Prescription Opioid Analgesic Dependence and Addiction: Experience in the United States

October 10, 2013

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Prescription Opioid Misuse & Diversion

- Outline of Presentation
  - Brief Epidemiology
  - Brief RADARS® System Methodology
  - Trends with abuse deterrent formulations & market changes
Prescription Drug Abuse in the United States
Prescription Drug Associated Deaths

Unintentional Drug Overdose Deaths by Major Type of Drug, United States, 1999-2008

- Opioid Analgesic
- Cocaine
- Heroin

Number of Deaths

Australia - Intentional and Unintentional Exposure Rates By Opioid and Year

Acknowledgement: Naren Gunja and Jared Brown (NSW Poisons Information Centre, Sydney)
WHICH OPIOIDS ARE ABUSED AND DIVERTED?
More Drug Production = More Drug Abuse

Dasgupta, et al. Drug Alcohol Depend, 2005
### What Drugs Are Most Abused?

#### 2011 v. 2012 Population Rate (Ranked Highest-Lowest)

<table>
<thead>
<tr>
<th>Poison Center</th>
<th>Opioid Treatment</th>
<th>Drug Diversion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2011</strong></td>
<td><strong>2012</strong></td>
<td><strong>2011</strong></td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Oxycodone</td>
<td>Oxycodone</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Hydrocodone</td>
<td>Oxycodone</td>
</tr>
<tr>
<td>Methadone</td>
<td>Methadone</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>Methadone</td>
<td>Morphine</td>
<td>Methadone</td>
</tr>
<tr>
<td>Morphine</td>
<td>Hydromorphone</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>Buprenorphine</td>
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<td>Hydromorphone</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Fentanyl</td>
<td>Oxymorphone</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Oxymorphone</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Oxymorphone</td>
<td>Oxymorphone</td>
</tr>
</tbody>
</table>
### What Drugs Are Most Desired?

#### 2011 v. 2012 URDD Rate (Ranked Highest-Lowest)

<table>
<thead>
<tr>
<th>Poison Center</th>
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<tr>
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</tr>
<tr>
<td>Methadone</td>
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<td>Methadone</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Oxymorphone</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>Morphine</td>
<td>Buprenorphine</td>
<td>Morphine</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Hydromorphone</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Morphine</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Oxycodone</td>
<td>Tramadol</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Oxycodone</td>
<td>Hydrocodone</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Hydrocodone</td>
<td>Tramadol</td>
</tr>
</tbody>
</table>
• Population
  – Any person in US, UK or Canada 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

StreetRx
www.streetrx.com
Example of Validation
Comparison of StreetRx, RADARS System Drug Diversion and Silk Road

## Street Price of Drugs

<table>
<thead>
<tr>
<th>Product</th>
<th>Median (IQR)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opana® ER (new, hard to crush)</td>
<td>$1.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>($0.40,$1.00)</td>
<td></td>
</tr>
<tr>
<td>Opana® ER (old, crushable)</td>
<td>$1.38</td>
<td>0.0580</td>
</tr>
<tr>
<td></td>
<td>($1.00,$2.67)</td>
<td></td>
</tr>
<tr>
<td>OxyContin® (new OP, hard to crush)</td>
<td>$0.63</td>
<td></td>
</tr>
<tr>
<td></td>
<td>($0.50,$1.00)</td>
<td></td>
</tr>
<tr>
<td>OxyContin® (old OC, crushable)</td>
<td>$1.00</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>($0.63,$1.25)</td>
<td></td>
</tr>
</tbody>
</table>
Underground Website Lets You Buy Any Drug Imaginable

End of Silk Road for drug users as FBI shuts down illicit website

Prosecutors arrest the alleged founder of Silk Road, an illicit online marketplace where users paid in Bitcoin virtual money.
WHERE DO ABUSERS GET THEIR DRUGS?
RADARS® System
Source of Abused Opioid, 2008

College Survey

Methadone Program

- Other
- Internet
- Theft
- Purchased Illegally
- Prescribed by Doctor
- Friends & Relatives
WHERE DO DIVERSION AND ABUSE OCCUR IN THE UNITED STATES?
Rx Abuse Occurs in Every 3 Digit Zip Code
WHICH ROUTES ARE USED TO ABUSE PRESCRIPTION OPIOIDS?
Intravenous Abuse is More Prevalent in Experienced Users
RADARS System through March 2011

<table>
<thead>
<tr>
<th>Source</th>
<th>College Survey (%)</th>
<th>OTP / SKIP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral or chew</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Inhale or snort</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>7</td>
<td>58</td>
</tr>
</tbody>
</table>
Route of Abuse

FIGURE 3. Initial route of abuse versus route of abuse at admission in a substance abuse treatment center. Source: Data from Hays et al. (21).

Can We Formulate a Solution to Rx Drug Abuse?
The Abuse Deterrent Formulations
OxyContin, Opana ER, Exalgo, Nucynta ER
Tamper Resistant Strategies

- Hard coatings which resist crushing
- Polymers which turn to viscous gel when heated
- Polymers which resist dissolving in water and alcohol
- Nasal tissue irritants
- Novel delivery systems (patches, implants, etc.)
Number of People Filling a Prescription for OxyContin® or Opana® ER

OxyContin®

Before

After ADF

Opana® ER

Before

After ADF

Year/Quarter
Drug Diversion Program
Abuse Deterrent Formulations

OxyContin

Opana ER
Poison Center Program
Abuse Deterrent Formulations

OxyContin

Opana ER
Poison Center Program
Route of Abuse

Intended Routes

Unintended Routes

Rate per 100,000 population

Year/Quarter
Treatment Programs
Abuse Deterrent Formulations

OxyContin

Opana ER
Oxymorphone: 
Squeezing the Balloon?
Intentional Abuse: An exposure resulting from intentional improper or incorrect use of a substance where the victim was likely attempting to gain a high, euphoric effect or some other psychotropic effect.

ORF = OxyContin ADF, CRF = Opana ER ADF
Conclusions

• Prescription drug abuse affects all countries
• Hydrocodone and oxycodone are the most prevalent drugs abuse
• Oxymorphone and methadone are most abused when drug supply in considered
• Abuse deterrent formulations appear to be effective
  – State Attorneys General
  – FDA