

The Evolution of Abuse Deterrent Drug Formulations: Testing Effectiveness from the Benchtop to the Real World

Richard C. Dart, MD, PhD

Director, Rocky Mountain Poison and Drug Center

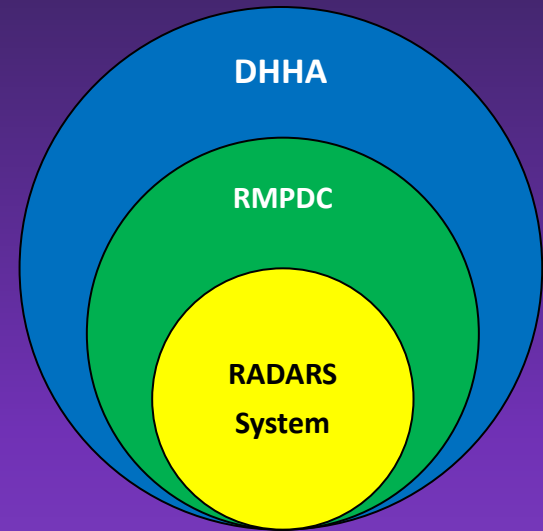
Executive Director, RADARS® System

Professor of Emergency Medicine, University of Colorado

What is the RADARS[®] System?

History

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



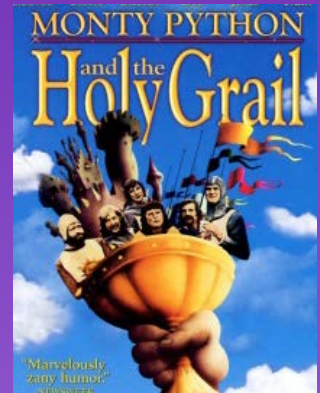
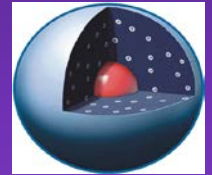
Conflict of Interest Statement

- 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. They do not have access to the raw data.
- Employees are prohibited from personal financial relationships with any company.

