

RADARS[®] SYSTEM

11th ANNUAL SCIENTIFIC MEETING

**Beyond the Label:
Prescription Opioid Abuse
May 12, 2017**

**Welcome
RADARS[®] System 2017**



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



RADARS System

11th Annual Scientific Meeting

105 Registrants

- Government 33
- Academic 26
- Industry/Pharma 35
- Other 11



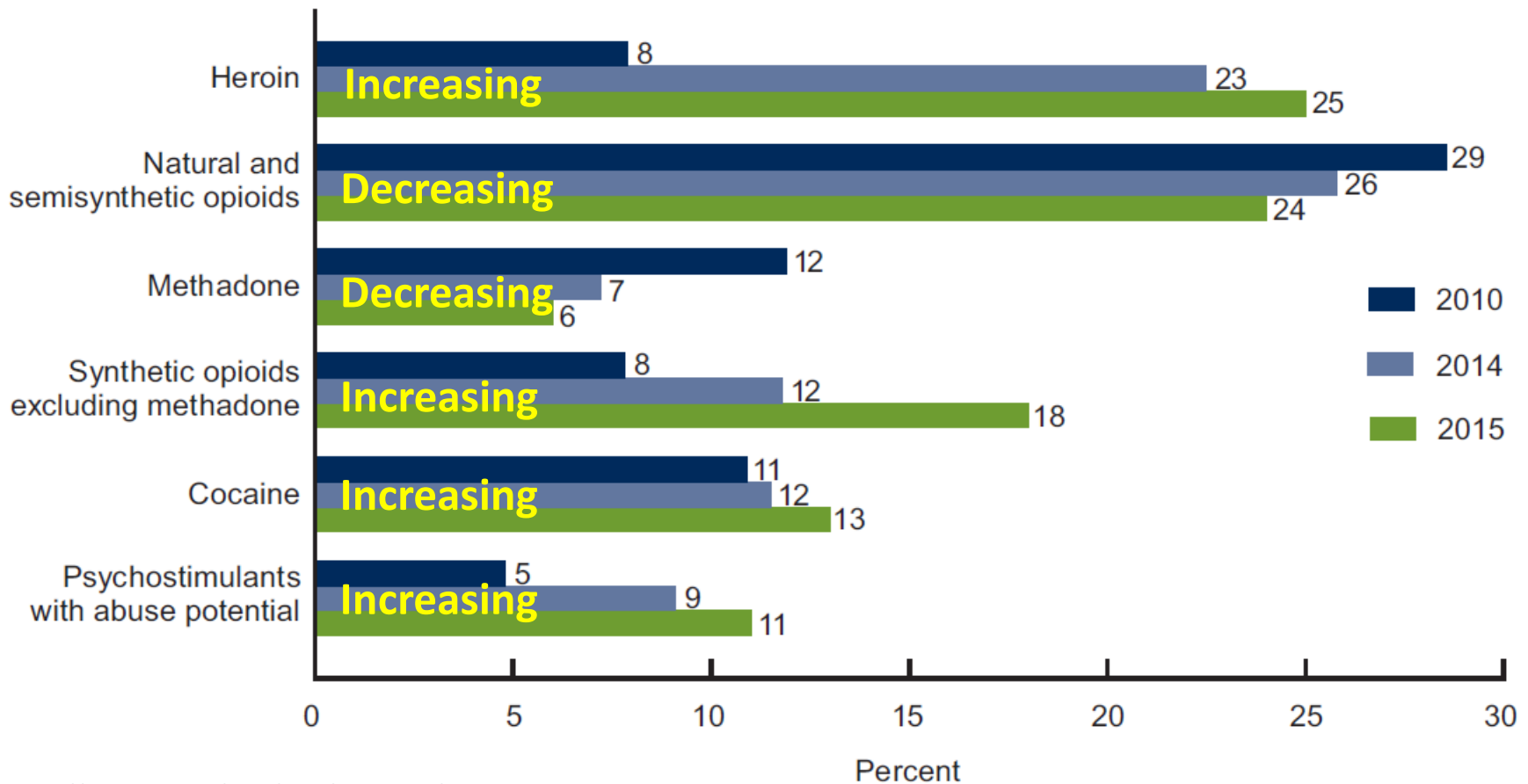
International Pre-Symposium

Global Insights in Prescription Drug Misuse



2016: A Year That Will Go Down in History

% Drug Overdose Deaths Involving Selected Drugs: 2010, 2014, 2015



<https://www.cdc.gov/nchs/data/databriefs/db273.pdf>

What Else Happened in 2016?

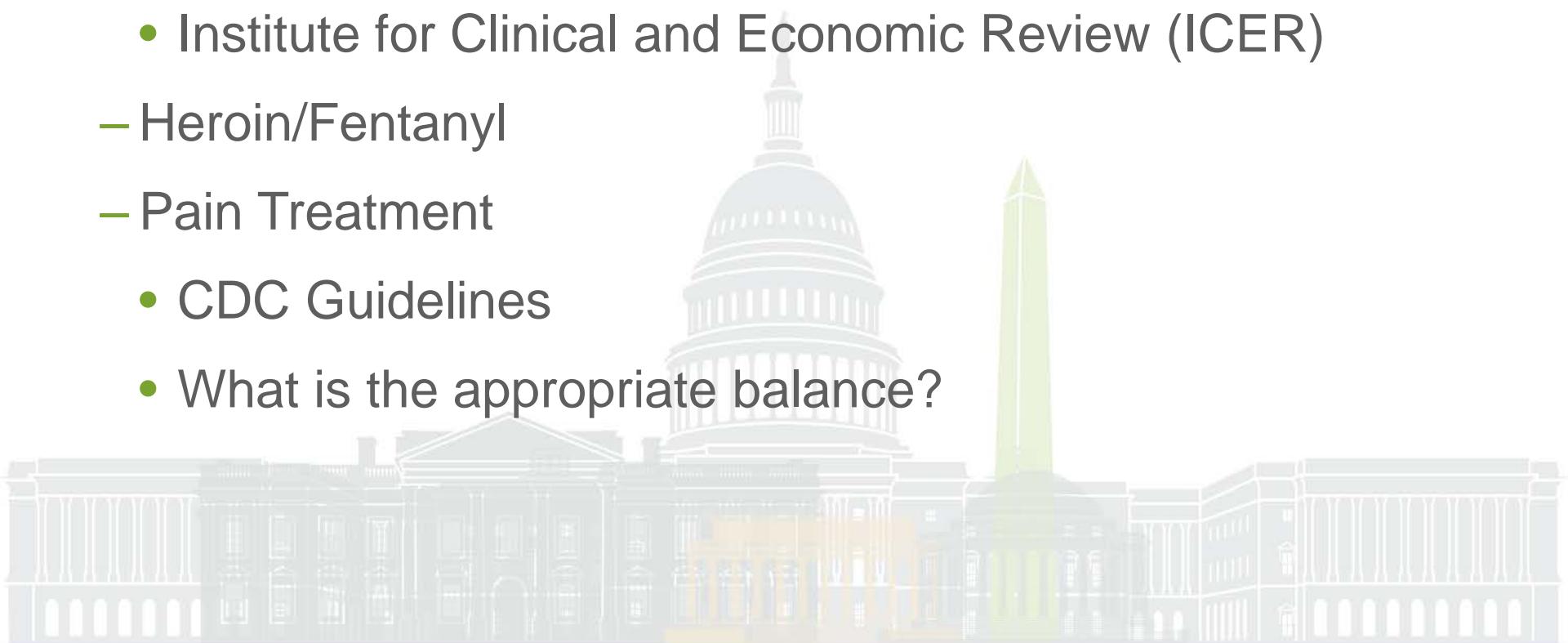
– ADFs

- Adcoms galore: Opana ER, RoxyBond and beyond
- FDA will continue to approve drugs with ADF
- Institute for Clinical and Economic Review (ICER)

– Heroin/Fentanyl

– Pain Treatment

- CDC Guidelines
- What is the appropriate balance?



RADARS[®] System

Scientific Advisory Board

Principal Investigators

Theodore J. Cicero, PhD
Washington University in St Louis



Richard C. Dart, MD, PhD
*Rocky Mountain Poison
& Drug Center, Denver Health*

Steven P. Kurtz, PhD
Nova Southeastern University



Mark W. Parrino, MPA
*American Association for the Treatment
of Drug Dependence*



Jody L. Green, PhD, CCRP
*Rocky Mountain Poison
& Drug Center, Denver Health*



Substance Abuse Experts

Herbert D. Kleber, MD
Columbia University



Sidney Schnoll, MD, PhD
PinneyAssociates



George Woody, MD
University of Pennsylvania



Epidemiology/Biostatistics

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

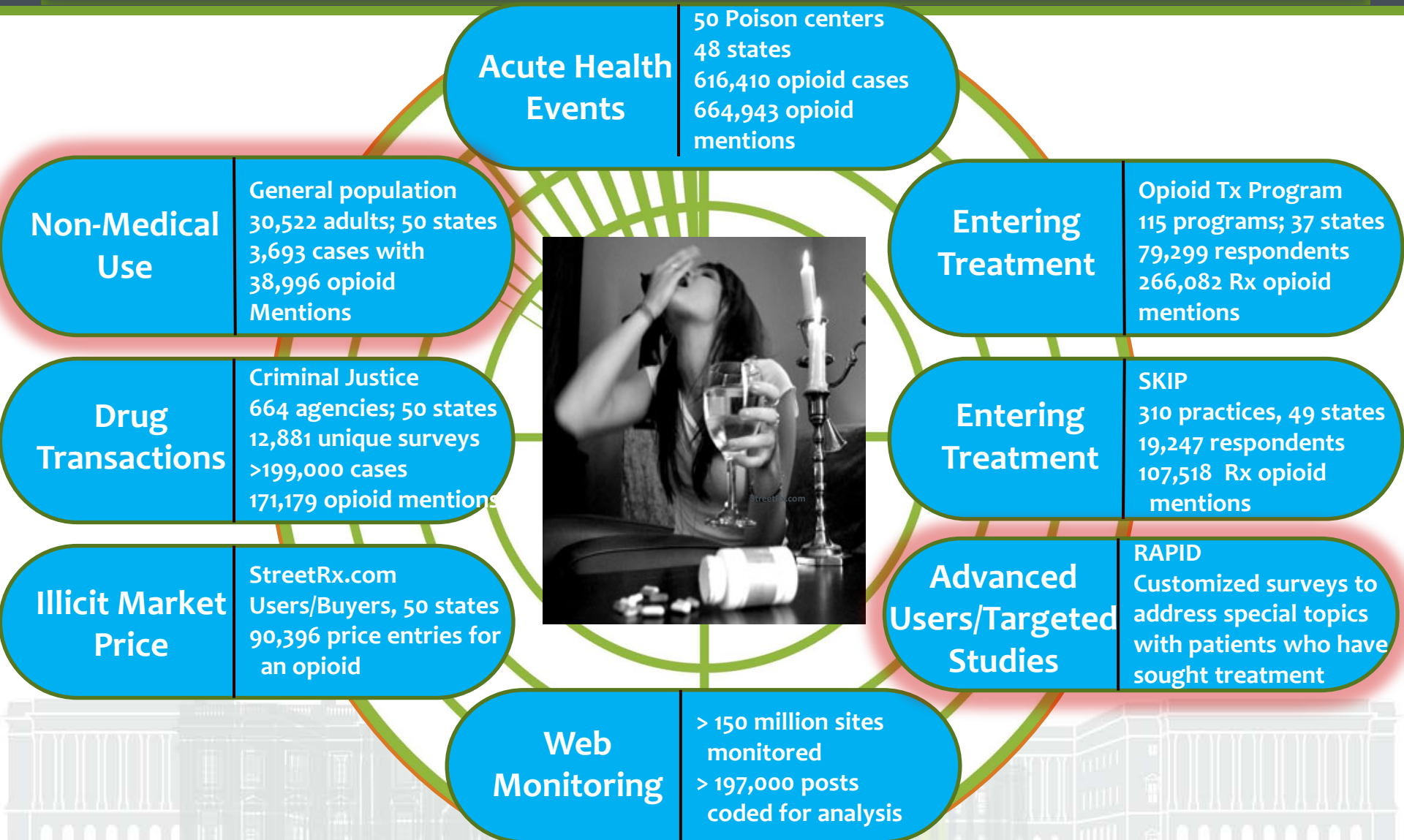


Law Enforcement

John Burke
*Pharmaceutical Diversion Education,
Inc.; International Health Facility
Diversion Association*

