Thursday, May 13, 2021

Postmarketing Surveillance: What’s the Next Move?
RADARS® System 15th Annual Scientific Meeting

Registrants n=131

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<td>Other</td>
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</table>
RADARS® System - Scientific Advisory Board

Principal Investigators

Theodore J. Cicero, PhD
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Pharmaceutical Diversion Education, Inc.; International Health Facility Diversion Association
RADARS® System Publications

- Citations Per Year
- Cumulative Citations
- Number of RADARS® Publications Per Year
News from RADARS® System

Monthly drug overdose deaths

Real World Evidence and Triangulation

Triangulation
More reliable answers by integrating results from several different approaches, each with different and unrelated key sources of potential bias.

Acute Health Effects
Substance Use Treatment
Drug Diversion
Population Survey
Street Price
Web Discussion
Mortality

SUBSTANCE ABUSE

Prescribing of Prescription Stimulants

Number of Stimulant Prescriptions Combined, 2020

The stimulants - amphetamine and related, methylphenidate, and modafinil

Source: IQVIA™ US-Based Longitudinal Prescription Data
Prescribing of Amphetamine, Methylphenidate

Number of Amphetamine Prescriptions, 2020

Number of Methylphenidate Prescriptions, 2020

Source: IQVIA™ US-Based Longitudinal Prescription Data
What is an “Endorsement”?

• Person endorses use of the drug
  – Not necessarily that they thought the drug was good
Non-Medical Use of Rx Stimulants, NMURx Program, 2018 - 2020

Cases per 100,000 Adults

NMURx Program

- Amphetamine
- Atomoxetine
- Modafinil
- Methylphenidate
RADARS System, Rx Stimulant Rates, 2008 - 2020

Poison Center Program

Cases per 100,000 population

Drug Diversion Program

2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020

2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
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2020

2008
2009
2010
2011
2012
2013
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2015
2016
2017
2018
2019
2020

Amphetamine
Methylphenidate

Amphetamine
Methylphenidate
Mortality related to medical stimulants is rising rapidly alongside illicit substances like cocaine and methamphetamine.

Interaction of Licit and Illicit Pharmaceuticals
Trends in Annual Opioid Prescribing Rates

Source: IQVIA™ US-Based Longitudinal Prescription Data
Non-Medical Use of Opioids, NMURx Program, 2018 - 2020

- Rx Opioids
- Heroin
- Illicit Fentanyl

Per 100,000 population

Yearly breakdown:
- 2018q3
- 2019q1
- 2019q3
- 2020q1
- 2020q3

Rx Opioids:
- Buprenorphine
- Fentanyl
- Hydromorphone
- Hydrocodone
- Methadone
- Morphine
- Oxymorphone
- Oxycodone
- Tramadol
Poison Center Program, Intentional Abuse, 2006 - 2020

Per 100,000 population

Includes:
- Buprenorphine
- Hydrocodone
- Hydromorphone
- Methadone
- Morphine
- Oxycodone
- Oxymorphone
- Tapentadol
- Tramadol

Includes:
- Oxycodone
- Hydrocodone
- Hydromorphone
- Morphine
- Oxymorphone
- Methadone
- Buprenorphine
- Tramadol

HC CII
Drug Diversion Program, 2006 - 2020

Invest. Opened Per 100,000 population

Includes:
- Buprenorphine
- Hydrocodone
- Hydromorphone
- Methadone
- Morphine
- Oxycodone
- Oxymorphone
- Tapentadol
- Tramadol

Oxycodone
Hydrocodone
Hydromorphone
Morphine
Methadone
Buprenorphine
Tramadol
Oxymorphone
Treatment Center Programs Combined, 2008 - 2020

Includes:
- Buprenorphine
- Hydrocodone
- Hydromorphone
- Methadone
- Morphine
- Oxycodone
- Oxymorphone
- Tapentadol
- Tramadol

Endorse. Per 100,000 population
Is Oxycodone Surging?
Oxycodone – Summary of Mosaic Evaluation

API-level Analysis of Oxycodone

- NMURx: Flat
- Treatment Centers: ↓↓
- Oxycodone API
- Diversion: ↓↓
- StreetRx: $1/mg Trend Flat
- Web Monitor: No change

