Risk Mitigation Strategies for Opioid Prescribing

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Disclosures

• Nothing to disclose
Conflict of Interest

No financial conflicts of interest to disclose

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Learning Objectives

1. Discuss monitoring strategies to ensure appropriate use of opioid prescriptions
2. Explore strategies to prevent opioid abuse by counseling patients on proper storage and disposal practice
3. Describe validated risk screening tools for aberrant drug taking behaviors as well as their utility and limitations
4. Select appropriate toxicology screening and appropriately interpret results to ensure safe use of opioids
The Problem......


Meet Richard

Richard consistently presents to your pharmacy requesting early refills of his tramadol prescription which he takes for chronic low back pain. You are concerned but aren’t sure how to proceed.
Is Richard “addicted”?

- **Aberrant drug taking behaviors**
  - any departure from prescription
- **Misuse**
  - departure with therapeutic intent
- **Abuse**
  - departure without therapeutic intent
- **Addiction**
  - now called *substance use disorder*
  - neurobiologic disease characterized by cravings, compulsion, withdrawal syndrome, and loss of control
- **Tolerance**
  - requiring increasing doses to garner the same effect
- **Hyperalgesia**
  - when noxious stimuli produces a heightened and non-proportional nociceptive response

# Diagnosis of Substance Use Disorder

<table>
<thead>
<tr>
<th>&lt; 2 symptoms = no disorder, 2-3 = mild disorder, 4-5 = moderate disorder, ≥ 6 = severe disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wanting to cut down or stop using, but not managing to</td>
</tr>
<tr>
<td>Spending a lot of time to get, use, or recover from use</td>
</tr>
<tr>
<td>Craving</td>
</tr>
<tr>
<td>Inability to manage commitments due to use</td>
</tr>
<tr>
<td>Continuing to use, even when it causes problems in relationships</td>
</tr>
<tr>
<td>Giving up important activities because of use</td>
</tr>
<tr>
<td>Continuing to use, even when it puts the user in danger</td>
</tr>
<tr>
<td>Continuing to use, even when physical or psychological problems are worsened</td>
</tr>
<tr>
<td>Increasing tolerance</td>
</tr>
<tr>
<td>Withdrawal symptoms</td>
</tr>
<tr>
<td>Using in larger amounts or for longer than intended</td>
</tr>
</tbody>
</table>

The “Addiction” Cycle

The end result...
Prescription opioids and heroin

- Quantitative questionnaire using street outreach, venue-recruitment, and needle-exchange advertisement (n = 123)
- Median age 29 yrs (75% male, 53% white, 28% hispanic, 19% black or other)
- 39.8% reported problematic prescription opioid use prior to first heroin use
- We are lacking data on true risk for first time exposure to opioids for an indication of pain

Risk Mitigation Strategies

• Prescription Drug Monitoring Programs
• Screening tools (prior to and during therapy)
• Random drug screening
• Opioid agreements
• Pill counts
• COMMUNICATION with prescribers, nurses, AND patients
  • Early requests
  • Erratic behaviors
## Validated Risk Assessment Tools

<table>
<thead>
<tr>
<th>Acronym of tool(^\alpha)</th>
<th>Number of questions</th>
<th>Completion</th>
<th>Time to complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOAPP®-R</td>
<td>24 items</td>
<td>Self-report</td>
<td>&lt; 10 minutes</td>
</tr>
<tr>
<td>DIRE</td>
<td>7 items</td>
<td>Clinician administered</td>
<td>&lt; 5 minutes</td>
</tr>
<tr>
<td>ORT</td>
<td>5 items</td>
<td>Clinician administered</td>
<td>&lt; 5 minutes</td>
</tr>
<tr>
<td>COMM</td>
<td>40 items</td>
<td>Self-report</td>
<td>&lt; 10 minutes</td>
</tr>
<tr>
<td>CAGE</td>
<td>4 items</td>
<td>Either</td>
<td>&lt; 5 minutes</td>
</tr>
<tr>
<td>PDUQ</td>
<td>42 items</td>
<td>Clinician administered</td>
<td>20 minutes</td>
</tr>
<tr>
<td>STAR</td>
<td>14 items</td>
<td>Self-report</td>
<td>&lt; 5 minutes</td>
</tr>
<tr>
<td>SISAP</td>
<td>5 items</td>
<td>Clinician administered</td>
<td>&lt; 5 minutes</td>
</tr>
<tr>
<td>PMQ</td>
<td>26 items</td>
<td>Self-report</td>
<td>&lt; 10 minutes</td>
</tr>
</tbody>
</table>

