Abuse, Misuse, and Diversion of Prescription Opioids:
Evaluating the Problem and Proposed Solutions

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Relationships

- Employed by the Denver Health and Hospital Authority
  - We operate the RADARS® System
- The RADARS System collects and analyzes data about prescription drug abuse, misuse, and diversion
  - Manufacturers subscribe to these data and use them for pharmacovigilance and regulatory reporting

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2

Relationships

- Through my employer, I also have research funding from
  - BTG International (snake venom)
  - McNeil Consumer Healthcare (non-prescription analgesics)
- Any margin supports DHHA
- No bonus or personal reward
- No personal conflicts

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Objectives

- Overview of data collection approaches used in the US

- Discuss some abuse / misuse / diversion prevention strategies currently employed in the US
  - Data evaluating effectiveness

A Fragmented System

- No unified medical record
- Multiple payors, including cash
  - No central administrative database
- Poor communication between prescribers
- No record of prescriptions written
- Many different legal entities involved

Major Official Data Sources

Data Source	Reporting Delay
Death Certificates	3 years
National Health and Nutrition Examination Survey	2 – 5 years
Drug Abuse Warning Network	2 – 3 years
Monitoring the Future	2 years
National Survey on Drug Use and Health	1 year
Drug Enforcement Administration	6 months
Claims databases (Medicaid, etc.)	Varies

Problems With Official Data

- Small samples
  - Coverage gaps & lack of geospecificity
- Chart review & survey issues
- Delay
- All exposure types may not be counted
- No formulation-specific data
  - At best, by active pharmaceutical ingredient

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A Study We Wish We Could Do

Social Assistance Patients
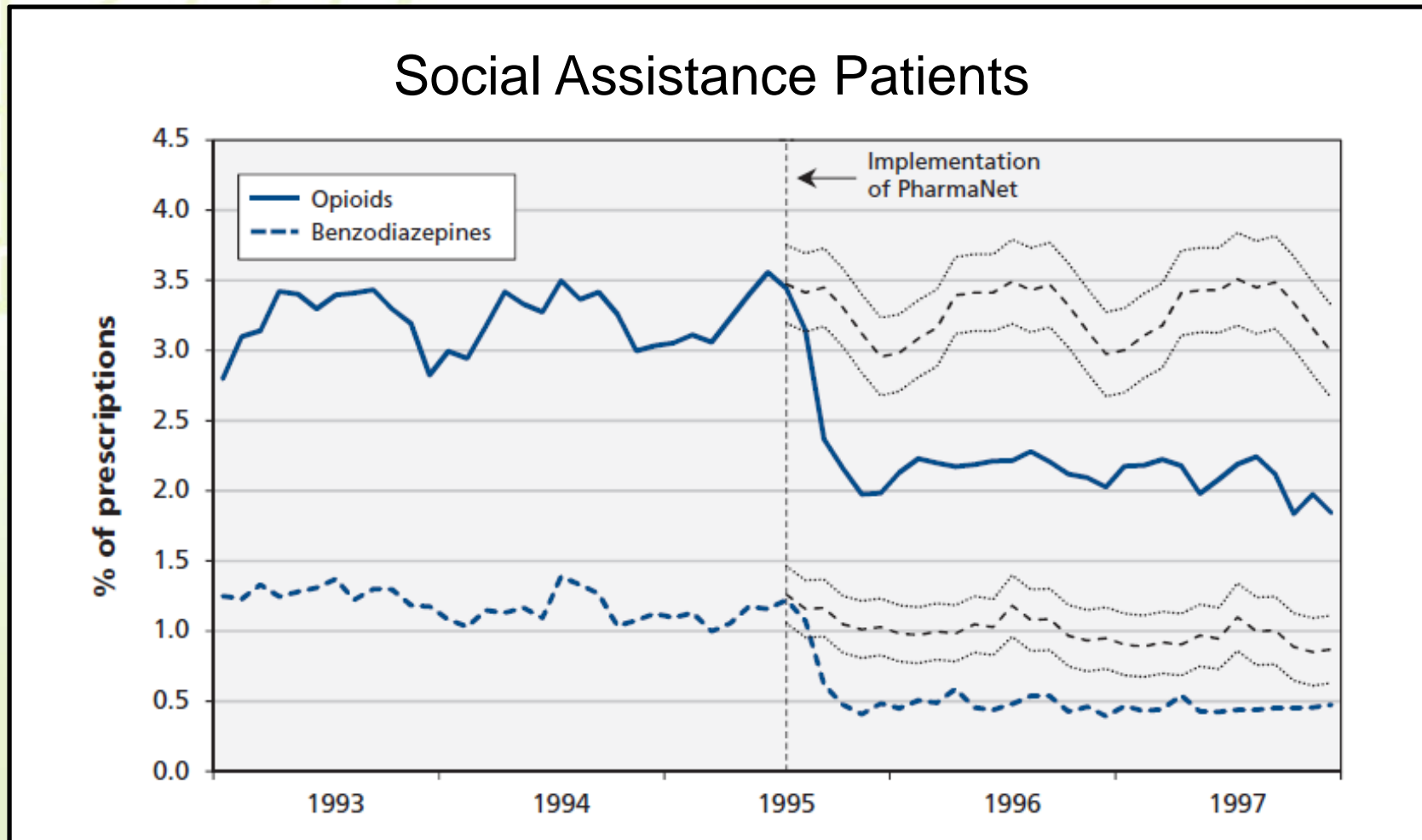
Dormuth CR *et. al.* Effect of a centralized prescription network on inappropriate prescribiing for opioid analgesics and benzodiazepines. *CMAJ*2012, ePub.

8

RADARS® System Mosaic Approach

Poison Center | Acute Events
51 centers
47 states

Drug Diversion | Law Enforcement
280 investigators
50 states

Opioid Tx Program (OTP) | Patients in Tx
73 programs
33 states

Survey of Key Informant Patients (SKIP) | Patients in Tx
125 pratices
50 states

College Survey | 2000 students
50 states
3x each year

**StreetRX (website)** | User/Buyers
Crowdsourcing
50 states

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9

How Specific?

- Geographic: 3-digit ZIP code
- Date: Year / quarter
- Age: Whole year (> 80 years combined)
- Formulation: Product and manufacturer
  - Some reports: Unclassifiable / NOS
  - "Roll-up" categories

Denominators

- Population
- Patients filling prescriptions for each formulation
  - A measure of availability
  - Unique Recipients of a Dispensed Drug, URDD

11

Extent of the US Problem
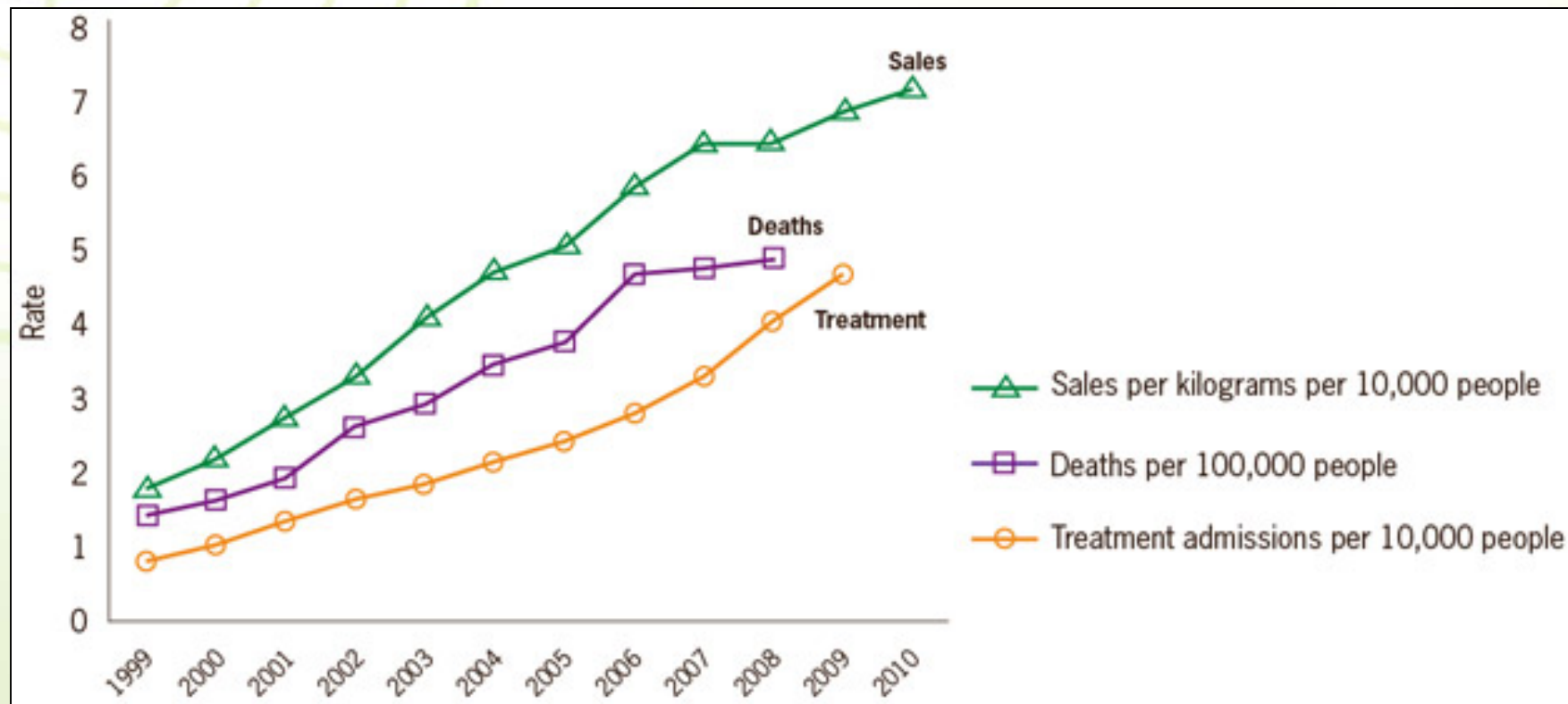
Most Abused Prescription Opioids
Population Rates, US, Jan - June 2012

Rank	PC	OTP	SKIP	DD	CS
1	Hydrocodone	Oxycodone	Hydrocodone	Oxycodone	Hydrocodone
2	Oxycodone	Hydrocodone	Oxycodone	Hydrocodone	Oxycodone
3	Tramadol	Methadone	Hydromorphone	Morphine	Morphine
4	Methadone	Morphine	Morphine	Buprenorphine	Tramadol
5	Morphine	Hydromorphone	Buprenorphine	Hydromorphone	Methadone
6	Buprenorphine	Oxymorphone	Methadone	Methadone	Fentanyl
7	Fentanyl	Buprenorphine	Fentanyl	Oxymorphone	Buprenorphine
8	Hydromorphone	Fentanyl	Oxymorphone	Tramadol	Hydromorphone
9	Oxymorphone	Tramadol	Tramadol	Fentanyl	Oxymorphone
10	Tapentadol	Tapentadol	Tapentadol	Tapentadol	Tapentadol

