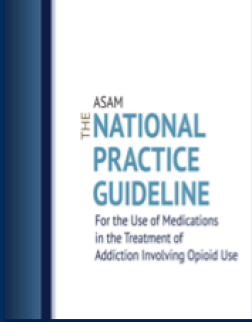


ASAM  
**THE NATIONAL  
PRACTICE  
GUIDELINE**

For the Use of Medications  
in the Treatment of  
Addiction Involving Opioid Use

## Slide 2. What?

The image shows the cover of the ASAM National Practice Guideline. The cover is white with a dark blue spine on the left. The text on the cover reads: "ASAM THE NATIONAL PRACTICE GUIDELINE For the Use of Medications in the Treatment of Addiction Involving Opioid Use".

**What?**

*The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use*

**AKA: The ASAM National Practice Guideline**  
1st to include all FDA-approved medications in single document

- ASAM developed this National Practice Guideline to provide information on evidence-based treatment of opioid use disorder (OUD).
- This is the first guideline publication to include all FDA-approved medications in a single document.
- Other existing guidelines typically do not include information on special populations (e.g. pregnant women, adolescents, etc)
- This presentation will introduce you to the National Practice Guideline, which identifies current practices and recommendations regarding the safe and effective use of medications for the treatment of opioid use disorder.
- Overall, the Practice Guideline contains recommendations for the evaluation and treatment of opioid use disorder, opioid withdrawal management, psychosocial treatment, special populations, and opioid overdose.
- The medications covered in the Guideline are mainly, but not exclusively, those that have been FDA-approved for the treatment of opioid dependence. They are Methadone, Buprenorphine, Naltrexone (in oral and extended-release injectable formulations), and Naloxone.
- The National Practice Guideline is intended primarily for clinicians involved in evaluating patients and providing authorization for pharmacological treatments at any level (physicians, prescribing healthcare providers, medical educators, and clinical care managers)

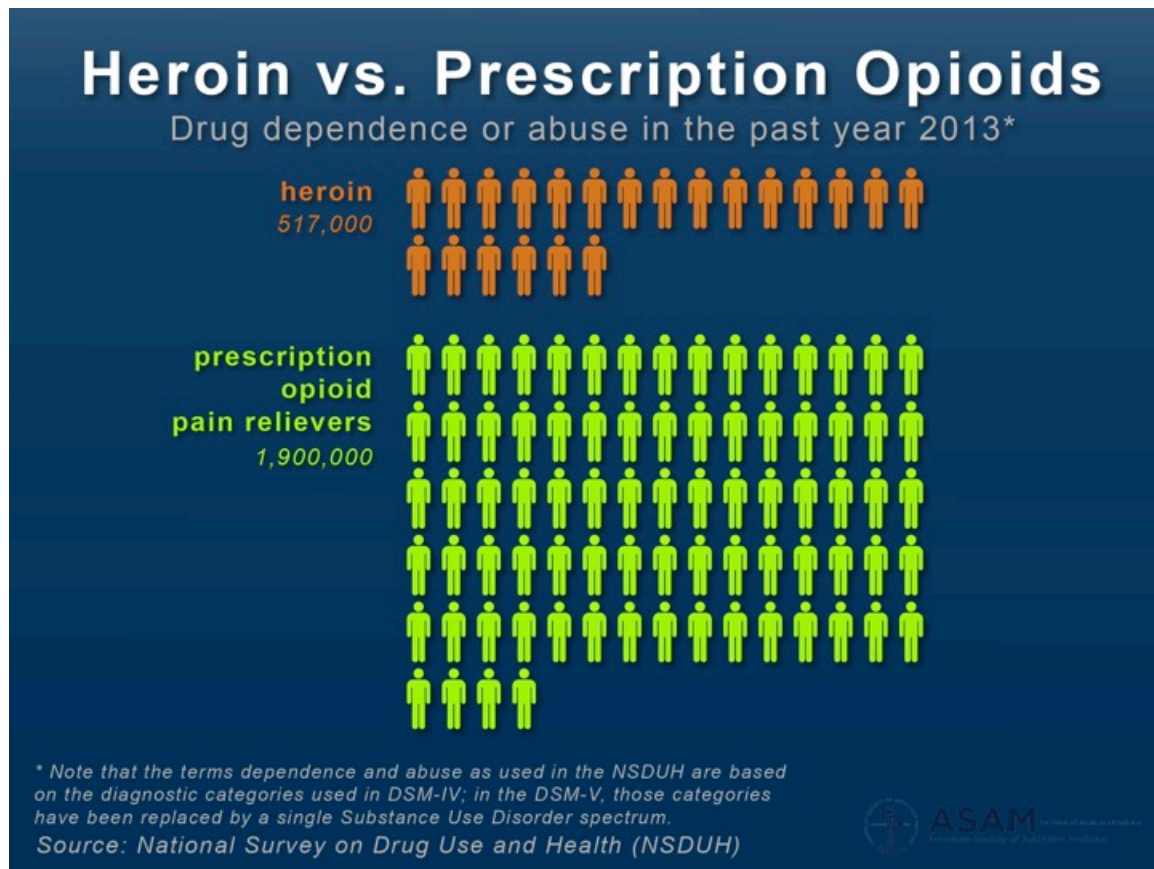
### Slide 3. Why?

# Why?



- 1.9 million people in the U.S. with Opioid Use Disorder (OUD)
- 517,000 with heroin use disorder
- Overdose deaths = deaths due to motor vehicle crashes
- Societal costs of opioid misuse ~ \$55 billion
- Opioid use is associated with increased mortality. The leading causes of death in people using opioids for nonmedical purposes are overdose and trauma.
- The number of unintentional overdose deaths from prescription opioids has more than quadrupled since 1999.
- Opioid use increases the risk of exposure to HIV, viral hepatitis, and other infectious agents through contact with infected blood or body fluids (e.g., semen) that results from sharing syringes and injection paraphernalia, or through unprotected sexual contact.

## Slide 4. Infographic Heroin vs. Prescription Opioids



Heroin vs. Prescription Opioid Use in the US

People living with heroin addiction: 517,000

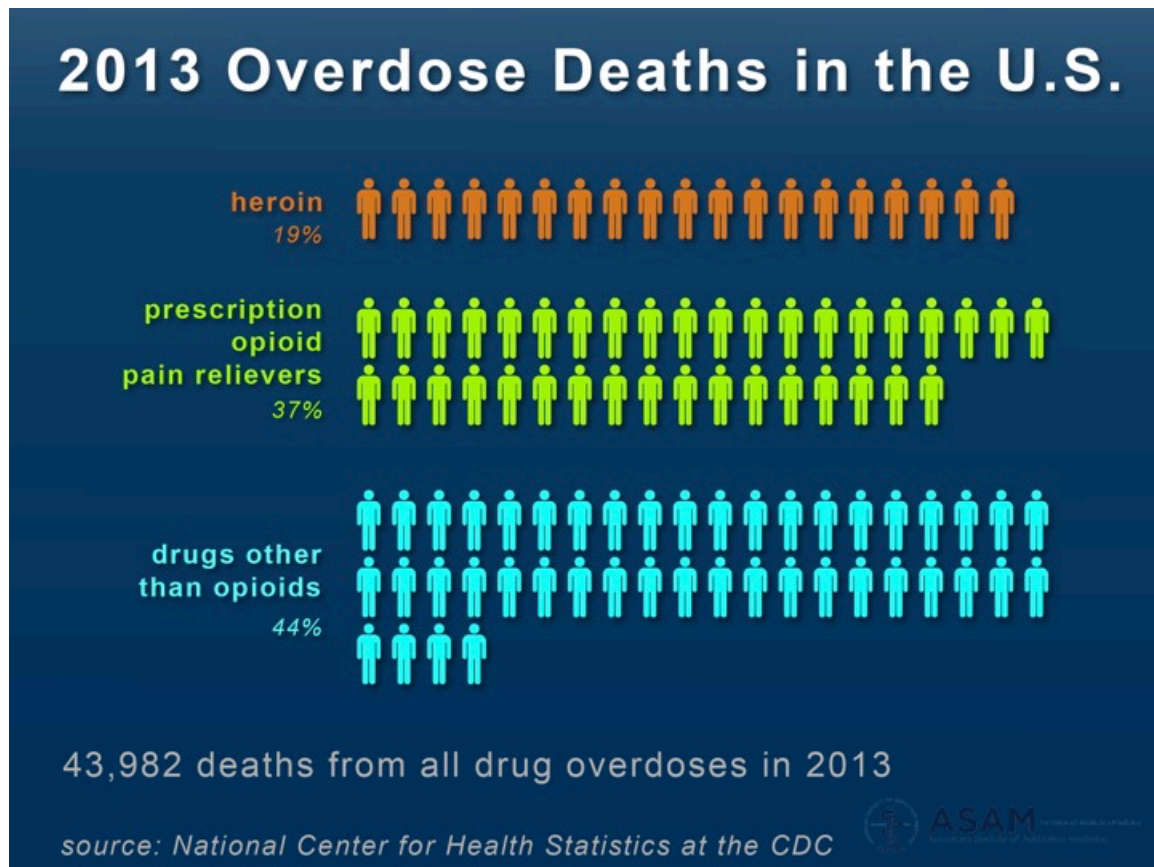
People living with addiction to prescription opioids: 1.9 million

In 2013, the *National Survey on Drug Use and Health (NSDUH)* estimated that 1.9 million Americans live with opioid pain reliever addiction and 517,000 are addicted to heroin. <http://www.samhsa.gov/data/sites/default/files/NSDUH-SR200-RecoveryMonth-2014/NSDUH-SR200-RecoveryMonth-2014.htm>

Note that the terms dependence and abuse as used in the NSDUH are based on the diagnostic categories used in DSM-IV; in the DSM-V, those categories have been replaced by a single Substance Use Disorder spectrum

Source: National Survey on Drug Use and Health (NSDUH)

Slide 5. Infographic Overdose Deaths in the U.S.



