RADARS® System

California Society of Addiction Medicine Opioid Pre-Conference Workshop

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Richard Dart, MD, PhD
Director – Rocky Mountain Poison and Drug Center
Professor, University of Colorado, Department of Emergency Medicine
Opioids and the Stars
Some celebrities have been publicly linked with use of these powerful painkillers (in several cases, with more than one such medication).

Reported past users of OxyContin, generic oxycodone, or Percocet (which consists of oxycodone and acetaminophen):
- Heath Ledger (actor; oxycodone was in his blood when he died)
- Rush Limbaugh (radio talk show host)
- Courtney Love (singer)

Reported past users of hydrocodone, which is chemically similar to oxycodone, including Vicodin (which consists of hydrocodone and acetaminophen):
- Jamie Lee Curtis (actress)
- Eminem (singer)
- Brett Favre (retired football star)

- Cindy McCain (businesswoman, wife of Sen. John McCain)
- Winona Ryder (actress)
- Steven Tyler (singer, American Idol judge)
- Walter Payton (late football legend)
- Matthew Perry (actor)
- Nicole Richie (reality TV personality)
Objectives

• Is Suboxone an abuse deterrent formulation?
• Misuse and abuse of buprenorphine in high risk populations
• What happens to innocent bystanders?
• Misuse and abuse of buprenorphine in California v. Nation
• Other abuse/tamper deterrent formulations
What is the RADARS® System?

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

• Purpose
  – Measure rates of misuse, abuse and diversion of prescription drugs
Mosaic Strategy for Postmarketing Surveillance of Medications
RADARS® System Process
Adding the Denominator

**Numerators compiled by each program**

**Two Denominators:**

1. **Population**
   - Tried and true - Disease burden on whole population
   - Does not account for drug availability

2. **Unique Recipients of Dispensed Drug (URDD)**
   - Number of unique people filling prescription for drug
   - Accounts for availability of drug in community
   - Relates events to corresponding patient benefit
   - Alternatives – pill count, total mgs of drug
RADARS® System

National Buprenorphine Rates
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

Number of Total Methadone and Buprenorphine Cases,
RADARS System Drug Diversion Program, 2002 - 2011
Availability of Buprenorphine has Expanded Unique Recipient of Dispensed Drug (URDD)
Buprenorphine Rates
Poison Center, Drug Diversion Programs
Population Rate (2006 – 2012)

Poison Center
Drug Diversion

Population Rate per 100,000

2006  2012

Suboxone Tablets
Suboxone Oral Film
Total SI buprenorphine
Total buprenorphine
Not otherwise specified buprenorphine

Poison Center
Drug Diversion
Opioid Treatment Program
Population Rate 2010 Q1 - 2012 Q1
Survey Key Informants’ Patients
Population Rate, 2010 Q1 - 2012 Q1

- Total buprenorphine
- SI buprenorphine tablets
- Not otherwise specified buprenorphine
- Suboxone® tablets
- Suboxone® oral film
Survey Key Informants’ Patients
Population v. URDD Rate, 2010 Q1 - 2012 Q1

- Total buprenorphine
- SI buprenorphine tablets
- Not otherwise specified buprenorphine
- Suboxone® tablets
- Suboxone® oral film
RADARS® System

Drug Diversion Program

&

Buprenorphine Street Price
Drug Diversion
Population v. URDD Rate, 2010 Q1 - 2012 Q1

- Total buprenorphine
- SI buprenorphine tablets
- Not otherwise specified buprenorphine
- Suboxone® tablets
- Suboxone® oral film

Population rate per 100,000

URDD rate per 1,000

2010 2012 2010 2012
Drug Diversion SPQ – Price Per mg (2012 Q1)
Drug Diversion SPQ – Price Per mg
(2010 Q1 - 2012 Q1)
Drug Diversion SPQ – Price per mg (Geometric Mean - 2010 Q4 - 2012 Q1)

- **Suboxone®**
  - 2010Q4: $0.00, n = 2
  - 2011Q1: $0.00, n = 4
  - 2011Q2: $1.00, n = 7
  - 2011Q3: $2.00, n = 10
  - 2011Q4: $4.00, n = 14
  - 2012Q1: $7.00, n = 14

- **Subutex®**
  - 2010Q4: $0.00, n = 14
  - 2011Q1: $0.00, n = 14
  - 2011Q2: $0.00, n = 14
  - 2011Q3: $0.00, n = 14
  - 2011Q4: $0.00, n = 14
  - 2012Q1: $0.00, n = 14

