MOD: Thank you for joining SCOPE of Pain: Safe and Competent Opioid Prescribing Education. I’m Judie Yuill, your moderator. This online activity is designed to help you manage patients in chronic pain using opioids when necessary, safely and competently.
Web-based Program

2 Modules
How to:
- determine when opioid analgesics are indicated
- assess for opioid misuse risk
- talk to patients about opioid risks and benefits
- monitor and manage patients on long-term opioid therapy

Case Study: Mary Williams
- 42 year old female
- Hypertension
- Type 2 diabetes with painful neuropathy
- Chronic low back pain

The web based program consists of two one hour modules that follow the case of Mary Williams, a forty-two year old female with hypertension, type two diabetes with painful diabetic neuropathy and chronic low back pain. Through the modules this case will elucidate how to assess chronic pain and opioid misuse risk, how to talk to patients about opioid risks and benefits, and how to monitor and manage patients on long term opioid therapy.
In these modules we’ll discuss the case with Doctor Daniel Alford, Associate Professor of Medicine, Assistant Dean of Continuing Medical Education and Director of the Clinical Addiction Research and Education Unit at Boston University School of Medicine and Boston Medical Center and with Doctor Seddon Savage, Director of the Dartmouth Center on Addiction Recovery and Education, Associate Professor of Anesthesiology at Dartmouth Medical School in Hanover, New Hampshire, Medical Director of the Chronic Pain and Recovery Center at Silver Hill Hospital in Connecticut and past President of the American Pain Society.
At the conclusion of this section, you will be better able to use universal precautions with patients on chronic opioid therapy including monitoring and documentation strategies and safely initiate, continue or modify opioid therapy as appropriate.
Now let’s catch up with Mary Williams. In module one we learned that Mary is diabetic, hypertensive, obese and a smoker with a remote history of an alcohol use disorder. She has chronic painful diabetic neuropathy and back pain. For the past year she has been on a regimen of gabapentin and immediate release, short acting oxycodone with acetaminophen for her pain. She has said that her pain and function have improved on this regimen but she gets the best benefit when she is able to take eight tablets per day.

Mary’s new provider has completed an initial assessment that includes screening for psychiatric comorbidities, substance abuse and opioid misuse risk. The provider found her pain to be moderate to severe with a significant impact on her function and quality of life and she has some opioid misuse risk due to her age, remote history of an alcohol use disorder and a family history of a substance use disorder.

Between her initial visit and this second visit one week later, her current provider was unable to contact her previous provider but did review her medical records and confirmed her history and medication lists. The clinician also received results from her urine drug test which as expected was positive for oxycodone only, and checked the state prescription drug monitoring program for her prescription history which showed only one prescriber and one pharmacy. There is no evidence of prescription opioid misuse in Mary Williams’ history. Now her PEG score is unchanged from the first appointment and at this point she has run out of her opioid prescription on schedule.
Doctor Savage, are there any steps that should be taken before initiating or changing opioid therapy? For example, when you’re taking care of a new patient who is already on opioids like Mary Williams?
SEDDON SAVAGE MD: Well, Judie, I think that’s a great question. There are in fact a number of things that need to be done to make sure that opioids are the right choice for an individual patient and to manage the opioids when you’ve elected to use them. I think the most important thing to remember first off is that pain, as discussed in module one, is a complex and very personal experience that is filtered through the entire bio-psycho-social context of the individual. So when we’re addressing a patient with chronic pain, it’s important to take a multi-dimensional approach to our care. And also to remember that pain is like other chronic conditions and we need to treat it as such. When we address a patient with diabetes or cardiac disease or other chronic illnesses, we always seek to engage them in a process of self-care and that’s equally important in the treatment of pain. Because we know that there are procedures and medications and treatments that can be provided. But most patients do best when they’re engaged in caring for their symptoms and in general for their health. When we’re treating patients with chronic pain, our goals are to reduce their pain but equally importantly to restore their function, particularly in valued areas of life. We also want to cultivate a sense of wellbeing and overall our goal is to improve the quality of life.

When I think of interventions for pain, I think of them as four basic domains. First there of course are the medications and there are many classes of medications, non-steroidal anti-inflammatories, acetaminophen, anticonvulsants, antidepressants, a variety of different topical agents, all can be very helpful in treating different types of pain. We have numerous procedures that we can do and selected appropriately, they can be very helpful to patients, nerve blocks, steroid injections, trigger point injections, implanted stimulators. Each have a role in certain types of pain for certain patients.
Physical approaches such as exercise or manual therapies, using orthotics or braces, application of electrical stimulation such as transcutaneous electrical nerve stimulation, use of heat, cold, stretch and other modalities can be very helpful for patients. And finally, I think very important for many patients is engaging them in psychological self-care. Often deep relaxation and meditation can be helpful, cognitive behavioral therapy, a series of psychoeducational groups about managing chronic pain for patients with co-occurring mental health issues, treatment of anxiety, depression and very important particularly when we’re talking about the use of opioids is addressing any co-occurring substance use challenges the individual may be dealing with. So overall taking a multi-dimensional approach to the treatment of pain is very important as a foundation for our care of the patient.
There are a number of resources that can be helpful in supporting patients. One that I think is particularly valuable is the American Chronic Pain Association. American Chronic Pain Association’s been active for over 30 years. It’s a very positive can-do oriented organization. They offer peer support and education to people who have pain. And also importantly to their support systems, their friends and families. There are self-guided, self-management tools. They give advice on talking to care providers. There’s information on medications and other treatments. And overall I think linking patients with this resource can be very helpful.
So if we do decide that opioids will be a component of the care of an individual with chronic pain, it’s very helpful to think about applying the concept of universal precautions. Opioids, we know, have special risks associated with them. All medications have benefits and have side effects and risks. But with opioids the stakes are particularly high. We know that these risks are present but predicting the risks for opioid misuse is pretty imprecise. So applying precautions universally protects all the patients that we are treating, each individual. And it also protects the public and the community health from opioids being diverted. If we apply universal precautions consistently, it reduces the stigma to our individual patients. Individuals don’t feel that they’re under particular scrutiny for diversion or misuse. We can simply conceptualize that this is something we apply to all patients and it standardizes our system of care.

