

Real World Data: Do ADFs Change Behavior?

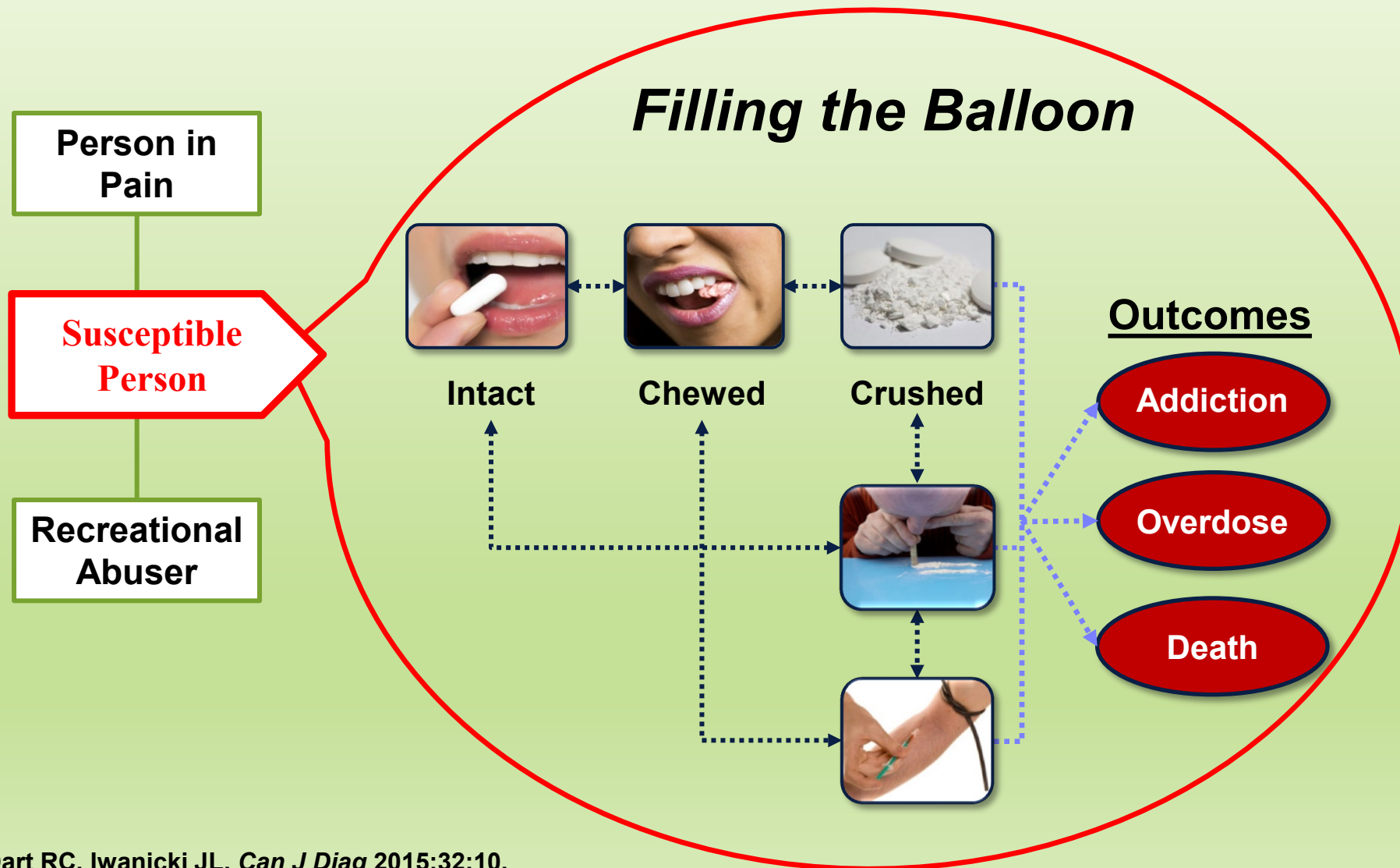
What Current Opioid Data Imply for Stimulants in the Future

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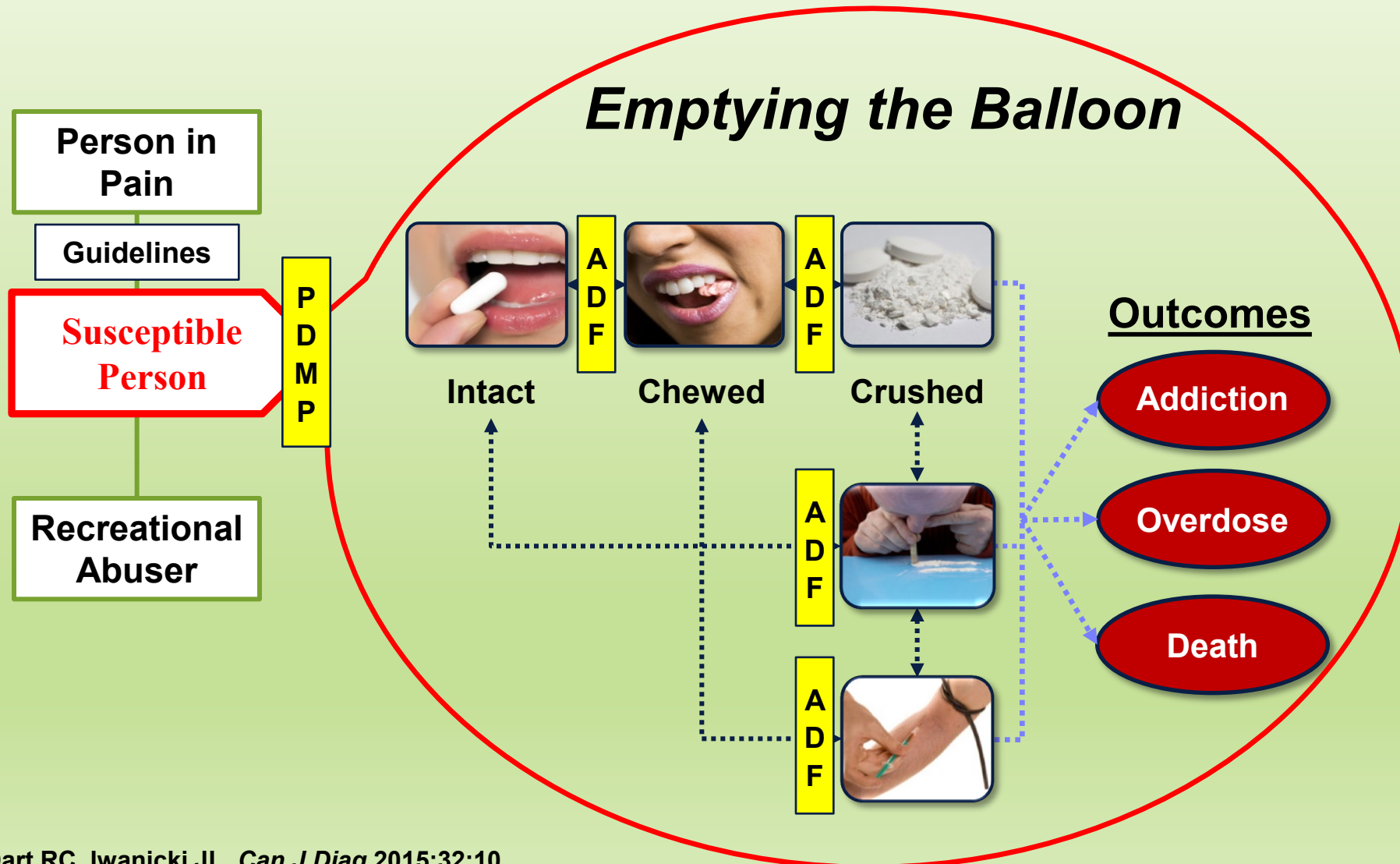
Roadmap

- Real-world data on ADF effectiveness
- Opana ER and its complicated history
- Effects of policy on behavior and trends
- Current prescription stimulant real-world data
- Lessons learned

