OVERVIEW

Peter D. Friedmann, MD, MPH, FASAM, FACP, and Jonna I. Gaberman, MD, provide their insights into the myriad challenges faced by clinicians in managing patients with opioid use disorder. The faculty discuss tools and factors to consider in the identification and assessment of persons with opioid use disorder. Treatment principles, including the importance of patient collaboration, comprehensive treatment, and harm reduction, are described that set the stage for detailed discussion of the roles, benefits, and limitations of medications approved for medication-assisted treatment. The faculty conclude by discussing the roles of primary care providers in the long-term management of patients with opioid use disorder.

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CONTENT AREAS

- Screening tools
- Assessment, including DSM-V criteria
- Treatment principles for opioid use disorder
- Efficacy/Safety of approved medications
- Roles of primary care providers

TABLE OF CONTENTS

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FACING OPIOID USE DISORDER

Connecting Primary Care to Patients Through Best Available Evidence

CE INFORMATION

Target Audience

This activity was developed for primary care providers, as well as addiction specialists, psychiatrists, nurse practitioners, physician assistants and other health care professionals who have an interest in opioid use disorder.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Implement screening tools to identify patients with opioid use disorder
- Describe the management principles, including goals, for opioid use disorder
- Initiate medication assisted therapy in patients diagnosed with opioid use disorder
- Employ a coordinated care model so as to decrease the risk of relapse for a patient with opioid use disorder

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Jonna Gaberman, MD

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FACING OPIOID USE DISORDER

Connecting Primary Care to Patients Through Best Available Evidence

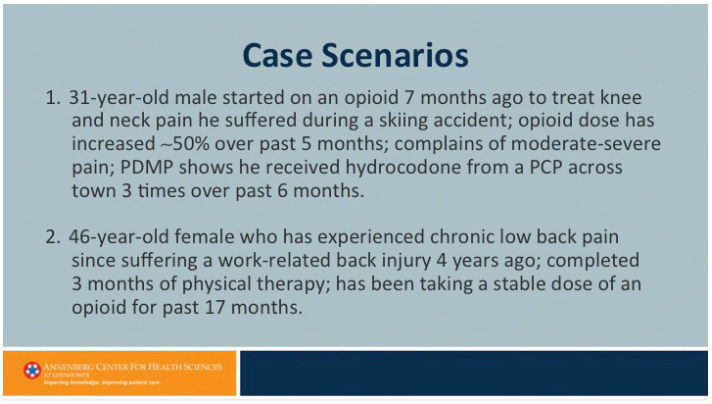
IDENTIFYING OPIOID USE DISORDER

I am Dr. Peter Friedmann, chief research officer and endowed chair for clinical research at Baystate Health and associate dean for research and professor of medicine at the University of Massachusetts-Baystate. I'm pleased to welcome you to "Office Perspectives: Facing Opioid Use Disorder. Connecting Primary Care Patients Through Best Available Evidence." My only faculty disclosure is that I have done some legal consulting for Endo Pharmaceuticals. Joining me in today's program is my colleague, Jonna Gaberman.

Dr. Gaberman: My name is Dr. Jonna Gaberman. I work at an academic community health center and practice outpatient internal medicine, along with the care of patients living with HIV infection and with substance use disorder. I do not have any conflicts of interest to disclose.

In Module 1, we will include discussion of different ways in which opioid use disorder can present. This is followed by a discussion of the risk factors of opioid use disorder and various validated screening tools that can be used to identify patients with opioid use disorder.

There are many ways in which persons with substance use disorder present. The cases in this slide speak to the connection between prescription opioids and the opioid

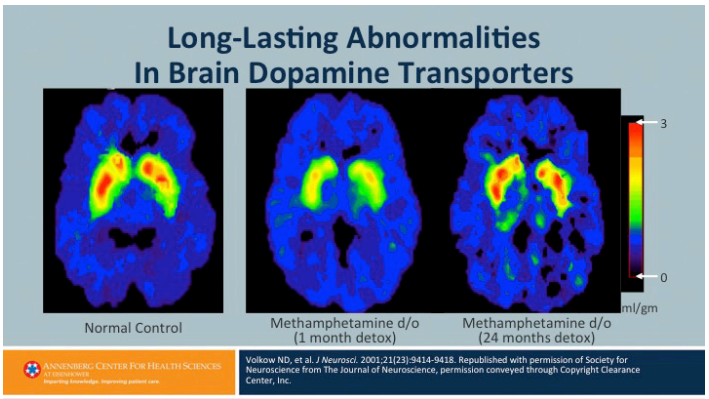


epidemic, contrasting concerning use with nonconcerning use. Case 1 raises red flags as this young man has pain lasting longer than expected after an injury. A pain medication dose which has been increasing despite a benign, nonprogressive condition, and evidence of opioid medicines from another physician by PMP, which is the Prescription Monitoring Program. This demonstrates a lack of control and increase in time spent pursuing pain medications.

Case 2 does not raise red flags and does not suggest substance use disorder. However, it is still important to note, over time, physiologic tolerance and dependence will develop. If the pain treatment is changed, the opioid must be carefully tapered off. There are adverse effects with long-term opioid use. So even with this patient's stable use, as prescribed, we may still want to pursue other classes of pain medication and other modalities, over time.

Dr. Friedmann, can you describe the physiology of substance use disorder, the criteria for diagnosis, and screening tools you recommend?

Dr. Friedmann: We'll be discussing opioid use disorder, which is one of the members of the family of substance use disorders. These disorders typically result from a process of behavioral conditioning in which, for example in our case, opioids activate the reward areas of the brain, typically the ventral tegmental area and the nucleus accumbens. This increased opioid activity leads to dopamine release. Dopamine is the main reward neurotransmitter. This increases in the nucleus accumbens and creates a good feeling. These good feelings are part of our very basic survival. These are the things that lead us to eat, to reproduce, and typically, the brain remembers these good feelings created by the dopamine and desires to repeat behaviors again to try to get these same good feelings. Over time, exposure to these opioids creates long-lasting abnormalities in brain dopamine transporters.

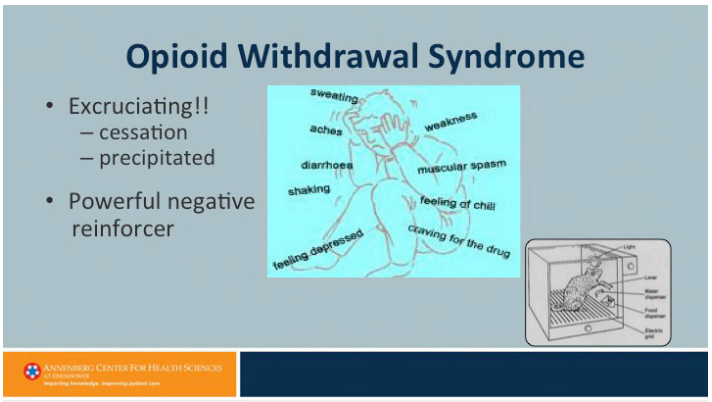


This slide happens to show the effects of methamphetamine, but the effects of opioids are very similar.[1] You see these parts of the brain that we were referring to previously. The ventral tegmental area and nucleus accumbens and, in a normal control, on the left, you see there is a lot of red on this PET scan indicating normal state of the brain dopamine transporters. What happens to people who've been exposed to chronic reinforcing compounds like methamphetamine or opioids is these transporters tend to be down-regulated,

which is what we see in the middle of the slide. After 1 month of detox you see there's not a lot of red, so not a lot of dopamine being created. This person is not feeling terribly well. What we see on the right is, after 24 months, those parts of the brain are starting to recover. So [it] really takes a very long time for people to come to the point where they start to feel normal. These long-lasting abnormalities in the reward system really are a major explanation for the remitting and relapsing nature of the substance use disorder syndrome.

The other part of the syndrome, which is unique in many ways to opioids, is the opioid withdrawal syndrome. If we think of the reward as being positive reinforcement, the way I like to talk about it is if you think of a rat that has an IV in its tail, and you train it to hit a lever and it gets the opioid or whatever the reinforcing compound is, it will continue to hit the lever until it dies. What withdrawal is not, [is] a positive reinforcer, but it's what's called a negative reinforcer.

At the bottom of this slide, this rat is in a cage and it's standing on an electrified grid, and if I turn on the electrified grid, I know it's very cruel, but they do studies like this, and



we drop the rat in it, it will sort of dance around like it has hot foot until it, by accident, hits the lever and then [the] electricity turns off. Then the electricity turns on again and it learns, over time, if I hit the lever that feeling of pain will go away. It's very different from punishment, in which a behavior creates an aversive [reaction].

In opioid use disorder, the withdrawal syndrome is a very prominent feature. It's excruciating! It's seen when people stop using opioids or if we give them . . . Or it's precipitated by giving them naloxone, which is Narcan, the reversal agent. But the way to think about withdrawal, and this is in the upper right part of the slide, is it really is, if you can imagine for a moment the very worst flu that you've ever had, upper respiratory infection. So you're achy, you're sweating, you're feeling terrible, you feel depressed. Then you combine that with the worst lower GI infection you've ever had. So, you're having diarrhea and stomach cramps and you're sort of curled up in a ball just like the fellow in this drawing. And you have craving for the drug and you have the knowledge in the back of your mind that if I just take a little bit of opioid, just a little bit, this misery will all go away very quickly.

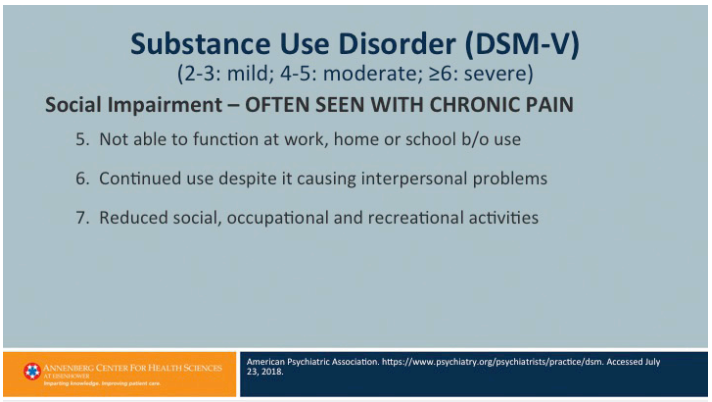
That is a very powerful pull for folks to go back to using. Our patients who have this disorder spend much of their lives just trying to feel normal. Over time, people stop getting the rewarding effects and the high of it, and really they're just trying to avoid withdrawal. Often that's the time when they come and seek treatment.

These neurobehavioral manifestations create what DSM-V calls the substance use disorder syndrome.[2] There are 11

features to the substance use disorder syndrome and the severity of one's disorder is based on a count. Two to 3 are mild, 4 to 5 are moderate, greater than 6 are severe. It's often difficult to think about all 11 categories so I often divide them into 4 parts.

