RADARS® System: Mosaic Approach to Opioid Surveillance & REMS Evaluation

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Objectives

• Describe the RADARS® System
  – The “mosaic” approach
  – Utilization for safety and risk mitigation analysis

• Prescription Drug Surveillance & REMS Evaluation
  – Importance of measuring the right outcome
RADARS System Fundamentals

• RADARS System History
  – 2001: Founded by Purdue Pharma
  – 2006: Independently owned and operated by Denver Health & Hospital Authority (Rocky Mountain Poison and Drug Center)
  – 2012: Serving 10 subscribers

• Independent Scientific Advisory Board

• Monitor over 120 different products
RADARS System Goals

• Measure rates of misuse, abuse and diversion of prescription drugs

• Identify sentinel events involving the misuse, abuse and diversion of prescription drugs nationwide

• Provide experienced and expert analysis and interpretation of the data
College Survey

- **Population**
  - College students (traditional and non-traditional)
- **Definition/Type of Cases**
  - Self-reported nonmedical use of prescription drugs in previous semester
- **Coverage**
  - 6,000 responders/year
  - 50 states across 4 regions
- **Reporting Timeframe**
  - Fall / Spring / Summer

**Participants by Age Range**

- 18-21
- 22-25
- 26-29
- 30-33
- 34-37
- >38
Poison Center (PC)

- **Population**
  - young children, adolescents, adults, elderly

- **Definition/Type of Cases**
  - Spontaneous reports of intentional exposure mentions of acute medical events associated with one or more prescription drugs

- **Coverage**
  - 50 of 57 PCs

- **Reporting Timeframe**
  - quarterly
Opioid Treatment Programs (OTP & SKIP)

• Population
  – Opioid dependent persons seeking treatment at public/private opioid treatment programs (OTP) and private substance abuse treatment programs (SKIP)

• Definition/Type of Cases
  – Self-reported use of prescription or illicit opioids to “get high” in the past 30 days
Opioid Treatment Programs (OTP & SKIP)

- Coverage
  - See map
- Reporting Timeframe
  - quarterly
Drug Diversion (DD)

- **Population**
  - Cases of prescription drug diversion

- **Definition/Type of Cases**
  - Number of new instances of pharmaceutical diversion investigated by drug diversion units or reported to state regulatory boards

- **Coverage**
  - 280 reporters from 50 states

- **Reporting Timeframe**
  - quarterly
StreetRx (www.streetrx.com)

- **Population**
  - Any person in US with access to the internet

- **Definition/Type of Cases**
  - Utilize crowdsourcing methodology to calculate average price of specific prescription drug in particular location
  - Validated by DD

- **Coverage**
  - All 50 states

- **Reporting Timeframe**
  - Quarterly
StreetRx (www.streetrx.com)

**Prices for Dilaudid, Exalgo, generic Dilaudid, hydromorphone, hydromorphone (generic Dilaudid), Palladone — USA**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Location</th>
<th>Price</th>
<th>Date</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilaudid, 8mg pill</td>
<td>Mesa, Arizona</td>
<td>$15</td>
<td>May 1</td>
<td>Pricey</td>
</tr>
<tr>
<td>Dilaudid, 8mg pill</td>
<td>Mesa, Arizona</td>
<td>$10</td>
<td>May 1</td>
<td>Reasonable</td>
</tr>
<tr>
<td>Exalgo, 16mg pill</td>
<td>Cincinnati, Ohio</td>
<td>$50</td>
<td>Apr 27</td>
<td>Rate:</td>
</tr>
<tr>
<td>Dilaudid, 2mg pill</td>
<td>Banning, California</td>
<td>$1.50</td>
<td>Apr 24</td>
<td>Not Bad</td>
</tr>
<tr>
<td>hydromorphone (generic Dilaudid), 4mg</td>
<td>Knoxville, Tennessee</td>
<td>$5</td>
<td>Apr 22</td>
<td>Rate:</td>
</tr>
<tr>
<td>Dilaudid, 2mg pill</td>
<td>Brewster, New York</td>
<td>$15</td>
<td>Apr 21</td>
<td>Rate:</td>
</tr>
</tbody>
</table>
RADARS® System Mosaic Approach

- College Survey
- Early Experimenters
- Poison Center
- Acute Events
- OTP (Opioid Tx Program)
- Patients in Treatment
- SKIP (Survey of Key Informant Pts)
- Patients in Treatment
- Drug Diversion
- Criminal Justice/Law Enforcement
- Street Price
- Users/Buyers
RADARS® System Process: A Tale of Two Denominators

