Opioids for Pain: Drug Seeking Behavior, Acute Pain Management, and Drug Monitoring Databases

Bryan D. Hayes, Pharm.D., DABAT, FAACT, FASHP
Nicole M. Acquisto, Pharm.D., FCCP, BCCCP
Zlatan Coralic, Pharm.D., BCPS
Disclosure

All planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.
Prescription Monitoring Databases

Zlatan Coralic, Pharm.D., BCPS
Emergency Medicine Clinical Pharmacist
Associate Clinical Professor
University of California San Francisco
RATE OF OPIOID-RELATED DEATHS QUADRUPLED SINCE 2000

1000 OPIOID ED VISITS PER DAY

91 AMERICANS DIE EACH DAY FROM OPIOID USE
Natural & Semi-Synthetic Opioid Overdose Death Rates

Age-adjusted deaths per 100,000 population for natural and semisynthetic opioids from 2014 to 2015, by census region of residence:

- **South***: 4.2 deaths; 5,374 deaths in 2015
- **West**: 3.8 deaths; 2,956 deaths in 2015
- **Northeast***: 3.3 deaths; 2,095 deaths in 2015
- **Midwest**: 3.3 deaths; 2,302 deaths in 2015
- **United States***: 3.8 deaths; 12,727 deaths in 2015

*Statistically significant at p<0.05 level.

## Heroin Use Has INCREASED Among Most Demographic Groups

<table>
<thead>
<tr>
<th>Category</th>
<th>2002-2004*</th>
<th>2011-2013*</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.4</td>
<td>3.6</td>
<td>50%</td>
</tr>
<tr>
<td>Female</td>
<td>0.8</td>
<td>1.6</td>
<td>100%</td>
</tr>
<tr>
<td><strong>AGE, YEARS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17</td>
<td>1.8</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>18-25</td>
<td>3.5</td>
<td>7.3</td>
<td>109%</td>
</tr>
<tr>
<td>26 or older</td>
<td>1.2</td>
<td>1.9</td>
<td>58%</td>
</tr>
<tr>
<td><strong>RACE/ETHNICITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>1.4</td>
<td>3</td>
<td>114%</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>1.7</td>
<td>--</td>
</tr>
<tr>
<td><strong>ANNUAL HOUSEHOLD INCOME</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>3.4</td>
<td>5.5</td>
<td>62%</td>
</tr>
<tr>
<td>$20,000–$49,999</td>
<td>1.3</td>
<td>2.3</td>
<td>77%</td>
</tr>
<tr>
<td>$50,000 or more</td>
<td>1</td>
<td>1.6</td>
<td>60%</td>
</tr>
<tr>
<td><strong>HEALTH INSURANCE COVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4.2</td>
<td>6.7</td>
<td>60%</td>
</tr>
<tr>
<td>Medicaid</td>
<td>4.3</td>
<td>4.7</td>
<td>--</td>
</tr>
<tr>
<td>Private or other</td>
<td>0.8</td>
<td>1.3</td>
<td>63%</td>
</tr>
</tbody>
</table>
WHAT WE HAVE TO DO

1. PREVENT ADDICTION
2. CONTROL ACCESS
3. TAKE CARE OF PATIENTS WITH ADDICTION
WHAT ARE PMPs (PDMPs)?

cdc.gov
WHO PAYS FOR PMPs?

- Board of Pharmacies (20)
- Departments of Health (16)
- Licensing Boards (6)
- Law Enforcement (5)
- Substance Abuse Programs (3)
- Consumer Protection (1)
WHO HAS PMPs?

Addiction. (2017) 112; 1773–1783
INFO* IN PMPs?

