Faculty Information

Yvonne D'Arcy, MS, CRNP, CNS, FAANP
Yvonne D'Arcy is a pain management & palliative care nurse practitioner with over 20 years of practice experience. She is the author of over 100 articles, ten books, and over 100 presentations. She has two AIN Book of the Year awards for her book on How to Manage Pain in the Elderly and The Compact Clinical Guide to Cancer Pain Management written with Pamela Davies. She speaks frequently on a variety of pain management topics. Yvonne is currently the co-chair of the AANP Pain Management Special Practice group.

DISCLOSURE:
None

Acknowledgement

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

This educational activity is supported by an independent educational grant from the Extended-Release/Long-Acting (ER/LA) Opioid Analgesic REMS Program Companies. Please see this document for a listing of the member companies. This activity is intended to be fully compliant with the ER/LA Opioid Analgesic REMS education requirements issued by the US Food and Drug Administration.
PRODUCTS COVERED BY THIS REMS

BRAND NAME PRODUCTS
- Arymo ER morphine sulfate ER tablets
- Avinza® morphine sulfate ER capsules
- Belbuca® buprenorphine buccal film
- Butrans® buprenorphine transdermal system
- Dilaudid® morphine hydrochloride tablets
- Duragesic® fentanyl transdermal system
- Embeda® morphine sulfate/naltrexone ER capsules
- Exalgo® hydromorphone hydrochloride ER tablets
- Hysingla® ER hydrocodone bitartrate ER tablets
- Kadian® morphine sulfate ER capsules
- MorphaBond® morphine sulfate ER tablets
- MS Contin® morphine sulfate CR tablets
- Nucynta® ER tapentadol ER tablets
- Opana® ER oxymorphone hydrochloride ER tablets
- OxyContin® oxycodone hydrochloride CR tablets
- Targiniq™ ER oxycodone hydrochloride/naloxone hydrochloride ER tablets
- Troxyca ER oxycodone hydrochloride/naltrexone capsules
- Vantrela ER hydrocodone bitartrate ER tablets
- Xtampza ER oxycodone ER capsules
- Zohydro® hydrocodone bitartrate ER capsules

GENERIC PRODUCTS
- Fentanyl ER transdermal systems
- Methadone hydrochloride tablets
- Methadone hydrochloride oral concentrate
- Methadone hydrochloride oral solution
- Morphine sulfate IR tablets
- Morphine sulfate ER capsules
- Oxycodone hydrochloride ER tablets
- Oxycodone hydrochloride tablets
- Methadone hydrochloride tablets
- Methadone hydrochloride oral solution
- Morphine sulfate tablets
- Morphine sulfate ER tablets
- Oxycodone hydrochloride ER tablets
- Morphine hydrochloride tablets
- Morphine hydrochloride oral concentrate
- Morphine hydrochloride oral solution
- Morphine sulfate ER tablets
- Morphine sulfate ER capsules
- Oxycodone hydrochloride ER tablets
- Oxycodone hydrochloride tablets
- Methadone hydrochloride tablets
- Methadone hydrochloride oral solution
- Morphine sulfate tablets
- Morphine sulfate ER tablets
- Oxycodone hydrochloride ER tablets
- Oxycodone hydrochloride tablets
- Methadone hydrochloride tablets
- Methadone hydrochloride oral solution
- Morphine sulfate tablets
- Morphine sulfate ER tablets
- Oxycodone hydrochloride ER tablets
- Oxycodone hydrochloride tablets
- Methadone hydrochloride tablets
- Methadone hydrochloride oral solution
- Morphine sulfate tablets
- Morphine sulfate ER tablets
- Oxycodone hydrochloride ER tablets
- Oxycodone hydrochloride tablets
- Methadone hydrochloride tablets
- Methadone hydrochloride oral solution
- Morphine sulfate tablets
- Morphine sulfate ER tablets
- Oxycodone hydrochloride ER tablets

CHAPTER 2
WHY ARE WE HERE?


SOURCE: MMWR, January 1, 2016/64(50);1378-82
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm

PRESCRIBING PATTERNS – WE PLAY A ROLE

OPIOID PRESCRIBING - THE PENDULUM SWINGS

PRESCRIBING BEHAVIORS
- Under-Prescribing
- Over-Prescribing
- Appropriate Prescribing

RESULTING OUTCOMES
- Unresolved Pain
- Adverse Outcomes
- Adequate Analgesia

BENEFITS VS. RISKS

BENEFITS
- Analgesia
  - Adequate pain control
  - Continuous, predictable (with ER/LAs)
  - Improved function
  - Quality of life

RISKS
- Overdose, especially as ER/LA formulations contain higher opioids than Immediate Release
- Life-threatening respiratory depression
- Abuse by patient or household contacts
- Misuse, diversion, and addiction
- Physical dependence and tolerance
- Interactions with other meds and substances
- Risk of neonatal opioid withdrawal syndrome
- Inadvertent exposure/ingestion by household contacts especially children

### Source of Most Recent Rx Opioids Among Past-Year Misusers 2015

Source where pain relievers were obtained for most recent misuse among 12.5 million people aged 12 or older who misused prescription pain relievers in the past year. Percentages, 2015

- 55% - Stolen, from friends or family
- 36% - Through a prescription or stolen from healthcare provider
- 5% - Bought from a dealer or stranger
- 5% - Some other way

### First Specific Drug Associated with Initiation of Illicit Drug Use 2013

2.8 million initiates of illicit drugs

- 70.3% - Marijuana
- 12.5% - Pain Relievers
- 6.3% - Inhalants
- 5.2% - Tranquilizers
- 2.7% - Stimulants
- 2.1% - Hallucinogens
- 0.5% - Sedatives and Cocaine

### The Federal Players

Many agencies involved

**Image:**

- Opioids
- Surgeon General
- CDC
- SAMHSA
- FDA

**Text:**

*We are here because of...*

### REMS: Risk Evaluation and Mitigation Strategy

- On July 9, 2012, the Food and Drug Administration (FDA) approved a Risk Evaluation and Mitigation Strategy (REMS) for extended-release (ER) and long-acting (LA) opioid medications
- First time FDA has ever used accredited CE/CME as part of a REMS

### Co*RE Statement

Misuse, abuse, diversion, addiction, and overdose of opioids has created a serious public health epidemic in the U.S.

When prescribed well and used as prescribed, opioids can be valuable tools to effectively treat pain.

This course does not advocate for or against the use of Immediate Release (IR) or Extended-Release/Long-Acting (ER/LA) opioids. Our purpose is to provide proper education about safe prescribing practices along with effective patient education.