2013 Overdose Deaths in the U.S.

Number of deaths from heroin in 2013 = 8,257

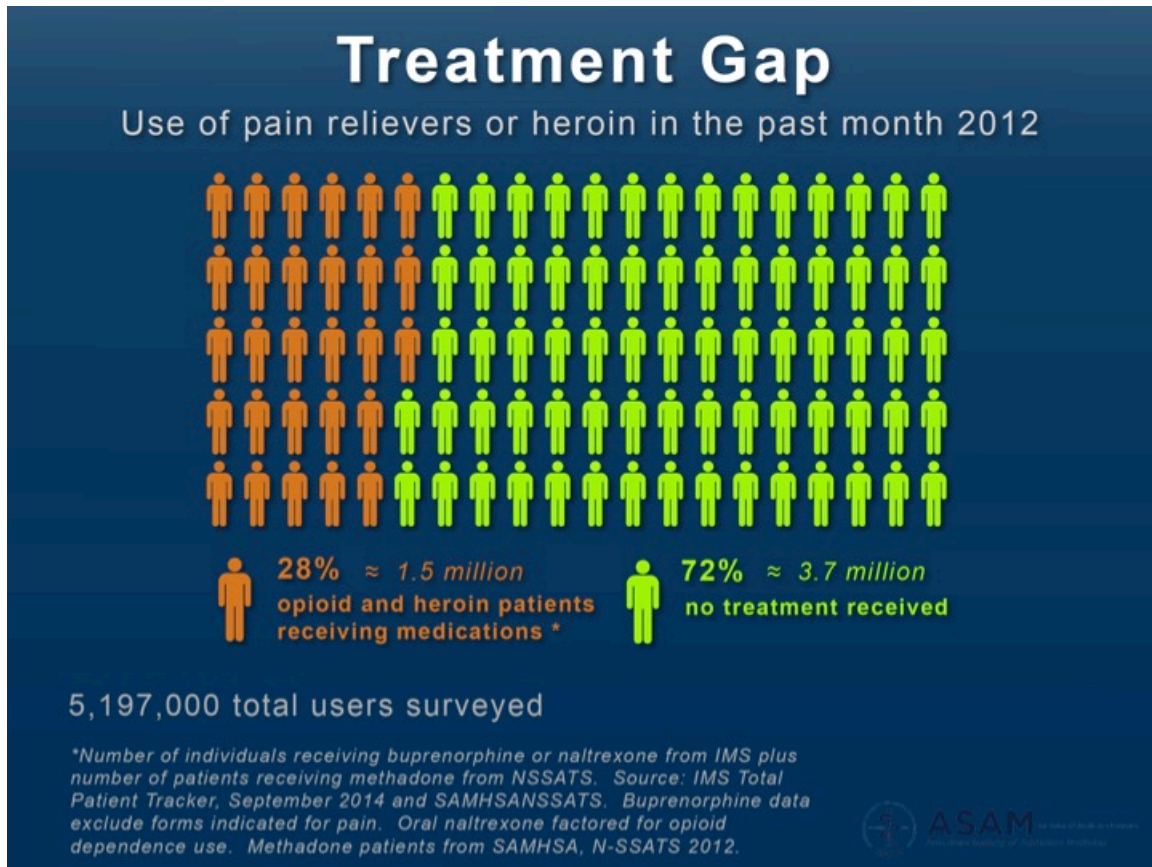
Number of deaths from prescription opioid pain relievers in 2013 = 16,235

Number of deaths from drugs other than opioids in 2013: 19,490

43,982 deaths (all drug overdoses) less the number for prescription opioids less the number for heroin)

Source: National Center for Health Statistics at the CDC

## Slide 6. Infographic Treatment Gap



The purpose of this infographic is to document the gap between those who need treatment and those who receive it. As you can see, there is a significant gap that needs to be closed.

Use of pain relievers or heroin in the past month 2012

Opioid & heroin patients receiving medications\* = 1,462,069 (28%)

Number of people using opioid pain relievers or heroin in the past month = 5,197,000

\* Number of individuals receiving buprenorphine or naltrexone from IMS plus number of patients receiving methadone from NSSATS.

Source: IMS Total Patient Tracker, September 2014 and SAMHSANSSATS.

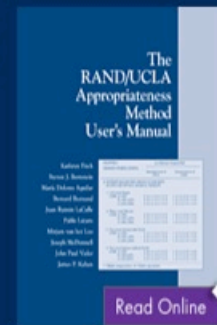
Buprenorphine data exclude forms indicated for pain. Oral naltrexone factored for opioid dependence use. Methadone patients from SAMHSA, N-SSATS 2012

## Slide 7. How?

# How?

Developed using RAND/UCLA Appropriateness Method (RAM)

- ♦ Consensus process combining scientific evidence with clinical knowledge
- ♦ Review of existing guidelines and literature
- ♦ Appropriateness ratings
- ♦ Necessity ratings
- ♦ Document development



This Practice Guideline was developed using the RAND/UCLA Appropriateness Method (RAM), a process that combines scientific evidence and clinical knowledge to determine the appropriateness of a set of clinical procedures. The RAM is a deliberate approach encompassing review of existing guidelines, literature reviews, appropriateness ratings, necessity reviews, and document development.

Slide 8. Who?

# Who?

- ◆ American Society of Addiction Medicine (ASAM)
- ◆ Treatment Research Institute (TRI)
- ◆ Guideline Committee: addiction medicine; psychiatry; obstetrics/gynecology; & internal medicine



For this project, American Association of Addiction Medicine (ASAM) selected an independent committee (known as the Guideline Committee) to oversee the development of the guideline.

The Guideline Committee was comprised of ten experts and researchers from multiple disciplines and specialties. The Guideline Committee was assisted by a technical team of researchers from the Treatment Research Institute (TRI), affiliated with the University of Pennsylvania and who also facilitated the RAND/RAM process.



## Slide 9. The Guideline Committee

### Guideline Committee Members

Sandra Comer, PhD  
Chinazo Cunningham, MD, MS  
Marc J. Fishman, MD, FASAM  
Adam Gordon, MD, MPH, FASAM  
Kyle Kampman, MD, Chair  
Daniel Langleben, MD  
Ben Nordstrom, MD, PhD  
David Oslin, MD  
George Woody, MD  
Tricia Wright, MD, MS  
Stephen Wyatt, DO



For this project, ASAM selected an independent committee to oversee guideline development, participate in review of treatment scenarios, and to assist in writing. ASAM's Quality Improvement Council, chaired by Margaret Jarvis, MD, oversaw the selection process for the independent development committee, referred to as the Guideline Committee.

The Guideline Committee was comprised of ten experts and researchers from multiple disciplines, medical specialties, and subspecialties including academic research, internal medicine, family medicine, addiction medicine, addiction psychiatry, general psychiatry, obstetrics/gynecology, pharmacology, and clinical neurobiology. Physicians with both allopathic and osteopathic training were represented in the Guideline Committee.

Note: Sandra Comer is a non-physician, PhD researcher

See [Practice Guideline](#), Appendix III, IV, and V for the qualifications, relationships and COI information for the Guideline Committee, Quality Improvement Council, and External Reviewers.

**Slide 10. Quality Improvement Council**

## Quality Improvement Council

John Femino, MD, FASAM

Margaret Jarvis, MD, FASAM, Chair

Margaret Kotz, DO, FASAM

Sandrine Pirard, MD, MPH, PhD

Robert J. Roose, MD, MPH

Alexis Geier-Horan, ASAM Staff

Beth Haynes, ASAM Staff

Penny S. Mills, MBA, ASAM, Executive VP

***External Reviewer***

Michael M. Miller, MD, FASAM, FAPA



See [Practice Guideline](#), Appendix III, IV, and V for the qualifications, relationships and COI information for the Guideline Committee, Quality Improvement Council, and External Reviewers.

## Slide 11. Treatment Research Institute

### Treatment Research Institute Technical Team Members

Amanda Abraham, PhD

Karen Dugosh, PhD

David Festinger, PhD

Kyle Kampman, MD, Principal Investigator

Keli McLoyd, JD

Brittany Seymour, BA


Abigail Woodworth, MS



The Guideline Committee was assisted by a technical team of researchers from the Treatment Research Institute (TRI) affiliated with the University of Pennsylvania and worked under the guidance of Dr. Kyle Kampman who led the TRI team as Principal Investigator in implementing the RAM.