3

Most Abused Prescription Opioids
## Population Rates, US, All Programs Combined
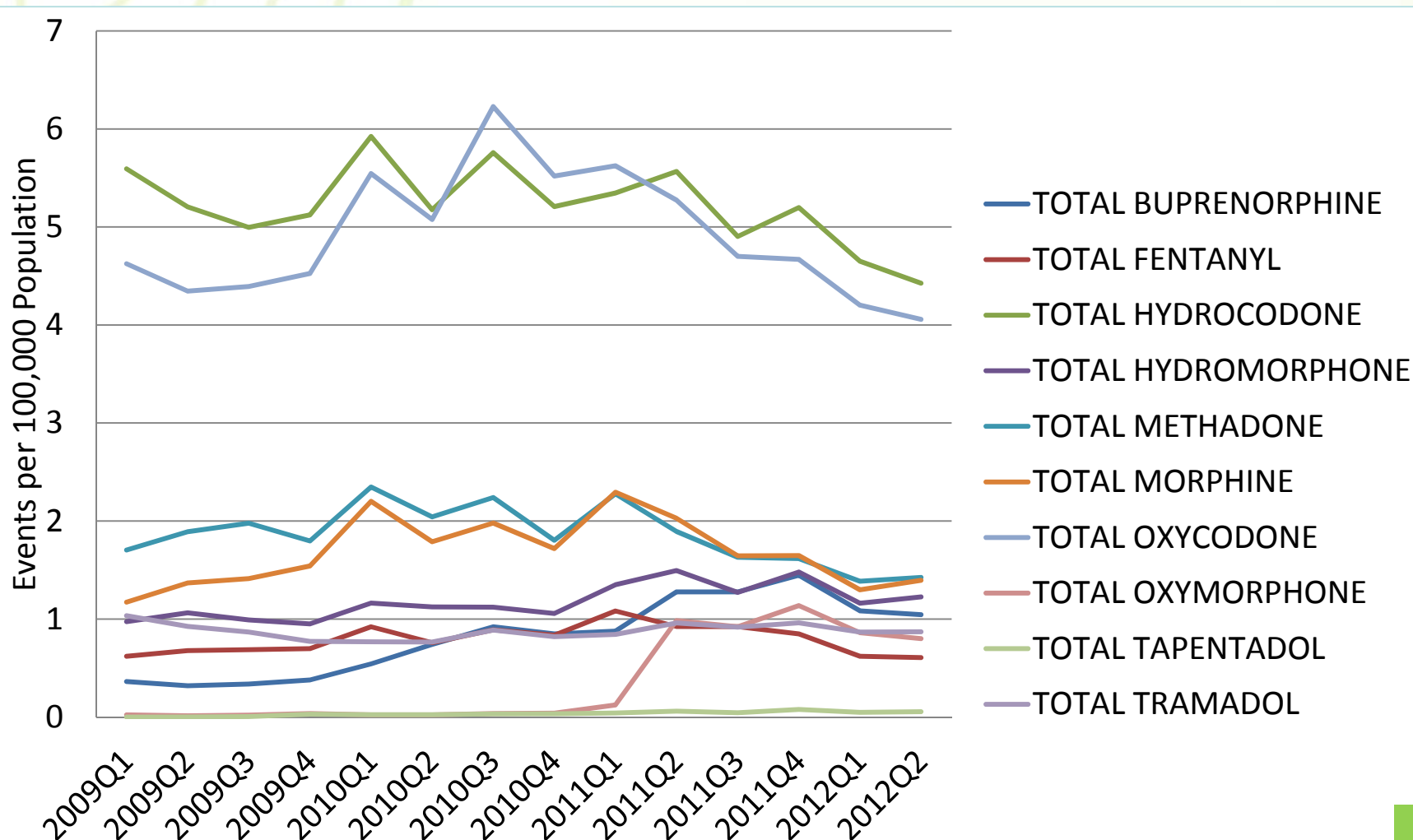
Most Abused Prescription Opioids
URDD Rates, US, Jan - June 2012

Rank	PC	OTP	SKIP	DD	CS
1	Methadone	Oxymorphone	Oxymorphone	Oxymorphone	Oxymorphone
2	Oxymorphone	Methadone	Hydromorphone	Hydromorphone	Methadone
3	Buprenorphine	Hydromorphone	Methadone	Methadone	Tapentadol
4	Hydromorphone	Morphine	Buprenorphine	Buprenorphine	Morphine
5	Morphine	Buprenorphine	Morphine	Morphine	Hydromorphone
6	Fentanyl	Fentanyl	Fentanyl	Oxycodone	Fentanyl
7	Tramadol	Oxycodone	Oxycodone	Fentanyl	Buprenorphine
8	Oxycodone	Tapentadol	Tapentadol	Hydrocodone	Oxycodone
9	Tapentadol	Hydrocodone	Hydrocodone	Tramadol	Tramadol
10	Hydrocodone	Tramadol	Tramadol	Tapentadol	Hydrocodone

5

Most Abused Prescription Opioids
URDD Rates, US, All Programs Combined
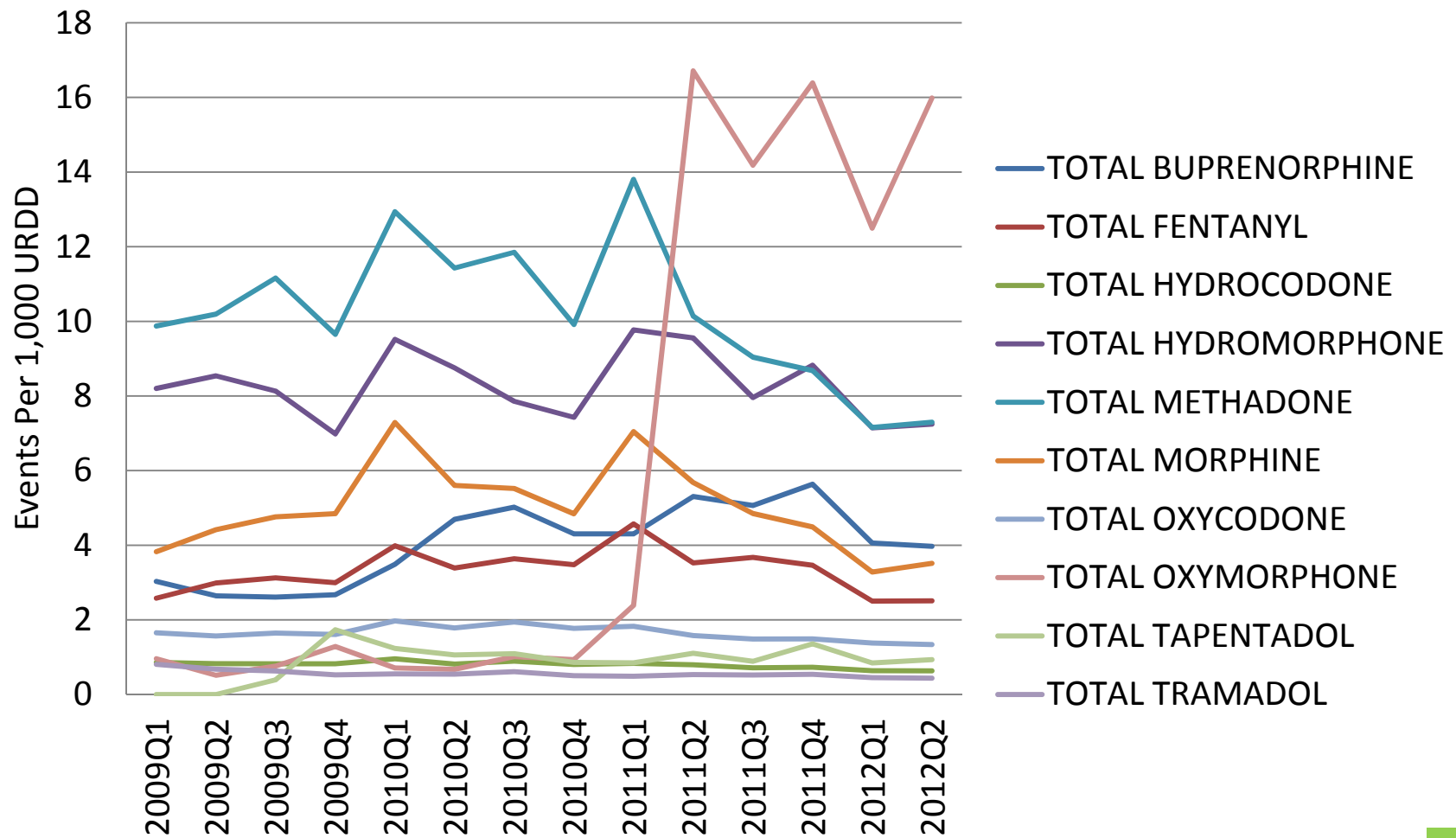
Interventions the US is Trying

- Abuse-deterrent and abuse-resistant formulations
- Prescription drug monitoring programs
- Community-based interventions

Tamper-Resistant and Abuse-Deterrent Formulations

- Hard coatings
- Polymers which turn to viscous gel when heated
- Polymers which resist dissolving in water and alcohol
- Novel delivery systems (patches, implants, etc.)
- Antagonists (naloxone)
- Aversive ingredients
- Nasal tissue irritants

Reformulated OxyContin

- August 2010

**OxyContin
OC**

**OxyContin
OP**

OxyContin Abuse Rates
Population Rates, Oct 2008 – June 2012
Poison Center Program – Intentional Abuse

