



Effect of Abuse-Deterrent Formulations and IR Opioids on Abuse, Overdose and Death from Rx Opioids

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Competing Interests

- RADARS System is owned by Denver Health and Hospital Authority, the public hospital for the City and County of Denver. The program is supported by subscriptions by pharmaceutical manufacturers of prescription opioid and stimulants.

Goals

- Describe types of abuse-deterrent formulations (ADFs)
- Trends in abuse and overdose rates of extended-release (ER) opioids as abuse-deterrent formulations (ADFs) were introduced into the group
- Role of immediate release (IR) and ER opioids in prescription opioid abuse and overdose
- Predict the public health implications of ADF opioid products

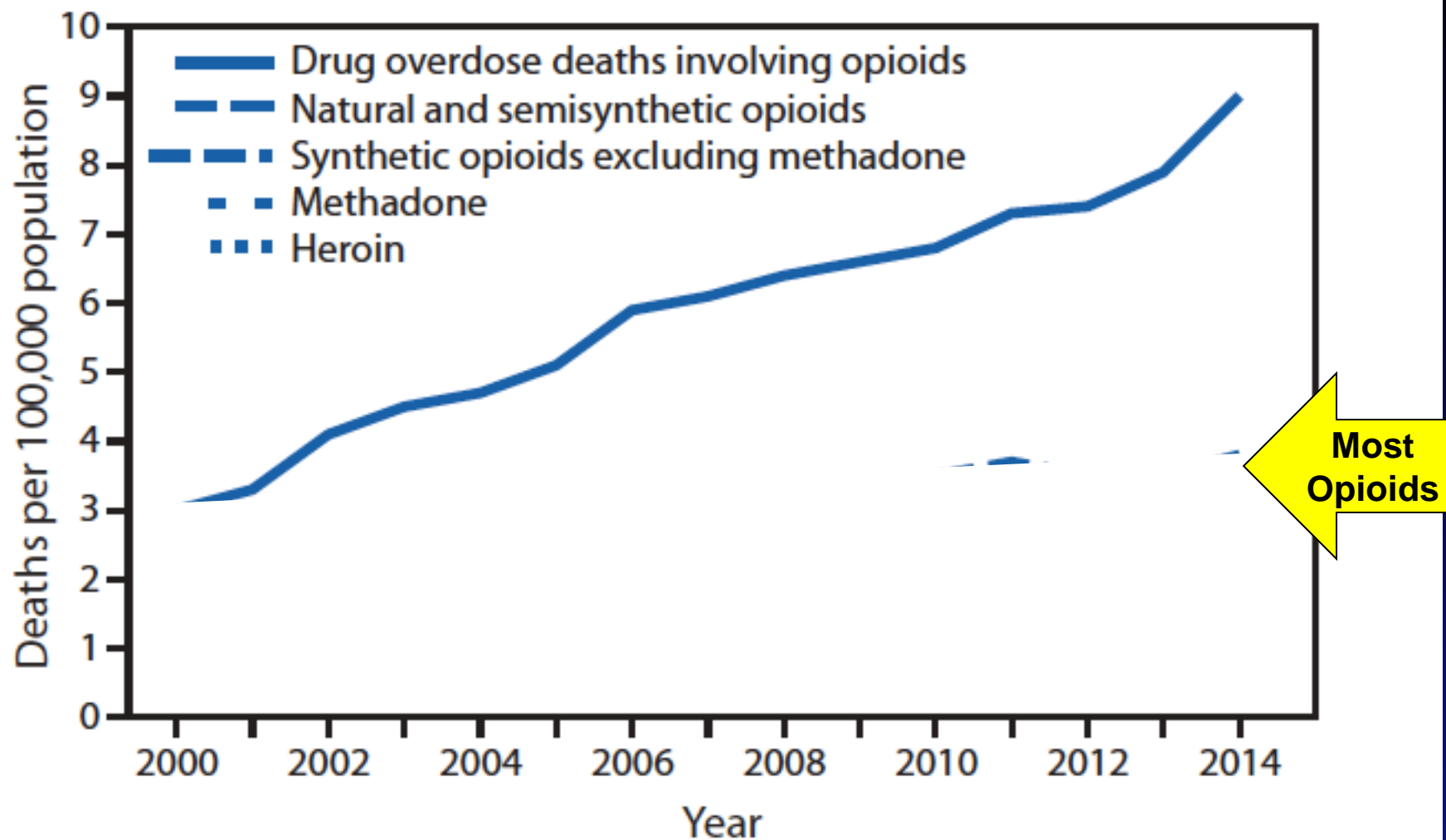


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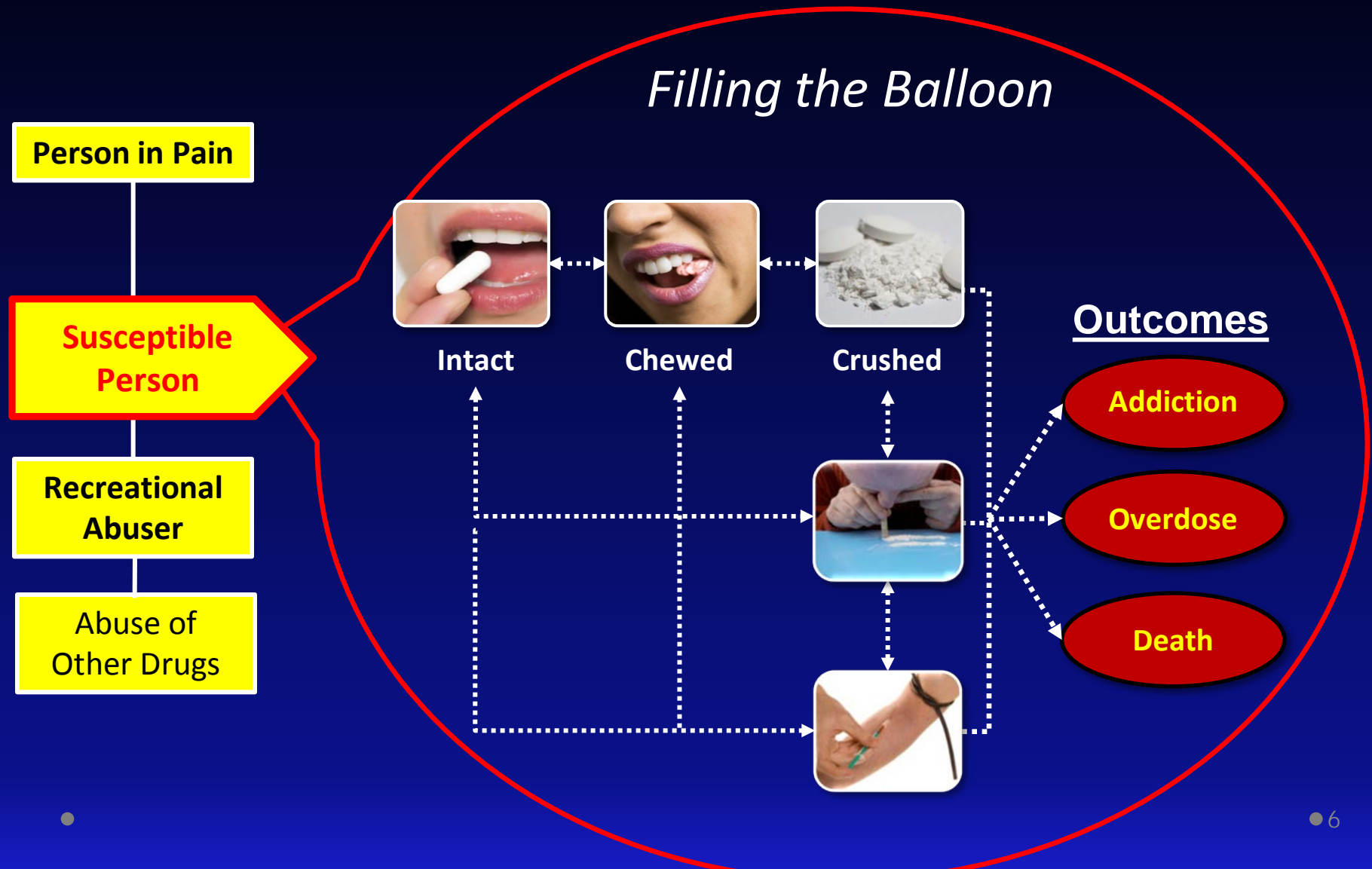


