SAFE AND EFFECTIVE MANAGEMENT OF NON-CANCER PAIN IN PRIMARY CARE

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Objectives

- Identify trends & consequences of the current opioid epidemic
- Review evidence & expert guidelines for prescribing controlled substances
- Identify challenges/solutions to implementation & adoption of guidelines
The use of therapeutic opioids—natural opiates and synthetic versions—increased 347% between 1997 and 2006, according to this U.S. Drug Enforcement data.
Epidemic of Chronic Pain

- Lasting >3 months
- Persists beyond what’s expected, given degree of pathology
- Elicited by injury/disease
- Likely perpetuated factors pathogenically & physically remote from original cause
- Prevalence of chronic pain in US
  - 10–25%
  - Rate increases with age/ chronic illness/obesity
  - Opioids recommended therapies for management of several types of non-cancer related pain
• No studies support benefit over other opioids
• Unprecedented Marketing
• Sales Reps trained “Risk of Addiction <1%”
• Original FDA Label– Risk of Abuse/Addiction
  – 1996 “Very Rare”
• Can be crushed, injected, inhaled or swallowed
• Risk of Abuse consistently minimized
• 2007 Purdue Pharma fined $634M
• 2009 OxyContin Sales $3B
5th Vital Sign

- Joint Commission Accreditation Hospital Organization (JCAHO)
Opioid Trends

- US consumes **80%** global oxycodone
- US consumes **>95%** global hydrocodone
- 1999–2010 Opiate Prescriptions quadrupled
- **15,500 Deaths** prescription OD (2009)
- More likely to die of Opiate OD than MVA
- 5,500 people took prescription pain meds non-medically for 1st time (2010)
- 4.8% use prescription pain pills non-medically
### Public Health Impact of Opioid Use

For every 1 overdose death in 2010, there were...

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>733</td>
<td>non-medical users</td>
</tr>
<tr>
<td>108</td>
<td>People abusing/dependent</td>
</tr>
<tr>
<td>26</td>
<td>ED visits for abuse</td>
</tr>
<tr>
<td>10</td>
<td>Abuse treatment admissions</td>
</tr>
</tbody>
</table>

Treatment admissions are for primary use of opioids from Treatment Exposure Data set. Emergency department visits are from DAWN (Drug Abuse Warning Network). Abuse/dependence and nonmedical use in the past month are from the National Survey on Drug Use and Health.
Emergency Department Visits Related to Drug Misuse or Abuse—United States, 2004-2010

Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010

CDC. MMWR 2011. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm60e1101a1.htm?s_cid=mm60e1101a1_w. Updated with 2009 mortality and 2010 treatment admission data.
MVA vs. Poisoning Deaths

NCHS Data Brief, December, 2011. Updated with 2009 and 2010 mortality data
High Opioid Dose and Overdose Risk

*Overdose defined as death, hospitalization, unconsciousness, or respiratory failure.

Method of Obtaining Prescription Pain Relievers
Reported by Past Month Nonmedical Users Ages 12 or Older
(2009 & 2010 Combined Annual Averages)

- From Friend or Relative for Free: 60.1%
- From One Doctor: 27.1%
- Bought from Friend or Relative: 26.8%
- Bought from Drug Dealer or Other Stranger: 11.5%
- Took from Friend or Relative without Asking: 11.2%
- Some Other Way: 6.5%
- From More Than One Doctor: 4.9%
- Bought on the Internet: 1.0%

National Survey on Drug Use and Health 2010.
Ensuring patients with pain are safely and effectively treated while reduce risks opioid abuse & overdose

- Complex
- Dynamic
- Subjective
- Time-consuming
- Emotional
- Social
- Difficult
Opioids have proven efficacy and (relative) safety for treating acute pain & pain during terminal illness


Opioids do NOT have proven efficacy or safety for treating chronic pain long–term

Meta–analysis 26 studies– Insufficient evidence on QOL or functional improvement for long–term opioids in chronic non–cancer pain
Opioid Efficacy

Comparison study of Chronic pain >6mo
Opioids vs non-opioids
Opioids poorer functional status, worse pain control & QOL
90% of Chronic Pain where opiates not proven helpful

Fibromyalgia

Axial low back pain w/o pathoanatomic diagnosis

Headaches
Clinical Guidelines

- Improve prescribing & treatment
- Basis for standard of accepted medical practice for purposes of licensure board actions
- Several consensus guidelines available
- Common themes among guidelines
Universal Precautions