See [Practice Guideline](#), Appendix III, IV, and V for the qualifications, relationships and COI information for the Guideline Committee, Quality Improvement Council, and External Reviewers.

## Slide 12. Definitions



### Definitions

- ◆ Opioid Use Disorder (OUD) is a chronic, relapsing disease defined in the DSM-5
- ◆ Bio-psycho-social-spiritual illness
- ◆ Addiction involving opioid use

All abbreviations and acronyms available in the ASAM National Practice Guideline



Opioid Use Disorder (OUD) is a chronic, relapsing disease. Many readers of this Practice Guideline may recognize the term “opioid use disorder” as it is used in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) developed by the American Psychiatric Association; others may be more familiar with the term “opioid dependence,” as used in previous editions of the DSM.

ASAM released its definition of addiction in 2011. It defines addiction as a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one’s behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

ASAM encourages the use of the term addiction. However, given the widespread use of the DSM’s categorization of disorders, the Practice Guideline, for the sake of brevity and convention, uses the term “opioid use disorder” (OUD).

See the [Practice Guideline](#) for a glossary and a complete list of abbreviations and acronyms.

## Slide 13. Our Premise

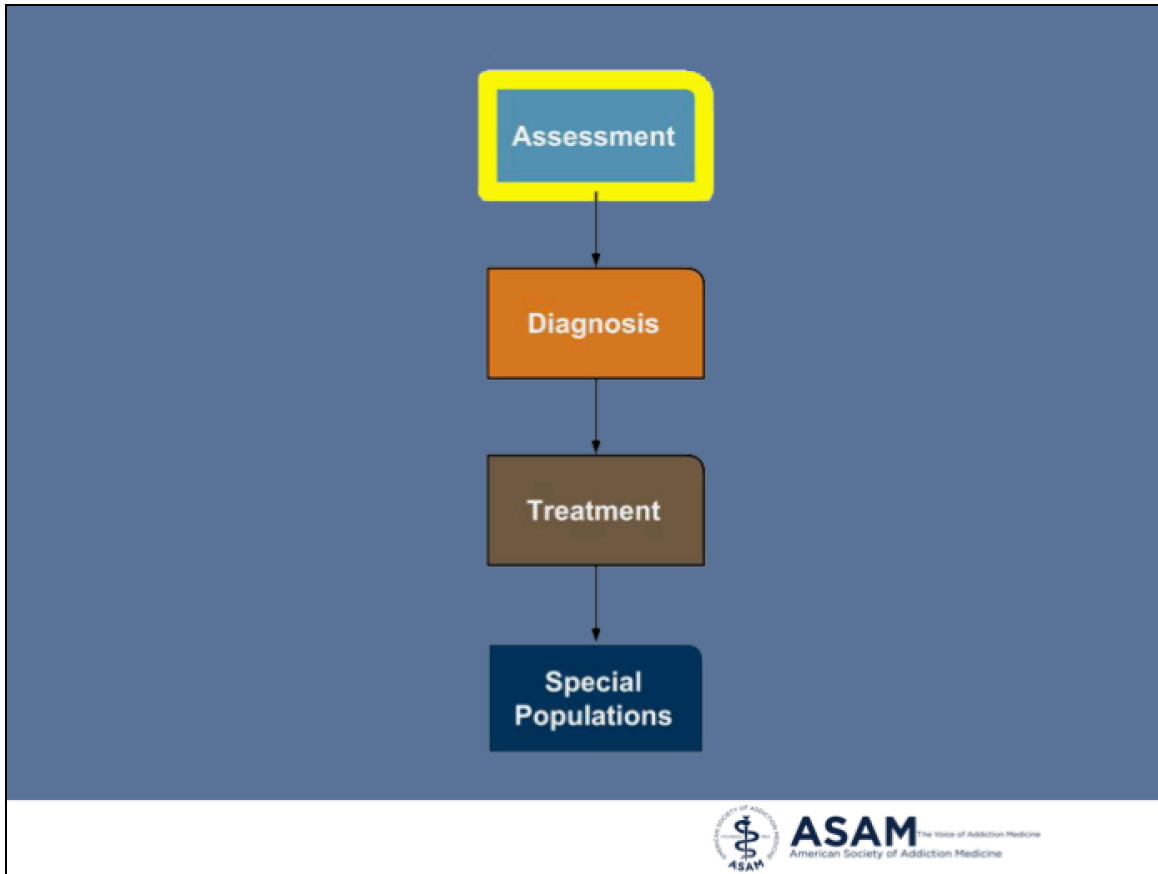
# Premise



- ◆ FDA-approved medications to treat OUD are clinical & cost-effective interventions
  - ◆ Saves lives, saves money
  - ◆ One component, along with psychosocial treatment
- ◆ 30% of treatment programs offer medication
- ◆ Less than half of eligible treatment program patients receive medications
- ◆ Missed opportunity to utilize most effective treatments

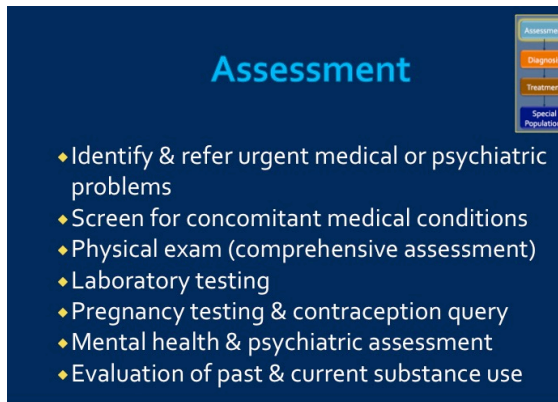


**Slide 14.**



At this point, you are moving into the Assessment portion of the slide deck.

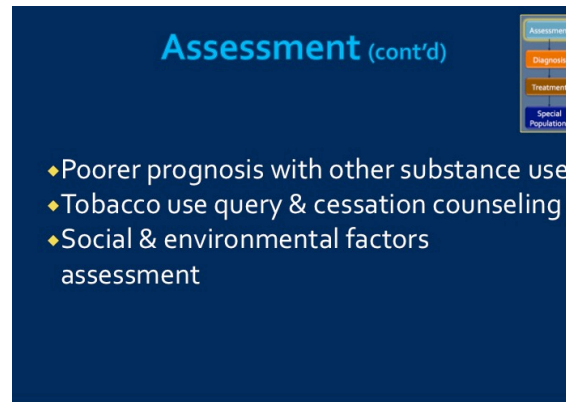
## Slides 15 & 16. Assessment



**Assessment**

- ◆ Identify & refer urgent medical or psychiatric problems
- ◆ Screen for concomitant medical conditions
- ◆ Physical exam (comprehensive assessment)
- ◆ Laboratory testing
- ◆ Pregnancy testing & contraception query
- ◆ Mental health & psychiatric assessment
- ◆ Evaluation of past & current substance use

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**Assessment (cont'd)**

- ◆ Poorer prognosis with other substance use
- ◆ Tobacco use query & cessation counseling
- ◆ Social & environmental factors assessment