### Learning Objectives

1. Accurately assess patients with pain for consideration of an opioid trial
2. Establish realistic goals for pain management and restoration of function
3. Initiate opioid treatment (IR and ER/LA) safely and judiciously, maximizing efficacy while minimizing risks
4. Monitor and re-evaluate treatment continuously; discontinue safely when appropriate
5. Counsel patients and caregivers about use, misuse, abuse, diversion, and overdose
6. Educate patients about safe storage and disposal of opioids
7. Demonstrate working knowledge and ability to access general and specific information about opioids, especially those used in your practice
You and Your Team can have an immediate and positive impact on this crisis while also caring for your patients appropriately.

OPIOID SITES OF ACTION IN THE BRAIN

UNDERSTANDING PAIN

The Impact of Pain

Pain Management Goals and Treatment Options: A Multi-Modal Approach
CHAPTER 3 - PEARLS FOR PRACTICE

- Explain neurophysiology of pain processing to patients
- When patients understand, their concerns are validated
- Pain has biological, psychological, social, and spiritual components

CHAPTER 4

PAIN ASSESSMENT

- Description of pain
  - Location
  - Intensity
  - Quality
  - Onset/Duratio
  - Variations/Pat terns/Rhythms
- What relieves the pain?
- What causes or increases pain?
- Effects of pain on physical, emotional, and psychosocial function
- Patient’s current pain and function

TREATMENT HISTORY

- Non-pharmacologic strategies and effectiveness
- Pharmacologic strategies and effectiveness
- Past use
  - Current use
    - Query state Prescription Drug Monitoring Program (PDMP) to confirm patient report
  - Dosage
    - For opioids currently prescribed: opioid, dose, regimen, and duration
    - Important to determine if patient is opioid tolerant
- General effectiveness

PAST MEDICAL HISTORY

- Illness relevant to (1) effects or (2) metabolism of opioids
  1. Pulmonary disease, constipation, nausea, cognitive impairment
  2. Hepatic, renal disease
- Illness possibly linked to substance use disorder (SUD):
  - Hepatitis
  - Trauma/Burns
  - HIV
  - Cardiac Disease
  - Tuberculosis
  - Pulmonary Disease
  - Cellulitis
  - STIs
  - Arthritis

CHALLENGE: THE EARLY REFILL

RED FLAG:
Is this misuse? Abuse?

Your patient requests an early refill for the second time in six months. Took extra medications for headache and again for toothache. Prescription is for lower back pain.

Action:
Evaluate potential misuse. Confirm patient’s understanding of each medication’s dosage, time of day, and maximum daily dose. Ask him/her to repeat these instructions back to you. Avoid clinical terms such as “prn”. Review treatment goals and expectations. Select and document a therapy plan that is compatible with patient’s individual needs, is safe, effective and balanced. Screen for risk with Current Opioid Misuse Measure (COMM) and, if indicated, refer to addiction specialist for treatment.

ASSESSMENT
The SOAPP® Monitoring Recommendations.

for chronic pain

Identifies patients as high, moderate, or low risk for misuse of opioids prescribed with pain (SOAPP® Screener and Opioid Assessment for Patients with Pain (SOAPP®)).

**RISK ASSESSMENT TOOLS**

- **Risk Factors for Opioid Abuse**
  - Controlled medications: prescribed or non-prescribed
  - Alcohol and tobacco
  - History of sexual abuse
  - Family history of substance abuse and psychiatric disorders
  - Age (16-45 YO)

Substance abuse history does not prohibit treatment with ER/LA opioids but may require additional monitoring and expert consultation/referral.

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

**Screening, Brief Intervention, and Referral to Treatment (SBIRT)**

- **Characterize Misuse Once Opioid Treatment Begins**
  - **PAIN**
    - Pain Intensity
  - **Assessment**
    - General assessment
  - **History**
    - Medical history
  - **Past Substance Use**
    - Substance abuse history

**Opioid Risk Tool (ORT)**

- Mark each box that applies

<table>
<thead>
<tr>
<th>Item</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of substance abuse</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Illegal drugs</td>
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<td>3</td>
</tr>
<tr>
<td>Prescription drugs</td>
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<td>4</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Age between 16 and 45 yrs</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>History of preadolescent sexual abuse</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Psychologic disease</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

**Pharmacological Assessment**

- **Screener and Opioid Assessment for Patients with Pain (SOAPP®)**
  - Identifies patients as high, moderate, or low risk for misuse of opioids prescribed for chronic pain

**Risk Assessment**

- **Physical Exam and Assessment**
  - **Components of the patient**
    - Musculoskeletal
    - Neurologic
  - **Order diagnostic tests** (appropriate to complaint)
  - **General vital signs, appearance, and pain behaviors**
  - **Cutaneous or trophic findings**

**RISK AND PAIN ASSESSMENT TOOL BOXES**

- **Pain Assessment**
  - Pain Assessment Tools (BP, etc.)
  - Functional Assessment (SF 36, PPS, geriatric assessment, etc.)
  - Pain intensity, Enjoyment of life, General activity (FPG)

- **Risk Assessment**
  - PDMP
  - UDT
  - Risk Assessment Tools (ORT or SOAPP®)

- **Mental Health Tools** (PHQ9, GAD7, etc.)
CONSIDER A TRIAL OF AN OPIOID?

**POTENTIAL BENEFITS ARE LIKELY TO OUTWEIGHT RISKS**

**FAILED TO ADEQUATELY RESPOND TO NON-OPIOID & NONDRUG INTERVENTIONS**

**PAIN IS MODERATE TO SEVERE**

**INITIATE TRIAL OF IR OPIOIDS**

INITIATING OPIOIDS: CDC GUIDELINE (2016)

- Begin with IR
- Prescribe the lowest effective dosage
- Use caution at any dosage, but particularly when:
  - Increasing dosage to ≤50 morphine milligram equivalents (MME)/day and carefully justify a decision to titrate dosage to ≤90 MME/day
- For acute pain, prescribe lowest effective dose of IRs, no more than needed
- Re-evaluate risks/benefits every 3–4 weeks of initiation or dose escalation
- Re-evaluate risks/benefits every 3 months; if benefits do not outweigh harms optimize other therapies, work to taper and discontinue
- Link to the Guideline: [https://www.cdc.gov/drugoverdose/prescribing/providers.html](https://www.cdc.gov/drugoverdose/prescribing/providers.html)

Cancer pain, hospice, and palliative care patients are not covered by CDC Guideline

INFORMED CONSENT

When initiating a trial of opioid analgesic therapy, confirm patient understanding of informed consent to establish:

<table>
<thead>
<tr>
<th>ANALGESIC AND FUNCTIONAL GOALS OF TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXPECTATIONS</td>
</tr>
<tr>
<td>POTENTIAL RISKS</td>
</tr>
<tr>
<td>ALTERNATIVES TO OPIOIDS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ALTERNATIVES TO OPIOIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs with long-term therapy (e.g., hyperalgesia, low testosterone, irregular menses or sexual dysfunction)</td>
</tr>
</tbody>
</table>

PATIENT PROVIDER AGREEMENT (PPA)

Document signed by both patient and prescriber at time an opioid is prescribed

- **CLARIFY TREATMENT PLAN AND GOALS OF TREATMENT WITH PATIENT, PATIENT’S FAMILY, AND OTHER CLINICIANS INVOLVED IN PATIENT’S CARE**
- **ASSIST IN PATIENT EDUCATION**
- **DISCUSS MEDICATION SAFE HANDLING, STORAGE, AND DISPOSAL**
- **DOCUMENT PATIENT AND PRESCRIBER RESPONSIBILITIES**

MONITOR ADHERENCE AND ABERRANT BEHAVIOR

- **REINFORCE EXPECTATIONS FOR APPROPRIATE AND SAFE OPIOID USE**
  - One prescriber
  - Consider one pharmacy
  - Safeguard
    - 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
  - Monitoring
    - Random UDT and pill counts
  - Refills
  - Identify behaviors for discontinuation
  - Exit strategy

- **ROUTINELY MONITOR PATIENT ADHERENCE TO TREATMENT PLAN**
  - Recognize and document aberrant drug-related behavior
    - In addition to patient self-report also use:
      - State PDMPs
      - UDT
        - Positive for non-prescribed drugs
        - Positive for illicit substance
        - Negative for prescribed opioid
      - Family member or caregiver interviews
      - Monitoring tools such as the COMRA, PADT, PMQ, or PDUQ
      - Medication reconciliation (e.g., pill counts)

PAIN= Pain Assessment and Documentation Tool
ADDRESS ABERRANT DRUG-RELATED BEHAVIOR

Behavior outside the boundaries of agreed-on treatment plan:

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

Any of these behaviors merits investigation. Proceed with caution.

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

CHAPTER 4 – PEARLS FOR PRACTICE

- Conduct a comprehensive and pain-focused history and physical
- Assess for risk of abuse and for mental health issues
- Determine if a therapeutic trial is appropriate
- Establish realistic goals for pain management and function
- Document EVERYTHING

CHALLENGE: THE DELAYED SURGERY

RED FLAG: Patient may be stalling to continue an opioid regimen

Ms. Jones says she needs opioids to manage her pain until she can have surgery. She reports continued delays in getting to surgery. You phone the surgeon and discover that no date has been set and that she has cancelled several appointments.

Action:
Set a time limit and expectation. Offer non-pharmacologic methods and non-opioid interventions for pain management. Communicate with the surgeon and advise patient to make appointment with surgeon for discussion of treatment plan.

Knowledge Test Question

1. Among the risk factors contained in screening tools for predicting aberrant drug-related behavior in patients receiving opioids for chronic pain are family and personal history of substance abuse, psychological problems, and pain-related H&P.

   A. Age (12-15 years)
   B. Age (16-45 years)
   C. Age (46-75 years)
   D. Age (≥ 76 years)
   E. Risk is even across age

   - Assess for risk of abuse and for mental health issues
   - Determine if a therapeutic trial is appropriate
   - Establish realistic goals for pain management and function
   - Document EVERYTHING

Correct answer: B. Age (16-45 years)

Rationale: Epidemiologic studies of prescription overdoses reveal risk factors include male sex, middle age, non-Hispanic white race, low income, and mental health problems. Rates of fatal overdose are lower at the extremes of age. The Opioid Risk Tool (ORT) lists age 16-45 as a risk factor. Fatal over dose rates are highest among people 45-54 years old for both unintentional and suicidal overdoses and those of undetermined intent.

References:
CHAPTER 5
MANAGEMENT
MONITORING AND DISCONTINUING

OPIOID SIDE EFFECTS

- Respiratory depression – most serious
- Opioid-Induced Constipation (OIC) – most common
- Sedation, cognitive impairment
- Falls and fractures
- Sweating, miosis, urinary retention
- Hypogonadism
- Tolerance, physical dependence, hyperalgesia
- Addiction in vulnerable patients

Prescribers should report serious AEs to the FDA:
www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf
or 1-800-FDA-1088

PART 1
MONITORING

OPIOID-INDUCED RESPIRATORY DEPRESSION

Chief hazard of opioid agonists, including ER/LA opioids
- If not immediately recognized and treated, may lead to respiratory arrest and death
- Greatest risk: initiation of therapy or after dose increase

Manifested by reduced urge to breathe and decreased respiration rate
- Shallow breathing
- CO₂ retention can exacerbate opioid sedating effects

Instruct patients/family members to call 911
Managed with
- Close observation
- Supportive measures
- Opioid antagonists
- Depending on patient’s clinical status

OPIOID-INDUCED RESPIRATORY DEPRESSION

MORE LIKELY TO OCCUR

- In elderly, cachectic, or debilitated patients
  - Contraindicated in patients with respiratory depression or conditions that increase risk
- If given concomitantly with other drugs that depress respiration
- Patients who are opioid-naïve or have just had a dose increase

REDUCE RISK

- Proper dosing and titration are essential
- Do not overestimate dose when converting dosage from another opioid product
  - Can result in fatal overdose with first dose
- Instruct patients to swallow tablets/capsules whole
  - Dose from cut, crushed, dissolved, or chewed tablets/capsules may be fatal, particularly in opioid-naïve individuals

WHEN TO MOVE FROM IR TO ER/LA OPIOIDS

PRIMARY REASONS

- Maintain stable blood levels (steady state plasma)
- Longer duration of action
- Multiple IR doses needed to achieve effective analgesia
- Poor analgesic efficacy despite dose titration
- Less sleep disruption

OTHER POTENTIAL REASONS

- Patient desire or need to try a new formulation
- Cost or insurance issues
- Adherence issues
- Change in clinical status requires an opioid with different pharmacokinetics
- Problematic drug-drug interactions
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
- Ant strength of transdermal fentanyl or hydromorphone ER
- Certain strengths/doses of other ER/LA products (check drug prescribing information)

MONITOR PATIENTS CLOSER 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 ER/LA analogs (opioids and non-opioids) if pain is not controlled during titration.