- **Suboxone Oral Film®**
  - 2010Q4: $0.00, n = 2
  - 2011Q1: $0.00, n = 3
  - 2011Q2: $0.00, n = 3
  - 2011Q3: $0.00, n = 3
  - 2011Q4: $0.00, n = 3
  - 2012Q1: $0.00, n = 3
RADARS® System
Poison Center Program –
Intentional Exposure Reasons and Medical Outcomes in Population
Poison Center Program
Medical Outcomes (2012 Q1)

- Single ingredient
  buprenorphine (%)
- Suboxone tablets (%)
- Suboxone oral film (%)

% of Total Medical Outcomes

No effect
Minor effect
Moderate effect
Major effect
Poison Center Program
Intentional Exposure Reasons (2012 Q1)

% of Total Intentional Exposures

- Intentional Abuse
- Intentional Misuse
- Intentional Suspected Suicide
- Intentional Unknown
- Withdrawal

- Single ingredient buprenorphine (%)
- Suboxone tablets (%)
- Suboxone oral film (%)

0.00 10.00 20.00 30.00 40.00 50.00 60.00
RADARS® System
Poison Center Program –
Exposure Rates and Medical Outcomes in Adolescents
Poison Center Program
Unintentional General, Population and URDD Rates
Children 0-12 Years (2009 Q4 – 2012Q1)
Poison Center Program
Unintentional General, Medical Outcome
Children 0-12 Years (2009 Q4 – 2012Q1)

Number of Unintentional General Outcomes

- No effect
- Minor effect
- Moderate effect
- Major effect
- Death

- Single ingredient buprenorphine
- Suboxone
- Suboxone Oral Film
RADARS® System
Poison Center Program –
Medical Outcomes
Methadone v. Buprenorphine
Poison Center Program
Medical Outcomes
Methadone v. Buprenorphine
2011 Q2 – 2012 Q1

Total Case Count

- No effect
- Minor Effect
- Moderate Effect
- Major Effect
- Death

Methadone Case Count

Buprenorphine Case Count
Poison Center Program
Medical Outcomes
Methadone v. Buprenorphine
2011 Q2 – 2012 Q1

% of Total Cases

- % of Total Methadone Cases
- % of Total Buprenorphine Cases

<table>
<thead>
<tr>
<th>Effect</th>
<th>No effect</th>
<th>Minor Effect</th>
<th>Moderate Effect</th>
<th>Major Effect</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Total Cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Conclusions

• Has availability of buprenorphine expanded?
  – Dramatic increase in people filling a prescription (URDD)
  – Marked increase of misuse and abuse in all systems
  – Street price is higher than other opioids
  – Single ingredient is on the rise, highest in OTP and SKIP

• Is Suboxone an abuse deterrent formulation?
  – Yes, endorsements are falling and lower than SI

• Misuse and abuse of buprenorphine in high risk populations (OTP and SKIP)
  – Total endorsements rising quickly
  – Single ingredient is generally preferred
RADARS® System

California Buprenorphine Rates Compared to National Rates
Buprenorphine Availability in California
Unique Recipient of Dispensed Drug (URDD)

- Suboxone Tablets
- Suboxone Oral Film
- Total SI
- Buprenorphine
- Total Buprenorphine
Poison Center Program
Average Population Rate per 100,000
2009 Q1 - 2012 Q1
Poison Center Program
Average URDD Rate per 1,000
2009 Q1 - 2012 Q1

[Bar chart showing average URDD rates for different types of buprenorphine and Suboxone products, with categories for Buprenorphine, Single Ingredient Buprenorphine Tablets, Suboxone, and Suboxone Sublingual Film, and two sets of data representing CA PC URDD Average and National PC URDD Average.]
Drug Diversion Program
Average Population Rate per 100,000
2009 Q1 - 2012 Q1

CA DD Population
Average

National DD
Population
Average
Drug Diversion Program
Average URDD Rate per 1,000
2009 Q1 - 2012 Q1
Opioid Treatment Program
Average Population Rate per 100,000
2010 Q1 - 2012 Q1

- Buprenorphine
- Single Ingredient Buprenorphine Tablets
- Nos Buprenorphine
- Suboxone
- Suboxone Sublingual Film

CA OTP Population Average
National OTP Population Average
Opioid Treatment Program
Average URDD Rate per 1,000
2010 Q1 - 2012 Q1

- Buprenorphine Tablets
- Single Ingredient Buprenorphine Tablets
- Suboxone
- Suboxone Sublingual Film

CA OTP URDD Average
National OTP URDD Average
SKIP Program
Average Population Rate per 100,000
2010 Q1 - 2012 Q1

CA SKIP Population Average
National SKIP Population Average
SKIP Program
Average URDD Rate per 1,000
2010 Q1 - 2012 Q1

