Opioid Risk Assessment, Mitigation, and Management

[1]Daniel P. Alford, MD, MPH
[1]Phillip Coffin, MD
[2]Melissa Weimer, DO, MCR

[1]These individuals were involved in the planning of the original 2017 content
[2] These individuals were involved in the 2021 review, update, and approved rerelease of this activity

Speaker acknowledgements for ACP video clip: Gregory Hood, MD

Educational Objectives

At the conclusion of this activity participants should be able to:

- Describe universal precautions and their role in opioid therapy
- Review monitoring and documentation strategies for opioid therapy
- Explain the fundamental principles of urine drug testing and interpretation
- List the differential diagnosis for drug misuse
- Describe when naloxone co-prescription should be considered

Case

- 45 year old man with hypertension, heart failure, and tobacco use who has been prescribed high dose opioids for chronic, non-specific testicular pain after a vasectomy 15 years ago and mechanical low back pain. You are seeing him for the first time after his previous PCP retired.
- Current total morphine equivalent dose prescribed is 390mg per day.
- He is also prescribed valium 5mg BID for muscle spasms.
- Prior medical records are sparse.
- Review of the prescription drug monitoring program show several early prescriptions over the last 3 months from his cardiologist who had agreed to prescribe for him while he found a new PCP.
- Patient tells you he has a family history of alcohol use disorder and a personal history of gambling disorder.

Universal Precautions in Pain Medicine

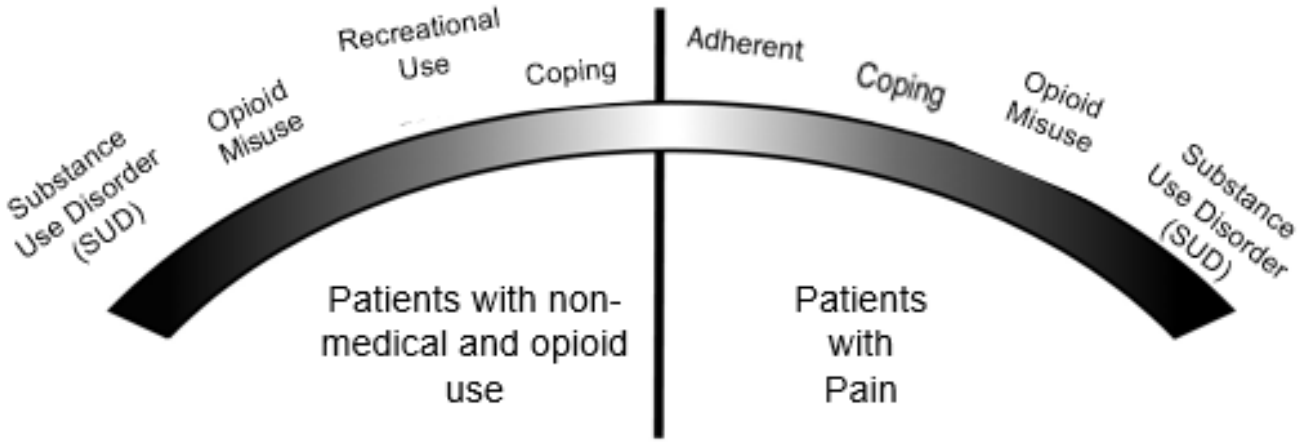
Part of an Office Controlled Substance Policy

- **Predicting opioid misuse is imprecise**
  - Protects all patients
  - Protects the public and community health
- **Consistent application of precautions**
  - Takes pressure off provider
  - Reduces stigmatization of individual patients
  - Standardizes system of care
- **Resonant with expert guidelines**
  - American Pain Society/American Academy of Pain Medicine
  - American Society of Interventional Pain Physicians
  - Federation of State Medical Boards
  - Canadian National Pain Centre

PCSS Providers Clinical Support System

Gourlay DL, Heit HA, Almahrezi A. Pain Med. 2005 Mar-Apr;6(2):107-12.

The Opioid Use Continuum



Providers Clinical Support System

Graphic adapted from Passik S D Mayo Clin Proc. 2009;84:593-601

Opioid Misuse in Primary Care

- Likely under recognized
- Published rates of prescription opioid misuse range from **4-26%**[1-4]
- In 2 hr interviews with 801 patients prescribed opioids by primary care physicians[2]
  - 26% purposeful sedation
  - 39% increasing dose w/o prescription
  - 8% obtaining from other physicians
  - 18% use for purposes other than pain
  - 20% drinking alcohol to relieve pain
  - 12% hoarding pain medications

1) Martell, et al. Ann Intern Med. 2007; 146: 116-27.
2) Fleming, et al. J Pain. 2007; 8: 573-82.
3) Boscarino, et al. Addiction. 2010; 105: 1776-82.
4) Banta-Green, et al. Drug Alcohol Depend. 2009: 104: 34-42.

Common Universal Precautions

- Comprehensive pain assessment including opioid risk assessment
- Formulation of pain diagnosis/es
- Opioid prescriptions should be considered a **test** or **trial**; continued or discontinued based on assessment and reassessment of risks and benefits
  - Decisions to continue or discontinue opioid therapy should be made regularly (i.e., every 2-3 months)
- Regular face-to-face visits
- Clear documentation

Federation of State Medical Boards Model Policy 2013. www.fsmb.org/grpol_policydocs.html
Gourlay DL, Heit HA, Almahrezi A. *Pain Med.* 2005;6(2):107-12.
Chou R, et al. *J Pain*. 2009;10(2):147-59.
Franklin GM. *Neurology*. 2014; 83:1277-1284

Common Universal Precautions

- **Patient Prescriber Agreements (PPA)**
  - **Informed Consent** (goals and risks)
  - **Plan of Care**
  - Signed by both patient and prescriber
  - Serves as a **Patient Counseling Document**
  - Efficacy not well established but no evidence of a negative impact on patient outcomes
- **Monitoring** for opioid adherence, opioid use disorder, and diversion
  - Urine drug testing
  - Pill counts
  - Prescription Drug Monitoring Program (PDMP) data

Fishman SM, Kreis PG. *Clin J Pain*. 2002;18(4 Suppl):S70-5.
Arnold RM, et al. *Am J Med*. 2006;119(4):292-6.
Starrels J, et al. *Ann Intern Med*. 2010;152(11):712-20.
Franklin GM. *Neurology*. 2014; 83:1277-1284

PPA Informed Consent

Realistic Goals

- Reduce pain, not eliminate
- Increase function (individualized and SMART goals)
  - Specific
  - Measureable
  - Action-oriented
  - Realistic
  - Time-sensitive

Potential Risks

- Side effects, physical dependence
- Drug interactions/over-sedation
- Potential for impairment e.g., driving
- Opioid use disorder, overdose
- Pregnancy
  - Significant risk of Neonatal Abstinence Syndrome
- Possible hyperalgesia (increased pain)
- Victimization by others seeking opioids

Nicolaidis C. *Pain Med.* 2011;12(6):890-7.
Paterick TJ, et al. *Mayo Clin Proc.* 2008;83(3):313-19.
Cheatle MD, Savage SR. *J Pain Symptom Manage.* 2012;44(1):105-16.
Tolia VN et al. *N Engl J Med* 2015;372:2118-26.

