counseling. So, it's something that is recommended. There are also other monitoring strategies that are recommended and can be very helpful, and these include urine drug testing, pill counts and use of your prescription drug monitoring program and these all align with CDC recommendations which advise us to use strategies to mitigate risks including Naloxone co-prescribing which we just mentioned, reviewing PDMP data and the use of urine drug testing.

76	**PPA Informed Consent** Now, specifically in these patient-provider agreements we also want to help our patients do a few things. First, we want to help them set realistic goals. I know in my clinic it's very common for me to ask patients what their goals are for their pain and for their response to be, "I want to be pain free." In acute pain that's probably a reasonable goal. But when we do get to the stage of patients having chronic pain, we want to make sure that we're helping them set expectations that are going to be achievable. In many cases with chronic pain the goal there is to reduce pain, but we may not be able to eliminate it. We also want to help shift the focus from pain control to function, and we can encourage the setting of smart goals. So these are goals that are specific, measurable, action-oriented, realistic, and time sensitive. For example, "I'd like to be able to walk my dog around one city block three times a day in the next month" would be an example of a smart goal that is focused on function. And we'd also like to be able to help our patients articulate the potential risks of their opioid medication. It's very common for patients without a use disorder to feel that these risks don't apply to them, and so, this is really your opportunity to talk to them about how opioid medications have risks for all patients, and specifically these could include the side effects of the medication. They can include physical dependence. We spoke earlier about drug interactions. Over sedation is one of the most concerning side effects that can occur. Talking about driving to your patients who drive is particularly important, and using caution, especially during dose adjustments, is recommended. There's of course the risk of misuse, overdose and overdose death, and women of childbearing age or women who may become pregnant there is a risk of neonatal opioid withdrawal syndrome if they have opioid exposure during their pregnancy. And then patients who are on opioids for a long period of time and those on high doses are at risk of a phenomenon called opioid hyperalgesia, which is actually a paradoxical worsening of pain in patients on opioid medication. And then finally, even patients who do not have a history of a use disorder and plan to use their medications as prescribed may find themselves sought out by other people in the community who are interested in their opioid prescription and that's something to talk about up front and just let patients know that in the current opioid crisis they may be approached for their opioid prescription and it is an expectation that their opioid prescription be used for them only and not shared with anyone else in the community. And these recommendations, again, are all consistent with the CDC guidelines that advise that before starting opioids one should establish realistic goals and continue opioids only if meaningful improvements outweigh the risks.

77	**PPA Plan of Care** This patient-provider agreement also gives you the chance to outline other aspects of your plan of care. In many cases this includes engagement in other non-opioid treatment modalities, for example, physical therapy, acupuncture. This is your chance to really set the stage with the patient that these other non-opioid therapies are an expected part of their treatment plan. This lets you outline your office's policies and procedures, including around when refills will happen, what the policies are around refills, and to state clearly your expectation that there be no illegal drug use while patients are on opioids and no other sedative use. I generally remind my patients that I'd like to be notified of all other sedating medications that they may be prescribed including if they were in an emergency room setting or seeing an outside provider. In my women of childbearing age I like to address birth control and discuss considerations around pregnancy and then I like to specify that when patients are prescribed opioid medications they are to be taken exactly as prescribed, exactly as the instructions are written on the pill bottle and we ask that there be no changes, no dose increases that haven't been discussed between the patient and provider. And then of course safe storage is very important. This becomes very important when there are children in the home. But we want medications to be stored in a safe place where they are protected from folks that might come into contact with them accidentally such as children, protected from potential theft and then again just as a reminder that the medications are not to be shared or sold.
78	**Monitoring for Benefits and Harm** So how is it that we monitor for benefits and harms? In the following slides we'll go through a few of these strategies. We can monitor for benefits, for example, by assessing and documenting PEG scores, by documenting changes in progress towards the smart goals that we've identified with our patients and we can assess for harms by using validated questionnaires like the Current Opioid Misuse measure or the COM, by pill counts, by urine drug screens, by use of the prescription drug monitoring program, by obtaining history from reliable family members and we say that with a brief word of caution because we do know that there are patients who can be targeted by folks looking out for their opioid prescription for secondary gain but history from reliable family members can be very helpful. And all of these strategies are in line with CDC recommendations, specifically recommendation number seven, to evaluate the benefits and harms within four weeks of starting and then at least every three months after starting an opioid prescription. And the CDC goes on to define clinically meaningful improvement as a 30 percent improvement in both pain and function.
79	**Office (face-to-face) Visits** In our office visits there are a few things we want to monitor for. We can think about the six A's, analgesia, activities, adverse effects, abhorrent behaviors, affect or mood and adherence. One other thing that can be helpful is to ask patients to describe to you how they're taking their medications. One helpful question can be, "Tell me how you're taking your medications" or just a 24-hour inventory where you say to the patient, "In the last 24 hours what time of day did you take your opioid pain prescription?"

