# *TRENDS OF OPIOID MISUSE AND DIVERSION: LESSONS FOR EUROPE FROM THE USA*

PROFESSOR ICRO MAREMMANI
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DR JODY GREEN
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# *WELCOME AND INTRODUCTIONS*

PROFESSOR ICRO MAREMMANI

University of Pisa, Italy

# *AGENDA*

| | | |
|---|---|---|
| 11:45–11:50 | Welcome and Introductions | Professor Icro Maremmani |
| 11:50 –12:30 | Trends of Opioid Misuse and Diversion: Lessons for Europe from the USA | Dr Jody Green |
| 12:30–12:45 | Question and Answer Session | Dr Jody Green Professor Icro Maremmani |

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- RBP had no influence on the scientific content of this presentation

- This presentation refers to medications that may not have been approved in all countries
- Please refer to your local prescribing information

# *TRENDS OF OPIOID MISUSE AND DIVERSION: LESSONS FOR EUROPE FROM THE USA*

DR JODY GREEN

Rocky Mountain Poison and Drug Center, USA

# Trends of Opioid Misuse and Diversion: Lessons for Europe from the United States

## *16 October 2012*

## Jody L. Green, PhD

*Research Director – Rocky Mountain Poison and Drug Center*

*Assistant Professor – Vanderbilt University Medical Center*

# Disclosure for Dr Jody Green

In compliance with COI policy,
ISAM requires the following disclosures to the session audience:

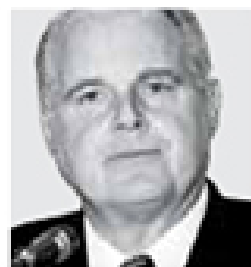| | |
|---|---|
| **Shareholder** | **No relevant conflicts of interest to declare** |
| **Grant / Research Support** | **No relevant conflicts of interest to declare** |
| **Consultant** | **No relevant conflicts of interest to declare** |
| **Employee** | **No relevant conflicts of interest to declare** |
| **Paid Instructor** | **No relevant conflicts of interest to declare** |
| **Speaker bureau** | **No relevant conflicts of interest to declare** |
| **Other** | **Reckitt Benckiser Pharmaceuticals and other opioid manufacturers subscribe to the RADARS System** |

# Opioids and the Stars

Some celebrities have been publicly linked with use of these powerful painkillers (in several cases, with more than one such medication).

**Reported past users of OxyContin, generic oxycodone, or Percocet**
(which consists of oxycodone and acetaminophen):

**Reported past users of hydrocodone, which is chemically similar to oxycodone, including Vicodin**
(which consists of hydrocodone and acetaminophen)
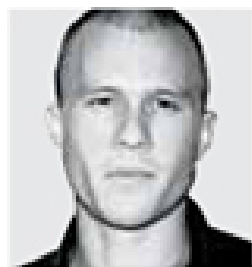
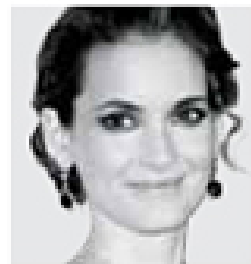**Heath Ledger**
(actor; oxycodone was in his blood when he died)

**Rush Limbaugh**
(radio talk show host)

**Courtney Love**
(singer)

**Jamie Lee Curtis**
(actress)

**Eminem**
(singer)
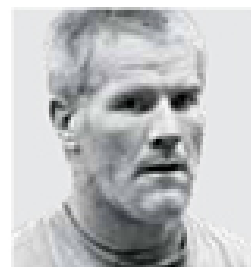
**Brett Favre**
(retired football star)

**Cindy McCain**
(businesswoman, wife of Sen. John McCain)

**Winona Ryder**
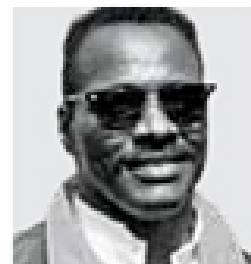(actress)

**Steven Tyler**
(singer, *American Idol* judge)

**Walter Payton**
(late football legend)

**Matthew Perry**
(actor)

**Nicole Richie**
(reality TV personality)

# Prescription Opioid Misuse & Diversion

- United States Experience
  - Deaths from opioid abuse have surpassed deaths caused by motor vehicle accidents
  - Abuse deterrent formulations
  - Increasing availability of generic products
  - Toll of accidental pediatric exposures

- Outline of Presentation
  - RADARS® System Methodology & General Results
  - Trends with abuse deterrent formulations & market changes
  - Medical outcomes following pediatric exposures
  - Lessons learned

# What is the RADARS® System?

- History
  - 2001: Created by Purdue Pharma
  - 2006: Denver Health and Hospital Authority/RMPDC
    - State sanctioned independent authority
    - Independently owned and operated program
    - Multiple pharmaceutical subscribers (cost-share model)
    - Scientific advisory board
    - Catalyst for bringing together industry, regulatory, academics

- Purpose
  - Measure rates of misuse, abuse and diversion of prescription drugs

# Mosaic Approach to Surveillance



| Poison Center | Acute Events<br>51 Centers<br>47 States |
| --- | --- |

| Drug Diversion | Criminal Justice<br>280 investigator<br>50 states |
| --- | --- |

| Opioid Tx Program (OTP) | Patients in Tx<br>73 programs<br>33 states |
| --- | --- |

| Survey of Key Informants' Patients (SKIP) | Patients in Tx<br>125 practices<br>50 states |
| --- | --- |

| College Survey | 2000 students<br>50 States<br>3x each year |
| --- | --- |

| StreetRx<br>www.streetrx.com | Users/Buyers<br>Crowdsourcing<br>50 states |
| --- | --- |

# RADARS® System Process
# A Tale of Two Denominators

| Drug Diversion | Poison Center | OTP | SKIP | College Survey |
|---|---|---|---|---|

**Numerators compiled by each program**
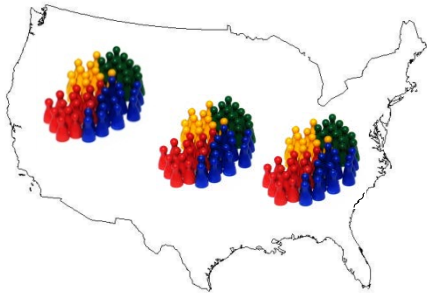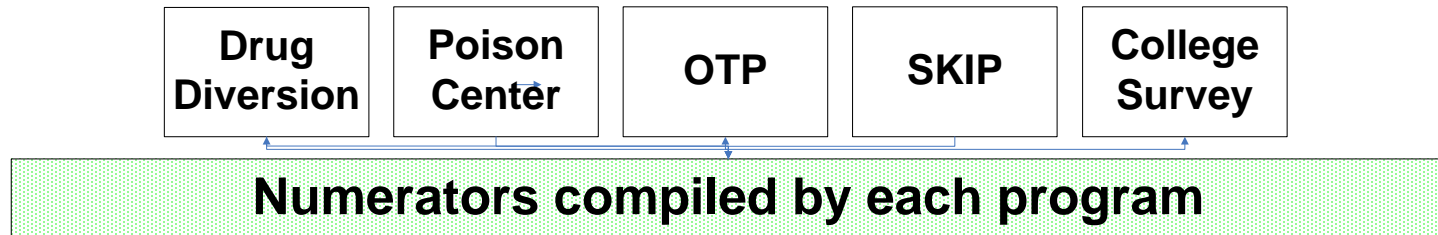
**POPULATION RATE =** $\dfrac{\text{Counts by System}}{\text{US Population}}$

- Disease burden on whole population
- Does not account for drug availability

**UNIQUE RECIPIENTS OF DISPENSED DRUG (URDD) RATE** $= \dfrac{\text{Counts by System}}{\text{URDD}}$

- Number of unique people filling prescription for drug (refills excluded)

