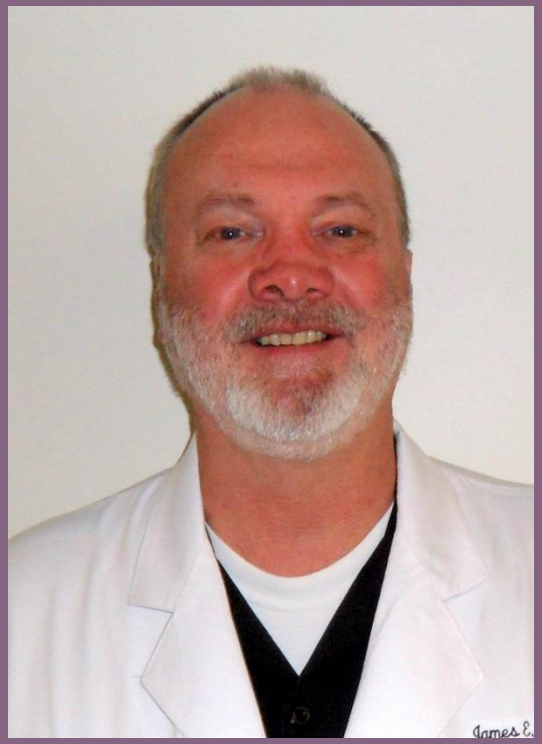
ER/LA OPIOID REMS:

Achieving Safe Use While Improving Patient Care

Presented by CO*RE
Collaboration for REMS Education
www.core-rems.org

Collaborative for
REMS Education

James Preston, D.O., FAODME



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DISCLOSURE:

Dr. Preston has nothing to disclose.

Collaborative for REMS Education

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.

Founded in June, 2010, the Collaborative on REMS Education (CO*RE), a multi disciplinary team of 10 partners and 3 cooperating organizations, has designed a core curriculum based on needs assessment, practice gaps, clinical competencies, and learner self-assessment to meet the requirements of the FDA REMS Blueprint.

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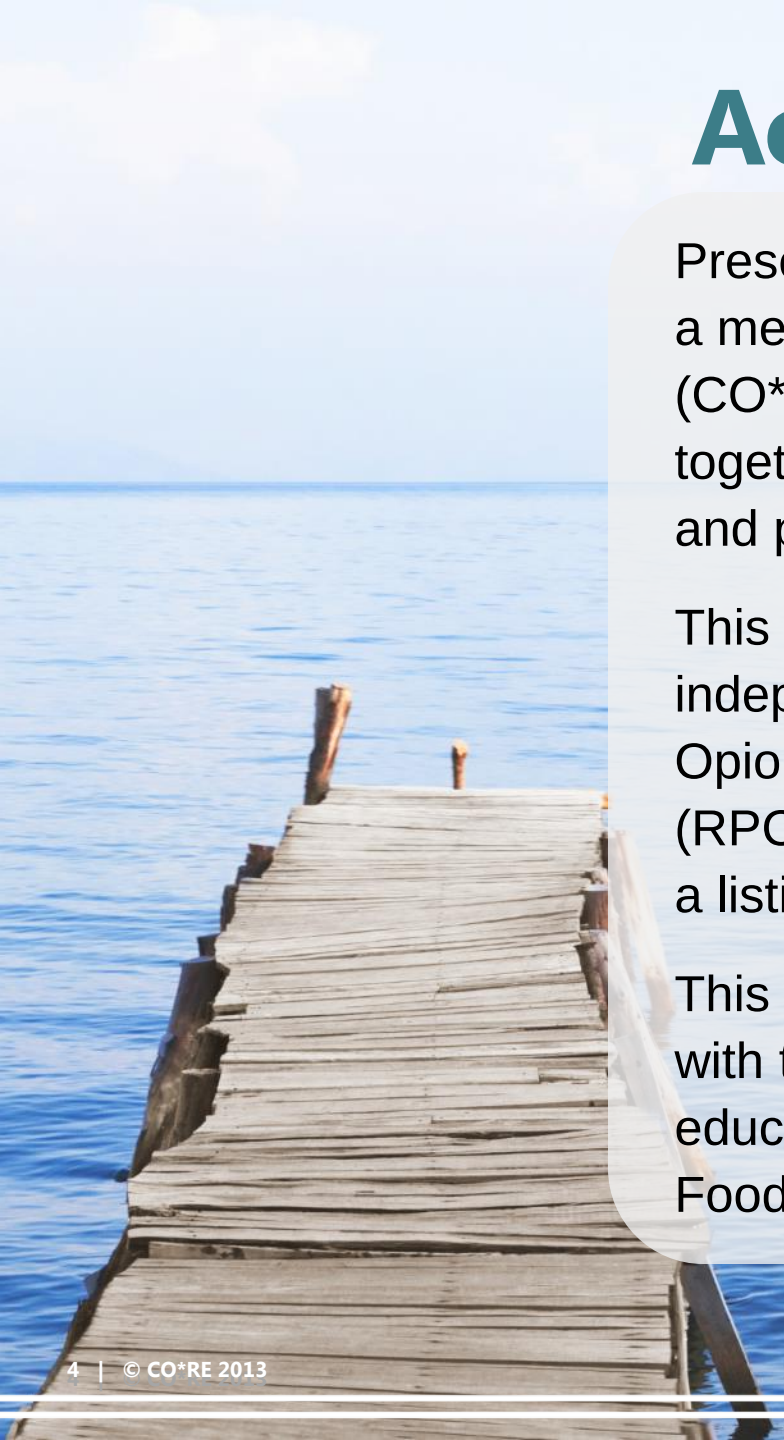
Acknowledgement



Presented by the American Osteopathic Association, a member of the Collaborative on REMS Education (CO*RE), 10 interdisciplinary organizations working together to improve pain management and prevent adverse outcomes.

This educational activity is supported by an independent educational grant from the ER/LA Opioid Analgesics REMS Program Companies (RPC). Please see www.er-la-opioidREMS.com for a listing of the member companies.

This activity is intended to be fully compliant with the ER/LA Opioid Analgesics REMS education requirements issued by the U.S. Food & Drug Administration.

Products Covered by this REMS

Brand Name Products

- Avinza® morphine sulfate ER capsules
- Butrans® buprenorphine transdermal system
- Dolophine® methadone hydrochloride tablets
- Duragesic® fentanyl transdermal system
- *Embeda® morphine sulfate/naltrexone ER capsules
- Exalgo® hydromorphone hydrochloride ER tablets
- Kadian® morphine sulfate ER capsules
- Methadose™ methadone hydrochloride tablets
- MS Contin® morphine sulfate CR tablets
- Nucynta® ER tapentadol ER tablets
- Opana® ER oxymorphone hydrochloride ER tablets
- OxyContin® oxycodone hydrochloride CR tablets
- †Palladone® hydromorphone hydrochloride ER capsules

Generic Products

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

* Not currently available due to voluntary recall (still approved);
† No longer marketed (still approved)

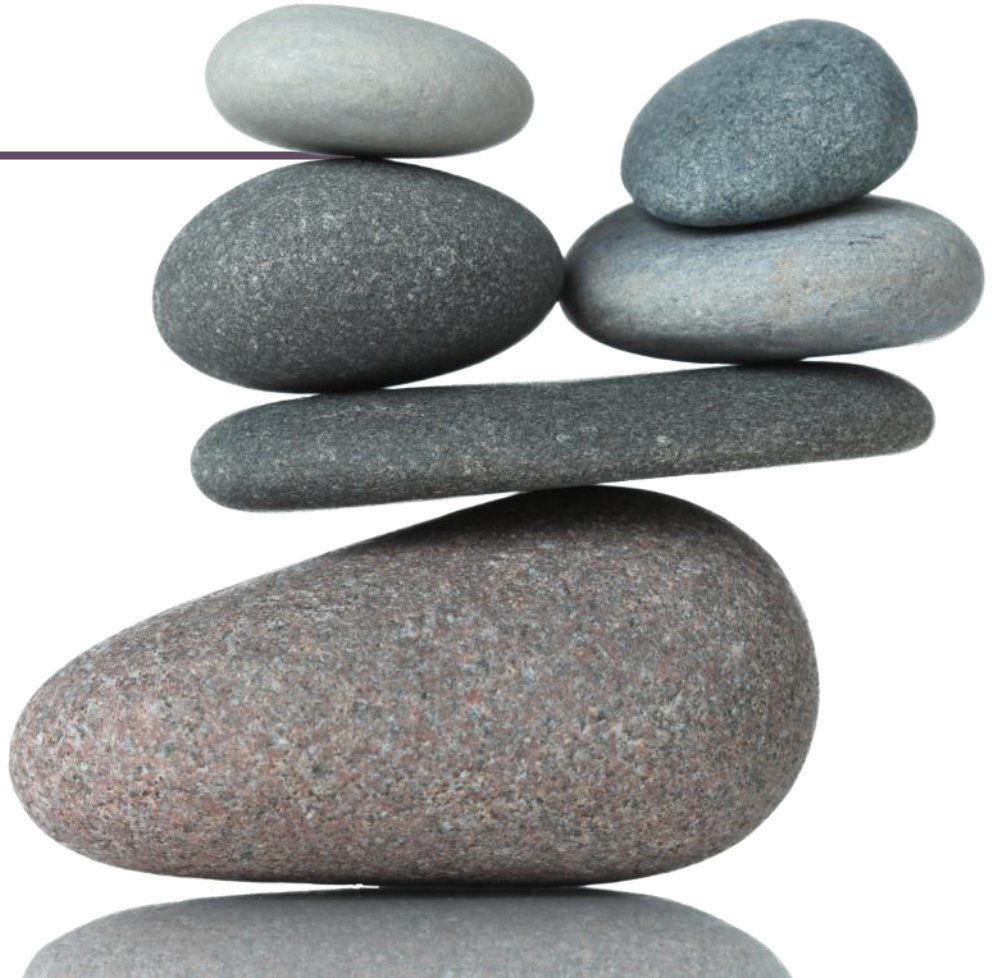
FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Heads Up: Zohydro

- Not yet officially included in FDA Blue Print
- Release approved by FDA in Fall, 2013
- Release set for March, 2014 though many seek to block its release
- Concerns revolve around
  - Potential misuse as Zohydro contains five times the amount of hydrocodone found in IR
  - Zohydro does not have built in abuse deterrence mechanism
- Stay tuned.

WHY PRESCRIBER EDUCATION IS IMPORTANT

Introduction



Prescribers of ER/LA Opioids Should Balance:

The benefits of prescribing ER/LA opioids to treat pain

The risks of serious adverse outcomes

Opioid Misuse/Abuse is a Major Public Health Problem

Improper use of any opioid can result in serious AEs including overdose & death

This risk can be greater w/ ER/LA opioids

ER opioid dosage units contain more opioid than IR formulations

In 2011

34.2 million Americans age ≥12 had used an opioid for nonmedical use some time in their life

Methadone is a potent opioid with a long, highly variable half-life

In 2010

425,247 ED visits involved nonmedical use of opioids

- *Methadone involved in 30% of prescription opioid deaths*

SAMHSA. (2012). *Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings*, NSDUH Series H-44, HHS Publication No. (SMA) 12-4713. Rockville, MD. SAMHSA. (2012). *The DAWN Report: Highlights of the 2010 Drug Abuse Warning Network (DAWN) Findings on Drug-Related Emergency Department Visits.* Rockville, MD. CDC. CDC Vital Signs. *Prescription Painkiller Overdoses. Use and abuse of methadone as a painkiller*. 2012. FDA. *Questions and Answers: FDA approves a Risk Evaluation and Mitigation Strategy for Extended-Release and Long-Acting Opioid Analgesics.* www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm309742.htm. 2012.

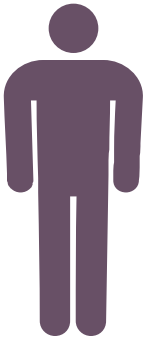
In 2009

39,147 Americans

DIED FROM DRUG POISONINGS

Nearly 14,800 Deaths involved prescriptions opioids

For every **1** death there are:



10 treatment admissions for abuse

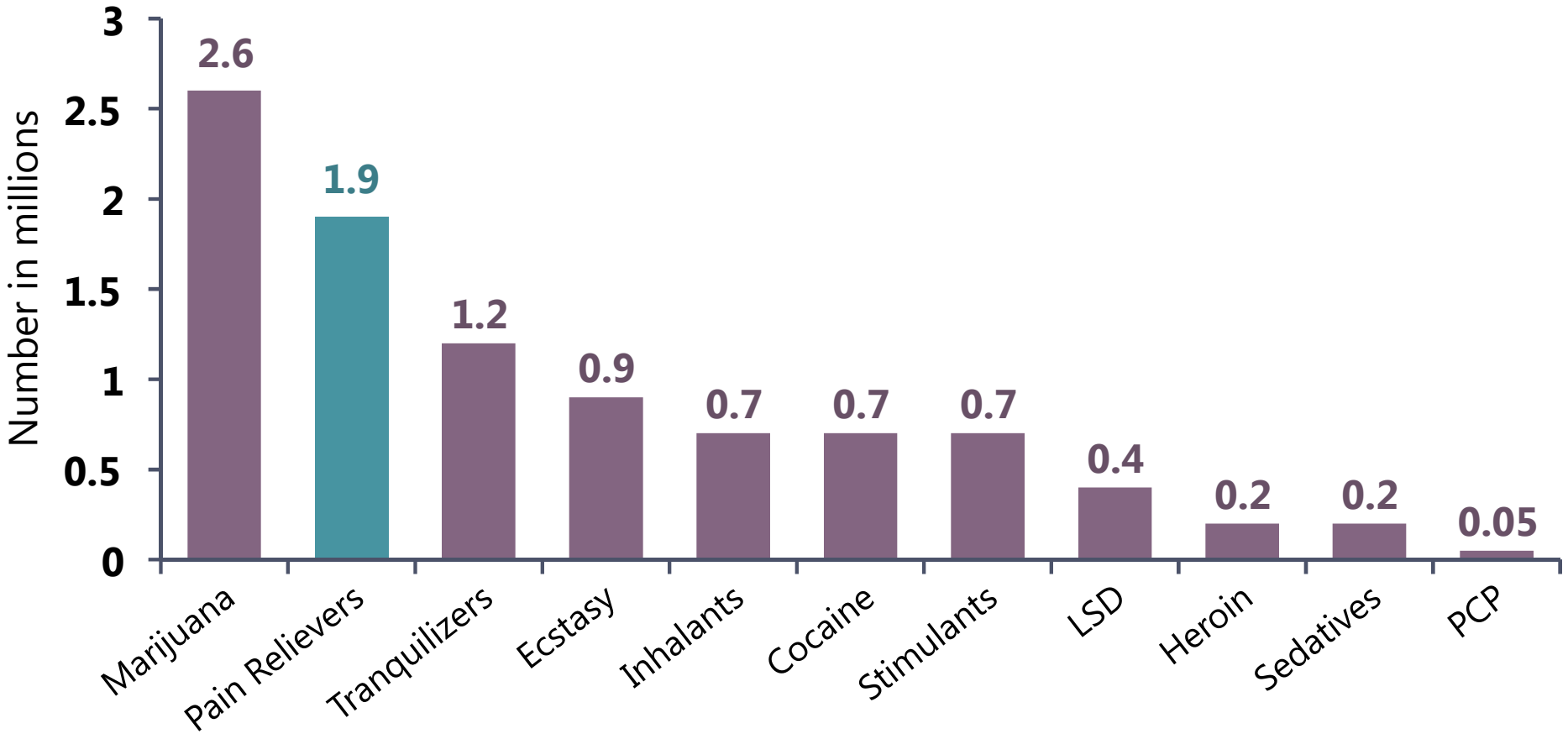
32 ED visits for misuse or abuse

130 people who abused or are addicted

825 Nonmedical users

Kochanek KD, et al. *National Vital Statistics Report* 2011;60:1-117. CDC Vital Signs. *Prescription Painkiller Overdoses. Use and abuse of methadone as a painkiller*. 2012. Warner M, et al. *Drug poisoning deaths in the United States, 1980-2008.* NCHS data brief, no 81. Hyattsville, MD: National Center for Health Statistics. 2011. National Center for Injury Prevention and Control. Division of Unintentional Injury Prevention. *Policy Impact. Prescription Painkiller Overdoses*. Nov 2011.

First-Time Use of Specific Drugs Among Persons Age ≥ 12 (2011)



SAMHSA. (2012). *Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings*, NSDUH Series H-44, HHS Publication No. (SMA) 12-4713. Rockville, MD.

Learning Objectives

Describe appropriate patient assessment for treatment with ER/LA opioid analgesics, evaluating risks and potential benefits of ER/LA therapy, as well as possible misuse.

Apply proper methods to initiate therapy, modify dose, and discontinue use of ER/LA opioid analgesics, applying best practices including accurate dosing and conversion techniques, as well as appropriate discontinuation strategies.

Demonstrate accurate knowledge about how to manage ongoing therapy with ER/LA opioid analgesics and properly use evidence-based tools while assessing for adverse effects.

Employ methods to counsel patients and caregivers about the safe use of ER/LA opioid analgesics, including proper storage and disposal.

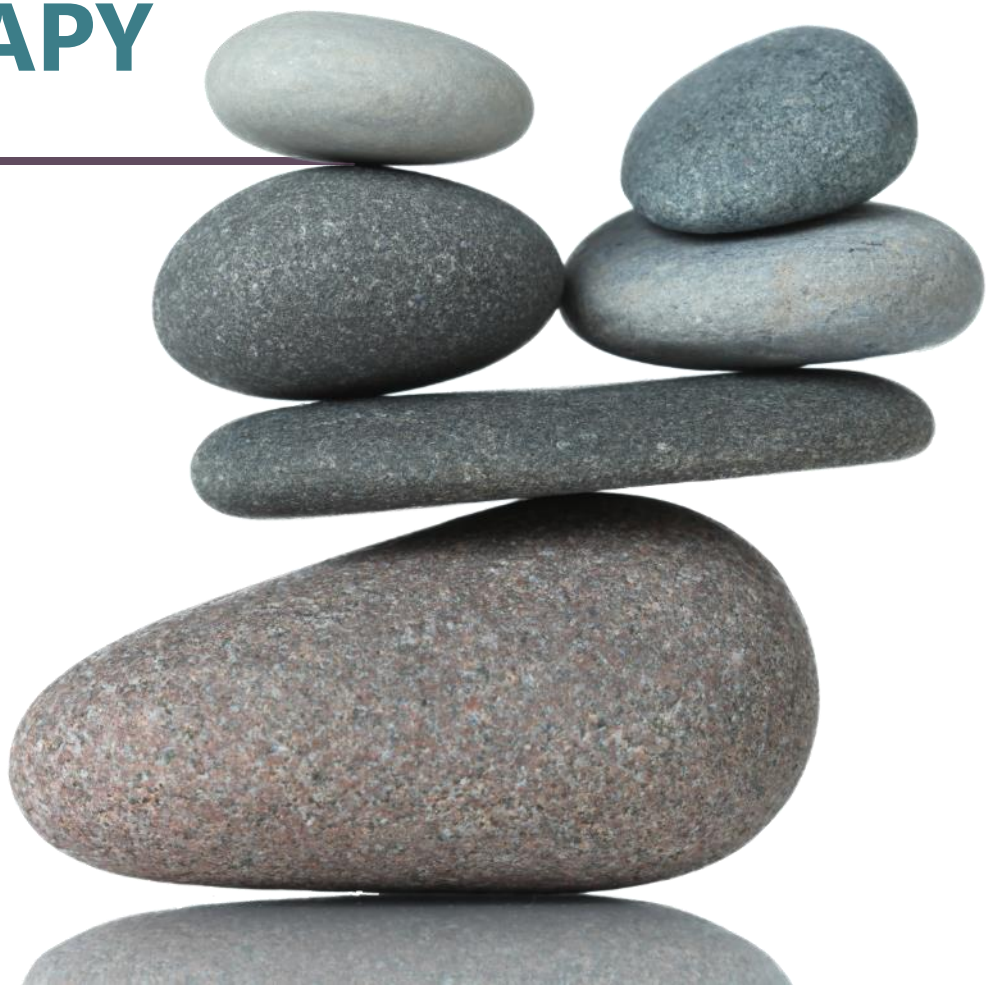
Review/assess general and product-specific drug information concerning ER/LA opioid analgesics and identifying potential adverse effects of ER/LA opioids.