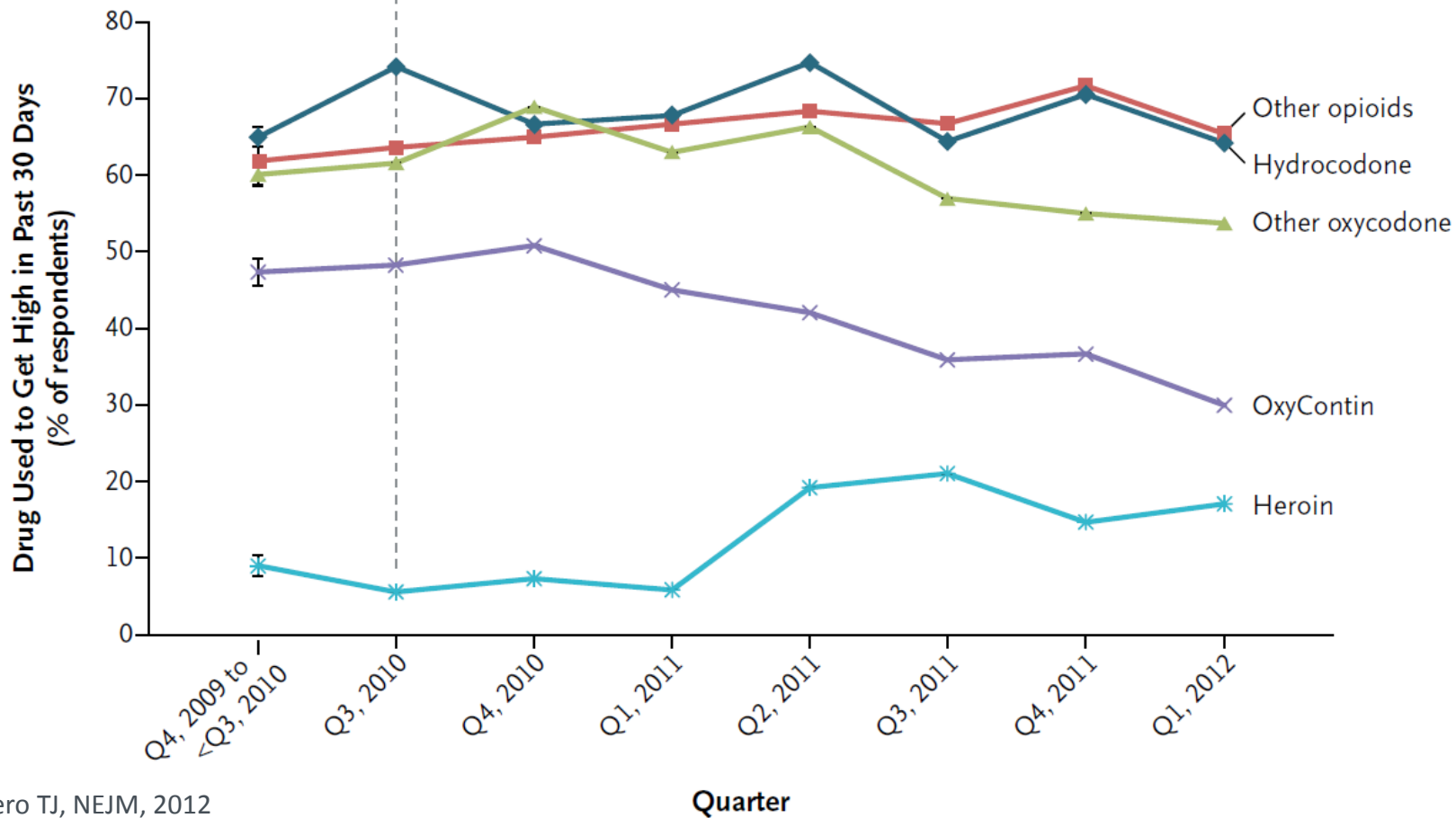


Mosaic Surveillance of Prescription Drug Abuse



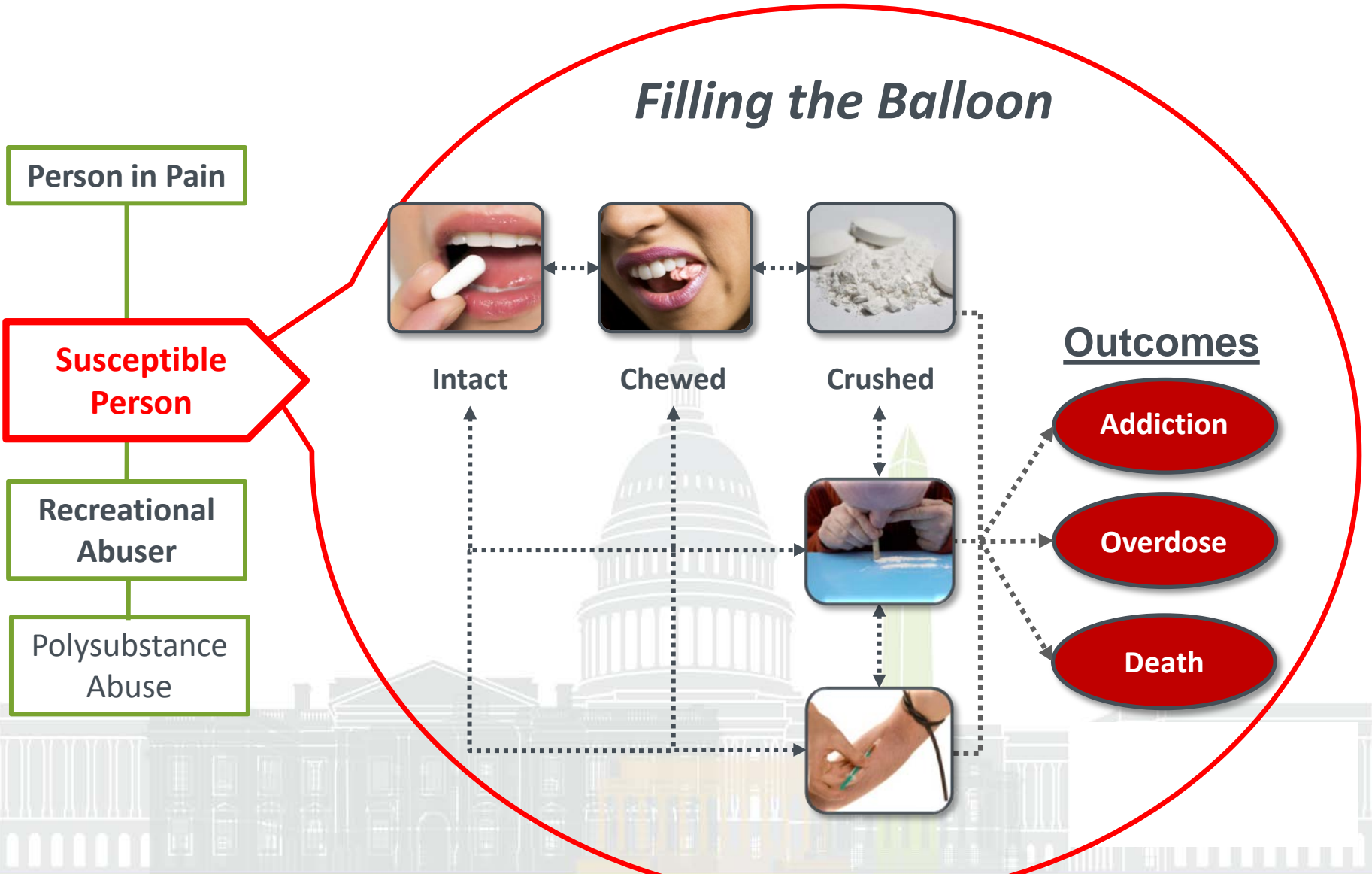
Cicero: Drugs Used to Get High in the Past 30 Days

