Surveillance of Psychoactive Drugs
Opioids, Psychedelics, and Cannabinoids

Wednesday, May 10, 2023
Surveillance of Psychoactive Drugs

- 2022 Annual RADARS® System review
  - Data
  - Methods and Changes
- New Challenges for PM surveillance of Prescription Drugs
  - Counterfeit or Falsified medications
  - Emergence of the psychedelic medications
RADARS® System Update
2006 through 2022
Registrants n=228

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government</td>
<td>51</td>
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<tr>
<td>Academic</td>
<td>128</td>
</tr>
<tr>
<td>Industry/Pharma</td>
<td>31</td>
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<tr>
<td>Other</td>
<td>18</td>
</tr>
</tbody>
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Thanks everyone for your interest (and your questions/comments) as we go through the meeting!
RADARS® System Publications - 2022

Citations Per Year
Cumulative Citations
Number of RADARS® Publications Per Year
RADARS® System: Real World Evidence and Triangulation
### Highlights - RADARS System Improvement 2020-2022

<table>
<thead>
<tr>
<th>Update</th>
<th>Description</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC Program</td>
<td>Improved quality review with industry best practices</td>
<td>2022</td>
</tr>
<tr>
<td>Treatment Centers</td>
<td>Created, validated and applied careless response process to exclude obvious fraudulent responses</td>
<td>2018</td>
</tr>
<tr>
<td>NMURx</td>
<td>Refined drug list to focus responses and control length of questionnaire</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>Created methods to follow-up with hard-to-reach populations</td>
<td>2020</td>
</tr>
<tr>
<td>Drug Diversion</td>
<td>Improved DBQA process, streamlined process for reporting</td>
<td>2022</td>
</tr>
<tr>
<td>StreetRx</td>
<td>Reorganized and categorized datasets to improve accuracy of analysis</td>
<td>2021</td>
</tr>
<tr>
<td>Web Monitoring</td>
<td>Implemented machine learning to identify invalid posts</td>
<td>2022</td>
</tr>
<tr>
<td></td>
<td>Implemented Dark Web tracking</td>
<td>2021</td>
</tr>
<tr>
<td></td>
<td>Created methodology for tampering “recipe-tracker”</td>
<td>2020</td>
</tr>
</tbody>
</table>
Drug-related Overdose Deaths in US, 2015-2022

Number of Deaths

10,000
20,000
30,000
40,000
50,000
60,000
70,000
80,000
90,000
100,000


Opioids
- Synthetic Opioids excl methadone
- Psychostimulants Cokeine
- Natural & Semisynth Heroin Methadone

Products - Vital Statistics Rapid Release - Provisional Drug Overdose Data (cdc.gov)
Trends in Opioid Prescribing Rates, 2010 - 2022

Source: IQVIA™ US-Based Longitudinal Prescription Data
NMURx, Non-Medical Use of Opioids, 2019 - 2022

*Drug NMU questions were redesigned for 2022 Q1 and Q3 surveys for better assessment of unknown formulations
Poison Center Program, Intentional Abuse
2012 - 2021

Major Opioids Combined

Per 100,000 population

Includes oxycodone, hydrocodone, hydromorphone, morphine, tramadol

COVID

Individual API Opioids

Oxycodone
Fentanyl
Hydrocodone
Hydromorphone
Morphine
Methadone
Buprenorphine
Tramadol
Tapentadol

COVID
Treatment Center Programs Combined
2012 - 2022

Major Opioids Combined

Endorse Per 100,000

Oxycodone, hydrocodone, hydromorphone, morphine, tramadol

COVID

Individual API Opioids

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

COVID
Drug Diversion Program
2012 - 2022

**Major Opioids Combined**

Invest. Opened Per 100,000 population

oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol

**Individual API Opioids**

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

COVID
Prescribing of Stimulants
2010 - 2022

Source: IQVIA™ US-Based Longitudinal Prescription Data
NMURx, Non-Medical Use of Rx Stimulants 2019 - 2022

