PEDIATRIC OPIOID REMS (RISK, EVALUATION, AND MITIGATION STRATEGIES)
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Objectives
• Define substance misuse, abuse, addiction, tolerance, physical dependence, and pseudo addiction
• Develop a plan of care for patients requiring opioids for treatment of pain, include: risk assessment, monitoring for misuse, adverse effects, and safe methods to discontinue opioids if ineffective or abuse identified
• Educate healthcare providers, patients, parents/guardians & the public on methods of securing, monitoring, and disposing of opioids.
What You Need to Know about Opioids
Opioids are indicated for severe pain and healthcare professionals must advocate for appropriate pain and risk assessment, optimal multimodal pain treatment, and monitor for adverse treatment effects including adverse effects from opioids, like sedation, respiratory depression, opioid use disorder and constipation.

Healthcare professionals are also instrumental in providing anticipatory guidance for safe opioid use at home.

### Rate of opioid prescriptions dispensed per 100 persons increases with age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 14</td>
<td>&gt; 1 million</td>
<td>1.7</td>
</tr>
<tr>
<td>15 to 19</td>
<td>&gt; 2 million</td>
<td>10.4</td>
</tr>
<tr>
<td>20 to 24</td>
<td>&lt; 3 million</td>
<td>13</td>
</tr>
<tr>
<td>25 to 34</td>
<td>&lt; 8 million</td>
<td>17.3</td>
</tr>
<tr>
<td>35 to 44</td>
<td>&gt; 8 million</td>
<td>20.5</td>
</tr>
<tr>
<td>45 to 54</td>
<td>&lt; 10 million</td>
<td>23.1</td>
</tr>
<tr>
<td>55 to 64</td>
<td>&gt; 11 million</td>
<td>26.3</td>
</tr>
<tr>
<td>65 +</td>
<td>&lt; 14 million</td>
<td>26.8</td>
</tr>
<tr>
<td>All</td>
<td>&lt; 57 million</td>
<td>17.4</td>
</tr>
</tbody>
</table>

**Children & adolescents are less likely to be prescribed opioids**
Pain management specialists have reassured patients and families that less than 1% of individuals treated for acute pain become addicted to opioids. This conclusion and belief was supported by two classic studies.

- Marks and Sachar in 1973 found that less than 1% of hospitalized patients receiving 100 mg of Meperidine IM every 4 hours became addicted.
- Porter and Jick in 1980 found that of 12,000 hospitalized medical inpatients who received at least one dose of an opioid analgesic, only 4 were diagnosed as addicts and all 4 had previous histories of substance abuse.

As opioid use for the treatment of pain became more common, prescription opioid use disorder did too.

A limitation of the classic studies that reassured patients and healthcare providers that pain was protective against the development of addiction and substance use disorders was lack of access to prescription opioids and lack of data regarding patients opioid use after hospital discharge.
The Opioid Epidemic

We were wrong.

Less than 1% of individuals treated for pain become addicted to opioids.

(Marks & Sachar, 1973; Porter & Jick, 1980)

Opioid misuse, opioid use disorder, and unintentional overdose deaths are significant public health problems. In 2015, overdose deaths increased 11% to 52,404. By comparison, the number of people who died in:

- car crashes increased by 12% to 37,757.
- gun–related homicides and suicides, rose 7% to 36,252.
Differentiate between the following terms:
• Drug abuse
• Addiction
• Drug diversion
• Drug misuse
• Nonmedical use
• Substance use disorder
• Tolerance
• Physical dependence
• Pseudo addiction

Type your answer here.
Clarify definitions

These terms are often used interchangeably despite their different definitions, which contributes to confusion among healthcare professionals.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Affected by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abuse</td>
<td>Use of a drug for nontherapeutic, recreational purposes (psychotropic or euphoric effects).</td>
</tr>
<tr>
<td>Addiction</td>
<td>A primary chronic neurobiological disease of reward, motivation, and memory and related circuitry, characterized by the “four Cs”: Compulsive use, impaired Control over use, Continued use despite harm, and strong Craving.</td>
</tr>
<tr>
<td>Drug diversion</td>
<td>The illicit redirection of legitimately prescribed drugs.</td>
</tr>
<tr>
<td>Misuse</td>
<td>Use of a drug prescribed for a medical purpose in a manner inconsistent with its intended purpose or prescribed use.</td>
</tr>
</tbody>
</table>
| Nonmedical use   | Use of a prescription drug  
|                  | • by someone other than the person for whom it was prescribed.  
|                  | • in a manner for which it was not prescribed—for example, to achieve a euphoric effect, increasing the dose without prescriber approval, unknowingly taking a larger dose than directed (misuse), or using the drug to attempt suicide or to make a suicidal gesture without really intending to commit suicide. |
Clarify definitions

