

Impact of Abuse-Deterrent Formulations

National Rx Drug Abuse Summit

Atlanta, Georgia

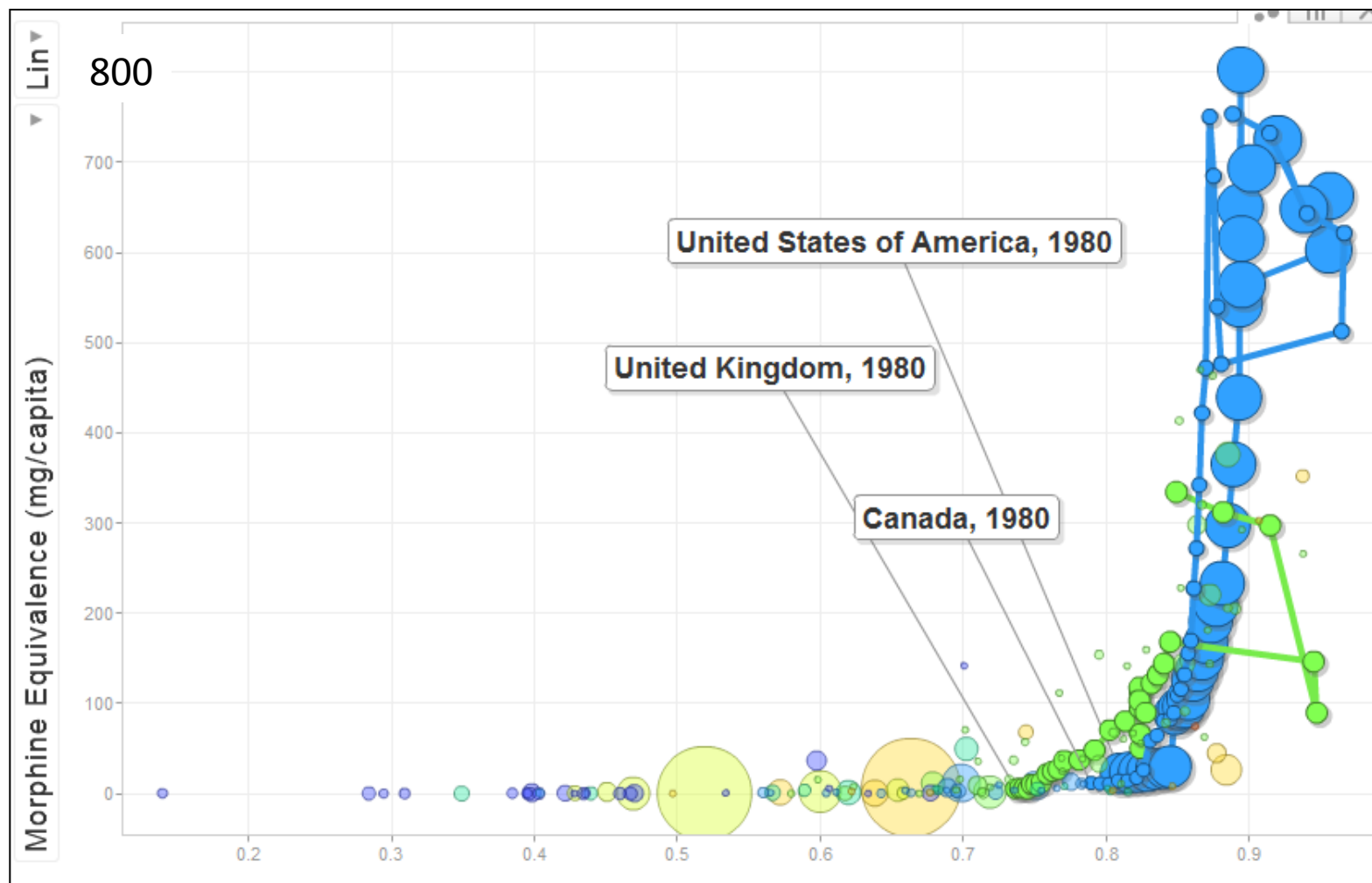
April 2014

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Director, Rocky Mountain Poison and Drug Center
Professor, University of Colorado

Disclosure Statement

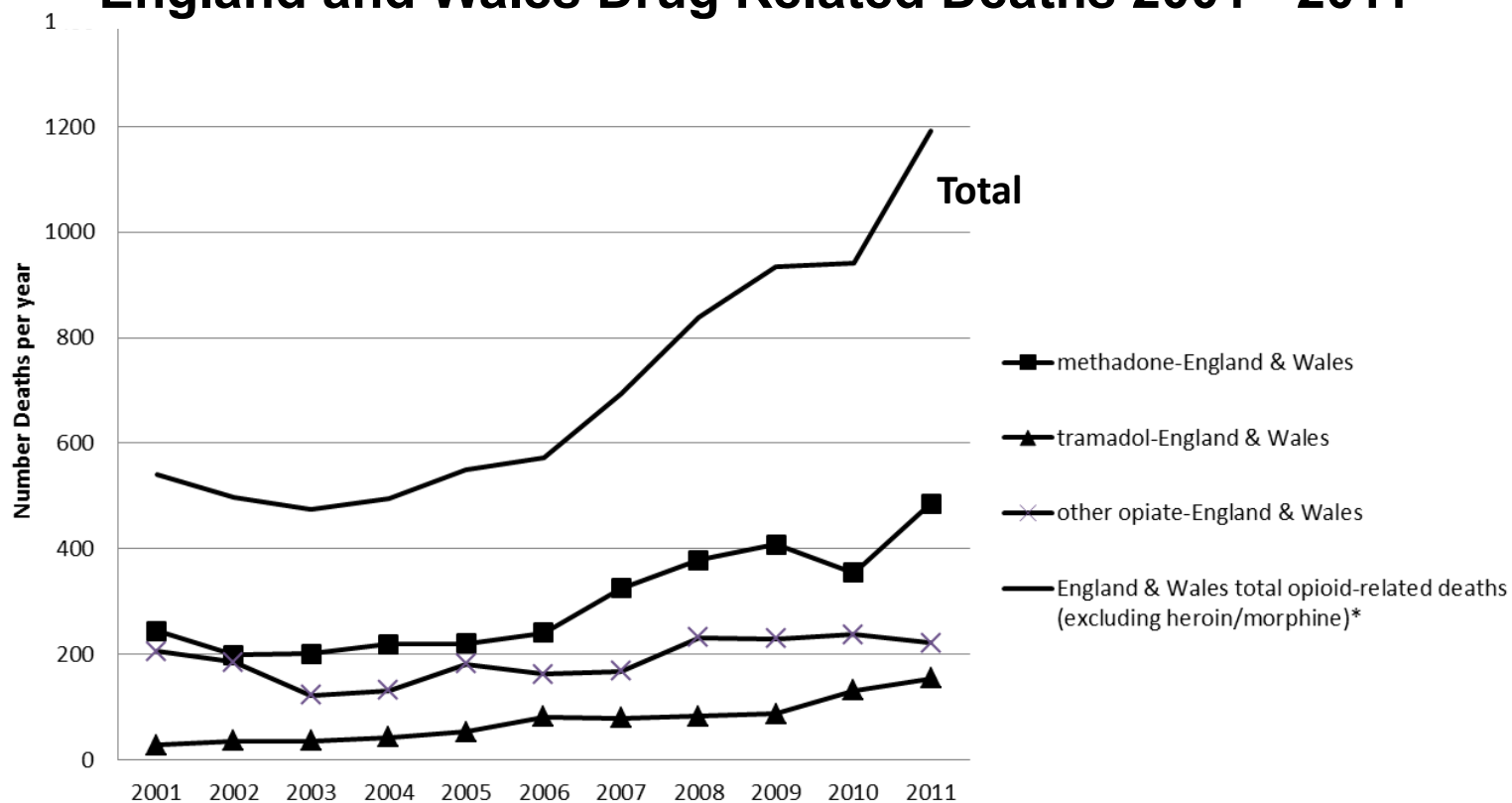
- "Richard Dart has financial relationships with proprietary entities that produce health care products and services."
- These financial relationships are research funding from McNeil Consumer Healthcare and Bioclon.
- The RADARS System is financially supported by subscriptions from most pharmaceutical companies that produce prescription opioids or stimulants.
- All relationships are with Denver Health and Hospital Authority, the public hospital for Denver, Colorado.
- Dr. Dart receives no individual compensation.

Total US Pharmaceutical Opioid Consumption 1980 – 2010, Morphine Equivalents (mg per capita)



<http://ppsg-production.herokuapp.com/chart>

England and Wales Drug Related Deaths 2001 - 2011



*Note: heroin and morphine are reported as one category in the data from England, Wales and Scotland; since the focus of this analysis is on prescription opioids, that category was not included in this analysis.