First, Do No Harm
Do your own evaluation

- History
  - Brief pain inventory, long pain inventory
- Physical Exam
- Old Records
- Order diagnostic testing as indicated
- Make Diagnosis
  - Add Chronic pain to specific diagnosis
Assess Risk for Abuse/Misuse

- COMM™ – Current Opioid Misuse Measure
- SOAPP® – Screener and Opioid Assessment for Patients in Pain
- Mental Health Evaluation
  - PHQ-2, PHQ-9, GAD-7

(Estimates Drug Abuse in Chronic Pain 18–41%)
Non-Opioid Treatments

• Optimize Sleep & Mood
• Weight loss (if indicated)
• Dietary/GI (if indicated)
• Surgical Eval (if indicated)
• Cold/Heat/TENS tx/Steroid injection/nerve block
• Physical therapy/accupuncture/massage/manipulation/
• New Mattress/Pillow/shoes/exercise/yoga
• Tylenol/NSAIDS/Topical anesthetics, topical antiinflammatory/muscle relaxant (acute)/Tramadol
Discuss expectations

- Non-judgmental, empathetic, respectful
- Strengthen physician–patient relationship
- Discuss realistic expectation (20–40% improvement in pain)
- **Functional Improvement** – End Goal
Opiate Prescriptions

- How taken
- Maximum pills/day
- Maximum pills/month

**Bad Example**
Hydrocodone 5/500
1–2 tabs every 4–6h prn pain
#60
2 refills

**Good Example**
Hydrocodone 5/500
1–2 tabs every 4–6h prn breakthrough pain (2pills/day)
#60/month
2 refills
Accept known risks

- Constipation
- sedation
- nausea
- vomiting
- Pruritis
- delayed gastric emptying
- hypogonadism
- muscle rigidity and myoclonus
- sleep disturbance

- pyrexia
- diminished psychomotor performance
- cognitive impairment
- hyperalgesia
- dizziness
- Tolerance
- Dependence
- Addiction
- Respiratory depression, death
Informed consent/ Treatment Agreement

- Goals of treatment decrease pain/improve function, not cure
- 1 prescribing physician
- 1 pharmacy
- Urine Drug Screening as requested
- No early refills/ call-ins
- Must adhere to tx plan & keep appt
- Medication cannot be shared, sold or given to another person
- Terms of violation of contract
Monitoring Aberrant Behaviour

- INSPECT state database
- Urine tox
- "Red Flags"...early refills, stolen scripts
- Adherence to treatment plan
Prescription Drug Monitoring Programs (PDMPs)

- Operational in 42 states
- Indiana INSPECT
- Focus PDMPs on
  - Patients at highest risk of abuse and overdose
  - Prescribers who deviate from accepted medical practice
Chronic Pain Maintenance

- 5 A’s – Documentation/ Ongoing Assessment
  - Activities Daily Living
  - Affect
  - Analgesia
    - Brief pain inventory
  - Adverse effects meds
  - Aberrent Behavoir
    - (INSPECT, Urine Tox)
Consider Consultation when..

- **High Risk**— mental illness/SUD
- **Suspect addiction** (Impaired control over drug use, Compulsive use, Continued use despite harm, Cravings)
- **Poor response to opioid escalations**
- **Opioid Dosing >100 Milliequivalents Morphine** (OD risk increased 7–9X)
- **Utilizing Methadone** (involved in 30% OD Deaths)
- **Treating w/ Opiates & Benzodiazepines**
- **Tx causing more problems than the condition**
- **Assistance in weaning**— especially benzos
Wean Opioids if

- No functional improvement
- Failure to comply with contract (not egregious violation)
- Significant ARD
Termination of Opiate

- Confirmed Diversion of prescribed opiate
- Forging Prescriptions
- Confirmed illicit drug use (ie cocaine, heroin)
- **ALWAYS** refer for Chemical Dependency Evaluation & Treatment

Objective • Non-judgemental • Empathatic

**Do not abandon patient**
AVOID

- Controlled substances & Alcohol
- Benzodiazepines & Opiates in same patient
- Writing a script without all information
Drug Testing

- Urine – preferred test
- Qualitative & Quantitative drug testing
- Understand potential false positives
- Understand potential false negatives
- Recognize when sample may be adulterated
- Utilize patient specific data to interpret urine drug test results
Urine Drug Testing

- Condition of treatment
- Good Screen for illicit drugs
- More limited detect adherence
- American Pain Society
  - Any patient receiving chronic therapy (> 30 days)
    - Consideration to periodic testing
  - History of substance abuse
  - High risk for abuse
  - Diversion suspected

*Postgraduate Medicine 2009;121(4):91-102*
Which test to order?