The first part being impaired control, which refers to requiring larger amounts or using for longer than the person

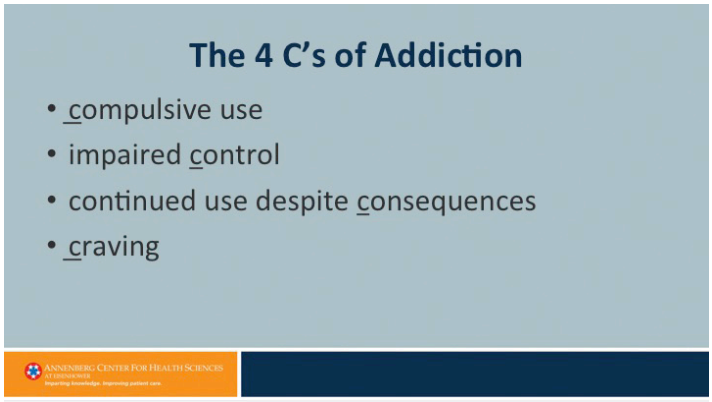
intended.[2] The second is about their desire to cut down, but inability to do so or, so to speak, their inability to control their use. Using a lot of time to obtain, use, or recover, and craving.



The next feature is social impairment.[2] Now, social impairment refers to how they function at work, home, or school. They continue to use despite having had problems in those areas, in interpersonal problems, and they reduce their social, occupational, or recreational activities and basically drug use becomes the only thing that they engage in.

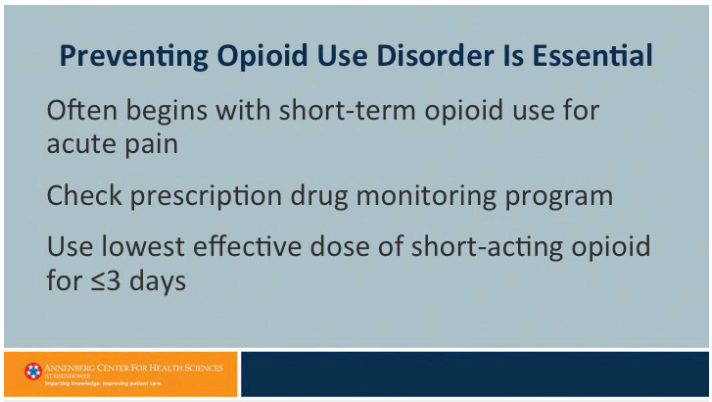
Risky use is using in dangerous circumstances, continued use despite having harms, particularly after overdose we see folks continue to use, and finally, the physiologic manifestations of tolerance and withdrawal.[2] Tolerance is requiring more to get the same effect or getting less effect with the same amount. With the withdrawal syndrome we talked about, and these physiologic manifestations, though they're important in the syndrome, I encourage you in making the diagnosis for folks on chronic opioids, sort of down play their significance. Folks on chronic opioids can manifest these physiologic manifestations.

Dr. Gaberman: I completely agree, Dr. Friedmann. Patients that are safely using opioids to control severe daily pain will often have these symptoms you describe because of dependence that develops physiologically. I think when we're trying to diagnose substance use disorder, opioid use disorder specifically, we really need to pay attention to the 4 "C's" which is compulsive use, impaired control, continued use despite adverse consequences, and ongoing cravings.

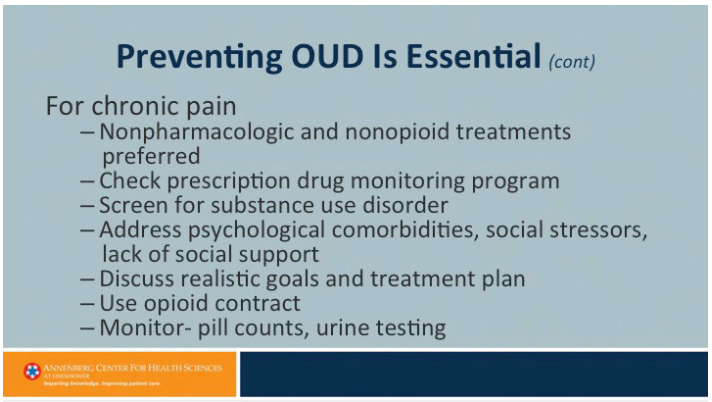


Dr. Friedmann: Yes, it's those manifestations of impaired control, sort of the compulsive quality of it, that really is what distinguishes it from legitimate opioid use for pain.

Dr. Gaberman: As primary care providers, we are front-line [in] evaluating and treating pain, especially chronic pain, and we cannot refrain from this treatment. However, being very cautious with opioid prescriptions is essential. Prior to writing an opioid prescription for acute or chronic pain, check the Prescription Drug Monitoring Program or PDMP, looking for evidence of uncontrolled use. With severe, acute pain, requiring opioid pain medication, try to use the lowest effective dose of short-acting medication and limit the supply, when possible, to 3 days. Most acute pain is resolved within that time frame.



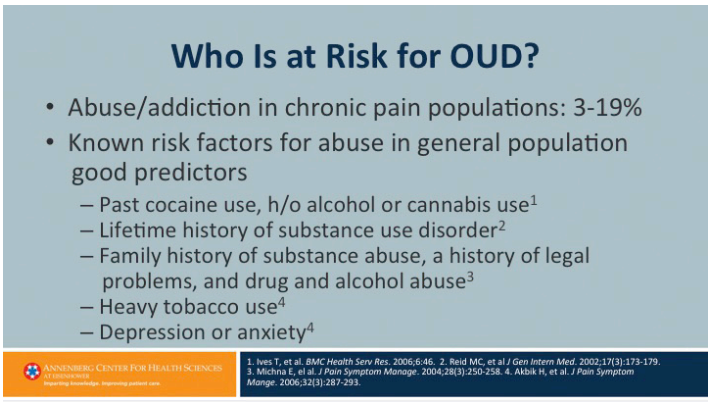
With chronic pain, first try nonpharmacologic and nonopioid treatments. These are preferred, given the risk of tolerance, dependence, and addiction with long-term opioid analgesic use, as well as other risks which I previously mentioned



ranging from opioid-induced hyperalgesia to overdose. Check the PDMP and screen for a history of substance use disorder. Address psychological comorbidities, social stressors, and lack of social support. Finally, it's very important to discuss realistic goals and create a treatment plan which includes discontinuation of the opioid pain medication if there's no improvement in function. Use that pain medication agreement which specifies for pill counts and urine toxicology screening.

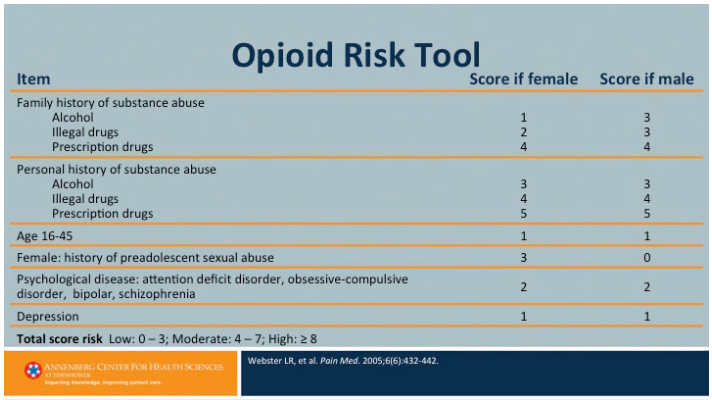
WHO IS AT RISK FOR OPIOID USE DISORDER

Dr. Friedmann: Who is at risk for opioid use disorder? This is an important thing to consider whenever you are thinking about initiating opioids for a patient with pain or another condition for which it's indicated. The literature suggests that somewhere between 3% and 19% of folks in chronic



pain populations will have abuse or addiction. The known risk factors are typically the same ones we see in the general population.[3] So those who have past substance use,[4] either current or lifetime history. Those with a strong family history of substance use disorder, legal problems.[5] Interestingly, heavy tobacco use is often a clue, and those that have psychiatric comorbidities, like depression or anxiety, are at a higher risk for developing these problems.[6]

To think of this in a formal sense, there are risk tools that are available. This is an example of one, the opioid risk tool, which gives a score.[7] So, you get points if you have a family



history of alcohol, illegal drug or prescription drug misuse, additional points if you have a personal history of those, if you are of younger age, women with a history of preadolescent sexual abuse, and those that have psychological disease, typically attention deficit hyperactivity disorder, obsessive-compulsive disorder, bipolar, schizophrenia, then depression. You get a score, and this sometimes can be helpful in determining who is at risk and who you need to watch closely. Again, it's often a relative contraindication. If somebody truly has pain and requires opioids for its management, this will sort of go into your calculus of risk and benefit. Like everything else in medicine, whether or not you start an opioid is a function of what you think the potential benefit will be for the person in terms of function vs what the risk is. Hopefully these tools, and thinking about the evaluation of their risk before coming into problems with addiction, that will help you think about the risks.

In evaluating folks for their risk of substance use disorder or their current status you'll need to do screening. Often, and I often think of this as case finding because typically these are folks that are coming in for a pain condition and are looking for opioid treatment and you're going to want to do an evaluation to understand what the risk part of the equation is. As you might imagine, people can be very challenged in doing these kinds of interviews. The way I find it most useful to do this is to ask permission, you know, "Do you mind if I ask you some personal questions about your substance use?" Try to avoid stigmatizing language.

FACING OPIOID USE DISORDER

Connecting Primary Care to Patients Through Best Available Evidence

Approach to Screening

- Ask permission
- Avoid stigmatizing language
- Use nonjudgmental approach
- Separate screening from feedback
- Embed screening questions in larger health assessment
- Probe about ranges
- Thank the patient

Typically, we want to use person first language. We'll talk more about that a little later in the presentation.

We try to avoid calling people addicts or thinking of them as clean or dirty. We really want to try to use a more medical language in approaching these disorders. You want to be nonjudgmental. It's very important to separate your screening from feedback. So if you're asking somebody about their use and they ask you a question like, "Oh, is that too much?" Or, "Is that bad?" It's really important to keep your counsel until the end, at such a time that you're going to want to give them specific advice.

Embedding the questions in a larger health assessment is useful. Probing about ranges, so if somebody says, "I use 2 to 3," it's useful to say, "Do you ever use 3 to 4?" Because people do tend to underreport their use. Then finally, thank the patient—that you understand that this can be challenging to talk about and you appreciate their honesty.

A number of tools have been validated. Many of them are long, and not very practical for a primary care or other medical setting, but some of the newer ones, the single item questions, are very useful. For illicit or prescription medication this one has been validated.[8] How many times in the past year have you used illegal drugs or prescription medication for nonmedical reasons? A positive screen is any answer greater than zero. Remember, it's a screen. It doesn't necessarily mean they have a substance use disorder, but it is an indication you need to do more assessment to understand that.

"Single Question Screen"

"How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" *(+ answer: > 0)*

Smith PC, et al. *Arch Intern Med.* 2010; 170(13):1155-1160.

