CARE OF THE ADDICTED PATIENT

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DISCLOSURE

• No financial relationships or conflicts of interest to disclose.

DRUGS

BECAUSE, WHY ELSE WOULD YOU VACUUM THE GRASS.
GOALS

• Review Traditional Toxidromes and associated drugs of abuse
• Review Emerging Drugs of Abuse
• Discuss the Current Opiate Epidemic
• Discuss care for the recovering/addicted patient.
SYMPATHOMIMETIC
SYMPATHOMIMETIC

- Cocaine, Amphetamines, LSD, Ectasy (MDMA)
SYMPATHETIC RESPONSE

- **Eyes** (Alpha 1): Pupil Dilation/Mydriasis
- **Heart** (Beta 1): Increased HR, Contraction, irritability
  - Often sinus tachycardia but at risk for arrythmias.
- **Lungs** (Beta2): Dilation of bronchial tree
- **Skin** (Alpha 1): Sweating, goose bumps
- **Muscles** (Beta2): Vasodilation-increased blood flow.
  - **Tachycardia, Hypertension, Hyperthermia**
SYMPATHETIC RESPONSE

• Physical Exam
  • Tremor, warm skin, diaphoresis, hypoactive bowel sounds.
  • Sympathetic stimulation $\rightarrow$ Epinephrine (adrenalin) release form the adrenal glands
  • “Fight or flight”
SYMPATHOMIMETIC-HYPERTHERMIA

- Hyperthermia
  - Increased motor tone generates heat
  - Can be exacerbated by dehydration and vasoconstriction
  - Temp >106 F documented → DIC and multisystem organ failure
- Treatment
  - Aggressive use of fluid and benzodiazepines.
  - Neuromuscular paralysis and intubation as needed.
  - Continuous monitoring of core temperature-rectal probe.
  - Wet sheets with large fans, pack groin and axilla with ice packs
  - Goal of 102 or less within 20 minutes
SYMPATHOMIMETIC-HYPERTENSION

• Hypertensive Emergencies
  • Aortic Dissection, Pulmonary Edema, Myocardial Ischemia/Infarction, Intracranial Hemorrhage, Intestinal Infarctions/mesenteric ischemia.
  • Pregnancy: Placental insufficiency and infarction of gravid uterus.

• Treatment
  • Benzodiazepines: Restore CNS inhibitory tone to peripheral nervous system.
  • IV nitroglycerin, nitroprusside.
  • Beta blockers may worsen hypertension
SYMPATHOMIMETIC-DYSRHYTHMIAS

- Cardiac Dysrhythmias
  - Sinus Tachycardia is most common.
  - Atrial fibrillation and other supraventricular tachycardias.
    - Result of catecholamine surge
  - Torsades DePointes or other wide complex tachycardias
    - Blockade of fast Na sodium channels in myocardium (cocaine only)
  - Ventricular dysrhythmias from hyperkalemia/rhabdomyolysis
- Treatment: Supraventricular- benzos, Ventricular-bicarb drip, amiodarone, lidocaine
SYMPATHOMIMETIC-COMPLICATIONS

- Oropharyngeal burns
  - High temp required to volatilize drug.
- Inhalational Barotrauma
  - Pneumothorax, pneumopericardium, pneumomediastinum.
- High risk of infection with IV use.
  - Bacteremia, abscess formation around injection site. Blood borne pathogens.
- “Crack Dancing”
  - Choreoathetoid movement disorder-abnormal dopaminergic tone
SYMPATHOMIMETIC-COMPLICATIONS

• "Cocaine Washout"
  • Profoundly sleepy but arousable and oriented.
• Dehydration and poor nutrition.
• MDMA- Life Threatening hyponatremia.
  • May worsen with fluids due to inability to retain sodium and increased free water.
SEDATIVE/HYPNOTIC

- Benzodiazepines, Barbiturates, GHB, Chloral hydrate, Ambien, Buspirone
- Mental Status: Sedation/confusion
- Pupils: Blurred vision, Miosis or mydriasis, may see nystagmus
- VS: Hypotension, hypothermia, bradypnea.
BARBITURATES
BARBITURATES

- Depress excitability of all excitable cells, particularly CNS via GABA.
  - Decrease neural transmission at autonomic ganglia, myocardium, GI tract and inhibit acetylcholine at neuromuscular junction.
- Dose related depressive effects
- Act directly on medulla to produce respiratory depression.
- Addictive, produce physical dependence and life threatening withdrawal.
- Pregnancy: Cross placenta with fetal levels approaching those of the mother.
  - Category D - associated with birth defects.
BARBITURATES-CLINICAL FEATURES

