INDUCTION – INITIATING
BUPRENORPHINE TREATMENT

Goal
To train providers to initiate patients on buprenorphine safely and effectively (induction) through appropriate preparation of the patient for induction, dosing principles, and responding to complications that may present during induction.

After completing this module, participants will be able to:
• Prepare patients to get ready to start taking buprenorphine successfully
• Demonstrate a thorough understanding of dosing guidelines to start patients on buprenorphine treatment
• Titrate buprenorphine dose to address the individual patient's needs
• Recognize, anticipate, and treat complications of buprenorphine use in your patients during induction

Professional Practice Gaps
Providers need to be able to prepare patients to start buprenorphine therapy, titrate the dose, and establish a final dose. Chapter 4 of TIP 40, later guidelines, and the FSMB Model policy describe this process in detail.

The FDA has produced an Appropriate Use checklist to follow for each patient that helps you make sure you follow the REMS guidelines for the medication with each patient. Items in the checklist pertaining to induction are explained in this training.
INDUCTION STAGE OVERVIEW

During induction, buprenorphine is started. Many providers conduct induction in-office because it requires a higher degree of attention and monitoring than later treatment.

**Goal Of Induction:**
Start buprenorphine treatment when the patient is in an appropriate state of withdrawal and to find your patient's ideal daily dose of buprenorphine

The patient should be in withdrawal as they take the first dose. This will avoid triggering severe withdrawal and also allow the titration of dose to an effective level for abstinence. The ideal daily dose minimizes both side effects and drug craving.

For most of your patients with opioid use disorder:
- The daily dose is 12 to 16 mg* buprenorphine/day
- Use the combination naloxone plus buprenorphine film or tablet
- Induction usually takes 2 to 4 days to complete

*Doses were established with the original Suboxone® sublingual tablets. Adjust dosage for the formulation you are prescribing.
**SCHEDULING OFFICE VISITS**

**Induction Day 1**
It is helpful to allow a 2-4 hour window on the first day of induction. After the initial dose of buprenorphine, you should monitor the patient for 1-2 hours and give an additional dose if withdrawal symptoms return. Consider follow-up with a phone call after the patient goes home. As you get more comfortable with the medication, the observation period will become more abbreviated.

**Induction Day 2**
On the second day, many patients will need a higher dose and will wake up in withdrawal, which is a reason to plan for a 2nd day induction phone call or visit dosing first thing in the morning. The second day of induction may take several hours as you increase the dose again and wait to see if withdrawal symptoms appear. Updated PCSS_MAT guidelines say that **day two monitoring and advising may happen by phone**. However, consider that some patients may benefit from in-person structure and guidance.

**Stabilization**
Ideally, there would be another appointment in 3-4 days.

**Maintenance**
After a maintenance dose is established, you should see patients weekly during the first month of treatment to monitor their toleration of the medication, their medication adherence, psychosocial stability, drug use, and adherence to counseling or recovery group involvement. Consider seeing them more frequently at first if they are high risk for relapse (many episodes of previous relapse, poor social support, mental health problems, etc.), have cognitive problems, have an atypical response, or have a particularly strong physical dependence. You should emphasize that treatment for opioid dependence involves more than just taking a pill.

**PRACTICE ACTION**
While conducting the pre-induction interview, it can be useful to have the patient describe their withdrawal symptoms in the order of typical appearance to use for comparison during induction. This information can be used later, on the day of induction, to predict when the patient will be ready, that is, insufficient withdrawal, to receive their first dose of buprenorphine.
PREPARE FOR INDUCTION

Prior Assessment
Elsewhere in the training, the following should have been completed:

• Screening and Detection of Opioid Use
• Diagnosis of Opioid Use Disorder
• Individualized Assessment of the Patient – including opioid use, medical status, other substance use, comorbidities and other key elements related to proper treatment with buprenorphine
• Physical and Laboratory assessment

Patient Interaction Steps Before Induction
1. Consent forms and treatment agreements
2. Determine when and where to start induction (clinic vs. home induction)
3. Provide patient education about the induction, stabilization, and maintenance processes
Case Study – Mr. Rossman Office Visit Prior to Induction

Name: Mr. Rossman
Age: 35 years old

Reason For Visit: Mr. Rossman began taking immediate-release oxycodone 20 mg for his back and developed moderate opioid use disorder. For the past year he has been taking 30 mg extended-release oxycodone, but 6 months ago, his provider tapered the dose and stopped prescribing it. His back has not been a problem for over a year, but he continues to take oxycodone ER daily getting it wherever he can. When he considered using heroin because of the difficulty maintaining a supply of oxycodone, he got scared of becoming a heroin addict and decided it was time to seek treatment. He came to you for help and together you have determined that he will start buprenorphine treatment. He is here for his pre-induction appointment and ready for patient education.

Mr. Rossman: So, how does this work?

Provider: You need to stop taking the extended-release oxycodone the day before. I'll give you a prescription to fill ahead of time, and I'd like you to bring it with you that day.

Mr. Rossman: I see. So, I just come here and take a pill and go?

Provider: It's pretty simple, but more involved than that. There are instructions to follow so that you absorb enough of the medication. You hold it in your mouth while it is absorbed rather than swallow it. We'll be monitoring your symptoms and use them to determine the right dose for you. If everything goes well, we'll probably just have you report your symptoms by phone the next day and we'll make a recommendation on how to adjust your dose. Often that is all that is needed. Then we just see you around a week later to make sure you're doing okay.

Mr. Rossman: Sounds good.

Provider: Next, I want to talk with you about safe storage and disposal of your medication.
SAFE MEDICATION STORAGE AND DISPOSAL

A guideline by the AMA (2017) recommends that providers:

- Talk to their patients about opioid misuse, letting them know that 70% of misused opioids come from family and friends

Proper storage of medications should start from the beginning and be revisited periodically throughout the course of treatment. This is to safeguard against potentially dangerous use by others.

- Any visitor can steal from a medicine cabinet and so it is not a good storage place.
- Individuals not tolerant of opioids can overdose on a relatively low dose.
- Risks to children should be emphasized; "Even very brief exposure to buprenorphine formulations can result in sedation, respiratory depression, cerebral anoxia, and death"². Following exposure of even a few seconds, children should receive immediate medical attention and observation for 24 hours.
- Proper disposal of medications should also be part of patient education.
- Document these discussions in the patient record.

**Quiz: Informed Consent**

An informed consent document discussed with and signed by the patient is a good way to reinforce practice policies and establish ground rules. Obtaining your patient's informed consent includes the following key steps:

1. Providing sufficient information
2. Your patient being able to process the information
3. Your patient's consent being freely granted

**What Are Some Areas Of Informed Consent That Are Unique To Buprenorphine? (Choose All That Apply)**

1. The success rates with weaning off the medication at a future date
2. The anticipated duration of treatment
3. The withdrawal that will be experienced if the medication is discontinued
INFORMED CONSENT QUIZ FEEDBACK

(1) The Success Rates With Weaning Off The Medication At A Future Date
Correct. It is important to inform patients that success rates of weaning off buprenorphine at a later date are low.

(2) The Anticipated Duration Of Treatment
Correct. The anticipated duration of treatment is a component of informed consent, and the typically indefinite duration for buprenorphine maintenance is unique to buprenorphine treatment.

(3) The Withdrawal That Will Be Experienced If The Medication Is Discontinued
Correct. Patients will experience withdrawal symptoms if they discontinue buprenorphine treatment and the sharing of this information is a component of informed consent in this instance. They must understand that they will be physically dependent on buprenorphine.
**Informed Consent**

Written and reviewed informed consent, signed by the provider and patient, should include the following elements:

**Treatment**

- Purpose of the treatment
- Alternative treatment options, including other medication-assisted treatment (e.g., methadone, naltrexone) and no medication assistance, and their relative risk for relapse
- Anticipated duration of treatment
- The success rates of buprenorphine maintenance and of weaning off buprenorphine at a future date
- The importance of seeking support from counseling and of a social support system

**Medication**

- Name of medication and what it does
- The mechanism by which buprenorphine treats opioid addiction: That one opioid dependence and addiction is basically being replaced by another dependence, buprenorphine, but not addiction. As part of explaining this topic, many of your patients will need an explanation of the difference between addiction, dependence, and the diagnosis of opioid use disorder.
- Risks and benefits:
  - Dependence on buprenorphine that will develop and withdrawal that would be experienced if it is stopped
  - The likelihood of relapse if treatment is discontinued
- Contraindications, warnings, adverse reactions, side effects, and drug interactions

**Confidentiality**

- Your patient's wishes regarding privacy (i.e., who can be told about treatment) ²³

**PRACTICE ACTIONS**

1. Document the informed consent in the patient's medical record.
2. Recommend that the patient be accompanied by someone who can help them recall instructions. This is a lot of information for patients to remember.
WITHDRAWAL AT INDUCTION

Objectively Assessing Withdrawal
Patient education prior to induction includes describing the target state of withdrawal that is needed before taking the first dose of buprenorphine. The target level of withdrawal is mild to moderate.

Immediately before induction, use an objective measure – like the Clinical Opioid Withdrawal Scale (COWS) – to evaluate your patient’s withdrawal symptoms. An objective measure is important, for example, because patients may exaggerate their symptoms to avoid discomfort. When patients have a mild to moderate COWS score of 12 to 16, they are ready for the first dose. Some providers go as low as 5 or as high as 24 on the COWS scale, but ideally > 10. Other withdrawal scales, such as the Subjective Opiate Withdrawal Scale (SOWS) and the Objective Opiate Withdrawal Scale (OOWS), may also be used.

Scale Components
The COWS measures withdrawal symptoms with observations of the following:

- Resting Pulse Rate
- Sweating
- Restlessness
- Pupil Size
- Bone or Joint Aches
- Running Nose or Tearing
- GI Upset
- Tremors
- Yawning
- Anxiety or Irritability
- Goose-flesh Skin

PRACTICE ACTION
Look for objective signs of withdrawal to help confirm reports of subjective symptoms.

Effect Of Opioid Type On Induction
Before induction day, determine the formulation your patient has been taking, short-acting vs. long-acting/extended release, because it can affect induction in several ways. Some opioids, including fentanyl, oxycodone, and morphine are available in both formulations. Warn patients that there will be a limited period of some discomfort from withdrawal that they will need to tolerate.

Short-Acting Opioids
- Buprenorphine treatment of dependence on short-acting opioids differs from treatment of dependence on long-acting opioids in a few ways. Most patients who present for buprenorphine treatment are dependent on short-acting opioids. Heroin and
many abused prescription narcotics are short-acting opioids. Specific formulation prescribing instructions may differ, for example, SuboxoneTM prescribing instructions recommend only "not less than 6 hours" since last short-acting opioid use, but recommend moderate withdrawal.

- Abstinence timing for short-acting is 12-16 hours.