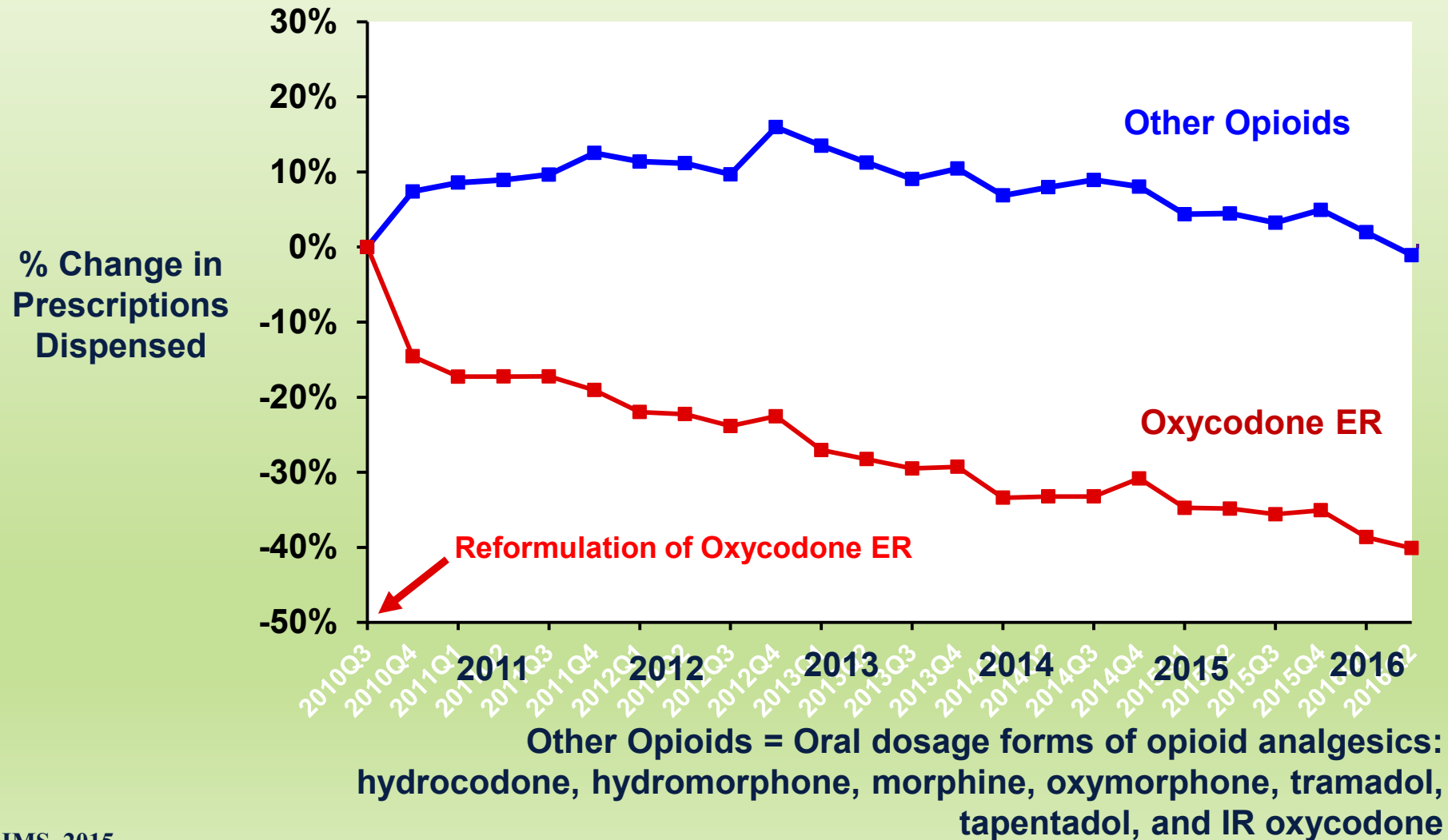
Biological Plausibility



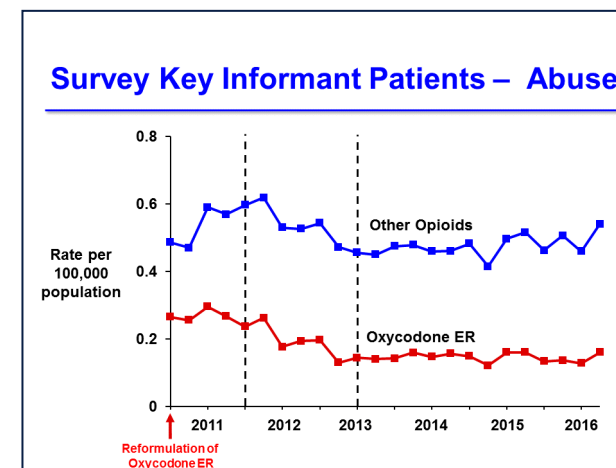
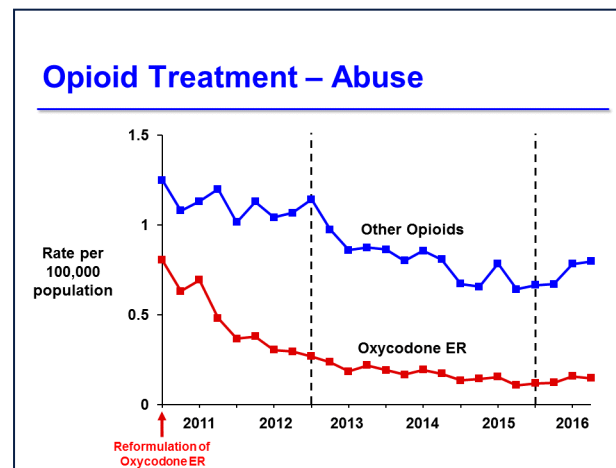
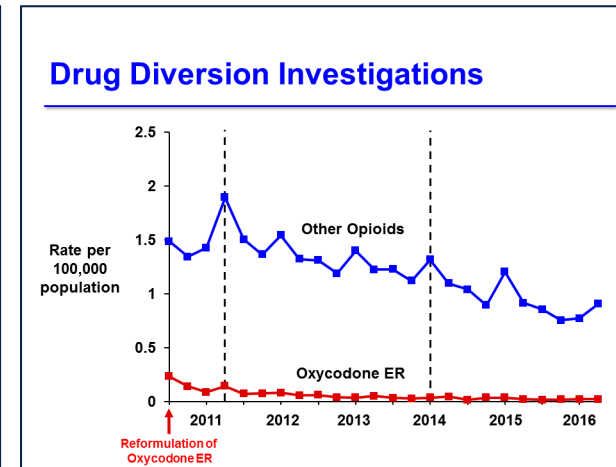
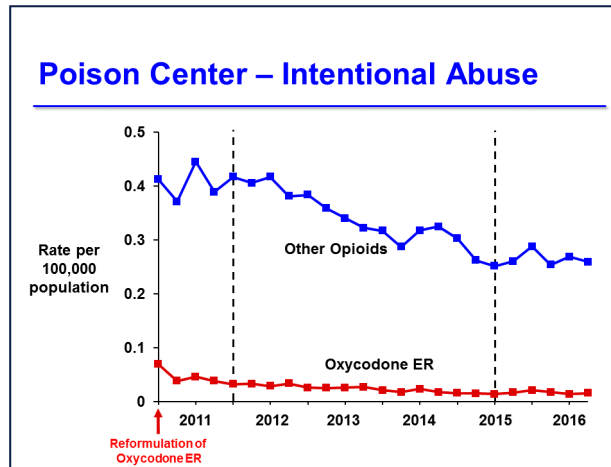
Intervening in Prescription Drug Abuse



Oxycodone ER Prescriptions Dispensed Decreased Promptly After Reformulation

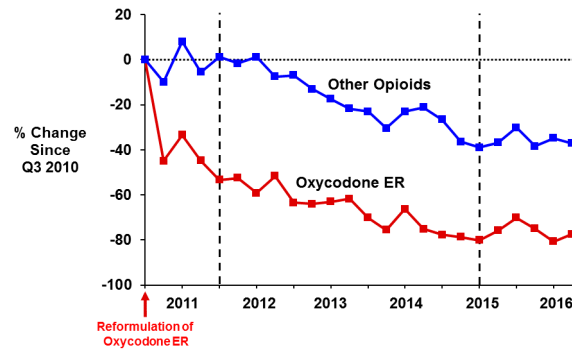


Temporality: 3 Phases of Oxycodone ER Abuse and Diversion, Adjusted for Population, 2010 – 2016Q2

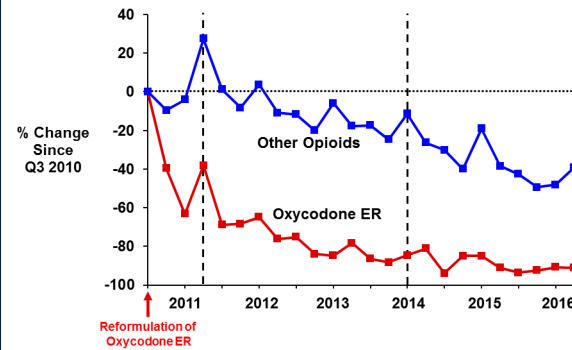


Effect Size: Oxycodone ER Abuse and Diversion, Adjusted for Population, 2010-2016

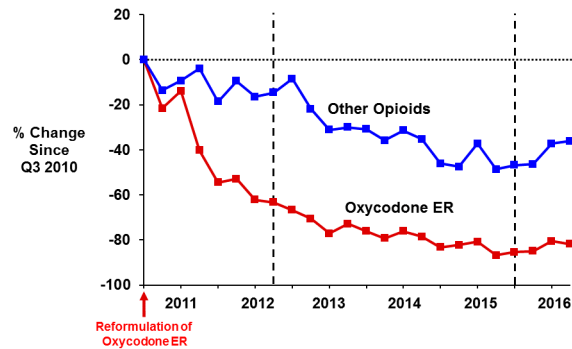
Poison Center – Intentional Abuse



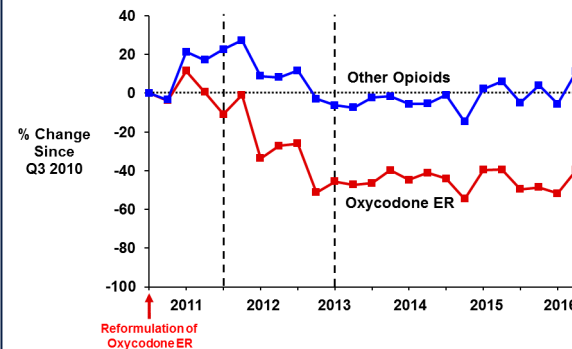
Drug Diversion Investigations



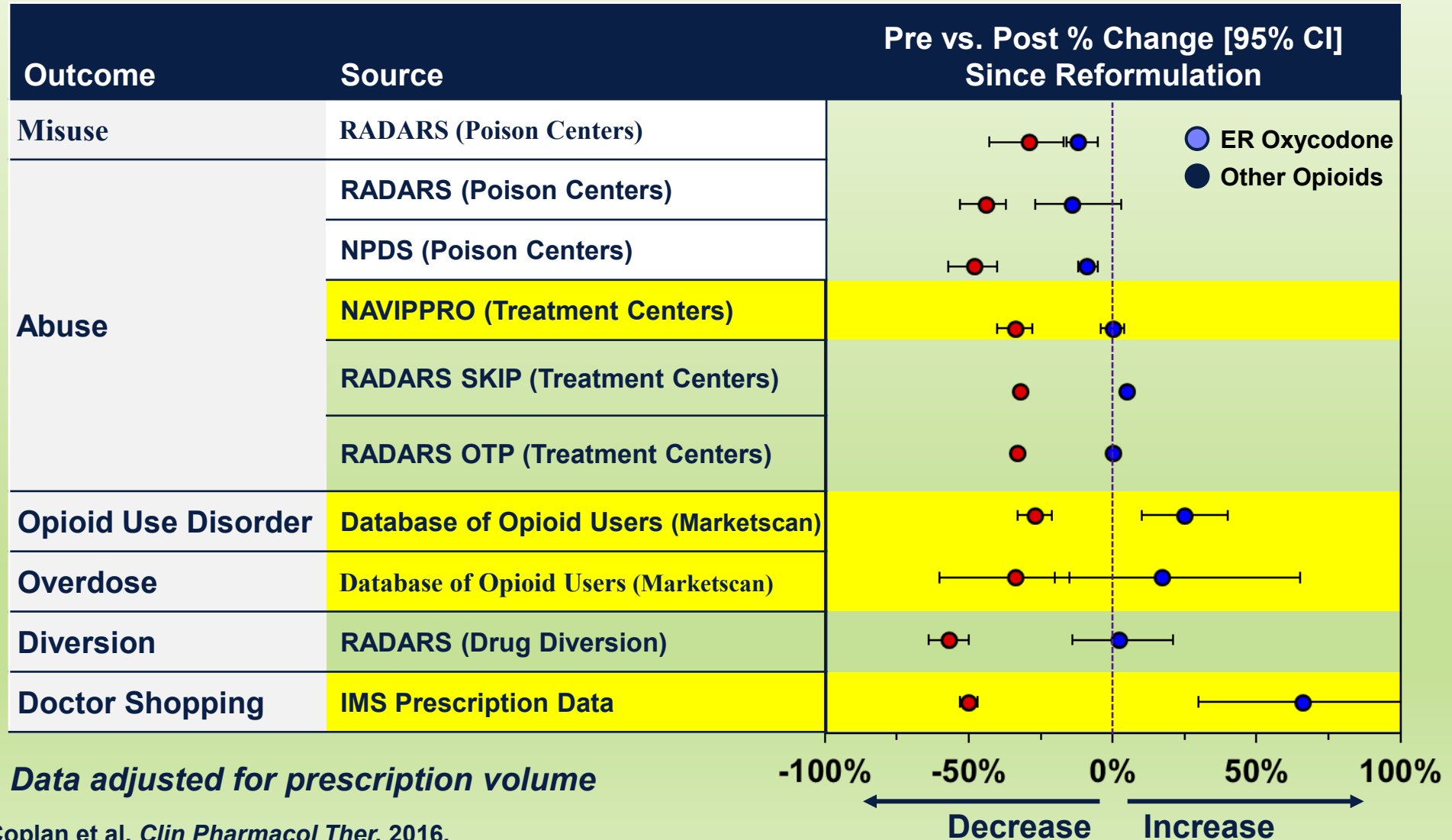
Opioid Treatment – Abuse



Survey Key Informant Patients – Abuse

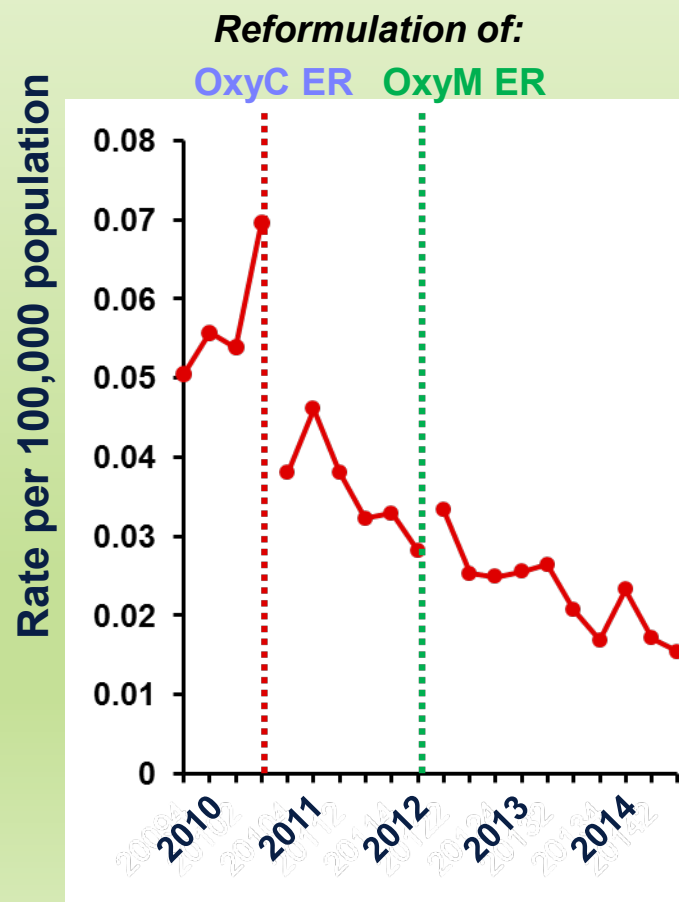


Consistency: Oxycodone ER Associated with Lower Rates Across Many Data Sources

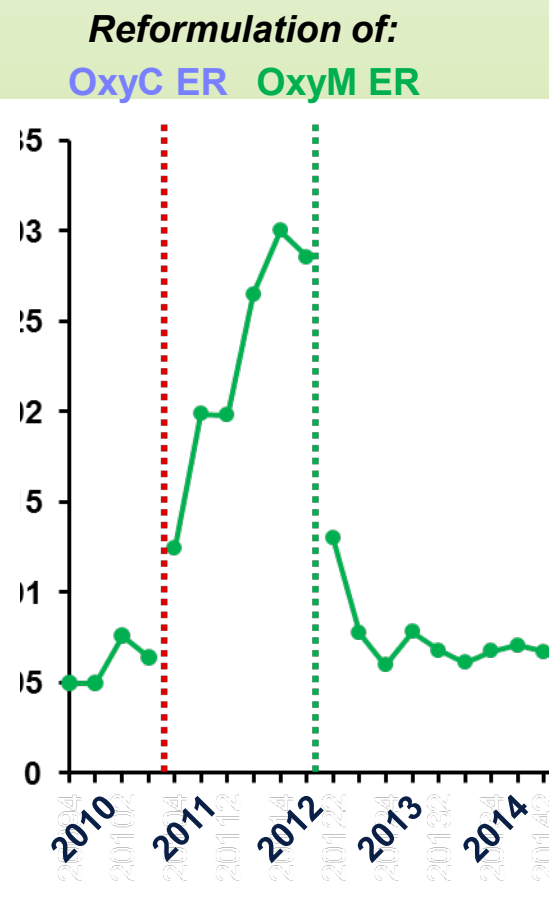


Poison Center Cases: Response to Reformulation of Oxycodone ER and Oxymorphone ER