Drug	Δ(%)
Oxycontin	-39.3%
Other Opioids	0.9%

Before Reformulation
After Reformulation

20
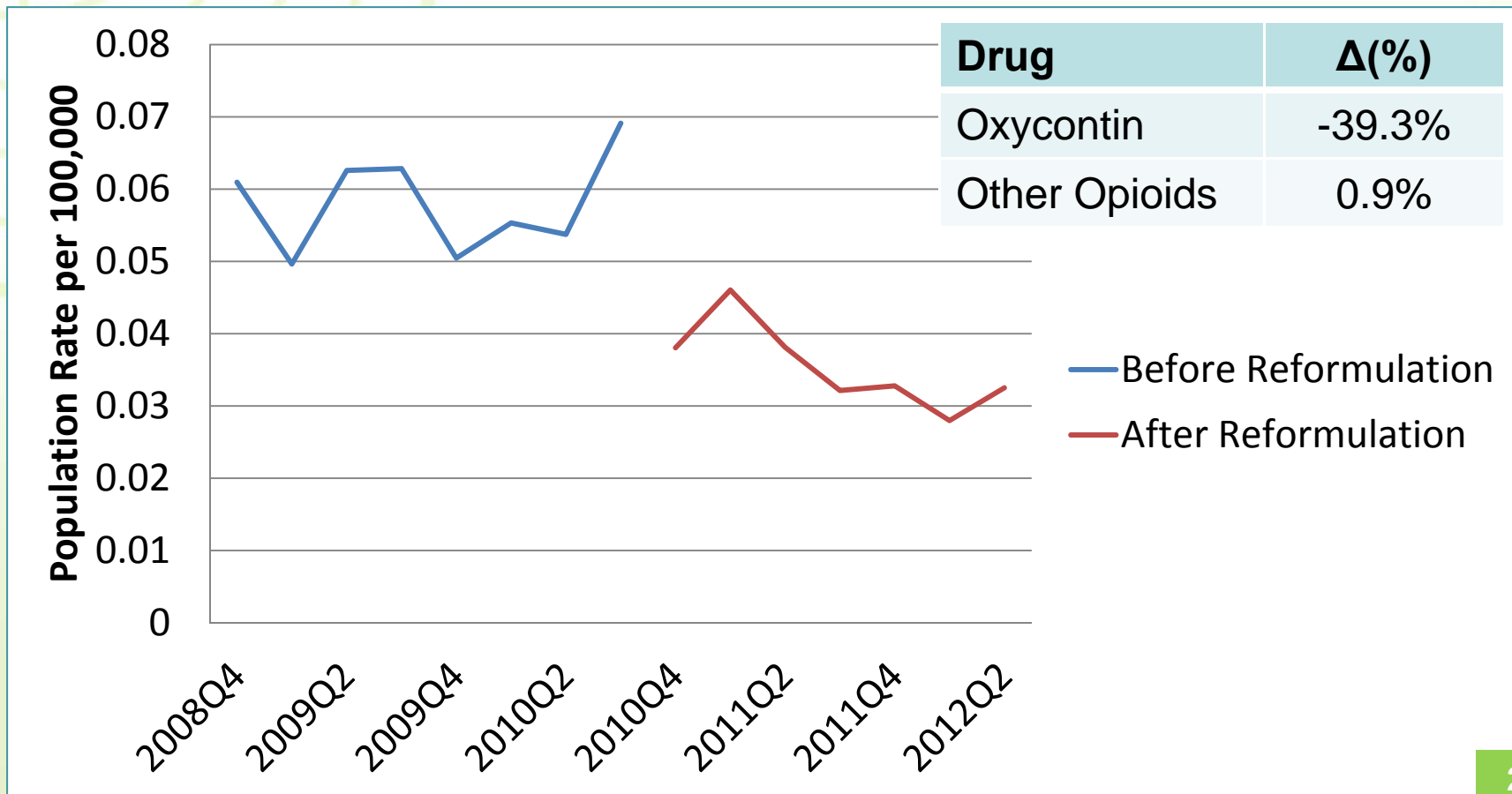
OxyContin Diversion Case Rates
Population Rates, Oct 2008 – June 2012
Drug Diversion Program
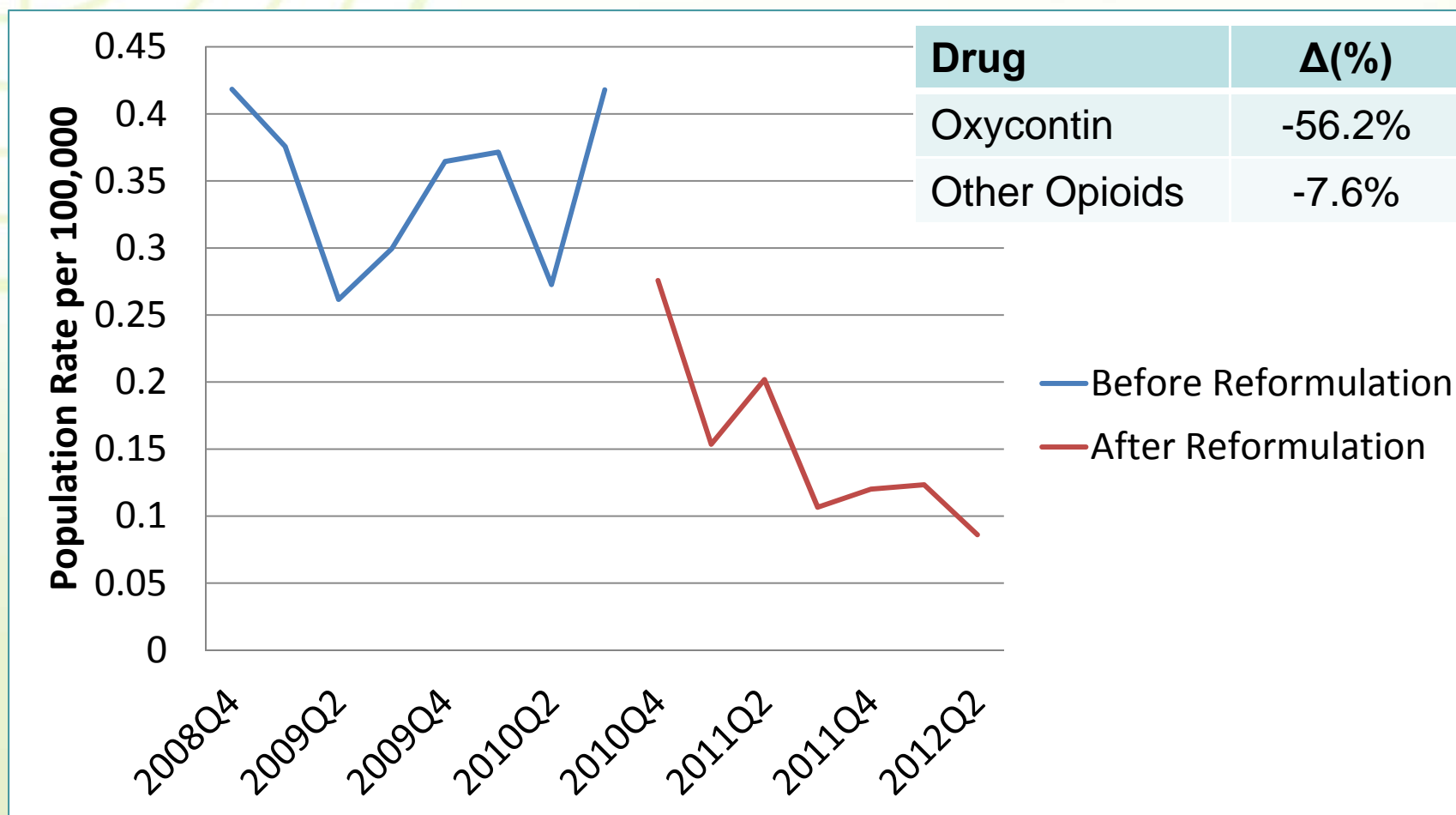
Drug	Δ(%)
Oxycontin	-56.2%
Other Opioids	-7.6%

Legend: Before Reformulation, After Reformulation

Y-axis: Population Rate per 100,000 (0 to 0.45)

X-axis: 2008Q4, 2009Q2, 2009Q4, 2010Q2, 2010Q4, 2011Q2, 2011Q4, 2012Q2

OxyContin Abuse Rates
Population Rates, Oct 2008 – June 2012
Opioid Treatment Program

Drug	Δ(%)
Oxycontin	-24.5%
Other Opioids	-9.5%

Before Reformulation

After Reformulation

OxyContin Abuse Rates
Population Rates, Oct 2008 – June 2012
Survey of Key Informants' Patients Program

Drug	Δ(%)
Oxycontin	-8.3%
Other Opioids	18.7%

Before Reformulation
After Reformulation
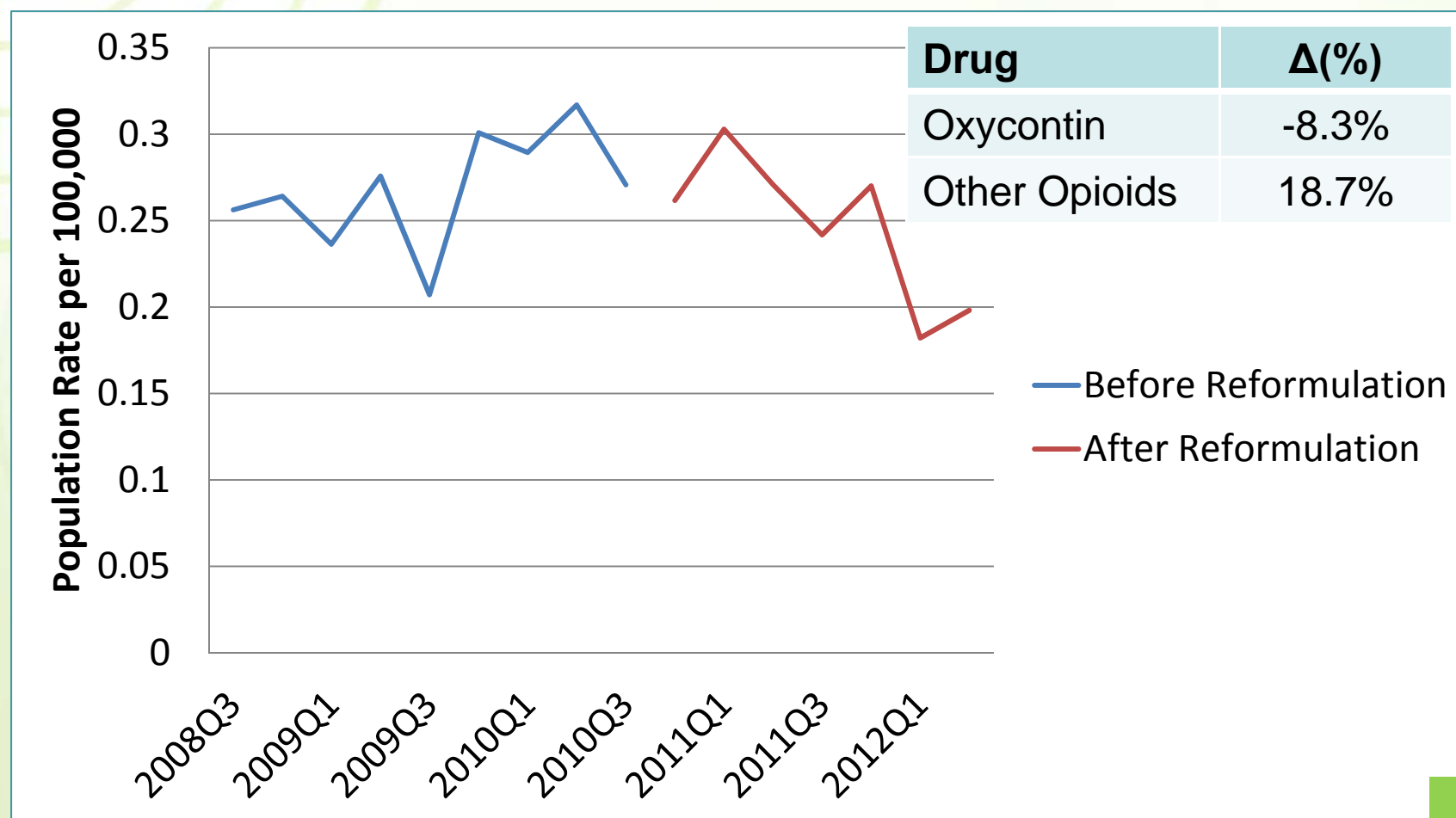
OxyContin Rates
URDD Rates, Oct 2008 – June 2012