**Intermediate-Acting**
For intermediate-acting opioids 17-24 hours of abstinence is needed.

**Long-Acting Opioids**
- Due to their longer action, patients on long-acting opioids must start abstaining from their medication for longer before their induction appointment to evoke withdrawal.
- Patients may need more "comfort" medicine (e.g., non-opioid analgesics, anxiolytic used sparingly and very carefully, antidiarrheal agents, antiemetics, antispasmodics) to help with remaining withdrawal after the first day until a stable daily dose is established.
- Differences in the activity of these two types of opioids at the mu opioid receptors make precipitated withdrawal much more likely for long-acting opioids than for short-acting opioids, so treat induction for long-acting opioids with care.
- Methadone is a long-acting opioid. Transferring from methadone requires some additional details and will be covered separately in another module in the section on special patients in this training activity.
- Abstinence timing for methadone is 30-48 hours.

**Dosage Guideline**
An expert panel developed the following consensus guidelines regarding dosage during induction:

- Make sure the patient is experiencing objective signs of withdrawal. Guidelines suggest that withdrawal symptoms are the more important indicator than a specific number of hours of abstinence.
- The maximum dose for day two, based on this consensus meeting was described as being between 8-16 mg. Other guidelines put 16 mg as the maximum dose for day 1 and suggest that going beyond 24 mg on day two and beyond gains little clinical effectiveness.
- Should be managed by experienced physicians.
- For patients previously on methadone: Monitor for withdrawal symptoms. If none are present within 24+ hours of last methadone treatment, wait prior to initiation.
INDUCTION: DAY 1

Before Starting Buprenorphine
When presenting for their first dose, your patients should be in mild/moderate withdrawal, which is a COWS score (12-16). Confiriming and documenting that your patient is in mild/moderate withdrawal before beginning induction will minimize the risk of precipitated withdrawal. Be honest with your patients about these withdrawal symptoms. Explain that this is an important step in the induction process and encourage them to wait it out. Having prepared the patient by going over the symptoms of mild to moderate withdrawal during the induction appointment, minimizes problems at this step.

PRACTICE ACTION
Have patients being inducted in the office stop at the pharmacy on the way to the appointment to pick up the first day's doses.

FYI
Remember: Formulations vary. Unless otherwise stated, dosages in this activity refer to the dosages and pharmacodynamics of generic buprenorphine or buprenorphine/naloxone combinations.

First Doses

Giving The First Dose
Start with a first dose of 4 mg* of the combination film or tablet. You may also start induction using the monotherapy tablets and then switch to the combination film or tablets after a few days. A lower starting dose of 2 mg* may be used if the patient is not currently physically dependent or uses methadone.

*Doses described were established for the original Suboxone or generic sublingual tablets; use equivalent doses for other formulations

After The First Dose
The recommendation for observation is to:

- Keep your patients in the office after the first dose
- Re-dose in 1-2 hour intervals (Gunderson 1+, Individior 2) with another 2 or 4 mg* buprenorphine if withdrawal symptoms persist or recur5,6.

[An earlier recommendation required a half-day of observation.]

After giving the second 4 mg dose, you can:

1. Observe your patients in the office for another 1+ hour and then re-dose if necessary
2. Have patients call in from home an hour later to report withdrawal symptoms
3. Allow patients to use their judgment to determine if they need an additional 4 mg buprenorphine

Maximum first day dose is now 16 mg4/ previously it was 8 mg1. Some patients do well on a lower dose and some formulations will require a lower dose, so individualized treatment is important. You should not exceed 16 mg buprenorphine on day one.

*Doses described were established for the original Suboxone or generic sublingual tablets; use equivalent doses for other formulations
FYI
Remember: Formulations vary. Unless otherwise stated, dosages in this program refer to the buprenorphine or buprenorphine/naloxone formulation in Suboxone.

Quiz: Case Study – Mr. Rossman Prior to Induction

Name: Mr. Rossman
Age: 35 years old

Review Of Case: Mr. Rossman is here for a pre-induction visit to treat his opioid use disorder. He is dependent on 30 mg oxycodone ER/day.

NEXT STEP
During his pre-induction office visit, you describe the level of withdrawal you would want him to be in at his induction visit.

Which Of The Following Is True Regarding Mr. Rossman’s Preparation For Induction? (Choose All That Apply)

1. He will need to take his last extended-release oxycodone at least an hour before induction so that his opioid blood levels are high enough at the time of induction.

2. A medical evaluation should include a history and physical; verification of his medications, alcohol use, and use of illicit drugs; a brief psychosocial assessment; and laboratory testing if there is a history of liver disease, alcohol, or illicit substance use.

3. Prior to induction, Mr. Rossman should be given a written medication guide for the formulation of buprenorphine that he will be prescribed.
CASE STUDY – MR. ROSSMAN PRIOR TO INDUCTION QUIZ FEEDBACK

(1) He Will Need To Take His Last Extended-release Oxycodone At Least An Hour Before Induction So That His Opioid Blood Levels Are High Enough At The Time Of Induction. This choice is inappropriate. Opioids should be cleared from his blood, not “high enough.” To start buprenorphine treatment, i.e., induction, the patient needs to be in a state of moderate withdrawal. This will avoid triggering severe withdrawal and also allow the titration of dose to an effective level for abstinence. Because Mr. Rossman is taking an extended-release opioid, he must start abstaining from his medication for longer before his induction appointment to evoke withdrawal, in comparison to a patient who is taking an immediate-release opioid. One hour will not be sufficient. The time needed for opioid abstinence before induction is likely to be around 24 hours or more.

(2) A Medical Evaluation Should Include A History And Physical; Verification Of His Medications, Alcohol Use, And Use Of Illicit Drugs; A Brief Psychosocial Assessment; And Laboratory Testing If There Is A History Of Liver Disease, Alcohol, Or Illicit Substance Use. While the first items in this list are all a part of medical evaluation prior to induction, laboratory testing should be completed for all patients starting buprenorphine. Lab tests for all patient should include liver function tests, urine toxicology, pregnancy test for women, and viral serologies for HIV and viral hepatitis.

(3) Prior To Induction, Mr. Rossman Should Be Given A Written Medication Guide For The Formulation Of Buprenorphine That He Will Be Prescribed. Correct. Mr. Rossman should be given a written medication guide that is specific for the formulation of buprenorphine that he will be prescribed, as part of his education prior to induction. Patient education prior to induction also includes the importance of being in withdrawal at induction, warning about sedating effects and recommending that he have someone with him to drive him home if induction will be in the clinic, all the usual components of informed consent including an understanding of the phases of treatment, alternative treatments, and anticipated duration of treatment, and ideally a written doctor-patient treatment agreement.

Medical evaluations are important for all buprenorphine patients, including, history and physical; verification of his medications, alcohol use, and use of illicit drugs; a brief psychosocial assessment and laboratory testing are all a part of medical evaluation prior to induction. Laboratory testing should include liver function tests, urine toxicology, pregnancy test, and viral serologies for HIV and viral hepatitis.

Quiz: Dose Day 1
Buprenorphine induction should be gradual. The patient’s dose should be increased slowly over the course of a few days.

What Is The Recommended First-day Total Dose (Suboxone Or Generic – Day 1 Of Induction)? (Choose One)

1. 2 mg/day
2. 4 mg/day
3. 8 mg/day
4. 16 mg/day
DOSE DAY 1 QUIZ FEEDBACK

(1) 2 Mg/day
The recommended FIRST DAY TOTAL dose is 8 mg buprenorphine (Generic or Suboxone, a little lower for other formulations) but many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.

(2) 4 Mg/day
4 mg is the recommended INITIAL dose (Suboxone or generic, a little lower for other formulations). The recommended first day TOTAL dose is 8 mg buprenorphine, but many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.

(3) 8 Mg/day
Correct. The recommended FIRST DAY TOTAL dose is 8 mg buprenorphine (Generic or Suboxone, a little lower for other formulations), but many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.

(4) 16 Mg/day
16 mg (generic or Suboxone, a little lower for other formulations) is the recommended total daily dose of buprenorphine AT THE END OF INDUCTION, not day 1. The recommended FIRST-DAY TOTAL dose is 8 mg buprenorphine. Many providers prescribe up to 12 mg total on the first day. And some patients may do well on 2, 4, or 6 mg.
**Evaluating Dosing**

When the patient is not exhibiting withdrawal symptoms and does not feel cravings for opioids, you may have established the daily dose – let your patient go overnight without additional doses. The next day, evaluate whether your patient was over-medicated, under-medicated, or medicated appropriately. Examination prior to the daily dose is important to identify medication status. According to updated PCSS-MAT guidelines recommended by SAMHSA (2016), this next day evaluation can happen via phone and the next in-office visit is recommended in 3-4 days.

- When your patients are **under-medicated**, they will experience craving or withdrawal between doses.
- When your patients are **over-medicated**, they will experience buprenorphine side effects.
- When your patients are **properly medicated**, they will have neither side effects nor craving or withdrawal between doses.

**Waiting Between Doses and Before Going Home**

Buprenorphine induction is often uncomfortable for patients because they have to enter into withdrawal before taking their first dose.

When patients come into the office and are in withdrawal, assess them right away and provide a dose of buprenorphine so as to keep them from being uncomfortable any longer than necessary. You may also want to have them get their initial buprenorphine doses from the pharmacy before the induction appointment so there is no wait time for the medication.

**Conducting Induction In Your Office**

- Symptom relief generally occurs in a little over an hour to two hours.
- Keep patients in a private room between doses if possible.
- You can provide books, magazines, videos, patient education materials, etc. to help them pass the time.

If a separate room is not possible, patients can wait in the general waiting room and should be told to inform staff immediately if their withdrawal symptoms worsen or return.

**Monitor patients for 1+ hours to assess their response to treatment before sending them home.** Some programs dismiss the patient when the COWS score goes below 4. Consider following with a phone call later.

**Combining Office And Home Induction**

Another option for induction is to have your patients come to the office for evaluation of withdrawal symptoms and to take the initial buprenorphine dose. Then they can leave the office and return home where they can have some privacy and comfort. You can then ask the patient to come back to the office 1-2 hours later for re-evaluation of withdrawal symptoms and another dose of medication. Trustworthy patients could be instructed to remain home and call into the office if withdrawal symptoms return. If needed, the additional dose can be approved over the phone.

**PRACTICE TIP**

The "Appropriate Use" checklist published by the FDA includes "Provided induction doses under appropriate supervision." If you do home induction, be sure to consider the patient and the circumstances to assure that this guideline is fulfilled.
Quiz: Case – Ms. Sanchez

Meet Your Patient

Name: Andrea Sanchez
Age: 32 years old
Reason For Visit: Ms. Sanchez is having trouble getting off Vicodin®. She saw your name on the SAMHSA locator list of providers who prescribe buprenorphine in her area.

Present History: Currently takes Vicodin daily. She had surgery for an ovarian cyst three years ago, and had trouble controlling pain in the weeks after the surgery. She ended up using 10 to 12 Vicodin tablets per day, always ran out too soon, and started looking forward to taking them. She is a schoolteacher and mother of two.

