

# **Innovations in Rx Technology: A Session on Abuse Deterrent Formulations – Coalition Operations Track**

## **Do ADFs Work?**

February 3, 2015

Richard C. Dart, MD, PhD

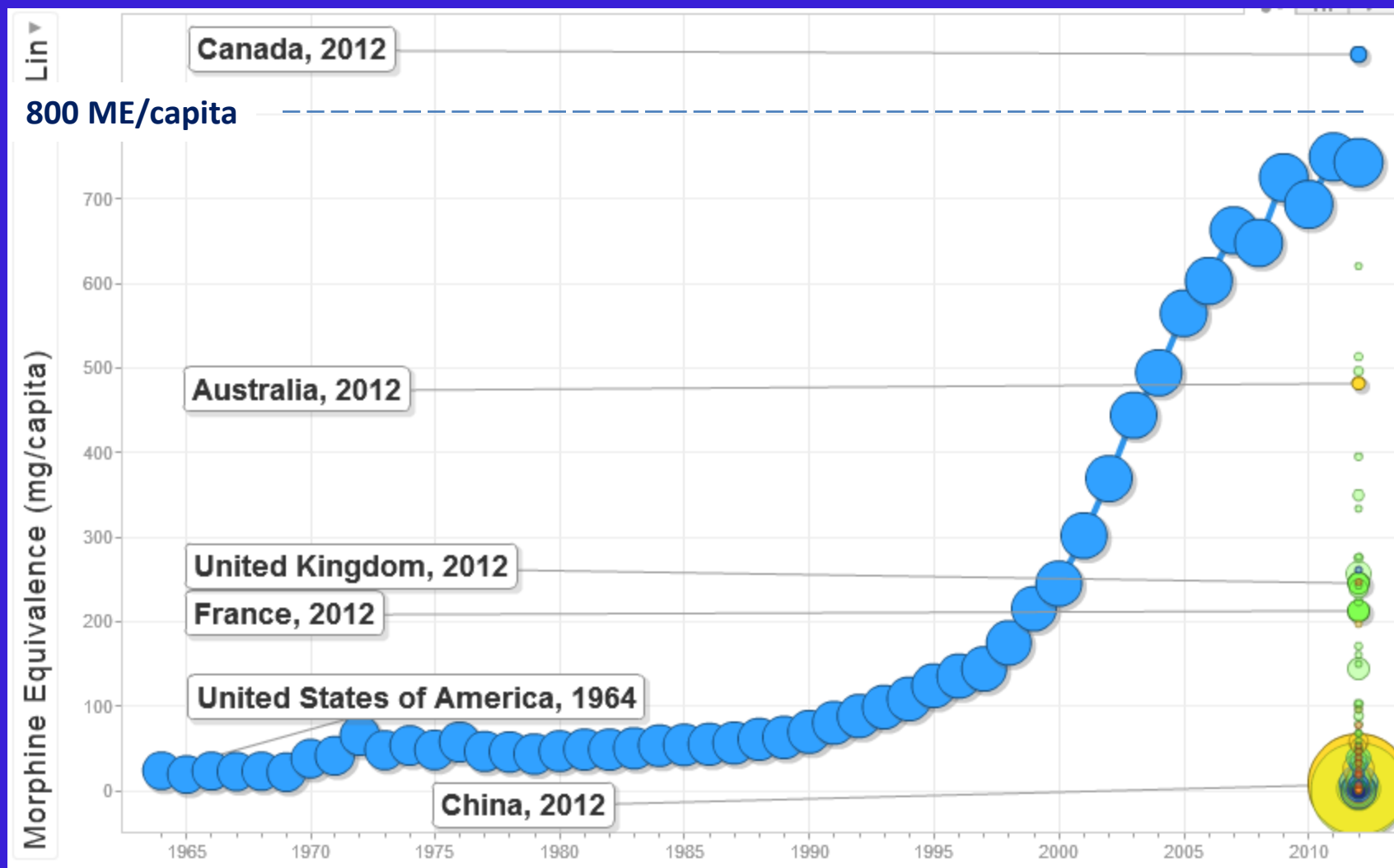
Director, Rocky Mountain Poison and Drug Center  
Professor, University of Colorado School of Medicine

# Outline

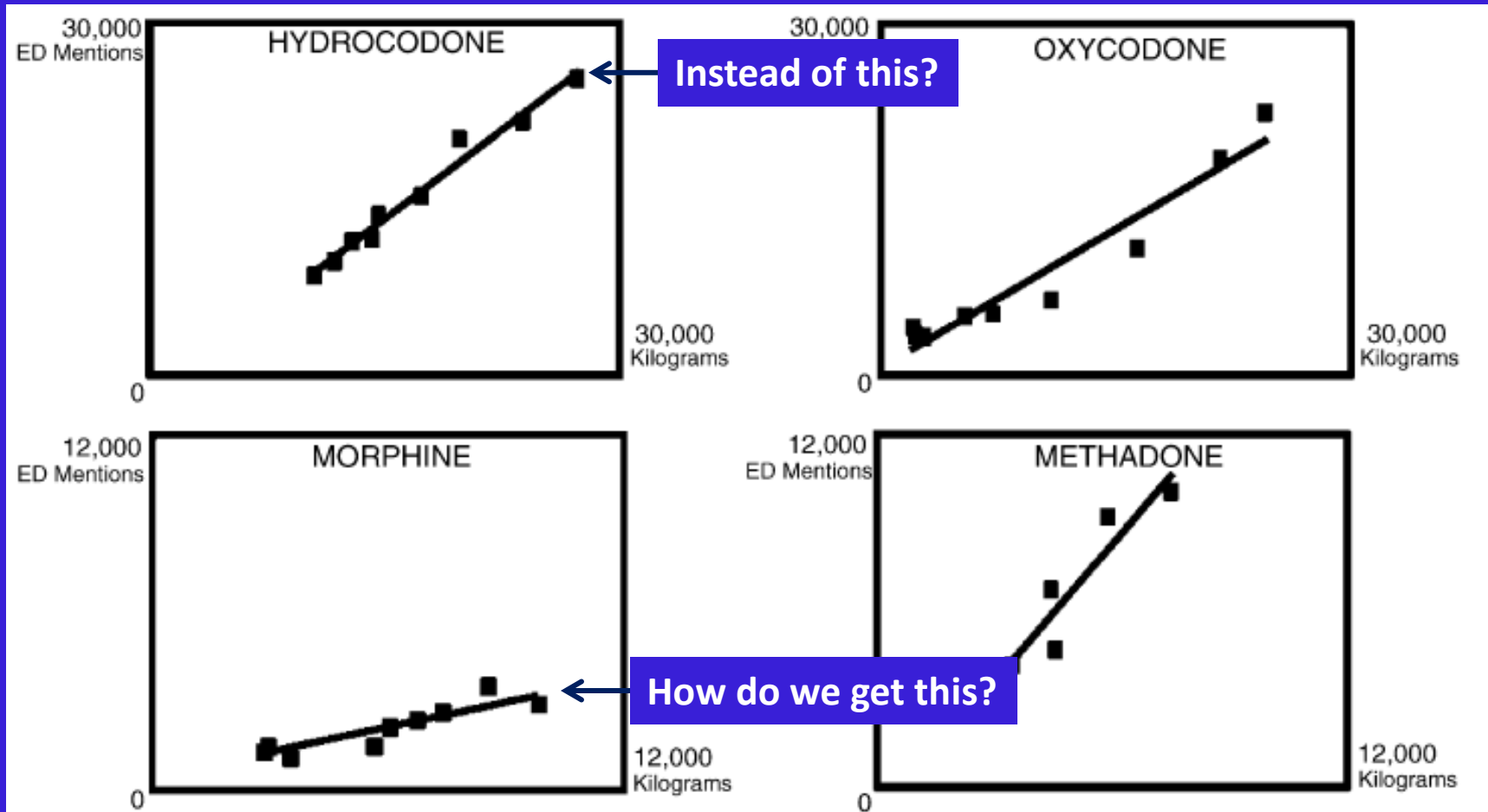
- Conceptual Framework for Abuse Deterrent Formulations
- Effectiveness of ADFs
- Unanticipated Consequences?