80	**Urine Drug Testing (1)** So urine drug testing is one tool that can help you monitor for harms in patients who are on opioid pain medications. They can help you confirm that patients are taking medications that you've prescribed, and they can help you confirm that patients do not have exposure to other prescribed or non-prescribed substances including illicit drugs. It's important to discuss urine drug testing openly with patients and again, to normalize it as a standard practice that you apply to all patients on pain medications that are opioids so that they don't feel stigmatized. Before you do a urine drug test it's important to ask patients when the last use of an opioid was so that you know what to expect in the urine screen. Screening can occur on a random or a scheduled basis or just when concerns arise. It's important to keep in mind though that urine drug testing is not a be all, end all. It's one data point that can be used in conjunction with all of the other data that you have about a patient's potential risks of opioid medication and it really should not be the only factor impacting medical treatment decisions. As with any in-office testing there is a small risk for lab error or mislabeling. We know that people that are dedicated to deceiving a urine drug test will find a way to do it, so it's an imperfect system.
81	**Urine Drug Testing (2)** Urine drug screening tests in general are immunoassays. These are the initial screens. Any positive or unexpected findings can then be confirmed with gas chromatography or a liquid chromatography and mass spectroscopy testing. But I think the most important thing that you can do is get to know your toxicologist or clinical pathologist in the clinic where you practice and really get a good understanding of what testing is available at your institution, who you can talk to when you have unexpected or difficult to interpret results so that you have the local resources that you need.
82	**Urine Drug Testing (3)** Just another word about the confirmatory testing, so GCMS or LCMS confirmatory testing is able to identify specific molecules. These are sensitive and specific, but they are more expensive and often take longer to return which is why most initial tests are immunoassay screenings. And it's worth noting that some of these tests do return with drug levels, not just qualitative positive or negative results. But these drug levels are not a validated way of knowing, for example, if your patient is taking all of their prescribed dose of a medication. Because there are so many person-specific differences in how opioid medications are metabolized we really should not use drug levels themselves to make treatment decisions. And as Dr. Alford mentioned earlier in this presentation, it's very important to know what metabolites to expect from the opioid that you're prescribing. Hydrocodone, for example, can break down into Hydromorphone and you would see both of those potentially in GCMS testing and it's important to know that so that you don't see something like Hydromorphone and think that your patient is taking a medication that they're not prescribed. So be familiar with the breakdown products of the medications that you're prescribing.

83	**Pill Counts** Now, a word about pill counts. Pill counts can be used to confirm medication adherence, to minimize diversion and there are a couple of strategies that can be effective. First and foremost, it's a good idea to prescribe a 28-day supply of medication and that's rather than a 30-day supply. What that does is that ensures that patients never run out of medication on a weekend day, on a day when you may not be available to provide a refill. It's recommended to prescribe so that patients actually have leftover medication, have not run out of their prescription on the day of their appointment so that you can do a pill count. I think very commonly we're writing prescriptions until the next clinic visit, but it can be a good idea to write for beyond the clinic visit so that you can then do a pill count when you see the patient. You can ask patients to bring medications to each of their visits and if you have concerns a higher level of monitoring is random pill counts where patients are called and asked to return with their pill bottles for an immediate count.
84	**Prescription Drug Monitoring Programs (PDMP)** Now, throughout our presentation we've mentioned prescription drug monitoring programs. These are pharmacy data that are available to prescribers and occasionally to other team members, and a majority of states now do require the use of PDMP programs before prescribing controlled substances. There's been some research on the impact of PDMP programs and we know that they can change prescriber behavior. We're still not quite sure whether prescription drug monitoring program implementation has an impact on overdoses. I think that remains to be seen. But it is something that is recommending and, depending on the state where you practice, may be required.
85	**Minimum Level of Monitoring Based on Risk (and State Laws)** This brings us to discussing what level of monitoring is appropriate for your patient. We've spoken today about how different patients may have different levels of risk for opioid medication. We have some data that can help guide us as far as how much monitoring is necessary and appropriate in different scenarios. This site here shows a number of different interventions that we've discussed, face-to-face visits, urine drug screens, pill counts and PDMP review as well as minimum levels of monitoring that are recommended based on patient risk categories. So, for example, if you're taking care of a patient who is felt to be low risk for complications of their opioid medication it would be appropriate to see that patient four times a year, to do a urine drug screen at least twice a year, to do pill counts at least twice a year and to check the PDMP at least twice a year. Now this might vary, again, by your state jurisdiction because different states have different laws governing how often the PDMP needs to be checked. In some states it needs to be checked before each and every prescription. But that's a place to start, and that's something that you will, of course, tailor based on the patient's risk. If patients have abhorrent behaviors or demonstrate themselves to be of higher risk then that would be something that you would intensify and you would see them more frequently and check screens more frequently. Dr. Alford, Can you talk about how we prevent this monitoring from compromising our relationships with our patients?