# RADARS System Opioid Abuse Trends
## Population Rate (Ranked Highest-Lowest) 2011

| Rank | Poison Center | Opioid Treatment | Survey of Key Informant Pts | Drug Diversion | College Survey |
|------|---------------|------------------|-----------------------------|----------------|----------------|
| 1 | **hydrocodone** | **oxycodone** | **hydrocodone** | **oxycodone** | **hydrocodone** |
| 2 | **oxycodone** | **hydrocodone** | **oxycodone** | **hydrocodone** | **oxycodone** |
| 3 | tramadol | methadone | morphine | morphine | morphine |
| 4 | methadone | morphine | hydromorphone | buprenorphine | tramadol |
| 5 | morphine | hydromorphone | methadone | methadone | fentanyl |
| 6 | buprenorphine | buprenorphine | buprenorphine | hydromorphone | methadone |
| 7 | fentanyl | fentanyl | fentanyl | tramadol | buprenorphine |
| 8 | hydromorphone | tramadol | tramadol | fentanyl | hydromorphone |

# RADARS System Opioid Abuse Trends
## URDD Rates (Ranked Highest-Lowest)
## 2011

| Rank | Poison Center | Opioid Treatment | Survey of Key Informant Pts | Drug Diversion | College Survey |
|---|---|---|---|---|---|
| 1 | methadone | methadone | hydromorphone | methadone | methadone |
| 2 | buprenorphine | hydromorphone | methadone | hydromorphone | hydromorphone |
| 3 | morphine | morphine | morphine | buprenorphine | morphine |
| 4 | hydromorphone | buprenorphine | buprenorphine | morphine | fentanyl |
| 5 | fentanyl | fentanyl | fentanyl | **oxycodone** | buprenorphine |
| 6 | tramadol | **oxycodone** | **oxycodone** | fentanyl | **oxycodone** |
| 7 | **oxycodone** | **hydrocodone** | **hydrocodone** | **hydrocodone** | **hydrocodone** |
| 8 | **hydrocodone** | tramadol | tramadol | tramadol | tramadol |

RADARS System Programs
URDD Rates by Active Ingredient
1st Quarter 2009 to 4th Quarter 2011

URDD: Unique recipients of dispensed drug

15
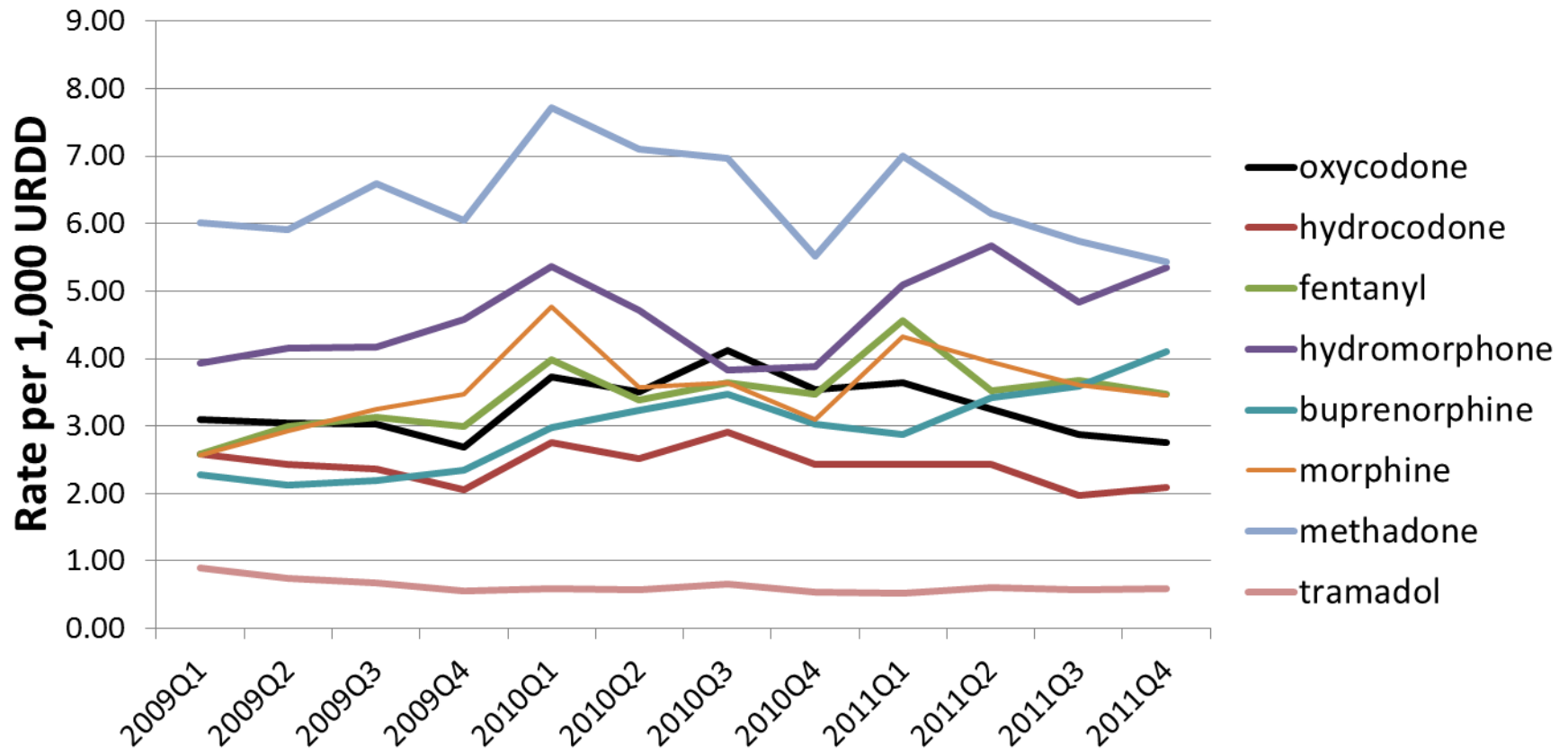
# RADARS System
# 2009 URDD Mortality Ranking

| Rank | RADARS System<br>Rate/100,000 URDD |
|---|---|
| 1 | methadone |
| 2 | morphine |
| 3 | fentanyl |
| 4 | buprenorphine |
| 5 | hydromorphone |
| 6 | oxycodone |
| 7 | hydrocodone |

# US CDC* Mortality Data

**Drug-related deaths involving opioids, by type of opioid — Drug Abuse Warning Network Medical Examiner System, 13 states, 2009**

| Opioid | No. | | Death rate/100kg MME | | RR | | (95% CI) | |
|---|---|---|---|---|---|---|---|---|
| | All deaths | Single drug deaths | All deaths | Single drug deaths | All deaths | Single drug deaths | All deaths | Single drug deaths |
| Buprenorphine | 20 | 2 | 0.8 | 0.1 | 0.02 | 0.01 | 0.01–0.04 | 0.00–0.03 |
| Fentanyl | 364 | 99 | 7.7 | 2.1 | 0.28 | 0.26 | 0.25–0.32 | 0.21–0.33 |
| Hydrocodone | 550 | 42 | 14.3 | 1.1 | 0.42 | 0.11 | 0.38–0.47 | 0.08–0.16 |
| Hydromorphone | 74 | 4 | 9.1 | 0.5 | 0.27 | 0.05 | 0.21–0.34 | 0.02–0.14 |
| Morphine | 824 | 153 | 20.2 | 3.8 | 0.64 | 0.41 | 0.58–0.70 | 0.34–0.50 |
| Oxycodone | 1,097 | 150 | 8.7 | 1.2 | 0.26 | 0.12 | 0.24–0.28 | 0.10–0. |
| Methadone | 1,034 | 298 | 33.6 | 9.7 | 1.00 | 1.00 | referent | referent |
| Total[†] | 3,294 | 748 | 10.4 | 2.4 | | | | |

MME = morphine milligram equivalent; RR = rate ratio; CI = confidence interval.
*Centers for Disease Control and Prevention
[†] Counts for each opioid might not sum to the total shown for all deaths because some deaths involved more than one opioid.

