Module II

Opioids 101
Module II: Opioids 101

Module II is designed to introduce participants to basic facts about opioids, including information on pharmacology, acute and long-term effects, and basic information about treatments for opioid addiction. This module contains background information necessary to understand the role of buprenorphine in the opioid treatment system. If the audience is already highly knowledgeable about opioid treatment, this module should be abbreviated or omitted.

Slide 1: Title Slide

The next module provides an overview of opioids and opioid treatment, setting the stage to see the role of buprenorphine in the treatment system.

Slide 2: Goals for Module II

We are now going to turn a little more directly to the issue of opioid addiction.

This module reviews the following:
- Opioid addiction and the brain
- Descriptions and definitions of opioid agonists, partial agonists, and antagonists
- Receptor pharmacology
- Opioid treatment options
### Slide 3: Opiate/Opioid: What’s the Difference?

*Throughout this training we are using the term opioid to define the class of drug with which we are dealing. It is important to understand what this term means.*

- **Opiate** refers only to drugs or medications that are derived directly from the opium poppy. Examples include heroin, morphine, and codeine.
- **Opioid** is a broader term referring to opiates and other synthetically-derived drugs or medications that operate on the opioid receptor system and produce effects similar to morphine. Examples include methadone, buprenorphine, meperidine, and fentanyl.

*Note to the Trainer(s): All opiates are opioids, but not all opioids are opiates.*

### Slide 4: Basic Opioid Facts

#### Description:
All opioids work basically the same way, regardless of their derivation.

#### Medical Uses:
There are benefits to using opioids; they are not just used recreationally.

#### Methods:
Bottom line – you can get opioids into your body in many ways.

### Slide 5: NIDA Brain Graphic

Opioids affect the brain globally, including areas that control:
- Autonomic bodily functions such as breathing, blood pressure, pulse;
- Emotions, especially the areas of the brain responsible for feeling pleasure;
- Pain – opioids block the transmission of pain messages from the body to the brain thereby diminishing or stopping the experience of the pain.

*Reference:*
Let's take the next few minutes to review some receptor pharmacology-related terms.

Receptor
A specific cell or place on a cell to which a specific molecule binds. There are unique receptors for many different molecules, including specific opioid receptors.

This Positron Emission Tomography (PET) scan image identifies the location of opioid receptors (mu and kappa) in the brain in normal, healthy volunteers (Kling et al. 2000).

PET scans are a nuclear imaging tool which produces a three-dimensional image or picture of the biological functions of the body. Physicians use them to pinpoint disease states in the body.

Note to the Trainer(s): This is an image of a single brain at different time intervals. The concentration of color indicates receptors located in the limbic reward system.

Reference:
Slide 8: Partial vs. Full Opioid Agonist and Antagonists

This slide graphically depicts the different types of opioids (whether they are prescribed medications such as Vicodin or methadone, or illicit substances like heroin).

Move forward to reveal first line (full agonist)

Full agonists (e.g., heroin, opium, Vicodin, methadone, etc.) fully activate the receptors so that the more you use, the more effect you experience. If someone continues to use, they will eventually experience overdose and, possibly, death.

The following metaphor may be helpful in explaining the differences between the types of opioids:

Opioid agonists work like having the right key to a door. You put the key in the lock, the lock turns and the door opens completely.

Move forward to reveal the next line (antagonists)

Opioid antagonists (e.g., naltrexone, naloxone) fill the receptors and block the action of other opioids. If the person has used an opioid agonist, the antagonist will replace it on the receptor and the person will experience withdrawal. If the person is stable on an antagonist, and uses another opioid, the antagonist will block the effects, preventing the user from experiencing the high.

The door metaphor continued:

Opioid antagonists work like having the wrong key to a door. You put the key in the lock; the door remains locked and will not open. Additionally, since the key is in the lock, no other key can be put in the lock (even if it is the right key for that door) until the wrong key is removed.

Move forward to reveal the last line (partial agonists)

Opioid partial agonists (e.g., buprenorphine) are in the middle.

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Slide 9: Opioid Agonists

Natural Derivatives

These substances are derived directly from the opium poppy. They are the drugs that we can also call opiates.

Note to the Trainer(s): Be sure to tell participants that the following pictures may serve as triggers and to act accordingly.
Slide 10: Opium

*Show picture for a few seconds and then move on.*

Reference:

Slide 11: Morphine

*Show picture for a few seconds and then move on.*

Reference:

Slide 12: Opioid Agonists

**Semi-synthetics**

These substances are derived from chemicals extracted from the opium poppy. They also fall into both the opiate and opioid categories.