The final reason to use universal precautions is it’s widely recommended by expert guidelines, American Pain Society, the Academy of Neurology, and importantly, the Federation of State Medical Boards, among others.
So what are the common universal precautions? There are a number of them. First, a comprehensive pain assessment with formulation of clear diagnoses of the contributors to the pain. Using a risk screening tool or interviewing carefully for risk of opioid misuse, and then adapting our care of the patient and particularly our prescribing of opioids, to accommodate the risks that we have perceived.

An important universal precaution is considering a trial of opioids as just that, a test or trial, that is paired with specific goals that the individual is seeking to achieve in terms of pain reduction or functional changes. We can stop opioids if they’re not effective. Seeing the patients on a regular basis in face to face visits so we can both interview and examine them is also important, and documenting our management of the patient, the specific interventions we are undertaking, and very importantly, our rationale for our decision making around the patient.

Other common universal precautions are the use of a patient prescriber agreement and monitoring for adherence, misuse and diversion.
Now, there’re two parts to a patient prescriber agreement and we’ll talk more about these in depth. There’s the informed consent and detailing the plan of care with the patient. Patient prescriber agreements often are signed by both the patient and the prescriber. It serves as a patient counseling document so that we are certain that we have gone over the appropriate details and risks and benefits with the patient. Now, the efficacy and outcomes of the use of patient prescriber agreements are not really well established scientifically, but there is no evidence of a negative impact on patients and most providers who use them find them extremely valuable in organizing care. Monitoring for adherence can include urine drug testing, pill counts and use of the prescription drug monitoring program and we’ll talk more about this in a minute.
In the informed consent, we want to help the individual develop realistic goals for the treatment, and also review individualized potential risks of the therapy.

Under realistic goals, usually the reduction of pain, not the elimination of pain, is one goal. To allow the patient to increase their function. It’s often helpful to develop specific goals with respect to function as well and the acronym SMART goals is helpful to think about. They should be specific, they should be measurable in a realistic time period and very action oriented, helping to engage them more in valued areas of their life and also realistic. And then review of the potential risk, both the physiologic side effects, the potential for the development of physical dependence if they’re on round the clock medications, important drug interactions that can occur, particularly with sedative hypnotics and others that may increase risk of overdose or negative consequences. The risk of over sedation or cognitive impairment and the need to be careful about driving or operating machinery until they know the effects of the medication on them. The risk of misusing or being led into the use of these medications for reward or euphoric effects, which in vulnerable individuals could lead to addiction. The risk of overdose with misuse is very important to establish with the patient. For women, it’s important to discuss pregnancy and the risk of babies or fetuses becoming physiologically dependent and developing neonatal abstinence syndrome at birth.

More and more we’re aware of the potential for patients to actually develop increased pain as a result of using opioids, so discussing the potential for opioid-induced hyperalgesia is important.

And finally, we know that others may seek opioids for misuse and thus the patient can become a victim of robbery or assault or home invasion. This is unfortunately not an infrequent occurrence.
So the second part of the patient provider agreement is the plan of care. Very important in the plan of care is engagement in other recommended treatments. You want to discuss your office policies for monitoring patients. It’s important to obtain permission to communicate with key others including both providers and often key significant others who sometimes can provide information that may be difficult for the patient to share. Indicating that there should be no use of illicit drugs and avoiding sedative use is important for safety purposes. We generally ask patients to notify the provider of all other medications that they are using and other drugs that they may be using. With women it’s important to discuss birth control, again concerns about fetuses developing a physiologic dependence on the opioids and periodically monitoring for pregnancy.

Then the final point in the plan of care is how the medications themselves should be managed, counseling patients to use them exactly as directed. Instructing patients in safe storage and protection from theft away from family visitors, workers who may be in the home, is important to emphasize. If at all possible, we advise patients to lock their medications. We counsel patients on safe disposal of medications when they are no longer using them or if the medication switched. And instructing patients not to sell or share their medications.
So it’s important when discussing these issues with patients and in thinking about our role in taking care of the patients to always embed our approach in the medical role. We are there to care for the patient. We are there to do the right thing for their health and for the public health. So it’s important to remember that we’re above all else care providers. There are many other people in society who are addressing the problem of opioid misuse and substance misuse more generally, who have a law enforcement or a justice role or deterrence role. Our role is taking care of our patients and protecting the public health.
If we always use a health oriented risk benefit framework while we are using the universal precautions, thinking always, do the benefits of the opioid treatment outweigh the potential risks and untoward side effects for this patient and for society, we will serve our patients well. Our role is not to determine whether the patient is good or bad or whether they deserve the opioids, if we should reward them for good behavior or punish them for bad behavior. Or even to consider whether we trust the patient. So we’re judging really the treatment and whether it’s beneficial or potentially harmful to the patient, not judging the patient.
Once we have engaged in the framework of universal precautions around opioids within a broader framework of comprehensive care of the individual’s chronic pain, we have to consider our opioid selection and dosing of the opioids. So what do we need to consider? Well, first we need to consider the pattern of the individual’s pain. Is it intermittent and rare? Is it intermittent and frequent? Or is it round the clock and constant? And then consider whether we want to use immediate release or whether we want to use sustained release long-acting opioids. It’s important that we begin therapy generally with short-acting opioids until a patient has developed tolerance, but we may settle into a pattern of use of long-acting opioids after a period of time. So the duration and onset of the drug is important to consider. One caveat is to remember that immediate release/short-acting opioids are pretty fast in onset and fast in offset so they’re a bit more rewarding to people who are vulnerable to those reward effects than the sustained release opioids.