The DSM-V combined the previous DSM-IV categories of substance abuse and dependence into a single disorder. With this new criteria, rates of opioid use disorder range from 0.7% to over 30%.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Affected by:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Substance use disorder</strong></td>
<td>A maladaptive pattern of substance use leading to clinically significant impairment or distress, demonstrated by a recurrence of two or more of the following events or behaviors within the previous 12 months</td>
</tr>
<tr>
<td></td>
<td>• failure to fulfill major role obligations</td>
</tr>
<tr>
<td></td>
<td>• hazardous use (of the substance or other substances, or of a motor vehicle while under the influence, for example)</td>
</tr>
<tr>
<td></td>
<td>• physiologic symptoms of withdrawal</td>
</tr>
<tr>
<td></td>
<td>• tolerance</td>
</tr>
<tr>
<td></td>
<td>• increasing use, or use over a longer period of time than intended</td>
</tr>
<tr>
<td></td>
<td>• unsuccessful attempts to quit or control use</td>
</tr>
<tr>
<td></td>
<td>• physical or psychological problems related to use</td>
</tr>
<tr>
<td></td>
<td>• investment of time in obtaining, using, and recovering from the substance</td>
</tr>
<tr>
<td></td>
<td>• cessation of activities to allow for use</td>
</tr>
<tr>
<td></td>
<td>• craving</td>
</tr>
<tr>
<td></td>
<td>• continued use despite social or interpersonal problems related to use</td>
</tr>
</tbody>
</table>
Opioid Misuse/Abuse
Opioid misuse/abuse & unintentional overdose deaths

Opioid prescribing began to decline after a peak in 2012; and unintentional opioid overdose deaths among 15-19 year olds also declined. This downward trend may have reflected decreased opioid prescribing; but in 2015, unintentional opioid overdoses rose.

https://www.cdc.gov/nchs/products/databriefs/db282.htm
Prescribing rates are now 19% below 2006 levels and doses have also decreased over time.

With a rate of 58.5 opioid prescriptions for every 100 Americans, it sounds like more than ½ of all Americans were prescribed opioids in 2017. Actually 17% of Americans had at least 1 opioid prescription filled, with an average of 3.4 opioid prescriptions dispensed per patient.

Average daily milligrams of morphine equivalents (MME)/prescription is 45 MME. This is >5 mg of hydrocodone every 4 hours, but <10 mg every 4 hours & <5 mg oxycodone every 4 hours.

The average number of days per prescription has increased to 18 days in 2017. This may not be an actual increase in number of days prescribed. Since opioid prescribing has decreased; this shift in average days may better reflect opioid prescribing for daily chronic and cancer pain.
Opioid misuse/abuse is a major public health problem

Almost 1 in 4 young adults report non-medical use of opioids during their lifetime.

<table>
<thead>
<tr>
<th>Age</th>
<th>Lifetime</th>
<th>Past Year</th>
<th>Past Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-17 years</td>
<td>9.4%</td>
<td>3.9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>18-25 years</td>
<td>24.4%</td>
<td>8.5%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

Nonmedical use of controlled medications is particularly concerning for adolescents and young adults. Over 1% of 12 to 17-year-olds report nonmedical opioid use in the past month, and almost 10% report nonmedical use during their short life-time.


Opioid misuse/abuse is a major public health problem

This analysis of the 772 unintentional opioid deaths of adolescents in 2015 recognizes that multiple drugs may have been involved, but attributes 70 of the deaths to cocaine, 126 to benzodiazepines, 82 to psychostimulants, and 494 to opioids.

The most significant increase in unintentional deaths from opioids was from heroin, with approximately 200 deaths. Deaths from synthetic opioids, such as tramadol and fentanyl increased to approximately 150 deaths; whereas the number of deaths from methadone were similar to cocaine at 70. Deaths from other opioids like oxycodone, hydrocodone, and hydromorphone were similar to those from benzodiazepines at about 120. These have been steadily decreasing as prescribing has decreased. Unfortunately, children may be turning to heroin and prescribers may be arming them with tramadol in an effort to treat pain without using stronger opioids. Tramadol and illicit fentanyl and heroin are killing adolescents in increasing numbers.
State Unintentional Death Reporting System (SUDORS)

Illinois Opioid-related SUDORS Data January-December, 2017

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>3</td>
<td>0.3</td>
</tr>
<tr>
<td>15 to 24</td>
<td>86</td>
<td>8.7</td>
</tr>
<tr>
<td>25 to 34</td>
<td>250</td>
<td>25.4</td>
</tr>
<tr>
<td>35 to 44</td>
<td>219</td>
<td>22.2</td>
</tr>
<tr>
<td>45 to 54</td>
<td>255</td>
<td>25.9</td>
</tr>
<tr>
<td>55 to 64</td>
<td>149</td>
<td>15.1</td>
</tr>
<tr>
<td>65 +</td>
<td>23</td>
<td>2.3</td>
</tr>
<tr>
<td>Total</td>
<td>985</td>
<td>100</td>
</tr>
</tbody>
</table>


