THE CARLAT REPORT
ADDICTION TREATMENT

A CE/CME Publication

CURRENT COVERAGE OF TOPICS IN ADDICTION MEDICINE

Daniel Carlat, MD
Editor-in-Chief

Volume 4, Number 2&3
March/April 2016
www.carlataddictiontreatment.com

IN THIS ISSUE

Focus of the Month:
Opiate Addiction

Learning Objectives

After reading these articles, you should be able to:

1. Identify the benefits of using a harm reduction approach and distributing naloxone directly to people that are addicted to opioids.
2. Describe the process of buprenorphine induction.
3. List the advantages of some of the main agents used in medication-assisted treatment for opioid addiction.

How to Treat Opiate Use Disorders

Michael Weaver, MD, FASAM. Dr. Weaver is a professor and medical director at the Center for Neurobehavioral Research on Addictions at the University of Texas Medical School.

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

Summary

- Successfully using motivational interviewing techniques during an evaluation can help patients move beyond denial and acknowledge opioid misuse problems.
- Medication-assisted treatment for patients misusing opioids can be used on an outpatient or inpatient basis.
- Buprenorphine (alone or in combination with naloxone) and methadone are the most commonly used medications for opioid addiction treatment.

Opiate use disorder is increasingly common, and it is important to develop a systematic approach for treating it. In this article, I will discuss some of the more important elements of treatment, starting with the need to address patients' denial and moving on to some of the nitty gritty aspects of medication-assisted treatment.

Continued on page 2

Q&A With the Expert

Naloxone and the Harm Reduction Approach

Eliza Wheeler, MA, MS

DOPE (Drug Overdose Prevention Education) project manager, San Francisco Bay Area

Ms. Wheeler has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CATR: What does harm reduction mean?
Eliza Wheeler: Harm reduction is a model for practicing public health that seeks to provide services in a nonjudgmental way. It seeks behavior change while acknowledging the need to meet a person where they are—especially in their particular journey through substance use. Abstinence is not a prerequisite for treatment or a condition that someone must meet to receive services.

CATR: Is this a fairly new model?
Eliza Wheeler: Not really. It was developed in Europe and started to take root in the U.S. in the mid- to late '80s. This was during the early days of hepatitis and HIV transmission when it was identified that those diseases were transmitted through the sharing of injection equipment. You had the old model, which was, "Everyone stop using injection drugs. You're going to get HIV." That was ineffective, because people don't just stop using drugs because they are told to.

CATR: Right. So what happened?
Eliza Wheeler: Early harm reduction activists, who were primarily drug users, public health workers, and people affected by HIV/AIDS, realized that there had to be a

Continued on page 4

How to Treat Opiate Use Disorders

Continued from page 1

Acknowledging the problem

In asking patients about their opiate use, I have encountered many forms of denial. Here are two of the more common ones.

"My problem isn't very serious."

Even people who acknowledge that they have a problem are very good at compartmentalizing—using both ambivalence and denial. They may say, "Well, I just need help with the physical part of my addiction. If I could do a quick detox I'd be fine. I don't need to do anything else beyond that." But in fact, most patients are unlikely to be successful without other support and will quickly relapse.

"I don't have a drug problem, I just use it sometimes to deal with stress."

Self-medicating is very common. People will use what they have at hand to self-treat their depression or anxiety symptoms without recognizing they are doing so. They may use their Vicodin in the same way others would "drown their sorrows" in alcohol.

Motivational interviewing

I often use motivational interviewing techniques during my initial evaluations (for details on the approach, see our interview with Dr. William Miller in *CATR,* October 2014). I start by helping people to recognize that there might be a problem. This usually involves helping them to see the discrepancy between where they are now and where they would like to be. Then I help them understand some of the things that they can work on to successfully achieve their goals.

One of the main challenges is to help people acknowledge what sort of pain they are using the drugs to address—physical pain, emotional pain, or both. Patients commonly end up abusing opiates after having received a narcotic prescription for a pain issue and then continuing to use it for other reasons. I try to help them recognize that there's a difference between emotional pain and physical pain. The medication may temporarily alleviate some symptoms of both of those things, but there are also negative aspects of using an opioid this way, and I help them to think this through.

Some patients readily admit that they use an opiate daily for emotional issues. If so, I might respond with, "Is this strategy giving you the kind of emotional stability that you want? After all, there are other ways to get through tough days. Have you really considered the potential consequences, including to your health, legal issues, and how others would perceive you for doing this sort of thing?" This will often lead to a discussion of alternative treatments, like counseling or psychiatric medications.

People often overestimate how much control they have over their use of opiates. Things may appear relatively stable from their point of view, but something unexpected may happen, causing more stress, and they escalate their use temporarily—only to realize they can't reduce their dose back to what they were taking before. And if they keep increasing the dose, tolerance and withdrawal symptoms appear. Such symptoms may drive people to do more egregious things to obtain their fix, and they may start to recognize that this is not how they want to live their lives.