OPIOID ROTATION

DEFINITION

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 (e.g., myoclonus)

RATIONALE

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
  - Patients show incomplete cross-tolerance to new opioid
    - Patient tolerant to first opioid can have improved analgesia from second opioid at a dose lower than calculated from an Equianalgesic Dosing Table (EDT)

EQUIANALGESIC DOSES (EDT)

Many different versions:
- PUBLISHED
- ONLINE
- ONLINE INTERACTIVE
- SMART-PHONE APPS

Vary in terms of:

Which opioids are included: May or may not include transdermal opioids, rapid-onset fentanyl, ER/LA opioids, or opioid agonist antagonists

EXAMPLE OF AN EDT FOR ADULTS

Equianalgesic Dose

<table>
<thead>
<tr>
<th>Drug</th>
<th>SC/IV</th>
<th>PO</th>
<th>Parenteral</th>
<th>PO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10 mg</td>
<td>30 mg</td>
<td>2.5-5 mg SC/IV</td>
<td>25 mg p.o.</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>0.5-1 mg SC/IV</td>
<td>0.5-1 mg p.o.</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>NA</td>
<td>20 mg</td>
<td>NA</td>
<td>10 mg q3-4h</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.5 mg)</td>
<td>(2.5 mg)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
<td>30 mg</td>
<td>NA</td>
<td>5 mg q3-4h</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.5 mg)</td>
<td>(2.5 mg)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5 mg</td>
<td>7.5 mg</td>
<td>0.2-0.5 mg SC/IV</td>
<td>1.5 mg q3-4h</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.2 mg SC/IV</td>
<td>(0.3 mg)</td>
</tr>
</tbody>
</table>

OPIOID TOLERANCE

If opioid tolerant caution should still be used at higher doses

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

Still requires caution when rotating a patient on an IR opioid to a different ER/LA opioid

EQUIANALGESIC DOSE TABLES (EDT)

Vary in terms of:

Whether ranges are used

Which opioids are included: May or may not include ER/LA opioids, rapid-onset fentanyl, opioid agonist antagonists

MU OPIOID RECEPTORS AND INCOMPLETE CROSS-TOLERANCE

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

May help explain:
- Inter-patient variability in response to mu opioids
- Incomplete cross-tolerance among mu opioids

Mu opioids bind to mu receptors

Many mu receptor subtypes:
- MU OPIOID RECEPTOR SUBTYPE

Drug 1

Drug 2

Potential

POTENCY
GUIDELINES FOR OPIOID ROTATION

Calculate equianalgesic dose of new opioid from EDT

- 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
  - Elderly or medically frail
- Closer to 25% reduction if patient is:
  - Does not have these characteristics
  - Is changing route of administration

*75%-90% reduction for methadone

GUIDELINES FOR OPIOID ROTATION (continued)

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

IF SWITCHING TO TRANSDERMAL:
- Fentanyl, calculate dose conversion based on equianalgesic dose ratios included in the PI
- Buprenorphine, follow instructions in the PI

BREAKTHROUGH PAIN (BTP)

PATIENTS ON STABLE ATC OPIOIDS MAY EXPERIENCE BTP
- Disease progression or a new or unrelated pain
- Target cause or precipitating factors
- Dose for BTP: using an IR is 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
- Risk for aberrant drug-related behaviors
- High-risk: only in conjunction w/frequent monitoring & follow-up
- Low-risk: w/routine follow-up & monitoring
- Non-opioid drug therapies
- Non-pharmacologic treatments

ATC = Around the Clock

RATIONAL FOR URINE DRUG TESTING (UDT)

- Urine testing is done FOR the patient not TO the patient
- Help to identify drug misuse/addiction
- Assist in assessing and documenting adherence

UDT FREQUENCY IS BASED ON CLINICAL JUDGMENT AND STATE REGULATIONS

BE READY TO REFER

SUBSTANCE USE DISORDER

SAMHSA substance abuse treatment facility locator
https://findtreatment.samhsa.gov/locator/home

SAMHSA mental health treatment facility locator
https://findtreatment.samhsa.gov/locator/home

HIGH RISK/COMPLEX PATIENTS
- Refer to pain management, check state regulations for requirements

SAMHSA = Substance Abuse and Mental Health Service Administration

TYPES OF UDT METHODS

Be aware of what you are testing and not testing

IMMUNOASSAY (IA) DRUG PANELS
- Either lab-based or point of care
- Identify substance as present or absent according to cutoff
- Many do not identify individual drugs within a class
- Subject to cross-reactivity and variability

GC/MS OR LC/MS
- Identify the presence and quantity of substance(s)
- Identify drugs not included in IA tests
- When results are contested

GC/MS = gas chromatography/mass spectrometry
LC/MS = liquid chromatography/mass spectrometry

SPECIFIC WINDOWS OF DRUG DETECTION

How long a person excretes drug and/or metabolite(s) at a concentration above a cutoff

DETECTION TIME OF DRUGS IN URINE

Governed by various factors; e.g., dose, route of administration, metabolism, fat solubility, urine volume and pH

<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>Marijuana/Pot</td>
<td>1-3 hours</td>
<td>1-7 days</td>
</tr>
<tr>
<td>Crack (Cocaine)</td>
<td>2-6 hours</td>
<td>3-3 days</td>
</tr>
<tr>
<td>Heroin (Opiates)</td>
<td>2-6 hours</td>
<td>3-3 days</td>
</tr>
<tr>
<td>Speed/Uppers</td>
<td>4-6 hours</td>
<td>2-3 days</td>
</tr>
<tr>
<td>(Amphetamine, methamphetamine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecstasy</td>
<td>2-7 hours</td>
<td>2-4 days</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>2-7 hours</td>
<td>3-4 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>6-12 hours</td>
<td>2-7 days</td>
</tr>
<tr>
<td>Oxycodone</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

URINE SPECIMEN INTEGRITY

SPECIMEN COLOR RELATED TO CONCENTRATION

Concentrated samples more reliable than dilute samples

TEMP WITHIN 4 MINUTES OF VOIDING IS 90-100ºF

pH FLUCTUATES WITHIN RANGE OF 4.5-8.0

CREATININE VARIES WITH HYDRATION

Normal urine: >20 mg/dL Dilute creatinine <20 mg/dL and specific gravity <1.003 Creatinine <2 mg/dL not consistent with human urine

INTERPRETATION OF UDT RESULTS

NEGATIVE RESULT

• Demonstrates recent use
  • Most drugs in urine have detection times of 1-3 days
  • Chronic use of lipid-soluble drugs: test positive for ≥1 week

• Does not diagnose
  • Drug addiction, physical dependence, or impairment
  • Does not provide enough information to determine
    • Exposure time, dose, or frequency of use

• Does not diagnose diversion
  • More complex than presence or absence of a drug in urine
  • May be due to maladaptive drug-taking behavior
  • Binging, running out early
  • Other factors: e.g., cessation of insurance, financial difficulties

POSITIVE RESULT

EXAMPLES OF METABOLISM OF OPIOIDS

<table>
<thead>
<tr>
<th>Codeine</th>
<th>Morphine</th>
<th>6-MAM*</th>
<th>Heroin</th>
<th>3-MAM*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6-25-30 MIN</td>
<td></td>
<td>3-5 MIN</td>
</tr>
</tbody>
</table>

CHALLENGE: THE OFFENDED PATIENT

RED FLAG:

You decide not to request routine risk assessment for fear of creating conflict

Mrs. Lane and her family have been your patients for years. She has chronic headache and back pain treatment. When you ask her to take a UDT, she becomes upset and accuses you of not trusting her. You decide against further risk assessments because you are concerned about damaging the relationship.