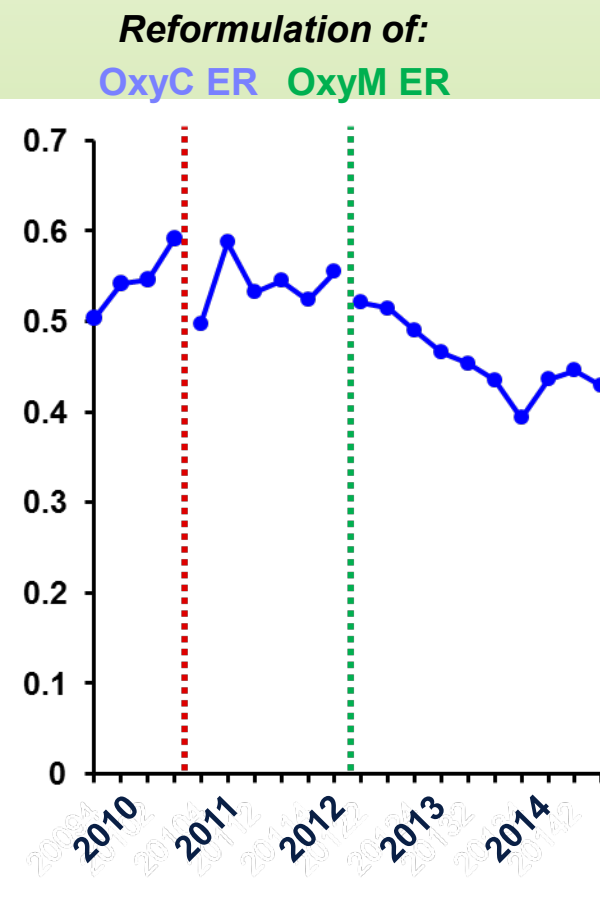
Oxycodone ER



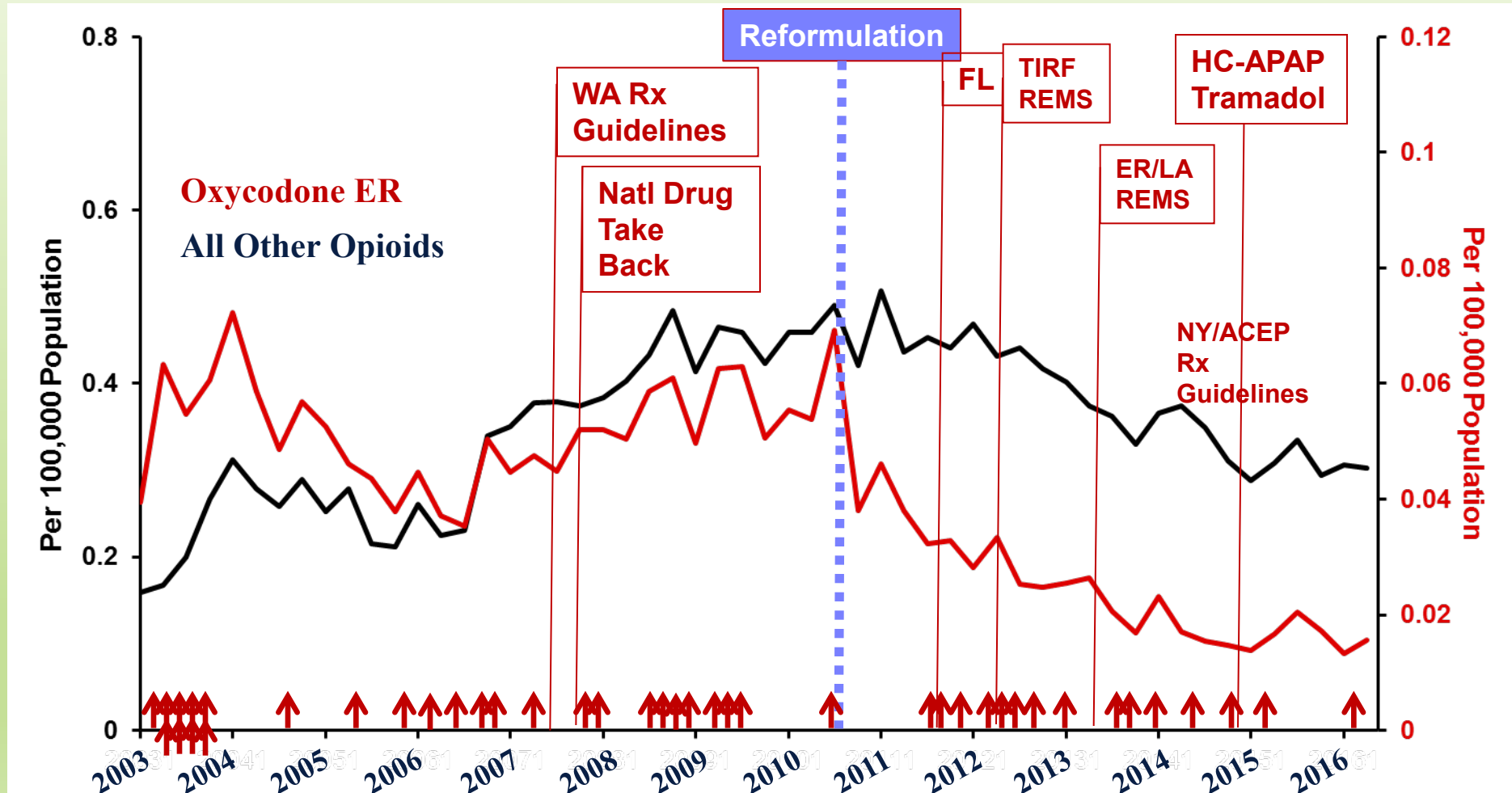
Oxymorphone ER



Other Opioids



Alternate Explanations Fail the Temporality and Specificity Criteria



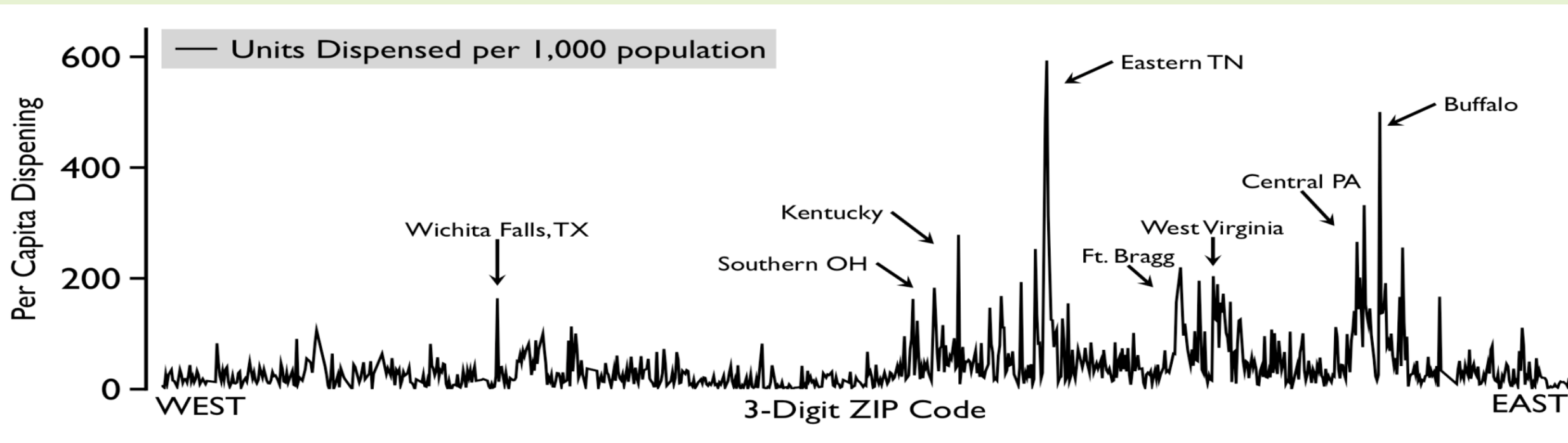
↑ PDMP Initiation

Opana ER

- Extended-release oxymorphone
- Oxymorphone developed in Germany 1914
- Patented 1955
- Opana ER formulation Initially approved in 2006
- Indications: moderate to severe pain requiring around-the-clock treatment
- Geographic distribution



Opana ER: Geographic distribution and heterogeneity



Time: 2009q3 – 2016q4

Source: IQVIA

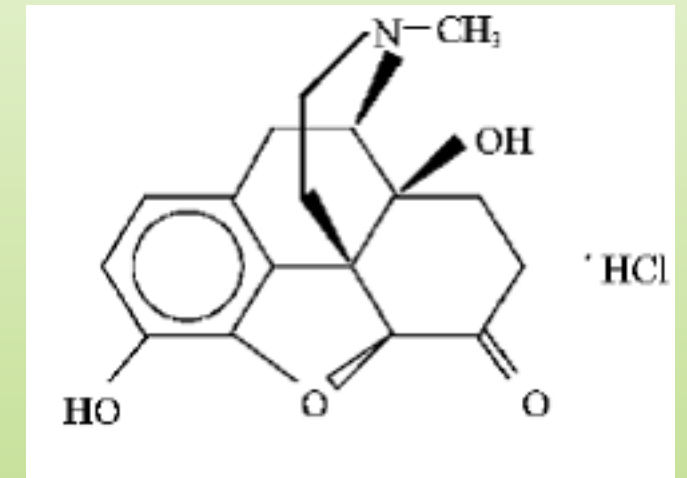
N: 360,432,541 units dispensed

Analysis unit: 3-digit ZIP

Metric: cumulative population-adjusted rate

Oxymorphone

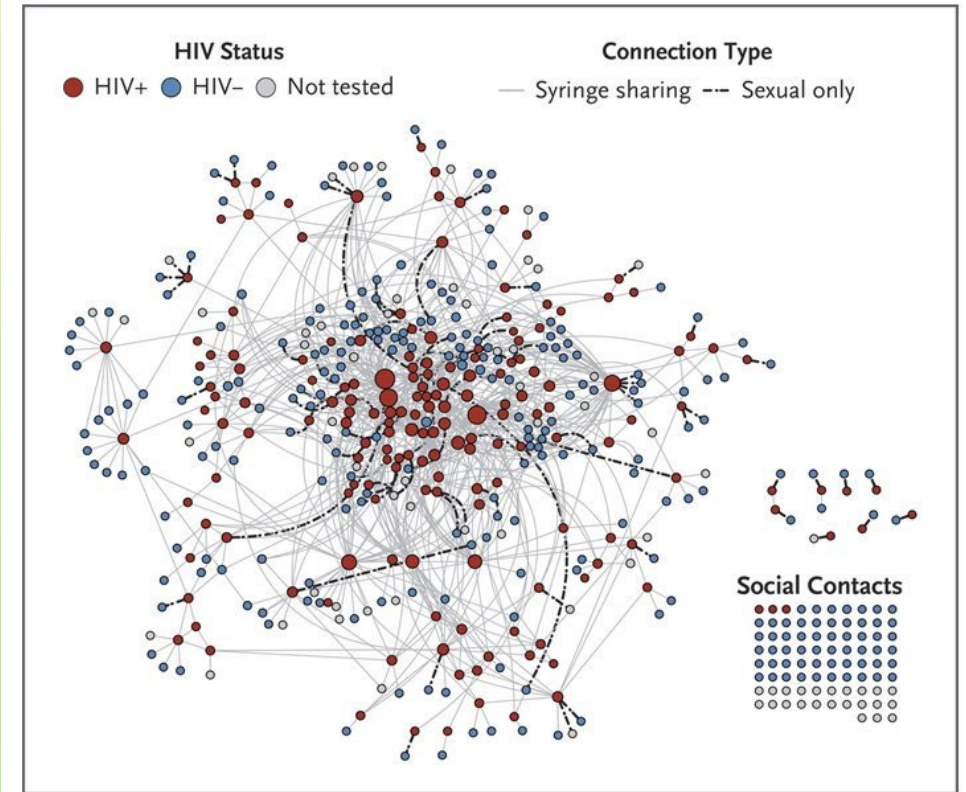
- Poor oral bioavailability
 - 10x more potent intravenously than orally
- Leads to unusual behaviors
 - Single 40mg pill = split into quarters
 - Each quarter = 2-4 users
 - Single pill leads to 8-16 doses intravenously
 - Each dose 50-75 MME