• Mild toxicity- mimics ethanol intoxication.
  • Drowsiness, slurred speech, ataxia, unsteady gait, nystagmus, impaired cognition
• Severe Toxicity
  • CNS depression from stupor to coma. Can see fluctuating level of consciousness
  • Diminished corneal and gag reflexes.
  • Flaccid muscle tone and diminished DTR’s.
  • Respiratory depression and arrest.
    • Breaths may be rapid but shallow, degree of hypoventilation may not be clinically apparent.
  • Hypotension, Noncardiogenic pulmonary edema.
• Supportive care
  • Intubation is often required.
  • Careful fluid replacement to maintain SBP > 90 and adequate urine output.
  • Monitor for fluid overload and pulmonary edema.
  • May need vasopressors to support BP.
BENZODIAZEPINES-CLINICAL FEATURES

- Enhance inhibitory actions of GABA.
- CNS depression ranging from mild drowsiness to coma.
- Respiratory depression can be seen in large overdoses.
- Ataxia is most common sign of toxicity.
- Profound coma or cardiopulmonary instability is rare and should prompt search for coingestants.
BENZODIAZEPINES-MANAGEMENT

- Manage expectantly with supportive care.
- Flumazenil
  - Precipitate acute withdrawal and seizures in chronic benzo user.
    - Cardiac dysrhythmias have been reported.
    - Seizure may be refractory and difficult to control.
OPIATES

- Fentanyl, Heroin, methadone, morphine, opium, hydrocodone, oxycodone, propoxyphene.
OPIATES

- Opioid B-endorphin stimulates µ-receptor, producing sensation of well being and general anesthesia.
  - Repetitive use makes B-endorphin system functionally deficient.
    - Decreased response to medication and withdrawal upon cessation.
• CNS depression.
  • Dysphoria and acute psychosis may occur with agonist/antagonist combination
• Respiratory
  • Decrease RR and tidal volume in dose dependent manner
  • Suppresses sensitivity to medullary respiratory center to hypercapnia.
• Eyes
  • Miosis- Stimulation of mu-receptor at CN III
OPIATES - CLINICAL FEATURES

- Gastrointestinal - Nausea and vomiting.
  - Delayed gastric emptying, Direct stimulation of chemoreceptor trigger zone and vestibular stimulation.
    - Antihistamines and anti-emetics generally effective treatment.
- GU
  - May cause urinary retention from urethral sphincter spasm and decreased detrusor tone.
  - Glomerulosclerosis and amyloidosis with long term abuse.
OPIATES-CLINICAL FEATURES

• Dermatologic
  • Pruritus, flushing and urticaria from histamine release-Not a true allergy. Eg morphine
    • Often localized to injection site and resolves with antihistamine.
    • Fentanyl- negligible amounts of histamine and good hemodynamic stability profile.

• Metabolic
  • Hypoglycemia and hypothermia have been reported
    • Mechanism unclear.
OPIATES-MANAGEMENT

- Attention to airway, ventilation and oxygenation.
- Usually can be managed with Narcan
  - Pure opiate antagonist.
  - 0.4 mg to 2 mg initial dose
    - May require up to 10 mg for some synthetic opiates.
  - Duration of action 1-2 hours, shorter than many opiates
    - Repeat dosing or infusion at 2/3 the effective initial dose per hour.
ANTICHOLINERGIC

- Cogentin, Dramamine, Benadryl, Atarax, Jimsonweed
ANTICHOLINERGIC-CLINICAL FEATURES

- Inhibit muscarinic Ach receptors both centrally and peripherally at end organ sites of parasympathetic nervous system.
- “Hot as a Hare” – Hyperthermia
- “Blind as a Bat” – Dilated pupils (mydriasis)
- “Dry as a Bone”–Dry skin
- “Red as a Beet” – Vasodilation causing flushed skin
- “Mad as a Hatter” – Agitation / Hallucinations
ANTICHOLINERGIC-CLINICAL FEATURES

• CNS
  • Agitated, confused, violent or incoherent. Visual hallucinations are common.
  • May see myoclonus or choreoathetoid movements.
  • Children more sensitive to CNS stimulant effects, more likely to have seizures
  • Massive ingestions associated with coma.

• Hyperthermia
  • Hepatic necrosis, rhabdomyolysis, myoglobinuric renal failure, cerebral edema, DIC
ANTICHOLINERGIC-MANAGEMENT

• Titrate sedation with benzodiazepine.
  • Prevent self injury, severe hyperthermia, myoglobinuric renal failure from muscle injury.
  • More thorough physical examination and diagnostic procedures.

• Hyperthermia
  • Measure core temp, Evaporative cooling with mist and fans, ice packs.
    • Antipyretics and simple cooling blankets ineffective.
ANTICHLINERGIC-MANAGEMENT

- Seizures
  - IV benzodiazepines.
    - Phenytoin is not useful in most toxin induced seizures.
- Physostigmine
  - Acetylcholinesterase inhibitor.
  - Reverses delirium in 87% and agitation in 90% of patients.
    - Compared to 24% reversal in agitation and no effect on delirium with benzodiazepines
ANTICHOLINERGIC-MANAGEMENT

- Physostigmine
  - In absence of anticholinergic blockade, can result in significant toxicity itself with cholinergic excess.
  - Seizures, muscle weakness, bradycardia, bronchoconstriction, bronchorhea, salivation, lacrimation, vomiting, diarrhea.
DISSOCIATIVES

• Ketamine, PCP,
  • Dextromethrophan
DISSOCIATIVES

- PCP
  - Agonist/antagonist actions at numerous sites
  - Intoxication usually 8-16 hours.
    - Longer in chronic users.
- Ketamine
  - Similar in structure
  - One tenth as potent as PCP and shorter duration and action.
- Dextromethorphan
  - Classified as opiate but blocks NMDA receptor at PCP binding site and blocks uptake of serotonin.
DISSOCIATIVES-CLINICAL FEATURES

- Wide spectrum of features
  - Behavior may be bizarre, lethargic, agitated, confused or violent.
  - Blank or catatonic stare is common.
  - Nystagmus may be present.
  - Moderate hypertension/tachycardia.
  - Hyperthermia
  - Violent Behavior and associated traumatic injuries.
DISSOCIATIVES-MANAGEMENT

• Haldol
  • Antagonizes CNS receptor site that is responsible for much of the violent behavior.
• Benzodiazepines for sympathomimetic features and seizures
• Aggressive treatment of hyperthermia.
• Aggressive fluids and monitor CK if suspect rhabdomyolysis.
• Dextromethorphan
  • Many preparations contain acetaminophen.
EMERGING DRUGS OF ABUSE
SYNTHETIC CANNABINOIDs

- K2, Spice
  - Other names: Bombay Blue, Blaze, Happy Tiger Incense, Bliss, Chaos Mint, Genie, Eclipse, Moon rocks
SYNTHETIC CANNABINOIDs

- Seven Main Categories based on Chemical Structure.
- Smoked, Oral or snorted.
  - Onset in minutes and duration typically 1 hour
- Acts on CB1 receptor in the CNS-psychoactive effects.
- Packaging notoriously contains little information regarding chemical composition and no standard exists.
  - Typically a mixture of dried vegetable material with SC substance sprayed onto the herbal mixture.
SYNTHETIC CANNABINOID CLINICAL FEATURES

- Wide variety of clinical effects reported.
  - CB1 agonism 2-800X more potent than typical THC
  - Euphoria, increased appetite, nystagmus, anxiety, paranoia, agitation, delusions, dizziness, confusion, hallucinations.
  - Toxicity: Hypertension, hyperthermia, cardiac ischemia, MI, seizures, dystonias, rhabdomyolysis, acute kidney injury.
- Lacks Cannabidiol
  - Anxiolytic/antipsychotic properties
SYNTHETIC CATHINONES-“BATH SALTS”
SYNTHETIC CATHINONES
SYNTHETIC CATHINONES

- Group of compounds with amphetamine like effects
  - Cathinone-naturally found in leaves of khat plant. Provides amphetamine like euphoria.
- Synthetic cathinones- various chemical alterations effecting pharmacokinetics and pharmacodynamics.
  - Route: Oral (powder, capsule, tablet), Gingival, nasal, IV, IM
  - Onset 15-30 minutes
  - Duration 2-48 hours.
SYNTHETIC CATHINONES

- Amphetamine like sympathomimetic effect.
  - Agitation, tachycardia, hallucination, hypertension, confusion, mydriasis, tremor, fever.
  - Rhabdomyolysis, hypertension, renal failure, seizures, arrhythmias.
2C AGENTS

• Basic Phenethylamine chemical structure.
  • Shared among catecholamines, amphetamines, synthetic cathinones and many other drugs.
  • Ecstasy, Molly.
  • Common among raves and music festivals.
  • Can be purchased on the internet listed as research chemicals.
2C AGENTS

• Stimulatory and hallucinogenic effects.
  • Nausea, vomiting, dizziness, diarrhea, headaches, muscle aches, confusion
2C AGENTS

• TWO DEAD, 57 HOSPITALIZED AFTER TAMPA’S SUNSET MUSIC FESTIVAL.
  • One of the victims’ mothers, Ms. Bermudez (Katie’s mother), was called to the hospital at 3 a.m. and claims that to her knowledge her daughter is not a heavy drug user. Katie suffered an extremely high fever and brain swelling before she passed away the following day at St. Joseph’s hospital.
2C AGENTS

- 24 people hospitalized for drug overdose at music festival.
  - Ohio, August 2014
OPIATE EPIDEMIC

Drug Overdose & Motor Vehicle Accident Deaths

Data: CDC
Drug Overdose Deaths in 2014

- Opioids: 18,893
- Heroin: 10,574
- Benzodiazepines: 7,945
- Cocaine: 5,415

Data: CDC
OPIATE EPIDEMIC

Heroin & Opioid Overdose Deaths

Data: CDC
Rate of Deaths from Heroin Overdoses, by Race

**WHITE**
- Increase from 2010–2014: 267%

**BLACK**
- Increase from 2010–2014: 213%

**HISPANIC or LATINO**
- Increase from 2010–2014: 137%

**NATIVE AMERICAN**
- Increase from 2010–2014: 236%

**ASIAN**
- Figures are too small to reliably calculate percentage increase.

Source: Centers for Disease Control
## Opiate Epidemic

### Overdose Deaths by Age in 2014 per 100,000 people

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Heroin</th>
<th>Opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24 years</td>
<td>3.3</td>
<td>3.1</td>
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<tr>
<td>25-34 years</td>
<td>8</td>
<td>9</td>
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<td>35-44 years</td>
<td>5.9</td>
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<td>45-54 years</td>
<td>4.7</td>
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<td>55-64 years</td>
<td>2.7</td>
<td>8.5</td>
</tr>
<tr>
<td>65-74 years</td>
<td>0.5</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Data: CDC
Twelve States have more opioid prescriptions than people.
- Alabama: 142.9 per 100 people
- Hawaii: 52 per 100 people.
- Nebraska: 79.4 per 100 adults
- South Dakota: 66.5 per 100 adults
- Iowa: 72.8 per 100 adults
OPIATE EPIDEMIC
OPIATE EPIDEMIC
OPIATE EPIDEMIC
Alberta Canada

- Manufactured to look like 80 mg OxyContin tablets.
- Forensics: research chemical called W-18.
  - Mu-receptor agonist.
  - 100X fentanyl, 10,000X morphine
OPIATE EPIDEMIC

• “Amped-up heroin blamed in 75+ overdoses in 2 states.”
  • Indiana and Ohio, August 2016
  • Heroin mixed with carfentanil.
    • Elephant tranquilizer, 10,000X morphine
    • Accidental exposure, required 100 mg narcan.
OPIATE EPIDEMIC

• Doctor convicted of murder for patients' drug overdoses gets 30 years to life in prison.

• Dr. Hsiu-Ying "Lisa" Tseng guilty of second-degree murder, the first time a doctor had been convicted of murder in the United States for overprescribing drugs, the district attorney’s office said.
• ACA
  • Pain control is part of survey in certain settings as a quality measure.
    • Goal to tie Medicare and Medicaid payments to the results of these surveys.
• Emergency Department Patient Experience of Care Survey
  • Under HCAHPs
  • Similar quality measures regarding pain control.
• Overprescribe to achieve patient satisfaction?
OPIATE EPIDEMIC

- Comprehensive Addiction and Recovery Act of 2016
  - Programs designed to curb abuse of all opiates.
    - 4 out of 5 new heroin users started out abusing prescription painkillers, often prescribed for acute pain or injury.
  - Task Fore
    - Review and provide recommendations on developing best practices in pain management.
    - Establish Grant programs to provide for purchase and distribution of naloxone as well as training first responders and other key community sectors.
OPIATE EPIDEMIC

• CARA
  
  • Create public awareness about links between prescription pain killers and heroin addiction.
  
  • Funds to carry out opiate abuse response effort.
    
    • Education, treatment and recovery.
    
    • Maintaining prescription drug monitoring programs.
OPIATE EPIDEMIC

- Nebraska
  - Current PDMP is facilitated through the states Health Information Initiative.
    - Participation by patients, physicians and other health care providers is voluntary.
    - Prescribers and Pharmacies must be paying members to check information
  - LB 471
    - All Pharmacies report to system when Rx is filled.
      - Applies to Rx filled outside NE with addresses in NE.
      - Eliminate patient opt-out.
      - Pharmacists and prescribers may check system prior to prescribing, though not required.
“State leaders hold opioid summit to prevent epidemic's spread to Nebraska.” OWH October 15, 2016

- 300 professionals from different fields.
- Nebraska Attorney General's office, NE DHHS, US Attorneys office, UNMC.

“This is a starting point for all of us to come together in a spirit of cooperation and collaboration and put together an effective plan that looks at prevention, law enforcement and treatment to stop this from becoming an epidemic in Nebraska,”
A new scientific review suggests that federal and state policies aimed at curbing inappropriate prescribing of opioids have not directly led to the recent increases in heroin use across the nation.

Researchers conducting an analysis of the relationship between prescription opioid and heroin abuse found that the transition to heroin use occurred before many policies, including public education efforts, prescription drug monitoring programs, increased enforcement and regulatory actions, and abuse-deterrent formulations, were enacted.
Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (i.e., based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (i.e., based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).

Level C recommendations. Other strategies for patient management that are based on Class III studies, or in the absence of any adequate published literature, based on panel consensus.
• 1. In the adult ED patient with noncancer pain for whom opioid prescriptions are considered, what is the utility of state prescription drug monitoring programs in identifying patients who are at high risk for opioid abuse?

• Level A recommendations. None specified.
Level B recommendations. None specified.
Level C recommendations. The use of a state prescription monitoring program may help identify patients who are at high risk for prescription opioid diversion or doctor shopping.
2. In the adult ED patient with acute low back pain, are prescriptions for opioids more effective during the acute phase than other medications?

Recommendations

Level A recommendations. None specified.
Level B recommendations. None specified.
Level C recommendations.

- (1) For the patient being discharged from the ED with acute low back pain, the emergency physician should ascertain whether nonopioid analgesics and nonpharmacologic therapies will be adequate for initial pain management.

- (2) Given a lack of demonstrated evidence of superior efficacy of either opioid or nonopioid analgesics and the individual and community risks associated with opioid use, misuse, and abuse, opioids should be reserved for more severe pain or pain refractory to other analgesics rather than routinely prescribed.

- (3) If opioids are indicated, the prescription should be for the lowest practical dose for a limited duration (eg, 1 week), and the prescriber should consider the patient's risk for opioid misuse, abuse, or diversion.
3. In the adult ED patient for whom opioid prescription is considered appropriate for treatment of new-onset acute pain, are short-acting schedule II opioids more effective than short-acting schedule III opioids?

- **Level A recommendations.** None specified.

- **Level B recommendations.** For the short-term relief of acute musculoskeletal pain, emergency physicians may prescribe short-acting opioids such as oxycodone or hydrocodone products while considering the benefits and risks for the individual patient.

- **Level C recommendations.** Research evidence to support superior pain relief for short-acting schedule II over schedule III opioids is inadequate.
• 4. In the adult ED patient with an acute exacerbation of noncancer chronic pain, do the benefits of prescribing opioids on discharge from the ED outweigh the potential harms?

• **Level A recommendations.** None specified.

  **Level B recommendations.** None specified.

  **Level C recommendations.**

  • (1) Physicians should avoid the routine prescribing of outpatient opioids for a patient with an acute exacerbation of chronic noncancer pain seen in the ED.

  • (2) If opioids are prescribed on discharge, the prescription should be for the lowest practical dose for a limited duration (eg, 1 week), and the prescriber should consider the patient’s risk for opioid misuse, abuse, or diversion.

  • (3) The clinician should, if practicable, honor existing patient-physician pain contracts/treatment agreements and
OPIATE EPIDEMIC
CDC PRESCRIPTION GUIDELINES

• 1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

• 2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
• 3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

• 4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

• 5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.
• 8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

• 9. Clinicians should review the patient’s history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.
QUESTIONS?