COUNTS BY SYSTEM = POPULATION RATE
UNITED STATES POPULATION

- Disease burden on whole population
- Does not account for drug availability

COUNTS BY SYSTEM = UNIQUE RECIPIENTS OF DISPENSED DRUG (URDD) RATE
URDD

- Number of unique people filling prescription for drug
Application of RADARS System Data

- Development of Interventions
  - How drugs are being abused, misused, diverted
  - Geographic specificity

- Ongoing surveillance
  - Monitoring trends over time due to market or regulatory changes

- Impact Assessment of Interventions – REMS Evaluation
  - Measuring the right outcome with product and geographic specificity
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<th>Opioid Treatment</th>
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<tbody>
<tr>
<td>1</td>
<td>hydrocodone</td>
<td>hydrocodone</td>
<td>hydrocodone</td>
<td>oxycodone</td>
<td>oxycodone</td>
</tr>
<tr>
<td>2</td>
<td>oxycodone</td>
<td>oxycodone</td>
<td>oxycodone</td>
<td>hydrocodone</td>
<td>hydrocodone</td>
</tr>
<tr>
<td>3</td>
<td>morphine</td>
<td>tramadol</td>
<td>morphine</td>
<td>methadone</td>
<td>morphine</td>
</tr>
<tr>
<td>4</td>
<td>tramadol</td>
<td>methadone</td>
<td>hydromorphone</td>
<td>morphine</td>
<td>buprenorphine</td>
</tr>
<tr>
<td>5</td>
<td>fentanyl</td>
<td>morphine</td>
<td>methadone</td>
<td>hydromorphone</td>
<td>methadone</td>
</tr>
<tr>
<td>6</td>
<td>methadone</td>
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</tr>
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<td>buprenorphine</td>
<td>fentanyl</td>
<td>fentanyl</td>
<td>fentanyl</td>
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</tr>
<tr>
<td>8</td>
<td>hydromorphone</td>
<td>hydromorphone</td>
<td>tramadol</td>
<td>tramadol</td>
<td>fentanyl</td>
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RADARS System Programs*  
Population Rates by API (2009 1Q to 2011 4Q)

*Includes College Survey, Poison Center, Opioid Treatment Program (OTP), Survey of Key Informants’ Patients (SKIP), and Drug Diversion.
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RADARS System Programs
URDD Rates by API (2009 1Q to 2011 4Q)

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Reformulated OxyContin®: Pre and Post-Analysis

OxyContin OC

OxyContin OP
Poison Center Program - Intentional Abuse Population Rate for OxyContin (2008 Q4 - 2011 Q4)

<table>
<thead>
<tr>
<th>Drug</th>
<th>∆ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyContin ORF</td>
<td>-34.4</td>
</tr>
<tr>
<td>Other Rx opioid</td>
<td>-2.8</td>
</tr>
</tbody>
</table>

- Before Introduction of OxyContin-reformulated
- After Introduction of OxyContin-reformulated
Drug Diversion Program
Population Rate for OxyContin (2008 Q4 - 2011 Q4)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyContin</td>
<td>-50.2</td>
</tr>
<tr>
<td>Other Rx opioid</td>
<td>-6.1</td>
</tr>
</tbody>
</table>

Before Introduction of OxyContin-reformulated

After Introduction of OxyContin-reformulated
Drug Diversion Program

OxyContin Street Price (2010 Q1 - 2011 Q4)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Street Price / mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyContin</td>
<td>$0.83</td>
</tr>
<tr>
<td>ORF</td>
<td>$0.68</td>
</tr>
</tbody>
</table>
REMS Evaluation

• Class-wide REMS
  – Measuring active pharmaceutical ingredient (API) level data
  – Indicative of overall trends for a class of drugs
  – NOT indicative of contributions of different formulations, routes or platforms
The RADARS® System SKIP Program
Percent Change in Abuse Rates per 100,000 population (2010 1Q to 2012 1Q)

Percent Change in Abuse Rates

- **Total buprenorphine**
- **Buprenorphine with naloxone**
- **Total single ingredient buprenorphine tablets**

DIA 2012
Collaborate to Innovate
Key Elements of the RADARS System

• 11 years of data
  – Maximum lag: 3 months
• Multifaceted ("mosaic") approach
  – Diversion & illicit sale
  – Misuse/Abuse/Addiction/Overdose
  – Medical outcomes
• Product & Geographic Specificity
  – National coverage of over 120 products
• Valuable system for surveillance and REMS evaluation