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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Opioid Addiction

Learning Objectives
After reading these articles, you should be able to:

1. Identify the benefits and drawbacks of Narcotics Anonymous (NA) for patients with opioid use disorder (OUD), as well as viable alternatives.

2. Describe the process of using medical management (MM) to treat patients with OUD.

3. Identify the benefits and drawbacks of medications currently used to treat OUD.

Narcotics Anonymous: What to Tell Your Patients

Most of us are pretty familiar with Alcoholics Anonymous (AA), and asking about AA attendance and participation is routine during appointments with patients trying to curb their alcohol use (see the November/December 2015 *CATR* for more info on AA). But what about Narcotics Anonymous (NA)? Is it just an opioid-focused version of AA? In this article, we'll summarize some basic info on NA and give you tips for how to educate your patients about it.

What is NA?
NA is a 12-step program founded in 1953. It was created to provide a simply written set of principles that patients can follow in their daily lives (see: https://www.na.org/admin/include/spaw2/uploads/pdf/handbooks/IGG.pdf). Meetings vary in structure and format and are not run by medically trained professionals; instead, they are conducted as a fellowship of people who volunteer to help one

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In Summary

- NA is a 12-step program that is available to people with substance use disorders.
- NA differs from AA in that it does not consider agonist treatment to be consistent with its abstinence model of recovery.
- Although evidence is limited, the outcome of NA corresponds to the degree with which a person participates.

Q&A With the Expert

Using Medical Management in Treating Opioid Use Disorder

Andrew Saxon, MD

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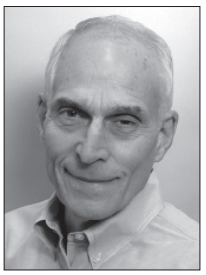
Dr. Saxon has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.



CATR: We often hear about an intervention called medical management (MM) for treating addiction. Could you tell us what MM is?
Dr. Saxon: To set the stage for understanding medical management, we need to go back about 20 years to the inception of the landmark COMBINE Study. This study was a very large clinical trial for alcohol use disorder (AUD) that compared naltrexone, acamprosate, and their combination, and also looked at two behavioral interventions. One of these interventions was MM, and the other was a very robust form of psychotherapy that included elements of motivational interviewing, cognitive behavioral therapy (CBT), and other skills building (Anton RF et al, *JAMA* 2006;295(17):2003-2017). MM was specifically developed for the COMBINE study.

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Narcotics Anonymous: What to Tell Your Patients

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another. Despite having "narcotics" in its title, NA is for anyone struggling with any addiction—this can include cocaine/stimulants, cannabis, alcohol, benzodiazepines, etc. If patients have multiple addictions, they can choose to attend either NA or AA, or even to attend both, in accordance with their personal preferences and their comfort level.

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What are NA meetings like?

Like AA, NA meetings are free to all comers and follow the 12-step philosophy. Meetings are led by members and take place in churches, community centers, hospitals, and similar places. Each meeting is slightly different, but there are typically 3 types. Speaker meetings feature speakers who tell the story of their recovery; topic meetings often focus on a particular NA step or recovery issue; and reading meetings begin with a reading from the library of 12-step literature (such as *Narcotics Anonymous,* which is often called the Basic Text, or *The Narcotics Anonymous Step Working Guide*) and proceed to a discussion of issues raised.

Unlike AA, which does not take any official position on agonist treatment with buprenorphine or methadone, NA explicitly considers such treatment to be inconsistent with its abstinence model of recovery, and NA culture discourages its use. While participants are not required to abandon agonist treatment, NA's official stance is that members on agonist treatment should not lead meetings, serve as speakers or sponsors, hold office in NA, or even share at meetings (https://www.na.org/?ID=bulletins-bull29). This can be an impediment to our patients, who often feel that they have to hide being on agonist treatment in NA meetings. Fortunately, some individual NA groups have recently adopted an open attitude toward agonist treatment.

Is NA effective?