<http://www.whitehouse.gov/blog/2014/02/10/5-things-know-about-opioid-overdoses>

Giraudon et al. Br J Clin Pharm 2013

FDA Draft Guidance

Abuse-Deterrent Opioids - Evaluation and Labeling

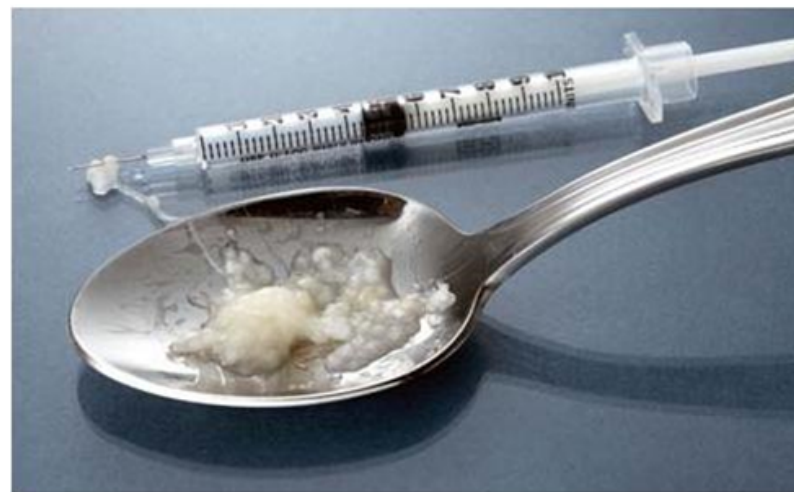
- Prescription opioid analgesics are an important component of modern pain management.
- Abuse and misuse of these products, however, have created a **serious and growing public health problem**.
- FDA has worked to address this problem while ensuring that patients in pain have **appropriate access** to opioid analgesics.

Conflicting Views

- ... FDA advisory committee voted against approval of a hydrocodone product lacking tamper-resistant technology.
 - "I would feel very uncomfortable approving a non-abuse-deterrent product," one of the panelists said at the time.
- Andrew Kolodny, MD, co-founder of PROP, expressed concern that labeling of abuse-resistant products could contribute to false marketing.
 - "If doctors are misled to believe that these formulations are less addictive, and if they develop a false sense of security about these products, that could possibly make the epidemic worse,"

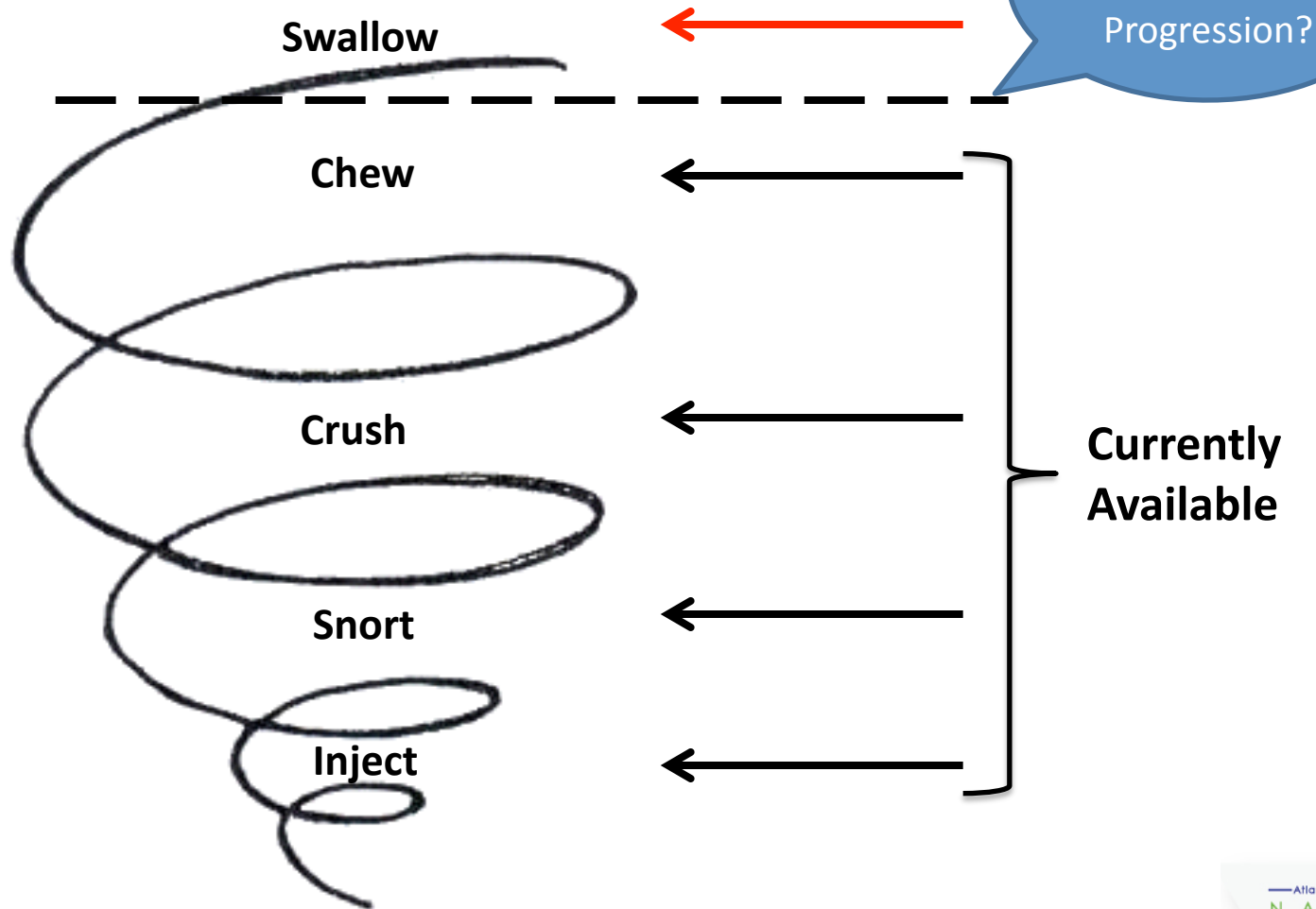
Abuse Deterrent Formulations in the United States

OxyContin, Opana ER, Exalgo, Oxecta, Nucynta ER



Abuse Deterrent Formulations

Site of Action



RADARS System

Results through December 31, 2013

What is the RADARS[®] System?

- History
 - Denver Public Safety Net Hospital for 150 years
 - State sanctioned independent authority
 - Created 2001 by Purdue Pharma
 - 2006, Denver Health and Hospital Authority (DHHA)
 - Independent program
 - Multiple pharmaceutical subscribers
 - Data can only be used for safety reporting
- Conflict of interest statement
 - None, other than running system for DHHA as noted above

Mosaic Surveillance for Surveillance of Prescription Drug Abuse

Acute Events

49 Poison centers
46 states

Drug Transactions

Criminal Justice
250 agencies
49 states

Entering Treatment

OTP
75 programs
37 states

Entering Treatment

SKIP
155 practices
47 states

New Initiates

College Survey
2000 students
50 states

Illicit Market Price

StreetRx.com
Users/Buyers
50 states



RADARS System

Scientific Advisory Board

Principal Investigators

- Theodore J. Cicero, PhD
Washington University at St. Louis
- Richard C. Dart, MD, PhD
Denver Health and Hospital Authority
- Hilary Surratt, PhD
Nova Southeastern University
- Mark W. Parrino, MPA
American Association for the Treatment of Opioid Dependence



Law Enforcement

- John Burke
National Association of Drug Diversion Investigators



Substance Abuse Experts

- Herbert D. Kleber, MD
Columbia University
- Sidney Schnoll, MD, PhD
Pinney Associates
- George E. Woody, MD
University of Pennsylvania



Epidemiology/Biostatistics

- Edgar Adams, ScD
Covance
- Nabarun Dasgupta, MPH
Founder – Epidemico
- Alvaro Muñoz, PhD
Johns Hopkins University