Oxymorphone

- Poor oral bioavailability
 - 10x more potent intravenously than orally
- Leads to unusual behaviors
 - Drug sharing
 - Unsafe injection practices
- Complications
 - HIV
 - Hepatitis C
 - TTP

Syringe-Sharing Network of Persons with Newly Diagnosed HIV Infection.



Opana ER: Interventions and Policy Changes

- 2011: Reformulation approved
 - Released in 2012
 - Tamper resistant, but did not achieve ADF labeling
- Concern for transition from intranasal to intravenous abuse
- Outbreaks associated with oxymorphone

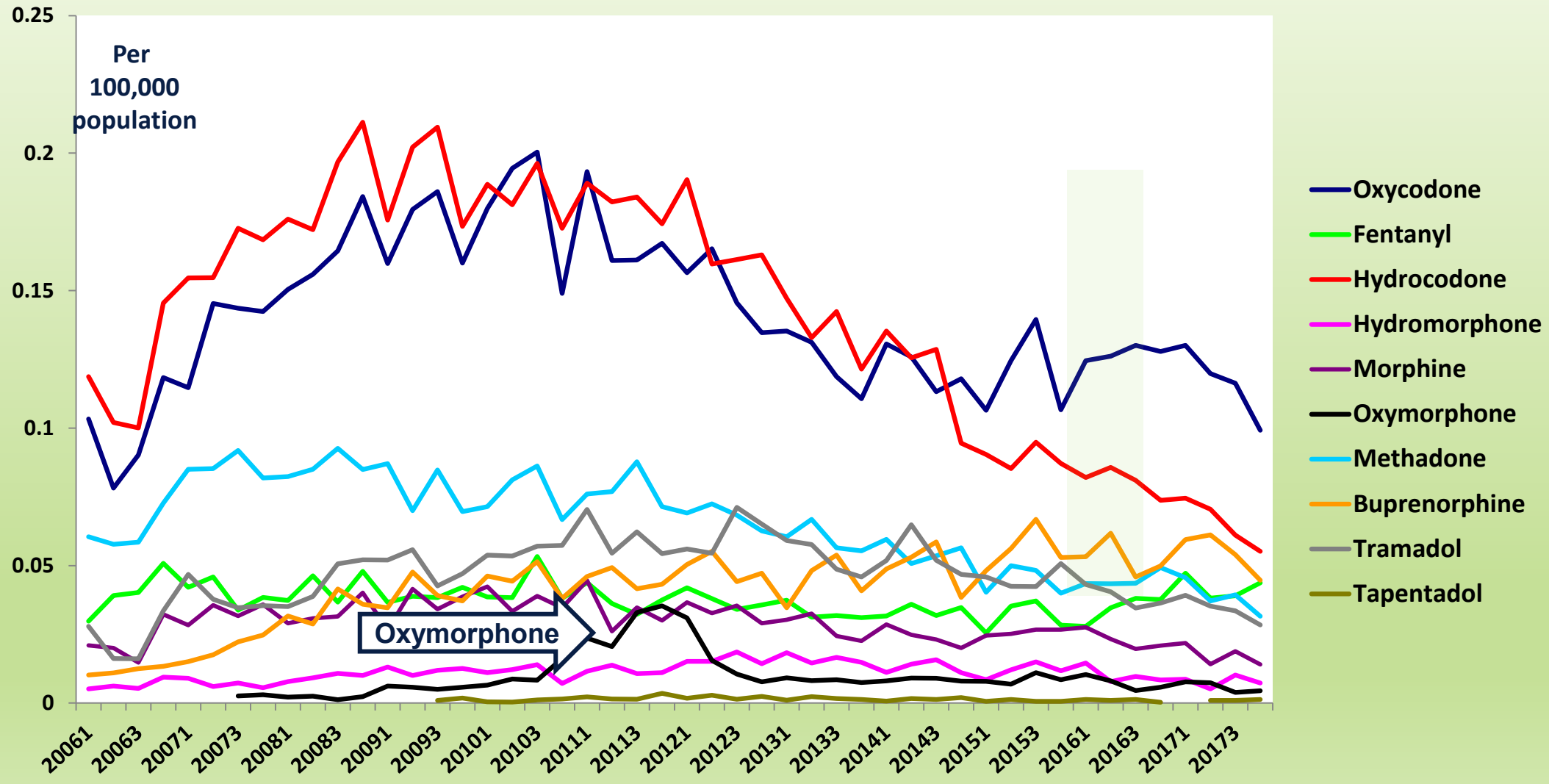


Opana ER: Interventions and Policy Changes

- March 2017:
 - FDA meeting
 - 18-8 vote, benefits no longer outweigh risks
- June 2017:
 - Recommended to be removed from market
- July 2017:
 - Opana ER removed
 - No change to generic forms or IR

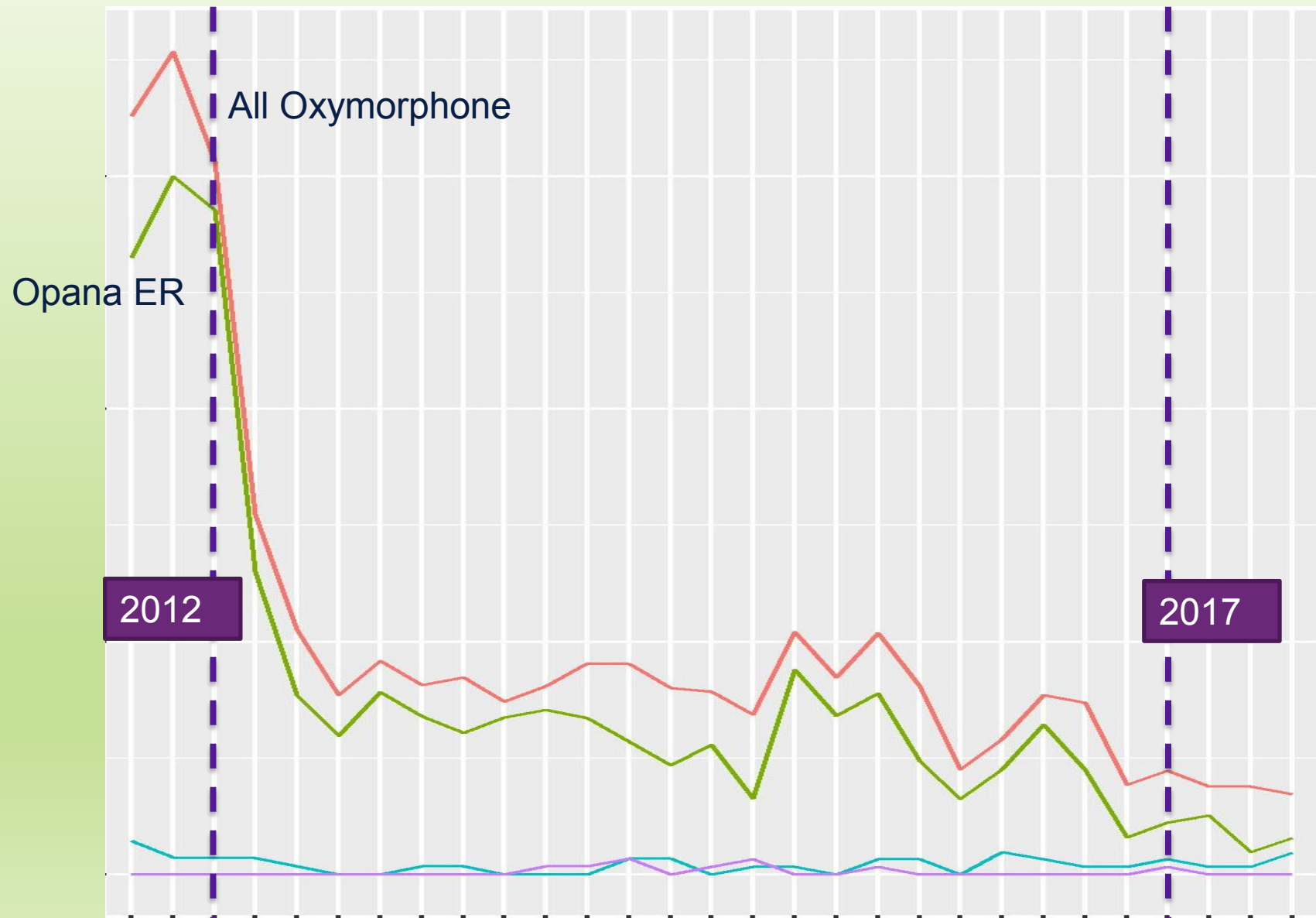


Oxymorphone: Big picture Poison Center Program



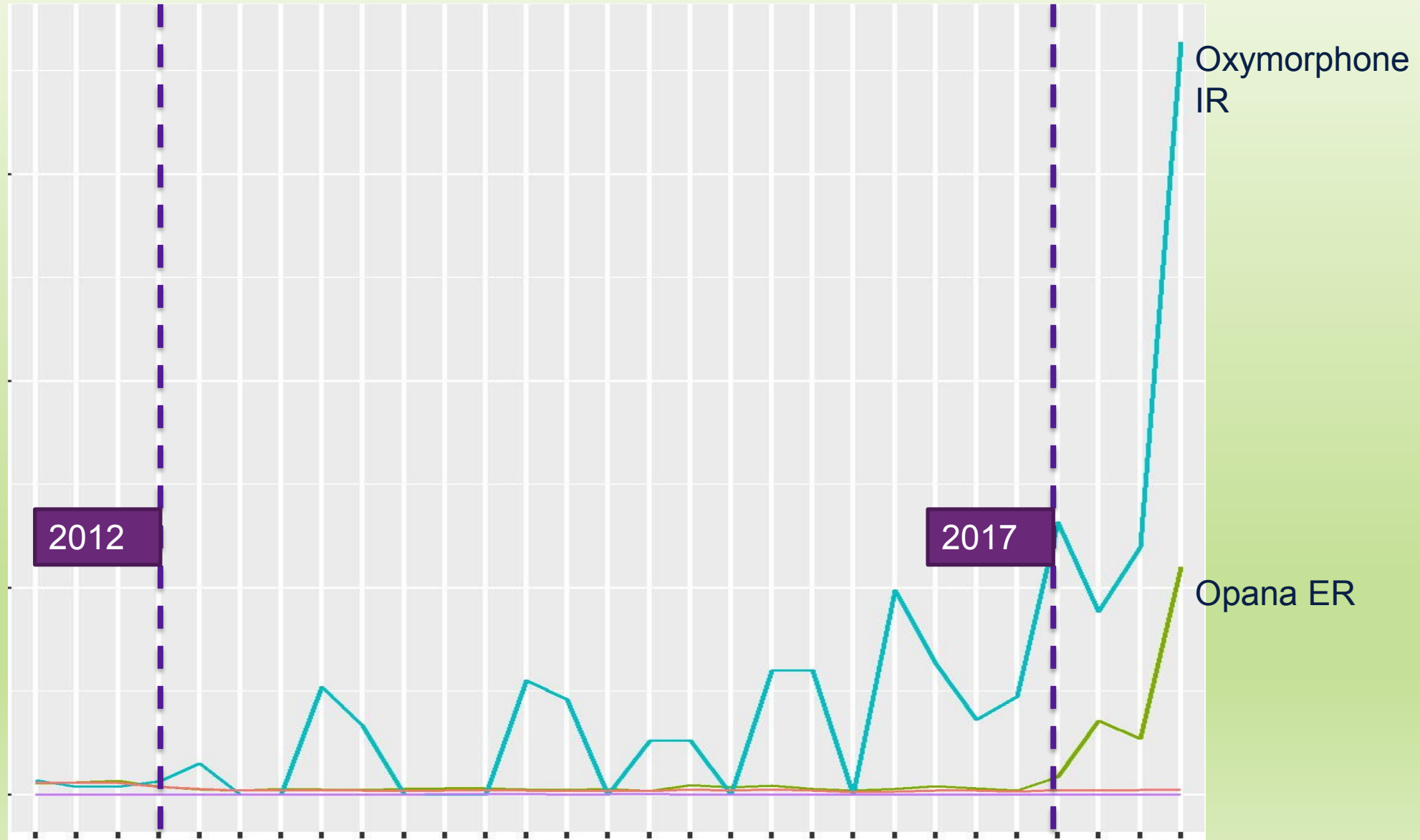
Opana ER: Effects of Policy on Behavior and Trends