There is more research for AA than NA, though neither have conclusive evidence of efficacy. Research on NA is not only scant, but also based on the relatively small numbers of patients who do not drop out of NA meetings early (80%–90% of patients drop out from NA within the first month). Nonetheless, the limited research has found that the outcome of NA correlates to the degree of a patient's participation. People who regularly attend meetings, who consider themselves to be "members," and who actively work through the 12 steps are more likely to have sustained abstinence greater than 1 year (Krentzman AR et al, *Alcohol Treat Q* 2010;29(1):75–84). Similarly, continuous weekly NA attendance for at least 3 years is associated with higher rates of sustained abstinence. Specific participation characteristics that are predictive of abstinence include having a sponsor, doing service in a manner that gives back to NA (eg, becoming a sponsor, hosting or coordinating a group meeting, etc), reading recovery literature, and contacting other members outside of meetings. Women may be more likely than men to benefit from NA meetings.

How to talk to your patients about NA

The bottom line is that while NA has limited evidence for its effectiveness, it is widely available and free, and will likely help your patients build up a network of people who will support their sobriety. Beware, however, of NA groups that pressure people to stop taking opioid use disorder (OUD) meds.

Here are some recommendations for points to make to your patients as you talk to them about NA:

1. Tell your patients that NA is a cost-free mutual-aid fellowship that provides consistent, dependable recovery-oriented support and can positively impact their social network.
2. Be honest with your patients about NA's philosophy of complete narcotic abstinence, which can be at odds with agonist treatment. Emphasize that agonist treatment saves lives, preserves health, improves quality of life, and is an essential component of recovery.
3. If you have patients on agonist treatment who opt for NA, be sure to ask about their participation in meetings and how they communicate their treatment to other members. Some choose to withhold that information, while others opt to share it.
4. Discuss finding meetings that welcome people on OUD meds. Patients can try different NA groups to see which ones they like, they can go to AA instead (though AA groups vary in their openness to non-alcohol addictions), or they can try alternatives such as Self-Management and Recovery Training (SMART) Recovery (https://www.smartrecovery.org), Women for Sobriety (https://womenforsobriety.org),

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Opioid Treatment Options

Opioid use disorder (OUD) treatment can be tricky, in part because it doesn't respond well to detox and counseling-only approaches. The overwhelming majority of people relapse after such attempts, or even become more vulnerable to overdose because of decreased tolerance after detoxing. And the trajectory in this country is worsening—in 2016, we averaged around 115 opioid overdose deaths per day; in 2017, that number was estimated at around 134 per day (https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates). But we do have effective and underutilized medications to treat OUD: buprenorphine, methadone, and extended release injectable naltrexone. Let's take a dive into these medication options.

Buprenorphine

While we used to tell our patients that both buprenorphine and methadone are first-line treatments, nowadays we increasingly think that buprenorphine should be the preferred agent, because it may be better at reducing mortality in the first month (Manhapra A et al, *BMJ* 2017;357:j1947). Buprenorphine has less associated stigma and poses fewer side effects (eg, QTc prolongation), drug interactions, and overdose risk than methadone. A special DEA waiver is required to prescribe it, but unlike methadone, buprenorphine can be prescribed through a regular office-based practice and doesn't require a specialized clinic, making it more convenient for patients.

The process of starting a patient on buprenorphine is called "induction," because the first step is introducing it at the right time during opioid withdrawal. When performing an induction, make sure your patient has used no opioid in at least 12–24 hours (or 24–48 hours for the longer-acting methadone)—this should put the patient into mild to moderate withdrawal. We usually look for a score on the Clinical Opiate Withdrawal Scale (COWS) of at least 8, though some guidelines suggest waiting until it reaches 12 (https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf). This waiting period is very important because giving buprenorphine too early can precipitate withdrawal. Pupil dilation may be the best way to assess for readiness to receive the first dose.