Poison Center
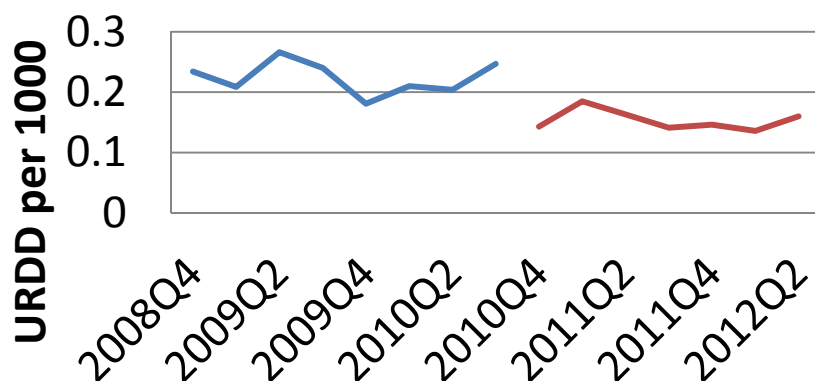
Drug	Δ(%)
Oxycontin	-31.3%
Other Opioids	-10.0%

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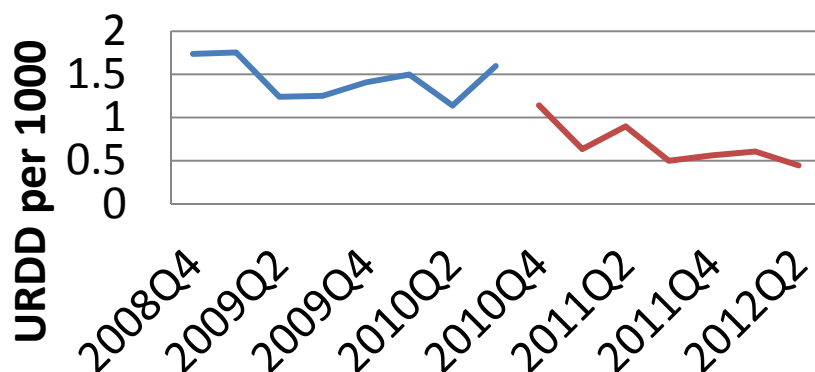
Drug	Δ(%)
Oxycontin	-52.9%
Other Opioids	-16.8%

OxyContin Rates
URDD Rates, Oct 2008 – June 2012

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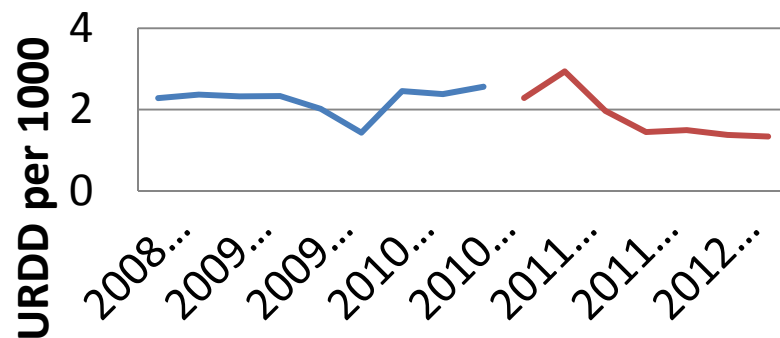
Drug	Δ(%)
Oxycontin	-14.8%
Other Opioids	-11.6%

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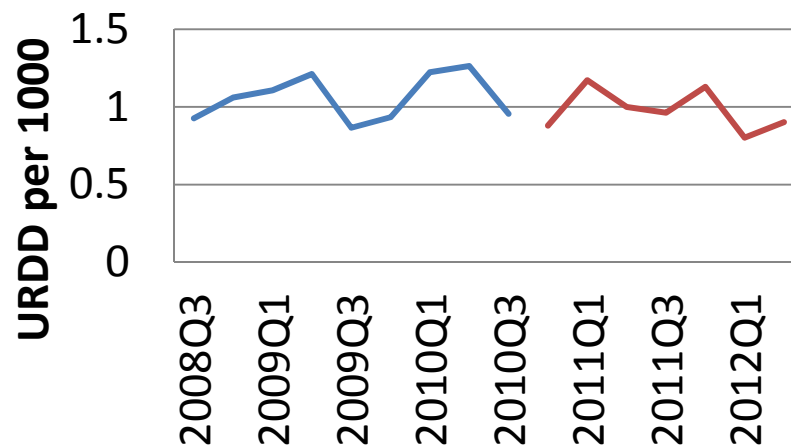
Drug	Δ(%)
Oxycontin	-9.4%
Other Opioids	7.6%

25

Street Price Down 18%

The RADARS® System Drug Diversion Program
OxyContin Street Price
1st Quarter 2010 to 4th Quarter 2011

$0.83/mg

$0.68/mg

OxyContin (old formulation)
OxyContin Reformulated
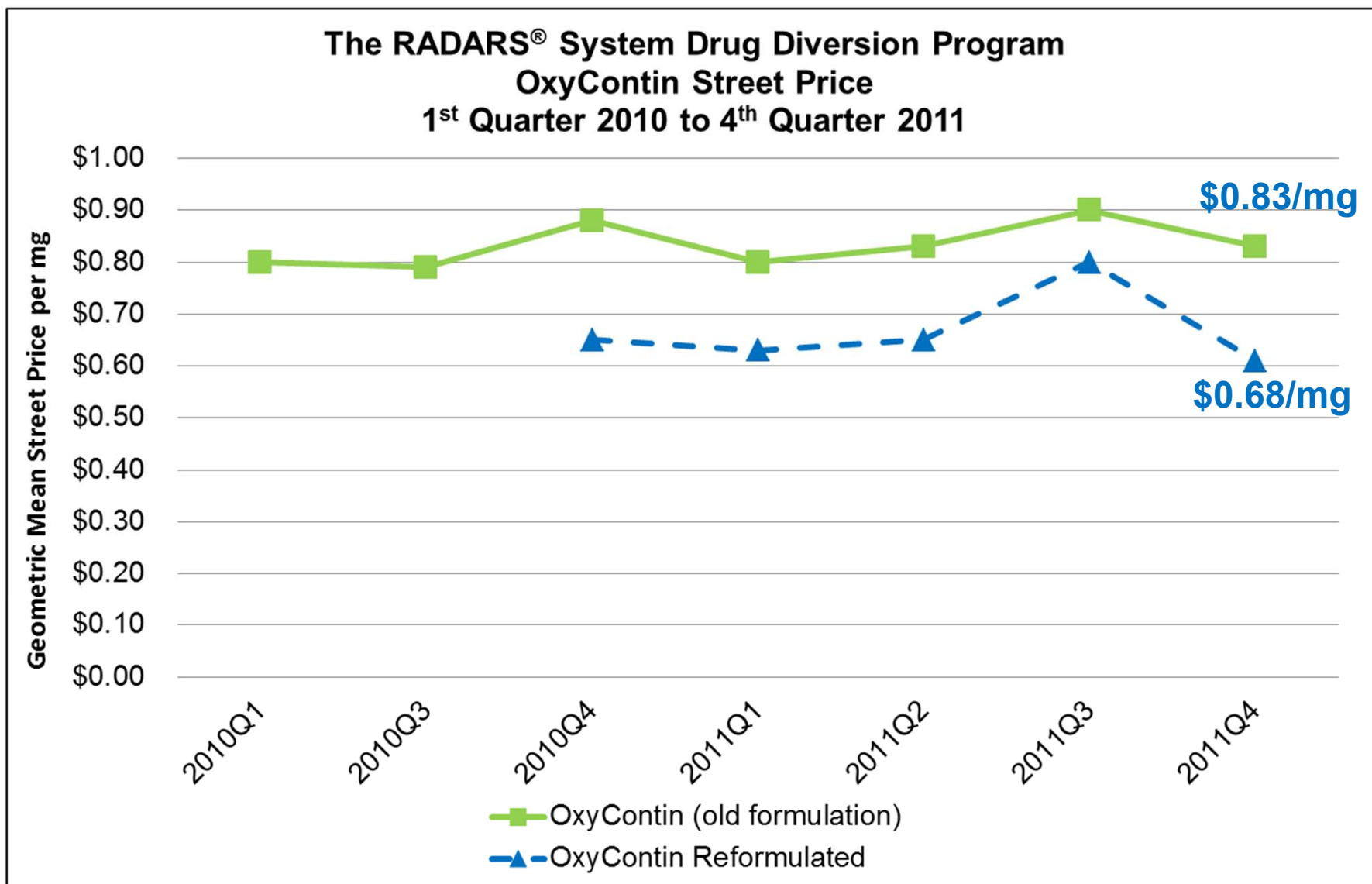
Evidence of OxyContin Abuse Deterrence

- Rates decreased in PC (abuse) and DD
  - More decrease than other opioids
  - Decrease in both population and URDD rates
- Effect less pronounced in treatment programs
  - Minimal in SKIP
- Price per mg less for new formulation
- Evidence of shifting to alternatives

Buprenorphine

- Single ingredient tablets
  - Formerly Subutex®; now generic only
- Naloxone combination tablets
  - Suboxone®, brand-only (for now)
- Naloxone combination film
  - Suboxone®, brand-only

28

Overall Buprenorphine Abuse is Increasing

The RADARS® System SKIP Program
Buprenorphine Abuse Rates per 100,000 Population
1st Quarter 2009 – 1st Quarter 2012