PPA Plan of Care

See also ACP Quality Connect: Chronic Pain Controlled Substance Agreements Video by Gregory A. Hood, MD, FACP

- Engagement in other recommended treatments
- Polices – monitoring, refills
- Permission to communicate with key others
- No illegal drug use, avoid sedative use
- Notifying provider of all other medications and drugs
- Discuss birth control, periodic monitoring for pregnancy
- Use as directed (dose, no adulteration of pills or patches, schedule, guidance on missed doses)
- Safe storage (away from family, visitors, pets)
- Safe disposal (read product specific information for guidance)
- No diversion, sharing or selling, protect from theft

Fishman SM, Kreis PG. *Clin J Pain.* 2002;18(4 Suppl):S70-5.
Arnold RM, Han PK, Seltzer D. *Am J Med.* 2006;119(4):292-6.

Discussing Monitoring

- Review the personal and public health (community health) risks of opioid medications
- Discuss your responsibility to look for early signs of harm
- Discuss agreements, pill counts, drug tests, prescription drug monitoring as ways that you are helping to protect patient from getting harmed by medications
  - ACE Inhibitor – renal functional analogy
- Use consistent approach, but set *level* of monitoring to match risk of opioid use disorder

Implementing Universal Precautions in Pain Medicine

Use a Health-Oriented, Risk Benefit Framework

NOT…

- **Is the patient good or bad?**
- **Does the patient deserve opioids?**
- **Should this patient be punished or rewarded?**
- **Should I trust the patient?**

RATHER…

Do the benefits of opioid treatment outweigh the untoward effects and risks for this patient (or society)?

Judge the opioid treatment NOT the patient

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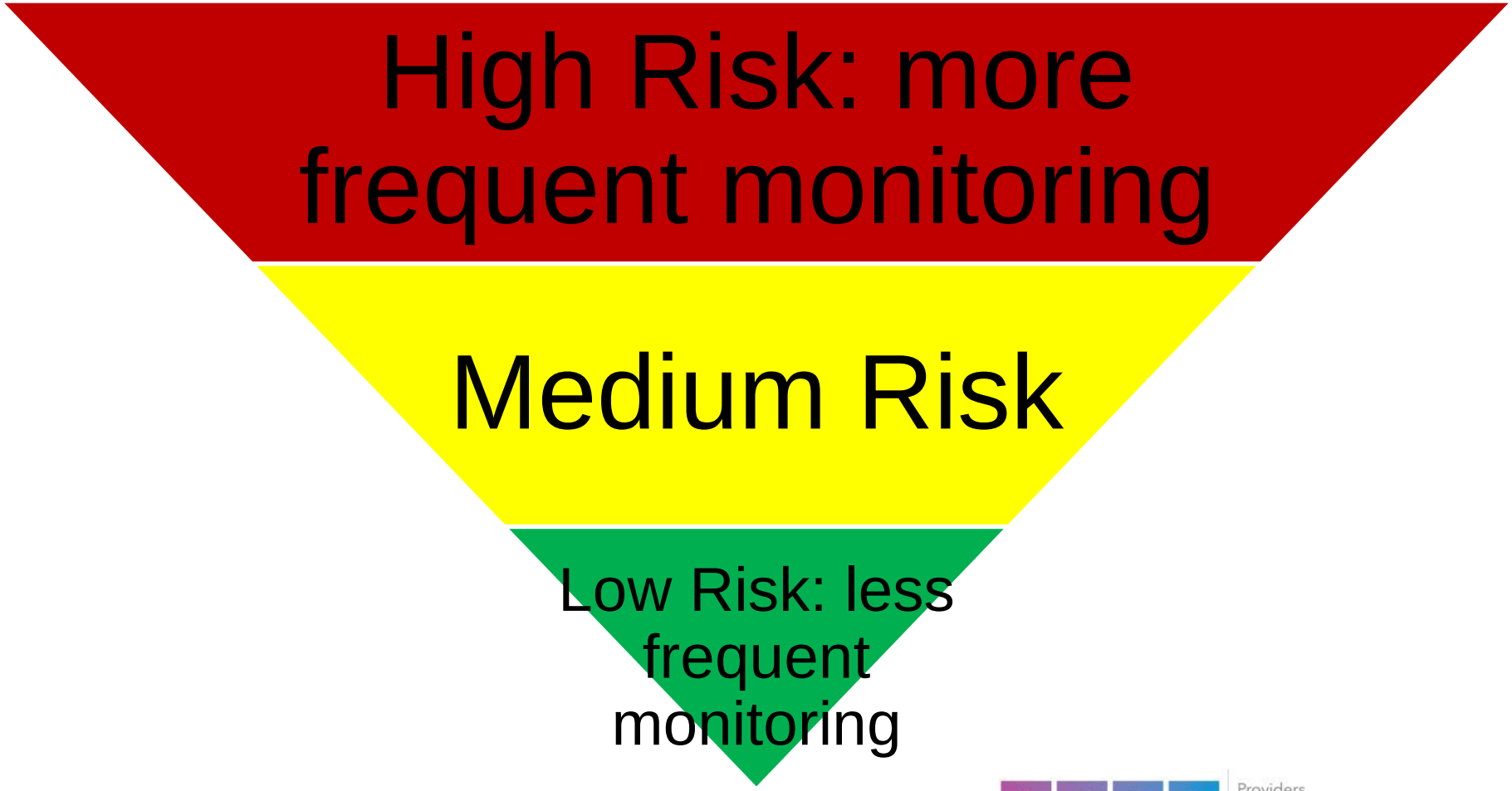
Nicolaidis C. *Pain Med.* 2011;12(6):890-7.

UNIVERSAL PRECAUTIONS IN PRACTICE

How do you determine level of monitoring?



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Opioid Misuse Risk Stratification

How should it be used?

Discuss level of concern with patient

- "Despite being in recovery from alcohol use disorder, you are at higher risk for developing problems with the opioid pain medication."

Level of monitoring that should be implemented

- Frequency of visits, urine drug testing, etc.
- High risk patients may need to agree to random call-backs

Need for pain and/or addiction consultant

- If available

Some patients may be too risky for opioids analgesics

- e.g., patient with recent opioid use disorder

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Opioid Misuse Risk Screening Tools

- **SOAPP**: Screener & Opioid Assessment for Patients w/ Pain
- **ORT**: Opioid Risk Tool
- **STAR**: Screening Tool for Addiction Risk
- **SISAP**: Screening Instrument for Substance Abuse Potential
- **PDUQ**: Prescription Drug Use Questionnaire

- **No "gold standard"**
- **Lack rigorous testing**

Webster et al. Pain Med. 2005
Butler et al. J Pain. 2008;
Adams et al. J Pain Symptom Manage, 2004

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Opioid Risk Tool (ORT)

		Female	Male
Family history of substance abuse			
	Alcohol	❑1	❑3
	Illegal drugs	❑2	❑3
	Prescription drugs	❑4	❑4
Personal history of substance abuse			
	Alcohol	❑3	❑3
	Illegal drugs	❑4	❑4
	Prescription drugs	❑5	❑5
Age between 16-45 years		❑1	❑1
History of preadolescent sexual abuse		❑3	❑0
Psychological disease			
	ADHD, OCD, bipolar, schizophrenia	❑2	❑2
	Depression	❑1	❑1

Scoring

0-3: low risk
4-7: mod risk
>8: high risk

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Webster LR, Webster RM. Pain Medicine, 2006

CASE: Opioid Risk Tool (ORT)

		Female	Male
Family history of substance abuse			
	Alcohol	❑1	☒3
	Illegal drugs	❑2	❑3
	Prescription drugs	❑4	❑4
Personal history of substance abuse			
	Alcohol	❑3	❑3
	Illegal drugs	❑4	❑4
	Prescription drugs	❑5	❑5
Age between 16-45 years		❑1	☒1
History of preadolescent sexual abuse		❑3	❑0
Psychological disease			
	ADHD, OCD, bipolar, schizophrenia	❑2	❑2
	Depression	❑1	☒1