• Controlled substance dispense information
• RX Theft/Loss Report
• Delegate assignment
• Epidemiological data

Date, Name, DOB, Address, Drug Name, Strength, Quantity, Day Supply, Pharmacy (#), Pharmacy DEA, Prescriber’s DEA, Prescriber Name, RX#, Refill#

*State specific
89,000 Rx for opioids

100,000 Missourians

900 Missourian OD deaths in 2016

2 Missourian neonates born daily with narcotic withdrawal
Senator Rob Schaaf (R)  
District 34  

“If they overdose and kill themselves, it just removes them from the gene pool.”
Governor Eric Greitens Announces Statewide Prescription Drug Monitoring Program

Home » News » News Archive

July 17, 2017
DO PMPs WORK?
↓ 1.4% reduction of opioid RX

↓ 2.5% reduction in opioid volume

↓ 5.6% in morphine equivalents per script

\( n = 40 \text{ million prescriptions} \)
States with PDMP vs States without
↓ MORTALITY
18% [1.6-29%]

States with liberal marijuana laws
↓ MORTALITY
16% [1-30%]

Addiction. (2017) 112; 1773–1783
IDEAL PMPs

- Universal access
- Real time
- Wealth of data
- Ease of use
- All prescription data
WHAT TO DO WITH PMPs?
THE ‘GOTCHA’ APPROACH
• 2nd opioid Rx = 2x risk of opioids at 1 year
• Risk of dependence ↑ w/day supply: starting with day 3
• Highest risk = XR or Rx for tramadol
Case

“Hey, this patient was discharged two days ago with a script for oxycodone. Says he lost the script. Should I write for a replacement script?” --ED Doc
## Case

<table>
<thead>
<tr>
<th>Date</th>
<th>Name</th>
<th>Drug</th>
<th>Dose</th>
<th>Qty</th>
<th>Days</th>
<th>Dr.</th>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/22</td>
<td>Patient</td>
<td>Oxy/APAP</td>
<td>5/325 mg</td>
<td>30</td>
<td>8</td>
<td>Dr. C</td>
<td>#1</td>
</tr>
<tr>
<td>8/11</td>
<td>Patient</td>
<td>Oxy/APAP</td>
<td>5/325 mg</td>
<td>24</td>
<td>2</td>
<td>Dr. A</td>
<td>#3</td>
</tr>
<tr>
<td>7/31</td>
<td>Patient</td>
<td>Oxy/APAP</td>
<td>5/325 mg</td>
<td>24</td>
<td>3</td>
<td>Dr. B</td>
<td>#2</td>
</tr>
<tr>
<td>7/29</td>
<td>Patient</td>
<td>Oxy/APAP</td>
<td>5/325 mg</td>
<td>20</td>
<td>10</td>
<td>Dr. A</td>
<td>#1</td>
</tr>
</tbody>
</table>
Pain Medications Are Harming You

Take control of your life. Get treated.

Call 1-800-662-HELP
SAMHSA’s National Helpline is a free, confidential treatment referral and information service for individuals and families facing mental health and/or substance use disorders, including pain medications and heroin.

24/7 365

1-800-662-HELP (4357)
(in English and Spanish)

www.samhsa.gov/find-help

Courtesy of Ruben Strayer, MD
Key Takeaways

- Opioid epidemic continues to claim lives
- PMPs are an imperfect but a useful tool available in all* states
- There is no standard on how to use PMPs for clinical decision making
- If you see a concerning pattern – speak up and offer resources.
Drug Seeking Behavior

Nicole M. Acquisto, Pharm.D., FCCP, BCCCP
Emergency Medicine Clinical Pharmacy Specialist
Associate Professor, Department of Emergency Medicine
University of Rochester Medical Center, Rochester, NY
“Only the medication with the ‘D’ works for me”

“I’m allergic to acetaminophen and NSAIDs. Oxycodone is fine”

“10/10 pain” (while eating a sandwich)
“Drug Seeking”

- Break the law to get controlled substances to sell on the street
- Deviant behavior to divert drugs as part of addiction
- Behaviors that appear to indicate addiction but actually reflect undertreated pain (pseudoaddiction)
- User/abuser
- Concerted effort to obtain a medication
- Seemingly inappropriate attempt to obtain opioids
Problems