Treatment

Effective treatment of any substance use disorder involves psychosocial interventions at the least, often with the addition of medication-assisted treatment. In this section, I'll focus on how to use medications such as methadone and buprenorphine to help your patients who are abusing opioids.

Detox

While we often think of detox as a short-term process, the official federal definition allows for up to a 6-month taper. Such a long detox can often be done on an outpatient basis. Some patients will opt for detox, while others will do better with maintenance treatment (defined as staying on a prescribed opiate for greater than 6 months). Some patients require inpatient detox, and the American Society of Addiction Medicine (ASAM) criteriacan help clinicians make that decision (see *CATR,* November 2015 for an entire issue explaining the ASAM criteria). In general, inpatient detox works best for patients with more severe addictions, those with psychiatric or medical issues, and those with challenging psychosocial situations, like homelessness and/or continued availability of substances at home.

Continued on page 3

How to Treat Opiate Use Disorders

Continued from page 2

Outpatient tapering

Some patients are able to gradually taper down their use of oral opioids without a specific detox protocol. For the most part, these are patients who have been able to obtain the medications legitimately. For example, patients may have started taking opioids because of some dental work, but later found that they became dependent, first psychologically then physically. They may have been obtaining it by going to multiple providers or perhaps one provider has continued to provide refills. In this context, it would be reasonable to try a therapeutic taper. In my experience, the taper will be most successful if you taper more slowly both at the beginning and at the end. For example, if a patient has become dependent on taking 8 to 10 Vicodin per day, you might reduce the dose by a half pill every few days initially, speed up the taper to a full pill per unit time, and then slow it back down to a half or a quarter pill at the end.

Switching to methadone as a tapering strategy

Another option is to switch your patient to a different opiate before doing the taper. One reason to do this is to interrupt the positive associations a patient might have made with a particular drug. In addition, switching to a longer-acting drug makes for less frequent dosing. The fewer daily choices people have between taking or not taking something, the more successful they'll be in following a tapering schedule. For example, one approach is to switch a patient from Vicodin to methadone, which has advantages because it is inexpensive, longer acting, and produces less euphoria than many of the other opioids. Not every pharmacy carries it, but many do, and it comes in a variety of forms, including liquid as well as tablets of different strengths.

Contrary to popular belief, you do not have to be part of a federally licensed treatment center to prescribe methadone. Any provider with a DEA license to prescribe Schedule II substances can prescribe methadone—as long as you are clear in your documentation that you are prescribing it for pain rather than for treatment of narcotic abuse. However, if the patient's opiate use is not related to pain, you will need to either refer to a narcotic treatment program for methadone maintenance or to a buprenorphine provider for office-based opioid treatment.

Conversion tables are available to help you determine the right dose of methadone to use when transitioning from opioids like hydrocodone or oxycodone. For example, see the Methadone Conversion and Dosing Information table online at http://www.iadur.org/sites/default/files/ghs-files/methadone-dosing.pdf.

Continued on page 6

Opiate Addiction Treatment: Some Helpful Online Resources

Resource	Description	Website
Providers' Clinical Support System for Medication Assisted Treatment	Free resource focusing on education and training of medical professionals on opioid misuse, including topics in medication-assisted treatment	http://pcssmat.org/
Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction	Consensus- and evidence-based best-practice guidelines about the use of buprenorphine to treat opioid addiction, with information on assessment and detailed protocols	http://buprenorphine.samhsa.gov/Bup_Guidelines.pdf
Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs	Best-practice training manual for counselors and clinical staff to understand and implement medication-assisted treatment of opioid addiction	http://buprenorphine.samhsa.gov/tip43_curriculum.pdf
Opioid Treatment Program Directory	Helps you to locate opioid treatment programs in your state	http://dpt2.samhsa.gov/treatment/directory.aspx
Buprenorphine Treatment Physician Locator	Helps you to locate clinicians authorized to treat opioid dependency with buprenorphine	www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator
Medication-Assisted Treatment website	Medication-assisted treatment directory of opioid-related resources and publications	http://www.samhsa.gov/medication-assisted-treatment

Expert Interview
Continued from page 1

different way to approach the issue. That's how the early interventions like syringe exchange were created, out of that idea that people are going to inject drugs, so what can we do that's more common sense and health focused. Providing an environment that at least provides safe injection equipment, along with education, support, and access to treatment makes sense. Since then, harm reduction has been integrated into many different public health programs. Methadone and Suboxone programs are examples.

CATR: You mention harm reduction as a less judgmental approach. How does it improve upon the traditional doctor/patient, client/provider relationship roles?

Eliza Wheeler: At its core, harm reduction deconstructs the power dynamics: this idea that doctors and case managers and clinicians know better about what other people are supposed to do, and that they have the power to get people to "stop doing" something that's bad for them. Harm reduction is a different orientation in which the people who are accessing services are the experts of their own lives and the providers are more like a conduit—people that can provide information and access to services for that person to engage at their own pace.