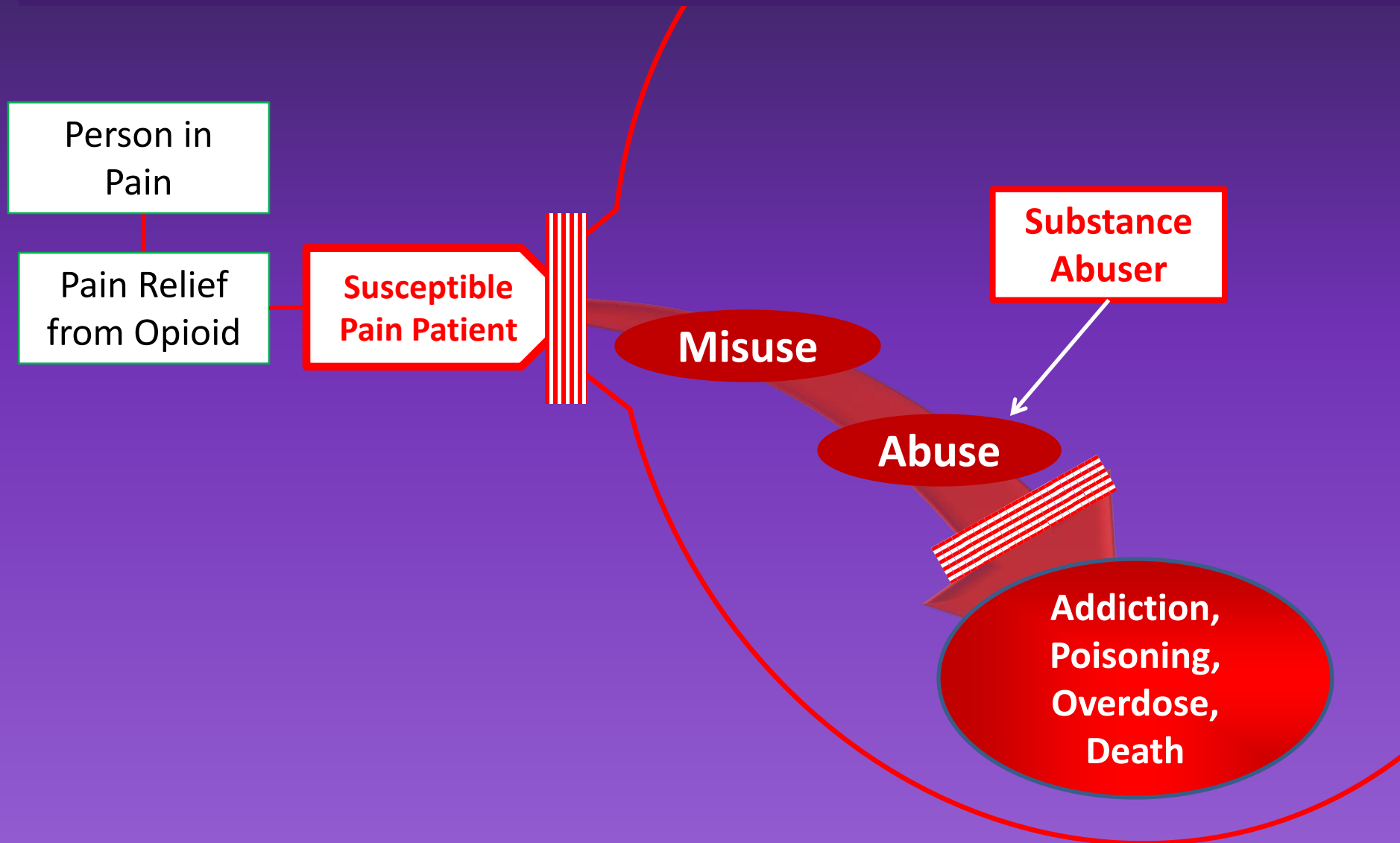
How Do Abuse Deterrent Formulations Work?