Slide 13: Heroin

Left-hand side picture – Mexican black tar heroin (mostly used in the Western U.S.)

Right-hand side top picture – South American white heroin (dominates the heroin market east of the Mississippi River)

Right-hand side bottom picture – Mexican brown heroin

Reference:
Heroin has been around for a long time and was originally marketed under the Bayer Label as a cough suppressant. This advertisement is from 1897. It is no longer considered to have any medical uses.

**Note:** In larger rooms the text of this slide is difficult to read and should therefore be read aloud.

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**Slide 15: Opioid Agonists**

*Show picture for a few seconds and then move on.*

Reference:


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**Slide 16: Opioid Agonists**

**Synthetics**

These substances are synthetically manufactured. They are considered opioids, but are NOT opiates.

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**Slide 17: Methadone/Darvocet**

*Show picture for a few seconds and then move on.*

Reference:

**Slide 18: Opioid Partial Agonists**

Buprenorphine/naloxone combination tablet (currently marketed as Suboxone®) and the buprenorphine-only tablet (currently marketed as Subutex®) are the formulations that are approved for the treatment of opioid addiction. Both medications are administered sublingually.

*It may be worth noting that buprenorphine is the only medication with FDA approval for the treatment of opioid addiction that is not schedule II (methadone is schedule II), and that only Suboxone® and Subutex® are approved. Using either of these medications for the treatment of pain is off label.*

*Although Buprenex® (injectable formulation of buprenorphine) and Talwin® (Pentazocine) are also partial opioid agonists and approved for the treatment of pain; they ARE NOT approved for the treatment of opioid addiction.*

Many medications can be used off label for purposes other than what they were originally studied for (this is known as off-label use). However, due to laws related to addiction treatment, it is illegal to use injectable buprenorphine (Buprenex®) and pentazocine (Talwin®) for treating opioid addiction.

**Slide 19: Buprenorphine/Naloxone Combination and Buprenorphine Alone**

This is what the two sublingual buprenorphine tablets currently being marketed look like.

**Slide 20: Opioid Antagonists**

As was previously stated, antagonists are those substances that block the effects of opioid agonists. Two examples are naloxone (the same medication in the buprenorphine/naloxone combination tablet) and naltrexone.
SMALL GROUP EXERCISE

Break the audience into small groups (3-4 people), and ask them to discuss the difference between dependence and addiction. After approximately 10 minutes, have the group reconvene and ask for a few volunteers to describe their discussions.

Slide 22: Dependence versus Addiction

Most providers use the term “addiction” to describe this pattern of problems. In order to keep this term distinct, we will use the term addiction (rather than dependence) throughout this training to refer to this pattern of problems resulting from use.

Reference:

Slide 23: Dependence versus Addiction

The term “dependence" is used to describe the body’s reaction to the presence of an addictive substance -that is physical dependence on the substance.

Physical dependence is one symptom of addiction, but it is important to remember that addiction can occur with or without physical dependence.

Physical dependence is defined by the presence of tolerance and/or withdrawal.

Let's look at the specific definitions of these terms.

Slide 24: Dependence versus Addiction

Tolerance

Tolerance deals with the body’s adaptation to a drug or medication. With repeated exposure, the response to the substance lessens. It therefore requires a higher dose to get the same effect.
Slide 25: Dependence versus Addiction

Withdrawal

This is another indicator of the body’s adaptation to the drug. This process occurs when the normal dose is reduced or stopped and the person experiences painful or uncomfortable symptoms, OR the person uses a similar substance in order to avoid these painful feelings (i.e. methadone or buprenorphine is used to address impending withdrawal).

*Let’s look at the problems that the DSM-IV-TR identifies.*

Slide 26: DSM-IV-TR Criteria for Substance Dependence

According to the DSM-IV-TR, substance use disorders occur on a continuum. The less severe form of the problem is called abuse and is defined as having repeated problems associated with use, but generally the individual is still at least somewhat functional in their lives. As the problem worsens, the person moves on to addiction (or what the DSM-IV-TR calls substance dependence) in which functioning is markedly impaired.

Addiction is based on clusters of behaviors and physical effects. It is defined as a “maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by three (or more) of seven symptoms occurring at any time during a 12-month period.”

*Read the bullets aloud.*

**Additional points to mention:**

Bullet #3: “taking larger amounts” – indicates a loss of control over moderating your drug use. “Over time” can also be stated as “longer periods than intended.”