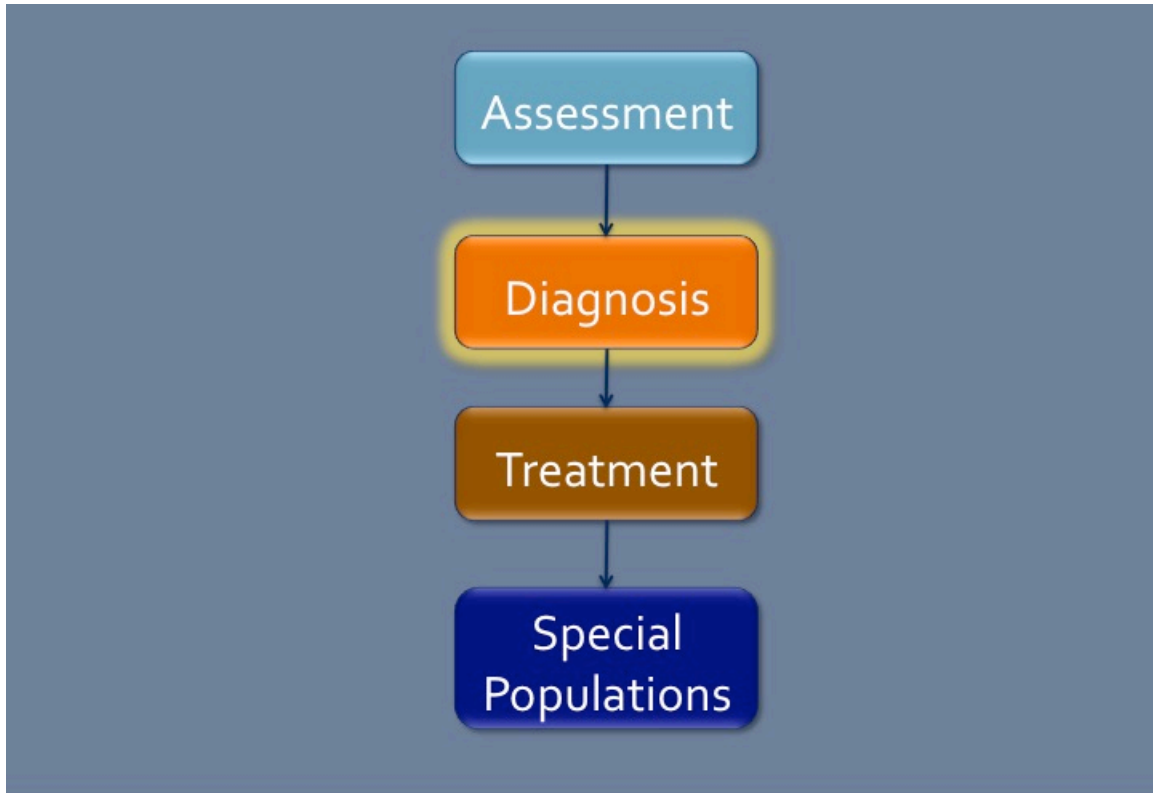
ASAM

- First clinical priority should be given to identifying and making appropriate referral for any urgent or emergent medical or psychiatric problem(s), including drug-related impairment or overdose.
- Completion of the patient's medical history should include screening for concomitant medical conditions including infectious diseases (hepatitis, HIV, and TB), acute trauma, and pregnancy.
- A physical examination should be completed as a component of the comprehensive assessment process. The prescriber (the clinician authorizing the use of a medication for the treatment of opioid use disorder) may conduct this physical examination him/herself, or, in accordance with the ASAM Standards, ensure that a current physical examination is contained within the patient medical record before a patient is started on a new medication for the treatment of his/her addiction.
- Initial laboratory testing should include a complete blood count, liver function tests, and tests for hepatitis C and HIV. Testing for TB and sexually transmitted infections should also be considered. Hepatitis B vaccination should be offered, if appropriate.
- The assessment of females presents special considerations regarding their reproductive health. Women of childbearing age should be tested for pregnancy, and all women of childbearing potential and age should be queried regarding methods of contraception given the increase in fertility that results from effective opioid use disorder treatment.
- Patients being evaluated for addiction involving opioid use, and/or for possible medication use in the treatment of opioid use disorder, should undergo (or have completed) an assessment of mental health status and possible psychiatric disorders (as outlined in the ASAM Standards).
- Opioid use is often co-occurring with other substance related disorders. An evaluation of past and current substance use as well as a determination of the totality of substances that surround the addiction should be conducted.

- The use of marijuana, stimulants, or other addictive drugs should not be a reason to suspend opioid use disorder treatment. However, evidence demonstrates that patients who are actively using substances during opioid use disorder treatment have a poorer prognosis. The use of benzodiazepines and other sedative hypnotics may be a reason to suspend agonist treatment because of safety concerns related to respiratory depression.
- A tobacco use query and counseling on cessation of tobacco products should be completed routinely for all patients, including those who present for evaluation and treatment of opioid use disorder.
- An assessment of social and environmental factors should be conducted (as outlined in the ASAM Standards to identify facilitators and barriers to addiction treatment, and specifically to pharmacotherapy. Before a decision is made to initiate a course of pharmacotherapy for the patient with opioid use disorder, the patient should receive a multidimensional assessment in fidelity with the ASAM Criteria. Addiction should be considered a bio-psycho-social-spiritual illness, for which the use of medication(s) is but only one component of overall treatment.



**Slide 17.**




At this point you are moving into the diagnosis portion of the slide deck.

## Slide 18. Diagnosis

# Diagnosis

- ◆ Provider confirms OUD diagnosis
- ◆ History & physical exam
- ◆ Scales measure OUD withdrawal symptoms
- ◆ Frequency of urine drug testing determined



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graph TD; A[Assessment] --> B[Diagnosis]; B --> C[Treatment]; C --> D[Special Populations];
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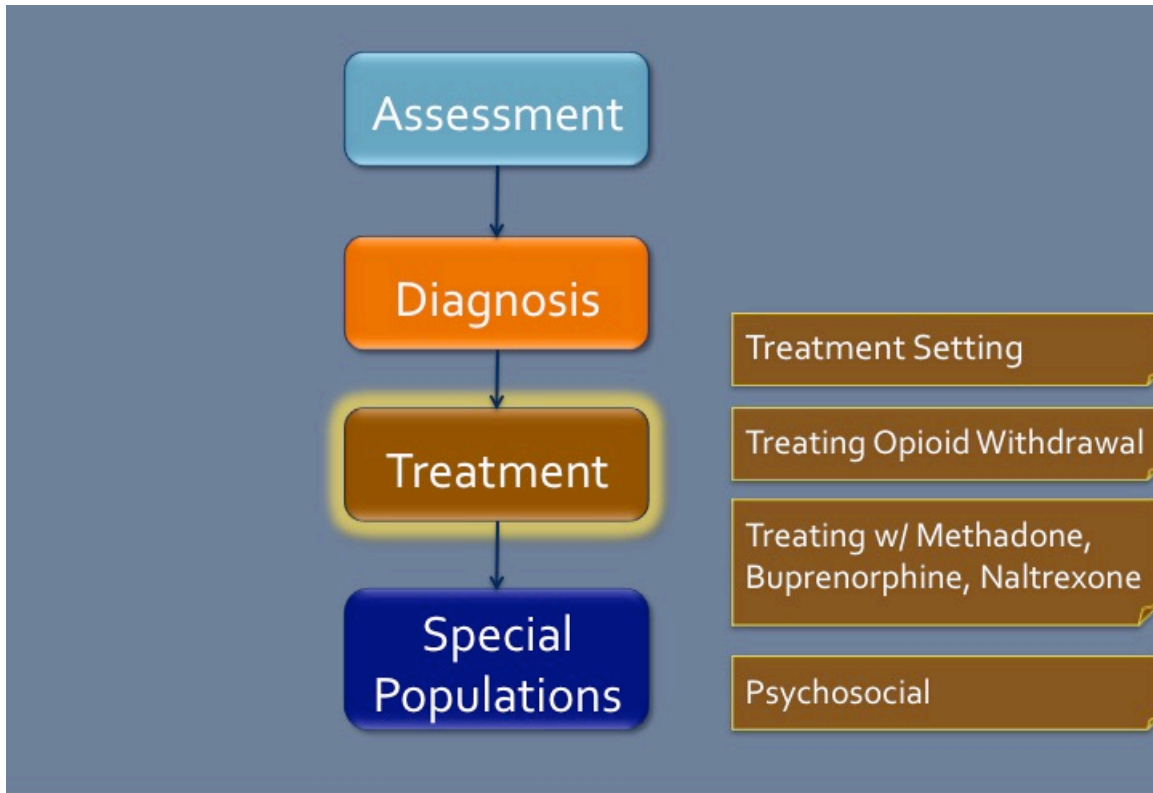
- Other clinicians may diagnose opioid use disorder, but confirmation of the diagnosis by the provider with prescribing authority and who recommends medication use, must be obtained before pharmacotherapy for opioid use disorder commences.
- Opioid use disorder is primarily diagnosed on the basis of the history provided by the patient and a comprehensive assessment that includes a physical examination.
- Validated clinical scales that measure withdrawal symptoms; e.g., the OOWS, SOWS, and the COWS may be used to assist in the evaluation of patients with opioid use disorder.
- Urine drug testing during the comprehensive assessment process, and frequently during treatment, is recommended. The frequency of drug testing is determined by a number of factors including: the stability of the patient, the type of treatment, and the treatment setting.

The diagnosis of opioid use disorder is based on criteria outlined in the DSM-5. The criteria describe a problematic pattern of opioid use leading to clinically significant impairment or distress. There are a total of 11 symptoms and severity is specified as mild (presence of 2-3 symptoms), moderate (presence of 4-5 symptoms) or severe (presence of 6 or more symptoms) within a 12-month period. Opioid use disorder

requires that at least two of the following 11 criteria be met within a twelve-month period: (1) taking opioids in larger amounts or over a longer period of time than intended; (2) having a persistent desire or unsuccessful attempts to reduce or control opioid use; (3) spending excess time obtaining, using or recovering from opioids; (4) craving for opioids; (5) continuing opioid use causing inability to fulfill work, home, or school responsibilities; (6) continuing opioid use despite having persistent social or interpersonal problems; (7) lack of involvement in social, occupational or recreational activities; (8) using opioids in physically hazardous situations; (9) continuing opioid use in spite of awareness of persistent physical or psychological problems; (10) tolerance, including need for increased amounts of opioids or diminished effect with continued use at the same amount – as long as the patient is not taking opioids under medical supervision; and (11) withdrawal manifested by characteristic opioid withdrawal syndrome or taking opioids to relieve or avoid withdrawal symptoms – as long as the patient is not taking opioids under medical supervision

More detail about diagnosing opioid use disorder is available in the *American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.

Slide 19.




At this point you are moving into the treatment portion of the slide deck.

