IMPACT OF OPIOID USE DISORDER

Goal
To familiarize providers with the extent of the opioid epidemic, the effect of opioid use disorder on the individual patient, and which individuals are at increased risk.

After completing this module, participants will be able to:

• Realize the likelihood of encountering heroin use and prescription opioid misuse in patients in the United States.
• Predict the potential impact of opioid use disorder on patients in terms of morbidity and mortality.
• Anticipate co-morbid negative health effects in patients having opioid use disorder.
• Recognize patients having dual diagnosis describe the interrelationships between opioid use disorder and mental illness.

Practice Gap
Physicians prescribing buprenorphine need an understanding of the impact of opioid used disorder on their patients and the population, including interactions between mental health and substance use disorders.1–4.

Patient-Centered Training Strategy
We will use cases to convey material and highlight a successful interaction strategy based on patient-centered practice. Viewing the opioid use problem from the patient perspective reveals a more complete appreciation of the impact of opioid addiction and the value of treatment.
EXAMPLE CASE – MR. HOWARD

The impact of opioid use disorder is devastating for the individuals it affects. Here is just one example:

Name: Mr. Howard
Age: 42 years old

Reason For Visit: Mr. Howard made an appointment with you, his primary care physician because he says that he is ready to get help for substance use problems.

Patient History: Mr. Howard has been physically dependent on heroin for 3 years. He also has mild alcohol use disorder and has been exposed to hepatitis C.

Is Mr. Howard A Good Candidate For Office-based Buprenorphine Treatment At This Time? (Choose The Best Answer)

1. No, patients who present with dual substance use disorder diagnoses are too complex and should automatically be sent to an addiction specialist instead.
2. No, because his exposure to hepatitis C could complicate opioid use disorder treatment; he should be sent to a hepatologist instead.
3. Yes, if you generally treat opioid and alcohol use disorders in your practice and you feel comfortable dealing with the complexities of the combination of these two diagnoses, you can treat him for these two problems.
4. Yes, but he should be sent to an inpatient rehabilitation facility first for complete detoxification and evaluation.
CASE FEEDBACK

1) No, Patients Who Present With Dual Substance Use Disorder Diagnoses Are Too Complex And Should Automatically Be Sent To An Addiction Specialist Instead.
Not necessarily. While most primary care providers would refer a patient who has a dual diagnosis of heroin and alcohol use disorder for specialty treatment, it is not "automatic." Each physician must evaluate his/her individual and office capabilities before deciding whether to treat such patients.

2) No, Because His Exposure To Hepatitis C Could Complicate Opioid Use Disorder Treatment; He Should Be Sent To A Hepatologist Instead.
Exposure to hepatitis C will not complicate current opioid use disorder treatment. However, it is good to remain aware of potential complicating factors during office-based treatment so specialist help can be obtained if needed. Whether he is referred to a hepatologist or not depends upon the scope of your practice.

3) Yes, If You Generally Treat Opioid And Alcohol Use Disorders In Your Practice And You Feel Comfortable Dealing With The Complexities Of The Combination Of These Two Diagnoses, You Can Treat Him For These Two Problems.
Correct. Primary care physicians who are comfortable doing so can provide treatment for dual-diagnosis patients like Mr. Howard. However, most would probably make a referral for specialty treatment. If you treat him in your practice, Mr. Howard should be referred to psychosocial services to round out his comprehensive addiction treatment. His hepatitis C exposure can be managed in your practice or referred, depending upon the scope of your practice.

4) Yes, But He Should Be Sent To An Inpatient Rehabilitation Facility First For Complete Detoxification And Evaluation.
You need to further evaluate Mr. Howard before sending him to detox. A patient starting on buprenorphine does not need to be completely detoxified from opioids before starting treatment. Primary care physicians who are comfortable doing so can provide treatment for dual-diagnosis patients like Mr. Howard.

This case illustrates just some of the potential impact of opioid misuse and opioid use disorder for individuals. The extent of the problem can be understood from looking at public health statistics.
THE OPIOID EPIDEMIC

Opioid misuse is more common than the figures for opioid use disorder and present a risk to your patients of developing addiction, as well as the dangers of overdose. The physical and mental health consequences of opioid misuse are significant and affect the full range of individuals.

"MISUSE" refers to using prescription opioids in any way other than as prescribed. Misuse includes both a person who takes a Percocet® every 2 hours instead of every 4, as well as the person who obtains medications illegally on the street or by stealing pills from a relative.

Opioid Misuse Statistics

The National Drug Use and Health survey of, found the following rates of opioid misuse among Americans:

- 11.8 million or 4.4% of the American population age 12 and over misused prescription pain reliever (includes any non-medically supervised use) in the year before a 2016 survey.\(^3\)
- 948,000 used heroin in the past year. Heroin use continues despite the known devastating effects. Past year heroin use rose from 2013 to 2016 to an all-time high rate of 0.4% of the population.\(^3\)
- The rate of overdose deaths is also steadily increasing. In 2015, over 22,000 deaths involved prescription opioids, an increase from 19,000 in 2014, which is nearly a 16% increase.\(^5\) In 2016, 63,600 drug overdose deaths involved an opioid, either prescription or heroin.\(^6\) There have been three waves in the increase of opioid deaths.

Relationship Between Opioid Prescribing and the Opioid Epidemic

Increases in opioid prescribing appear to be related to increases in opioid use disorder. A factor contributing to the epidemic is the high rate of chronic pain for which opioids are frequently prescribed. A high percentage of persons in treatment for opioid addiction started taking the drugs during pain treatment.\(^15\) For example, a sizable majority (84%) of a group of individuals in opioid addiction treatment received a prescription for opioids for pain at some point.\(^16\) The prescribing of opioids has increased in the past 20 years, in tandem with the increased frequency of opioid addiction.\(^2,17\) Over 289 million prescriptions for opioids are written per year.\(^14\) The CDC has published guidelines for prescribing opioids, which, if followed, would likely decrease the extent of this epidemic.\(^18\)

Only some patients who are prescribed opioids will become addicted. Becoming addicted after an opioid prescription is more common with chronic pain than with acute pain and with higher doses (MME 120+ mg, OR=122.45) than with lower doses (MME 1–36 mg, OR=14.92).\(^19\) Among primary care patients on chronic opioid therapy for pain, the CDC estimates the incidence of opioid use disorder was 3 to 26%\(^18\). Opioid use disorder in the context of having chronic pain is defined as using more than is needed for pain for purposes other than treating pain.\(^20\)

- The percentage of individuals who used an opioid analgesic stronger than morphine increased from 17.0% in 1999-2002 to 37.0% in 2011-2012.\(^8\)
- Opioid overdose deaths rose in parallel with an increase in opioid prescribing in the 1990s.
- Treatment for opioid use disorder increased steadily in parallel to sales of opioid pain relievers from 1999 to 2009.\(^9,10\)

Opioids Are Common Among Diverted Drugs Seized By DEA:

- Oxycodone and hydrocodone comprised the majority of the drugs seized by law enforcement in 2009.\(^12\)
The opioid maintenance medications, methadone and buprenorphine, together were 14% of the drugs seized.