Reference:

Slide 27: Dependence versus Addiction - Summary

For clarity, let’s review the terms again:

*Read slide aloud.*

Slide 28: Opioids and the Brain: Pharmacology and Half-Life (Transition Slide)

So now that you know which drugs and medications are included in the class known as opioids, let’s look at how they work.

Slide 29: Opioid Agonists: Pharmacology

*So how do opioids work?*

Opioids work by stimulating the opioid receptors in the brain and gastrointestinal (GI) tract. When they bind to the receptor, users experience relief from pain, cough suppression, feelings of euphoria, and they may become stuporous. If the dose is high enough, they may experience a slowing of respiration. This final symptom can lead to death.
Slide 30: Opioid Agonists: Pharmacology

**Acute effects** of opioids include:
- Constriction of the pupils so that they become very small (sometimes referred to as pinpoint pupils)
- Constipation
- An allergic-type reaction accompanied by itching and/or difficulty breathing
- Lower libido due to decreases in sex hormones.

With **chronic use**, tolerance and withdrawal symptoms develop and the above symptoms may become more significant.

**Cross tolerance**: We have already discussed the definition of tolerance. With opioids, you also see cross-tolerance. This means that once tolerance develops for one substance (e.g., heroin) you will see tolerance for other opioids, as well (e.g., codeine or Demerol). If the person is receiving treatment with an opioid medication (either as a treatment for opioid addiction or for other medical indications), the dose will need to be adjusted depending upon the level of tolerance.

In a person who is otherwise generally healthy, withdrawal from an opioid agonist is not life threatening. However, it is characterized by drug cravings and marked distress, including flu-like symptoms, joint pain, sweating, runny nose, diarrhea, nausea, and anxiety. It is also frequently associated with relapse to drug use. Once the immediate withdrawal from the drug is over (usually after a few days), there are residual emotional and physical symptoms that place the patient at significant risk for relapse.

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Slide 31: Possible Acute Effects of Opioid Use

**Summarize the symptoms associated with acute effects, chronic use, and withdrawal.**

**Bullet #1**: Rush is generally reported with administration by injection or smoking. It is not commonly associated with oral administration.

**Bullet #5**: Drowsiness is commonly referred to as “nodding out.”
### Consequences of Opioid Use

- **Addiction**
- **Overdose**
- **Death**
- **Use-related (e.g., HIV infection, malnutrition)**
- **Negative consequences from injection:***
  - Infectious diseases (e.g., HIV/AIDS, Hepatitis B and C)
  - Collapsed veins
  - Bacterial infections
  - Abscesses
  - Infection of heart lining and valves
  - Arthritis and other rheumatologic problems

The first three consequences (addiction, overdose, and death) refer to opioid use in general. There are also consequences from behaviors that may be associated with substance use such as infections resulting from unprotected sexual behaviors, malnutrition, etc.

Many of the consequences refer specifically to injection drug use:

- **Collapsed veins** resulting from repeated injections.

  **Ask trainees:** What do people do if their veins collapse?  
  *(Answer: find another place).*

- **Viral Infections** such as HIV or Hepatitis C, resulting from sharing injection equipment with people.

- **Bacterial infections** may be caused by not cleaning the injection site properly or by using needles that have been exposed to bacteria. This can introduce bacteria into the bloodstream.

- **An abscess** is a subcutaneous infection. If untreated, an abscess can rupture and lead to sepsis or even death.

- **Blood infections** can be contracted from bacteria transferred into the bloodstream via dirty needles/ syringes. The bacteria settles in the heart, causing an infection of the heart lining (endocarditis) or a breakdown of heart valves (which causes them to become less effective at bringing blood to and from the heart).

- **Arthritis and other rheumatologic problems** may develop as a result of chronic infections and muscle/tissue inflammation.
Once the body becomes accustomed to the drug being on board, it may react if the drug is removed. The intensity of the withdrawal symptoms will depend on the level of use (dose and type of opioid) and the frequency and duration of use (chronicity).

Withdrawal symptoms are basically a rebound effect; those functions that have been depressed or altered by the opioid suddenly emerge again. Withdrawal symptoms are often the opposite of symptoms seen when actively using the opioid (e.g., people get constipated when taking opioids and have diarrhea when withdrawing).

First signs of withdrawal occur shortly before the next scheduled dose of buprenorphine.

- Length of the withdrawal depends upon the half-life. Half-life is the time it takes for half a given amount of a substance, such as a drug, to be removed from living tissue through natural biological activity. The slower the medication is removed from the body, the longer the experience lasts. Usually the next dose of a medication is taken at about one half-life.

