Evolution of the Opioid Overdose Epidemic

Richard C. Dart, MD, PhD
Executive Director, RADARS® System
Denver Health and Hospital Authority
95 Registrants

- Government 26
- Academic 14
- Industry/Pharma 28
- Other 28

International Pre-Symposium

International Landscape of Prescription Medication Misuse

Betsy Nugent
RADARS System
Scientific Advisory Board

Principal Investigators

Theodore J. Cicero, PhD
Washington University in St Louis

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Nova Southeastern University

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American Association for the Treatment of Drug Dependence

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George Woody, MD
University of Pennsylvania

Epidemiology/Biostatistics

Nabarun Dasgupta, MPH
Rocky Mountain Poison & Drug Center, Denver Health

Law Enforcement

John Burke
Pharmaceutical Diversion Education, Inc.; International Health Facility Diversion Association
Petty died at 66 of "cardiopulmonary arrest due to: fentanyl, oxycodone, temazepam, alprazolam, citalopram, acetylfentanyl, and despropionyl fentanyl."

Artist: Jason Mecier
ARS Question

- Which of these celebrities died from fentanyl contained in a counterfeit medication?
  - Heath Ledger
  - Michael Jackson
  - Tom Petty
  - Whitney Houston
Fentanyl deaths now outpace prescription painkiller overdoses, study finds

Counterfeit hydrocodone tablets seized in the investigation of a rash of fentanyl overdoses in northern California in April 2016. / REUTERS/DRUG ENFORCEMENT ADMINISTRATION
What Happened in 2017?

Figure 4. Age-adjusted drug overdose death rates, by opioid category: United States, 1999–2016
**T40.2 National and semisynthetic opioids: oxycodone, morphine, hydromorphone, oxymorphone, others**

**RADARS System opioids: oxycodone, hydrocodone, morphine, hydromorphone, and oxymorphone.**

Deaths include cases followed to a known medical outcome whose death was related to the reported
Opioid Prescribing Declining Since 2010

Source: IQVIA National Prescription Audit, data extracted 2016-2018

NVSS Synthetic

NVSS Nat/Semi

NVSS Nat/Semi w/o Heroin/Fent

NVSS Deaths Per 100,000 population

Graph showing the increase in deaths per 100,000 population from 2006 to 2016.
Deaths from Prescription Opioids are Decreasing Substantially

NVSS Deaths Per 100,000 population

PC Deaths Per 100,000 population

NVSS – Heroin T40.1 + Synth T40.4

NVSS – Nat/Semi

NVSS – Nat/Semi w/o Fent-Heroin

PC - Nat/Semi
NEWS FROM RADARS SYSTEM
Mosaic Surveillance of Prescription Drug Abuse

- **Acute Health Events**: 50 Poison centers, 48 states, 616,410 opioid cases, 664,943 opioid mentions.

- **Entering Treatment**: Opioid Tx Program, 115 programs; 37 states, 79,299 respondents, 266,082 Rx opioid mentions.

- **Entering Treatment**: SKIP practices, 49 states, 19,247 respondents, 107,518 Rx opioid mentions.

- **Non-Medical Use**: General population, 30,522 adults; 50 states, 3,693 cases with 38,996 opioid mentions.

- **Drug Transactions**: Criminal Justice, 664 agencies; 50 states, 12,881 unique surveys, >199,000 cases, 171,179 opioid mentions.

- **Illicit Market Price**: StreetRx.com Users/Buyers, 50 states, 90,396 price entries for an opioid.

- **Web Monitoring**: >150 million sites monitored, >197,000 posts coded for analysis.

- **Advanced Users/Targeted Studies**: RAPID Customized surveys to address special topics with patients who have sought treatment.

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Poison Center Program
All Opioids, Intentional Abuse, 2006 - 2017

Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol
Drug Diversion Program
All Opioids, Diversion, 2006 - 2017

Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol
Treatment Center Programs Combined
All Opioids, Abuse, 2006 - 2017

Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol
Poison Center Program
API, 2006-2017

Per 100,000 population

Methadone

HC

Oxycodone
Fentanyl
Hydrocodone
Hydromorphone
Morphine
Oxymorphone
Methadone
Buprenorphine
Tramadol
Tapentadol
Drug Diversion Program
API, 2006-2017

Per 100,000 population

- Oxycodone
- Fentanyl
- Hydrocodone
- Hydromorphone
- Morphine
- Oxymorphone
- Methadone
- Buprenorphine
- Tramadol
- Tapentadol