**Cost To Society:**
- Total U.S. societal costs of prescription opioid abuse have been estimated at over $55 billion\(^\text{13}\).
- The health care component of the cost for prescription opioid abuse accounted for nearly half of the societal cost.
- The criminal justice costs accounted for 9% of the cost.

![Societal Costs of Prescription Opioid Abuse in the US](image)
PREVALENCE OF OPIOID MISUSE

The current rate of prescription opioid misuse of persons over age 12 reporting past-month misuse of pain relievers (1.2% of the population) is higher than past month heroin use (0.2% of the population). Trends for prescription pain relievers are more difficult to establish because of changing definitions in surveys. However, both prescription opioid misuse and heroin have increased over the past 10 years, according to most measures.

Prevalence of Opioid Pain Reliever Misuse

Opioid misuse continues to be very common and rising in most ways. The following evidence and status reports describe trends in the misuse of pain relievers:

- A majority, 62.3% of individuals 12 or older who misuse pain reliever, misuse pain relievers for pain relief; that is, they use it to relieve pain but without medical supervision. That leaves around 7.2 million people who misuse pain relievers for reasons other than pain relief.
- Opioid misuse is more common than opioid use disorder: For example, 11.5 million people misused prescription pain relievers in the past year vs. only 2.1 million meeting diagnostic criteria for prescription medication disorder.
- Prescription drugs containing hydrocodone, methadone, oxycodone, and morphine are among the more commonly abused prescription opioids.
- Hydrocodone combination medications, e.g., Vicodin, Lortab, were moved to Schedule II in 2014 because of the high potential for abuse.
- An increase in heroin overdose deaths starting around 2010 went from 1 per 100,000 to 4.9 per 100,000 in 2016.
- An increase in deaths from synthetic opioid overdose, especially fentanyl, starting around 2013.

Prevalence Of Heroin Use

Heroin use is not just an urban problem. Previously prevalent in low socioeconomic, urban settings, heroin usage among suburban, middle-class individuals has also increased in the past two decades. It can no longer be assumed that heroin users will fit the addict stereotype.

- 626,000 individuals over age 12 or 0.7% of the population had heroin disorder in 2016.
- Heroin overdose deaths per 100,000 rose from 1.0 in 2010 to 4.9 in 2016.
- The number of past users of heroin is around 828,000. This is higher than most years from 2002 through 2009 but similar to years since then.
Heroin is often one of the drugs involved in polysubstance use. Most heroin users also have misused prescription opioid pain medications.

**Discuss Mr. Howard’s Heroin Use**

**Name:** Mr. Howard  
**Age:** 42 years old

**Provider:** Do you use any other opioids besides heroin?

**Mr. Howard:** No, I started with taking some opioids I had left over from a dental procedure and then getting more for friends just to relax or get high once in a while. But, next thing I knew, I needed to keep taking them and had no way to get them that I could afford. I found that heroin was much cheaper.

**Provider:** And you say you are ready to get help for your heroin use and alcohol use problem now. What led you to seek help at this time?

**Mr. Howard:** Two things. I have a good job now and don't want to risk losing it from being caught doing something that is illegal. And the other is that I had an overdose and they needed to give me naloxone to reverse that. I survived that time and I didn't get arrested. I don't want to ever take that risk again.

**Provider:** That's understandable!
RISKS FOR OPIOID MISUSE

People Misuse Opioids In Order To:
- Intoxication, euphoria
- Self-medicate to treat pain
- Improve their mood (chemical coping)
- Divert opioids to other people, who use them for the above purposes

Use Of Opioids Can Lead To Addiction In Vulnerable Individuals, Which Includes People With:
- History of substance abuse
- Mental health disorder
- Younger age
- Pre-adolescent sexual abuse
- Family history of substance abuse

By Demographics

Opioid Misuse By Age
Current Use By Youths Aged 12 To 17 In 2016:
- Past month misuse of pain relievers in this age group was 1.0%, which is a little less than the population as a whole (1.2%)
- Past month heroin use in this age group was 0.1%, which is less than the population as a whole (0.2%)

Young Adults Aged 18 To 25:
- Past month misuse of pain relievers was 1.8%, a little higher than the population as a whole (1.2%)
- Past month heroin was 0.3% in this age group, which is higher than any other age group – the rate for the population as a whole is 0.2%

Opioid Misuse By Race, Gender, And Socioeconomic Status

Opioid use affects all races, genders, and socioeconomic statuses. Heroin use is no longer an isolated problem of poor, urban neighborhoods.

National survey data show significant gender differences in the misuse of prescription opioids. From 2007-2012, use of prescription opioid analgesics was higher among women at 7.2%, compared to men at 6.3%. However, males and females have reported lifetime use at 15.9% & 11.2%, respectively.

Significant racial differences exist in prescription opioid misuse. American Indians/Alaska Natives and non-Hispanic whites show the highest rates of opioid abuse.
Opioid Misuse Quiz

Which Has A Higher Prevalence Rate In The U.S.: Prescription Opioid Misuse Or Heroin Use?

1. Prescription opioid misuse
2. Heroin use
3. Prevalence rates are similar
OPIOID MISUSE QUIZ FEEDBACK

(1) Prescription Opioid Misuse
Correct. The percent of the U.S. population using heroin in the past year in 2016 was only 0.4. Past year prescription opioid misuse was far more prevalent at 4.4% of the population.

(2) Heroin Use,
(3) Prevalence Rates Are Similar
The percent of the U.S. population using heroin in the past year in 2016 was only 0.4. Past year prescription opioid misuse was far more prevalent at 4.4% of the population.
Impact of Opioid Use Disorder

OPIOID OVERDOSE

Opioid Overdose Rates High From Heroin and (Even More Often) Prescription Opioids

There has been an increase in overdose deaths from both heroin and prescription opioids that corresponds to an increase in their use\(^1^5\).

