

RADARS® SYSTEM 10th ANNUAL SCIENTIFIC MEETING



Lessons from the Downward Spiral aka The Bubble Slide

May 6, 2016

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The Anti-ADF Movement: Can ADFs contribute to reducing prescription drug abuse?



Home Issues Topic collections

CMAJ June 29, 2015
10.1503/cmaj

I want everyone in this Chamber to understand this: "Abuse-deterrent opioid" is an oxymoron..."
Senator Markey, MA

<https://www.congress.gov/congressional-record/2016/2/11/senate-section/article/s883-3>

CDC >

CDC [Monitoring Opioids for Chronic Pain – United States, 2016](#)



FDA's Throckmorton: Future for AD Opioids. Where are we headed?

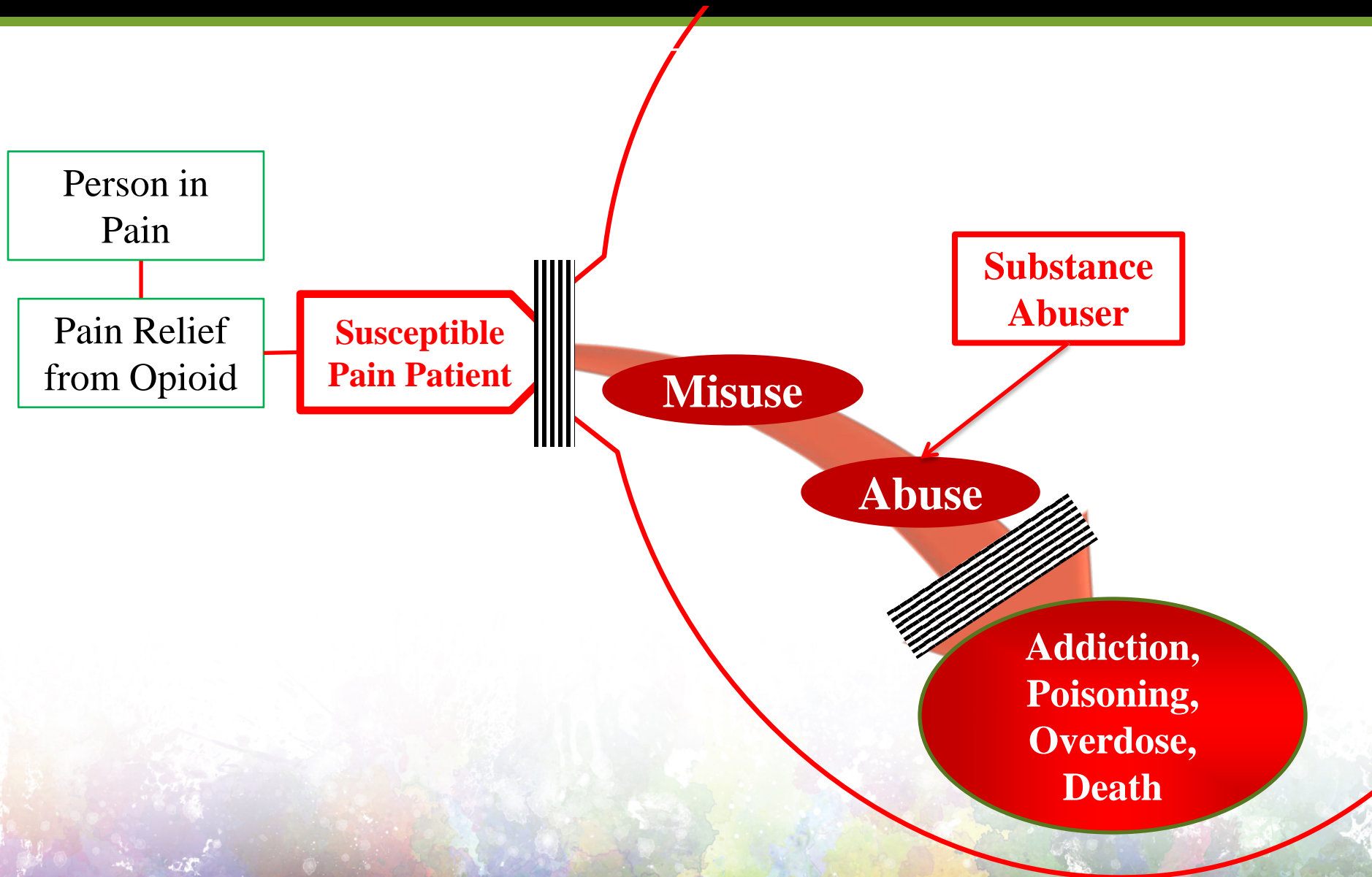
- Early: market has a small number of AD products using early AD technology
 - Case by case decision-making
- Intermediate: multiple products approved as abuse deterrent using various technologies
 - Fuller set of regulator issue identified.
 - Guidance outlining FDA's approach for brand name and generic development is refined
 - Actions potentially shift to class-wide scope
- Late: AD formulations of all major opioids marketed
 - Focus is on supporting iterative improvements in AD technologies.