HC

Methadone

Bup
Changes in Prescription Drug Abuse, 2017

• After substantial improvement from 2010 to 2016, abuse and diversion seem to have plateaued.
  – Buprenorphine a concern?
    • Generally safer than methadone
  – Rescheduling of hydrocodone effective although seems to have affected oxycodone abuse

• Lots of room for improvement

• How do we do that without compromising the care of pain patients?
Poison Center Program
Prescription Stimulant Rates, 2007 - 2017

Per 100,000 population

- Methylphenidate
- Amphetamine
Drug Diversion Program
Prescription Stimulant Rates, 2007 - 2016

Per 100,000 population

20073 20084 20101 20112 20123 20134 20151 20162 20173

Methylphenidate
Amphetamine

[Graph showing the prescription stimulant rates for Methylphenidate and Amphetamine per 100,000 population from 2007 to 2016]
Poison Center Program
Route of Administration, 3Q 2017

Use via inhalation

% Int. Abuse Cases

Use via injection

Methylphenidate Amphetamines Oxycodone Hydrocodone
1. Trends in intentional abuse or misuse of benzodiazepines and opioid analgesics and the associated mortality reported to poison centers across the United States from 2000 to 2014.


3. Racial/ethnic differences in prevalence trends for heroin use and non-medical use of prescription opioids among entrants to Opioid Treatment Programs, 2005-2016. *Subst Use Misuse*


8. The demand side of the prescription opioid epidemic: does the initial source of opioids matter? *Drug Alcohol Depend*.

9. Increased use of heroin as an initiating opioid of abuse. *Addict Behav*.

10. Increases in self-reported fentanyl use among a population entering drug treatment. *Drug Alcohol Depend*.

11. Psychoactive substance use prior to the development of iatrogenic opioid abuse: analysis of opioid abusers. *Addict Behav*.


### National Poison Data System (NPDS) 2007-2014

<table>
<thead>
<tr>
<th>Generic Code</th>
<th>Intentional Abuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>51275</td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td>18182</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>13833</td>
</tr>
<tr>
<td>Carisoprodol</td>
<td>8633</td>
</tr>
<tr>
<td>Atypical Antipsychotics</td>
<td>8556</td>
</tr>
<tr>
<td>Other Sedative/Hypnotic/Anti-Anxiety or Anti-Psychotic</td>
<td>8150</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>5927</td>
</tr>
<tr>
<td>Other SSRI</td>
<td>5185</td>
</tr>
<tr>
<td>Other Antihistamines</td>
<td>5155</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>3662</td>
</tr>
<tr>
<td>Other Antidepressant</td>
<td>3173</td>
</tr>
<tr>
<td>Trazodone</td>
<td>3124</td>
</tr>
<tr>
<td>Other Muscle Relaxant</td>
<td>2989</td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>2948</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>1373</td>
</tr>
<tr>
<td>Phenothiazines</td>
<td>1288</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>1271</td>
</tr>
<tr>
<td>Clonidine</td>
<td>1159</td>
</tr>
</tbody>
</table>
Cicero TJ, Ellis MS, Kasper ZA. Increases in self-reported fentanyl use among a population entering drug treatment: the need for systematic surveillance of illicitly manufactured opioids. *Drug Alcohol Depend.*
Summary

1. Abuse of prescription stimulants and other non-opioid drugs may be increasing
2. Non-oral routes of abuse surprisingly high for prescription stimulants
Abuse of other drugs is on the rise
Illicit fentanyl is our biggest challenge
Survey of Non-Medical Use of Rx Drugs (NMURx) Coverage

- UK: 3Q14
- Singapore: 3Q15
- US, Canada: 3Q16
- France, Italy: 2Q17
- Germany, Spain: 4Q17
Survey of Non-Medical Use of Prescription Drugs (NMURx)