Opioids with short half-lives (e.g., heroin) have acute withdrawal symptoms that peak at 3-4 days and then subside by days 3-7. Opioids with longer half-lives (e.g., methadone – half-life of 24 hours) have longer acute withdrawal periods.

It is important to note that unlike methadone, buprenorphine has a fairly short half-life. However, it still has a very long duration of action. In this case, the duration of action results from high receptor affinity or the strength with which a medication binds to a receptor.

Regardless of the length of the acute withdrawal, there are protracted withdrawal symptoms (e.g., aches and pains, general malaise) that persist for weeks or months after use ceases.
### Slide 34: Opioid Withdrawal Syndrome: Acute Symptoms

Acute withdrawal symptoms are the opposite of acute intoxication symptoms.

**Summarize the acute withdrawal symptoms.**

Note regarding the term “gooseflesh”: This symptom is where the phrase “going cold turkey” comes from.

<table>
<thead>
<tr>
<th>Acute Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupillary dilation</td>
</tr>
<tr>
<td>Lacrimation (watery eyes)</td>
</tr>
<tr>
<td>Rhinorrhea (runny nose)</td>
</tr>
<tr>
<td>Muscle spasms (“kicking”)</td>
</tr>
<tr>
<td>Yawning, sweating, chills, gooseflesh</td>
</tr>
<tr>
<td>Stomach cramps, diarrhea, vomiting</td>
</tr>
<tr>
<td>Restlessness, anxiety, irritability</td>
</tr>
</tbody>
</table>

### Slide 35: Opioid Withdrawal Syndrome: Protracted Symptoms

Protracted withdrawal symptoms are less severe than the acute symptoms, but are still experienced as extremely disruptive and uncomfortable.

**Summarize the protracted withdrawal symptoms.**

- **Anorgasmia** = inability to have an orgasm
- **Anhedonia** = overall lack of pleasure (everything is gray)

<table>
<thead>
<tr>
<th>Protracted Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep muscle aches and pains</td>
</tr>
<tr>
<td>Insomnia, disturbed sleep</td>
</tr>
<tr>
<td>Poor appetite</td>
</tr>
<tr>
<td>Reduced libido, impotence, anorgasmia</td>
</tr>
<tr>
<td>Depressed mood, anhedonia</td>
</tr>
<tr>
<td>Drug craving and obsession</td>
</tr>
</tbody>
</table>

### Slide 36: Treatment of Opioid Addiction (Transition Slide)

Anyone who takes opioids for a period of time will develop a physical dependence. For instance, a patient who is taking Vicodin over a period of time for pain will experience withdrawal symptoms if they suddenly stop taking them. As previously discussed, this does not mean that they are addicted. It just means that their body has adapted to the medication. Generally, the prescribing physician will help the patient gradually taper down on the dose once the medication is no longer needed.

However, if a person has an addiction to opioids—that is he/she has lost control over his/her use, and/or has developed the problems associated with addiction (whether or not physical dependence is present)—it is unlikely that he/she is going to stop using without some sort of treatment.

The next section of the training will examine the treatment options available for opioid addiction.
The successful treatment for opioid addiction requires both management of physical withdrawal symptoms and behavioral and cognitive changes that encourage the patient to abstain from using the drug of abuse in the future. Providing psychosocial and counseling services along with pharmaceutical treatment increases the likelihood of achieving long-term, comprehensive lifestyle changes and preventing relapse. You want to help the patient restore a degree of normalcy to brain function and behavior, thereby leading to increased employment rates, reduced criminal behavior, and lowered risk of HIV, hepatitis C, and other diseases.

**Note to the Trainer(s):** Bullet #3: Stress the importance of combining both treatment approaches and tailoring treatment to meet the particular needs of the patient (e.g., deciding between inpatient and outpatient, behavioral and pharmacological, etc.).
Slide 38: How Can You Treat Opioid Addiction?

**Medically-Assisted Withdrawal**

The individual is systematically withdrawn from addicting drugs. Medications (e.g., methadone, buprenorphine, and clonidine) are used to alleviate withdrawal symptoms while the person gradually returns to an opioid-free state. It can be done successfully in inpatient or outpatient settings.

Generally, a medical provider supervises the withdrawal to monitor medical safety and administer medications to relieve discomfort.

This approach is not sufficient by itself to transition someone to maintaining an ongoing opioid-free life. Longer-term treatment that helps the person to develop new behaviors and strategies for coping is critical.

Patients who are not successful in withdrawing or who choose not to withdraw from opioids should be considered for treatment with medications as part of the treatment plan.

Reference:

How Can You Treat Opioid Addiction?