Action:

Require all patients receiving opioids to follow a treatment plan and adhere to defined expectations. Create office policy for performing UDT for patients receiving opioids beyond two weeks. Practice universal precautions. Explain to patient that you must meet the standards of care that include evaluation of risk in all patients, use of PRAs, and other tools.
PART 2
DISCONTINUING

REASONS FOR DISCONTINUING OPIOIDS

PAIN LEVEL DECREASES IN STABLE PATIENTS
INTOLERABLE AND UNMANAGEABLE AEs
NO PROGRESS TOWARD THERAPEUTIC GOALS

MISUSE
• 1 or 2 episodes of increasing dose without prescriber knowledge
• Sharing medications
• Unapproved opioid use to treat another symptom (e.g., insomnia)

ABERRANT BEHAVIORS
• Use of illicit drugs or unprescribed opioids
• Repeatedly obtaining opioids from multiple outside sources
• Prescription forgery
• Multiple episodes of prescription loss
• Diversion

TAPER DOSE WHEN DISCONTINUING

• Minimize withdrawal symptoms in opioid-dependent patient, consider medications to assist with withdrawal
• May use a range of approaches from slow 10% dose reduction per week to more rapid 25%-50% reduction every few days
• If opioid use disorder or a failed taper, refer to addiction specialist or consider opioid agonist therapy
• Counseling and relaxation strategies needed

CHAPTER 5 – PEARLS FOR PRACTICE

• Establish informed consent and PPA at the beginning
• Educate the whole team: patients, families, caregivers
• Refer if necessary
• Anticipate opioid-induced respiratory depression and constipation
• Follow patients closely during times of dose adjustments
• Periodically evaluate functional outcomes
• Discontinue opioids slowly and safely

CHALLENGE: IS THIS A LAB ERROR?

RED FLAG:
The questionable Urine Drug Test

Donald has been prescribed oxycodone for six months to treat back pain. His UDT at six months comes back negative in all areas. He tells you that he is taking his meds.

Action:
Do not discharge the patient as the first action. Contact the lab and discuss the test and any metabolite or specimen integrity issues. Ask: Is this the right lab test? Repeat the UDT and document everything. Discuss with the patient.

CHALLENGE: PATIENTS WHO ARE NOT WHO THEY APPEAR

RED FLAG:
Patient wants to control their pill mg dose and taper plan

Tom has back pain. He is managed by taking oxycodone (40 mg BID) but wants to decrease his dose when he can, thus he requests only 20 mg pills. He often brings in unused meds to show how he is trying to reduce his dose. He resists any change.

Action:
Do not allow patient to taper on their own. Create an endpoint for the taper. See patient once a week with a seven-day supply for the tapering until they are off opioids. Document teaching, patient’s comments about the plan, UDT, pill counts, non-pharmacological modalities for pain management, and their adherence to this plan.
Knowledge Test Question

2. Which of the following is most important to consider when determining a starting dosage of an extended-release/long-acting opioid?

A. Results of urine drug test
B. Patient preference
C. Cost of the medications
D. Assessment of individual needs
E. Starting dosage listed in the package insert

Rationale: Opioid selection, initial dosing, and titration should be individualized according to the patient’s health status, previous exposure to opioids, attainment of therapeutic goals and predicted or observed harms. Genetic differences are increasingly understood to help explain individual differences in analgesic response and tolerance to various opioids.

References:

Correct answer: D. Assessment of individual needs

Knowledge Test Question

3. A 55-year-old man who is being treated for chronic low back pain after undergoing laminectomy comes for follow-up evaluation. A trial of oxycodone ER therapy is planned. Completion of which of the following is the most appropriate step before initiation of therapy?

A. Oswestry Disability Index
B. Roland Morris Disability Questionnaire
C. Patient-Prescriber Agreement
D. MRI of the lumbar spine
E. Routine blood tests

Rationale: Informed consent and patient-prescriber agreements are important strategies to ensure that patients understand treatment goals and potential opioid risks.

References:

Correct answer: C. Patient-Prescriber Agreement

OLDER ADULTS

RISK FOR RESPIRATORY DEPRESSION

- Age-related changes in distribution, metabolism, excretion; absorption less affected

MONITOR

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

ROUTINELY INITIATE A BOWEL REGIMEN
KNOW THE REPRODUCTIVE PLANS AND PREGNANCY STATUS OF YOUR PATIENTS

- 40% of women with childbearing potential are prescribed opioids
- Opioid exposure during pregnancy causes increased risk for fetus
- Most women do not know they are pregnant in first few weeks
- Therefore all women of childbearing age are at risk
- No adequate nor well-controlled studies of opioids for pain in pregnancy

WOMEN WITH CHILDBEARING POTENTIAL

THE PREGNANT PATIENT

Potential risk of opioid therapy to the newborn is neonatal opioid withdrawal syndrome

GIVEN THESE POTENTIAL RISKS, CLINICIANS SHOULD:

- Counsel women of childbearing potential about risks and benefits of opioid therapy during pregnancy and after delivery
- Encourage minimal/no 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

- If chronic opioid therapy is used during pregnancy, anticipate and manage risks to the patient and newborn
- If using opioids on a daily basis, consider methadone or buprenorphine

CHILDREN AND ADOLESCENTS: HANDLE WITH CARE

JUDICIOUS USE OF IR FOR BRIEF THERAPY

SAFETY AND EFFECTIVENESS OF MOST ER/LA OPIOIDS ESTABLISHED

- Pediatric analgesic trials pose challenges
- Transdermal fentanyl approved in children aged ≥2 yrs
- Oxycodone ER dosing changes for children ≥11 yrs

ER/LA OPIOID INDICATIONS ARE PRIMARILY LIFE-LIMITING CONDITIONS

WHEN PRESCRIBING ER/LA OPIOIDS TO CHILDREN:

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

CHALLENGE: VULNERABILITY IN CO-DEPENDENT OLDER ADULTS

RED FLAG: Questionable family diversion

78-year-old Thelma comes into clinic, accompanied by grandson, who is in the exam room with you and Thelma. Thelma says her oxycodone 10 mg tablets q 4 hours is no longer working for her back pain. She asks for more medicine. You ask grandson to leave the exam room so you can examine her privately.