Start with a small dose of buprenorphine, usually 2 mg–4 mg. Monitor the

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The Many Varieties of Buprenorphine for Treating OUD

Generic Name (Brand Name) Year FDA Approved (Rx status) [G] denotes generic availability	Formulation and Available Strengths (mg)	Usual Dosage Range (mg)	Comments
Buprenorphine (formerly Subutex) [G] 2002 (C-III)	Sublingual tablet: 2, 8	4–24 QD	Original mono version; very inexpensive and effective, but since it does not contain naloxone, it carries a higher risk of being ground up and injected.
Buprenorphine/naloxone [G] 2002 (C-III)	Sublingual tablet: Bup/Nx: 2/0.5, 8/2	4–24 QD	The first combination buprenorphine/naloxone agent. Long track record; inexpensive, but some complain about the taste.
Buprenorphine/naloxone (Suboxone) [G] 2010 (C-III)	Sublingual film: Bup/Nx: 2/0.5, 4/1, 8/2, 12/3	4–24 QD	Faster absorption than tablets; easy to taper gradually because film can be cut into small sizes. Packaging makes it more difficult for kids to open, but there may be more diversion potential because the films can easily be mailed. Relatively high cost, though generics are newly available.
Buprenorphine/naloxone (Cassipa) 2018 (C-III)	Sublingual film: Bup/Nx: 16/2	4–24 QD	The higher dose formulation offers convenience of fewer films for those on higher doses, but relatively higher cost.
Buprenorphine/naloxone (Bunavail) 2014 (C-III)	Buccal film: Bup/Nx: 2.1/0.3, 4.2/0.7, 6.3/1	2.1–12.6 QD	High bioavailability, fast absorption, less constipation; very high cost. More convenient than other preparations because it sticks to the cheek while dissolving, allowing patients to talk, but less dosing flexibility because cutting may decrease the medication's ability to stick to the cheek mucosa.
Buprenorphine/naloxone (Zubsolv) 2013 (C-III)	Sublingual tablet: Bup/Nx: 0.7/0.18, 1.4/0.36, 2.9/0.71, 5.7/1.4, 8.6/2.1, 11.4/2.9	2.9–17.2 QD	Menthol flavor; higher bioavailability than generics, but also higher cost.
Buprenorphine implant (Probuphine) 2016 (C-III)	Rods implanted subdermally in the upper arm; each rod contains 74.2 mg of buprenorphine	Rods release the equivalent of 320 mg of buprenorphine over 6 months	Provides coverage for up to 6 months; consistent dosing; good bioavailability, but invasive, as it requires surgical implantation that may lead to scarring. Appropriate only for stable patients maintained on buprenorphine 8 mg/day or lower. Used for up to 6 months only; expensive.
Extended release buprenorphine (Sublocade) 2017 (C-III)	Injection: 100 mg/0.5 mL and 300 mg/1.5 mL provided in a prefilled syringe with a 19-gauge 5/8-inch needle	2 monthly initial doses of 300 mg followed by 100 mg monthly maintenance doses	Once-a-month subcutaneous injection provides a controlled dose with no need for daily maintenance and reduces risk of misuse, accidental ingestion, and diversion; however, it is substantially more expensive than traditional sublingual applications.

Buprenorphine/naloxone products are not bioequivalent. Comparable brand-name doses: 8mg/2 mg SL film = 5.7 mg/1.4 mg SL tab = 4.2 mg/0.7 mg buccal film. The brand-name SL film is equivalent to generic tablets.
Buprenorphine implant is equivalent to 8 mg or less daily SL films.
Extended release buprenorphine dosed 300/300/100 mg is equivalent to around 16 mg–24 mg daily SL films, and dosed 300/300/300 mg is equivalent to around 24 mg–32 mg daily SL films.