# The Epidemic

# US Consumption of Prescription Opioids, 1964 - 2012



# More Drug Production = More Drug Abuse But - the Slope Varies by Drug



# How Do Abuse, Addiction and Death Occur?

**Population with Addiction Risk**



**Exposed to Opioid**  
Recreational Use or Pain Treatment

**Swallow**  
**Misuse/Abuse**

**Chew**

**Crush**

**Snort**



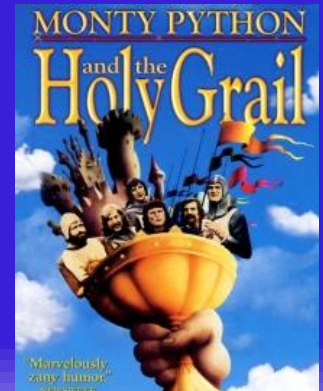
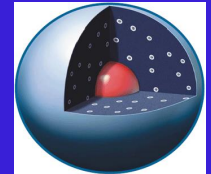
**Increasing**  
**Rate of**  
**Abuse,**  
**Addiction,**  
**Death**

# Abuse Deterrent Formulations



# Strategies for Abuse Deterrence

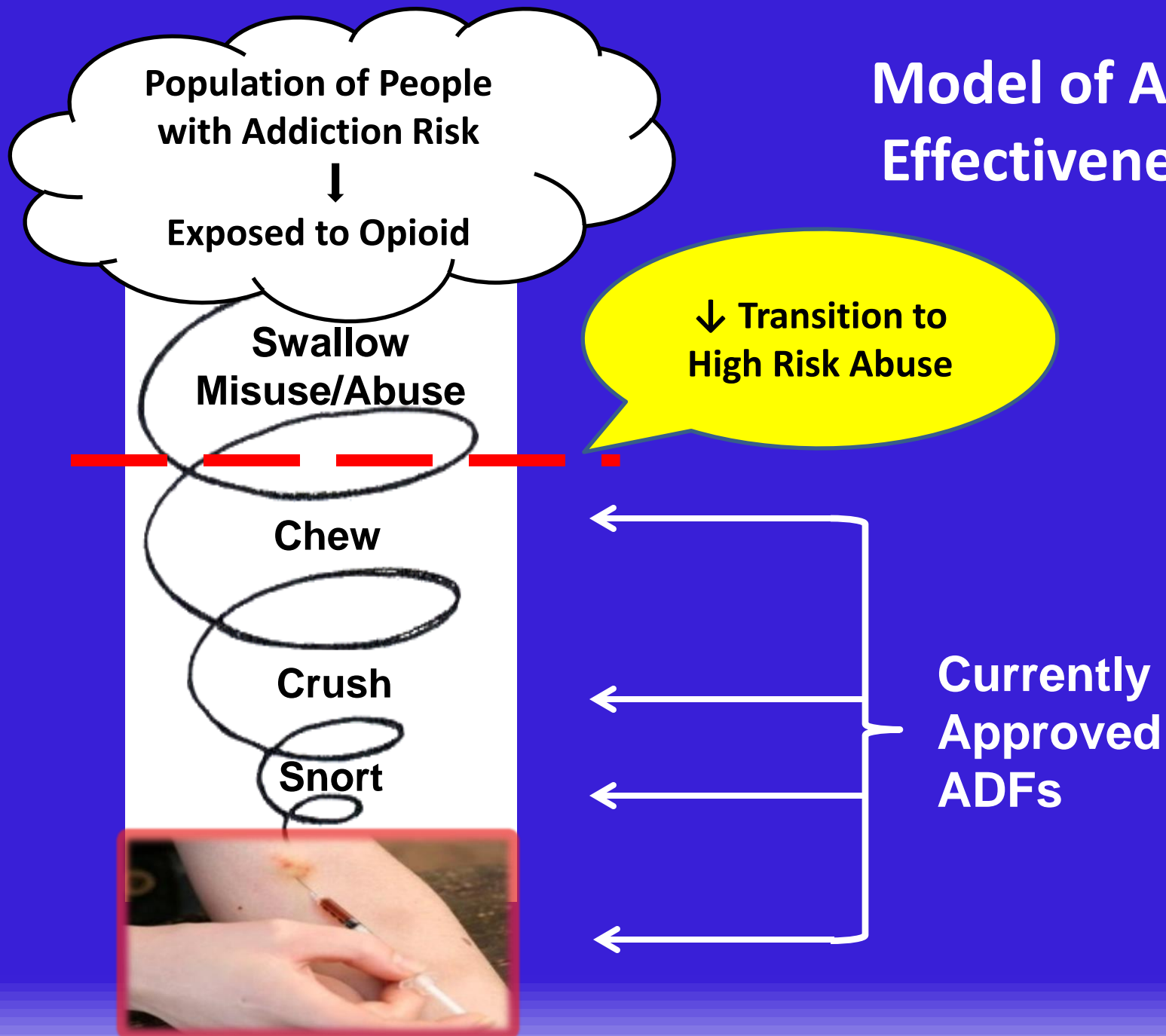
- ***Physical/Chemical barriers*** - physical form of an oral drug is less amenable to abuse.
- ***Agonist/Antagonist combinations*** - interfere with euphoria
- ***Aversion agents*** - unpleasant effect if dosage form is manipulated or a higher dosage is used.
- ***Delivery System*** depot/implants to reduce release (e.g. SR depot SQ injectable formulation).
- ***Prodrug*** lacks opioid activity until transformed (e.g. GI tract).
- ***Combination*** – Two or more methods combined
- ***Holy Grail*** - Overdose only releases therapeutic amount.