• An online, cross-sectional survey that assesses prescription drug use in the general adult population
• 10,000 - 30,000 unique individuals twice annually
• Same survey
  – Canada
  – United Kingdom
  – Germany
  – France
  – Spain
  – Italy
# Survey of Non-Medical Use of Prescription Drugs (NMURx) and National Survey of Drug Use and Health (NSDUH)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NMURx 2016</th>
<th>NSDUH 2015</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Weighted N=247,773,709 % (95% CI)</td>
<td>Weighted N=242,801,072 % (95% CI)</td>
</tr>
<tr>
<td>18-25 yrs</td>
<td>13.9 (13.4-14.4)</td>
<td>14.4 (14.1-14.7)</td>
</tr>
<tr>
<td>26-34</td>
<td>16.5 (16.1-16.9)</td>
<td>15.8 (15.4-16.2)</td>
</tr>
<tr>
<td>35-49</td>
<td>24.4 (23.9-24.9)</td>
<td>24.9 (24.3-25.4)</td>
</tr>
<tr>
<td>50-64</td>
<td>25.9 (25.4-26.4)</td>
<td>25.7 (25.0-26.4)</td>
</tr>
<tr>
<td>65+</td>
<td>19.3 (18.8-19.7)</td>
<td>19.2 (18.6-19.9)</td>
</tr>
<tr>
<td>Gender - Female</td>
<td>51.3 (50.7-51.9)</td>
<td>51.8 (51.1-52.5)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>77.1 (76.6-77.7)</td>
<td>64.7 (64.1-65.4)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>7.2 (6.8-7.5)</td>
<td>11.8 (11.4-12.2)</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>0.6 (0.5-0.7)</td>
<td>0.5 (0.4-0.6)</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
<td>3.6 (3.4-3.8)</td>
<td>5.5 (5.1-5.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8.9 (8.5-9.2)</td>
<td>15.6 (15.1-16.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5.9 (5.6-6.2)</td>
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### Survey of Non-Medical Use of Prescription Drugs (NMURx) and National Survey of Drug Use and Health (NSDUH)

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<th>Residential Region</th>
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<tr>
<td>Northeast</td>
<td>17.9 (17.4-18.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Midwest</td>
<td>21.1 (20.6-21.6)</td>
<td>NA</td>
</tr>
<tr>
<td>South</td>
<td>37.5 (36.9-38.1)</td>
<td>NA</td>
</tr>
<tr>
<td>West</td>
<td>23.5 (23.0-24.0)</td>
<td>NA</td>
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<table>
<thead>
<tr>
<th>Total Household Income</th>
<th>NMURx 2016</th>
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<tbody>
<tr>
<td>&lt; $20,000</td>
<td>12.4 (12.0-12.8)</td>
<td>17.9 (17.3-18.4)</td>
</tr>
<tr>
<td>$20,000-49,999</td>
<td>29.5 (29.0-30.1)</td>
<td>30.0 (29.4-30.7)</td>
</tr>
<tr>
<td>≥$50,000</td>
<td>52.2 (51.6-52.8)</td>
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</tr>
</tbody>
</table>

| Student Enrollment‡   | 11.1 (10.7-11.6)    | 8.4 (8.1-8.7)       |
| Current Healthcare Professional | 5.1 (4.9-5.4) | NA               |
| Served in Armed Forces | 10.6 (10.3-10.9)   | 9.1 (8.7-9.6)      |
| Lifetime Substance Abuse Treatment§ | 6.3 (6.0-6.6) | 6.2 (5.9-6.5)     |
Survey of Non-Medical Use of Prescription Drugs (NMURx) and National Survey of Drug Use and Health (NSDUH)
NMURx: Opioids, BDZ, Stimulants, GABA, Illicit Drugs, 2017 Q3
Non-Medical Use Around the World, 2017

% Respondents

- Pain Reliever Use
- Pain Reliever NMU
Non-Medical Use Around the World, 2017

% Respondents

Rx Stim Use
Rx Stim NMU
Effectiveness of ADFs in the Real World

Richard C. Dart, MD, PhD

Executive Director, RADARS System, Denver Health and Hospitals
Professor, University of Colorado School of Medicine

Abuse Deterrent Formulations of Prescription Opioid Analgesics

Hon. Earl “Buddy” Carter

U.S. Representative (R-GA, 1st District)
Understanding Changes in the US ‘Heroin’ Market: Notes from the Field

Dan Ciccarone MD, MPH

Professor of Family and Community Medicine, UCSF
Principal Investigator, Heroin in Transition Study (NIH/NIDA)

The Illicit Injection of Prescription Opioids—Risks and Rewards

Jon E. Zibbell, PhD
Senior Public Health Scientist – Behavioral Health, RTI International
Getting to Category IV
FDA’s Current Approach to the Postmarket Evaluation of Opioid Analgesic Products with Properties Intended to Deter Abuse

Tamra E. Meyer, PhD, MPH
Lead Epidemiologist, Division of Epidemiology II, Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, Food and Drug Administration

A Causal Approach to Understanding Abuse in the Community

Nabarun Dasgupta, MPH, PhD
Senior Scientist – RADARS System, Denver Health and Hospitals

John Schwarz, PhD
Director of Biostatistics – RADARS System, Denver Health and Hospitals
Thinking Outside the Opioid Box: Non-Opioid Pharmaceutical Abuse

Janetta L. Iwanicki, MD

Associate Medical Director – Rocky Mountain Poison & Drug Center, Denver Health and Hospital Authority

Panel Discussion and Summary
End