# RADARS System vs CDC 2009 Mortality Data

| Rank | RADARS System Rate/100,000 URDD | CDC Death rate/100kg MME |
|---|---|---|
| 1 | methadone | methadone |
| 2 | morphine | morphine |
| 3 | fentanyl | hydrocodone |
| 4 | buprenorphine | hydromorphone |
| 5 | hydromorphone | oxycodone |
| 6 | oxycodone | fentanyl |
| 7 | hydrocodone | buprenorphine |

MME = morphine milligram equivalent
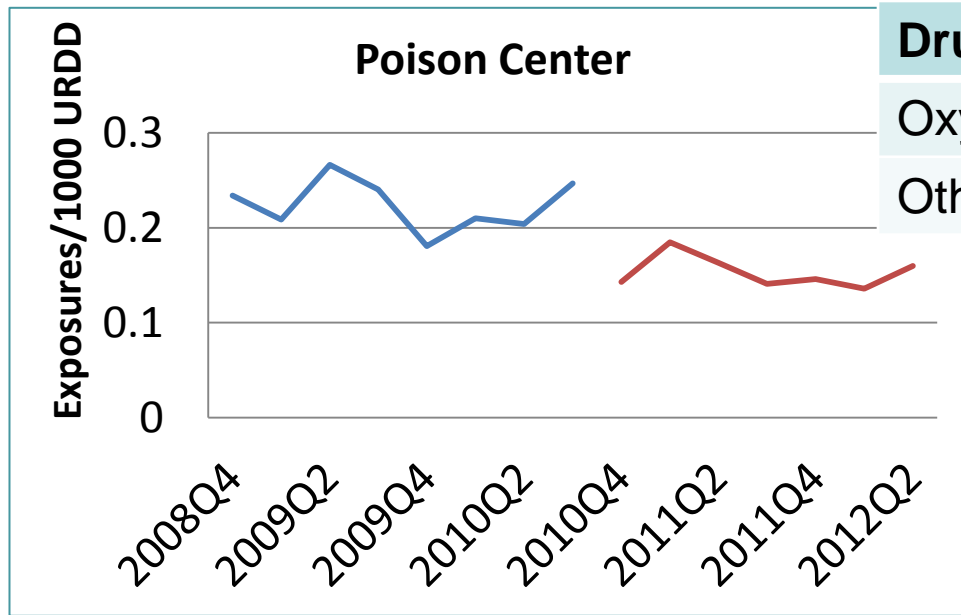URDD = unique recipient of dispensed drug

***Spearman rank correlation is fairly strong (p=0.052) in the ranks of the two estimates..***

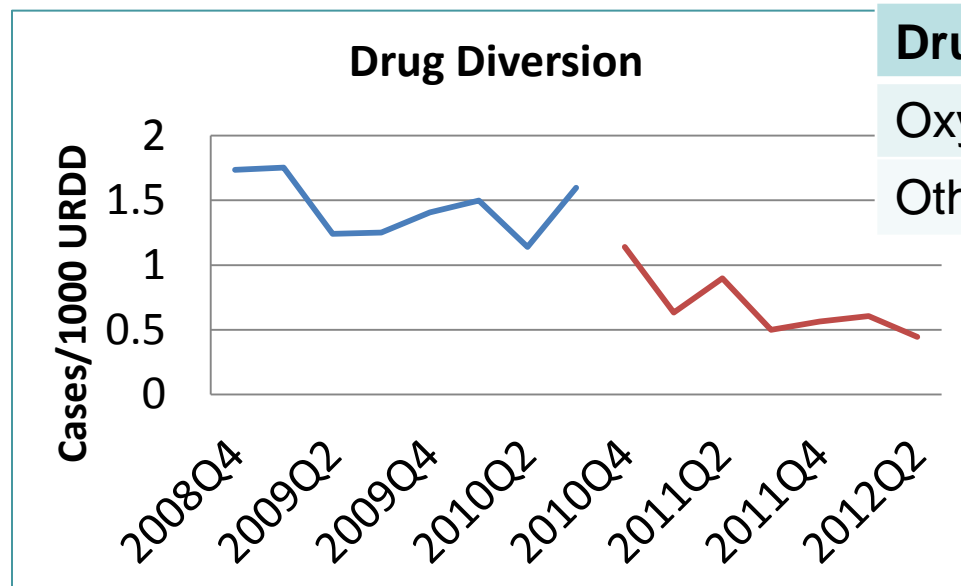# "Abuse Deterrent Formulations"

- OxyContin
- Exalgo
- Suboxone

# OxyContin® URDD Rates per 1,000

### Poison Center



| Drug | Δ(%) |
|------|------|
| Oxycontin | -31.3% |
| Other Opioids | -10.0% |

| | |
|---|---|
| —— (blue) | Before Reformulation |
| —— (red) | After Reformulation |

### Drug Diversion



| Drug | Δ(%) |
|------|------|
| Oxycontin | -52.9% |
| Other Opioids | -16.8% |

URDD: Unique recipients of dispensed drug

# OxyContin® URDD Rates per 1,000



**Opioid Treatment Program**
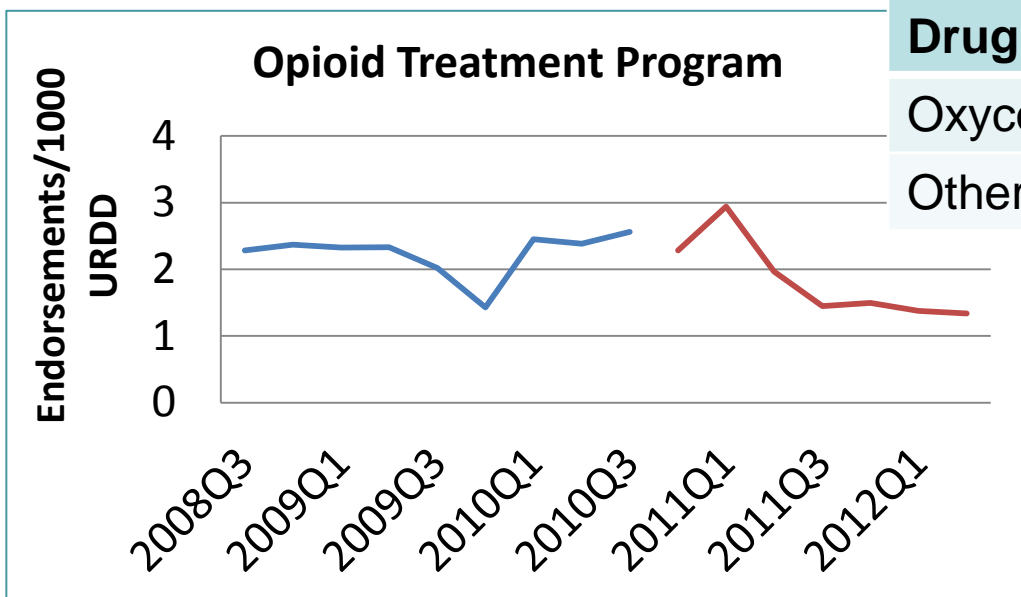
| Drug | Δ(%) |
|------|------|
| Oxycontin | -14.8% |
| Other Opioids | -11.6% |