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CATR: Interesting. What was the "active ingredient" in MM?
Dr. Saxon: The idea was that MM would approximate what could be done in primary care by a healthcare provider while also prescribing a medication for AUD, but without the need to be a trained psychotherapist. MM simply involved monitoring the patient and taking vital signs, talking about medication adherence, talking about alcohol use, providing support and, very importantly, reinforcing any positive steps the patient was making. It also included encouraging mutual-help group attendance.
CATR: So, how did MM fare in this comparison?
Dr. Saxon: Well, the punch line is that in this study if you got a pill and you got MM, there was no advantage to adding on the more robust psychotherapy. So that was a strong encouragement that the healthcare provider working with a patient with a substance use disorder (SUD) and prescribing medication could achieve good results without extensive additional treatment.
CATR: These are encouraging results. Can MM also be used for opioid use disorder (OUD)?
Dr. Saxon: Yes, David Fiellin and his colleagues at Yale adapted MM for OUD. The sessions include a few extra things like checking urine toxicology and monitoring psychiatric and medical issues. But it's basically the same idea: You check in with the patient; make sure the medication is being taken, problem solve if it's not, find out about the substance use, help the patient to come up with a brief plan for reducing or discontinuing the substance use, and encourage attending a mutual-help group.

"People with OUD who leave treatment are at very high risk for overdose and death. A lot of providers feel that the ultimate goal is to taper people off medication, but we need to reeducate them on this. The goal is to keep people on medication, not to get them off."

Andrew Saxon, MD

CATR: I've heard that the easy way to remember MM is to think of it as the four A's: Abstinence, Adherence, and AA attendance.
Dr. Saxon: Yes, that's a perfect framework to present it.
CATR: To simplify it even further, one can ask, "What's so special about doing that? Wouldn't we do something very similar in treating diabetes or depression or any chronic condition?"
Dr. Saxon: That's exactly right. It's sort of that ideal physician visit that's going to take 15 or 20 minutes, in most cases, and cover all that territory. I think we have always underestimated how meaningful that is to patients to have that time with their healthcare provider.
CATR: That sounds like a good pharmacotherapy visit to me. I'm wondering, though—why do we even have to have a special name for it by calling it MM?
Dr. Saxon: You could call it whatever you want, but you know what happens: When something gets a name, it's very hard to change that name. We don't need to call it MM, but that's what people know it as.
CATR: Seems practical and pretty straightforward. So, we don't have to refer patients to specialty addiction care?
Dr. Saxon: Not necessarily. It's similar to what healthcare providers would do when treating any chronic condition. If we think about the opioid crisis and the millions of people who need help, even if the patients were willing to go to specialty programs, there is not enough space to treat everyone. We have to treat them in non-specialty settings. And MM becomes the tool to achieve that.
CATR: What are your thoughts on enhancing MM with other psychosocial interventions for OUD?
Dr. Saxon: A few studies have been done comparing MM alone and MM combined with various psychosocial interventions, such as drug counseling, CBT, and contingency management (Ling W et al, *Addiction* 2013;108(10):1788–1798). None of these interventions improved on the effectiveness of basic MM. But before concluding that we shouldn't offer therapy to these patients, we have to realize that these are aggregate results—thus, some people could have had a good response to the added psychotherapy. Besides, often the more challenging patients don't get into these studies. So we are talking about the average patient in the average office setting who is probably going to do just fine with MM and medication without anything more elaborate, but there could still be some patients who would benefit from more.
CATR: How do you decide who might benefit from more than just office-based meds plus MM?
Dr. Saxon: You just have to make a clinical judgment; if the patient is doing great with MM, why use up precious healthcare resources adding something that's unnecessary? But if the patient is unstable and struggling, then we have to start looking for other interventions to try and get that patient on track. The idea is to start with the simplest, least costly, and most direct intervention. In most cases, that is office-based buprenorphine, or for some patients it might be extended release naltrexone. For the patients who respond well to that, you've found the treatment modality for them. For the patients who are not doing well, you can step up the level of care.
CATR: Let's talk about OUD meds for a bit. Do you reserve buprenorphine, methadone, and extended release naltrexone for patients in the moderate to severe range of OUD? Or do you intervene even with the mild OUD when only 2 or 3 DSM-5 criteria are met?
Dr. Saxon: I may have a skewed perspective, but in my experience there are very few patients who come to clinical attention who have mild OUD. But I would treat all forms of OUD with medication. It would be a conversation with the patient who has mild OUD, and I would generally recommended extended release naltrexone for those people, presuming that their ability to withdraw from opioids would not be much of a challenge. And if they have substantial withdrawal and have a hard

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time stopping the opioids, then they are probably going to move at least into the moderate range. So, I think for mild OUD, extended release naltrexone would be my preference.