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.**



Role of Abuse Deterrent Formulations



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.**

RADARS Examines Prescription Drug Abuse from Multiple Perspectives

Poison Center Data

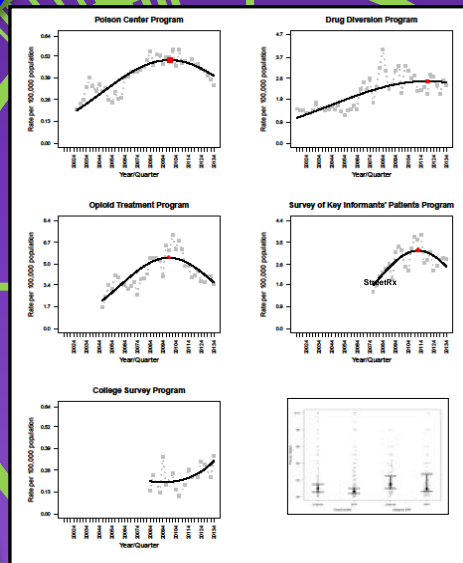
Drug Diversion Program

**OTP and SKIP
Substance Abuse
Treatment**

**College Student
Survey**

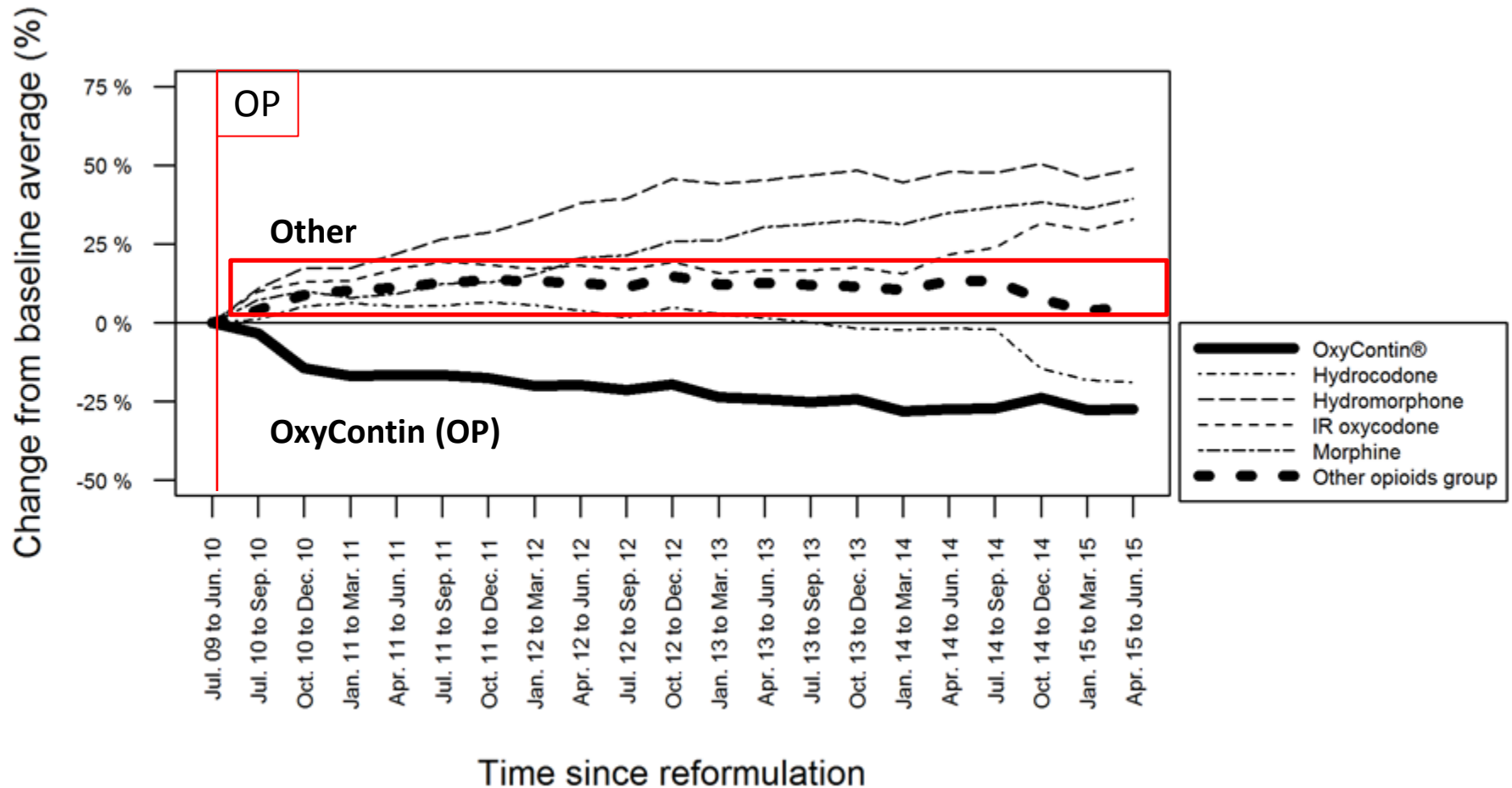
**StreetRx.com
Illicit Market Price**

Web Monitoring

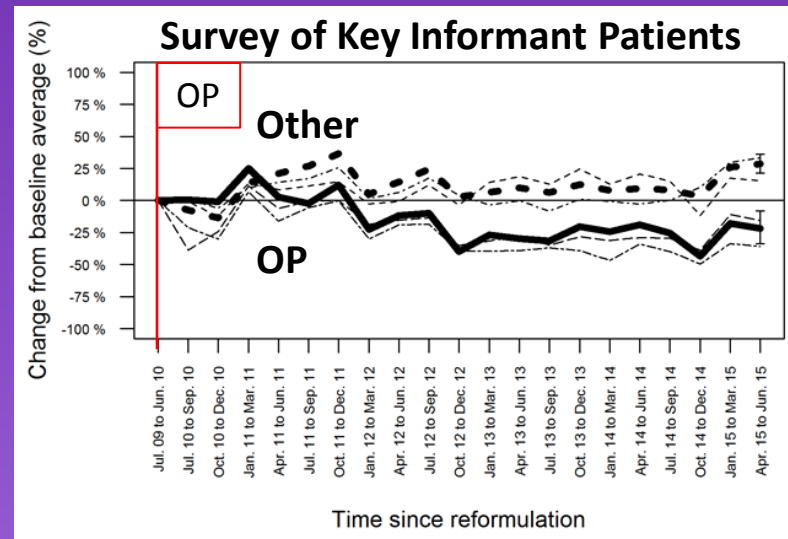
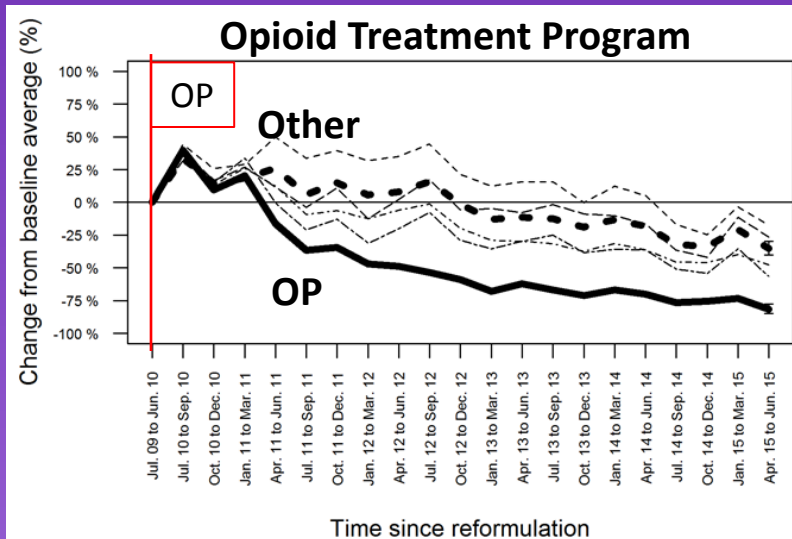
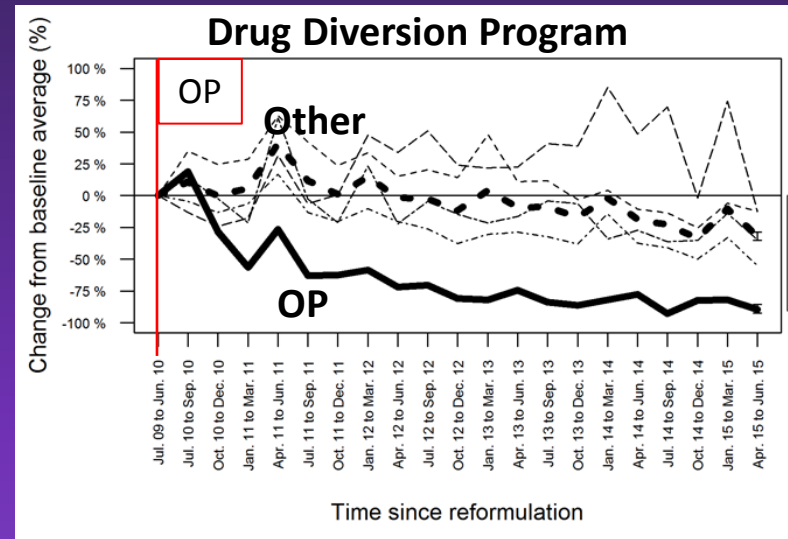
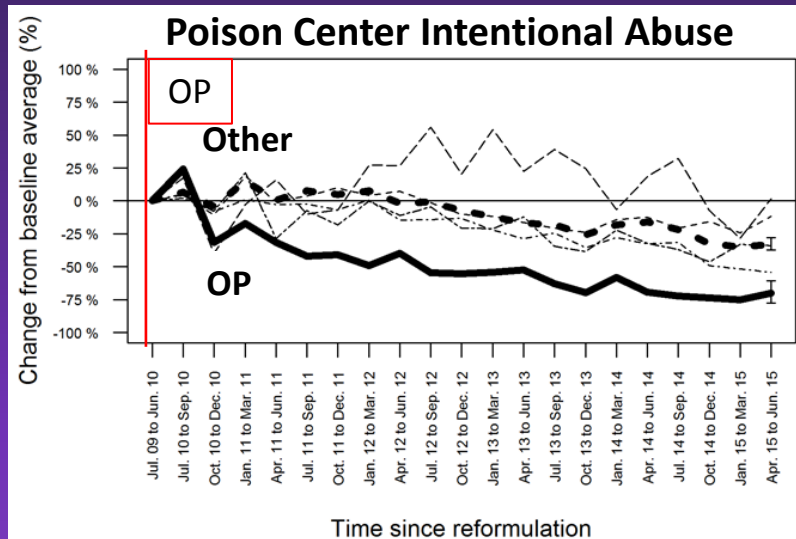