Action: Based on exam findings and her request for more medication:

- UDT and PDMP check
- Discuss whether or not it is possible her grandson, or another family member, might be using her medications.
- Patient education: Do not give opioids to another person. Store in secure place—locked. Let you know if medications are not secure or if she feels any pressure about sharing medications.

FEDERAL AND STATE REGULATIONS

Comply with federal and state laws and regulations that govern the use of opioid therapy for pain

FEDERAL

- Code of Federal Regulations, Title 21 Section 1306: rules governing the issuance and filling of prescriptions pursuant to section 309 of the Act (21 USC 829)
  www.deadiversion.usdoj.gov/21cfr/21usc/829.htm

STATE

- Database of state statutes, regulations, and policies for pain management
  www.medscape.com/resource/pain/opioid-policies
- www.medstats.medscape.com/medstats/policies

KNOW YOUR FEDERAL AND STATE LAWS

CHAPTER 7

FEDERAL

- Code of Federal Regulations, Title 21 Section 1306: rules governing the issuance and filling of prescriptions pursuant to section 309 of the Act (21 USC 829)
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  www.medstats.medscape.com/medstats/policies
**Opioid Prescribing: Safe Practice, Changing Lives**

**State Specific Information**

**Texas**

www.dshs.texas.gov/

Created: September 2016

Updated: December 2017

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

**PDMP: Prescription Drug Monitoring Program**

- Texas Prescription Monitoring Program
  - Administered by the Board of Pharmacy
  - Schedule II-V are monitored
  - Dispensers and Prescribers are required to register and input data
  - Before prescribing, there is not an obligation to review under certain circumstances

**General**

- Prescribers; dispensers; state regulatory boards and law enforcement
- Prescribers can authorize a registered delegate

**Access**

- Must be entered into PDMP by next business day after dispensing
- Unsolicited reports/alerts are sent to law enforcement only
- Texas 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

**Reporting**

- Existing prescriptions not reported by patient
- Multiple prescribers/pharmacies
- Drugs that increase overdose risk when taken together
- Patient pays with cash (vs insurance) for controlled meds

**PDMP BENEFITS**

- Provides full accounting of prescriptions filled by patient
- Opportunity to discuss with patient

**Content Outline**

- Prescription Drug Monitoring Program (PDMP)
- Prescriber Status and Education Requirements
- Naloxone Regulation
- Medical and Recreational Marijuana Status
- Patient Prescriber Agreement & Treatment Programs

**Prescriber Status and Education Requirements**

<table>
<thead>
<tr>
<th>Physician</th>
<th>Physician Assistant</th>
<th>Advanced Practice Nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed</td>
<td>Schedule II-V</td>
<td>Schedule III-V</td>
</tr>
</tbody>
</table>

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

Effective date • September 2015

Criminal Immunity
• Prescribers: Yes
• Dispensers: Yes
• Lay People: Yes

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

Carried by First Responders • Yes

Marijuana Status

Medical

Recreational Not legal for recreational use in Texas

Patient Prescriber Agreement and Treatment Programs

- A Patient Prescriber Agreement (PPA) is recommended or required
- For a list of treatment programs in this state:

Patient Prescriber Agreement and Treatment Programs

Patient Prescriber Agreement and Treatment Programs

Patient Prescriber Agreement and Treatment Programs

Patient Prescriber Agreement and Treatment Programs

Patient Prescriber Agreement and Treatment Programs

Patient Prescriber Agreement and Treatment Programs

Patient Prescriber Agreement and Treatment Programs

Knowledge Test Question

4. A 63-year-old woman with a history of spinal stenosis and peripheral neuropathy secondary to breast cancer treatment comes for evaluation because of increasingly severe back pain. She describes the pain as a constant ache after doing yard work. She underwent chemotherapy 12 years ago. Medications include an opioid. Which of the following is the most appropriate next step?

A. Assure the patient that the heightened sensitivity to pain is to be expected
B. Reevaluate the underlying medical condition
C. Refer the patient to physical therapy and administer a short-acting opioid as necessary
D. Increase extended-release/long-acting opioid therapy dosage for up to one month
E. Consider adding an adjuvant analgesic for neuropathic pain

Correct answer: B. Reevaluate the underlying medical condition

Rationale: A change in pain or new pain may indicate significant progression in a disease or a new underlying medical disorder that warrants further medical evaluation. New or worsening pain, especially if worse at night or with recumbency in the cancer survivor is concerning for return of malignancy.

References:

Knowledge Test Question
Knowledge Test Question

5. Use of ER/LA opioids in pediatric patients <18 years of age deserves special consideration because
   A. Safety & effectiveness of most ER/LA opioids has not been established in this population
   B. Many children experience chronic pain
   C. Starting doses of opioids are reduced
   D. Opioid risk screening tools have not been validated in this population
   E. Many state laws require consultation with a pediatric pain specialist or pain clinic

   • Conduct a comprehensive and pain-focused H&P
   • Assess for risk of abuse and for mental health issues
   • Establish realistic goals for pain management and function
   • Document EVERYTHING

Knowledge Test Question

6. A 59 year-old with long-standing hypertension and stage 3 chronic kidney disease continues treatment with disease-modifying anti-rheumatic drugs (DMARDs) for rheumatoid arthritis (RA). Recently she has experienced increasing pain and further functional decline likely due to progression of RA and osteoarthritis of the hips, knees, and feet as well. She continues to be employed and able to take a short walk to visit a friend. The following is the best next step for addressing this patient’s pain.
   A. Acetaminophen 650 mg two tabs q 4 hours prn
   B. Duloxetine 20 mg daily
   C. Oxycodone IR 5 mg q 4 hours prn
   D. Morphine sulfate ER 15 mg q 8 hours
   E. Ibuprofen 600 mg q 4 hours prn

   • Establish realistic goals for pain management and function
   • Document EVERYTHING

CHAPTER 8
COUNSELING PATIENTS AND CAREGIVERS

Knowledge Test Question

Correct answer: A. Safety & effectiveness of most ER/LA opioids has not been established in this population

Rationale: Opioid use in children deserves special consideration because the safety and effectiveness of most ER/LA opioids has not been established in this population. Opioid use in children is based on off-label use.

