Thursday, May 16, 2019
13th Annual Scientific Meeting
Transforming Post-Marketing Surveillance of Prescription Drugs
RADARS System
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Mac Miller
NEWS FROM RADARS SYSTEM
RADARS System – 103 Publications in Scientific Literature

RADARS System Publications Cited over Time

- Number of Citations per Year
- Cumulative Citations
- Number of Publications

Number of Publications:
- 2005: 2
- 2006: 4
- 2007: 8
- 2008: 1
- 2009: 7
- 2010: 6
- 2011: 7
- 2012: 6
- 2013: 9
- 2014: 8
- 2015: 8
- 2016: 8
- 2017: 11
- 2018: 10

Number of Citations:
- 2005: 0
- 2006: 4
- 2007: 12
- 2008: 20
- 2009: 49
- 2010: 88
- 2011: 126
- 2012: 176
- 2013: 288
- 2014: 408
- 2015: 578
- 2016: 772
- 2017: 1116
- 2018: 1648

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Trends in Annual Opioid Prescribing Rates

IQVIA Transactional Data Warehouse
Perspective

No Shortcuts to Safer Opioid Prescribing

Deborah Dowell, M.D., M.P.H., Tamara Haegerich, Ph.D., and Roger Chou, M.D.

https://healthprofessionalsforpatientsinpain.org/
Poison Center Program
Intentional Abuse, 2006 - 2018

Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol

Oxycodone
Fentanyl
Hydrocodone
Hydromorphone
Morphine
Methadone
Buprenorphine
Tramadol
Oxymorphone
Drug Diversion Program, 2006 - 2018

Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol
Treatment Center Programs Combined, 2008 - 2018

Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol

Oxycodone
Fentanyl
Hydrocodone
Hydromorphone
Morphine
Methadone
Buprenorphine
Tramadol
Heroin
Oxymorphone
Treatment Center Programs, 2008 - 2018

Opioid Treatment Program

Survey of Key Informants’ Patients Program

% Respondent

0 10 20 30 40 50 60 70 80


Oxycodone
Fentanyl
Hydromorphone
Hydrocodone
Methadone
Morphine
Buprenorphine
Methadone
Tramadol
Heroin

Poison Center Program
Prescription Stimulant Rates, 2008 - 2018

Cases per 100,000 population

- Methylphenidate
- Amphetamines

2008-2018
Drug Diversion Program
Prescription Stimulant Rates, 2008 - 2018

Per 100,000 population

Methylphenidate
Amphetamines
DECREASING RX OPIOID ABUSE, BUT INCREASING DEATHS?
The Opioid Epidemic

Wave 1: Rise in Prescription Opioid Overdose Deaths
Wave 2: Rise in Heroin Overdose Deaths
Wave 3: Rise in Synthetic Opioid Overdose Deaths

National Vital Statistics System, Centers for Disease Control, 2017
Is Total Substance Abuse Increasing?

National Survey of Drug Use and Health. US Centers for Disease Control, 2017
Opioid Epidemic - Epidemic of Opioid Deaths

Wave 1: Rise in Prescription Opioid Overdose Deaths
Wave 2: Rise in Heroin Overdose Deaths
Wave 3: Rise in Synthetic Opioid Overdose Deaths

National Vital Statistics System, Centers for Disease Control, 2017
Anything that reduces Opioid Drug Supply will increase use of Heroin

Alcohol - Nicotine

Marijuana

Polysubstance Abuse

### Opioids
- Heroin
- Fentanyl
- Rx analgesics
- Loperamide

### Benzodiazepines
- Alprazolam
- Diazepam

### Antipsychotics
- Quetiapine
- Olanzapine

### AEDs
- Pregabalin
- Gabapentin

### Stimulants
- Cocaine
- Amphetamine
- Methylphenidate

### Hallucinogens
- Ketamine
- LSD

### NPS/synthetics
- Mephedrone
- Cathinones
- Synthetic cannabinoids
Former US drug czar says national focus on opioid epidemic is overlooking real culprit

Bill Bennett
Needed: Better Data on Prescription Drug Abuse
Needs: A Dataset for the Evaluation of Rx Drug Abuse

• To assess safety
  – Product / API specificity
  – Dosage form, formulation
  – Respondent behaviors, motivation
  – Longitudinal data
  – Large numbers?