Oxycodone ADF – Reduced Use

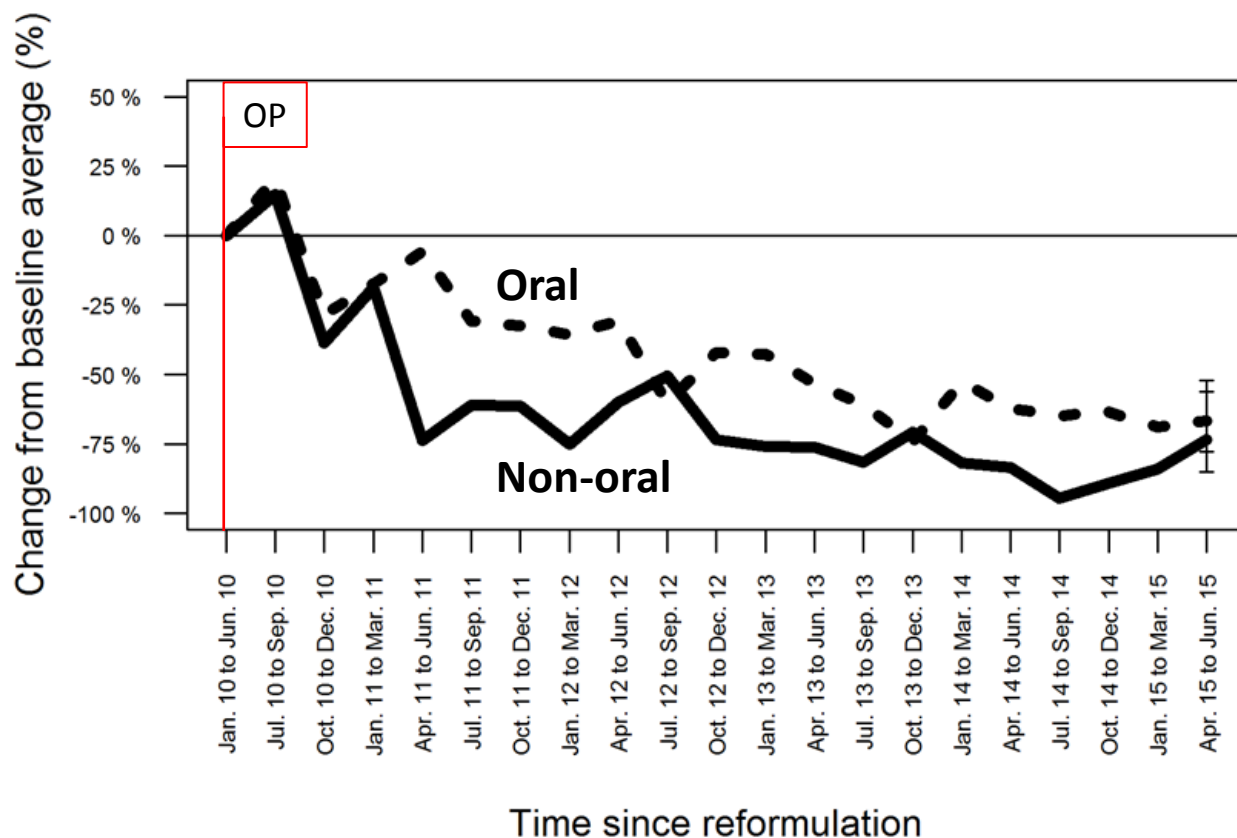
Number of People Filling Prescriptions