Poison Center Program, rate per population



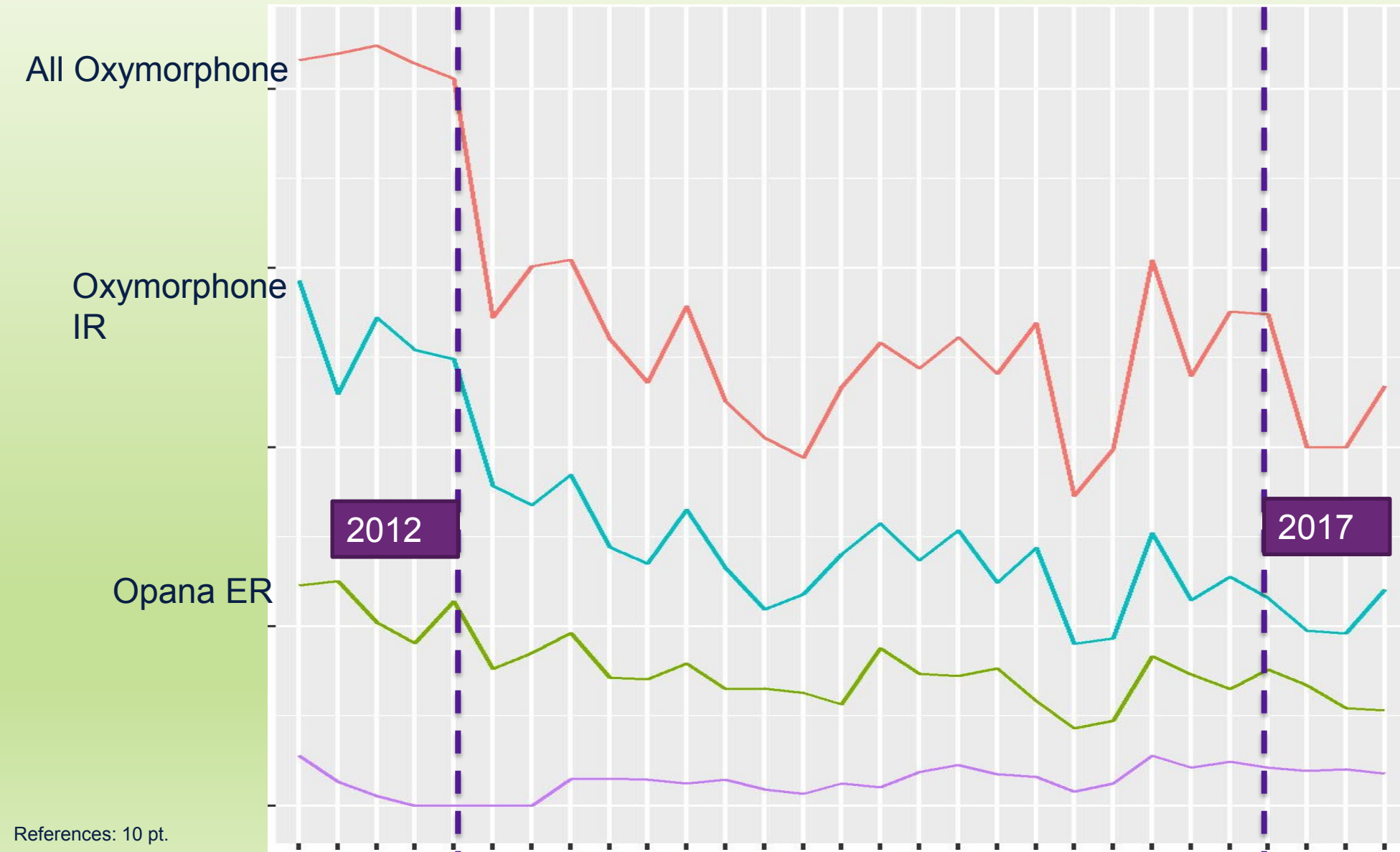
Opana ER: Effects of Policy on Behavior and Trends

Poison Center Program, rate per prescriptions



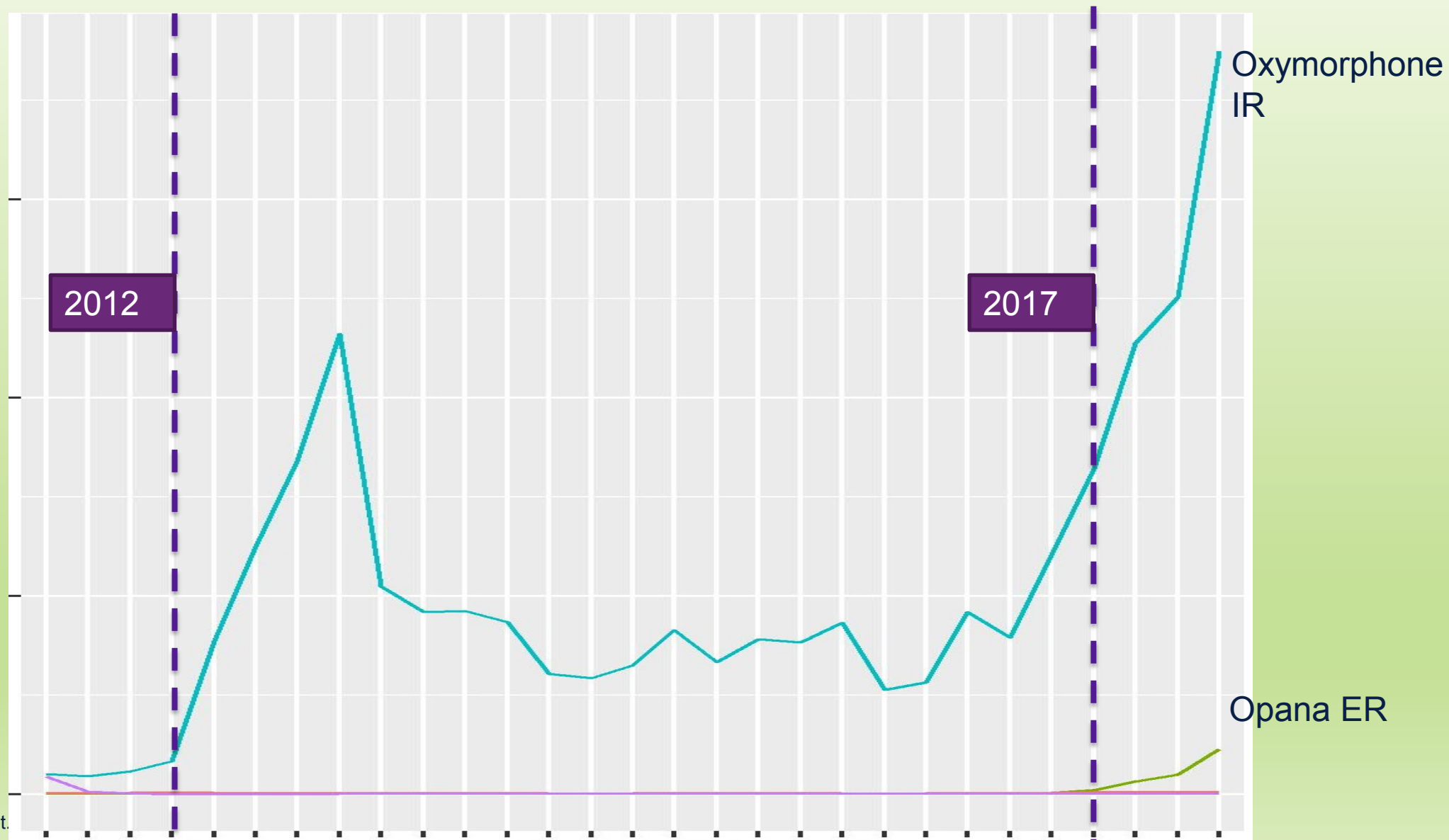
Opana ER: Effects of Policy on Behavior and Trends

Treatment Center Programs, rate per population



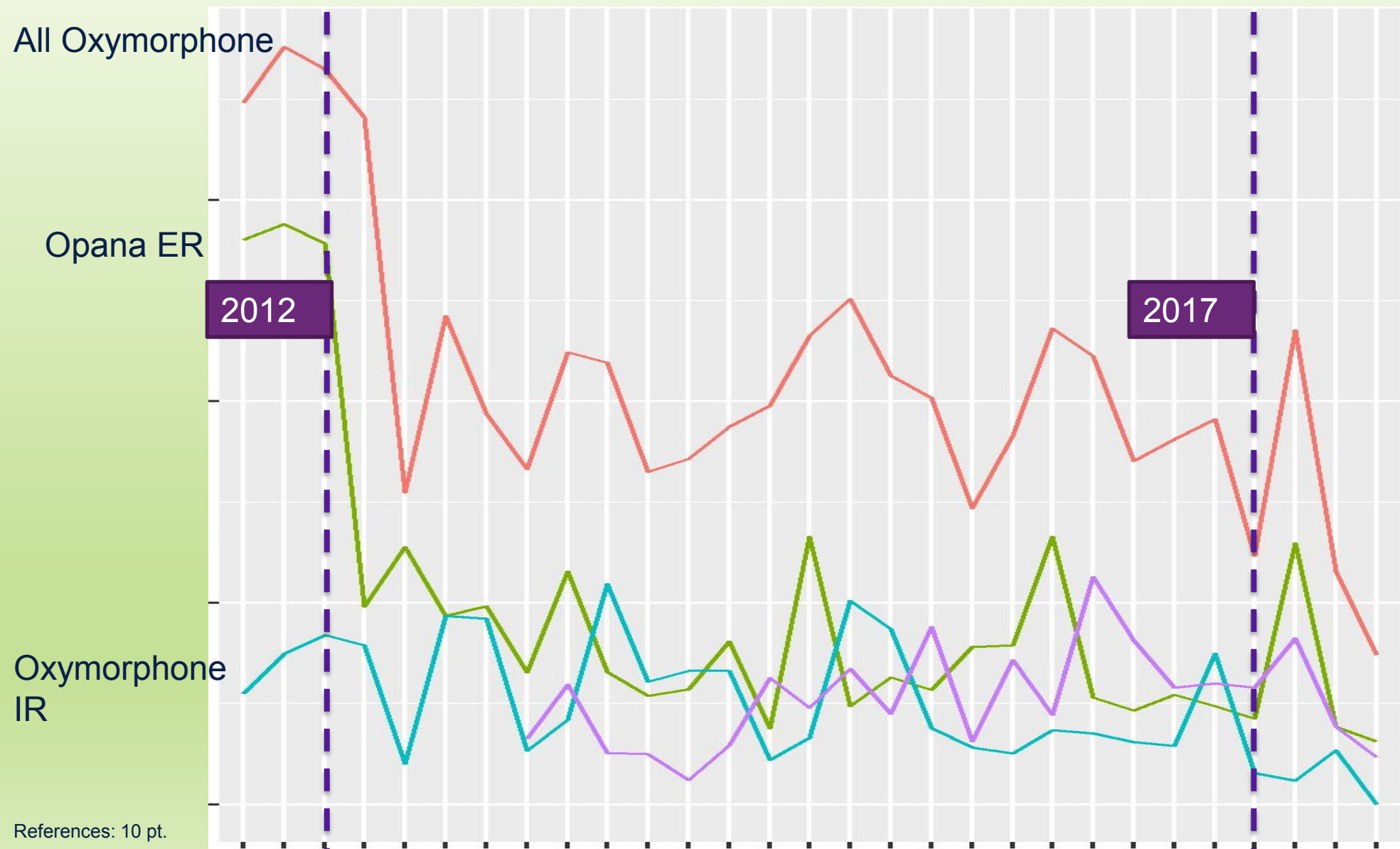
Opana ER: Effects of Policy on Behavior and Trends