The National Institute on Drug Abuse has created a modification of the single item screen. So this the NIDA-modified ASSIST.[9] The ASSIST is a longer screening instrument that they have modified to a shortened version. This is the quick screen on this slide. Ask, "In the past year how often have you used alcohol, tobacco, drugs?" So it asks for the different categories of substance use. Again, anything more than "never" is a positive screen.

NIDA-Modified ASSIST

NIDA *Quick Screen* Question: In the past year, how often have you used the following?	Never	Once or Twice	Monthly	Weekly	Daily or Almost Daily
Alcohol • For men, 5 or more drinks a day • For women, 4 or more drinks a day					
Tobacco Products					
Prescription Drugs for Non-Medical Reasons					
Illegal Drugs					

National Institute on Drug Abuse. https://www.drugabuse.gov/sites/default/files/pdf/nmassist.pdf. Accessed June 25, 2018.

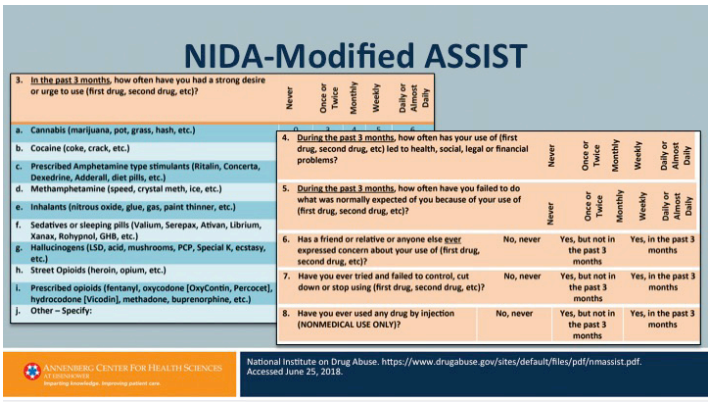
NIDA-Modified ASSIST

Question 1 of 8, NIDA-Modified ASSIST: In your *LIFETIME*, which of the following substances have you ever used? *Note for Physicians: For prescription medications, please report nonmedical use only.*	Yes	No
a. Cannabis (marijuana, pot, grass, hash, etc.)		
b. Cocaine (coke, crack, etc.)		
c. Prescription stimulants (Ritalin, Concerta, Dexedrine, Adderall, diet pills, etc.)		
d. Methamphetamine (speed, crystal meth, ice, etc.)		
e. Inhalants (nitrous oxide, glue, gas, paint thinner, etc.)		
f. Sedatives or sleeping pills (Valium, Serepax, Ativan, Xanax, Librium,Rohypnol, GHB, etc.)		
g. Hallucinogens (LSD, acid, mushrooms, PCP, Special K, ecstasy, etc.)		
h. Street opioids (heroin, opium, etc.)		
i. Prescription opioids (fentanyl, oxycodone [OxyContin, Percocet], hydrocodone [Vicodin], methadone, buprenorphine, etc.)		
j. Other – specify:		

Question 2 of 8, NIDA-Modified ASSIST: In the past three months, how often have you used the substances you mentioned (first drug, second drug, etc)?	Never	Once or Twice	Monthly	Weekly	Daily or Almost Daily
• Cannabis (marijuana, pot, grass, hash, etc.)	0	2	3	4	6
• Cocaine (coke, crack, etc.)	0	2	3	4	6
• Prescription stimulants (Ritalin, Concerta, Dexedrine, Adderall, diet pills, etc.)	0	2	3	4	6
• Methamphetamine (speed, crystal meth, ice, etc.)	0	2	3	4	6
• Inhalants (nitrous oxide, glue, gas, paint thinner, etc.)	0	2	3	4	6
• Sedatives or sleeping pills (Valium, Serepax, Ativan, Librium, Xanax, Rohypnol, GHB, etc.)	0	2	3	4	6
• Hallucinogens (LSD, acid, mushrooms, PCP, Special K, ecstasy, etc.)	0	2	3	4	6
• Street opioids (heroin, opium, etc.)	0	2	3	4	6
• Prescription opioids (fentanyl, oxycodone [OxyContin, Percocet], hydrocodone [Vicodin], methadone, buprenorphine, etc.)	0	2	3	4	6
• Other – Specify:	0	2	3	4	6

National Institute on Drug Abuse. https://www.drugabuse.gov/sites/default/files/pdf/nmassist.pdf. Accessed June 25, 2018.

The ASSIST goes on to look at different categories of drugs from cannabis to prescription opioids and everything in between.[9] It looks at both lifetime use and last 3-month use. Then, this other part to look at, urges and cravings in the last 3 months, whether the person has had health, social, legal or financial consequences, again, trying to get at some of these DSM categories.[9] Whether they've had some issues around role functioning, whether there's any family concern, attempts to control or cut down. Again, trying to get at that issue of loss of control. Finally, a question about injection.



Injection is often, for me, a sign that someone has developed tolerance. Typically, you go from snorting or smoking to a more vial available form, which would be injection. As you develop tolerance and need more and more drug delivered to the receptor, more quickly, in order to get the effect.

Dr. Gaberman: Urine toxicology tests are an added tool when screening for substance use disorder. The majority of time, persons using unprescribed substances will not exhibit aberrant behavior. When ordering a urine tox screen I try to use that time to open up discussion and ask patients what we will see. Our opioid pain medication agreement allows for random urine toxicology screening, as well as routine screening at specified time intervals, based on the patient's stability.

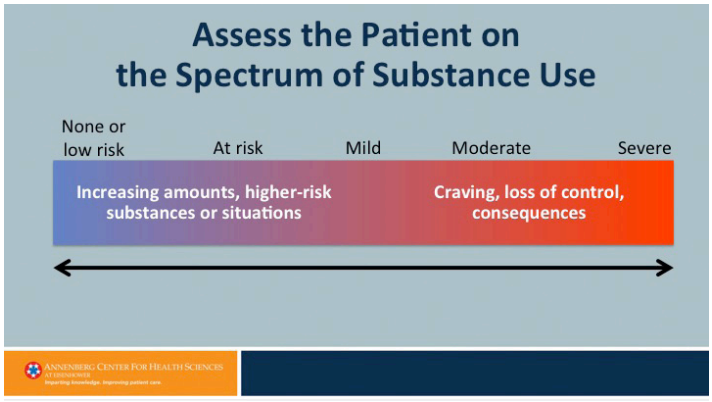
We always expect the prescribed pain medication will be present on the toxicology screen. It is important to note that fentanyl and oxycodone will not show up on a routine opiate urine tox screen and must be specifically ordered. Clonazepam is variable with benzodiazepine urine tox screening, so I recommend checking with your lab.

Dr. Friedmann: In summary, opioid use disorder is a neurobehavioral disorder characterized by loss of control in use, despite consequences. This syndrome is not the same as physiologic dependence, which can be seen in folks who are using opioids appropriately. Commonly, opioid use disorder is sparked with opioid treatment for a pain condition and sometimes that treatment can blossom into opioid use disorder. It's important for you to assess the person's risk for developing that syndrome and using validated tools to screen them for that risk.

PATIENT ASSESSMENT

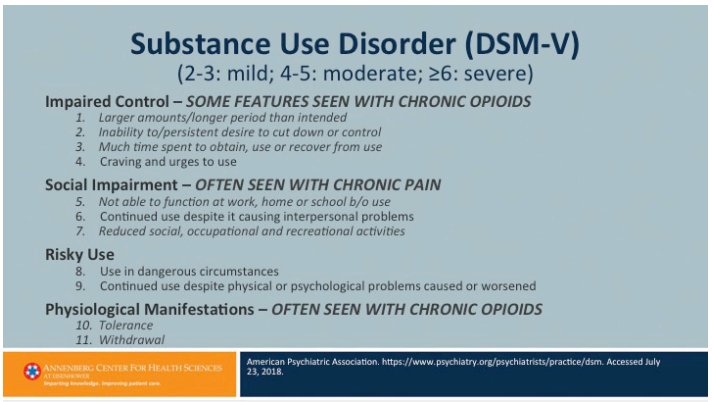
Dr. Friedmann: In Module 2, we discuss the steps to take to assess for the presence of opioid use disorder in a patient who screens positive. Topics will include the DSM-V, the 4 C's, characteristics of addiction, and assessing readiness for treatment.

As we alluded to in the previous module, substance use disorder exists now on a spectrum. This is very different than the old DSM thinking about addiction as being either abuse or dependence. Rather than these discrete categories, this really reflects our current understanding of substance use

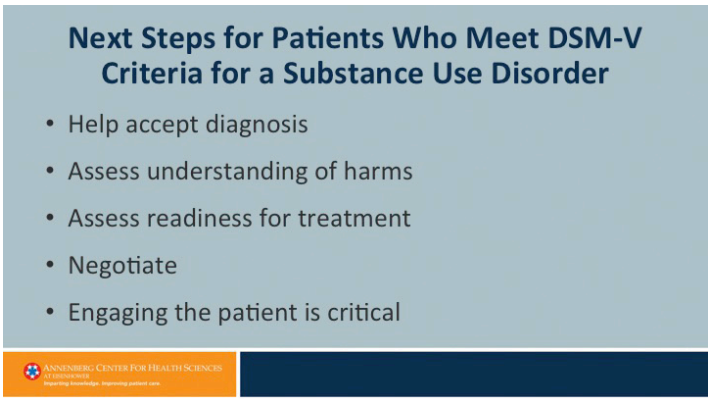


that it's a spectrum from low-risk to severe, moving from left to right. Increasing amounts and higher risk substances to the development of actual craving, loss of control, and consequences.

For the person who's screened positive, understanding where they fit on the spectrum is an important task for the clinician. Substance use disorder in DSM-V, as we previously discussed, there are 11 criteria and you would categorize in an assessment their impaired control, social impairment, risk of use, and physiologic manifestations. These 11 dimensions and sort of accounts from mild, moderate, severe. Typically, those who have moderate to severe are folks that we strongly consider for medication for opioid use disorder.

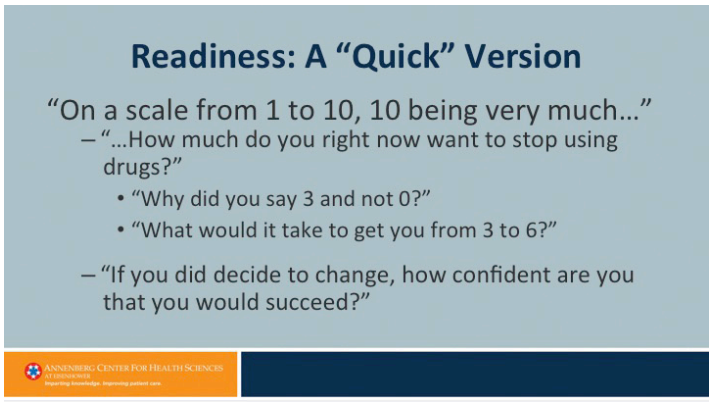


If the person meets DSM-V criteria, it's often a challenge to help them accept the diagnosis that they've had a pain condition and now I'm concerned that they have another condition, opiate use disorder. It's important that you assess their understandings of what the harms are they've experienced, their readiness for treatment. You're going to enter a process of negotiating with them about what kinds of treatment folks will accept. The thing to remember is that engagement, working with a person over time, really is one of the most important things that you can do for these patients.