Opioid overdose deaths in the U.S. increased from July 2016 to September 2017 by 30% in many areas. Increases in this period in many cities were as high as 54% and in the Midwest were as high as 70%\(^2^6\). In 2016, there were 63,632 opioid overdose deaths from a combination of prescription and illicit opioids\(^1^2\). Increases in emergency department visits for overdose and an increase in prescription opioid misuse corresponds to an increase in the prescribing of opioids\(^1^4,2^7\).

In 2014 there were 10,574 heroin overdoses\(^1^5\). Heroin overdoses more than tripled from 2011 to 2014.

Injury cases that never make it to the emergency room and cases in which the link to opioids is not noted, make actual morbidity rates significantly higher.

PRACTICE TIP

Make patients aware of the high rate of opioid overdose during patient education. Patient knowledge of this risk may help serve as a motivator to start treatment or stay abstinent.

Overdose Risk and Mortality

Opioid Overdose Mortality

Opioid overdose can cause respiratory suppression, leading to cardiac arrest. Opioids, including heroin and prescription opioids, rank as either the most common or second most common drugs implicated in drug-related deaths\(^2^8\).

Overdose from prescription drugs is an epidemic, according to the CDC: 33,091 people died from opioid overdose in 2015, which is up 16% from 2014\(^2^9\). Opioid analgesics, like oxycodone, hydrocodone, and methadone, were involved in about 16,651 pharmaceutical overdose deaths. Overdose deaths involving prescription opioids were largely responsible for a doubling of the death rate by poisoning in the U.S. between 1999 and 2006\(^3^0\).

Prescription opioid overdose deaths have been increasing substantially since 1999. American Indian or Alaska natives and non-Hispanic white persons have seen a particularly alarming increase in opioid overdoses\(^3^1\).

Opioid Overdose Risk Factors

Overdose is more likely when the patient\(^3^2\):

- Has a history of substance abuse
Impact of Opioid Use Disorder

- Is on concurrent sedative-hypnotic medications
- Is depressed
- Has a new prescription or refill
- Is on a high dose

**Practice Action**

Because of the high risk of overdose in patients on chronic opioid therapy, if you prescribe it for a patient, you should consider also prescribing a means to treat overdose, such as a naloxone kit, and describe for the patient and family how to use it.
OPIOID PRESCRIBING GUIDELINES

Introduction
If you prescribe opioids for pain, it is important to know the evidence and expert consensus-based guidelines for how to prescribe so as to keep the risk of patients developing opioid use disorder to a minimum. You may also interact with other providers who refer patients to you for treatment of opioid use disorder and have the opportunity to guide them in how to minimize the risk of contributing to opioid use disorder developing in their patients.

CDC Guidelines For Prescribing Opioids
The CDC produced clinical guidelines for all patients based on an analysis of the literature and expert input. Following these guidelines would reduce the rate at which opioids are currently prescribed and therefore would likely help decrease the rate of opioid use disorder. The CDC’s guidelines are paraphrased below.

Evidence Levels Explained
- Evidence level 2 means evidence from clinical trials with limitations or exceptionally strong evidence from observational guidelines.
- Evidence level 3 means evidence from observational studies or randomized clinical trials with notable limitations.
- Evidence level 4 means it comes from clinical experience or observations or studies with important or major limitations.

Determine When To Initiate Or Continue Chronic Opioids
1. **Use other treatments first if possible:** Non-opioid pharmacologic medication and nonpharmacologic therapy are preferred treatment for chronic pain. Only consider opioids if benefits for both pain and functioning are likely to outweigh risks. If opioids are prescribed, minimize their use by combining with non-opioids and non-pharmacological therapy. *Evidence level 3.*

2. **Use treatment goals:** Set realistic treatment goals for pain and function at the outset. Explain that treatment will continue only if the risk vs. benefit ratio is favorable with "clinically meaningful improvement." *Evidence level 4.*

3. **Discuss risks with patient:** Discuss known risks and realistic benefits of opioid therapy before starting. Define patient and clinician responsibilities for managing therapy. *Evidence level 3.*

Opioid Selection, Dose, Duration, Follow-up, Discontinuation
1. **Use immediate release, not extended-release/long-acting opioids (ER/LAs)** when starting opioid therapy for chronic pain. Evidence level 4. The FDA's REMS (Risk Evaluation and Mitigation Strategy) for ER/LA opioids requires that the pharmaceutical companies provide special training for prescribers of ER/LA opioids. The requirement is of the company, but it seems important for the providers prescribing ER/LA opioids to take it.

2. **Use lowest possible dose:** Reassess benefits vs risks carefully when considering a dosage increase to ≥50 morphine milligram equivalents (MME)/day. Avoid increasing the dose to ≥90 MME/day or carefully justify. *Evidence level 3.*

3. **Prescribe only a 3 day supply for most acute pain, rarely more than 7-day supply:** The supply should be only for the duration of pain requiring opioids, not the duration of the pain. Prescribe the lowest effective dose of immediate-release opioids. *Evidence level 4.*
4. **Evaluation of benefits vs. risks is ongoing**: Evaluate benefits and risks with patients within 1 to 4 weeks of starting opioid therapy or a dose increase. Reevaluate at least every 3 months. Taper to a lower dosage or discontinue opioids if benefits do not exceed risks. Evidence level 4. Most patients can tolerate around a 10% reduction of the original dose per week.33

**Assessing Risk And Addressing Harms Of Opioid Use**

1. **Ongoing evaluation for opioid-related risk and harm**: This should include strategies to mitigate risk, especially of overdose, in which case, offering naloxone should be considered. Factors that increase risk for opioid overdose are history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use. *Evidence level 4.*

2. **Consult prescription drug monitoring program database before prescribing and during treatment**: Look at total opioid doses and dangerous drug combinations. Check the database at least every 3 months and consider checking at every prescription. *Evidence level 4.*

3. **Use urine drug testing before and during treatment**: Test prior to prescribing and at least annually for the prescribed medications, controlled prescription drugs, and illicit drugs. Drug testing may vary depending on the individual clinician/clinic and/or patient situation. Evidence level 4

4. **Avoid prescribing opioids together with benzodiazepines**: Avoid concurrent prescribing whenever possible. *Evidence level 3*

5. **Treat opioid use disorder**: Treat or arrange treatment for opioid use disorder, usually with medication-assisted treatment, i.e., buprenorphine or methadone, in combination with behavioral therapy. *Evidence level 2.*

**PRACTICE ACTION**

Patients will better understand, retain, and comply with your buppractice policies if they are put in writing. The effect may be further enhanced if the information is put in the form of a treatment agreement that is signed by both you and the patient.