# How Can We Prove an ADF Works?

- Draft Guidance Abuse-Deterrent Opioids Evaluation and Labeling, 2013
  - High public health priority
  - Recognizes the value of opioid analgesics in pain treatment
- Premarketing Studies
  - Category 1 - Laboratory-based in vitro manipulation and extraction studies
  - Category 2 - Pharmacokinetic studies
  - Category 3 - Clinical abuse potential studies
- **Category 4 - Postmarketing Studies - Postmarketing data to assess the impact of an ADF on actual abuse.**

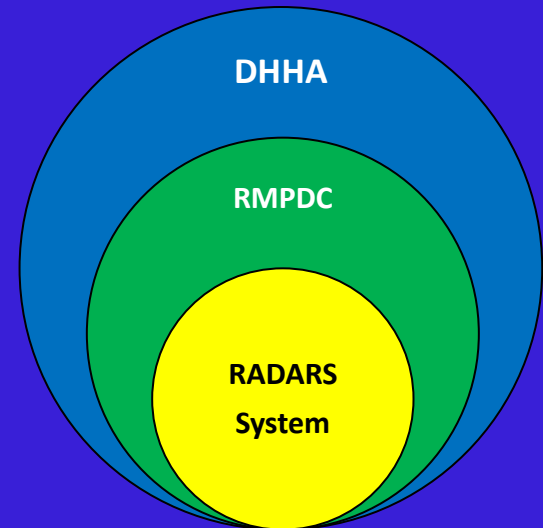
# Model of ADF Effectiveness



# What is the RADARS<sup>®</sup> System?

## History

- 2002, Purdue Pharma
- 2006, Denver Health and Hospital Authority
  - Rocky Mountain Poison and Drug Center
  - Denver Public Hospital for 150 years
  - State sanctioned independent authority



## Conflict of Interest Statement

- Most manufacturers of prescription opioids or stimulants subscribe to RADARS System.
- RADARS System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado.
- Subscribers receive information, but do not participate in developing the System, data collection, or analysis of the data. They do not have access to the raw data.
- Employees are prohibited from personal financial relationships with any company.

# Mosaic Surveillance of Prescription Drug Abuse - 2013

## Acute Health Events

49 Poison centers  
491,874 opioid mentions

## Drug Transactions

Criminal Justice  
260 agency  
146,786 opioid mentions

## Entering Treatment

Opioid Tx Program  
66 programs  
183,573 mentions

## Entering Treatment

Survey Key Informant Pts - 109 practices, 45 states  
64,678 mentions

## New Initiates

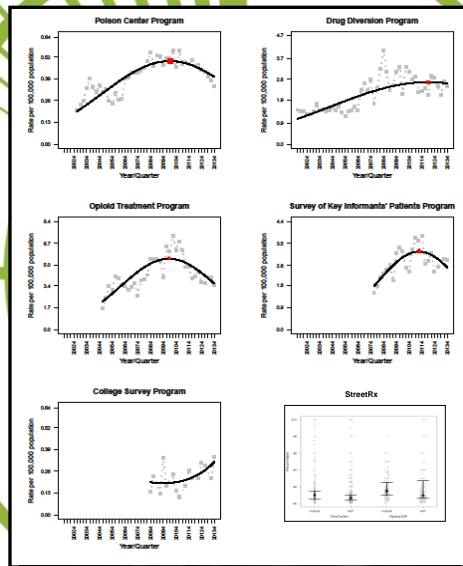
College Survey  
2000 students  
11,871 mentions

