



## Post-Marketing Surveillance: Lessons Learned and Recommendations for the Future

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# + Conflicts of Interest/Disclosure



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# + Conflicts of Interest (<\$10,000)

## ■ Conflict of Interest

- Member, Scientific Advisory Board for the Researched Abuse, Diversion and Addiction Related Surveillance (RADARS®) System, which collects subscription fees from 14 pharmaceutical firms.
- Consultant, Pfizer Pharmaceuticals



# + Regulatory Approaches to Opioid Abuse





# Limitations of Data Sources Currently Used by Regulatory Agencies



- Data available only months or years later.
- Late in uncovering a problem.
- Most are passive reporting systems.
- Use of restrictive quantitative measures.



# Traditional Post-Marketing Programs



- DAWN: Drug Abuse Warning Network
- TEDS: Treatment Episode Data Set
- NFLIS: National Forensic Laboratory Information
- NSDUH: National Household Survey on Drug Use and Health
- MTF: Monitoring the Future



# Proactive Post-Marketing Surveillance



- Most programs seek out abuse in vulnerable populations.
- RADARS: Researched Abuse, Diversion and Addiction Related Surveillance
- NAVIPPRO: National Addictions Vigilance Intervention and Prevention



Identification of risk  
is fairly easy.





Mitigation is difficult.