The patient’s prior experience should be considered. We know that there are receptor polymorphisms for Mu opioids and that some patients get better analgesic response to some opioids. In addition to receptor polymorphisms, there are differences in opioid metabolism.

We have to consider the patient’s level of opioid tolerance, as I mentioned, before starting long-acting/sustained release opioid formulations. Considering the route of administration is important. The cost and insurance coverage is clearly important for some individuals and we should take that in consideration as well. It’s important to remember that chronic pain is just that, a chronic condition. We can start at low doses and go very slowly in making changes, a little improvement can go a long way when somebody’s been living with chronic pain.
Applying rational polypharmacy can also be a potent strategy in relieving pain. We know that different classes of pain medications act on different parts of the pain pathways. For example, use of nonsteroidal anti-inflammatory agents or topical agents such as Lidocaine may relieve peripherally-mediated pain, whereas tricyclic antidepressants and some anticonvulsants such as gabapentin, as well as opioids may act at the spinal cord and at the brain. So sometimes by combining different classes of medications we can get improved analgesia even at lower doses of each medication.
So here is an example of one way we can exploit the synergistic interaction of different medications. If we draw our attention to the table on the left, we see the baseline level of pain, which improves somewhat with the administration of a placebo. If we administer gabapentin, we see a greater effect in reduction of pain. Morphine alone has a greater effect in reduction of pain. But when we combine morphine and gabapentin, we get the greatest drop in pain intensity.

So turning our attention to the table on the right, we see that the dose of gabapentin required to achieve pain relief when it’s used as a single agent, is far higher than the dose that’s required when we combine it with morphine. And similarly for morphine, the dose of morphine required to achieve pain relief is higher when it’s used alone and lower when it’s in combination. So combining these two medications may be very effective improving analgesia, at the same time we reduce the required dose of each medication.
After reviewing the Patient Provider Agreement with Mary Williams, she and the provider sign it. Because Mary Williams has constant, around the clock severe pain and takes up to eight short acting oxycodone tablets daily, her provider changes her medication regimen to extended release oxycodone to try to stabilize her analgesia and minimize possible opioid withdrawal mediated pain. With more stable blood levels Mary’s pain control might improve with lower total daily oxycodone doses, going from forty milligrams to thirty milligrams per day. In addition, the provider increases her gabapentin to take advantage of the synergy between gabapentin and opioids.
Doctor Savage, can you describe the monitoring strategies you put into place in order to keep your patients on chronic opioid therapy safe?
SEDDON SAVAGE MD: Yes, the monitoring strategies that we use when using opioids for the treatment of chronic pain flow naturally from our goals. Often we use the six A’s as a way of guiding our monitoring of patients. First we look at analgesia, is the pain in fact improved or is the patient seeming to require more and more medications but complaining that the pain is worse and worse. We want to look at activities or the level of function. So we want to see if there’re any adverse effects of the medications, either side effects or other adverse effects. Are they engaging in what has been termed aberrant behaviors? For example, not showing up for medication refills in person, calling for early renewals, reporting lost scripts. How is their affect, their mood? And finally, are they adhering to the plan of treatment or are there important deviations that need our attention?

Another helpful strategy in understanding how a patient is adhering to the plan of care is to ask them to describe their use of opioids over the last 24 hours. This review can be very enlightening and it can help us revise or shape our care.

The collection of objective information is also a critically important part of monitoring opioid therapy of chronic pain. Let’s talk a little more about urine drug tests, pill counts and use of the prescription drug monitoring program.
So why do urine drug testing? Well, there’re a number of important reasons. Urine drug testing can give us important information that helps confirm that the individual is using the medication that we’re prescribing to them and can help identify use or nonuse of illicit drugs. Self-reported drug use among patients with pain and among patients generally can be very unreliable.

How do we find out about drug use if the patient doesn’t tell us? Well, we can observe behaviors, but sometimes these observations don’t tell us the whole story and testing the urine can provide the piece that we’re missing.

Urine drug testing can be very helpful for some patients to improve their adherence, particularly patients who have had a history of substance misuse in the past. And finally, it’s an evolving standard of care, one that’s really expected as part of the care of persons on opioid therapy.
Let’s talk about how to implement urine drug testing. First of all, we can do it on a random basis, which is often recommended so that patients can’t prepare in advance. But it can also be done on a scheduled basis. If somebody’s truly losing control over their medications or other drugs, they’re not likely to be able to prepare for a scheduled appointment on a routine basis. It’s important to do however, when concerns arise, if we’re concerned that the patient isn’t taking the medications that we prescribed, or if they maybe are exhibiting behaviors that suggest that they’re using illicit drugs. We can call them in and ask them to present within 24 hours to get a urine drug screen.

We can discuss the urine drug testing openly with the patient. We’ll often say to a patient, “if I send your urine out right now, what am I going to find in it? Will there be any surprises?” And patients will often be quite open.