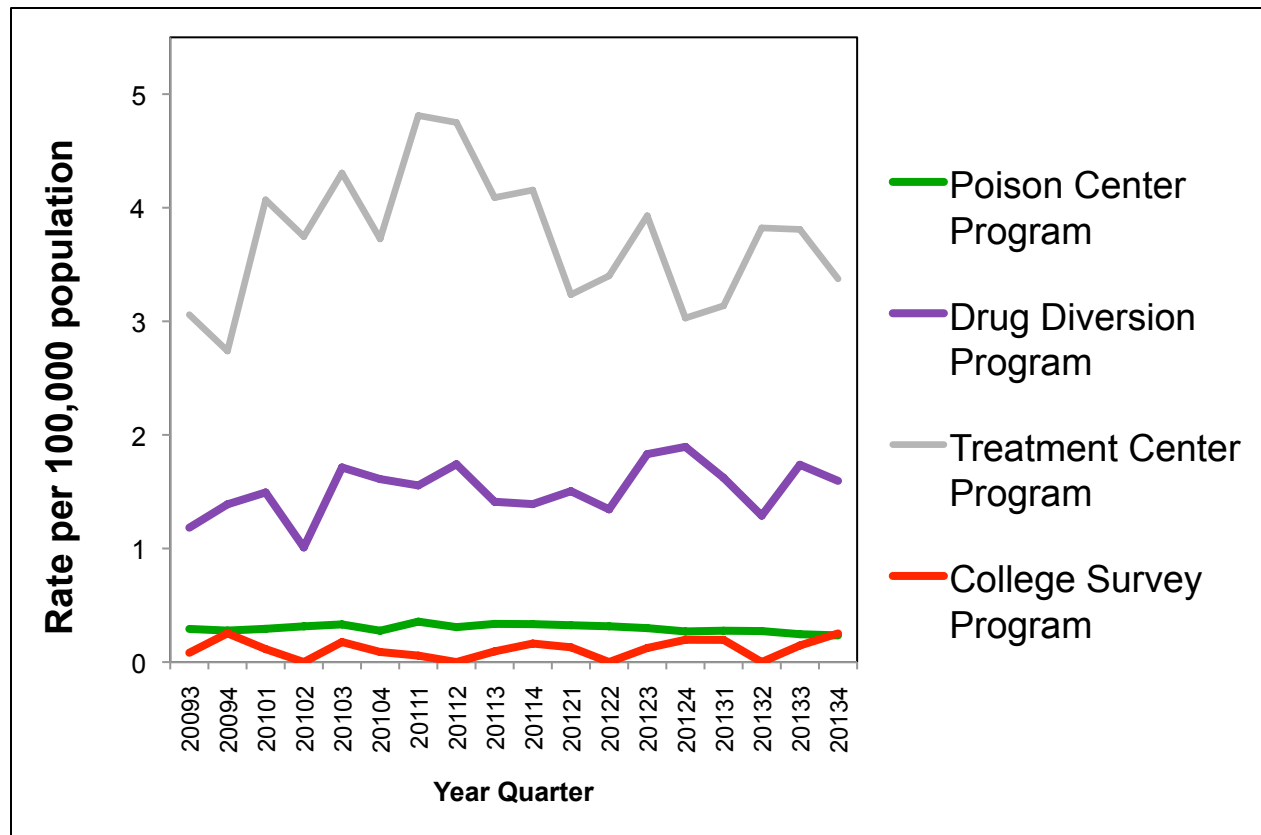
Show Me The Data

- Do ADFs decrease abuse?
 - OxyContin[®] (polyethylene oxide), Opana ER[®] (Intac[®]), Nucynta ER (Intac[®])
 - Exalgo[®], Oxecta[®], Embeda[®]
 - Suboxone[®], buprenorphine/naloxone combos
- Do they affect outcome?
 - Injection?
 - Mortality?