Sometimes folks won't meet the full criteria, but if you think the opioid use is problematic it would be useful for you to increase the structure of treatment, either by seeing them more often, giving them shorter prescriptions, increasing the amount of monitoring, urine testing, etc, augmenting the nonopioid modalities and support in terms of their pain management, and considering whether or not a taper is appropriate, particularly if you're not seeing a lot of functional benefit from the medication. If you're not seeing benefit, and they're continuing to display risky behavior, that would be an indication that maybe this is not an appropriate medication for them.

Readiness for treatment is important to assess. A quick way to do this is to ask someone on a scale from 1 to 10, 10 being very much, "How much do you, right now, want

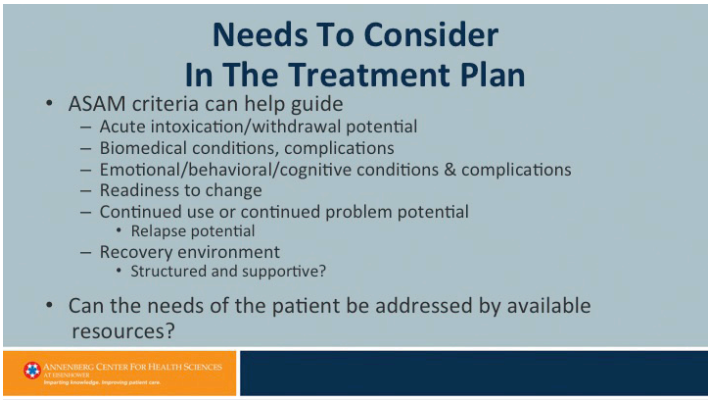


to stop using?" If the person, for example, 10 being very much and 1 being zero, the person says 3, for example, the question we naturally want to ask is, "Why are you not a 10?" But that's not the question that should be asked! The question that should be asked is, "Why are you not a zero?" In other words, "Why are you not totally unready?" Because in some ways they said 3 because they recognize that there may be something about it. If you can get them to articulate what it is they're concerned about that made them a 3, that's what's called a self-motivating statement and can help move them along in terms of their readiness.

Another question you could ask is, "What would it take to get you from a 3 to a 6?" Again, a 6 is not a 10, but to be a little more ready and what kinds of things we can do. You can do similar things around confidence, particularly for those who've tried to quit before but haven't been successful. They often lack confidence and a lot of your work as a clinician is going to be a coach for them, to inspire hope, to let them know that they can do this and to sort of work with them to help move them forward.

There are other needs that you're going to want to consider in your assessment as you're thinking about what treatment plan is going to be appropriate. The American Society of Addiction Medicine, or ASAM, has a series of criteria formerly called the "Patient Placement Criteria" that can help guide thinking about the treatment plan. They define 6 areas that you want to think about in defining what kinds of services a person might need and what kind of setting they might need in order to enter recovery.

What is their potential for acute intoxication or withdrawal? If they're acutely intoxicated, you're going to want to stabilize. If they're early on and they're going to potentially

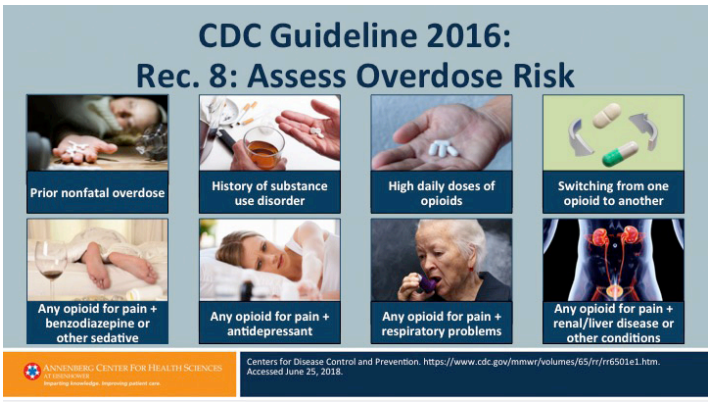


develop withdrawal you'll want to manage those symptoms, put them in a setting where those symptoms will be able to be managed. Similarly, if they have biomedical conditions or complications from their use, those will need to be managed. Those both are a risk to their health, but they also can be things that will trigger relapse, particularly pain or other kinds of symptoms. Do they have emotional behavioral cognitive conditions or complications? This sort of speaks to their mental health state. Very common for there to be co-occurrence of mental health conditions and substance use disorders. Often, those emotional issues can be triggers for use. When someone feels sad they use, when they feel depressed they use. You, again, will want to address those issues either yourself or referring them to an appropriate provider or setting that can address those issues as part of their treatment plan.

Readiness to change, we sort of talked about. You want to assess what their readiness is and how often you're going to see them and what kind of structure they need in their treatment that will determine their continued use or continued problem potential. Again, have they had multiple relapses in the past? Are they hopeful and confident about their ability to do it this time? Depending on what you've assessed in that area, you may or may not need a residential or a more structured setting for them. Finally, the domain that I often turn to as being the most important to think about, if you were to just pick one for me, it's recovery environment. Recovery environment has 2 dimensions; it's structure and it's support. Structure sort of refers to the idea that do they have something to do every day in a structured way? That's sort of the addiction medicine version of, "Idle hands are the devil's workshop," which is to say that if the person doesn't have structure, doesn't have something to do every day they're going to get into mischief. Employment is really, really important and that's probably the best thing that they can do, but it's often challenging for our patients, so we often substitute meetings or treatment as something stable for them to do that's highly scheduled.

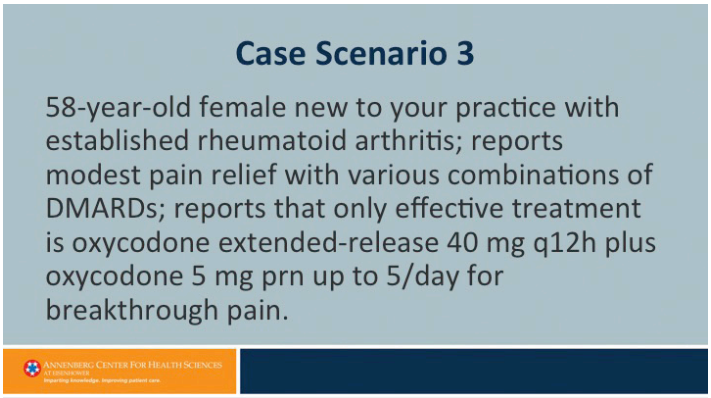
The supportive dimension refers to the kind of environment they live in. Are there other people using drugs? Are their family and friends supportive of them entering recovery or they don't have any people in their social network who don't use? Typically, [for] those folks, again, recovery groups like AA can be useful as a place for those folks to go to meet people who are struggling with the same issues that they are and to try to meet folks who are on their way to sobriety as opposed to continuing to use.

The other question you need to ask yourself is whether the needs of this patient can be met by the resources that you have, and if not, then you need to look around your community for resources that will be able to help this patient.



The CDC guideline recommends assessing overdose risk.[10] This is more important than ever now, given the fentanyl that Dr. Gaberman talked about, out there. Very high overdose risk. People on their first relapse can die. We want to be sure they don't, so folks who have prior overdoses, all our patients with substance use disorder, those using high daily doses of prescribed opioids, those who are switching if you're doing location. Any prescription benzo or sedatives or antidepressants, those with respiratory issues, or anything that can affect metabolism. All of those folks you really need to assess their overdose risk. We're going to talk about that a little bit more in one of the future modules. Dr. Gaberman has brought a case that would be good for us to talk a little bit about.

Dr. Gaberman: This case is about a patient newly presenting to you. Continuing this patient on opioid analgesics which were previously prescribed requires investigation to verify doses and safe use. Abruptly stopping the pain medications in the new patient would throw that patient into withdrawal and should not be done, but before writing a script, it is essential to check the prescription drug monitoring program. There are times when the patient's old prescriptions do not show up on this, possibly because she or he is coming from



another state, but then it's important to contact the patient's old prescriber or pharmacy to verify the dosing.

The patient's high dose of oxycodone in this case raises a red flag as it seems very high for a chronic condition, that even when severe, can often be brought under control with biologics; however, the limited information we possess in this description does not suggest a substance use disorder. To investigate this further we would need to review old records of RA treatment and disease control as well as prior pain medications tried, doses used, and we would also need to speak with this patient about psychological comorbidities, social stressors, day-to-day functioning, and send a urine toxicology screen.

Signs of impaired control, social impairment and risky use are really necessary before diagnosing substance use disorder. Even without a diagnosis of substance use disorder in this case, after getting to know the patient better, I would recommend planning a slow taper down to a safer daily dose. Dr. Friedmann just reviewed the CDC's recommendations for preventing overdose with opioid use.

This patient's total daily use of oxycodone, 105 mg, is equivalent to 160 mg of morphine using a factor of 1.5 to make this conversion from oxycodone to morphine. A morphine equivalent daily dose of 50 mg and especially over 90 mg poses a marked increased risk for overdose. Indications to taper the opioid dose here would be lack of a significant improvement in pain and function over time on this dose and a daily dose over 50 mg morphine equivalent, but remember that tapering plans should be individualized and discussed with a patient, and minimize symptoms of withdrawal while maximizing nonpharmacologic therapy and nonopioid medication.

Tapering 10% of their original dose per week can be done, but patients on chronic opioids usually need to go slower, and they will often find a decrease of 10% per month much easier. Tapering should be done in coordination with the patient's rheumatologist in this case, and with an appropriate psychosocial support. You will often find that tapering does lead to improved function without worsening pain and you may be surprised that sometimes patients even experience less pain over time.

Dr. Friedmann: Jonna, We have patients who come and ask for only hydromorphone (Dilaudid) works for me, or only this or only that. Do you find that to be a red flag in working with folks like this?

Dr. Gaberman: I do, but I also try to step back and be careful and respect what the patient is saying and take it at face value but know that I need to do further investigation. That's why I mention it's very important to not only check the PDMP but to really try hard, when a patient is on such a high dose of opioids, to speak to the prior prescriber, to find out from the pharmacy what the pattern of use was.

Dr. Friedmann: In summary, if the person screens positive, you're going to need to assess for substance use disorder, for example, opioid use disorder. As part of that, you'll want to understand their readiness for treatment, their severity and treatment needs, particularly in other domains that can affect the course of their recovery and you'll need to make a decision about whether you can treat those needs yourself or whether you're going to need to make a referral for appropriate services.