86	**What is the Clinician's Role?** Sure. I think it's important to remember what our role is, and our role is to be a clinician. We're not supposed to be police officers or DEA agents or judges for that matter. And the way we maintain the clinician role is to judge the treatment, not the patient, by using a risk-benefit framework.
87	**Discussing Monitoring** So we want to make sure we discuss monitoring with our patients by reviewing the personal as well as the public and community health risks of opioid medications, discuss that it's your responsibility to look for and manage early signs of harm and discuss agreements, pill counts and urine drug testing as a way to keep your patients safe and avoid harm. We need to use a consistent approach, but we should apply it individually to match that patient's risk.
88	**Managing Harm: Opioid Adverse Effects** Now it's not just risk of overdose. It's certainly risk of adverse effects that we're also monitoring for. For instance, nausea and vomiting. That will usually resolve within a few days or we can use antiemetics or switch to a different opioid. If the person is sedated, however, we really need to decrease the dose. Constipation, you can use Senna laxatives, bowel stimulants or peripherally acting opioid antagonists or switch to a different opioid. We really should avoid bulking agents because you have a hypodynamic bowel, which can be made worse, if you fill it with fiber. Pruritis, you can switch to a different opioid or use a non-sedating antihistamine. And urinary retention, especially our male patients who maybe had BPH, this can tip them over to urinary retention and in those cases you really need to switch to a different opioid.
89	**Collateral Opioid Risk** We need to think about collateral risk. Dr. Taylor mentioned safe storage and disposal and it's really about the risk to young children who may ingest and overdose, or adolescents who may experiment leading to overdose and addiction, or any other household context. And as was alluded to before, we can mitigate that risk with safe storage and disposal, educating family members about the risk, having the Poison Control number readily available, co-prescribing Naloxone and if you want to learn more about co-prescribing Naloxone I encourage you to go to PrescribeToPrevent.org to find out information about specific laws within your state that may pertain to Naloxone co-prescribing.
90	So as you've heard, this is a lot of work.

91	**Optimize Office Systems** So there are several strategies that can help you optimize your office systems to support safe opioid prescribing. First, as we've discussed, it's helpful to have standardized policies throughout your practice that are really supported by all of the clinicians in your group so that systems are applied in a fair and predictable way to all patients. It also can be helpful to maintain a patient registry, which allows practice managers to track office-wide adherence to the guidelines that you have agreed upon with your colleagues, and there are HEDIS measures that are helping some practices support safe opioid prescribing in their groups. More information is available online at the website here on the slide. It's also important to get your non-prescriber staff involved, so specifically involved nurses, medical assistants, pharmacists and behavioral health providers can help support safe prescribing and all of the policies that we've described. Finally, it is helpful to maintain a list of up-to-date local resources including pain clinic referrals, mental health providers and substance use disorder treatment services so that those are really at your fingertips when you're in clinic working with a patient. And if you'd like more information on how to optimize your office systems, we have more details at scopeofpain.org under supplemental training.
92	**Documentation: Rationale for All Decisions** Let's say another word about documentation. We've touched on this briefly in other sections of our training today, but it is very important to document the rationale for all of your treatment decisions. This is really to protect the prescriber when any concerns arise. So you want to document a number of things, including subjective reports from the patient, from family, from other care providers and always circle back to the six A's that we mentioned, analgesia, activities, adverse effects, abhorrent behaviors, affect and adherence. Including this information will really help you document in a robust way that will make your decision making clear. You also want to include the objective information that we've discussed around urine drug screen results, pill counts and prescription drug monitoring program data and then be sure to list your clinical and diagnostic impressions. Finally, it's important to know both your local state as well as federal guidelines around documentation in the area of opioid and other controlled substances and we list here a number of websites that may be helpful.
93	In the ensuing couple of months, Kathy reports somewhat more consistent pain relief and denies sedation. But about nine hours after her dose her pain increases and that interferes with her concentration. Dr. Alford decides to increase the ER/LA oxycodone from 15 milligrams to 20 milligrams every twelve hours to reduce end of dose failure. In one week his nurse contacts Kathy and confirms that this has been effective in improving pain relief without any sedation or other adverse effects. She is more active and able to concentrate on her work.

94	Then, 2 months later, she presents to the Emergency Department of her local hospital after injuring her ankle. **Kathy:** OWWWW! Oh my gosh that hurts! I was running to catch my bus to work, but I tripped… I'm so clumsy! Oh wow… I can't even stand on that foot! I'm pretty sure it's broken. The pain was just so bad that I took a Vicodin that my husband got from his dentist a while back. Can you please prescribe a narcotic for this? Nothing else ever works on my pain. **Dr. Taylor:** Well I can see lots bruising and swelling and you're very tender on exam, but luckily your X-ray came back negative for a fracture. This looks like it will be a really bad sprain. But I see from the state database that you're already taking oxycodone, and that you got your last prescription 2 weeks ago. Dr. Taylor, how should an Emergency Department provider manage Kathy's acute pain?
95	**Treating Acute Pain in the Emergence Department** Acute pain is, of course, a very common presentation in the emergency department. Over the last several decades the number of ED visits in which an opioid was prescribed has increased substantially from about 21 percent around 2001 to 31 percent in 2010. We also know that, like other care settings, there is wide variety in opioid prescribing practices among emergency department physicians. And we know that being seen in the emergency department and being prescribed an opioid is associated with the transition to long-term opioid pain medication use. Among opioid naïve patients, for example, who filled an opioid prescription, almost 20 percent were still taking an opioid pain medication one year later. And as we've alluded to earlier today as well, we know that patients presenting with certain types of acute pain may not have benefit from opioid pain control compared to non-opioid pain control strategies.
96	Kathy was discharged from the Emergency Department with a treatment plan consisting of rest, ice, compression, and elevation. She was also given an ankle brace. The ED provider talked to Kathy about the risks of taking someone else's prescription opioids, and prescribed a combination of ibuprofen and acetaminophen. Kathy was extremely upset as she left and still insisted that she needed something stronger for her pain. On follow up, Kathy's ankle pain improved and she returned to work in 10 days.
97	Now, let's discuss **four potential scenarios** for this case of Kathy James being treated with opioids for chronic pain.
98	Kathy seemed to be doing well on her pain treatment plan including opioid therapy for her painful diabetic neuropathy and chronic hip pain for the next eleven months…