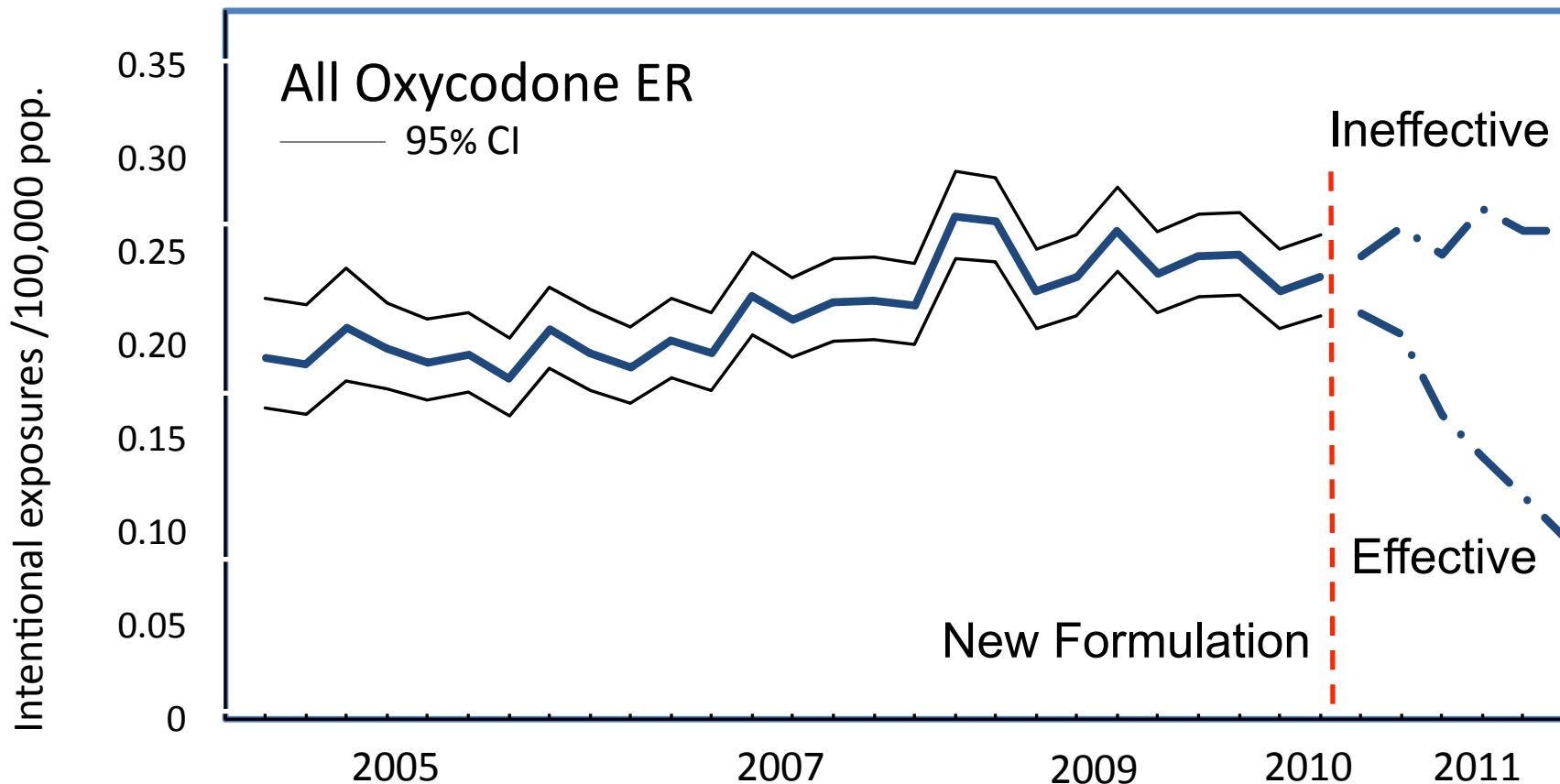
RADARS System

Schedule II Excluding Oxycodone ER Population

Rates by Program, 2009-2013

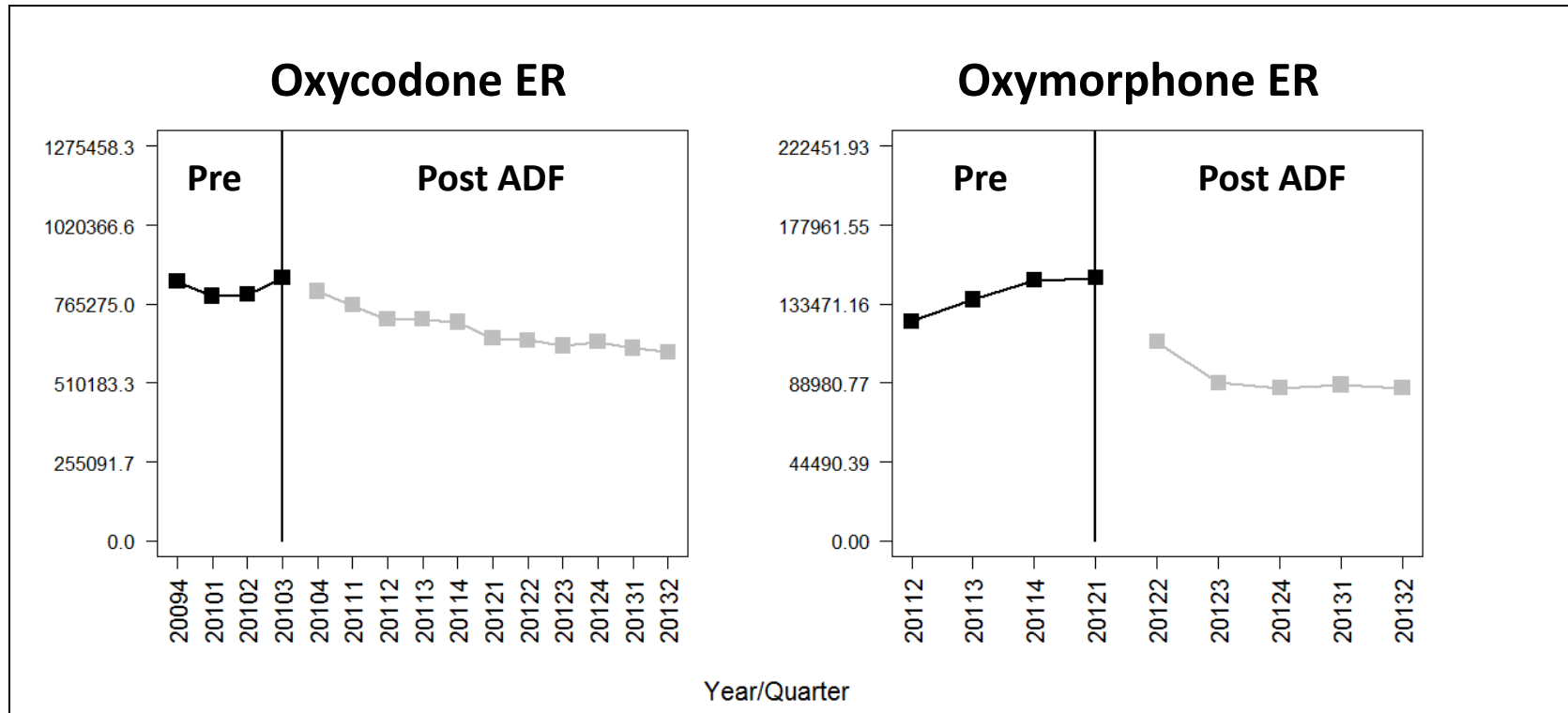


Model for Oxycodone Extended Release RADARS System Poison Centers

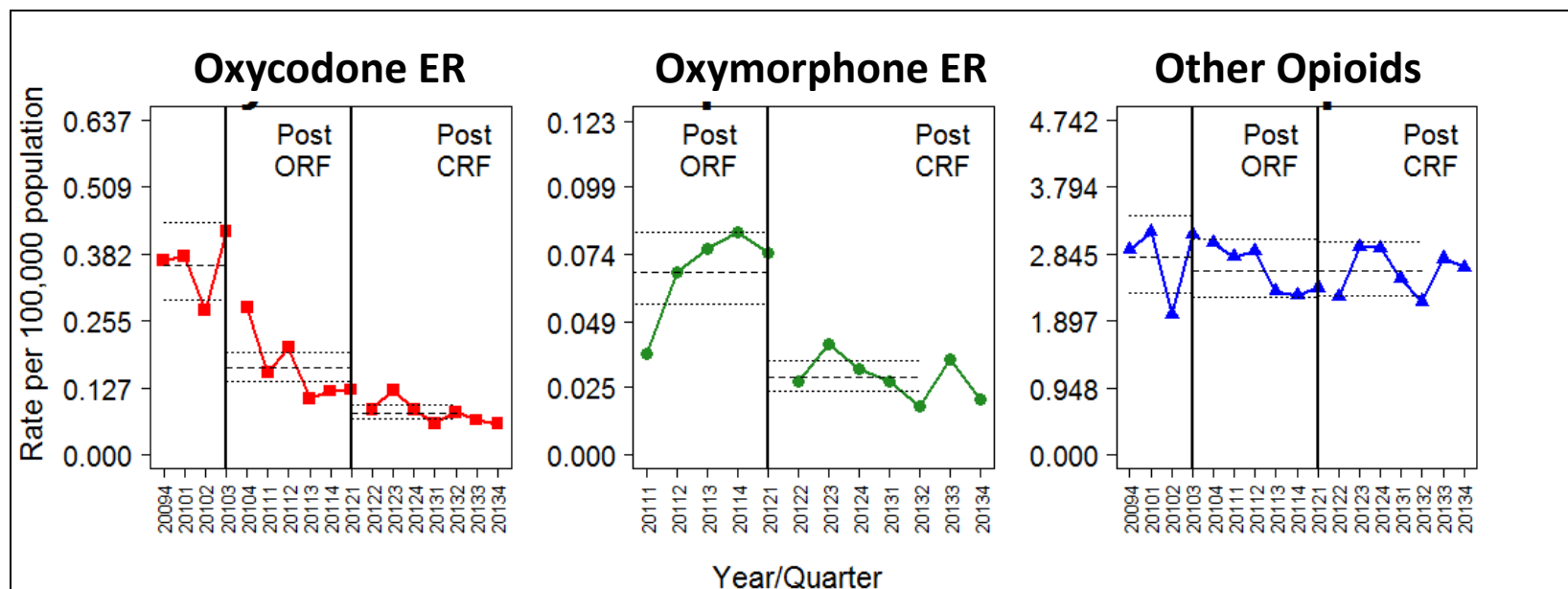


October 21-22, 2010: Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting Announcement

ADFs–Demand Reduction People Filling Prescriptions

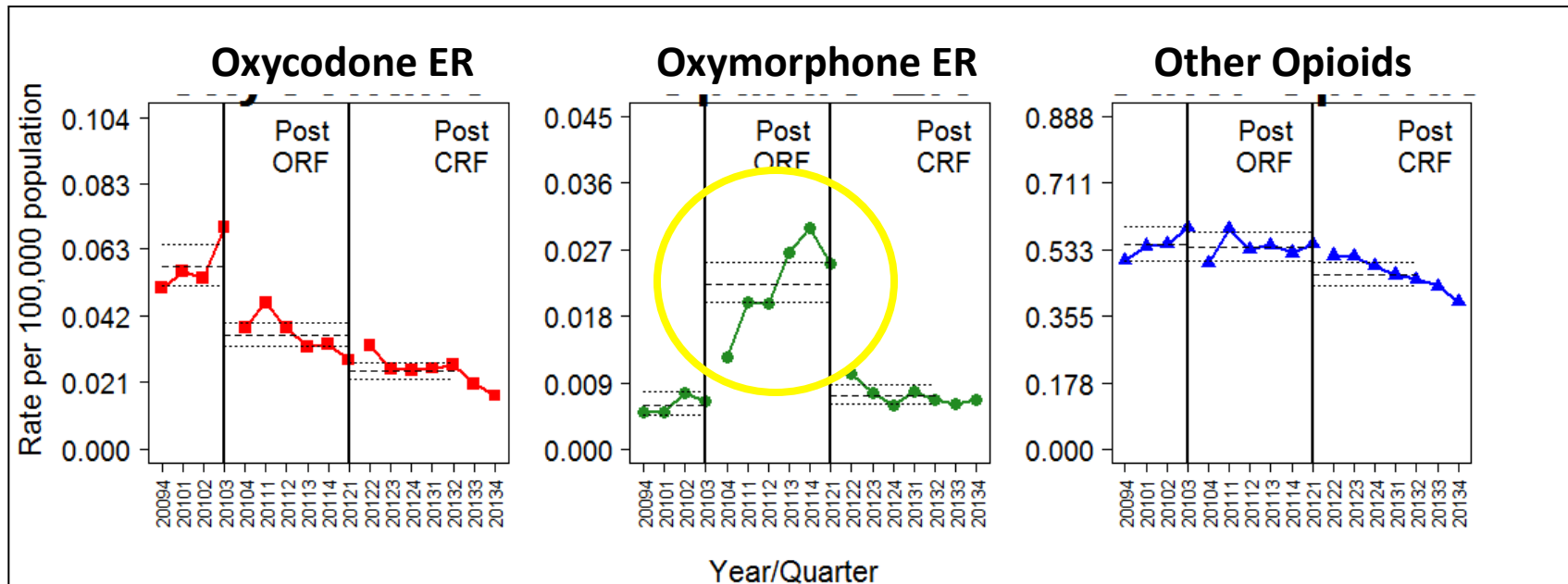


Drug Diversion Program Population Rate, 2009-2013



*Other opioids excluding ER oxycodone and ER oxymorphone.