What Additional Information Would Help You Decide Whether Buprenorphine Treatment Is Indicated For Ms. Sanchez? (Choose All That Apply)

1. More information about signs of her physical dependence on opioids
2. More information about any current pain
3. Her state of mind
4. What she expects from buprenorphine treatment
CASE – MS. SANCHEZ QUIZ FEEDBACK

(1) More Information About Signs Of Her Physical Dependence On Opioids
(2) More Information About Any Current Pain
(3) Her State Of Mind
(4) What She Expects From Buprenorphine Treatment

Correct. These items and more are among the information to obtain prior to initiating buprenorphine treatment.
Ms. Sanchez – Further Evaluation

About: Opioid Use Disorder
To discover if she meets criteria for opioid use disorder, you ask Ms. Sanchez whether she has experienced any withdrawal symptoms and if she feels she is giving up significant work or family time to use or to obtain hydrocodone/acetaminophen.

**Ms. Sanchez:** I'm not a junkie, I don't get sick if I stop taking Vicodin®. I do notice that I'm crabby and I'm sluggish at work if I don't take it. I just can't stand how I feel, so I take one. Then I take more to keep going. My husband is very supportive and puts up with a lot while I was cutting my dose down, but I haven't told him I'm still using.

About: Pain
To learn more information about her pain, you ask Ms. Sanchez whether her pain recurs when she reduces her dosage, if her pain interferes with her work or family activities, or if she has chronic intractable pain.

**Ms. Sanchez:** I don't have pain anymore, although my hips ache a little after my morning run. I do some stretches and the achiness goes away.

About: State Of Mind
To screen for depression, you ask Ms. Sanchez whether she has been or is currently depressed, if she has experienced loss of energy, or has feelings of hopelessness. You also ask what it means when she says she can't get through the day.

**Ms. Sanchez:** I just love my family and my life. I was in therapy for years, but I don't need therapy. Of course, I get tired since I have kids and a busy job. Yes, I do notice that when I take Vicodin® I feel more energy and I'm nicer. Don't worry, I'm not depressed, and I'm certainly not suicidal or anything.

About: Treatment Expectations
To learn what she expects from buprenorphine treatment, you ask Ms. Sanchez if she would be able to participate in the counseling and monitoring necessary to treat addiction. It is crucial to determine whether her request for buprenorphine is actually for treatment of her opioid use disorder, or whether it is really part of drug-seeking behavior (i.e., just another way to get a prescription for an opioid), whether she expects that buprenorphine will magically dissolve her addiction.

**Ms. Sanchez:** I just want to get rid of this addiction. When I was drinking, I just decided to stop, and I did. I've been in AA ever since. I thought quitting Vicodin would be like that, but it wasn't as simple. I heard that buprenorphine will help you get off opiates. I don't need any more therapy since I was in therapy for years. Do I really need a urine test? I'm not a junkie. I told you what I'm taking.

Ms. Sanchez – Additional Concerns
Ms. Sanchez seems to meet the criteria for buprenorphine treatment. However, her case should be examined a bit more closely first.

Before prescribing buprenorphine, it is important to examine the reasons why Ms. Sanchez may be having trouble stopping her use of hydrocodone/acetaminophen. Also, it is important to examine her motivation and pre-conceptions about addiction treatment. On the surface she appears to be addiction-savvy, having gone to AA. However, on closer inspection, she is resisting counseling and testing. She has superficial expectations about buprenorphine, considering it a way to simply eliminate her opioid use problem.
She does not have chronic pain currently and does meet DSM 5 criteria for opioid use disorder*. She may or may not have underlying depression. It would certainly be something to evaluate further if she continues to use hydrocodone/acetaminophen or other opioid even when the addiction is properly addressed.

In spite of flowery statements about family and work, she is not finding her husband fully supportive at this point. These “wonderful” parts of her life may actually be stressful and triggers to use. It could be helpful to have her name individuals who will be her support system when she stops using.

*Review of the diagnosis, opioid use disorder: The DSM 5 diagnosis, opioid use disorder, requires a minimum of two criteria for a diagnosis*. A patient who meets 2-3 criteria has a mild case, 4-5 moderate, and 6-7 severe.

**Quiz: Ms. Sanchez – Induction Dose**

**Preparing for Induction**

You review the treatment options with Ms. Sanchez, including psychosocial components of addiction treatment. You explain that at such a low dose of hydrocodone/acetaminophen, she may be able to discontinue opioids with few physical problems, but she needs some support to carry this out. You discuss the requirements of your office-based buprenorphine treatment with Ms. Sanchez, which includes at least one counseling session with a physician assistant. Together you decide to try to first stabilize her medically on buprenorphine, so she can stop her Vicodin® use. She reluctantly agrees to the counseling session and a urine drug screen.

You go over patient education with Ms. Sanchez and review the patient-provider treatment agreement for her to sign.

You perform a urine drug test and upon receiving the results instruct her on correct usage of the Suboxone® film (e.g., holding the edges).

Ms. Sanchez will start home induction the next day.

**What Should Be Ms. Sanchez's Initial Buprenorphine Dose, Considering That She Is Dependent On A Relatively Low Dose Of Opioids? (Choose All That Apply)**

1. 2 mg
2. 4 mg
3. 8 mg
4. See if she can get through Day 1 without buprenorphine; she may not really need it
MS. SANCHEZ – INDUCTION DOSE QUIZ FEEDBACK

(1) 2 Mg
This is one possible option. Most prescribers start with a 4 mg dose on Day 1; however a low level of physical dependence is an indication for starting with 2 mg. If started with 4 mg, Ms. Sanchez may not need another dose increase on Day 2.

(2) 4 Mg
Correct. This is the usual recommended first dose for Day 1. Ms. Sanchez may not need another dose increase on Day 2.

(3) 8 Mg
This is not the best answer. Start with a 4 mg dose on Day 1. 2 mg also may work as an initial dose with increments of 2 mg. With 4 mg starting dose, she may or may not need a dose increase on Day 2.

(4) See If She Can Get Through Day 1 Without Buprenorphine; She May Not Really Need It
This is not the best option. She shows signs of being physically dependent and has struggled in past attempts to cut back without buprenorphine. For home induction, she could wait for her subjective (psychological) withdrawal symptoms to appear (craving, vague irritability, fatigue) before self-administering the first dose. It isn't clear whether 2 mg or 4 mg dose increments are best.
PATIENT INSTRUCTION

Patient Education About Induction and Ongoing Treatment

Review patient education in detail before induction day and repeat the key points on induction day. Follow a checklist to assure that all patient education points are reviewed with all of your patients. (See: Appropriate Use Checklist, under Resources)

The following patient education points are important to emphasize before induction and again on induction day:

1. **Be in withdrawal at induction:** Advise your patients not to use opioids for the appropriate amount of time to be in withdrawal at induction in order to prevent precipitated withdrawal. This may be 12 to 24 hours for many opioids and potentially longer for long-acting opioids. Patients often know the timing from experiences with running out of the drug they take.

2. **Come with a driver:** Recommend your patient get a friend/family member to drive them home when doing clinic-based induction.

3. **Review medication guide:** Provide your patients with a written Medication Guide that is specific for the buprenorphine formulation you will prescribe.

Patient Instruction On How To Take Buprenorphine

Review Key Patient Education Points

Remind patients of key points relevant to successful induction covered the day of _induction_. These include:

- The possibility of taking recommended comfort medications for residual withdrawal symptoms or requesting additional comfort medications as needed
- Taking doses as directed; not taking a dose on their own unless this has been carefully explained and authorized by you
- Reminders of the importance to abstain from the opioid they were using and other substances

Tips For Taking Buprenorphine Sublingually

There is a specific approach to sublingual administration that will improve absorption of buprenorphine.

Below are some tips you can provide to your patients when taking sublingual buprenorphine. Advise patients that:

- Each buprenorphine tablet or film will take some time to dissolve under their tongues, but the film dissolves more quickly than generic tablets.
  - The mean time for generic tablets is 7 to 12.4 minutes; the mean time for Suboxone®* film is 5 to 6.6 minutes; the relatively newer, smaller, sublingual tablet, Zubsolv® and the buccal film, Bunavail™, dissolve faster.
  - With the buccal film formulation, two films can be applied in their mouths simultaneously, one inside each cheek.
- They should grasp the film by the edges and place under their tongues at the base, just to the side of the center.
- While the medication is dissolving, they should not talk, drink, or swallow.
• While the tablet is dissolving, they will salivate a lot, so they will need to tilt their heads forward to avoid swallowing the saliva.
• Suggest rinsing their mouths or eating a mint prior to taking buprenorphine to help with the taste.
• Patients with higher buprenorphine doses might find it more comfortable to take their medication sequentially rather than all at once.
  • A film can be placed on the left and right base of tongue; if a third film is needed, it should be taken after the first two films have dissolved.
  • Your patients should not try to take more than two tablets at one time.
*We are using brand names since there is a difference in the product that is not reflected in the generic name. We are not advocating one brand or the other.

Sedating Effects
Sedation effects are most obvious in early stages of treatment (induction, titration of dose).²
• Use caution with psychomotor activities (e.g., driving a car).
• Instructions to avoid other sedating medications and alcohol are particularly important in this phase.

PRACTICE TIP
Some patients crush the tablets and pour them under their tongue to speed absorption. This approach is not listed as a method of administering buprenorphine, but it has become popular in inpatient settings due to easier monitoring and assuring that patients take their medication.

Quiz: Mr. Rossman Induction: Day 1

Mr. Rossman
Age: 35 years old

Summary To Date: Mr. Rossman presents for day 1 of buprenorphine induction. He has moderate opioid use disorder and is dependent on extended-release oxycodone. He presented for his induction appointment with mild withdrawal and when symptoms were mild to moderate, was given an initial dose of buprenorphine.

Next Step
Mr. Rossman has been given an initial dose of 4 mg and remained the in office. After one hour, you re-evaluate him and he feels better, but is still experiencing some withdrawal symptoms.

What Is The Correct Next Dose (still On Day 1 Of Induction) To Give Mr. Rossman In Order To Reduce His Withdrawal Symptoms? (Choose One)

1. 2 mg
2. 4 mg
3. 6 mg
4. 8 mg
Mr. Rossman Induction: Day 1 Quiz Feedback

(1) 2 Mg
This is a little low. While gradual increase is advisable, subsequent doses of buprenorphine should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

(2) 4 Mg
**Correct.** The dosage should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

(3) 6 Mg
This is a little high. Gradual increase is advisable; subsequent doses of buprenorphine should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.

(4) 8 Mg
Gradual increase is advisable. Subsequent doses of buprenorphine should be increased by 4mg until withdrawal symptoms are reduced or maximum dosage is met.
Medical Management of Remaining Withdrawal Symptoms

After day 1 dosing, a single dose of buprenorphine can be sent home with the patient for remaining spontaneous withdrawal (withdrawal from stopping the opioid of dependence) symptoms. Remaining symptoms can also be managed medically with non-opioid medications. However, most of the time it is not necessary. Sometimes called "comfort meds", they are most often needed by patients transferring from long-acting opioids and include:

- Anxiolytics (use very carefully and in limited quantities)
- Non-opioid pain relievers (NSAIDs or acetaminophen)
- Antidiarrheal agents
- Antiemetics
- Antispasmodics
INDUCTION: DAY 2+

Evaluating your Patient on Day 2
On the second day, evaluate your patient's response to the first day's dose.