• Terminology can be stigmatizing
  – Causes a patient’s actual pain or other issues to be undertreated
  – Pain and misusing opioids is not mutually exclusive
• Defamation claims
• Interference with insurance coverage
• Possibility of misdiagnosis
Behaviors to Describe Drug Seeking:

- Going to different EDs for opioids
- Telling inconsistent stories about pain/medical history
- Lost/stolen prescription

Drug Seeking Defined As:

- Addicted to opioids
- Abusing pain medication
- Manipulative

Epidemiology

- Opioid/heroin epidemic
- 30% opioid prescriptions diverted for illegal use
- 44 million pain-related visits annually to US EDs (42.6%)
- ED visits for nonmedical use of opioids increased 111% 2004-2008
- Subjective and difficult to quantify drug seeking behavior
- ED volume 75,000/yr → 262 (4%) drug-seekers/month
  - Age ~ 34.3 years, ~ 13 ED visits/year, ~ 4 different hospitals, ~2 different aliases

Classic Behaviors

- Allergies to non-narcotic pain medications; everything other than drug of choice
- Requests opioids, benzos or muscle relaxants by name; claim other medications do not work
- Requests IV opioids
- Requests increased dose
- Preoccupation with opioids
- Lost/stolen medications
- Multiple visits for pain and same complaint

- 10/10 pain
- Suspicious history
- Angry when questioned closely about pain symptoms
- Symptoms out of proportion to examination
- No primary care physician
- Specific about which physician they want to see
- Increases doses without provider’s instruction
- Uses aliases

<table>
<thead>
<tr>
<th>“Classic” Behaviors</th>
<th>Total (n = 178)</th>
<th>% Total Visits (n = 2,486)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/10 pain</td>
<td>724</td>
<td>29.1</td>
<td>27.3-30.9</td>
</tr>
<tr>
<td>Headache</td>
<td>539</td>
<td>21.7</td>
<td>20.1-23.2</td>
</tr>
<tr>
<td>Back pain</td>
<td>516</td>
<td>20.8</td>
<td>19.2-22.4</td>
</tr>
<tr>
<td>Med by name</td>
<td>377</td>
<td>15.2</td>
<td>13.8-16.6</td>
</tr>
<tr>
<td>Out of medication</td>
<td>235</td>
<td>9.5</td>
<td>8.3-10.6</td>
</tr>
<tr>
<td>Need refill</td>
<td>174</td>
<td>7</td>
<td>6-8</td>
</tr>
<tr>
<td>Request IV</td>
<td>106</td>
<td>4.3</td>
<td>3.5-5.1</td>
</tr>
<tr>
<td>Dental pain</td>
<td>45</td>
<td>1.8</td>
<td>1.3-2.3</td>
</tr>
<tr>
<td>10+ pain</td>
<td>44</td>
<td>1.8</td>
<td>1.3-2.3</td>
</tr>
<tr>
<td>Lost medication</td>
<td>15</td>
<td>0.6</td>
<td>0.3-0.9</td>
</tr>
</tbody>
</table>

Mixed Methods Study

• Video vignettes (n = 192 PCPs)
  – Active request for a medication or more general request for help with back pain as a new complaint in an established patient

• Assessment of “drug-seeking”
  – 21% active request vs. 3% general request, p <0.001
  – Active request: OR 8.1 (95% CI 2.1-31.2)
  – More likely to inquire about substance abuse
  – 50% recognized potential for misuse and evaluated risk/benefit