Supply AND Demand  
need to be understood

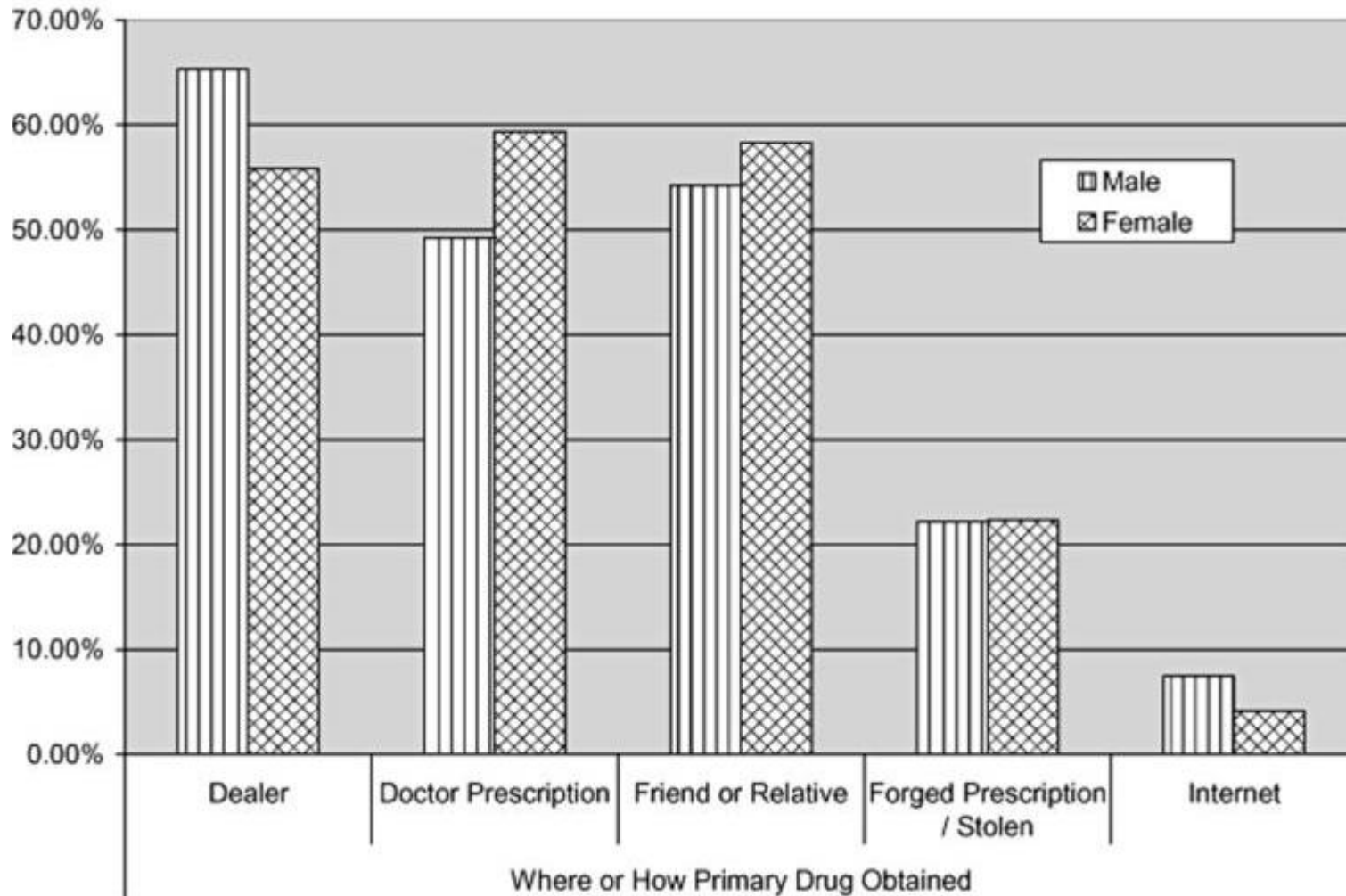


Most post-marketing  
surveillance systems  
fail to examine mitigation



Current focus only on  
SUPPLY

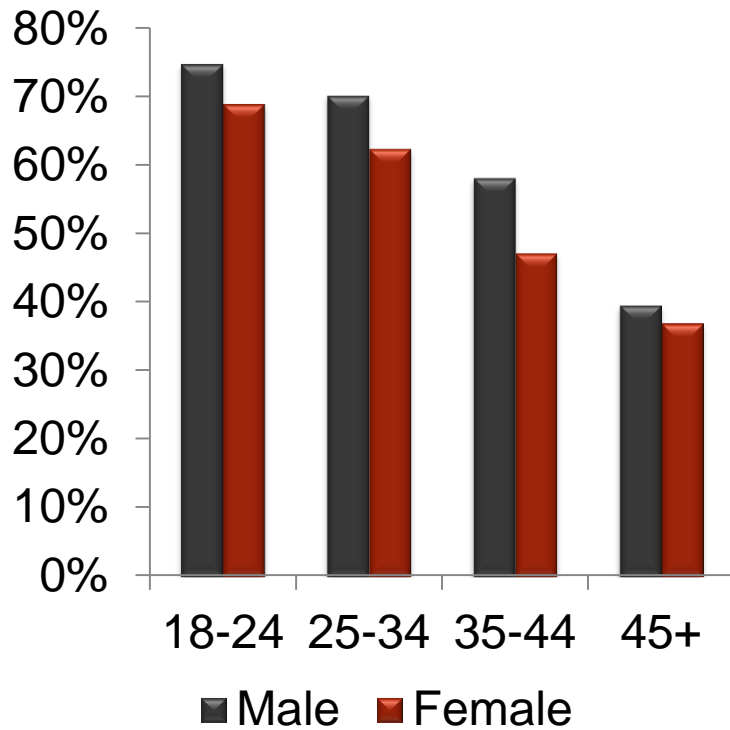
# + Sources of Diversion



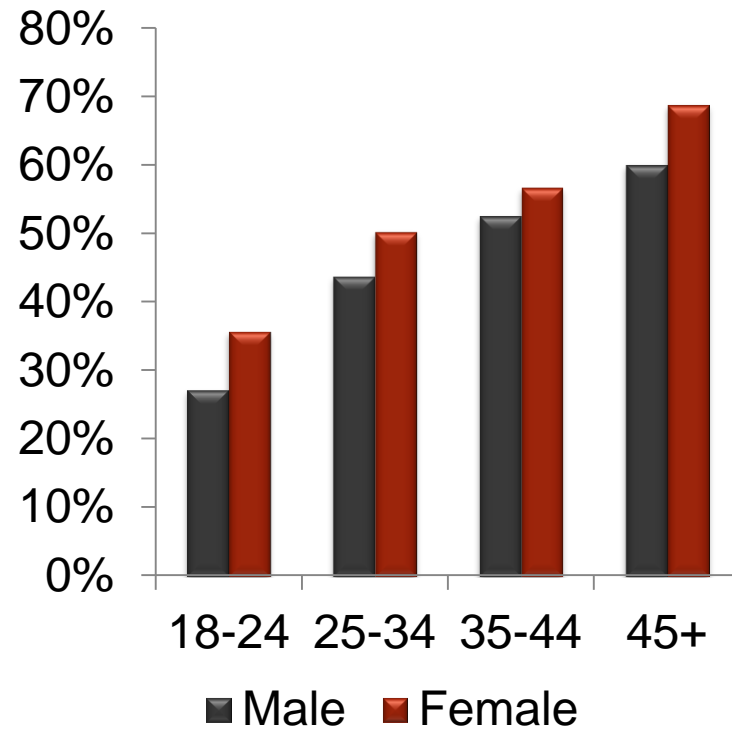
# + Sources of Diversion



## DEALER



## PHYSICIAN





# Supply-Side Interventions

# + Supply-Side Interventions: Physician-Focused

- Prescription Monitoring Programs (PMPs).
- Crackdown on 'pill mills' and 'script doctors.'
- Physician Education.
- CDC Prescribing Guidelines.