Misuse, abuse, divergence and overdose of ER/LA opioids is a major public health crisis.

YOU and **YOUR TEAM** ***can*** have an immediate and positive impact on this crisis while also caring for your patients appropriately.

ASSESSING PATIENTS FOR TREATMENT WITH ER/LA OPIOID ANALGESIC THERAPY

Unit 1



Balance Risks Against Potential Benefits

Conduct thorough H&P and appropriate testing

Benefits Include

- Analgesia
  (adequate pain control)
- Improved Function

Comprehensive benefit-to-harm evaluation

Risks Include

- Overdose
- Abuse by patient or household contacts
- Misuse & addiction
- Physical dependence & tolerance
- Interactions w/ other medications & substances
- Inadvertent exposure by household contacts, especially children

Chou R, et al. *J Pain*. 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain*. 2010. FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics*. Modified 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Adequately **DOCUMENT** all patient interactions, assessments, test results, & treatment plans

Clinical Interview: Patient 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 abuse, e.g.:

Hepatitis	**HIV**	**Tuberculosis**	**Cellulitis**
STIs	**Trauma, burns**	**Cardiac disease**	**Pulmonary disease**

Chou R, et al. *J Pain*. 2009;10:113-30. Zacharoff KL, et al. *Managing Chronic Pain with Opioids in Primary Care*. 2nd ed. Newton, MA: Inflexion, Inc., 2010. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain*. 2010.

Clinical Interview: Pain & Treatment History

Description of pain

Location

Intensity

Quality

Onset/ Duration

Variations / Patterns / Rhythms

What relieves the pain?

What causes or increases pain?

Effects of pain on physical, emotional, and psychosocial function

Patient's pain & functional goals

Heapy A, Kerns RD. Psychological and Behavioral Assessment. In: Raj's Practical Management of Pain. 4th ed. 2008;279-95. Zacharoff KL, et al. Managing Chronic Pain with Opioids in Primary Care. 2nd ed. Newton, MA: Inflexion, Inc., 2010.

Clinical Interview: Pain & Treatment History, cont'd

Pain Medications

Past use

Current use

- Query state **PDMP** where available to confirm patient report
- Contact past providers & obtain prior medical records
- Conduct **UDT**

Dosage

- For opioids currently prescribed: opioid, dose, regimen, & duration
  - Important to determine if patient is **opioid tolerant**

General effectiveness

Nonpharmacologic strategies & effectiveness

Perform Thorough Evaluation & Assessment of Pain

Seek objective confirmatory data

Components of patient evaluation for pain

Order diagnostic tests (appropriate to complaint)

General: vital signs, appearance, posture, gait, & pain behaviors

Neurologic exam

Musculoskeletal Exam

- Inspection
- Palpation
- Percussion
- Auscultation
- Provocative maneuvers

Cutaneous or trophic findings

Lalani I, Argoff CE. History and Physical Examination of the Pain Patient. In: *Raj's Practical Management of Pain*. 4th ed. 2008;177-88. Chou R, et al. *J Pain*. 2009;10:113-30.

Assess Risk of Abuse, Including Substance Use & Psychiatric Hx

Obtain a complete Hx of current & past substance use

- Prescription drugs
- Illegal substances
- Alcohol & tobacco
  - Substance abuse Hx does not prohibit treatment w/ ER/LA opioids but may require additional monitoring & expert consultation/referral
- Family Hx of substance abuse & psychiatric disorders
- Hx of sexual abuse

Social history also relevant

Employment, cultural background, social network, marital history, legal history, & other behavioral patterns

Chou R, et al. *J Pain.* 2009;10:113-30. SAMHSA. *Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders.* Treatment Improvement Protocol (TIP) Series 54. HHS Publication No. (SMA) 12-4671. 2011. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.* 2010.

Risk Assessment, cont'd

Be knowledgeable about risk factors for opioid abuse	Understand & use addiction or abuse screening tools	Conduct a UDT
• Personal or family Hx of alcohol or drug abuse • Younger age • Presence of psychiatric conditions	• Assess potential risks associated w/ chronic opioid therapy • Manage patients using ER/LA opioids based on risk assessment	• Understand limitations

Chou R, et al. *J Pain.* 2009;10:113-30.

Risk Assessment Tools: Examples

Tool	# of items	Administered By
Patients considered for long-term opioid therapy:		
ORT Opioid Risk Tool	5	patient
SOAPP® Screener & Opioid Assessment for Patients w/ Pain	24, 14, & 5	patient
DIRE Diagnosis, Intractability, Risk, & Efficacy Score	7	clinician
Characterize misuse once opioid treatments begins:		
PMQ Pain Medication Questionnaire	26	patient
COMM Current Opioid Misuse Measure	17	patient
PDUQ Prescription Drug Use Questionnaire	40	clinician
Not specific to pain populations:		
CAGE-AID Cut Down, Annoyed, Guilty, Eye-Opener Tool, Adjusted to Include Drugs	4	clinician
RAFFT Relax, Alone, Friends, Family, Trouble	5	patient
DAST Drug Abuse Screening Test	28	patient
SBIRT Screening, Brief Intervention, & Referral to Treatment	Varies	clinician

Opioid Risk Tool (ORT)

Mark each box that applies	Female	Male
1. Family Hx of substance abuse		
Alcohol	☐ 1	☐ 3
Illegal drugs	☐ 2	☐ 3
Prescription drugs	☐ 4	☐ 4
2. Personal Hx of substance abuse		
Alcohol	☐ 3	☐ 3
Illegal drugs	☐ 4	☐ 4
Prescription drugs	☐ 5	☐ 5
3. Age between 16 & 45 yrs	☐ 1	☐ 1
4. Hx of preadolescent sexual abuse	☐ 3	☐ 0
5. Psychologic disease		
ADD, OCD, bipolar, schizophrenia	☐ 2	☐ 2
Depression	☐ 1	☐ 1

Scoring Totals:

Administer

On initial visit

Prior to opioid therapy

Scoring *(risk)*

0-3: low

4-7: moderate

≥8: high

Webster LR, Webster RM. *Pain Med.* 2005;6:432-42.

Screener & Opioid Assessment for Patients with Pain (SOAPP)®

Identifies patients as at high, moderate, or low risk for misuse of opioids prescribed for chronic pain

How is SOAPP® administered?

Usually self-administered in waiting room, exam room, or prior to an office visit

May be completed as part of an interview w/ a nurse, physician, or psychologist

Prescribers should have a completed & scored SOAPP® while making opioid treatment decisions

SOAPP® Monitoring Recommendations. https://painedu.org/soapp/SOAPP_Monitoring_Recommendations.pdf
The SOAPP® Version 1.0 Tutorial. https://painedu.org/soapp-tutorial_01.asp

Optional Slide

SOAPP® : Available in 4 Formats to Assess Misuse Risk

SOAPP® 1.0 24Q version (original)	14Q version	5Q (short-form) version	SOAPP-R 24Q version (revised)
24 questions (14 used to score tool)	14 questions*	5 questions*	24 questions
Add ratings for 14 "screening" questions	Add ratings for each question		
Score ≥12: high risk 8-11: moderate risk <8: low risk	Score ≥12: high risk 8-11: moderate risk <8: low risk	Score ≥4: increased risk	Score ≥22: high risk 10-21: moderate risk ≤9: low risk
<10 min. to complete 10 "unscored" questions provide background	<8 min. to complete	<5 min. to complete	<10 min. to complete

*Questions from SOAPP V.1.0 Patients rate all questions on scale of 0-4

SOAPP® Monitoring Recommendations. painedu.org/soapp/SOAPP_Monitoring_Recommendations.pdf The SOAPP® Version 1.0 Tutorial. painedu.org/soapp-tutorial_01.asp *SOAPP® Frequently Asked Questions.* painedu.org/soapp-development.asp painedu.org. *SOAPP® Version 1.0-SF.* painedu.org *SOAPP® Version 1.0-14Q.* painedu.org *SOAPP®-R.* painedu.org

When to Consider a Trial of an Opioid

Potential benefits are likely to outweigh risks

Failed to adequately respond to nonopioid & nondrug interventions

Continuous, around-the-clock opioid analgesic is needed for an extended period of time

Pain is chronic and severe

No alternative therapy is likely to pose as favorable a balance of benefits to harms

Chou R, et al. *J Pain.* 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain*. 2010.

When to Consider a Trial of an Opioid, cont'd

60-yr-old w/ chronic disabling OA pain

- Nonopioid therapies not effective, IR opioids provided some relief but experienced end-of-dose failure
- No psychiatric/medical comorbidity or personal/family drug abuse Hx
  - High potential benefits relative to potential risks
  - Could prescribe opioids to this patient in most settings w/ routine monitoring

30-yr-old w/ fibromyalgia & recent IV drug abuse

- High potential risks relative to benefits (opioid therapy not 1st line for fibromyalgia)
- Requires intensive structure, monitoring, & management by clinician w/ expertise in both addiction & pain
  - Not a good candidate for opioid therapy

Chou R, et al. *J Pain.* 2009;10:113-30.

When to Consider a Trial of an Opioid, cont'd

Selection of patients between these 2 extremes requires:

Careful assessment & characterization of patient risk

Structuring of care to match risk

In patients w/ Hx of substance abuse or a psychiatric comorbidity, this may require assistance from experts in managing pain, addiction, or other mental health concerns

In some cases opioids may not be appropriate or should be deferred until the comorbidity has been adequately addressed

– Consider referral

Chou R, et al. *J Pain.* 2009;10:113-30.

Referring High-Risk Patients

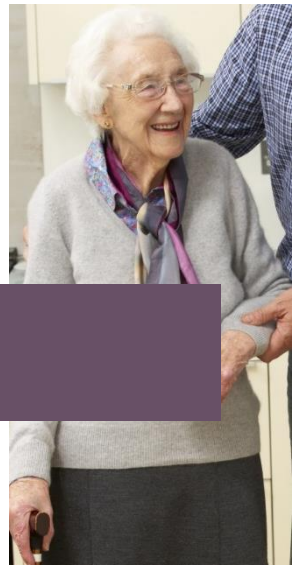
Prescribers should

Understand when to appropriately refer high-risk patients to pain management or addiction specialists

Also check your state regulations for requirements

Chou R, et al. *J Pain.* 2009;10:113-30.

Special Considerations: Elderly Patients



Does patient have medical problems that increase risk of opioid-related AEs?

Respiratory depression more likely in elderly, cachectic, or debilitated patients

- Altered PK due to poor fat stores, muscle wasting, or altered clearance
- Monitor closely, particularly when
  - Initiating & titrating ER/LA opioids
  - Given concomitantly w/ other drugs that depress respiration
- Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
- Titrate dose cautiously

Older adults more likely to develop constipation

- Routinely initiate a bowel regimen before it develops

Is patient/caregiver likely to manage opioid therapy responsibly?

American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. *J Am Geriatr Soc.* 2009;57:1331-46. Chou R, et al. *J Pain.* 2009;10:113-30.

Special Considerations: Children (<18 years)

Safety & effectiveness of most ER/LA opioids unestablished

Pediatric analgesic trials pose challenges
Transdermal fentanyl approved in children aged ≥2 yrs

Most opioid studies focus on inpatient safety

Opioids are common sources of drug error

Opioid indications are primarily life-limiting conditions

Few children with chronic pain due to non-life-limiting conditions should receive opioids

When prescribing opioids to children:

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

Berde CB, et al. *Pediatrics.* 2012;129:354-64. Gregoire MC, et al. *Pain Res Manag* 2013;18:47-50.
Mc Donnell C. *Pain Res Manag.* 2011;16:93-8. Slater ME, et al. *Pain Med.* 2010;11:207-14.

Optional Slide

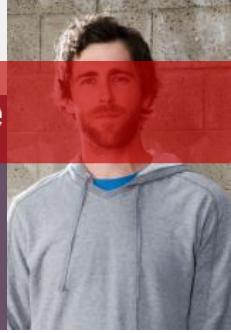
Case:

Peter
25-Year-Old Male

Case:

Optional Slide

Peter



New to area, presents at 4:45 PM on Friday

- Chronic left knee pain from a MVA 5 yrs ago
- Wants oxycodone ER & oxycodone IR for "rescue"

Hx

- 3 knee surgeries—last was 18 mo ago
- Persistent ambulatory dysfunction—granted disability
- Prior therapies: medications, supporting devices, & PT
  - Only oxycodone ER works
    - Allergic to acetaminophen & NSAIDs
    - Morphine & codeine make him throw up
  - PT sessions not helpful

Physical examination of knee

- No erythema, swelling, or bruising; surgical scars present
- Left quadriceps has signs of atrophy compared to right side
- Limited ROM on flexion of left knee

Peter: Assess Abuse Risk w/ 5-Q SOAPP

Optional Slide

How often:	Never= 0	Seldom= 1	Sometimes= 2	Often= 3	Very often=4
1. Do you have mood swings?		☑			
2. Do you smoke a cigarette within an hr after you wake up?					☑
3. Have you taken medication other than the way that it was prescribed?	☑				
4. Have you used illegal drugs (e.g., marijuana, cocaine) in past 5 yrs?		☑			
5. In your lifetime, have you had legal problems or been arrested?		☑			

After further questioning:

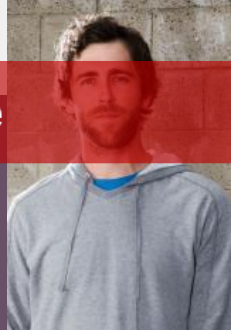
- Admits smoking 1 cigarette pack/d for 10 yrs
- Claims occasional marijuana use, not for last 2 yrs

Total Score: 7

(Cutoff is 4)=high risk for prescription opioid misuse

Optional Slide

Peter: Assess Abuse Risk



Ask for contact details of prior regular physician

- No info w/ him—can get it on Monday if you give him a prescription now

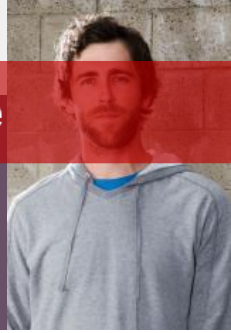
Ask Peter to provide a urine sample for testing

- He accuses you of not trusting him
- Explain it is your office policy for a new patient being considered for a controlled substance
  - He goes with your nurse

Access your state's PDMP: 6-month report

- Received 28 prescriptions from 4 physicians, using 5 pharmacies
  - Left quadriceps has signs of atrophy compared to right side
- Some paid for w/ insurance, others w/ cash

Optional Slide



Peter: UDT & Results

POC immunoassay cup tests for THC, cocaine, opiates, methamphetamine, & amphetamine

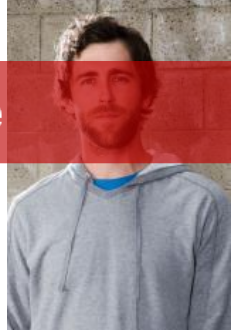
- Only detects naturally occurring opiates – morphine & codeine
- **Semisynthetic oxycodone not reliably detected**
  - Included in some, but not all panels – always check

POC test positive for THC & negative for other substances

Second sample sent to laboratory, w/ request for a pain management profile that includes oxycodone

- Adulterant panel, THC, cocaine, opiates, & oxycodone

Optional Slide



Peter: What Now? Should You:

1. Write a 4-day supply of ER & IR oxycodone, to last until you contact his previous prescriber on Monday

2. Not write a prescription today, since he lied about prescribers & drug use. Untreated addiction prevents you from addressing his pain; refer to a pain management physician w/ addiction expertise

3. Write 30-day prescriptions for ER & IR oxycodone while you carry out diagnostic tests on his injury, obtain his prior medical records, & review test results

Answer 2 is correct

Optional Slide

Peter: Case Summary

Several red flags raised:

- PDMP report revealed probable doctor shopping
- UDT positive for recent marijuana use, which he denied
- SOAPP score suggests risk for prescription drug misuse
- DEA identified modus operandi used by a drug-seeking patient
  - Wants appointment toward end of office hrs
  - Requests specific controlled substance
  - Claims nonopioid analgesics do not work or allergy
  - Reluctant to give name of primary physician
- Younger age

Peter may have a pain problem:

- Beyond your scope of practice to manage while his addiction is untreated
- Refer to pain management or addiction specialist

Challenge: The Friday Afternoon Patient

Optional Slide

Red Flag:

Adjusting a prescription without performing appropriate evaluation or screening

It is 4 pm on Friday and you are four patients behind schedule. Mr. Kingston asks you to increase his current dosage of hydrocodone, because he says it is not relieving his pain. It would take you two minutes to say yes.

Action: Check your local PDMP. Employ practice management strategies that maximize efficiency.

- Patient-administered screening tools
- Office staff to administer and score tools, document results, and communicate to the prescriber

Merrill, et al., 2002; Wilsey et al., 2008) (Sehgal, et al., 2012; Chou, et al., 2009a

Optional Slide

Challenge: The Delayed Surgery

Red Flag:

Patient may be stalling to continue an opioid regimen

Ms. Van Buskirk 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 expectations for time limitations. Offer non-medicine and non-opioid options for pain management. Consider referral to addiction specialist.

Gourlay, Heit, & Amahregi, 2005; Stanos, 2012

Pearls for Practice

Document EVERYTHING

Conduct a Comprehensive H&P

General and pain-specific

Assess Risk of Abuse

Compare Risks with Expected Benefits

Determine Whether a Therapeutic Trial is Appropriate

INITIATING THERAPY, MODIFYING DOSING, & DISCONTINUING USE OF ER/LA OPIOID ANALGESICS

Unit II

Federal & State Regulations

Comply w/ federal & state laws & regulations that govern the use of opioid therapy for pain

Federal

- Code of Federal Regulations, Title 21 Section 1306: rules governing the issuance & filling of prescriptions pursuant to section 309 of the Act (21 USC 829)
  - www.deadiversion.usdoj.gov/21cfr/cfr/2106cfrt.htm
- United States Code (USC) - Controlled Substances Act, Title 21, Section 829: prescriptions
  - www.deadiversion.usdoj.gov/21cfr/21usc/829.htm

State

- Database of state statutes, regulations, & policies for pain management
  - www.medscape.com/resource/pain/opioid-policies
  - www.painpolicy.wisc.edu/database-statutes-regulations-other-policies-pain-management

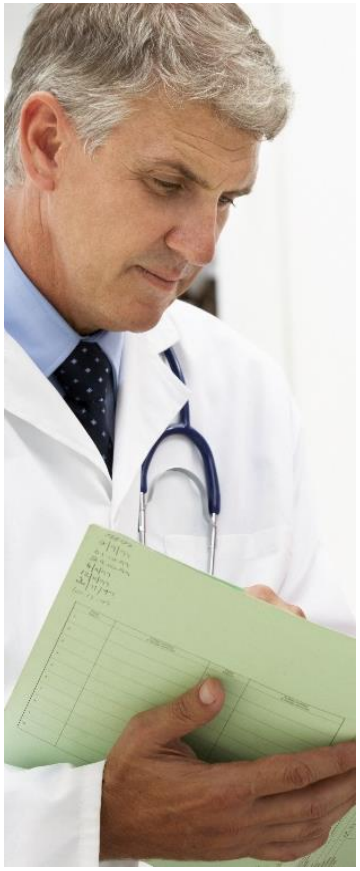
Initiating Treatment

Prescribers should regard initial treatment as a therapeutic trial

May last from several weeks to several months

Decision to proceed w/ long-term treatment should be intentional & based on careful consideration of outcomes during the trial

- Progress toward meeting therapeutic goals
- Presence of opioid-related AEs
- Changes in underlying pain condition
- Changes in psychiatric or medical comorbidities
- Identification of aberrant drug-related behavior, addiction, or diversion



Chou R, et al. *J Pain.* 2009;10:113-30

ER/LA Opioid-Induced Respiratory Depression

Chief hazard of opioid agonists, including ER/LA opioids

- If not immediately recognized & treated, may lead to respiratory arrest & death
- Greatest risk: initiation of therapy or after dose increase

Manifested by reduced urge to breathe & decreased respiration rate

- Shallow breathing
- CO_2 retention can exacerbate opioid sedating effects

Instruct patients/family members to call 911*

- Managed w/ close observation, supportive measures, & opioid antagonists, depending on patient's clinical status

Chou R, et al. *J Pain.* 2009;10:113-30. FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

ER/LA Opioid-Induced Respiratory Depression

More likely to occur

- In elderly, cachectic, or debilitated patients
  - **Contraindicated** in patients w/ respiratory depression or conditions that increase risk
- If given concomitantly w/ other drugs that depress respiration

Reduce risk

- Proper dosing & titration are essential
- **Do not overestimate** dose when converting dosage from another opioid product
  - Can result in fatal overdose w/ 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

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Initiating & Titrating: Opioid-Naïve Patients

Drug & 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 PI)

Monitor patients closely for respiratory depression

Especially within 24-72 h of initiating therapy & increasing dosage

Individualize dosage by titration based on efficacy, tolerability, & presence of AEs

Check ER/LA opioid product PI for minimum titration intervals

Supplement w/ IR analgesics (opioids & nonopioid) if pain is not controlled during titration

The ER/LA Opioid Analgesics Risk Evaluation & Mitigation Strategy. *Selected Important Safety Information. Abuse potential & risk of life-threatening respiratory depression.* www.er-la-opioidrems.com/IwgUI/rems/pdf/important_safety_information.pdf. 2012. Chou R, et al. *J Pain.* 2009;10:113-30. FDA. *Blueprint for Prescriber Education for ER/LA Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafety InformationforPatientsandProviders/UCM311290.pdf

Initiating: Opioid-Tolerant Patients

If opioid tolerant – no restrictions on which products can be used

Patients considered opioid tolerant are taking at least

- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/hr
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid

For 1 Wk Or Longer

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

The ER/LA Opioid Analgesics Risk Evaluation & Mitigation Strategy. *Selected Important Safety Information. Abuse potential & risk of life-threatening respiratory depression.* www.er-la-opioidrems.com/IwgUI/rems/pdf/important_safety_information.pdf. 2012.