## Drug-Seeking Defined by PDMP

<table>
<thead>
<tr>
<th>Behaviors</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requests for opioids by name</td>
<td>1.9</td>
<td>1.1-3.2</td>
</tr>
<tr>
<td>Multiple visits for same complaint</td>
<td>2.5</td>
<td>1.5-4.2</td>
</tr>
<tr>
<td>Suspicious history</td>
<td>1.9</td>
<td>1.1-3.2</td>
</tr>
<tr>
<td>Symptoms out of proportion to examination</td>
<td>1.8</td>
<td>1.1-3</td>
</tr>
</tbody>
</table>

\[ \geq 4 \text{ opioid prescriptions from } \geq 4 \text{ providers in 12 months} \]

Emergency Department as a Target

• Always open
• Visit/history might be brief
• No verification of past medical history
• Minimal time to sort out drug-seeking
• Frequent visits might go unnoticed (different EDs)
Difficulty in Managing Patients

Pain “Control”

Protect susceptible patients from consequences of drug abuse/addiction

Pain and misusing opioids are not mutually exclusive
Patient Approach

• Use prescription monitoring program data
• Explain why the prescription pattern is a problem
• Clarify the treatment plan from the beginning
• Reinforce that patients are best served by having their pain managed comprehensively as outpatients
ED Strategies

- Patient photos
- Opioid policies/guidelines
- Prescription drug monitoring programs
- Treatment pathways
  - Pain management with history of substance abuse
- Patient agreements
- Care coordination/case managers
- E-prescribing

Meditech Nurse Advisory Committee.
Practice recommendations (treatment in the ED)

- Alternative modes for symptom management (non-pharmacologic and pharmacologic) should be trialed as first-line approach to pain management before opioids
  - Refer to adult and pediatric non-opioid treatment pathways for specific disease states
- Opioids are not indicated for:
  - Abrasions
  - Burns (minor)
  - Cellulitis
  - Chest pain
  - Contusions
  - Cough
  - Dental pain without acute trauma
  - Dysuria
  - Ear pain
  - Hemorrhoids
  - Lacerations
  - Neck pain
  - Sexual transmitted diseases
  - Sprains/strains
  - Throat pain

- Patients should be educated regarding appropriate expectations for pain control in the ED
<table>
<thead>
<tr>
<th>High-risk Criteria for Opioid Addiction</th>
<th>High-risk Factors for Opioid Related Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal or family history of substance abuse (alcohol, illicit drugs, prescription drugs)</td>
<td>Extremes of age (infant or elderly)</td>
</tr>
<tr>
<td>Age between 16 and 45</td>
<td>Pulmonary comorbidities (COPD, sleep apnea)</td>
</tr>
<tr>
<td>Mental health/psychological history (e.g. depression, attention deficit disorder, bipolar disorder, schizophrenia)</td>
<td>Cardiac comorbidities (CHF)</td>
</tr>
<tr>
<td>History of sexual abuse</td>
<td>Organ dysfunction (renal or hepatic)</td>
</tr>
</tbody>
</table>
### The Dangers of Opioids (Information in talking with patients)

<table>
<thead>
<tr>
<th>Common side effects</th>
<th>Serious side effects of chronic use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/vomiting</td>
<td>Cardiac abnormalities, including prolonged QTc and torsades de pointes</td>
</tr>
<tr>
<td>Constipation</td>
<td>Sudden cardiac death with concomitant use of benzodiazepines and methadone</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Hormonal disruptions, including decreased testosterone in males</td>
</tr>
<tr>
<td>Euphoria</td>
<td>Decreased LH and FSH and fertility in women</td>
</tr>
<tr>
<td>Respiratory depression, particularly with the simultaneous use of alcohol, benzodiazepines, antihistamines, muscle relaxants, or barbiturates</td>
<td>Musculoskeletal compromise, including increased risk of osteoporosis</td>
</tr>
<tr>
<td>Lightheadedness</td>
<td>Immunosuppression</td>
</tr>
<tr>
<td>Dry mouth</td>
<td></td>
</tr>
</tbody>
</table>

- Hyperalgesia (upregulation of receptors and increased tolerance)