• Characteristics
  – Accuracy
  – Fast
  – General population + special populations
    • Power for subpopulation assessment
  – Cost effective
  – Understanding of strengths and weaknesses
Survey of Non-Medical Use of Prescription Drugs Program (NMURx), United States

Study Design

- Online, Cross-sectional
- Self-administered, Anonymous
- Semi-annual - 60,000 responses
  - 30,000 twice annually
- Acknowledgement

Lori Crane, PhD
University of Colorado
NMURx Key Design Features

- **Revised NMU definition**
  - Simpler definition
  - Better orientation (examples included)
  - Similar to NSDUH

- **12 Month Focus**
  - Enhanced recall
  - Better estimates of current state

- **Ease of use**
  - Fewer questions per screen
  - Simplified language
  - Easy navigation
  - Clear instructions

- **Device Compatibility**
  - Better representation
  - Sustainable sample pool
  - Redesign: 30% smartphone
    - 7% tablet
  - 64% desktop

- **Randomization**
  - Drug classes, API
  - Reason, route, source
  - Illicit drugs

- **Advanced flow / skip logic**
  - Fewer questions; 10.5 minutes
  - Avoid adapting to question flow
Gender, age, income, location, veteran and student status
Use, NMU, Abuse of Rx drugs (product-specific)
Co-ingestants, use of illicit drugs/alcohol
Reason for non-medical use (e.g. treat pain, to get high, curiosity)
Routes of administration
Source of drug, price paid if purchased
Hx chronic/acute pain and Rx drug therapy
NMURx Program Coverage

- North America
  - US
  - Canada
- Europe
  - UK
  - France, Italy
  - Germany, Spain
- Singapore
Order Effect is a Large Source of Inaccuracy in Web-based Surveys

Without randomization, the survey would underestimate as position decreased

- 7.7% of respondents endorsed lifetime use of any product in position 1.
- For position 42, it was 4.3%
- Opioids: effects are about the same.
  - Fentanyl, 8.0% of respondents in 1st position; 4.6% in last position
  - Oxycodone, 39.7% in first position; 29.5% in last position
NMURx Estimates vs National Probability Surveys

Calibration Weighting for Representative Estimates

NHIS - National Health Interview Survey
NHANES - National Health and Nutrition Examination Survey
NSDUH - National Survey of Drug Use and Health
Cannabis Users Non-Medical Use and DAST-10
NMURx, United States, 3Q 2018

<table>
<thead>
<tr>
<th>Category</th>
<th>Cannabis Users</th>
<th>Cannabis Non-Users</th>
<th>Cigarette Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-NMU with Opioids</td>
<td>14.9 (13.9, 15.9)</td>
<td>3.8 (3.5, 4.0)</td>
<td>17.0 (16.1, 17.9)</td>
</tr>
<tr>
<td>Co-Use with Illicits</td>
<td>19.0 (17.8, 20.1)</td>
<td>3.8 (3.5, 4.0)</td>
<td>16.5 (15.6, 17.4)</td>
</tr>
<tr>
<td>Injection of pain reliever pills</td>
<td>1.6 (1.3, 1.9)</td>
<td>0.28 (0.21, 0.34)</td>
<td>2.8 (2.4, 3.1)</td>
</tr>
</tbody>
</table>

DAST-10 Category

- None, 0: 32.3 (70.4, 43.4)
- Low, 1-2: 50.3 (27.4, 39.7)
- Moderate, 3-5: 13.5 (1.7, 11.3)
- Substantial, 6-8: 3.9 (0.41, 0.33)
- Severe, 9-10: 1.1 (0.11, 0.06)

Mean DAST Score: 1.51 (0.40, 1.34)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Adults</th>
<th>No. Adults (%)</th>
<th>Adults</th>
<th>No. Adults (%)</th>
<th>Adults</th>
<th>No. Adults (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR Oxycodone</td>
<td>4,192,762</td>
<td>(96)</td>
<td>569,364</td>
<td>(14)</td>
<td>198,952</td>
<td>(5)</td>
</tr>
<tr>
<td>ER Oxycodone</td>
<td>2,388,787</td>
<td>(93)</td>
<td>339,715</td>
<td>(14)</td>
<td>115,941</td>
<td>(5)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>5,649,317</td>
<td>(96)</td>
<td>532,801</td>
<td>(10)</td>
<td>185,367</td>
<td>(3)</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>573,092</td>
<td>(87)</td>
<td>185,356</td>
<td>(32)</td>
<td>106,705</td>
<td>(19)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>580,896</td>
<td>(80)</td>
<td>149,046</td>
<td>(26)</td>
<td>107,220</td>
<td>(18)</td>
</tr>
<tr>
<td>Morphine</td>
<td>1,356,376</td>
<td>(97)</td>
<td>251,661</td>
<td>(18)</td>
<td>260,810</td>
<td>(19)</td>
</tr>
<tr>
<td>Tramadol</td>
<td>2,752,051</td>
<td>(96)</td>
<td>227,689</td>
<td>(8)</td>
<td>159,192</td>
<td>(6)</td>
</tr>
<tr>
<td>Codeine</td>
<td>3,563,103</td>
<td>(97)</td>
<td>275,683</td>
<td>(8)</td>
<td>164,890</td>
<td>(5)</td>
</tr>
</tbody>
</table>