Artist: Jason Mecier

FIGURE 2. Drug overdose deaths* involving opioids,^{†,§} by type of opioid[¶] — United States, 2000–2014

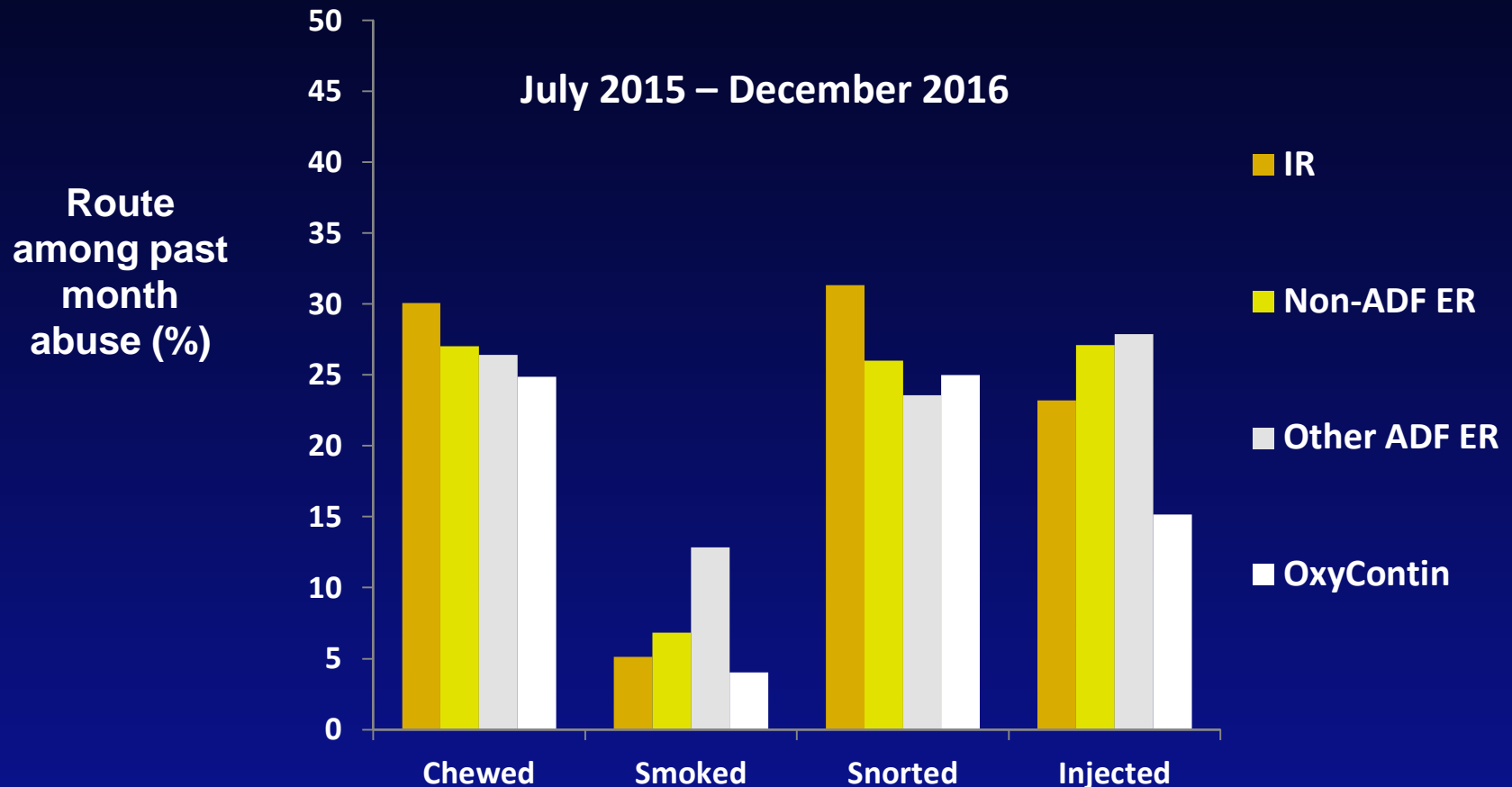


Progression of Rx Drug Abuse

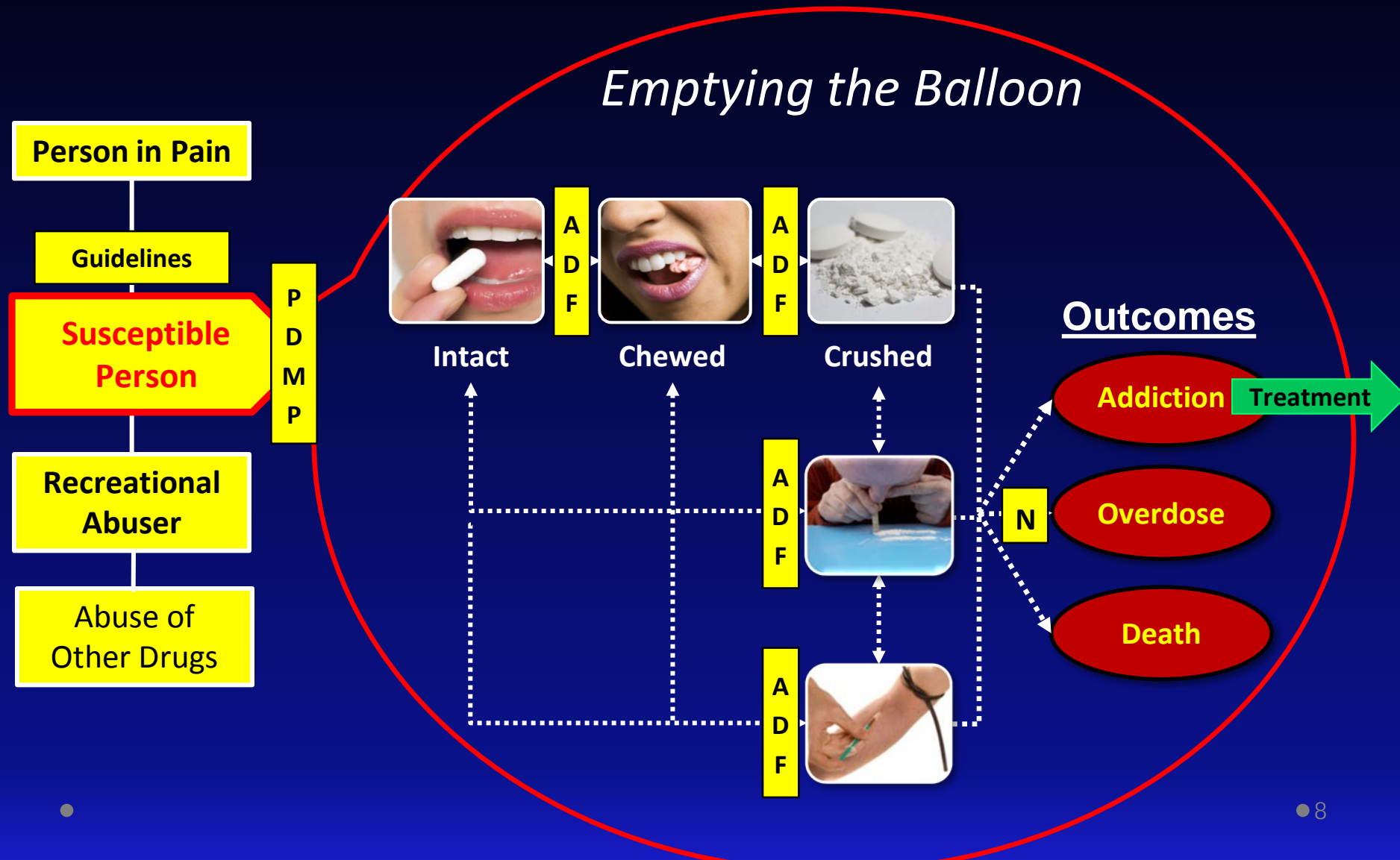


Who Cares About Chewing?