**American Pain Society (APS) Clinical Guidelines for Chronic Opioid Therapy**

Clinical guidelines for the use of chronic opioid therapy overlap to a large extent with the more recent CDC guidelines presented on the previous page, but do include a few additional guidelines:

1. **Pain should be moderate or severe** in order to prescribe opioids

2. **Patient/provider treatment agreements**: Consider use of written agreements that describe responsibilities of both the patient and prescribing provider and the treatment structure that helps prevent addiction, misuse, and diversion. Include patient education on using as directed, safe storage, keeping appointments, etc.

3. **Increase treatment structure for higher risk patients**: For example, more frequent appointments and urine drug testing with higher risk.

4. **Plan for stopping opioid treatment before starting**: Describe a plan that includes the conditions under which treatment will be stopped, and a plan for tapering and providing psychosocial supports when stopping.

These guidelines will be described further in the following pages.
**Black Box Warning**

Because of the risks of misuse, abuse, addiction overdose, and death, the FDA enhanced the warnings for immediate release opioids\(^{34}\). The FDA had enhanced the warnings for extended-release/long-acting opioids (ER/LA) for the same reasons in 2014\(^{35}\).

**Immediate Release Opioids**

A boxed warning is required on immediate-release (IR) opioids to warn of the safety issues of "misuse, abuse, addiction, overdose, and death"\(^{34}\):

- "IR opioids should be reserved for pain severe enough to require opioid treatment and for which alternative treatment options (e.g., non-opioid analgesics or opioid combination products, as appropriate) are inadequate or not tolerated."
- Product information should be consulted for required information on patient monitoring and drug administration including initial dosage and dosage changes during therapy.
- Physically dependent patients should be warned not to stop taking opioids abruptly.

**Extended-Release/Long-Acting Opioids**

A boxed warning is required on ER/LA opioids to warn of the safety issues of "misuse, abuse, addiction, overdose, and death"\(^{35,36}\):

- "ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate."
- "Because of the risks of addiction, abuse, and misuse, even at recommended doses, and because of the greater risks of overdose and death, these drugs should be reserved for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain; ER/LA opioid analgesics are not indicated for as-needed pain relief."

**Enhanced Warnings For All Opioids**

Both IR and ER/LA opioids require a warning of the risk of neonatal opioid withdrawal syndrome. Chronic use of IR and ER/LA opioids taken during pregnancy "can result in neonatal opioid withdrawal syndrome (NOWS), which may be life-threatening if not recognized and treated"\(^{34}\).

Both IR and ER/LA opioids are affected by the relatively more recent, enhanced safety warnings for all opioids, including warning of risk for serotonin syndrome, adrenal insufficiency, and decreased sex hormone levels with chronic use\(^{34}\).

**Did You Know?**

Regarding the effectiveness of chronic opioid therapy, the CDC concluded that the body of evidence was insufficient to recommend for or against chronic opioid therapy\(^{19}\). They found "no study of opioid therapy versus placebo; no opioid therapy, or nonopioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration."

**Practice Response**

1. Maximize your use of non-opioid pain management in chronic pain management and use a high level of caution if you prescribe chronic opioid therapy.
2. The SPCA of 2018 law will require screening all new Medicare patients for opioid use problems. Because of the high rate of opioid use disorder, consider screening all patients for opioid use problems.

3. Unsafe injection drug use and unsafe sexual practices linked to drug use contribute to the spread of HIV, hepatitis B and C, and other infectious diseases.
OPIOID USE DISORDER AND OTHER PSYCHIATRIC ILLNESS

Recognizing mental health disorders in patients is important. Opioid misuse may cause or exacerbate several types of psychiatric disorders and mental impairment. Mental illness may also predispose patients to substance use. Thus, the chronology of both must be obtained.

Further psychiatric illness is associated with worse outcomes for buprenorphine treatment.

Example Case – MS. NELSON

Ms. Nelson started taking opioids for chronic back pain but now feels that she has become addicted. She says that the impact on her life is "almost unbearable."

Name: Ms. Nelson
Age: 47 years old
Reason For Visit: Back pain.

Patient History: She has been a patient at your primary care clinic for the past 10 years, although she has not been in the office for over 2 years.

Patient Interview: When asked how she was feeling, she burst into tears and revealed that she has become addicted to prescription opioids. She ran out of pills yesterday and came in today in the hope of getting a prescription from you. As she was in the waiting room, she realized that she could not let this problem go on any longer.

Ms. Nelson – Initial Patient Interview

Ms. Nelson relates the following to you during her appointment:

Ms. Nelson: I'm sorry for crying. It just hit me how desperate I've become. I think I'm addicted to painkillers.

Provider: It is good that you recognize the issue and are looking for help now. When do you think your addiction started?

Ms. Nelson: Right after my mom died last summer. She had been suffering a long time, so her death was almost a relief, but I was still a wreck afterward. I just couldn't keep it together. Right before the funeral, I found some leftover pain pills in her medicine cabinet, so I took them during those first few tough days. They gave me some relief, but I stopped when I ran out of pills.

Provider: But you were able to acquire more medication at a later time?

Ms. Nelson: Yes. I went back to work a few weeks later, even though I was still grieving. A woman at work offered me some oxycodone to help perk me up. That was around Labor Day. By Halloween, I was hooked. By January, I finally felt at peace with my mother's death, but I couldn't stop taking the pills. Lately, I've been crying all the time again, and I don't know why.

Provider: And you have continued to acquire the oxycodone?

Ms. Nelson: I always got my pills through the woman at work, which was easy. But then she was away this week with a family emergency, and I started to panic when I ran out of pills. I knew this was a problem. So, here I am.

Provider: It is good that you now recognize the issue of taking this medication long-term and the addictive nature of them.
Ms. Nelson: For a long time I convinced myself that it was harmless, just the little boost that I needed to get through the day. I tried to stop a few times, but I could never go without it for more than a day. It’s been almost a year now and...I think I’m finally ready to face up to this and get some help.
INCREASED RISK OF COMORBID MENTAL ILLNESS

People with opioid use disorder are at an increased risk for mental illness. Many psychiatric disorders are associated with substance use disorders, and a dual diagnosis of opioid use disorder with other forms of mental illness is common. Opioid misuse is associated with later development of generalized anxiety disorder (hazard ratio 2.8, 95% CI=2.2 to 3.6) and bipolar I disorder (hazard ratio 3.6, 95% CI=2.6 to 4.9).