Number Adults Who NMU

- Amphetamines
- Methylphenidate
- Atomoxetine
- Modafinil

COVID
Poison Center Program, Rx Stimulants
2012 - 2021

Cases per 100,000 population

Amphetamine

Methylphenidate

COVID
Drug Diversion Program, Rx Stimulants
2012 - 2022

Invest. per 100,000 population

Amphetamine

Methylphenidate

COVID
Summary of Trends through 2022

• Prescribing, use and misuse of prescription opioids
  – Improved, but still a substantial source of drug that is misused/abused.
• Prescribing, use and misuse of prescription stimulants are similar although amphetamine is still gradually rising.
• Illicit opioids and stimulants remain dominant in terms of abuse and mortality.
• If we take our eye off the ball, Rx medications will worsen.
Challenges Ahead
Challenges Ahead

- Counterfeit/Falsified Drugs
- Psychedelic medications
Falsified Drugs in RADARS Drug Diversion Program

Invest. Opened Per 100,000 population

RADARS System Drug Diversion Program

- Other oxycodone
- Other known IR oxycodone

https://www.dea.gov/onepill
Use of Falsified Drugs in the US Among People Who Endorse Drug Diversion

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Falsified Products % (95%)</th>
<th>NMU of Rx Opioids/Stimulants % (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Prevalence</td>
<td>1.8 (1.7, 1.9)</td>
<td>6.7 (6.4, 6.9)</td>
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<tr>
<td>Male</td>
<td>62.8 (59.4, 66.2)</td>
<td>52.4 (50.5, 54.2)</td>
</tr>
<tr>
<td>18-24 yrs of age</td>
<td>22.7 (18.9, 26.5)</td>
<td>12.3 (10.7, 14.0)</td>
</tr>
<tr>
<td>Bachelor/higher</td>
<td>48.1 (44.6, 51.7)</td>
<td>44.7 (42.8, 46.5)</td>
</tr>
<tr>
<td>Current HCP</td>
<td>20.8 (18.3, 23.3)</td>
<td>6.2 (5.3, 7.1)</td>
</tr>
<tr>
<td>DAST Score 3+</td>
<td>36.5 (33.2, 39.8)</td>
<td>10.3 (9.1, 11.4)</td>
</tr>
</tbody>
</table>

Users of Falsified Products
- Lower prevalence
- Male
- Younger
- + Current HCP
- Higher DAST

Research supported by the US Food and Drug Administration (FDA) award 75F40120C00151
Perceptions and Identification of Counterfeit Medications by Adults Using Diverted Drugs

• Goal
  • Describe how counterfeit drugs are identified and used in people who endorse diverted drugs

• Methods
  • Mixed method design using the RADARS® System NMURx methodology to identify a cohort of users of diverted drugs.

30,003 total respondents
2022 Q3 NMURx survey
  1992
Endorsed Use of Diverted Drug - NMURx
  257
  Took the NMURx Express survey
  82
Encountered a suspected falsified drug
Wall Street Backs New Class of Psychedelic Drugs

Psychedelic-therapy industry gets a reality trip as investors focus on treatments costing less time and money

By Matt Wirz
Feb. 23, 2023
Psychedelic Clinical Trials: Count 1994-2020 (excludes ketamine)

Alex Belser, Yale University Founding President, Nautilus Sanctuary Chief Clinical Officer, Adelia Therapeutics Chief Clinical Advisor, Cybin https://isctm.org/public_access/17th_Annual/Presentation/Belser_Session2.pdf
MDMA TRIALS: CLINICAL DEVELOPMENT

Source: ClinicalTrials.gov, Accessed 5/16/22
The Rise of the Psychedelic Medications

- Smoking cessation
- Alzheimer's
- Anorexia nervosa
- Depression and AUD
- Lyme disease
- Obsessive-Compulsive disorder
- Anxiety, depression, PTSD
- Romantic relationships

https://www.hopkinsmedicine.org/psychiatry/research/psychedelics-research.html
Many Addictive Medications Started Out as “Safer”

- Heroin
- Methadone
- Cocaine
- Amphetamine
- Traditional postmarketing surveillance takes years to detect adverse effects.
Turn on, Tune in, Drop Out

Respected Therapeutic Intervention? Dangerous Drug of Abuse?