- Sleep disturbances

- Delayed or inhibited gastric emptying, increased sphincter tone, and blockade of peristalsis
• **Patients on chronic opioids:**
  - Should receive opioid medications from one practice. EM providers should coordinate care with a patient’s primary pain treatment physician whenever possible.
  - Should not be prescribed additional opioids through the ED
  - Should not have opioid regimens adjusted for chronic conditions and should not be routinely prescribed narcotics for acute exacerbations of non-chronic pain

• **Patients at high risk for misuse (Table 1):**
  - May need to be given smaller supplies of controlled substances
  - Benefit from earlier follow-up with a PCP or appropriate specialist for ongoing management

• The ED will not refill lost, chronic, stolen, or otherwise missing opioid prescriptions or controlled substances

• When considering opioids, the lowest effective dose in the shortest appropriate duration (e.g. ≤ 3 days) should be prescribed

• Long-acting or extended release opioid products should not be used for relief of acute pain
Care Plan Utilization

Mean ED visits/year

1 yr before: Male (n = 32) - 9.5, Female (n = 28) - 5.9
1 yr after: Male (n = 32) - 3, Female (n = 28) - 2.1
2 yr after: Male (n = 32) - 1.9, Female (n = 28) - 1.2

P = 0.009

“Only the medication with the ‘D’ works for me”

“I’m allergic to acetaminophen and NSAIDs. Oxycodone is fine”

“10/10 pain” (while eating a sandwich)
Drug Seeking Behaviors

- Evaluate previous history/ED visits/PDMP history
- Discuss pattern with patient
- Discuss risks of opioids with patient
- Risk/benefit evaluation for medication therapy to treat current pain
- Discuss appropriate expectations for pain control
- Case management if necessary
Key Takeaways

• Several classic behaviors associated with opioid misuse
• Implement strategies to decrease drug seeking behavior
• Pain and opioid misuse are not mutually exclusive
• Risk/benefit evaluation if necessary
  – Utilize resources available in the ED
Thank You!

University of Rochester Medical Center
Opioid Alternatives for Treatment of Acute Pain

Bryan D. Hayes, Pharm.D., DABAT, FAACT, FASHP
Attending Pharmacist, EM & Toxicology, MGH
Assistant Professor of EM, Harvard Medical School

@PharmERToxGuy
TRAMADOL
Which of the following problems may be associated with tramadol?

- A. Warfarin interaction
- B. Hypoglycemia
- C. Seizures
- D. Erratic metabolism
‘Messy’ pharmacology

Erratic metabolism

Leppert W. Pharmacology 2011;87(5-6):274-85.
DOES IT WORK?

Osteoarthritis: modest

Neuropathic: comparable to alternatives

IN THE ED

MS: ↓ hydroc/APAP
Ankle: = hydroc/APAP

22% of first-seizure pts had recent tramadol use

1. Mean total tramadol dose in last 24 hours (reported): 140 mg

2. Duration of tramadol use less than 10 days: 84.5%

3. Seizure within 6 hours of tramadol consumption: 74%
Hypoglycemia

Warfarin Interaction

A 30 year old male presents with acute back pain after playing basketball. Which dose of ketorolac is appropriate?

A  60 mg IM
B  30 mg IM
C  30 mg IV
D  15 mg IV
Ceiling Effect
Comparison of Intravenous Ketorolac at Three Single-Dose Regimens for Treating Acute Pain in the ED: A Randomized Controlled Trial


240 pts w/ acute pain

Ketorolac IV 10 vs. 15 vs. 30 mg

Pain score, VS, AE @ 15, 30, 60, 90, 120 min

Morphine 0.1 mg/kg rescue at 30 min

Outcome: ↓ pain score at 30 min
Comparison of Intravenous Ketorolac at Three Single-Dose Regimens for Treating Acute Pain in the ED: A Randomized Controlled Trial


**Pain score - no difference**
- 10 mg: 7.7 to 5.2
- 15 mg: 7.5 to 5.1
- 30 mg: 7.8 to 4.8

**Rescue morphine - no difference**

**AE - no difference**

**Limitations:** No placebo + box plot variability
Ketorolac 10-15 mg = 30 mg (or 60)

↑ dose = ↑ AE

Ibuprofen ceiling 400-600 mg

Anti-inflammatory
A 30 year old male presents with acute back pain after playing basketball. Which dose of ketorolac is appropriate?