With dual diagnoses, the relationship with opioid misuse to mental health disorders can be difficult to discern. For example, post-traumatic stress disorder may both be a risk for and a result of opioid use disorder.

Preexisting Mental Health Disorders

Certain mental illnesses appear to increase the risk for developing opioid misuse. Preexisting psychiatric disorders (mood disorders, major depressive disorder, bipolar I disorder, anxiety disorders, panic and generalized anxiety disorders) were associated with an increased risk opioid misuse (hazard ratio 2.2 for any anxiety disorder to 3.1 for bipolar I disorder). Furthermore, with psychiatric disorders, opioid misuse is more likely to lead to full opioid use disorder.

Some patients may have a dual diagnosis, that is, a psychiatric diagnosis that may contribute to their opioid use disorder. These patients may benefit more from the reverse treatment sequence. In these patients, stabilization of the psychiatric illness should be considered prior to buprenorphine treatment.

PRACTICE TIPS

Other substance-induced disorders may be reduced when the patient is treated for opioid use disorder.

Treat patients with opioid-independent mental health disorders for both their opioid use problem and their psychiatric disorder.

Induced Psychiatric Disorders

Criteria that can help differentiate opioid-induced from opioid-independent mental disorders include the following:

Order Of Onset

A psychiatric disorder is not considered to be caused by opioid misuse if it developed before the patient started using opioids (opioid independent). If the psychiatric disorder developed after the patient began using opioids, it is more likely to be caused by opioids (opioid dependent).

Family History

A family history of mental illness increases the likelihood that mental illness is independent of opioid misuse.

Symptoms During Abstinence

Psychiatric disorders that persist during periods of abstinence (from both opioids and all other substances of abuse) are much more likely to be independent of opioid misuse.

Treatment For Opioid-Induced Psychiatric Disorders

With opioid-induced mental disorders (particularly depression), psychiatric symptoms often resolve once opioid use stops.
In opioid-induced psychiatric disorder cases, addiction treatment stability is the first therapeutic step\textsuperscript{40}. Psychiatric treatment for the disorder is necessary only in severely affected patients, such as those who are suicidal.

**Ms. Nelson – History and Physical**

Let's return to Ms. Nelson as an example to further explore how to discern between substance use problems and depression and the contribution of each.

By midway through the intake appointment, you have obtained the following history from Ms. Nelson and her medical records:

**Vitals**
- Pulse: 90; BP: 134/80; Resp: 18; T: 100.1; height: 5' 7"; weight: 120 lb.

**Health History**
- History of ovarian cysts, but no current known problems

**Psychiatric History**
- No history of treatment for psychiatric disorders or mental illness

**Substance Abuse History**
- None prior to opioid use one year ago

**Personal History**
- Never married; family members are deceased or have left the area

**Social History**
- Ms. Nelson has several close female friends who "are like family" to her. She works as an office manager with the local (county) government and reports that the job is "her life." Also of note is that she was introduced to opioids by a coworker.

**Ms. Nelson – Initial Impression**

**Symptoms Of Opioid Use Disorder**

In speaking further with Ms. Nelson, you can make the diagnosis of Opioid Use Disorder based on DSM 5 criteria. She is exhibiting the following criteria for this diagnosis:

- Tolerance
- Withdrawal
- Has taken opioids in larger amounts and over a longer period than was intended
- Has unsuccessfully tried to cut down or control opioid use
- Has reduced important social, occupational, or recreational activities because of opioid use

**Symptoms Of Opioid Withdrawal**

As noted, she appears to be in withdrawal, which is expected, assuming that she last took oxycodone approximately 20 hours ago as reported. Her current withdrawal symptoms include the following:

- Rhinorrhea (runny nose)
- Lacrimation
- Pupillary dilation
• Elevated pulse
• Slight fever
• Anxiety

**Quiz: Ms. Nelson - Tentative Diagnosis**

There is more to Ms. Nelson's story than just opioid use disorder. She also appears to have psychiatric symptoms that could interfere with her treatment, and that should be addressed.

**From What You Know So Far, Which Of The Following Diagnoses Seem Likely? (Choose All That Apply)**

1. Antisocial Personality Disorder
2. Borderline Personality Disorder
3. Major Depressive Episode or Persistent Complex Bereavement
4. Anxiety disorders
5. Post-traumatic Stress Disorder
MS. NELSON – TENTATIVE DIAGNOSIS QUIZ FEEDBACK

(1) Antisocial Personality Disorder
No evidence of antisocial personality disorder so far. Patients with ASPD exhibit behaviors, such as deceitfulness, lying, repeated instances of breaking the law, lack of remorse for one's actions, etc. Ms. Nelson seems quite the opposite – she shows signs of remorse, a concern for how her actions have affected her own well-being, and conscientiousness.

(2) Borderline Personality Disorder
No evidence of borderline personality disorder (BPD) so far, but it is probably too early to say for sure. You may want to ask discretely probing questions during your clinical interview or need some more time to get to know her better. However, her history of visits at your clinic over the last decade does not suggest BPD.

(3) Major Depressive Episode Or Persistent Complex Bereavement
Correct. Ms. Nelson described herself as crying all the time for no apparent reason. She was also 'stressed and depressed' right before she began abusing opioids. Grief over her mother's death may have contributed to her depression. Some people start abusing opioids as a way to cope with grief or depression.

Other symptoms that also could be consistent with major depression and/or her opioid abuse include her low body weight. However, many of her symptoms may also be the result of an anxiety disorder, such as PTSD or GAD. You will need to gather additional information during your interview in order to better clarify if/how her depressive symptoms are related to opioid use disorder and what treatment(s) she needs. Persistent Complex Bereavement Disorder is another possibility.

(4) Anxiety Disorders
Correct. Some of Ms. Nelson's symptoms may be a result of anxiety disorder, such as generalized anxiety disorder or post-traumatic stress disorder (PTSD). She certainly seems anxious during the interview, but some of that may be attributed to opioid withdrawal. Additionally, some of her other symptoms, such as crying all the time for no apparent reason, could be consistent with major depression. You will need to gather additional information to clarify the clinical picture and determine if/how her anxiety symptoms are related to her opioid use disorder and what treatment(s) she needs.