As Dr. Gaberman and I have both emphasized, it's really important in this day and age that we assess overdose risk as we'll talk about in future modules, and that we address that risk.

TREATMENT PRINCIPLES

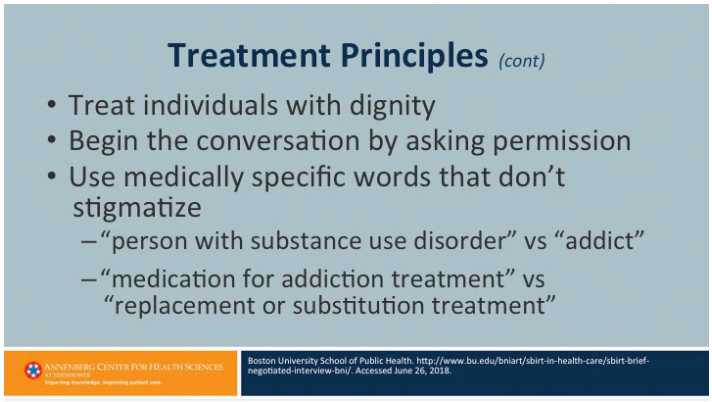
Dr. Gaberman: Module 3 includes discussion of the management principles of opioid use disorder. Also discussed are suggestions for talking with the patient with an opioid use disorder and we talk about the importance of harm reduction as well as the continued treatment of the pain disorder.

Opioid use disorder is a chronic illness. As we spoke about in the earlier modules, primary prevention involves careful prescribing of pain medications, and secondary prevention involves intervening when there appears to be the beginning of risky behavior, as Dr. Friedmann just described.

In this module, we will begin to discuss tertiary prevention of opioid use disorder using medication addiction treatment, or what we call MAT. MAT helps patients interrupt use, enter into remission, and return to remission when they relapse. With opioid use disorder, MAT has been shown over decades to be lifesaving. It helps patients prevent an infectious complication and death from overdose. This is not the case with abstinence or nonmedication treatment, including short-term detox or rehab. These have never been shown effective in treating opioid use disorder long term, and may actually increase the likelihood of overdose death due to the elimination of tolerance.

In interrupting intravenous opioid use, MAT reduces the risk of numerous complications including endocarditis, cellulitis, osteomyelitis, scarring of the veins, HIV infection, and viral hepatitis. And in all cases of opioid use, it reduces the risk of overdose death.

A harm reduction approach says to a patient I care enough to meet you where you're at, to reduce your risk for infection and overdose.[11] Harm reduction involves implementing strategies to reduce the negative consequences of drug use and acknowledging that there's a continuum of drug-using behaviors and some are safer than others. This includes utilizing nasal naloxone to prevent overdose and also providing information on needle exchange and teaching safe needle use to prevent infection for those who are not fully in remission or who have relapsed.



A harm reduction approach treats patients with dignity.[12] Conversations include asking permission first. People feel respected when asked permission and are more likely to be open. The approach also involves using nonstigmatizing language, as Dr. Friedmann beautifully described in the earlier module.

Dr. Friedmann: When we talk about conveying the dignity of the patient, that is something that asking permission does. It conveys respect for them, for their autonomy. It empowers them. They do have the ability to say, "No, I don't really want to talk about this." I have never in my 25 plus years being in this field, I have never had a patient say no. What this does, in combination with using nonstigmatizing approaches, particularly language, [is] that [it] develops [a] therapeutic alliance. You are on the patient's side, you are working together towards whatever the goal is. And numerous studies have shown that having a strong therapeutic alliance with the patient really is the most important factor in helping them achieve behavioral change.

Dr. Gaberman: I completely agree. Medications are optimally paired also with counseling and social support to address co-occurring mental health concerns and social problems.[12] This is important because substance use disorder is highly associated with social exclusion, isolation, joblessness, and housing insecurity. So again, just reinforcing why it's so important to treat patients with respect and dignity.

I want to add a brief example of a case where [the] harm reduction model really hit home for me. When we first began our buprenorphine (Suboxone) program I had a patient who sniffed heroin and smoked crack cocaine. She was dependent on both and she did well on our buprenorphine

FACING OPIOID USE DISORDER

Connecting Primary Care to Patients Through Best Available Evidence

Treatment Principles *(cont)*

- Comprehensive treatment goes beyond medication addiction treatment to include psychosocial support
  - Important due to high occurrence of social exclusion, isolation, joblessness, housing insecurity

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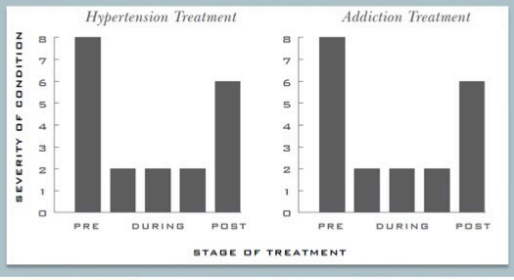
Boston University School of Public Health. http://www.bu.edu/bniart/sbirt-in-health-care/sbirt-brief-negotiated-interview-bni/. Accessed June 26, 2018.

(Suboxone) program and entered into remission for her opioid use disorder, though she continued to use cocaine. After about a year of intensifying support through counseling and an intensive outpatient program, we discharged her from our buprenorphine (Suboxone) program and let her know she was welcome to come back when she was ready to be fully sober or substance-free. But over the ensuing 6 months off of medication addiction treatment, she relapsed with opioids, but now had moved from sniffing heroin to IV drug use with mixed heroin and cocaine. Her risk of death markedly increased. Fortunately, she's now back in our program. She continues to smoke crack cocaine and we are trying to address that, and she's working to reenter remission for opioid use disorder, but fortunately, also she's no longer using needles. Through a harm reduction lens, I now see treating her various forms of substance use as no different from treating hypertension and diabetes, for example. I would never think about stopping antihyperglycemics on a patient drinking a liter of Coca-Cola a day, who doesn't have control of their sugars, nor should I have stopped buprenorphine (Suboxone) in someone in full remission from opioid use disorder, even though they continued to use cocaine.

This slide, with a graph showing control of the chronic condition and stage of treatment, beautifully illustrates

Goals Are Those for a Chronic Disorder



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NIDA. Principles of Drug Addiction Treatment. Published 2012. https://www.drugabuse.gov/sites/default/files/podat_1.pdf. Accessed July 12, 2018.

the case that I just relayed to you. It just shows that while somebody is on treatment, their chronic condition is controlled.[9] When they go off of the treatment they lose control of this condition, whether it be hypertension, whether it be diabetes or medication addiction treatment.

Treatment Principles *(cont)*

- Nonjudgmental, appreciative inquiry
- Set expectations upfront
  - Written treatment agreement for medication and monitoring
- Shared decision-making
- Contingency management model

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In terms of management principles, it's so important to use a nonjudgmental approach. Make sure to set up expectations up front with a written treatment agreement that allows for pill or film counts and urine toxicology screenings. Make sure to emphasize progress and used shared problem-solving. Use a contingency management model to respond to a patient doing well with the longer duration prescriptions. On the other hand, respond to a patient with relapse substance use by shortening the interval of the prescription from 14 days to 7 days, for example. Add support with counseling and even a recovery coach, if available. With continued substance use, discuss with the patient intensifying care, which could include an intensive outpatient program, for example.

Harm Reduction Strategies for Individual and Community

- Bystander prevention and family training
- Safe needle and syringe use and disposal
- Safe medication storage
- Screen/Vaccinate for hepatitis B
- Part of holistic patient management

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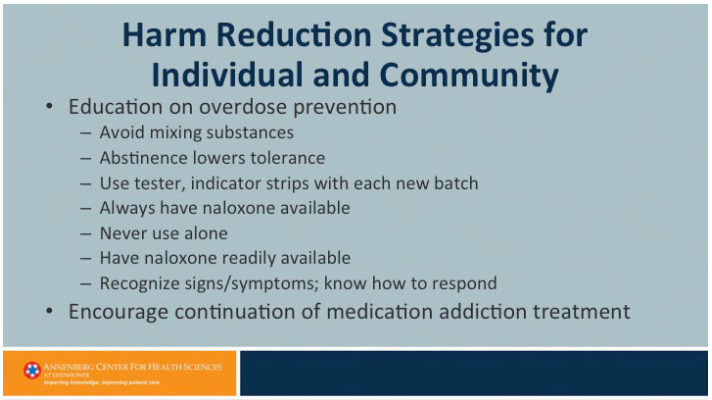
Important harm reduction strategies for the patient and his or her close family and friends include counseling on safe needle use, needle exchange, and safe disposal of needles. We've had family members in our clinic who've come in with needle sticks because needles were not disposed of safely.

It is critical to let patients know where they can dispose of their needles, at home, in the interim, and then in the community. It also includes secure storage of medication for addiction treatment in the home. The last thing we want is for children or people without opioid tolerance to get in contact with these medications. It is beneficial as well to screen for hepatitis B immunity, and to offer vaccination to anybody not immune.

Dr. Friedmann: The idea that you are treating the person holistically, all of their conditions, their risk for hepatitis, their vaccine needs, again that conveys your respect for their personhood and again, important in developing therapeutic alliance. Again, not extra to their recovery but really an important addition to it.

Dr. Gaberman: I also, as a primary care doctor, would say that that's why I think treating addiction in the primary care setting is so important because we treat the whole patient and to the patient that's really important. They may come in with pain issues, or diabetes or other issues, then we address the whole patient and all the problems they're dealing with.



So, with overdose prevention, it is helpful to involve a family [member] or close friend, anyone who might be looking out for the patient when he is using opioids. Important advice, specifically for the patient, includes not mixing opioids with other drugs, sedatives or alcohol. Also, being aware that abstinence lowers tolerance. Some of the highest risk times for overdose death are when someone relapses after being late for injectable naltrexone or Vivitrol, after being released from prison, and also in the immediate postpartum period after refraining from use during pregnancy. These times are critical and it's so important for people with opioid use disorder to know that these are risky times.

The other important counseling is to let patients know they should try a test dose of whatever substance they are going to use and even use a fentanyl indicator strip if available. Both are very important because of the large amount of inexpensive, highly-potent fentanyl and even carfentanil on the street. Caution patients never to use alone. With fentanyl, the risk of overdose death is in minutes. It does not help if the family member is downstairs. Keep nasal naloxone on hand and remember to continue to encourage patients to use medication addiction treatment to help enter into long-term remission.

Family members and close friends can be taught how to respond in the event of an overdose. Discuss with them how to recognize overdose. Make sure they know to call 911 immediately for help and how to administer nasal naloxone. There are many ways one can prescribe naloxone and one of them is nasal naloxone or nasal Narcan, which is the one we use. In the syllabus, you'll find details on how to prescribe other forms of naloxone. With fentanyl on the uptick, responding to overdose must be quick, whereas with heroin one might have had up to an hour to respond. With fentanyl, it is only minutes. In addition, the fentanyl effect can last much longer beyond the duration of 2 doses of nasal naloxone. So the initial call to 911 is absolutely essential.