99	Then, Dr. Alford was notified that Kathy was seen in the emergency room of a local hospital, requesting an early refill of her oxycodone after running out early. The ED physician noted that she was in moderate to severe opioid withdrawal and gave her a prescription for enough oxycodone pills to last until her next appointment with Dr. Alford in one week.
100	**Dr. Alford:** Hello Kathy. Wow, I was surprised to get a call from the emergency room doctor about your visit last week requesting an early refill of your oxycodone. **Kathy:** Yeah, well, my foot pain has been so much worse that I started taking an extra pill in the afternoon, so I ran out. I think I've gotten used to this dose, and it doesn't work the way it used to. But now I've got my husband telling me I'm addicted, and I'm not! But the pain is so bad that it's hard to get to work, and I can't sleep because even the sheets hurt. I think I need a higher dose. Dr. Alford, what do you think is happening with Kathy, and how will you respond to her request?
101	**Consider the Differential Diagnosis** The first thing to do is to take a deep breath and consider the entire differential diagnosis of this behavior. And, I like to think of it, as is this pain relief seeking or substance seeking? Has her disease progressed? Has her neuropathy gotten worse or maybe she has poorly opioid responsive pain or maybe she's developed opioid analgesic tolerance? Maybe it's opioid withdrawal mediated pain, which I'll talk more about or maybe she's developed that paradoxical response called opioid induced hyperalgesia. But on the other side, maybe she has developed an opioid use disorder or addiction. Possibly she's treating some other psychiatric symptom. We know that opioids make people feel better. Maybe she's treating a depression or an anxiety disorder or maybe there's criminal intent. Maybe she is selling her opioids and we know that these opioids have a street value. Unfortunately, it's usually more complicated than that and it can be a combination of many of the things we just talked about. For example, it could be a patient with chronic pain with a comorbid opioid use disorder who's taking some of their opioids for pain and maybe selling some for income.
102	**Opioid Withdrawal Mediated Pain** So I mentioned opioid withdrawal mediated pain and this is just a figure to show exactly what I'm talking about, and that is we had mentioned earlier that people who are on chronic opioids will become physically dependent. And when their level of opioid drops below a certain level they're going to go through withdrawal, and the first thing they're going to feel is worsening pain. So you can see this cycle here where they're comfortable. The level drops to a certain level where they feel pain. They take their opioid. They feel better. But are they treating their withdrawal mediated pain or are they treating their pain? And I think that is the theory behind putting someone like this on a long-acting opioid to try to avoid these ups and downs during the day to avoid withdrawal mediated pain.

103	**Opioid-Induced Hyperalgesia (OIH)** And then there's opioid induced hyperalgesia that Dr. Taylor had mentioned as well, and it's a paradoxical enhanced pain sensitivity in some patients on chronic opioid therapy. Unfortunately, the underlying pathophysiology is complex and not clearly understood and we don't know the true incidence as well. And, unfortunately there's no official criteria or guidelines for diagnosing it. But clinically what we see is kind of a generalized, diffuse, ill-defined pain not like the pain that we're treating perhaps. If we're treating back pain but now everything hurts I start to think about opioid induced hyperalgesia. An increased dose might improve the analgesia but only temporarily and there are no studies looking at opioid taper. However, if the person has this problem we really need to decrease the dose or stop the opioid over time because their pain has worsened.
104	**Addiction (Opioid Use Disorder)** In terms of substance seeking, has the person developed an opioid use disorder or addiction? It's really a clinical syndrome that presents as loss of control, impulsive use, continued use despite harm or craving, and what do I mean? Loss of control: the person cannot take the medication as prescribed. They keep running out early, showing up in the emergency room, calling the on-call service. Compulsive use is a preoccupation with the opioid. That is, they don't want to hear anything else about pain control. They just want more opioids so anything else you recommend, they dismiss. Continued use despite harm: so even though they're having adverse effects they want more opioid. They should want less. And craving: that's this urge. They wake up in the morning. The only thing they think about is getting more opioid. And these behaviors are worrisome behaviors and we worry about both the pattern and severity. So if someone escalates their dose on more than one occasion after you've educated them, that's a pattern that's very worrisome. But it only takes once for me to get called from the pharmacy that someone has altered their prescription for me to say this is a problem. Remember that addiction or an opioid use disorder is a behavioral maladaptation, which is different than physical dependence, which is a physiologic adaptation to being exposed to this molecule, namely an opioid.
105	**Discussing Possible Addiction (OUD)** How do we discuss possible addiction or opioid use disorder with our patients? We want to be specific and timely with our feedback, tell our patients, which behaviors raise our concern that there's possibly a use disorder, things that they did that made us worried about loss of control, compulsive use, continued use despite harm. Remember that patients may suffer from both chronic pain and a use disorder, and sometimes we just need to agree to disagree with a patient if they disagree with our clinical decision-making. Remember that if you're worried about an opioid use disorder that the benefits of an opioid can no longer outweigh the risks and you can say things like, "I cannot responsibly continue prescribing an opioid as I feel it will cause you more harm than good" and if you think the person has a use disorder remember to refer them to addiction treatment. They may not be willing to accept that referral, but we should at least talk to them about the referral and the need for treatment.