Similar to that, it’s important to document the time of last medication use so that we know when the patient is taking their medication, rather than if there’s no medication, and having the patient say, “Oh, well, I hadn’t taken it for a day because I was traveling,” or some other explanation. It’s important to recognize urine drug testing is simply one medical data point that we need to integrate with our observations of the patient, with other data points we have about their medication use, their function, their pain, and other clinical facts. We can’t discriminate, if we find something that is unexpected, for example, the medication is not in their urine or they’re using an illicit substance, we can’t discriminate between elective use, whether they have become addicted or whether, if the medication’s missing in their urine, whether they’re diverting it or just forgot to take it. We need to again, integrate this piece of information with other information that we have about the patient.
Also important to recall that there is a small risk for mislabeling or other lab error or unusual metabolic pathways sometimes can explain why medications we expect to be there are not there. For that reason, I think it’s important to have a good relationship with the lab or a toxicologist who we can talk to when unexpected findings occur, particularly if we’re going to take action based on them or revise the treatment plan.

Now, none of this can prevent dedicated deceivers from beating the system. But for most patients, implementation of urine drug testing, as we’ve discussed, can be very helpful in supporting safety.
There are two different broad categories of urine drug tests: are urine drug screens and urine confirmation screens. The drug screens are usually immunoassays – they’re convenient, they can be done quite quickly at point of care or in a lab. They’re relatively inexpensive. It’s important to know however what’s included in the testing panel. There’s a risk of false negatives in urine drug screens because most labs have cutoffs and only report when the concentration is above a certain level. There’s also with immunoassays a risk of false positives due to cross reactions of different drugs. So whenever we get an unexpected finding with an immunoassay, it’s important that the same urine be sent for a confirmation test.
Confirmation testing is usually done by gas chromatography/mass spectroscopy. This type of testing identifies specific molecules. It’s highly sensitive, it’s highly specific, but it’s quite a bit more expensive so it’s not generally recommended to be done on a routine basis.

There is not good evidence that measurement of urine drug levels is a valid method of determining the amount of an opioid that an individual has ingested.

To interpret urine drug testing findings it’s important to be aware of certain common opioid metabolic pathways. For example, codeine metabolizes into both morphine and hydrocodone. In turn, hydrocodone and morphine metabolize into hydromorphone. So for example, if you find hydromorphone in the urine it could be a result of using hydromorphone as a prescribed opioid or it could be the result of metabolism of codeine, morphine or hydrocodone. Similarly, oxycodone metabolizes into oxymorphone. Now heroin may be an issue for some of our patients, not prescribed, but used from the street. And it metabolizes into 6-monoacetylmorphine, but that’s only in the blood and therefore captured in the urine for a very brief moment in time. So more commonly we will see heroin picked up as morphine in the urine. Bear in mind that some individuals have idiosyncratic metabolic pathways as well, which may alter findings in a urine drug screen. Consulting with a toxicologist is very important before taking action based on the findings.
Another strategy that can be valuable in monitoring opioid therapy is the use of pill counts. Pill counts provide objective information that can help confirm medication adherence and can help minimize diversion. One strategy that is often used for routine pill counts is the use of a 28-day supply rather than a 30-day supply so that the renewal dates fall on a regular day during the week rather than landing on a weekend periodically. And prescribing the medications so that the patient should have several days of residual medication when they arrive for the appointment, then asking the patient to bring the medications in at each visit and having the prescribing clinician or another member of the staff routinely count the medications at the visit.

Pill counts can also be used if concerns or risks arise in care of the patient. The individual can be called and asked to come in for a random pill count at any point during the month. For example, if somebody has been alleged to be diverting their medications or you are concerned that they are not using them as prescribed.
Increasingly states have prescription drug monitoring programs and it is a very powerful resource that’s substantially underutilized by many clinicians. Some states, because of the underutilization of this resource, are beginning to mandate use. In any event, most clinicians who use it on a regular basis, find it to be very, very valuable. The prescription drug monitoring programs are a statewide electronic database of all controlled substances that are dispensed by pharmacists. The data is available to prescribers and pharmacists and in some states available also to law enforcement in the context of investigations. There is good evidence evolving that suggests that regular use of the PDMP has positive outcomes that improve prescribing and also reduce prescription drug abuse and diversion of controlled substances. So I would really encourage people to begin using it on a routine basis.
Now again, in discussing all these various strategies for monitoring, some patients may feel somewhat skeptical and wonder why pill counts and drug tests and checking databases is being done. It’s not done with other medications. But embedding this again in the health paradigm that we’re seeking to protect all individuals in the practice and the public health, reviewing the risks of opioid medications when they are misused and the fact that misuse of opioids can sneak up on people very subtly over time and that our responsibility is to look for and to manage any early signs that a harmful pattern of use may be evolving. Most patients readily understand this and appreciate the extra care we’re taking in monitoring them. Using a consistent approach, universal precautions with all patients and then importantly tailoring the application of these precautions to individuals is very important.
MOD: In our case study, Mary Williams had a remote history of an alcohol use disorder which puts her at higher risk of opioid misuse. So do you have to monitor her differently? And if so, how?
SEDDON SAVAGE MD: It’s important to apply universal precautions with all patients to whom we’re prescribing opioids, but it’s also important to consider the patient’s individual risk and to adjust our care to better support their particular needs. With patients who have a past history of addiction or substance use disorder of any kind it’s important to acknowledge that history rather than avoiding talking about it as sometimes our inclination is. Framing addiction is a challenging health issue, congratulating the patient on their recovery or getting past that challenge, expressing admiration for their work in doing that, can be very, very helpful, and most people who are in recovery, will tell you they never want to go there again. So acknowledging their desire to stay in recovery can be very, very helpful.