<table>
<thead>
<tr>
<th>Product</th>
<th>CA SKIP URDD Average</th>
<th>National SKIP URDD Average</th>
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</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single Ingredient Buprenorphine Tablets</td>
<td>3.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Suboxone</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Suboxone Sublingual Film</td>
<td>0.5</td>
<td>1.0</td>
</tr>
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College Survey Program
Average Population Rate per 100,000
2009 Q1 - 2012 Q1

Average Population Rate per 100,000
2009 Q1 - 2012 Q1

CA CS Population Average
National CS Population Average
RADARS® System
Poison Center Program –
Intentional Exposure Reasons and
Medical Outcomes in
California Population
Poison Center Program
Medical Outcomes in California (2012 Q1)

% of Total Medical Outcomes

- Suboxone oral film (%)
- Suboxone (%)
- Single ingredient buprenorphine (%)
Poison Center Program
Intentional Exposure Reasons in California (2012 Q1)
Conclusions

• Availability of buprenorphine has expanded in California
  – URDD trends match National trends

• Misuse and abuse of buprenorphine in high risk populations (SKIP)
  – Total endorsements for California are higher than National average for both Population and URDD rates
  – Suboxone and not-otherwise-specified buprenorphine are most frequently endorsed

• Misuse and abuse of buprenorphine in college students
  – Single ingredient most frequently endorsed and above National average
RADARS System
Other Abuse/Tamper Deterrent Formulations
Reformulated OxyContin

OxyContin OC

OxyContin OP
Poison Center Intentional Exposures
Population rate for OxyContin
2008 Q4 - 2012 Q1

<table>
<thead>
<tr>
<th>Drug</th>
<th>Δ (%)</th>
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<tbody>
<tr>
<td>OxyContin</td>
<td>-23.1%</td>
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<tr>
<td>Other Rx opioid</td>
<td>2.5%</td>
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</tbody>
</table>

Before Reformulated OxyContin®

After Reformulated OxyContin®
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>-51.9</td>
</tr>
<tr>
<td>Other Rx opioid</td>
<td>-7.1</td>
</tr>
</tbody>
</table>

Before Reformulated OxyContin®
After Reformulated OxyContin®
Opioid Treatment Program
Population rate for OxyContin
2008 Q4 - 2011 Q4

<table>
<thead>
<tr>
<th>Drug</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyContin</td>
<td>-24.4</td>
</tr>
<tr>
<td>Other Rx opioid</td>
<td>-9.3</td>
</tr>
</tbody>
</table>

Before Reformulated OxyContin®
After Reformulated OxyContin®
Survey of Key Informants Patients (SKIP)
Population rate for OxyContin
2008 Q4 - 2011 Q4

Before Reformulated OxyContin®
After Reformulated OxyContin®
OxyContin URDD Rates
All Programs

Poison Centers

Drug Diversion

Opioid Treatment Program

Survey Key Informant Patients
Street Price Quotient
Oxycontin® Reformulation Analysis

- **Before introduction of reformulated ER oxycodone**
- **During transition to reformulated ER oxycodone**
- **After reformulated ER oxycodone transition**

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Average Price per Milligram</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR Oxycodone</td>
<td>$0.85</td>
</tr>
<tr>
<td>ER Oxycodone-original formulation</td>
<td>$0.97</td>
</tr>
<tr>
<td>Reformulated ER Oxycodone</td>
<td>$0.69, $0.70</td>
</tr>
</tbody>
</table>
Reformulated OxyContin
Conclusions

• Data support that reformulated OxyContin is tamper and abuse deterrent
  – Total PC cases, PC abuse cases, DD cases and street price have decreased greatly
  – OxyContin rates decreased at a much higher percentage than other opioids over the same time period
  – Decrease in both Population and URDD rates indicates that both decreased availability and decreased desirability may be involved.

• New formulation is still abused
  – OTP, SKIP show minimal effect
Hydromorphone: Exalgo Introduction
Drug Diversion Program
Population Rate for Hydromorphone
2006 Q3 - 2012 Q1

Introduction of Exalго
Drug Diversion Program
URDD Rate for Hydromorphone
2006 Q3 - 2012 Q1

Rate per 1,000 URDD

Introduction of Exalgo

Rate per 1,000 URDD
Opioid Treatment Program
Population Rate for Hydromorphone
2006 Q3 - 2012 Q1

Introduction of Exalgo
Opioid Treatment Program
URDD Rate for Hydromorphone
2006 Q3 - 2012 Q1

Rate per 1,000 URDD

Introduction of Exalgo
Exalgo / Hydromorphone
Conclusions

• Hydromorphone misuse abuse and diversion rates per population and URDD have been increasing over time

• Release of Exalgo in March 2010 corresponded with changes in these trends
  – Post-Exalgo release trends declining or remaining stable
  – Trends in abuse among high risk populations (OTP) were statistically significant after release

• Further study of overall changes in trend patterns continue in RADARS System
Thank You!