Treatment Center Programs, rate per prescriptions



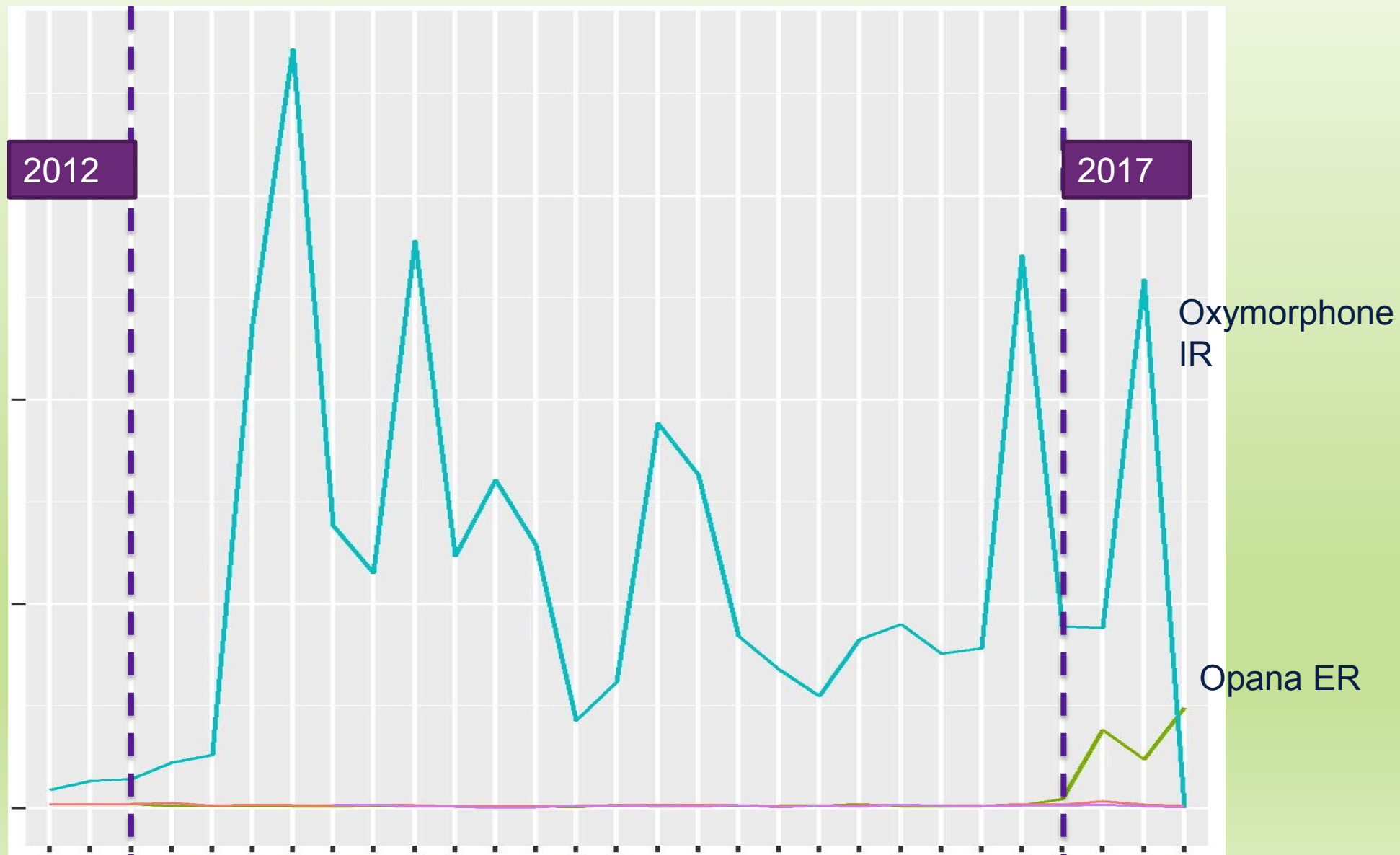
Opana ER: Effects of Policy on Behavior and Trends

Drug Diversion Program, rate per population



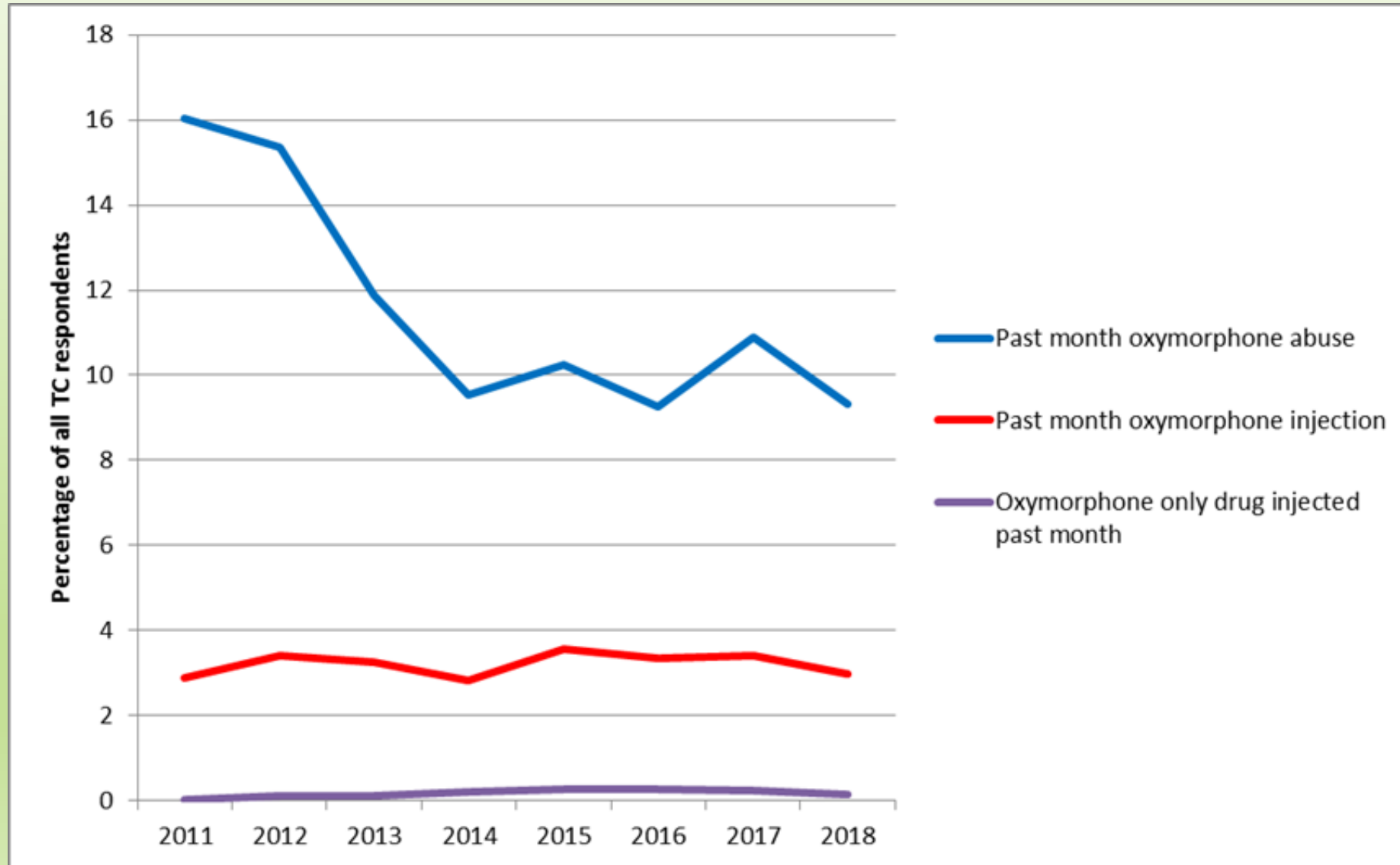
Opana ER: Effects of Policy on Behavior and Trends

Drug Diversion Program, rate per prescriptions



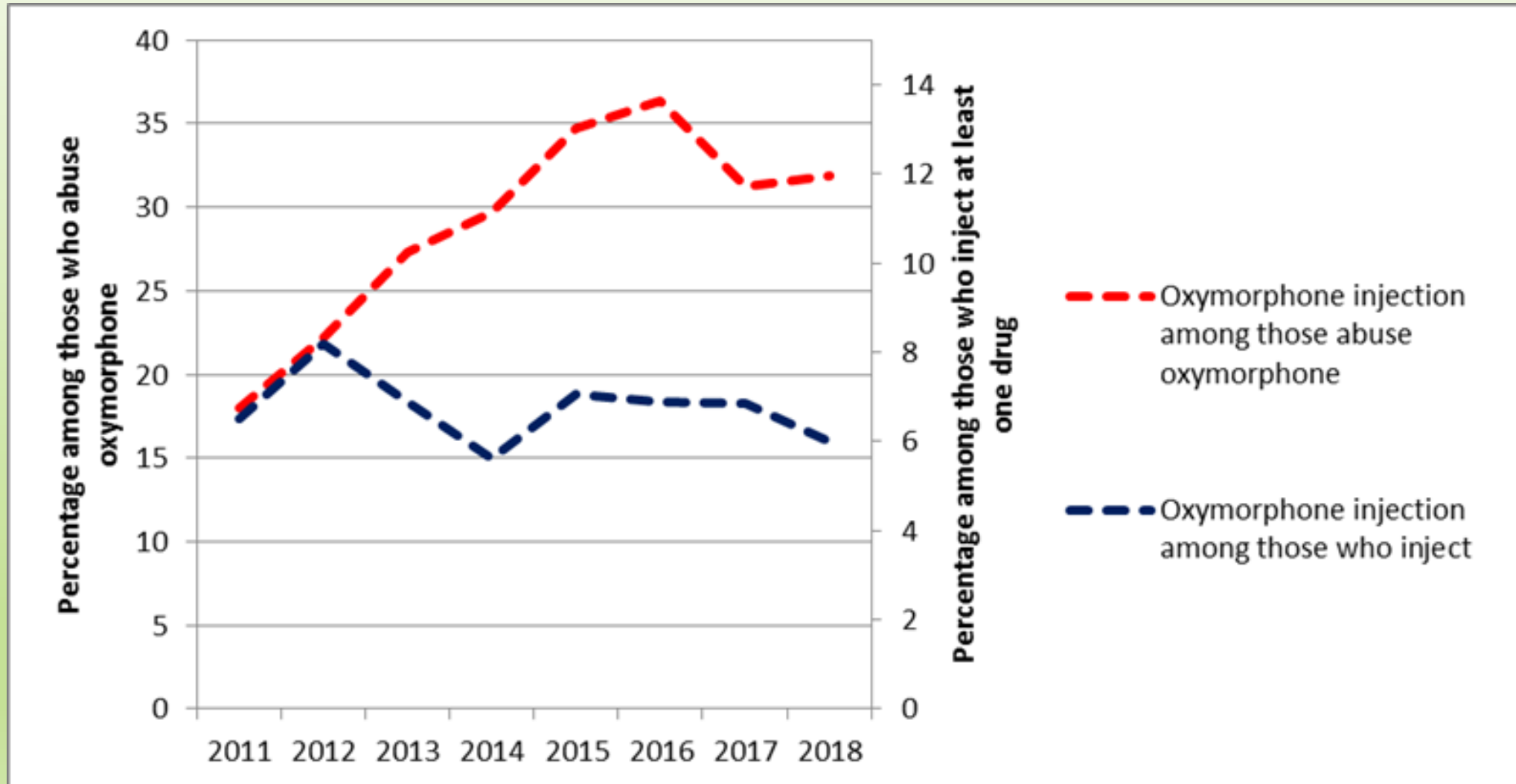
Opana ER: Effects of Policy on Behavior and Trends

Did injection behavior change?