Intentional Abuse of Psilocybin
US National Poison Data System, 2018 - 2022

Psychedelic Drugs

2018 2019 2020 2021 2022

Psilocybin

Ketamine
Ketamine
Special K, Green K, Super K, Super acid, Jet, and Cat Valium

The Benefits of Ketamine Therapy:

- Relatively safe: while ketamine does have some side effects (most notably, hallucinations), they are usually mild and short-lived.
- Few side effects when used in low doses; high doses of ketamine can cause serious side effects, such as coma or death.
- Fast-acting: it takes effect within minutes and lasts up to four hours.

https://treatmentindiana.com/
RADARS® System: Esketamine in 2022

Poison Center Program
Esketamine - No abuse/misuse reports
Ketamine - 47 abuse cases

Treatment Center Program
Esketamine - 2 cases, 0.0007938 cases/100,000
Ketamine: 61 cases, 0.02421 cases/100,000

Drug Diversion Program
Esketamine - no cases of diversion
Ketamine - 5 cases of diversion

NMURx
Esketamine - Prescriptions too low
Ketamine: National prevalence 0.19%

StreetRx
Esketamine – No reports
Ketamine - 35 cases entered

Web Monitoring
Esketamine: No reports
Ketamine: 91 reports

Mortality
Postmarket Surveillance of Psychedelics

- Patient
  - Treatment seeking vs. experience seeking
- Drug
  - Approved pharmaceutical product vs. illegal
- Provider
  - High school training vs. experience lay person vs. addiction psychiatrist
- Setting
  - Living room vs. religious setting vs. medical facility
The Heart of the Matter

RADARS® System Evidence Generators
- 51 US Poison Centers
- 150 Treatment Centers
- 197 Drug Diversion Programs
- 60,000 respondents NMURx

The RADARS® System Team Members
- Kate Reynolds, Research Director
- Joshua Black, PhD
- Rick Olson, MA
- Jennifer Jewell, PhD
- Kari Rockhill, PhD
- Numerous chart reviewers, data managers
- Nabarun Dasgupta, PhD
- Andrew Monte, MD, PhD
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President, Canadian Consumer Product and Pharmaceutical Safety Inc.

Professor of Emergency Medicine, Medical Toxicology and Pharmacology, University of Colorado

Surveillance of Psychoactive Drugs
Opioids, Psychedelics, and Cannabinoids
Application of socioecological framework of drug abuse to psychedelic drugs

Mohammad Jalali, PhD
Assistant Professor, Harvard Medical School
Senior Lecturer, MIT Sloan
Policy Needs to Address the Safety of Psychedelic Drugs

Brian Anderson, MD, MSc

Assistant Clinical Professor, UCSF

Principal Investigator, Community Uses of Psychedelics and Safety Study (FDA)
Assessing Polysubstance Use of Licit (Gabapentin, Xylazine) and Illicit Substances

Sandra Comer, PhD

Professor of Neurobiology, Columbia University

Director the Opioid Laboratory in the Division of Substance Use Disorders
Cannabis: Lessons Learned from Public Experience in Colorado

Mike Van Dyke, PhD, CIH
Associate Professor, Center for Health, Work & Environment
Department of Environmental and Occupational Health
Colorado School of Public Health, CU Anschutz Medical Campus
Fireside Chat: The Evidence Generation System in Postmarket Surveillance

Robert M. Califf M.D., MACC
Commissioner of Food and Drugs, Food and Drug Administration
Defining Polysubstance Use in a National Population-based Survey

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Biostatistician III
Rocky Mountain Poison & Drug Safety
Satisfying the Craving for Novel Psychoactive Post-Market Surveillance

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