Formulation-level Analysis of Oxycodone

- NMURx: Flat
- PC: ↑↑↑
- Treatment Centers: ↓↓
- By Formulation
- StreetRx: IR>>ER Trend Flat
- Web Monitor: No change
- Diversion: Flat
Postmarketing Surveillance of “Small” Drugs

- How do we interpret drugs with low exposure (low prescription volume)
  - Sufentanil
  - Esketamine
  - MDMA (Ecstasy)
  - Oxymorphone
- Any drug will garner a small number of endorsements
  - Careless endorsements
  - Innate variability
- What is the relation between drugs with low prescription volumes and use?
Quantifying the Relation: Rx Dispensing and Estimates of NMU

• **Methods**
  • Data source – NMURx Program
  • 37 API
  • Joinpoint regression
  • Test – Retest to estimate reliability

• **Results**
  • 4 waves: 106,404 respondents
  • Demographics stable

<table>
<thead>
<tr>
<th>Pain Relievers</th>
<th>Sedatives</th>
<th>Stimulants</th>
<th>Cannabinoids</th>
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<td>Buprenorphine</td>
<td>Alprazolam</td>
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<tr>
<td>Codeine</td>
<td>Baclofen</td>
<td>Methylphenidate</td>
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<td>Oxazepam</td>
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<td>Quazepam</td>
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<td>Tramadol</td>
<td>Zaleplon</td>
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Black, *et al.* Results

Validity of Model

Number Adults Used/Year

Prescriptions Dispensed/Year

Intercept: 170 Adults

High Volume vs. Low Volume Pharmaceuticals

- Higher Volume Pharmaceuticals (above threshold)
  - Quantitative prevalence and trend analysis
- Lower Volume Pharmaceuticals (below threshold)
  - Non-representative national sample
  - Analyze individual cases
  - Qualitative methods
  - Example oxymorphone
- Contact individuals in f/u to Poison Center, NMURx, and Survey of Key Informants’ Patients Programs
2021 Program

Postmarketing Surveillance: What’s the Next Move?

Richard C. Dart, MD, PhD

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

Meeting the Challenges of COVID-19 in Postmarketing Surveillance

Janetta L. Iwanicki, MD

Chief Scientific Officer, Research and Consulting, Rocky Mountain Poison & Drug Safety, Denver Health and Hospital Authority
Defining Populations of Interest for Postmarketing Studies

Nabarun Dasgupta, PhD

Senior Scientist and Innovation Fellow, Gillings School of Global Public Health, University of North Carolina in Chapel Hill
Consultant – RADARS® System

The Rest of the Story: Other Drugs Misused in the United States

Janetta Iwanicki, MD

Chief Scientific Officer, Research and Consulting, Rocky Mountain Poison & Drug Safety, Denver Health and Hospital Authority
Prescribing and Over-The-Counter Drugs; A Vast Range of Misusing Opportunities

Professor Fabrizio Schifano
Chair in Clinical Pharmacology and Therapeutics
Consultant Psychiatrist (Addictions); Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit, School of Life and Medical Sciences, University of Hertfordshire, UK

Understanding Stimulant Use in the General Population: Prevalence and Patterns of Non-Medical Use

Joshua C. Black, PhD
Senior Research Scientist, Rocky Mountain Poison & Drug Safety, Denver Health and Hospital Authority
It’s Not Easy Being Buprenorphine: Identifying Unique Substance Use Patterns Associated with Buprenorphine

Matthew Ellis, PhD(c)

*Principal Investigator, RADARS® System Survey of Key Informants’ Patients*
*Research Faculty Instructor, Washington University School of Medicine*

Changes in Diversion of Buprenorphine and Gabapentin in the U.S.

Mance E. Buttram, PhD

*Associate Professor, Nova Southeastern University*
*Associate Director, Center for Applied Research on Substance Use and Health Disparities*
FDA’s Holistic Approach to Addressing Polysubstance Use and the Drug Overdose Crisis

Marta Sokolowska, PhD
Associate Director for Controlled Substances, Office of the Center Director, Center for Drug Evaluation & Research, Food & Drug Administration

Panel Discussion and Summary