B

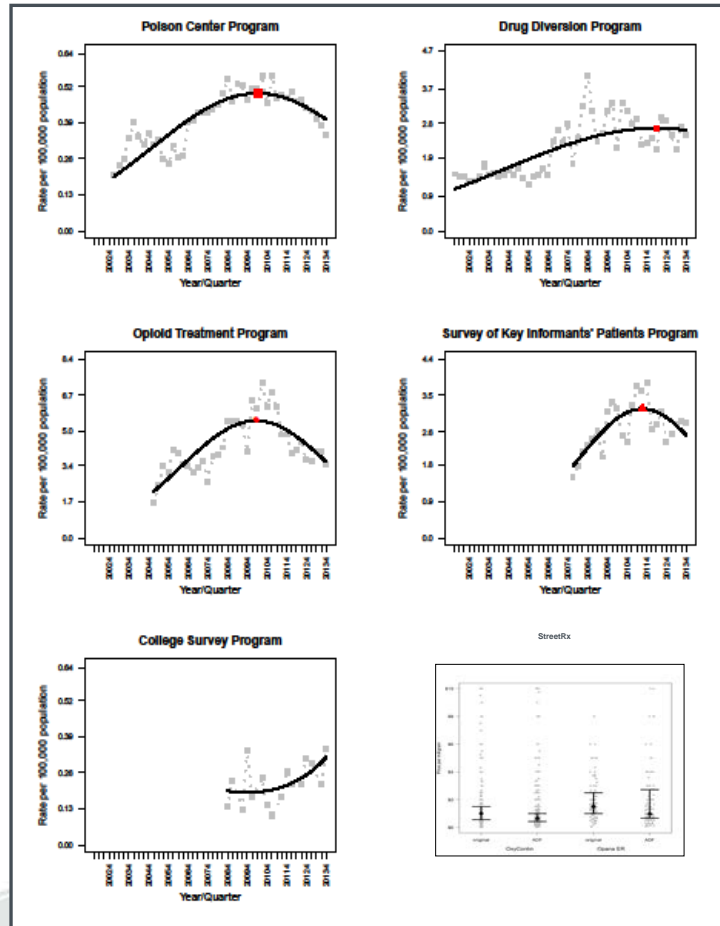


Cicero TJ, NEJM, 2012

30,000 Feet – Progression of Rx Drug Abuse

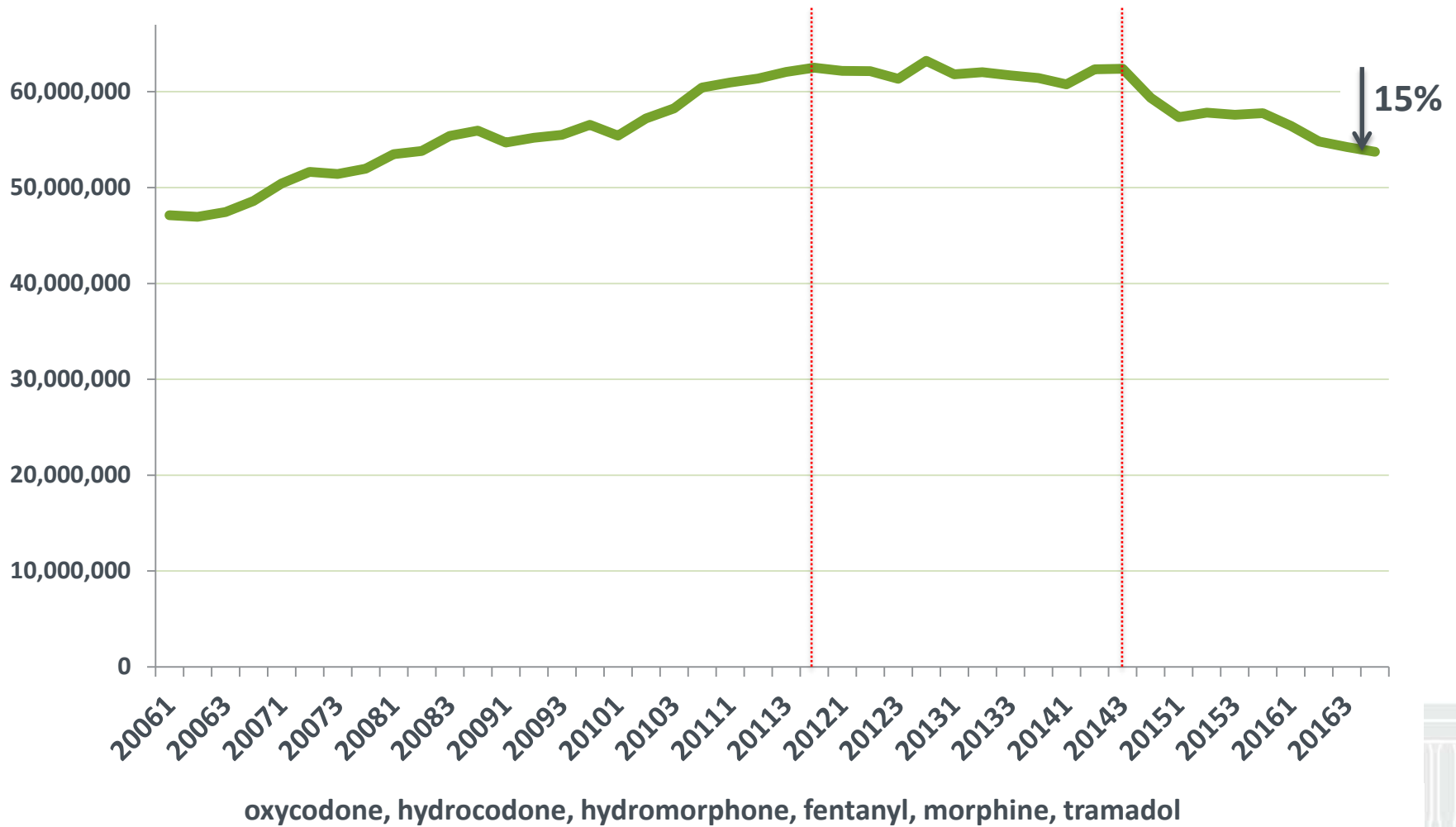


30,000 Feet: General Trends in Prescription Opioid Abuse, 2003 - 2013



Trends in Opioid Analgesic Abuse and Mortality in the United States.
N Engl J Med 2015;372:241-8

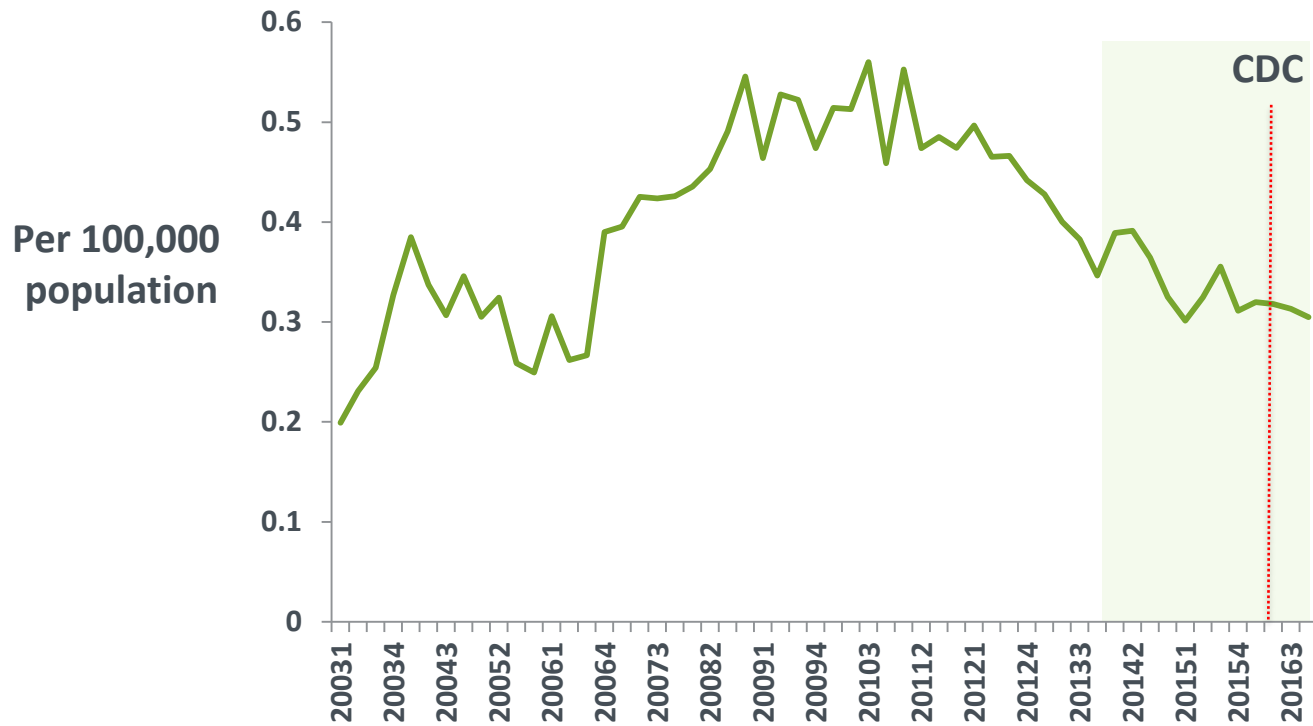
Prescriptions Dispensed for Opioid Analgesics, 2005-2016.



oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol

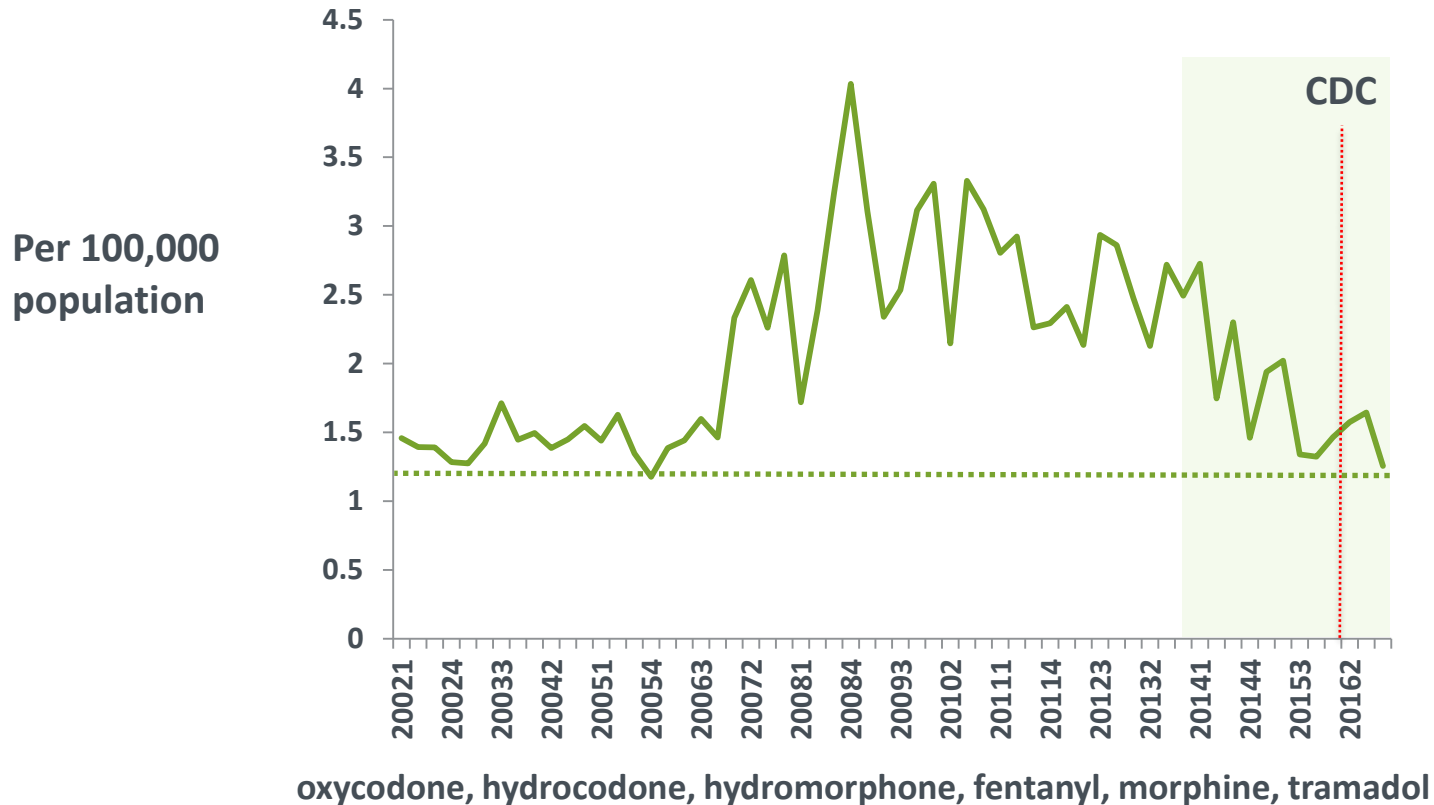
Source: IMS

RADARS System Poison Center Program All Opioids, Intentional Abuse, 2003 - 2016



oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol

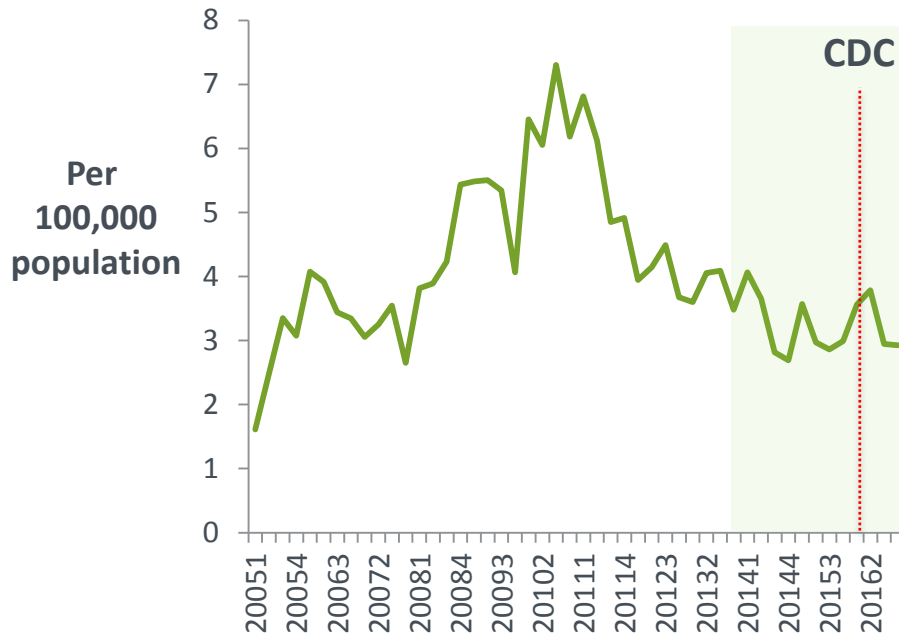
RADARS System Drug Diversion Program All Opioids, Intentional Abuse, 2002 - 2016