- If your patient was over-medicated at the end of the first day, decrease the dose.
- If your patient experienced withdrawal symptoms or opioid cravings after leaving the office on the first day, increase the dose.

In most cases, you can do patient monitoring over the phone on day 2. When your patient leaves the office at the end of day 1, schedule a time to talk to your patient first thing the following morning.

Then ask a series of questions to gauge how your patient is feeling and to determine if the dose needs to be adjusted:

- How are you feeling now?
- How do you feel physically?
- What did you have for dinner last night? (having a good dinner is indicative of how they felt all day)
- How did you sleep?
- Did you eat breakfast yet? If not, why not? (if patient has upset stomach, then patient may be going back to withdrawal – in which case may need dose increase)
- Have you had any cravings?

Dosing On Day 2
If your patient reports feeling unwell, then evaluate for withdrawal again and increase the dose by another 4 mg. So, a patient who took a total of 8 mg (two 4 mg doses) on day 1 and who requires a dose increase would start day 2 with a 12 mg dose. If symptoms persist after an hour, you can increase the dose by another 4 mg buprenorphine.

The maintenance dose for most patients is generally in the range of 4 mg to 24 mg buprenorphine. Clinical advantage has “not been demonstrated” for doses higher than 24 mg. The required dosage varies. Patients who were dependent on higher doses of opioids may require a higher daily dose.

Next few days: Many of your patients will be stabilized by day 2, and almost all will be stabilized by day 3.

PRACTICE ACTION
On day 2 be sure to emphasize that, although you are not requiring an office visit, your patients should not adjust the dose on their own.

Day 3 And Beyond
Repeat the same protocol for dosing on day 3.

- Start the day with a phone appointment
- Evaluate cravings and withdrawal
- Determine if a dose increase is needed
You can safely prescribe up to 32 mg/day, but there is a ceiling effect around 16 mg and higher doses will do little to decrease cravings. Patients who insist on a high dose should be re-evaluated at the time of induction and/or monitored throughout treatment for diversion.
Ms. Sanchez – Stabilization

Patient: Ms. Sanchez

Recall Ms. Sanchez who completed home induction for opioid use disorder related to dependence on a low dose of Vicodin.

Most likely Ms. Sanchez will be maintained on at least 8 mg. Because she is dependent on such a low dose of hydrocodone/acetaminophen, her physical withdrawal symptoms may be minimal. Instead, she could wait for her subjective (psychological) withdrawal symptoms to appear (craving, vague irritability, fatigue) before self-administering the first dose.

Ms. Sanchez took two 4 mg doses on day 1, as guided, and did not experience any physical or psychological cravings in subsequent days. On day 2, she continued to do well at the same total dose of 8 mg, so she was stabilized on an 8 mg dose.
Case Example – Mr. Allen

Patient: Mr. Allen
You are preparing to treat Mr. Allen for dependence on heroin (a short-acting opioid).

Prior to Induction Day
After consultation, you decided that Mr. Allen is a suitable candidate for buprenorphine treatment. You meet with him the day before you plan to begin induction. You impress upon him that he needs to be in mild/moderate opioid withdrawal before beginning buprenorphine treatment (COWS score of around 12 to 16) and, therefore, should abstain from heroin for around 12 to 16 hours before beginning treatment. You also explain that there is a risk of greater discomfort and the treatment not working properly if he comes to the first induction appointment and is not in withdrawal.

Induction, Day 1
Mr. Allen shows up on time for his appointment the following day. He affirms that he has not taken heroin in 12 hours. Your patient’s behavior and physical signs are consistent with someone in mild/moderate opioid withdrawal (COWS = 12).

- You go ahead and give Mr. Allen his first 4 mg dose of medication, sublingual Suboxone® film. You advise him not to talk or swallow until the medication is all gone. You check under his tongue to make sure it is completely gone and ask him to remain in the office for monitoring for an hour or so.
- After 30 minutes, Mr. Allen reports that he is beginning to feel relief from withdrawal, but he still reports (and shows signs of) being under-medicated. His COWS is reduced to 9.
- After 60 minutes, it is clear that while Mr. Allen has responded further to the buprenorphine, he is still under-medicated. He continues to show signs of withdrawal (a little flushing and slightly elevated pulse). Upon questioning, he confirms that he feels calmer but still feels some mild flu-like pain and stomach cramps of withdrawal (COWS=5). Accordingly, you give him an additional 4 mg dose. Following this dose, Mr. Allen leaves the office.
- Mr. Allen calls an hour later and reports that all symptoms are resolved except some mild generalized pain (COWS=1) so you do not recommend an additional 1st-day dose. You recommend he take acetaminophen (500 mg) if needed and call your office in the morning.

Quiz: Mr. Allen Induction Day 2
After induction on Day 1 with a dose of 8 mg, Mr. Allen calls the office for dosing at the scheduled time on the morning of Day 2. His withdrawal symptoms have increased a little from the previous evening. The physician assistant confirmed that Mr. Allen did not take any heroin and other opioids overnight and reminded him of the importance of being candid. Your evaluation confirms he still has some minor withdrawal symptoms (COWS is 3-4).

What Dose Changes, If Any, Would You Make At This Time? (Choose One)
1. No additional buprenorphine needed. Have him take his day 1 dose of 8 mg and call in 1-2 hours.
2. Add 4 mg for a total dose of 12 mg and ask him to call back in 1-2 hours.
3. Add 8 mg for a total dose of 16 mg and ask him to call back in 1-2 hours.
4. Add 12 mg for a total dose of 20 mg and ask him to call back in 1-2 hours.
**Mr. Allen Induction Day 2 Quiz Feedback**

(1) No Additional Buprenorphine Needed. Have Him Take His Day 1 Dose Of 8 Mg And Call In 1-2 Hours.
Mr. Allen needs additional buprenorphine from his day 1 dose of 8 mg. Leaving the patient with withdrawal symptoms is likely to lead to relapse.

(2) Add 4 Mg For A Total Dose Of 12 Mg And Ask Him To Call Back In 1-2 Hours
Correct. Because of his continued withdrawal symptoms, Mr. Allen needs additional buprenorphine. Increments of 4 mg are recommended.

(3) Add 8 Mg For A Total Dose Of 16 Mg And Ask Him To Call Back In 1-2 Hours
Because of his continued withdrawal symptoms, Mr. Allen needs additional buprenorphine from his day 1 dose of 8 mg. The goal is to titrate him to the lowest dose needed to prevent symptoms and return to opioid use.

(3) Add 12 Mg For A Total Dose Of 20 Mg And Ask Him To Call Back In 1-2 Hours
Because of his continued withdrawal symptoms, Mr. Allen needs additional buprenorphine. However, increments of 4 mg are recommended. The goal is to titrate him to the lowest dose needed to prevent symptoms and return to opioid use.
**Mr. Allen – Days 2 and 3**

**Induction, Day 2 (continued)**

As described in the previous quiz, on Day 2, Mr. Allen called the office with some increase in withdrawal symptoms, from the previous night, a COWS score of 3-4. He had not had any other opioids since before starting induction. After evaluating him and confirming some withdrawal symptoms, you prescribed Mr. Allen a 12 mg dose (8 mg dose established on Day 1, plus an increase of 4 mg) and ask him to call in around an hour.

A short time later, Mr. Allen felt much calmer and most signs of withdrawal appeared to have abated or disappeared. Mr. Allen called after an hour saying he does not feel like he's about to go into withdrawal anymore. It appears that you may have found Mr. Allen's daily dose. You tell him to call again after two hours to report how he is doing, which he does and reports no problems.

**Induction, Day 3**

The next morning (induction day 3) you re-evaluate Mr. Allen via phone. He reports no problems with withdrawal symptoms and that he is not aware of drug craving. He says that he “feels good”. He also reports that he went to a support group the night before and that it went “really well.” It appears that you have found a therapeutic daily dose for him. You prescribe him a week's worth of buprenorphine at a 12 mg/day dose. He makes an appointment to meet with you again in 3-4 days for his first follow-up appointment.
QUIZ: CASE – MS. COLLIER

Name: Yolanda Collier
Age: 47 years old

Reason For Visit: Now that she has grandchildren, Ms. Collier would like to "stop using illegal drugs." She would like to try buprenorphine.

Medical History: She is currently heroin-dependent. Ms. Collier has a 20-year history of opioid (heroin) dependence. She also has a history of asymptomatic hepatitis C; her liver function tests from a year ago showed only mild abnormalities.

Treatment History: She had tried methadone treatment for almost a year, five years ago, but could not maintain it due to her work and family commitments.

Next Step
During her visit, you learn that Ms. Collier is mentally stable and complete blood tests and learn that her liver function is unchanged. Otherwise, she is apparently healthy and has a good understanding of buprenorphine treatment and its benefits. The day before induction, you complete patient education and the written, signed patient-provider treatment agreement.

What Is The Best Next Step For Ms. Collier? (Choose One)
1. Refer her to a hepatologist for a thorough hepatitis C evaluation
2. Refer her to an opioid treatment program since she has had a period of success with methadone maintenance in the past.
3. Induct her onto buprenorphine
CASE – MS. COLLIER QUIZ FEEDBACK

(1) Refer Her To A Hepatologist For A Thorough Hepatitis C Evaluation
This is not the best answer. Ms. Collier’s hepatic function test is unchanged. It is a good idea, however, to get Ms. Collier’s consent to allow you to discuss her opioid treatment with her hepatologist.

(2) Refer Her To An Opioid Treatment Program Since She Has Had A Period Of Success With Methadone Maintenance In The Past.
This is not the best answer. Ms. Collier was maintained on methadone successfully for a while, but ultimately this treatment approach failed, for a variety of reasons. In some cases, a patient's treatment history makes them an unlikely candidate for success with buprenorphine treatment, but this does not appear to be the situation in Ms. Collier’s case.

(3) Induct Her Onto Buprenorphine
Correct. If her blood and urine results come back as expected, Ms. Collier seems to be an appropriate candidate for buprenorphine induction.

Quiz: Ms. Collier – Induction
Prior to Induction: Ms. Collier wants to try buprenorphine and agrees to the terms of your treatment agreement. She seems committed to getting clean and has a better support system around her than she has in past years. Together, you decide to induct her onto buprenorphine.

Ms. Collier expresses concern about going into withdrawal; she says she always gets severely nauseated. To treat this, you prescribe an antiemetic, dolasetron (commonly used, serotonin (5-HT3) antagonist), to start taking an hour before she anticipates withdrawal symptoms would start.

Induction Day: On induction day, Ms. Collier arrives at your office at 9:00 am. She reports that her last heroin use was 14 hours ago. She reports chills, nasal stuffiness, and having some difficulty sitting still, although she appears able to do so. She denies pain or gastrointestinal complaints. She says she is anxious, slightly irritable, and feels a tremor in her hands, although it is not visible to others. Her vitals are stable (BP 120/70, P 77), pupils are normal, and she is without diaphoresis, flushing, yawning, rhinorrhea, lacrimation, or piloerection.