TOTAL = 5

Scoring

0-3: low risk
4-7: mod risk
>8: high risk

Webster LR, Webster RM. Pain Medicine, 2006

Case: Level of Risk Assessment

- Opioid Risk Tool Total = 5
- Does not take into account
  - Personal history of gambling disorder
  - Early refill requests
  - High opioid dose
  - Co-prescription of benzodiazepines
  - Apparent poor benefit of opioids and poor pain coping
- All together, risk is assessed to be HIGH
- Your monitoring approach
  - 14 day prescriptions with no refills
  - Urine drug testing every 1-2 months
  - Random Pill Counts
  - Close monitoring of prescription drug monitoring program with refills

Example Monitoring Approach

See also ACP Quality Connect: Chronic Pain
Minimizing the Risk of Abuse by Gregory A. Hood, MD, FACP

	Low Risk	Medium Risk	High Risk
Patient Provider Agreement	Once every other year	Once every other year	Once year
Pain Visit with Functional Goal & Side Effect Assessment	Every 3-6 months	Every 3 months	Every month – 2 weeks
Random Urine Drug Testing	Every 6-12 months	Every 6 months	Every few weeks to month
Pill Count	Once year	Every 6 months	Monthly to semi-monthly
Prescription Refill Allowance	28 days	28 days	7-14 days

MONITORING STRATEGIES

- See also ACP Quality Connect: Chronic Pain Minimizing the Risk of Abuse by Gregory A. Hood, MD, FACP

Office Visit Monitoring

Monitoring for:

Six A's

- **A**nalgesia
- **A**ctivities
- **A**dverse effects
- **A**berrant behaviors
- **A**dherence
- **A**ffect

Also:

- Review opioid use
  - How is patient actually using prescribed opioids?
    - 24-hour inventory
  - Objective information
    - Signs of medication misuse
    - Prescription Drug Monitoring Program
    - Urine drug tests
    - Pill counts
- Revise treatment as indicated

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Passik SD, et al. Clin Ther. 2004;26(4):552-61.

Urine Drug Tests

Objective information that can provide:

- **Evidence of therapeutic adherence**
- **Evidence of use or non-use of illicit drugs**

- Discuss urine drug testing openly with patient
  - If I send your urine right now, what will I find in it…
- Document time of last medication use
- Random, scheduled and/or when concerns arise
- One medical data point to integrate with others
  - Cannot discriminate elective use, addictive use and diversion
- Small risk for mislabeling, adulteration, other error
- **Consult toxicologist/clinical pathologist before acting if patient disputes findings**
- Dedicated deceivers can beat the system

Heit HA and Gourlay DL. J *Pain Symptom Manage.* 2004;27(3):260-7.
Christo PJ et al. *Pain Physician.* 2011;14(2):123-43.

Why Drug Test?

Self-reported drug use among patients with pain is unreliable

- Fleming MF, et al. J Pain 2007.
- Fisbain DA, et al. Clin J Pain 1999.
- Berndt S, et al. Pain 1993.

Behavioral observations detects only some problems

- Wasan AJ, et al. Clin J Pain 2007.
- Katz NP, et al. Anesth Analg 2003.

May improve adherence (e.g., decreased illicit drug use)

- Pesce A, et al. Pain Physician 2011.
- Starrels J, et al. Ann Intern Med 2010.
- Manchikanti L, et al. Pain Physician 2006.

Evolving standard of care

- Chou R, et al. J Pain 2009.
- Tescot AM, et al. Pain Physician 2008.
- FSMB 2013

Introducing UDT

- As part of treating pain with opioids, I order urine tests to help me understand how safe they are for patients
- The test measures a number of medications and drugs that could interfere with your treatment
- This is something I do with ALL patients on these medications and it doesn't mean that I don't trust you.
- If I find something unexpected, we'll talk about it and work together to address it.

Urine Drug Testing

- Urine drug **screens** are usually immunoassays
  - Can be done at point of care or in a lab
  - Quick and relatively inexpensive
  - Need to know what is included in testing panel
  - Risk of false negatives due to cut offs
  - Risk of false positives due to cross reactions

All unexpected findings should be sent for confirmation by GC/MS
(Gas Chromatography/Mass Spectroscopy)

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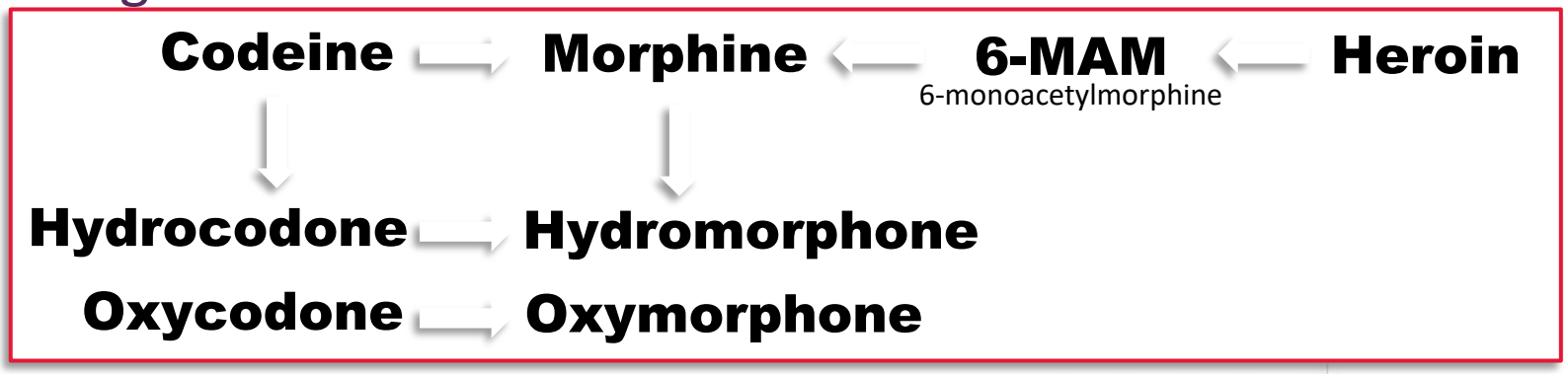
Reisfield GM et al. *Bioanalysis.* 2009;1(5):937-52.

Urine Drug Testing

- GC/MS **confirmation**
  - Identifies specific molecules
  - Sensitive and specific
  - More expensive
  - Must be aware of opioid metabolism to interpret
  - **NOTE:** GC/MS measurement of urine drug levels is not a valid method of determining the amount of opioid ingested



Peppin JF et al. *Pain Med.* 2012; 13:886-96.
Heit HA, Gourlay DL. J *Pain Symptom Manage.* 2004;27(3):260-7.
Heit HA, Gourlay DL, Caplan YH. Urine Drug Testing in Clinical Practice; Pharmacom Group Inc., May 2010.