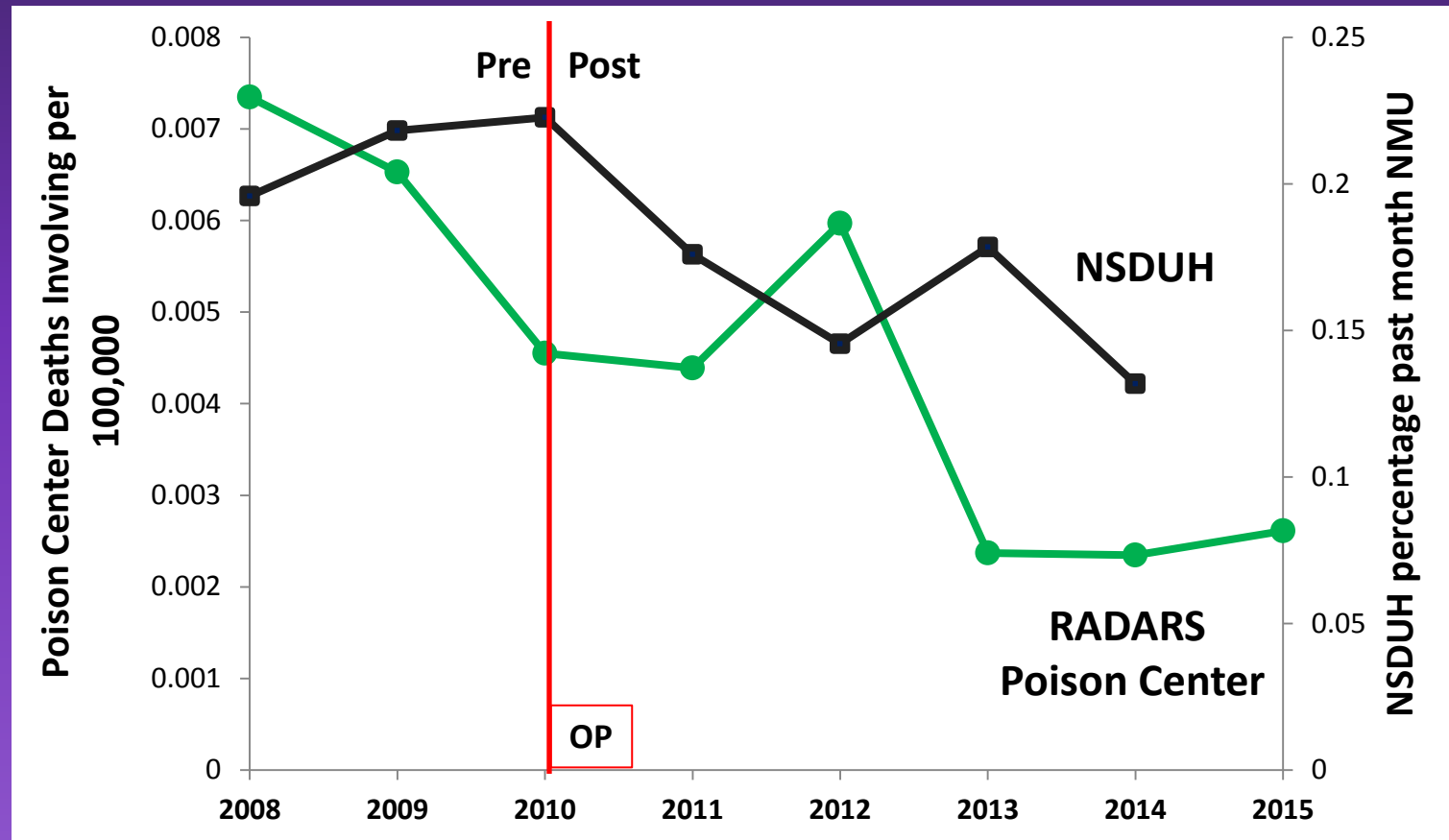
RADARS System, Abuse and Diversion, 2009 - 2015