How Would You Characterize Her Degree Of Withdrawal? What Is Her Score On The Clinical Opioid Withdrawal Scale? (Choose One)
1. COWS 2 points: Little to no withdrawal
2. COWS 5 points: Mild withdrawal
3. COWS 14 points: Moderate withdrawal
4. COWS 28 points: Moderately severe withdrawal
Ms. Collier – Induction Quiz Feedback

(1) COWS 2 Points: Little To No Withdrawal,
(3) COWS 14 Points: Moderate Withdrawal,
(4) COWS 28 Points: Moderately Severe Withdrawal

In scoring the COWS, one point would be added for each of the mild symptoms she has: subjective chills, restlessness, nasal stuffiness, subjective tremor, and anxiety/mild irritability. This equals a total of five points which corresponds to Mild Withdrawal (5 to 12 points). She does not have any of the moderate or severe symptoms that score more points in the COWS, such as piloerection, which is 3 points.

(2) COWS 5 Points: Mild Withdrawal
Correct. In scoring the COWS, one point would be added for each of the mild symptoms she has: subjective chills, restlessness, nasal stuffiness, subjective tremor, and anxiety/mild irritability. This equals a total of five points which corresponds to Mild Withdrawal (5 to 12 points). She does not have any of the moderate or severe symptoms that score more points in the COWS, such as piloerection, which is 3 points.

Discussion: Mild/moderate withdrawal or a COWS score of 12 to 16 is recommended before starting induction (PCSS-MAT guidelines). Ms. Collier should be in at least this level of withdrawal in order to prevent precipitated withdrawal. Also, it would be better to observe some objective evidence of withdrawal (e.g., diaphoresis, dilated pupils), rather than rely on subjective symptoms as reported by the patient.

Case: At this point, you express concern to Ms. Collier that her degree of withdrawal is not sufficient and explain the risk of precipitated withdrawal. You offer her a quiet room in which to wait, but she says she has things to do. You ask her to return to your office in a couple of hours for induction.

When she returns 2 hours later, Ms. Collier is still experiencing chills, nasal congestion, and mild tremor and now reports escalating restlessness and anxiety. She also is having mild, diffuse pain and is nauseated. On exam, she appears more anxious but does not appear to be fidgety. Her pulse is 90, and she is flushed. Her pupils are moderately dilated. Her exam and symptoms are otherwise unchanged.

Quiz: Ms. Collier

Would You Start Buprenorphine Induction Now? (Choose One)

1. Yes, her withdrawal is adequate to begin the induction.
2. No, withdrawal is not adequate to begin induction.
Ms. Collier Quiz Feedback

(1) Yes, Her Withdrawal Is Adequate To Begin The Induction. This is the best option. Currently, Ms. Collier appears in adequate withdrawal to initiate induction. Her score on the COWS would be a 13, indicating mild to moderate withdrawal:

- Pulse: 90 (1)
- Sweating: flushed (2)
- Restlessness: subjective restlessness but still (1)
- Pupils: moderately dilated (2)
- Bone/Joint Aches (1)
- Runny nose or tearing (1)
- GI Upset: nausea (2)
- Tremor: still mild, subjective tremor (1)
- Yawning: none
- Anxiety: observable (2)
- Gooseflesh: none

TOTAL: 13 Mild/moderate withdrawal

(2) No, Withdrawal Is Not Adequate To Begin Induction. No, this is not the best option. Currently, Ms. Collier appears in adequate withdrawal to initiate induction. Her score on the COWS would be a 13, indicating mild to moderate withdrawal.
Ms. Collier – Continue Induction

Initiating Treatment And Assessing Via Phone

Day One

- You initiate treatment with a 2.8 mg dose of the Zubsolv® formulation of buprenorphine/naloxone (two 1.4 mg tablets). You chose Zubsolve because you are concerned about her ability to be patient enough for a more slowly dissolving formulation. This is similar to starting her with 4 mg of Suboxone.
- One hour later, Ms. Collier reports that she no longer is nauseated or having chills. She is much less anxious and her pain is almost gone. Her vitals are BP 116/78, P 76, and she is no longer flushed. Her cravings have decreased, but are still present slightly.
- You give her an additional 2.8 mg dose prior to leaving the clinic (equivalent to adding 4 mg Suboxone).
- Later in the afternoon, you speak on the phone, and Ms. Collier reports that she is feeling well, without withdrawal or cravings. Her total first-day dose was 5.7 mg Zubsolv, the equivalent to 8 mg Suboxone.

Day Two

The next morning you assess Ms. Collier via phone. She is having some cravings and slight withdrawal symptoms. You increase her dose of buprenorphine to 8.5 mg (equivalent to 12 mg Suboxone). She reports feeling good for the rest of the day. She does not need another dose increase.

Day Three

She awakes on Day 3 feeling good. She calls the office reporting no cravings or withdrawal symptoms, so you have established her daily dose of buprenorphine (Zubsolv® formulation) at 8.5 mg. Medication information states that the typical target dose is 11.4 mg and range is 2.8 to 17.1 mg\textsuperscript{11}
HOME INDUCTION

Many clinicians now complete induction for a substantial portion of their buprenorphine patients at home. At-home buprenorphine induction is a safe and convenient option for some patients. Several studies found at-home induction to be as effective as office-based induction\(^{12,13}\). Patients who have been on buprenorphine previously may be comfortable with home re-induction. However, in an expert consensus opinion, ASAM recommends home induction be offered only by a provider who is experienced with buprenorphine treatment\(^{14}\).

The "Appropriate Use" checklist published by the FDA states that the following should be completed for each patient starting buprenorphine induction: "Provided induction doses under appropriate supervision"\(^{8}\). Providers should consider their availability to provide "appropriate supervision" as needed for a patient (for example, by talking to them on the phone).

Preparing for At-Home Induction

Before deciding upon at-home induction, your patients must come into the office for an initial consultation, assessment, physical exam, lab work, etc. In other words, the process leading up to induction is the same. You should provide patients who are going to be inducted at home with thorough patient education about the process. Here are some more specific guidelines:

- Confirm that your patients do not have any complicating medical or psychiatric problems
- Verify that your patients have support from family and friends and that someone can be at home with them on induction day
- Review instructions with the patient, asking them questions to confirm their understanding and giving them the opportunity to ask questions
  - Educate your patients on how to recognize signs and symptoms of withdrawal and how to rate it so that they have sufficient withdrawal
  - Educate your patients about precipitated withdrawal
  - Educate your patients about correct administration of buprenorphine formulation prescribed
  - Send instructional materials home with your patients and ensure that they understand procedures
- Prescribe only a limited supply of buprenorphine to start until the dose is established
- Put dose amount and timing in writing

Protocol for Home Dosing

Assuring Adequate Withdrawal In Home Induction

With at-home dosing, your patients are responsible for:

- Assessing their own symptoms
- Taking their first dose when they are in mild/moderate withdrawal

You can refer them to the COWS scale if needed to objectively assess their withdrawal symptoms.

Recommend that your patients have a friend or relative assist them, because withdrawal is uncomfortable, and your patients might be tempted to take their first dose prematurely.
Dosing Guidelines For At Home Induction
Dosing protocols for at-home induction follow a similar protocol as office induction:

- Start with a 4 mg* (sublingual tablets or equivalent of other formulations) buprenorphine dose.

After the first dose, patients should continue to monitor their withdrawal symptoms and take 1 or 2 more 4 mg doses as needed on Day 1.

- Check on process via phone and document in patient record.
- Maximum dose of 8 mg day one; allow up to 16 mg total dose first day if approved by phone⁴.

Follow the same dosing protocols as would be used for patients who are inducted in the office.

- Day 2: Maximum of 16 mg, but allow up to 24 mg if approved by phone.
- Day 3: Same as for in-office induction.

Schedule a follow-up office visit for 3-7 days⁴.

Monitoring And Follow-up For At Home Induction
Your comfort level and that of your patient will determine how much monitoring is likely to be most effective during the at-home induction process. If you are a newer prescriber, you might want to have your patient call-in to the office and have their withdrawal symptoms assessed over the phone before taking the first dose or subsequent doses. Or, patients who are concerned about precipitated withdrawal may feel more comfortable checking in with a nurse before taking the first dose. Each clinician should set practice guidelines accordingly.

- Follow-up visit is recommended; between 3 and 7 days has been recommended⁴.

PRACTICE TIP
Having another individual, who reviews the guidelines, observe the home induction process, may improve the outcome⁴.

Poll: After reading about home vs. office-visit inductions, do you plan to do any home inductions?
- Yes
- No
- Unsure
- Later, after I have more experience
- Does not apply to me

How about you? Take the poll yourself!
https://bup.clinicalencounters.com/induction-poll/
COMPLICATIONS DURING INDUCTION

Having A Mentor To Consult
Before starting your buprenorphine practice, you may want to establish a relationship with another buprenorphine provider in your area as a mentor. Alternatively, you could choose a Physician Clinical Support System-Medication Assisted Treatment (PCSS-MAT) mentor (see sidebar) to consult if questions or problems arise.

Patients Presenting Without Withdrawal
One of the most common problems in buprenorphine inductions is that patients present for their first dose without being in withdrawal. Many addicted patients have a fear of going into withdrawal.

In this situation, you must decide if your patient is going to be in withdrawal soon or if the induction needs to be rescheduled.

It is also appropriate to question your patient further about their:

- Commitment to seeking treatment
- Recent opioid use – Some patients may not know what medications are included in opioids. Patients sometimes do not understand that you meant for them to stop all opioids, even those in combination with other medications, like Vicodin®.

Managing Precipitated Withdrawal
Precipitated withdrawal occurs from not having gone long enough without the opioid of dependence before starting buprenorphine. Patients should be warned in advance about the possibility of precipitated withdrawal if they take an opioid while going into withdrawal for induction.

If withdrawal symptoms get worse instead of better after you give the first dose, it is possible that precipitated withdrawal has occurred. You may be able to determine if it is precipitated withdrawal from the severity of symptoms or by re-asking your patient about their abstinence schedule, reassuring them you just need the information to help them. Taking a problem-solving approach, try to identify if the patient inadvertently swallowed the buprenorphine rather than letting it be slowly absorbed. Another possibility is that they may have taken an opioid, intentionally or not, while they were trying to abstain.

Even if you proceed slowly with induction, precipitated withdrawal may still occur, but infrequently.

Precipitated withdrawal can be managed in two ways:

1. Continue induction with additional doses of buprenorphine until withdrawal abates, up to the recommended target dose of the formulation but with the minimal dose needed to manage withdrawal, using the COWS scale sequentially as a guide. Precipitated withdrawal will not get worse by continuing and the withdrawal symptoms may be alleviated by additional buprenorphine. There is no formal clinical guideline, but expert consensus supports continuing induction. Further, your patient will have fewer opioid receptors available for illicit opioids. This will present less of a risk for overdose from self-medicating with drugs to treat withdrawal symptoms.