## Slide 20. Treatment Setting

# Treatment Setting

- ◆ Clinician & patient share treatment option decisions
- ◆ Consider patient preferences & treatment history & setting to determine medication
- ◆ Venue as important as medication selected
- ◆ Office treatment may not be suitable for patients with selected drug addiction issues
- ◆ OTPs offer daily dosing and supervision



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graph TD; A[Assessment] --> B[Diagnosis]; B --> C[Treatment]; C --> D[Special Populations];
```




- The choice of available treatment options for addiction involving opioid use should be a shared decision between clinician and patient.
- Clinicians should consider the patient's preferences, past treatment history, and treatment setting when deciding between the use of methadone, buprenorphine, and naltrexone in the treatment of addiction involving opioid use. The treatment setting described as Level 1 treatment in the ASAM Criteria may be a general outpatient location such as a clinician's practice site. The setting as described as Level 2 in the ASAM Criteria may be an intensive outpatient treatment or partial hospitalization program housed in a specialty addiction treatment facility, a community mental health center, or another setting. The ASAM Criteria describes Level 3 or Level 4 treatment respectively as a residential addiction treatment facility or hospital.
- The venue in which treatment is provided is as important as the specific medication selected. Opioid Treatment Programs (OTPs) offer daily supervised dosing of methadone, and increasingly of buprenorphine. In accordance with federal law (21 CFR §1306.07), OBOT, which provides medication on a prescribed weekly or monthly basis, is limited to buprenorphine. Naltrexone can be prescribed in any setting by any clinician with the authority to prescribe any medication. Clinicians

should consider a patient's psychosocial situation, co-occurring disorders, and risk of diversion when determining whether OTP or OBOT is most appropriate.

- OBOT may not be suitable for patients with active alcohol use disorder or sedative, hypnotic, or anxiolytic use disorder (or who are in the treatment of addiction involving the use of alcohol or other sedative drugs, including benzodiazepines or benzodiazepine receptor agonists). It may also be unsuitable for persons who are regularly using alcohol or other sedatives but do not have addiction or a specific substance use disorder related to that class of drugs. The prescribing of benzodiazepines or other sedative-hypnotics should be used with extreme caution in patients who are prescribed methadone or buprenorphine for the treatment of an opioid use disorder.
- Methadone is recommended for patients who may benefit from daily dosing and supervision in an OTP, or for patients for whom buprenorphine for the treatment of opioid use disorder has been used unsuccessfully in an OTP or OBOT setting.
- Oral naltrexone for the treatment of opioid use disorder is often adversely affected by poor medication adherence. Clinicians should reserve its use for patients who would be able to comply with special techniques to enhance their adherence; e.g. observed dosing. Extended-release injectable naltrexone reduces, but does not eliminate, issues with medication adherence.

## Slide 21 and 22. Opioid Withdrawal Management

### Opioid Withdrawal Management



- ◆ Medications for withdrawal preferred to abrupt cessation
- ◆ Advise patients medications alone for opioid withdrawal not a complete treatment method
- ◆ Medical history & physical exam focus on withdrawal signs & symptoms
- ◆ Methadone withdrawal symptom management in OTP or inpatient setting



### Opioid Withdrawal Management (cont'd)

- ◆ Buprenorphine can be used to manage withdrawal symptoms
- ◆ Combination buprenorphine & low dose oral naltrexone to manage withdrawal & facilitate ER injectable naltrexone shows promise
- ◆ Clonidine to support opioid withdrawal
- ◆ Anesthesia ultra-rapid opioid detoxification (UROD) is NOT recommended - too high risk
- ◆ Increased risk of OD or death with stopping agonist therapy & resuming opioid use



- Using medications for opioid withdrawal management is recommended over abrupt cessation of opioids. Abrupt cessation of opioids may lead to strong cravings, which can lead to continued use.
- Patients should be advised about risk of relapse and other safety concerns from using opioid withdrawal management as standalone treatment for opioid use disorder. Opioid withdrawal management on its own is not a treatment method.
- Assessment of a patient undergoing opioid withdrawal management should include a thorough medical history and physical examination focusing on signs and symptoms associated with opioid withdrawal.
- Opioid withdrawal management in cases in which methadone is used to manage withdrawal symptoms must be done in an inpatient setting or in an OTP. For short acting opioids, tapering schedules that decrease in daily doses of prescribed methadone should begin with doses between 20 mg to 30 mg per day and should be completed in 6 to 10 days.
- Opioid withdrawal management in cases in which buprenorphine is used to manage withdrawal symptoms should not be initiated until 12 to 18 hours after the last dose of a short-acting agonist such as heroin or oxycodone, and 24 to 48 hours after the last dose of a long-acting agonist such as methadone. A dose of buprenorphine sufficient to suppress withdrawal symptoms is given (this can be 4 mg to 16 mg per day) and then the dose is tapered. The duration of the tapering schedule can be as brief as 3 to 5 days or as long as 30 days or more.
- The use of combinations of buprenorphine and low doses of oral naltrexone to manage withdrawal and facilitate the accelerated introduction of extended-release injectable naltrexone has shown promise. More research will be needed before this can be accepted as standard practice.
- The Guideline Committee recommends, based on consensus opinion, the inclusion of clonidine as a recommended practice to support opioid withdrawal. Clonidine is not FDA-approved for the treatment of opioid withdrawal but it has been extensively used off-label for this purpose. Clonidine may be used orally or trans-

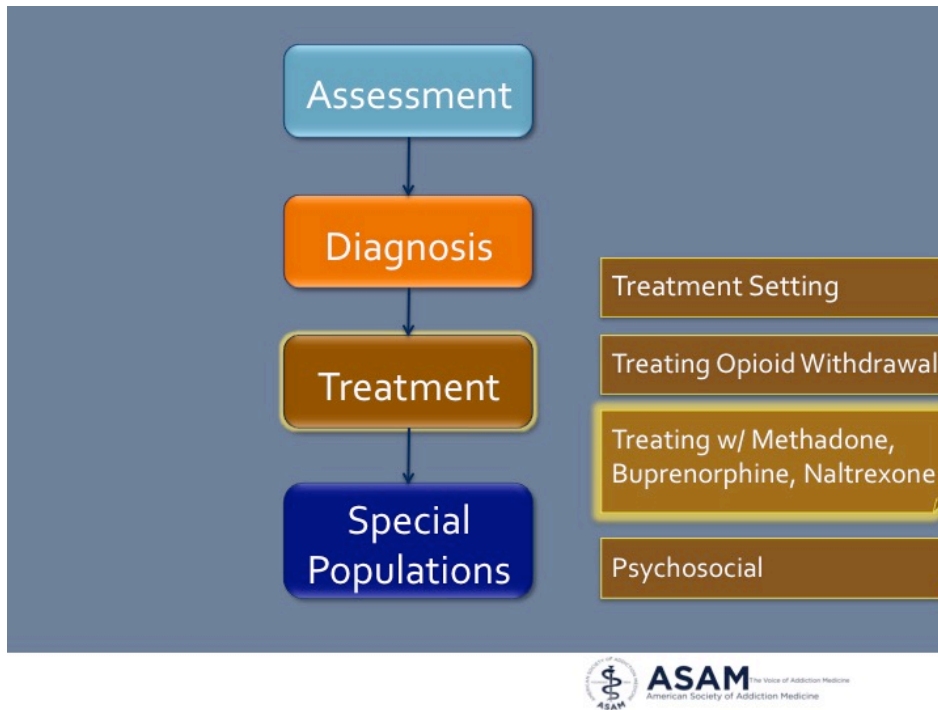
dermally at doses of 0.1 to 0.3 mg every 6 to 8 hours with a maximum dose of 1.2 mg daily to assist in the management of opioid withdrawal symptoms. Its hypotensive effects often limit the amount that can be used. Clonidine can be combined with other nonnarcotic medications targeting specific opioid withdrawal symptoms such as benzodiazepines for anxiety, loperamide for diarrhea, acetaminophen or NSAIDs for pain, and ondansetron or other agents for nausea.

- Opioid withdrawal management using anesthesia UROD is not recommended due to high risk for adverse events or death. Naltrexone-facilitated opioid withdrawal management can be a safe and effective approach but should be used only by clinicians experienced with this clinical method and in cases in which anesthesia or conscious sedation are not being employed.

There are a number of useful opioid withdrawal scales that can assist the clinician in evaluating patients with opioid use disorder by identifying and quantitating the severity of opioid withdrawal symptoms. The Objective Opioid Withdrawal Scale (OOWS), which relies on clinical observation, is useful in measuring and documenting the objectively measurable symptoms of opioid withdrawal. The Subjective Opioid Withdrawal Scale (SOWS) records the patient's rating of opioid withdrawal on a 16-item scale. Finally, the Clinical Opioid Withdrawal Scale (COWS) includes 11 items and contains signs and symptoms of opioid withdrawal, which are both objective and subjective in nature.