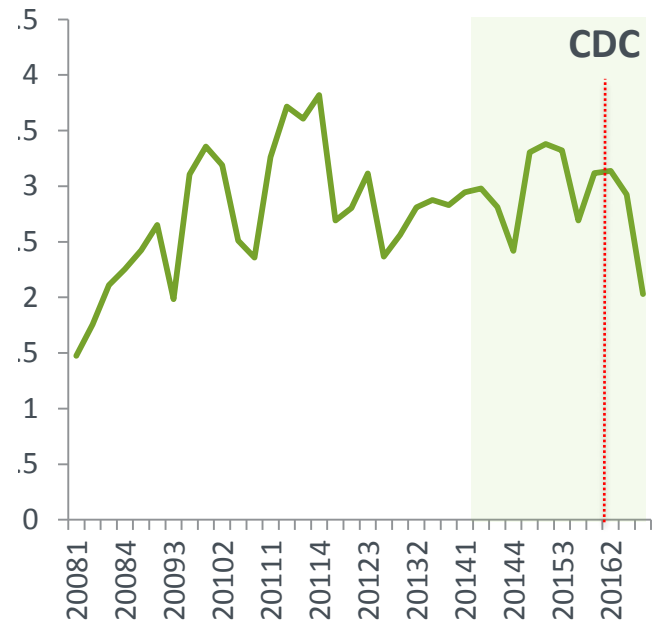
RADARS System Treatment Programs

All Opioids, Intentional Abuse

Opioid Treatment Program

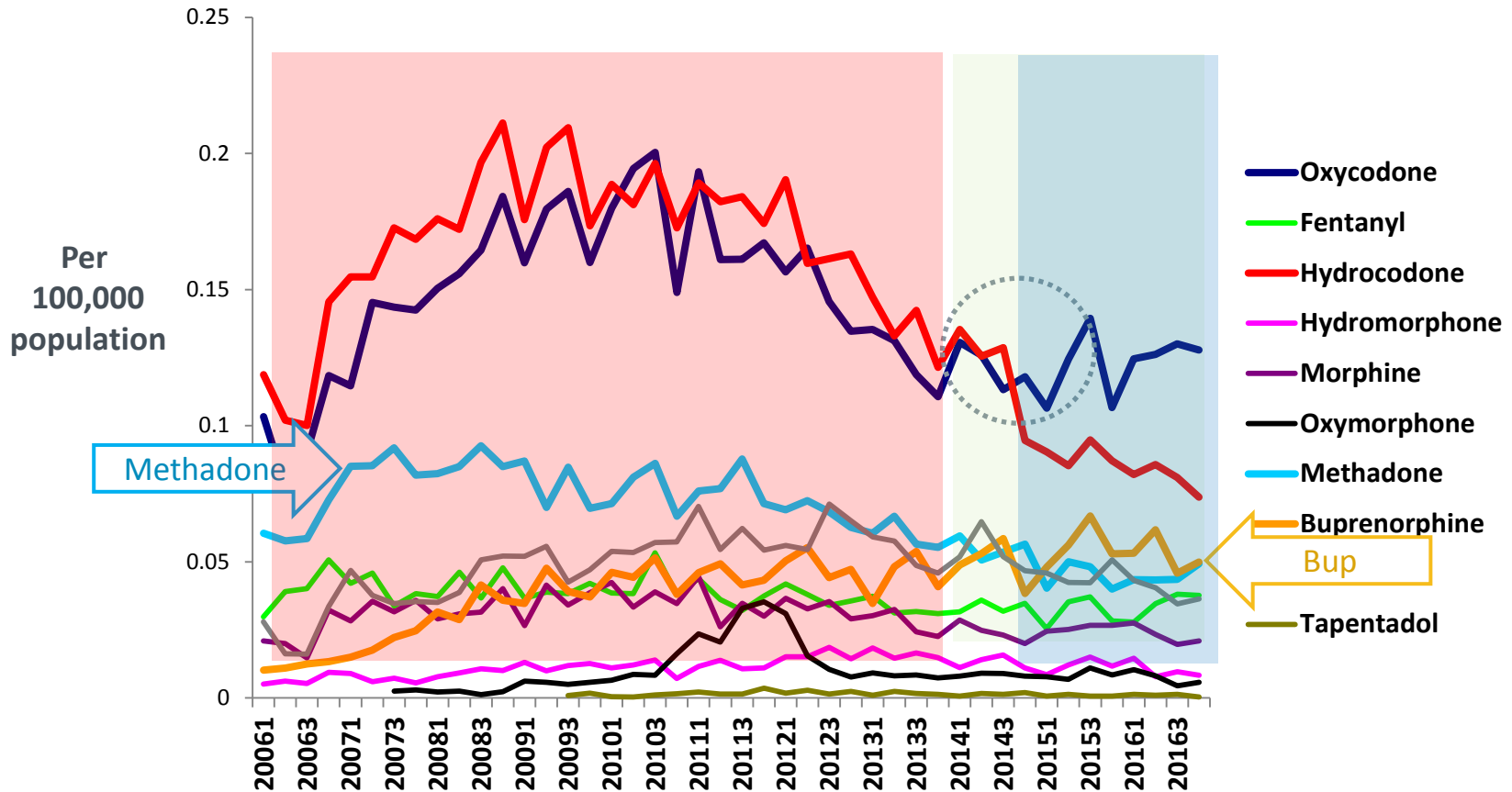


Survey Key Informant Patients

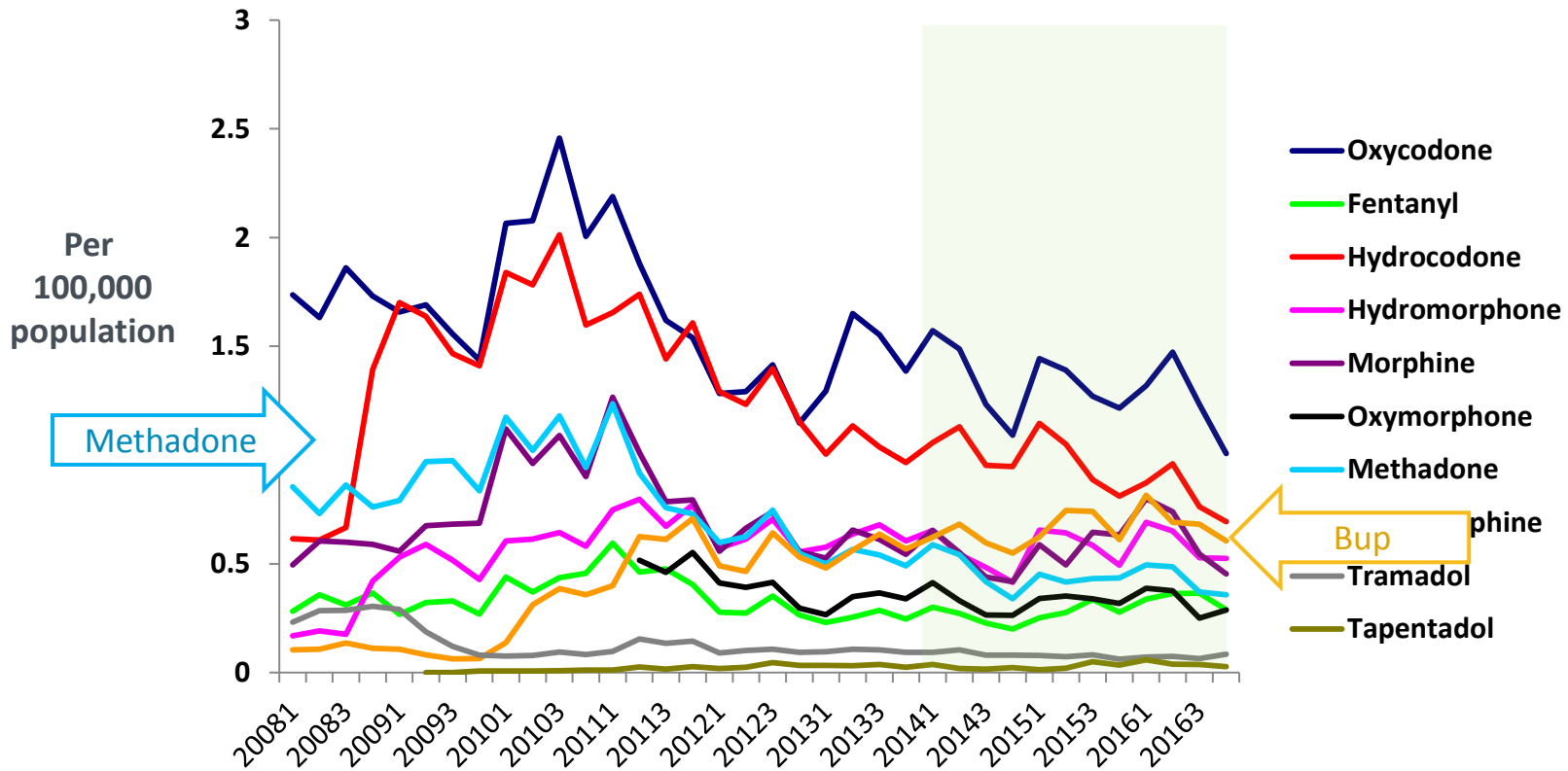


oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, tramadol

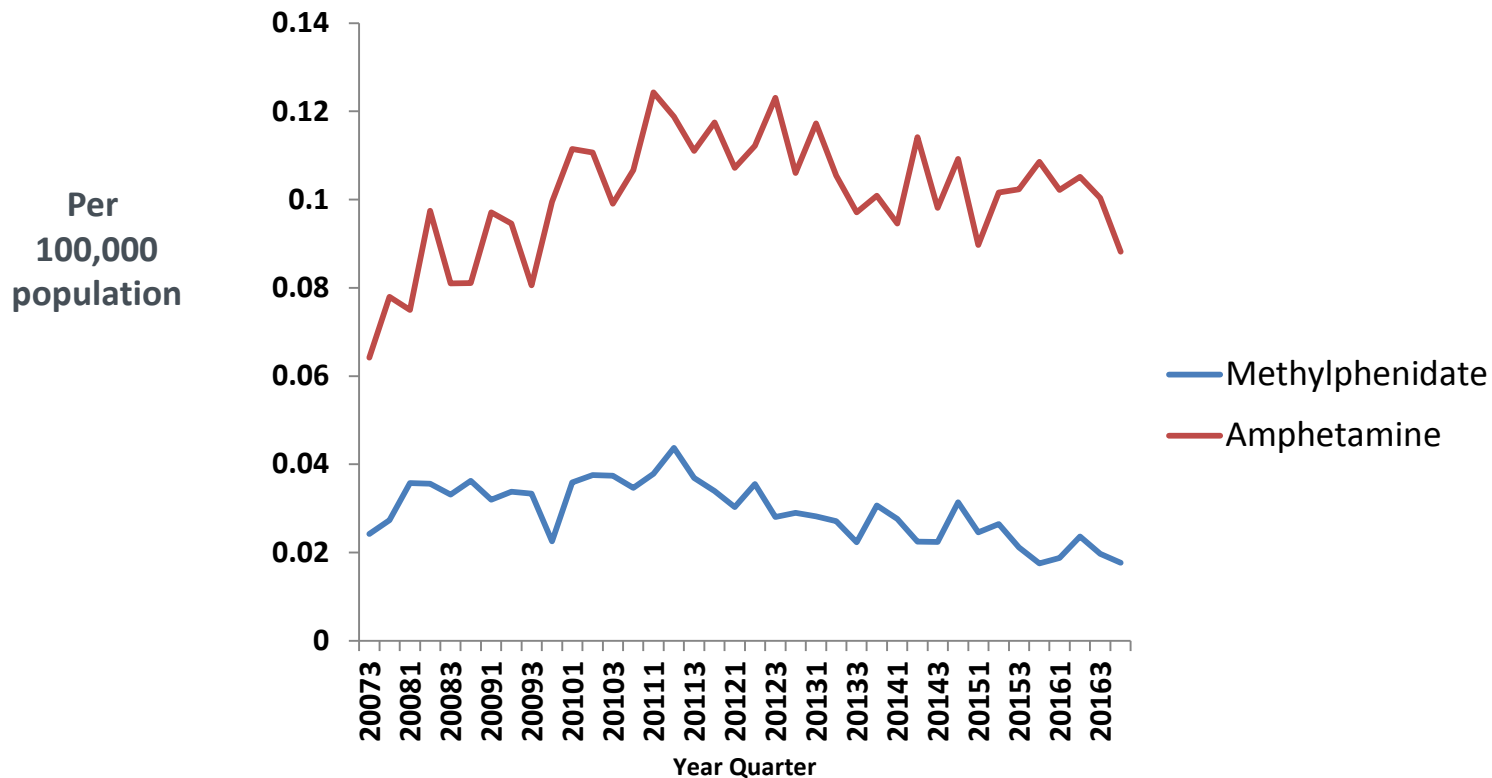
20,000 Feet - RADARS System Poison Center Intentional Abuse, 2006 - 2016