106	**Lack of Benefit** Now if we think the person has either lost benefit or there just isn't any benefit from the opioid, what are the next steps? Well, the first thing is to reassess the factors affecting their pain and re-attempt to treat the underlying disease that may be making their pain worse or any of the comorbidities that we talked about earlier. We could consider adding or increasing non-pharmacological treatment like acupuncture or CBT. We could add or increase adjuvant medications for synergy. We could also add breakthrough medications or consider something called opioid rotation, which I'm going to talk about.
107	**Consider Breakthrough Medication** In terms of breakthrough medications remember the first choice is really no breakthrough medication. You shouldn't assume that somebody who's put on a long-acting medication is going to need breakthrough medications. But if it turns out that they do the next important message is that the first choice is a non-opioid. So even though they're on a long-acting opioid you would start with a non-opioid for breakthrough medication including NSAIDs, Acetaminophen and adjuvant medications. But if that doesn't work you could use a short-acting opioid, either the same molecule or a different molecule or one of the dual mechanism opioids that we talked about, the Fentanyl or Tramadol.
108	**Consider Opioid Rotation** Now if that doesn't work and you're thinking about an opioid rotation that is switching to a different opioid to, one, restore analgesic efficacy or to limit adverse effects and decrease the overall Morphine milligram equivalents. This is based on large intra-individual variation or response to different opioids, remembering that there are different variants to the mu-opioid receptors and it's really based on surveys and anecdotal evidence and it is promising but needs validation.
109	**Opioid Conversion Tables** But if you're going to do it and you're going to switch someone from one opioid to another you'll go to an opioid conversation table and you'll notice if you've done that before that there's no two opioid conversion tables that are exactly the same, so there's lots of variation. Why is that? Well, they're derived from relative potency ratios using single-dose analgesic studies in opioid naïve patients. And they were based on limited doses and limited ranges of doses and they really don't reflect the realities of our patients who may be on chronic opioids for many years and have tolerance and physical dependence, and they're not reliable due to individual pharmacogenetic differences. So, most tables do not adjust for incomplete cross tolerance.

110	**Kathy James: Opioid Rotation** Let's use our case of Ms. James and talk about rotating her from Oxycodone to long-acting Morphine. I like this online program when I'm doing a rotation called GlobalRPH.com, and what it allows you to do is to put in the person's current opioid, in this case Oxycodone, the total daily dose. In this case remember she's on 20 twice a day so 40mg. Then, you reduce for incomplete cross tolerance the person's tolerance for sedation, respiratory depression. Oxycodone is not going to be equivalent to those same adverse effects with Morphine. We want to decrease the equivalent dose to avoid adverse effects. We're going to decrease by 50 percent. Most recommendations are somewhere between 25 to 75 percent, so it's not an exact science. So I generally pick 50 percent, and if you do that and you put in Morphine as the new medication, she'll end up on 30mg per day or 15mg twice a day. You can see in this case we've gone from 60 Morphine milligram equivalents to 30 Morphine milligram equivalents.
111	Over the next eighteen months Kathy James's condition improved on a stable morphine dose of fifteen milligrams twice per day and she had no recurrent aberrant medication taking behavior. Along with the morphine her gabapentin was titrated up. Ibuprofen was added for breakthrough pain and low dose nortriptyline was added at night for her neuropathic pain. Kathy continued acupuncture therapy, and joined a monthly chronic pain support group. Her individual PEG scores remained between five and six on the ten point scale. She remained employed and remained adherent with treatment and monitoring. She continued with her regularly scheduled follow-up visits.
112	In the second scenario, after being rotated to morphine and maintained on gabapentin, ibuprofen and nortriptyline, Kathy's pain remained out-of-control with PEG scores between 9 and 10 out of 10.
113	Despite small incremental morphine dose increases, on each visit she demanded that she be changed back to oxycodone and at a higher dose. After being converted back to oxycodone her pain did not improve. She is now on medical leave from her job and according to her husband spends most of the day in bed. She has been adherent with urine drug testing and pill counts. Clinic staff reported on multiple occasions that she was rude and confrontational when they asked her to leave a urine test and when she tried to be seen without an appointment. Dr. Alford, what should be the next steps in managing this patient's pain and opioid use?
114	**Continued Lack of Benefit** Well this is clearly a case of a patient with continued lack of benefit. So remember that not all chronic pain is opioid responsive, that more opioid is not always better, that more opioid may increase risk of adverse effects and some patients with chronic pain actually improve after opioid taper.