Before Reformulation
After Reformulation

**Survey of Key Informant Patients**
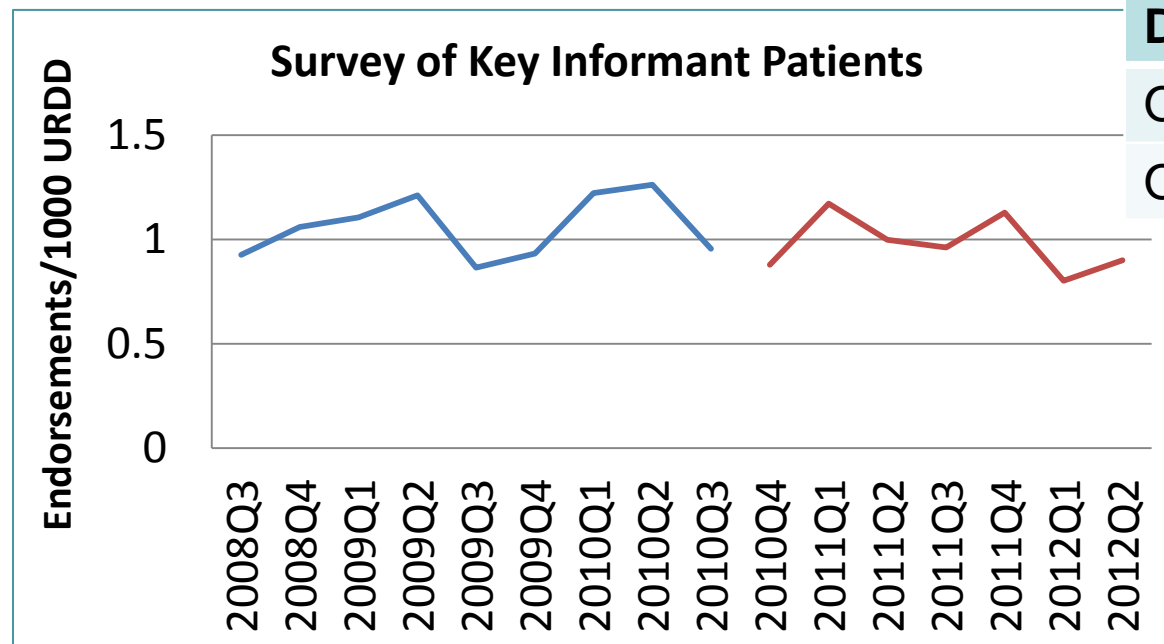
| Drug | Δ(%) |
|------|------|
| Oxycontin | -9.4% |
| Other Opioids | 7.6% |

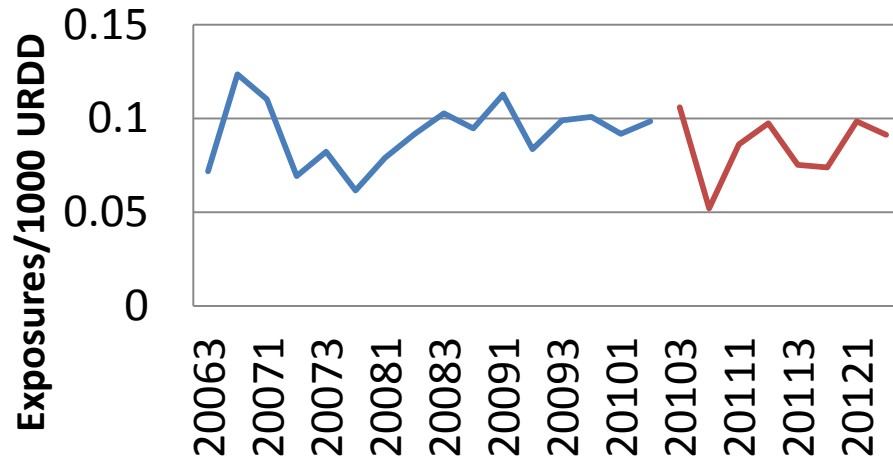URDD: Unique recipients of dispensed drug

# Reformulated OxyContin Conclusions

- Data support that reformulated OxyContin is tamper and abuse deterrent
  - Poision Center abuse, Drug Diversion and Opioid Treatment Program cases have decreased
  - OxyContin rates decreased at a much higher percentage than other opioids over the same time period
  - Decrease in both Population and URDD rates suggests reduction in both availability and desirability
- Reformulated OxyContin may be abuse deterrent for opioids in general
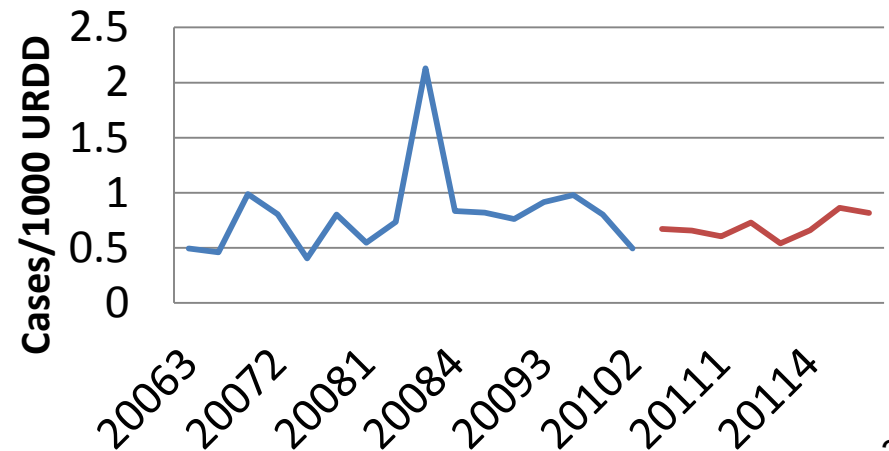- New formulation still is abused
  - SKIP data show minimal effect

URDD: Unique recipients of dispensed drug; SKIP: Survey of key informants' patients

# Hydromorphone (Class) URDD Rates per 1,000



URDD: Unique recipients of dispensed drug

# Hydromorphone (Class) URDD Rates per 1,000



URDD: Unique recipients of dispensed drug

# Exalgo / Hydromorphone Conclusions

- Hydromorphone misuse, abuse and diversion rates per population and URDD have been increasing over time

- Release of Exalgo in March 2010 corresponded with changes in these trends
  - Post-Exalgo release trends declining or remaining stable
  - Decreasing trends in abuse among high risk populations (OTP) were statistically significant after release