Total_Buprenorphine

29
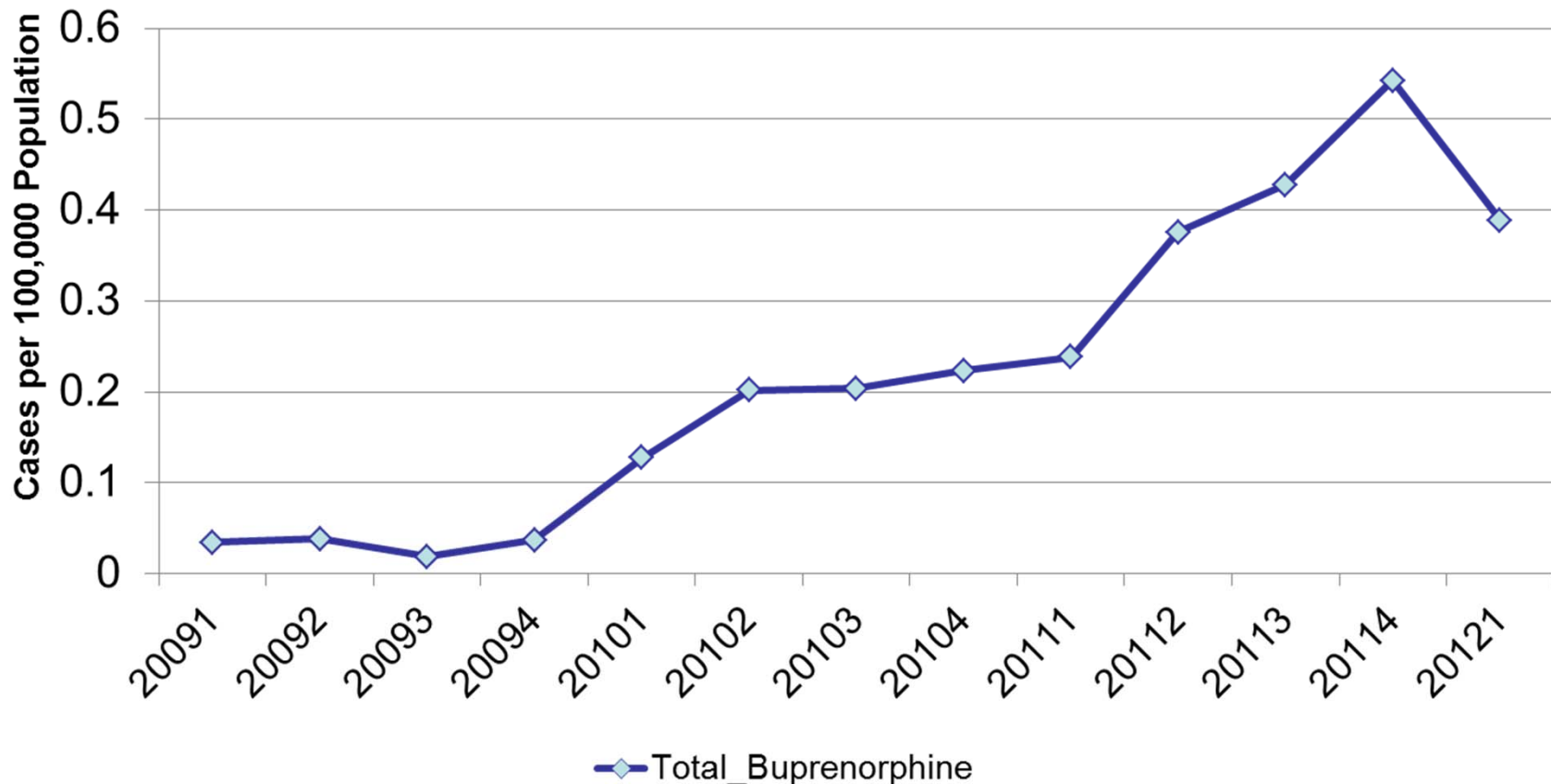
Single-Ingredient Buprenorphine URDD Rates Rising

Poison Center Program
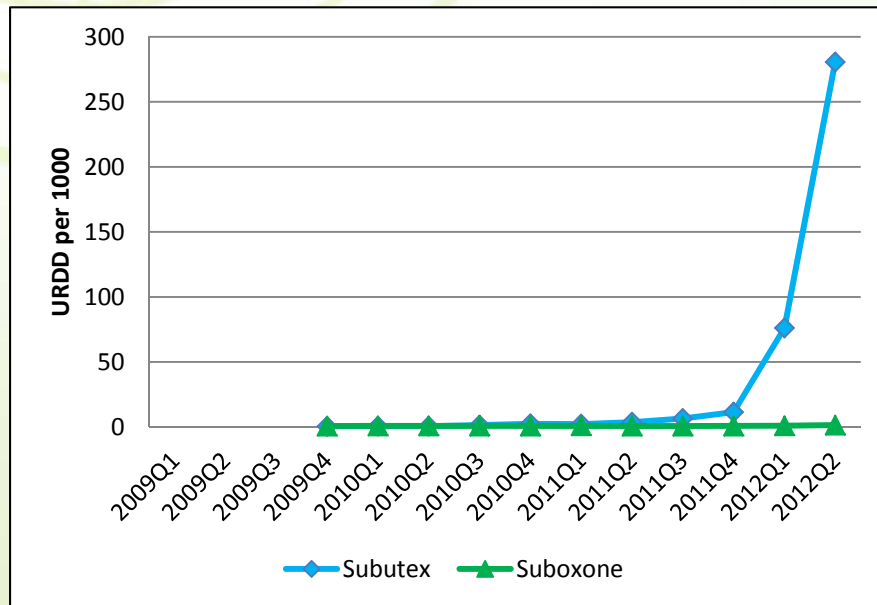
Drug Diversion Program
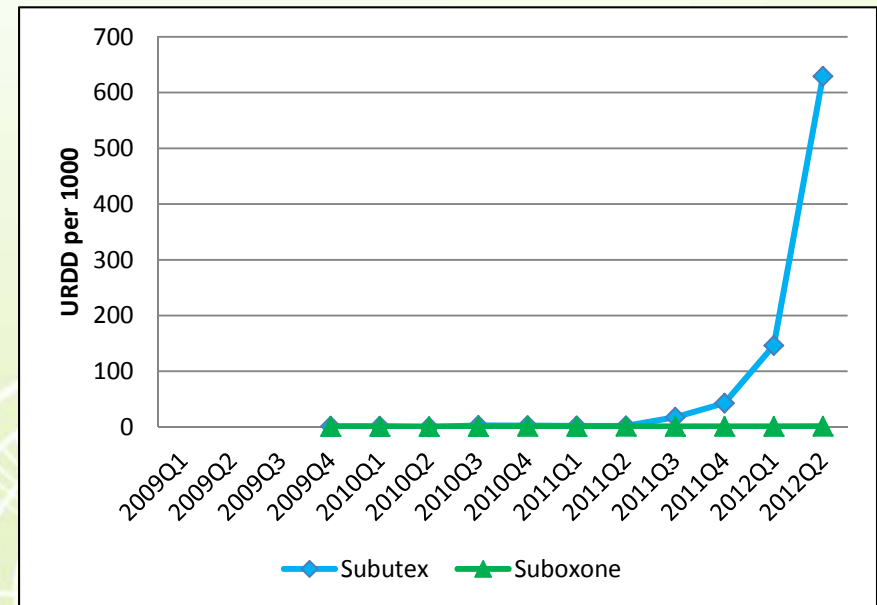
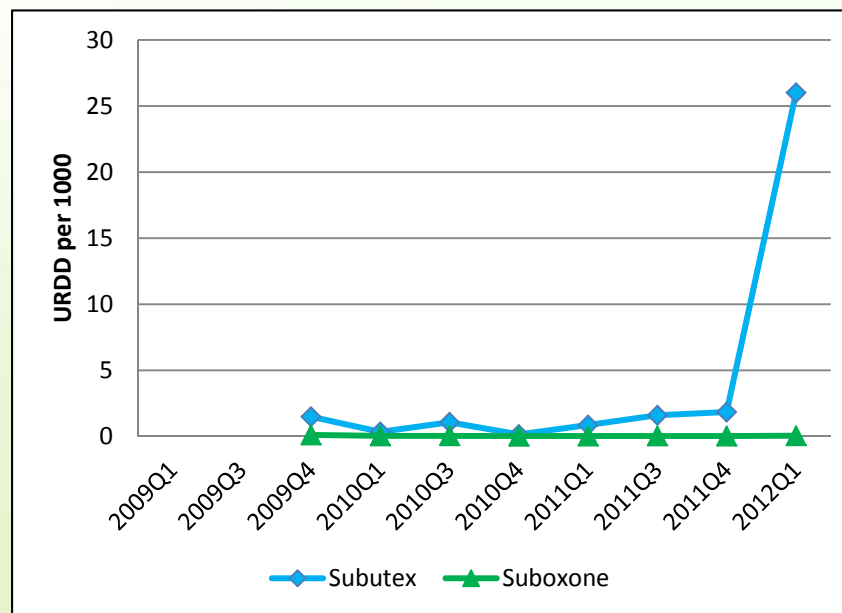# Single-Ingredient Buprenorphine URDD Rates Rising