Current ADFs in the United States

- **OxyContin**, an ER oxycodone tablet formulation, was reformulated in 2010 to deter abuse; the current product is more difficult to crush, break, or dissolve than the original, and when dissolved forms a viscous gel that is difficult to inject through a hypodermic needle.
- **Embeda** is formulated as capsules of ER morphine pellets that contain a sequestered core of the opioid antagonist naltrexone. If the pellets are swallowed, the morphine is gradually released and absorbed, while the naltrexone core passes through the gut intact. If the pellets are crushed, chewed, or dissolved, naltrexone is released, blocking morphine-induced euphoria.
- **Hysingla ER** is an ER hydrocodone tablet formulation; when dissolved it forms a viscous gel that is difficult to inject through a hypodermic needle.
- **Targiniq ER** is an opioid agonist/antagonist combination containing ER oxycodone and naloxone, has been approved by the FDA with claims of abuse deterrence in the labeling, but is not yet commercially available.

The Downward Spiral

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- Draft Guidance Abuse-Deterrent Opioids Evaluation and Labeling, 2013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

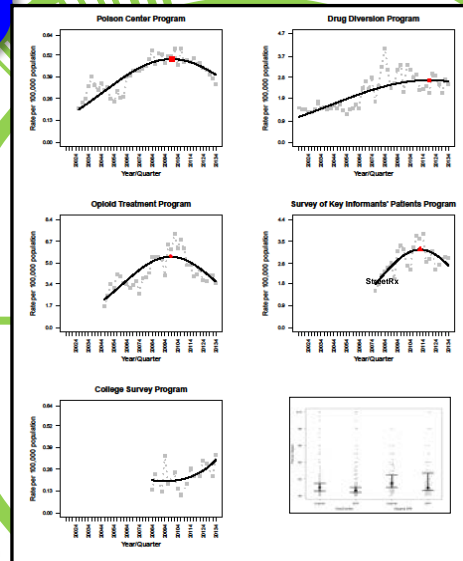
Drug Diversion Program

OTP and SKIP
Substance Abuse
Treatment

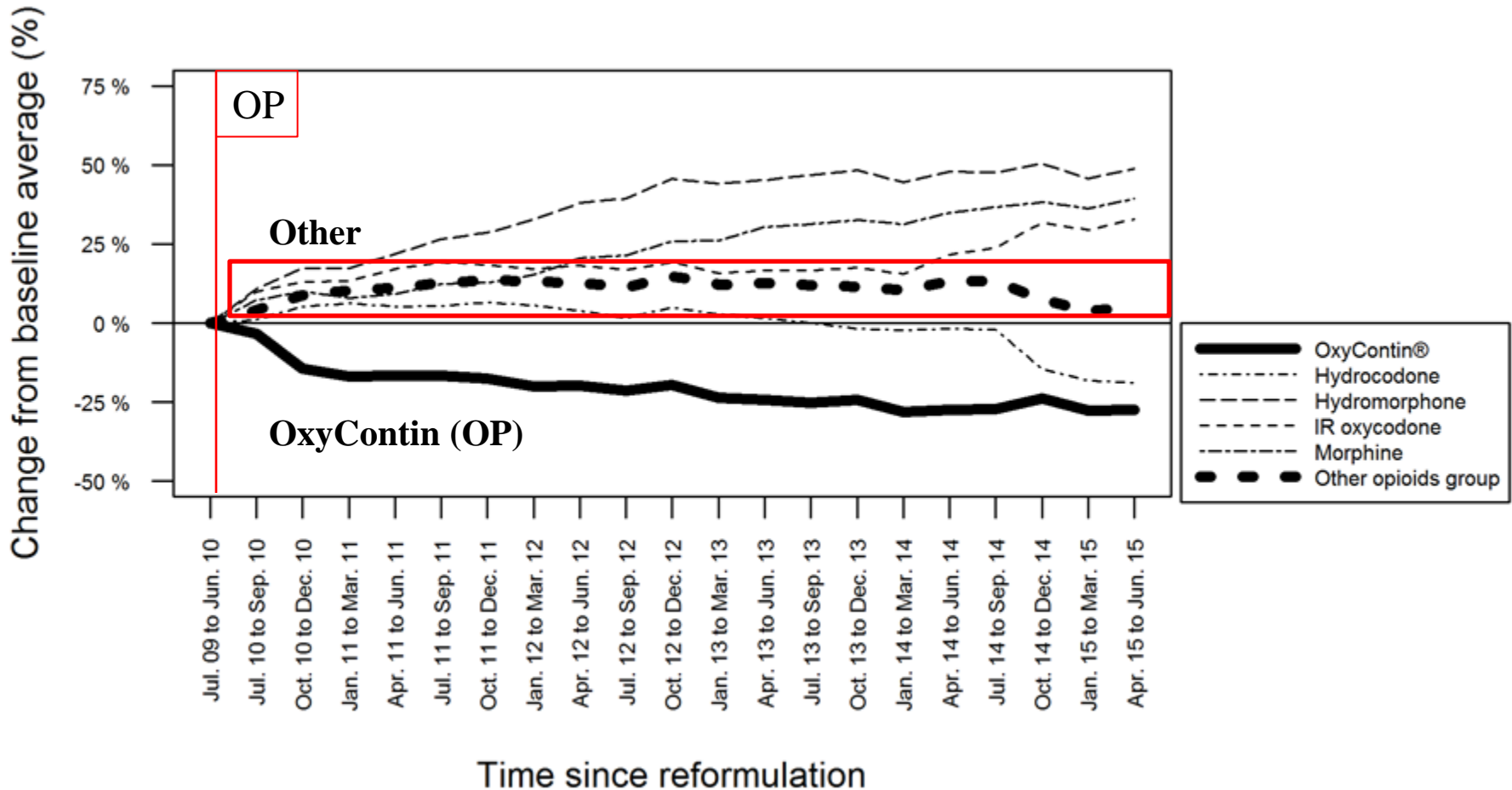
College Student
Survey

StreetRx.com
Illicit Market Price

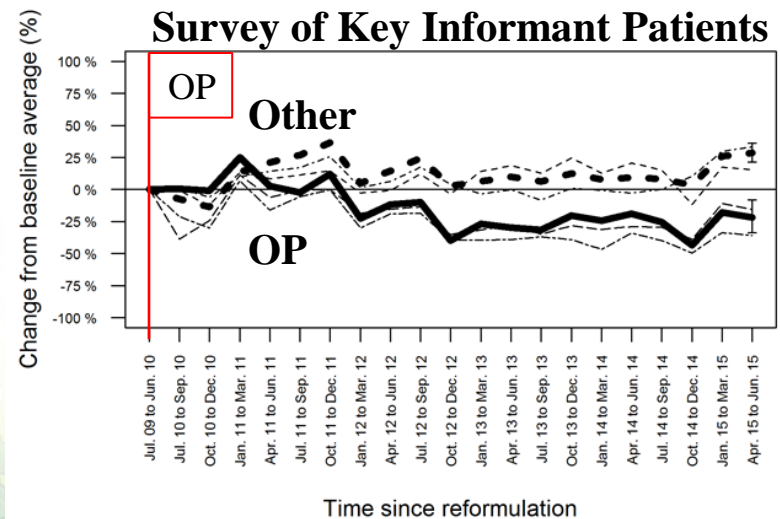
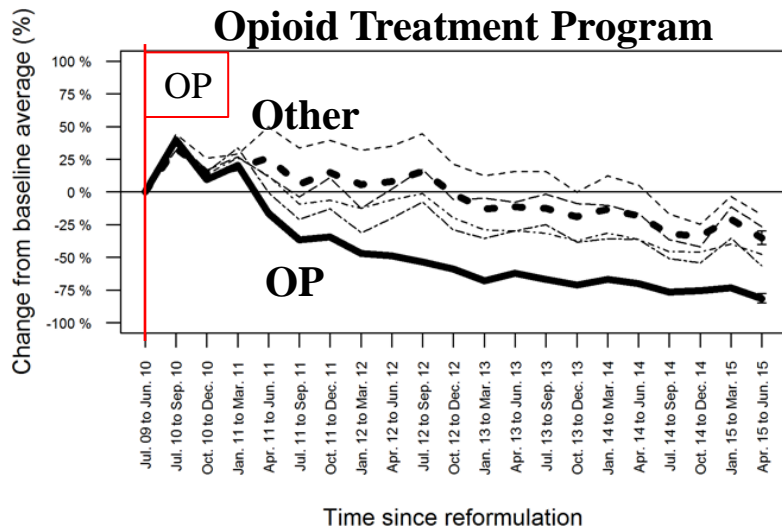
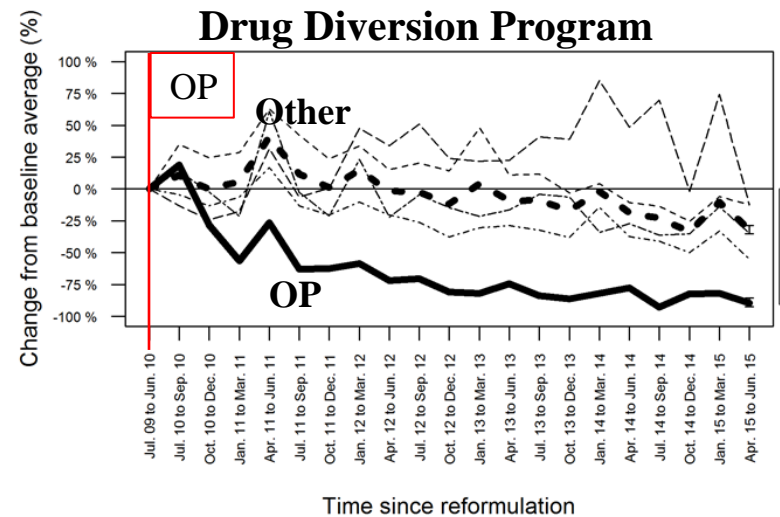
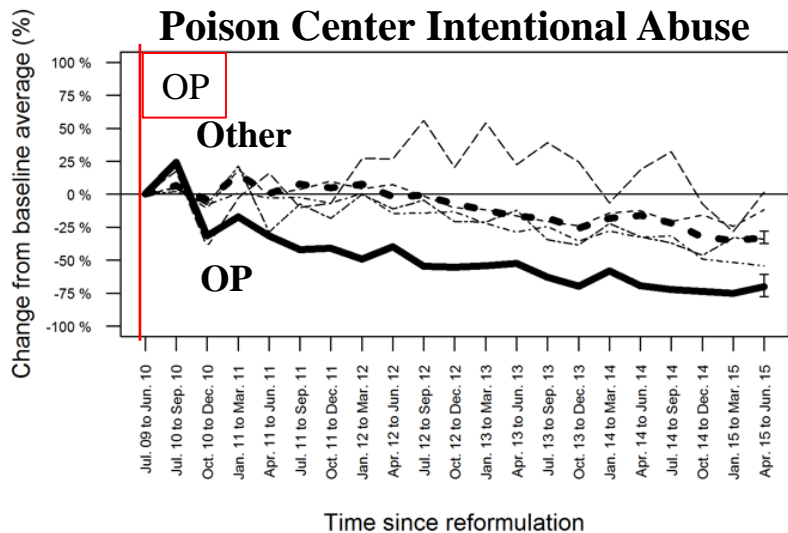
Web Monitoring