   • Conduct a comprehensive and pain-focused H&P
   • Assess for risk of abuse and for mental health issues
   • Establish realistic goals for pain management and function
   • Document EVERYTHING

Knowledge Test Question

Correct answer: C. Oxycodone IR 5 mg q 4 hours pm

Rationale: Adding an immediate release opioid is the next best step for this patient experiencing moderate to severe pain. Adding another opioid, such as oxycodone, would be appropriate and effective for this patient’s pain.

   • Conduct a comprehensive and pain-focused H&P
   • Assess for risk of abuse and for mental health issues
   • Establish realistic goals for pain management and function
   • Document EVERYTHING

USE PATIENT COUNSELING DOCUMENT

DOWNLOAD:

ORDER HARD COPIES:
www.minneapolis.cenveo.com/pcc/submit ORDER HARD COPIES:
www.er relieves the pain of arthritis and inflammation. It is important to discuss the potential side effects and benefits with the patient and their caregiver. The counseling document can be downloaded for free from the website provided.
COUNSEL PATIENTS ABOUT PROPER USE

EXPLAIN

- Product-specific information about the IR or ER/LA opioid (especially when converting)
- Take opioid as prescribed
- Adhere to dose regimen
- How to handle missed doses
- Notify prescriber if pain not controlled
- Call prescriber for options on side effect management

INSTRUCT PATIENTS/ CAREGIVERS TO

- Read the ER/LA opioid Medication Guide received from pharmacy every time an ER/LA opioid is dispensed

OPIOIDS SHOULD BE STORED IN A SAFE AND SECURE PLACE

- Away from children, family members, visitors, and pets
- Safe from theft

OPIOIDS CAN CAUSE DEATH EVEN WHEN TAKEN PROPERLY

- Signs/symptoms are respiratory depression, gastrointestinal obstruction, allergic reactions

WARN PATIENTS

Never break, chew, crush, or snort an oral ER/LA tablet/capsule, or cut or tear patches prior to use
- May lead to rapid release of ER/LA opioid causing overdose and death
- If unable to swallow a capsule whole, refer to PI to determine if appropriate to sprinkle contents on applesauce or administer via feeding tube
- Use of CNS depressants or alcohol with ER/LA opioids can cause overdose & death
- Use with alcohol may result in rapid release and absorption of a potentially fatal opioid dose—"dose dumping"
- Other depressants include sedative-hypnotics and anxiolytics, illegal drugs

OPIOIDS ARE SCHEDULED UNDER Controlled Substances Act and can be misused and abused

Use of CNS depressants or alcohol with ER/LA opioids can cause overdose & death
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- Other depressants include sedative-hypnotics and anxiolytics, illegal drugs

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

Naloxone:
- An opioid antagonist administered by injection or intranasally, or IV
- Reverses acute opioid-induced respiratory depression but will also reverse analgesia

Available as:
- Naloxone kit (with syringes, needles)
- Injectable
- Nasal spray

What to do:
- Discuss an "overdose plan"
- Involve and train family, friends, partners, and/or caregivers
- Check with pharmacy if they are prescribing
- Check expiration dates and keep a viable dose on hand
- In the event of known or suspected overdose, administer naloxone and call 911

Consider offering a naloxone prescription to all patients prescribed IR and ER/LA opioids

### Substances Parents Have Discussed with Teens*

<table>
<thead>
<tr>
<th>Substance</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer/Alcohol</td>
<td>30%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>15%</td>
</tr>
<tr>
<td>Cocaine/club</td>
<td>15%</td>
</tr>
<tr>
<td>Re-pain reliever w/ doctor’s Rx</td>
<td>21%</td>
</tr>
<tr>
<td>Any Rx drug used w/ doctor’s Rx</td>
<td>21%</td>
</tr>
<tr>
<td>Heroin</td>
<td>10%</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>10%</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>10%</td>
</tr>
<tr>
<td>Non-Rx cold/cough medicine to get high</td>
<td>15%</td>
</tr>
<tr>
<td>Stimulants w/ doctor’s Rx</td>
<td>10%</td>
</tr>
<tr>
<td>Inhalants</td>
<td>10%</td>
</tr>
</tbody>
</table>

*As reported by teens

### RX Opioid Disposal

New “Disposal Act” expands ways for patients to dispose of unwanted/expired opioids

**Decreases Amount of Opioids Introduced into the Environment, Particularly into Water**

<table>
<thead>
<tr>
<th>Collection receptacles</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Call DEA Registration Call Center at 1-800-882-9539 to find a local collection receptacle</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mail-back packages</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtained from authorized collectors</td>
<td></td>
</tr>
</tbody>
</table>

Look for local take-back events:
- Conducted by Federal, State, tribal, or local law enforcement
- Partnering with community groups

**Voluntarily maintained by:**
- Law enforcement
- Authorized collectors, including:
  - Manufacturer
  - Distributor
  - Reverse distributor
  - Retail or hospital/clinics pharmacy
    - Including long-term care facilities

### Other Methods of Opioid Disposal

**If collection receptacle, mail-back program, or take-back event unavailable, throw out in household trash**

- Take drugs out of original containers
- Mix with undesirable substance
- Place in sealable bag, can, or other container
- Remove identifying info on label

### FDA: Prescription Drug Disposal

**Flush down sink/toilet if no collection receptacle, mail-back program, or take-back event available**

- As soon as they are no longer needed
- Includes transdermal adhesive skin patches
  - Used patch (3 days) still contains enough opioid to harm/kill a child
  - Dispose of used patches immediately after removing from skin
- Fold patch in half so sticky sides meet; then flush down toilet
- Do NOT place used or unneeded patches in household trash
- Butrans (buprenorphine transdermal system)
  - Exception: can seal in Patch-Disposal Unit provided and dispose of in the trash

### Chapter 8 – Pearls for Practice

- Use formal tools (PPAs, counseling document) to educate patients and caregivers
- Emphasize safe storage and disposal to patients and caregivers
- Consider co-prescribing naloxone
7. An **inappropriate** method to dispose of unused opioid medication is:
   - A. Return the medication to a pharmacy
   - B. At a law-enforcement sponsored drug take back event
   - C. Mix into an undesirable substance
   - D. Dispose of medication in the regular trash
   - E. Flush down the toilet

   **Correct answer:** D. Dispose of medication in the regular trash

   **Rationale:** Recommendations from FDA, package inserts, and the literature for best methods of disposal vary, but all agree that simply throwing away medications is inappropriate.

8. The most important reason a patient should be counseled to never break, cut, chew, or crush a ER/LA opioid tablet or cut or tear patches is because:
   - A. The medicine will expire
   - B. It is against the law
   - C. The dose will be less than prescribed
   - D. The patient may die
   - E. None of the above

   **Correct answer:** D. The patient may die

   **Rationale:** Tablets should not be chewed, crushed or dissolved. Crushing or dissolving the tablet results in the immediate release of the dosage leading to overdose which can result in respiratory depression and death.