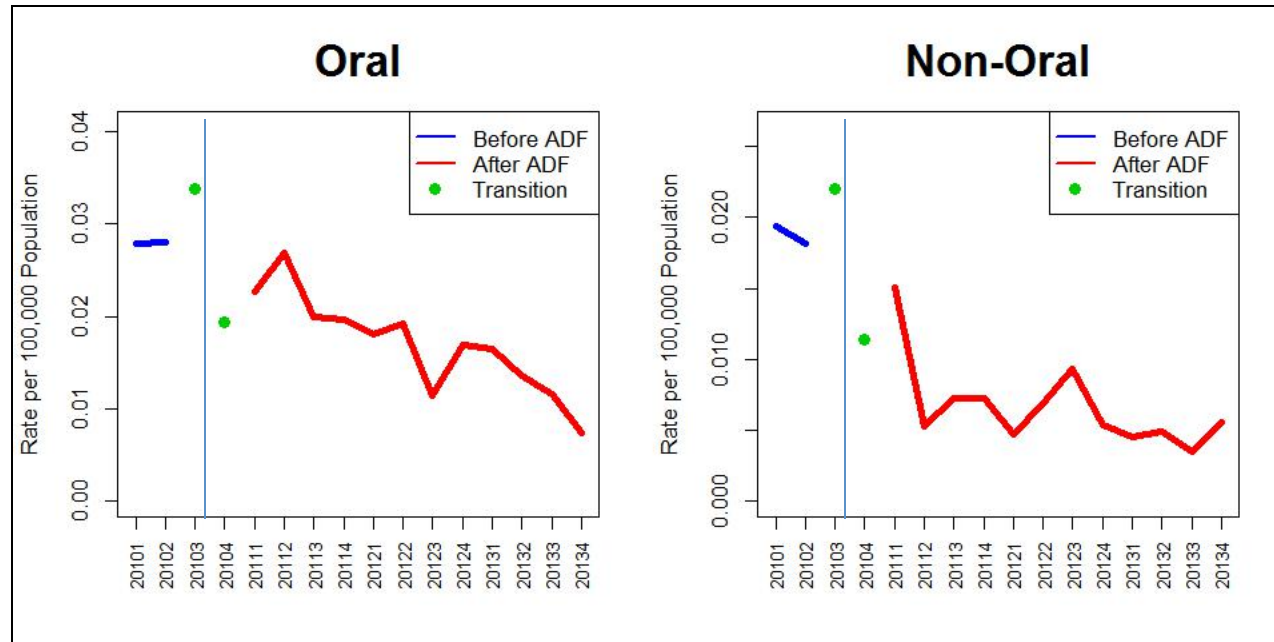
Poison Center Program Population Rate, 2009-2013



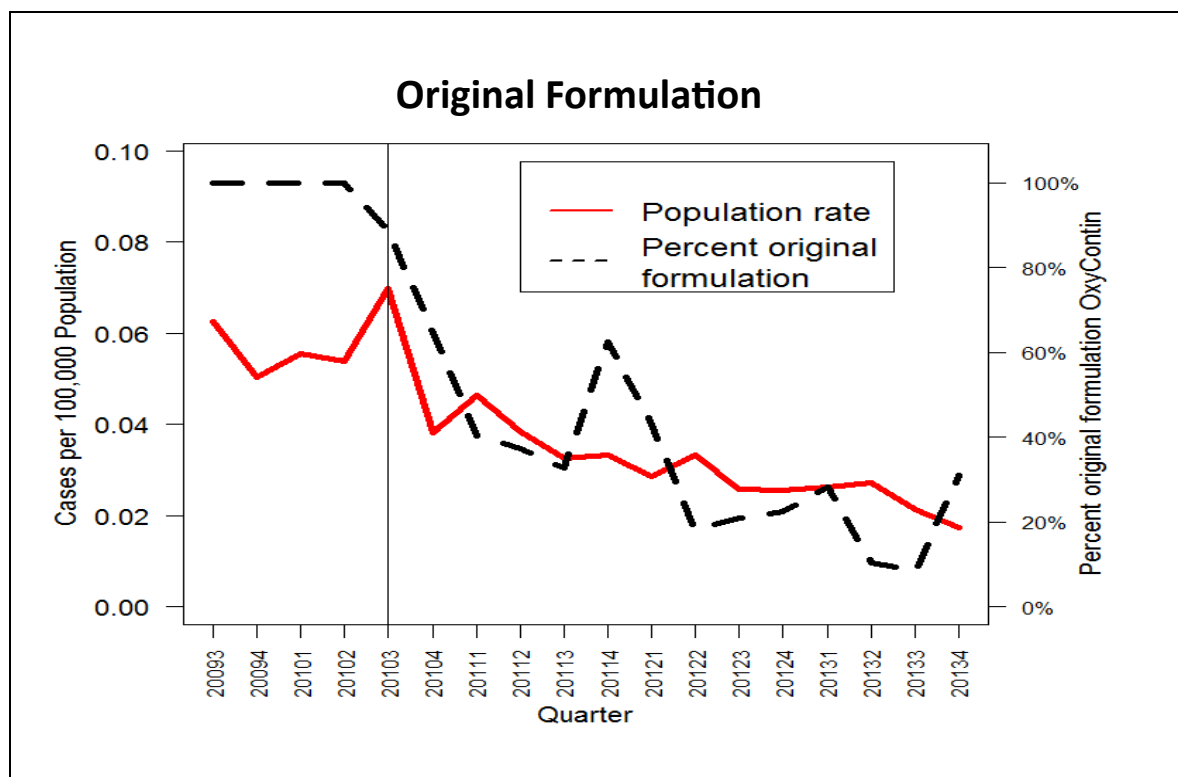
*Other opioids excluding ER oxycodone and ER oxymorphone