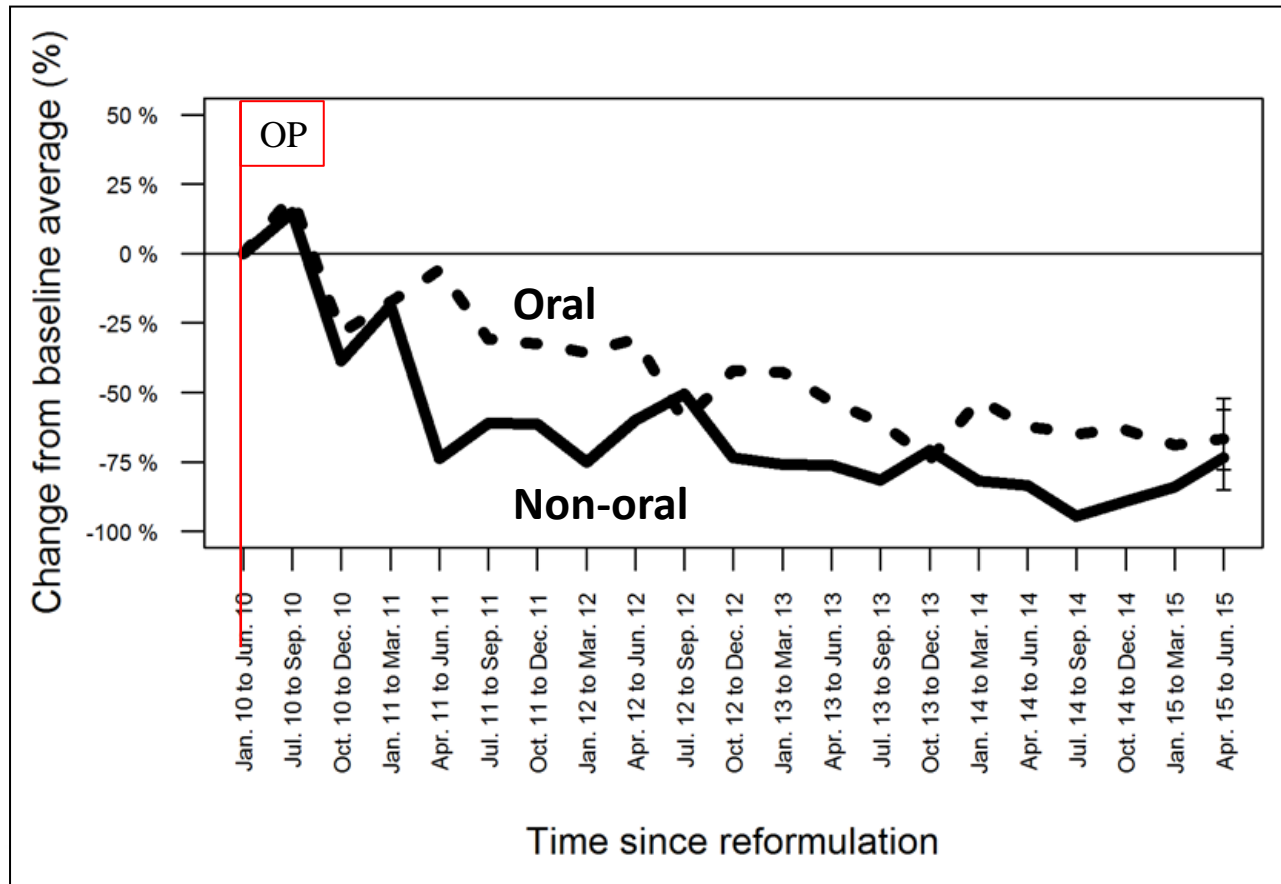
Oxycodone ADF – Reduced Use Number of People Filling Prescriptions