Prescription vs. Illicit Opioid*

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rx only</td>
<td>134</td>
<td>14.0</td>
</tr>
<tr>
<td>Illicit only</td>
<td>637</td>
<td>66.4</td>
</tr>
<tr>
<td>Rx/Illlicit combination</td>
<td>149</td>
<td>15.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>39</td>
<td>4.1</td>
</tr>
<tr>
<td>Total</td>
<td>959</td>
<td>100</td>
</tr>
</tbody>
</table>

Mean number of substances detected by toxicology=8.13

The most recent data from Illinois shows the majority of overdose deaths are from illicit drugs. Please note that these are rarely single drug overdoses.
State Unintentional Death Reporting System (SUDORS)

<table>
<thead>
<tr>
<th>Drug Present*</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl/Any fentanyl analogs</td>
<td>653</td>
<td>66.3</td>
</tr>
<tr>
<td>Heroin or 6-MAM</td>
<td>364</td>
<td>37.0</td>
</tr>
<tr>
<td>Alcohol</td>
<td>267</td>
<td>36.5</td>
</tr>
<tr>
<td>Cocaine</td>
<td>353</td>
<td>35.8</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>343</td>
<td>34.8</td>
</tr>
<tr>
<td>Methadone</td>
<td>70</td>
<td>7.1</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>38</td>
<td>3.9</td>
</tr>
</tbody>
</table>

*Not Mutually Exclusive
Mean number of substances detected by toxicology=8.13

Heroin is metabolized to morphine
Both will be found in toxicology reports
6-mam is the intermediate metabolite from heroin to morphine.

What are you doing to prevent overdose from these drugs?
Where do they get the drugs? 

Type your answer here.
Prescribing Patterns & Processes
Sources of prescription opioids among past-year non-medical users

Opioids previously prescribed for acute pain are a commonly identified source of misused opioids

Left-over prescription opioids are the primary source for misused prescription opioids.

- >80% of teens report opioid misuse is “to relieve pain”
- 35% confess “to get high” is their primary motivation for misuse

Have you been given or given a left over RX to a friend or relative?
Where do you store prescription opioids and other dangerous drugs?
Prescribing patterns

Of 749 oxycodone and hydrocodone pills dispensed to 49 adolescents after appendectomy:
• 67.5 (24%) were reportedly used as prescribed,
• 53.5 pills (8%) were unaccounted for by pill count, and
• 488 pills (68%) over 2/3 of the number prescribed, were returned to families for disposal.


• Legitimately prescribed opioid use before high school graduation is independently associated with a 33% increase in risk of future opioid misuse as a young adult (before 23 years of age).

• This association is strongest among young adults who reported little to no previous history of drug use and ardent disapproval of illegal drug use as teens.

• Of grave concern is teens’ transition from taking thoughtfully prescribed opioids for the treatment of acute pain to compulsive drug misuse.

Opioids are prescribed to teenagers, 15-19 years of age, at over 5% of their emergency department (ED) visits, including 15% of visits for injuries.
Opioid dosing: ROSTERS

- Risk assessment
- Optimize multimodal for opioid-sparing effect
- Start low, go slow
- Titrate to effect
- Evaluate efficacy
- Reevaluate continued need for opioids
- Secure, monitor, and dispose

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Risk factors for substance abuse have been identified but are not predictive. Opioid abuse risk assessment tools have been developed to help healthcare professionals identify and weigh these risk factors.

In addition, researchers have found adolescents who engaged in nonmedical use of opioids for sensation-seeking were more likely to report other problem behaviors than those adolescents who were non-medical users, medical users (were prescribed and used opioids as prescribed) or self-treaters (engaged in nonmedical use of opioids for self-treatment).

Sensation seekers were more likely to have also used illicit drugs, gambled, report binge drinking, sexual activity and depression in the last year than non-medical users, medical users, and self-treaters.

Sensation seekers were more likely to report problems with impulsivity in the last year than non-medical users and medical users, but not self-treaters. There was no difference in the reporting of being disciplined among Sensation seekers, non-medical users, medical users, and self-treaters. This perhaps suggests these kids are not being screened for high-risk behaviors and they are not getting caught.

Those at a higher risk for prescription opioid addiction

Adolescents with a history of:

- substance abuse with prescription drugs,
- use of Illegal substances,
- alcohol use
- family history of substance abuse or psychiatric disorders.

- tobacco use
- sexual abuse,
- psychiatric disorders

Risk of opioid-respiratory depression

Incidence of respiratory depression is estimated at less than 0.5-1%. Respiratory depression is a serious adverse opioid event and fear of respiratory depression has been implicated as a significant contributor to the under-treatment of pediatric pain.

**Pediatric patients at risk for opioid-related respiratory depression include:**
- premature infants and neonates
- preexisting pulmonary disease
- known or suspected sleep-disordered breathing problems
- anatomic oral or airway abnormalities
- treatment with other sedative
- significant systemic disease, renal, or hepatic impairment.