2. Stop induction and treat withdrawal symptomatically (especially clonidine, antidiarrheals, antiemetics, nonsteroidal anti-inflammatory drugs). Have your patient continue abstinence from the opioid of dependence and re-induce on buprenorphine the next day.
Dealing With Other Adverse Reactions
Headache and sweating are commonly experienced.

Severe adverse reactions to buprenorphine during induction are exceedingly rare. Complications can arise when patients are taking medications that interact with buprenorphine. Take a thorough history and conduct urinalysis prior to induction to reduce the likelihood of such problems occurring.

Key Point
Precipitated withdrawal can be treated by lowering the buprenorphine dose and with several other supportive therapies.
**Case: Mr. Frank – Methadone Transfer to Buprenorphine**

**Reason for visit:** Mr. Frank comes in seeking buprenorphine treatment instead of his current methadone treatment.

**History:** He has been maintained on a moderate dose of methadone (75 mg) for 6 months.

Mr. Frank is adamant about wanting to transfer to buprenorphine. He wants a new provider closer to home and says he is tired of driving 20 miles to and from the opioid treatment program (OTP) every day.

Is Mr. Frank a good candidate for buprenorphine induction?

**Evaluating Patients for Transfer from Methadone**

Reasons patients may choose to switch from methadone to buprenorphine include:

- Potential convenience of being treated in primary care rather than at a drug clinic that may be farther away or carry perceived stigma
- To reduce hypogonadism they experience with chronic use of methadone

Patients who are seeking a transfer from methadone to buprenorphine should be carefully evaluated:

- Encourage patients who are stable on methadone to stay on methadone, if possible, especially on higher doses
- Suitable candidates should have no complicating medical or psychiatric issues
- Work closely with the patient's opioid treatment program (OTP) before starting buprenorphine induction

The induction protocol differs in slight but important ways for patients who are dependent on long-acting opioids, including methadone, in comparison to short-acting opioids.

Feasibility of outpatient transfer from low to moderate doses of methadone to buprenorphine has been demonstrated in a number of clinical trials. For patients switching from methadone, because the process is somewhat complicated, providers would ideally have:

- Experience working with methadone maintenance patients
- Good understanding of the pharmacokinetics of methadone

**PRACTICE ACTIONS**

Because patients switching from methadone to office-based buprenorphine treatment are going from a program having a higher level of structure to a lower level of structure, be sure that there are adequate psychosocial supports in place to minimize a potential relapse.
METHADONE TAPER BEFORE THE TRANSFER

Case: Mr. Frank
Mr. Frank and his wife come to the office in the morning for buprenorphine induction. He took his last methadone 35 mg dose 48 hours ago.
Mr. Frank says that he “feels terrible” and is having cravings.
Physical exam confirms that he is in moderate withdrawal (COWS: 14).
Based on his current status, is Mr. Frank ready for induction?

Precipitated Withdrawal.
One concern in methadone-to-buprenorphine transfer is the potential for precipitated withdrawal\(^7\). In order to minimize this risk, you should taper your patients who are maintained on high doses of methadone\(^17\). Taper them down to a 30 mg methadone daily dose (ideally) prior to transfer and maintain them on this dose for a week. Patients at doses lower than 30 mg have less discomfort in the transfer.

- Conduct the methadone taper, in conjunction with the opioid treatment program (OTP), over several days or weeks. The long taper is because of tissue stores of methadone built up over time.
- Prepare your patient for some discomfort and withdrawal symptoms during this time.
- Adjunctive medications are often needed to address withdrawal symptoms during the tapering period.
- Many patients will feel anxiety about withdrawal during this time.

Patients on high doses of methadone (60+ mg) may experience significant pain or discomfort during the tapering period, which puts them at risk for relapse. It will also take these patients longer to be able to tolerate buprenorphine without withdrawal symptoms. Carefully monitor these patients and resume methadone maintenance if needed – a transfer may not be appropriate\(^18\).

Induction – Methadone Transfer to Buprenorphine

Timing
Because of tissue stores of methadone built up over time, patients need a relatively longer wait after stopping opioids. Patients coming off a methadone taper need to abstain from opioids for 36 to 72 hours before taking their first buprenorphine dose\(^7\). They should be in mild to moderate withdrawal before taking their first dose, as determined by the COWS.

Timing of the first dose can be a challenge with methadone transfer patients:

- Patients who have never missed a methadone dose will be unaware of how long it takes them to start to experience withdrawal symptoms.
- Methadone is stored in the body longer and metabolized more slowly, so it is more difficult to predict how quickly withdrawal symptoms will start after the last dose of methadone.
- Each person metabolizes methadone differently, so there is no “absolute.”

Induction Process
In order to minimize the risk of precipitated withdrawal during buprenorphine induction, Mr. Frank's daily dose of methadone should be tapered down to 30 mg. Buprenorphine rarely precipitates withdrawal in patients taking 30 mg/day or less of methadone. You discuss the plan with the director of his Opioid Treatment Program, and Mr.
Frank is able to taper down to 35 mg over a period of 3 weeks. Guidelines say to keep him at the lowered dose for a week prior to inductions. However, his withdrawal and cravings symptoms are more severe below a 35 mg dose per day.

After 3 days at the 35 mg daily dose of methadone, Mr. Frank is ready for induction. Because he is experiencing more severe withdrawal symptoms at this lower dose, you agree to expedite the buprenorphine transfer.

After the patient is in withdrawal, the induction process is the same as for short-acting opioids:

1. Patients should be inducted starting with 4 mg of buprenorphine initial dose. Lower starting doses of around 0.8 mg buprenorphine have been associated with less withdrawal discomfort; however, higher doses of around 32 mg buprenorphine have resulted in shorter duration of symptoms. The 4 mg initial dose is chosen as a balance between these two benefits.
2. Then given additional 4 mg doses when withdrawal symptoms reappear.

**Induction Dosing Schedule**
The buprenorphine dosing guidelines are the same for long-acting and short-acting opioids. As a refresher, here is the dosing schedule for the induction period (Doses described were established for Suboxone or generic sublingual tablets; use equivalent doses for other formulations):

- Day 1 total dose: 8-16 mg (should not be within 24 hrs of last methadone dose). Less withdrawal discomfort has been reported when starting with lower doses, however shorter duration of symptoms was associated with higher doses.
- Day 2 total dose: 12-24 mg (dependent on first-day dose)
- Day 3+ total dose: up to 32 mg
- Maximum daily increase: 8 mg
- Target daily dose: 12-16 mg
- Maximum daily dose: 32 mg

Patients withdrawing from long-time methadone maintenance seem to take longer to get comfortable. They often require higher doses of buprenorphine (more than 16 mg) on day 1 to treat withdrawal symptoms. These patients should be titrated down to a lower dose after a few days.

**PRACTICE TIP**
Some clinicians induce methadone transfer patients with a smaller first dose, as low as 2 mg, to decrease the chances of precipitated withdrawal, and to minimize its effects should it occur. If there is no precipitated withdrawal, then it is safe to increase the dose soon thereafter.

Remember that patients can be placed back on methadone if they do not tolerate buprenorphine, as long as their methadone clinic permits this.
PREPARING FOR INDUCTION – METHADONE TRANSFER TO BUPRENORPHINE

Quiz: Case Study – Mr. Cole

Name: Mr. Cole
Age: 50 years old
Reason For Visit: He wants to try buprenorphine maintenance instead of methadone.
Medical History: Mr. Cole developed opioid use disorder almost a decade ago after taking prescription opioids for several months following a workplace injury to his back and groin. When he was unable to get prescription opioids, he started buying heroin, which he uses intranasally along with oxycodone, if he can obtain it. Currently, he has mild to moderate, intermittent pain.
Treatment History: Mr. Cole has been off and on methadone maintenance 3 times during the past 8 years. Twice Mr. Cole was tapered off of methadone successfully at his own request and then later relapsed after 3 months to a year and a half; and once he started using heroin while still being maintained on methadone.

When he was not working Mr. Cole did not feel like going all the way to the methadone maintenance treatment (MMT) clinic every day, so he decided to "manage" his treatment himself. He said that he can buy methadone on the street or from a friend who shares his daily methadone dose with him; they each take 25 mg/day. He wants to switch to buprenorphine.

Provider: What is making you want to switch from methadone to buprenorphine?

Mr. Cole: It feels like I get judged for being on it. Plus, the daily methadone clinic visits are a hassle, and I don't want to risk getting in trouble for how I've been getting my methadone, you know. I thought I could try switching to buprenorphine instead.

From What You Know So Far, Are You Inclined To Think That Mr. Cole Is A Good Candidate For Buprenorphine Treatment? (Choose One)

1. Definitely Yes
2. Definitely No
3. Possibly, but this is not enough information
CASE STUDY – MR. COLE QUIZ FEEDBACK

(1) Definitely Yes,
(2) Definitely No
At this time you do not have enough information to assess fully whether or not Mr. Cole is a suitable candidate for buprenorphine treatment, but you should not rule it out. Gather more information to get a clearer picture and make a well-informed clinical judgment.

(3) Possibly, But This Is Not Enough Information
Correct. At this time you do not have enough information to assess fully whether or not Mr. Cole is a suitable candidate for buprenorphine treatment, but you should not rule it out. Gather more information to get a clearer picture and make a well-informed clinical judgment.
Patient Education In Transfer From Methadone To Buprenorphine

Advise patients transferring from methadone to buprenorphine about what to expect during the induction and maintenance periods:

- The risks and benefits of transferring
- Information on how the maintenance therapies differ
- You might wish to include an additional consent form detailing the methadone-to-buprenorphine transfer process

Mr. Cole – Additional History

Further Treatment History

During the clinical interview, you further explore Mr. Cole’s history and current situation.

Mr. Cole: All of my relapses were directly related to stressful events in my life: losing my job, an arrest for assault that I didn’t even do, and the death of my brother. Even though I had the relapses, I did pretty well on methadone. Other than those 3 times, I’ve always had negative urine test results.

Provider: Have you had any counseling or participated in a support group?

Mr. Cole: Yes. I have attended Narcotics Anonymous group meetings, and I saw a counselor at the clinic a few times.

Psychiatric History: Mr. Cole was treated for depression with SSRIs for 6 months after his brother died. He does not think that they helped and that over time he just started to “move on.”

Social and Work History: Mr. Cole recently was married for the second time to his longtime girlfriend. She is very supportive of him seeking buprenorphine treatment. He recently reunited with his large extended family as well, most of whom live in the same town as Mr. Cole.

Mr. Cole has two children from his first marriage and two with his current wife. He is currently on seasonal unemployment from his job as a carpenter, a job which offers him health insurance with medication coverage.

Physical Exam Findings: Physical exam is unremarkable.

Quiz: Mr. Cole – Induction Issues

Mr. Cole and his wife are relieved that, after a thorough evaluation, you agreed to induct Mr. Cole onto buprenorphine using combination generic sublingual tablets. He says he is committed to stopping drug use for the last time.

His case is somewhat complicated by the fact that he has been abusing both short-acting (heroin, oxycodone) and long-acting (methadone) opioids simultaneously.