Opioid Rotation

Definition:

Change from an existing opioid regimen to another opioid w/ 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 & AEs of different mu opioids vary among patients
- Patients show incomplete cross-tolerance to new opioid
  - Patient tolerant to 1st opioid can have improved analgesia from 2nd opioid at a dose lower than calculated from an EDT

Fine PG, et al. *J Pain Symptom Manage*. 2009;38:418-25. Knotkova H, et al. *J Pain Symptom Manage*. 2009;38:426-39.
Pasternak GW. *Neuropharmacol*. 2004;47(suppl 1):312-23.

Mu Opioid Receptors & Incomplete Cross-Tolerance

Optional Slide

Mu opioids bind to mu receptors

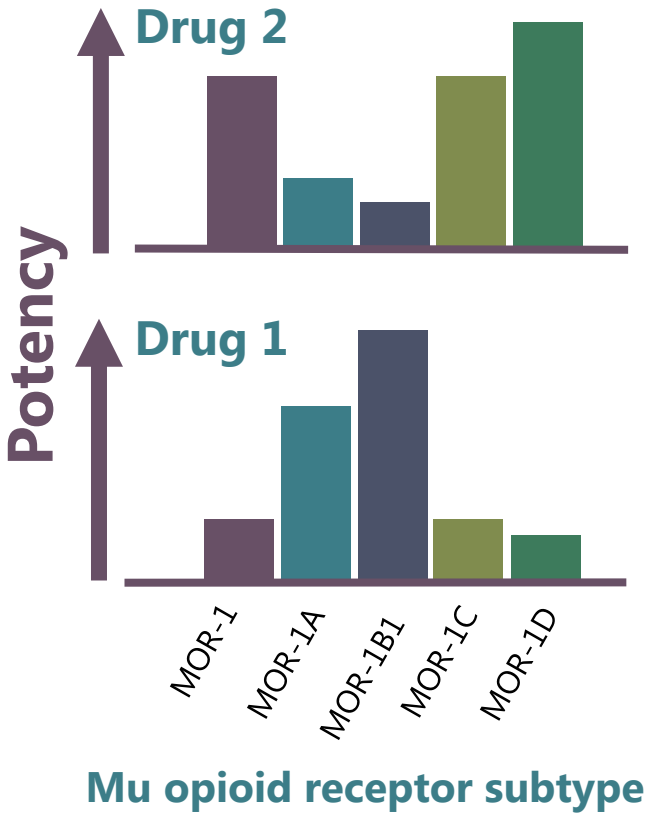
Many mu receptor subtypes:

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

May help explain:

Inter-patient variability in response to mu opioids

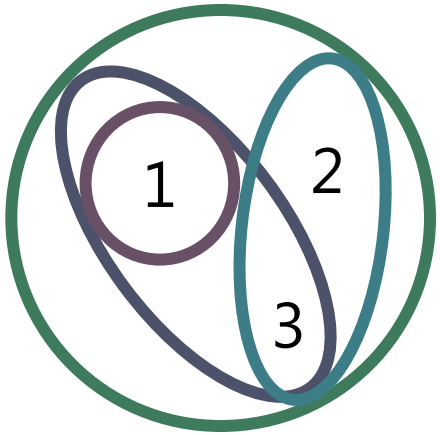
Incomplete cross-tolerance among mu opioids



Pasternak GW. *Pain Med.* 2012;13 Suppl 1:S4-11.

Incomplete Cross-Tolerance

Optional Slide



Drug	Receptor Subtype Selectivity
A	1+3
B	2+3
C	1
D	1+2+3

Challenge drug:

	Cross-tolerance if tolerant to drug:			
	A	B	C	D
A	-	Partial	Partial	Yes
B	Partial	-	No	Yes
C	Yes	No	-	Yes
D	Partial	Partial	Partial	-

Pasternak GW. *Trends Pharmacol Sci.* 2001;22:67-70.

Reasons for Opioid Rotation

Optional Slide

Poor opioid responsiveness:

- Dose titration yields intolerable / unmanageable AEs
- Poor analgesic efficacy despite dose titration

Other potential reasons:

- Patient desire or need to try a new formulation
- Cost or insurance issues
- Adherence issues
- Concern about abuse or diversion
- Change in clinical status requires an opioid w/ different PK
- Problematic drug-drug interactions

Fine PG, et al. *J Pain Symptom Manage.* 2009;38:418-25. Knotkova H, et al. *J Pain Symptom Manage.* 2009;38:426-39. Cruciani R, et al. *Oncology.* 2005;19:1-4.

Equianalgesic Doses

Opioid rotation requires calculation of an approximate equianalgesic dose

Equianalgesic dose is a construct derived from relative opioid potency estimates

- Potency refers to dose required to produce a given effect

Relative potency estimates

- Ratio of doses necessary to obtain roughly equivalent effects
- Calculate across drugs or routes of administration
- Relative analgesic potency is converted into an equianalgesic dose by applying the dose ratio to a standard

Fine PG, et al. *J Pain Symptom Manage*. 2009;38:418-25. Knotkova H, et al. *J Pain Symptom Manage*. 2009;38:426-39.

Equianalgesic Dose 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

Knotkova H, et al. *J Pain Symptom Manage.* 2009;38:426-39. Shaheen PE, et al. *J Pain Symptom Manage.* 2009;38:409-17.
Webster LR, et al. *Pain Med.* 2012;13:562-70. Haffey F, et al. *Drug Saf.* 2013;36:111-7.

Example of an EDT for Adults

	Equianalgesic Dose		Usual Starting Doses	
Drug	**SC/IV**	**PO**	**Parenteral**	**PO**
Morphine	10 mg	30 mg	2.5-5 mg SC/IV q3-4hr (◆1.25 – 2.5mg)	5-15 mg q3-4hr (IR or oral solution) (◆2.5-7.5 mg)
Oxycodone	NA	20 mg	NA	5-10 mg q3-4 (◆2.5 mg)
Hydrocodone	NA	30 mg	NA	5 mg q3-4h (◆ 2.5 mg)
Hydromorphone	1.5 mg	7.5 mg	0.2-0.6 mg SC/IV q2-3hr (◆0.2mg)	1-2 mg q3-4hr (◆0.5-1 mg)

UniPAC3_Table9(AAHPM)(2012)

Limitations of EDTs

Single-dose potency studies using a specific route, conducted in patients w/ limited opioid exposure

Did Not Consider

Chronic dosing	High opioid doses	Other routes
Different pain types	Comorbidities or organ dysfunction	Gender, ethnicity, advanced age, or concomitant medications
Direction of switch from 1 opioid to another	Inter-patient variability in pharmacologic response to opioids	Incomplete cross-tolerance among mu opioids

Fine PG, et al. *J Pain Symptom Manage.* 2009;38:418-25. Knotkova H, et al. *J Pain Symptom Manage.* 2009;38:426 -39. Shaheen PE, et al. *J Pain Symptom Manage.* 2009;38:409-17. Webster LR, et al. *Pain Med.* 2012;13:562-70.

Utilizing Equianalgesic Doses

Incomplete cross-tolerance & inter-patient variability require use of conservative dosing when converting from one opioid to another

Equianalgesic dose a starting point for opioid rotation

Intended as General Guide

Calculated dose of new drug based on EDT must be reduced, then titrate the new opioid as needed

Closely follow patients during periods of dose adjustments

Follow conversion instructions in individual ER/LA opioid PI, when provided

Fine PG, et al. *J Pain Symptom Manage.* 2009;38:418-25.
Knotkova H, et al. *J Pain Symptom Manage.* 2009;38:426-39.

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	Closer to 25% reduction if patient
• Receiving a relatively high dose of current opioid regimen • Elderly or medically frail	• Does not have these characteristics • Is switching to a different administration route of same drug

***75%-90% reduction for methadone**

Fine PG, et al. *J Pain Symptom Manage.* 2009;38:418-25.

Guidelines for Opioid Rotation, cont'd

If switching to **methadone:**

- Reduce calculated equianalgesic dose by **75%-90%**
- For patients on very high opioid doses (e.g., ≥1,000 mg morphine equivalents/d), be cautious converting to methadone ≥100 mg/d
  - Consider inpatient monitoring, including serial EKG monitoring

If switching to **transdermal:**

- **Fentanyl**, calculate dose conversion based on equianalgesic dose ratios included in the PI
- **Buprenorphine**, follow instructions in the PI

Fine PG, et al. *J Pain Symptom Manage*. 2009;38:418-25.

Guidelines for Opioid Rotation, cont'd

Have a strategy to frequently assess analgesia, AEs and withdrawal symptoms

Titrate new opioid dose to optimize outcomes & safety

Dose for breakthrough pain (BTP) ***using a short-acting, immediate release preparation*** is 5%-15% of total daily opioid dose, administered at an appropriate interval

If oral transmucosal fentanyl product is used for BTP, begin dosing lowest dose irrespective of baseline opioid dose

NEVER use ER/LA opioids for BTP

Fine PG, et al. *J Pain Symptom Manage*. 2009;38:418-25.

Guideline for Opioid Rotation: Summary

Optional Slide

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	Equinalgesic 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‡

*If switching to transdermal fentanyl, 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

Fine PG, et al. *J Pain Symptom Manage*. 2009;38:418-25.

Breakthrough Pain in Chronic Pain Patients

Patients on stable ATC opioids may experience BTP	Therapies	Consider adding
Disease progression or a new or unrelated pain	• Directed at cause of BTP or precipitating factors • Nonspecific symptomatic therapies to lessen impact of BTP	• 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 • Nonopioid drug therapies • Nonpharmacologic treatments

Chou R, et al. *J Pain.* 2009;10:113-30.

Optional Slide

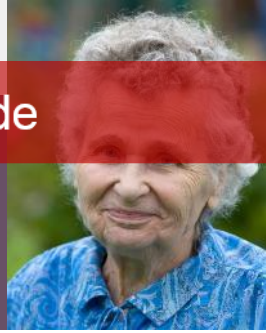
Case:

Wilma
73-Year-Old Female

Case:

Optional Slide

Wilma



Advanced Colon Cancer

- w/ peritoneal & liver metastases

Presents w/ increasing abdominal pain

- Wakes frequently at night in severe pain

Regimen: oxycodone IR 5 mg q6h + 1 at bedtime

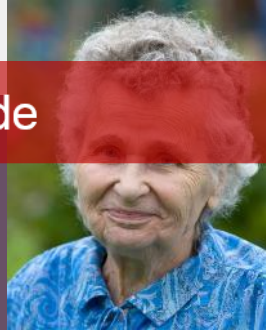
- She has some resistance to opioids
  - Morphine means she's about to "die" & methadone is for "addicts"
  - Does not like to take a lot of pills

Consider rotating to an ER/LA opioid: fewer pills & may allow her to sleep through the night

- Her total current oxycodone dose is 25 mg/d
- She is NOT opioid tolerant
  - Would require 30 mg oral oxycodone/d for a wk or longer

Optional Slide

Rotation Options for Wilma



No option for hydromorphone ER or transdermal fentanyl

Only for opioid-tolerant patients

Avoid morphine & methadone due to her resistance

Consider oxymorphone ER: calculate equianalgesic dose

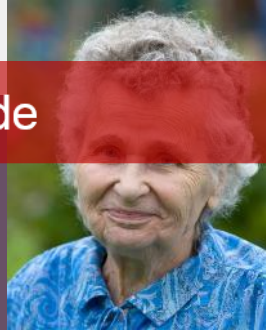
20/10=25 mg/X
10x25=250=20X **X=12.5 mg oxymorphone/d**

Reduce by 25% for safety=9.4 mg oxymorphone ER/d

Wilma was on low dose of oxycodone so 25% reduction is reasonable

Start oxymorphone ER 5 mg q12h w/ oxycodone IR 5 mg PRN for BTP

Optional Slide

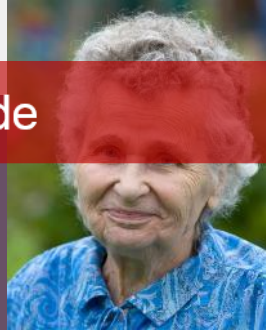


Rotation Options for Wilma
cont'd

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	Equinalgesic 24 Hr Dose of New Opioid	By 25% – 50%

Optional Slide

Educating Wilma to Take ER/LAs Safely



Advise Wilma to call

- Tomorrow to check in
- Any time to let you know…
  - If her pain worsens
  - She needs >2 doses of BTP medication/d
  - She experiences AEs

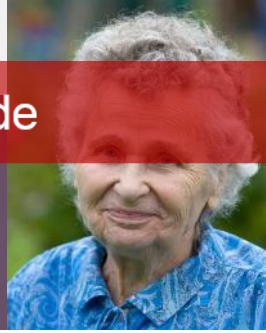
Caution Wilma*

- Store securely to prevent accidental exposure or theft
  - May result in serious harm/death (especially children) & can be abused
- Do not share w/ others
- Swallow whole: do not crush, chew, or dissolve
- Do not consume alcohol or use prescription or OTC products w/ alcohol
- Take Patient Counseling Document to any doctor visits

* Go over the Patient Counseling Document

Optional Slide

Titrate Wilma's Oxymorphone ER Dose



After 1 week, pain was improved, but still moderate

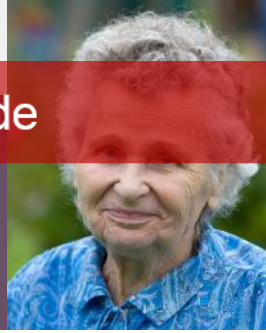
- She is reluctant to take oxycodone IR for BTP
  - "Too many pills"
- Steady-state plasma oxymorphone ER levels occur within 3 d
  - Dosage may be adjusted every 3 to 7 d
- Increase oxymorphone ER to 7.5 mg q12h w/ oxycodone IR for "emergencies"

Follow-up call the next day

- Pain was much improved
- Able to sleep through the night

Continue to re-evaluate analgesia & AEs

Optional Slide



Wilma: Case Summary

Good candidate for rotation to an ER/LA opioid:	Choice of ER/LA opioid was limited:	Educate:	Continue to monitor her & titrate if necessary
Pain not well controlled	Not opioid tolerant so cannot rotate to hydromorphone ER or transdermal fentanyl	ER/LA opioids are harmful to people for whom they are not prescribed	
Pain prevents her sleeping through the night			
Does not like to take a lot of pills	Reluctant to take morphine or methadone	Safeguard her medications	

Reasons for Discontinuing ER/LA Opioids

No progress toward therapeutic goals

Intolerable & Unmanageable AEs

Pain level decreases in stable patients

Nonadherence or unsafe behavior

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

Aberrant behaviors suggestive of addiction &/or diversion

- Use of illicit drugs or unprescribed opioids
- Repeatedly obtaining opioids from multiple outside sources
- Prescription forgery
- Multiple episodes of prescription loss

Chou R, et al. *J Pain.* 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.* 2010.

Taper Dose When Discontinuing

Optional Slide

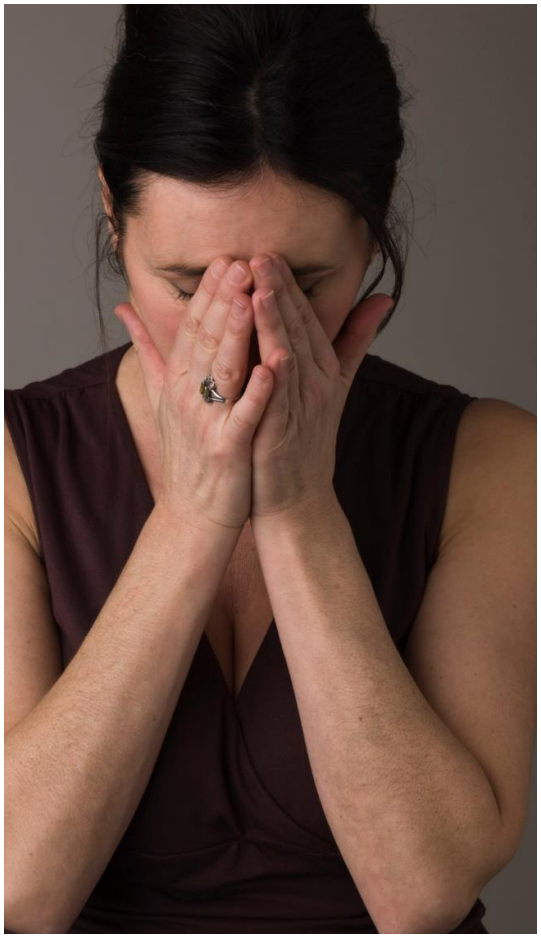
Taper dose to avoid withdrawal symptoms in opioid dependent patient

Recommend outpatient setting for patients without severe medical or psychiatric comorbidities

Recommend rehabilitation setting for patients unable to reduce opioid dose in less structured settings

- When aberrant drug-related behaviors continue, may need to enforce tapering efforts

May use a range of approaches from slow 10% dose reduction per week to more rapid 25%-50% reduction every few days



Chou R, et al. *J Pain.* 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy*

Taper Dose When Discontinuing
cont'd

Optional Slide

Factors that influence the reduction rate:

- Reason for decision to discontinue the opioid
- Presence of medical & psychiatric comorbidities
- Dose
  - Initial rate more rapid at high doses (e.g., >200 mg/d morphine equivalent)
  - Slower rate at low doses (e.g., 60-80 mg/d morphine equivalent)
- Occurrence of withdrawal symptoms as taper is initiated

After taper, continue, substance use, or:

- Continue to treat pain w/ nonopioids analgesics.
- Continue to treat psychiatric disorders.
- If aberrant behaviors may be due to addiction
  - Addiction treatment resources should be made available
  - Motivate patient to seek addiction treatment.

Chou R, et al. *J Pain.* 2009;10:113-30.

Optional Slide

Case:

Ernesto
53-Year-Old Male

Case:

Optional Slide

Ernesto

Workplace back injury at age 41 causes chronic back pain

- Partial diskectomy & subsequent L4-5 fusion
- He continues to work in a modified position

Presents for follow-up medication management

- Stable regimen of oxycodone ER 30 mg q12h + hydrocodone/ acetaminophen IR 5 mg/500 mg q6h prn for BTP
  - Effectively controls his pain
- You write prescriptions for oxycodone ER & hydrocodone IR
  - Stress he safeguard medication in a locked medication safe
- Ernesto states he rarely takes hydrocodone IR for BTP
  - Not necessary in the last month
  - Has not filled a hydrocodone IR prescription for 6 months

Optional Slide

Ernesto: What Now?