What are the variables of care that we can structure in a way to support our patients who are in recovery from substance use disorders? Well, there are a number of them. First of all, consider the setting of care. What is the setting of care where they can get the best care coordination and the best expertise to support their recovery? Then considering the specific supports we’re offering for their recovery; what will best support their recovery from co-occurring conditions? Considering the selection of our treatments is important. Organizing opioid therapy in a way that is less rewarding; supplementing opioids, if they’re required, with other non-rewarding medications or treatments can be important. We also should consider the supply of medications. And finally, intensifying our supervision of the individual, perhaps seeing them more frequently, doing more frequent pill counts or urine drug testing or other monitoring and supports can be very helpful in supporting a person’s recovery when they have a history of substance use disorder.
MOD: How can a provider do all this monitoring during a fifteen minute office visit?
Optimize Office Systems

**Saves Time and Stress**

Develop and implement:

- Office controlled substance policies, reflected in PPA
- Management flow sheet
- Patient registry
- Utilize other staff (*nurses, medical assistants, pharmacist, psychologists*)
- Lists of referral and support resources (*pain, mental health, addiction*)

SEDDON SAVAGE MD: It is a lot of work but management of patients with complex chronic conditions often is a lot of work. And just as we do for patients with diabetes, or who are using Coumadin, we need to engage our entire office system and co-care providers in management of the patient. Having controlled substance policies that are reflected in the patient provider agreement is one important step in doing that. Having a management flow sheet or checklist to make sure that you’re meeting all the policies that you’ve set up for yourselves and are managing patients – each patient – exactly how you would ideally manage them, is very, very helpful. Having a patient registry that allows you to look at your management of this group of patients can be very, very helpful. Many of the strategies that we have discussed can be implemented by other staff, and this can save valuable time for the prescribing clinician.

It’s also very helpful to have a list of referral and support resources including such things as pain treatment providers, mental health providers, addiction counselors, and others can be critically important.
MOD: In the ensuing months, Mary Williams 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. The provider decides to increase the ER/LA oxycodone from fifteen milligrams to twenty milligrams every twelve hours to reduce end of dose failure. In one week the provider’s nurse contacts her, confirms that this has been effective in improving pain relief and again, denies any sedation or other adverse effects. She is more active and able to concentrate on her work.
With all the monitoring and medication changes, what sort of documentation is required in the patient’s file?
SEDDON SAVAGE MD: Documentation of opioid therapy is particularly important. It needs to be comprehensive and it needs to be very thoughtful. We need to document both our management of the patient and the rationale for all our decision making. So we need to include the subjective reports that we’re getting from patients, from family members and from co-care providers. It’s important to document all the standard screening tests that we perform, laboratory tests, drug tests, the objective information that we’ve obtained, as well as our clinical and diagnostic impressions and our recommendations and the rationale for those recommendations.

It’s also important, of course, that we know federal and relevant state guidelines and regulations and that we work within those guidelines and regulations. And all the resources that we’ve discussed in these modules can be found at scopeofpain.org.

In terms of our discussion of how therapy is going, how the patient is doing, remember, document the six A’s: analgesia, activities and function, any adverse effects or side effects, any aberrant behaviors or concerns that are arising, the affect, mood and general wellbeing of the patient, as well as their adherence to the plan of care.
MOD: Could you summarize what we’ve discussed here today?

SEDDON SAVAGE MD: Certainly. So most importantly I think we need to remember that opioids are just one tool that we can elect to use when they’re indicated in a comprehensive and multimodal approach that includes self-care and a variety of synergistic treatments. If we do elect to use opioids in the care of patients with chronic pain, it’s important to employ universal precautions at the same time we individualize the application of these strategies. We should initiate opioid treatment as a trial or a test aimed at clear, functional goals and we can continue or discontinue the opioid therapy based on the patient’s response and on the clinical indications for continuation or discontinuation. It’s critical that we assess the benefits for the patient and the risks or harms that they’re experiencing and that we document these very clearly to justify our continuation or discontinuation of the treatment.
MOD: Mary Williams seemed to be doing well on her opioid therapy for the next eleven months. The provider is then surprised to find out that Miss Williams was seen in the emergency room of a local hospital, requesting an early refill of her oxycodone after running out early. The ER 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 her provider in one week.
At this point, Mary’s primary care provider must think about a number of things:

- How should Mary’s recent aberrant medication-taking behavior be addressed?
- Has Mary developed an addiction?
- Has she developed tolerance to the opioid?
- How should the provider accurately assess and manage this new worrisome behavior?
- How should the provider communicate about these issues with Mary at her next visit?
We’ll turn back to Doctor Alford now to discuss how to assess and manage aberrant medication taking behavior.
At the conclusion of this final section you will be better able to assess the differential diagnosis for aberrant medication taking behavior, assess lack of benefit, and/or increased risk or harm, and determine whether and how to continue, modify or discontinue opioid therapy.
This visit is an early follow-up after her ER visit where she requested an early refill of her oxycodone. She reports that over the past month her pain has worsened. She is concerned that her body has become used to her current dose. She’s upset that her husband has accused her of being addicted. Her work has been affected and she’s having trouble sleeping. She wants to increase her dose of oxycodone.

Doctor Alford, is this a problem with unrealistic expectations? Is she correct that she has developed tolerance to her oxycodone dose or is her husband correct that she has become addicted to oxycodone?
DANIEL ALFORD MD: Whenever a patient exhibits aberrant medication taking behaviors it’s always useful to readdress their expectations of the medications because if the patient is expecting that the opioids “eliminate their pain” they may think that more opioids will equal more pain relief. That will lead to unsanctioned dose escalation and/or continue to request for higher doses.