How Should Mr. Cole Prepare For Induction? (Choose One)

1. Abstain from heroin and oxycodone for 12 hours or more
2. Abstain from methadone for at least 48 hours
3. Abstain from ALL opioids for at least 48 hours
4. Abstain from heroin and oxycodone for 12 hours or more AND abstain from methadone for at least 48 hours
MR. COLE – INDUCTION ISSUES QUIZ FEEDBACK

(1) Abstain From Heroin And Oxycodone For 12 Hours Or More
This is not the best option. Guidelines do recommend abstaining from short-acting opioids for at least 12 hours or more as tolerated to ensure that the patient is in adequate withdrawal prior to buprenorphine induction. However, Mr. Cole also has been using methadone daily, and guidelines recommend that patients should abstain from these longer-acting opioids for at least 48 hours in order to avoid precipitated withdrawal. Mr. Cole says that he is taking 25 mg of methadone per day, so tapering down his methadone dose will not be necessary prior to induction.

(2) Abstain From Methadone For At Least 48 Hours
This is not the best option. It is correct that Mr. Cole should stop using methadone at least 48 hours prior to induction in order to avoid precipitated withdrawal. Mr. Cole says that he is taking 25 mg of methadone per day, so tapering down his methadone dose will not be necessary. However, guidelines ALSO recommend abstaining from short-acting opioids for at least 12 hours or more as tolerated. Abstaining from them for 48 hours will probably lead to severe withdrawal, so 12-24 hours is probably a more realistic time frame.

(3) Abstain From ALL Opioids For At Least 48 Hours
This is not the best option. Guidelines recommend abstaining from short-acting opioids for at least 12 hours or more as tolerated, but abstaining from them for 48 hours will probably lead to severe withdrawal. However, Mr. Cole should stop using methadone at least 48 hours prior to induction in order to avoid precipitated withdrawal. Mr. Cole says that he is taking 25 mg of methadone per day, so tapering down his methadone dose will not be necessary.

(4) Abstain From Heroin And Oxycodone For 12 Hours Or More AND Abstain From Methadone For At Least 48 Hours
This is the best option. Guidelines recommend abstaining from short-acting opioids for at least 12 hours or more as tolerated to ensure that the patient is in adequate withdrawal prior to buprenorphine induction. Regarding methadone, guidelines recommend that patients abstain from these longer-acting opioids for at least 48 hours before induction, in order to avoid precipitated withdrawal. Mr. Cole says that he is already only taking 25 mg of methadone per day, so tapering down his methadone dose will not be necessary prior to induction. So, he can simply stop taking methadone 48 hours before induction, without tapering first. Then he would stop using short-acting opioids 12 to 24 hours prior to induction.
**Continuing Treatment – Methadone Transfer To Buprenorphine**

**Induction, Day 2**
On Day 2, you assess Mr. Frank via phone. He says that he awoke with significant cravings and feeling nauseated. After his initial dose (12 mg) and some ondansetron for nausea, he started to feel better. He required two more 4 mg doses of buprenorphine on Day 2.

**Induction, Day 3**
On Day 3, Mr. Frank felt better in the morning. He said that he felt good the night before, too, and finally had a good dinner and good night's sleep.

On Day 3, he started with an initial dose of 20 mg and said that he felt pretty good throughout the day; he did not require another buprenorphine dose increase. The next day, he again took 20 mg in the morning and felt good all day. His maintenance dose was then set at 20 mg/day.

**FYI: Buprenorphine To Methadone Transfer**
When switching in the opposite direction, that is, going from buprenorphine to methadone, there is no need for a time delay. Adding methadone, which is a full mu-opioid agonist to buprenorphine, which is a partial agonist, typically does not produce an adverse reaction\(^\text{14}\).

**Poll: When you are waived, are you willing to transfer your patients from methadone to buprenorphine?**
- Yes, I am willing to transfer my patients to buprenorphine at this time
- I might be willing to transfer my patients to buprenorphine, with additional training and information
- No, I am not willing to transfer my patients to buprenorphine

What do you think? Take the poll yourself!

https://bup.clinicalencounters.com/methadone-poll/

**Mr. Cole – Proceeding With Induction**

**Talking With Mr. Cole**
Mr. Cole follows your instructions about abstaining but goes about it in his own way. His wife brings him into the clinic for induction.

*Mr. Cole: I decreased my methadone and then stopped taking it completely a week ago, but I doubled my oxycodone and heroin at the same time. I took my last heroin two days ago and last dose of oxycodone 24 hours ago.*

*Provider: Are you experiencing any withdrawal?*

*Mr. Cole: Definitely!*

You test and find that he is in moderate withdrawal (*COWS: 12*).

Additional information sources may be a good idea in his case as well. Consider talking with his wife, with permission. Keep in mind that occasionally a partner's "support" may be to get the medication for themselves.

**Proceed Slowly**
Proceeding slowly with Mr. Cole's induction, using smaller doses with more time between doses, seems prudent given his recent substance use history. He may not have been completely honest about the time of last use, for
example. Adjunctive medications can be used to ease any withdrawal during induction and increase Mr. Cole's chances of success during the stabilization period.
ILLICIT BUPRENORPHINE USERS

Prevalence Of Illicit Buprenorphine Use
Many of your patients starting buprenorphine are already taking buprenorphine illicitly.

The number of people taking buprenorphine illicitly is increasing. In one study of around 250 people using diverted buprenorphine:

- 9.6% were using it daily
- 50.6% used it infrequently (1-2 uses over a 6-month period)

People taking buprenorphine illicitly often use other drugs as well. Urine drug testing of over 1,000 persons on parole or probation in Maryland found that of the 9.2% who tested positive for buprenorphine, 45% contained 2 or more other drugs – most often morphine (45%), cocaine (27%), and benzodiazepines (19%).

Obtain A Detailed History Of Illicit Buprenorphine Use
Ask all patients whether they are already taking buprenorphine, even illicit use, before induction. For those already using buprenorphine, determine if they have a regular, established dose of buprenorphine that might affect how treatment is started.

Possible reasons for illicit buprenorphine use include:

- Not able to purchase their usual opioid of abuse due to a supply not being available
- Became dependent during pain management, and not able to obtain a legitimate prescription for various reasons
- Curious whether buprenorphine might help them quit
- Lower cost than the drug to which they are addicted
- For the high (unlikely for heroin users, as the high does not compare)
- Ask your patients starting buprenorphine treatment if they use unprescribed buprenorphine and establish whether it is:
  - Regular or occasional use
  - What dose is being used
- Determine whether buprenorphine is the only drug your patients are taking or whether they are taking other opioids as well; the latter is typically the case.

Up to 1-2 mg of buprenorphine may be taken recreationally without developing tolerance, especially when used intermittently, although individual response varies.

Patients Already Using Buprenorphine Illicitly
If a new patient is already taking buprenorphine regularly, buprenorphine can simply be continued if the following conditions are met:

- The dose is in the therapeutic range.
- The patient is not on any other drugs, verified by drug test.

The picture becomes more complicated when:

- Other opioids are being taken at the same time as illicit buprenorphine.
- The dose of buprenorphine is not in the therapeutic range.
• Buprenorphine is abused intermittently.

The buprenorphine dose will need to be titrated during the induction. The dose at which the titration is started might be modified if there is already some regular use of buprenorphine. Consultation with a more experienced buprenorphine prescriber can be helpful in determining the most appropriate approach to induction in a particular case. More experienced prescribers can be found through the PCSS-MAT mentor program.

**Take Steps To Prevent Additional Diversion**

Treatment structure is especially important with patients in this category, in order to minimize the risk for buprenorphine diversion. Treatment structure may include urine drug tests, frequent follow-up visits, limited supply, and written treatment agreements.
MEDICALLY SUPERVISED WITHDRAWAL

Requesting Medically Supervised Withdrawal (Detoxification)
Detoxification, or medically supervised withdrawal (MSW), involves using a medication such as buprenorphine to take a patient from an opioid-dependent to an opioid-free medication-free and drug-free state. Patients who want to stop using opioids, but do not want to be maintained on buprenorphine, may request MSW.

Research has shown buprenorphine to be an effective medication in helping patients detoxify from other opioids, superior to clonidine alone, and relatively equal to methadone in relieving withdrawal symptoms\(^{22-24}\). Buprenorphine is relatively equal to methadone in relieving signs and symptoms of withdrawal.

Risks Of Medically Supervised Withdrawal
Relapse is a significant concern when conducting MSW. It is extremely common and, in some cases, can lead to overdose. The implications of relapse and possible risk of overdose should be carefully explained to patients who are requesting MSW. Also, the benefits of maintenance therapy should be discussed. Detoxification-based treatments have a low likelihood of long-term success as compared to medication maintenance treatments\(^{25}\), which is not surprising given our understanding of addiction as a chronic relapsing disease.

Inpatient Detoxification With Office-Based Maintenance
Hospitals, typically do not admit a person specifically to transfer them from methadone to buprenorphine. However, some patients who already are hospitalized for other reasons might be able to do so. Advantages include that they can be monitored and treated symptomatically in a safe and secure setting\(^{10}\). Patients can be inducted at an inpatient detox center and then, upon discharge, can make a seamless transfer to the outpatient setting, if they were evaluated prior to admission.

Detoxification Protocol

Patients Should Be Closely Monitored For Medically Supervised Withdrawal
If patients in detoxification become unstable, they should be:

- Carefully monitored
- Offered appropriate psychosocial support
- Offered medication maintenance treatment, such as buprenorphine

Detoxification is often conducted in an inpatient setting.

Clinical Guidelines
There is no absolute standard for how fast or slowly to detoxify a patient using buprenorphine. The general guideline is to detoxify as gradually as possible to minimize symptoms of withdrawal.

Conducting medically supervised withdrawal involves inducting the patient onto buprenorphine and then tapering the patient back off of buprenorphine. The buprenorphine/naloxone combination formulation should be used in most cases.

Dosing Schedule For Medically Supervised Withdrawal
In some instances the medically supervised withdrawal process can be completed in a week:

1. Induction on days 1 to 3
2. Tapering on days 4 to 7
In all instances, you should work closely with your patient to determine a realistic time frame for conducting medically supervised withdrawal.

**Further Guidance**
Detailed information about rapid detoxification is beyond the scope of this module. However, should you wish to learn more about protocols or how to implement such programs in your practice, you may wish to seek advice from a more experienced buprenorphine provider. You can find a waived mentor through the *Physician Clinical Support System-MAT*. 
STABILIZATION

The stabilization period is the next few weeks after induction during which patients should be maintained at their established dose, and continues until your patient is no longer experiencing withdrawal symptoms or intense cravings. This typically occurs at about 6-8 weeks following induction. Side effects should be minimal or none.

Continue monitoring patients to see how treatment is incorporated into their lives and whether use of other opioids is controlled.

**Goal Of Stabilization:**
Eliminate opioid use other than the partial agonist buprenorphine, as noted by patient reports and confirmed by urine drug testing.