1. His pain is perfectly controlled w/ oxycodone ER 30 mg q12h, which you continue to prescribe
2. His low back condition has improved—may be possible to control pain w/ a lower dose of oxycodone ER
3. His low back condition has improved—may no longer need around-the-clock treatment w/ oxycodone ER

To determine course of action, initiate a trial taper:

Closely monitor pain & withdrawal symptoms	No concerns about Ernesto seeking drugs or displaying aberrant behaviors, so a slow taper is appropriate	Help prevent withdrawal symptoms

Optional Slide

Ernesto: Taper Schedule – Month 1

Current opioid dose is oxycodone 60 mg/d	Prescribe oxycodone ER 20 mg q12h (#60) + oxycodone IR 5 mg (#60) w/ instructions:

Day	Oxycodone ER 20 mg tablet	Oxycodone IR 5 mg tablet	Total daily dose (mg)	Call on day:
1-7	20 mg q12h	q8h	55 (9% decrease)	2: pain controlled, no withdrawal symptoms
8-14	20 mg q12h	q12h	50 (9% decrease)	9: pain controlled, no withdrawal symptoms
15-28	20 mg q12h	q12h prn	40 (20% decrease if prn not used)	16: pain controlled, no withdrawal symptoms

Follow-up office visit

Pain is well controlled	Has not needed to use IR oxycodone	No withdrawal symptoms

Optional Slide

Ernesto: Taper Schedule – Month 2

Current dose is oxycodone 40 mg/d			Prescribe oxycodone ER 10 mg q12h (#60) + oxycodone IR 5 mg (#90) w/ instructions:	
Day	**Oxycodone ER 10 mg tablet**	**Oxycodone IR 5 mg tablet**	**Total daily dose (mg)**	**Call on day:**
1-7	10 mg q12h	q12h	30 (25% decrease)	2: pain controlled, no withdrawal symptoms
8-14	10 mg q12h	q12h prn	20 (30% decrease if PRN not used)	9: pain controlled, no withdrawal symptoms
15-21	–	q8h	15 (25% decrease)	16: pain controlled, no withdrawal symptoms
22-30	–	q12h	10 (30% decrease)	23: pain controlled, no withdrawal symptoms

Optional Slide

Ernesto: Follow Up

Follow-up visit

- Pain well controlled & no withdrawal symptoms
- Replace scheduled oxycodone IR w/ oxycodone IR 5 mg (#30) as needed for pain if ibuprofen is not effective
- Instruct him to dispose of remaining oxycodone ER & hydrocodone IR
  - **DEA National Prescription Drug Take-Back Day** scheduled next Saturday

1-month follow-up visit

- Has not needed to use oxycodone IR
- Reports good function w/ no pain
- Instruct him to dispose of remaining oxycodone IR
  - No upcoming **DEA National Prescription Drug Take Back Day**
  - You enter his zip code at **http://rxdrugdropbox.org/**
    - A prescription drug drop box is located in police department of the town in which he works
  - Reassure him if pain recurs, you will manage it

Optional Slide

Ernesto: Case Summary

Not needing BTP opioid suggests pain condition may have improved	Slow taper is appropriate, because there is no urgency	Dispose of unneeded medications from the home
Determine if he no longer needs oxycodone ER or if a lower dose would be effective	• Goal: minimize withdrawal symptoms while assessing effect on pain • Engage patient during taper to monitor pain & withdrawal symptoms	Ensure they are not available to children, pets, & household acquaintances to avoid serious risks from unintended exposure

Optional Slide

Challenge: The Broken Stereotype

Red Flag:

Making assumptions about a patient's risk factors without objective evidence

Ms. Yeun seems like a "good" patient. She has never abused opioids previously. She has been in the practice a long time, has never been a problem, and in fact, is rather enjoyable. She always brings Christmas cookies for the staff around the holidays.

Action: Require all patients receiving opioids to follow a treatment plan and adhere to defined expectations. Evaluate risk in all patients. Use patient-provider agreements, contracts, or other tools.

Gourlay & Heit, 2005; Stanos, 2012

Challenge: The Early Refill

Optional Slide

Red Flag:

Patient requests an early refill every month.

You have prescribed Mr. Arias a long-acting opioid for low back pain and a short-acting PRN opioid for breakthrough pain. Every month he requests a refill for both prescriptions 3-8 days early. Upon questioning, Mr. Arias tells you that he takes both pills whenever he feels he needs them.

Action: Make sure that patients understand each medication's dosage, time of day, and maximum daily dose. Ask them to repeat these instructions back to you. Avoid clinical terms such as "PRN" that the patient may not understand.

Chou, et al., 2009a; Ballantyne, J.C., 2012; Stanos, 2012

Pearls for Practice

Treat Initiation of Opioids as a Therapeutic Trial

Anticipate ER/LA Opioid-Induced Respiratory Depression

It can be immediately life-threatening

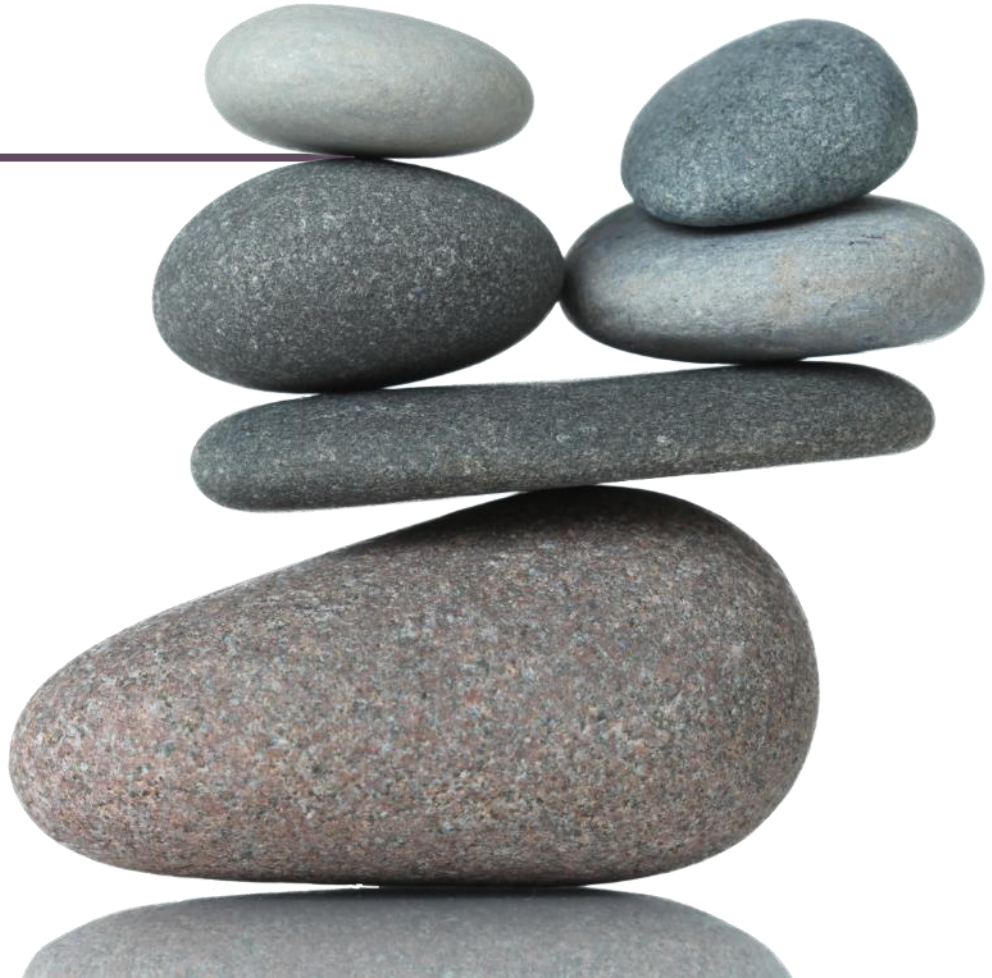
Be Conservative and Thoughtful In Dosing

When initiating, titrating, and rotating opioids
First calculate equinalgesic dose, then reduce dose appropriately

Discontinue ER/LA opioids slowly and safely

MANAGING THERAPY WITH ER/LA OPIOID ANALGESICS

Unit III



Informed Consent

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

- **Analgesic & functional goals of treatment**
- **Expectations**
- **Potential risks**
- **Alternatives to opioids**

The potential for & how to manage:

- Common opioid-related AEs (e.g., constipation, nausea, sedation)
- Other serious risks (e.g., abuse, addiction, respiratory depression, overdose)
- AEs after long-term or high-dose opioid therapy (e.g., hyperalgesia, endocrinologic or sexual dysfunction)

Chou R, et al. *J Pain.* 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.* 2010.

Patient-Prescriber Agreement (PPA)

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

- **Clarify treatment plan & goals of treatment w/ patient, patient's family, & other clinicians involved in patient's care**
- **Assist in patient education**
- **Inform patients about the risks & benefits**
- **Document patient & prescriber responsibilities**

Chou R, et al. *J Pain*. 2009;10:113-30.

Consider a PPA

Reinforce expectations for appropriate & safe opioid use

- Obtain opioids from a single prescriber
- Fill opioid prescriptions at a designated pharmacy
- Safeguard opioids
  - Do not store in medicine cabinet
  - Keep locked (e.g., use a medication safe)
  - Do not share or sell medication
- Instructions for disposal when no longer needed

- Commitments to return for follow-up visits
- Comply w/ appropriate monitoring
  - E.g., random UDT & pill counts
- Frequency of prescriptions
- Enumerate behaviors that may lead to opioid discontinuation
- An exit strategy

Chou R, et al. *J Pain*. 2009;10:113-30.

Monitor Patients During Opioid Therapy

Therapeutic risks & benefits do not remain static	Identify patients	Periodically assess continued need for opioid analgesic
Affected by change in underlying pain condition, coexisting disease, or psychologic/ social circumstances	• Who are benefiting from opioid therapy • Who might benefit more w/ restructuring of treatment or receiving additional services (e.g., addiction treatment) • Whose benefits from treatment are outweighed by risks	Re-evaluate underlying medical condition if clinical presentation changes

Chou R, et al. *J Pain.* 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.* 2010.

Monitor Patients During Opioid Therapy, cont'd

Periodically evaluate:

- Pain control
  - Document pain intensity, pattern, & effects
- Functional outcomes
  - Document level of functioning
  - Assess progress toward achieving therapeutic goals
- Health-related QOL
- AE frequency & intensity
- Adherence to prescribed therapies

Patients requiring more frequent monitoring include:

- High-risk patients
- Patients taking high opioid doses

Chou R, et al. *J Pain.* 2009;10:113-30. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain.* 2010.

Anticipate & Treat Common AEs

Constipation — most common AE; does not resolve with time

- Initiate a bowel regimen before constipation develops
- Increase fluid & fiber intake, stool softeners, & laxatives
- Opioid antagonists may help prevent/treat opioid-induced bowel dysfunction

Nausea & vomiting — tend to diminish over days or weeks

Oral & rectal antiemetic therapies as needed

Drowsiness & sedation — tend to wane over time

Counsel patients about driving, work & home safety as well as risks of concomitant exposure to other drugs & substances w/ sedating effects

Pruritus & myoclonus — tend to diminish over days or weeks

Treatment strategies for either condition largely anecdotal

Chou R, et al. J Pain. 2009;10:113-30

Monitor Adherence and Aberrant Behavior

Routinely monitor patient adherence to treatment plan

- Recognize & document aberrant drug-related behavior
  - In addition to patient self-report also use:
    - State PDMPs, where available
    - UDT
      - Positive for nonprescribed drugs
      - Positive for illicit substance
      - Negative for prescribed opioid
- Family member or caregiver interviews
- Monitoring tools such as the COMM, PADT, PMQ, or PDUQ
- Medication reconciliation (e.g., pill counts)

PADT=Pain Assessment & Documentation Tool

Chou R, et al. *J Pain*. 2009;10:113-30.

Address Aberrant Drug-Related Behavior

Behavior outside the boundaries of agreed-on treatment plan:

Behaviors that are **less** indicative of aberrancy

- **Unsanctioned dose escalations or other noncompliance w/ therapy on 1 or 2 occasions**
- **Unapproved use of the drug to treat another symptom**
- **Openly acquiring similar drugs from other medical sources**

Behaviors that are **more** indicative of aberrancy

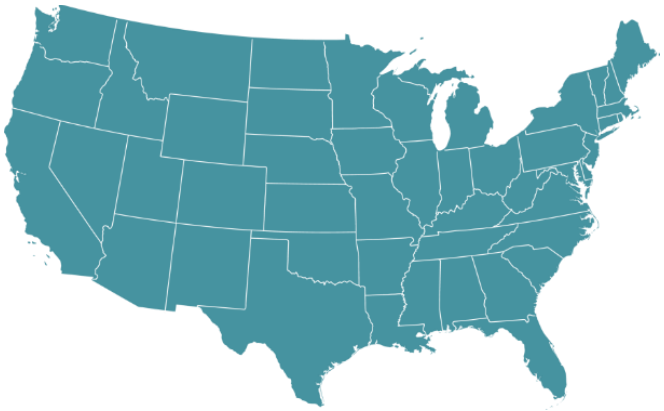
- **Multiple dose escalations or other noncompliance w/ therapy despite warnings**
- **Prescription forgery**
- **Obtaining prescription drugs from nonmedical sources**

Fleming MF, et al. *Pain Med.* 2008;9:1098-106. Passik SD, et al. *J Pain Symptom Manage.* 2011;41:116-25. Portenoy RK. *J Law Med Ethics.* 1996;24:296-309. Passik SD, et al. *Clin J Pain.* 2006;22:173-81. Chou R, et al. *J Pain.* 2009;10:113-30.

Prescription Drug Monitoring Programs (PDMPs)

49 states & 1 territory have legislation authorizing a PDMP

43 states have an operational PDMP



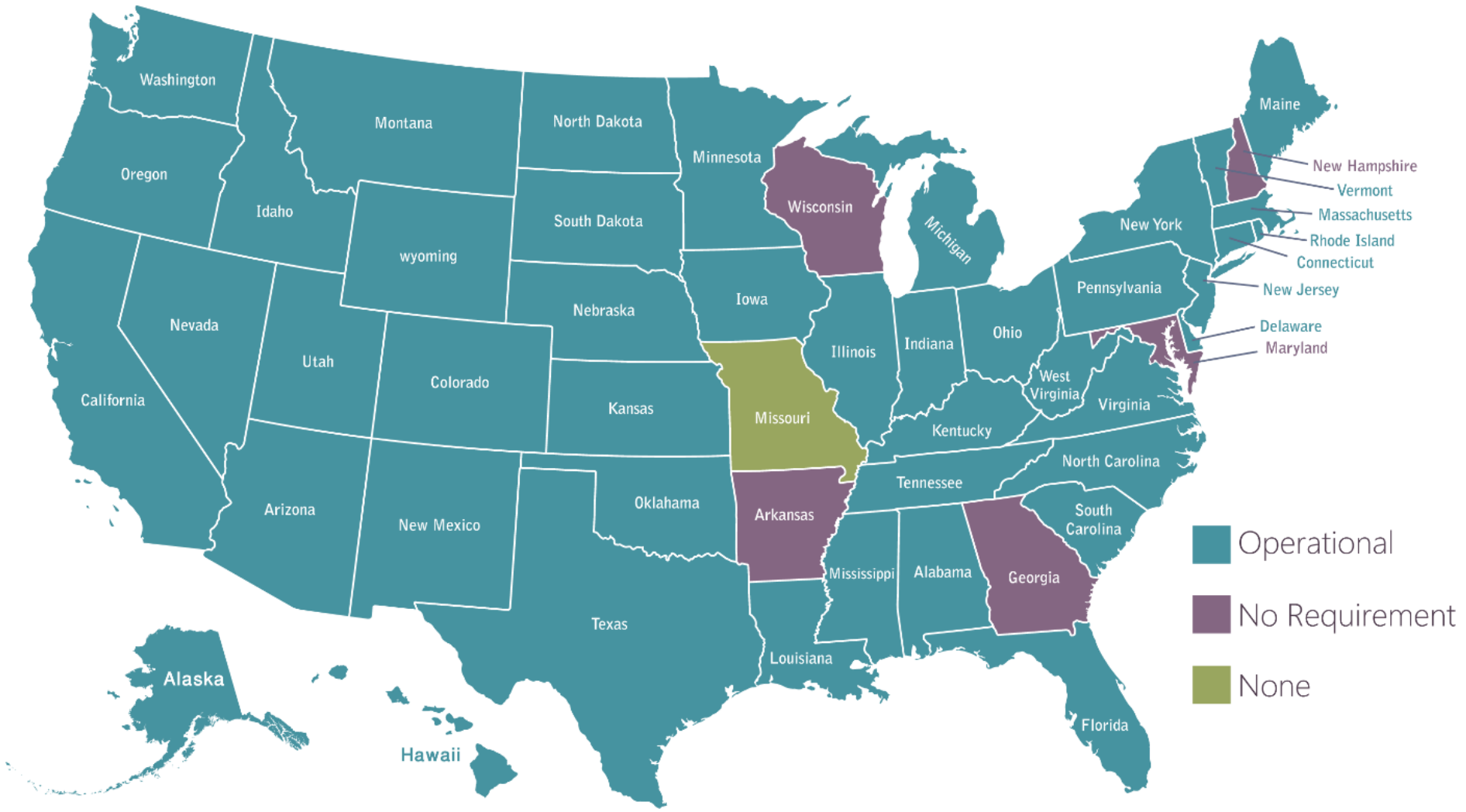
National Alliance For Model State Drug Laws. Status of Prescription Drug Monitoring Programs. www.namsdl.org/documents/PMPProgramStatus01022013.pdf Alliance of States with Prescription Monitoring Programs. www.pmpalliance.org/pdf/pmp_status_map_2012.pdf Alliance of States with Prescription Monitoring Programs. Prescription Monitoring Frequently Asked Questions (FAQ). www.pmpalliance.org/content/prescription-monitoring-frequently-asked-questions-faq

Individual state laws determine

- Who has access to PDMP information
- Which drug schedules are monitored
- Which agency administers the PDMP
- Whether prescribers are required to register w/ the PDMP
- Whether prescribers are required to access PDMP information in certain circumstances
- Whether unsolicited PDMP reports are sent to prescribers