Poison Center Program

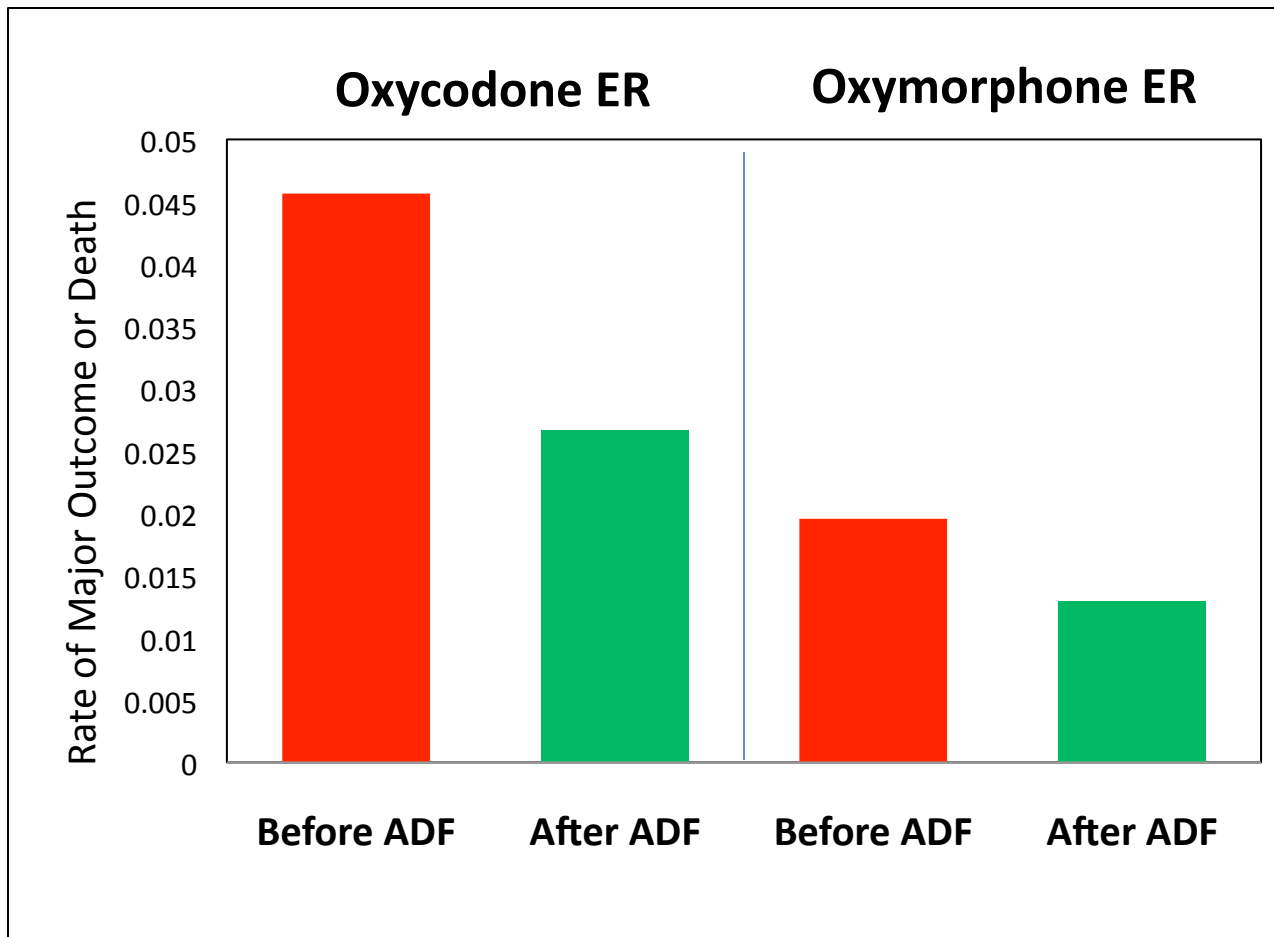
Route of Administration, OxyContin



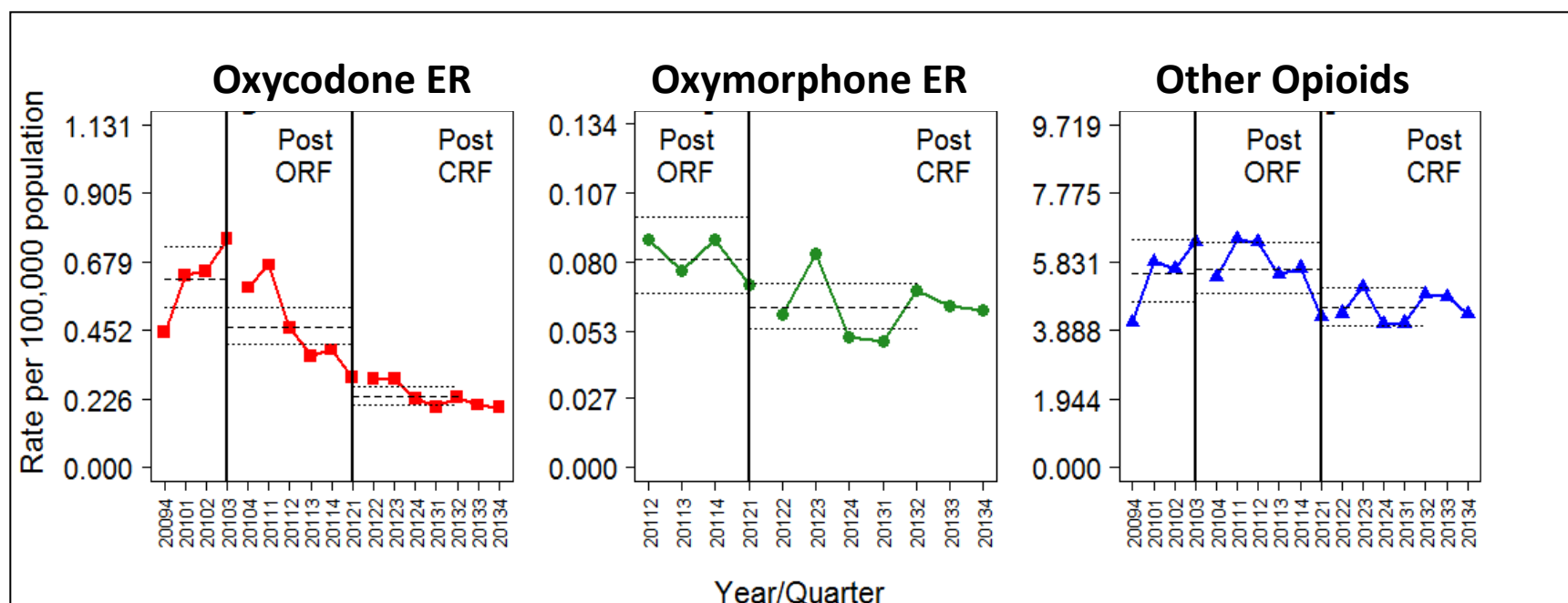
Relation of Original OxyContin and Mentions in Poison Center Program



Case Outcome in Poison Center Program - Major Outcome or Death



Treatment Programs Combined 2009-2013



*Other opioids excluding ER oxycodone and ER oxymorphone.

StreetRx.com

Submissions are anonymous

DID YOU GET a good deal?

Name of drug*

City State*

\$ Price*

Show me:

All

Most Popular

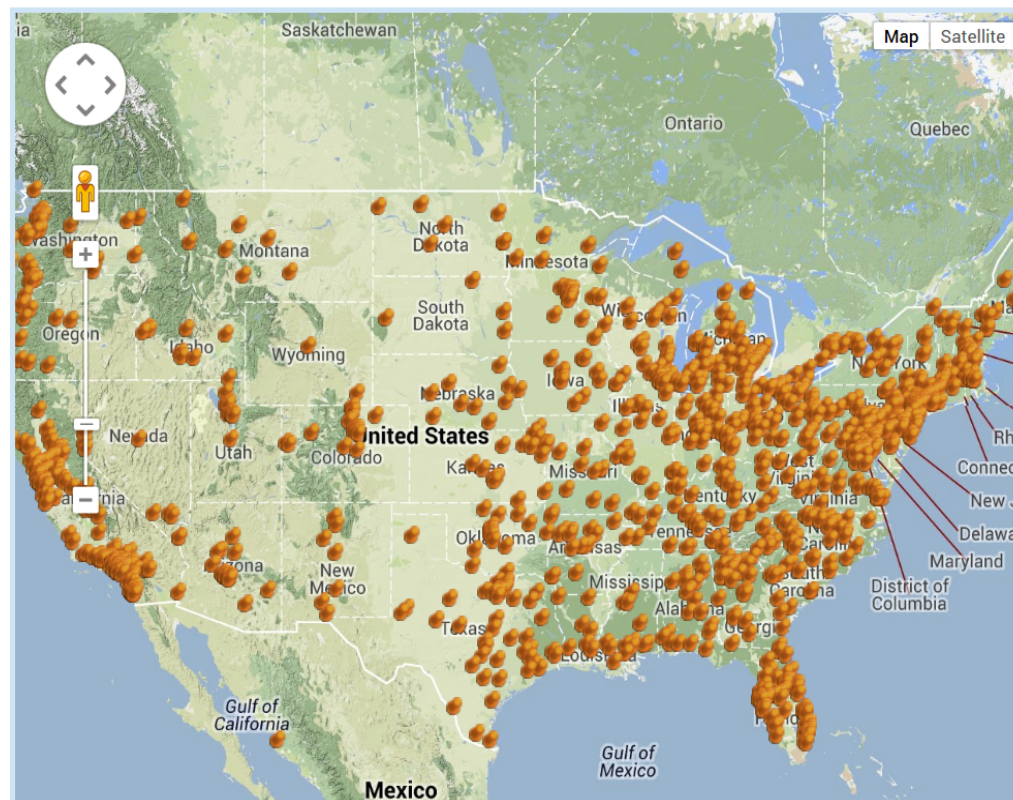
Best Price

Latest prices

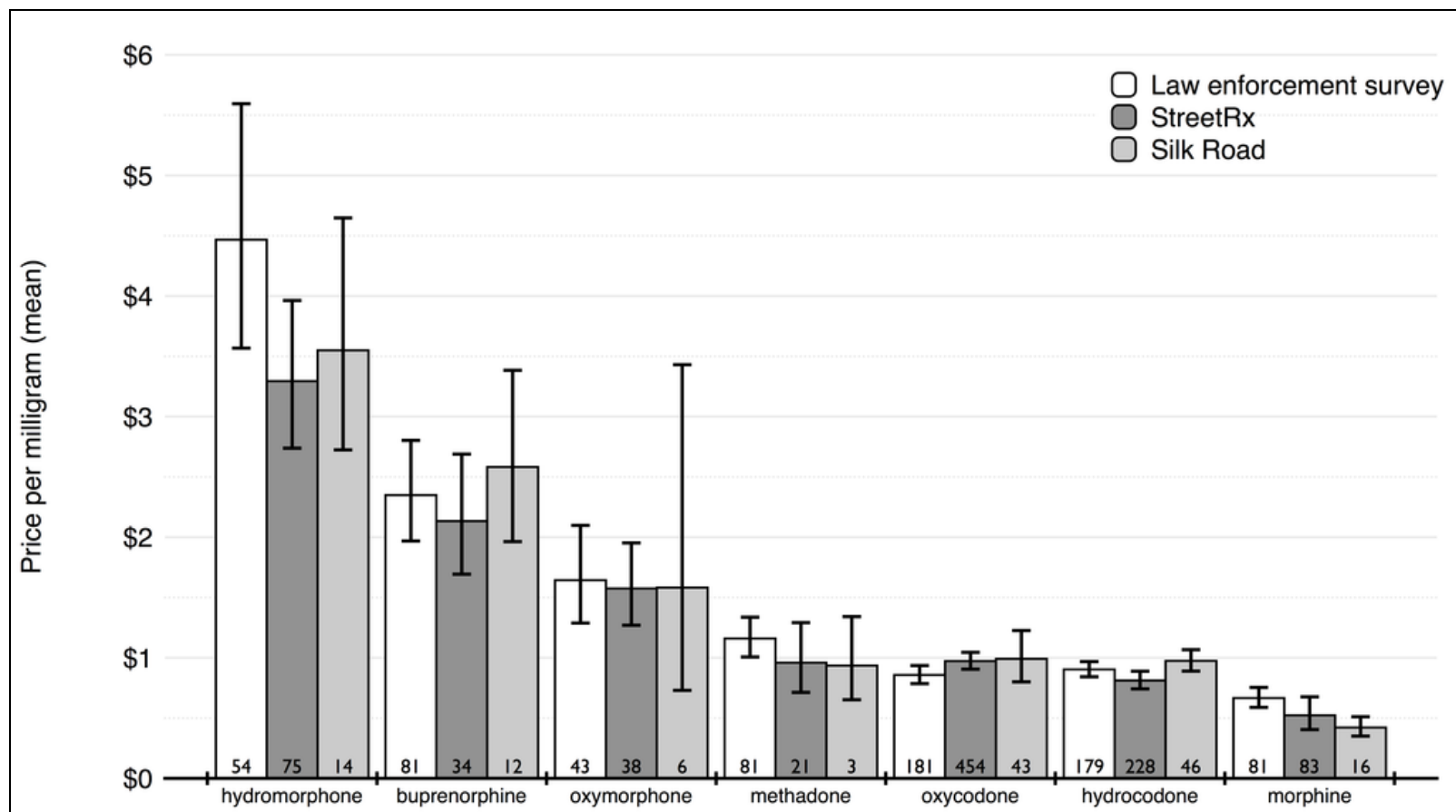
Drug	Location	Price	Date	Rating
Norco hydrocodone, 10/325mg pill	Indianapolis, Indiana	\$8	Apr 4	Rate: \$ \$ \$ \$ \$
oxycodone, 30mg pill	Denver, Colorado	\$30	Apr 4	Reasonable \$ \$ \$ \$ \$
Adderall XR, 30mg pill	Lockport, New York	\$1.50	Apr 4	Not Bad \$ \$ \$ \$ \$
Adderall XR, 30mg pill	Harrisonburg, Virginia	\$12	Apr 4	Rate: \$ \$ \$ \$ \$
hydrocodone (generic Vicodin), 5mg pill	San Marcos, Texas	\$5	Apr 4	Rate: \$ \$ \$ \$ \$

