Are Abuse Deterrent Formulations Effective?

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Professor, University of Colorado
• **Venue:** The Fairfax Embassy Row Hotel, November 18, 2013, **Time:** 0915-1015 (15 min Q&A)

• **Key objectives:** To understand the current level of misuse and diversion from the national RADARs data and the changing profile dependent on the increasing use of mono-buprenorphine

• **Topics/Evidence to be addressed:**
  
  • Misuse and diversion – is this a common problem worldwide, examples in the OPD population, comparisons?
  • Recent FDA decisions on morphine (rejected due to no abuse deterrence) and generic Oxycontin (not approved due to no abuse deterrence)
  • Impact of abuse deterrent formulations on misuse and abuse
  • Why it is important to favour abuse deterrent formulations and is it important in the OPD population?
  • Diversion reflects the treatment system of the particular country/ access to treatment
  • Diversion/drug street price = local demand
  • Can we identify which patient will divert?
  • Abuse deterrent formulations (in relation to overdose/mortality) – risk of different treatment
Prescription Opioid Deaths are Rising Internationally

United Kingdom Drug Related Deaths 2001 - 2011

*Note: heroin and morphine are reported as one category in the data from England, Wales and Scotland; since the focus of this analysis is on prescription opioids, that category was not included in this analysis.

Source: RADARS® System, Denver Health and Hospitals
What is the RADARS® System?

• History
  – 2006, Denver Health and Hospital Authority (DHHA)
  – Multiple pharmaceutical subscribers
  – Independent program
  – Denver Public Safety Net Hospital for 150 years
  – State sanctioned independent authority

• Conflict of Interest Statement
  – None, other than running system for DHHA as noted above.
RADARS System
Scientific Advisory Board

**Principal Investigators**
- Theodore J. Cicero, PhD  
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- Richard C. Dart, MD, PhD  
  *Denver Health and Hospital Authority*
- Hilary Surratt, PhD  
  *Nova Southeastern University*
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  *American Association for the Treatment of Opioid Dependence*

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- Sidney Schnoll, MD, PhD  
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**Epidemiology/Biostatistics**
- Edgar Adams, ScD  
  *Covance*
- Nabarun Dasgupta, MPH  
  *Founder – Epidemico*
- Alvaro Muñoz, PhD  
  *Johns Hopkins University*
Challenges of Prescription Drug Abuse Surveillance

- Clandestine behavior
- Geographical variability
- Changes rapidly
- Multiple age groups
- Product specificity
  - 15 active pharmaceutical ingredients (API)
    - Opioids: Hydrocodone, oxycodone, hydromorphone, oxymorphone, morphine, fentanyl, tapentadol, tramadol, buprenorphine, methadone
    - Stimulants
  - Dozens of specific products (Vicodin, OxyContin, Opana ER, Suboxone, Subutex, etc.)
RADARS System Mosaic

Acute Events: 53 Poison Centers, 46 States

Drug Transactions: Criminal Justice, 280 investigator, 50 states

Entering Treatment: OTP, 73 programs, 33 states

Entering Treatment: SKIP, 125 practices, 50 states

New Initiates: College Survey, 2000 students, 50 States

Illicit Market Price: StreetRx.com, Users/Buyers, 50 states

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RADARS® System Process
Two Denominators

- **Drug Diversion**
- **Poison Center**
- **OTP**
- **SKIP**
- **College Survey**

Numerator compiled by each program

**POPULATION RATE** = \( \frac{\text{Event Count by Area}}{\text{Population}} \)

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

**UNIQUE RECIPIENTS OF DISPENSED DRUG (URDD) RATE**

\[ \frac{\text{Event Count by Area}}{\text{URDD}} \]

- URDD = Number of unique people filling prescription for drug (refills excluded)
TRENDS IN PRESCRIPTION OPIOID ABUSE IN THE UNITED STATES