So first we need to start with reeducating our patients about realistic goals and potential opioid risks.
How do we monitor them for opioid misuse? Well there’s certainly questionnaires such as the Current Opioid Misuse Measure (or COMM) which is a self-administered seventeen item questionnaire that patients can complete in the waiting room, which predicts current opioid misuse. But there are other strategies. Ones that we’ve already talked about. Pill counts and urine drug testing and prescription drug monitoring program data.

But also it’s helpful to get a history from reliable family members. But remember that some family members may have secondary gain for giving inaccurate information. So we really need to know who the family member is and I think it’s helpful to have the family member come to the visit with the patient in order to talk about their concerns.
So, when patients exhibit aberrant medication-taking behaviors, there is a differential diagnosis that we should consider. I think it’s helpful to divide these behaviors into pain relief seeking or drug seeking. For pain relief seeking, is this disease progression? Has her neuropathy worsened or her spinal stenosis worsened or does she have poorly opioid response with pain? Or has she developed withdrawal mediated pain, opioid analgesic tolerance or opioid induced hyperalgesia? Or is it drug seeking? Has she developed an opioid use disorder or addiction? Or is she self-medicating some other psychiatric diagnosis? We know that opioids make people feel better. Is she self-medicating anxiety or depression with that opioid? Or is she actually selling the medication with criminal intent, that is, diversion? And I would argue, for some of the patients that we’re most worried about, it’s a combination of all of the above. For example, the patient with chronic pain with comorbid addiction taking some of the medication for pain and diverting some of the medication for income. So let’s talk a little bit more about some of these pain relief seeking and drug seeking behaviors.
As far as pain relief seeking let’s talk about opioid analgesic tolerance. This would be a right shift of the dose response curve. We know that analgesic tolerance has been demonstrated in animal models. We know that in human studies opioid doses can be stabilized over long periods of time. Therefore I suggest that we assume opioid analgesic tolerance is not common but that it may happen. Clinically if you increase the dose it should overcome the decreased analgesia due to tolerance.
What about pain relief seeking due to opioid induced hyperalgesia? Well this is a paradoxical enhanced pain sensitivity in patients on chronic opioid therapy. And the underlying pathophysiology is complex and really not clearly understood. The true incidence of opioid induced hyperalgesia is unknown. There are no official criteria or guidelines for diagnosing hyperalgesia and really, clinically, what we see is pain that is generalized, diffuse, ill-defined and not necessarily located at the source of the original pain.

With hyperalgesia increasing the dose may improve analgesia but only temporarily. And there are no studies looking at opioid taper and opioid induced hyperalgesia and there are some case studies showing improved analgesia with opioid rotation; that is, switching to a different opioid which we’ll talk more about.
What about on the drug seeking side, opioid use disorder? When I'd like to go to the DSM-V and make a diagnosis using those symptoms; however, despite the DSM-V now saying if someone’s prescribed opioids you cannot use tolerance or withdrawal as part of your diagnosis (which is an important new addition to DSM-V, improved over DSM-IV). But if you look at the other symptoms like using larger amounts or duration than intended, persistent desire to cut down, a great deal of time spent obtaining and using opioids. All these may apply to our patients with chronic pain on opioids without an addiction. So we need to be careful even applying the opioid use disorder criteria from the DSM-V when it applies to our patients with chronic pain on long term opioid therapy.
So we’re pretty much left with using a clinical syndrome presenting as the three C’s: loss of control, compulsive use and continued use despite harm. So what do I mean by loss of control? Well that is the person who keeps running out early or escalating their dose or showing up at the emergency room or calling the on call service or losing their prescription. Compulsive use. It’s a preoccupation with their opioid. They’re totally focused on getting more opioid and everything else that you recommend for pain management they want nothing to do with it. They just want more of the drug. And then continued use despite harm. Even though the person is sedated, slurring their words with no improvement in function they want more. They should actually want less. They should be telling you, this medication isn’t working. I want something different.

And really what we’re looking for is a pattern. So if the person loses control once, it is different than the person who’s losing control repeatedly. Although it also depends on the severity. It only takes one time for me to get called from the pharmacy that someone has altered the prescription for me to say that they have lost control and therefore cannot take this medication safely. Remember that addiction is not the same as physical dependence, which is the biological adaptation to being exposed to opioids. Whereas addiction is really the behavioral maladaptation.
Now there’s a spectrum of these aberrant behaviors and I have them classified here as yellow to red flags. And so moving from yellow to red I would say: request for increased opioid dose: well that could mean disease progression or it could mean that they’re addicted. So it’s really a yellow flag, not necessarily a red flag. Requests for a specific opioid by name, “brand name only”: well this could be the patient just telling you what worked in the past or it could be a patient who is selling their prescription and knows that brand name only carries a higher street value because it’s more recognizable. Non-adherence with other recommended therapies: well again it’s a yellow flag, not necessarily red flag but it’s something to be concerned about. Running out early; resistance to changed therapy despite adverse effects; deterioration of function at home and work are starting to get more into the orange to red flag zone. Certainly non-adherence with monitoring: that is the person is non-compliant with pill counts or urine drug testing. Multiple lost or stolen opioid prescriptions is now turning into a red flag, as well as illegal activities, forging scripts, selling opioid prescriptions. So again it depends on the circumstance of your individual patient, how well you know the patient and if there’s a pattern and the severity of these behaviors.
MOD: Doctor Alford, how would your clinical approach differ if you think Mary’s aberrant medication taking behavior is due to lack of benefit versus addiction, versus diversion? What are the next steps? Should she be referred to a pain or an addiction specialist?
### Lack or Loss of Benefit

**What are the next steps?**

- Reassess factors affecting pain
- Re-attempt to treat underlying disease and co-morbidities
- Consider...
  - adding or increasing non-pharmacologic treatment (e.g., acupuncture, CBT)
  - adding or increasing adjuvant medications for synergy
  - adding breakthrough medications
  - opioid rotation