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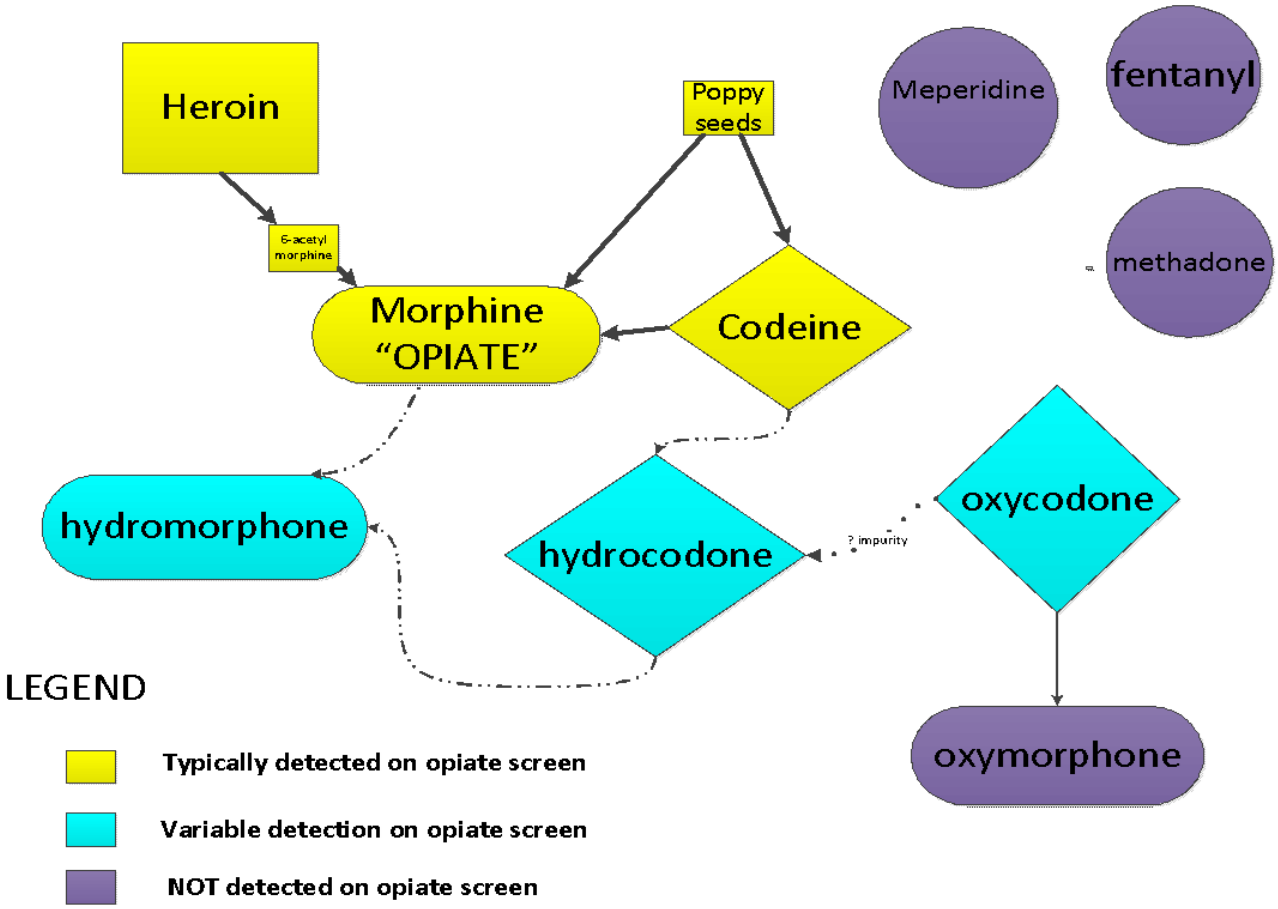
Opioid Metabolic Pathways



From Warner E, Starrels J Liebschutz J, Lorch E. SGIM 35th Annual Meeting. Urine Drug testing in the primary care setting, 2012.

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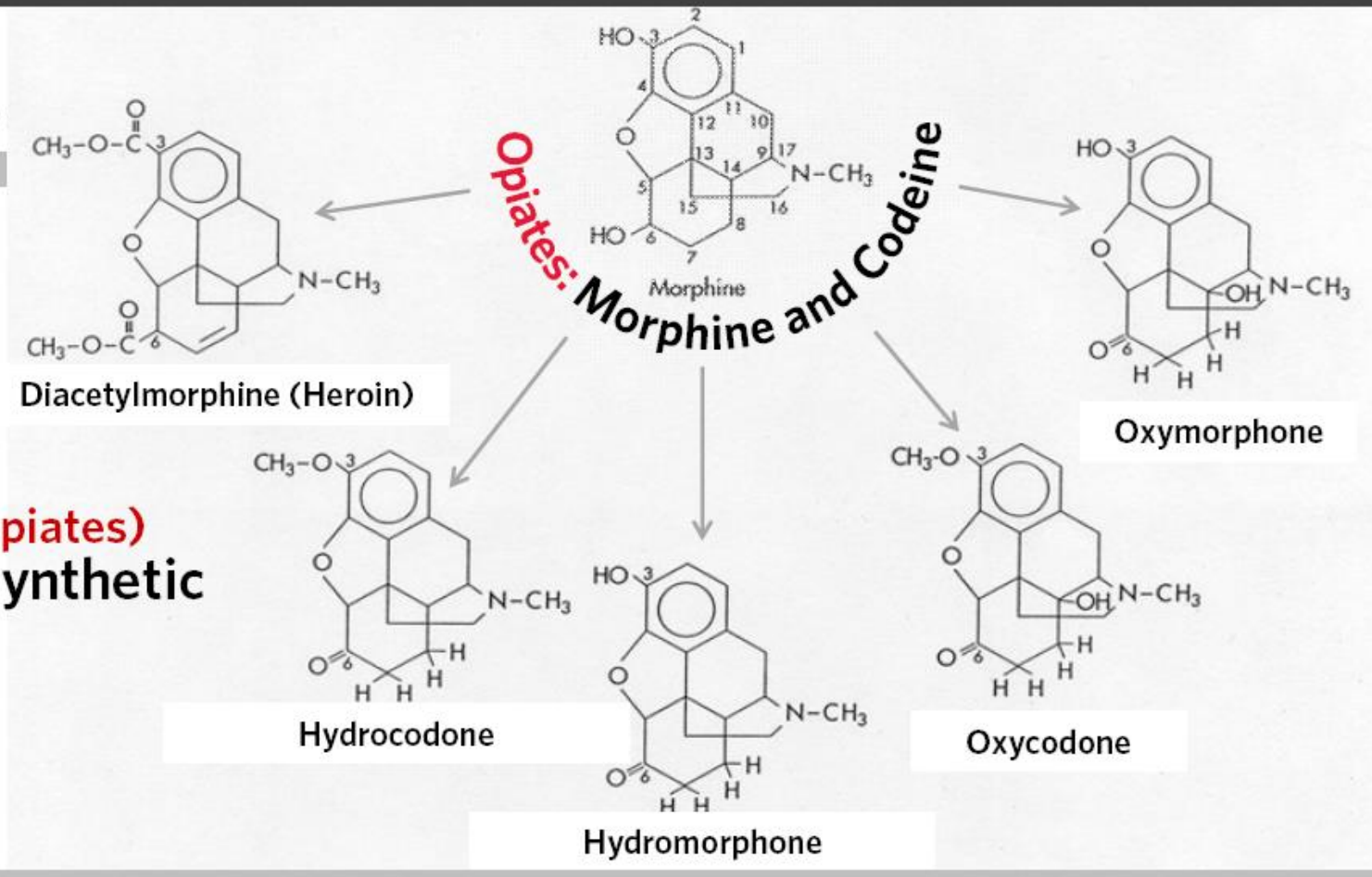
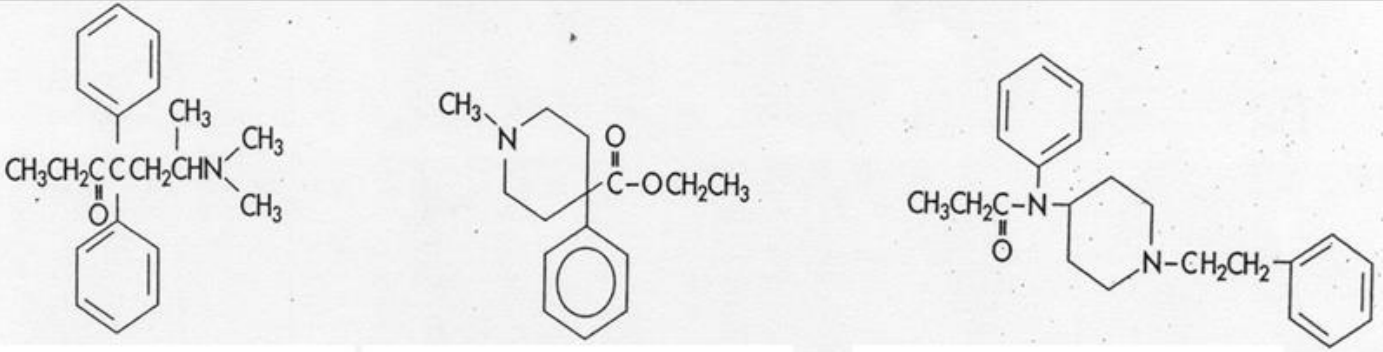
Opioids