CATR: Let's talk more specifically about syringe exchange programs. How do they work?

Eliza Wheeler: We provide people a place to dispose of their dirty syringes and pick up clean ones. While it is legal in most places for people to purchase clean syringes over the counter at pharmacies, many people don't have enough money, or they fear the stigma they'll face in approaching a pharmacy. Also, some pharmacies refuse to participate despite the legality. Even if they do, they're not going to provide any harm reduction information or treatment services.

CATR: And most of these places provide other services in addition to syringe exchange?

Eliza Wheeler: Absolutely. They do HIV and hepatitis testing; some programs provide case management, therapists, wound care doctors—it depends on the program and the funding and how established they are. Some of the oldest studies of syringe exchange show that drug users who engaged in syringe exchanges were significantly more likely to actually access treatment than people who weren't engaged in syringe exchange. Because of the ongoing contact they had with a person and with a program that worked with them, users were able to progress through the stages of behavior that led directly to recovery in some cases.

CATR: How successful are syringe exchange programs?

Eliza Wheeler: Syringe exchange programs reduce the spread of communicable disease among users and the community. They are the only evidence-based intervention that reduces the spread of HIV and hepatitis among injection drug users [Ed. Note: An excellent summary of this evidence is available at http://goo.gl/f5QPSI].

CATR: I understand that syringe exchange programs also provide naloxone, an opiate antagonist used to reverse opiate overdoses. I think many physicians, myself included, originally thought of naloxone as being something that only ER doctors or first responders would use. Tell us a little bit about the evolution of distributing naloxone directly to lay people.

Eliza Wheeler: For as long as there has been drug use, drug users have been developing methods of trying to save whoever it is that they're with when they're using. There are street methods that are passed along from person to person throughout drug-using communities. They are well intentioned but not always the most effective ways, like throwing people in showers and injecting them with stimulants or putting ice on them. But naloxone actually works, so it makes sense to provide it to drug users themselves, who are most likely to be the very first responders to an overdose. They are the people who are with each other when they're using drugs.

CATR: And people have been able to use naloxone successfully?

Eliza Wheeler: Yes. We have almost 20 years of experience distributing naloxone to lay people—mostly drug users—in various programs throughout the country. In an *MMWR* study I participated in, we reported that these programs have trained over 150,000 people and received about 26,000 reports of overdose reversals (Wheeler EJ et al, *MMWR Morb Mortal Wkly Rep* 2015;64(23);631–635).

CATR: In your study, did you determine who was most likely to administer the naloxone?

Eliza Wheeler: Yes, we found that 83% of reversals were administered by people who used drugs, and about 9% were from non-drug using friends and family.

CATR: So the bottom line is that naloxone should definitely be given to drug users. Were these primarily injectable versions of naloxone?

Eliza Wheeler: Yes, and currently the majority of programs nationally are still distributing the low-cost injectable naloxone.

CATR: But I assume the landscape is changing now, with the introduction of easier-to-use versions of Narcan.

Eliza Wheeler: Yes, it's all shifting. The Evzio product is an auto-injector that makes it very easy for lay people to inject, and it has been out now for about two years. We distribute that as well as the regular vial and syringe injectable naloxone. We used to

Continued on page 5

Expert Interview

Continued from page 4

distribute the off-label, adapted device but had to phase it out when the manufacturer doubled the price, and we probably won't be able to give out the recently approved Narcan nasal spray either because of cost. Most distribution programs are operating on fixed amounts of money from grants or private donations, so we are pretty bound by wholesale distribution costs of naloxone.

CATR: So if I have a patient who I believe would benefit from naloxone, cost-wise am I better off writing a prescription or sending them to a program?

Eliza Wheeler: If the patient has insurance, you can write a prescription and have them go fill it at the pharmacy, and their insurance will cover the cost. Also, with third party prescribing, which is legal in most states, a person can get naloxone for a family member or friend if that person is at risk for opioid overdose. Legal info can be found on your specific state at the Public Health Law Research website (http://www.lawatlas.org/query?dataset=laws-regulating-administration-of-naloxone). In addition, there are many states that now don't require a prescription in order to dispense naloxone at a pharmacy. You can check the most recent legislation for your state on the same Website mentioned above. Alternatively, you can check your city or state's Department of Public Health website. You'll find information about syringe exchanges and drop-in centers, places like that. The North American Syringe Exchange Network also provides a directory of syringe exchange programs that can be searched by state (https://nasen.org/directory/). Then there's the distribution programs, the HIV prevention programs; they're the full-service harm reduction programs.

"At its core, harm reduction deconstructs the power dynamics: this idea that doctors and case managers and clinicians know better about what other people are supposed to do, and that they have the power to get people to 'stop doing' something that's bad for them."

Eliza Wheeler, MA, MS

CATR: Is the process easy?

Eliza Wheeler: Yes. The patient fills out a little bit of paperwork and then sits with somebody to learn how to use the drug; the training takes about 5–10 minutes.