- Further study of overall changes in trend patterns continue in RADARS System

URDD: Unique recipients of dispensed drug; OTP: Opioid treatment program

# Availability of Buprenorphine has Expanded
## Unique Recipient of Dispensed Drug (URDD)



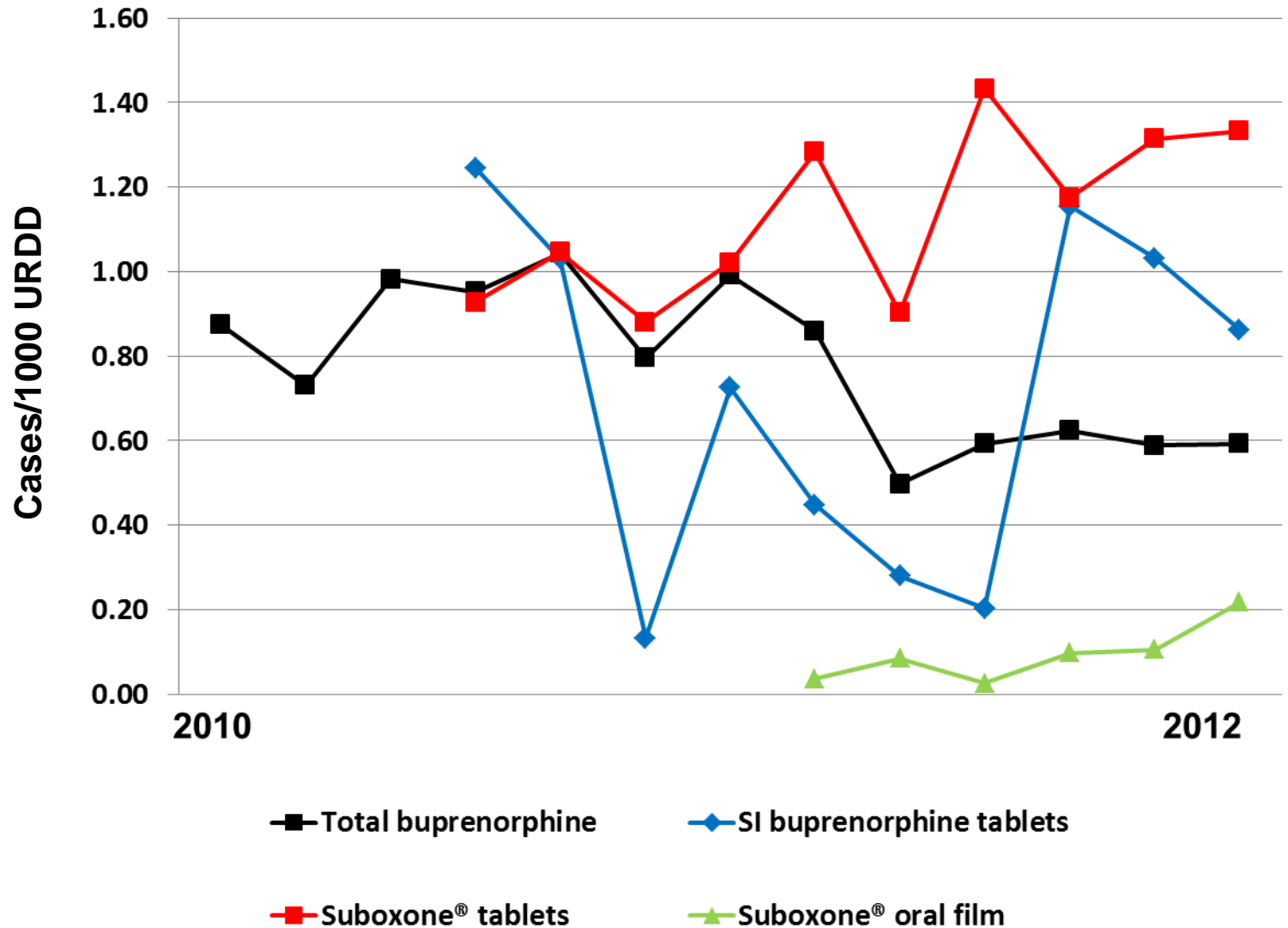URDD: Unique recipients of dispensed drug