Natural (Opiates) and Semisynthetic



Synthetic



From prior PCSS-O presentation

Typical Detection Time in Urine

See also: Urine Drug Testing Appendix

Medication/Substance	Common Detection Time
Amphetamine Methamphetamine	1-3 days 1-3 days
Barbiturate (short-acting) Barbiturate (long-acting)	24 hours Up to 21 days
Benzodiazepine (short-acting) Benzodiazepine (long-acting)	3 days Up to 30 days
Cocaine metabolites	1-4 days
Marijuana (single use) Marijuana (moderate use—4x/week) Marijuana (daily use) Marijuana (long-term)	3 days 5-7 days 10-15 days >30 days
Opioids (codeine, hydrocodone, morphine, etc) Opioids (heroin)	1-3 days 1-3 days

Cone EJ, Caplan YH. Postgrad Med 2009:121 (4): 91-102.
Smith HS. Opioid metabolism. Mayo Clinic Proc. 2009:84(7): 613-624.
Tenore P. Advanced urine toxicology testing. J Addictive Diseases 2010:29(4): 436-448.
Warner EA, et al. *Principles of Addiction Medicine*.2009:295-304.

Potential Harms of Urine Drug Testing

- Incorrect interpretation of urine drug tests could result in adverse consequences
  - Unwarranted discontinuation of opioids
  - Damage to physician-patient relationship
- Potential for false reassurance
  - Tampering
  - Alteration of behavior in anticipation of urine drug testing
- More evidence needed to understand the effects of urine drug testing on patient outcomes

Urine Drug Testing Pearls

- Oxycodone and synthetic opioids do not show up as “opiates”
- Methadone needs specific methadone test
- Oxycodone and oxymorphone need specific test
- Fentanyl needs specific fentanyl test
- Certain drugs may cause false positives on screening, but not gas chromatography confirmation
- Benzodiazepines may be false negative

Urine Drug Testing: Step 1

- **Anticipate the results of your test**
  - Identify which medications your patient is taking
  - When did patient last take his/her medications?
  - Document information in your note

From Warner E, Starrels J Liebschutz J, Lorch E.
SGIM 35th Annual Meeting.
Urine Drug testing in the primary care setting, 2012.

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Step 2:Select the Appropriate Test

- Screening
  - Panel or individual drugs
  - Point of care vs laboratory

- Confirmation
  - Automatic reflex on positives
  - For all positive and negative tests
  - Only when clinician requests

From Warner E, Starrels J Liebschutz J, Lorch E.
SGIM 35th Annual Meeting.
Urine Drug testing in the primary care setting, 2012.

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Step 3: Assess Specimen Validity

- Assess color
- Temperature 90-100 F.
- Urine pH ranges 4.5-8.5
- Creatinine concentration should be >20 mg/dL (<20 mg/dL is dilute, < 5mg/dL is not human specimen).
- Specific gravity

From Warner E, Starrels J Liebschutz J, Lorch E.
SGIM 35th Annual Meeting.
Urine Drug testing in the primary care setting, 2012.

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Step 4: Compare to Expected Results

Drug	Screening: Opiate immunoassay	Confirmation: GC/MS
Codeine	Positive	Codeine Morphine
Fentanyl	Negative	Fentanyl
Heroin	Positive	Morphine
Hydrocodone	Positive	Hydrocodone, hydromorphone
Hydromorphone	Positive	Hydromorphone
Methadone	Negative	Methadone
Morphine	Positive	Morphine Codeine
Oxycodone	Negative	Oxycodone Oxymorphone
Oxymorphone	Negative	Oxymorphone

From Warner E, Starrels J Liebschutz J, Lorch E. SGIM 35th Annual Meeting.

Urine Drug testing in the primary care setting, 2012.

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Differential Diagnosis

UDT Result	Differential for Unexpected Results
Positive	Use of non-prescribed medications Use of illicit drugs Use of previously prescribed medications (hoarding) Cross-reaction (food, OTC, herbal products)* Contamination Laboratory error
Negative	Diversion Didn't take within time frame to make test positive (ran out early, prn med, etc.) Fast metabolizer Laboratory processing error Extreme dilution of urine Malabsorption Hoarding/Binging

***Should occur only on screen, and not on confirmatory test with exception of poppy seeds.**

Case

- Patient is prescribed morphine and valium
  - Screening Expected results: + opiates, + benzodiazepines
  - GC/MS results: + morphine, + codeine, + diazepam

- If patient were prescribed oxycodone
  - Screening Expected results: + oxycodone, + benzodiazepines (negative opiates)
  - GC/MS results: + oxycodone, + oxymorphone, + Diazepam

Pill Counts

Objective information that can:

- Confirm medication adherence
- Minimize diversion

28 day supply (rather than 30 days)

Prescribe so that patient should have residual medication at appointments

Ask patient to bring in medications at each visit

For identified risks or concerns, can request random call-backs for immediate counts

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Prescription Drug Monitoring Programs (PDMP)

- Statewide electronic database on dispensed controlled substance prescriptions
- Prescription data available to prescribers and pharmacists (usually for the past year, and including information on date dispensed, patient, prescriber, pharmacy, medicine, and dose)
- A substantially underutilized resource
- 49 states including District of Columbia and Guam have an active PDMP. Missouri is the only state without an active PDMP.[1]
- 40 states have an active prescriber mandated use of PDMP provision in statute or rule (as of Jan 2019) [2]
- Several studies* suggest association between PDMP use and positive outcomes related to improving prescribing and reducing prescription drug abuse

[1] AANP Policy Brief 2018
[2] National Alliance for Model State Drug Laws 2019
Haffajee RL et al. Mandatory use of prescription drug monitoring programs. *JAMA.* 2015

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Discussing Monitoring

- Review the personal and public health (community health) risks of opioid medications
- Discuss your responsibility to look for and manage early signs of harm
- Discuss agreements, pill counts, drug tests, etc. as ways that you are helping to protect patient from getting harmed by medications