CATR: One of the interesting questions for prescribers is how often we should be prescribing naloxone. Clearly, opiate overdoses are a growing threat, and some unknown percentage of our patients are using or abusing opiates in one form or another. How wide of a net should we be casting on our patients in terms of prescriptions for naloxone?

Eliza Wheeler: It is a tricky issue. According to the National Center for Health Statistics for the Center for Disease Control and Prevention, in 2014, the most recent year for which we have figures, there were over 47,000 deaths from drug overdoses in the U.S., over 29,000 of which were opioid related (http://goo.gl/TbD8BF). This includes heroin, but the majority were due to prescription opioids of various types. There are millions of people taking prescription opioids; in 2012, 259 million prescriptions for opioid painkillers were written, more than enough for each American adult to have their own bottle of pills (http://www.cdc.gov/vitalsigns/opioid-prescribing). So a relatively small proportion of those people who take prescription opioids die from overdose, whereas a relatively large proportion of heroin users die from overdose. This means that prescribing naloxone to heroin users is important, but it's not as clear that providing every prescription opioid user with naloxone will make a significant impact or be cost-effective. However, there are problems with trying to determine who should or should not receive naloxone. We are learning as we go with this intervention in terms of offering it to prescription drug users.

CATR: And often, we see patients who are substance abusers and may deny opioid use, yet we don't know if we can believe them. We might be tempted to prescribe all of them naloxone, just in case.

Eliza Wheeler: Right, and there are risk matrices available to help prescribers decide which patients are most at risk for overdose. They include factors like whether patients are on benzodiazepines and/or alcohol, whether they have chronic pain, chronic obstructive pulmonary disease, liver issues, and so on (See our table "Risk Factors for Opioid Overdose" on page 10). Depending on these variables, the matrices estimate the probability that the patient might overdose. Here in San Francisco, all of our Department of Public Health medical clinics prescribe naloxone to anyone who's on chronic pain management with opioids. So if you are on an ongoing prescription of opioids, for any reason, you get a naloxone prescription.

CATR: Regardless of whether the patient is a drug abuser?

Eliza Wheeler: Yes, because they've found that that was the best way to go about it—focus on risky drugs rather than risky people, which removes the hyper focus on patients who are "badly behaved" in terms of their opiate use. So the clinicians here started offering a discussion on opiate safety to all chronic opioid users and stopped calling it overdose prevention.

CATR: How did this change in language improve matters?

Eliza Wheeler: It changed the conversation, because you'd have these chronic pain patients on prescription opioids, some of whom were using their meds in risky ways, taking benzodiazepines and/or drinking. But generally they did not consider

Continued on page 10

How to Treat Opiate Use Disorders
Continued from page 3

On a cautionary note, since methadone is long-acting, patients may not notice the effects as quickly as they are used to, and might be tempted to take extra doses initially. The danger is that these doses can catch up to them all at once, and people may accidentally overdose on methadone because of their inexperience in using it.

Buprenorphine for maintenance or detox treatment

Buprenorphine is a semisynthetic opioid that has been available as a narcotic since 1981. It has long been used as an option for treating severe pain and comes in different forms, including injectable, sublingual, and as a skin patch.

How did buprenorphine end up playing such a central role in treating opiate abuse? Unlike all other opiate products such as codeine, hydrocodone, oxycodone, methadone, and even heroin, buprenorphine is an opioid agonist/antagonist. The agonist property activates opioid receptors, while the antagonist property tends to modulate that activation. For this reason, the medication helps patients feel normal rather than high.

The bottom line is that buprenorphine, with its push/pull agonist/antagonist properties, is less likely to be abused than its opiate cousins. This in itself makes it a good choice for maintenance treatment. The buprenorphine mono product (without naloxone, brand name Subutex) has been generic for a few years and is relatively cheap; some insurance companies have it on their preferred formulary list. For some addiction specialists, plain old buprenorphine is the treatment of choice for opiate maintenance or detox.

In order to be able to prescribe buprenorphine (with or without naloxone), you need a waiver from the Department of Health and Human Services—a system that was established as part of the Drug Addiction Treatment Act of 2000 (DATA2000). To obtain this waiver, you need to go through an 8-hour training, which will enable you to prescribe buprenorphine to up to 30 patients in the first year and as many as 100 patients in the second year. New federal legislation will soon allow for treatment of up to 200 patients after the second year.

Buprenorphine is a Schedule III controlled substance, so it's less restricted than methadone (which is Schedule II). Patients can get a one-month prescription from a buprenorphine provider with up to 5 refills, although most experts recommend at least monthly visits. One of the reasons buprenorphine is less restricted is because of its safety profile—as an opioid agonist/antagonist, it's more difficult to overdose on buprenorphine than it is on methadone.