## Illicit Market Price

StreetRx.com  
Users/Buyers, 50 states  
8,441 price entries

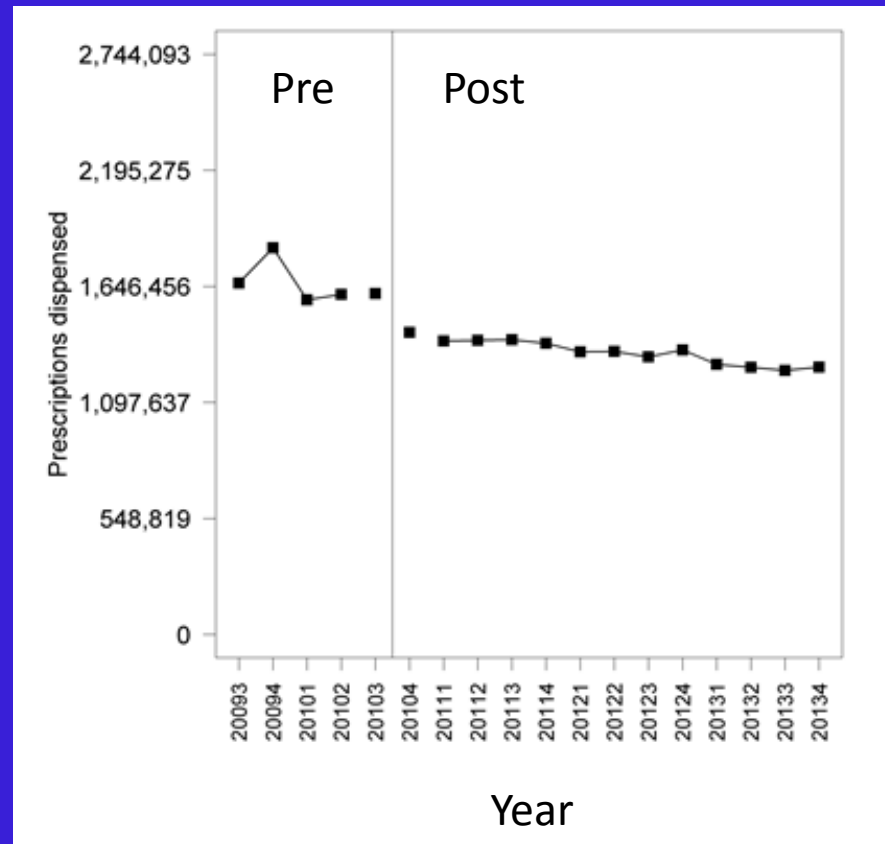
## Web Monitoring

> 150 M sites  
> 35,000 posts coded for analysis



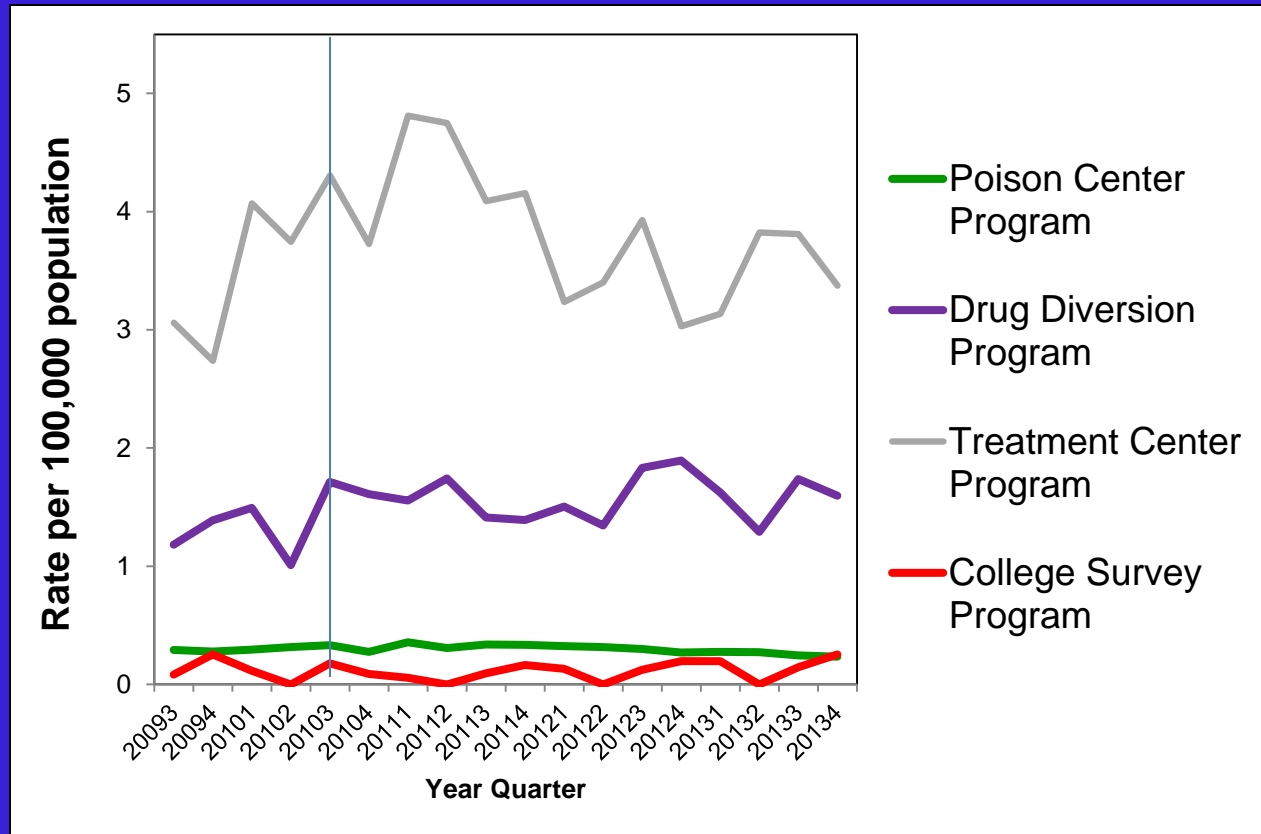
# Oxycodone ADF – Reduced Use

## Number of People Filling Prescriptions



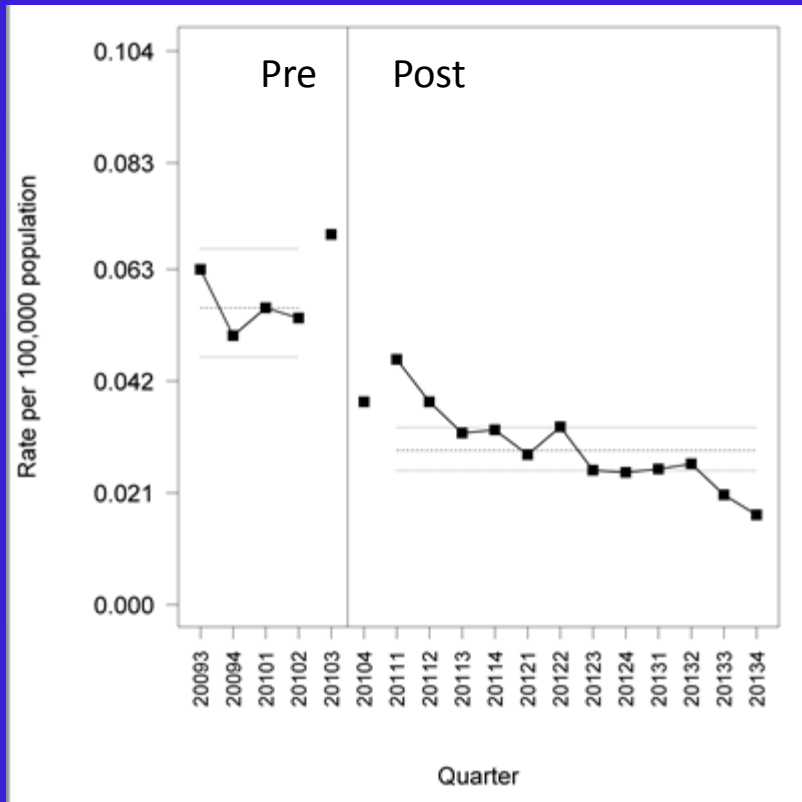
# RADARS System

## Schedule II Excluding Oxycodone ER Population Rates by Program, 2009-2013



# Poison Center Program

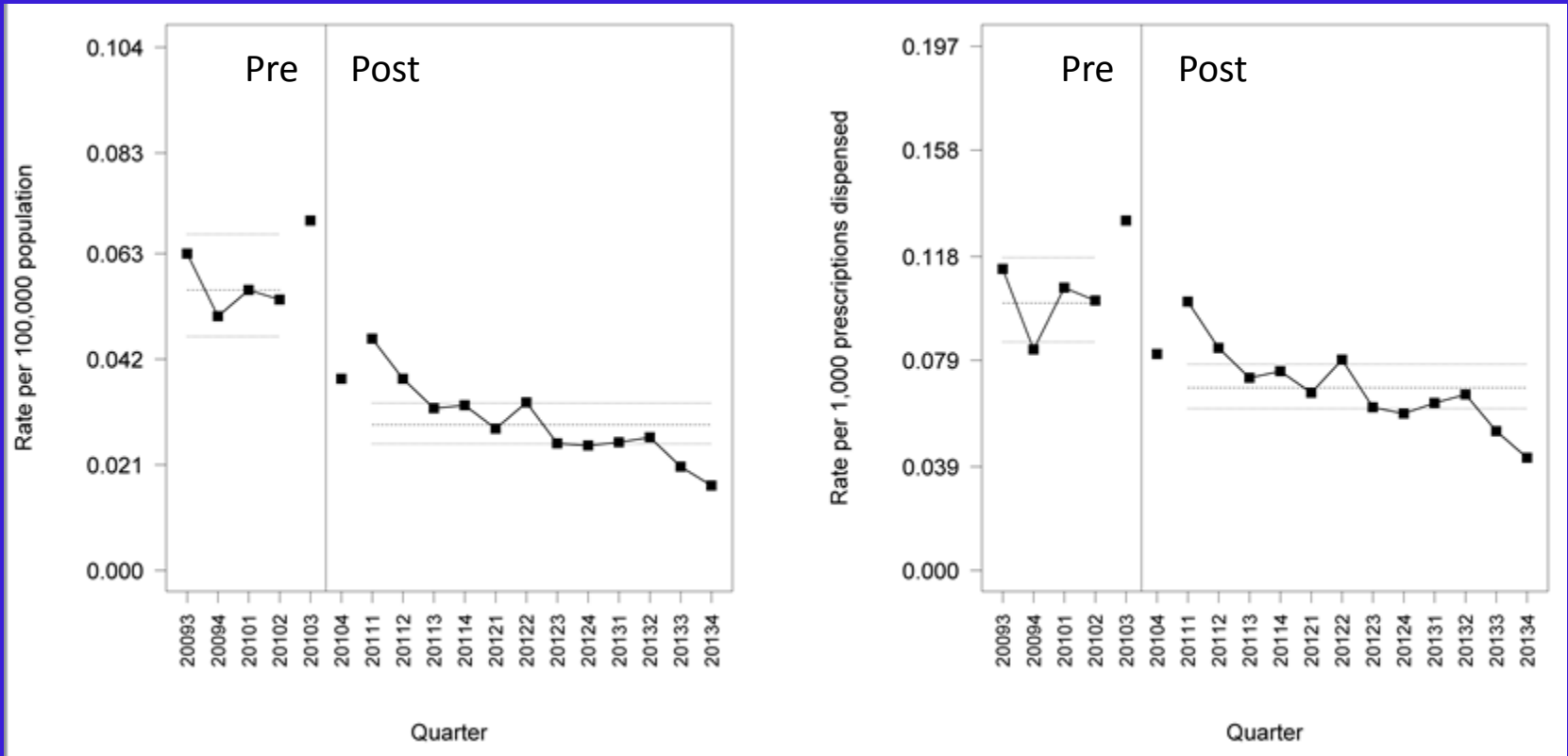
## Oxycodone ER Population Rate, 2009-2013