Use consistent approach (Universal Precautions)

BUT apply it individually to match risk

Monitoring is a lot of work… Engage office staff

- Educate all staff on protocols and policies
  - How and when prescriptions will be dispensed
  - Appointments, program expectations
  - Pain management and addiction
- Be consistent: send the same message
- Engage the entire team to:
  - Help educate and monitor patients
  - Remind patients of policy and treatment agreement
  - Manage refills
  - Monitor for adherence

MANAGING DRUG MISUSE-RELATED BEHAVIORS

Case

- Patient calls to request a refill 8 days early stating that his daughter is in the hospital in another state.
- had been in the hospital for 3 days during his current prescription, so refill would actually be 11 days early.
- *What do you do?*

Opioids and Unrealistic Expectations

Patients often have unrealistic expectations that…

…lead to the belief that opioids will always relieve pain, *therefore* more opioids equal more relief

…leading to unsanctioned dose escalation or continued requests for higher doses

Re-educate about realistic goals and potential opioid risks

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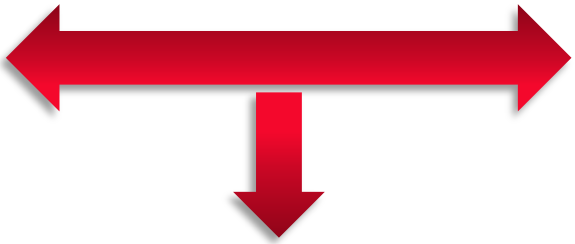
Alford DP. *JAMA.* 2013;309(9):919-25.

Monitoring for Opioid Misuse

- Patient questionnaire
  - **Current Opioid Misuse Measure (COMM)**
    Self-administered 17 items
- Other strategies
  - Pill counts (scheduled vs random)
  - Urine drug tests (scheduled vs random)
  - PDMP data
- History from “reliable” family members
  - Beware of family members with secondary gain for giving inaccurate information

Differential for Opioid Misuse



n Relief Seeking

- Disease progression
- Poorly opioid responsive pain
- Withdrawal mediated pain
- Opioid analgesic tolerance
- Opioid-induced hyperalgesia

[redacted]

For example, patient with chronic pain, with co-morbid addiction, taking some for pain and diverting some for income

[redacted]

- Opioid use disorder/Addiction
- Other psychiatric diagnosis
- Criminal intent (diversion)

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Alford DP. *JAMA.* 2013;309(9):919-25.

DDx: Pain Relief Seeking

Opioid Analgesia Tolerance

- Right shift of the dose-response curve
  - Analgesic tolerance demonstrated in animal models
  - Human studies find opioid doses stabilize long-term
  - Therefore, assume opioid analgesic tolerance is not common but may happen
- Increased dose overcomes decreased analgesia

Schug SA, et al. *Drug Safe* 1992;7(3):200-13.
Portenoy RK and Foley KM. *Pain.* 1986;25(2):171-86.
Chang G, et al. *Med Clin North Am.* 2007;91(2):199-211.
Joseph EK, et al. *J Neurosci.* 2010;30(13):4660-6.

DDx: Pain Relief Seeking

Opioid-Induced Hyperalgesia

- Enhanced pain sensitivity to same opioid dose
- Paradoxically more opioid will worsen pain
- Central and peripheral sensitization of *pronociceptive* process
- Increased dose may improve analgesia but only temporarily

Chang G, et al. *Med Clin North Am.* 2007;91(2):199-211.
Lee M et al. *Pain Physician* 2011;14:145-161
Eisenberg E et al. *J Pain Symptom Manage.*2015

DDx: Drug Seeking

Opioid Use Disorder (OUD)/Addiction

- ✔ *Tolerance
- ✔ *Withdrawal
- ✔ **Use in larger amounts or duration than intended**
- ✔ **Persistent desire to cut down**
- ✔ Giving up interests to use opioids
- ✔ **Great deal of time spent obtaining, using,** or recovering from **opioids**
- ✔ Craving or strong desire to use opioids
- ✔ Recurrent use resulting in failure to fulfill major role obligations
- ✔ **Recurrent use in hazardous situations**
- ✔ Continued use despite social or interpersonal problems caused or exacerbated by opioids
- ✔ **Continued use despite physical or psychological problems**

*This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision

Mild OUD: 2-3 Criteria
Moderate OUD: 4-5 Criteria
Severe OUD: ≥6 Criteria

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.)

DDx: Drug Seeking

Addiction

Clinical syndrome presenting as…

Loss of **C**ontrol

Compulsive use

Continued use despite harm

} **Medical Misuse**
(pattern and severity)

Addiction is **NOT** the same as Physical Dependence

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Savage SR, et al. *J Pain Symptom Manage.* 2003;26:655-667.

Concerning Behaviors for Opioid Use Disorder

Spectrum: Yellow to Red Flags

- ☐ Requests for increase opioid dose
- ☐ Requests for specific opioid by name, “brand name only”
- ☐ Non-adherence w/other recommended therapies (e.g., PT)
- ☐ Running out early (i.e., unsanctioned dose escalation)
- ☐ Resistance to change therapy despite AE (e.g. over-sedation)
- ☐ Deterioration in function at home and work
- ☐ Non-adherence w/monitoring (e.g. pill counts, UDT)
- ☐ Multiple “lost” or “stolen” opioid prescriptions
- ☐ Illegal activities – forging scripts, selling opioid prescription

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Modified from Portenoy RK. *J Pain Symptom Manage*. 1996;11(4):203-17.

Case: Responding to the Early Refill

- See patient at an office visit
- Perform Urine Drug Test
- Perform Pill Count
- Confirm story with a family member

Goals:

- Re-establish goals and expectations
- Reassess risks and benefits

MEDICATIONS TO AVOID WITH OPIOIDS

High Risk Medications to Avoid

- Alcohol – advise against *any* use
  - May rapidly release opioid (dose dump) when certain ER/LA opioids are exposed to alcohol
- Benzodiazepines and sedative hypnotics
  - Highest risk of unintentional overdose
  - Potentiating effect on sedation and respiratory depression
- Certain muscle relaxers (Carisoprodal)
- Marijuana
- Medications that interact with methadone
  - Multiple medications
- Medications that interact with tramadol or tapentadol
  - SSRI or SNRIs