Buprenorphine/naloxone

Given that buprenorphine alone is an effective treatment for opioid addiction, why did drug makers create Suboxone, the combination of buprenorphine and naloxone? Wouldn't naloxone—an opiate blocker used to reverse opioid overdoses—neutralize buprenorphine's effectiveness, rendering it useless as a treatment? Not if it's taken sublingually, as directed. When buprenorphine is absorbed through the mouth's mucosal lining, it works fine—but naloxone is then inactivated. But if you choose to grind the combination pill and dissolve in saline to inject it, the naloxone is very much active, and will prevent you from getting high. So naloxone was added to reduce the potential for abuse by injection.

How to start patients on buprenorphine: Induction

Induction refers to the somewhat complicated process of starting an opioid-dependent patient on buprenorphine (by "buprenorphine" I am referring to any of the preparations, whether mono or combined with naloxone). It can be done in an outpatient setting, and the process usually takes 1–2 days.

I start by emphasizing to patients that they should not use opioids for about 24 hours before presenting for induction—otherwise the first dose will cause an unpleasant withdrawal experience. For those of you who need a review, the early symptoms of opiate withdrawal are anxiety, craving, nausea, aches in the lower back areas and legs, some muscle cramps, and possibly some diarrhea. Later, it gets progressively worse to the point where patients have a runny nose, watery eyes, intestinal cramps, vomiting, muscle twitches, and the famous "cold turkey" goose flesh.

Once they're in the early stage of withdrawal, start with low doses of buprenorphine, 2–4 mg, and then every hour or two give them additional doses until they're comfortable. I check on patients every hour or so. We have a waiting room with wi-fi, a DVD player, and magazines, and I tell them, "You're going to be hanging out for a while. There's a bathroom very close by." Medical personnel, myself or my nurse, are checking on them regularly, and they can get someone's attention right away.

After the second dose, most people are feeling much better physically, so then it's just a matter of titrating up to where they feel comfortable without "feeling like a zombie"—in other words, too sedated.

Depending on their tolerance, typical doses are between 12 and 16 mg a day. Some people do fine with 10 mg, while some people need more like 20 mg; it just depends on individual tolerance. If they're feeling sleepy or a little lightheaded, stop dosing wherever they are. I've seen a lot of variability in dosing needs. Someone who has been using 8 or 10 Vicodin a day may get by with 8 mg of buprenorphine. But the patient who is injecting a fair amount of heroin multiple times a day may require

Continued on page 7

How to Treat Opiate Use Disorders
Continued from page 6

up to 16 mg or more that first day.

At the end of the first day of induction, I make sure patients have someone who can drive them home. I will usually give them a prescription to pick up a small amount of buprenorphine at the pharmacy. If they absolutely need it, they can take a dose at home. They will rarely actually need it because buprenorphine is long-acting, and once you get the initial dose up during the course of a day, the cumulative effects will get them through at least the next 12 hours or so.

The next morning, the patients come back and we pick up where we left off the day before. I give them the first day's dose all at once to start with and make sure they can tolerate it, and then if necessary go up from there. It usually takes us two days to find the right dose, but occasionally it takes longer.

The maximum recommended dose of buprenorphine or buprenorphine/naloxone is 32 mg per day. Due to the agonist/antagonist properties of the drug, doses higher than 32 mg may start to cause some opioid withdrawal symptoms, which is known as the "ceiling effect." Patients who have been using high doses of opioids, either prescription opioid analgesics or heroin, may need a higher overall opioid dose than can be provided with buprenorphine due to this effect. In that case, these patients would benefit more from methadone maintenance because methadone does not have a ceiling effect. There's no set upper limit for methadone—the final maintenance dose is based on tolerance and can be affected by other medications that enhance methadone metabolism (such as some of the antiretroviral medications to treat HIV).

After the induction, I will generally see patients weekly, which allows me to make more dosage adjustments as needed. I will increase the dose if there are still cravings and withdrawal symptoms, or reduce it if there are opioid side effects, such as constipation or oversedation.

Life after induction

Maintenance vs. tapering

Once we have arrived at a stable dose of buprenorphine, I begin talking to patients about how long they will need to stay on it. Some people need more time on the medication—many months to years—because of the severity of their addiction and the harsh consequences of relapse. Having such patients on a maintenance dose for many months allows them time to work on the behavioral components that they are learning in therapy or in 12 step programs.

On the other hand, other patients don't have as severe a problem with opiates, and if they have good social supports, they might be ready for a taper fairly soon after they start. The taper is fairly straightforward. The smallest dosage strength is 2 mg, and people can cut pills or strips in half and taper down in 1-mg increments. I'll have them decrease the dose anywhere from every few days to every few weeks depending on the time available and the patient's physical and psychological comfort level. A typical outpatient taper will take around 2 months, and this time can be lengthened depending on the patient's readiness and starting dose.

Psychosocial interventions

In addition to prescribing medication, I make sure that my patients are engaged in some kind of psychosocial intervention. This might be individual counseling, a group program, or involvement with a 12 step self-help group. I want them to be working on relapse prevention skills, coping skills, and refusal skills. And in their home environment, I encourage them to rally as much support as possible from family and friends who are not using drugs.