Key elements of the stabilization phase include:

- Regular and frequent clinic visits until the patient stabilizes medically and psychosocially.
- Monitor patients weekly, or more frequently for the first month, adjusting for the patient's behavior:
  - Adjust dosing if needed
  - Recommend starting psychosocial therapies along with medication assisted therapy
    - Adherence to the treatment plan
    - Being responsible with their medication supply
    - No high-risk behaviors/diversion risks
  - Patient education about and starting psychosocial treatment
  - Limit medication supply until the next appointment time with no early prescriptions
  - Require that patients attend clinic visits to get next prescription

Following stabilization, visits can be less often, usually monthly, and larger supplies of medication can be provided.

**Dosage Guideline**
Most of your patients will have already stabilized at a dose of between 8 and 24 mg per day. Rarely, a dose of 32 mg may be needed for high opioid tolerance. Further dose adjustments are considered minor ‘tweaks,’ but usually are not a big part of stabilization.

Guidelines for dose adjustments in the uncommon case that it needs adjusting:

- Adjust the dose in no more than 2-4 mg per week in increments of no more than 2 mg at a time.
- Allow 5 days between adjustments, due to long plasma half-life and longer duration of action
- Daily dose is established when patient is no longer using illicit opioids, withdrawal symptoms are not present, and the patient is not experiencing cravings and has the best possible functional status.

Source: *Practice Guidance for Buprenorphine for the Treatment of Opioid Use Disorders*
PRACTICE ACTIONS
1. Your patients who are maintained on high doses of buprenorphine can take their doses sequentially, taking no more than 16 mg at one time.
2. During stabilization, observe your patients for possible complications of buprenorphine use and counsel patients to be aware of potential complications.

FYI
Remember: Formulations vary. Unless otherwise stated, dosages in this program refer to film or generic tablet formulations.

Long-term effects from opioid addiction, even after treatment, may include problems with executive control functions and ability to focus on a task. These symptoms underscore the benefit of long-term follow-up in the treatment of opioid addiction.

Follow-Up Timetable
The following timetable can be used as a guideline, assuming adherence to treatment, no treatment complications, and no opioid use:

- Weekly follow-up or more often if needed, for around the first 4 to 6 weeks post-induction
- Every other week follow-up for around the next 6 to 8 weeks
- Monthly follow-up indefinitely
- Quarterly follow-up for very stable, long-term patients

One possible guide for when to change from weekly to monthly visits is to change when the patient has three negative random urine drug tests in a row. If the patient de-stabilizes, resume weekly visits.

Protocol At Follow Ups
During follow-up sessions, you should:

- Assess any medical complaints your patient may have
- Adjust your patient’s daily dose if he or she appears to be over- or undermedicated
- Direct your patient toward psychosocial services and thereafter assess whether the patient is using these services
- Monitor for signs of buprenorphine misuse or diversion
- Conduct random urine drug screens (weekly during the first 2 months) to monitor for continued abuse of other opioids and other drugs and for proper use of buprenorphine (if concerned)

PRACTICE TIP
Some providers, rather than seeing the patient weekly themselves, have the patient go to counseling weekly. The provider checks with the psychosocial provider regularly, but sees the patient in person less often.
LOOKING AHEAD – MAINTENANCE PHASE

Ms. Sanchez continued at 8 mg for three months with no side effects and no cravings.

**Quiz: Looking Ahead To Maintenance**

Which Of The Following Are Recommendations For Providers During The Maintenance Phase Of Buprenorphine Therapy? (Choose All That Apply)

1. Adjust patients' daily dose if they are either over- or undermedicated
2. Assess patients for readiness to discontinue buprenorphine use, and discontinue most patients
3. Remain vigilant for signs of resumed opioid abuse
4. Assess the patients' medical complaints
LOOKING AHEAD TO MAINTENANCE QUIZ FEEDBACK

An expert panel developed the following consensus guidelines regarding dosage during maintenance: 16 mg or greater or the equivalent is effective at suppressing illicit opioid use. The dose range for effectiveness is usually 4 to 24 mg buprenorphine. Source: *Practice Guidance for Buprenorphine for the Treatment of Opioid Use Disorders*

(1) Adjust Patients' Daily Dose If They Are Either Over- Or Undermedicated
Correct. Providers are encouraged to adjust patients' buprenorphine doses as appropriate.

(2) Assess Patients For Readiness To Discontinue Buprenorphine Use, And Discontinue Most Patients
Most patients should be encouraged to continue buprenorphine use indefinitely, given the very high relapse rate for patients who discontinue pharmacotherapy.

(3) Remain Vigilant For Signs Of Resumed Opioid Abuse
Correct. Providers are encouraged to monitor for resumed opioid abuse.

(4) Assess The Patients' Medical Complaints
Correct. Providers are encouraged to assess patients' medical complaints.
KEY POINTS

• Induction or starting of buprenorphine can be completed at home or in the office, as determined by patient characteristics (including ability to follow instructions).

• The patient should stop their opioid use around a half day prior to induction and be in a state of mild to moderate withdrawal when taking their first dose.

• The first day or two is typically used to titrate the dose upward from an initial dose of around 2 to 4 mg in order to determine an optimal dose that controls withdrawal symptoms.

• A common maintenance dose is 12 to 16 mg.
**SUMMARY**

Buprenorphine treatment phases are: Induction, Stabilization, Maintenance

**Formulations**
- Buprenorphine is available as buprenorphine/naloxone combination therapy. The form that should be prescribed for most patients, and buprenorphine monotherapy.
- Sublingual film, buccal film, or sublingual tablet are available currently for induction. Other long-acting formulations (implant, injection) are only used after a stable maintenance dose is established.

**General Induction Guidelines**
- Induction can be conducted in the office or at home. Consider that the "Appropriate Use" checklist published by the FDA includes "Provided induction doses under appropriate supervision" and that some patients may benefit from the guidance and monitoring of an in-office visit.
- Patients should be in mild/moderate withdrawal (COWS score of 12-16), typically achieved by 12 to 16 hours of abstinence if dependent on short-acting opioids, 17-24 hours for intermediate-acting, and 30-48 hours for methadone and other long-acting opioids.\(^4\)
- Initial dose is 2 mg to 4 mg buprenorphine, typically with the corresponding dose of naloxone.
- Monitor the patient for around 1+ hour for response to dose should occur at induction, followed by increments of 2 to 4 mg, followed by another 1+ monitoring.
- Maximum dose day 1 is 16 mg.
- Follow-up by phone that day and for each day of induction until the maintenance dose is established.
- Recommended maintenance daily dose is 4 to 24 mg\(^4\). Most commonly, the maintenance dose is 12 to 16 mg (Suboxone, generic, or equivalent doses for Zubsolv or Bunavail), which is as effective as 60 mg of methadone.
- After maintenance dose is established, have an office visit in 3-4 days.
- Dose adjustments potentially occur during all 3 phases of treatment but are far less common after induction.

**Standard Induction Protocol**
- First-day maximum dose can range from 8-16 mg (Suboxone or equivalent doses for Zubsolv or Bunavail), given in 4 mg increments.
- After day 1, dose can be increased a maximum of 8 mg per day, to a ceiling dose of 32 mg.
- Daily dose is established when the patient is neither undermedicated nor overmedicated. Average daily dose is 16 mg.
- During induction, treat withdrawal symptomatically.

**Stabilization**
- The stabilization period lasts several weeks following induction. Patients should receive a limited supply of medication during stabilization and return for regular follow-up; weekly for the first month.
Medically Supervised Withdrawal
Buprenorphine can be used to ease acute symptoms of withdrawal for patients who want complete detoxification followed by taking no medication-assisted treatment or opioids. It generally has poorer success rates than continued medication-assisted treatment.
**RESOURCES**

**AMA Guide: Promote safe storage and disposal of opioids and all medications:** AMA Task Force to Reduce Opioid Abuse produced a brief flier with 3 steps providers should take to promote safe storage and disposal of opioids and all medications with links to resources for patients.

**Appropriate Use Checklist:** Reminder of the safe use conditions and monitoring requirements for prescribing buprenorphine-containing transmucosal products for opioid dependence.

**Buprenorphine Product Formulations Comparison:** Describes the different formulations of buprenorphine for treatment of opioid use disorder. Includes Brand Names, How Supplied, Dosage, Maintenance Target Dose, and Instructions for Use.

**Buprenorphine Product Formulations Comparison:** Compares the different formulations of buprenorphine products made by different drug companies.

**Clinical Opioid Withdrawal Scale (COWS):** This PDF Document contains the Clinical Opioid Withdrawal Scale (COWS), a common instrument used to assess a patient's opioid withdrawal severity.

**Home Buprenorphine / Naloxone Induction in Primary Care:** This abstract discusses a study done on the feasibility of an unobserved buprenorphine induction protocol. The study involved 103 patients who were heroin users and prescription opioid misusers and discusses safety and rates of complications from induction through follow-up.

**Información sobre la Buprenorfina (The Facts about Buprenorphine for Treatment of Opioid Addiction (en Español)):** Ofrece información a los pacientes sobre la buprenorfina y los tratamientos con ayuda de medicamentos para tratar la adicción a los opioides, y también describe la adicción y los síntomas del síndrome de abstinencia. Además, explica cómo funciona la buprenorfina, su uso apropiado, sus efectos secundarios y cómo se la utiliza en conjunto con la consejería en el proceso de recuperación.

**Models of Buprenorphine Induction:** A learning activity that includes the different clinical models of buprenorphine induction, the associated evidence, and the pros and cons of each.

**Objective Opiate Withdrawal Scale (OOWS):** The Objective Opiate Withdrawal Scale (OOWS) contains 13 physically observable signs, rated present or absent, based on a timed period of observation of the patient by a rater.

**Patient Handout: The Facts about Buprenorphine for Treatment of Opioid Addiction:** This patient booklet is free to download from the Substance Abuse and Mental Health Services Administration (SAMHSA). It gives patients information on buprenorphine and medication-assisted treatment for opioid addiction. Describes addiction and withdrawal, how buprenorphine works, its proper use, its side effects, and how it fits with counseling in the recovery process.

**Patient Rights: Confidentiality and Consent:** This is a patient handout to inform patients about their rights when undergoing office-based buprenorphine treatment.

**Physician Clinical Support System – Clinical Coaching:** This website is designed to provide coaching for providers in treating chronic pain, and substance use disorders including opioid use disorder.

**Sample Consent Form:** This is a sample of a consent form that can be used when initiating buprenorphine treatment for a new patient.

**Side Effect Management:** This form provides a list of possible symptoms that a patient may have during buprenorphine treatment, possible causes, and recommended management of the symptoms.
**Subjective Opiate Withdrawal Scale (SOWS):** Annex of opioid withdrawal scales for downloading includes the Subjective Opiate Withdrawal Scale (SOWS). The SOWS contains 16 symptoms whose intensity the patient rates on a scale of 0 (not at all) to 4 (extremely).

**TIP 40 Chapter 4: Treatment Protocols:** Discusses protocols for office-based buprenorphine treatment, including the administering of the drug itself, devising a treatment plan, and choosing an appropriate frequency for visits.

**Withdrawal Versus Precipitated Withdrawal:** Two types of withdrawal are associated with mu opioid agonist dependence: withdrawal and precipitated withdrawal.
REFERENCES