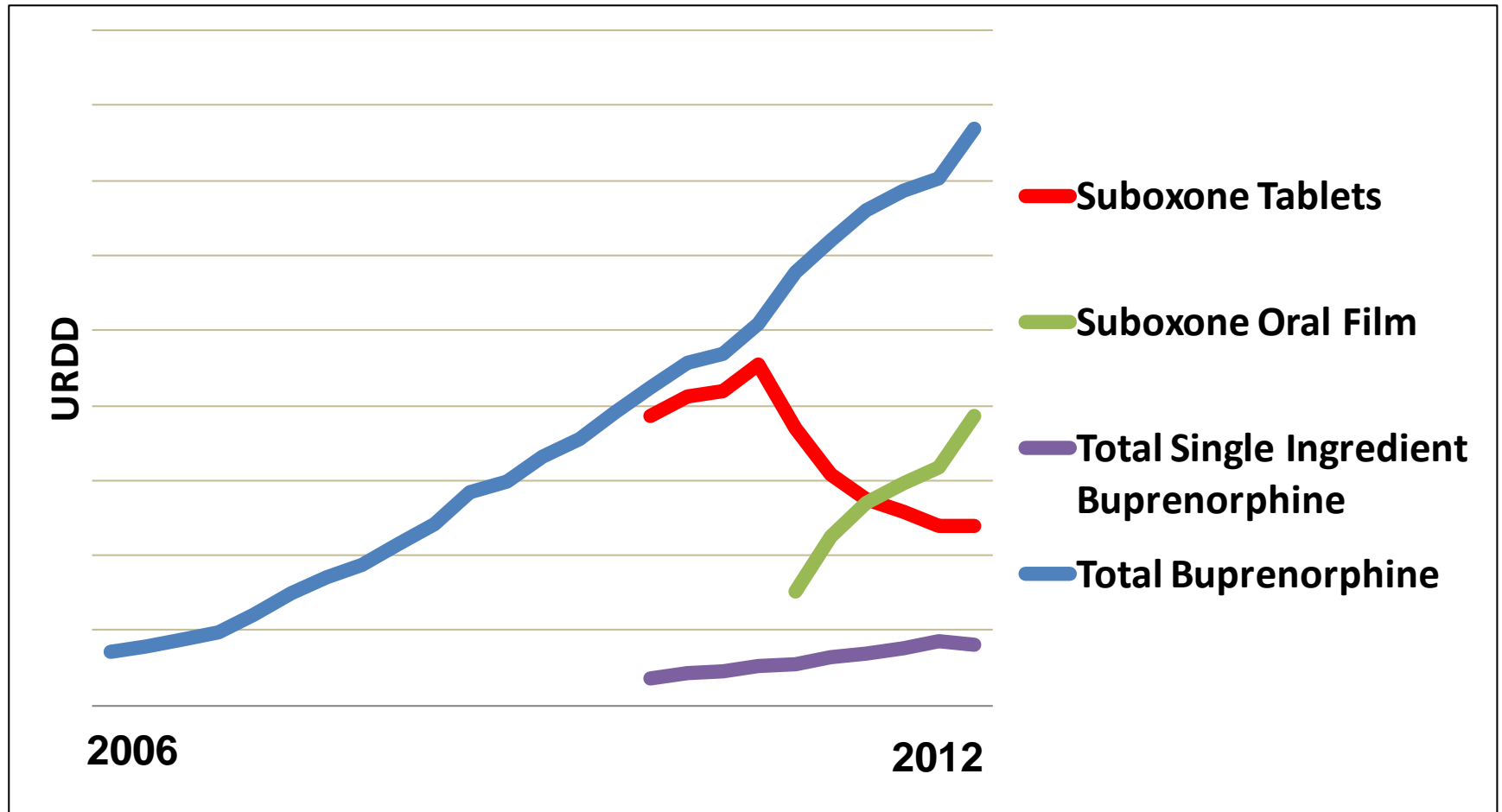
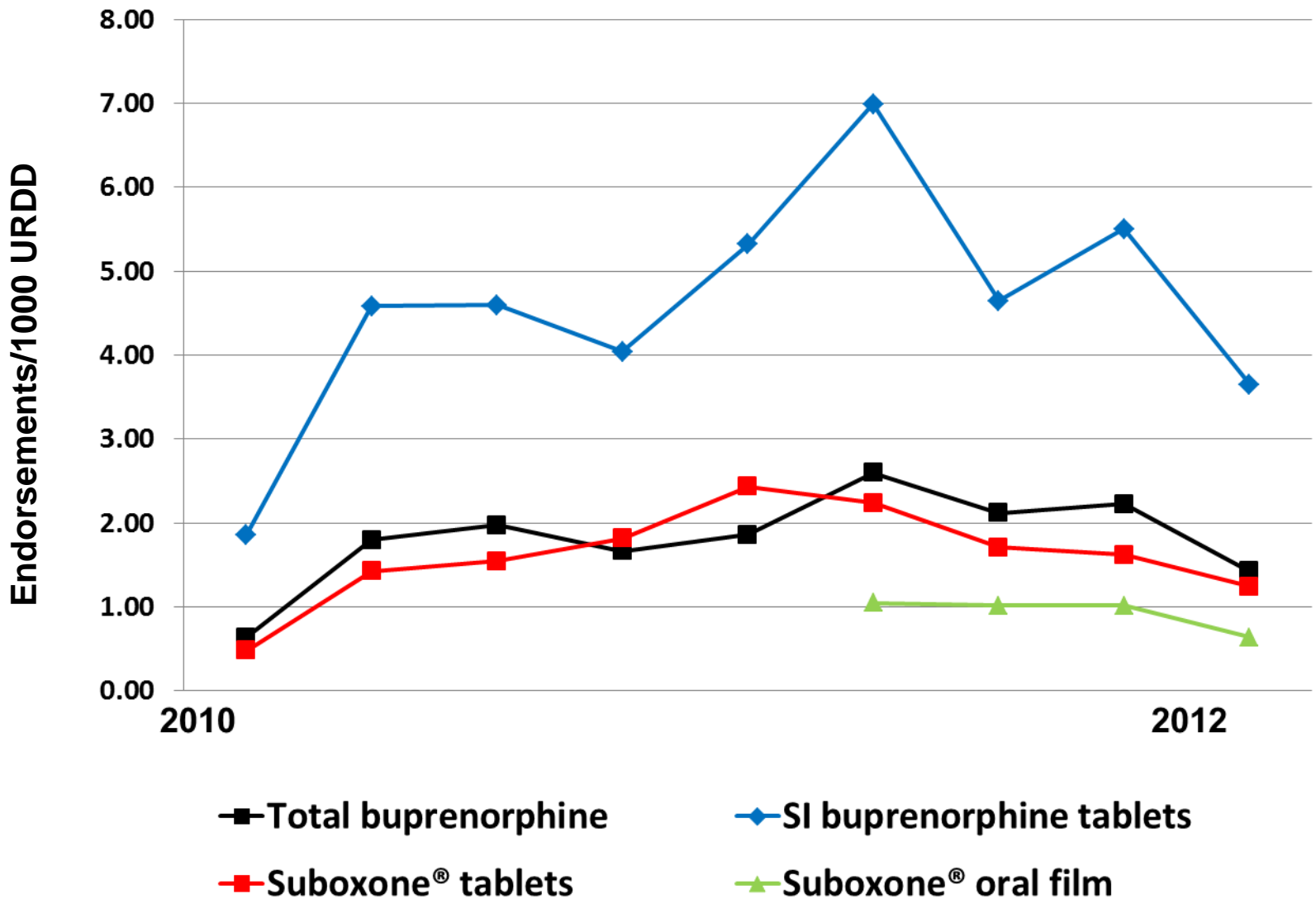# Poison Center
## URDD Rate, 2010 Q1 – 2012 Q1
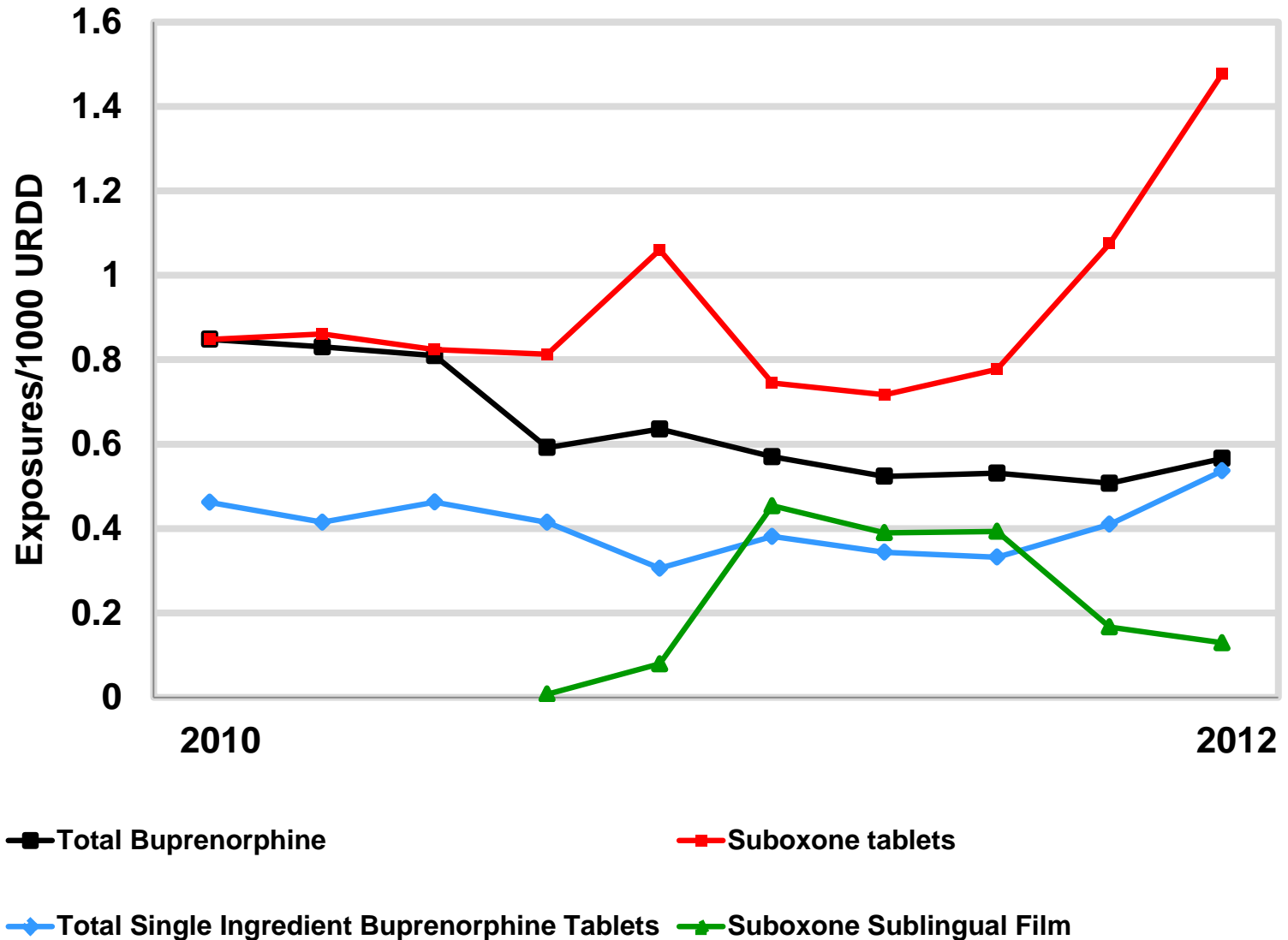
# Drug Diversion
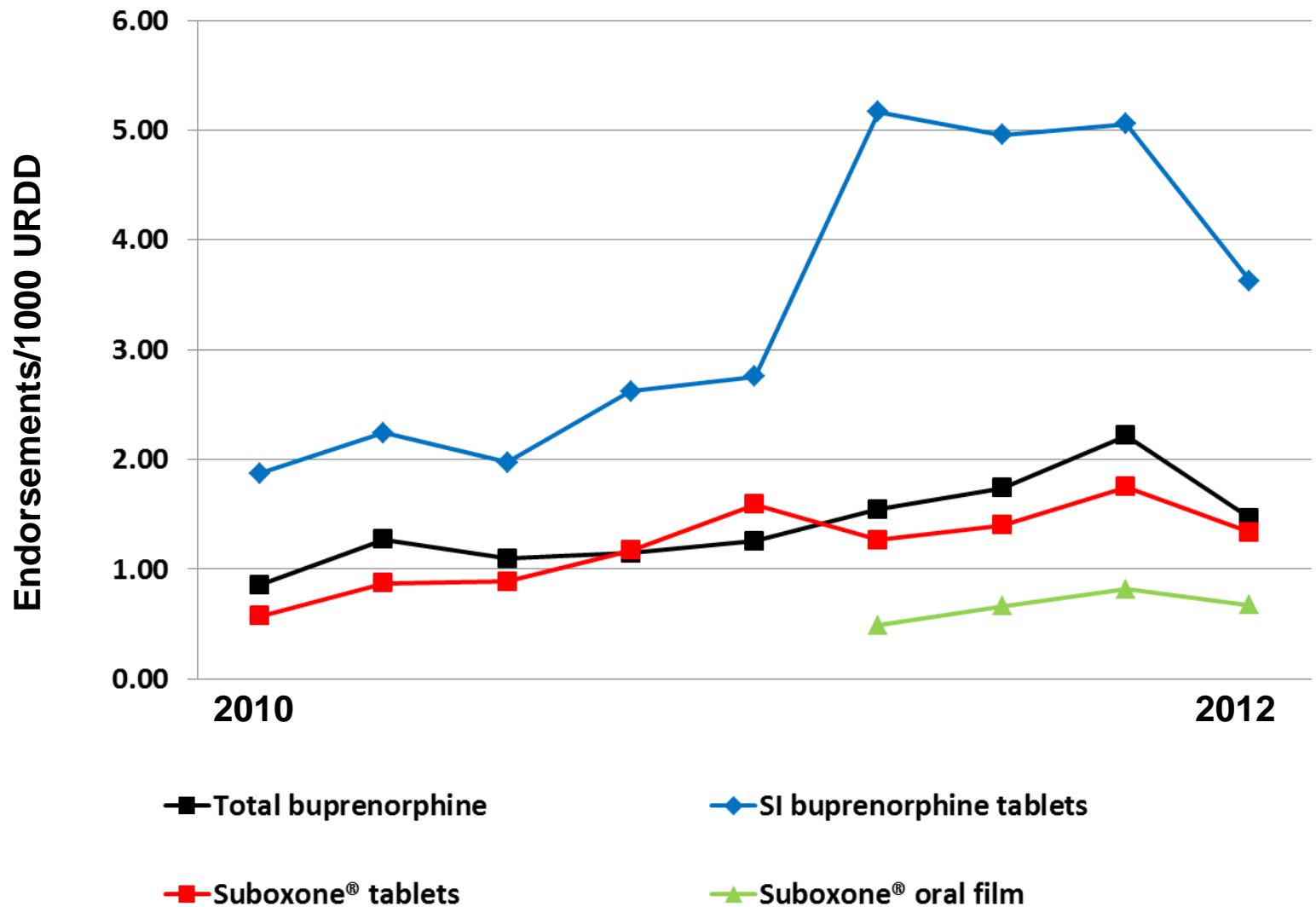## URDD Rate, 2010 Q1 – 2012 Q1