So with all this, Dr. Friedman, I wanted to ask you how you treat pain, especially acute pain, in patients that are on medication addiction treatment?

Dr. Friedmann: That's a great question that folks are often very concerned about. It really depends on the type of medication addiction treatment they're on. It's typically folks who have chronic pain syndrome. Naltrexone is relatively contraindicated. For those who are on agonist treatment,

either with methadone or buprenorphine, you need to treat their opioid debt to prevent withdrawal. So the baseline amount of methadone that you're giving once a day is not enough to treat their pain. That's often a mistake. You need

to add medication on top of that.

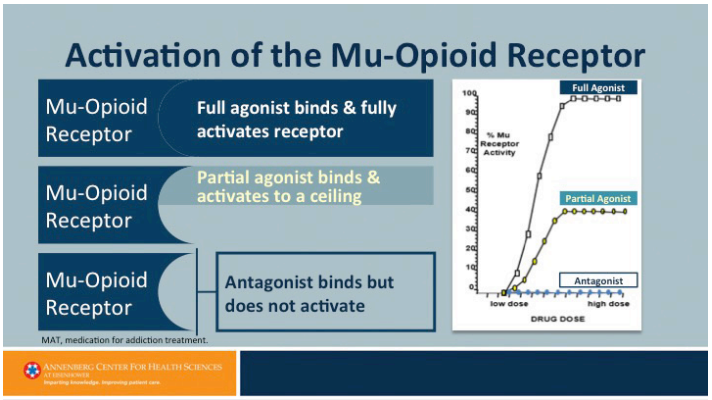
What's true of these medications also is that analgesic effect is much shorter-acting so you'll need to . . . whereas for example, you give buprenorphine once a day for the addiction treatment, you may need to give it 3 or 4 times a day to treat pain. What we often do for folks who are on buprenorphine who are, say, going to undergo a dental extraction or something, is we will continue their buprenorphine but we will divide their dose 3 times a day, maybe increase the dose slightly, make it 3 times a day. Some folks do add another short-acting opioid because the thinking is not all of the receptors are occupied all the time and that some short-acting opioid for pain control may be useful.

As we mentioned, this is different for naltrexone. For those folks, you probably, if they're going to undergo a painful procedure, you'll probably need to use other modalities for pain management or take them off the naltrexone . . . In an elective process, it can be overridden by anesthesiologists using high doses of pharmaceutical fentanyl, but typically it's more challenging with naltrexone.

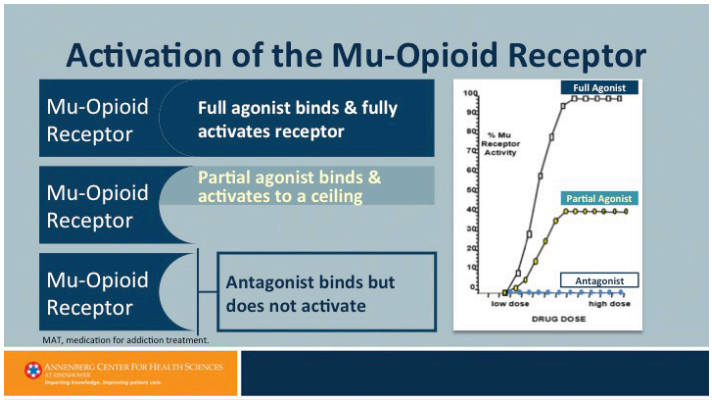
Dr. Gaberman: Management of opioid use disorder should take into account the patient's readiness for change. Approach the patient with concern and compassion, as behavioral change is very hard and many have relapsed in the past and lack hope. Use patient-centered, nonstigmatizing language, incorporate harm-reduction and motivational principles, and continue to treat pain conditions as needed.

MEDICATION-ASSISTED THERAPY

Dr. Friedmann: Module 4 focuses on the use of medication for addiction treatment, or MAT, for opioid use disorder. Beginning with a description of how these medications work. Details have been provided about the efficacy of available medications. For example, methadone, buprenorphine, the combination of buprenorphine-naloxone, and naltrexone. The rewarding aspects of opioids come through activation of the μ-opioid receptor and the μ-opioid receptor in these reward areas of the brain, their intrinsic activity, which is shown on the graph on the right side of the slide. What happens with a full agonist, at the top, is that it binds and fully activates the receptor. Now, if a full agonist is relatively short-acting and has a very rapid onset, that will give the feeling of the rush, the high, the euphoria. Those typically are the most abused substances. However, if you give something that is very long-acting and has a very slow onset, but occupies that receptor in a competitive way against the short-acting, that will build tolerance and so the person, in order to achieve the euphoria, will need to have a very high dose of a short-acting agonist. That's sort of how methadone works. It occupies the receptor; it competes against the short-acting agonist over a very long period of time. It also negates the negative reinforcing effects, so it reduces the withdrawal that folks experience.



At the other end of the spectrum are the antagonists. An antagonist at the bottom binds the receptor but does not activate it. So that's illustrated by the straight line at the very bottom of the graphic. The example of that is naltrexone. [With] naltrexone you get no pain-relieving effect from it, you get no feeling of being normal from it, it has absolutely no abuse potential because there's no way to get any euphoria from it. So typically, when it was introduced orally, patients wouldn't take it because there was nothing reinforcing the medication-taking behavior. This is the reason why now it's used in a monthly injectable form to be sure that folks are adhering to the medication.



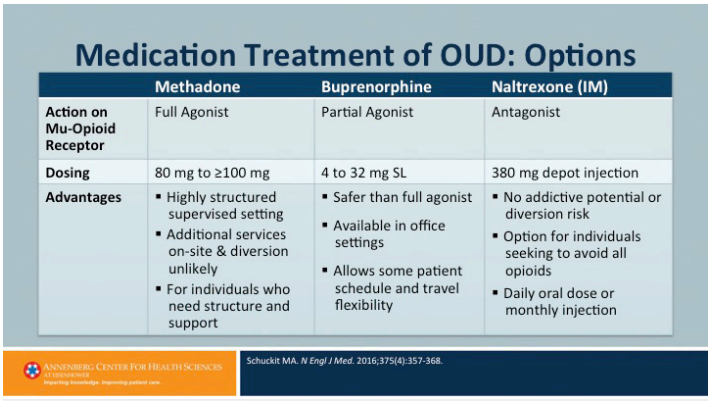
Sort of in between, in the middle of this slide are the partial agonists that bind and activate to a ceiling—that's what buprenorphine is. You'll see at the lower end of the drug dose on the left, it acts very similarly to the full agonist, right? There is an increase in intrinsic receptor activity, so

there is a little bit of a positive feeling that folks get. But it's not so much that they're feeling high. It's enough that they're feeling normal, that it's relieving the withdrawal symptoms. But then it hits the ceiling, and once it hits that ceiling there's no more increase of intrinsic activity and that's what makes it safer. So there's less risk of respiratory depression, less risk of misuse. That's how the 3 medications tend to work.

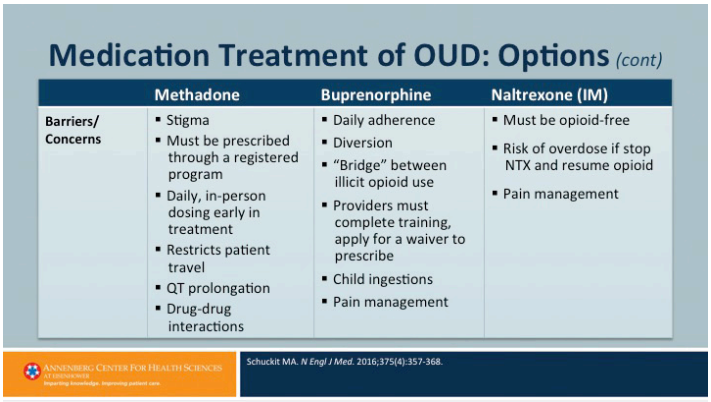
[Regarding] the medication treatment of opioid use disorder, there have been decades of very well-done randomized trials showing that they're effective in reducing relapse, overdose, infections, and other harms. As we mentioned, the 3 options are agonists therapy with methadone, partial agonists with buprenorphine, and antagonists with naltrexone. The thing to bear in mind is all these medications have been studied in the context of other counseling. So clearly, to do that, a team approach is best to address those co-occurring medical and psychiatric and social issues that our patients experience.

Dr. Gaberman: Dr. Friedman, I just want to add that we've found in our health center that patients don't usually stay on injectable naltrexone. We've received some patients coming from prison who received it there, but once they've had the first injection with us they don't tend to stay on it and tend to transition over to buprenorphine. I've also found that it's very difficult to start in an outpatient setting because it can throw patients into withdrawal. Patients need to be off of all substances, off of all opioids for at least 7 days, and when transitioning from methadone, even longer. So, the startup is incredibly difficult. They would need to take oral naltrexone first, to make sure they're safe, and then transition to injectable. It's very challenging.

Dr. Friedmann: I think the experience with naltrexone bears that out. However, it is a useful tool and there are people who want that approach, and I view all of these as the things we have in our . . . some people say tool belt, I like to say bat utility belt. This notion that 1 medication is going to work for everybody is a fallacy. Clearly, there are many different roads to recovery and there are many different ways a medication can be used.



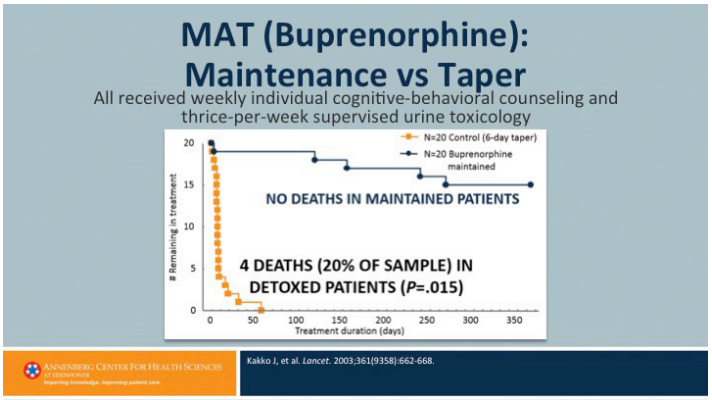
Methadone has to be done in a very highly-structured, supervised setting.[13] For folks who need that kind of support, for folks who need more agonist activity in order to overcome the craving, methadone is an important option that really needs to be available to folks. Buprenorphine is safer. It can be used in the office setting with less restrictions than methadone. It allows the patient some flexibility and so that's a good option for patients who have a relatively good prognosis. Then, naltrexone is useful for folks who really want to seek to avoid opioids, it's just given once monthly and it's also useful if someone decides to taper, for example, off some of the others. During that period where they're first off of everything, it's sometimes a useful tool to help in that transition.