**Slide 23.**



At this point you are moving to the portion of the slide deck that addresses specific pharmacotherapy treatment options.

The medications covered in this National Practice Guideline all have ample evidence supporting their safety and efficacy and are mainly those that have been approved by the FDA for the treatment of opioid dependence as defined in prior versions of the DSMIII and DSM-IV and not necessarily the definition contained in the current version of the manual, the DSM-5.

Here are the medications that will be discussed:

- \* **Methadone** (mu agonist) for opioid use disorder treatment and withdrawal management
- \* **Buprenorphine** (partial mu agonist) for opioid use disorder treatment and withdrawal management
- \* **Naltrexone** (antagonist) for relapse prevention
- \* **Naloxone** (antagonist) to treat overdose

Each section of the Guideline that addresses a medication to treat OUD is organized in an identical manner and covers the following: (1) background; (2) patient selection and treatment goals; (3) course of treatment; (4) switching treatment medications; (5) summary of recommendations; and (6) areas for further research.

## Slide 24 and 25. Methadone

**Methadone**

- ◆ Methadone for physiological dependence with psychosocial intervention
- ◆ Methadone in monitored program setting
- ◆ Psychosocial treatment with methadone
- ◆ Recommended initial dose 10-30 mg; usual daily dosage from 60-120 mg
- ◆ Methadone for relapse or at risk for relapse
- ◆ Relapse prevention strategies part of comprehensive treatment

**Methadone (cont'd)**

- ◆ May switch from methadone to other medication if side effects or other issues
- ◆ Low doses of methadone first if switching to buprenorphine
- ◆ Complete withdrawal from methadone before switching to oral or ER naltrexone
- ◆ No recommended/optimal treatment duration (depends on patient response)

- Methadone is a treatment option recommended for patients who are physiologically dependent on opioids, able to give informed consent, and who have no specific contraindications for agonist treatment when it is dispensed in the context of an appropriate plan that includes psychosocial intervention
- The recommended initial dose ranges for methadone are from 10 mg to 30 mg with reassessment in 3 to 4 hours and a second dose not to exceed 10 mg on the first day if withdrawal symptoms are persisting. Federal law mandates that the initial dose cannot exceed 30 mg and not exceed 40 mg in one day.
- The usual daily dosage of methadone ranges from 60 mg to 120mg. Some patients may respond to lower doses and some patients may need higher doses.
- Higher methadone doses may be associated with increased risk of adverse effects, including prolongation of QT interval & other arrhythmias (torsades de pointes). Clinicians, in consultation with patients, may need to consider the relative risk of adverse events with methadone as compared to the risk of morbidity and mortality of an untreated OUD.
- Dosage increases in 5 to 10 mg increments applied no more frequently than every 7 days (depending on clinical response), are necessary to avoid over-sedation, toxicity, or even iatrogenic overdose deaths.
- The administration of methadone should be monitored because unsupervised administration can lead to misuse and diversion. OTP regulations require monitored medication administration until the patient's clinical response and behavior demonstrates that the prescribing of non-monitored doses is appropriate.
- Methadone should be reinstated immediately if relapse occurs, or when an assessment determines that the risk of relapse is high for patients who previously received methadone in the treatment of opioid use disorder but who are no longer prescribed such treatment.
- Patients on low doses of methadone (30 – 40mg per day or less) generally tolerate the transition to buprenorphine with minimal discomfort; whereas patients on higher doses of methadone may find that switching causes significant discomfort.

- Patients should be closely monitored during such a switch since there is a risk that stable methadone patients may become unstable when switching to buprenorphine. Patients switching from methadone to naltrexone need to be completely withdrawn from methadone and other opioids. This can take up to 14 days but can be typically achieved in 7 days. A naloxone challenge may be useful.
- Patients who discontinue agonist therapy with methadone or buprenorphine and then resume opioid use should be made aware of the risks associated with opioid overdose, and especially the increased risk of death.

## Slides 26 and 27. Buprenorphine

**Buprenorphine**

- ◆ Mild to moderate opioid withdrawal symptoms before buprenorphine
- ◆ Start with 2-4 mg; increase dosage in 2-4 mg increments
- ◆ Observe patients in office during induction, home inductions if experienced physician or patient
- ◆ After induction  $\geq 8$  mg a day; 4-8 mg increases w/ continued opioid use (daily dose 12-16 mg or higher)
- ◆ Psychosocial treatment with buprenorphine


**Buprenorphine**

- ◆ Reduce buprenorphine diversion
- ◆ Frequent urine drug tests (including buprenorphine)
- ◆ Frequent visits until stable
- ◆ If/when taper, should be slow & monitored
- ◆ 7-14 days between buprenorphine to naltrexone
- ◆ Buprenorphine to methadone no time delay
- ◆ No recommended time limit for treatment

- For this guideline, recommendations using the term “buprenorphine” will refer generally to both the buprenorphine only and the combination buprenorphine/naloxone formulations. When recommendations differ by product, the term buprenorphine monoproduct will be used and the combination product will be called “combination buprenorphine/naloxone.”
- The guideline acknowledges that there are multiple formulations of buprenorphine currently in the market and that these multiple formulations have different bioavailability and have different buprenorphine/naloxone dose strengths. The guideline document includes bioequivalence charts. Because of the possibility of slight differences in bioavailability between the different formulations of buprenorphine, patients switching from one form of buprenorphine to another should be monitored for adverse effects.
- Generally, buprenorphine initiation should occur at least 6 to 12 hours after the last use of heroin or other short-acting opioids, or 24 to 72 hours after their last use of long-acting opioids such as methadone.
- Clinicians should observe patients in their offices during induction. Emerging research suggests, however, that many patients need not be observed and that home buprenorphine induction may be considered. Home-based induction is recommended only if the patient or prescribing physician is experienced with the use of buprenorphine. This is based on the consensus opinion of the Guideline Committee.
- Regarding dosing – the FDA approves dosing to a limit of 24 mg per day, and there is limited evidence regarding the relative efficacy of higher doses. In addition, the use of higher doses may increase the risk of diversion.
- Patients who discontinue agonist therapy and resume opioid use should be made aware of the risks associated with an opioid overdose, and especially the increased risk of death.

## Slide 28. Naltrexone

# Naltrexone



- ◆ Naltrexone rec to prevent relapse
- ◆ Psychosocial treatment with naltrexone
- ◆ Oral naltrexone taken daily in 50 mg doses or 3x weekly in two 100 mg doses, followed by one 150 mg dose
- ◆ Naltrexone ER administered every 4 weeks at set dosage of 380 mg/injection
- ◆ No recommended length of treatment