See what OTHERS paid

e.g. dilaudid california



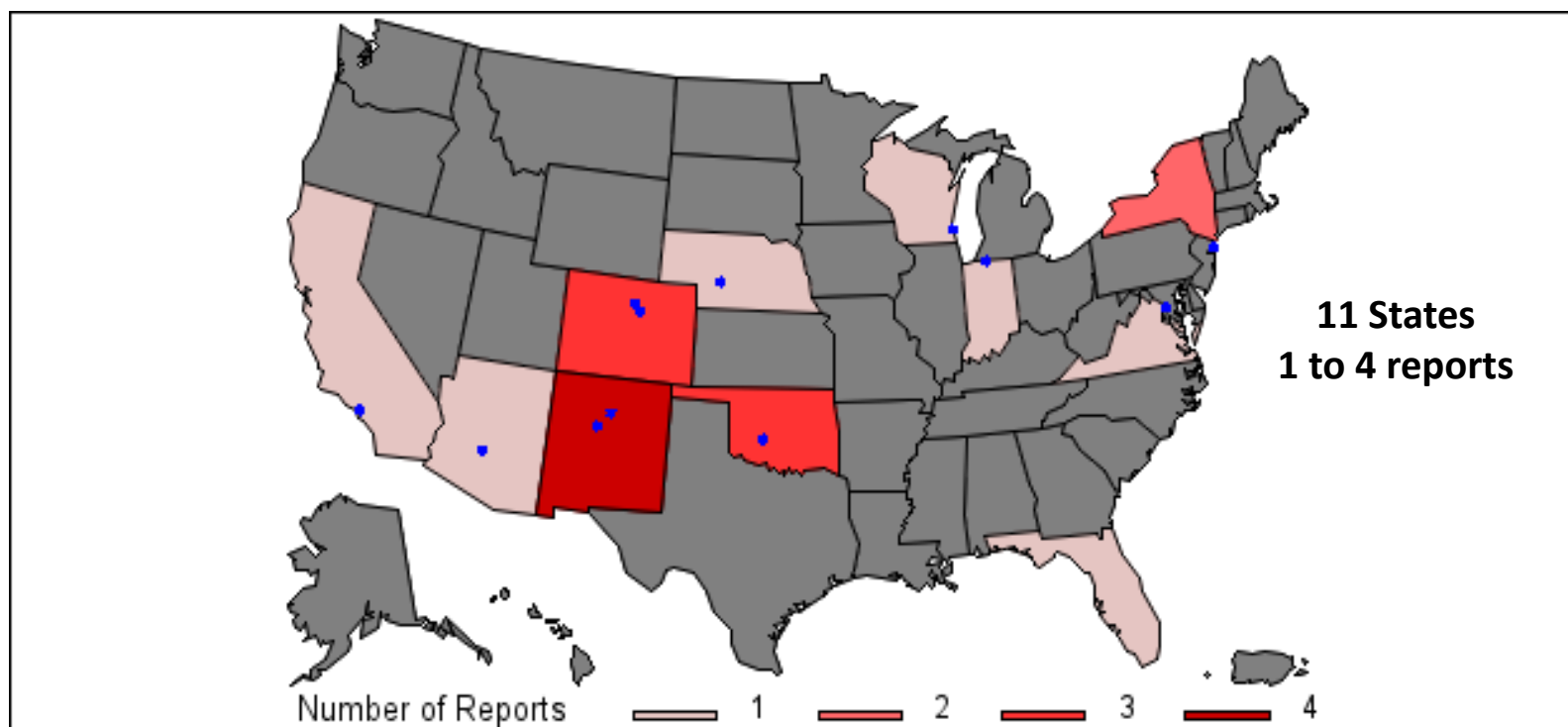
StreetRx, RADARS System Drug Diversion and Silk Road – Price per milligram drug



Dasgupta, Suratt, et al, J Med Internet Res, 2013

US StreetRx

Endorsement of Canadian Oxycodone Products in United States



Oxycodone ER in US and Canada

Formulation	United States		Canada	
	Number reports	Reported Median Price per mg, US Dollar (range)	Number reports	Reported Median Price per mg, Canadian Dollar (range)
Crushable “Old OxyContin”				
Apo-Oxycodone CR	24	1.00 (0.15 – 16.80)	1	1.00 (NR)
OxyContin®	93	1.00 (0.06 – 10.00)	16	1.00 (0.54 – 6.00)
Co-Oxycodone CR	11	1.00 (0.30 – 4.00)	0	NR
Teva-Oxycodone CR	4	0.88 (0.10 – 3.75)	0	NR
Average		1.00		1.00
Abuse Deterrent “New OxyContin”				
Oxycodone ER (OxyContin in US, OxyNEO in Canada)	277	0.63 (0.03 – 10.00)	15	0.75 (0.38 – 1.40)
Average		0.63		0.75

Other Data Sources

Navipro Treatment Centers

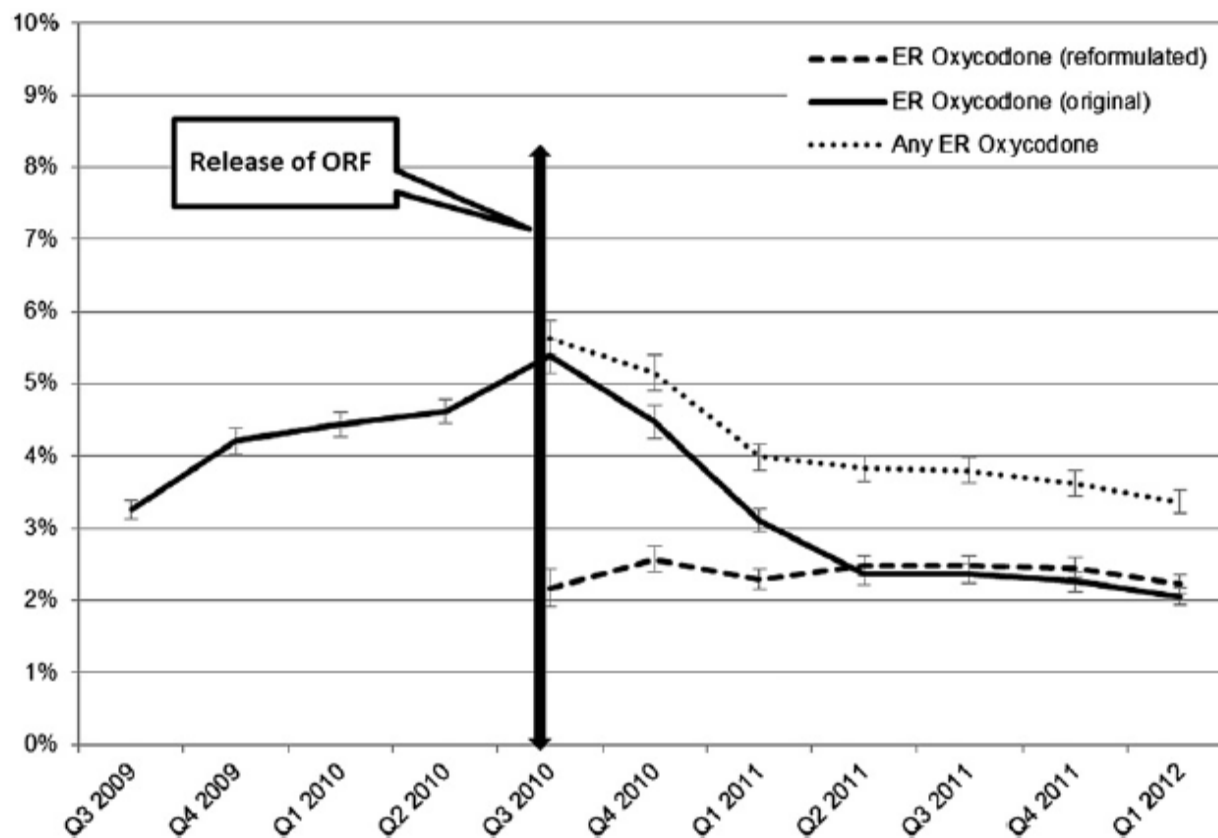


Figure 1. Quarterly prevalence of past-30-day abuse for original ER oxycodone, reformulated ER oxycodone (ORF), or any ER oxycodone (OC or ORF) among individuals assessed for substance abuse treatment.