# Opioid Treatment Program
## URDD Rate 2010 Q1 - 2012 Q1

# Survey Key Informants' Patients
## URDD Rate, 2010 Q1 – 2012 Q1

# Buprenorphine Conclusions

- Has availability of buprenorphine expanded?
  - Dramatic increase in people filling a prescription (URDD)
  - Marked increase of misuse and abuse in all systems
- Is Suboxone an abuse deterrent formulation?
  - Yes, endorsements are falling and lower than single ingredient in most programs
- Misuse and abuse of buprenorphine in high risk populations (OTP and SKIP)
  - Total endorsements rising quickly
  - Single ingredient is generally preferred

URDD: Unique recipients of dispensed drug; OTP: Opioid treatment program; SKIP: Survey of key informants' patients

# The Underrecognized Toll of Prescription Opioid Abuse on Young Children

J. Elise Bailey, MSPH
Elizabeth Campagna, MS
Richard C. Dart, MD, PhD
The RADARS System Poison
  Center Investigators*

From the Rocky Mountain Poison and Drug Center–Denver Health, Denver, CO (Bailey, Campagna, Dart); and the University of Colorado School of Medicine, Denver, CO (Dart).
[Ann Emerg Med. 2009;53:419-424.]

*Bailey et al*                                    Prescription Opioid Exposures in Children

**Table 1.** Characteristics and outcomes of childhood (<6 years of age) exposures by opioid analgesic.

| Characteristic | Buprenorphine (n=176) | Fentanyl (n=123) | Hydrocodone (n=6,003) | Hydromorphone (n=68) | Methadone (n=415) | Morphine (n=419) | Oxycodone (n=2,036) | Total (n=9,240) |
|---|---|---|---|---|---|---|---|---|
| **Age, y** | | | | | | | | |
| Median (range) | 2.0 (0.8–5.0) | 1.9 (0.2–5.0) | 2.0 (0.0–5.5) | 2.0 (0.8–5.0) | 2.0 (0.1–5.0) | 2.0 (0.1–5.0) | 2.0 (0.1–5.5) | 2.0 (0.0–5.5) |
| Male, No. (%)* | 99 (56.3) | 64 (52.5) | 3,232 (53.9) | 33 (48.5) | 232 (56.7) | 224 (53.5) | 1,081 (53.5) | 4,965 (53.9) |
| **Outcome, No. (%)[†]** | | | | | | | | |
| No effect | 40 (32.0) | 51 (64.6) | 2,673 (77.3) | 32 (74.4) | 173 (62.2) | 171 (64.8) | 916 (78.4) | 4,056 (74.9) |
| Minor effect | 55 (44.0) | 17 (21.5) | 708 (20.5) | 11 (25.6) | 55 (19.8) | 64 (24.2) | 186 (15.8) | 1,096 (20.2) |
| Moderate effect | 25 (20.0) | 8 (10.1) | 71 (2.1) | 0 | 34 (12.2) | 24 (9.1) | 52 (4.4) | 214 (4.0) |
| Major effect | 5 (4.0) | 3 (3.8) | 6 (0.2) | 0 | 14 (5.0) | 5 (1.9) | 10 (0.8) | 43 (0.8) |
| Death | 0 | 0 | 2 (0.1) | 0 | 2 (0.7) | 0 | 4 (0.3) | 8 (0.1) |
| Unknown[§] | 47 | 44 | 2,385 | 22 | 127 | 136 | 779 | 3,540 |
| Confirmed nonexposure | 4 | 0 | 158 | 3 | 10 | 19 | 89 | 283 |

