Induction – Initiating Buprenorphine Treatment (Cases Only)

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 (didactic + cases), 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[1], later guidelines[2], and the FSMB Model policy[3] 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.

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.*

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.

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.

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[9]. 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
Incorrect; 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

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.

CASE EXAMPLE – MR. ALLEN

Prior To Induction Day

You are preparing to treat Mr. Allen for dependence on heroin (a short-acting opioid). After consultation, you decided that he is a suitable candidate for buprenorphine treatment.

You meet with Mr. Allen 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 -[4]). 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)[11]

METHADONE TRANSFER TO BUPRENORPHINE

Case: Mr. Frank – Methadone Transfer to Buprenorphine

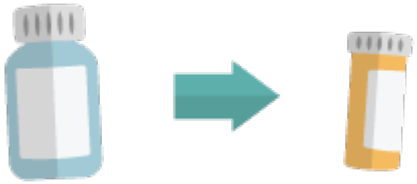
Reason for visit: Mr. Frank comes in seeking buprenorphine treatment instead of his current methadone treatment.

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[16]

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[17]. 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.

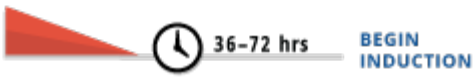
One concern in methadone-to-buprenorphine transfer is the potential for precipitated withdrawal[7]. In order to minimize this risk, you should taper your patients who are maintained on high doses of methadone[17]. Taper them down to a 30 mg methadone daily dose (ideally) prior to transfer and maintain 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[17]. 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[17]. Less withdrawal discomfort has been reported when starting with lower doses, however shorter duration of symptoms was associated with higher doses[17]
- 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[10]. 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[10].

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.

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[14].

Poll: When you are waivered, 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.

MS. SANCHEZ – STABILIZATION

Most likely she 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. She was stabilized on an 8 mg dose.

LOOKING AHEAD – MAINTENANCE PHASE

Ms. Sanchez continued at 8 mg for three months with no side effects and no cravings. We will pick up her case again in the Maintenance module.

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[2]. The dose range for effectiveness is usually 4 to 24 mg buprenorphine. Source: *Practice Guidance for Buprenorphine for the Treatment of Opioid Use Disorders*[26]

(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.