Population Rate

Availability Rate (URDD)
### RADARS System Opioid Abuse Trends

**URDD Rates ( Ranked Highest-Lowest )**

#### 2012

<table>
<thead>
<tr>
<th>Rank</th>
<th>Poison Center</th>
<th>Opioid Treatment</th>
<th>Survey of Key Informant Pts</th>
<th>Drug Diversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methadone</td>
<td>Oxymorphone</td>
<td>Oxymorphone</td>
<td>Oxymorphone</td>
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<tr>
<td>2</td>
<td>Oxymorphone</td>
<td>Methadone</td>
<td>Hydromorphone</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>3</td>
<td>Buprenorphine</td>
<td>Hydromorphone</td>
<td>Methadone</td>
<td>Methadone</td>
</tr>
<tr>
<td>4</td>
<td>Hydromorphone</td>
<td>Buprenorphine</td>
<td>Buprenorphine</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>5</td>
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<td>Morphine</td>
<td>Morphine</td>
<td>Morphine</td>
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<tr>
<td>6</td>
<td>Fentanyl</td>
<td>Fentanyl</td>
<td>Fentanyl</td>
<td>Oxycodone</td>
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<tr>
<td>7</td>
<td>Tramadol</td>
<td>Tapentadol</td>
<td>Tapentadol</td>
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<td>8</td>
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<tr>
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<td>10</td>
<td>Hydrocodone</td>
<td>Tramadol</td>
<td>Tramadol</td>
<td>Tapentadol</td>
</tr>
</tbody>
</table>
BUPRENORPHINE AND METHADONE DATA FOR THE UNITED STATES
How Many Patients Fill a Prescription?
Unique Recipients of dispensed drug (URDD)
2009Q1 - 2012Q4

Methadone
Combination Buprenorphine Tablets
SI Buprenorphine Tablets
Combination Buprenorphine Film
Buprenorphine Data Comparison
RADARS System & CESAR Fax

Estimated Number of Total Methadone and Buprenorphine Reports,
U.S. Law Enforcement-Seized Drug Exhibits Analyzed by Forensic Laboratories, 2003-2010

RADARS System Drug Diversion Program
Diversion Reports 2002 - 2012

CESAR = Center for Substance Abuse Research
Opioid Treatment Program
Past 30 Day Endorsements, 2009-2012

Population Rate

- Methadone high, but decreasing
- Bup-Single Ingredient Increasing slightly
- Bup-Naloxone Film Strip increasing slightly
- Bup-Naloxone Combination Decreasing Slightly

Availability Rate (URDD)

- Bup-Single Ingredient Highest, Increased, Flat
- Methadone Decreasing
- Bup-Naloxone Combination Lower, Flat
- Bup-Naloxone Film Strip Lowest, Decreasing
Survey of Key Informant Patients
Past 30 Day Endorsements, 2009-2012

Population Rate

- Methadone high, but decreasing
- Bup-Single Ingredient Increasing
- Bup-Naloxone Combination Increasing Flat
- Bup-Naloxone Film Strip Increasing slightly
- Bup-Single Ingredient Increasing Dramatically
- Methadone Slight Decrease
- Bup-Naloxone Combination Increasing
- Bup-Naloxone Film Strip low, flat
RADARS System Drug Diversion Cases 2009-2012

- **Population Rate per 100,000**: Methadone high, but decreasing slightly
- **Bup-Naloxone Combination**: Decreasing Slightly
- **Bup-Naloxone Film Strip**: Increasing
- **Bup-Single Ingredient**: Increasing

- **Availability Rate (URDD) per 1,000**: Bup-Naloxone Combination Increasing Greatly
- **Bup-Single Ingredient**: Increasing Greatly
- **Methadone Slight Decrease**: Bup-Naloxone Film Strip increasing slightly
Why Are Endorsements of Buprenorphine Strip So Low?

• The quickly replaced tablet in United States before generic tablets became available.
• But the rate of abuse endorsement was low
• Potential explanations
  – Misidentification
  – Serial numbers
  – Different packaging (child proof)
  – Others?
• **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

StreetRx

www.streetrx.com
Comparison of StreetRx, RADARS System Drug Diversion and Silk Road – Price per milligram of drug

Death Cases in Poison Center Program
All Ages, 2009Q1 - 2012Q4

- Total Methadone
- Total Combination Buprenorphine Tablets
- Total Single Ingredient Buprenorphine Tablets
- Total Buprenorphine Oral Films
Death Cases in Poison Center Program
Ages under 12 years, 2009Q1 - 2012Q4
Conclusions

• Prescription opioid abuse in the US may be plateauing, but still causes 16,000 deaths per year

• Methadone
  – Endorsements in treatment programs decreasing
  – More deaths than any other opioid
  – But many deaths involve pills (treatment of pain)

• Buprenorphine
  – Endorsements are relatively flat, but there is dramatic shift of products involved
  – Abuse is increasing quickly perhaps due to generic availability
    • Single-ingredient “Subutex”
    • Combination tablet (Bup-naloxone; “Suboxone”)
  – Exceptional safety in all groups
  – Endorsement of buprenorphine strip has been very low. Diversion has also been low.
  – Why is the price of buprenorphine so high
Thank you!