9. To avoid inadvertent overdose and death a patient should be counseled to avoid co-administration of an extended-release opioid with which of the following?
   - A. Alcohol
   - B. Diphenhydramine
   - C. St. John’s wort
   - D. Aspirin
   - E. Methamphetamine

   **Correct answer:** A. Alcohol

   **Rationale:** Use of other CNS depressants such as sedative-hypnotics and antianxiety drugs, alcohol, or illegal drugs with ER/LA opioid can cause overdose leading to death.
Knowledge Test Question

10. Which of the following extended-release/long-acting opioids is most likely to induce a peak respiratory depression that occurs later and persists longer than the analgesic effect?

A. Fentanyl transdermal patch
B. Hydromorphone ER
C. Methadone
D. Oxycodone CR
E. Tapentadol ER

Correct answer: C. Methadone

Rationale: Methadone has a long, biphasic elimination half-life. It may take up to 10 days to reach steady-state serum levels. The analgesic effect occurs more quickly than the peak respiratory depression, which may occur later and persist longer than the analgesic effect of methadone. Methadone is a highly lipophilic drug. Tissue binding predominates over binding to plasma proteins, and accumulation of the drug occurs in the tissues with repeated dosing. Methadone reabsorption from the tissue may continue for weeks after administration has ceased.

References:

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

CNS depressants can potentiate sedation and respiratory depression

Some ER/LA products rapidly release opioid (dose dump) when exposed to alcohol

Use with MAOIs may increase respiratory depression

Can reduce efficacy of diuretics

Certain opioids with MAOIs can cause serotonin syndrome

Drugs that inhibit or induce CYP enzymes can increase or lower blood levels of some opioids

Methadone and buprenorphine can prolong QTc interval

DRUG INTERACTIONS COMMON TO OPIOIDS

- Concurrent use with other CNS depressants can increase risk of respiratory depression, hypotension, profound sedation, or coma
- Reduce initial dose of one or both agents
- Avoid concurrent use of partial agonists* or mixed agonist/antagonists† with full opioid agonist
- May reduce analgesic effect and/or precipitate withdrawal

- May enhance neuromuscular blocking action of skeletal muscle relaxants and increase respiratory depression
- Concurrent use with anticholinergic medication increases risk of urinary retention and severe constipation
- May lead to paralytic ileus

*Buprenorphine, Naltrexone, naldorphine, butorphanol
 †Buprenorphine, pentazocine, nalbuphine, butorphanol
SPECIFIC CHARACTERISTICS

Know for opioid products you prescribe:

- Drug substance
- Formulation
- Strength
- Dosing interval
- Key instructions
- Use in opioid-tolerant patients
- Product-specific safety concerns
- Relative potency to morphine
- Specific information about product conversions, if available

SUMMARY

Prescription opioid abuse and overdose is a national epidemic. Clinicians must play a role in prevention.

Knowledge Test Question

11. When using an equianalgesic table to rotate opioids other than methadone, an important step to account for incomplete cross-tolerance among mu opioids includes:

A. Initiate the new opioid at the calculated equianalgesic dose
B. Increase the calculated equianalgesic dose by 10%
C. Reduce calculated equianalgesic dose by 25%
D. Convert and total all opioids to oral morphine equivalents
E. Refer to the package insert for appropriate supplemental rescue dose

Correct answer: C. Reduce calculated equianalgesic dose by 25%

Rationale: Equianalgesic doses are approximate and most are based on single dose studies. The doses are to be used only when converting to a different opioid. Patients can become tolerant to the analgesic and side effects of a given opioid but not exhibit the same tolerance to another opioid. This is called incomplete cross-tolerance; meaning caution must be used when switching to a different opioid. When switching to a different opioid, it is recommended that a dose reduction of 25-50% should be made depending on the clinical situation.

Knowledge Test Question

12. A 72 year-old grandfather with severe persistent abdominal pain from colon cancer has been taking an immediate release opioid every four hours around the clock. He and his wife care for their two young grandchildren, and he states that he can no longer help with their care due to his pain level. He wants to increase the dose of his medication and asks what else he might do to control the pain.

A. More consistent plasma concentrations
B. Less need for ongoing monitoring
C. Less pain
D. Less need for nonopioid analgesics
E. More oral administration

Correct answer: D. Less need for nonopioid analgesics

Rationale: An ER/LA opioid offers more consistent plasma concentration. It would not offer fewer adverse events. A therapeutic trial is a risk for all opioids. Opioid treatment IR or ER requires ongoing monitoring. When switching to a different opioid, it is recommended that a dose reduction of 25-50% should be made.
13. A 67-year-old female with severe knee osteoarthritis has recently been converted from an immediate release opioid for pain control. She has chronic obstructive pulmonary disease that has made her a poor surgical candidate. In addition to extended release opioid, which second prescription would you consider?
A. naloxone
B. nortriptyline
C. duloxetine
D. acetaminophen

Correct answer: A. Naloxone
Rationale: Naloxone is appropriate for co-prescribing with all opioid prescriptions. The addition of the other medications may be appropriate in the future, but medications changes are best done one at a time. Naloxone prescribing is strictly for safety and reversal of adverse side effects, particularly respiratory depression particularly in this patient with underlying pulmonary disease.

14. A positive result of hydromorphone of a urine drug toxicology test for a patient on prescribed morphine can be interpreted as
A. Use of heroin in past month
B. Proof of supplemental hydromorphone
C. Presence of the oxycodone metabolite
D. Presence of the morphine metabolite
E. Presence of semisynthetic opioids

Correct answer: D. Presence of the morphine metabolite
Rationale: In certain cases, small amounts of opioid metabolites may appear in the urine (hydrocode from codeine, hydromorphone from hydrocodeone or morphine, oxymorphone from oxycodone) and should not be interpreted as evidence of the use of nonprescribed agents. Though heroin metabolizes to morphine and could ultimately produce hydromorphone metabolites, the quantities that would appear in the urine would be much smaller than those seen with the use of heroin. Thus, detecting a morphine metabolite in a urine drug screen is often associated with natural processes and is not reliably identified as evidence of non-prescribed agents.

YOUR PARTICIPATION IS IMPORTANT

Thank you for completing the post-activity assessment for this CO*RE session. Your participation in this assessment allows CO*RE to report de-identified numbers to the FDA. A strong show of engagement will demonstrate that clinicians have voluntarily taken this important education and are committed to patient safety and improved outcomes.

THANK YOU!