Status of State PDMPs

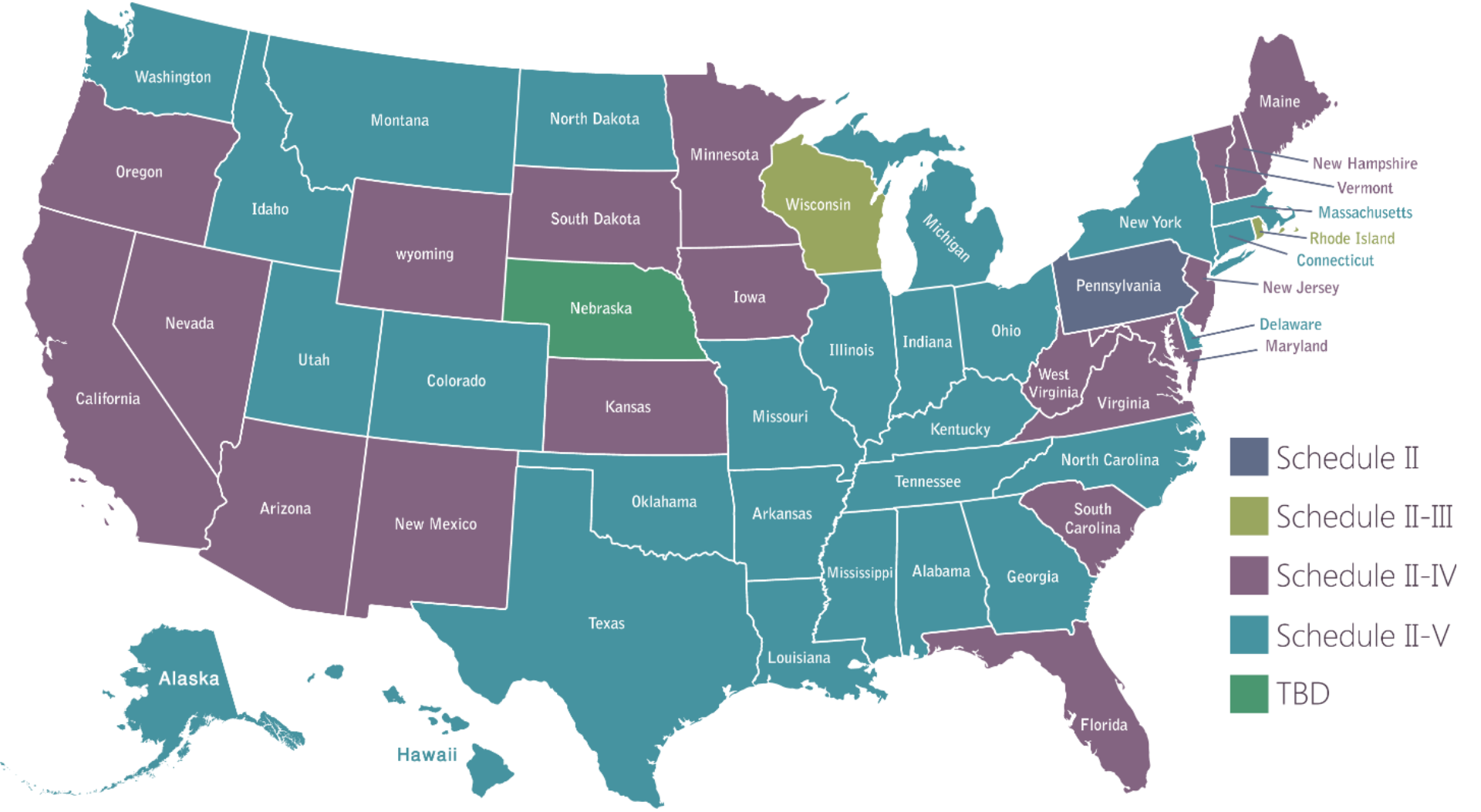
Optional Slide



National Alliance For Model State Drug Laws. Status of Prescription Drug Monitoring Programs. www.namsdl.org/documents/PMPProgramStatus01022013.pdf

Optional Slide

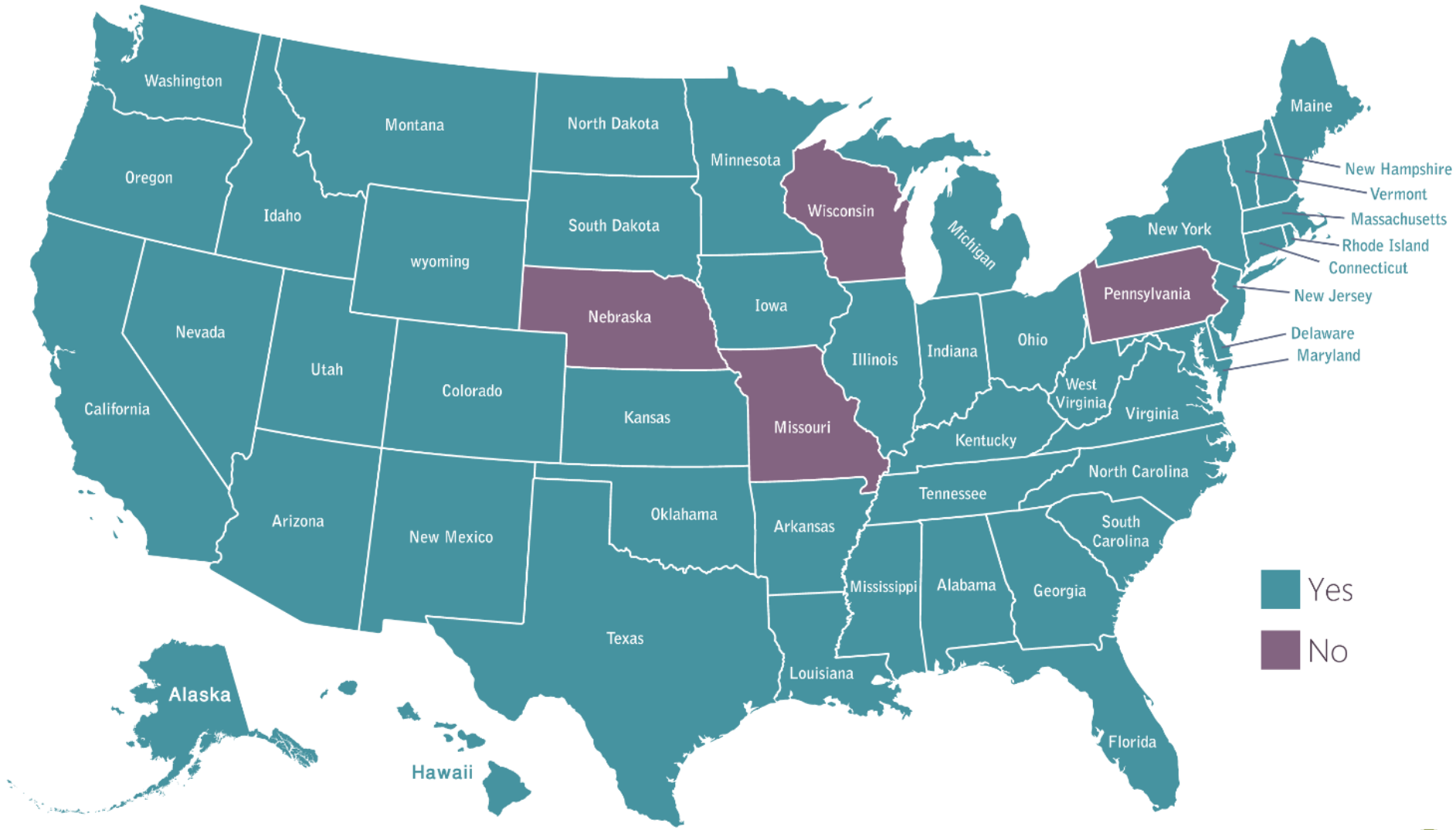
PDMPs: Substances Monitored



Alliance of States with Prescription Monitoring Programs . Prescription Monitoring Frequently Asked Questions (FAQ). www.pmpalliance.org/content/prescription-monitoring-frequently-asked-questions-faq

PDMPs Providing Database Access to Prescribers

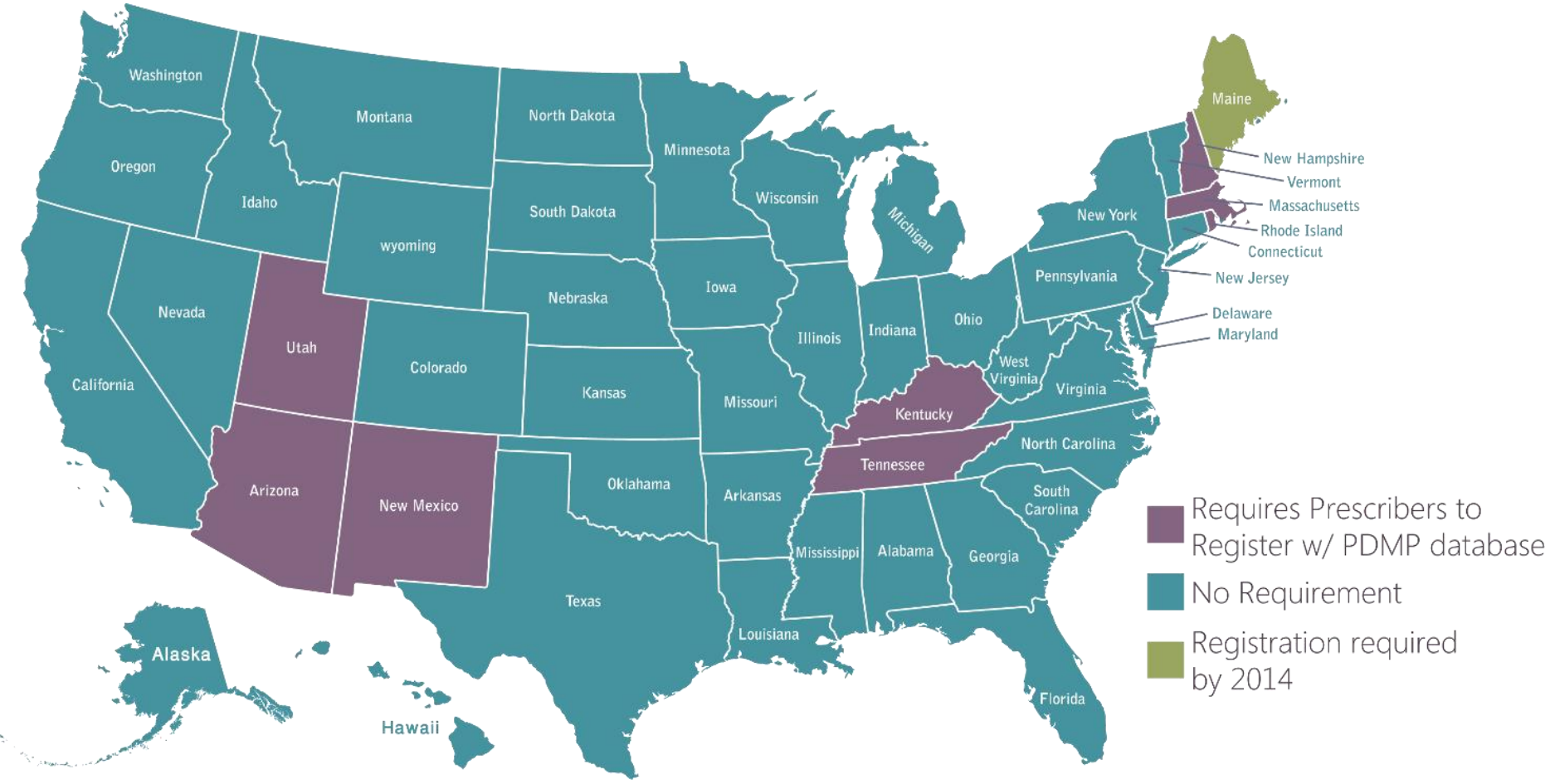
Optional Slide



National Alliance For Model State Drug Laws. Compilation of State Prescription Monitoring Programs. Maps. www.namsdl.org/documents/CompilationofPMPMaps01022013.pdf

PDMPs: Requirements for Prescribers to Register

Optional Slide



National Alliance For Model State Drug Laws. Compilation of State Prescription Monitoring Programs. Maps. www.namsdl.org/documents/CompilationofPMPMaps01022013.pdf

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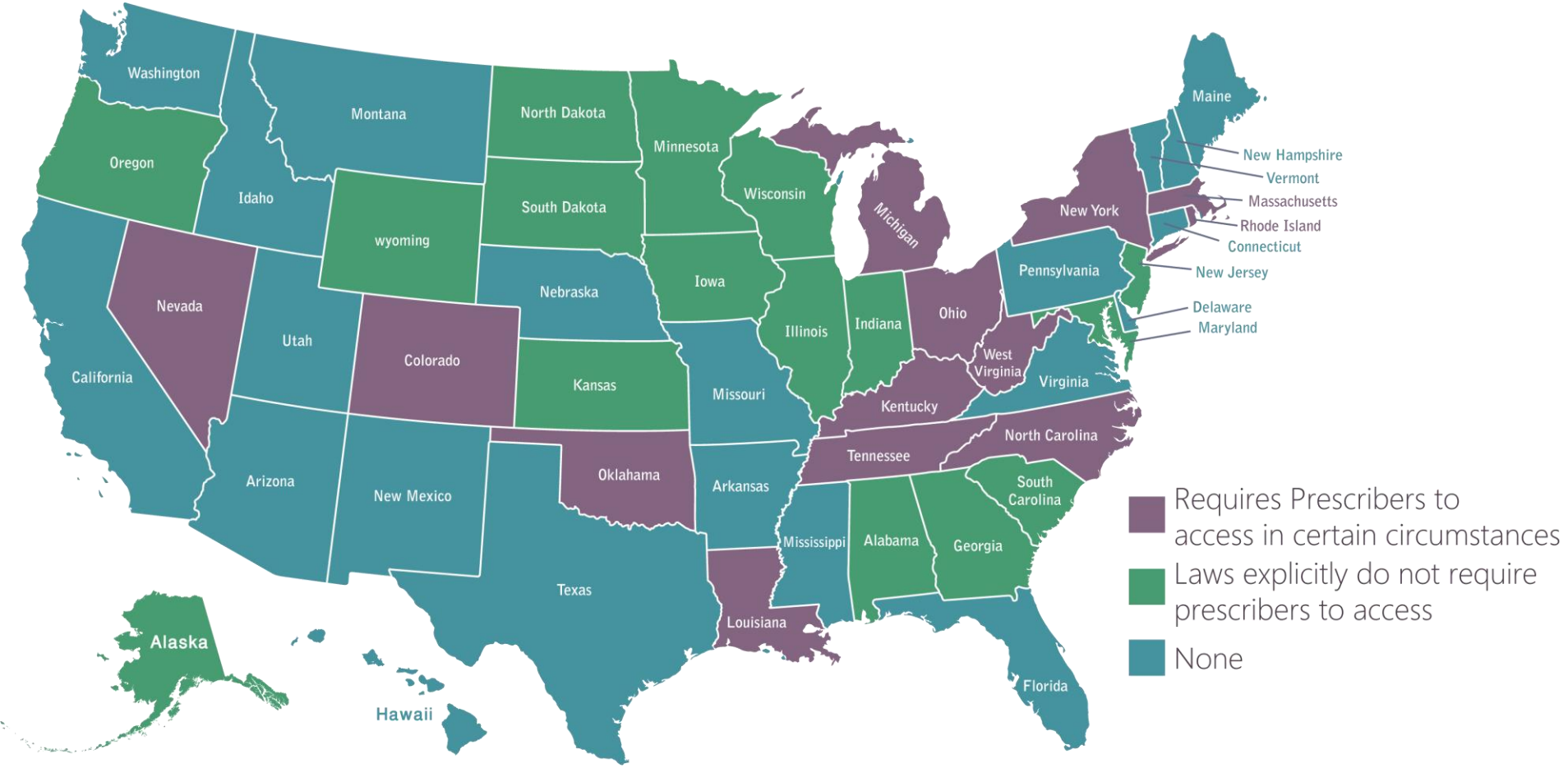
PDMPs: Requirements for Prescribers to Access



National Alliance For Model State Drug Laws. Compilation of State Prescription Monitoring Programs. Maps. www.namsdl.org/documents/CompilationofPMPMaps01022013.pdf

PDMP Benefits

Record of a patient's controlled substance prescriptions

- Some are available online 24/7
- Opportunity to discuss w/ patient

Provide warnings of potential misuse/abuse

- Existing prescriptions not reported by patient
- Multiple prescribers/pharmacies
- Drugs that increase overdose risk when taken together
- Patient pays for drugs of abuse w/ cash

Prescribers can check their own prescribing Hx

Perrone J, et al. *N Engl J Med.* 2012;366:2341-3. Gugelmann HM, et al. *JAMA.* 2011;306:2258-9. Clark T, et al. *Prescription Drug Monitoring Programs: An Assessment of the Evidence for Best Practices.* 2012. The Prescription Drug Monitoring Program Center of Excellence, HellerSchoolfor Social Policy & Management, Brandeis University. www.pdmpexcellence.org/sites/all/pdfs/Brandeis_PDMP_Report_final.pdf.

JOHN SMITH *Patient RX History Report* Optional Slide Date: 02-18-2012

This report may contain another person's controlled substance information. Review the "Patients that Match Search Criteria" section below to ensure all prescriptions belong to the requested individual.

Search Criteria: ((Last Name Begins 'smith' AND First Name Contains 'john') AND (D.O.B = '12/09/1965' AND State = 'CT')) AND Request Period = '08/11/2011' to '02/18/2012'

Patients that match search criteria

Name	DOB	Address
JOHN SMITH	12/09/1965	56 West First Street CT 06457
JOHN SMITH	12/09/1965	21 Hill Road Wallingford CT 06492
JOHN SMITH	12/09/1965	92 Pecan Dr Ivoryton CT 06442
JOHN SMITH	12/09/1965	16 Forest St Haddam CT 06438

Prescribers for prescriptions listed

DAV RI69	RICHARD DAVIS Jones Family Practice 19 Peach St Durham CT 06422
NEU SH62	SHAUN NEUTON NP 12 Crescent Ave Derby CT 06418
JON MI81	MICHAEL JONES MD 63 Clinton Medical Center Essex CT 06426
FIE JA79	JAMES FIELDING MD 12 Crescent Ave Derby CT 06418
JOR BR77	BRIAN JORDAN NP 30 Lexington Dr Hartford CT 06102

Pharmacies that dispensed prescriptions listed

IJXXXX	DBA: CVS/PHARMACY #1100; 12 Swan St New Britain CT 06053
GHXXXX	DBA: CVS/PHARMACY #2222; 95 Eastern Dr Middletown CT 06457
LMXXXX	DBA: CVS/PHARMACY #3333; 45 Westerley Ave Hartford CT 06114
EFXXXX	DBA: RITE AID PHARMACY #9960; 55 River Road Essex CT 06426
ABXXXX	DBA: WALGREENS #22; 999 First Ave Deep River CT 06417
CDXXXX	DBA: WALGREENS #4441; 600 Eastern Ave Middletown CT 06457

JOHN SMITH

Patient RX History Report

Optional Slide

Date: 02-18-2012

Fill	Product, Str, Form	Qty	Days	Prescriber	Written	Rx#	N/R	Pharm	Pay
1/20/12	FENTANYL PATCH 100MCG C-II, TRANSDERMAL PATCH	20	30	JON MI81	1/06/12	134XX	N	ABXXX	04
1/06/12	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	270	34	JON MI81	1/06/12	123XX	N	ABXXX	04
12/21/11	FENTANYL PATCH 100MCG C-II, TRANSDERMAL PATCH	20	30	JON MI81	12/20/11	431XX	N	ABXXX	04
12/08/11	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	270	34	JON MI81	12/08/11	654XX	N	ABXXX	04
11/28/11	FENTANYL PATCH 100MCG C-II, TRANSDERMAL PATCH	15	25	JON MI81	11/16/11	221XX	N	ABXXX	04
11/19/11	CLONAZEPAM, 1 MG, TABLET	90	90	JON MI81	11/16/11	334XX	N	EFXXX	01
11/09/11	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	240	30	JON MI81	11/09/11	645XX	N	GHXXX	03
11/09/11	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	30	3	JON MI81	11/09/11	879XX	N	GHXXX	01
10/20/11	OXYCODONE HYDROCHLORIDE, 15 MG, TABLET	120	20	DAV RI69	10/20/11	991XX	N	CDXXX	04
10/18/11	FENTANYL PATCH 100MCG C-II, TRANSDERMAL PATCH	10	30	JON MI81	10/14/11	824XX	N	CDXXX	04
10/14/11	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	270	34	JON MI81	10/14/11	632XX	N	CDXXX	04
9/22/11	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	120	20	DAV RI69	9/22/11	491XX	N	CDXXX	04
9/22/11	OXYCODONE HYDROCHLORIDE, 15 MG, TABLET	120	20	DAV RI69	9/22/11	533XX	N	CDXXX	04
9/22/11	FENTANYL PATCH 100MCG C-II, TRANSDERMAL PATCH	10	30	DAV RI69	9/22/11	222XX	N	CDXXX	04
9/20/11	CLONAZEPAM, .5 MG, TABLET	60	30	DAV RI69	6/02/11	477XX	N	CDXXX	01
8/30/11	OXYCODONE HYDROCHLORIDE, 30 MG, TABLET	30	6	JOR BR77	8/30/11	784XX	N	LMXXX	03
8/25/11	FENTANYL PATCH 75MCG C-II, 75MCG TRANSDERMAL PATCH	10	30	FIE JA79	8/25/11	599XX	N	CDXXX	04
8/20/11	CLONAZEPAM, .5 MG, TABLET	60	30	DAV RI69	6/02/11	216XX	N	CDXXX	01
8/15/11	OXYCODONE HYDROCHLORIDE TABLETS, 30 MG, TABLET	180	23	NEU SH62	8/15/11	705XX	N	IJXXXX	03
8/11/11	FENTANYL PATCH 100MCG C-II, TRANSDERMAL PATCH	10	30	FIE JA79	7/26/11	447XX	N	CDXXX	04

N/R: N=New R=Refill
Pay: 01=Private Pay 02=Medicaid 03=Medicare 04=Commercial Ins. 05=Military Inst. & VA 06=Workers Comp 07=Indian Nations 99=Other

PDMP Unsolicited Patient Threshold Reports

Reports automatically generated on patients who cross certain thresholds when filling prescriptions. Available in some states.