RADARS SKIP - Adults meeting DSM-IV criteria for substance abuse with a primary drug that is an opioid



Progression of Rx Drug Abuse



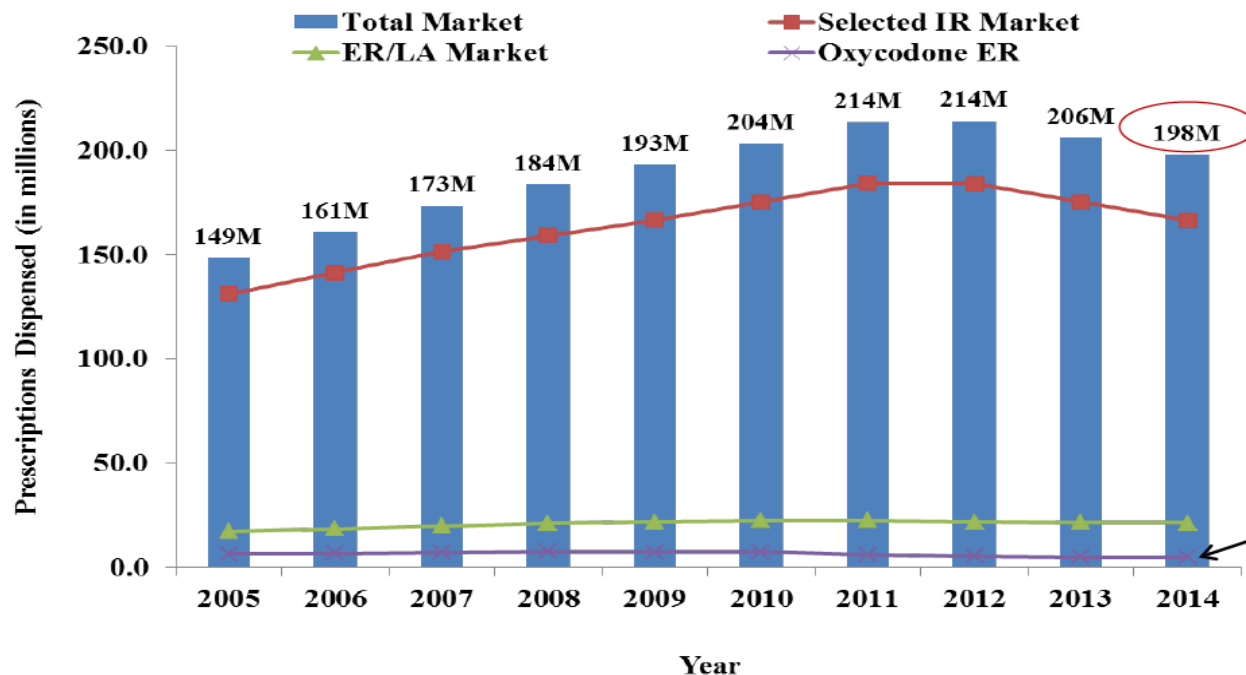
10 FDA-approved ADFs:

All physical/chemical or agonist/antagonist

Product	Drug Substance	Sponsor	Approval	Marketed
Oxycontin	oxycodone	Purdue	4/4/2010	YES
Targiniq ER	oxycodone + naloxone	Purdue	7/23/2014	NO
Embeda	morphine + naltrexone	Pfizer	10/17/2014	YES
Hysingla ER	hydrocodone	Purdue	11/20/2014	YES
Morphabond	morphine	Inspirion	10/2/2015	NO
Xtampza ER	oxycodone	Collegium	11/6/2015	YES
Troxyca ER	oxycodone + naltrexone	Pfizer	8/22/2016	NO
Arymo ER	morphine	Egalet	1/9/2017	Limited
Vantrela ER	hydrocodone	Teva	1/18/2017	NO
RoxyBond	oxycodone	Inspirion	4/26/2017	NO