Psychiatric medications for other symptoms

Antidepressants and other medications for anxiety can be very helpful in supporting recovery, and just about any of the SSRIs and SNRIs are appropriate. Both gabapentin and hydroxyzine are effective anti-anxiety medications that are not controlled substances. For insomnia, there are medications like trazodone.

Benzodiazepines are not ideal for these patients. For one, they can produce a high that may lead to craving and relapse to opiates. In addition, it's hard to overdose on buprenorphine alone, the combination of buprenorphine and benzodiazepines can more readily lead to overdose. It's important to let patients know about this risk.

Typical causes of failure of buprenorphine treatment

Lack of support

Lack of good support in the immediate home environment is a big reason why patients may have significant problems remaining abstinent. They need to have family or close non-using friends for encouragement and to help them deal with the emotional and physical ups and downs of being in early recovery.

Using other drugs

Some people don't want to give up their marijuana or their alcohol, which is another reason for relapse back to opioids. I do random drug testing, and I let people know that the goal is going to be abstinence from all the substances that could cause problems.

Even though maintenance methadone or buprenorphine only target withdrawal from and cravings for opioids as a class, most people will also reduce their intake of other drugs of abuse. This is because the behavioral components of the recovery program are universal, not specific to opioids.

Continued on page 9

Agents Used in Medication-Assisted Treatment (MAT) for Opioid Addiction			
Generic Name (Brand Name) Year FDA Approved (Rx status) ***[G] denotes generic availability***	**Formulation and Available Strengths (mg)**	**Usual Dosage Range (mg)**	**Advantages/Disadvantages**
Buprenorphine (formerly Subutex) [G] 2002 (C-III)	Sublingual tablets: 2, 8	4–24 QD	Advantages: Original mono version; has a long track record; very inexpensive. Many experts find it to be just as effective as agents that include naloxone. Disadvantage: Since it does not contain naloxone, can be ground up and injected.
Buprenorphine and naloxone [G] 2002 (C-III)	Sublingual tablets: Bup 2/Nx 0.5, 8/2	4–24 QD	Advantages: First combination buprenorphine/naloxone agent. Long track record; inexpensive. Disadvantage: Some complain about the taste.
Buprenorphine and naloxone (Suboxone) [G] 2010 (C-III)	Sublingual strips: Bup 2/Nx 0.5, 4/1, 8/2, 12/3	4–24 QD	Advantages: 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. Disadvantages: More diversion potential because you can easily mail the strips; relatively high cost.
Buprenorphine and naloxone (Bunavail) 2014 (C-III)	Buccal film: Bup 2.1/Nx 0.3, 4.2/0.7, 6.3/1	2.1–12.6 QD	Advantages: High bioavailability, fast absorption, less constipation; more convenient than other preparations because it sticks to the cheek while dissolving, allowing patients to talk. Disadvantages: Very high cost; may be more difficult to cut than Suboxone film, because cutting may decrease its sticking ability to cheek mucosa.
Buprenorphine and naloxone (Zubsolv) 2013 (C-III)	Sublingual tablets: Bup 1.4/Nx 0.36, 2.9/0.71, 5.7/1.4, 8.6/2.1, 11.4/2.9	2.9–17.2 QD	Advantages: Menthol flavor; higher bioavailability than generics. Disadvantage: Higher cost than generics.
Methadone [G] (Dolophine, Methadose) 1947 (C-II)	Oral tablets: 5, 10, 40 Oral liquid: 10 mg/mL, 10 mg/5 mL, 5 mg/5 mL	20–120 QD	Advantages: Long track record; daily dosing requirement may be good for those needing closer supervision. Disadvantages: Daily dosing is inconvenient for those with job or family duties; many drug interactions; high risk of respiratory depression.
Naltrexone ER (Vivitrol) 2006 (Rx)	IM injection: 380	380 Q 4wk	Advantages: Monthly injection decreases worries about compliance; beneficial for alcohol use disorder. Disadvantages: Shot can be painful; patients may not return for repeat injections; patients must go through longer period of withdrawal before starting treatment.

Buprenorphine/naloxone products are not bioequivalent. Comparable doses: 2mg/0.5 mg SL strip = 1.4 mg/0.36 mg SL tab; 4 mg/1 mg SL strip = 2.1 mg/0.3 mg buccal film; 8 mg/2mg SL strip = 4.2 mg/0.7 mg buccal film or 5.7 mg/1.4 mg SL tab; 12 mg/3 mg SL strip = 6.3 mg/1 mg buccal film

How to Treat Opiate Use Disorders

Continued from page 7

How to choose among the different formulations of buprenorphine

There are several different formulations of buprenorphine available (see our table, "Agents Used in Medication-Assisted Treatment (MAT) for Opioid Addiction, on page 8). Suboxone is the most common combination product and the only one that is FDA approved for induction. It was originally available in sublingual tablets, and now it's available as strips or films, which are also sublingual. There's also a different brand name of tablet (Zubsolv), which is a more bioavailable form of buprenorphine. Higher bioavailability means that a larger fraction of the drug is absorbed, which in turn allows for a lower number of milligrams to achieve the same effect. A more recent alternative is Bunavail, a buccal film that is also highly bioavailable and which dissolves on the inside of the cheek as opposed to under the tongue.