E-mailed to prescribers to whom prescriptions were attributed

Prescribers review records to confirm it is your patient & you wrote the prescription(s) attributed to you

If inaccurate, contact PDMP

If you wrote the prescription(s), patient safety may dictate need to discuss the patient w/ other prescribers listed on report

- Decide who will continue to prescribe for the patient & who might address drug abuse concerns.

Clark T, et al. *Prescription Drug Monitoring Programs: An Assessment of the Evidence for Best Practices*. 2012. The Prescription Drug Monitoring Program Center of Excellence, Heller School for Social Policy & Management, Brandeis University. www.pdmpexcellence.org/sites/all/pdfs/Brandeis_PDMP_Report_final.pdf.

Rationale for Urine Drug Testing (UDT)

Help to identify drug misuse/addiction

- Prior to starting opioid treatment

Assist in assessing adherence during opioid therapy

- As requirement of therapy w/ an opioid
- Support decision to refer

UDT frequency is based on clinical judgment

Depending on patient's display of aberrant behavior and whether it is sufficient to document adherence to treatment plan

Check state regulations for requirements

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4. SAMHSA. *Clinical Drug Testing in Primary Care.* Technical Assistance Publication (TAP) 32. HHS Publication No.(SMA) 12-4668. Rockville, MD: SAMHSA, 2012. Chou R, et al. *J Pain.* 2009;10:113-30. Gourlay DL, et al. Compliance monitoring in chronic pain management. In: *Bonica's Management of Pain. 4th ed.* Gourlay DL, et al. *Pain Med.* 2009;10 Suppl 2:S115-23.

Main Types of UDT Methods

Initial testing w/ IA drug panels:

- Classify substance as present or absent according to cutoff
- Many do not identify individual drugs within a class
- Subject to cross-reactivity
- Either lab based or at POC

Identify specific drugs &/or metabolites w/ sophisticated lab-based testing; e.g., GC/MS or LC/MS*

- Specifically confirm the presence of a given drug
  - e.g., morphine is the opiate causing a positive IA*
- Identify drugs not included in IA tests
- When results are contested

* GC/MS=gas chromatography/ mass spectrometry
IA=immunoassay
LC/MS=liquid chromatography/ mass spectrometry

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4. Cone EJ, et al. *Postgrad Med.* 2009;121:91-102. SAMHSA. *Clinical Drug Testing in Primary Care.* Technical Assistance Publication (TAP) 32. HHS Publication No.(SMA) 12-4668. Rockville, MD: SAMHSA, 2012.

Detecting Opioids by UDT

Most common opiate IA drug panels

- Detect "opiates" morphine & codeine, but doesn't distinguish
- Do not reliably detect semisynthetic opioids
  - Specific IA panels can be ordered for some
- Do not detect synthetic opioids (e.g., methadone, fentanyl)
  - Only a specifically directed IA panel will detect synthetics

GC/MS or LC/MS will identify specific opioids

- Confirm presence of a drug causing a positive IA
- Identify opioids not included in IA drug panels, including semisynthetic & synthetic opioids
- Identify opioids not included in IA drug panels, including semisynthetic & synthetic opioids

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4.

Optional Slide

Specific Windows of Drug Detection

How long a person excretes drug &/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, & pH

For most drugs it is 1-3 days

Chronic use of lipid-soluble drugs increases detection time; e.g., marijuana, diazepam, ketamine

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4.
Vandevenne M, et al. *Acta Clin Belg.* 2000;55:323-33.

Optional Slide

Specific Windows of Drug Detection, cont'd

Drug in urine	Time
Amphetamines	≤3 d
THC (depending on grade & frequency of use) – Single use – Chronic use	 1-3 d ≤ 30 d
Benzoylecgonine after cocaine use	2-4 d
Opiates (morphine, codeine)	2-3 d
Methadone – EDDP (methadone metabolite)	≤3 d ≤6 d
Benzodiazepines (depending on drug & dose)	Days to wks

EDDP=2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4.

Characteristics of Urine: Assessing Specimen

Optional Slide

Specimen color related to concentration

Concentrated samples more reliable than dilute samples

Temp within 4 min of voiding is 90-100°F

pH fluctuates within range of 4.5-8.0

Creatinine varies w/ hydration

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

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4. Cook JD, et al. *J Anal Toxicol.* 2000;24: 579-88. Cook JD, et al. *J Anal Toxicol.* 2007;31:486-96. DHHS SAMHSA. *Fed Regist.* 2008;73:71858-907.

Interpretation of UDT Results

Positive Result

Demonstrates recent use

- Most drugs in urine have detection times of 1-3 d
- Chronic use of lipid-soluble drugs: test positive for ≥1 wk

Does not diagnose

- Drug addiction, physical dependence, or impairment

Does not provide enough information to determine

- Exposure time, dose, or frequency of use

Negative Result

Does not diagnose diversion

- More complex than presence or absence of a drug in urine

May be due to maladaptive drug-taking behavior

- Bingeing, running out early
- Other factors: eg, cessation of insurance, financial difficulties

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* 2010. Ed 4. SAMHSA. *Clinical Drug Testing in Primary Care.* TAP 32. HHS Publication No.(SMA) 12-4668. 2012. Gourlay DL, et al. Pain Med. 2005;6:107-12. Gourlay D, et al. *Clin J Pain.* 2010;26:358. Nafziger AN, et al. *Clin J Pain.* 2009;25:73-9.

Interpretation of UDT Results, cont'd

Be aware

Testing technologies & methodologies evolve

Differences exist between IA test menu panels vary

- Cross-reactivity patterns
  - Maintain list of all patient's prescribed & OTC drugs
    - Assist to identify false-positive result
- Cutoff levels

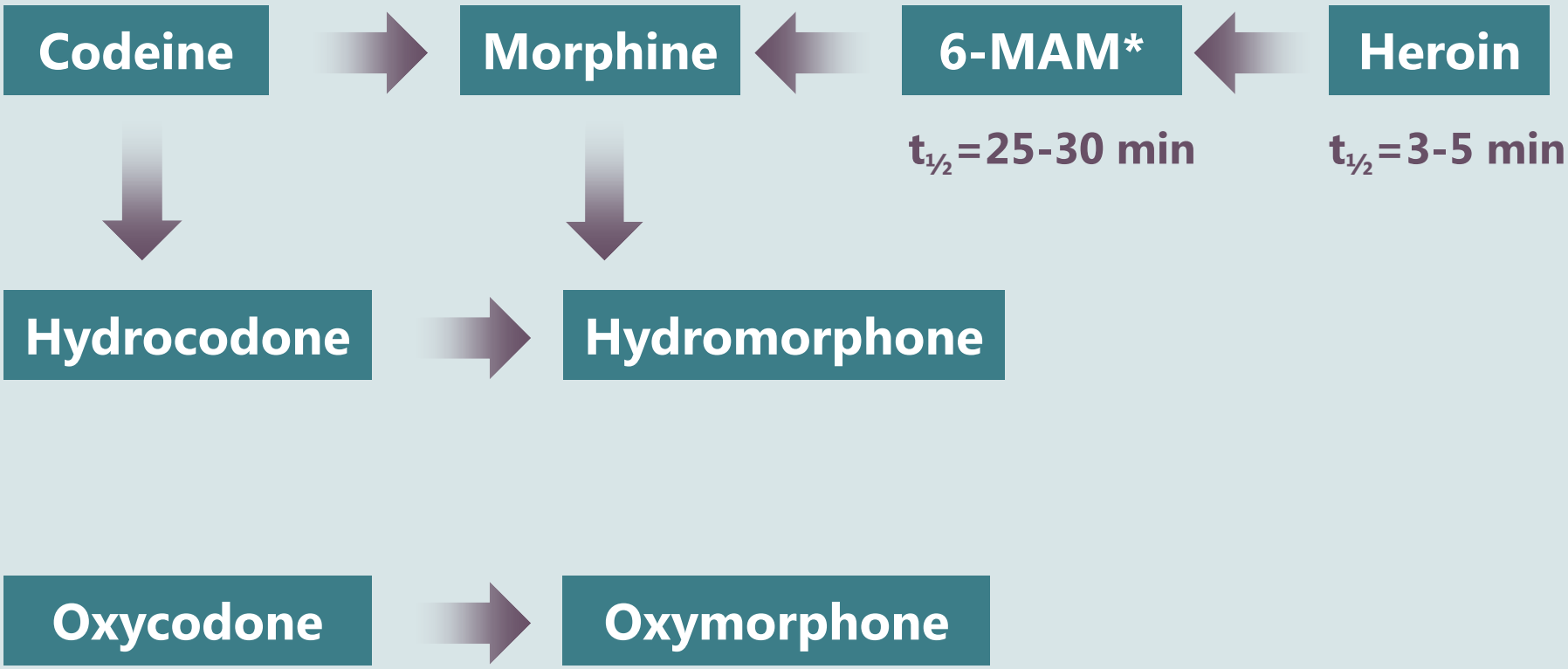
Time taken to eliminate drugs

- Document time of last use & quantity of drug(s) taken

Opioid metabolism may explain presence of apparently unprescribed drugs

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* Ed 4. 2010.

Examples of Metabolism of Opioids



*6-MAM=6-monoacetylmorphine

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* Ed 4. 2010.

Interpretation of UDT Results

Use UDT results in conjunction w/ other clinical information

Investigate unexpected results

Discuss w/ the lab

Schedule appointment w/ patient to discuss unexpected/abnormal results

Chart results, interpretation, & action

Do not ignore the *unexpected* positive result

May necessitate closer monitoring &/or referral to a specialist

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice. The Art & Science of Patient Care.* Ed 4. 2010.

Be Ready to Refer

Be familiar w/ referral sources for abuse or addiction that may arise from use of ER/LA opioids

SAMHSA substance abuse treatment facility locator

http://findtreatment.samhsa.gov/TreatmentLocator/faces/quickSearch.jspx

SAMHSA mental health treatment facility locator

http://findtreatment.samhsa.gov/MHTreatmentLocator/faces/quickSearch.jspx

Optional Slide

Challenge: The Insistent Patient

Red Flag:

Patient refuses to consider non-opioid treatment options

Mr. Lee's daily function has improved significantly over the past two years. You suggest titrating his dosage down or trying alternative pain management options. He is extremely resistant and tells you "Nothing else relieves my pain."

Action: Work with your patient to set treatment goals and expectations. Select and document a therapy plan or use a patient-provider agreement. Evaluate Mr. Lee for potential addiction; consider referral to psychiatry or addiction medicine.

Merrill, et al., 2002; Wilsey et al., 2008) (Sehgal, et al., 2012; Chou, et al., 2009a

Pearls for Practice

Anticipate and Treat Common Adverse Effects

Use Informed Consent and Patient Provider Agreements

Use UDT and PDMP as Valuable Sources of Data About your Patient

However, know their limitations

Monitor Patient Adherence, Side Effects, Aberrant Behaviors, and Clinical Outcomes

Refer Appropriately if Necessary

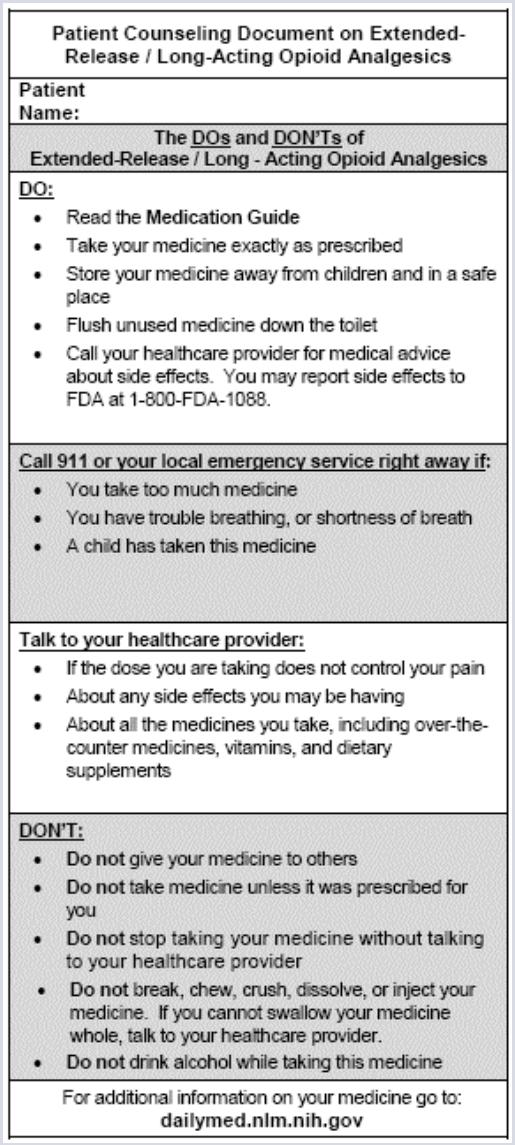
COUNSELING PATIENTS & CAREGIVERS ABOUT THE SAFE USE OF ER/LA OPIOID ANALGESICS

Unit IV

Use **Patient Counseling Document** to help counsel patients

Download:
www.er-la opioidrems.com/IwgUI/rems/pdf/patient_counseling_document.pdf

Order hard copies:
www.minneapolis.cenveo.com/pcd/SubmitOrders.aspx



Patient Counseling Document on Extended-Release / Long-Acting Opioid Analgesics

Patient Name:

The DOs and DON'Ts of Extended-Release / Long - Acting Opioid Analgesics

DO:

- Read the Medication Guide
- Take your medicine exactly as prescribed
- Store your medicine away from children and in a safe place
- Flush unused medicine down the toilet
- Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Call 911 or your local emergency service right away if:

- You take too much medicine
- You have trouble breathing, or shortness of breath
- A child has taken this medicine

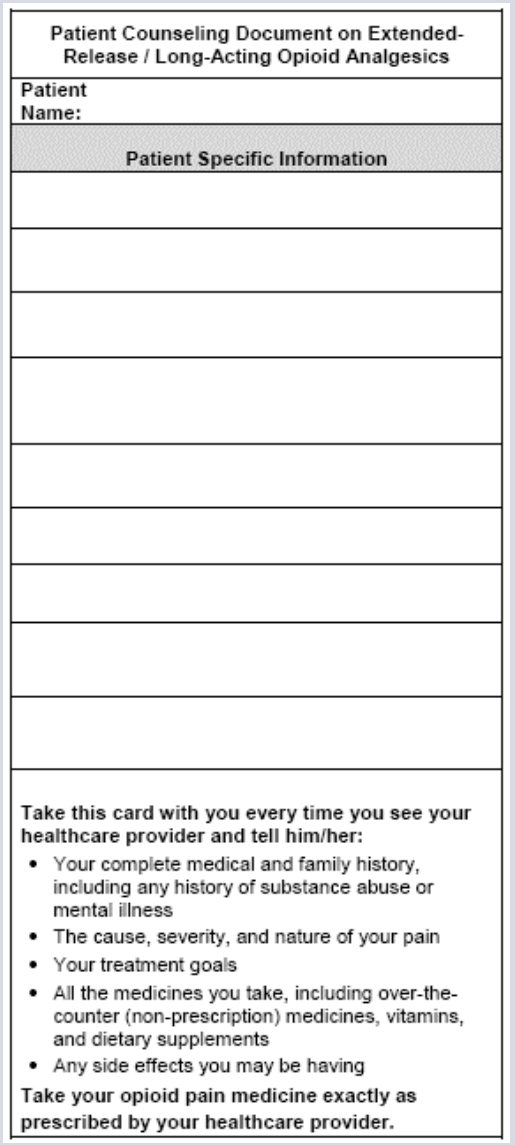
Talk to your healthcare provider:

- If the dose you are taking does not control your pain
- About any side effects you may be having
- About all the medicines you take, including over-the-counter medicines, vitamins, and dietary supplements

DON'T:

- Do not give your medicine to others
- Do not take medicine unless it was prescribed for you
- Do not stop taking your medicine without talking to your healthcare provider
- Do not break, chew, crush, dissolve, or inject your medicine. If you cannot swallow your medicine whole, talk to your healthcare provider.
- Do not drink alcohol while taking this medicine

For additional information on your medicine go to: **dailymed.nlm.nih.gov**



Patient Counseling Document on Extended-Release / Long-Acting Opioid Analgesics

Patient Name:

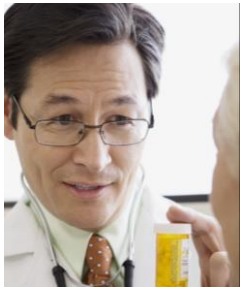
Patient Specific Information

Take this card with you every time you see your healthcare provider and tell him/her:

- Your complete medical and family history, including any history of substance abuse or mental illness
- The cause, severity, and nature of your pain
- Your treatment goals
- All the medicines you take, including over-the-counter (non-prescription) medicines, vitamins, and dietary supplements
- Any side effects you may be having

Take your opioid pain medicine exactly as prescribed by your healthcare provider.

Counsel Patients About Proper Use



Explain

- Product-specific information about the prescribed ER/LA opioid
- How to take the ER/LA opioid as prescribed
- Importance of adherence to dosing regimen, handling missed doses, & contacting their prescriber if pain cannot be controlled

Instruct patients/ caregivers to

- Read the ER/LA opioid **Medication Guide** received from pharmacy **every time** an ER/LA opioid is dispensed
- At every medical appointment explain all medications they take

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. Available at www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf
The ER/LA Opioid Analgesics Risk Evaluation & Mitigation Strategy. *Selected Important Safety Information. Abuse potential & risk of life-threatening respiratory depression.* www.erlopioidrems.com/IwgUI/rems/pdf/important_safety_information.pdf.

Counsel Patients About Proper Use, cont'd

Counsel patients/caregivers:

- On the most common AEs of ER/LA opioids
- About the risk of falls, working w/ heavy machinery, & driving
- Call the prescriber for advice about managing AEs
- Inform the prescriber about AEs

Prescribers should report serious AEs to the FDA:

www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082725.pdf

or **1-800-FDA-1088**

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Warn Patients

Never break, chew, or crush 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 & death
- When a patient cannot swallow a capsule whole, prescribers should refer to PI to determine if appropriate to sprinkle contents on applesauce or administer via feeding tube

Use of CNS depressants or alcohol w/ ER/LA opioids can cause <u>overdose & death</u>

- Use with alcohol may result in rapid release & absorption of a potentially fatal opioid dose
- Other depressants include sedative-hypnotics & anxiolytics, illegal drugs

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Warn Patients, cont'd

Misuse of ER/LA opioids can lead to death

- Take **exactly** as directed
- Counsel patients/caregivers on risk factors, signs, & symptoms of overdose & opioid-induced respiratory depression, GI obstruction, & allergic reactions
- Call **911** or poison control **1-800-222-1222**

Do not abruptly stop or reduce the ER/LA opioid use

- Discuss how to safely taper the dose when discontinuing

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Optional Slide

POISON Help
1-800-222-1222

WARNING:

A person who at first only seems to be overmedicated may get much worse. **They should be kept awake & watched closely.**

If a child or pet ever swallows an opioid that was not prescribed for them, it is ***always an emergency***. Call for help immediately.

Signs to Watch For - Overmedication or Overdose?

(Share this with your caregivers.)

Overmedication Warning - Call Healthcare Provider

U.S. residents also can call the National Poison Hotline at 1-800-222-1222.