- **HC**: Hydrocodone
- **IR Oxy**: Immediate Release Oxycodone
- **Codeine**: Codeine
- **Tramadol**: Tramadol
- **ER Oxy**: Extended Release Oxycodone
- **Morphine**: Morphine
- **OM**: Oral
- **HM**: Inhalation
- **Other**: Other routes

The diagram shows the comparison of Adults and No. Adults for different routes of administration (Oral, Inhalation, Injection, Other).
Drug Use in Pregnancy
NMURx, Q3 2018

• 228,291 (9.4% of pregnant women ages 18-49 years) used an illicit drug or non-medically used a prescription drug in the past month
  – Men 18.6%
  – Non-pregnant women ages are 16.5%.
  – Largely driven by illicit drug use (8.9%) specifically cannabis with past month use prevalence of 7.5%

• Prescription drug classes examined
  – 2.1% prevalence for stimulant NMU
  – 1.6% pain relievers
  – 1.5% sedatives
Summary

• Prescription drug abuse continues to decrease even as opioid deaths increase
• Methadone decreasing and buprenorphine increasing
• Abuse of prescription stimulants and other non-opioid drugs are increasing
• Anything that restricts the opioid drug supply will increase heroin abuse
• Illicit fentanyl is our biggest challenge
Transforming Post-Marketing Surveillance of Prescription Drugs

Richard C. Dart, MD, PhD

Executive Director, RADARS® System, Denver Health and Hospital Authority
President, Canadian Consumer Product and Pharmaceutical Safety Inc.

Project Lazarus: Local Solutions to National Opioid Crisis; What They Need to Know

Fred Wells Brason II, Chaplain

President and CEO, Project Lazarus
Speaker, U.S. Department of State U.S. Speaker Program,
The Bureau of International Information Programs
The Epidemiology of Prescription Opioid Abuse: A Regulatory Perspective

Gerald J. Dal Pan, MD, MHS

Director, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, US Food and Drug Administration
The Dead Speak: How Can Mortality Data Improve Drug Safety?

The Evolution of Mortality Data in the United States

Richard C. Dart, MD, PhD

Executive Director, RADARS® System, Denver Health and Hospital Authority
President, Canadian Consumer Product and Pharmaceutical Safety Inc.

Mortality Involving Prescription Drugs

Joshua C. Black, PhD

Associate Research Scientist, Rocky Mountain Poison & Drug Center, Denver Health and Hospital Authority
Lessons from Opana® ER: Policy, Behavior, and Reality

Janetta L. Iwanicki, MD

Scientific Director of Research and Surveillance, Rocky Mountain Poison & Drug Center, Denver Health and Hospital Authority
The Route to Utilization of Trend-in-Trend

Introduction: Remember Quinoa?

John Schwarz, PhD

Director of Biostatistics, Rocky Mountain Poison & Drug Center, Denver Health and Hospital Authority

Comment: Using Trend-in-Trend to Evaluate Drug Abuse

Rose Radin, PhD, MPH

Epidemiologist, Division of Epidemiology, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, United States Food and Drug Administration

Next Steps: Evaluating Routes and Comparators

John Schwarz, PhD
Drug Diversion in Healthcare Facilities: Our Nation’s Little Secret

John J. Burke

President, Pharmaceutical Diversion Education Inc.

President and Co-Founder, International Health Facility Diversion Association

Panel Discussion and Summary

Richard C. Dart, MD, PhD (Moderator)

Executive Director, RADARS® System, Denver Health and Hospital Authority

President, Canadian Consumer Product and Pharmaceutical Safety Inc.
End