CATR: What if the patient says, "No, I really don't want naltrexone; I prefer buprenorphine."

Dr. Saxon: You have to take it on a case-by-case basis, but I think that would probably be okay, because even with a mild form of the disorder there is still a risk for overdose and inadvertent death if the patient is using opioids, so it's better to be on the medication.

CATR: On the flipside, can people who do well on buprenorphine for a while be switched to extended release naltrexone?

Dr. Saxon: I wouldn't do that unless it was at the patient's request, because if they are doing well on their regimen, I'm not going to rock the boat. But there may be some patients who want to switch, and then that can be a good idea. And if they go on extended release naltrexone and are not doing well, they can always go back to the buprenorphine.

CATR: What about completely detoxing patients off opioids? The FDA recently approved lofexidine for that purpose.

Dr. Saxon: Unfortunately, while complete detox sounds compelling intuitively, it rarely works. Patients with OUD are at very high risk for relapse and overdose if you try to detox them and treat them with behavioral intervention and no medication. This is the treatment that the vast majority of patients with OUD get in our country, and it's not evidence-based. The only reason for withdrawing patients from opioids is if they want to get on extended release naltrexone. So there's a real role for lofexidine in helping to make that transition from opioid use to extended release naltrexone—that transition is very difficult, and a large proportion of the patients who attempt withdrawal don't successfully navigate it. So maybe lofexidine (or its close relative, clonidine) can help with our success there, but again, don't do it unless the patient wants to go on extended release naltrexone, because if the plan is to go on buprenorphine or methadone, you don't need to completely withdraw people.

CATR: We hear a lot about rehabs that do not accept patients on OUD meds. What are your thoughts on that?

Dr. Saxon: I think most Americans think if you have an addiction problem, you go to a 28-day program and go drug-free. And of course, these programs are in competition with buprenorphine and methadone clinics. In fact, most people don't need the 28-day programs, though some of them can be helpful if they accept people on methadone or buprenorphine.

CATR: Some would say that being on a medication for OUD doesn't mean that the person will necessarily completely stop using, but that at least the person is using less, and we can work on harm reduction strategies (see the Q&A "Naloxone and the Harm Reduction Approach" in the March/April 2016 *CATR*). Can that be done as part of MM?

Dr. Saxon: Yes, that can be part of MM. If a patient is coming to appointments and still using opioids or other drugs, but is trying to get better, then you should keep working with the patient. Often the problem is that we've got these good treatments, but people drop out because we put too many demands on them or perhaps because they can't afford the medication. We know that if people stay on medication, they are less likely to die, so we want to keep people on it. We also want to make sure that all patients with OUD get prescribed naloxone and, ideally, that their family members receive education on using it. Syringe exchange programs aren't widely available, but we should talk to patients who inject about where they can get clean needles and syringes. I think that is a great harm reduction tool to help preserve health and limit the spread of infectious diseases.

CATR: Any additional thoughts on providing meds in the context of MM for treating OUD?

Dr. Saxon: I want to emphasize that medication treatment is the treatment for OUD. It's very important to remain in treatment because when people with OUD leave treatment, they are at very high risk for overdose and death. A lot of providers feel that the ultimate goal is to taper people off medication, and we need to reeducate them that the goal is to keep people on medication, not to get them off. So if you are doing MM with patients on buprenorphine and they've been on it for several years, and their lives are going well, and they have good functional status, you want to keep it going; you don't want to stop the medication. And if you achieve that, you have real treatment success that you can feel very good about.

CATR: Thank you for your time, Dr. Saxon.