(5) Post-Traumatic Stress Disorder
No evidence of PTSD so far but, it is probably too early to evaluate. PTSD is very common among patients who abuse opioids. Nothing Ms. Nelson has said so far is a red flag for PTSD other than the presence of anxiety, but further discussion will allow you to rule out this diagnosis.
DEPRESSION

Depression And Treating Opioid Use Disorder

**Prevalence:** Depression is the most common mood disorder among patients with opioid use disorder. An estimated 44% to 54% of patients with opioid use disorder have suffered from major depression at some point in their lifetime. At any time, up to 30% of patients with opioid use disorder are currently depressed.

**Impact of Treatment:** Patients with depression are less likely to respond well to treatment for opioid use disorder as compared to patients without a comorbid disorder. They are also more likely to relapse to opioid use. However, patients with comorbid depression do respond well to psychiatric intervention.

Sometimes what appeared to be major depression remits rapidly after patients cease opioid misuse, because it was actually a substance use disorder. Persistent cases that are independent of opioid use disorder can be treated readily with psychotherapy or pharmacotherapy.

**PRACTICE TIP**
The U.S. Preventive Services Task Force has indicated that all adults should be screened for depression. This recommendation has been expanded from past suggestions to now include pregnant and postpartum women, as well as those who do not indicate prior evidence of depression.

Screening tools suggested in guidelines include the "Patient Health Questionnaire," the "Hospital Anxiety and Depression Scales" in adults, the "Geriatric Depression Scale" in older adults, and the "Edinburgh Postnatal Depression Scale" in postpartum and pregnant women.

Suicidality and Treating Opioid Use Disorder

Because of a relatively high rate of suicidality among patients with opioid use disorder, it is important to monitor patients for risk factors.

**Prevalence:** By some reports, almost half of opioid users have a past suicide attempt. Mortality attributable to suicide in individuals with opioid use disorder is estimated to be up to around a third higher than in the general population; up to 7% of those with opioid use disorder die from suicide each year.

**Impact of Treatment:** Treatment for opioid use disorder decreases the risk of suicide. Methadone maintenance treatment significantly decreased suicidal ideation and attempts. Some forms of psychosocial treatment appear to be even more effective.

**Assessment:** When suicidality is reported or suspected, you should assess patients' relative risk of committing suicide. Specifically, try to determine if the patient actively wants to kill himself or herself, has access to lethal means of suicide, and "has a plan."
MS. NELSON CLARIFYING THE DIAGNOSIS

Symptoms
At this stage, Major Depression and Generalized Anxiety Disorder are potential diagnoses worth exploring further.

Current Depressive Symptoms
- Anhedonia (inability to feel pleasure)
- Poor concentration
- Insomnia
- Weight loss

Current Anxiety Symptoms
- Anhedonia
- Poor concentration
- Insomnia
- Restlessness
- Muscle tension/aches

These symptoms are still not sufficient to make a psychiatric diagnosis. You would need to ask Ms. Nelson a few more questions in order to make a more definitive diagnosis.

Further Interview with Ms. Nelson

Provider: So, you felt depressed at first when your mom died, but then felt at peace with it after a few months. Have you continued to feel depressed?

Ms. Nelson: I'm not sure. I gradually started to feel better, around January. But then I never really got back to my old self and continued to have trouble concentrating, sleeping, and eating. I didn't feel as sad about my mom anymore, but I didn't feel like myself, and I still don't. I definitely feel sad and depressed a lot.

Provider: Do you feel sad every day?

Ms. Nelson: I guess so, almost.

Provider: And is your sadness getting in the way of your daily life?

Ms. Nelson: Well, I don't do all of the things that I used to do. I just don't have the energy or motivation. Many days I can't even bring myself to shower or eat much.

Provider: Are you currently feeling anxious about anything?

Ms. Nelson: I feel really anxious right now, but I don't remember feeling a lot of stress and anxiety before I decided to come to you today.
QUIZ: MS. NELSON – MENTAL HEALTH DIAGNOSIS

What Mental Health Diagnosis Would Be The Most Logical And Likely With This Much Additional Information? (Choose One)

1. Generalized Anxiety Disorder
2. Major Depressive Episode
3. Opioid-Induced Depressive Disorder
4. None of the above
MS. NELSON – FINAL DIAGNOSIS QUIZ FEEDBACK

(1) Generalized Anxiety Disorder
This is not the best choice. Ms. Nelson's anxiety-related symptoms appear to be acute and are most likely related to opioid withdrawal. A diagnosis of Generalized Anxiety Disorder requires 6 months or more of poorly controlled anxiety and worry, and Ms. Nelson reports that she has not felt much stress or anxiety as of late.

(2) Major Depressive Episode
This is not the best choice. Ms. Nelson does appear to meet most of the DSM diagnostic criteria for major depression. She has been experiencing multiple depressive symptoms for at least a month. These symptoms occurred months after her mother's death, so go beyond bereavement. A confounding feature is that she took opioids for her mood, which sounded depressed. However, for a diagnosis of Major Depressive Episode, the symptoms must not be related to substance use. You cannot definitively determine the cause of her depressive symptoms and their relationship to her opioid dependence.

(3) Opioid-Induced Depressive Disorder
Correct. Ms. Nelson took opioids for her mood, which sounded depressed. However, for a diagnosis of Major Depressive Episode, the symptoms must not be related to substance use.

At this time, you cannot definitively determine the cause of her depressive symptoms and their relationship to her opioid dependence, so the best diagnosis until further observation (during abstinence and treatment) is Opioid-Induced Depressive Disorder. Regarding anxiety, Ms. Nelson's anxiety-related symptoms appear to be acute and are most likely related to opioid withdrawal.

(4) None Of The Above
Opioid-Induced Depressive Disorder is a possibility.
ANXIETY DISORDERS

Anxiety Disorders In General And Treating Opioid Use Disorder

**Prevalence:** Anxiety disorders are common in patients with opioid use disorder, with a lifetime prevalence of 8% to 27%\(^48\). Generalized anxiety disorder occurs in about 5% of this population; phobia in 2-9%\(^48\).

**Impact on Buprenorphine Treatment:** Routine treatment of anxiety disorders with pharmacotherapy and psychotherapy would be appropriate for treating anxiety in the context of buprenorphine treatment, however, caution is needed regarding use of benzodiazepines:

- Benzodiazepines in combination with buprenorphine are associated with risk of respiratory depression and increase the risk of buprenorphine overdose\(^49\).