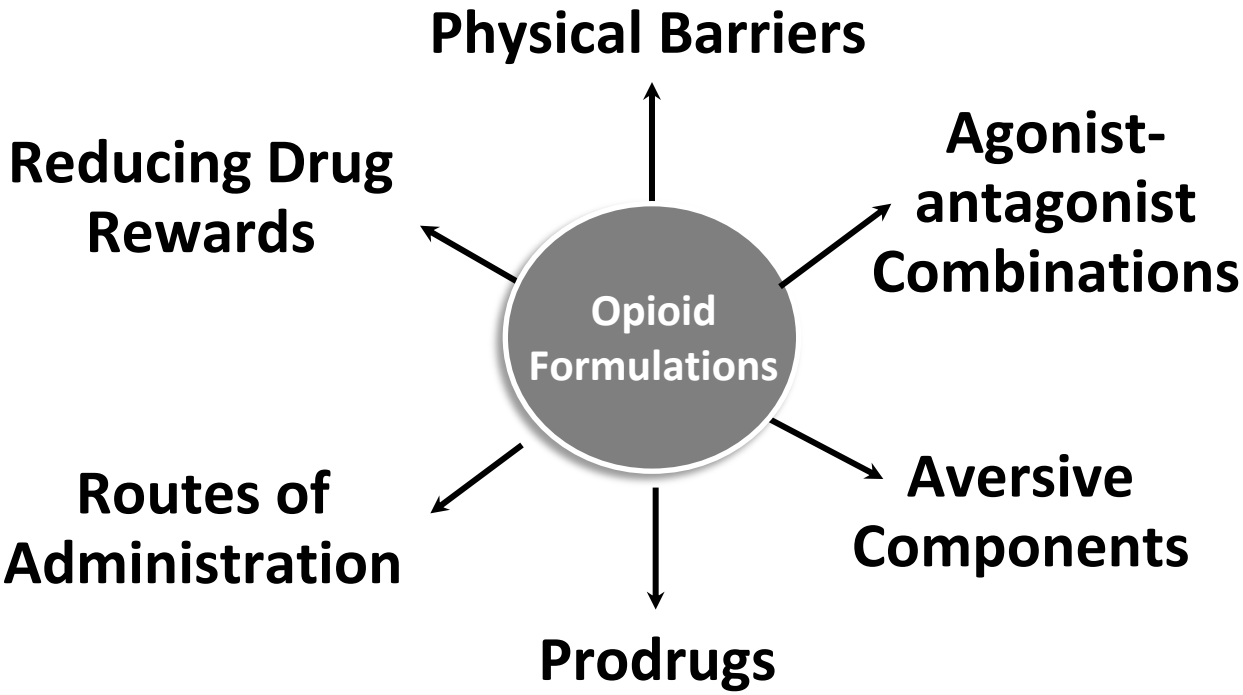
ABUSE-DETERRENT OPIOID FORMULATIONS

Abuse-deterrent Opioid Formulations

- Abuse deterrent opioid formulations recently approved by FDA or undergoing FDA approval process
  - Designed to be tamper-resistant or co-formulated with medications that reverse opioid effects or produce noxious side effects when tampered with
  - Effectiveness for reducing misuse and improving clinical outcomes yet to be established
  - Likely to be primarily effective in patients who crush or inject opioids
  - Some patients may seek other prescription or illicit opioids[a]

[a]Cicero et al. NEJM 2012

Abuse Deterrent/Resistant Formulations



Currently there are NO PROVEN abuse deterrent/resistant opioids or formulations

FDA 2013 Guidance for Industry Abuse Deterrent Opioids – Evaluation and Labeling
www.fda.gov

Passik SD. *Mayo Clin Proc.* 2009;84(7):593-601.
Stanos SP, et al. *Mayo Clin Proc*. 2012;87(7):683-94.
Larochelle MR et al. *JAMA Intern Med*. 2015;175(6):978-987
Michna E et al. *Curr Med Res Opin*. 2014.
Cassidy TA et al. *Pain Med* 2014;15(3):440-51.

NALOXONE CO-PRESCRIPTION SLIDES ADAPTED FROM DR. PHILLIP COFFIN

Overdose Risk Factors

- Prior overdose
  - Overdose in any 1 year predicts a 6-fold increased likelihood of overdose in next year
  - Any history of opioid overdose predicts a 4-fold increased risk of mortality
- Concomitant use of other substances
  - Sedatives, alcohol, cocaine
- Reduced tolerance

Darke, S, et al. Drug Alcohol Rev. 2007 Jan; 26(1):49-54.
Binswanger, et al. Ann Int Med, 2013.

Opioid Overdose Risk Management Plan

- Consider in the following situations
  - High dose opioids (MED >50 mg)
  - History of opioid overdose (intentional or unintentional)
  - Use of benzodiazepines or other sedative hypnotics
  - Opioid use disorder
  - Heroin use

Concept of Lay Naloxone

- Overdose usually witnessed
- Death takes a while
- EMS not routinely accessed
- Naloxone is safe and effective
- May decrease the need for advanced respiratory support
- Possible behavior change

Naloxone and the Law

- Naloxone is not a controlled substance; no different than prescribing other routine medications to your patients
- Some states have added legal protections
  - Prescribing to a bystander
  - Administration of naloxone by lay bystanders
  - Prescribing or dispensing based on standing order or directly from pharmacies

How to Prescribe Naloxone

- Injectable
  - Vial
    - Naloxone 0.4mg/1mL IM if overdose
    - IM syringes (3 mL 25g 1” syringes are recommended
  - Autoinjector: Evzio®, 0.4mg naloxone
- Intranasal
  - Naloxone 2mg/2mL prefilled syringe, spray ½ into each nostril if overdose
  - MAD (Mucosal Atomization Device) nasal adaptor

	Injectable (and intranasal- IN) generic[1]	Intranasal branded[2]	Injectable generic[3]	Injectable generic	Auto-injector branded
Brand name		Narcan Nasal Spray			Evzio Auto-Injector
Product comparison					
					
FDA approved Labeling includes instructions for layperson use	X (for IV, IM, SC)	X X	X	X	X X
Layperson experience	X		X		X
Assembly required	X		X	X	
Fragile	X				
Can titrate dose	X		X	X	
Strength	1 mg/mL	4 mg/0.1 mL	0.4 mg/mL OR 4 mg/10 mL	0.4 mg/mL	0.4 mg/0.4mL
Total volume of kit/package	4 mg/4 mL	8 mg/ 0.2 mL	0.8 mg/2 mL OR 4 mg/10 mL	0.8 mg/2 mL	0.8 mg/0.8 mL
Storage requirements (All protect from light)	Store at 59-86 °F Fragile: Glass.	Store at 59-77 °F Excursions from 39-104 °F	Store at 68-77 °F Breakable: Glass.	Store at 68-77 °F Breakable: Glass.	Store at 59-77 °F Excursions from 39-104 °F
Cost/kit[4]	$$	$$	$	$	$$$[3]
Prescription variation					
Refills	Two	Two	Two	Two	Two

Talking about “opioid safety”

- People who use prescription opioids, including patients with opioid use disorder in remission, may not perceive their own “overdose” risk
- Consider focusing on “opioid safety” with language such as
  - Opioids can sometimes slow or even stop your breathing
  - Naloxone is the antidote to opioids – to be [sprayed in the nose/injected] if there is a bad reaction where you can’t wake up
  - Naloxone is for opioid medications like an Epi-Pen is for someone with an allergy

Resources for providers

- Naloxone Program Implementation Manual
  - www.harmreduction.org/issues/overdose-prevention/tools-best-practices
- AHRQ description of Massachusetts naloxone program
  - www.innovations.ahrq.gov/content.aspx?id=3912
- Clinic-based prescribing information and guidelines
  - www.prescribetoprevent.org
  - Reversing the Overdose Epidemic in Oregon: A Toolkit for Oregon's Physicians, PAs, and other Prescribers
- Pharmacy resources: www.stopoverdose.org
- Advocacy film and materials: Reach for Me: Fighting to end the American Drug Overdose Epidemic: www.hri.global/contents/1386
- Research updates and other overdose-related news: www.overdosepreventionalliance.org

SAMHSA websites:http://www.samhsa.gov/capt/tools-learning-resources/opioid-overdose-prevention-toolkit
http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit-Updated-2016/SMA16-4742

Summary

- Evaluating a patient's risk of opioid misuse should be done universally on all patients prescribed long term opioids.
- The level and frequency of opioid monitoring depends on his or her initial risk evaluation.
- Opioid monitoring involves several steps and helps determine whether the benefits of ongoing treatment outweigh the risks.
- Urine drug testing is a key monitoring component.
- Naloxone co-prescription should be considered in patients prescribed high dose opioids.