115	**Discussing Continued Lack of Benefit** It's important to stress with the patient how much you still believe that they have terrible pain and be empathic about their suffering and the impact the pain is having on their life. Express frustration that the treatment plan didn't work and focus on the patient's strengths and their ability to cope with their pain and show a commitment to continue caring for them even without opioids, schedule close follow-up during and after a taper.
116	**Discontinuing Opioids** If you've decided to discontinue the opioids you really don't need to prove with 100 percent certainty that the person has an addiction or a use disorder or that they're diverting. You only really need to assess and reassess the risk-benefit ratio. So if the patient's unable to take the opioid safely or is nonadherent with monitoring then discontinuing opioids is completely appropriate even in a setting of benefits. You really need to determine how urgent to discontinue based on the severity of the risks and harms. Document your rationale for discontinuing the opioids. You need to determine if the person has physical dependence and determine whether or not a taper is required. An important take home message here is that you are not abandoning the patient here. You're abandoning the opioid.
117	**Risk Benefit Framework** The risk-benefit framework becomes incredibly helpful when the patient responds, "But I really need opioids" or "Don't you trust me?" or "I thought we had a good relationship. I thought you cared about me" or "If you don't give them to me, I'll drink or use drugs or hurt myself" or "Can't you give me enough until I find a new doctor?" And your response is going to be, "I cannot continue to prescribe a medication that is not helping you or is hurting you, or both".
118	Despite Dr. Alford's best efforts to explain to Kathy why the treatment plan will include tapering off opioids due to lack of adequate benefit and focusing on nonopioid pain treatments including cognitive behavioral therapy, Kathy keeps on insisting that she needs higher dose oxycodone. **Dr. Alford:** Ms. James, it seems that we are not going to agree on the treatment plan moving forward. To make sure I know that you understand why I am making this change can you please tell me in your own words why I want to taper your oxycodone and try other treatments. **Kathy:** Well, it's because you don't think it's helping me, but I disagree…all I need is a higher dose of oxycodone…but it seems that you don't understand me so I'm going to need to find a new doctor…. **Dr. Alford:** Well ultimately that's your choice. But I just want you to know that if you change your mind, I'm happy to continue caring for you and trying to control your pain but not with opioids… Ms. James storms out of the office and states that she will be calling patient advocacy…

119	**In the third scenario, Kathy seemed to be doing well on her pain treatment plan including oxycodone for her painful diabetic neuropathy and chronic hip pain for the next eleven months…** but then she started to struggle and become frustrated with the "rules" and stigma of taking opioids.
120	**Kathy:** Oh my gosh, I am so glad you were able to squeeze me in for an appointment on such short notice! The pharmacy wouldn't refill the oxycodone you wrote for me! They said that they can't put it through my insurance…new rules I guess… The company just refuses to pay even though I have been on this medication for a while! I'm just so sick of this… everyone treats me like I'm a criminal or a suspect just 'cause I need these meds… even my husband is giving me the side-eye now. I hate being put through the ringer by people here – c'mon, drug tests?? Dr. Robertson never made me do that! These things are ruining my life. I just tried to stop taking them myself, but my god I just got so sick… I just want to get off them!!!! Dr. Alford: OK, Kathy. I completely understand your frustration, and the insurance company paperwork sure doesn't help. Let's talk about how we can taper you off the medications safely, to minimize the side effects…and try you on other treatments for your pain.
121	**Opioids and Pain: Qualitative Study on Clinician and Patient Perspectives** This is not an uncommon scenario. We certainly see patients becoming frustrated with monitoring, but also frustrated with insurance companies and the ability to get their opioids on a schedule. And this was a qualitative study that looked at clinicians' attitudes as well as patient perspectives and they came up with themes. So the patient themes included: patients who are on opioids felt that there were threats to their trustworthiness and iatrogenic suffering by clinicians demonstrating lack of care empathy which caused further suffering. Another theme was communicating the invisible and subjective condition of chronic pain was difficult. Clinicians did not accept reports of pain on face value. Another theme was motive, honesty and testimony, where patients perceived an untrustworthiness by their clinicians. And then finally, stigmatized identities: that patients who had chronic pain that influenced their own perceived trustworthiness. Clinician themes included challenges of the practice context. For example, they recalled difficult interactions and the impact that those had on their approach to care for other patients. And finally, complicated clinical relationships. That is, they did not see their role as a collaborative partner, but instead saw themselves in a defensive role as interrogators.