- Intoxicated behavior - confusion, slurred speech, stumbling.
- Feeling dizzy or faint.
- Feeling or acting very drowsy or groggy, or nodding off to sleep.
- Unusual snoring, gasping, or snorting during sleep.
- Difficulty waking-up from sleep and becoming alert or staying awake.

Overdose Poisoning - Call Emergency Services

Dial 911 in the US or Canada

- Person cannot be aroused or wakened, or is unable to talk if awakened.
- Any trouble with breathing; such as shortness of breath, slow or light breathing, or stopped breathing.
- Gurgling noises coming from mouth or throat.
- Body is limp, seems lifeless. Face is pale, clammy.
- Fingernails or lips turned blue/purple.
- Slow or unusual heartbeat or stopped heartbeat.

Opioids911-Safety: Help for Safely Using Opioid Pain Relievers. Pain Treatment Topics.
http://opioids911.org/emergencies.php

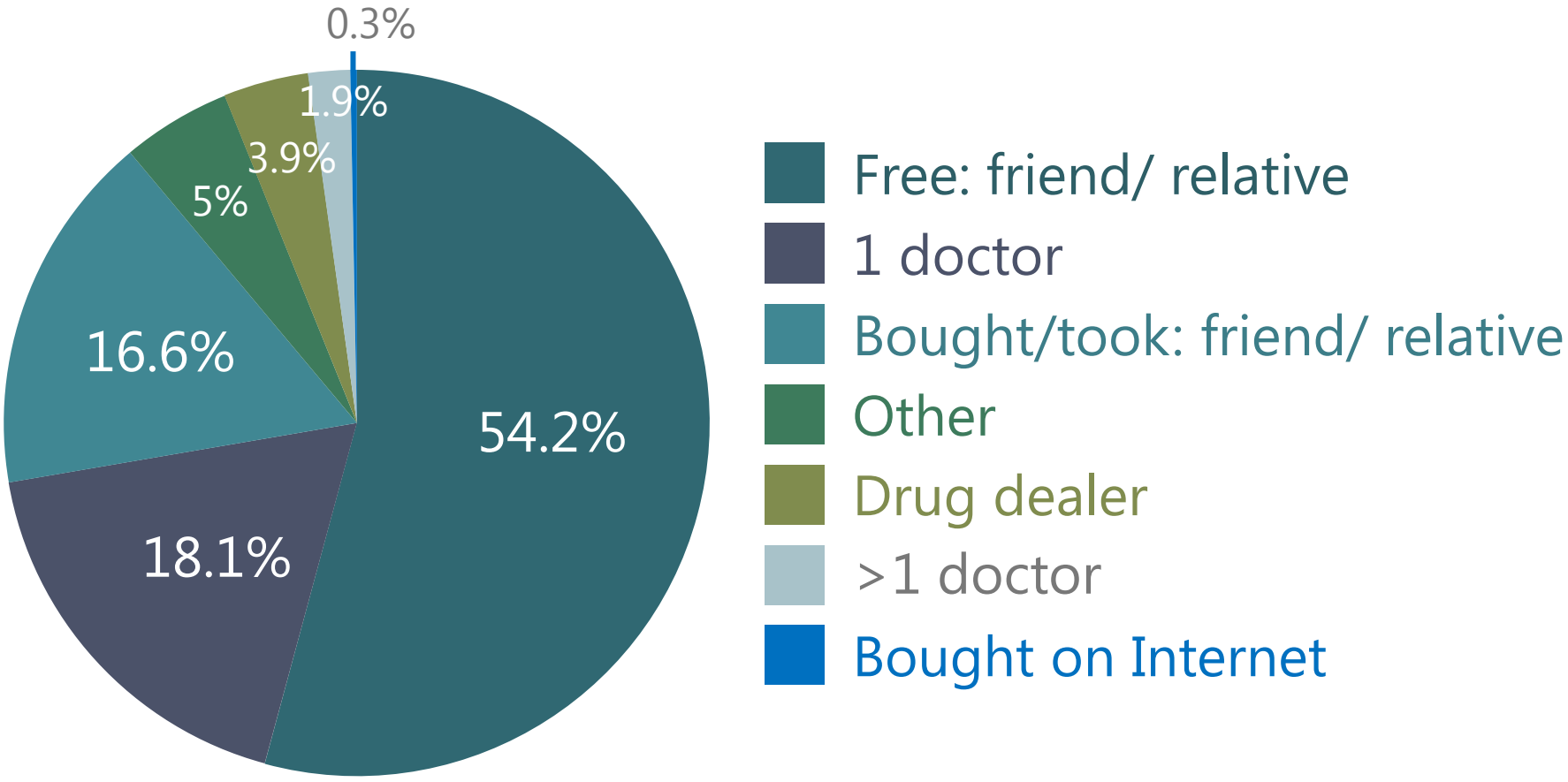
Protecting the Community

Caution Patients

- **Sharing ER/LA opioids w/ others may cause them to have serious AEs**
  - Including death
- **Selling or giving away ER/LA opioids is against the law**
- **Store medication safely and securely**
- **Protect ER/LA opioids from theft**
- **Dispose of any ER/LA opioids when no longer needed**
  - Read product-specific disposal information included w/ ER/LA opioid

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Source of Most Recent Rx Opioids Among Past-Year Users



SAMHSA. (2012). *Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings*, NSDUH Series H-44, HHS Publication No. (SMA) 12-4713. Rockville, MD.

Educate Patients & Families

Rx medicines should only be taken when prescribed to you by a provider

- **Taking a pill prescribed for someone else is drug abuse and illegal, "even just once"**

Misusing Rx drugs can be as dangerous as illegal "street" drugs

Mixing Rx opioids w/ alcohol or w/ sedatives / hypnotics is potentially fatal

Apa-Hall P, et al. *J Sch Nurs.* 2008;24(suppl):S1-16. Paulozzi LJ, et al. *Pain Med.* 2012;13:87-95.
Webster LR, et al. *Pain Med.* 2011;12 Suppl 2:S26-35.

Parents Should Set Good Examples & Educate Teens

Optional Slide

Parent Survey

- 45% of parents have taken pain medications w/o a prescription at some point
- 14% have given their children pain medications w/o a prescription

Teen Survey

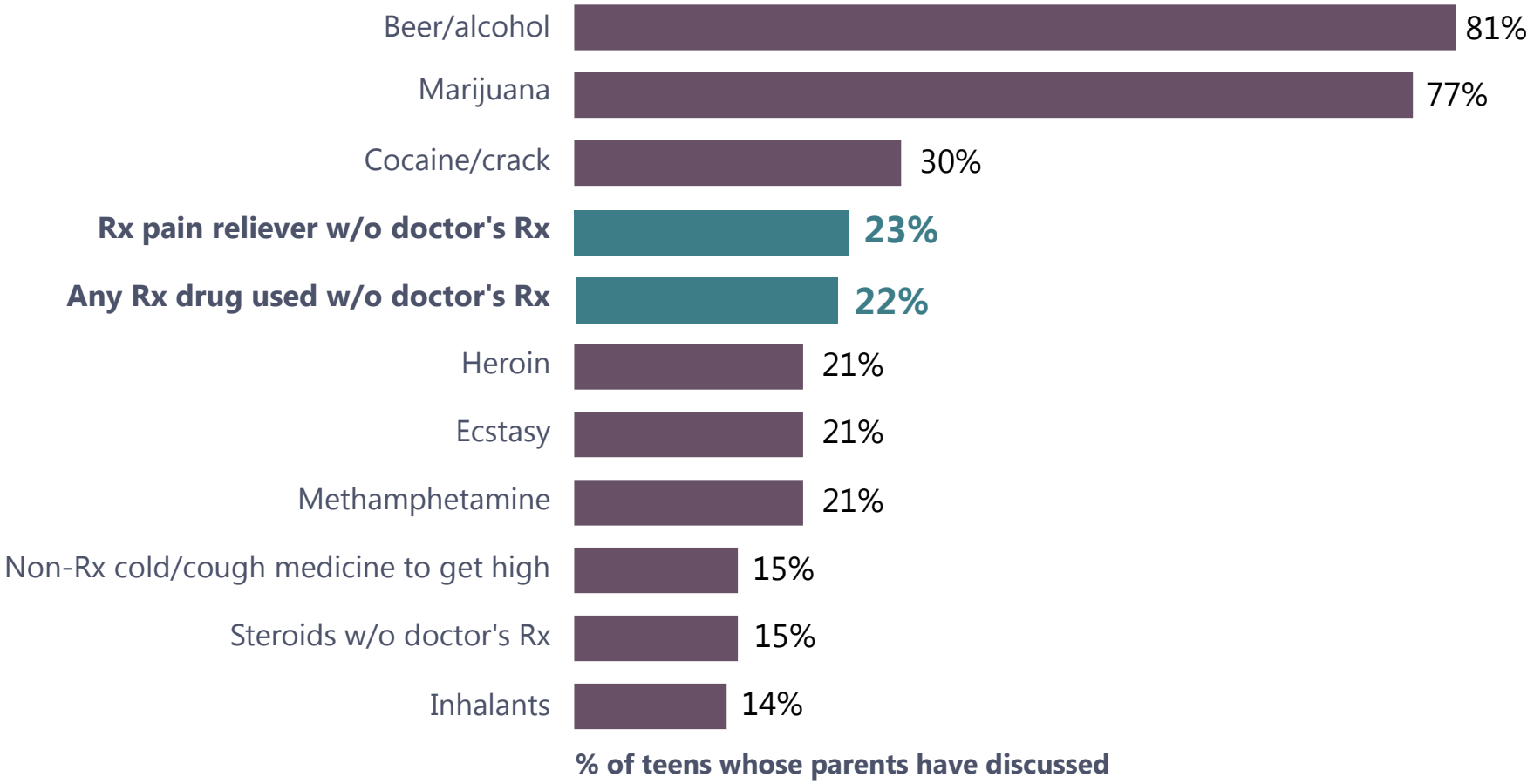
Teens continue to report that their parents do not talk to them about the risks of prescription drugs at the same levels of other abused substances

The Partnership at DrugFree.org. *Abuse of Prescription Pain Medicine in Massachusetts: Attitudes and Behavior Among Parents of Teens*. October, 2011. The Partnership at DrugFree.org. *2010 Partnership Attitude Tracking Survey. Teens and Parents.* 2011.

Optional Slide

Substances Parents Have Discussed With Teens*

*As reported by teens



The Partnership at DrugFree.org. *2010 Partnership Attitude Tracking Survey. Teens and Parents.* 2011.

Educate Parents: Not in My House

Step 1: Monitor

- Note how many pills in each prescription bottle or pill packet
- Keep track of refills for all household members
- If your teen has been prescribed a drug, coordinate & monitor dosages & refills
- Make sure friends & relatives—especially grandparents—are aware of the risks
- If your teen visits other households, talk to the families about safeguarding their medications

The Partnership at DrugFree.org. *Rx Abuse: Not in My House.* http://notinmyhouse.drugfree.org/steps.aspx

Educate Parents: Not in My House, cont'd

Step Two: Secure

- Do not store prescription meds in the medicine cabinet
- Keep meds in a safe place (e.g., locked cabinet)
- Tell relatives, especially grandparents, to lock meds or keep in a safe place
- Encourage parents of your teen's friends to secure meds

Step Three: Dispose

- Take inventory of all prescription drugs in your home
- Discard expired or unused meds

The Partnership at DrugFree.org. *Rx Abuse: Not in My House.* http://notinmyhouse.drugfree.org/steps.aspx

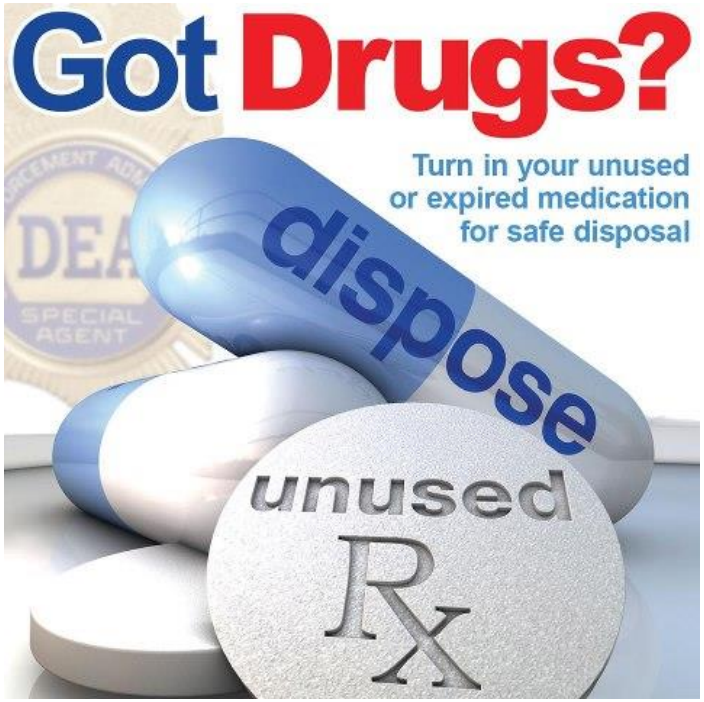
ER/LA Opioid Drug Disposal

National Prescription Drug Take-Back Day: "Got Drugs?"

Dates and Locations TBA
Check back at
http://www.deadiversion.usdoj.gov/drug_disposal/takeback/index.html

Drug drop boxes in some local police departments, to find a box near you:

- http://rxdrugdropbox.org/ or
- www.americanmedicinechest.com/ or
- www.takebacknetwork.com/local_efforts.html



Prescription drug disposal when a program or drop box is unavailable:

If take-back program or drop box unavailable, throw out in household trash

- Take drugs out of original containers
- Mix w/ undesirable substance, e.g., used coffee grounds or kitty litter
  - Less appealing to children/pets, & unrecognizable to people who intentionally go through your trash
- Place in sealable bag, can, or other container
  - Prevent leaking or breaking out of garbage bag
- Before throwing out a medicine container
  - Scratch out identifying info on label

FDA. *How to Dispose of Unused Medicines.* 2011. www.fda.gov/downloads/Drugs/ ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm107163.pdf SMAR$_x$T Disposal. A prescription for a healthy planet. www.smarxtdisposal.net/index.html

Prescription Drug Disposal

**FDA lists especially harmful medicines –
in some cases fatal w/ just 1 dose –
if taken by someone other than the patient**

- Instruct patients to check medication guide

Flush down sink/toilet if no take-back program available

- **As soon as they are no longer needed**
  - So cannot be accidentally taken by children, pets, or others
- **Includes transdermal adhesive skin patches**
  - Used patch worn for 3d 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**
  - Exception is Butrans: can seal in Patch-Disposal Unit provided & dispose of in the trash

www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicines/ucm186187.htm

Disposal Updates

In Dec 2012, DEA published a Notice of Proposed Rulemaking for Disposal of Controlled Substances

- The Secure & Responsible Drug Disposal Act of 2010 would expand options to collect controlled substances from ultimate users for disposal to include:
  - Take-back events
  - Mail-back programs
  - Collection receptacle locations

Check back at
www.deadiversion.usdoj.gov/drug_disposal/

DEA. *Federal Register*. 2012; 77(246):75783-817. Proposed Rules. Disposal of Controlled Substances. www.deadiversion.usdoj.gov/fed_regs/rules/2012/fr1221_8.htm

Optional Slide

Case:

Anne
47-Year-Old Female

Case:

Optional Slide

Anne

Anne has ovarian cancer

Stable disease based on recent imaging

Stable pain management for 1 yr w/hydromorphone ER 12 mg q24h

Last 2 months she asked for a renewal prescription 5-7 days early

- When questioned did not realize she was requesting refills early

Query your state PDMP: she has not been doctor shopping

Collect urine sample: send to lab for pain management panel that includes hydromorphone, opiates, & drugs of abuse

She reports no change in her pain control

- Current regimen is still effective

Optional Slide

Anne: What Would You Do Next?

1. Refuse to give her a refill until the "correct" time
2. Make her next prescription for only 2 weeks & have her bring in her pill bottles for a count at next visit
3. Ask where she keeps her medications & how she secures them

Answer 3 is correct

Optional Slide

Anne: Interview

Anne reports that she keeps her medications in her purse on top of the refrigerator

Further questioning reveals that her niece & nephews have recently visited her home more often than usual

Anne: What Now? Should You:

Optional Slide

1. Only prescribe 2 wks of hydromorphone ER at a time & request she brings in her prescription bottles for pill counts at each visit
2. Stress to her the safety concerns when ER/LA opioids are taken by someone for whom they are not prescribed; request she brings her prescription bottles for pill count next visit
3. Call the police

Answer 2 is correct

Optional Slide

Anne: Case Summary

Explain to Anne

- ER/LA opioids are extremely harmful—can be fatal w/ just 1 dose—if taken by someone other than the patient
- She is responsible for storing medication in a safe & secure place away from children, family members, & visitors
- If she cannot safeguard her medications, you will consider an alternative therapy

You will not provide early renewal of prescription again

At the next visit

- UDT positive for hydromorphone (negative other drugs)
- Anne reports she
  - Purchased a medication safe that same day
  - Counts her medication daily
  - Spoke to her sister regarding concerns about her niece/nephews

Optional Slide

Challenge: The Offended Patient

Red Flag:

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

Mrs. Jorgensen has been your patient for eight years and has never caused any problems. When you ask her to under urine drug testing, she becomes upset and accuses you of not trusting her.

Action: Describe UDT as a routine part of medication monitoring rather than a "drug test". Create an office policy for performing UDT on all ER/LA opioid patients. Practice by following universal precautions. Use a patient-provider agreement to clarify expectations of treatment.

Chou, et al., 2009a; Ballantyne, J.C., 2012; Stanos, 2012

Optional Slide

Challenge: The Daughter's Party

Red Flag:

Patients do not safeguard their opioid medications correctly

Your patient's daughter, Jody, stole her father's opioids from his bedside drawer to take to a "fishbowl party". Her best friend consumed a mix of opioids and alcohol and died of an overdose.

Action: Always counsel patients about safe drug storage; warn patients about the serious consequences of theft, misuse, and overdose. Tell your patients that taking another person's medication, even once, is against the law.

Chou, et al., 2009a; Ballantyne, J.C., 2012; Stanos, 2012

Pearls for Practice

Establish Informed Consent

Counsel Patients about Proper Use

Appropriate use of medication

Consequences of inappropriate use

Educate the Whole Team

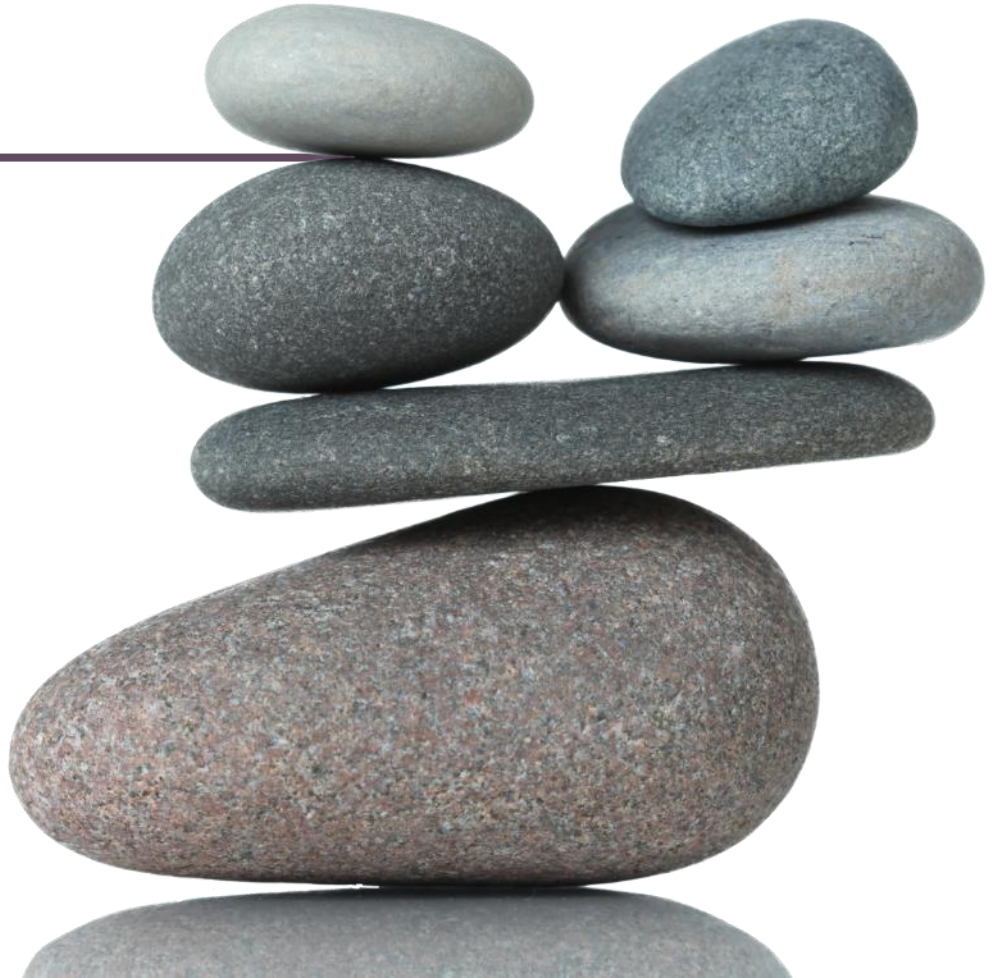
Patients, families, caregivers

Tools and Documents Can Help with Counseling

Use them!