**Long-Term Residential Treatment**
- Provides a highly structured environment, including 24-hour care and lengths of stay from 6-12 months
- May employ a variety of models, including Therapeutic Communities and cognitive behavioral therapy

**Outpatient Psychosocial Treatment**
- Patients involved in outpatient psychosocial treatment continue to live in the community while receiving their treatment allowing them to continue to hold jobs and make use of social supports in the community
- Less costly than residential treatment
- Varies in types and intensity of services offered
- Group counseling is emphasized
- Medically-assisted withdrawal is offered; generally done with clonidine and other non-narcotic medications. Patients report being very uncomfortable during the withdrawal process when clonidine is used, consequently, many leave treatment prematurely.

Reference:

Behavioral Therapies

Behavioral therapies are designed to help individuals change their thought patterns around drug use and learn new behaviors to help them stop using and to avoid relapse. Two general strategies have shown a great deal of promise:

Contingency management:

- Helps the patient to adopt new behaviors by reinforcing behaviors that move them toward their recovery goals.

Research has shown that motivational incentive programs that use low-cost reinforcement (prizes, vouchers, clinic privileges, etc.), delivered in conjunction with on-site urine screening, promotes higher rates of treatment retention and abstinence from drug abuse.

The *Promoting Awareness of Motivational Incentives (PAMI)* Blending Product, developed through the Blending Initiative, is based on the positive research outcomes and lessons learned from the NIDA CTN study, Motivational Incentives for Enhanced Drug Abuse Recovery (MIEDAR). The tools contained in this training package are designed to build awareness of motivational incentives as a research-based therapeutic strategy within the addiction treatment field.

This Blending Product is available at:

www.drugabuse.gov/Blending/

www.attcnetwork.org
Behavioral Therapies

Cognitive-behavioral interventions:
- Help the patient to change the way they think and behave with regards to drug use;
- Increase positive coping strategies.

Many different types of behavioral therapies have been used successfully for substance abuse disorders. These include:
- Motivational Enhancement Therapy
- The Matrix Model
- Cognitive and Cognitive-Behavioral Therapy
- Community Reinforcement Approach
- Self-Help Programs

Note to the Trainer(s): The following resources can be obtained free of charge:

SAMHSA’s Treatment Improvement Protocol (TIP) series includes a number of documents that contain best-practice guidelines for the provision of interventions and therapies for individuals with substance abuse disorders.

The Principles of Drug Addiction Treatment: A Research-Based Guide (a.k.a., the NIDA Blue Book) reviews treatment approaches that have empirical support for their efficacy.

Reference:

How Can You Treat Opioid Addiction?

Agonist Maintenance Treatment

Agonist maintenance helps to stabilize people so that they don't constantly experience the cycles of use and withdrawal. This allows them to function more normally, engage in treatment, and diminish the negative behaviors associated with use.

These treatments have been conducted primarily on an outpatient basis in specific opioid treatment programs, traditionally using methadone. With the addition of buprenorphine to the treatment system, patients can also receive treatment through physicians in the offices.

Maintenance programs are most effective if they are combined with an effective behavioral treatment program.

Additionally, patients may need treatment for other medical or psychological conditions. They may also need a variety of social support services including:

- Vocational rehabilitation
- Employment
- Education
- Housing
- Case management
- Parenting
- Socialization skills
- Anger management

Reference:


Benefits of Methadone Maintenance Therapy

- Used effectively and safely for over 30 years
- Not intoxicating or sedating, if prescribed properly
- Effects do not interfere with ordinary activities
- Suppresses opioid withdrawal for 24-36 hours

Review and summarize bullet points.

- Bullet #1: Used effectively and safely for over 30 years.
- Bullet #2: Not intoxicating or sedating, if prescribed properly
- Bullet #3: Effects do not interfere with ordinary activities
- Bullet #4: Suppresses opioid withdrawal for 24-36 hours
Antagonist Maintenance Treatment

Use of opioid antagonists can also be effective. As with agonist treatment, antagonist treatment is generally conducted through an outpatient setting.

The antagonist is prescribed after medical withdrawal from opioids is complete. If antagonists are administered before complete withdrawal, the person may experience immediate and intense withdrawal.

Antagonists block the effects of any illicit opioid. Over time, this helps the person to break the pattern and desire of use.

One problem with antagonist treatment is that patients stop taking them because they want to get the experience of taking an agonist.

Effective antagonist maintenance therefore requires:

- A positive therapeutic relationship with the treatment provider
- Ongoing counseling
- Monitoring of medication to determine level of compliance.

Reference: