FACULTY INFORMATION

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DISCLOSURE:
Dr. Carron has nothing to disclose.

ACKNOWLEDGMENTS

Presented by AOA, a member of the Collaborative for Risk Evaluation and Mitigation Strategy (REMS) Education (CO*RE), nine interdisciplinary organizations working together to improve pain management and prevent adverse outcomes.

This activity is supported by an independent educational grant from the Opioid Analgesic REMS Program Companies (RPC). Please see this document for a list of REMS Program Companies. This activity is intended to be fully compliant with the Opioid Analgesic REMS education requirements issued by the U.S. Food and Drug Administration.
CO*RE COLLABORATION

BY THE END OF THIS SESSION YOU WILL BE ABLE TO

• Describe the pathophysiology of pain as it relates to the concepts of pain management.
• Accurately assess patients in pain.
• Develop a safe and effective pain treatment plan.
• Identify evidence-based non-opioid options for the treatment of pain.
• Identify the risks and benefits of opioid therapy.
• Manage ongoing opioid therapy.
• Recognize behaviors that may be associated with opioid use disorder.
WHY ARE WE HERE?

CO*RE STATEMENT

Misuse, abuse, diversion, addiction, and overdose of opioids in the United States have created a serious public health epidemic.

When prescribed well, and used as prescribed, opioids can be valuable tools for effective pain management.

There is potential for unintended consequences of inadequately managed pain from far-reaching prescribing restrictions.

This course is in alignment with the FDA Opioid Analgesics REMS Education Blueprint.

This course does not advocate for or against the use of opioids. We intend to help healthcare providers manage pain without putting vulnerable patients at risk for misuse or opioid use disorder. The goal is to keep our patients, our communities, and ourselves SAFE.

PRESCRIBING PATTERNS AND OPIOID-RELATED DEATHS
DEA SCHEDULED DRUGS

<table>
<thead>
<tr>
<th>SCHEDULE</th>
<th>DESCRIPTION</th>
<th>EXAMPLES</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>High potential for abuse; no currently accepted medical use</td>
<td>Heroin, LSD, cannabis, ecstasy, peyote</td>
</tr>
<tr>
<td>II</td>
<td>High potential for abuse, which may lead to severe psychological or physical dependence</td>
<td>Hydrocodone, methadone, meperidine, oxycodeine, fentanyl, morphine, oxymorphone, comitine, hydrocodone conbination products</td>
</tr>
<tr>
<td>III</td>
<td>Potential for abuse, which may lead to moderate or low physical dependence or high psychological dependence</td>
<td>Products containing ≤ 60 mg codeine per dose, buprenorphine, benzphetamine, phendimetrazine, ketamine, anabolic steroids</td>
</tr>
<tr>
<td>IV</td>
<td>&quot;Low potential&quot; for abuse</td>
<td>Alprazolam, benzodiazepines, carisoprodol, clonazepam, clorazepate, diazepam, fentanyl, haloperidol, lorazepam, temazepam, tramadol</td>
</tr>
<tr>
<td>V</td>
<td>Low potential for abuse</td>
<td>Cough preparations containing ≤ 200 mg codeine/100 ml</td>
</tr>
</tbody>
</table>

Complete list of products covered under the Opioid Analgesic REMS available at: https://opioidanalgesicrems.com/RpcUI/products.u

FENTANYL AND FENTANYL ANALOGUES

OO deaths from fentanyl and fentanyl analogues, such as carfentanil, have increased 540% in three years.

Street fentanyl is illegally manufactured. It is generally NOT a diverted pharmaceutical product.

Two causes of fentanyl OD death: opioid-induced respiratory depression and rigid chest wall syndrome; higher or repeated doses of naloxone are required to reverse a fentanyl overdose.

Fentanyl is also found in heroin, cocaine, and methamphetamine.

RISKS VERSUS BENEFITS

RISKS
- Misuse, diversion, and addiction
- Abuse by patient or household contacts
- Interactions with other meds and substances
- Risk of maternal abstinence syndrome
- Inadvertent exposure/ingestion by household contacts, especially children
- Life-threatening respiratory depression
- Overdose, especially as ER/LA formulations contain more MME than IR

BENEFITS
- Analgesia
- Reliable pain control
- Quick analgesia (particularly with IRs)
- Continuous, predictable (with ER/LAs)
- Improved function
- Improved quality of life

THE NEUROMECHANISMS OF PAIN

Peripheral Pain Modulators:
- Enkephalin
- Norepinephrine
- Prostaglandins
- Cytokines
- Bradykinin
- Substance P
- Others

Descending Neurotransmitters:
- Serotonin
- Norepinephrine
- Endogenous opioids
- Others

MEDIATORS OF PERIPHERAL NOCICEPTION

Feeling physical pain is vital for survival: pain is the body’s early warning system.
Types of Pain

- **Nociceptive / Inflammatory**
  - Pain in response to an injury or stimuli; typically acute

- **Nociplastic**
  - Pain that arises from altered nociceptive function; typically chronic

- **Neuropathic**
  - Pain that develops when the nervous system is damaged; typically chronic

- **Mixed Types (Nociceptive / Neuropathic)**
  - Primary injury and secondary effects

Possible development of chronic pain after an acute injury.

Biopsychosocial Spiritual Context of Pain

- **Biological**
  - Nutritional status
  - Inflammation
  - Pain
  - Sleep/fatigue

- **Social**
  - Family
  - Intimacy
  - Relationships

- **Psychological**
  - Depression
  - Anxiety
  - Grief

- **Spiritual**
  - Religious faith
  - Spiritual distress

*ACEs = Adverse Childhood Experiences

Experience of Pain
PAIN CATASTROPHIZING

- "Tell me about your pain..."
  - Listen for rumination, feelings of hopelessness, or anticipation of negative outcomes.
  - These feelings are important to identify because they can prolong and intensify pain; or lead to higher levels of suffering and altered perception of pain.
  - If identified, shift to "tell me about your life."

CHAPTER 2
TERMINOLOGY

WORDS MATTER: LANGUAGE CHOICE CAN REDUCE STIGMA

"If you want to care for something, you call it a flower; if you want to kill something, you call it a weed."
—Don Coyhis

<table>
<thead>
<tr>
<th>Commonly Used Term</th>
<th>Preferred Term</th>
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<tbody>
<tr>
<td>Addiction</td>
<td>Substance use disorder (SUD) [from the DSM-5]</td>
</tr>
<tr>
<td>Drug-seeking, aberrant/problematic behavior</td>
<td>Using medication not as prescribed</td>
</tr>
<tr>
<td>Addict</td>
<td>Person with substance use disorder (SUD)</td>
</tr>
<tr>
<td>Clean/dirty urine</td>
<td>Positive/negative urine drug screen</td>
</tr>
</tbody>
</table>
WORDS MATTER: DEFINITIONS

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Misuse</td>
<td>Use of a medication in a way other than the way it is prescribed</td>
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<tr>
<td>Abuse</td>
<td>Use of a substance with the intent of getting high</td>
</tr>
<tr>
<td>Tolerance</td>
<td>Increased dosage needed to produce a specific effect</td>
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<tr>
<td>Dependence</td>
<td>State in which an organism only functions normally in the presence of a</td>
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<tr>
<td></td>
<td>substance</td>
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<tr>
<td>Diversion</td>
<td>Transfer of a legally controlled substance, prescribed to one person, to</td>
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<tr>
<td></td>
<td>another person for illicit (forbidden by law) use</td>
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<tr>
<td>Withdrawal</td>
<td>Occurrence of uncomfortable symptoms or physiological changes caused</td>
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<td></td>
<td>by an abrupt discontinuation or dosage decrease of a pharmacologic agent</td>
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<tr>
<td>MME</td>
<td>Morphine milligram equivalent; a standard opioid dose value based on</td>
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<tr>
<td></td>
<td>morphine and its potency; allows for ease of comparison and risk</td>
</tr>
<tr>
<td></td>
<td>evaluations</td>
</tr>
<tr>
<td>Chronic non-</td>
<td>Any painful condition that persists for ≥ 3 months, or past the time of</td>
</tr>
<tr>
<td>cancer pain</td>
<td>normal tissue healing, that is not associated with a cancer diagnosis</td>
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<tr>
<td>(CNCP)</td>
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</tbody>
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World Health Organization, Ensuring Balance in National Policies on Controlled Substances.
https://www.who.int/medicines/areas/quality_safety/GLs_Ens_Balance_NOCP_Col_EN_sanend.pdf

HOW IS PAIN RESOLVED?
PAIN ASSESSMENT

DESCRIPTION OF PAIN

- Location
- Intensity
- Quality
- Onset/duration
- Variations/patterns/rhythms

WHAT RELIEVES THE PAIN?

WHAT CAUSES OR INCREASES THE PAIN?

EFFECTS OF PAIN ON PHYSICAL, EMOTIONAL AND PSYCHOSOCIAL FUNCTION

PATIENT'S CURRENT LEVEL OF PAIN AND FUNCTION

PAST MEDICAL AND TREATMENT HISTORY

NONPHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

RELEVANT ILLNESSES

PAST AND CURRENT OPIOID USE

- Query your state’s Prescription Drug Monitoring Program (PDMP) to confirm patient report
- Contact past providers and obtain prior medical records
- For opioids currently prescribed, note the opioid, dose, regimen, and duration
- Determine whether the patient is opioid-tolerant

GENERAL EFFECTIVENESS OF CURRENT PRESCRIPTIONS

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

PDMPs are state-run, electronic databases that track controlled substance prescriptions in a state.

PDM DATABASES

- Provide a full accounting of the controlled substance prescriptions filled by a patient
- Nearly all are available online 24/7
- Required in most states; know your state laws

BENEFITS

- Identify potential drug misuse/abuse
- Discover existing prescriptions not reported by patient
- Opportunity to discuss with patient
- Determine if patient is using multiple prescribers/pharmacies
- Identify drugs that increase overdose risk when taken together


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- Identify potential drug misuse/abuse
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**Obtain a Complete Social and Psychological History**

**Social History**
- Employment, cultural background, social network, relationship history, legal history, and other behavioral patterns

**Psychological History**
- Screen for:
  - Mental health diagnoses, depression, anxiety, PTSD, current treatments
  - Alcohol, tobacco, and recreational drug use
  - History of adverse childhood experiences
  - Family history of substance use disorder and psychiatric disorders
  - Depression and anxiety can be predictors of chronic pain

**Physical Exam and Assessment**
- Seek objective data
- Conduct physical exam and evaluate for pain
- Order diagnostic tests (appropriate to complaint)

- General: vital signs, appearance, and pain behaviors
- Musculoskeletal exam
  - Inspection
  - Range of motion

- Neurologic exam
- Cutaneous or trophic findings

**Pain Assessment Tool Box**
  - Pain Assessment Tools: BPI or 5 A's
  - Functional Assessment: SF-36, PPS, Geriatric Assessment
  - Pain intensity, Enjoyment of life, General activity
  - PEG
  - Childhood Trauma Questionnaire
  - ACE
  - Assessment in Advanced Dementia
  - Psychological Measurement Tools (PHQ-9, GAD-7, etc.)
CHAPTER 4
CREATING THE PAIN TREATMENT PLAN

COMPONENTS OF A MULTIMODAL TREATMENT PLAN FOR PAIN

- All Self-Working as a Treatment Team
- Cognitive Behavioral Therapy
- Physical & Occupational Therapy
- Pharmaco Therapy

PAIN MANAGEMENT GOALS AND TREATMENT OPTIONS: A MULTIMODAL APPROACH

- Reduce Pain
  - Cognitive Behavioral Therapy
  - Interventional Treatments
- Cultivate Well-Being
  - Physical Treatments
  - Pharmacotherapy
- Self-care
  - Provider care
- Improve Quality of Life
  - Reduce function
EVIDENCE-BASED NONPHARmacologic TREATMENTS

- Tai Chi
- Yoga
- CBT and ACT
- Acupuncture
- PT/OT/aquatic
- Mindfulness meditation
- OMT
- Massage therapy
- Chiropractic
- Neuromodulation or surgical approaches (in some situations)

CBT = cognitive-behavioral therapy; ACT = acceptance commitment therapy; OMT = osteopathic manipulative therapy

What is appropriate for your patient?

PHARMACologic TREATMENTS BY TYPE OF PAIN

NOciceptive / inFLammatory

- Antihistamines
- IR opioids
- Nerve blocks
- NSAIDs
- Topical / transdermal

NOcIPlastic

- Anticholinergics
- Anticonvulsants
- TCA and SNRIs
- Other serotonin agents

NEUropathIC

- Anticonvulsants
- IR and ER/LA opioids
- Nerve blocks
- TCA and SNRIs
- Transdermal opioids

CONTINUE EFFECTIVE NONPHARMACOLOGIC OPTIONS

POTENTIAL SITES OF ACTION FOR ANALGESIC AGENTS

Pain perception requires brain activity, however pain can be blocked in the periphery.

Peripherally Mediated Pain:
- Acetaminophen
- Antihistamines
- NSAIDs
- Opioids
- Topical anesthetics

Centrally Mediated Pain:
- Alpha-2 agonists
- Anticonvulsants
- Ca2+ channel antagonists
- NMDA RAs
- Opioids
- TCA/SNRI antidepressants
### Drug Characteristics to Consider Before Prescribing

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Formulation</th>
<th>Strength</th>
<th>Dosing interval</th>
<th>Key instructions (indications, uses, contraindications)</th>
<th>Specific drug interactions</th>
<th>MOA*</th>
<th>Product-specific safety concerns</th>
<th>Specific information about product conversions, if available</th>
<th>Use in opioid-tolerant patients</th>
<th>Relative potency to morphine</th>
</tr>
</thead>
</table>

*MOA = Mechanism of action

Opioid product information available at [https://opioidanalgesicsrems.com/RpcUI/products.u](https://opioidanalgesicsrems.com/RpcUI/products.u)

### Consider an Opioid Only When:

- Potential benefits are likely to outweigh risks
- Patient has failed to adequately respond to non-opioid and nonpharmacological interventions
- Patient has neuropathic or nociceptive pain that is moderate to severe
- Begin as a therapeutic trial


### Opioid Misuse Risk Assessment Tools


**Tools for Patients Considered for Opioid Therapy**

- ORT-OUD Opioid Risk Tool
- SOAPPT Screener and Opioid Assessment for Patients with Pain
- DIRE Diagnostic, Intractability, Risk, and Efficacy score

**Tools for Substance Use Disorder**

- CAGE-AID: Cut down, Annoyed, Guilty, Eye-Opener tool, Adapted to Include Drugs
- RAPIT Relate, Alone, Friends, Family, Trouble
- DAST Drug Abuse Screening Test
- CTQ Childhood Trauma Questionnaire
- ACES Adverse Childhood Experiences
A CLOSER LOOK AT THE ORT-OUD

Substance use disorder history does not prohibit treatment with opioids, but may require additional monitoring and expert consultation or referral.

Scoring:
- ≤ 2: low risk
- ≥ 3: high risk

OPIOID SIDE EFFECTS AND ADVERSE EVENTS

<table>
<thead>
<tr>
<th>SIDE EFFECTS</th>
<th>ADVERSE EVENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory depression</td>
<td>Death</td>
</tr>
<tr>
<td>Opioid-induced constipation (OIC)</td>
<td>Addiction</td>
</tr>
<tr>
<td>Myoclonus (twitching or jerking)</td>
<td>Overdose</td>
</tr>
<tr>
<td>Sedation, cognitive impairment</td>
<td>Hospitalization</td>
</tr>
<tr>
<td>Sweating, moist, urinary retention</td>
<td>Disability or permanent damage</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td>Falls or fractures</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td></td>
</tr>
<tr>
<td>Tolerance, physical dependence, hyponogonadism</td>
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</tbody>
</table>

Prescribers should report serious AEs and medication errors to the FDA:
https://www.fda.gov/media/76299/download
or 1-800-FDA-1088

OPIOID-INDUCED RESPIRATORY DEPRESSION

MORE LIKELY TO OCCUR:
- In elderly, cachectic, or debilitated patients
- If given concomitantly with other drugs that depress respiration (such as benzodiazepines)
- In patients who are opioid-naive or have just had a dose increase
- Opioids are contraindicated in patients with respiratory depression or conditions that increase risk

HOW TO REDUCE RISK:
- Ensure proper dosing and titration
- Do not overestimate dose when converting dosage from another opioid product
- Can result in fatal overdose with first dose
- Avoid co-prescribing benzodiazepines
- Instruct patients to swallow tablets/capsules whole
- Dose from cut, crushed, dissolved, or chewed tablets/capsules may be fatal, particularly in opioid-naive individuals
**TRANSDERMAL/TRANSMUCOSAL DOSAGE FORMS**

- Do not cut, damage, chew, or swallow
- Prepare skin: clip (not shave) hair and wash area with water
- Rotate location of application
- Do not apply buccal film products if film is cut, damaged, or changed in any way — use the entire film
- Note that metal foil backings are not safe for use in MRIs
- Monitor patients with fever for signs or symptoms of increased opioid exposure
- Note that exertion or exposure to external heat can lead to fatal overdose

**FOR SAFER USE: KNOW DRUG INTERACTIONS, PK, AND PD**

- CNS depressants can potentiate sedation and respiratory depression
- Opioid use with MAOIs may increase respiratory depression
- Certain opioids with MAOIs can cause serotonin syndrome
- Many opioids can prolong QTc interval, check the PI; methadone requires extra caution
- Opioid use can reduce efficacy of diuretics
- Drugs that inhibit or induce CYP enzymes can increase or lower blood levels of some opioids
- Some ER/LA products rapidly release opioid dose during (when exposed to alcohol) or without (dose dumping)

**OPIOIDS AND CYP450 ENZYME INTERACTIONS**

- Metabolism of several commonly used opioids occurs through the cytochrome P450 system
- Be aware of potential inhibitors (e.g., macrolides, azole antifungals) and inducers (e.g., carbamazepine)
- Genetic and phenotypic variations in patient response to certain opioids
- Refer to product-specific information in the drug package insert before prescribing

**DRUG INTERACTIONS COMMON TO OPIOIDS**

**Other CNS Depressants**
- Increased risk of respiratory depression, hypotension, profound sedation, or coma
- Reduce initial dose

**Partial Agonists* or Mixed Agonist/Antagonists †**
- Avoid concurrent use with full opioid agonist
- May reduce analgesic effect and/or precipitate withdrawal

**Skeletal Muscle Relaxants**
- Concurrent use may enhance neuromuscular blocking action and increase respiratory depression

**Anticholinergic Medication**
- Concurrent use increases risk of urinary retention and severe constipation
- May lead to paralytic ileus

*Remembrate: *specifications, abbreviations, subheadings*

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**SPECIAL POPULATIONS**

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**OLDER ADULTS**

**RISK FOR RESPIRATORY DEPRESSION**
- Age-related changes in distribution, metabolism, excretion, absorption less affected

**ACTIONS**
- Monitor
  - Initiation and titration
  - Concomitant medications (polypharmacy)
  - Falls risk, cognitive change, psychosocial status
  - Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
  - Start low, go slow, but GO
  - Routinely initiate a bowel regimen
  - Patient and caregiver reliability risk of diversion

Neonatal opioid withdrawal syndrome is a potential risk of opioid therapy for women using opioids on a daily basis. ACOG recommends methadone or buprenorphine. Given this potential risk, clinicians should:

- Discuss family planning, contraceptives, breastfeeding plans with patients.
- Counsel women of childbearing potential about risks and benefits of opioid therapy during pregnancy and after delivery.
- Encourage minimal opioid use during pregnancy, unless potential benefits outweigh risks to fetus.
- Refer to a high-risk OB/Gyn who will ensure appropriate treatment for the baby.

- Perform universal screening to avoid maternal abstinence syndrome.
- For women using opioids on a daily basis, ACOG recommends methadone or buprenorphine.

Handle with care: judicious & low-dose use of IR for brief therapy:

- Pediatric analgesic trials pose challenges.
- Transdermal fentanyl approved in children ≥ 2.
- Oxycodone ER dosing changes for children ≥ 12.

- ER/LA opioid indications are primarily life-limiting conditions.

- Consult pediatric palliative care team or pediatric pain specialist or refer to a specialized multidisciplinary pain clinic.

Other populations needing special treatment considerations:

- Persons with sleep disorders or sleep-disordered breathing (sleep apnea).
- Persons with dementia/nonverbal patients.
- Persons with obesity.
- Persons with renal/hepatic impairment.
- Persons with psychiatric disorders.
- Persons at end-of-life.
- Persons with substance use disorders.
WHEN TO CONSIDER A TRIAL OF AN OPIOID

Non-malignant pain
- 68 y/o male with Osteoarthritis in multiple joints, interfering with ability to golf
- PMH- HTN, Diabetes
- Failed Acetaminophen, NSAIDS, Lidoderm patch

Malignant pain
- 76 y/o female with metastatic ovarian cancer
- New onset LLE pain
- Taking Acetaminophen currently for back pain

INFORMED CONSENT

When initiating a pain treatment plan, confirm patient understanding of informed consent to establish:

- Analgesic and functional goals of treatment
- Expectations
- Potential risks
- Alternatives
- Patient's understanding
- Patient's decision

PATIENT PROVIDER AGREEMENT (PPA)

Reinforce expectations for appropriate and safe opioid use

- Clarify treatment plans and goals
- One prescriber
- Consider one pharmacy
- Safeguards
  - Do not store in medicine cabinet
  - Keep locked (medication safe)
  - Do not share or sell
- Instructions for disposal when no longer needed
- Prescriber notification for any event resulting in a pain medication prescription
- Follow-up plan
- Monitoring
  - Random UDT and pill counts
- Refill procedure
- Identify behaviors indicating need for discontinuation
- Exit strategy
- Signed by both
PPA NONADHERENCE

Behavior outside the boundaries of agreed-on treatment plan

- Unsanctioned dose escalations or other noncompliance with therapy on 1 or 2 occasions
- Unapproved use of the drug to treat another symptom
- Openly acquiring similar drugs from other medical sources
- Multiple dose escalations or other noncompliance with therapy despite warnings
- Prescription forgery
- Obtaining prescription drugs from nonmedical sources

Any of these behaviors merits investigation; proceed with caution.

CHAPTER 5
MANAGING PATIENTS ON OPIOID ANALGESICS

INITIATING OPIOIDS

- Begin a therapeutic trial with an IR opioid
- Prescribe the lowest effective dosage
- Use caution at any dosage, but particularly when:
  - Increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day
  - Carefully justify a decision to titrate dosage to ≥ 90 MME/day
- Always include dosing instructions, including daily maximum
- Be aware of interindividual variability of response
- Have PPA, baseline UDT, and informed consent in place
- Co-prescribe naloxone (if indicated) and bowel regimen
- Re-evaluate risks/benefits within 1–4 weeks (could be as soon as 3–5 days) of initiation or dose escalation
- Re-evaluate risks/benefits every 3 months; if benefits do not outweigh harms, optimize other therapies and work to taper and discontinue

There are differences in benefit, risk and expected outcomes for patients with chronic pain and cancer pain, as well as for hospice and palliative care patients.
ONGOING AND LONG-TERM MANAGEMENT OF PATIENTS ON OPIOID ANALGESICS

PERIODIC REVIEW OF PAIN

• Is the patient making progress toward functional goals?
• Reset goals if required or indicated; develop reasonable expectations
• Monitor for breakthrough pain
• Review adverse events/side effects at each visit
  • Evaluate bowel function
  • Screen for endocrine function as needed
  • Report adverse events to the FDA website
• Implement opioid rotation, as indicated

Prescribers should report serious AEs and medication errors to the FDA:
https://www.fda.gov/media/76299/download
or 1-800-FDA-1088

ONGOING AND LONG-TERM MANAGEMENT OF PATIENTS ON OPIOID ANALGESICS

MONITORING FOR SAFETY

• Check PDMP (when clinically indicated or legally mandated)
• Use urine drug testing (UDT)
• Reassess risk of SUD and/or OUD
• Monitor adherence to the treatment plan
  • Medication reconciliation
  • Evaluate for nonadherence

DISCONTINUING AND TAPERING

• When is opioid therapy no longer necessary?

MONITORING PAIN AND SUBSTANCE USE DISORDER

PAIN – 5 A’s

• Analgesia
• Activity/Function
• Aberrant/Problematic behavior, not present
• Adverse events
• Affect

SUD – 5 C’s

• Control, loss of
• Compulsive use
• Craving drug
• Continued use
• Chronic problem
WHEN TO MOVE FROM IR TO ER/LA OPIOIDS

<table>
<thead>
<tr>
<th>PRIMARY REASONS</th>
<th>OTHER POTENTIAL REASONS</th>
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<tbody>
<tr>
<td>- Maintain stable blood levels</td>
<td>- Patient desires or need to try a new formulation</td>
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<tr>
<td>(steady state plasma)</td>
<td>- Cost or insurance issues</td>
</tr>
<tr>
<td>- Longer duration of action</td>
<td>- Adherence issues</td>
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<tr>
<td>- Multiple IR doses needed to</td>
<td>- Change in clinical status requiring an opioid with</td>
</tr>
<tr>
<td>achieve effective analgesia</td>
<td>different pharmacokinetics</td>
</tr>
<tr>
<td>- Poor analgesic efficacy</td>
<td>- Problematic drug-drug interactions</td>
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<tr>
<td>despite dose titration</td>
<td></td>
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<tr>
<td>- Less sleep disruption</td>
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CONSIDERATIONS FOR CHANGE FROM IR TO ER/LA OPIOIDS

- DRUG AND DOSE SELECTION IS CRITICAL
  - Some ER/LA opioids or dosage forms are only recommended for opioid-tolerant patients
  - ANY strength of transdermal fentanyl or hydromorphone ER
  - Certain strengths/doses of other ER/LA products (check drug prescribing information)

- MONITOR PATIENTS CLOSELY FOR RESPIRATORY DEPRESSION
  - Especially within 24 – 72 hours of initiating therapy and increasing dosage

- INDIVIDUALIZE DOSAGE BY TITRATION BASED ON EFFICACY, TOLERABILITY, AND PRESENCE OF AEs
  - Check ER/LA opioid product PI for minimum titration intervals
  - Supplement with IR analgesics (opioid and non-opioid) if pain is not controlled during titration

EMERGENCE OF OPIOID-INDUCED HYPERALGESIA

- An increased sensitivity to pain
- Usually occurs at high MME dosages and over long periods of time
- A physiological phenomenon that can happen to anyone
- Consider this explanation if:
  - Pain increases despite dose increases
  - Pain appears in new locations
  - Patient becomes more sensitive to painful stimuli
  - Patient is not improving in the absence of underlying cause progression

Patients considered opioid tolerant are taking at least:
- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/hour
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid

Also use caution when rotating a patient on an IR opioid to a different ER/LA opioid.

Products restricted to opioid tolerant individuals include transdermal fentanyl (Duragesic) and hydromorphone (Exalgo).

**OPIOID TOLERANCE VERSUS PHYSICAL DEPENDENCE**

**TOLERANCE**
- Occurs when increased dose is needed to maintain the functional status no longer achieved by current dose
- CNS and respiratory depression can develop with dose increase

**PHYSICAL DEPENDENCE**
- Occurs when an organism only functions normally in the presence of the substance
- Abrupt discontinuation or dosage decrease causes uncomfortable symptoms of withdrawal

Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure and DO NOT equal addiction or opioid use disorder.

**OPIOID ROTATION**

**DEFINITION**
A change from an existing opioid regimen to another opioid with the goal of improving therapeutic outcomes or to avoid AEs attributed to the existing drug.

**RATIONALE**
Used when differences in pharmacologic or other effects make it likely that a switch will improve outcomes
- Effectiveness and AEs of different mu-opioids vary among patients
- Patient tolerant to first opioid might have improved analgesia from second opioid at a dose lower than calculated from an Equianalgesic Dosing Table (EDT)
EQUIANALGESIC DOSING TABLES (EDT)

Many different versions:
- Published
- Online
- Online interactive
- Smart-phone apps

Vary in terms of:
- Equianalgesic values
- Whether ranges are used
- Which opioids are included: May or may not include transdermal opioids, rapid-onset fentanyl, ER/LA opioids, or opioid agonist-antagonists

START WITH AN EDT FOR ADULTS

<table>
<thead>
<tr>
<th>EQUIANALGESIC DOSE</th>
<th>USUAL STARTING DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRUG</td>
<td>SCI/IV</td>
</tr>
<tr>
<td>Morphine</td>
<td>10 mg</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 mg</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MU-OPIOID RECEPTORS AND INCOMPLETE CROSS TOLERANCE

MU-OPIOIDS BIND TO MU RECEPTORS

MANY MU RECEPTOR SUBTYPES

Mu-opioids produce subtly different pharmacologic responses based on distinct activation profiles of mu receptor subtypes

MAY HELP EXPLAIN:
- Interpatient variability in response to mu-opioids
- Incomplete cross tolerance among mu-opioids
GUIDELINES FOR OPIOID ROTATION

REDUCE CALCULATED EQUIANALGESIC DOSE BY 25% – 50%*

SELECT % REDUCTION BASED ON CLINICAL JUDGMENT

CLOSER TO 50% REDUCTION IF PATIENT
- Is receiving a relatively high dose of current opioid regimen
- Is elderly or medically frail

CLOSER TO 25% REDUCTION IF PATIENT
- Does not have these characteristics
- Is changing route of administration

*Slight modification from original text: use equianalgesic dose ratios provided in PI
† If switching to methadone, reduce dose by 75% – 90%
‡ If oral transmucosal fentanyl used as rescue, begin at lowest dose irrespective of baseline opioid

GUIDELINES FOR OPIOID ROTATION (continued)

IF SWITCHING TO METHADONE:
- Standard EDTs are less helpful in opioid rotation to methadone
- For opioid tolerant patients, methadone doses should not exceed 30 – 40 mg/day upon rotation
- Consider inpatient monitoring, including serial EKG monitoring
- For opioid-naïve patients, do not give methadone as an initial drug

IF SWITCHING TO TRANSDERMAL:
- Fentanyl: calculate dose conversion based on equianalgesic dose ratios included in the drug package insert

GUIDELINES FOR OPIOID ROTATION: SUMMARY

VALUES FROM EDT*

PATIENT OPIOID VALUES

SOLVE FOR X

AUTOMATICALLY REDUCE DOSE

Value of current opioid

Value of new opioid

24-hr dose of current opioid

X amount of new opioid

Equianalgesic 24-hr dose of new opioid

By 25% – 50%†

Frequently assess initial response

Titrate dose of new opioid to optimize outcomes

Calculate supplemental rescue dose used for titration at 5% – 15% of total daily dose‡
BREAKTHROUGH PAIN (BTP)

PATIENTS ON STABLE ATC OPIOIDS MAY EXPERIENCE BTP
- Due to disease progression or a new or unrelated pain
- Target cause or precipitating factors
- Dose for BTP: Using an IR, 5% – 15% of total daily opioid dose, administered at an appropriate interval
- Never use ER/LA for BTP

CONSIDER ADDING
- PRN IR opioid trial based on analysis of benefit versus risk
  - There is a risk for aberrant/problematic drug-related behaviors
  - High-risk: Add only in conjunction with frequent monitoring and follow-up
  - Low-risk: Add with routine follow-up and monitoring
- Consider non-opioid drug therapies and nonpharmacologic treatments

ABUSE-DETERRENT FORMULATION (ADF) OPIOIDS
- Response to growing non-medical-use problem
- An ER/LA opioid with properties to meaningfully deter abuse, even if they do not fully prevent abuse
  - Less likely to be crushed, injected, or snorted
- Consider as one part of an overall strategy
- Mixed evidence on the impact of ADF on misuse
- Overdose is still possible if taken orally in excessive amounts
- These products are expensive with no generic equivalents

URINE DRUG TESTING (UDT)
- Urine testing is done FOR the patient, not TO the patient
- Helps to identify drug misuse/addiction
- Assists in assessing and documenting adherence

CLINICAL CONSIDERATIONS
- Recommend UDT before first prescription (baseline) then intermittently, depending on clinical judgment and state regulations
- Document time and date of last dose taken
- Be aware of possible false positives or negatives
- Clarify unexpected results with the lab before confronting patient to rule out poor specimen or error
SCREENING VERSUS CONFIRMATORY UDTS

<table>
<thead>
<tr>
<th>Analysis technique</th>
<th>Screening (Office-based)</th>
<th>Confirmatory (Send to lab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (low or none when testing for semi-synthetic or synthetic opioids)</td>
<td>Low or none</td>
<td>High</td>
</tr>
<tr>
<td>Specificity (can result in false positives or false negatives)</td>
<td>Varies</td>
<td>High</td>
</tr>
<tr>
<td>Turnaround</td>
<td>Rapid</td>
<td>Slow</td>
</tr>
<tr>
<td>Other</td>
<td>Intended for a drug-free population, may not be useful in pain medicine</td>
<td>Legally defensible results</td>
</tr>
</tbody>
</table>

GC-MS = gas chromatograph-mass spectrometry; HPLC = high-performance liquid chromatography

WINDOWS OF SPECIFIC DRUG DETECTION

<table>
<thead>
<tr>
<th>Drug</th>
<th>How soon after taking drug will there be a positive drug test?</th>
<th>How long after taking drug will there continue to be a positive drug test?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis</td>
<td>1 – 3 hours</td>
<td>1 – 7 days</td>
</tr>
<tr>
<td>Crack (coca)</td>
<td>1 – 6 hours</td>
<td>2 – 3 days</td>
</tr>
<tr>
<td>Heroin (opiates)</td>
<td>2 – 6 hours</td>
<td>1 – 3 days</td>
</tr>
<tr>
<td>Speed/upsers (amphetamine, methamphetamine)</td>
<td>4 – 6 hours</td>
<td>2 – 3 days</td>
</tr>
<tr>
<td>Angel dust/PCP</td>
<td>4 – 6 hours</td>
<td>7 – 14 days</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>2 – 7 hours</td>
<td>2 – 4 days</td>
</tr>
<tr>
<td>Benzedrine</td>
<td>2 – 7 hours</td>
<td>1 – 4 days</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>2 – 4 hours</td>
<td>1 – 3 weeks</td>
</tr>
<tr>
<td>Methadone</td>
<td>3 – 8 hours</td>
<td>1 – 3 days</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>4 – 12 hours</td>
<td>2 – 7 days</td>
</tr>
<tr>
<td>Codeine</td>
<td>1 – 3 hours</td>
<td>1 – 2 days</td>
</tr>
</tbody>
</table>

SOURCE: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/DrugsofAbuseTests/ucm125722.htm

EXAMPLES OF OPIOID METABOLISM

- POPPY SEEDS
- CODEINE
- MORPHINE
- HYDROCODONE
- HYDROMORPHONE
- OXYCODONE
- OXYMORPHONE

*6-MAM=6-Monoacetylmorphine

Tₚᵥ=25 – 30 Min
Tᵥ=3 – 5 Min
**REASONS FOR DISCONTINUING OPIOIDS**

<table>
<thead>
<tr>
<th>Pain Level Decrease in Stable Patients</th>
<th>Intolerable and Unmanageable AE’s</th>
<th>No Progress Toward Therapeutic Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>• One or two episodes of increasing dose without prescriber knowledge</td>
<td>• Use of illicit drugs or unprescribed opioids</td>
<td></td>
</tr>
<tr>
<td>• Sharing medications</td>
<td>• Repeatedly obtaining opioids from multiple outside sources</td>
<td></td>
</tr>
<tr>
<td>• Unapproved opioid use to treat another symptom (e.g., insomnia)</td>
<td>• Prescription forgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Multiple episodes of prescription loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Diversion</td>
<td></td>
</tr>
</tbody>
</table>

**MISUSE OR ABERRANT BEHAVIORS**

- One or two episodes of increasing dose without prescriber knowledge
- Sharing medications
- Unapproved opioid use to treat another symptom (e.g., insomnia)
- Use of illicit drugs or unprescribed opioids
- Repeatedly obtaining opioids from multiple outside sources
- Prescription forgery
- Multiple episodes of prescription loss
- Diversion

**OUD/SUD RISK ASSESSMENT TOOLS**

- PMQ Pain Medication Questionnaire
- COMM Current Opioid Misuse Measure
- PDUQ Prescription Drug Use Questionnaire
- SBIRT Screening, Brief Intervention, and Referral to Treatment

Even at prescribed doses, opioids carry the risk of misuse, abuse, opioid use disorder, overdose, and death

**TAPER DOSE WHEN DISCONTINUING**

- No single approach is appropriate for all patients
- May use a range of approaches from a slow 10% dose reduction per week to a more rapid 25% – 50% reduction every few days
- To minimize withdrawal symptoms in patients physically dependent on opioids, consider medications to assist with withdrawal (clonidine, NSAIDs, antihistamines, antidiarrheal agents)
- If opioid use disorder or a failed taper, refer to an addiction specialist or consider opioid agonist therapy
- Counseling and relaxation strategies needed
CONSULTING A PAIN SPECIALIST

- Appropriate when you feel you cannot provide the level of care needed
- First ensure you have a reliable specialist to refer to
- To find a pain specialist in your area:
  - Consult with state boards
  - Consult with colleagues
  - Use online resources
  - Consult payment source
- Prior to referral, contact the specialist and ask what is needed for referral

Adequately DOCUMENT all patient interactions, assessments, test results, and treatment plans.

CHAPTER 6
EDUCATING YOUR PATIENTS AND THEIR CAREGIVERS
COUNSEL PATIENTS ABOUT PROPER USE

- Take opioid as prescribed
- Adhere to dose regimen
- Use lowest amount of medication necessary for shortest time
- Do not abruptly discontinue or reduce dose; taper safely to avoid withdrawal symptoms
- Properly handle unused doses
- Notify HCP if pain is uncontrolled
- Manage side effects
- Inform HCP of ALL meds being taken
- Never share or sell opioids: can lead to others’ deaths, against the law
- Use caution when operating heavy machinery and driving
- Read the opioid drug package insert received from the pharmacy every time an opioid is dispensed

USE PATIENT COUNSELING DOCUMENT

USE PATIENT COUNSELING DOCUMENT

- Respiratory depression: most serious
- Opioid-induced constipation (OIC): most common
- Sexual dysfunction and other endocrine abnormalities
- Tolerance, physical dependence, hyperalgesia
- Allergic reactions
- Sedation, cognitive impairment
- Falls and fractures
- Sweating, miosis, urinary retention
- Hypogonadism
- Myoclonus (twitching or jerking)
- Addiction in vulnerable patients
- Overdose and death
WARN PATIENTS

Never break, chew, crush, or snort an opioid tablet/capsule, or cut or tear patches or buccal films prior to use
- May lead to rapid release of opioid, causing overdose and death
- If patient is unable to swallow a capsule whole, refer to drug package insert to determine if appropriate to sprinkle contents on applesauce or administer via feeding tube

Use of CNS depressants or alcohol with opioids can cause overdose and death
- Use with alcohol may result in rapid release and absorption of a potentially fatal opioid dose, known as “dose dumping”
- Use with other depressants such as sedative-hypnotics (benzodiazepines), anxiolytics, or illegal drugs can cause life-threatening respiratory depression

If not immediately recognized and treated, may lead to respiratory arrest and death
More likely to occur in opioid naive patients during initiation or after dose increase

Greatest risk: when co-prescribed with a benzodiazepine

OPIOID-INDUCED RESPIRATORY DEPRESSION

Instruct patients/family members to:
- Screen for shallow or slowed breathing
- Deliver naloxone
- CALL 911

Instructions may differ if patient is on hospice or near end of life

SIGNS OF OVERDOSE POISONING CALL 911
- Person cannot be aroused or awakened or is unable to talk
- Any trouble with breathing, heavy snoring is warning sign
- Gurgling noises coming from mouth or throat
- Body is limp, seems lifeless; face is pale, clammy
- Fingernails or lips turn blue/purple
- Slow, unusual heartbeat or stopped heartbeat
NALOXONE

What it is:
• An opioid antagonist administered intranasally (most common) or parenterally
• Reverses acute opioid-induced respiratory depression but will also reverse analgesia; may precipitate acute opioid withdrawal
• No abuse potential

What to do:
• Discuss an overdose plan with patients
• Consider offering a naloxone prescription to all patients prescribed opioids; some states require co-prescribing
• Involve and train family, friends, partners, and/or caregivers in the proper administration of naloxone
• Check to see if pharmacy dispenses it
• Check expiration dates and replace expired naloxone
• In the event of known or suspected overdose call 911 and administer naloxone

NALOXONE OPTIONS

• Available as auto-injector, intramuscular injection, or nasal spray
• Cost and insurance coverage vary
• Make use of tutorial videos to demonstrate administration
• Store at room temperature
• Dispose of used containers safely

SAFE OPIOID STORAGE AND DISPOSAL

STEP 1: MONITOR
• Note how many pills are in each prescription
• Keep track of dosage and refills
• Make sure everyone in the home knows

STEP 2: SECURE
• Keep meds in a safe place (locked cabinet or box)
• Store away from children, family, visitors, and pets
• Encourage parents of your teen’s friends to secure their prescription

STEP 3: DISPOSE
• Discard expired or unused meds
• Consult drug package insert for best disposal method
WHERE AND HOW TO DISPOSE OF UNUSED OPIOIDS

Authorized Collection Sites
- Use the DEA disposal locator website to find sites near you:
  https://apps.deadiversion.usdoj.gov/pubdispsearch
- Search Google Maps for "drug disposal nearby"

Options
- Drug take-back days (local pharmacies or local law enforcement)
- Flush
  - Fold patch in half so sticky sides meet, then flush
- Trash (mix with noxious element)

Mail-Back Packages
- Obtain from authorized collectors


CHAPTER 7
UNDERSTANDING OPIOID USE DISORDER (OUD)

OPIOIDS
PAIN
OUD
• Risk of opioid use disorder in patients on chronic opioid therapy (COT) for chronic non-cancer pain (CNCP) is up to 26%

• Risk is always highest with past history of substance use disorder (SUD) or psychiatric comorbidity

WHAT IS ADDICTION?

OFFICIAL ASAM DEFINITION:
Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

PRACTICAL DEFINITION:
Addiction is the continued use of drugs or activities, despite knowledge of continued harm to one’s self or others.

SUBSTANCE USE DISORDER: DSM-5 CRITERIA

1. Tolerance*
2. Withdrawal

LOSS OF CONTROL
3. Using larger amounts and/or for longer periods
4. Inability to cut down on or control use
5. Increased time spent obtaining, using, or recovering
6. Craving/compulsion

USE DESPITE NEGATIVE CONSEQUENCES
7. Role failures at work, home, school
8. Interpersonal problems
9. Reducing social, work, recreational activity
10. Physical hazards
11. Physical or psychological harm

* Not valid if opioid is taken as prescribed

2 – 3 = mild
4 – 5 = moderate
≥6 = severe

Not valid if opioid is taken as prescribed
The DSM-5 criteria for opioid use disorder may be misleading in the context of prescribed opioids for the treatment of pain. Harm may be masked under these conditions. Clinical judgement is key.

Physical dependence or tolerance doesn't necessarily equal OUD/addiction. Doesn't necessarily equal aberrant or problematic behavior.
THE CYCLE OF SUBSTANCE USE DISORDER

NEUROTRANSMITTERS
- Dopamine
- Opioid peptides
- Corticotropin-releasing factor (CRF)
- Dynorphin
- Glutamate

EVERYONE IS VULNERABLE, BUT WHO IS MOST VULNERABLE TO OPIOID MISUSE OR OUD?

- Those with a genetic predisposition to substance abuse (family history)
- Those with psychiatric comorbidities
- Those with low hedonic tone
- The probability of long-term opioid use increases most sharply in the first days of therapy, particularly after 5 days or 1 month of opioids has been prescribed.

TREATMENT OF OPIOID USE DISORDER

- Medication options for addiction treatment (MAT)
  - Methadone (Schedule II)
  - Buprenorphine (Schedule III)
  - Naltrexone (not a controlled substance)
- Supplementary psychosocial and recovery support services
  - Housing, childcare, support groups, employment services
- Temporal considerations
  - Frequency of administration (daily versus long-acting formulations)
  - Length of treatment
  - No recommended time period for treatment
  - Patients who discontinue and resume risk overdose and death
TREATING PAIN IN THE PATIENT WITH OUD

- Remember that untreated pain is a trigger for relapse
- Must address both pain and opioid use disorder
- Avoid other potentially problematic medications
- Consider a multidisciplinary pain program
- Consider buprenorphine for both pain and OUD
- Consider using opioids that do not metabolize to other prescribed medications
- Enlist patient’s family significant other to secure and dispense opioids
- Recommend an active recovery program
- Remember to use UDT, PDMP, pill counts, PPA


OPIOID ANALGESICS WITH BENZODIAZEPINES, NICOTINE, AND ALCOHOL

- More than 30% of opioid overdoses involve benzodiazepines (BZDs); both are CNS depressants (avoid concurrent prescribing)
- Nicotine and alcohol use are risk factors for misuse of prescribed opioids
- Nicotine users are co-prescribed BZDs and muscle relaxants (MRs) with opioids to a greater extent than non-nicotine users


BUPRENORPHINE

- If using for pain, you don’t need a waiver
- If using to treat OUD, you need a waiver
- The most commonly prescribed pharmacotherapy for the treatment of OUD
- Partial mu-agonist with “plateau effect” for respiratory depression
- Good efficacy and safety profile
- FDA-approved buprenorphine products for pain:
  - Butrans: 7-day transdermal patch
  - Belbuca: buccal mucosal film; BID dosing
Content Outline

- Opioid Prescribing Rates and Overdose Deaths
- Prescription Drug Monitoring Program (PDMP)
- Prescribing Limits, Status and Education Requirements
- Naloxone Regulation
- Medical and Recreational Marijuana Status

Opioid Prescribing Rates & Overdose Deaths

<table>
<thead>
<tr>
<th>State</th>
<th>Prescribing Rates (per 100 people)</th>
<th>Opioid Overdose Deaths</th>
</tr>
</thead>
</table>

Updated: April 2019
The CO*RE State Information Hub is updated three times per year. Since opioid/prescribing policies, laws and regulations change rapidly, please refer to your state’s regulations for the most up-to-date information.

State Specific Information
Iowa
https://idph.iowa.gov/

Updated: April 2019
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### PDMP: Prescription Drug Monitoring Program

**General**
- Iowa Prescription Monitoring Program: [https://pharmacy.iowa.gov/prescription-monitoring-program](https://pharmacy.iowa.gov/prescription-monitoring-program)
- Administered by the Board of Pharmacy
- Schedule II-IV are monitored
- Dispensers are required to register and input data
- Before prescribing, there is an obligation to review under certain circumstances
- Prescribers can authorize a registered delegate

**Reporting**
- Must be entered into PDMP by the next business day after dispensing
- Unsolicited reports/alerts are sent to prescribers and dispensers
- Iowa does share data with other states’ PDMP
- Out-of-state pharmacies are required to report to the patient’s home state
- Patient will not be notified if their record has been accessed

---

### Prescribing Limits, Status & Education Requirements

**Initial prescribing limits for acute pain:** None

<table>
<thead>
<tr>
<th>Prescriber Status</th>
<th>Physician</th>
<th>Physician Assistant</th>
<th>Advanced Practice Nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Licensed</td>
<td>II-V</td>
<td>Schedule II-V</td>
</tr>
<tr>
<td>Education Requirements</td>
<td>2 hrs./5 yrs.</td>
<td>2 hrs./2 yrs.</td>
<td>2 hrs./3 yrs.</td>
</tr>
</tbody>
</table>

---

### Naloxone Regulation

**Effective date:** April 2016

**Criminal Immunity**
- Prescribers: No
- Dispensers: No
- Lay People: No

**Also Available**
- Without Prescription: Yes
- To 3rd Party: Yes
- By Standing Order: Yes

**Carried by First Responders:** Yes

---
Marijuana Status

Medical

Use of Marijuana for Medicinal Purposes

Recreational

Not legal for recreational use in Iowa

© 2017 The National Alliance for Model State Drug Laws (NAMSDL)

REFERRALS AND TREATMENT CENTERS

ASAM, SAMHSA, and AAAP are all helpful referral resources.

ASAM resources: https://www.asam.org/resources/resource-links
SAMHSA locator: https://findtreatment.samhsa.gov/locator
AAAP locator: https://www.aaap.org/patients/find-a-specialist/

Our session stops here, but your review continues...

For detailed information, prescribers can refer to prescribing information available online via DailyMed at www.dailymed.nlm.nih.gov or https://opioidanalgesicrems.com/RpcUI/products.u

Please visit the CO*RE Tools Repository http://core-rem.s.org/opioid-education/tools/
YOUR PARTICIPATION IS IMPORTANT

Thank you for completing the post test for this CO*RE session.

Your participation in this test allows CO*RE to report de-identified numbers to the FDA.

Strong test participation will demonstrate that clinicians have voluntarily engaged with this important material and are committed to patient safety and improved outcomes.

THANK YOU!

WWW.CORE-REMS.ORG