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Opioid Treatment Options
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COWS after the buprenorphine dose, and if it's still elevated after 2 hours, you can give another 2 mg or 4 mg. Continue this process until withdrawal subsides. Most patients find relief on 8 mg or less, but some may require 12 mg. Schedule regular office visits to monitor lingering withdrawal symptoms in the first days—nighttime body aches and sweats are common and can be addressed by dose adjustment. Clinicians can also do "home inductions": Basically, if your patient isn't in enough withdrawal in your office, you can prescribe the buprenorphine and instruct the patient how to start it at home when enough withdrawal is being experienced, and to contact you as needed. This is safe because although opioid withdrawal is uncomfortable, it is not usually medically dangerous.

After induction and stabilization on an effective dose, you shift to the maintenance phase and can gradually reduce visit frequency, based on how well your patient does. Keep in mind that people with OUD who are at high risk for return to use but have not been recently using (eg, after release from incarceration), and are therefore not physically dependent on opioids, should be inducted and titrated more slowly and with lower doses.

Buprenorphine is usually combined with naloxone. While naloxone is an opioid blocker, it isn't active when taken sublingually or orally—only if it's snorted or injected into the bloodstream. Therefore, it's included in the buprenorphine preparations to reduce the potential for misuse.

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News of Note

FDA Approves Lucemyra—But Is It Better Than Clonidine?

On May 16, 2018, the FDA announced its approval of Lucemyra (lofexidine) as a drug to help patients withdraw from opioids. Like clonidine, lofexidine is an alpha-2 agonist, but it is touted as causing less orthostatic hypotension and therefore being somewhat safer to use.

To put this in perspective, it's important to note that buprenorphine is the preferred agent for opioid detox because of its superior treatment retention and ability to be continued as maintenance therapy. But buprenorphine is not available in many settings, such as jails or any setting that doesn't have buprenorphine-waivered physicians. Thus, clonidine remains the backbone of many opioid detox protocols. So why do we need another detox medication? The main reason seems to be lofexidine's claimed decrease in orthostatic hypotension compared with clonidine.

FDA approval was based on 2 randomized, double-blind, placebo-controlled, non-inferiority trials of 866 adults who met DSM-IV criteria for opioid dependence. Participants were physically dependent on opioids and were undergoing abrupt opioid discontinuation. The primary outcome was withdrawal symptom severity on both a clinician-rated scale (the MHOWS) and a self-rated scale (the SOWS-G). In the first study, done in 2008 and lasting 11 days, lofexidine decreased day 5 MHOWS scores (19.5) compared to placebo (30.9), p = .0019 (*Drug Alcohol Depend* 2008;97(1–2):158–168). But scores on the self-reported SOWS-G scale did not separate from placebo.

In a second study of 264 patients, completed in 2017 over 8 days, lofexidine decreased SOWS-G scores (6.32) compared to placebo (8.67), p = .0212 (Gorodetzky CW et al, *Drug Alcohol Depend* 2017;176:79–88). Retention was better for lofexidine than placebo in both studies, but did not exceed 38.2% in either study. This means over 60% of participants quit before reaching the 11- or 8-day mark, respectively.

If you prescribe lofexidine, start with 3 0.18 mg tabs every 5–6 hours during peak withdrawal, then increase to 4 tabs/dose up to a maximum of 16 tabs daily. Lower dosing is recommended for patients over 65. Lofexidine's most common adverse effects are very similar to clonidine—not surprising, since the two are close chemical relatives—and include bradycardia, hypotension, dizziness, and dry mouth. In addition, rebound hypertension can occur when the drug is withdrawn abruptly. The FDA has mandated 15 postmarketing studies, so we're likely to learn more about the side effects of lofexidine over the next few years.

CATR'S TAKE

Will lofexidine change how US doctors treat opioid withdrawal? It's hard to say. Lofexidine is not a new drug; it was developed more than 40 years ago and has been used for opioid withdrawal in the United Kingdom since 1992 (Vartak AP, *Expert Opin Drug Discov* 2014;9(11):1371–1377). It's become especially popular in the UK for ultra-rapid detox, sometimes in combination with naltrexone.