References

- Adams et al. (2004) Development of a self-report screening instrument for assessing potential opioid medication misuse in chronic pain patients. J Pain Symptom Manage; 27(5):440-59.
- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC
- Alford DP. (2013) Chronic back pain with possible prescription opioid misuse. JAMA;309(9):919-25.
- Arnold RM, et al. (2006) Opioid contracts in chronic nonmalignant pain management: objectives and uncertainties. Am J Med;119(4):292-6.
- Banta-Green, et al. (2009) Opioid use behaviors, mental health and pain--development of a typology of chronic pain patients.Drug Alcohol Depend;104(1-2): 34-42.
- Berndt S, et al. (1993) Polymedication and medication compliance in patients with chronic non-malignant pain. Pain;52(3):331-9.
- Binswanger, et al. (2013) Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. Ann Intern Med; 159(9):592-600.
- Boscarino, et al. (2010) Risk factors for drug dependence among out-patients on opioid therapy in a large US health-care system. Addiction; 105(10): 1776-82.
- Butler et al. (2013) Abuse rates and routes of administration of reformulated extended-release oxycodone: initial findings from a sentinel surveillance sample of individuals assessed for substance abuse treatment. J Pain.14(4):351-8.
- Cassidy TA et al. (2014) Changes in prevalence of prescription opioid abuse after introduction of an abuse-deterrent opioid formulation. Pain Med;15(3):440-51.
- Chang G, et al. (2007) Opioid tolerance and hyperalgesia. Med Clin North Am.;91(2):199-211.
- Cheatle MD, Savage SR. (2012) Informed consent in opioid therapy: a potential obligation and opportunity. J P&SM. 44(1):105-116
- Chou R, et al. (2009) Research gaps on use of opioids for chronic noncancer pain: findings from a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. J Pain;10(2):147-159.
- Christo PJ et al. (2011) Urine drug testing in chronic pain. Pain Physician;14(2):123-43.
- Cicero TJ, et al. (2014). The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years. JAMA Psychiatry;71(7):821-826
- Darke, S, et al. (2007) The Australian Treatment Outcome Study (ATOS): what have we learnt about treatment for heroin dependence? Drug Alcohol Rev; 26(1):49-54.
- Eisenberg, E, et al. (2015). Opioid-induced hyperalgesia (OIH): a real clinical problem or just an experimental phenomenon? J Pain Symptom manage; 49(3): 632-6.
- Federation of State Medical Boards Model Policy 2013. www.fsmb.org/grpol_policydocs.html
- Fisbain DA, et al. (1999) Chronic pain disability exaggeration/malingering and submaximal effort research. Clin J Pain; 15(4):244-74.
- Fishman SM, Kreis PG. (2002) The opioid contract. Clin J Pain;18(4 Suppl):S70-5.

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References

- Fleming, MF, et al. (2007). Substance use disorders in a primary care sample receiving daily opioid therapy. J Pain; 8(7): 573-582.
- Franklin GM. (2014) Opioids for chronic noncancer pain: a position paper of the American Academy of Neurology. Neurology; 83:1277-1284
- Gourlay DL, et al. (2005) Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. Pain Med;6(2):107-12.
- Haffajee RL et al. (2015) Mandatory use of prescription drug monitoring programs. *JAMA; 313(9):891-2.*
- Heit HA, Gourlay DL. (2004) Urine drug testing in pain medicine. J *Pain Symptom Manage*;27(3):260-7.
- Heit HA, et al. (2010) Urine Drug Testing in Clinical Practice; Pharmacom Group Inc.
- Joseph EK, et al. (2010) Shared mechanisms for opioid tolerance and a transition to chronic pain. *J Neurosci*;30(13):4660-6.
- Katz NP, et al. (2003) Behavioral monitoring and urine toxicology testing in patients receiving long-term opioid therapy. Anesth Analg; 97(4):1097-102.
- Larochelle MR et al. (2015) Rates of opioid dispensing and overdose after introduction of abuse-deterrent extended-release oxycodone and withdrawal of propoxyphene. *JAMA Intern Med*.;175(6):978-987
- Lee M, et al. (2011) A comprehensive review of opioid-induced hyperalgesia. Pain Physician;14;145-161.
- Manchikanti L, et al. (2006) Controlled substance abuse and illicit drug use in chronic pain patients: An evaluation of multiple variables. Pain Physician; 9(3):215-25.
- Martell, et al. (2007) Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. Ann Intern Med; 146(2): 116-27.
- Michna, E, et al. (2014) Use of prescription opioids with abuse-deterrent technology to address opioid abuse. Curr Med Res Opin; 30(8):1589-98.
- Nicolaidis C. (2011) Police officer, deal-maker, or health care provider? Moving to a patient-centered framework for chronic opioid management. Pain Med.12(6):890-7.
- Passik SD, et al. A new tool to assess and document pain outcomes in chronic pain patients receiving opioid therapy. Clin Ther. 2004;26(4):552-61.
- Passik SD. (2009) Issues in long-term opioid therapy: unmet needs, risks, and solutions. Mayo Clin Proc;84(7):593-601.
- Paterick TJ, et al. Medical informed consent: general considerations for physicians. *Mayo Clin Proc*;83(3):313-19.
- Pesce A, et al. (2011) Illicit drug use in the pain patient population decreases with continued drug testing. Pain Physician; 14(2):189-93.
- Peppin JF et al. (2012) Recommendations for urine drug monitoring as a component of opioid therapy in the treatment of chronic pain. *Pain Med*; 13:886-96.
- Portenoy RK. (1996) Opioid therapy for chronic nonmalignant pain: a review of the critical issues. *J Pain Symptom Manage*;11(4):203-17.
- Portenoy RK and Foley KM. (1986) Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. *Pain*;25(2):171-86.
- Reisfield GM et al. (2009) 'False-positive' and 'false-negative' test results in clinical urine drug testing. *Bioanalysis*;1(5):937-52.
- Tescot AM, et al. (2008) Opioid pharmacology. Pain Physician; 11(2):S133-53.
- Tolia VN et al. (2015). Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. *N Engl J Med*;372:2118-26.
- Starrels J, et al. (2010) Systematic review: treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. Ann Intern Med;152(11):712-20.
- Schug SA, et al. (1992) Adverse effects of systemic opioid analgesics. *Drug Safe*;7(3):200-13.
- Wasan AJ, et al. (2007) Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. Clin J Pain; 23(4):307-15.
- Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med; 6(6): 432-42.
- Savage SR, et al. *(2003)* Definitions related to the medical use of opioids: evolution towards universal agreement. *J Pain Symptom; 26(1)*:655-667.
- Stanos SP et al. (2012) Strategies to reduce the tampering and subsequent abuse of long-acting opioids: potential risks and benefits of formulations with physical or pharmacologic deterrents to tampering. Mayo Clin Proc;87(7):683-694.
- Webster, et al. (2005) Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med;6(6):432-442.

PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.
- PCSS Mentors are a national network of providers with expertise in **addictions, pain, evidence-based treatment including medications for opioid use disorder (MOUD)**.
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

For more information visit:

https://pcssNOW.org/mentoring/

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Ask a Colleague

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American Academy of Family Physicians	American Society for Pain Management Nursing
American Academy of Pain Medicine	Association for Multidisciplinary Education and Research in Substance use and Addiction
American Academy of Pediatrics	Council on Social Work Education
American Pharmacists Association	International Nurses Society on Addictions
American College of Emergency Physicians	National Association of Social Workers
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