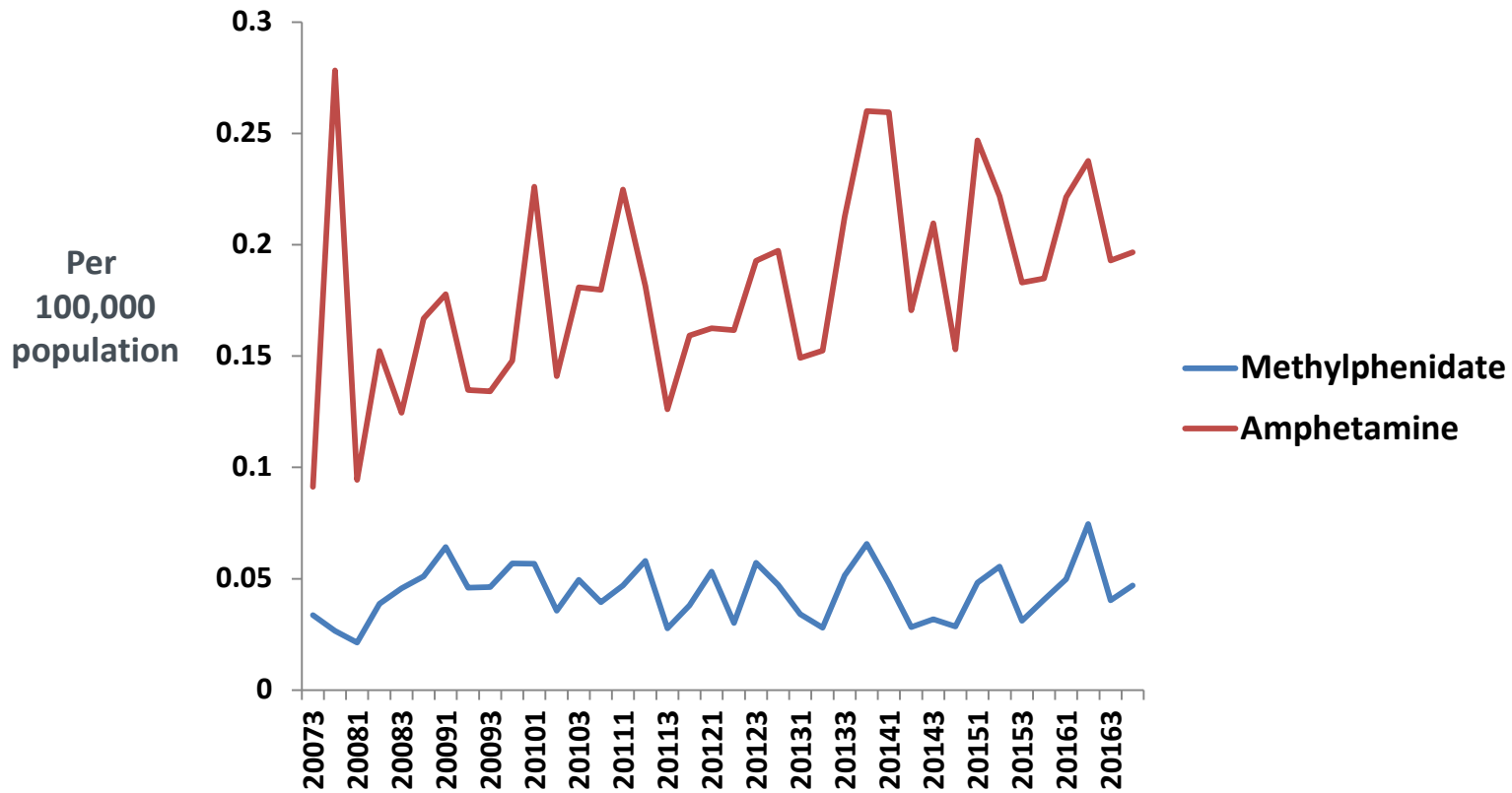
RADARS System Treatment Programs Combined, 2008 - 2016



Poison Center Program Prescription Stimulant Rates 2007 - 2016

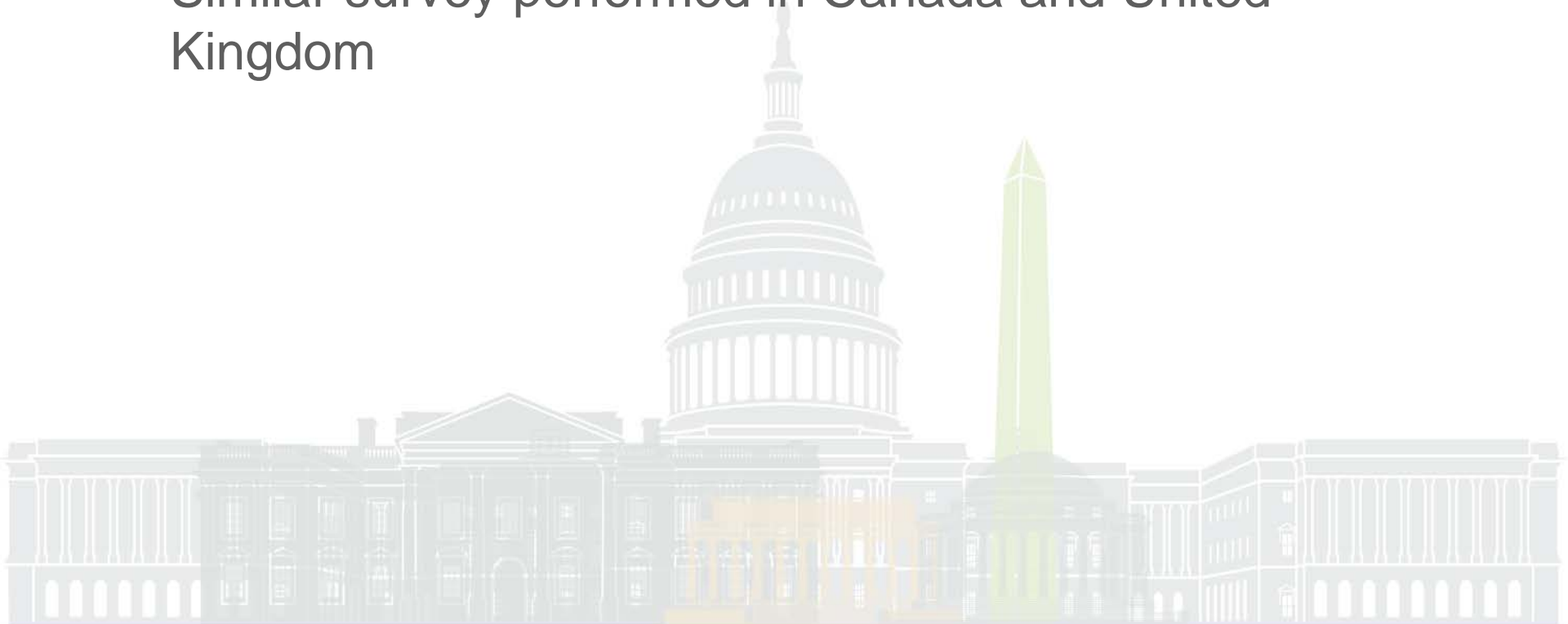


Drug Diversion Program Prescription Stimulant Rates, 2007 - 2016

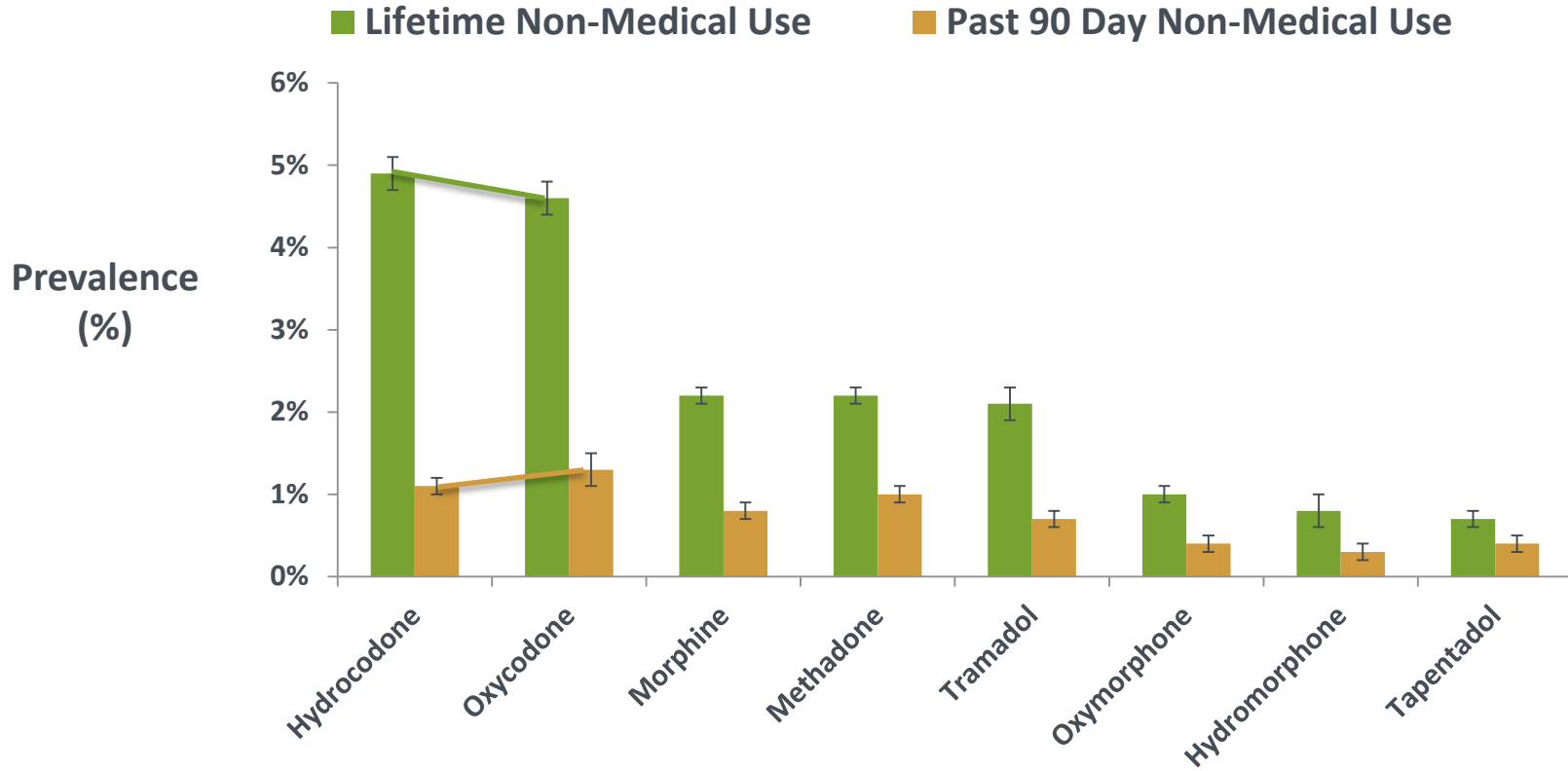


NMURx - Survey of Non-medical Use of Prescription Drugs Program

- An online, cross-sectional survey that assesses prescription drug use in the general adult population
- 30,000 people twice annually
- Similar survey performed in Canada and United Kingdom