However, clonidine is inexpensive, readily available, and effective for many patients. Moreover, buprenorphine works even better for relieving opioid withdrawal and retaining patients—and best of all, it can be continued as maintenance therapy. Whatever agent you chose, it's important to remember that detox alone increases the risk of fatal overdose. Thus, treating opioid withdrawal should be followed by pharmacotherapy with buprenorphine, methadone, or extended release naltrexone.

—Joshua Sonkiss, MD. Dr. Sonkiss has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Opioid Treatment Options

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There are only a couple of practical reasons to use a buprenorphine-only product: if there is a documented allergy to naloxone, or if the patient is pregnant (to minimize exposing the developing fetus to medications, and to lower the potentially higher risk of withdrawal if the combination product is injected or snorted).

There are several available formulations of buprenorphine (see table on page 3).

A long-acting buprenorphine subdermal implant called Probuphine became available in 2016. However, it's only recommended for patients who have been stabilized on a sublingual film dose equivalent to 8/2 mg or less for 3 months. Buprenorphine implants require special provider training to prescribe and insert them into the arm, and they must be removed and replaced every 6 months. While this option may seem attractive because it avoids missed doses and lowers risk for diversion, clinical trials showed no difference in relapse rates compared to the traditional sublingual formulations (Rosenthal RN et al, *Addiction* 2013;108(12):2141–2149). Buprenorphine implants might be especially helpful for patients who travel abroad for extended periods, especially to places where access to continued buprenorphine treatment is limited.

The newest buprenorphine preparation is potentially better, and comes as a monthly extended release subcutaneous injection branded as Sublocade. Patients have to be stabilized on a transmucosal dose of another buprenorphine product for only 7 days prior to administering the injectable. Recommended induction is 2 monthly injections at 300 mg, then a maintenance dose of 100 mg each month.

Methadone

Whether first-line or not, good old methadone has a secure position in treating OUD. Consider methadone for patients who strongly prefer it, or who don't do well on buprenorphine—for example, those with more severe OUD for whom even high doses of buprenorphine don't provide enough coverage. Methadone should also be considered if observed dosing is warranted to enhance compliance and reduce the risk of diversion—though buprenorphine dosing can also be observed in a similar manner. Methadone can only be dispensed from federally regulated opioid treatment programs (OTPs). Methadone is dispensed daily to new patients, with take-home doses earned after a period of weeks to months depending on the clinic. OTPs are required to

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CE/CME Post-Test

This CME test is only available to active subscribers. Tests must be completed within a year from each issue's publication date. If your subscription expires before that date, you will not have access to the test until your subscription is renewed. To earn CME or CE credit, you must read the articles and then take the post-test at www.TheCarlatReport.com. You must answer 75% of the questions correctly to earn credit. You will be given two attempts to pass the test. As a subscriber to *CATR*, you already have a username and password to log onto www.TheCarlatReport.com. To obtain your username and password, please email info@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this month's CE/CME post-test. This page is intended as a study guide. Please complete the test online at www.carlataddictiontreatment.com. Note: Learning objectives are listed on page 1.

1. Your 35-year-old patient has been in recovery from opioid use disorder (OUD) for 6 weeks and tells you that he is feeling isolated. You recommend that he try Narcotics Anonymous (NA) to connect with a network of people who will continue to support his sobriety. Which of the following statements about NA is true? (LO #1)
   [ ] a. Approximately 10%–20% of people drop out of NA meetings within the first month
   [ ] b. People who attend bimonthly NA meetings have higher rates of sustained abstinence after 6 months
   [ ] c. NA participants who actively work through the 12 steps are more likely to have sustained abstinence greater than 1 year
   [ ] d. Men ages 35–50 who attend monthly NA meetings for 1 year benefit from greater rates of sustained abstinence than women in the same age group