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DANIEL ALFORD MD: Let’s start with lack or loss of benefit. What are the next steps? The first thing to do is to reassess the factors that are affecting the pain and then reattempt to treat any underlying disease and comorbidities. We should then consider adding or increasing non-pharmacological treatment such as acupuncture or cognitive behavioral therapy, or adding or increasing adjuvant medications for synergy or even adding breakthrough medications or opioid rotation and we’re going to talk more about those.
The first choice is really non-opioid therapy. And so gone are the days where we assumed just because somebody is on extended release/long acting opioids that they need an immediate relief short acting opioid for breakthrough pain. We should actually assume that they don’t need that and that we should try an NSAID or acetaminophen or some adjuvant medication for breakthrough medication as a first choice. However, if that doesn’t work you certainly could use an immediate release/short acting opioid, either the same molecule as the extended release/long acting opioid that they’re on or a different molecule. And then finally we could use one of the dual mechanism opioids, tapentadol or tramadol, for breakthrough medication.
In terms of considering opioid rotation, this is really a relatively new concept and that is switching to another opioid as a means of restoring analgesic efficacy or limiting adverse effects. It’s really based on large inter-individual variation in response to different opioids based on different variants of the Mu opioid receptor, based on surveys and anecdotal evidence and it really is promising but needs validation.
So if you decide to rotate to a different opioid you’re going to go to an opioid conversion table. So we need to talk about the limitations of these tables and the first is that these tables are derived from relative potency ratios using single dose analgesic studies in opioid naïve patients. They’re based on limited doses or ranges of doses and they really don’t reflect the clinical realities of chronic opioid administration. They’re also not reliable due to individual pharmacogenetic differences and that most tables do not adjust for incomplete cross tolerance.
So let’s see how an opioid rotation would work in Mary Williams’ case. So let’s say she’s rotated off extended release/long acting oxycodone and switched to extended release/long acting morphine. Well you could use a conversion table or you could use a website like the one listed here, that is an opioid converter. And you put in the oxycodone and you put in the dose. In this case, forty milligrams. You account for incomplete cross tolerance and they say the usual range is a twenty-five to seventy-five percent reduction and I generally pick fifty percent reduction. And then you select the opioid that you’re switching to, in this case morphine, and it gives you the conversion. So with a fifty percent reduction in conversion due to incomplete cross tolerance, her morphine dose would be thirty milligrams total. So that would be fifteen milligrams BID.
After you made changes if there’s still a continued lack of benefit, how do you manage that situation?
Well first of all remember that not all chronic pain is opioid responsive and that more opioid is not always better. In fact more opioid may increase risk of adverse effects.
So when should you refer to a pain specialist? Well certainly if you’re unsure of the pain diagnosis or you’re unsure if there are other treatment options that you haven’t thought about, or if you want a second opinion on opioid therapy for this individual patient. How do you find a pain specialist? Well some state medical association websites list pain specialists, but you could go to the national site of the American Academy of Pain Medicine website where they list pain specialists around the country. And you really need to know what are the services that your pain specialist offers. Now if you can’t find a pain specialist you can always get a second opinion from your colleague who could look with fresh eyes at this patient either during a visit or just review your chart and give you an opinion as to whether or not the opioids seem to be helping or not.

And the finally there is a free mentoring program available to you called the Providers Clinical Support System for Opioid Therapies and their website is listed here. It’s a free, federally funded program for individuals who would like mentoring and education around opioid prescribing.
How do you discuss continued lack of benefit with your patient? Well first stress how much you believe and empathize with the patient’s pain severity and the impact on their life. Express frustration that the medication didn’t work as you had hoped that it would. Focus on the patient’s strengths. Encourage therapies for coping with pain and show a commitment to continue caring for this patient and their pain even without opioids. And schedule close follow-ups during and after the taper.
Managing Opioid Risks and Harms

Now let’s move on to managing opioid risks and harms.
Always stay in the risk/benefit mindset. If you think the person has developed an addiction give them specific feedback as to why you think they’re developed an addiction. What are the behaviors that raise your concern for possible addiction? What have they done to make you think they’ve lost control or that they’re using it in a compulsive way or that they’re continuing to use the opioid despite harm? Be specific. Remember that patients may suffer from both chronic pain and addiction. Sometimes we just need to agree to disagree with the patient who doesn’t believe our diagnosis of addiction. We need to remember that in these cases the benefits no longer outweigh the risk and we can say statements such as, “I cannot responsibly continue to prescribe opioids as I feel it would cause you more harm than good.” Always offer a referral to addiction treatment.
When do you refer to an addiction specialist? When the patient is using illicit drugs or they’re experiencing problems with other prescription medication such as benzodiazepines prescribed by somebody else, or they’re abusing or are addicted to alcohol, or if the patient agrees that they have an opioid addiction and want help such as a referral to medication-assisted treatment which would be methadone, buprenorphine or naltrexone or if they have a dual trio diagnosis of pain addiction and psychiatric disease.
How do you find an addiction specialist? Well certainly you could go to a national website of the Substance Abuse and Mental Health Service Administration or SAMHSA which has a treatment locator and the website is listed here. Or you can go to your state resources usually put out by the Department of Public Health. They will list acute treatment services such as detoxes or residential treatment or a methadone maintenance treatment program; office-based opioid treatment with buprenorphine programs, and always AA and NA are freely and widely available and effective for our patients.