Nonmedical Opioid Use in the Survey of Nonmedical Use of Prescription Drugs (NMURx), 3Q 2016, United States

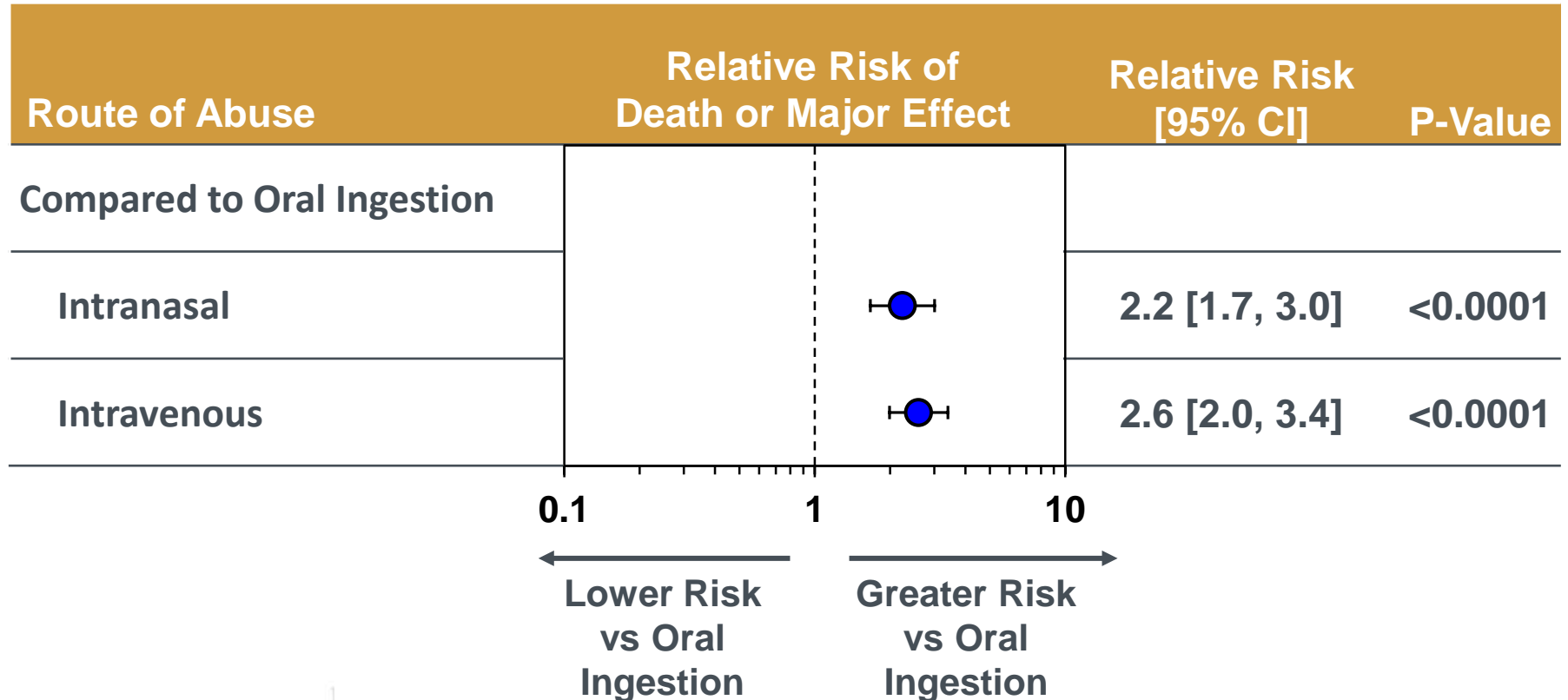


10,000 Feet and Lower Details on What's Happening in Prescription Drug Abuse

AND V

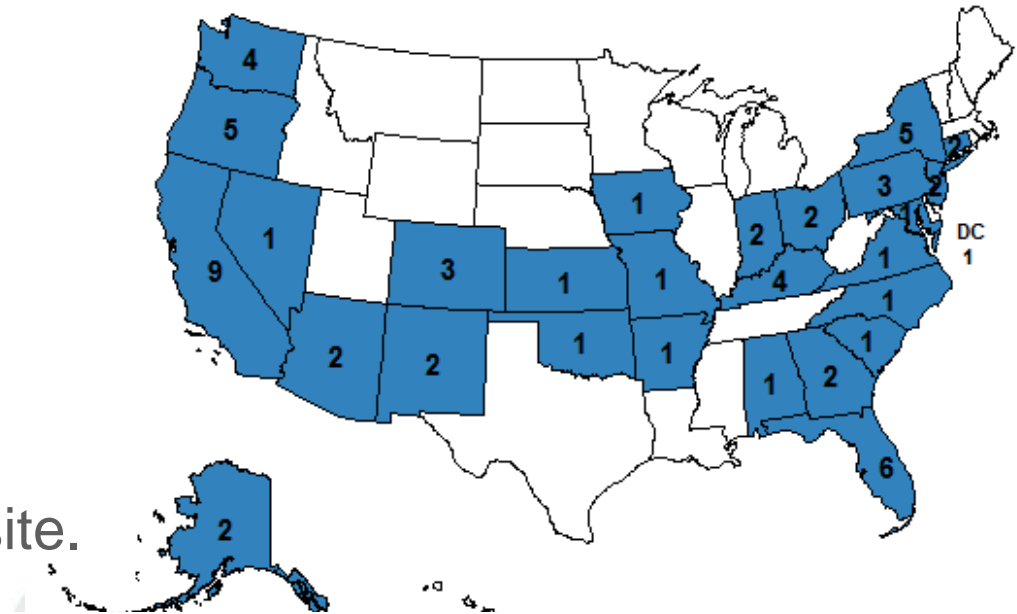
A stylized, light-colored illustration of a government building, likely the Virginia State Capitol, featuring a prominent dome and a tall, slender spire. The building is rendered in a minimalist, line-art style with some color accents in shades of green and orange. The text 'AND V' is overlaid on the building's facade.

IV and Intranasal Opioid Abuse Associated With Higher Risk of Death or Major Effects



If the Prescription Drug Market is Decreasing, Where is the Drug Coming From?

- Counterfeit Rx analgesics
 - Fentanyl containing
- Importation (Web, other)
- Illicit Drug (Heroin)
- 4 months: 67 reports of Rx oxycodone from Canada reported to US StreetRx website.



- 51 (76%) confirmed that the drug was acquired in the US.
- 9 (13%) - the drug was acquired in Canada but used in the US.
- 7 (10%) did not report the country of acquisition.
- 62 (92.5%) reports of crushable oxycodone products
- 5 (7.5%) reports of OxyNEO, the only difficult to crush (tamper-resistant) oxycodone product in our analysis.
- Geographically diverse, but 16 (24%) cases from states bordering Canada

The Big Box Effect

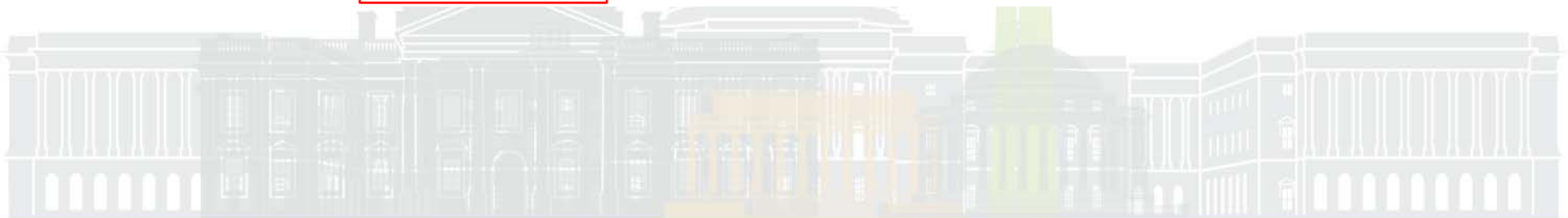
| Drug | Formulation | Dosage strength mg/tablet | N | Geometric mean price US dollar/mg (95% CI) | Median price US dollar/mg (IQR) |
|-----------|--|------------------------------|------|---|------------------------------------|
| Oxycodone | Total | | 5611 | 0.59 (0.58, \$0.60) | 1.25 (1.18, 1.31) |
| | Crush-resistant Reformulated OxyContin® | 15 or less | 665 | 0.75 (0.70, \$0.79) | 1.00 (\$0.50, \$1.00) |
| | | 20 – 40 | 1487 | 0.54 (0.52, \$0.56) | 0.63 (\$0.38, \$1.00) |
| | | 60 or more | 772 | 0.36 (0.34, \$0.38) | 0.44 (\$0.25, \$0.63) |
| | Crushable Original OxyContin®, generic oxycodone ER, and oxycodone IR | 15 or less | 896 | 0.84 (0.79, \$0.88) | 1.00 (\$0.60, \$1.00) |
| | | 20 – 40 | 1548 | 0.67 (0.64, \$0.70) | 0.83 (\$0.50, \$1.00) |
| | | 60 or more | 243 | 0.34 (0.30, \$0.40) | 0.50 (\$0.25, \$0.75) |