Opioid Treatment Program
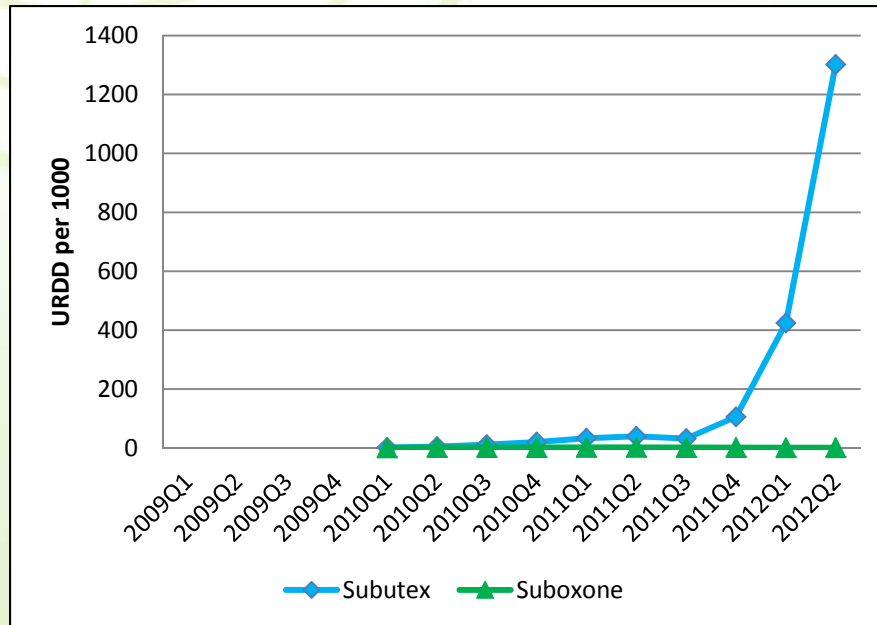
Survey of Key Informants' Patients Program
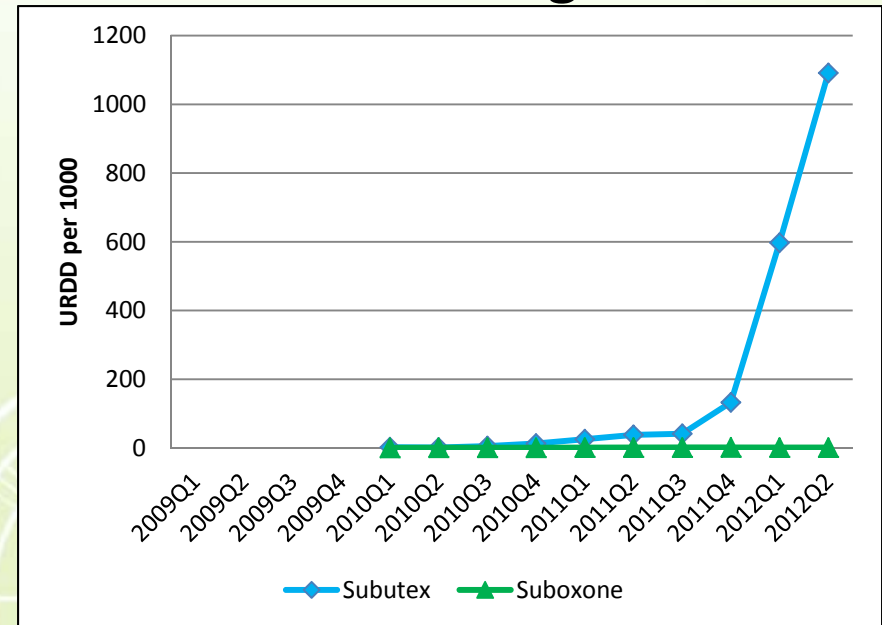
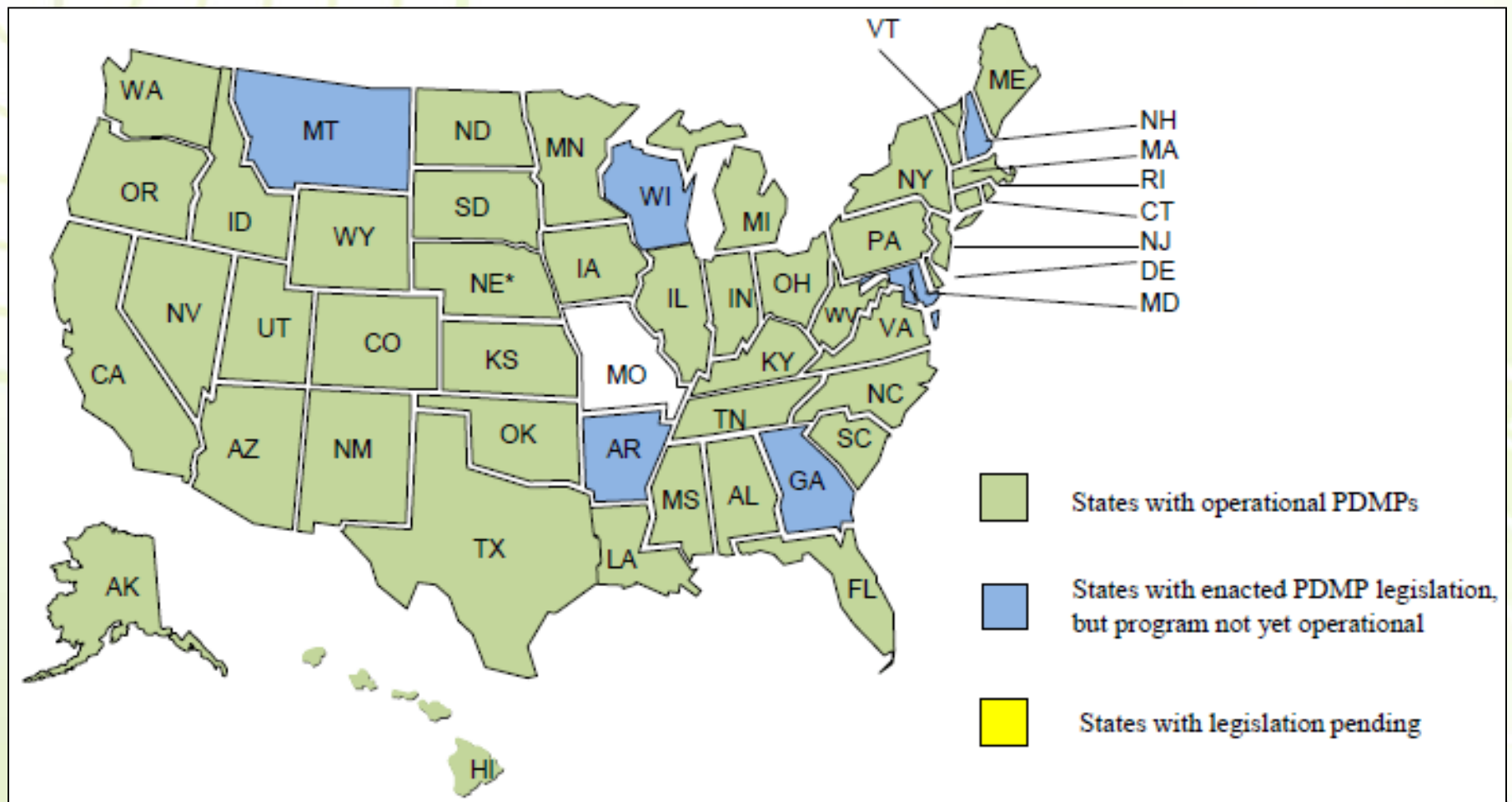# Single-Ingredient Buprenorphine URDD Rates Rising

College Survey Program

Buprenorphine

- Dramatic increase in prescribing makes population rates hard to interpret
- Abuse occurs (not just "street detox")
- Naloxone combination products are less preferred by abusers
- Dramatic increase in diversion / abuse of single ingredient tablets
  - Out of proportion to URDD

Prescription Drug Monitoring Programs

- State-based with federal funding
- Monitor patient and provider behavior
- Wide variety in:
  - Governance & intent
  - Ease of use
- No national integration
- White House designated priority strategy

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34

PDMPs Operational in 43 States

States with operational PDMPs

States with enacted PDMP legislation, but program not yet operational

States with legislation pending

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35

Limitations of PDMPs

- Not all PDMPs cover hydrocodone, codeine, and tramadol
- Cannot account for all sources of supply
  - Methadone maintenance programs
  - Veterans Administration
  - Indian Health Service
- Require prescriber to submit a query
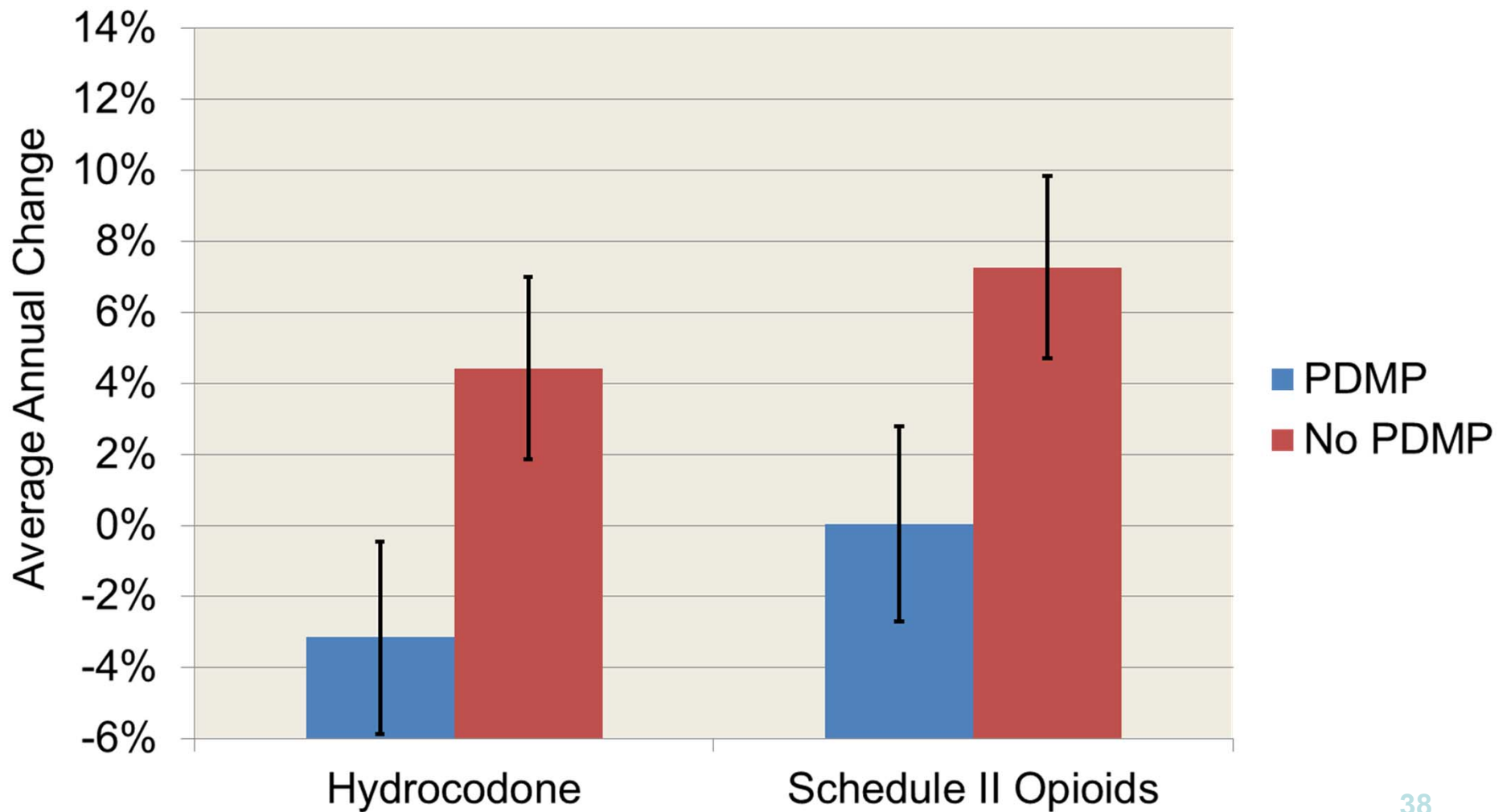 - Time consuming → unterutilization