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



Nonmedical Use and Outcomes Associated with Oxycodone ER have Decreased, 2008 - 2015



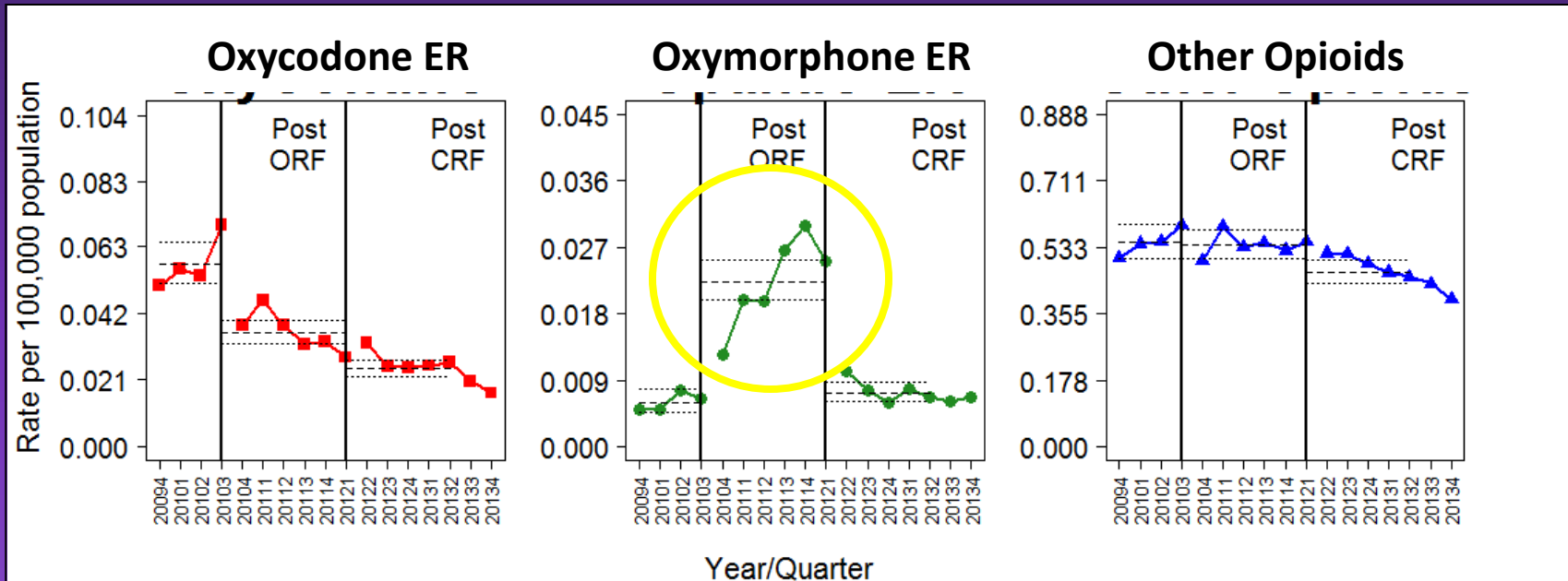
Abuse Deterrent Formulation Reduces Street Price 2013 - 2014