122	**Tapering Opioids 1** How do we taper opioids? Well, there are no validated protocols in patients on opioids for chronic pain. There was a recent systematic review that found very low-quality evidence that suggested that several types of opioid tapers may be effective and that pain, function and quality of life may improve for some patients with opioid dose reduction.
123	**Tapering Opioids 2** Another study found that 62 percent of patients in a pain clinic who remained in a voluntary, not an involuntary but a voluntary patient-centered opioid taper over four months were able to decrease their Morphine milligram equivalents by half. The likelihood of decreasing their opioid by half was not predicted by starting dose, baseline pain intensity, years prescribed opioids or any other psychosocial variable. However, those that were successful in decreasing their opioid dose, neither pain intensity nor pain interference increased with that opioid reduction.
124	**Opioid Tapering – General Approach** A more general approach to opioid tapering is first, decide on how quickly you want to do it and it depends. If you're worried about lack of benefit you can taper over weeks to months. If you're worried about apparent harm or risk, you should really taper over days to weeks. The first step is to reduce the medication dose to the smallest dosage unit. The second step would be to increase the amount of time between doses. You might need to convert an extended release long-acting opioid to a short-acting opioid to get to even smaller dosage increments. Remember, you can always use an alpha-adrenergic agonist like Clonidine or Tizanidine off-label to treat the withdrawal symptoms. Remember to build up alternative pain treatment modalities while you're tapering the opioid because their pain will increase during that opioid taper.
125	Over six months, Kathy successfully tapered off the oxycodone. Her neuropathic pain was moderately controlled on a combination of nortriptyline, gabapentin, and capsaicin cream. Kathy joined a monthly chronic pain support group. Her individual PEG scores remained between five and six on the ten point scale. She remained employed and remained adherent with treatment and monitoring. She continued with her regularly scheduled follow-up visits.
126	**In the final scenario, Kathy seemed to be doing well on her pain treatment plan including oxycodone for her painful diabetic neuropathy and chronic hip pain for the next eleven months…** Her urine drug tests consistently returned expected results, except once, when the UDT was opiate positive but negative for oxycodone, raising concerns for opioid misuse (including possible diversion).

127	**Kathy:** I have no idea why the test results came back that way. I've been taking the meds exactly like you told me to, and I never gave any of the oxy to anyone else! **Dr. Alford:** Unfortunately I was not able to do a confirmatory screening, but I do want to tell you I'm worried that this is not the first concern I have: Remember that the last couple of appointments you were supposed to bring in your pill bottles so I could do a pill count and you told me you forgot them. As we discussed early on, this puts you at greater risk for harm from these potentially dangerous medications, so I'm going to need to monitor you more closely, including doing urine tests more frequently. There were no additional unexpected test results over the next two months. Dr. Taylor, how do you talk to patients who you are worried may be diverting some of their opioid pain medications?
128	**Discussing Possible Diversion** When we think of diversion we think of it as one form of opioid misuse, meaning giving, selling or trading a prescription medication to another person. In discussing this with patients it's really important to zero in on the behaviors that have made you feel worried. Specifically, a urine drug test that's negative for a prescribed opioid or nonadherence with pill counts. By focusing on the behaviors it can help eliminate some of the stigma that can sometimes creep into these conversations and it's important to outline to patients that when you do see behaviors that raise concern for diversion it actually threatens your ability to continue to prescribe their medication.
129	Two months later, Kathy is brought to the Emergency Department after suffering an overdose. Her husband explains that he found her on the bathroom floor, and administered naloxone, to which she responded, and then called 911. Her husband reports that Kathy's pain has increased recently, resulting in her taking extra oxycodone pills AND taking some of her father's morphine. She has been sleeping a lot, and calling in sick to work. He acknowledges that he's been denying Kathy's problem to himself, as he's immersed himself in work and childcare. He had no idea that she had become addicted to her pain pills. He is terrified of losing her, and begs for help from the ED provider. Dr. Taylor, how should the Emergency Department clinician manage Kathy?

130	**Treatment Gaps following Opioid Overdose** Here we know that patients like Miss James experience very substantial treatment gaps after an opioid overdose. We know that patients who have an opioid overdose in the overwhelming majority of cases go on to receive further opioid prescriptions. In fact, 91 percent of patients who have had a non-fatal opioid overdose receive a subsequent opioid prescription. Seven percent of those patients go on to have another overdose, and at two years the rate of repeat overdose is about 17 percent. As we mentioned earlier in the training, a prior overdose is a very potent risk factor for a subsequent overdose. We also know that, unfortunately, very few patients presenting with a non-fatal opioid overdose are connected to opioid use disorder treatment. In fact, less than one-third of people who suffer a non-fatal opioid overdose receive medications for an opioid use disorder in the following year which is a tremendous missed opportunity because medications for opioid use disorder are associated with decreased all-cause and opioid-related mortality in this population.
131	**Opioid Use Disorder (OUD) Primer** And so when we think about opioid use disorder we again want to think about a chronic relapsing brain disorder that is characterized by compulsive drug use, use despite consequences and that involves changes to the brain and the reward pathway involving stress and self-control. We know that these changes in the brain do persist after stopping drug use, and we know that like other chronic diseases opioid use disorder can involve cycles of relapse and remission. We also know that opioid use disorder is a potentially fatal illness. Without treatment it is progressive and can result in disability or premature death. With this in mind, the CDC recommends that we offer a range of evidence-based treatment, typically Buprenorphine or Methadone in combination with behavioral therapies for patients who have an opioid use disorder.
132	**DSM-5 Opioid Use Disorders** In terms of diagnosing an opioid use disorder, the DSM-V criteria are an agreed upon set of criteria that allow you to assess your patients. So these evaluate tolerance and withdrawal, though it's important to note that these first two criteria may be seen in patients on prescribed opioids and do not necessarily by themselves constitute a use disorder, and the 11 criteria go on to assess for loss of control and for continued use despite negative consequences. And patients can be stratified into a mild, moderate or severe opioid use disorder based on how many criteria out of these 11 that they meet.