*First dose, first dose increase, first 24 hours of routine treatment, any dose or interval change.*

Oral routes can result in respiratory depression, but rapid IV push fentanyl can result in chest rigidity.
Check the PDMP

Before prescribing an opioid, check the prescription drug monitoring program (PDMP)

- Record of a patient’s controlled substance prescriptions dispensed
- Some are available online 24/7
- Opportunity to discuss with 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 abusable drugs with cash
- Prescribers can check their own prescribing history

## Opioid dosing: ROSTERS

### When opioid treatment is appropriate

- Optimize multimodal approach.
- Start with the recommended initial dose for size and age and titrate slowly to effect.
- Evaluate efficacy and reevaluate continued need for opioids to treat pain.
- Educate patients and families in the risk of unintentional death from opioid misuse and monitor the patient.

<table>
<thead>
<tr>
<th>R</th>
<th>O</th>
<th>S</th>
<th>T</th>
<th>E</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk assessment</td>
<td>Optimize multimodal for opioid-sparing effect</td>
<td>Start low, go slow</td>
<td>Titrate to effect</td>
<td>Evaluate efficacy</td>
<td>Reevaluate continued need for opioids</td>
</tr>
</tbody>
</table>
Monitoring for sedation and respiratory depression

**Sedation precedes opioid-related respiratory depression.**

Therefore, monitoring of patients receiving opioids should include the purposeful and systematic serial assessments of sedation level and respiratory quality, depth, rate, and effectiveness. Technology can enhance respiratory monitoring, but it does not replace the need for vigilant systematic nursing assessments.

58% of all sentinel events (loss of life or limb or significant risk of loss) from opioids are the result of improper monitoring.

*(The Joint Commission, 2010)*
The Pasero-Opioid-Induced Sedation Scale is the most specific validated opioid-induced sedation assessment tool.

No action other than continued monitoring is necessary for patients who are awake and alert, slightly drowsy, or asleep but easily aroused. With progressive sedation, the patient may drift off to sleep while talking. This level of sedation should prompt increased monitoring and consideration of decreasing opioid dose. When patients are somnolent or unresponsive to verbal and physical stimulation, opioids should be stopped.

Patients should respond to touch even when asleep. Look for a head turn or position change, some movement from the child who appears to be asleep. Patients who don’t react to touch or blood pressure cuff inflation may be overly sedated. To prevent respiratory depression, stimulate the patient more vigorously. Discuss the importance of this assessment early in the night shift. Explain that the goal is safety, not to awaken the child, but that the child may awaken when level of sedation is being assessed.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Asleep, easy to arouse</td>
<td>Vigilantly monitor</td>
</tr>
<tr>
<td>1</td>
<td>Awake and alert</td>
<td>Routine monitoring</td>
</tr>
<tr>
<td>2</td>
<td>Slightly drowsy, easily aroused</td>
<td>Vigilantly monitor</td>
</tr>
<tr>
<td>3</td>
<td>Frequently drowsy, arousable, drifts off to sleep during conversation</td>
<td>Increased monitoring, consider decreasing opioid dose</td>
</tr>
<tr>
<td>4</td>
<td>Somnolent, minimal or no response to verbal and physical stimulation</td>
<td>Stop opioids, stimulate patient, consider opioid antagonist</td>
</tr>
</tbody>
</table>

How does one determine asleep, easy to arouse?
CDC guidelines NOT intended for Children

CDC Guideline for Prescribing Opioids for Chronic Pain

In 2015, the CDC published guidelines for primary care settings for prescribing opioids to adult patients with chronic pain greater than 3 months. The CDC specifically noted these guidelines were not intended for use with children.

**Purpose:** to provide recommendations for the prescribing of opioid pain medication for patients 18 and older in primary care settings.

Recommendations focus on the use of opioids in treating pain lasting:
- longer than 3 months or
- past the time of normal tissue healing

**Exclusion:** The guidelines are not intended for adults with cancer, being treated for cancer, palliative care, and end-of-life care.

https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1er.htm

Average days supply per prescription increased from 2006 to 2016.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13.3</td>
<td>13.9</td>
<td>14.5</td>
<td>15.0</td>
<td>15.5</td>
<td>16.0</td>
<td>16.4</td>
<td>16.9</td>
<td>17.2</td>
<td>17.7</td>
<td>18.1</td>
</tr>
</tbody>
</table>

But the guidelines state WITHOUT REFERENCE that prescriptions for acute pain should be limited to 3 days or less and more than 7 days is rarely needed.

**Problem:** Too many days  
**Solution:** Fewer days

Even at low doses, taking an opioid for >3 months, increases the risk of substance use disorder **15-fold**

For acute pain, prescriptions should be for the expected duration of pain severe enough to need opioids.
Prescribing patterns

Although not intended for pediatrics, some 3rd party payers, pharmacies, and states reference the CDC guidelines for their adoption of a 3-7 day limit for dispensing prescribed opioids to all patients, including pediatric patients.


Navy vertical bars indicate the number of patients who took at least one prescribed opioid on that postoperative day
Multiple colored vertical bars indicate the highest pain score (Red is 5 on 0-5 scale) each patient reported each postoperative day by patients who reported pain.