\(^\alpha\) - SOAPP®-R (Screen and Opioid Assessment for Patient’s in Pain-revised); DIRE (Diagnosis, Intractability, Risk, and Efficacy); ORT (Webster’s Opioid Risk Tool); COMM (Current Opioid Misuse Measure); CAGE (Cut-down, Annoyed, Guilt, Eye-opener); PDUQ (Prescription Drug Use Questionnaire); STAR (Screening Tool for Addiction Risk); SISAP (Screening Instrument for Substance Abuse Potential); PMQ (Pain Medication Questionnaire)
Opioid Risk Tool

<table>
<thead>
<tr>
<th>Family history of substance abuse</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>1 point</td>
<td>3 points</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>2 points</td>
<td>3 points</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>4 points</td>
<td>4 points</td>
</tr>
<tr>
<td><strong>Personal History of Substance abuse</strong></td>
<td><strong>Female</strong></td>
<td><strong>Male</strong></td>
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<tr>
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<td>4 points</td>
</tr>
<tr>
<td>Prescription Drugs</td>
<td>5 points</td>
<td>5 points</td>
</tr>
<tr>
<td>Age (16 yrs to 45 yrs)</td>
<td>1 point</td>
<td>1 point</td>
</tr>
<tr>
<td>Preadolescent sexual abuse</td>
<td>3 points</td>
<td>0 points</td>
</tr>
<tr>
<td>Depression</td>
<td>1 point</td>
<td>1 point</td>
</tr>
<tr>
<td>ADD, OCD, Bipolar, or Schizophrenia</td>
<td>2 points</td>
<td>2 points</td>
</tr>
</tbody>
</table>

Low Risk 0 – 3 points, Moderate Risk 4 – 7 points, High Risk > 8 points

Is Richard Low, Med, or High Risk?

- 56 years old
- Father abused EtOH
- Past medical history of Bipolar disorder
- Previously treated with buprenorphine for medication assisted therapy

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</tr>
<tr>
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Urine Drug Screening

• Immunoassay
  • Fast results
  • Inexpensive
  • High sensitivity, low specificity

• Gas chromatography / mass spectrometry
  • Slower results
  • Expensive
  • High sensitivity, high specificity

• Interpretation
  • Pharmacists ideally positioned to interpret presence or absence of metabolites
  • What would you expect if patient is on hydrocodone? Oxycodone?

UDS Interpretation

Decision tree may be downloaded free of charge from the Society of Palliative Care Pharmacists

www.palliativepharmacist.org
Opioid Agreements

• No data to support their efficacy in reducing misuse / abuse
• Standard of care
• Many include stipulations for patient conduct
• Should be used as informed consent

CDC Key Recommendations

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

6. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

9. Clinicians should review the patient’s history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.
Assessing morphine equivalents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Parenteral</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Codeine</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
<td>NA</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>NA</td>
<td>30</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Meperidine</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>NA</td>
<td>20</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Tramadol</td>
<td>NA</td>
<td>120</td>
</tr>
</tbody>
</table>

Richard takes 8 tramadol 50mg tablets PO daily.
What is his MEDD?

\[
x/30mg = 400mg/120mg
\]
\[
x = 100mg \text{ of MEDD}
\]

Richard’s tramadol use is equivalent to 100mg MEDD
What non-opioid alternatives could we offer Richard?

