Researched Abuse, Diversion, and Addiction Related Surveillance (RADARS® System)

Introduction and Selected Results

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Outline

• Background
• Overview of Methods
• Results
  – Trends in opioid misuse, abuse and diversion
  – Role and value of denominators
  – Abuse deterrent formulations
• Outstanding issues and questions
RADARS System Background
What is the RADARS® System?

History

– 2002, Purdue Pharma
– 2006, Denver Health and Hospital Authority
  – Denver Public Hospital for 150 years
  – State sanctioned independent authority
– Most companies with an opioid product on the US market are subscribers.

Conflicts of Interest Statement

• Most manufacturers of prescription opioids or stimulants subscribe to RADARS System.
• RADARS System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado.
• Subscribers receive information, but do not participate in developing the System, data collection, or analysis of the data. They do not have access to the raw data.
• Employees are prohibited from personal financial relationships with any other company.
RADARS System Timeline

Key Informant Program

Opioid Treatment Program

SKIP Program

1st Site Audit

StreetRx Program

New Programs
- Int’l Programs
- Pain Patients?
- National Survey?
- Coroners?

RADARS® System Timeline
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
- 2011
- 2012
- 2013
- 2014

Drug Diversion Program

RADARS® System acquired by DHHA

College Survey Program

Web Monitoring Program

Poison Center Program
Mosaic Surveillance of Prescription Drug Abuse

- **Acute Health Events**: 49 Poison centers, 46 states, 456,610 cases, 491,874 opioid mentions
- **Drug Transactions**: Criminal Justice, 260 agency; 49 states, 145,090 cases with 146,786 opioid mentions
- **Entering Treatment**: Opioid Tx Program, 66 programs; 34 states, 41,031 cases with 183,573 opioid mentions
- **Entering Treatment**: SKIP, 109 practices, 45 states, 10,214 cases with 64,678 opioid mentions
- **New Initiates**: College Survey, 2000 students, 50 states, 3,564 cases with 11,871 opioid mentions
- **Illicit Market Price**: StreetRx.com Users/Buyers, 50 states, 8,441 price entries for an opioid
- **Web Monitoring**: > 150 million sites monitored, > 35,000 posts coded for analysis

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**Illegal Market**

- Price: StreetRx.com
- Users/Buyers, 50 states
- 8,441 price entries for an opioid

**New Initiates**

- College Survey
- 2000 students, 50 states
- 3,564 cases with 11,871 opioid mentions

**Entering Treatment**

- Opioid Tx Program
- 66 programs; 34 states
- 41,031 cases with 183,573 opioid mentions

**Drug Transactions**

- Criminal Justice
- 260 agency; 49 states
- 145,090 cases with 146,786 opioid mentions

**Acute Health Events**

- 49 Poison centers
- 46 states
- 456,610 cases
- 491,874 opioid mentions

**Illicit Market**

- Price
- StreetRx.com
- Users/Buyers
- 50 states
- 8,441 price entries for an opioid
RADARS System Strengths

• Product specificity
  – Specific product identity provided
  – Can categorize by common characteristics (ADF, IR, ER, etc.)
  – Dosage strength in some programs

• Geographic specificity
  – Any combination of 3 digit ZIP codes

• Timeliness – current data to 2014 Q1
  – Real time data available in Poison Center, Survey of Key Informant Patients programs

• Unique data sources
  – Difficult to access populations: children, diverters, alternate routes of use, etc.
  – Abuse related risks - Medical outcome including death

• Detailed custom surveys can be performed in Drug Diversion and Survey of Key Informant Patients Programs
RADARS System Limitations

- De-identified data: source can’t be verified, additional information cannot be obtained.
- Self-reporting: PC, OTP, SKIP, CS, StreetRx, Web Monitoring
- Spontaneous reporting: PC, StreetRx, Web Monitoring
- Geographical coverage is not universal, but is widespread
Bending the Curve
Opioid Analgesic Trends in the United States, 2014 Q1

Analgesic group: oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, and tramadol
Opioid Analgesic Trends in the United States, 2014 Q1

Poison Center Program

Drug Diversion Program

Opioid Treatment Program

Survey of Key Informant Patients

College Survey Program

Confidential

Analgesic group: oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, and tramadol
Denominators
# Denominator Options to Calculate Rates of Abuse, Misuse and Diversion of Prescription Drugs

