Urine Drug Monitoring in Chronic Non-Cancer Pain: A Review of Outcome Studies and Gaps in the Literature

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This presentation

- Why perform UDM in clinical care?
- Our systematic review
- Gaps in the literature
Opioids for chronic pain

- Increasing use for musculoskeletal pain: 1980 to 2000

- 6% of all primary care visits in 2001

Increasing opioid misuse and negative consequences

• ↑ incidence misuse\textsuperscript{1,2}
• ↑ admissions for addiction treatment\textsuperscript{3}
• ↑ ED visits\textsuperscript{4}
• ↑ overdose deaths\textsuperscript{5}

1. MTF; 2. NSDUH; 3. TEDS; 4. DAWN; 5. CDC
Annual sales of Rx opioids and unintentional overdose death
1990 - 2006

Source: Paulozzi, CDC, Congressional testimony, 2007
Sources of misused opioids

- 19% directly from a doctor
- 56% given for free by a friend or relative
  - 81% of those friends/relatives received them from a doctor
- 9% bought from a friend or relative
- 4% from a drug dealer or stranger

http://oas.samhsa.gov/nsduh/2k6nsduh/2k6Results.pdf
UDM recommended

• Federation of State Medical Boards
• American Pain Society
• American Academy of Pain Management
• American Society of Addiction Medicine
• Department of Veterans Affairs

• But what is the evidence?
Conceptual Model: Potential reasons to use UDM in CNCP

**Influences**
- Concern about opioid misuse, addiction, and overdose
- Clinician risk management
- Guidelines
- Policies (state or practice)
- Education and training
- Clinical experience

**Outcomes**
- Identify opioid misuse, addiction, and overdose
- Reduce opioid misuse, addiction, overdose
- Identify illicit drug use
- Confirm appropriate opioid use
- Reduce legal vulnerability
- Improve clinician comfort
Conceptual Model: Potential reasons to use UDM in CNCP

Influences

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Research Questions

1. Is UDM effective in identifying opioid misuse, addiction, or overdose?
2. Is UDM effective in reducing opioid misuse, addiction, or overdose?
3. What is the prevalence of UDM in the primary care setting?
Search Strategy

• Primary Search: MEDLINE, PsycINFO, EMBASE, Cochrane (through 3/08)
  – English, Spanish, or French
  – Combining 4 Topic Areas (with “AND”)
    1. Opioids
    2. Chronic Pain
    3. Urine Drug Testing
    4. Substance Abuse

• Secondary Search: References from selected articles and relevant reviews, and through correspondence with experts
<table>
<thead>
<tr>
<th>Topic Area</th>
<th>MeSH term (Medline, Embase, Cochrane)</th>
<th>Key words (Medline, Embase) or Text words (Cochrane, PsychInfo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Opioids</td>
<td>Narcotics</td>
<td>opi$, narcotic$, buprenorphine, butorphanol, codeine, dihydromorphine, fentanyl, heroin, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, nalbuphine, oxycodone, oxymorphone, propoxyphene</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Analgesics, opioid</td>
</tr>
<tr>
<td>2. Chronic Pain</td>
<td>Pain</td>
<td>Pain$.mp</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic disease, Chronic pain, pain management, non-cancer pain, pain syndrome, pain treatment, pain control, non-malignant pain</td>
</tr>
<tr>
<td>3a. Opioid Agreements</td>
<td>Contracts</td>
<td>Agreement$, contract$</td>
</tr>
<tr>
<td>3b. Urine Drug Testing</td>
<td>Substance Abuse Detection</td>
<td>Drug test$, Drug screen$, Urine test$, Urine screen$</td>
</tr>
<tr>
<td>4. Substance Abuse</td>
<td>Substance-related disorders</td>
<td>Addict$, dependen$, abus$, misus$, substance us$, drug us$, drug habit$</td>
</tr>
<tr>
<td></td>
<td>Opioid-related disorders</td>
<td>Narcotic$, opi$ dependence</td>
</tr>
<tr>
<td></td>
<td>Behavior, addictive</td>
<td>Addict$, behavior, Misuse behavior, ABC, addiction behavior checklist, COMM, current opioid misuse measure, PDUQ, prescription drug use</td>
</tr>
</tbody>
</table>
Study Selection and Analysis

• Exclusion Criteria:
  – Not in English, French, or Spanish
  – Not relevant to study questions
  – Not original research
  – Cancer patients only
  – Surgical or post-op patients only
  – Case report or case series where n<20

• Quality assessment and data extraction
• Data synthesis +/- meta-analysis
Electronic Database Search (MEDLINE, EMBASE, PsycINFO and Cochrane CTN) (N=2063)

Excluded (N=1933)
Duplicate (N=286)
Irrelevant (N=1512)
Not original analysis (N=125)
Cancer pts only (N=5)
Post-op or surgical (N=2)
Case report/series <20 (N=3)

Abstracts reviewed (N=2063)

Full text articles reviewed (N=130)

Excluded (N=TBD)

Eligible articles

Opioid Agreements
Urine Drug Monitoring (N=13)
Risk Assessment Tools
Outcomes assessed

• 5 on UDM for identifying opioid misuse
  – 3 monitoring for opioids
  – 2 monitoring for illicit drugs
• 1 on UDM for reducing opioid misuse
• 2 on UDM for reducing illicit drug use
• 0 assessed outcomes of addiction or overdose

• 4 on prevalence of UDM in PC
Study quality

- 0 RCT
- 2 prospective
- 2 with follow-up at least 6 months
- 1 with control group (historical)
- 3 with multivariate analysis
- N (range) 60-801
- GRADE scores: 2 moderate, 6 low, 5 very low
Is monitoring urine for **opioids** effective in identifying prescription opioid misuse?