Most Opioids Available in US are IR

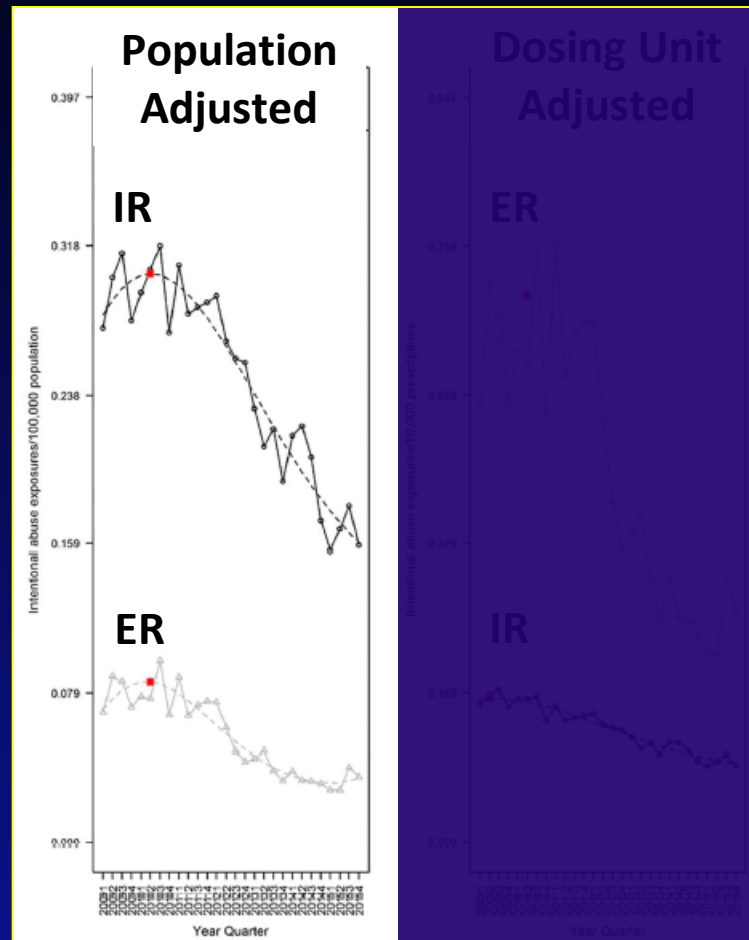
IR and ER/LA Opioid



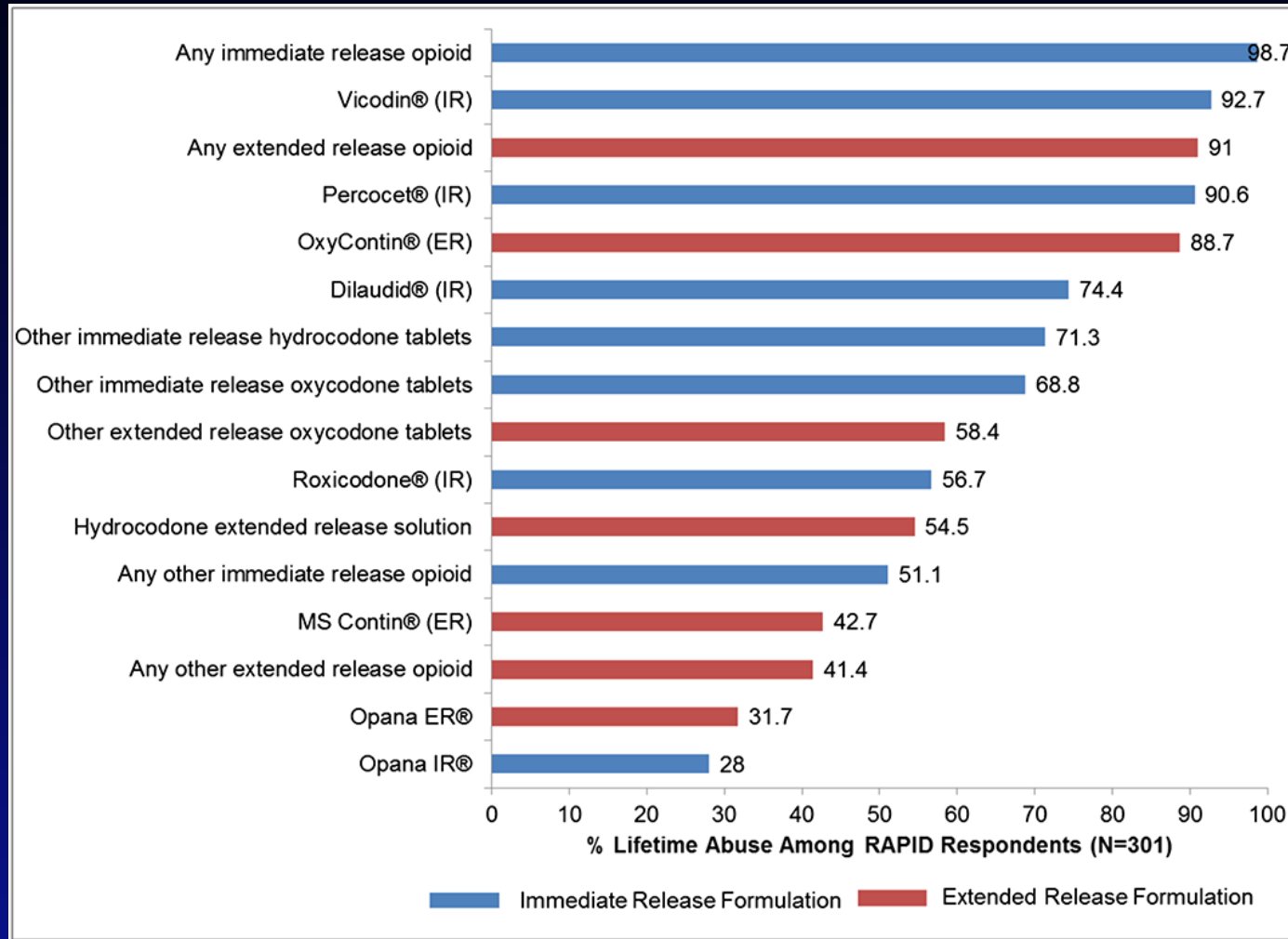
Nationally estimated number of prescriptions dispensed for selected IR and ER/LA opioid analgesics from U.S. outpatient retail pharmacies

Source: IMS Health, National Prescription Audit™ Extracted May and August 2015

IR Opioids Abused Preferentially



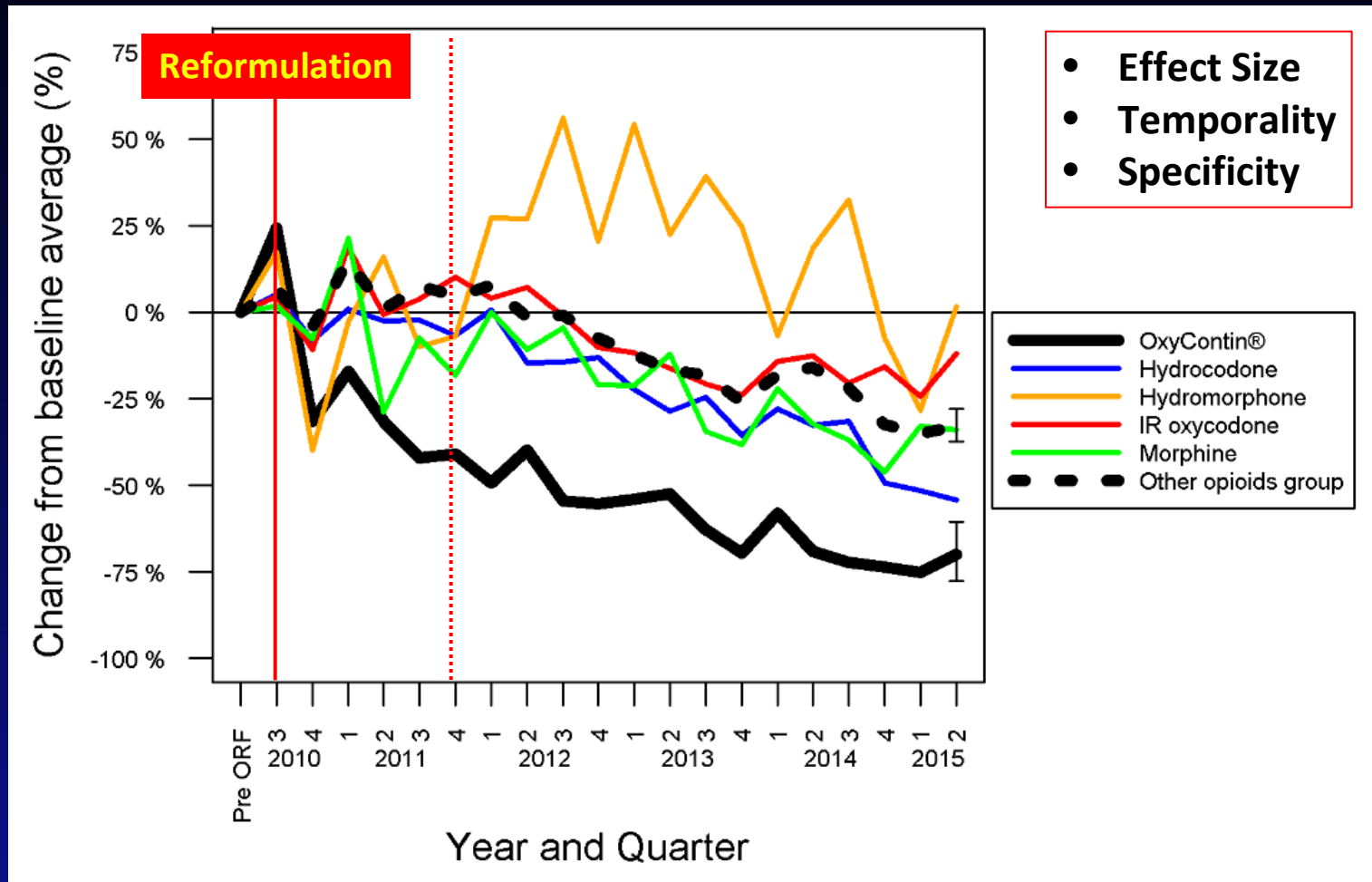
Preferences in abuse of IR vs ER opioids in treatment-seeking opioid abusers