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

Limited Impact Unless Most Opioid Analgesics are Abuse Deterrent



Poison Center Program Population Rate, 2009-2013

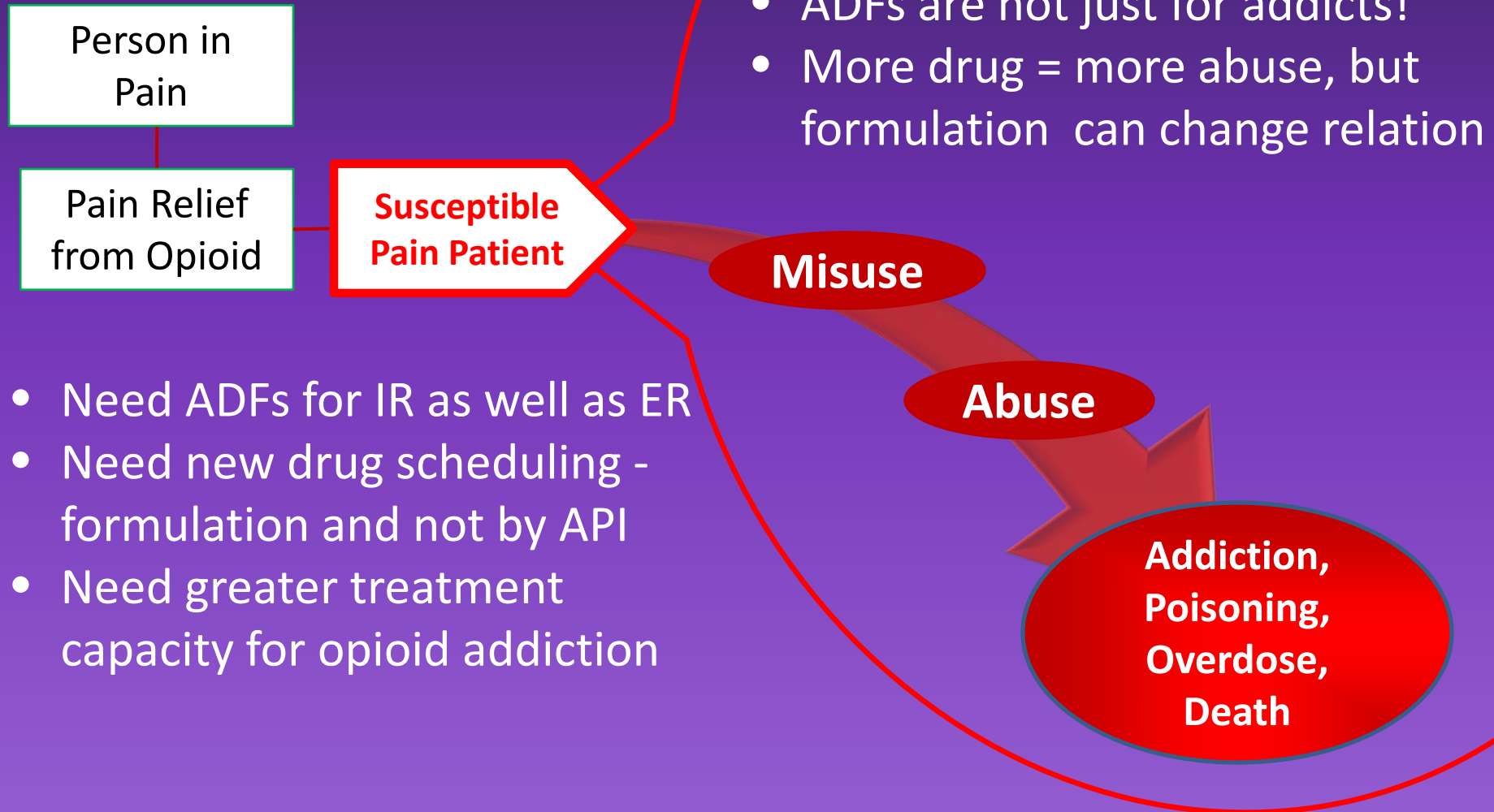


*Other opioids excluding ER oxycodone and ER oxymorphone

Battle of the ADFs



Summary



Questions?