CBT: cognitive behavioral therapy
NSAIDs: nonsteroidal antiinflammatory drugs
TCAs: tricyclic antidepressants
SNRIs: serotonin norepinephrine reuptake inhibitors
SMRs: skeletal muscle relaxants

Multimodal Analgesia

- CBT
- Physical Therapy
- Acupuncture
- Chiropractic
- Anticonvulsants
- Anesthetics
- SNRIs
- TCAs
- NSAIDs
- SMRs
NSAIDs

Non-acetylated salicylates
- Diflunisal
- Salsalate
- Choline Mg trisalicylate

Propionic acids
- Ibuprofen
- Naproxen
- Oxaprozin
- Flurbiprofen
- Ketoprofen

Acetic acids
- Diclofenac
- Etodolac
- Tolmetin
- Sulindac
- Ketorolac

Enolic acids
- Meloxicam
- Piroxicam

Others
- Celecoxib
- Nabumetone
- Meclofenamate
Serotonin Norepinephrine Reuptake Inhibitors

- **Venlafaxine**
  - positive data in post-mastectomy neuropathy, diabetic peripheral neuropathy
- **Desvenlafaxine**
  - no data to date
- **Duloxetine**
  - FDA-approved for diabetic peripheral neuropathy, fibromyalgia, musculoskeletal pain
- **Milnacipran**
  - FDA-approved for fibromyalgia syndrome
  - Positive date in neuropathic pain
- **Levomilnacipran**
  - no data to date

Tricyclic Antidepressants

<table>
<thead>
<tr>
<th>Tertiary Amines</th>
<th>Secondary Amines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline</td>
<td>Amitriptyline</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Imipramine</td>
</tr>
<tr>
<td>Protriptyline</td>
<td>Clomipramine</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>Doxepin</td>
</tr>
</tbody>
</table>

Combined Ki of Serotonin and Norepinephrine

Antihistaminergic Activity, $K_i$ (nM)

Anticonvulsants with data in pain (excluding animal models)

<table>
<thead>
<tr>
<th>1st Generation</th>
<th>2nd Generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Eslicarbazepine</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Ezogabine</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>Felbamate</td>
</tr>
<tr>
<td></td>
<td>Gabapentin</td>
</tr>
<tr>
<td></td>
<td>Lacosamide</td>
</tr>
<tr>
<td></td>
<td>Lamotrigine</td>
</tr>
<tr>
<td></td>
<td>Levetiracetam</td>
</tr>
<tr>
<td></td>
<td>Oxcarbazepine</td>
</tr>
<tr>
<td></td>
<td>Pregabalin</td>
</tr>
<tr>
<td></td>
<td>Topiramate</td>
</tr>
<tr>
<td></td>
<td>Zonisamide</td>
</tr>
</tbody>
</table>

MeSH terms used included "drug name" combined with "pain" or "neuropathy"
All entries reviewed via [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
Search performed 24 Dec 2016

Skeletal Muscle Relaxants

• Antispasmodics
  • Cyclobenzaprine
  • Metaxalone
  • Methocarbamol
  • Orphenadrine citrate
  • Carisoprodol

• Antispasticity Agents
  • Tizanidine
  • Baclofen
  • Diazepam
  • Dantrolene

• All equally effective for short-term relief of low back pain
• Not more effective than NSAIDs for acute low back pain
• Poor supporting data

NMDA Glu Receptor Antagonists

- Dextromethorphan
- Ketamine
- Memantine

Topical Analgesics

- Lidocaine
- Capsaicin
- Diclofenac
- Nitroglycerin
- Select opioids*
- Ketamine*
- Amitriptyline*
- Gabapentin*
- Baclofen*
- Many others with no supporting data

* must be compounded

Standardizing Care

CDM Principles

Risk assessment
- Opioid risk tools
- Psychiatric screens
- Previous record review

Policies and expectations
- Office visits
- Nursing utilization
- ED utilization
- Refill policies
- Non-pharm adherence

Education / referral
- Individual
- Group

Treatment agreements
- Consent
- Educational
- Punitive
- Conduct agreements

Risk management
- PMP review
- Drug screening
- Pill count
- Case discussion

Assessment
- Validated scales
- The 4 “A”s
- Frequency of visits
- Case discussion

Efficacy
- Evidence-based
- Financially feasible
- Patient appropriate

VAS: visual analog scale; NRS: numeric rating scale; BPI: Brief Pain Inventory; MPQ: McGill Pain Questionnaire; NPRS: Neuropathic Pain Rating Scale
Conclusions

1. Opioid analgesics possess numerous risks including substance use disorder
2. Numerous screening tools exist to predict problematic opioid use prior to developing substance use disorder
3. Prescribers and pharmacists have a responsibility to ensure safe and legitimate use of opioid analgesics
4. Numerous non-opioid analgesics are available when risks of opioids outweigh their anticipated benefit