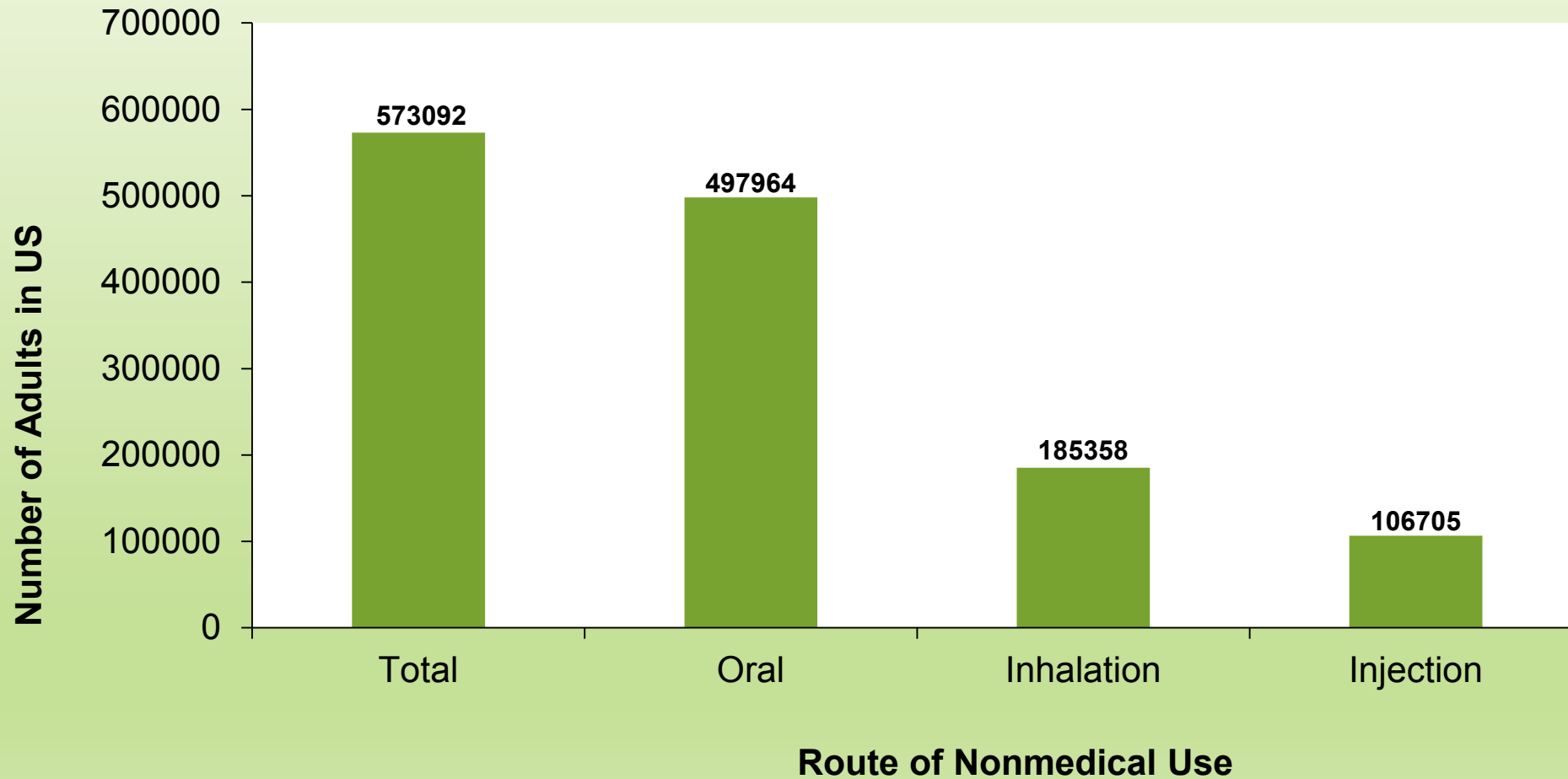
Opana ER: Effects of Policy on Behavior and Trends

Did injection behavior change?



Opana ER: Effects of Policy on Behavior and Trends

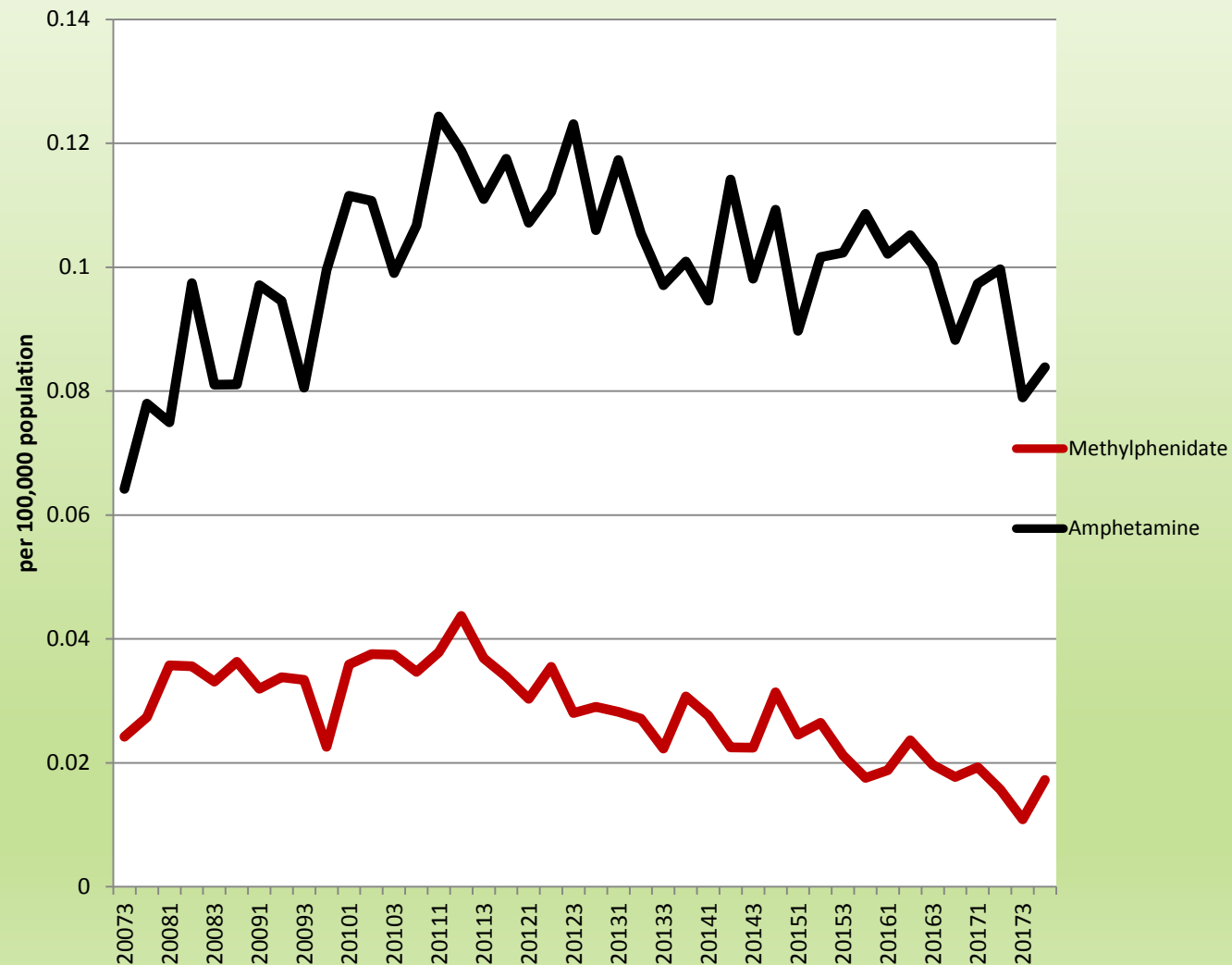
Did injection behavior change? NMURx data



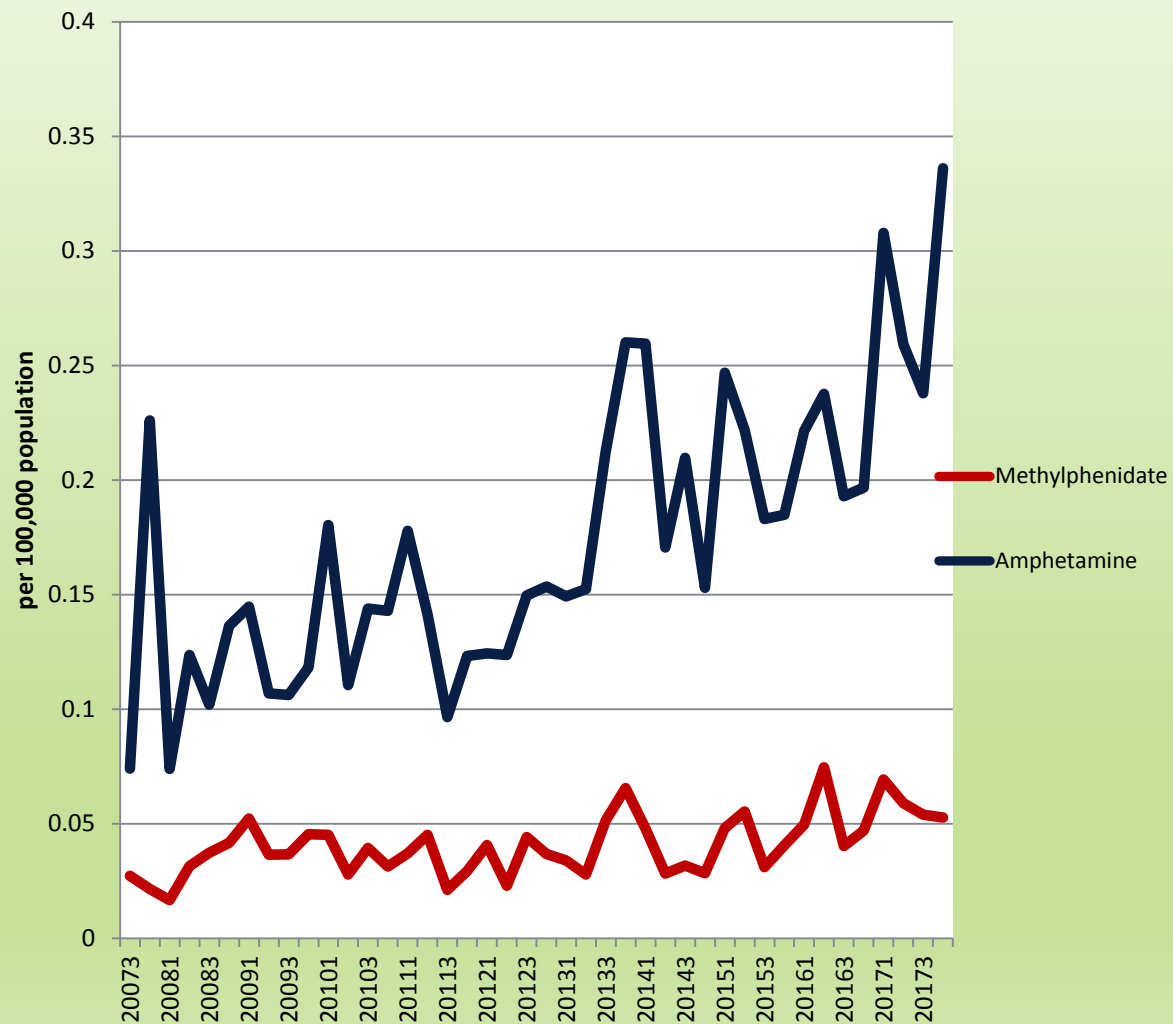
Stimulants

- Used as single substance or polysubstance
 - Pharmaceutical "speedball" effect
- Highest rates in teenage and young adult population
- Rates of intentional abuse stable, but diversion increasing