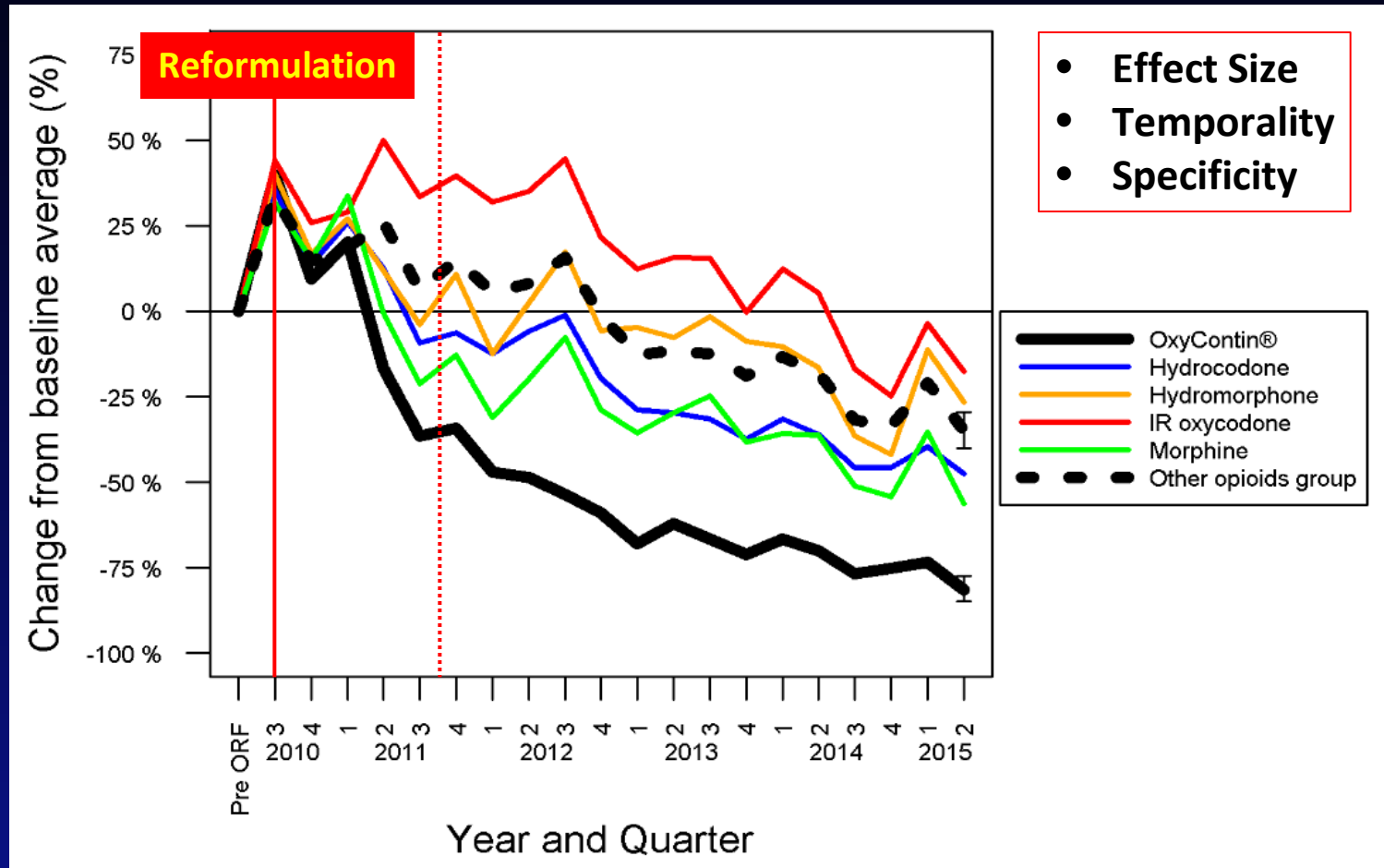
Systematic Review of Abuse Deterrent (Tamper Resistant) Formulations

- Question: What is the evidence that opioid analgesics with abuse deterrent labeling improve outcomes (abuse, misuse, overdose, death)?
- 44 reports on opioids with abuse deterrent labeling
 - Hydrocodone (n=7)
 - Morphine (n=5)
 - Oxycodone (n=32)*
- Hill Criteria
- Also assessed confounding factors and bias

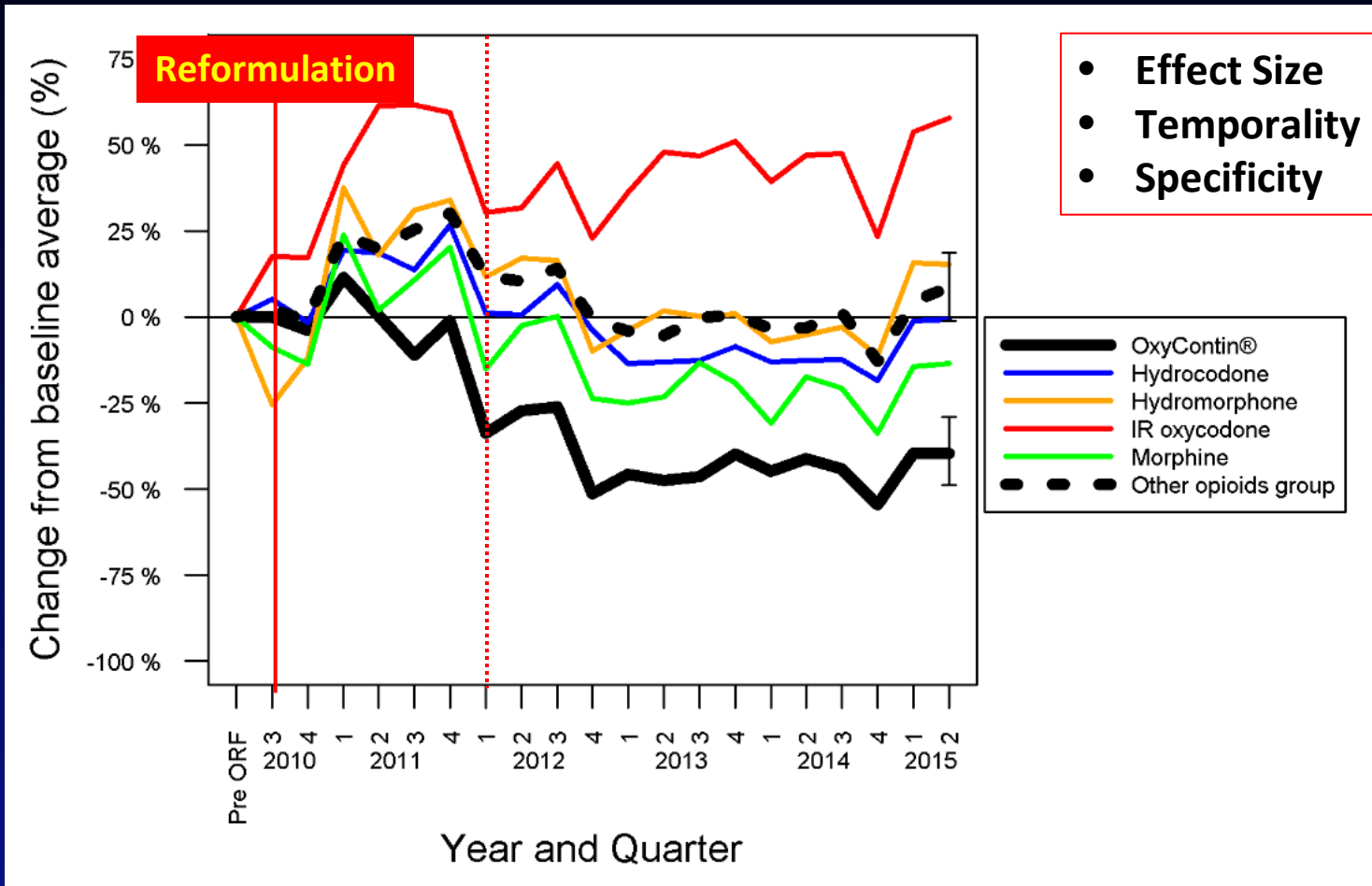
Cases Involving Intentional Abuse, Poison Center Program