However, remember those appendectomy patients? This graph shows patient pain score and opioids use by day after discharge home.

Indeed less than half needed opioids on the 4th day home, but some were still using opioids on the 8th day.

And there were reports of pain of 4 out of 5 on day 8, 11, and 13!
Monitor for possible drug abuse

Healthcare providers need to monitor for possible drug abuse

**Personal appearance changes:**
- Messy, careless appearance
- Red, flushed cheeks or face
- Poor hygiene
- Burns or soot on fingers or lips

**Behavioral changes:**
- Unusually clumsy, stumbling, lack of coordination
- Hostility or anger
- Decreased motivation
- Loud or obnoxious behavior
- Being deceitful or secretive

Recognize possible drug abuse

- New friends, secretive about the new peers
- Loss of interest in old hobbies/sports
- Lying about new interests and activities
- Demanding more privacy: locking doors; avoiding eye contact; sneaking around
- Money/valuables missing from home
Monitor opioid use

Obtain random urine drug test (UDT) to:

- Help to identify drug misuse/addiction prior to starting opioid treatment
- Assist in assessing adherence during opioid therapy
- Support decision to refer.

Testing frequency is based on clinical judgment.

If patient displays aberrant behavior, UDT alone is not sufficient to document adherence to treatment plan.

Check state regulations for requirements.
### Drug class-specific windows

Drug and drug metabolites in urine only reflect recent drug use

<table>
<thead>
<tr>
<th>Drug in urine</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>≤3 d</td>
</tr>
<tr>
<td>THC (depending on grade &amp; frequency of use)</td>
<td></td>
</tr>
<tr>
<td>- Single use</td>
<td>1-3 d</td>
</tr>
<tr>
<td>- Chronic use</td>
<td>≤ 30 d</td>
</tr>
<tr>
<td>Benzoylecgonine after cocaine use</td>
<td>2-4 d</td>
</tr>
<tr>
<td>Opiates (morphine, codeine)</td>
<td>2-3 d</td>
</tr>
<tr>
<td>Methadone</td>
<td>≤3 d</td>
</tr>
<tr>
<td>- EDDP (methadone metabolite)</td>
<td>≤6 d</td>
</tr>
<tr>
<td>Benzodiazepines (depending on drug &amp; dose)</td>
<td>Days to wks</td>
</tr>
</tbody>
</table>

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


Meaning of UDT results

<table>
<thead>
<tr>
<th>Positive result</th>
<th>Negative result for prescribed opioid</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Demonstrates recent use</td>
<td>• Does not diagnose diversion</td>
</tr>
<tr>
<td>• Does not diagnose</td>
<td>• More complex than presence or absence of a drug in urine</td>
</tr>
<tr>
<td>• Drug addiction, physical dependence, or impairment</td>
<td>• May be due to maladaptive drug-taking behavior</td>
</tr>
<tr>
<td>• Does not provide enough information to determine exposure time, dose, or frequency of use</td>
<td>• Bingeing, running out early</td>
</tr>
<tr>
<td></td>
<td>• Other factors: e.g., no insurance</td>
</tr>
</tbody>
</table>

Be aware

Testing technologies and methodologies evolve. Differences exist in panels, cross-reactivity patterns.

Maintain list of all patient’s prescribed & OTC drugs

• Assist to identify false-positive results
• Cutoff levels
• Time taken to eliminate drugs
• Document time of last use & quantity of drug(s) taken
• Opioid metabolism may explain presence of apparently un-prescribed drugs.
Prescribed Use or Abuse?
Examples of opioid metabolism

Not comprehensive pathways, but may explain presence of apparently un-prescribed drugs.

- Codeine → Morphine → 6-MAM → Heroin
  - Hydrocodone → Hydromorphone
  - Oxycodone → Oxymorphone
  - t½=25-30 min
  - t½=3-5 min

6-MAM=6-monoacetylmorphine
**Medication prescribed:** Oxycodone

Oxycodone is indicated as the prescribed medication. You would expect UDT to be opiate positive if oxycodone was taken in last 2-3 days. However oxycodone is negative and hydrocodone and it’s metabolite hydromorphone are in the urine. This suggests the patient has taken hydrocodone. Since hydromorphone is the metabolite, the patient may be taking this drug as well.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Results</th>
<th>Comment</th>
<th>Cut-off</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
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<td></td>
<td>500</td>
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</tr>
<tr>
<td>Barbiturates</td>
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<td></td>
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</tr>
<tr>
<td>Benzodiazepines</td>
<td>Negative</td>
<td></td>
<td>75</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Buprenorphine/metabolite</td>
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<td></td>
<td>5</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>Negative</td>
<td></td>
<td>20</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Cocaine metabolite</td>
<td>Negative</td>
<td></td>
<td>150</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Negative</td>
<td></td>
<td>1.0</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Methadone metabolite</td>
<td>Negative</td>
<td></td>
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<td>ng/mL</td>
</tr>
<tr>
<td>Opiates</td>
<td>POSTIVE</td>
<td>INCONSISTENT 165</td>
<td>10</td>
<td>ng/mL</td>
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<td>• Hydrocodone, Quant</td>
<td>POSITIVE</td>
<td>INCONSISTENT 68</td>
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</tr>
<tr>
<td>• Hydromorphone, Quant</td>
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<td>INCONSISTENT</td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Oxycodone</td>
<td>Negative</td>
<td>INCONSISTENT</td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Oxymorphone</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Alcohols</td>
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<td></td>
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<td>%</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>ug/mL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Normal</td>
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<td>50</td>
<td>mg/dL</td>
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<tr>
<td>pH</td>
<td></td>
<td></td>
<td>6.8</td>
<td></td>
</tr>
</tbody>
</table>
Medication prescribed: Oxycodone