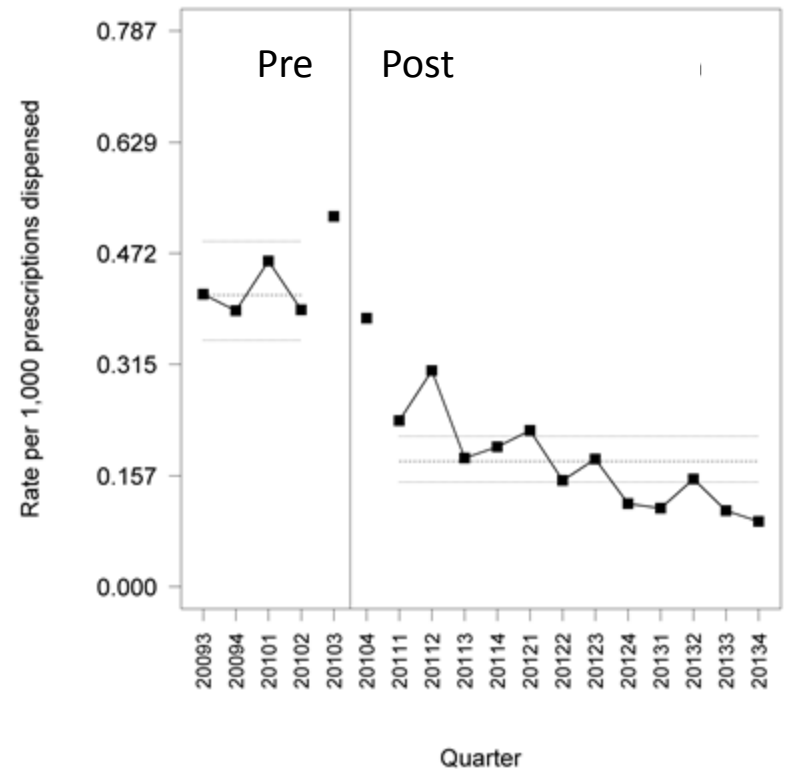
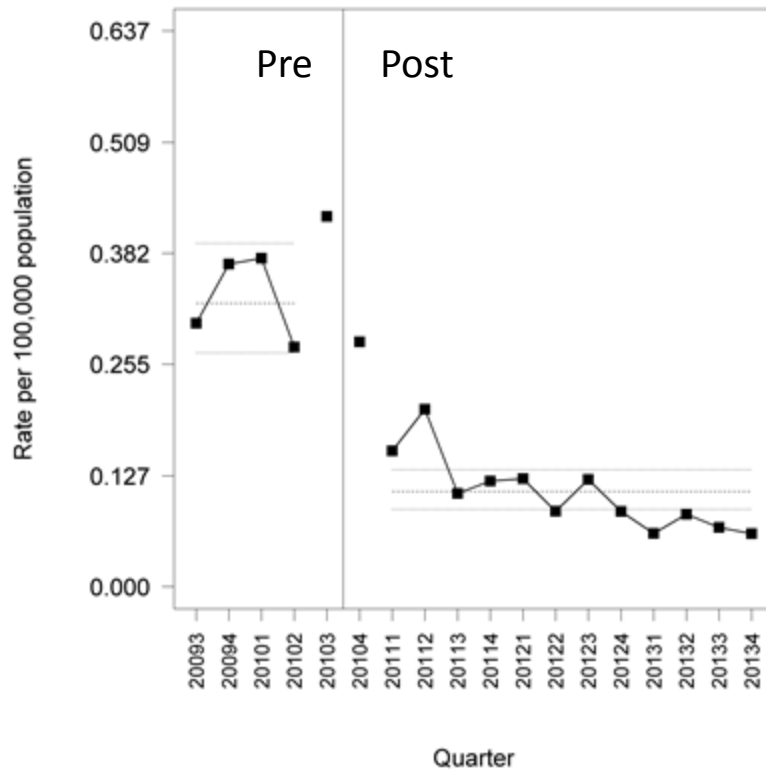
# Poison Center Program

## Oxycodone ER Population and Prescription Rates, 2009-2013

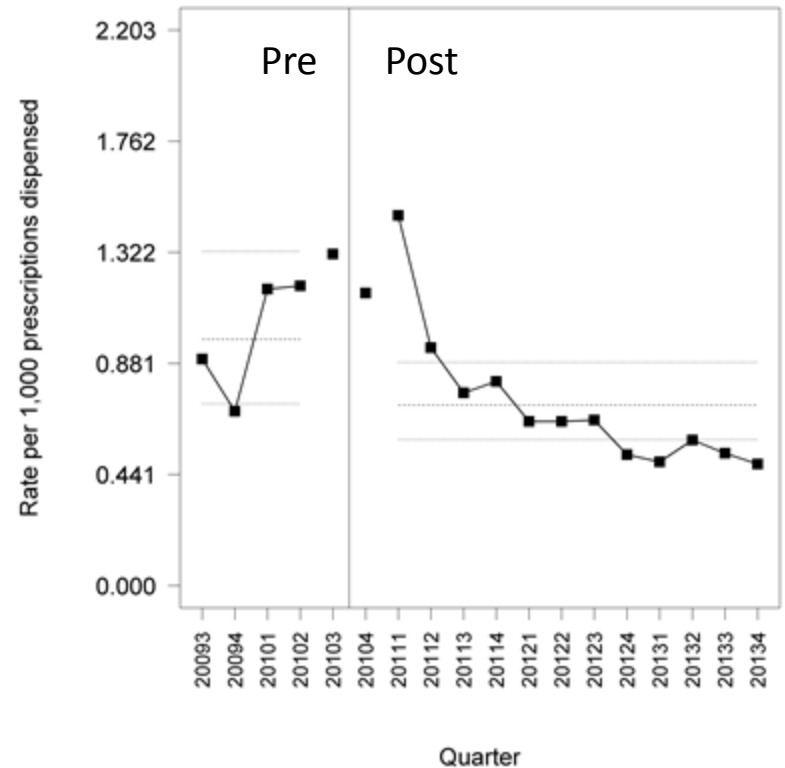
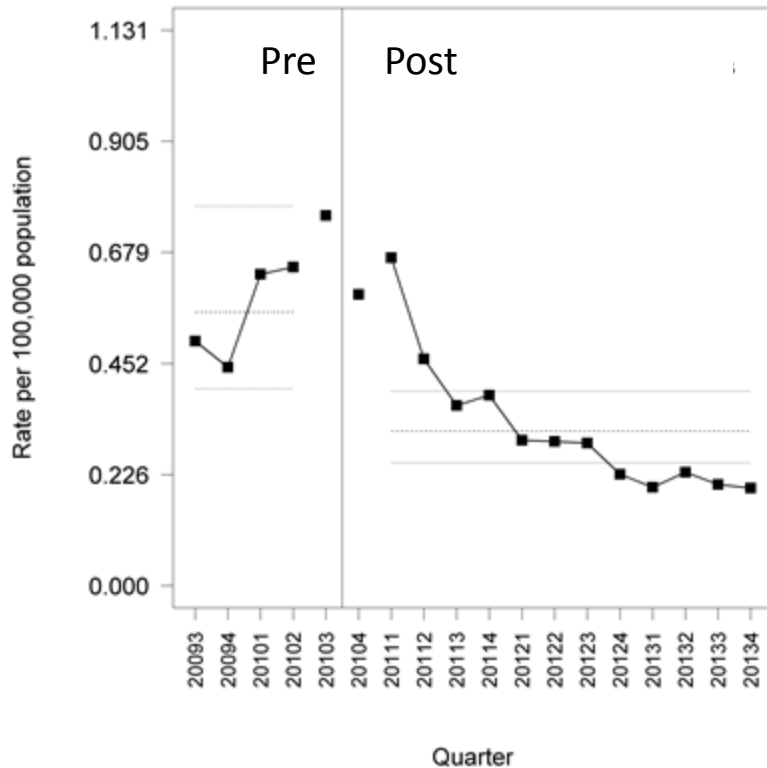