Butler S, et al, J Pain 2012

Other Data Sources

National Survey of Drug Use and Health

Good News – Bad News

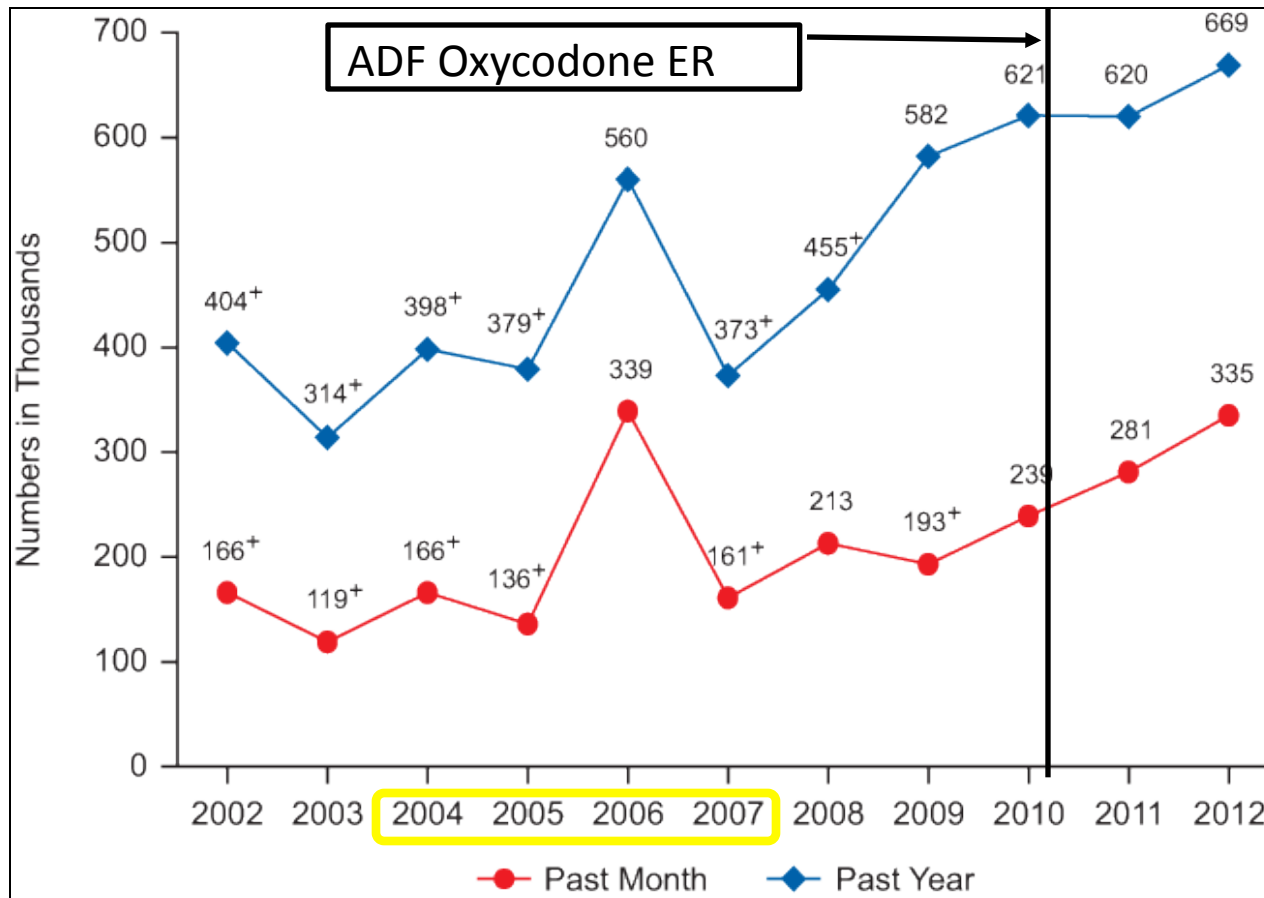
“The number of persons aged 12 or older who were current nonmedical users of the pain reliever OxyContin declined from 566,000 in 2010 to 358,000 in 2012.”

Yes, Abuse Deterrent Formulations Can
Reduce the Diversion and Abuse of an Opioid
Analgesic, but...

Some Important Questions Remain!

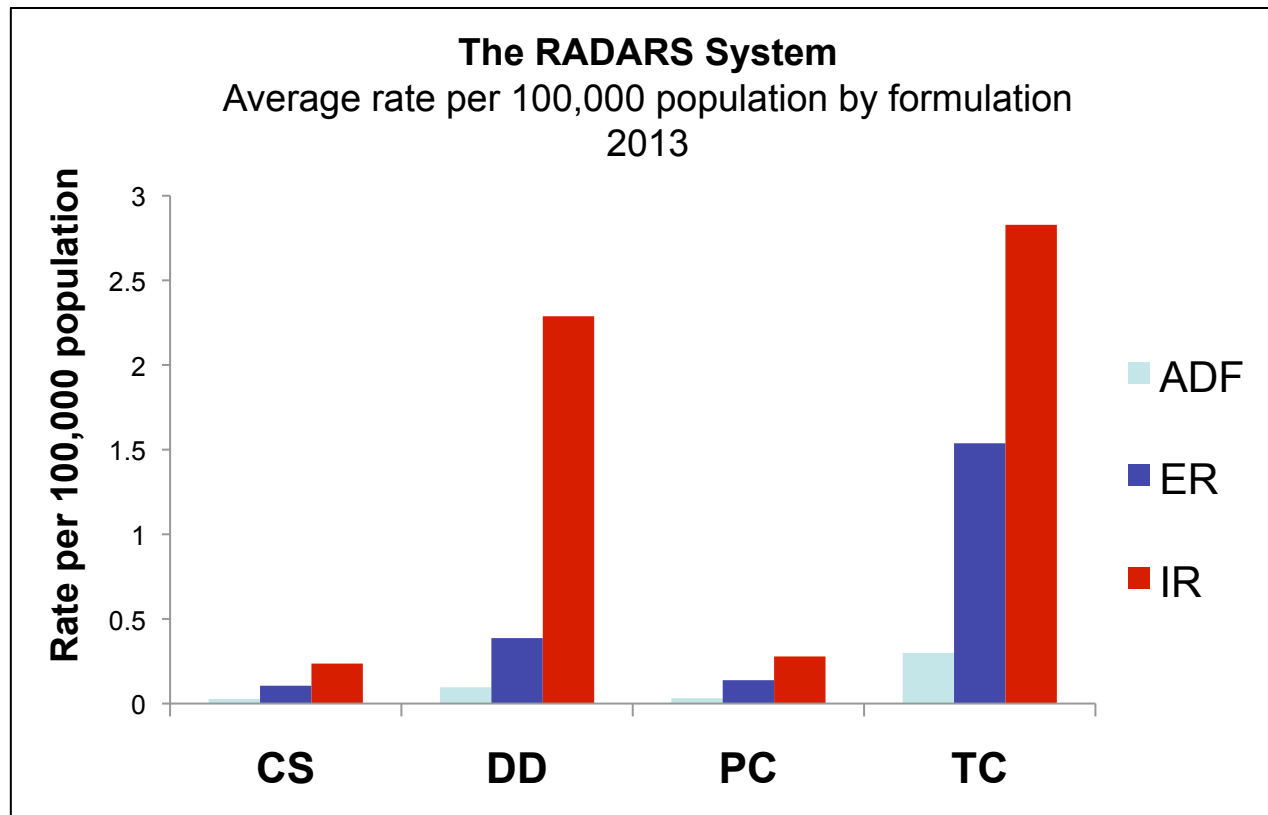
Squeezing the Balloon

Heroin - Past Month, Past Year



NSDUH Report 2012

Can ADFs Bend the Curve?



- CS – College Survey
- DD – Drug Diversion
- PC – Poison Center
- TC – Treatment Centers combined
- Methadone, buprenorphine, liquids, injectables excluded

Conclusions

- Formulations that resist crushing and forming injectable solutions can reduce diversion, abuse and the sequelae of abuse of that particular drug.
- The potential impact of ADF technology would be greater if more products used technology.
- However, the “market” will adjust to the new barriers.

Thank You!