Post-Traumatic Stress Disorder (PTSD) And Treating Opioid Use Disorder

**Prevalence:** PTSD is common among people with substance use disorders: 40.6% of drug dependent people reported symptoms of PTSD and were diagnosed with PTSD\(^50\). Also, PTSD has a significant positive relationship to severity of drug problems\(^50\).

**Impact on Buprenorphine Treatment:** Like many other psychiatric disorders, the symptoms of PTSD can overlap with those of opioid withdrawal. There is strong evidence that opioid use may be a kind of self-medication for PTSD\(^39\). Therefore, patients with PTSD should be treated for the PTSD, and this treatment should be integrated with treatment for opioid use disorder.
PERSONALITY DISORDERS

It is important to recognize personality disorders in patients having opioid use disorder because comorbid personality disorders increase the difficulty of treating opioid use disorder.

**Prevalence:** Comorbid personality disorders are very common among patients with opioid use disorder. An estimated 30% to 75% of patients with opioid use disorder have a lifetime diagnosis of a personality disorder.\(^5^1\) This statistic is more than 4 times the prevalence in the general population. The most common are borderline personality disorder (around 50%)\(^5^2\) and antisocial personality disorder (around 40%)\(^5^3\). Some experienced providers have noted that many addicted individuals exhibit at least some antisocial behavior\(^5^4\).

**Impact of Treatment:** The presence of a personality disorder may interfere with a patient's thoughts and actions and strain the doctor-patient relationship. Many personality disorders affect interpersonal relationships negatively\(^2^1\). Therefore, consider the following:

- Additional time learning a patient's individual challenges
- Consultation with a mental health provider, for more severe personality disorders
- Additional care in communications and efforts to build trust
- A written treatment agreement and additional treatment structure, especially more frequent office visits
- Referring these patients to a higher level of care if the above precautions are not possible in your practice or are ineffective

In addition, patients who are both addicted to opioids and have a personality disorder:

- May not respond as well to, or may even deteriorate as a result of, treatment for opioid use disorder\(^5^5\)
- Are less likely to complete treatment\(^5^1\)
- Are more prone to relapse to opioid misuse after successful treatment\(^5^1\)
OTHER PSYCHIATRIC DISORDERS

Having other psychiatric disorders also impacts the outcome of substance use disorder treatment.

Attention Deficit Hyperactivity Disorder (ADHD) And Treating Opioid Use Disorder

Patients with ADHD may require the following, in addition to routine treatment:

- More careful instructions when instructing patients on correct buprenorphine usage and dosing, considering the patient's attention span.
- Additional treatment structure, as there are often surrounding factors, such as emotional problems and the externalization of other issues in ADHD patients, which may negatively affect their treatment outcomes.
- Additional follow-up phone calls during induction and stabilization.
- Additional psychosocial support, such as participation in a 12 step program, to provide support for impulsive behavior. That support may need to continue throughout maintenance.

Polysubstance Use

Polysubstance use is very common among those who abuse opioids. Cocaine use is most common among heroin addicts (around 75% reported concurrent use), and alcohol is commonly abused by licit and illicit drug users.

Quiz: Comorbidities

It Is Very Common For Patients Having Substance Use Disorders To Present With Comorbidities. Which Of The Following Statements Is True?

1. Mental illness is a risk factor for opioid use disorder.
2. Opioid use disorder is a risk factor for mental illness.
3. Both answers are true.
4. Neither 1 nor 2 is true.
CASE: COMORBIDITIES QUIZ FEEDBACK

(1) Mental Illness Is A Risk Factor For Opioid Use Disorder,
(2) Opioid Use Disorder Is A Risk Factor For Mental Illness:
These choices are true, but not the best answer because both answers are correct. Opioid use disorder is a risk for mental illness, especially depression and anxiety, and mental illness, especially depression and anxiety increased the risk of opioid use disorder. The 2 conditions, mental health illness and opioid use disorder, are often self-reinforcing.

(3) Both Answers Are True.
Correct. Opioid use disorder is a risk for mental illness, especially depression and anxiety, and mental illness, especially depression and anxiety increased the risk of opioid use disorder. The 2 conditions, mental health illness and opioid use disorder, are often self-reinforcing.

(4) Neither Is True.
Opioid use disorder may be a risk for mental illness or mental illness a risk for opioid use disorder. In many cases, the 2 conditions are self-reinforcing.
MS. NELSON – SUMMARY AND PLAN

Summary
Ms. Nelson has been diagnosed with Opioid Use Disorder and Opioid-Induced Depressive Disorder. At this time, it is difficult to determine if Ms. Nelson's depression is a result of or related to her opioid abuse (as currently diagnosed) or if it is an independent psychiatric problem. The situation will be more apparent after she has been abstinent from opioids for several days and begun treatment.

Plan for Ms. Nelson

Buprenorphine Treatment:
Ms. Nelson is a good candidate for buprenorphine therapy. She could even start induction today because she is already in withdrawal from opioids.

Depression Treatment:
Consider referring her to supportive psychosocial services to complement the buprenorphine treatment. Psychosocial services will provide a forum to further address her feelings of depression and anxiety as well as substance abuse issues. If her depression does not abate during treatment, she could be treated safely with SSRIs while taking buprenorphine.

Patient Education:
Remember to review patient education with her (including the Medication Guide for the formulation of buprenorphine that you prescribe) and the patient-provider treatment agreement.

Practice Response
1. Screen patients having opioid use disorder for mental health problems.
2. Treat underlying mental health disorders to improve chances for good outcomes from substance use treatment and vice versa.
OTHER HEALTH IMPACT

Treating opioid use disorder greatly decreases associated health risks including HIV transmission, suicide, and neonatal mortality. Untreated, these disorders decrease the quality of life and increase the risk of suicide.

The other major health effects of opioid misuse, aside from addiction, are:

- Neonatal abstinence syndrome
- Infections
- Side Effects

Neonatal Abstinence Syndrome

Infants born to mothers dependent on opioids have a syndrome called neonatal abstinence with withdrawal symptoms including dysfunction of the autonomic nervous system, GI system, and respiratory system. This syndrome occurs in infants of over half of opioid-dependent mothers\(^\text{57}\). Precise figures on the prevalence of this syndrome are not available because the infant's condition is often compounded by other factors, such as poor maternal health and malnutrition. However, neonatal intensive care unit days attributed to neonatal abstinence increased from 0.6% to 4% in the years from 2004 to 2013. Figures describing the prevalence of opioid use disorder in this chapter do not include these infants.

