Abuse, Misuse, and Diversion of Prescription Opioids: Evaluating the Problem and Proposed Solutions

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Associate Director, Rocky Mountain Poison & Drug Center Denver Health and Hospital Authority
Associate Professor, Department of Emergency Medicine
University of Colorado School of Medicine
Relationships

• Employed by the Denver Health and Hospital Authority
  – We operate the RADARS® System

• The RADARS System collects and analyzes data about prescription drug abuse, misuse, and diversion
  – Manufacturers subscribe to these data and use them for pharmacovigilance and regulatory reporting
Relationships

• Through my employer, I also have research funding from
  – BTG International (snake venom)
  – McNeil Consumer Healthcare (non-prescription analgesics)
• Any margin supports DHHA
• No bonus or personal reward
• No personal conflicts
Objectives

- Overview of data collection approaches used in the US
- Discuss some abuse / misuse / diversion prevention strategies currently employed in the US
  - Data evaluating effectiveness
A Fragmented System

- No unified medical record
- Multiple payors, including cash
  - No central administrative database
- Poor communication between prescribers
- No record of prescriptions written
- Many different legal entities involved
## Major Official Data Sources

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Reporting Delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death Certificates</td>
<td>3 years</td>
</tr>
<tr>
<td>National Health and Nutrition Examination Survey</td>
<td>2 – 5 years</td>
</tr>
<tr>
<td>Drug Abuse Warning Network</td>
<td>2 – 3 years</td>
</tr>
<tr>
<td>Monitoring the Future</td>
<td>2 years</td>
</tr>
<tr>
<td>National Survey on Drug Use and Health</td>
<td>1 year</td>
</tr>
<tr>
<td>Drug Enforcement Administration</td>
<td>6 months</td>
</tr>
<tr>
<td>Claims databases (Medicaid, etc.)</td>
<td>Varies</td>
</tr>
</tbody>
</table>
Problems With Official Data

• Small samples
  – Coverage gaps & lack of geospecificity
• Chart review & survey issues
• Delay
• All exposure types may not be counted
• No formulation-specific data
  – At best, by active pharmaceutical ingredient
**RADARS® System Mosaic Approach**

| Poison Center | Acute Events  
| 51 centers  
| 47 states |
| Opioid Tx Program (OTP) | Patients in Tx  
| 73 programs  
| 33 states |
| College Survey | 2000 students  
| 50 states  
| 3x each year |
| Drug Diversion | Law Enforcement  
| 280 investigators  
| 50 states |
| Survey of Key Informant Patients (SKIP) | Patients in Tx  
| 125 practices  
| 50 states |
| StreetRX (website) | User/Buyers Crowdsourcing  
| 50 states |
How Specific?

• Geographic: 3-digit ZIP code
• Date: Year / quarter
• Age: Whole year (> 80 years combined)
• Formulation: Product and manufacturer
  – Some reports: Unclassifiable / NOS
  – “Roll-up” categories
Denominators

- Population
- Patients filling prescriptions for each formulation
  - A measure of availability
  - Unique Recipients of a Dispensed Drug, URDD
Extent of the US Problem

[Graph showing trends in sales, deaths, and treatment over time from 1999 to 2010.]
<table>
<thead>
<tr>
<th>Rank</th>
<th>PC</th>
<th>OTP</th>
<th>SKIP</th>
<th>DD</th>
<th>CS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hydrocodone</td>
<td>Oxycodone</td>
<td>Hydrocodone</td>
<td>Oxycodone</td>
<td>Hydrocodone</td>
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<tr>
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<td>Hydrocodone</td>
<td>Oxycodone</td>
<td>Hydrocodone</td>
<td>Oxycodone</td>
</tr>
<tr>
<td>3</td>
<td>Tramadol</td>
<td>Methadone</td>
<td>Hydromorphone</td>
<td>Morphine</td>
<td>Morphine</td>
</tr>
<tr>
<td>4</td>
<td>Methadone</td>
<td>Morphine</td>
<td>Morphine</td>
<td>Buprenorphine</td>
<td>Tramadol</td>
</tr>
<tr>
<td>5</td>
<td>Morphine</td>
<td>Hydromorphone</td>
<td>Buprenorphine</td>
<td>Hydromorphone</td>
<td>Methadone</td>
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<tr>
<td>6</td>
<td>Buprenorphine</td>
<td>Oxymorphone</td>
<td>Methadone</td>
<td>Methadone</td>
<td>Fentanyl</td>
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<tr>
<td>7</td>
<td>Fentanyl</td>
<td>Buprenorphine</td>
<td>Fentanyl</td>
<td>Oxymorphone</td>
<td>Buprenorphine</td>
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<tr>
<td>8</td>
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<td>Fentanyl</td>
<td>Oxymorphone</td>
<td>Tramadol</td>
<td>Hydromorphone</td>
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<td>Tramadol</td>
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<tr>
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</table>
Most Abused Prescription Opioids
Population Rates, US, All Programs Combined
# Most Abused Prescription Opioids