# Drug Diversion Program

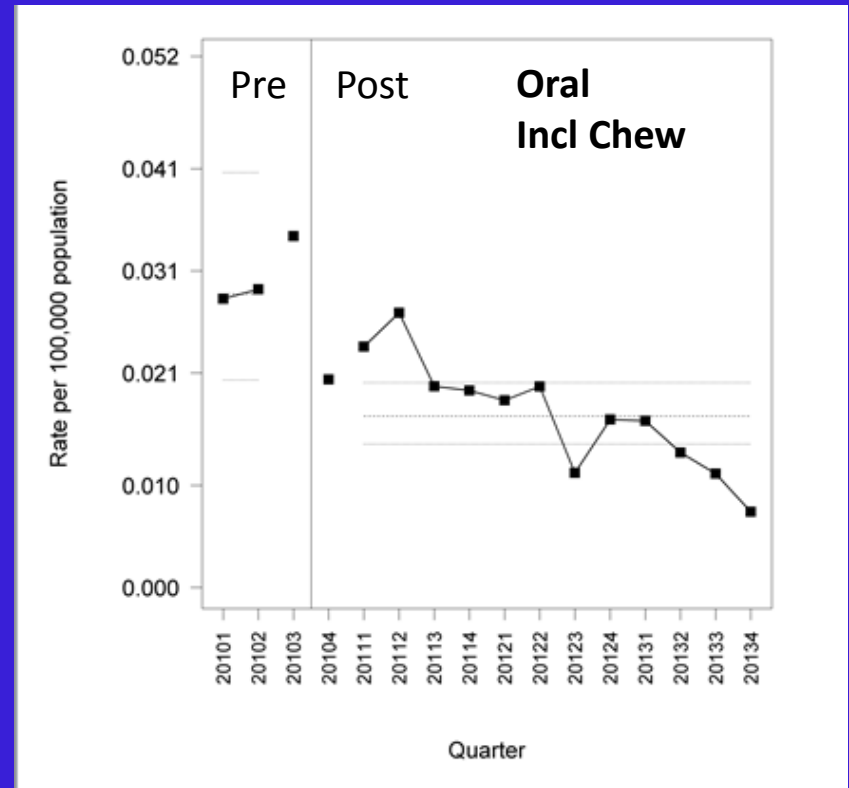
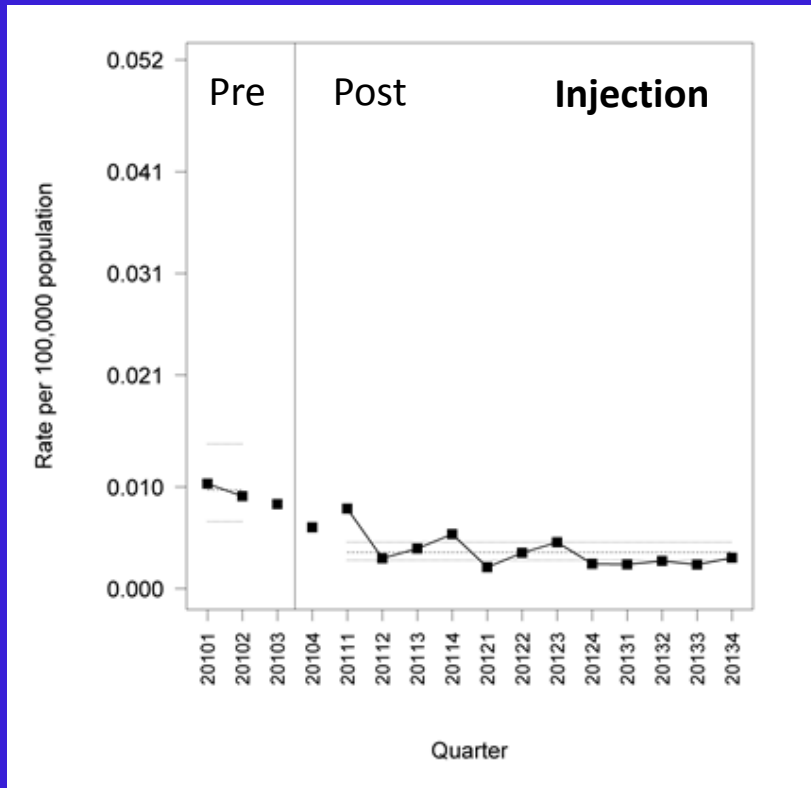
## Oxycodone ER Population and Prescription Rates, 2009-2013