Comparative Rates of Serious Adverse Outcomes Among Opioid Analgesics

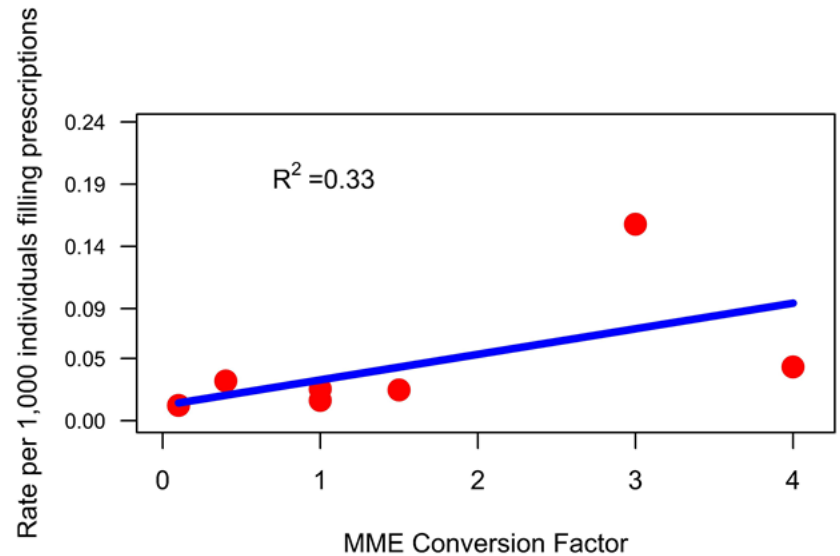
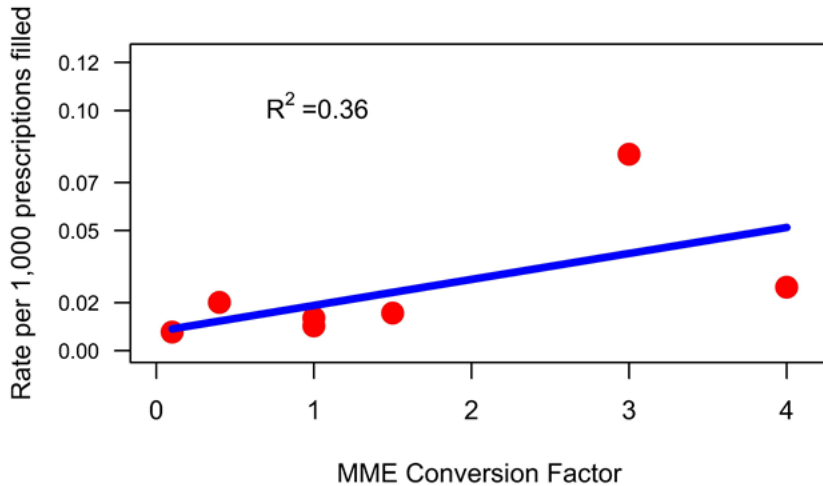
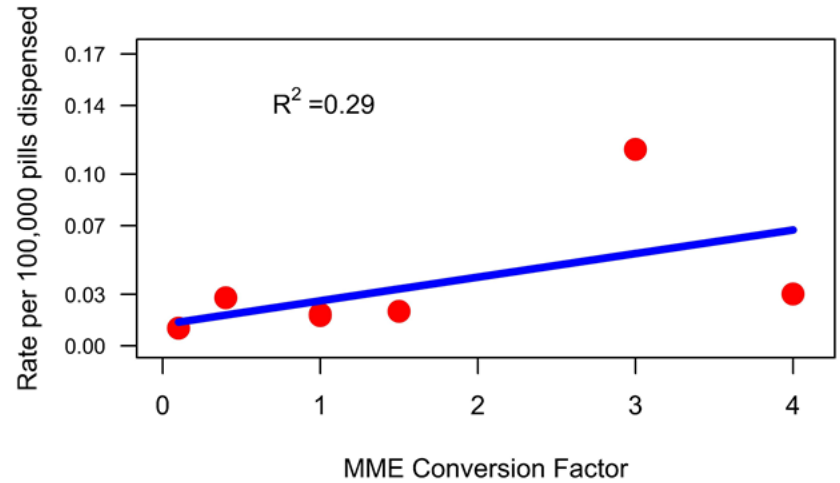
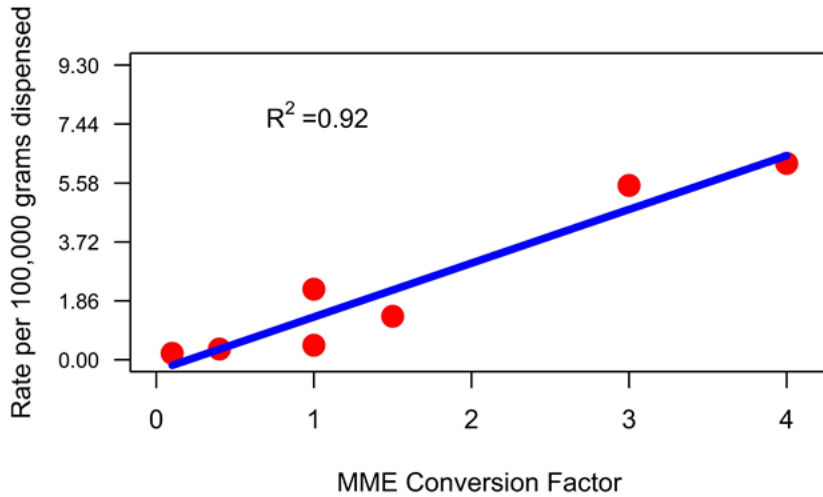
- Hypothesis – Serious Adverse Outcomes occur at different rates among commonly prescribed opioid analgesics
- Serious Adverse Events in RADARS System Poison Center Program
 - Death, major medical effect, or hospitalization following exposure to tablets containing
 - Oxycodone, hydrocodone, morphine, hydromorphone, oxymorphone, tapentadol, and tramadol
 - 2010 - 2014
- Adjusted for availability through outpatient dispensing data and regressed on morphine milligram equivalents (MME)

Retail Pharmacy Prescription Dispensing Data for Commonly Prescribed Opioid Analgesics, 2010 - 2014

| Drug name | Grams dispensed | Dosage units dispensed | Prescriptions dispensed | Individuals filling prescription |
|---------------|-----------------|------------------------|-------------------------|----------------------------------|
| Hydromorphone | 5,724,736 | 1,179,372,325 | 13,467,269 | 8,228,737 |
| Oxymorphone | 7,926,067 | 381,084,087 | 5,329,702 | 2,763,057 |
| Hydrocodone | 265,856,002 | 33,733,714,726 | 573,941,422 | 366,732,970 |
| Oxycodone | 290,383,569 | 19,789,381,382 | 254,188,658 | 161,873,589 |
| Morphine | 105,820,455 | 2,636,964,926 | 35,814,511 | 19,059,945 |
| Tapentadol | 23,228,541 | 279,757,288 | 3,892,220 | 2,444,324 |
| Tramadol | 652,779,439 | 12,930,489,500 | 172,778,391 | 109,273,930 |

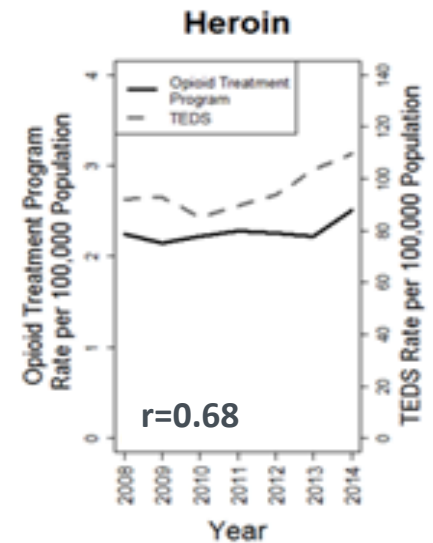
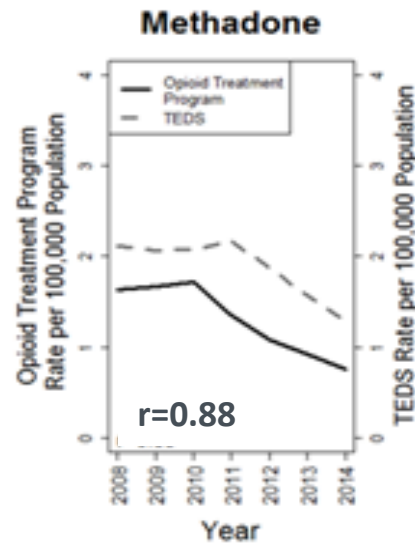
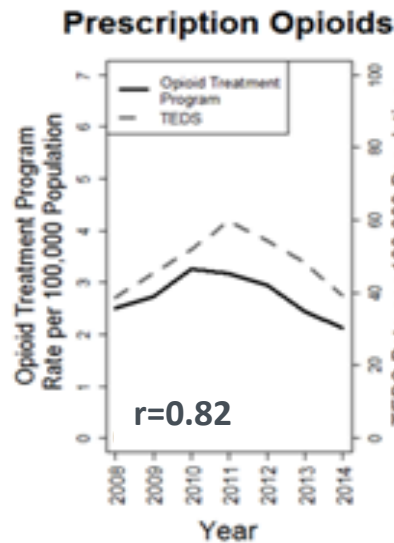


Correlation of Rate (Death, Hospitalization, Major Effect) and Relative Opioid Potency, 2010 - 2014

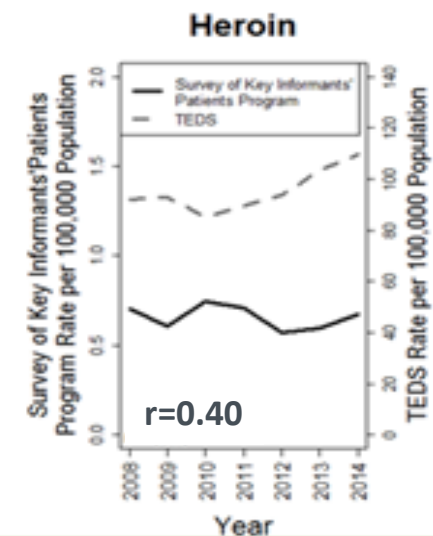
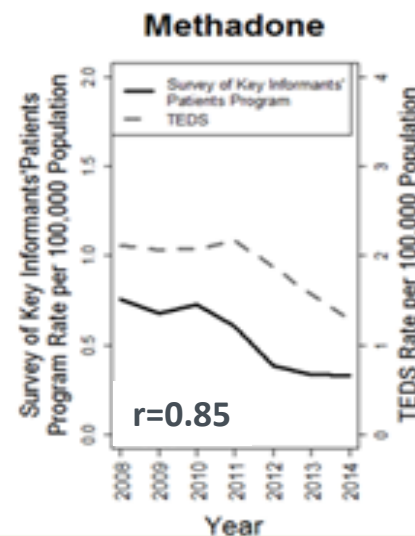
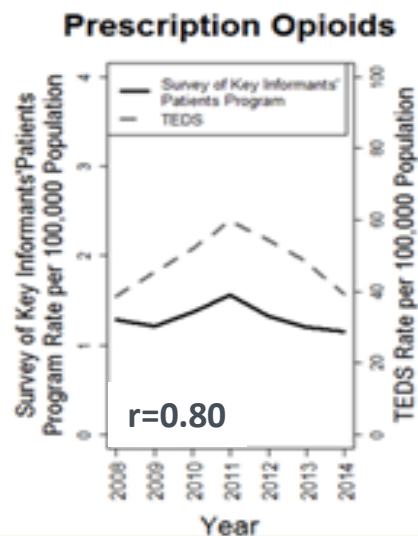


RADARS System Opioid Treatment Program (OTP) and Survey of Key Informant Patients (SKIP) and Treatment Episode Data Set (TEDS)