Oxycodone is indicated as the prescribed medication. You would expect UDT to be opiate positive if oxycodone was taken in last 2-3 days. UDT is positive for opiate, oxycodone, and it’s metabolite oxymorphone. Therefore, UDT is consistent with a patient taking the oxycodone prescribed. However, urine opioid levels can not be used to determine whether the dose and frequency of oxycodone taken is consistent with the dose and frequency prescribed.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Results</th>
<th>Comment</th>
<th>Cut-off</th>
<th>Unit</th>
</tr>
</thead>
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<td>Amphetamines</td>
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<td></td>
<td>500</td>
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</tr>
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<td>Barbiturates</td>
<td>Negative</td>
<td></td>
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<td>Benzodiazepines</td>
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<td></td>
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</tr>
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<td>ng/mL</td>
</tr>
<tr>
<td>Cannabinoids</td>
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<td></td>
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<td>ng/mL</td>
</tr>
<tr>
<td>Cocaine metabolite</td>
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<td></td>
<td>150</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Negative</td>
<td></td>
<td>1.0</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Methadone metabolite</td>
<td>Negative</td>
<td></td>
<td>100</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Opiates</td>
<td>POSTIVE</td>
<td></td>
<td>50</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Hydrocodone</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Hydromorphone</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Oxycodone, Quant</td>
<td>POSTIVE</td>
<td>CONSISTENT, 52</td>
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<td>ng/mL</td>
</tr>
<tr>
<td>• Oxymorphone, Quant</td>
<td>POSTIVE</td>
<td>CONSISTENT, 36</td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Alcohols</td>
<td>Negative</td>
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<td>%</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Negative</td>
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<td>10</td>
<td>ug/mL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Normal</td>
<td></td>
<td>50</td>
<td>mg/dL</td>
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<tr>
<td>pH</td>
<td></td>
<td></td>
<td>6.8</td>
<td></td>
</tr>
</tbody>
</table>
**Medication prescribed:** Morphine

Morphine is indicated as the prescribed medication so we would expect UDT to be opiate positive if morphine was taken in last 2-3 days. However, 6-monoacetylmorphine is the metabolite for heroin – so this patient is using heroin. Refer to immediate treatment.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Results</th>
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<th>Cut-off</th>
<th>Unit</th>
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<td>ng/mL</td>
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<td>Negative</td>
<td></td>
<td>200</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Negative</td>
<td></td>
<td>75</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Buprenorphine/metabolite</td>
<td>Negative</td>
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<td>Cannabinoids</td>
<td>Negative</td>
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<td>ng/mL</td>
</tr>
<tr>
<td>Cocaine metabolite</td>
<td>Negative</td>
<td></td>
<td>150</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Negative</td>
<td></td>
<td>1.0</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Methadone metabolite</td>
<td>Negative</td>
<td></td>
<td>100</td>
<td>ng/mL</td>
</tr>
<tr>
<td>Opiates</td>
<td>POSITIVE</td>
<td></td>
<td>50</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Morphine, Quant</td>
<td>POSITIVE</td>
<td>CONSISTENT, 10,000</td>
<td>10</td>
<td>ng/mL</td>
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<tr>
<td>• 6-monoacetylmorphine, Quant</td>
<td>POSITIVE</td>
<td>INCONSISTENT, 985</td>
<td>10</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Codeine, quant</td>
<td>Negative</td>
<td>INCONSISTENT, 852</td>
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<td>ng/mL</td>
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<tr>
<td>Alcohols</td>
<td>Negative</td>
<td></td>
<td>0.02</td>
<td>%</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>ug/mL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Normal</td>
<td></td>
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<td>mg/dL</td>
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<tr>
<td>pH</td>
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<td></td>
<td>6.8</td>
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</tr>
</tbody>
</table>
Methadone is indicated as the prescribed medication and is found in the urine, but the metabolite EDDP is not – suggesting the patient slipped some drug into the urine specimen. Oxycodone is also in the urine, suggesting the patient has been taking oxycodone, a drug that was not prescribed.