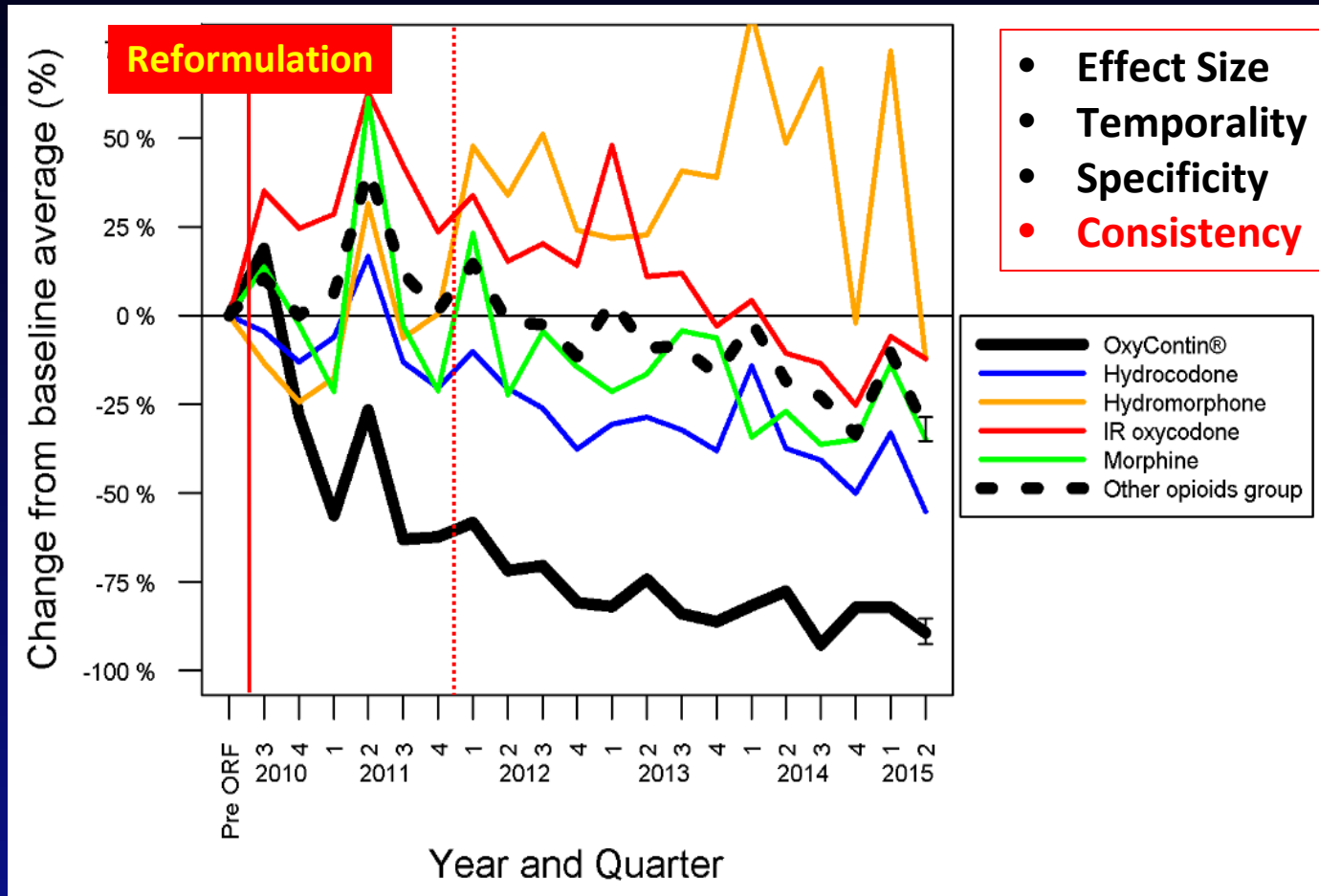
Investigations Opened, Drug Diversion Program



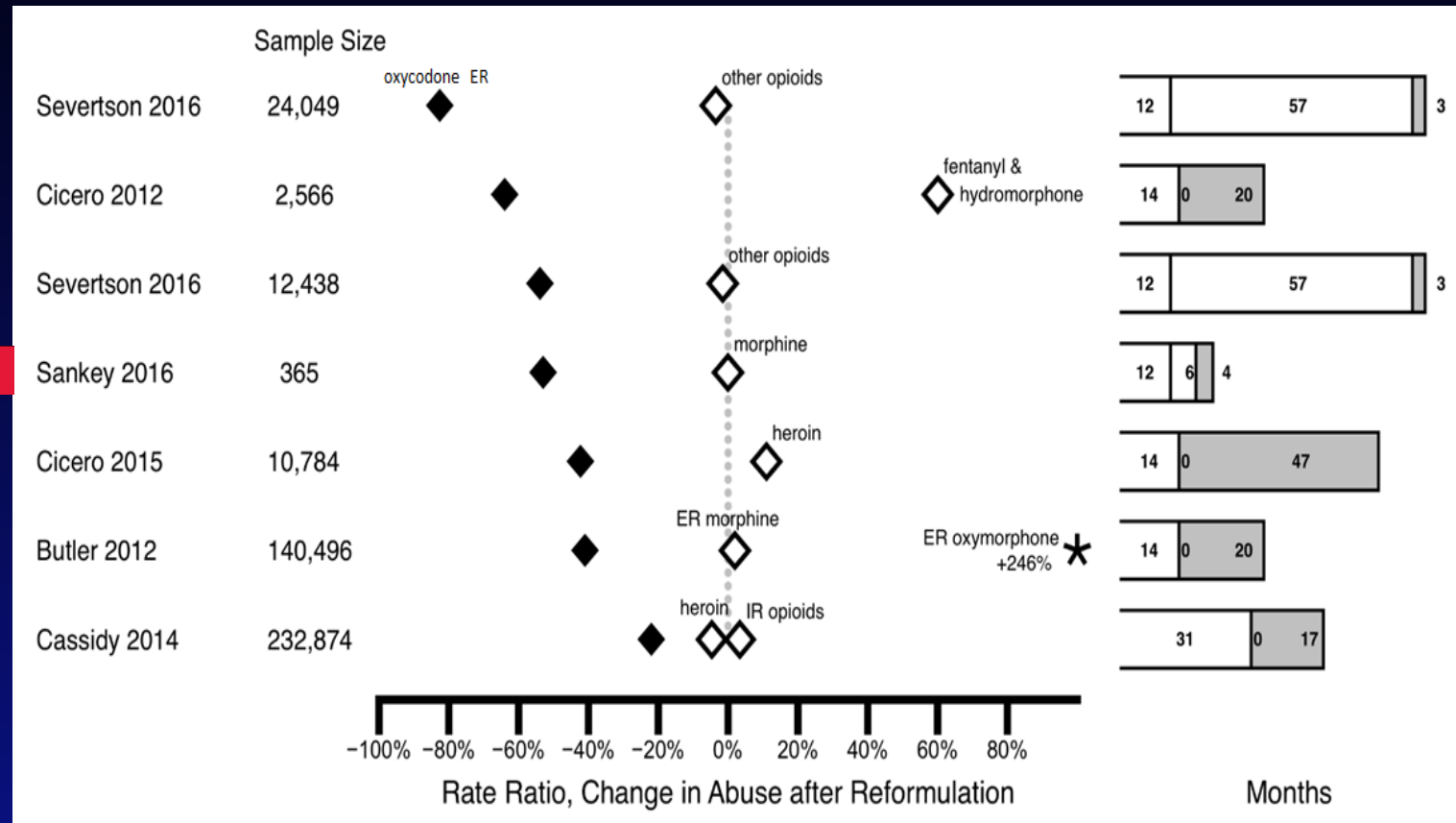
Drugs Used in Past 30 Days, Opioid Treatment Program