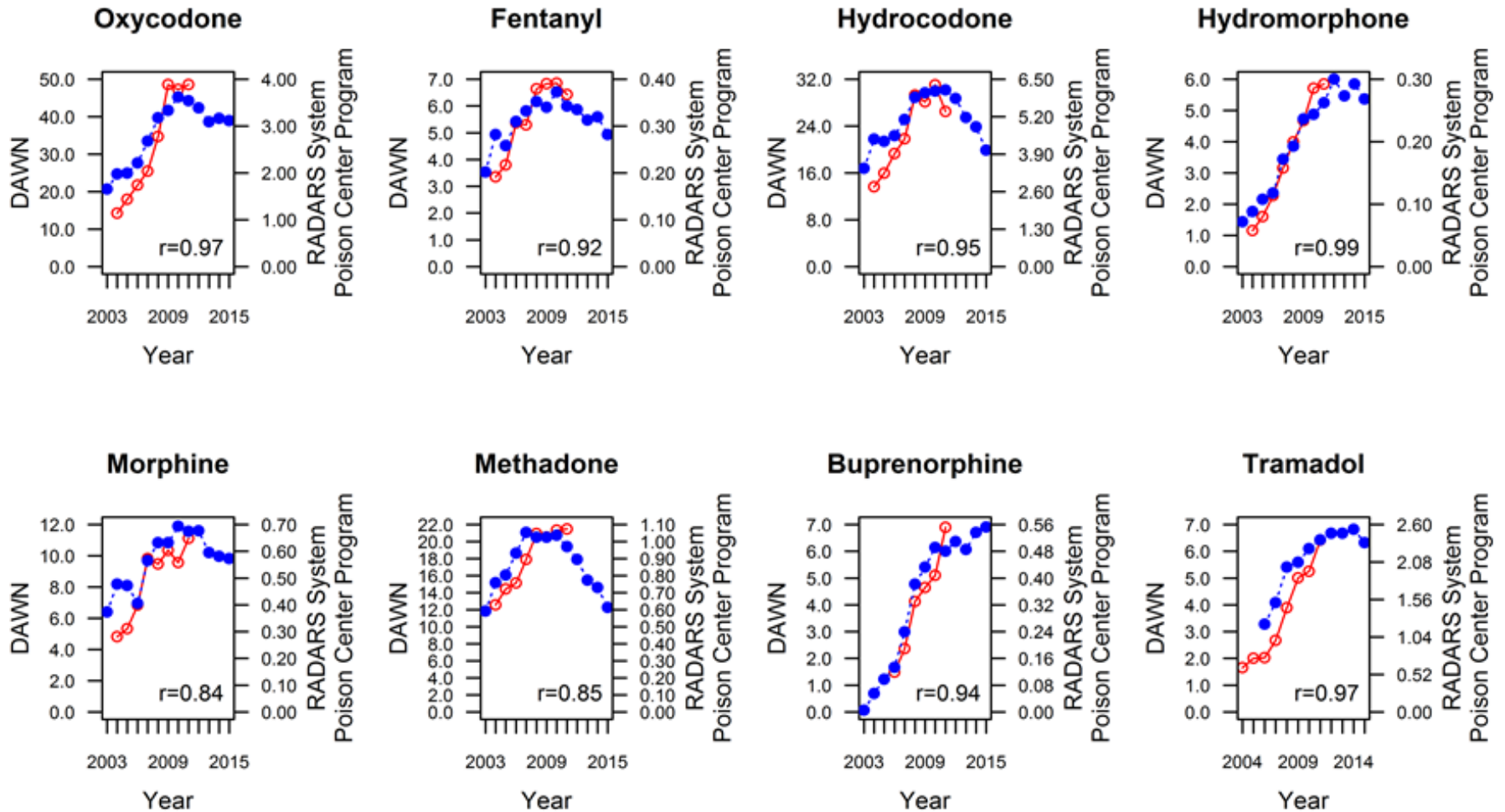
OTP



SKIP



DAWN vs. RADARS System Poison Center Program



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

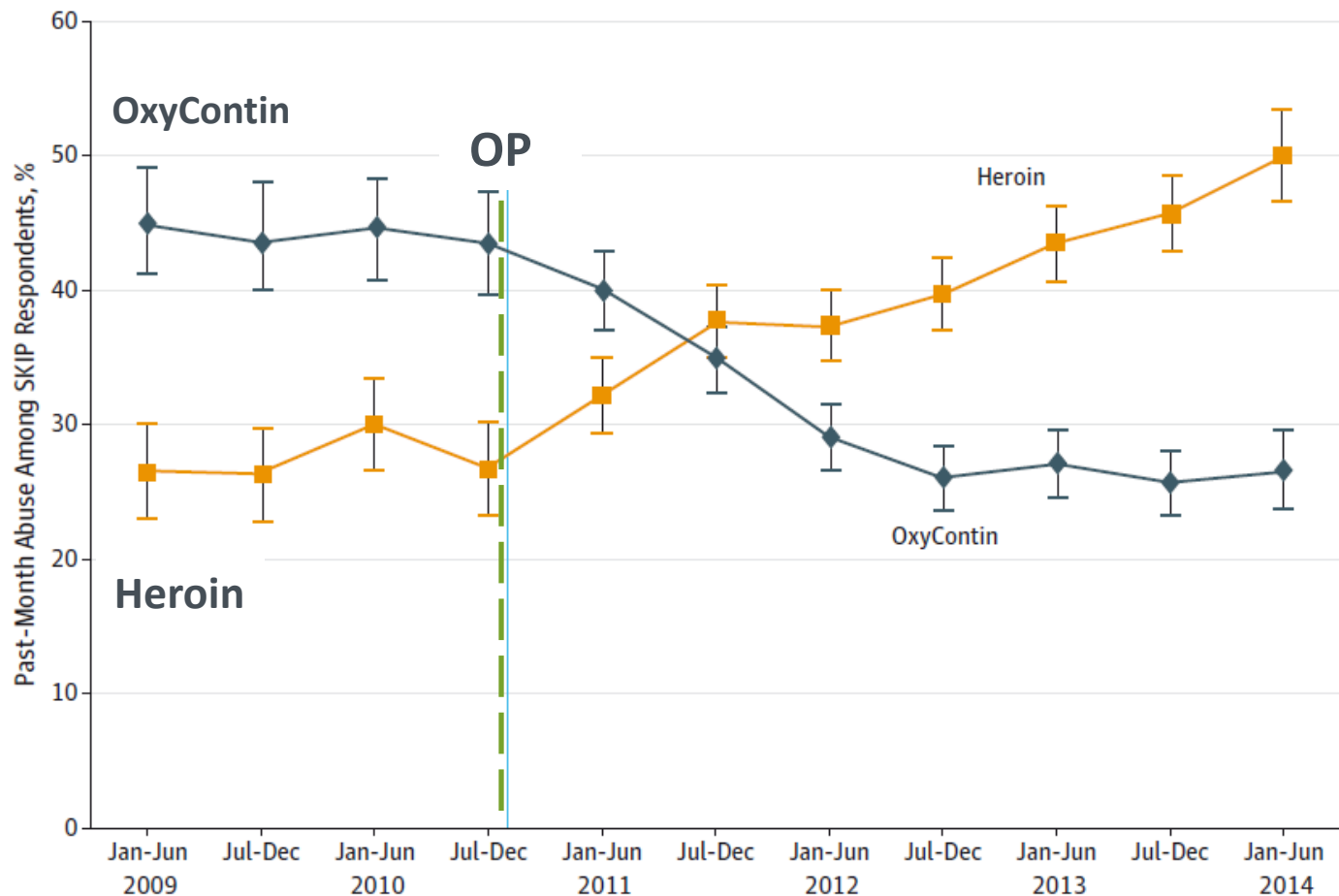
Dan L. Longo, M.D., *Editor*

Relationship between Nonmedical Prescription-Opioid Use and Heroin Use

Wilson M. Compton, M.D., M.P.E., Christopher M. Jones, Pharm.D., M.P.H.,
and Grant T. Baldwin, Ph.D., M.P.H.



Past-Month Use of Oxycodone (OP) or Heroin Before and After Reformulation

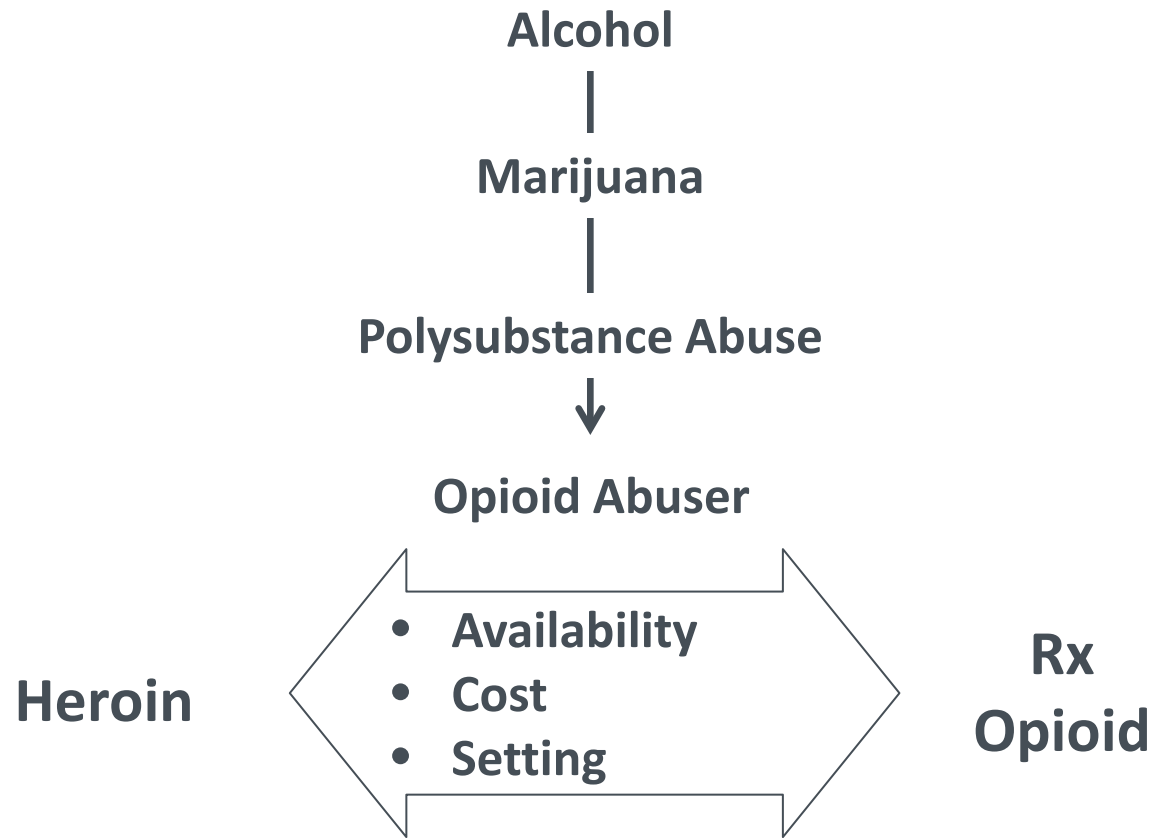


Other Factors

- Cost
 - Every \$100 decrease in price of pure gram of heroin resulted in a 2.9% increase in number heroin overdose hospitalizations
 - Price point phenomenon
- Availability (*Dreamland*)
- Many abusers use multiple opioids
- Other opioids
 - Hydrocodone-acetaminophen
 - Oxycodone-acetaminophen
 - Morphine
 - Hydromorphone
 - Oxymorphone
- Other Drugs



Heroin - Push? Or Pull?



2017 Program

- **Behind the Opioid Epidemic – Fentanyl, Immediate-Release Opioids, and Mortality**
 - Janetta Iwanicki, MD
 - Associate Medical Director, Rocky Mountain Poison and Drug Center, Denver Health and Hospital Authority
- **Darknet Drug Markets: Supply Chains, Stakeholders, and Opportunities for Public Health**
 - Michael Gilbert, MPH, *Epidemico*
 - Nabarun Dasgupta, MPH, PhD
 - *Senior Scientist, RADARS® System, Denver Health and Hospital Authority*



2017 Program

- **ICER's Report on Comparative Value of Abuse Deterrent Formulations of Opioids: Draft Results**
 - Richard Chapman, PhD
 - *Director of Health Economics – Institute for Clinical and Economic Review (ICER)*
- **Evaluating the Impact of Abuse Deterrent Formulations: Methodological Challenges in Postmarketing Data**
 - Judy Staffa, PhD, RPh
 - *Associate Director for Public Health Initiatives, Office of Surveillance and Epidemiology – U.S. Food and Drug Administration*



2017 Program

- **Findings from the Australian National Opioid Medications Abuse Deterrence (NOMAD) Study: Monitoring the Impact of a Potentially Tamper-Resistant Formulation of Controlled-Release Oxycodone, Reformulated OxyContin®**
 - Louisa Degenhardt, PhD
 - *NHMRC Principal Research Fellow, National Drug & Alcohol Research Centre – University of New South Wales*
- **RAPID Analysis of Routes of Administration: Oral to Non-Oral Transitions**
 - Theodore J. Cicero, PhD
 - *John P. Feighner Professor of Psychiatry, Department of Psychiatry – Washington University in St. Louis School of Medicine*