- Urine drug screen – qualitative (Immunoassay) – $  
  - Most common: initial screening  
  - Generally used by ER, OB/GYN, and work–place physicals

- Comprehensive urine drug screen – quantitative (GC–MS) – $$$$$  
  - Confirmatory testing  
  - Compliance testing

Postgraduate Medicine 2009;121(4):91–102  
Urine Drug Test—Qualitative (aka Immunoassay)

Pro’s
- Presence/absence of drug class
- Cheap
- Point-of-care
  - Within minutes
  - Help guide therapy

Con’s
- Will not tell specific medication
- False positives
- True negative
  - Semi-synthetic or synthetic opioids
  - Benzodiazepines
  - Concentration dependent
    - Must know detection thresholds for test used
- May require confirmation
- Know limitations

Postgraduate Medicine 2009;121(4):91–102
Comprehensive Urine Drug Test—Quantitative (aka—GC–MS testing)

- **Pros**
  - Standard for confirmatory testing
  - Presence or absence
  - Specific drug and/or metabolite
  - Most accurate, sensitive and reliable
  - Preferred test if looking for specific medication

- **Cons**
  - Time-consuming (~ 1 week turnaround time)
  - Send-out lab
  - Cost ~ $250
  - Identification of drugs based on test design
    - Fentanyl
    - Clonazepam

Postgraduate Medicine 2009;121(4):91–102
### Length of Time Drugs of Abuse Can Be Detected in Urine

<table>
<thead>
<tr>
<th>Substance</th>
<th>Detection Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>7–12 hours</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>48 hours</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>48 hours</td>
</tr>
<tr>
<td>Barbiturate</td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td>24 hours</td>
</tr>
<tr>
<td>Long-acting</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td>3 days</td>
</tr>
<tr>
<td>Long-acting</td>
<td>30 days</td>
</tr>
<tr>
<td>Cocaine metabolites</td>
<td>2–4 days</td>
</tr>
<tr>
<td>Marijuana</td>
<td></td>
</tr>
<tr>
<td>Single use</td>
<td>3 days</td>
</tr>
<tr>
<td>Moderate use</td>
<td>(4 times/wk) 5–7 days</td>
</tr>
<tr>
<td>Daily use</td>
<td>10–15 days</td>
</tr>
<tr>
<td>Long-term heavy smoker</td>
<td>&gt; 30 days</td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>48 hours</td>
</tr>
<tr>
<td>Heroin (morphine)</td>
<td>48 hours</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>2–4 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>3 days</td>
</tr>
<tr>
<td>Morphine</td>
<td>48–72 hours</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2–4 days</td>
</tr>
</tbody>
</table>

## Summary of Agents Contributing to False Positive Results by Immunoassay

<table>
<thead>
<tr>
<th>False Positive</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol</strong></td>
<td>Short-chain alcohols (e.g. isopropyl alcohol)</td>
</tr>
<tr>
<td><strong>Amphetamines</strong></td>
<td>Amantadine, Benzphetamine, Bupropion, Chlorpromazine, Clobenzorex, l-Deprenyl, Desipramine, Dextroamphetamine, Ephedrine, Fenproporex, Isometheptene, Isoxsuprine, Labetalol MDMA, Methamphetamine, l-Methamphetamine (Vick’s inhaler), Methylphenidate, Phentermine, Phenylephrine, Phenylpropanolamine, Promethazine, Pseudoephedrine, Ranitidine, Ritodrine, Selegiline, Thioridazine, Trazodone, Trimethobenzamide, Trimipramine</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td>Oxaprozin, Sertraline</td>
</tr>
<tr>
<td><strong>Cannabinoids</strong></td>
<td>Dronabinol, Efavirenz, Hemp-containing foods, NSAIDs, Proton pump inhibitors, Tolmetin</td>
</tr>
<tr>
<td><strong>Cocaine</strong></td>
<td>Coca leaf tea, Topical anesthetics containing cocaine</td>
</tr>
<tr>
<td><strong>Opioids, opiate</strong></td>
<td>Dextromethorphan, Diphenhydramine, Heroin, Opiates (codeine, hydromorphone, hydrocodone, morphine), Poppy seeds, Quinine, Quinolones, Rifampin, Verapamil</td>
</tr>
<tr>
<td><strong>Phencyclidine</strong></td>
<td>Dextromethorphan, Diphenhydramine, Doxylamine, Ibuprofen, Imipramine, Ketamine, Meperidine, Mesoridazine, Thioridazine, Tramadol, Venlafaxine, O-desmethyldenlafaxine</td>
</tr>
<tr>
<td><strong>Tricyclic antidepressants</strong></td>
<td>Carbamazepine, Cyclobenzaprine, Cyproheptadine, Diphenhydramine, Hydroxyzine, Quetiapine</td>
</tr>
</tbody>
</table>