- ◆ Plan and monitor naltrexone to agonist switches




- Oral formula naltrexone may be considered for patients where adherence can be supervised or enforced. Extended-release injectable naltrexone may be more suitable for patients who have issues with adherence.
- The efficacy of naltrexone use in conjunction with psychosocial treatment has been established, whereas the efficacy of extended-release injectable naltrexone without psychosocial intervention has not been established.
- Because there is no physical dependence associated with naltrexone, it can be stopped abruptly without withdrawal symptoms.
- Switching from naltrexone to methadone or buprenorphine should be planned, considered, and monitored. Switching from an antagonist such as naltrexone to a full agonist (methadone) or a partial agonist (buprenorphine) is generally less complicated than switching from a full or partial agonist to an antagonist because there is no physical dependence associated with antagonist treatment and thus no possibility of precipitated withdrawal. Patients being switched from naltrexone to buprenorphine or methadone will not have physical dependence on opioids and thus the initial doses of methadone or buprenorphine used should be low. Patients should not be switched until a significant amount of the naltrexone is no longer in their system, about 1 day for oral naltrexone or 30 days for extended-release injectable naltrexone.
- Patients who discontinue antagonist therapy and resume opioid use should be made aware of the increased risks associated with an opioid overdose, and especially the increased risk of death.

## Slides 29 and 30. Psychosocial in Conjunction with Medications


### Psychosocial in Conjunction with Medications

- ♦ Recommended with any pharmacological treatment – at a minimum should include:
  - ♦ Psychosocial needs assessment
  - ♦ Supportive counseling
  - ♦ Links to existing family support
  - ♦ Referrals to community services



### Psychosocial in Conjunction with Medications (cont'd)

- ♦ Collaboration with behavioral provider
- ♦ Psychosocial treatment generally recommended for patients receiving opioid agonist treatment
- ♦ Offered with oral and extended-release injectable naltrexone



- Extensive literature reviews were conducted on psychosocial treatment with medications. Most recommendations for psychosocial treatments are not correlated with any specific pharmacological approach.
- Treatment planning should include collaboration with qualified behavioral health care providers to determine the optimal type and intensity of psychosocial treatment and for renegotiation of the treatment plan for circumstances in which patients do not adhere to recommended plans for, or referrals to, psychosocial treatment.
- While not considered by ASAM to be a psychosocial treatment on its own, mutual help (e.g., NA, SMART, AA, etc.) compliments professional treatment but is not a substitute for professional treatment. Many providers recommend mutual help programs but there is anecdotal information to suggest that some of these programs may be less accepting of patients receiving medications for OUD.

Slide 31. Medications for OUC Treatment

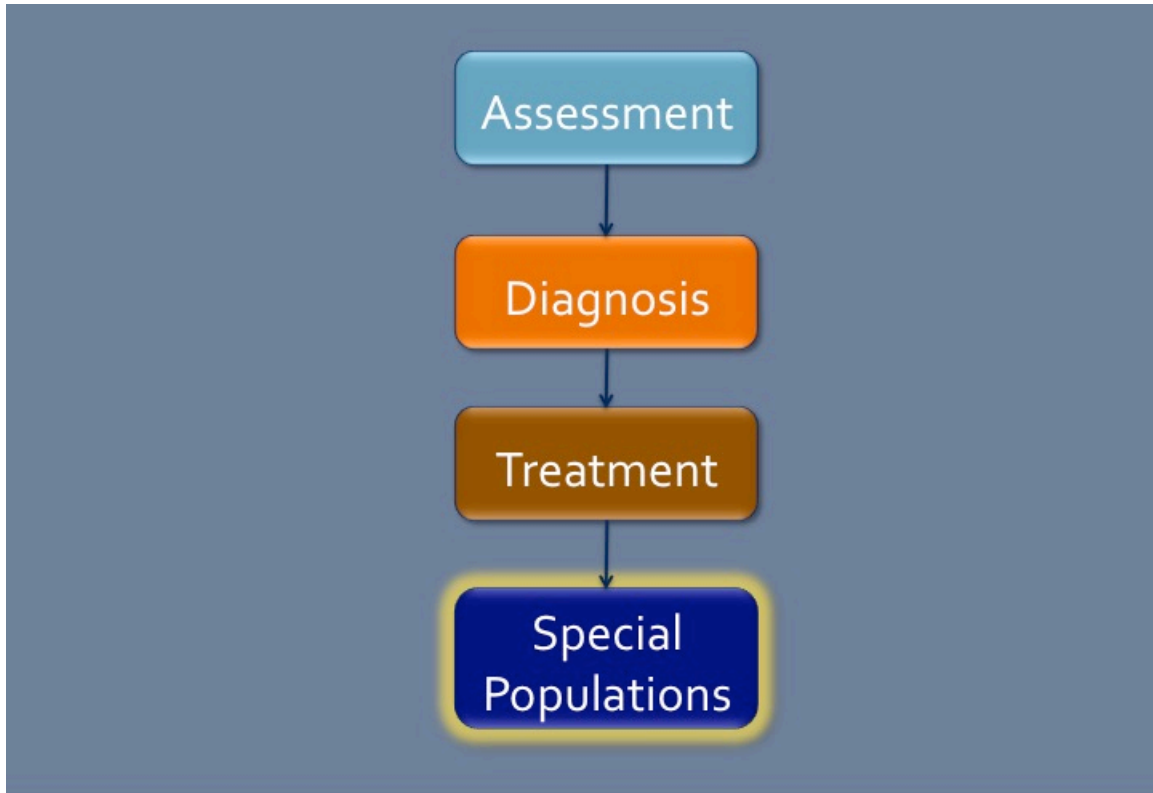
## Medications for OUD Treatment

Agent	Dose	Dosing
Buprenorphine sublingual film, tablets (generic)	PO: 2 mg, 8 mg film and tablets	Initial: 2–4 mg (Increase by 2–4 mg) Daily: ≥8 mg Max: 24 mg/day
Methadone tablets/liquid (generic)	PO: 5 mg, 10 mg, tablets; 10 mg/mL liquid	Initial: 10-30 mg (Reassess in 3–4 hours, add ≤10 mg PRN) Daily: 60-120 mg <sup>a</sup>
Naltrexone XR injection ( <i>Vivitrol</i> ®)	IV/IM: 380 mg in 4 cc	Every 4 weeks
Naltrexone tablets (generic)	PO: 50 mg	Daily: 50 mg (May give 2–3 daily doses at once on M–W–F.)

<sup>a</sup>The dose should be individualized and may be higher or lower than this usual dosage.




**Slide 32.**



At this point you are moving into the special populations portion of the slide deck.




## Slides 33 and 34. Pregnant Women



### Pregnant Women

- ◆ Identify & refer urgent medical conditions
- ◆ Medical & psychosocial examination
- ◆ OB/Gynecologists be alert to signs of OUD
- ◆ Psychosocial treatment is recommended
- ◆ HIV & hepatitis (B & C) testing & counseling
- ◆ With patient consent, urine testing for opioids and other drugs
- ◆ Treat OUD women w/methadone or buprenorphine rather than abstinence



### Pregnant Women

- ◆ Co-managed w/ OB/GYN & addiction specialist
- ◆ Pregnancy affects pharmacokinetics
- ◆ Methadone treatment initiated ASAP
- ◆ Buprenorphine monotherapy is alternative to methadone
- ◆ Discontinue naltrexone if relapse risk low
- ◆ No naloxone unless overdose
- ◆ Breastfeeding encouraged with methadone and buprenorphine



- Obstetricians and gynecologists should be alert to signs and symptoms of opioid use disorder. Pregnant women with opioid use disorder are more likely to seek prenatal care late in pregnancy, miss appointments, experience poor weight gain, or exhibit signs of withdrawal or intoxication.
- Counseling and testing for HIV should be provided in accordance with state law. Tests for hepatitis B and C and liver function are also suggested. Hepatitis A and B vaccination is recommended for those whose hepatitis serology is negative.
- State laws differ on reporting substance use during pregnancy. Laws that penalize women for use and for obtaining treatment serve to prevent women from obtaining prenatal care and worsen outcomes.
- Hospitalization during initiation of methadone and treatment with buprenorphine may be advisable due to the potential for adverse events, especially in the third trimester.
- In an inpatient setting, methadone should be initiated at a dose range of 20 mg to 30 mg. Incremental doses of 5 mg to 10 mg are given every 3 to 6 hours, as needed, to treat withdrawal symptoms.
- After induction, clinicians should increase the methadone dose in 5 mg to 10 mg increments per week. The goal is to maintain the lowest dose that controls withdrawal symptoms and minimizes the desire to use additional opioids.
- Twice daily dosing is more effective and has fewer side effects than single dosing but may not be practical because methadone is typically dispensed in an outpatient clinic.
- Pharmacokinetics of methadone are affected by pregnancy. With advancing gestational age, plasma levels of methadone progressively decrease and clearance increases. Increased or split doses may be needed as pregnancy progresses. After childbirth, doses may need to be adjusted.
- Buprenorphine monopreparation is reasonable and recommended alternative to methadone. While there is evidence of safety, there is insufficient evidence to recommend the combination buprenorphine/naloxone formulation.
- If a woman becomes pregnant while she is receiving naltrexone, it is appropriate to discontinue the medication if the patient and doctor agree that the risk of relapse is low. If the patient is highly concerned about relapse and wishes to continue naltrexone, she should be informed about the risks of staying on naltrexone and provide her consent for ongoing treatment. If the patient wishes to discontinue naltrexone but then reports relapse to opioid use, it may be appropriate to consider treatment with methadone or treatment with buprenorphine.