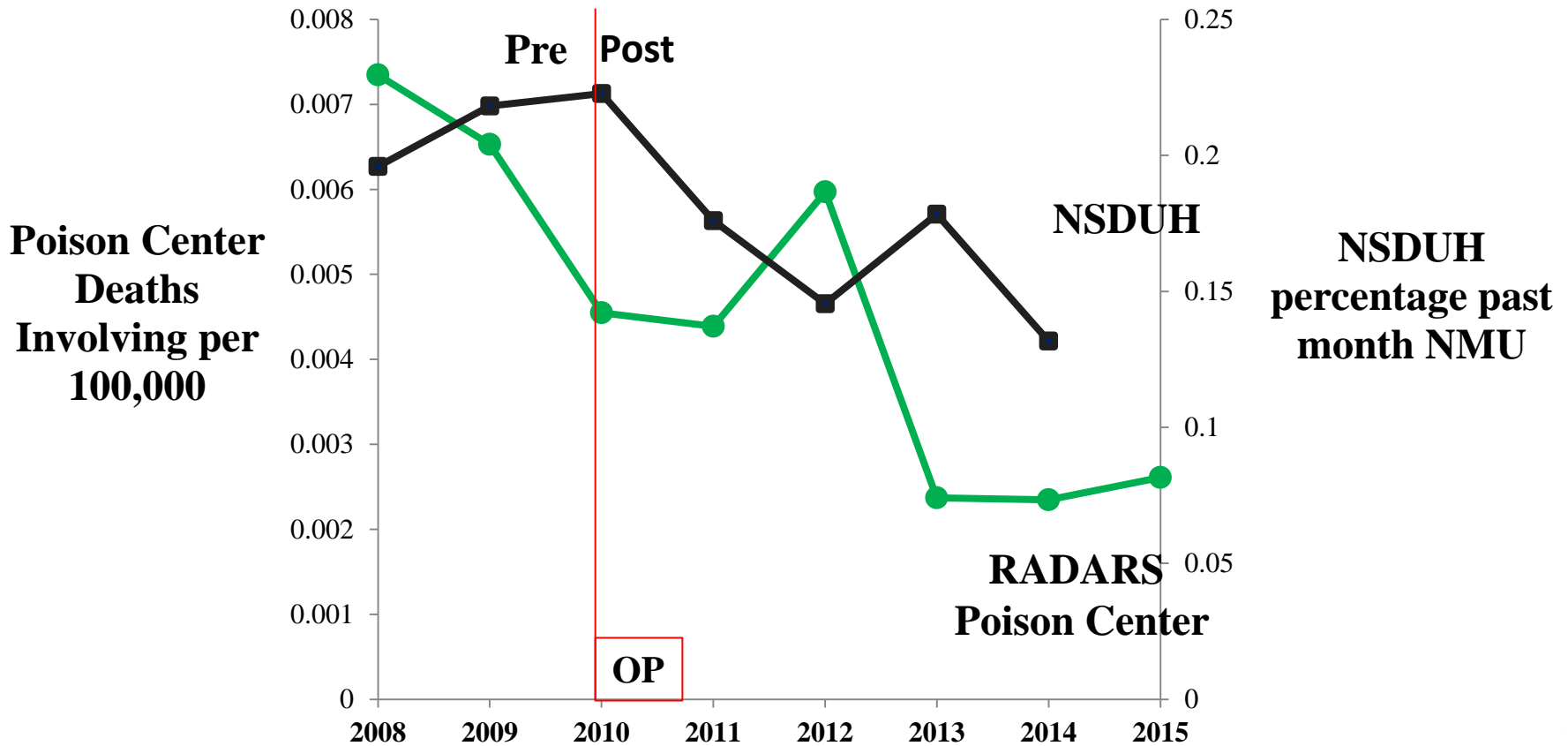
RADARS System, Abuse and Diversion, 2009 - 2015