GENERAL DRUG INFORMATION FOR ER/LA OPIOID ANALGESIC PRODUCTS

Unit V



General ER/LA Opioid Drug Information

Prescribers should be knowledgeable about general characteristics, toxicities, & drug interactions for ER/LA opioid products:

ER/LA opioid analgesic products are scheduled under the Controlled Substances Act & can be misused & abused

Respiratory depression is the most serious opioid AE

Can be immediately life-threatening

Constipation is the most common long-term AE

Should be anticipated

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

For Safer Use: Know Drug Interactions, PK, & PD

CNS depressants can potentiate sedation & respiratory depression

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

Some drug levels may increase without dose dumping

Use w/ MAOIs may increase respiratory depression

Certain opioids w/ MAOIs can cause serotonin syndrome

Can reduce efficacy of diuretics

Inducing release of antidiuretic hormone

Methadone & buprenorphine can prolong QTc interval

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

Opioid Tolerant

Tolerance to sedating & respiratory-depressant effects is critical to safe use of certain ER/LA opioid products, dosage unit strengths, or doses

Patients must be opioid tolerant before using

- Any strength of transdermal fentanyl or hydromorphone ER
- Certain strengths or daily doses of other ER products

Opioid-tolerant patients are those taking at least

- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/hr
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid

FOR 1 WK OR LONGER

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012 www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf
The ER/LA Opioid Analgesics Risk Evaluation & Mitigation Strategy. *Selected Important Safety Information. Abuse potential & risk of life-threatening respiratory depression.* www.er-la-opioidrems.com/IwgUI/rems/pdf/important_safety_information.pdf. 2012.

Key Instructions: ER/LA Opioids

Individually titrate to a dose that provides adequate analgesia & minimizes adverse reactions

Times required to reach steady-state plasma concentrations are product-specific

Refer to product information for titration interval

Continually re-evaluate to assess maintenance of pain control & emergence of AEs

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Key Instructions: ER/LA Opioids, cont'd

During chronic therapy, especially for non-cancer-related pain, periodically reassess the continued need for opioids

If pain increases, attempt to identify source, while adjusting dose

When an ER/LA opioid is no longer required, gradually titrate dose downward to prevent signs & symptoms of withdrawal in physically dependent patients

Do not abruptly discontinue

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Common Drug Information for This Class

Limitations of usage	Dosage reduction for hepatic or renal impairment	Relative potency to oral morphine
• Not for use as an as-needed analgesic • Not for mild pain or pain not expected to persist for an extended duration • Not for use in treating acute pain	See individual drug PI	• Intended as general guide • Follow conversion instructions in individual PI • Incomplete cross-tolerance & inter-patient variability require conservative dosing when converting from 1 opioid to another – Halve calculated comparable dose & titrate new opioid as needed

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Transdermal Dosage Forms

Do not cut, damage, chew, or swallow

Exertion or exposure to external heat can lead to fatal overdose

Rotate location of application

Prepare skin: clip - not shave - hair & wash area w/ water

Monitor patients w/ fever for signs or symptoms of increased opioid exposure

Metal foil backings are not safe for use in MRIs

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf
The ER/LA Opioid Analgesics Risk Evaluation & Mitigation Strategy. *Selected Important Safety Information. Abuse potential & risk of life-threatening respiratory depression.* www.er-la-opioidrems.com/IwgUI/rems/pdf/important_safety_information.pdf. 2012.

Drug Interactions Common to this Class

Concurrent use w/ other CNS depressants can increase risk of respiratory depression, hypotension, profound sedation, or coma

Reduce initial dose of one or both agents

Avoid using partial agonists & mixed agonist/antagonist analgesics† together, may reduce analgesic effect or precipitate withdrawal

May enhance neuromuscular blocking action of skeletal muscle relaxants & increase respiratory depression

Concurrent use w/ anticholinergic medication increases risk of urinary retention & severe constipation

May lead to paralytic ileus

†Buprenorphine, pentazocine, nalbuphine, butorphanol

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Drug Information Common to This Class

Use in opioid-tolerant patients

- See individual PI for products which:
  - Have strengths or total daily doses only for use in opioid-tolerant patients
  - Are only for use in opioid-tolerant patients at all strengths

Contraindications

- Significant respiratory depression
- Acute or severe asthma in an unmonitored setting or in absence of resuscitative equipment
- Known or suspected paralytic ileus
- Hypersensitivity (e.g., anaphylaxis)
- See individual PI for additional contraindications

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Pearls for Practice

Patients MUST be opioid-tolerant in order to safely take most ER/LA opioid products

Be familiar with drug-drug interactions, pharmacokinetics and pharmacodynamics of ER/LA opioids

Central nervous system depressants (alcohol, sedatives, hypnotics, tranquilizers, tricyclic antidepressants) can have a potentiating effect on the sedation and respiratory depression caused by opioids.

Optional Slide

Challenge: The Patient in the ER

Red Flag:

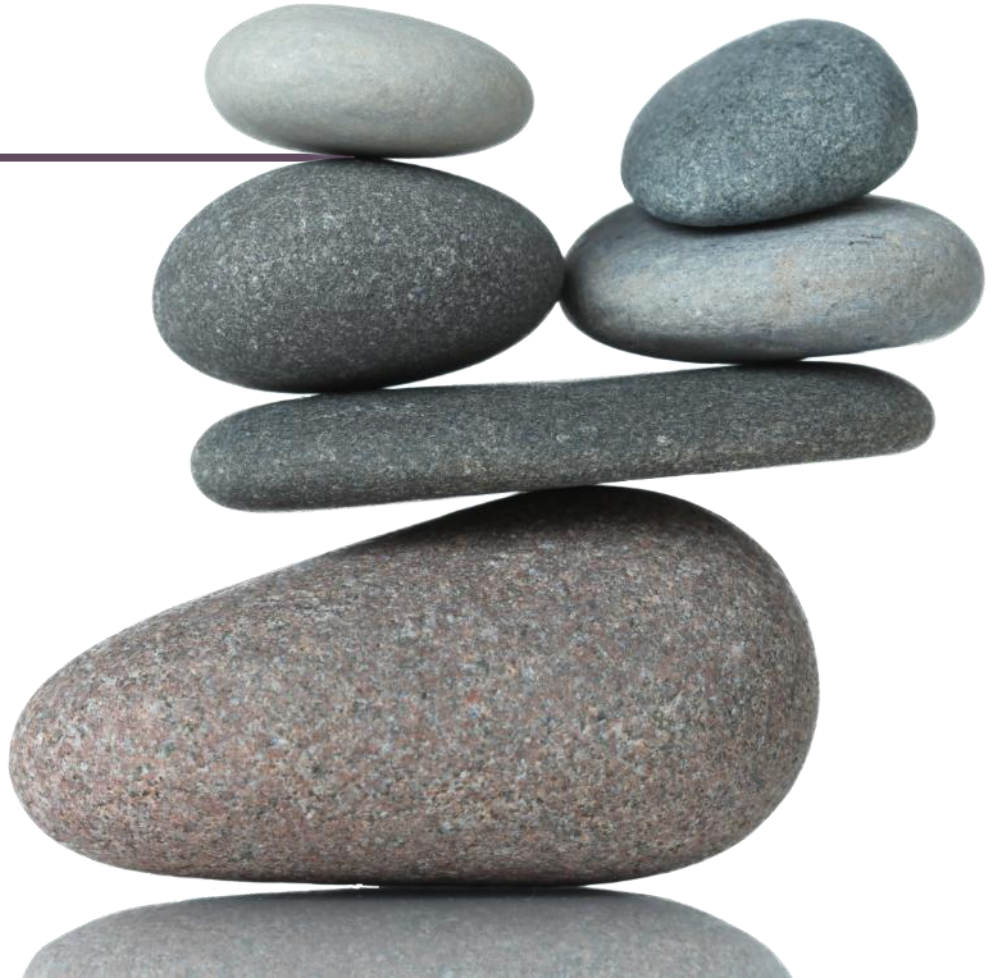
You are woken by a telephone call at 2 am reporting that your patient, Mr. Diallo, is in the ER with apparent respiratory depression.

Action: Be familiar with risk factors for respiratory depression and know when opioids are contra-indicated. Anticipate possible risks and develop contingency plans. Teach patients, family, and caregivers about respiratory depression and its symptoms.

Merrill, et al., 2002; Wilsey et al., 2008) (Sehgal, et al., 2012; Chou, et al., 2009a

SPECIFIC DRUG INFORMATION FOR ER/LA OPIOID ANALGESIC PRODUCTS

Unit VI



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
- Specific drug interactions

For detailed information, refer to online PI:
DailyMed at www.dailymed.nlm.nih.gov Drugs@FDA at www.fda.gov/drugsatfda

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012.
www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Morphine Sulfate ER Capsules (Avinza)

Dosing interval	• Once a day
Key instructions	• Initial dose in opioid non-tolerant patients is 30 mg • Titrate using a minimum of 3-d intervals • Swallow capsule whole (do not chew, crush, or dissolve) • May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing; use immediately • MDD:* 1600 mg (renal toxicity of excipient, fumaric acid)
Drug interactions	• Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose • PGP* inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold
Opioid-tolerant	• 90 mg & 120 mg capsules for use in opioid-tolerant patients only
Product-specific safety concerns	• None

* MDD=maximum daily dose; PGP= P-glycoprotein

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Buprenorphine Transdermal System (Butrans)

Dosing interval	• One transdermal system every 7 d

Key instructions	• Initial dose in opioid non-tolerant patients on <30 mg morphine equivalents & in mild-moderate hepatic impairment: 5 mcg/h
	• When converting from 30 mg-80 mg morphine equivalents, first taper to 30 mg morphine equivalent, then initiate w/ 10 mcg/h
	• Titrate after a minimum of 72 h prior to dose adjustment
	• Maximum dose: 20 mcg/h due to risk of QTc prolongation
	• Application
	  • Apply only to sites indicated in PI
	  • Apply to intact/non-irritated skin
	  • Prep skin by clipping hair; wash site w/ water only
	  • Rotate application site (min 3 wks before reapply to same site)
	  • Do not cut
	• Avoid exposure to heat
	• Dispose of patches: fold adhesive side together & flush down toilet

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Buprenorphine Transdermal System (Butrans) cont'd

Drug interactions	• CYP3A4 inhibitors may increase buprenorphine levels • CYP3A4 inducers may decrease buprenorphine levels • Benzodiazepines may increase respiratory depression • Class IA & III antiarrythmics, other potentially arrhythmogenic agents, may increase risk of QTc prolongation & torsade de pointe
Opioid-tolerant	• 10 mcg/h & 20 mcg/h for use in opioid-tolerant patients only
Drug-specific safety concerns	• QTc prolongation & torsade de pointe • Hepatotoxicity • Application site skin reactions
Relative potency: oral morphine	• Equipotency to oral morphine not established

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Methadone Hydrochloride Tablets (Dolophine)

Dosing interval	• Every 8 to 12 h
Key instructions	• Initial dose in opioid non-tolerant patients: 2.5 to 10 mg • Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose & death. Use low doses according to table in full PI • High inter-patient variability in absorption, metabolism, & relative analgesic potency • Opioid detoxification or maintenance treatment only provided in a federally certified opioid (addiction) treatment program (CFR, Title 42, Sec 8)
Drug interactions	• Pharmacokinetic drug-drug interactions w/ methadone are complex – CYP 450 inducers may decrease methadone levels – CYP 450 inhibitors may increase methadone levels – Anti-retroviral agents have mixed effects on methadone levels • Potentially arrhythmogenic agents may increase risk for QTc prolongation & torsade de pointe • Benzodiazepines may increase respiratory depression

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Methadone Hydrochloride Tablets (Dolophine) cont'd

Opioid-tolerant	• Refer to full PI
Drug-specific safety concerns	• QTc prolongation & torsade de pointe • Peak respiratory depression occurs later & persists longer than analgesic effect • Clearance may increase during pregnancy • False-positive UDT possible
Relative potency: oral morphine	• Varies depending on patient's prior opioid experience

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Fentanyl Transdermal System (Duragesic)

Dosing interval	• Every 72 h (3 d)

Key instructions	• Use product-specific information for dose conversion from prior opioid
	• Hepatic or renal impairment: use 50% of dose if mild/moderate, avoid use if severe
	• Application
	  – Apply to intact/non-irritated/non-irradiated skin on a flat surface
	  – Prep skin by clipping hair, washing site w/ water only
	  – Rotate site of application
	  – Titrate using no less than 72 h intervals
	  – Do not cut
	• Avoid exposure to heat
	• Avoid accidental contact when holding or caring for children
	• Dispose of used/unused patches: fold adhesive side together & flush down toilet

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Fentanyl Transdermal System (Duragesic), cont'd

Key instructions	**Specific contraindications:** • Patients who are not opioid-tolerant • Management of – Acute or intermittent pain, or patients who require opioid analgesia for a short period of time – Post-operative pain, out-patient, or day surgery – Mild pain
Drug interactions	• CYP3A4 inhibitors may increase fentanyl exposure • CYP3A4 inducers may decrease fentanyl exposure
Opioid-tolerant	• All doses indicated for opioid-tolerant patients only
Drug-specific safety concerns	• Accidental exposure due to secondary exposure to unwashed/unclothed application site • Increased drug exposure w/ increased core body temp or fever • Bradycardia • Application site skin reactions
Relative potency: oral morphine	• See individual PI for conversion recommendations from prior opioid

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Morphine Sulfate ER-Naltrexone Tablets (Embeda)

Dosing interval	• Once a day or every 12 h
Key instructions	• Initial dose as first opioid: 20 mg/0.8 mg • Titrate using a **minimum of 3-d intervals** • Swallow capsules whole (do not chew, crush, or dissolve) • Crushing or chewing will release morphine, possibly resulting in fatal overdose, & naltrexone, possibly resulting in withdrawal symptoms • May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately
Drug interactions	• Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose • PGP inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold
Opioid-tolerant	• 100 mg/4 mg capsule for use in opioid-tolerant patients only
Product-specific safety concerns	• None

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Hydromorphone Hydrochloride ER Tablets (Exalgo)

Dosing interval	• Once a day
Key instructions	• Use conversion ratios in individual PI • Start patients w/ moderate hepatic impairment on 25% dose prescribed for patient w/ normal function • Renal impairment: start patients w/ moderate on 50% & patients w/ severe on 25% dose prescribed for patient w/ normal function • Titrate using a minimum of 3 to 4 d intervals • Swallow tablets whole (do not chew, crush, or dissolve) • Do not use in patients w/ sulfite allergy (contains sodium metabisulfite)
Drug interactions	• None
Opioid-tolerant	• All doses are indicated for opioid-tolerant patients only
Product-specific adverse reactions	• Allergic manifestations to sulfite component
Relative potency: oral morphine	• ~5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in individual product information

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Morphine Sulfate ER Capsules (Kadian)

Dosing interval	• Once a day or every 12 h
Key instructions	• PI recommends not using as first opioid • Titrate using minimum of 2-d intervals • Swallow capsules whole (do not chew, crush, or dissolve) • May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately
Drug interactions	• Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose of morphine • PGP inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold
Opioid-tolerant	• 100 mg & 200 mg capsules for use in opioid-tolerant patients only
Product-specific safety concerns	• None

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Morphine Sulfate CR Tablets (MS Contin)

Dosing interval	• Every 8 h or every 12 h
Key instructions	• Product information recommends not using as first opioid. • Titrate using a minimum of 2-d intervals • Swallow tablets whole (do not chew, crush, or dissolve)
Drug interactions	• PGP inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold
Opioid-tolerant	• 100 mg & 200 mg tablet strengths for use in opioid-tolerant patients only
Product-specific safety concerns	• None

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Tapentadol ER Tablets (Nucynta ER)

Dosing interval	• Every 12 h
Key instructions	• 50 mg every 12 h is initial dose in opioid non-tolerant patients • Titrate by 50 mg increments using minimum of 3-d intervals • MDD: 500 mg • Swallow tablets whole (do not chew, crush, or dissolve) • Take 1 tablet at a time w/ enough water to ensure complete swallowing immediately after placing in mouth • Dose once/d in moderate hepatic impairment (100 mg/d max) • Avoid use in severe hepatic & renal impairment
Drug interactions	• Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of a potentially fatal dose of tapentadol • Contraindicated in patients taking MAOIs
Opioid-tolerant	• No product-specific considerations
Product-specific safety concerns	• Risk of serotonin syndrome • Angio-edema
Relative potency: oral morphine	• Equipotency to oral morphine has not been established

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Oxymorphone Hydrochloride ER Tablets (Opana ER)

Dosing interval	• Every 12 h dosing, some may benefit from asymmetric (different dose given in AM than in PM) dosing
Key instructions	• Use 5 mg every 12 h as initial dose in opioid non-tolerant patients & patients w/ mild hepatic impairment & renal impairment (creatinine clearance <50 mL/min) & patients >65 yrs • Swallow tablets whole (do not chew, crush, or dissolve) • Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth • Titrate using a minimum of 2-d intervals • Contraindicated in moderate & severe hepatic impairment
Drug interactions	• Alcoholic beverages or medications w/ alcohol may result in absorption of a potentially fatal dose of oxymorphone
Opioid-tolerant	• No product-specific considerations
Product-specific safety concerns	• None
Relative potency: oral morphine	• Approximately 3:1 oral morphine to oxymorphone oral dose ratio

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Oxycodone Hydrochloride CR Tablets (OxyContin)

Dosing interval	• Every 12 h
Key instructions	• Opioid-naïve patients: initiate treatment w/ 10 mg every 12 h • Titrate using a minimum of 1 to 2 d intervals • Hepatic impairment: start w/ ⅓-½ usual dosage • Renal impairment (creatinine clearance <60 mL/min): start w/ ½ usual dosage • Consider other analgesics in patients w/ difficulty swallowing or underlying GI disorders that predispose to obstruction. Swallow tablets whole (do not chew, crush, or dissolve) • Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth
Drug interactions	• CYP3A4 inhibitors may increase oxycodone exposure • CYP3A4 inducers may decrease oxycodone exposure
Opioid-tolerant	• Single dose >40 mg or total daily dose >80 mg for use in opioid-tolerant patients only
Product-specific safety concerns	• Choking, gagging, regurgitation, tablets stuck in throat, difficulty swallowing tablet • Contraindicated in patients w/ GI obstruction
Relative potency: oral morphine	• Approximately 2:1 oral morphine to oxycodone oral dose ratio

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Summary

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

Understand how to assess patients for treatment w/ ER/LA opioids

Be familiar w/ how to initiate therapy, modify dose, & discontinue use of ER/LA opioids

Know how to manage ongoing therapy w/ ER/LA opioids

Know how to counsel patients & caregivers about the safe use of ER/LA opioids, including proper storage & disposal

Be familiar w/ general & product-specific drug information concerning ER/LA opioids

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!

Thank you!

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