2. Relapse rates in patients with OUD who are treated with the long-acting buprenorphine subdermal implant are about equal compared to those using the traditional sublingual formulations. (LO #3)
   [ ] a. True [ ] b. False

3. According to studies in buprenorphine treatment for OUD, psychosocial interventions combined with medical management (MM) show which of the following results? (LO #2)
   [ ] a. Psychosocial interventions with MM are approximately 8% more effective than MM alone
   [ ] b. Psychosocial interventions with MM are approximately 18% more effective than MM alone
   [ ] c. Psychosocial interventions with MM are only effective if patients continue both for at least 2 years
   [ ] d. Psychosocial interventions have not been shown to improve the effectiveness of basic MM

4. Your patient has had difficulty stopping opioid use for even a few days and has relapsed multiple times. Extended release naltrexone (XR-NTX) would be a good first-line medication choice for this patient's treatment. (LO #3)
   [ ] a. True [ ] b. False

5. What is NA's official stance regarding agonist treatment? (LO #1)
   [ ] a. NA does not take any official position on agonist treatment
   [ ] b. People who receive agonist treatment are encouraged to follow the 12 steps online but are barred from attending NA meetings in person
   [ ] c. People who receive agonist treatment can attend, share at, or be a speaker at meetings but should not serve as NA sponsors within their first year of attendance
   [ ] d. People who receive agonist treatment should not lead NA meetings, serve as speakers or sponsors, or hold office

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provide a package of services, including counseling. Methadone prolongs QTc, so be sure to check an electrocardiogram for patients with cardiac risk factors and limit other QTc-prolonging medications.

Extended release naltrexone (XR-NTX)

XR-NTX is administered through a monthly intramuscular injection. Oral naltrexone isn't really a viable option—people stop taking it and relapse (Minozzi S et al, *Cochrane Database Syst Rev* 2011(2):CD001333). XR-NTX has had a slew of good data, including a 2017 study showing equal effectiveness to buprenorphine/naloxone over 12 weeks (Tanum L et al, *JAMA Psychiatry* 2017;74(12):1197–1205). But getting patients on it remains a challenge, and it still is considered second-line. Patients are typically required to stop using opioids for a full week or more before taking XR-NTX, providing plenty of time to relapse before even starting the medication. A recent *Lancet* study covered in the January/February 2018 *CATR* showed that 28% of XR-NTX patients dropped out of the induction period, compared to only a 6% dropout rate during buprenorphine induction (Lee JD et al, *Lancet* 2018;391(10118):309–318). But once patients were stable on XR-NTX, relapse rates were similar between the medications. Consider XR-NTX for highly motivated patients who prefer a non-opioid medication option. And be sure to counsel them that their risk of overdose greatly increases if they stop taking it, because of the high risk of relapse in addition to loss of opioid tolerance.

Naloxone

For any patient with OUD, prescribe intranasal or injectable naloxone for potential overdose reversal. Educate

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THE CARLAT REPORT:
ADDICTION TREATMENT

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This Month's Focus:
Opioid Addiction

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patients and their loved ones about overdose risk, prevention, and identification, and about how to use naloxone and respond to an overdose. More information for prescribers as well as patients and families is available by accessing the SAMHSA website at https://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA18-4742, or the Prescribe to Prevent website at http://prescribetoprevent.org. We also refer you to our coverage of naloxone in the March/April 2016 *CATR*.

CATR VERDICT: Buprenorphine, methadone, and XR-NTX are effective medications and should be an integral part of treatment for most of our patients with OUD.

Narcotics Anonymous: What to Tell Your Patients

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or Secular Organizations for Sobriety (SOS) (http://www.sossobriety.org). For more information on alternatives to 12-step programs, see the June/July 2017 *CATR*.

CATR VERDICT: NA is a free and widely available recovery fellowship, but it has a hard-line philosophy that may pressure patients to come off buprenorphine and methadone. Refer patients to groups that welcome people on OUD meds, whether they are NA groups that have an accepting attitude toward meds, AA groups, or increasingly widespread alternatives.