<table>
<thead>
<tr>
<th>Author Year</th>
<th>N</th>
<th>Design</th>
<th>Results</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Inappropriate NEG</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Inappropriate POS</strong></td>
<td></td>
</tr>
<tr>
<td>Berndt 1993</td>
<td>109</td>
<td>Cross-sectional</td>
<td>--</td>
<td>6% codeine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>New referrals</td>
</tr>
<tr>
<td>Fishbain 1999</td>
<td>226</td>
<td>Cross-sectional</td>
<td>7.5% any opioid</td>
<td>0.4% any opioid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14% refused UDT</td>
</tr>
<tr>
<td>Katz 2003</td>
<td>122</td>
<td>Retros. cohort</td>
<td>--</td>
<td>6.5% opioid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21% without behavioral issues had POS UDT</td>
</tr>
</tbody>
</table>
Is monitoring urine for illicit drugs effective in identifying prescription opioid misuse?

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Setting</th>
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<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manchikanti 2003</td>
<td>PM</td>
<td>150</td>
<td>Cross-sectional UDT</td>
<td>34% POS illicit drugs in opioid abusers</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>14% POS illicit drugs in opioid non-abusers</td>
</tr>
<tr>
<td>Fleming 2007</td>
<td>PC</td>
<td>801</td>
<td>Interviews and UDT</td>
<td>24% POS illicit drug</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Not significant predictor of opioid use disorder</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>MJ: aOR 1.4 (0.5-3.9), p=.516</td>
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<tr>
<td></td>
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<td></td>
<td>Cocaine: aOR 1.65 (0.42-6.42), p=.47</td>
</tr>
</tbody>
</table>
Is UDM effective in reducing misuse, addiction, or overdose?

- 0 studies of the effect on addiction or overdose
- 1 study addresses effectiveness of UDM in reducing misuse
  - Wiedemer 2007
    - Multi-disciplinary, structured intervention
    - Resolution in 45% of pts referred for aberrant drug-related behavior
Does UDM in chronic pain management reduce illicit drug use?

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<th>N</th>
<th>Design</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Manchikanti 2006</td>
<td>PM</td>
<td>500</td>
<td>Prospective cohort</td>
<td>POS illicit drug test in 16% vs 22% in control group.</td>
</tr>
<tr>
<td>Wiedemer 2007</td>
<td>PC</td>
<td>335</td>
<td>Retrospective cohort</td>
<td>45% of those referred for aberrant drug-related behaviors resolved</td>
</tr>
</tbody>
</table>
What is the prevalence of UDM in primary care?

<table>
<thead>
<tr>
<th>Author Year</th>
<th>N</th>
<th>Sample</th>
<th>Resp. rate</th>
<th>Design</th>
<th>% Providers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams 2001</td>
<td>74</td>
<td>12 FP practices</td>
<td>--</td>
<td>Chart review</td>
<td>8%</td>
</tr>
<tr>
<td>Bhamb 2006</td>
<td>248</td>
<td>FP and IM</td>
<td>74%</td>
<td>Written questionnaire</td>
<td>6.9% -- for new pts, 15% -- for estab. Pts</td>
</tr>
<tr>
<td>Boulanger 2007</td>
<td>100</td>
<td>Canadian GPs and FP</td>
<td>23%</td>
<td>Telephone survey</td>
<td>30%</td>
</tr>
<tr>
<td>Reisfield 2007</td>
<td>60</td>
<td>FP at review course</td>
<td>75%</td>
<td>Written questionnaire</td>
<td>73% -- sometimes</td>
</tr>
</tbody>
</table>
Conclusions

• UDM is infrequently used in PC
• Little to no evidence that UDM reduces Rx opioid misuse
• Some evidence that monitoring urine for opioids is effective at identifying misuse in PM
• Equivocal evidence that testing for illicit drugs helps identify Rx opioid misuse
• Most research is low quality
Gaps in the Literature

1. Determine clinical effectiveness
2. Evaluate potential harm
3. Evaluate across clinical practice settings
4. Define best practices
5. Disseminate best practices
Gaps in the Literature

1. Determine clinical effectiveness
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Determine clinical effectiveness

• Does UDM in CNCP reduce opioid misuse, diversion, addiction, and/or overdose?

• Need:
  – Prospective, longitudinal studies
  – Standardized definitions of misuse and addiction
  – Use of validated instruments to classify opioid misuse and addiction in CNCP
Evaluate potential harm

- Misinterpretation of results may lead to accusation and/or discharge
- Impact on doctor-patient relationship unknown
- Loss to follow-up may affect other preventative care or chronic disease management
- Inadequate response to urine result may put clinician at risk
Evaluate across clinical settings

- How does variability across practice settings alter the benefits and risks of UDM?
  - How does primary care differ from pain management?

- Consider variability in:
  - Feasibility of UDM
  - Clinician proficiency in ordering and interpreting
  - Prevalence of misuse
  - Cost-effectiveness
  - Availability of assays
Acknowledgements

- Dan Alford, Barbara Turner, Alok Kapoor, Robin Williams
- PRISM (Program of Research Integrating Substance Use Information into Mainstream Healthcare) and SGIM
- Robert Wood Johnson Foundation
- NIDA
- SAMHSA
- Treatment Research Institute
Define best practices

• Many questions remain:
  – When in the course of treatment should UDM be performed?
  – In every patient or those deemed high risk?
  – What drugs should we test for?
  – Using which assays?
  – How should we respond to results?

• Need to develop quality measures
Disseminate best practices

• Evaluate ways to:
  – Educate clinicians about ordering and interpreting UDM
  – Educate clinicians about talking to patients about addiction
• Create a national opioid management support system
• Publish in general medical journals