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36

Poison Center Program
Intentional Abuse Exposures
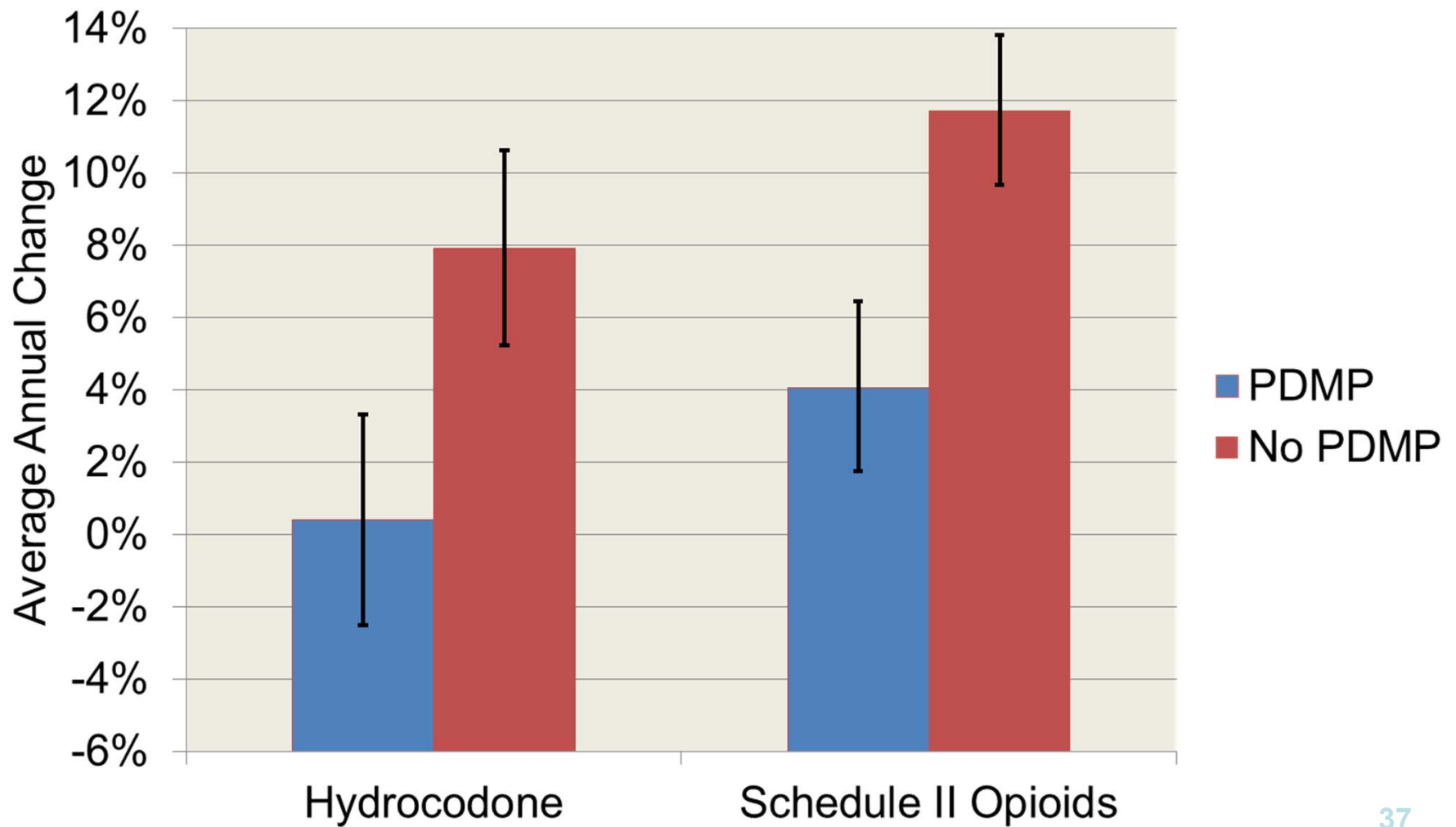
Poison Center Program
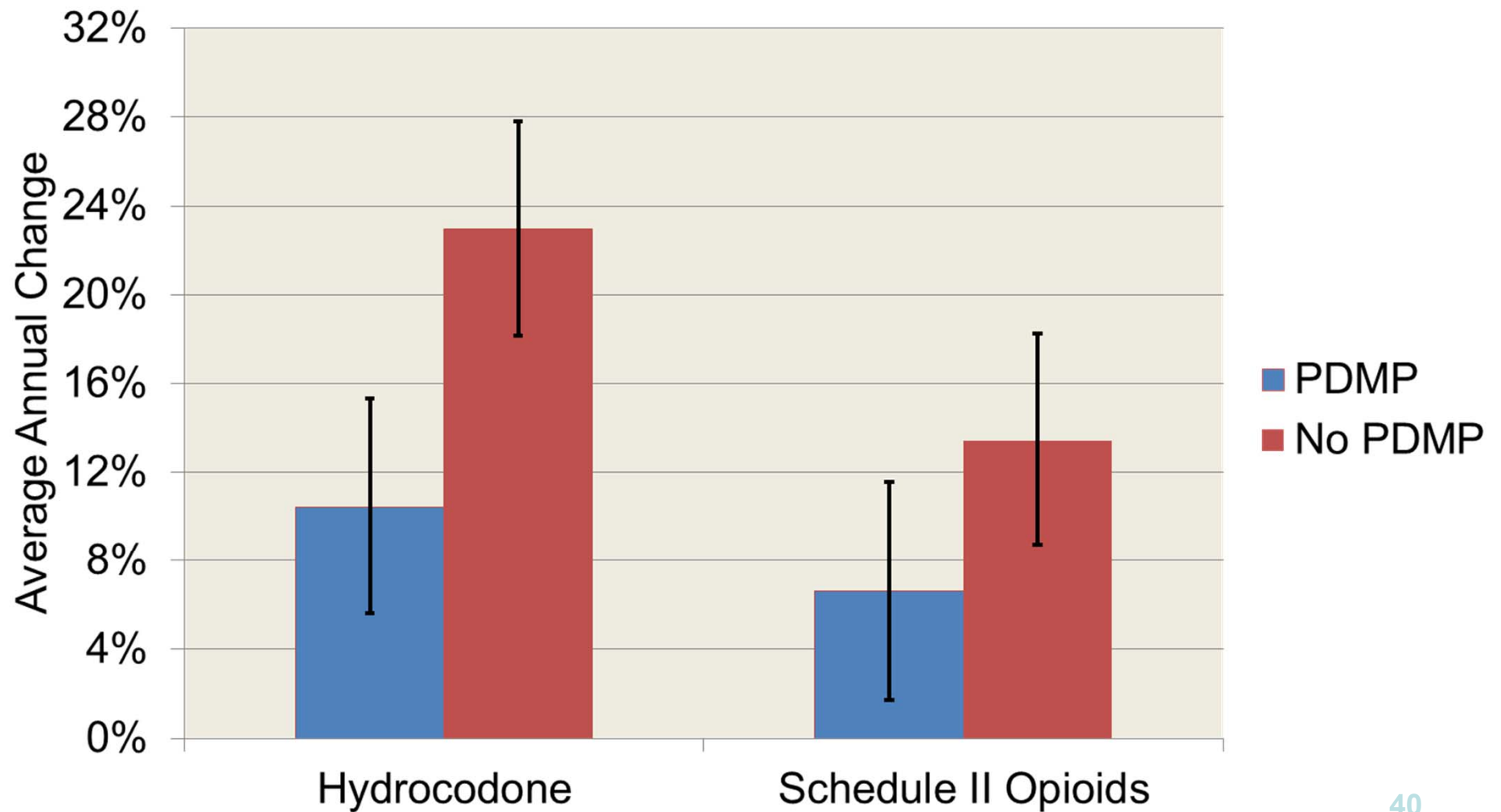## *Intentional Abuse Exposures, Adjusted for Drug Supply*