133	**Medications for Treating Opioid Use Disorders (MOUD)** Fortunately, we do have very effective medications for opioid use disorder. The goals with using these medications are, number one, to alleviate physical withdrawal, to achieve opioid blockade, which may reduce the risk of overdose death when other opioids are used concurrently, to reduce cravings for opioids and to help normalize the brain changes that result from opioid use disorder. As we've alluded to, we have very strong evidence for medications for opioid use disorder, including Methadone, Buprenorphine and Naltrexone, and the way these medications work is different. Methadone is a full opioid agonist, whereas Buprenorphine is a partial agonist and Naltrexone is an antagonist or a blocker at the mu-opioid receptor. The use of these medications has a variety of benefits, including retaining patients in treatment, increased employment, decreased rates of relapse, decreased infections including HIV and Hepatitis C seroconversion and most importantly, decreased mortality. They are incredibly effective potent treatments. But unfortunately, in spite of the efficacy of these treatments we have a very large gap between the patients that need opioid use disorder treatment and those who are able to access medications for their use disorder.
134	**Addiction Treatment Referrals and Resources** On this slide we direct you to a number of resources that may help you connect to treatment programs in your area, including the SAMHSA treatment locator. We've also found that State Department of Public Health websites can connect you with local acute treatment services, residential programs, Methadone maintenance treatment programs and office-based treatment programs for Buprenorphine or Naltrexone and mutual self-help organizations such as Alcoholics Anonymous and Narcotics Anonymous are both free, widely available and have been widely studied.

135	**Patients on MOUD and Pain Management** Now, patients with an opioid use disorder who have concurrent pain present several challenges. In the case of a patient who has both an opioid use disorder and chronic pain, there are certain Buprenorphine formulations that can be prescribed to treat both the chronic pain in an off-label manner as well as the opioid use disorder, though it's worth noting that the use of Buprenorphine for opioid use disorder does require special training and a special waiver under the Drug Addiction Treatment Act of 2000. The other important notation here is that Buprenorphine, when used for the treatment of opioid use disorder, has a duration of up to 24 hours. However, its analgesic properties only last about 8 to 12 hours. When you're treating someone with concurrent opioid use disorder and chronic pain, you may wish to consider TID dosing of the medication whereas in patients who have only an opioid use disorder and no pain you might be able to dose Buprenorphine once or twice a day. And we know from systematic reviews that studies do report effectiveness of Buprenorphine in treating chronic pain in this population, though the quality of evidence has room to improve. Acute pain presents different challenges in patients on medications for opioid use disorder. It's important to remember that patients who are physically dependent on opioid such as Methadone or Buprenorphine for their substance use disorder treatment must be maintained on a daily equivalent of the medication that they are used to before any pain control benefits are realized. Pain control requirements in patients who have been maintained on chronic opioids are often higher than patients who are opioid naïve due to increased pain sensitivity and opioid cross-tolerance.
136	The ED physician initiates buprenorphine for Kathy's OUD; this treatment is continued by her PCP, who is waivered to prescribe buprenorphine for the treatment of OUD. The PCP changes buprenorphine dosing to three times daily to treat both chronic pain and OUD. Kathy attends Narcotics Anonymous meetings and outpatient addiction counseling. Her PEG scores remain between five and six on the 10-point scale. She remains employed, and continues with regularly scheduled follow up visits. Dr. Alford and Dr. Taylor, can you please summarize what we've learned during these modules?
137	**Summary Points: Part 2 (1)** In part two we've reviewed the importance of using universal precautions as an approach to patients on opioid pain control medication, but to also individualize care based on risk. We discussed continuing or modifying opioid treatment based on the clinical indication and the response to therapy and we discussed strategies to optimize office systems to involve the entire healthcare team. We discussed documenting benefits, risks and harms and rationale for the plan of care.

138	**Summary Points: Part 2 (2)** We talked about how worrisome opioid taken behavior can signify pain relief or substance seeking behaviors or a combination of both, and that it's important to fully assess and then respond to these worrisome behaviors. The decisions to continue or discontinue opioids should be based on a reassessment of the risks and benefits of the treatment and should be well-documented, and that medication-based treatment is highly effective in treating opioid use disorders but it's not universally available.
139	Thank you for participating in the Scope of Pain online activity. Please complete the post-test and an evaluation and you'll be able to download your certificate.
140	Also, be sure to visit our resources page where you'll find additional educational modules, tools to help you implement what you've learned into your practice and videos that model challenging clinical interactions.