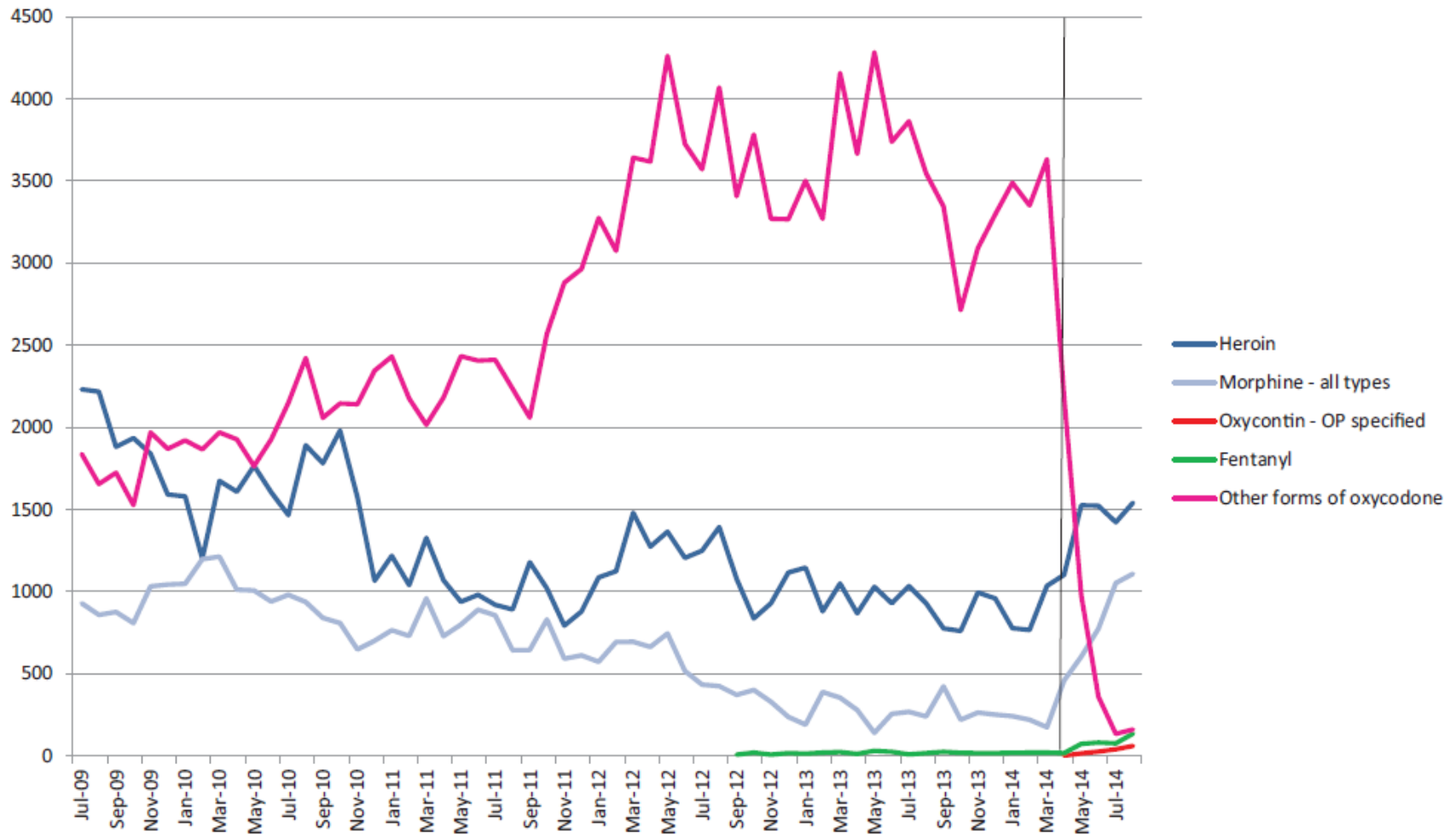
Drugs Used in Past 30 Days, Survey of Key Informant Patients



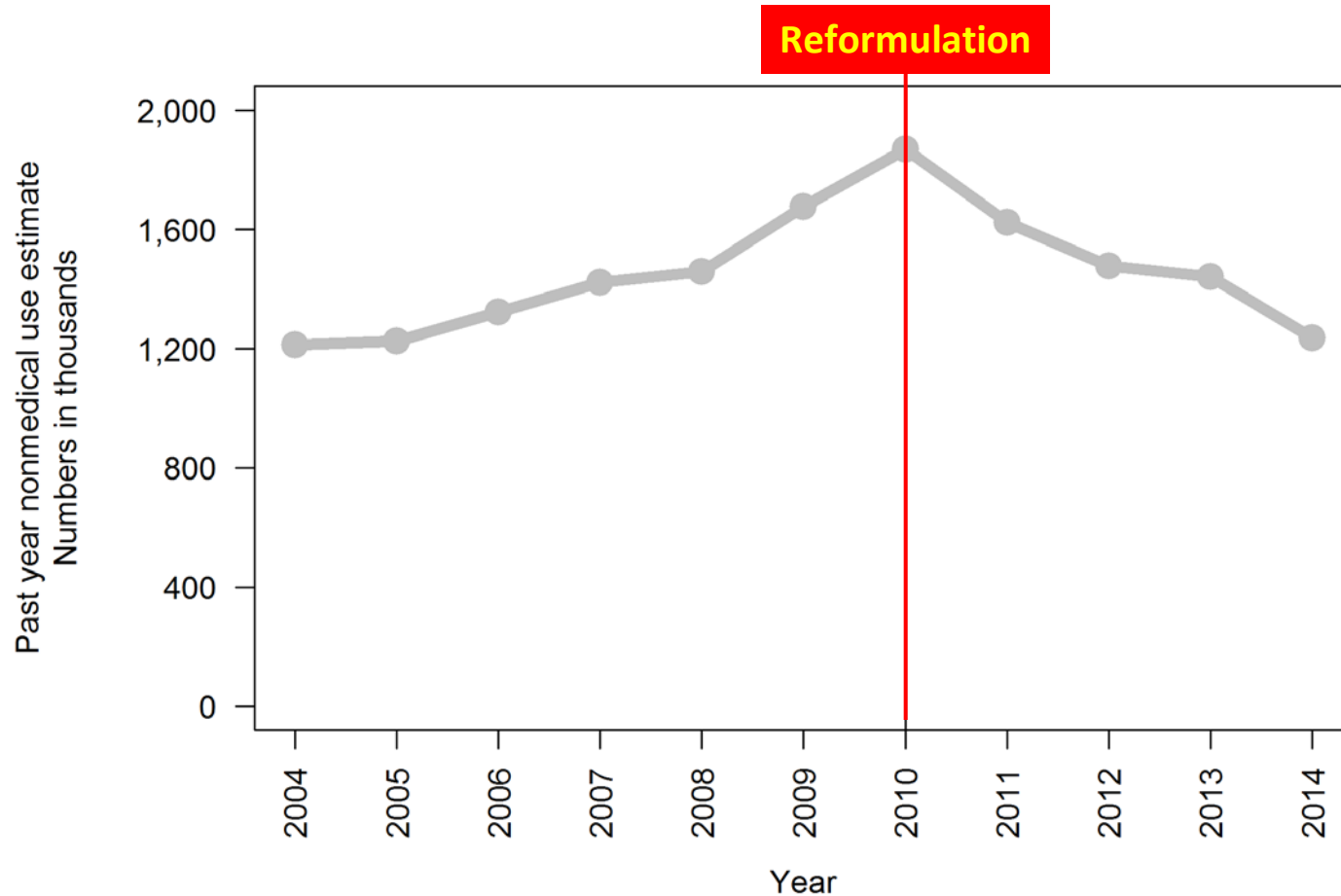
Reported Change in Treatment Measures of Abuse After Reformulation of Oxycodone ER