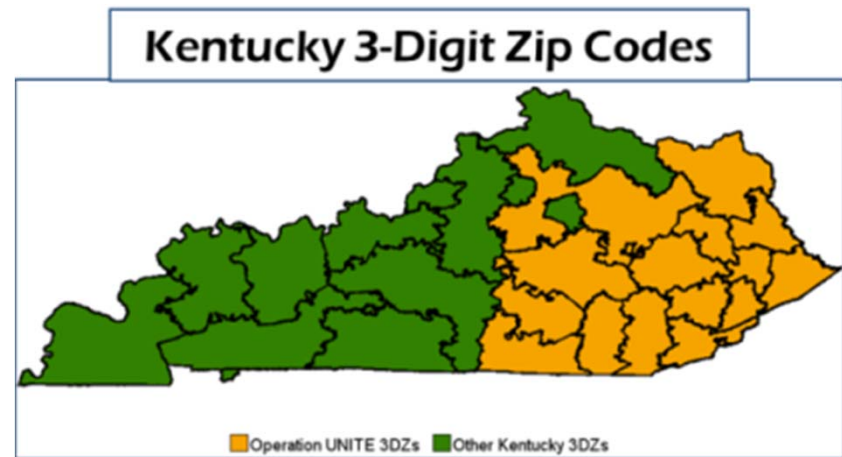# Treatment Programs
Opioid Abuse Mentions
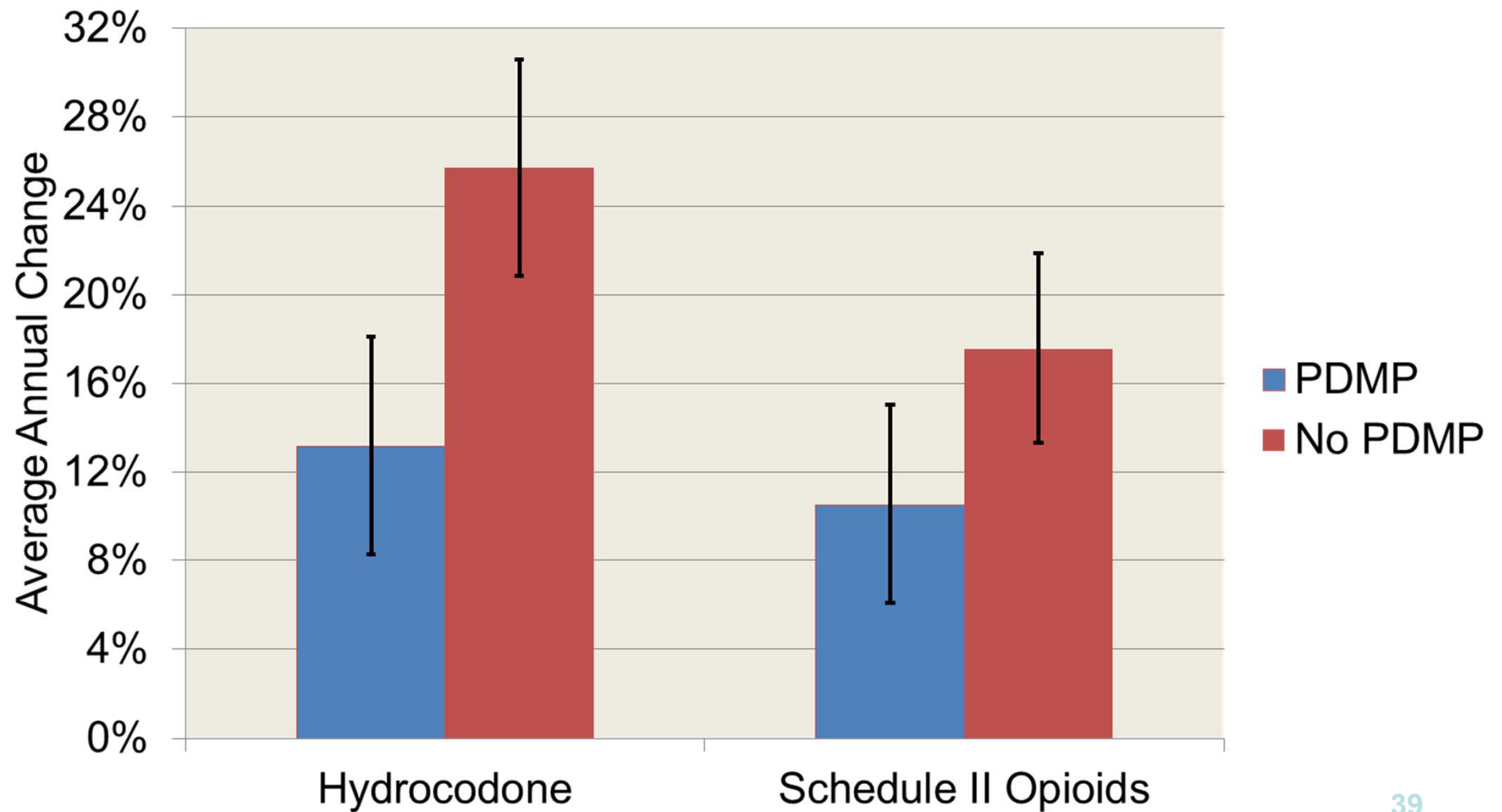
Treatment Programs
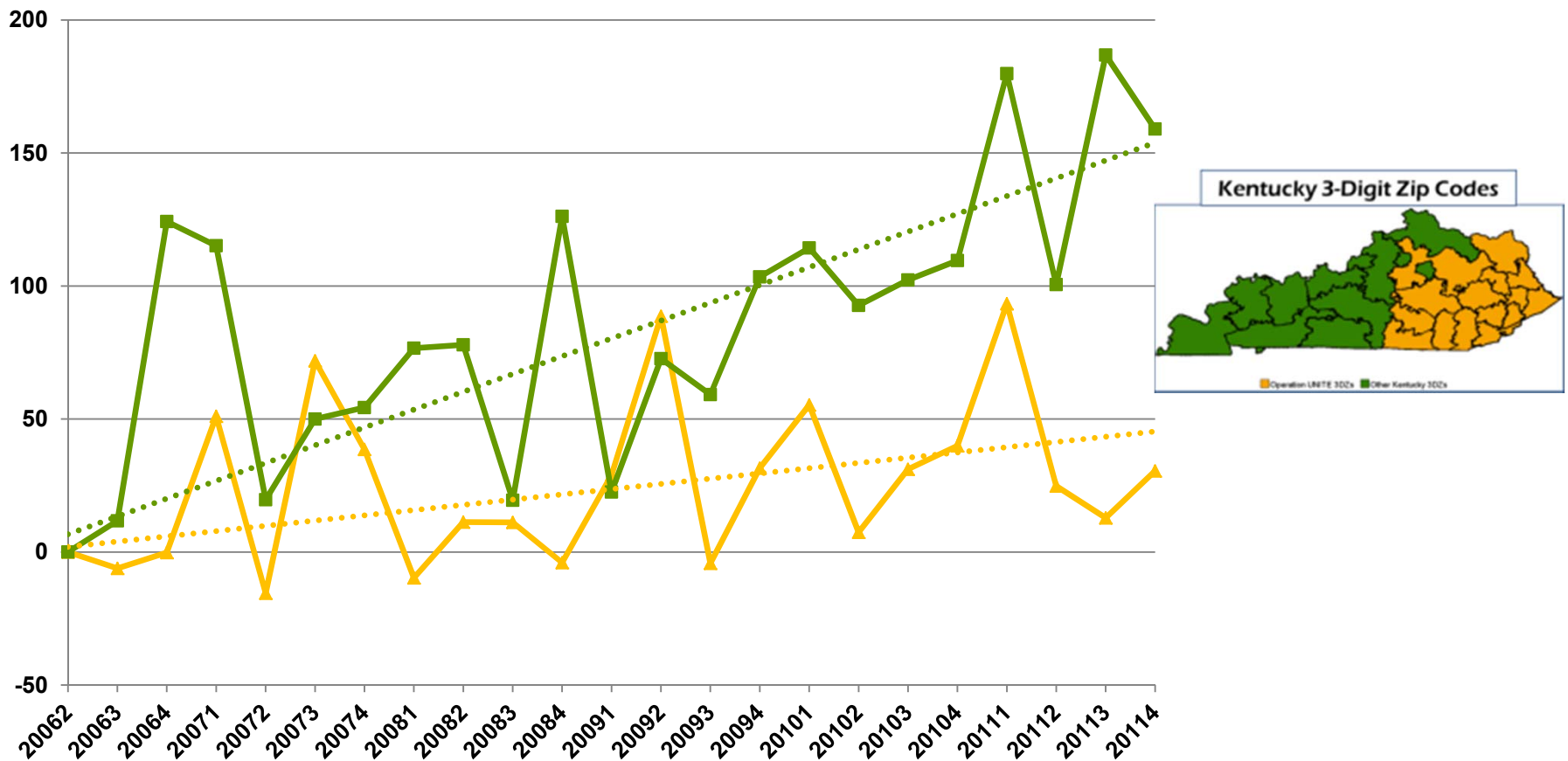## *Opioid Abuse Mentions, Adjusted for Drug Supply*

Operation UNITE

- "Unlawful Narcotics Investigations, Treatment and Education"
- Three-pronged intervention
  - Education
  - Enforcement
  - Treatment

Kentucky 3-Digit Zip Codes

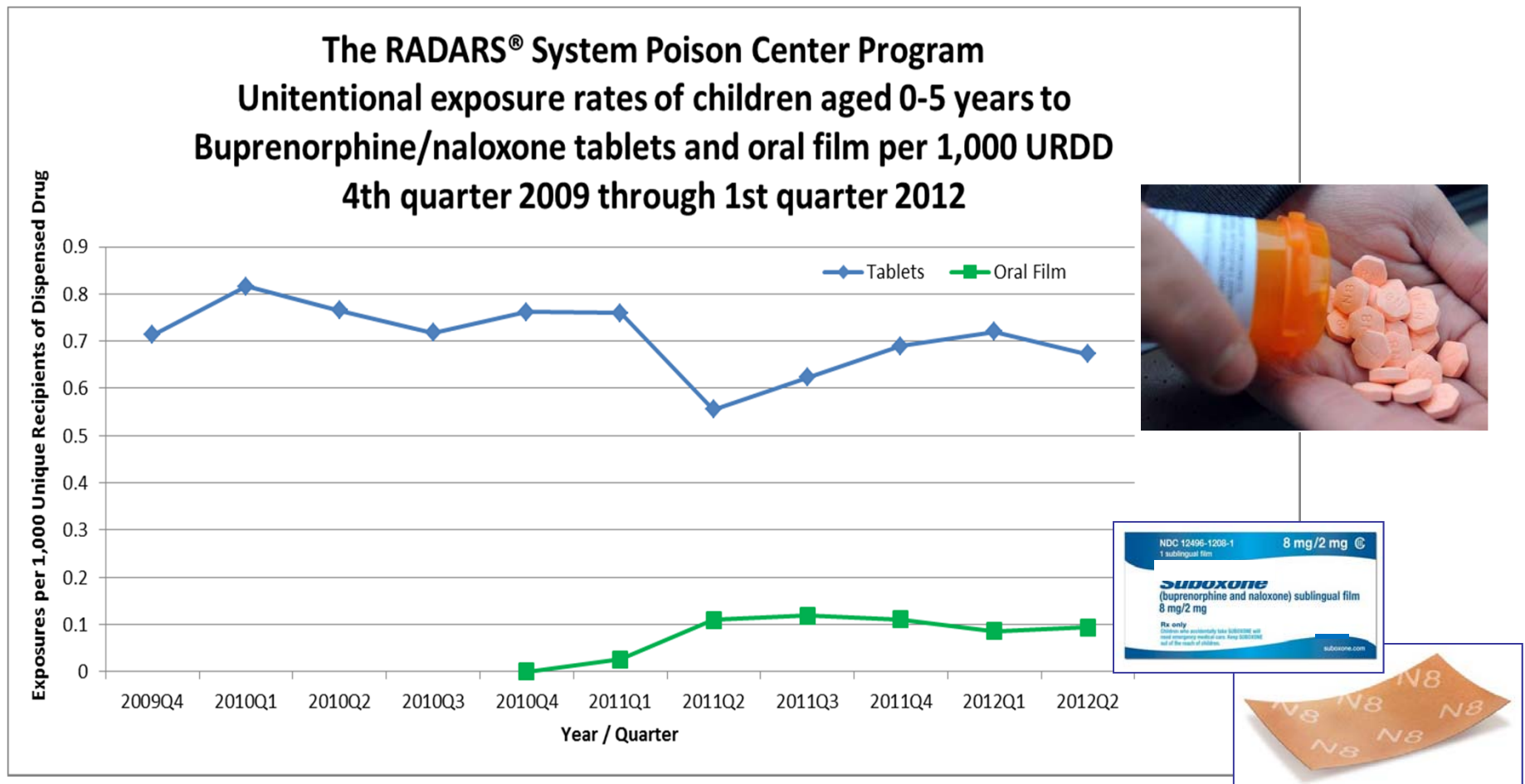Operation UNITE 3DZs   Other Kentucky 3DZs

Rise in Abuse Less in Operation UNITE Region

The RADARS® System Poison Center Program
Intentional Abuse Population Rates – All Opioids 2nd Quarter 2006 to
4th Quarter 2011, Percent Change from Baseline

Pediatric Unintentional Exposures

The RADARS® System Poison Center Program
Unitentional exposure rates of children aged 0-5 years to
Buprenorphine/naloxone tablets and oral film per 1,000 URDD
4th quarter 2009 through 1st quarter 2012

What the Future Holds

- Pharmaceutical innovations
  - Less abuse-prone active ingredients
  - Tamper- and abuse-deterrent formulations

- Regulatory strategies
  - Risk Evaluation and Mitigation Strategy requirements
  - Expanded role for Prescription Drug Monitoring Programs

- Measuring impact
  - Multimodal ("mosaic") approach
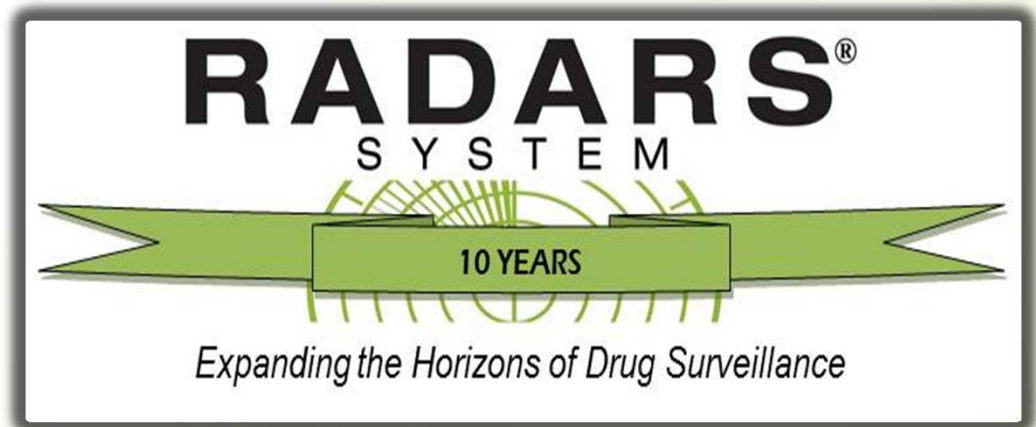
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