A. 60 mg IM
B. 30 mg IM
C. 30 mg IV
D. 15 mg IV
WARNING KETAMINE
Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the ED: A Randomized Controlled Trial


45 pts - IV ketamine 0.3 mg/kg (8.6)

45 pts - IV morphine 0.1 mg/kg (8.5)

Abdominal pain ~70%
Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the ED: A Randomized Controlled Trial


Pain score 30 min:
Ketamine 4.1 vs. Morphine 3.9 ($p = 0.97$)

Rescue fentanyl: no difference

Ketamine: ↑ minor AE
Low-dose ketamine
State/institution RN regs
Discharge meds?
A prospective randomized, double-dummy trial comparing IV push low dose ketamine to short infusion for treatment of pain in the ED


Ketamine 0.3 mg/kg IV push vs. 15-min

Pain score, VS, AE @ 5, 15, 30, 60, 90, 120 min

SERSDA and RASS scales
A prospective randomized, double-dummy trial comparing IV push low dose ketamine to short infusion for treatment of pain in the ED


24 patients in each group

SERDSA: IV push 3.0 vs infusion 0.0 \( (p = 0.001) \)

RASS: IV push -2.0 vs. infusion 0.0 \( (p = 0.01) \)

Pain, VS, AE: no difference
Dilute in 100 mL NS
Infuse over 15 min

Use outside ED
Still may need opioids
3-6% risk of dependence?  
(Shah, MMWR 2017)

IN ketamine
LIDOCAINE

Topical or IV

Na\textsuperscript{+} Channel
Renal colic
Headache
Post-surgery
Post-herpetic neuralgia
Bolus: 1-2 mg/kg

Infusion: 0.5-3 mg/kg/hr
SAFE + EFFECTIVE

Lidocaine > morphine

* NSAIDS?

PATCH

4% = $1.67

5% = $9

Sample Acute/Chronic Back Pain Protocol

**Oral/Topical Regimen**
- Ibuprofen 400-800 mg
- Acetaminophen 500-1000 mg
- Muscle Relaxant: Diazepam 5 mg or Methocarbamol 500-1500 mg
- Lidocaine patch-5% no more than 2 patches per 12h

**Parenteral Regimen**
- IV Ketamine infusion: 0.3 mg/kg bolus over 15 min, 0.15-0.25 mg/kg/hr infusion with titration q30 min by 5 mg
- IV Lidocaine (preservative-free): 1.5 mg/kg over 10 min (Max 200 mg)
- IV Ketorolac (only if cannot tolerate po) 10-15 mg

**If no improvement-admit for observation**
- IV Ketamine: 0.3 mg/kg bolus over 15 min, 0.15-0.25 mg/kg/hr infusion with titration q30 min (no more than 24h)
- IV Lidocaine: 2.5 mg/kg/hr (100 mg IV bolus over 20 min, if no side effects, start infusion at 2.5 mg/kg/hr)
Topical analgesics
Trigger Point Inj
Nitrous Oxide
Summary

1. Tramadol is not safe
2. NSAID ceiling for pain
3. Ketamine may reduce opioids
4. Lidocaine IV or topical
Opioid Alternatives for Treatment of Acute Pain

Bryan D. Hayes, Pharm.D., DABAT, FAACT, FASHP
Attending Pharmacist, EM & Toxicology, MGH
Assistant Professor of EM, Harvard Medical School
PharmERToxGuy.com