Infection Risk

Infection Associated With Injected Opioids

The route by which a drug is misused will have some effect on the health effects. Many prescription opioids that are misused are not taken via the traditional route, i.e., swallowed. The most common routes of administration of diverted opioids are, in order from most common to least common:

1. Injection
2. Ingestion (Sublingual administration)
3. Inhalation\(^\text{58,59}\)

Be sure to consider that patients who inject prescription opioids are at increased risk for infectious disease.

Heroin Effects Overview

Heroin users—particularly injection drug users—are at increased risk for multiple infectious diseases and so should be evaluated for them.

HIV/AIDS

**Prevalence:** About one-third of the 1 million HIV-positive cases in America are linked with injection drug use\(^\text{60}\). About 2.8% of injection drug users are HIV positive\(^\text{61}\). Non-injecting heroin users are also at increased risk for contracting HIV through risky sexual behavior\(^\text{62}\). A higher incidence of HIV infection may explain part of the high incidence of renal disease and failure in heroin users\(^\text{63}\).

**Impact of Buprenorphine Treatment:** Treatment for opioid use disorder and adherence to treatment lowers the risk of contracting HIV\(^\text{64}\). This effect has been studied most extensively in methadone maintenance treatment\(^\text{64}\). Patients receiving office-based buprenorphine treatment were less likely to engage in risky behaviors, such as sharing needles and having multiple sexual partners in one study\(^\text{65}\).
**Hepatitis C**

**Prevalence:** Up to 90% of injection drug users have been infected at one time with hepatitis C (HCV); 85% of those ever exposed to HCV will develop the chronic form of the disease. Studies of non-injecting drug users have found ever-infected prevalence rates to be as low as 6%.

**Impact of Buprenorphine Treatment:** Opioid and other substance treatment programs are among the control measures that can improve the outcome for hepatitis patients and those at risk of contracting hepatitis. An estimated 5% to 6% of new cases of end-stage renal disease in the United States are attributed to heroin use. The higher incidence of HCV in this group is a likely contributor. Other possible reasons include bacterial contaminants and toxins used to dilute the drug and rhabdomyolysis (skeletal muscle damage) after non-fatal overdose.

**Other Infectious Diseases**

**Tissue infections:** Unsterile injection practices put injection drug users at heightened risk for a variety of tissue infections, both local and systemic. Skin abscesses at injection sites are common among injection drug users, as are endocarditis, cellulitis, and deltoid abscesses.

**Lung disease:** People who misuse opioids are at increased risk for lung diseases, including pneumonia and tuberculosis.

**PRACTICE RESPONSE**

Liver function tests are indicated for patients in buprenorphine treatment prior to induction and periodically during maintenance treatment. There are additional, specific guidelines for treating patients who have Hepatitis C.

**Opioid Side Effects**

Side effects of chronic prescription opioid use, whether prescribed or illicit, include the following, and vary based on length of use and dose:

- **Common side effects for short-term and low dose use include:** constipation, nausea, sedation
- **Possible side effects from high dose use include:** low blood pressure and respiratory depression
- **Potential side effects with long-term, high dose use include:** hyperalgesia, endocrinologic dysfunction including hypogonadism, sexual dysfunction, immune dysfunction, and sleep apnea.

**PRACTICE TIPS**

Patient education highlighting the side effects of chronic opioid misuse may help keep patients motivated to start or remain abstinent on buprenorphine treatment.
KEY POINTS

• Despite efforts to prescribe opioids less frequently, the problem of opioid addiction continues at epidemic levels and has not waned.

• If clinicians who prescribe opioids for their patients’ pain followed the precautions of current guidelines designed to decrease opioid addiction, such as the CDC Guidelines for Prescribing Opioids, fewer individuals would develop opioid use disorder.

• Depression, anxiety, and other mental health problems are often comorbid with opioid use disorder. It can be challenging to determine which came first. Patients often do better with their buprenorphine treatment if any underlying mental health problem is also treated.
Summary

Prevalence of Opioid Use Disorder and Other Misuse
- About 14% of the population have misused prescription opioids in their lifetimes. At least 2 million people have opioid use disorder.
- Both heroin use and prescription opioid misuse increased in recent years. Oxycodone and hydrocodone are the most commonly misused prescription opioids.

Availability of Treatment for Opioid Use Disorder
- Only a small number of patients who have opioid use disorder or abuse opioids receive the treatment.
- About twice as many patients are now maintained on buprenorphine compared to methadone.

Morbidity and Mortality Associated with Opioid Misuse and Opioid Use Disorder
- Prescription opioids are a factor in around five times more ER cases than heroin.
- Heroin and prescription opioids rank as the most common drugs implicated in drug-related deaths.

Medical Comorbidities and Risk Factors
- Injection drug users are at an increased risk of HIV and Hepatitis C. Treatment for opioid use is effective at reducing risk factors for HIV.
- History of substance abuse, mental health disorder, or sexual abuse are all risk factors for opioid misuse turning into opioid use disorder. Young adults age 18-25 are also at greater risk.

Psychiatric Comorbidities
- Psychiatric disorders that are especially associated with substance use disorders include depression, anxiety, and personality disorder. Suicide risk and rates are much higher among substance abusers than in the general population.
- Before starting treatment, differentiate between opioid-induced vs. opioid-independent mental health disorders and treat opioid-independent disorders in addition to the opioid use disorder.
- Patients with psychiatric comorbidities are less likely to respond to opioid treatment and more likely to relapse.
RESOURCES

CDC Guideline for Prescribing Opioids for Chronic Pain
Clinical guidelines, literature review, and analysis of the evidence on the use of opioids for chronic pain. Recommendations are also made for prescribing opioids for acute pain.

DSM 5 Criteria for Opioid Withdrawal
Lists the DSM 5 Criteria for Opioid Withdrawal (APA, 2013).

Monitoring of liver function tests and hepatitis in patients receiving buprenorphine/ naloxone
This web page provides brief recommendations for monitoring patients undergoing buprenorphine treatment using liver function tests, and the proper actions to take if a patient develops hepatitis.

Signs and Symptoms of Opioid Intoxication and Withdrawal
A description of the signs of opiate withdrawal useful for physicians in determining withdrawal during medically supervised detoxification.
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