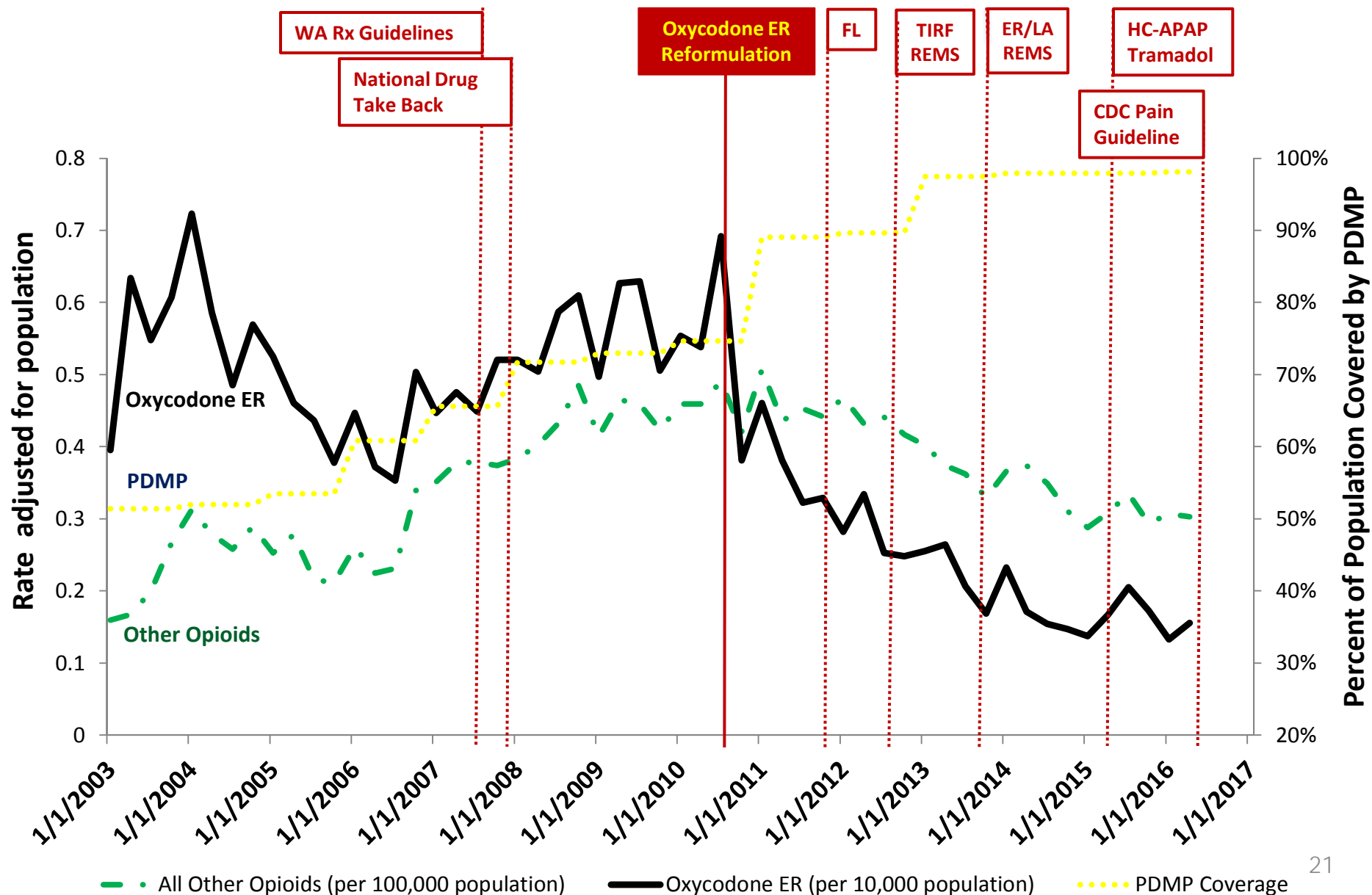
Client visits per month, Sydney Medically Supervised Injecting Centre



Nonmedical Use of OxyContin®, National Survey of Drug Use and Health, 2006 – 2014



Timeline of Interventions vs. Oxycodone ER



Institute for Clinical and Economic Review (ICER)

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Overall Approach

- Compared a hypothetical cohort of 100,000 adult non-cancer chronic pain patients who were newly prescribed either:
 - a) extended-release (ER) ADF opioids, or
 - b) ER non-ADF opioids
- Time horizon: 5 years (with 1 year cycle length)
- Perspective: third-party payer covering commercially-insured population

Results: Cost Neutrality Threshold Analysis

- In 2nd threshold analysis, varied ADF opioid drug cost to achieve cost-neutrality
 - Kept base case incidence of abuse in each opioid cohort constant
- Average daily ADF opioid costs would need to be reduced from \$11.60 to \$7.04 at 90mg MED per day to achieve cost neutrality
 - 39% discount from current pricing

	Base-case cost	Cost to attain cost-neutrality	Percentage difference
ADF opioid average daily drug cost*	\$11.60	\$7.04	-39.3%

Scenario Analysis: Diversion

- Using estimate of 1.25 cases of diverted abuse for every case of prescription opioid abuse, ADF cohort has additional spending of ~\$521 million over 5 years.
- To achieve cost-neutrality, diversion in the ADF cohort would need to decrease by approximately 57% relative to the non-ADF cohort.
- Reducing the rate of diversion to 1:1 and 0.75:1 ratios required greater reductions in diversion risk to achieve cost neutrality.

Summary

- Our results suggest ADF opioids substantially reduce incidence of opioid abuse relative to non-ADF formulations among patients initially prescribed these drugs for therapeutic purposes, but with increased costs to the health system.
- Further research is required to ascertain how the balance of reduced diversion of prescribed opioids versus increased use of other legal and illicit opioids affects clinical and economic outcomes in these populations.

Societal cost savings from abuse deterrent formulations for prescription opioids in Canada

Conclusion

The expected reduction in the NMU rate for RxO that would result from mandating adoption of ADF across all opioids, would very likely produce significant net societal cost savings.

Results Skinner, 2017

- Total Canadian societal economic costs from non-medical use of prescription opioids - \$4.3 billion/year.
- The median ADF effectiveness reducing NMU rates by between 45.1% and 64%.
- 2012 to 2015 savings ranged from \$560 million to \$16.9 billion (\$140 million to \$4.2 billion per year).
- Median estimate about \$9.3 billion for the entire period (averaging \$2.3 billion per year).

http://www.canadianhealthpolicy.com/product_articles/societal-cost-savings-from-abuse-deterrent-formulations-for-prescription-opioids-in-canada.html#sthash.RVzHMLli.dpuf

Summary

- Reformulation of oxycodone ER was followed by improved outcomes specific to oxycodone ER
- The initial decrease contrasted with increases for most other opioids during the first 18 months, but was then followed by decreases for almost all opioids
- Similar results in 3 different countries with different baseline conditions, measurements and timeframes
- Multiple sources of bias and confounding are present
- We conclude that the evidence available doesn't indicate this affected the results.
- We need wider application of abuse deterrent preparations, particularly for immediate release products.

Questions?