Stimulants, RADARS Poison Centers



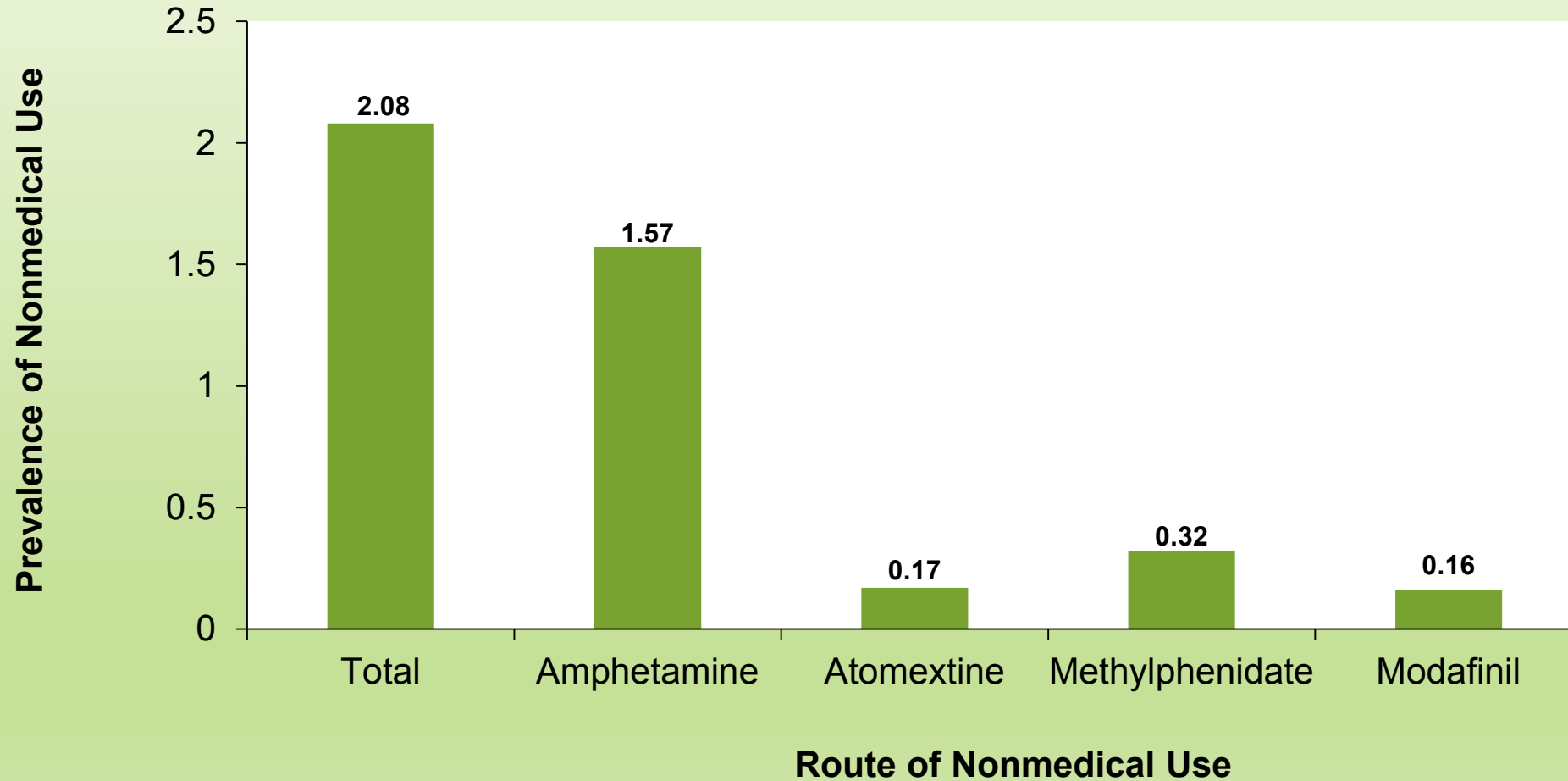
Stimulants, RADARS Drug Diversion



Prescription Stimulants: Prevalence of Nonmedical Use

NMURx data

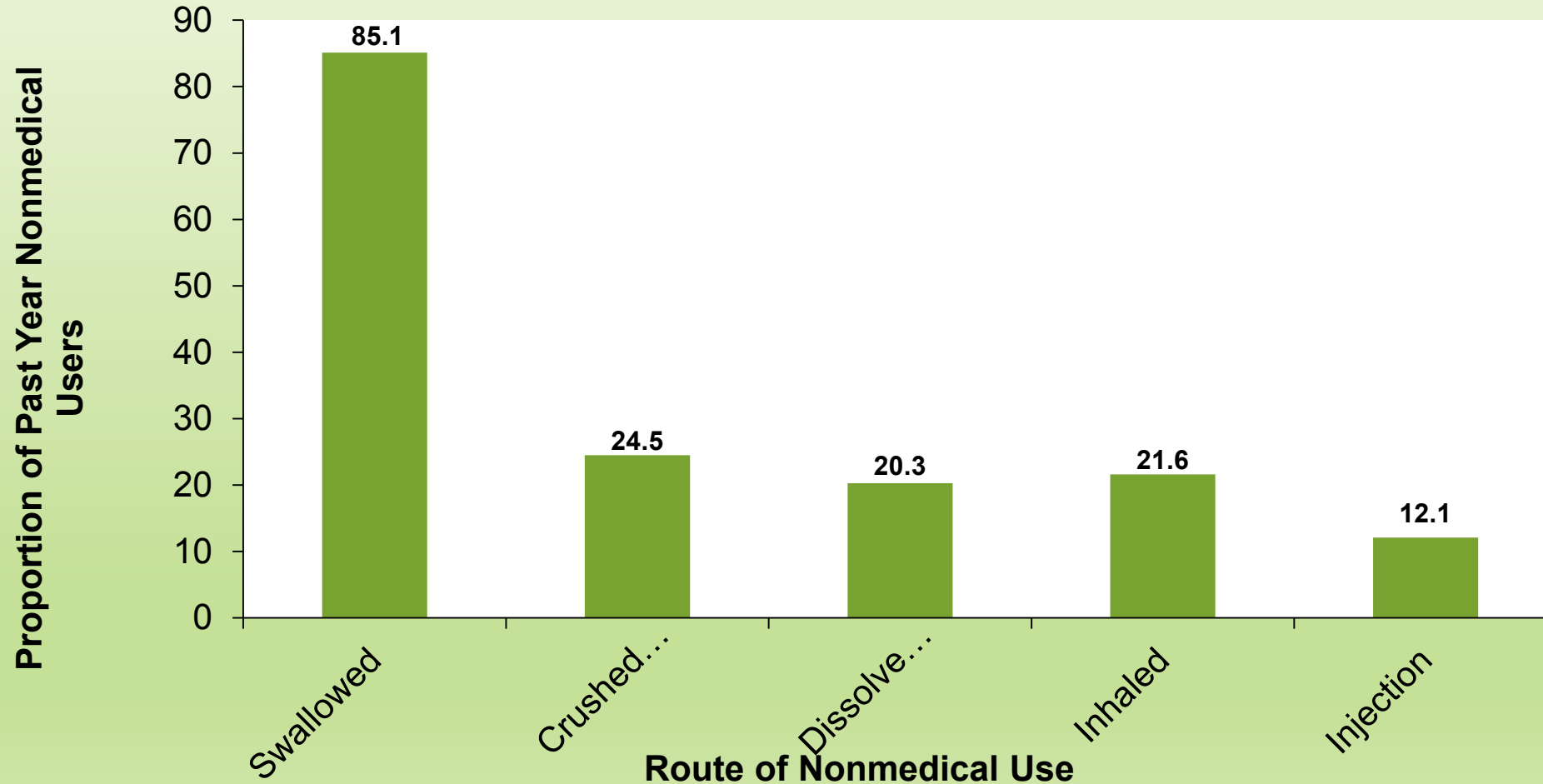
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Prescription Stimulants: Routes of Nonmedical Use

NMURx data

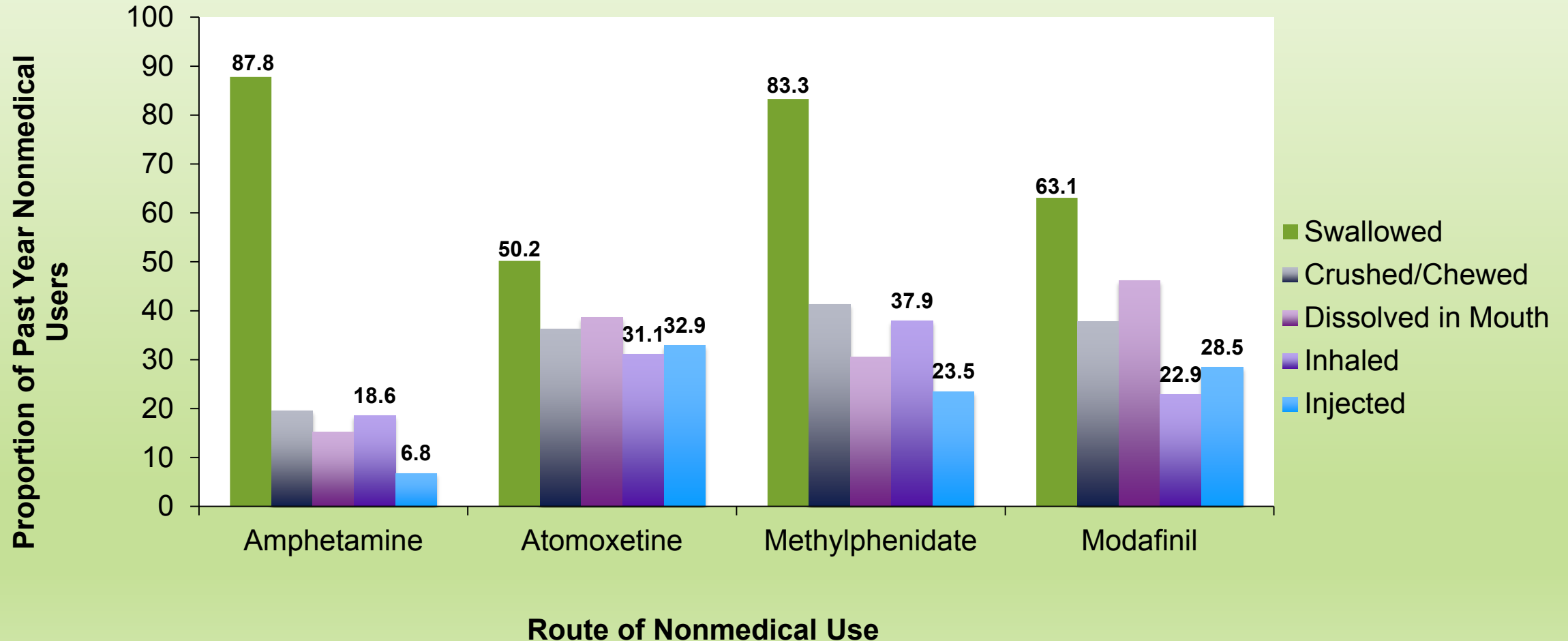
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Prescription Stimulants: Routes of Nonmedical Use

NMURx data

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Conclusions

- ADF preparations do appear to decrease overall abuse
 - Biggest impact likely in those who do not yet have severe opioid use disorder
- ADF preparations may impact route of abuse
 - Transition from IN to IV seen with oxymorphone
- Oxymorphone as a molecule lends itself to dangerous behaviors
 - Low oral bioavailability, high intravenous potency
 - Sharing behaviors are common

Conclusions and Discussion

- Rising prescription stimulant nonmedical use, abuse, diversion
 - Approx 5 million adults in US currently nonmedically use
 - Potential for early warning of issues to come
- Trajectories of stimulant use poorly understood
 - Will the balloon apply?
- Non-oral routes of stimulant abuse suggest potential for ADF utility
 - Will need to address both inhalation and injection
 - Beware unintended consequences

Questions?

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