The medications have their pluses and minuses.[13] Methadone is highly stigmatized. People don't want to go to the programs. There's a lot of daily dosing, particularly at the beginning of treatment. So it's really very restrictive. Some people need that structure. There can be issues with QTc prolongation and drug interactions.

Buprenorphine has fewer of those issues because it's given in the office, it has to be given daily. There are more issues with diversion with buprenorphine and, of course, providers need to complete a training in order to get a waiver to do it. Naltrexone, as Dr. Gaberman mentioned, you really need to be opioid-free. It's difficult to do an outpatient induction onto it. Dr. Gaberman also mentioned the risk of overdose if folks stop it and resume use. Again, the issues around pain are challenging.

The thing to bear in mind, though, is even given all of these challenges, it's still far superior to the medication-free treatments that we see. So, a huge effect size has been seen



for medication vs tapering. There's a very well-cited study from 2003 in *The Lancet*[14] that compared a buprenorphine maintenance protocol to a 6-day taper, and what we see in this graphic is that very few folks remained in treatment after the buprenorphine was stopped. The thing [is] that it was not powerful . . . It was a small study, only 20 patients, they received sort of state-of-the-art Cadillac counseling. Twenty patients in each arm. There were no deaths in the maintained patients and 4 deaths in the detox patients, which reached statistical significance. So that suggests that really it's a huge, huge effect size. This has been borne out in many studies. This is not a simple thing like getting a 2 or 3 percentage point reduction in myocardial infarction (MI), like you get with statins. This is really a huge life-saving treatment that we see and it's been consistently shown.

The other thing that's been shown is that this is a chronic disease that's relapsing and recurring. But the number of relapses and treatment in this study by Robin Clark at [the] University of Massachusetts[15] shows that those who get nonmedication treatment have many, many more relapses over the course of treatment than those who are treated with medication. The thing to bear in mind, in this day and age, is that every [time] somebody relapses, they're at risk to die. Right? Because the elicit supply on the street is really risky and there's a lot of fentanyl out there. So, relapse does occur in these folks. Dr. Gaberman, can you tell us a little about your experience with relapse for folks who have been on medication?

Dr. Gaberman: As we spoke about, opioid use disorder—all substance abuse disorders—are chronic medical

conditions. So, though medication treatment helps people enter into remission, there are still episodes of relapse. Patients may also still struggle with other substance use such as cocaine, [as] in the case that I relayed to you earlier. When you're working with patients who are in a medication addiction treatment program, it's important to use behavioral contingencies, because contingency management can be helpful. In fact, with cocaine, where there isn't a medication to treat cocaine-use disorder, often times that's the only thing we have to offer.

When patients are doing well and are in remission and are remaining off of opioids, we oftentimes will extend their prescriptions for medication, such as buprenorphine to 28 days which allows them much more flexibility so that they can go on with their life and live the life that they value and do the things they want. When patients are struggling, and having episodes of relapse, we shorten the interval of the prescription, as I mentioned earlier, to 7 days. Some programs do it even to twice a week. We're not able to do that. Again, the plan has to make sense for the patient, but also for you and your office, and it depends on what you can accommodate.

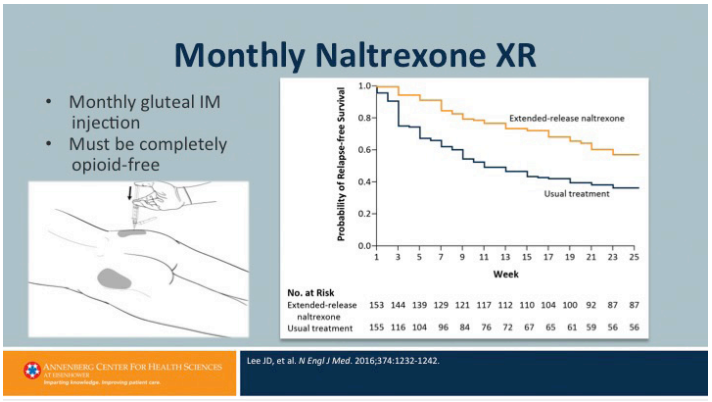
When patients relapse, we try to see them every week, we increase the amount of urine toxicology screening we do, and we really push for them to keep their counseling visits, and to work with a counselor closely. If their relapse continues and they don't respond to this, then we start talking to them about higher level of care. I will always bring up methadone maintenance with patients. A lot of

patients are very resistant to that and I don't push them if it's something that they won't do, but it does offer more structure, and some patients find they do better going on methadone maintenance. We also offer people referrals to intensive outpatient programs or partial hospitalization.

Dr. Friedmann: These are often challenging, challenging patients. The cocaine issue is often difficult, and I also use these same approaches that you really want to intensify treatment. I think you really want to emphasize to the patient that this is not a punishment, but really this is to try to get them back on track and help them develop some skills to be able to deal with some of the temptations that are out there.

Dr. Gaberman: I agree.

Dr. Friedmann: [For] some of these folks who've relapsed, some of these longer-term medications might be useful. Those who are either struggling with recurrent use or whom you might be concerned about diversion, folks who use cocaine I'm always concerned about diversion, I'm always concerned that folks are selling part of their buprenorphine dose or bartering to buy cocaine. Some of those folks might be appropriate for the injectables. So we've talked a little

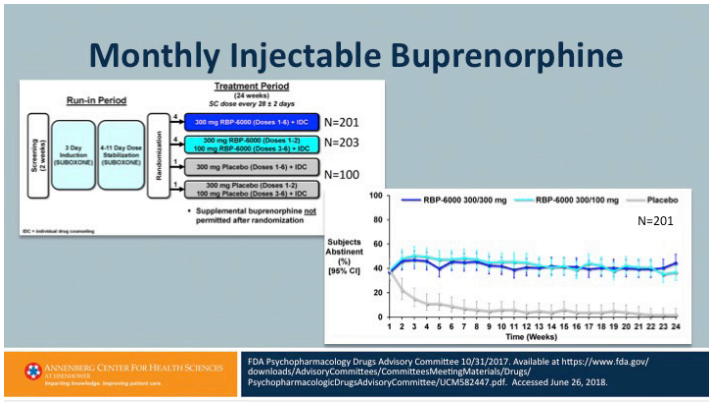


about the monthly injectable, naltrexone.[16] There have been a number of studies that have shown . . . As we mentioned, they have to be completely opioid-free. It's very challenging for the induction. Often, they need to be in an inpatient detox or incarcerated in a completely drug-free setting before they're able to do this. There are some outpatient protocols that use increasing doses of oral naltrexone to get folks started. I have not used any of those. Have you used any of those oral protocols, Dr. Gaberman?

Dr. Gaberman: I have not. I think our concern is also diversion, but on the other hand, I think we need to step back and look at the graphs, the studies that you just presented and how important it is to treat patients with these medications for their opiate use, and often times I think they need to be addressed separately, quite honestly. I haven't found naltrexone helpful. I think that patients at greater risk . . . the greatest risk for overdose . . . are often the people that are poly substance-users, so pushing those patients onto naltrexone, where I think they're going to lose their tolerance and have a higher risk of overdose, I would be very concerned about.

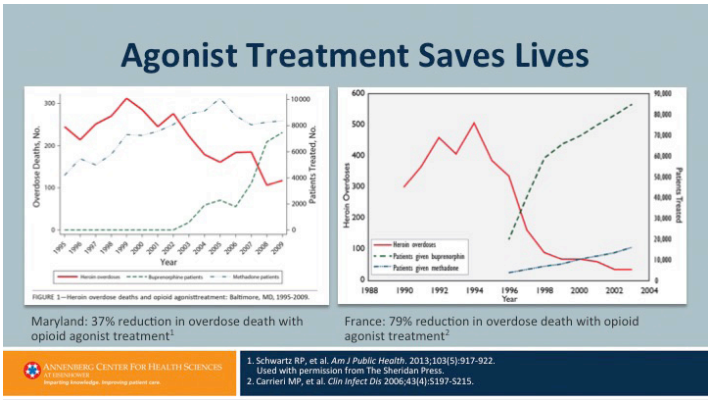
Dr. Friedmann: This sort of bears out what we've been talking about.[17] Once folks are able to get onto the medication, they do as well as folks on buprenorphine, but really the challenge on the left side of this graph—the intent to treat population, is that a lot of people are not successful in getting into the opioid-free state that allows them to get onto the medication. But once they do, they tend to do pretty well.

In terms of opioid craving, what the study also showed—comparing extended-release naltrexone to buprenorphine—[it] demonstrated that amongst those that are on the medication, there is [a] slightly less, but significant decrease in craving early in treatment amongst those that are on extended-release naltrexone.[17] Those effects tend to fade over 24 weeks. The thinking may have to do with what's happening at the level of the opioid receptor. In point of fact, this is in the per-protocol, not the intention to treat. This is amongst the people who received the treatment. Again, it doesn't negate the challenge of getting folks on the treatment.



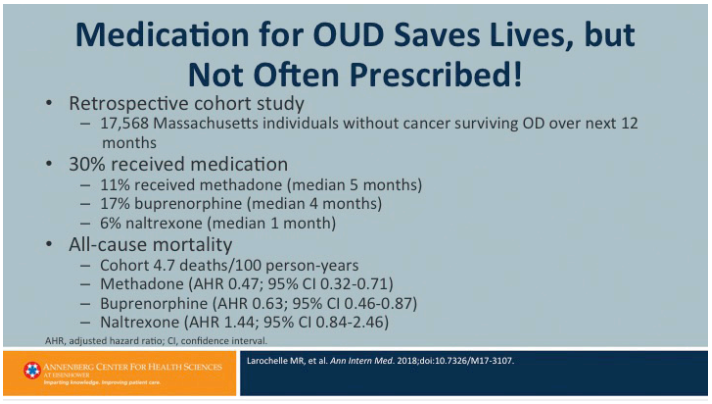
One of the tools that many of us are very excited about is the monthly injectable. Monthly injectable buprenorphine,[18] which has been recently marketed and that's going to be a useful tool, again, for folks that we think are having trouble with adherence to daily medication. Those folks might do better coming in for a monthly injection.

The overall message is that agonist treatment saves lives. This graph shows 2 studies that have dramatically shown this. The one on the left is from Baltimore.[19] During the period where the rest of the country saw an increase in



overdoses, Baltimore saw a decrease in overdoses over the 2000s, largely because of a very aggressive program of increasing access to primarily buprenorphine, but there was also a more gradual increase in methadone. Similarly, in France, when they undertook a program of aggressive use of buprenorphine in primary care settings for opioid use disorder, they saw a change from an increasing amount of overdoses on the left, this is on the right-hand graph.[20] On the left-hand side of that graph you see there were increases in overdose deaths, and once they implemented an aggressive buprenorphine program in primary care, there was a dramatic drop in lifesaving effects.