The main factor influencing the choice of formulation tends to be what the patient's insurance policy covers. Some companies simply cover the cheapest product—which is the generic mono product, buprenorphine without naloxone. Other companies will preferentially cover the combination product, typically the Suboxone strips.

In general, I favor the combination product over the mono product, in part because it is more available in pharmacies. Some patients and their families request the combination because they believe having the naloxone adds a measure of safety, although in my experience the scenario the naloxone is meant to prevent (injection abuse) is rarely a concern. The mono product should always be used, however, for pregnant women in order to reduce exposure to medications overall, including naloxone.

Among the combination formulations, Suboxone has been around the longest and is most familiar to patients. The strips tend to be more easily dissolvable than the former Suboxone tablets, which are no longer marketed. It takes about 5 minutes to dissolve under the tongue, and during that time, the patient shouldn't talk or swallow (not a fun way to start the day).

The mono buprenorphine tablets take at least 5 minutes to dissolve, and it can take longer if you need two or more tablets. I tell my patients to rinse their mouth out really thoroughly, and then to get it nice and moist before putting the tablet under the tongue, because that will help everything to dissolve.

The Bunavail product is the most recent one to come to market. The claim is that it dissolves the fastest and allows you to talk and eat with the patch on the inside of your cheek.

For each strength of Suboxone film, there is an equivalent strength Zubsolv tablet or Bunavail buccal film, but the equivalent strength does not mean the same number of milligrams of buprenorphine/naloxone due to differences in bioavailability between the different products. The conversion charts tell practitioners what dose of Zubsolv or Bunavail to use for a known dose of Suboxone being taken by your patient. That helps to reduce confusion.

Vivitrol

Vivitrol is a long-acting injectable form of naltrexone, which like naloxone is an opiate receptor blocker. Before an injection with Vivitrol, people have to abstain from opioids for at least several days, preferably about one week. You may have to do a detox with methadone or buprenorphine to get patients off their preferred opiates, and then have them stop for a few days. The injections are every 4 weeks, and they can't be done at home. They are deep gluteal intramuscular injections, and the manufacturer sends kits to the physician's office. You don't need any special licensing to administer it; any psychiatrist or primary care practitioner can do it in the office.

Vivitrol is certainly effective to extinguish opioid use, but the potential problem is that people may not show up for subsequent injections. In a psychiatric setting, giving someone who has a dual diagnosis an injection can give both the provider and the patient some peace of mind for a while, so that can be a part of discharge planning.

Conclusion

While the opiate epidemic is serious, we have some excellent tools for helping patients decrease their use of the more dangerous drugs, and in some cases patients can successfully end their opiate use completely. According to the latest follow-up studies, buprenorphine retention rates at 1 year are around 60%–66% (Fiellin et al, *N Engl J Med* 2006;355:365–374). As far as methadone maintenance, those rates are as high as 80%, according to one recent study (Hser YI et al, *Addiction* 2014;109(1):79–87). Medication-assisted treatment for opiate addiction works and should be part of our therapeutic repertoire.

❖ ❖ ❖

Expert Interview

Continued from page 5

themselves to be drug addicts. So when their providers said to them, "We're going to talk to you about overdose prevention and prescribe you Narcan," these people would get angry and say, "What are you accusing me of?" So clinicians shifted the conversation to opioid safety and started saying, "We've started this new initiative where we talk to all our patients that take opioids about safety, and one of the safety things that we do is that we provide you the antidote if you stop breathing or have trouble breathing from your medications. You can pick it up at the pharmacy along with your prescription for your opioid medication." And instead of being resistant, people were more likely to respond, "Great. Thanks for the information." They felt taken care of vs. judged.

CATR: So how would we apply this approach in our psychiatric practices? Let's say I have a patient to whom I'm prescribing a benzodiazepine and I know that in the past this person has used prescription opiates.

Eliza Wheeler: Just say, "You might be prescribed opiate drugs like Vicodin or Percocet, and I'm wondering if you know about some of the risks of mixing these types of drugs. I'm concerned about that interaction, and there's a medication I want to show you how to use; it's really easy. I'd like to have you keep it on hand or have a friend keep it on hand or know how to use it in case you ever have trouble breathing from the mixture of medications." Something like that. Keep it focused on the medications.

CATR: That non-judgmental, harm reduction approach is certainly something most psychiatrists are used to, so I think it's an easy strategy to adopt.

Eliza Wheeler: It's interesting to see how much more positively people react when you de-emphasize the term "overdose." People associate overdose with people who inject heroin, and they don't associate it with the more common scenario, which is the person who drinks and takes a bunch of Vicodin. In these cases, the respiration slows, the heart rate slows, respiratory failure occurs, and the heart stops. That's a much more common kind of overdose death than the proverbial heroin user who is found with a needle sticking in the arm.