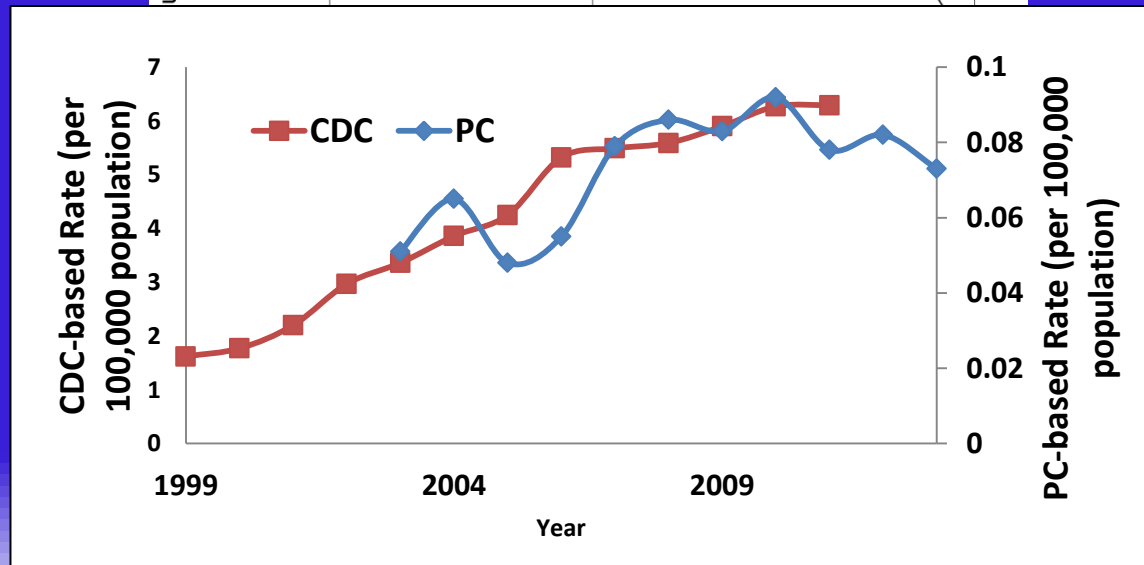
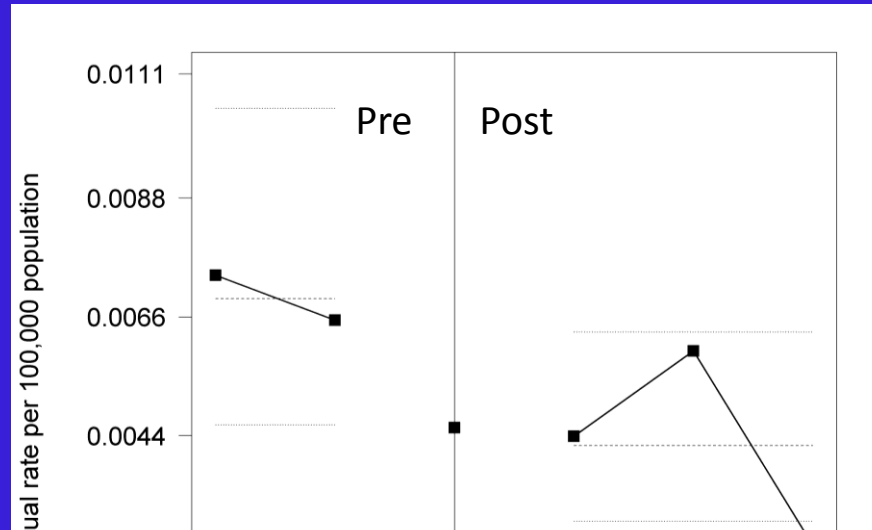
# Treatment Centers Combined Oxycodone ER Population and Prescription Rates, 2009-2013



# Oral and Non-oral Abuse Decrease after Oxycodone ADF - Poison Center Program



# Death Associated with Oxycodone ER have Decreased Poison Center Program, 2008 - 2013



# Abuse Deterrent Formulation Reduces Street Price 2013 - 2014

	United States		Canada	
	Number reports	Median Price/mg, US Dollar (range)	Number reports	Median Price/mg, Canadian Dollar (range)
<b>Crushable “Old OxyContin”</b>				
<b>Median</b>	<b>283</b>	<b>1.00</b>	<b>50</b>	<b>1.00</b>
<b>Abuse Deterrent “New OxyContin”</b>				
<b>Median</b>	<b>364</b>	<b>0.70</b>	<b>23</b>	<b>0.63</b>

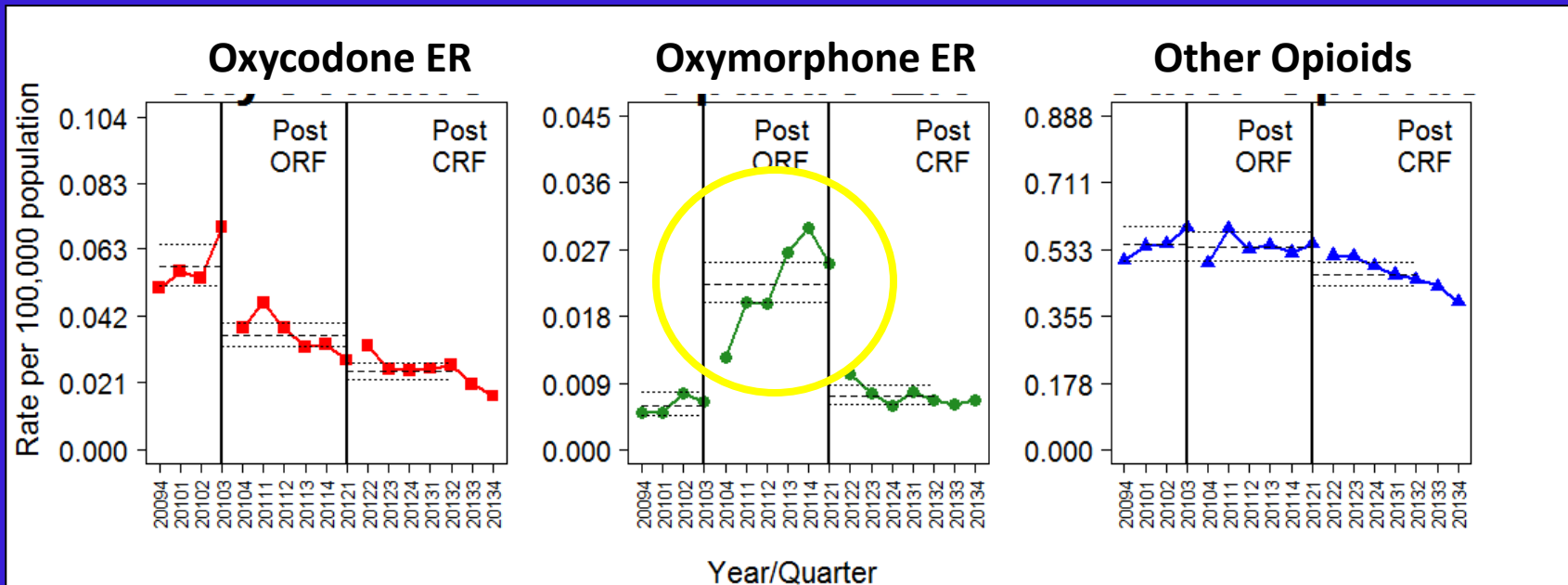
# **Refining Our Understanding of Abuse Deterrent Formulations**