### Analyte Results Comment Cut-off Unit

<table>
<thead>
<tr>
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<tr>
<td>Fentanyl</td>
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<td>ng/mL</td>
</tr>
<tr>
<td>Methadone metabolite, Quant</td>
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<td>CONSISTENT, &gt;50,000</td>
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<td>ng/mL</td>
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<td>INCONSISTENT</td>
<td>50</td>
<td>ng/mL</td>
</tr>
<tr>
<td>• Oxycodone</td>
<td>POSITIVE</td>
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<td>10</td>
<td>ng/mL</td>
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</tbody>
</table>
Iatrogenic Withdrawal Syndrome (IWS)

Increased risk after 5 days of continuous opioid or benzodiazepine infusion
Onset 1 to 48 hours after tapering or discontinuing infusion

**Signs:**

- **Neurologic:** irritability, anxiety, tremors, clonus, yawning, sneezing, delirium, seizures, hallucinations, and mydriasis
- **Gastroenteric:** feeding intolerance with vomiting, diarrhea, uncoordinated sucking
- **Activation of sympathetic nervous system:** tachycardia, hypertension, tachypnea, sweating, fever, and cough

**Standardized instruments**

Use of standardized assessment instruments is recommended to differentiate sources of distress and to target interventions appropriately (Harris et al., 2016). This table provides examples of instruments recommended for use in the literature.

<table>
<thead>
<tr>
<th>Concept</th>
<th>Instrument(s)</th>
<th>When to use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iatrogenic Withdrawal Syndrome</td>
<td>• Withdrawal Assessment Tool version 1 (WAT-1) (ICU only)</td>
<td>• When weaning opioids or benzodiazepines infused ≥ 5 days</td>
</tr>
<tr>
<td></td>
<td>• Sophia Observation withdrawal Symptoms-scale (SOS)</td>
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<tr>
<td></td>
<td>• Modified Finnegan</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Neonatal abstinence scale</td>
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</tr>
</tbody>
</table>
Iatrogenic Withdrawal Syndrome

**Increased risk of tolerance and physical dependence with prolonged infusions of short-acting opioids**

- Tolerance: need for increased medication to achieve consistent therapeutic effects. Rare when opioid therapy < 72 hours
- Tolerance, escalating doses, prolonged treatment are coupled with the development of physiologic dependence.
- Physical dependence: “physiologic and biochemical adaptation of neurons such that removing a drug precipitates withdrawal or an abstinence syndrome” (Anand et al., 2010)

Once tolerance and dependence present, ending therapy abruptly or weaning too quickly precipitates IWS.

**Strongest risk factors**: longer duration, higher cumulative dose. Abrupt discontinuation and rapid weaning precipitates symptoms.
Management of opioid withdrawal

It has been suggested that nurse-controlled sedation/analgesia protocols may reduce cases of IWS (Kanwaljeet, 2010), however this was not the case in a recent randomized clinical trial in US PICUs (Curley, 2016). However PICU patients were exposed to fewer days of opioids and sedative classes.

**Procedure**

- Prevent or delay tolerance
- Titrate opioids to adequate pain management, adjust to minimum effective dose
- Frequently re-evaluate if continued use needed
- Use longer acting opioids for persistent pain
- Consider daily interruption of sedatives
- Gradual weaning for patients at risk
- Recommendations range from 10% of current dose every other day to 20% of total dose every day)
- Pharmacological treatments such as methadone, and clonidine (alternatives e.g. dexmedetomidine, buprenorphine)
The hospital assesses and manages the patient’s pain and minimizes the risks associated with treatment.

The hospital educates the patient and family on discharge plans related to pain management including the following:

- Pain management plan of care
- Side effects of pain management treatment
- Activities of daily living, including the home environment, that might exacerbate pain or reduce effectiveness of the pain management plan of care, as well as strategies to address these issues

Safe use, storage, and disposal of opioids when prescribed

*In 2018, the Joint Commission mandates education of patients and families on safe use, storage, and disposal of opioids.*
Education about Opioids
What do you tell families about opioids on discharge from the hospital or ED?

Type your answer here.
Educate patients and families

Teach patients and families the intended and appropriate use of the opioids for the patient’s specific need. Include:

- Use of multimodal approach to treat pain
- Potential weaning strategies
- When to call provider if pain persists.
- Have patients and families repeat back instructions to ensure understanding
- Answer questions or concerns about addiction or risk factors.

Caution patients and families

Sharing opioids with others may cause them to have serious adverse effects, including death

Selling or giving away opioids is against the law.

Storage

- Store opioids in a safe and secure place away from children, family members, household visitors, & pets (e.g., a medication safe)
- Dispose of any opioids when no longer needed
- Read product-specific disposal information included
- May be flushed down toilet if Drug take-back program not immediately available.

FDA. Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. 8-28-2012.
The ready availability of prescription medications in teens’ own homes highlights the need for increased educational efforts targeting parents and other family members regarding safeguarding and monitoring prescription medications in the home, so that they do not act as “unintentional enablers.”

**Step 1: MONITOR**

Parents are in an influential position to immediately help reduce teen access to prescription drugs because these drugs are found in the home.