CATR: And I could imagine that this information might be surprising to some of my patients. They might be thinking that they have a small but manageable problem. They take a couple of Vicodin a day and they have a few drinks. They may not realize that on a given day they might drink a little too much and they take a couple of extra Vicodin, and that might be enough to tip them over the edge into an overdose.

Eliza Wheeler: Absolutely. These less threatening conversations can also open up a larger discussion about the use of opiates in general, and can keep people more engaged in treatment.

CATR: Are there any good training resources for readers who might want to learn more about this approach?

Eliza Wheeler: Yes, there is the Prescribe to Prevent website (www.prescribetoprevent.org), which has some training videos and links to webinars to help providers learn about these discussions, and there is practical information on exactly how to write the prescriptions for naloxone, and scripts to help you tell the patients how to use the drug if needed.

CATR: Thank you for all of this helpful information, Ms. Wheeler.

Risk Factors for Opioid Overdose

Research has shown that the following patient characteristics are associated with an increased risk of eventual opioid overdose.

1. Substance abuse, dependence, and/or addiction
2. A history of accidental exposure and unintentional opioid misuse (includes members of a patient's household who may discover and use the prescribed opioid inappropriately)
3. A morphine equivalent dose (MED) ≥20 mg per day
4. Switching to another opioid
5. Chronic obstructive pulmonary disease
6. Sleep apnea
7. Asthma
8. Chronic kidney and/or liver impairment
9. Use of CNS depressants, including benzodiazepines and alcohol
10. Use of certain medications for depression, including monoamine oxidase inhibitors (MAOIs)

CE/CME Post-Test

To earn CE or CME credit, you must read the articles and log on to www.CarlatAddictionTreatment.com to take the post-test. You must answer at least four questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be taken by April 30, 2017. As a subscriber to *CATR,* you already have a username and password to log on www.CarlatAddictionTreatment.com. To obtain your username and password or if you cannot take the test online, please email info@thecarlatreport.com or call 978-499-0583.

The Carlat CME Institute is approved by the American Psychological Association to sponsor continuing education for psychologists. Carlat CME Institute is also accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Carlat CME Institute maintains responsibility for this program and its content. Carlat CME Institute designates this enduring material educational activity for a maximum of two (2) *AMA PRA Category 1 Credit*™ or 2 CE for psychologists. Physicians or psychologists should claim credit commensurate only with the extent of their participation in the activity.

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. Naloxone reverses the effects of all of the following drugs except: (Learning Objective #1)
   - [ ] a. Prescription opioids
   - [ ] b. Benzodiazepines
   - [ ] c. Heroin
   - [ ] d. Methadone

2. Buprenorphine without naloxone is preferable to the combination product for which of the following clinical situations? (LO #2)
   - [ ] a. High opioid maintenance dose requirements
   - [ ] b. Pregnancy
   - [ ] c. Suspected buprenorphine diversion
   - [ ] d. Hepatitis C virus positive

3. It is legal in the U.S. to prescribe naloxone to a patient that is an established opioid user. (LO #1)
   - [ ] a. True
   - [ ] b. False

4. The process of induction onto buprenorphine is best started in which of the following situations? (LO #2)
   - [ ] a. The patient has just taken a small dose of a prescription opiate
   - [ ] b. Only after the patient has been taking an antidepressant for one week
   - [ ] c. The patient has just begun to notice opioid withdrawal symptoms
   - [ ] d. In intensive care unit settings

5. Naloxone has been distributed to drug users in the U.S. since which year? (LO #1)
   - [ ] a. 2010
   - [ ] b. 1996
   - [ ] c. 2016
   - [ ] d. 2001

6. What is the main disadvantage of buprenorphine without naloxone? (LO #3)
   - [ ] a. Taste
   - [ ] b. High cost
   - [ ] c. Can be ground up and injected
   - [ ] d. Long withdrawal necessary before treatment

7. Which group is the primary recipient of naloxone distribution programs? (LO #1)
   - [ ] a. Parents of drug users
   - [ ] b. Law enforcement
   - [ ] c. Drug users
   - [ ] d. Service providers and other professionals (shelter workers, treatment programs staff)

8. Bunavail is a form of buprenorphine/naloxone that dissolves very quickly with sublingual administration. (LO #2)
   - [ ] a. True
   - [ ] b. False

PLEASE NOTE: WE CAN AWARD CE/CME CREDIT ONLY TO PAID SUBSCRIBERS

THE CARLAT REPORT:
ADDICTION TREATMENT

P.O. Box 626
Newburyport, MA 01950

PRSRT STD
US Postage
PAID
Nashville, TN
Permit 989

This Month's Focus:
Opiate Addiction

Next month in *The Carlat Addiction Treatment Report:* Benzodiazepines