There is also a free mentoring program and educational program for those interested in learning more about medication assisted treatment; that would be methadone and buprenorphine and naltrexone. And that’s again through the Providers Clinical Support System, with the website listed here.
If you’re worried that the patient is actually diverting their opioids, discuss why you’re concerned about diversion. Maybe it’s non-adherence with pill counts or the urine drug test was negative for the prescribed opioid. And discuss your inability to continue to prescribe opioids if the opioid is being given or sold to others.
MOD: If tapering opioids is the best choice, what is the best way to go about it? How quickly can you taper someone off and are there different recommendations for tapering short acting versus long acting opioids? Is there ever a time when you would not need to taper a patient off opioids? Are you at risk of being accused of abandoning your patient if you decide to stop the opioid analgesics?
**Discontinuing Opioids**

- Do not have to prove addiction or diversion - only assess and reassess the risk-benefit ratio
- If patient is unable to take opioids safely or is nonadherent with monitoring then discontinuing opioids is appropriate even in setting of benefits
- Need to determine how urgent the discontinuation should be based on the severity of the risks and harms
- Document rationale for discontinuing opioids
- Determine if the opioid needs to be tapered due to physical dependence

### You are abandoning the opioid therapy
**NOT** the patient

**DANIEL ALFORD MD:** So how to discontinue opioids is one of the most frequently asked questions that I receive. The first thing is you do not need to prove that the person absolutely is addicted or that they’re diverting and frankly it’s sometimes hard to be a hundred percent certain when you’re only seeing the patient in your clinical office. But you really only need to assess and reassess the risk/benefit ratio. If based on your observations the patient is unable to take opioids safely or is not adherent with monitoring then discontinuing opioids is appropriate even in the setting of benefit.

Determining how urgent to discontinue the opioids is really based on the severity of the risks and harms. You should always document the rationale for discontinuing opioids and determine if the opioids even need to be tapered at all; if there’s physical dependence or not. Some patients on a few short acting opioids a day will not have physical dependence and therefore don’t need tapering. Or if the patient has a urine drug test that’s negative for the opioid you’re prescribing and they’re not in physical withdrawal then you don’t need to taper it.

Remember that when you do decide to discontinue opioids you are not abandoning the patient. You are abandoning the opioid therapy, and that’s a really important take home message here. Again, we’re going to continue caring for this patient. They may abandon you and fire you but you’re not abandoning them. You’re willing to continue treating them and treating their pain but just not with opioids.
So how do we taper immediate relief/short acting opioids? Well again, first decide whether you need to taper at all. Is there physical dependence? And then your tapering is really going to be based on the strength and number of tablets that the person is on and you’re going to decrease the strength of the tablets and decrease the number of tablets maybe on a weekly basis or every two weeks, depending on how quickly you want to do it.

For instance if the person is being tapered because of lack of benefit you can do it over months. If the person is being tapered because you’re worried about their safety, you’re going to be doing it over weeks. Remember to build up alternative pain treatment modalities at the exact same time that you’re tapering.
What about tapering extended release/long acting opioids? You’re pretty much limited by the size of these medications in terms of their dose and their formulation. But the general recommendation is to decrease by ten to twenty percent each week. So as I had mentioned, long acting pill formulations are really going to dictate the increments of dose decrease that are possible. Remember that individuals should not be breaking these pills in half because you disrupt the long acting formulation. The rate of decrease is going to be again determined by the circumstance of withdrawal, whether it’s an emergency taper or controlled taper over months. And sometimes you need to use the immediate release/short acting opioids to treat breakthrough symptoms. You can also use centrally-acting alpha-adrenergic agonists like clonidine or tizanidine to treat withdrawal. Now these are off label uses of these medications. Again, build up alternative pain treatment modalities at the same time of the taper.
So the risk/benefit framework that we’ve been talking about can be incredibly useful when you’re making decisions about continuing or discontinuing the opioids and they can be incredibly helpful when the patient responds to your plan to discontinue opioids with the following comments. “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.” “If you don’t give them to me, I will drink/use drugs/hurt myself.” “Can you just give me enough to find a new doc?” And your response should be, “I cannot continue to prescribe a medication that is not helping you (or is hurting you or both)” and then move on. But really I think when a patient continually asks despite that statement, you should ask them in their own words to explain why you’re planning to discontinue their opioids. If they say that it’s because you don’t believe that I have terrible pain then they really haven’t heard anything you’ve had to say about risks and benefits. If they say you’re discontinuing it because you don’t think they’re helping me, that’s fine. They understand at least and they can disagree with what you have to say but you’re going to continue with your plan of action. But again, as I had mentioned before, you’re not abandoning the patient. You’re abandoning the therapy because either it’s not working or it’s harming them.
Next Steps

MOD: Over the next eighteen months...
...Mary Williams’ 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 amitriptyline was added at night for her neuropathic pain. Mary also joined a monthly chronic pain support group. Her 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. Doctor Alford, could you summarize what we’ve learned in this section?
**Summary Points: Essential Content 2b**

- Aberrant medication taking behavior can signify pain-relief or drug seeking behaviors or a combo of both
- It is important to fully assess and then respond to aberrant behaviors
- Decisions to continue or discontinue opioids should be based on reassessment of the risks and benefits of the treatment

DANIEL ALFORD MD: The summary points for this section are that aberrant medication taking behaviors can signify pain relief or drug seeking behaviors or a combination of both. And it’s important to fully assess and respond to all aberrant medication taking behaviors. And finally 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.

MOD: Thank you for participating in The Scope of Pain online activity. Please complete the final posttest in an evaluation and download your certificate worth two AMA PRA category one credits or two nursing contact hours. Also be sure to visit our resources page where you’ll find more information, tools to help you implement what you’ve learned into your practice and videos that model challenging clinical interactions.