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

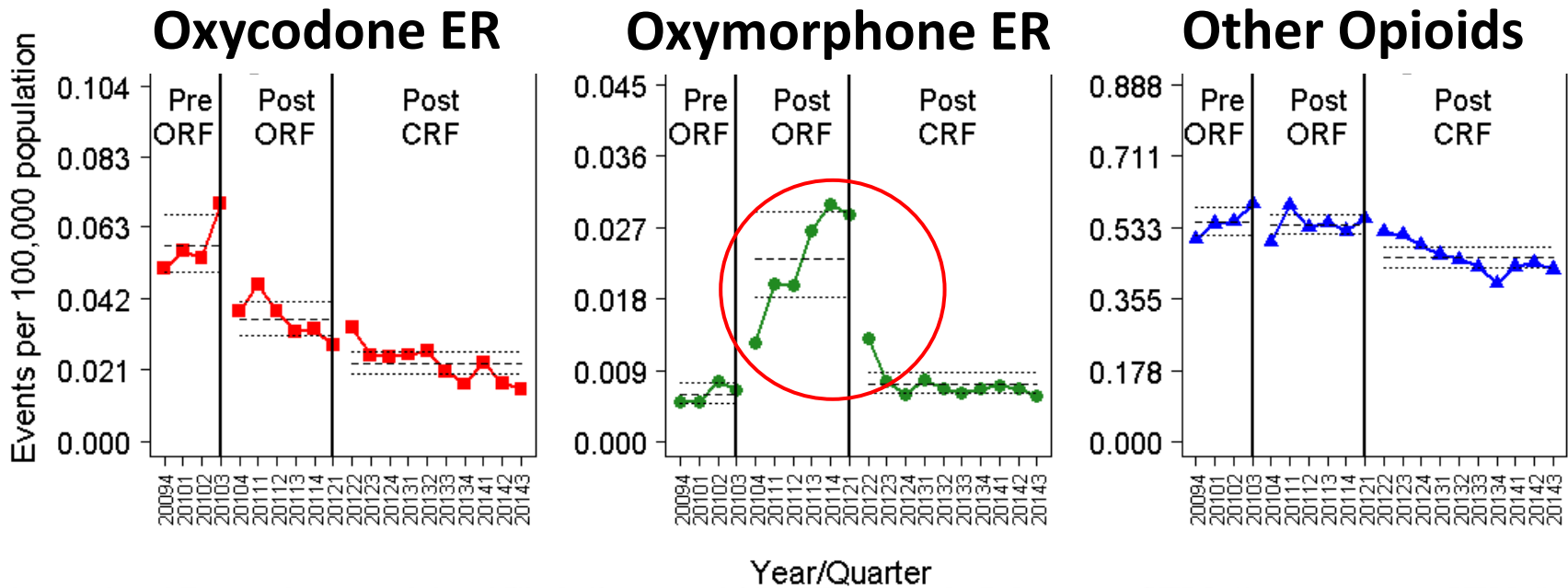
	United States		Canada	
	Number reports	Median Price/mg, US Dollar (range)	Number reports	Median Price/mg, Canadian Dollar (range)
Crushable “Old OxyContin”				
Median	283	1.00	50	1.00
Abuse Deterrent “New OxyContin”				
Median	364	0.70	23	0.63

Limited Impact Unless Most Opioids Analgesics are Abuse Deterrent



Changes in Abuse Indicators Following Introduction of Abuse Deterrent Formulations

Poison Center Intentional Abuse



Battle of the ADFs



Niacin



Prodrug



Crush
Resistance

Summary

- Lots of controversy
 - Cost
 - Fear of increased prescribing
 - Alternatives are plentiful
- Won't be able to tease out the minor differences until most of the market is ADF
- Then the fun will begin
 - But only if health care payers decide to pay.