<table>
<thead>
<tr>
<th>Denominator</th>
<th>Source</th>
<th>Definition</th>
<th>Can tell us...</th>
<th>Limitations/ Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>US Census</td>
<td>Population of the areas covered by program</td>
<td>Overall public health burden</td>
<td>Does not account for drug availability, which vary in the volume of drug produced</td>
</tr>
<tr>
<td>Unique Recipients of Dispensed Drug</td>
<td>IMS Health</td>
<td>Number of people filling a prescription during specified time</td>
<td>Risk per person who fills a prescription</td>
<td>Measures patient volume, does not measure drug volume</td>
</tr>
<tr>
<td>Prescription Counts</td>
<td>IMS Health</td>
<td>Number of prescriptions dispensed during the specified time</td>
<td>Risk per prescription dispensed</td>
<td>Does not account for variability in how much drug is dispensed (e.g. 3 days vs. 30 day supply or 5 mg tablets vs. 80 mg tablets)</td>
</tr>
<tr>
<td>Dosage Units Dispensed</td>
<td>IMS Health</td>
<td>Number of prescriptions multiplied by the number of dosage units dispensed</td>
<td>Risk per dosage unit dispensed</td>
<td>“Dose” is not the same across prescriptions (e.g. “take 1-2 tablets...”); dosage units within the same form can vary (e.g. tablets can be 10 mg v. 80 mg); not applicable to liquid products</td>
</tr>
<tr>
<td>Milligrams Dispensed</td>
<td>IMS Health</td>
<td>Dosage units multiplied by the content (mg) of each unit dispensed</td>
<td>Risk per unit weight dispensed</td>
<td>One milligram in not equivalent across all active ingredients; dosage units are not applicable to liquid products</td>
</tr>
<tr>
<td>Morphine-equivalent Milligrams</td>
<td>IMS; convert</td>
<td>Mg dispensed multiplied by the morphine-equivalent conversion factors</td>
<td>Risk per “standard” potency unit dispensed</td>
<td>Morphine equivalence conversion factors may vary by source; morphine equivalence measures are a difficult concept to convey to most audiences</td>
</tr>
</tbody>
</table>
Poison Center Intentional Abuse Rates
IR vs. ER Opioid Solid Dosage Units, 2009-2013

Number Rx
Population
Unique Recipients (URDD)
Prescriptions

Conversion Factors
Hydrocodone 1
Hydromorphone 4
Methadone 3
Morphine 1
Oxycodone 1.5
Oxymorphone 3
Tramadol 0.1
Von Korff, 2008

Units Dispensed
Milligrams Dispensed
Morphine-equivalent dispensed

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Poison Center Intentional Abuse Rates
API Opioid Solid Dosage Units, 2009-2013

Number Rx

Population

Unique Recipients (URDD)

Prescriptions

Units Dispensed

Milligrams Dispensed

Morphine-equivalent dispensed

- Hydrocodone
- Hydromorphone
- Methadone
- Morphine
- Oxycodone
- Oxymorphone
- Tramadol

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Denominators

• Selection of denominator depends on the question to be answered
  – Example – Responsible prescriber should decrease number of scripts to some degree and number of tablets per Rx. Which denominator?
• Units dispensed a problem when non-tablet units are involved
• We need to understand the conditions for selecting a denominator.
• What process could provide this information to sponsors and regulators internationally?
Abuse Deterrent Formulations
Abuse Deterrent Formulations

Population of People with Addiction Risk
↓
Exposed to Opioid

Swallow

Chew

Crush

Snort

Can ADFs Minimize Progression?

Currently Approved ADFs

Currently Approved ADFs

Inject
Mosaic Surveillance on Opana ER and OxyContin

Poison Center Program

Drug Diversion Program

Treatment Programs COMBINED

StreetRx

Population vs. Price per milligram

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Mosaic Surveillance on Opana ER and OxyContin

- Poison Center Program
- Drug Diversion Program
- Treatment Programs COMBINED
- StreetRx

URDD – Unique Recipients of Dispensed Drug

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Drug Diversion Program
ER oxymorphone diversion cases by state and time period
January 2011 through June 2013

![Graphs showing diversion rates for OxyContin®, Opana® ER, and Other Opioids over time.](image)
Drug Diversion Program
ER oxymorphone diversion cases by state and time period
January 2011 through June 2013

Before Reformulation

0 cases
11 to 20 cases
1 case
2 to 10 cases
21 to 50 cases
More than 50 cases

Participating Agency

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Drug Diversion Program
ER oxymorphone diversion cases by state and time period
January 2011 through June 2013

Before Reformulation

After Reformulation

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Validation

Prescription Opioid Mortality Rates are Similar for CDC, RADARS Poison Centers

Add methods from tech report
Poison Center Calls Predict ED Visits in DAWN ED Data

StreetRx, RADARS Drug Diversion and Silk Road Provide Similar Estimates of Street Price for Prescription Opioids

US StreetRx
Endorsement of Canadian Oxycodone Products in United States

11 States
1 to 4 reports
## Cost of Oxycodone ER in US and Canada – StreetRx

<table>
<thead>
<tr>
<th>Formulation</th>
<th>United States</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reported Median Price per mg, US Dollar (range)</td>
<td>Reported Median Price per mg, Canadian Dollar (range)</td>
</tr>
<tr>
<td>Crushable “Old OxyContin”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apo-Oxycodone CR</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>(0.15 – 16.80)</td>
<td>(NR)</td>
</tr>
<tr>
<td>OxyContin®</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>(0.06 – 10.00)</td>
<td>(0.54 – 6.00)</td>
</tr>
<tr>
<td>Co-Oxycodone CR</td>
<td>1.00</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>(0.30 – 4.00)</td>
<td></td>
</tr>
<tr>
<td>Teva-Oxycodone CR</td>
<td>0.88</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>(0.10 – 3.75)</td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Abuse Deterrent “New OxyContin”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone ER</td>
<td>0.63</td>
<td>0.75</td>
</tr>
<tr>
<td>(OxyContin in US, OxyNEO in Canada)</td>
<td>(0.03 – 10.00)</td>
<td>(0.38 – 1.40)</td>
</tr>
<tr>
<td>Average</td>
<td>0.63</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Future Work

• Surveillance of prescription drug abuse requires multiple perspectives and timely, product-specific data.

• Tantalizing to think that the US may be making progress on prescription opioid abuse.

• Further validation to understand relation of different perspectives to drug abuse is needed.
  – What types? What programs?
THE END