**URDD Rates, US, Jan - June 2012**

<table>
<thead>
<tr>
<th>Rank</th>
<th>PC</th>
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</tr>
</thead>
<tbody>
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</tr>
<tr>
<td>6</td>
<td>Fentanyl</td>
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<td>Fentanyl</td>
<td>Oxycodone</td>
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<td>Hydrocodone</td>
</tr>
</tbody>
</table>
Most Abused Prescription Opioids
URDD Rates, US, All Programs Combined
Interventions the US is Trying

• Abuse-deterrent and abuse-resistant formulations
• Prescription drug monitoring programs
• Community-based interventions
Tamper-Resistant and Abuse-Deterrent Formulations

- Hard coatings
- Polymers which turn to viscous gel when heated
- Polymers which resist dissolving in water and alcohol
- Novel delivery systems (patches, implants, etc.)
- Antagonists (naloxone)
- Aversive ingredients
- Nasal tissue irritants
Reformulated OxyContin

- August 2010

OxyContin OC

OxyContin OP
OxyContin Abuse Rates
Poison Center Program – Intentional Abuse

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyContin</td>
<td>-39.3%</td>
</tr>
<tr>
<td>Other Opioids</td>
<td>0.9%</td>
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</tbody>
</table>

Drug Abuse Rates
Poison Center Program – Intentional Abuse
OxyContin Diversion Case Rates
Drug Diversion Program

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycontin</td>
<td>-56.2%</td>
</tr>
<tr>
<td>Other Opioids</td>
<td>-7.6%</td>
</tr>
</tbody>
</table>

Drug Diversion Program

Population Rate per 100,000

- Blue line: Before Reformulation
- Red line: After Reformulation

Population Rate per 100,000

- 0.45
- 0.4
- 0.35
- 0.3
- 0.25
- 0.2
- 0.15
- 0.1
- 0.05
- 0

2008Q4 2009Q2 2009Q4 2010Q2 2010Q4 2011Q2 2011Q4 2012Q2
OxyContin Abuse Rates
Opioid Treatment Program

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycontin</td>
<td>-24.5%</td>
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<tr>
<td>Other Opioids</td>
<td>-9.5%</td>
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</table>

Drug Abuse Rates
Population Rates per 100,000

Before Reformulation
After Reformulation

0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0

2008Q3  2009Q1  2009Q3  2010Q1  2010Q3  2011Q1  2011Q3  2012Q1
OxyContin Abuse Rates
Survey of Key Informants’ Patients Program

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycontin</td>
<td>-8.3%</td>
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<tr>
<td>Other Opioids</td>
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The graph shows the population rates per 100,000 for Oxycontin and Other Opioids before and after reformulation.
OxyContin Rates
URDD Rates, Oct 2008 – June 2012

**Poison Center**

<table>
<thead>
<tr>
<th>URDD per 1000</th>
<th>2008Q4</th>
<th>2009Q2</th>
<th>2009Q4</th>
<th>2010Q2</th>
<th>2010Q4</th>
<th>2011Q2</th>
<th>2011Q4</th>
<th>2012Q2</th>
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<tbody>
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<tr>
<td>2009Q2</td>
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<td>0.1</td>
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<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
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<tr>
<td>2011Q2</td>
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<td>0.2</td>
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<td>0.2</td>
<td>0.1</td>
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**Drug Diversion**

<table>
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<th>2009Q4</th>
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<th>2011Q2</th>
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<td>1.0</td>
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</tbody>
</table>

**Drug ∆(%)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>∆(%)</th>
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</thead>
<tbody>
<tr>
<td>Oxycontin</td>
<td>-52.9%</td>
</tr>
<tr>
<td>Other Opioids</td>
<td>-16.8%</td>
</tr>
</tbody>
</table>
**OxyContin Rates**

URDD Rates, Oct 2008 – June 2012

**Survey of Key Informant Patients**

<table>
<thead>
<tr>
<th>Period</th>
<th>URDD per 1000</th>
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<tbody>
<tr>
<td>2008Q3</td>
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<td>2012Q1</td>
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</table>