Understanding metabolism pathway key to interpreting results

metabolites to ensure correct interpretation
## Interpreting Immunoassay (POC) Results

<table>
<thead>
<tr>
<th>Medication</th>
<th>POC category</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam (Xanax)</td>
<td>Benzodiazepines</td>
<td>Alprazolam and most other benzos are likely to be detected via iCup if the patient is using the medication chronically as opposed to as needed. Clonazepam is a difficult benzodiazepine to detect via both iCup and GC-MS testing. Clonazepam may reveal a negative result in an adherent patient.</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Natural opioids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tylenol with codeine (Tylenol #3)</td>
<td>Opiates</td>
<td>Likely to be detected via iCup, especially scheduled chronic dosing.</td>
</tr>
<tr>
<td>Morphine (MS Contin)</td>
<td>Opiates</td>
<td></td>
</tr>
<tr>
<td><strong>Semisynthetic opioids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone (Oxycontin)</td>
<td>Oxycodone Opiates (requires much higher concentration for +)</td>
<td>Less likely than natural opioids to be detected, especially with PRN usage. May see (+) oxycodone panel and (-) opiate panel in a patient taking semisynthetic opioids. GC-MS can allow for specific interpretation of opiate metabolites, possibly indicating other drug use.</td>
</tr>
<tr>
<td>Hydrocodone/APAP (Vicodin)</td>
<td>Oxycodone Opiates (requires much higher concentration for +)</td>
<td></td>
</tr>
<tr>
<td><strong>Synthetic opioids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl (Duragesic)</td>
<td>Not detected</td>
<td>Fentanyl is not tested via the iCup opiate panel.</td>
</tr>
<tr>
<td>Methadone (Methadose)</td>
<td>Methadone</td>
<td>Methadone is very difficult to accurately assess via iCup due to being a synthetic opioid.</td>
</tr>
<tr>
<td>Tramadol (Ultram)</td>
<td>Not detected</td>
<td>Tramadol, a non-narcotic, is not detected via the iCup.</td>
</tr>
<tr>
<td><strong>Non-BZD hypnotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zolpidem (Ambien), Eszopiclone (Lunesta), Zaleplon (Sonata)</td>
<td>Not detected</td>
<td>Sleep agents are not detected via the iCup (with the exception of benzodiazepines used for this purpose).</td>
</tr>
</tbody>
</table>
Urine Drug Testing

Patient on Controlled Medications

UDT (in-office)

Positive

Positive for non-prescribed or illicit drugs. Discuss with patient preliminary positive test result, consider patient discrepancy or admission. Does preliminary test match patient report?

Negative

Review sensitivity limitation list for prescribed medication. Assess for RED FLAGS, e.g. early refills, Inspect Report.

Is it Reconcilable?

Yes

Expected Result
No further testing

No

UnExpected Result
Proceed with GC/MS Confirmatory Testing

Patient NOT on Controlled Medications

UDT (in-office)

Positive

Review false-positive interactions table. Discuss with patient discrepancy between expected results and actual results

Negative

Prescribe as indicated. No further action needed.

Insurance

Payer Source

Self-Pay

Send-out for GC/MS confirmatory
Urine Toxicology

- Interpretation is complex
- Urine toxicology is one piece of information
- Care–termination decisions should not be based on single piece of information
Challenges in Providers’ adoption of Opiate Guidelines

- Lack of Time
- Lack of knowledge
- Patient expectations
- Decreased patient satisfaction
- Strain physician–patient relationship
- Physician belief that opiates are safe
- Physician belief that not necessary
• Online Provider Toolkit to be published—Spring 2013
• Summary of evidence & expert opinion
• Copy/Link to validated tools to help providers practice w/in guidelines
• Guidance for safe prescribing of prescription drugs
• Patient education