Medication for opioid use disorder saves lives, but it's not often prescribed. Recently, Marc LaRochelle from Boston Medical Center published in the *Annals of Internal Medicine*, an impressive study using retrospective data from



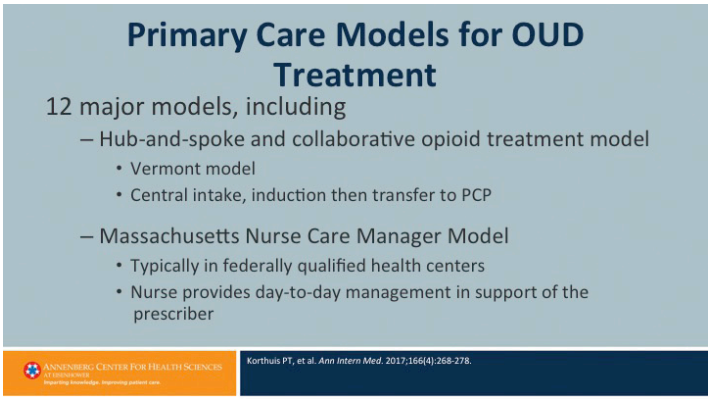
Massachusetts.[21] Over 17,000 individuals who survived overdose and looked at what happened to them. Only 30% of them received medication. The highest risk for death after an overdose is having had a prior overdose. What they saw was that individuals' all-cause mortality was greatly reduced by methadone and buprenorphine and they did not detect an effect of naltrexone. Again, bearing out that we really need to do more to get medication out there.

[In] the Surgeon General's report, the science is really clear — MAT works.[22] The Surgeon General says, "The use of opioid agonist medication to treat opioid use disorders has always had its critics." This slide is sort of a long statement. This is not substituting one substance for another. The abstinence-only philosophy, or the medication-free philosophy, as I prefer it, really is detrimental to people's lives, I think, as a large cause of a lot of the deaths that we're seeing. We have decades of research that show the benefits of medication outweigh its risks.

In summary, medication treatment extinguishes the out-of-control drug-using behavior. Remember we said it blocks those receptors and competes against the short-acting, and [in] doing so, reduces the drug-using behavior, the consequences, and craving. We have 3 types of medication; they're all efficacious, but as of now, only methadone and buprenorphine have been demonstrated to be lifesaving and really those should be first-line.

MINIMIZING RELAPSES

Module 5 focuses on strategies to consider in employing a coordinated-care model involving primary care providers to decrease the risk of relapse for people with opiate use disorder. There's an excellent review by Todd Korthuis.[23] It was in the *Annals of Internal Medicine* in 2017 that outlined 12 primary care models for opiate use disorder that are in existence. I really wanted to speak about 2 of them. One of them is the Hub-and-Spoke Collaborative Opioid Treatment Model. This is also called the Vermont Model, in which there is a central intake, usually at an opioid treatment program.



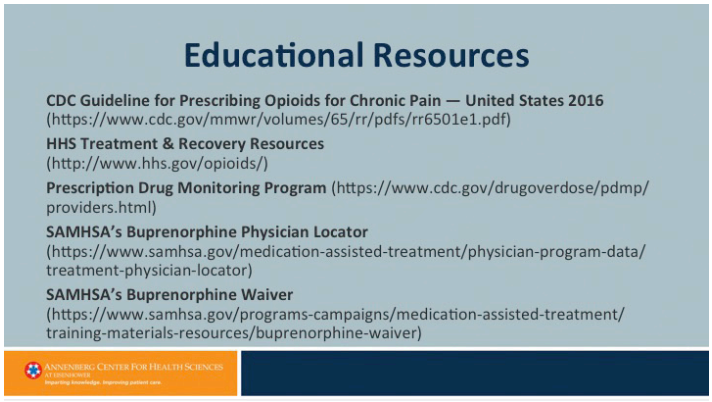
There is a centralized induction that occurs, so starting with buprenorphine and, of course, assessment, and all these other kinds of things that we talked about earlier occur. Then those folks are transferred to the "spoke" which is usually a primary care provider that will provide the ongoing care. This model has been very successful in Vermont, it's being replicated in Maine. There was also a big project in California to replicate it, as well, and it's seen a lot of success.

The model that Dr. Gaberman in my program has developed is called the Massachusetts Nurse Care Manager Model and this is a model in which there is a dedicated nurse supporting the prescriber in a health center. Typically, these are federally qualified, ours is a look-alike, but the principle is the same, that there is support staff who is responsible for the day-to-day management of these patients in support of the prescriber.

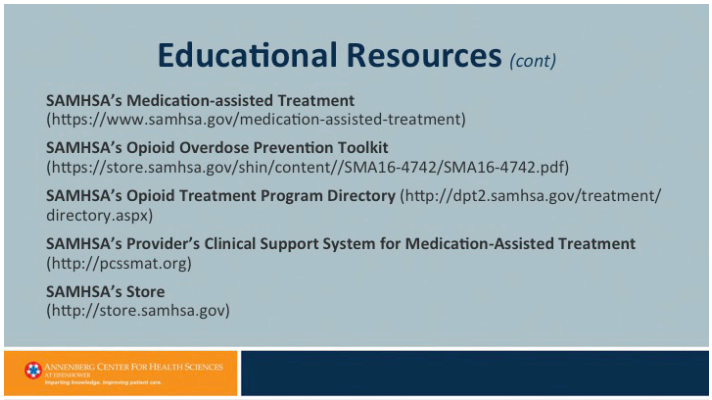
I urge you to pull the article and look at the other models. Again, there's variation, but they all have 4 major components.[23] Pharmacotherapy is a key piece of it.

Medication works, as we talked about. Educational interventions. Educating both patients and families, but also staff, about the chronic relapsing nature of the illness and the need for effective medication. Coordination and integration with other medical and psychosocial needs is a big part of it. Many of these studies use case management, a number are increasingly using recovery coaches, and peer-support interventions. Again, to help support people and to help coordinate their care to meet the multidimensional needs and deficits they experience. Finally, the delivery of psychosocial services. This typically involves either delivering counseling on site, integrated into the program, or by referral, and ensuring that folks are getting to where they need to be.

Dr. Gaberman: Providing this addiction treatment, within the primary care office, makes it much more accessible to patients and allows the primary care provider to collaborate and coordinate with other members of the patient's



care team. This syllabus has many useful links. I want to particularly highlight that there's a link to prescription drug monitoring programs, to the buprenorphine physician locator, and to the buprenorphine waiver program. Please look through them. They are all very useful links.



Several models of coordinated care have been developed for primary care settings. I want to just emphasize that nearly 80% of Americans with opioid use disorder currently do not receive effective treatment with medication. It's a huge number. Primary care providers have the opportunity

to broadly increase access to this lifesaving treatment. The benefits of the treatment are dramatic and the work is very rewarding. I encourage all of you, if you have not already done so, to sign up for a buprenorphine waiver course, which takes a total of 8 hours, and provides you with the ability to prescribe office-based addiction treatment for those in need.

REFERENCES

1. Volkow ND, Chang L, Wang GJ, et al. Loss of dopamine transporters in methamphetamine abusers recovers with protracted abstinence. *J Neurosci*. 2001;21(23):9414-9418.
2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Published 2018. https://www.psychiatry.org/psychiatrists/practice/dsm. Accessed July 24, 2018.
3. Ives TJ, Chelminski PR, Hammett-Stabler CA, et al. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC Health Serv Res*. 2006;6:46.
4. Reid MC, Engles-Horton LL, Weber MB, Kerns RD, Rogers EL, O'Connor PG. Use of opioid medications for chronic noncancer pain syndromes in primary care. *J Gen Intern Med*. 2002;17(3):173-179.
5. Michna E, Ross EL, Hynes WL, et al. Predicting aberrant drug behavior in patients treated for chronic pain: importance of abuse history. *J Pain Symptom Manage*. 2004;28(3):250-258.
6. Akbik H, Butler SF, Budman SH, Fernandez K, Katz NP, Jamison RN. Validation and clinical application of the Screener and Opioid Assessment for Patients with Pain (SOAPP). *J Pain Symptom Manage*. 2006;32(3):287-293.
7. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med*. 2005;6(6):432-442.
8. National Institute on Alcohol Abuse and Alcoholism. Clinician's Guide to Helping Patients Who Drink Too Much. Published 2005. https://pubs.niaaa.nih.gov/publications/practitioner/CliniciansGuide2005/guide.pdf. Accessed June 25, 2018.
9. National Institute on Drug Abuse. Principles of Drug Addiction Treatment. A Research-Based guide. Published 2012. https://www.drugabuse.gov/sites/default/files/podat_1.pdf. Accessed July 12, 2018.
10. Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. Published 2016. https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm. Accessed June 25, 2018.
11. Harm Reduction Coalition. Principles of harm reduction. Published 2018. http://harmreduction.org/about-us/principles-of-harm-reduction. Accessed June 26, 2018.
12. Boston University School of Public Health. The brief negotiated interview (BNI). Published 2018. http://www.bu.edu/bniart/sbirt-in-health-care/sbirt-brief-negotiated-interview-bni/. Accessed June 26, 2018.
13. Schuckit MA. Treatment of opioid-use disorders. *N Engl J Med*. 2016;375(4):357-368.
14. Kakko J, Svanborg KD, Kreek MJ, Heilig M. 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. *Lancet*. 2003;361(9358):662-668.
15. Clark RE, Baxter JD, Aweh G, O'Connell E, Fisher WH, Barton BA. Risk factors for relapse and higher costs among medicaid members with opioid dependence or abuse: Opioid agonists, comorbidities, and treatment history. *J Subst Abuse Treat*. 2015;57:75-80.
16. Lee JD, Friedmann PD, Kinlock TW, et al. Extended-release naltrexone to prevent opioid relapse in criminal justice offenders. *N Engl J Med*. 2016;374(13):1232-1242.
17. Lee JD, Nunes EV, Jr., Novo P, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. *Lancet*. 2018;391(10118):309-318.
18. US Food and Drug Administration. FDA briefing document. Joint Meeting of Psychopharmacologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee. October 31, 2017. Published 2017. https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM582447.pdf. Accessed June 26, 2018.
19. Schwartz RP, Gryczynski J, O'Grady KE, et al. Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. *Am J Public Health*. 2013;103(5):917-922.
20. Auriacombe M, Fatseas M, Dubernet J, Daulouede JP, Tignol J. French field experience with buprenorphine. *Am J Addict*. 2004;13(Suppl 1):S17-S28.
21. Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: A cohort study. *Ann Intern Med*. 2018;doi:10.7326/M17-3107.
22. US Department of Health and Human Services. Facing Addiction in America. The Surgeon General's Report on Alcohol, Drugs, and Health. Published 2016. https://addiction.surgeongeneral.gov/sites/default/files/surgeon-generals-report.pdf. Accessed June 25, 2018.
23. Korthuis PT, McCarty D, Weimer M, et al. Primary care-based models for the treatment of opioid use disorder: A scoping review. *Ann Intern Med*. 2017;166(4):268-278.