## Slides 36 and 37. Individuals with Pain

 <h3>Individuals with Pain</h3> <ul style="list-style-type: none"><li>◆ Correct diagnosis &amp; target suitable for treatment identified</li><li>◆ Try non-narcotic medications first</li><li>◆ Consider methadone or buprenorphine for patients with active OUD not in treatment</li><li>◆ Pharmacotherapy with psychosocial counseling</li><li>◆ OUD methadone patients will require opioids in addition to regular methadone dose</li><li>◆ Methadone w/short-acting opioid for surgery</li><li>◆ Increase buprenorphine for mild acute pain</li></ul> 	 <h3>Individuals with Pain</h3> <ul style="list-style-type: none"><li>◆ Discontinue buprenorphine, start high potency opioid for severe acute pain</li><li>◆ Consult w/surgeon &amp; anesthesiologist before discontinuing buprenorphine for surgery</li><li>◆ Treat naltrexone patients with mild pain NSAIDs and with ketorolac for severe pain</li><li>◆ Discontinue naltrexone 72 hours prior to surgery; ER naltrexone 30 days prior</li></ul> 
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- If pharmacological treatment is considered for individuals with pain, non-narcotic medications such as acetaminophen and NSAIDs should be tried first.
- For severe acute pain, discontinuing buprenorphine and commencing on a high potency opioid (such as fentanyl) is advisable. Patients should be monitored closely and additional interventions such as regional anesthesia should also be considered.
- The decision to discontinue buprenorphine prior to an elective surgery should be made in consultation with the attending surgeon and anesthesiologist. If it is decided that buprenorphine should be discontinued prior to surgery, this should occur 24 to 36 hours in advance of surgery and restarted post-operatively when the need for full opioid agonist analgesia has passed.

## Slide 38. Adolescents



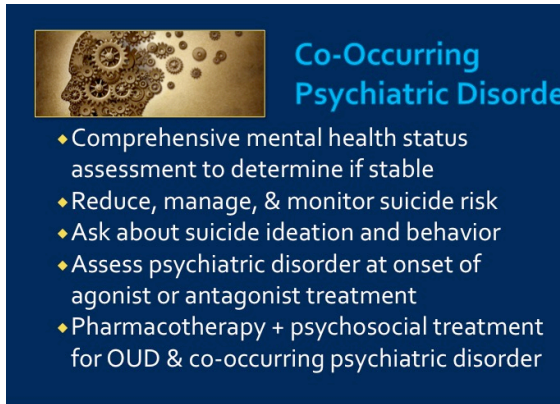
# Adolescents

- ◆ Consider all treatment options
- ◆ Opioid agonists, antagonists use appropriate
- ◆ Psychosocial treatment recommended
- ◆ Concurrent practices to reduce infection from STDs and blood-borne viruses
- ◆ Benefit from treatment in specialized facilities with multidimensional services



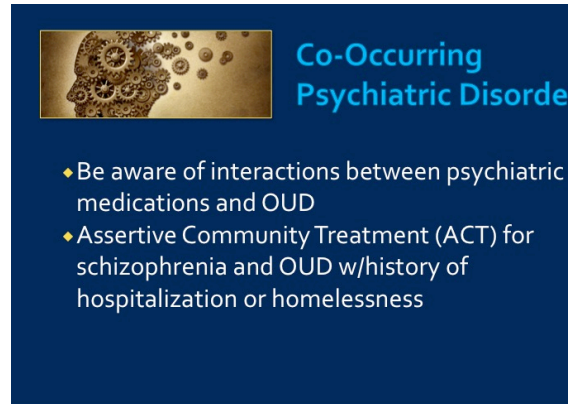
- Clinicians should consider treating adolescents who have opioid use disorder using the full range of treatment options, including pharmacotherapy.
- Opioid agonists (methadone and buprenorphine) and antagonists (naltrexone) may be considered for treatment of opioid use disorder in adolescents. Age is a consideration in treatment, and federal laws and FDA approvals need to be considered for patients under age 18.
- Buprenorphine is FDA-approved for patients 16 and older
- There are no controlled trials evaluating methadone for the treatment of OUD in adolescents under the age of 18. However, the federal code on opioid treatment, offers an exception for patients aged 16 and 17 who have a documented history of at least two prior unsuccessful withdrawal management attempts, and have parental consent.
- Naltrexone may be considered for young adults aged 18 and older with OUD.
- Confidentiality is of particular importance in treatment adolescents. Adolescents have reported that they are less likely to seek treatment if services are not confidential. There are many clinical and legal responsibilities when young person requests confidentiality. More than half the states in the US, by law, permit adolescents less than 18 to consent to addiction treatment without parental consent.

## Slides 39 and 40. Co-Occurring Psychiatric Disorders



Slide 39 features a blue background with a golden gear-like brain graphic on the left. The title "Co-Occurring Psychiatric Disorders" is in light blue. The content is a bulleted list of five items.

- ◆ Comprehensive mental health status assessment to determine if stable
- ◆ Reduce, manage, & monitor suicide risk
- ◆ Ask about suicide ideation and behavior
- ◆ Assess psychiatric disorder at onset of agonist or antagonist treatment
- ◆ Pharmacotherapy + psychosocial treatment for OUD & co-occurring psychiatric disorder



Slide 40 features a blue background with a golden gear-like brain graphic on the left. The title "Co-Occurring Psychiatric Disorders" is in light blue. The content is a bulleted list of two items.

- ◆ Be aware of interactions between psychiatric medications and OUD
- ◆ Assertive Community Treatment (ACT) for schizophrenia and OUD w/history of hospitalization or homelessness



- A comprehensive assessment including determination of mental health status should evaluate whether the patient is stable. Patients with suicidal or homicidal ideation should be referred immediately for treatment and possibly hospitalization.
- Management of patients at risk for suicide should include: a) reducing immediate risk; b) managing underlying factors associated with suicidal intent; and c) monitoring and follow-up.
- Assessment for psychiatric disorder should occur at the onset of agonist or antagonist treatment. Reassessment using a detailed mental status examination should occur after stabilization with methadone, buprenorphine or naltrexone.

## Slide. 41. In the Criminal Justice System



### In Criminal Justice System

- ◆ Pharmacotherapy effective regardless of length of sentenced term
- ◆ Should get some type of pharmacotherapy and psychosocial treatment
- ◆ Opioid agonists and antagonists may be considered for treatment
- ◆ Pharmacotherapy initiated minimum 30 days prior to release



- There is insufficient evidence to recommend any one treatment (agonist or antagonist) as superior to another for prisoners or parolees.

## Slide 42. Naloxone for Opioid Overdose

# Naloxone for Opioid Overdose



- ◆ Naloxone should be given for opioid overdose
- ◆ Naloxone to save life of pregnant mother
- ◆ OUD patients & family given prescriptions and trained on use of naloxone
- ◆ Police, medical 1st responders & firefighters trained & authorized to administer naloxone



- There are few studies comparing the superiority of naloxone by route of administration including: intranasal, intramuscular or intravenous.
- The currently available intranasal naloxone formulation is not dispensed in a preloaded syringe and this may affect its usefulness.
- The development of a more convenient administrative device for intranasal naloxone could improve the effectiveness of this form of naloxone.

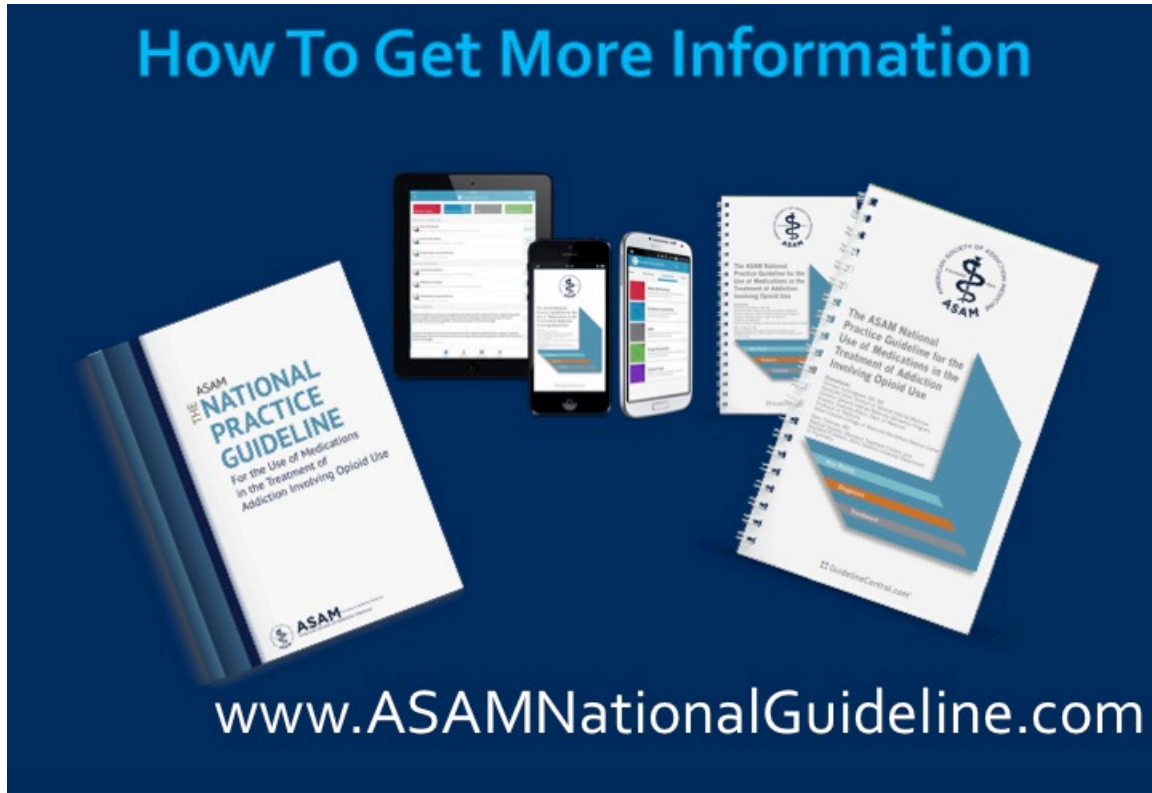
Slide 43. Opioid Overdose Medications

## Opioid Overdose Medications

Agent	Dose	Dosing
Naloxone injection		
<i>Evzio</i> ® (auto-injector)	0.4mg/0.4mL	For emergency treatment of overdoses
<i>Narcan</i> ® (generic) <sup>a</sup>	(various)	Opioid depression, diagnosis of suspected opioid overdose ↓BP in septic shock

<sup>a</sup>There is not yet an FDA-approved intranasal formulation. There are only kits made available to deliver the injectable formulation intranasally.

## Slide 44. How To Get More Information

A promotional graphic for the ASAM National Practice Guideline. It features a dark blue background with the title "How To Get More Information" in large, light blue, sans-serif font at the top. Below the title, there are images of the guideline materials: a hardcover book on the left, a tablet and two smartphones in the center showing the guideline's website interface, and a spiral-bound pocket guide on the right. The book and pocket guide covers both feature the ASAM logo and the title "The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use". At the bottom of the graphic, the website address "www.ASAMNationalGuideline.com" is written in white, sans-serif font. The ASAM logo, a caduceus inside a circle with "ASAM" below it, is also present in the bottom right corner of the graphic area.

The National Practice Guideline website: [www.ASAMNationalGuideline.com](http://www.ASAMNationalGuideline.com)

The ASAM website: [www.asam.org](http://www.asam.org)

The website includes links to the Pocket Guide, phone application, *Journal of Addiction Medicine* (JAM) article and supplement, and information about future educational webinars on the Guideline.