**Opioid Treatment Program**

<table>
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<tr>
<th>Period</th>
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</thead>
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<tr>
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<td>2011...</td>
<td>2.0</td>
</tr>
<tr>
<td>2012...</td>
<td>2.0</td>
</tr>
</tbody>
</table>

**Drug** | **Δ(%)**
---|---
Oxycontin | -14.8%
Other Opioids | -11.6%

**Drug** | **Δ(%)**
---|---
Oxycontin | -9.4%
Other Opioids | 7.6%
Street Price Down 18%

The RADARS® System Drug Diversion Program
OxyContin Street Price
1st Quarter 2010 to 4th Quarter 2011

Geometric Mean Street Price per mg

- $0.83/mg
- $0.68/mg

OxyContin (old formulation)
OxyContin Reformulated
Evidence of OxyContin Abuse Deterrence

- Rates decreased in PC (abuse) and DD
  - More decrease than other opioids
  - Decrease in both population and URDD rates
- Effect less pronounced in treatment programs
  - Minimal in SKIP
- Price per mg less for new formulation
- Evidence of shifting to alternatives
Buprenorphine

- Single ingredient tablets
  - Formerly Subutex®; now generic only
- Naloxone combination tablets
  - Suboxone®, brand-only (for now)
- Naloxone combination film
  - Suboxone®, brand-only
Overall Buprenorphine Abuse is Increasing
Single-Ingredient Buprenorphine
URDD Rates Rising

Poison Center Program

Drug Diversion Program
Single-Ingredient Buprenorphine URDD Rates Rising

Opioid Treatment Program

Survey of Key Informants’ Patients Program

Subutex

Suboxone
Single-Ingredient Buprenorphine
URDD Rates Rising

College Survey Program

![Graph showing URDD rates for Subutex and Suboxone over time]

- URDD per 1000
- Years: 2009Q1 to 2012Q1
- Subutex
- Suboxone
Buprenorphine

- Dramatic increase in prescribing makes population rates hard to interpret
- Abuse occurs (not just “street detox”)
- Naloxone combination products are less preferred by abusers
- Dramatic increase in diversion / abuse of single ingredient tablets
  - Out of proportion to URDD
Prescription Drug Monitoring Programs

• State-based with federal funding
• Monitor patient and provider behavior
• Wide variety in:
  – Governance & intent
  – Ease of use
• No national integration
• White House designated priority strategy
PDMPs Operational in 43 States

Source: National Association of Model State Drug Laws
Last updated 9/11/2012; accessed 9/15/2012
Limitations of PDMPs

• Not all PDMPs cover hydrocodone, codeine, and tramadol
• Cannot account for all sources of supply
  – Methadone maintenance programs
  – Veterans Administration
  – Indian Health Service
• Require prescriber to submit a query
  – Time consuming → unterutilization
Poison Center Program

*Intentional Abuse Exposures*

![Bar chart showing average annual change in intentional abuse exposures for Hydrocodone and Schedule II Opioids with and without PDMP.]
Poison Center Program

Intentional Abuse Exposures, Adjusted for Drug Supply

Average Annual Change

<table>
<thead>
<tr>
<th></th>
<th>PDMP</th>
<th>No PDMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>-6%</td>
<td>-2%</td>
</tr>
<tr>
<td>Schedule II Opioids</td>
<td>-4%</td>
<td>2%</td>
</tr>
</tbody>
</table>
Treatment Programs

Opioid Abuse Mentions

Average Annual Change

Hydrocodone

Schedule II Opioids

PDMP

No PDMP
Treatment Programs

Opioid Abuse Mentions, Adjusted for Drug Supply

Average Annual Change

- Hydrocodone
- Schedule II Opioids

PDMP
No PDMP
Operation UNITE

• “Unlawful Narcotics Investigations, Treatment and Education”

• Three-pronged intervention
  • Education
  • Enforcement
  • Treatment
Rise in Abuse Less in Operation UNITE Region

The RADARS® System Poison Center Program
Intentional Abuse Population Rates – All Opioids 2nd Quarter 2006 to 4th Quarter 2011, Percent Change from Baseline
Pediatric Unintentional Exposures

The RADARS® System Poison Center Program
Unintentional exposure rates of children aged 0-5 years to
Buprenorphine/naloxone tablets and oral film per 1,000 URDD
4th quarter 2009 through 1st quarter 2012

Data available at:
What the Future Holds

• Pharmaceutical innovations
  • Less abuse-prone active ingredients
  • Tamper- and abuse-deterrent formulations

• Regulatory strategies
  • Risk Evaluation and Mitigation Strategy requirements
  • Expanded role for Prescription Drug Monitoring Programs

• Measuring impact
  • Multimodal (“mosaic”) approach