- Start by taking note of how many pills are in each of your prescription bottles or pill packets.
- Keep track of your refills. This goes for your own medication, as well as for your teens and other members of the household. Needing to refill medication more often than expected could indicate a problem.
- If your teen has been prescribed a drug, be sure you control the medication and monitor dosages and refills.
- Make sure your friends and relatives—especially grandparents—are also aware of the risks. Encourage them to regularly monitor their own medicine cabinets.
- If there are other households your teen has access to, talk to those families as well about the importance of helping safeguard their medications.
Educate parents

Step 2: SECURE

Teens abuse prescription drugs because they are easily accessible and either free or inexpensive. Approach securing your prescriptions the same way you would other valuables in your home, like jewelry or cash.

- Take prescription medications out of the medicine cabinet and hide them in a place only you know about.
- If possible, keep all medicines in a safe place, such as a locked cabinet your teen cannot access.
- Tell relatives, especially grandparents, to lock their medications or keep them in a safe place.
- Talk to the parents of your teenager’s friends. Encourage them to secure their prescriptions.

However, in the survey of Massachusetts parents by the Partnership at DrugFree.org, 34% of respondents say that grandparents use prescription pain relievers, but only 19% have spoken to grandparents about safeguarding their medications.

Safely disposing of expired or unused prescription medications is a critical step to decrease the opportunity for your teens or their friends to abuse your medications.

Step 3: DISPOSE

After taking an inventory of all of the prescription drugs in your home, discard expired or unused prescription drugs when your teens are not home.
How do you dispose of opioids?

Type your answer here.
Prescription drug disposal

The website for DEA approved take back sites: www.deadiversion.usdoj.gov

Search for an Authorized Collector Location

Then type in zip code or city and state
How to dispose of opioids

If a take back program or site is not immediately available.

“While FDA and the EPA take the concerns of flushing certain medicines in the environment seriously, there has been no indication of environmental effects due to flushing.”

Video demonstration: www.smarxtdisposal.net/index.html


Prescription drug disposal

What are you going to do now to prevent opioid use disorders and opioid overdose deaths?

TONIGHT:
Dispose of all unused medications

TOMORROW:
Tell your patients, your friends, and your relatives to dispose of all unused medications

FDA lists especially harmful medicines—in some cases fatal with just 1 dose—if taken by someone other than the patient.

All opioids are such drugs!

Flush down sink/toilet if no available take-back program exists as soon as they are no longer needed so the opioids cannot be accidentally taken by children, pets, or others.

Transdermal patches
This includes transdermal adhesive skin patches.
• A used patch worn for 3 d 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: Butrans
You can seal in Patch-Disposal Unit provided and dispose of in the trash.
Be ready to refer

Be familiar with referral sources for abuse or addiction.
- SAMHSA substance abuse treatment facility locator
  https://findtreatment.samhsa.gov/

Behavioral Health Treatment Services Locator

Welcome to the Behavioral Health Treatment Services Locator, a confidential and anonymous source of information for persons seeking treatment facilities in the United States or U.S. Territories for substance abuse/addiction and/or mental health problems.

PLEASE NOTE: Your personal information and the search criteria you enter into the Locator is secure and anonymous. SAMHSA does not collect or maintain any information you provide.

Enter a starting location:

Or Call
SAMHSA’s National Helpline
1-800-662-HELP (4357)
1-800-487-4889 (TTY)

Or Watch
Video Tutorials
Click here for instructional help using the Locator.
In Summary...
Key Points

Opioids are indicated for severe pain and healthcare professionals must advocate for appropriate pain assessment, optimal pain treatment and monitor for adverse treatment effects including adverse effects from opioids.

There is an opioid epidemic
- Almost 1 in 4 young adults report non-medical use of opioids during their lifetime.

Before prescribing an opioid, check the prescription drug monitoring program (PDMP)

Opioid dosing: ROSTERS
- Risk assessment
- Optimize multimodal for opioid-sparing effect
- Start low, go slow
- Titrate to effect
- Evaluate efficacy
- Reevaluate continued need for opioids
- Secure, monitor, and dispose

Educate parents on how to:
- Monitor opioid usage
- Secure the medications
- Dispose of unused drugs
Appendix
**References**


Disposal of Unused Medicines: What You Should Know

FDA. Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. 8-28-2012.


Fortuna, RJ, Robbins, BW, Caiola, E, Joynt M, & Halterman JS. Prescribing of controlled medications to teens and young adults in the United States Pediatrics 2010;126;1108. DOI: 10.1542/peds.2010-0791.


The Joint Commission, 2018. https://www.jointcommission.org/issues/article.aspx?Article=T4iS%2BGolXqWgV%2BRgHcgHI7uKHH03zjhc5kD9sTYF4ww%3D&print=y


SMARxT Disposal. A prescription for a healthy planet. www.smarxtdisposal.net/index.html


US Food & Drug Administration. Safe Disposal of Medicines