# Poison Center Program
# Unintentional General, Medical Outcome
## Children 0 – 6 Years (2009 Q4 – 2012 Q2)
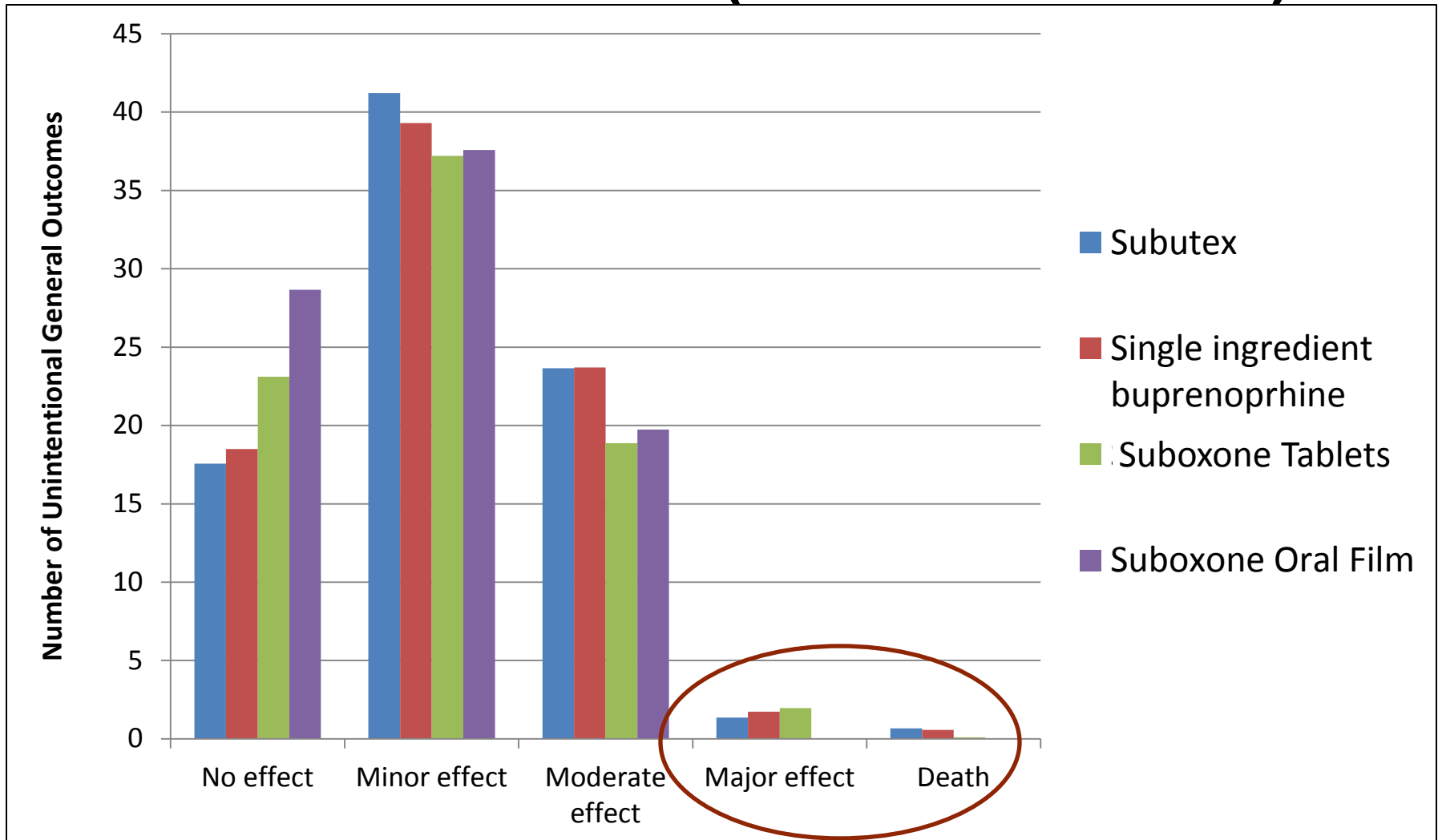
# Moving Forward: USA

- **Pharmaceutical strategies**
  - Improve physical tamper resistance (i.e. OxyContin®, Exalgo®)
  - Decrease abuse potential chemically (i.e. Suboxone®)

- **Regulatory strategies**
  - FDA Approval of Extended Release (ER) & Long Acting (LA) opioid Risk Evaluation Mitigation Strategy (REMS) in July 2012; other class-wide REMS in draft
  - Introduction of Prescription Monitoring Programs (PMP) across US

- **Measuring impact of these strategies**
  - RADARS® System Data Trending
  - Mosaic approach

# RADARS® System
# Global Prescription Drug Surveillance

# Poison Center Studies

- Global Poison Center Collaboration
  - Harmonization of poison center data from 7 countries from 2007 through 2010
    - United States, United Kingdom, Germany, Italy, Netherlands, Switzerland, Australia

- Objective
  - Characterize human exposures to prescription opioids and stimulants reported to poison centres

# Opioid Treatment Studies

- European Opiate Addiction Treatment Association (Europad) Pilot

- Principal Investigator: Icro Maremmani
  - Currently collecting data from opioid treatment facilities in 4 countries
    - Italy, Spain, France, and Germany
  - Data collection to continue through the spring 2013
  - Minimum of 250 surveys from each country

# **Future Plans**

- Expansion of surveillance of EU opioid treatment programs
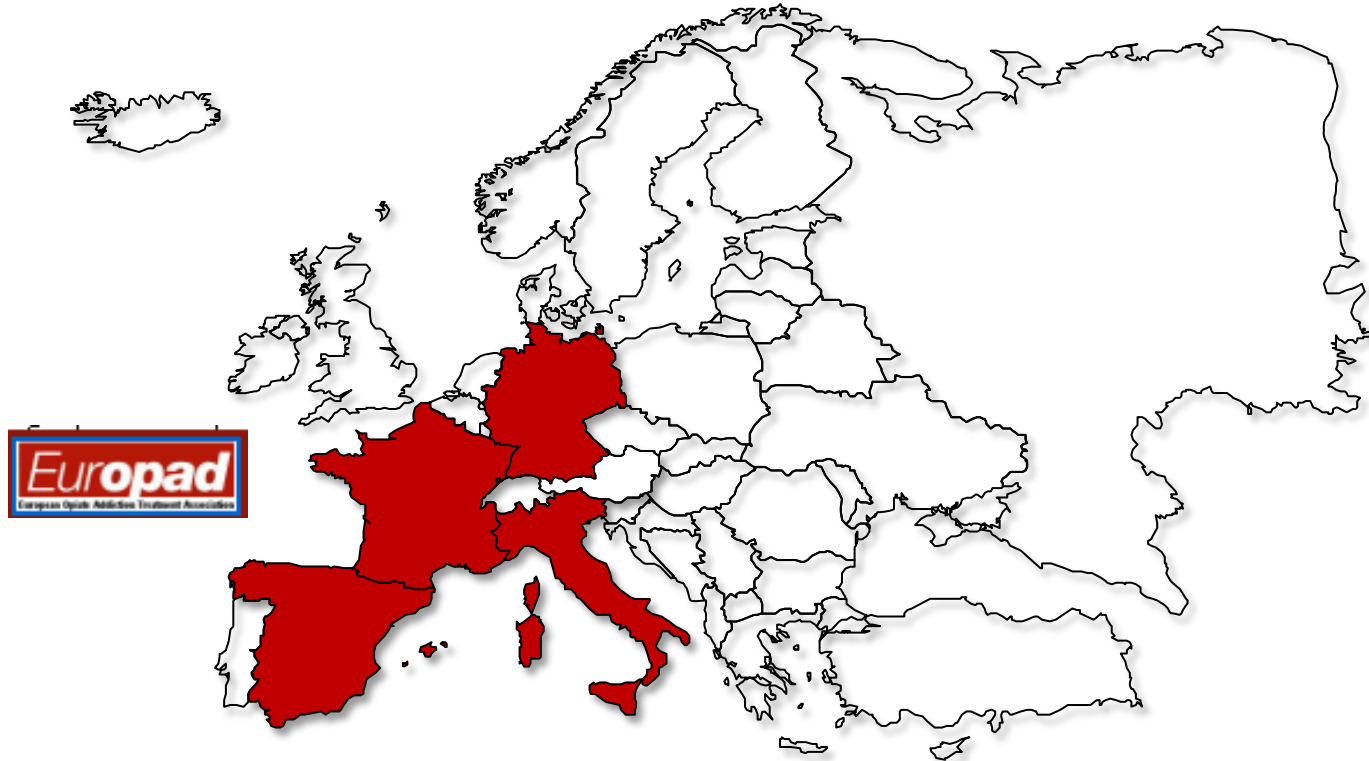
# Lessons Learned

- Important to employ mosaic approach
  - No one data source is perfect
  - Different sources answer different questions
  - Triangulation and validation of external data sources

- Abuse deterrent of tamper resistant formulations <u>can</u> impact misuse and diversion of prescription opioids
  - Dependent upon how drug is misused
  - Important to monitor consequence of "squeezing the balloon"

- Systematic measurement to gauge impact of interventions is critical
  - Baseline data to understand trends
  - Consistent methodology

# Thank You!

**For further information or questions:**

**jody.green@rmpdc.org**

**www.radars.org**

# *Q&A SESSION*

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