# Limited Impact Unless Most Opioids Analgesics are Abuse Deterrent



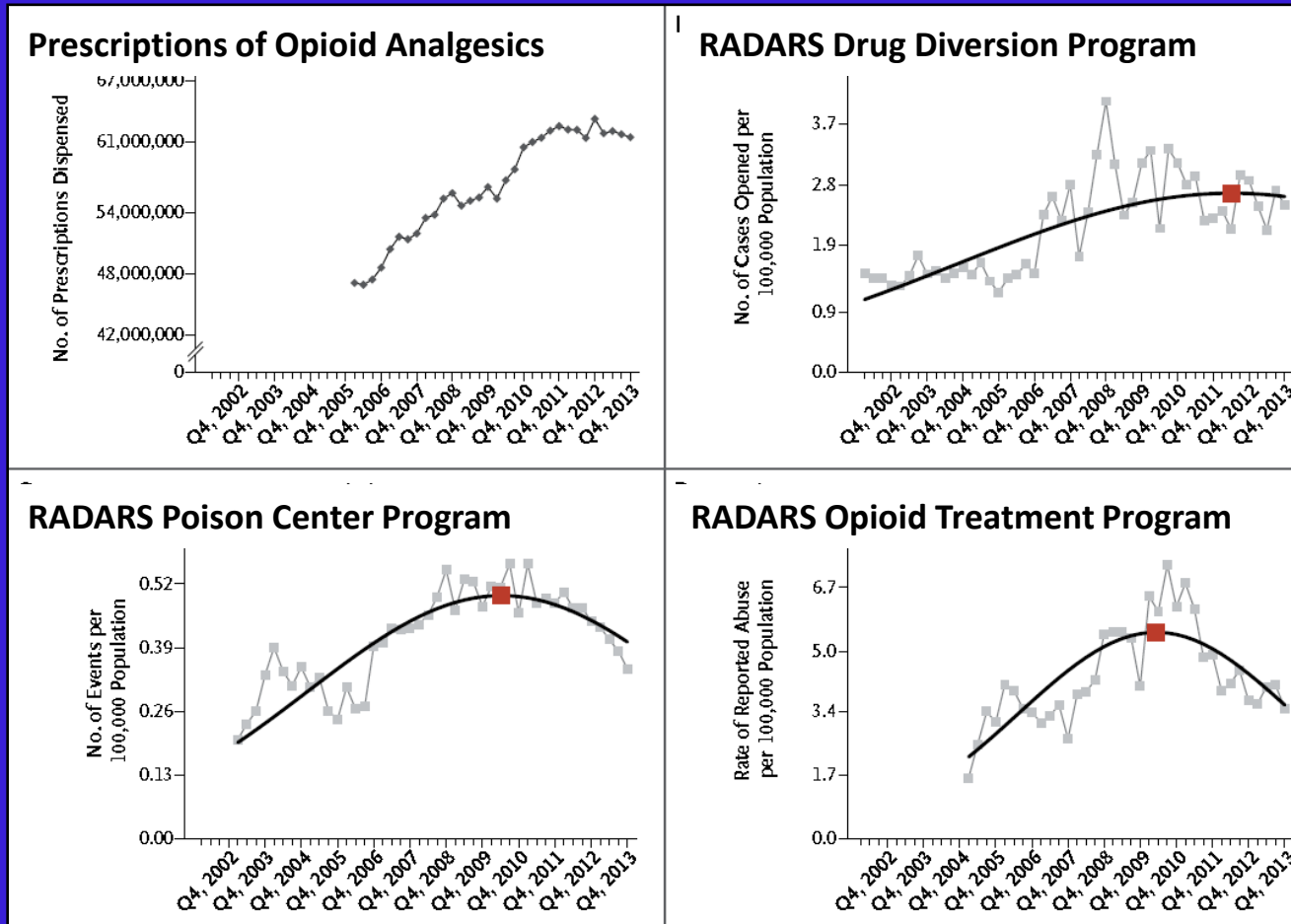


# Poison Center Program Population Rate, 2009-2013



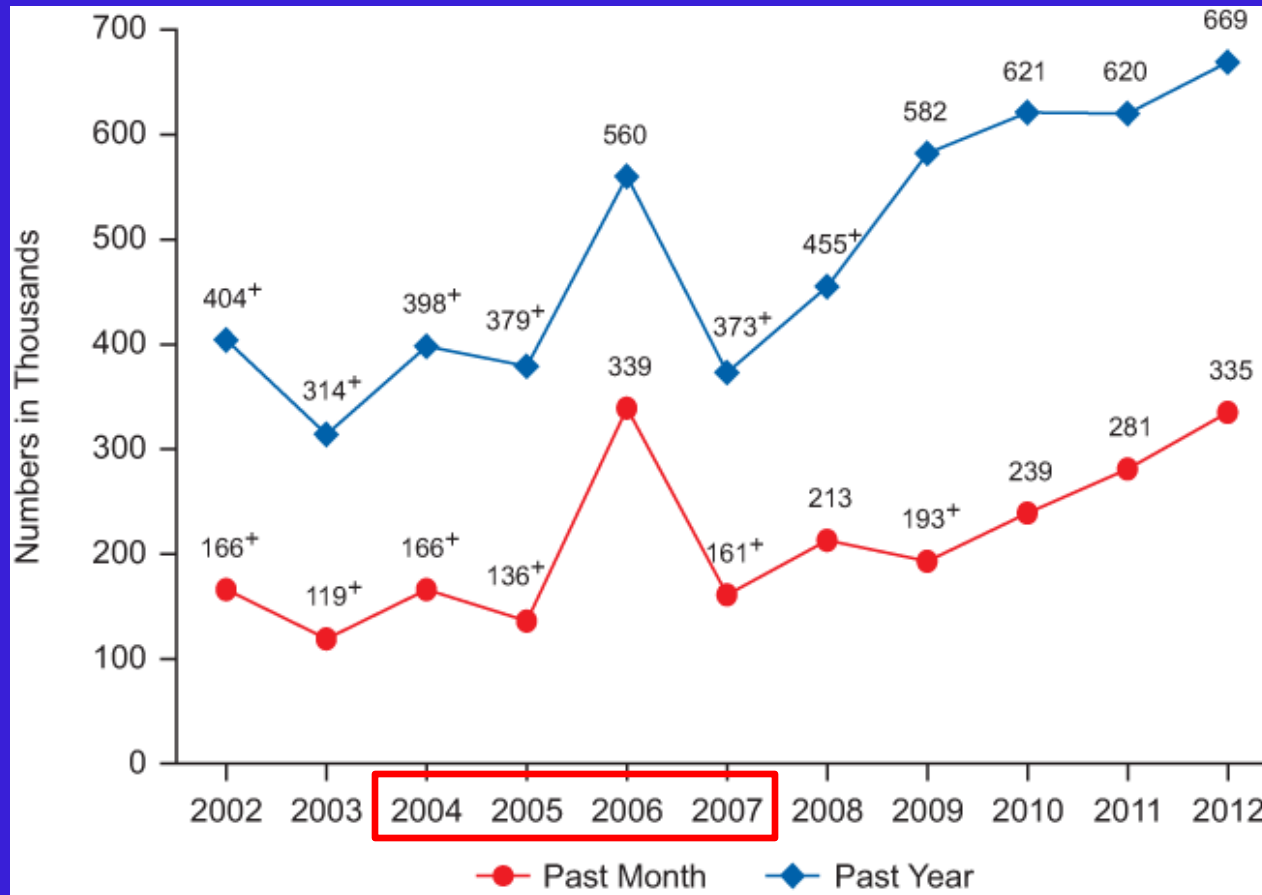
\*Other opioids excluding ER oxycodone and ER oxymorphone

# National Trends in Opioid Abuse and Diversion



# Endorsement of Heroin Use

## National Survey of Drug Use and Health



# Battle of the ADFs





# Summary

Population with Addiction Risk



Exposed to Opioid  
Recreational Use or Pain Treatment

Swallow  
Misuse/Abuse

Chew

Crush

Snort

↓ Transition to  
High Risk Abuse

- ADFs are not for addicts
- More drug = more abuse, but formulation can change relation
- Need ADFs for IR as well as ER
- Need new drug scheduling - formulation and not by API
- Need greater treatment capacity for opioid addiction



Questions?