Innovations in Rx Technology: A Session on Abuse Deterrent Formulations – Coalition Operations Track

Do ADFs Work?

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Outline

• Conceptual Framework for Abuse Deterrent Formulations
• Effectiveness of ADFs
• Unanticipated Consequences?
The Epidemic
US Consumption of Prescription Opioids, 1964 - 2012

http://www.painpolicy.wisc.edu/global
More Drug Production = More Drug Abuse
But - the Slope Varies by Drug

Instead of this?

How do we get this?

How Do Abuse, Addiction and Death Occur?
Population with Addiction Risk

\[\downarrow\]

Exposed to Opioid

Recreational Use or Pain Treatment

Swallow

Misuse/Abuse

Chew

Crush

Snort

Increasing Rate of Abuse, Addiction, Death
Abuse Deterrent Formulations
Strategies for Abuse Deterrence

- **Physical/Chemical barriers** - physical form of an oral drug is less amenable to abuse.
- **Agonist/Antagonist combinations** - interfere with euphoria
- **Aversion agents** - unpleasant effect if dosage form is manipulated or a higher dosage is used.
- **Delivery System** depot/implants to reduce release (e.g. SR depot SQ injectable formulation).
- **Prodrug** lacks opioid activity until transformed (e.g. GI tract).
- **Combination** – Two or more methods combined
- **Holy Grail** - Overdose only releases therapeutic amount.
How Can We Prove an ADF Works?

  - High public health priority
  - Recognizes the value of opioid analgesics in pain treatment
- Premarketing Studies
  - Category 1 - Laboratory-based in vitro manipulation and extraction studies
  - Category 2 - Pharmacokinetic studies
  - Category 3 - Clinical abuse potential studies
- Category 4 - Postmarketing Studies - Postmarketing data to assess the impact of an ADF on actual abuse.

Population of People with Addiction Risk
\[ \downarrow \]
Exposed to Opioid

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\[ \downarrow \text{Transition to High Risk Abuse} \]

Currently Approved ADFs

Model of ADF Effectiveness
What is the RADARS® System?

**History**
- 2002, Purdue Pharma
- 2006, Denver Health and Hospital Authority
  - Rocky Mountain Poison and Drug Center
  - Denver Public Hospital for 150 years
  - State sanctioned independent authority

**Conflict 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 company.
Mosaic Surveillance of Prescription Drug Abuse - 2013

- **Acute Health Events**: 49 Poison centers, 491,874 opioid mentions
- **Drug Transactions**: 260 agency, 146,786 opioid mentions
- **Entering Treatment**: Opioid Tx Program, 66 programs, 183,573 mentions
- **Entering Treatment**: Survey Key Informant Pts, 109 practices, 45 states, 64,678 mentions
- **New Initiates**: College Survey, 2000 students, 11,871 mentions
- **Illicit Market Price**: StreetRx.com Users/Buyers, 50 states, 8,441 price entries
- **Web Monitoring**: > 150 M sites, > 35,000 posts coded for analysis

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Oxycodone ADF – Reduced Use
Number of People Filling Prescriptions
RADARS System
Schedule II Excluding Oxycodone ER Population Rates by Program, 2009-2013
Poison Center Program
Oxycodone ER Population Rate, 2009-2013

Pre  Post
Poison Center Program
Oxycodone ER Population and Prescription Rates, 2009-2013
Drug Diversion Program
Oxycodone ER Population and Prescription Rates, 2009-2013
Treatment Centers Combined
Oxycodone ER Population and Prescription Rates, 2009-2013
Oral and Non-oral Abuse Decrease after Oxycodone ADF - Poison Center Program
Death Associated with Oxycodone ER have Decreased Poison Center Program, 2008 - 2013

![Graph showing the change in death rates associated with oxycodone ER before and after the Poison Center Program from 2008 to 2013. The graph compares CDC-based rates and PC-based rates, with a clear decrease in rates post-program implementation.]
Abuse Deterrent Formulation Reduces Street Price 2013 - 2014

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<thead>
<tr>
<th></th>
<th>United States</th>
<th>Canada</th>
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<tbody>
<tr>
<td></td>
<td>Number reports</td>
<td>Median Price/mg, US Dollar (range)</td>
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<td>Crushable “Old OxyContin”</td>
<td>283 1.00 50</td>
<td>1.00</td>
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<tr>
<td>Abuse Deterrent “New OxyContin”</td>
<td>364 0.70 23</td>
<td>0.63</td>
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Refining Our Understanding of Abuse
Deterrent Formulations
Limited Impact Unless Most Opioids Analgesics are Abuse Deterrent
Poison Center Program
Population Rate, 2009-2013

*Other opioids excluding ER oxycodone and ER oxymorphone
National Trends in Opioid Abuse and Diversion

Prescriptions of Opioid Analgesics

RADARS Drug Diversion Program

RADARS Poison Center Program

RADARS Opioid Treatment Program

Endorsement of Heroin Use
National Survey of Drug Use and Health

[Graph showing the numbers in thousands of heroin users from 2002 to 2012, with data points for past month (red) and past year (blue). The years 2004 and 2007 are highlighted.]
Battle of the ADFs

Bob and Paul are hiking when they encounter a bear.

Bob starts putting on his tennis shoes.

Paul says, "What? You can't outrun a bear!"

Bob says, "I don't have to outrun the bear — I just have to outrun you!"

Niacin

Crush Resistance

Prodrug
Population with Addiction Risk

↓ Exposed to Opioid Recreational Use or Pain Treatment

Swallow
Misuse/Abuse

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↓ Transition to High Risk Abuse

• ADFs are not for addicts
• More drug = more abuse, but formulation can change relation
• Need ADFs for IR as well as ER
• Need new drug scheduling - formulation and not by API
• Need greater treatment capacity for opioid addiction
Questions?