# + Supply-Side Interventions: Drug-Focused

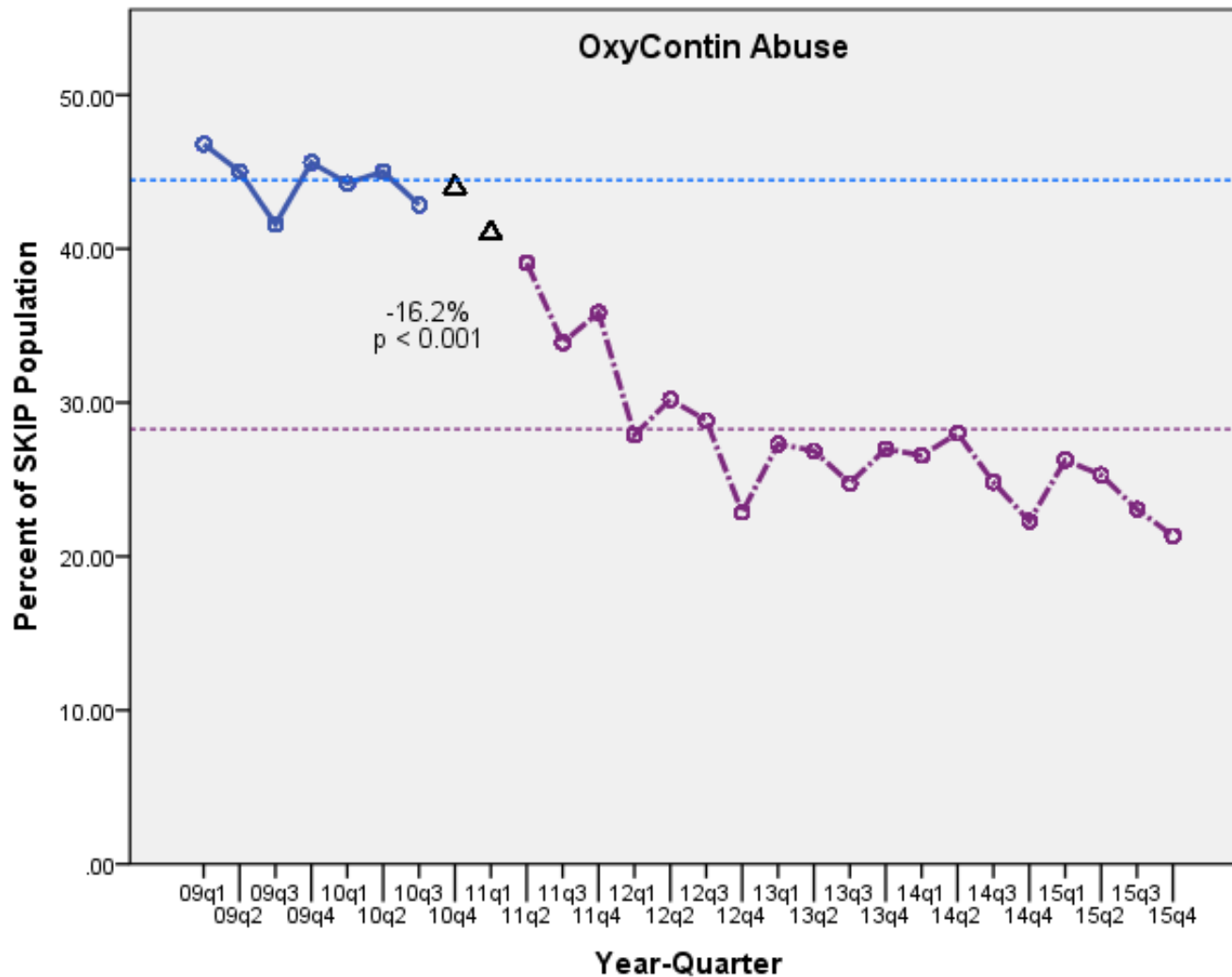
- Abuse-Deterrent Formulations



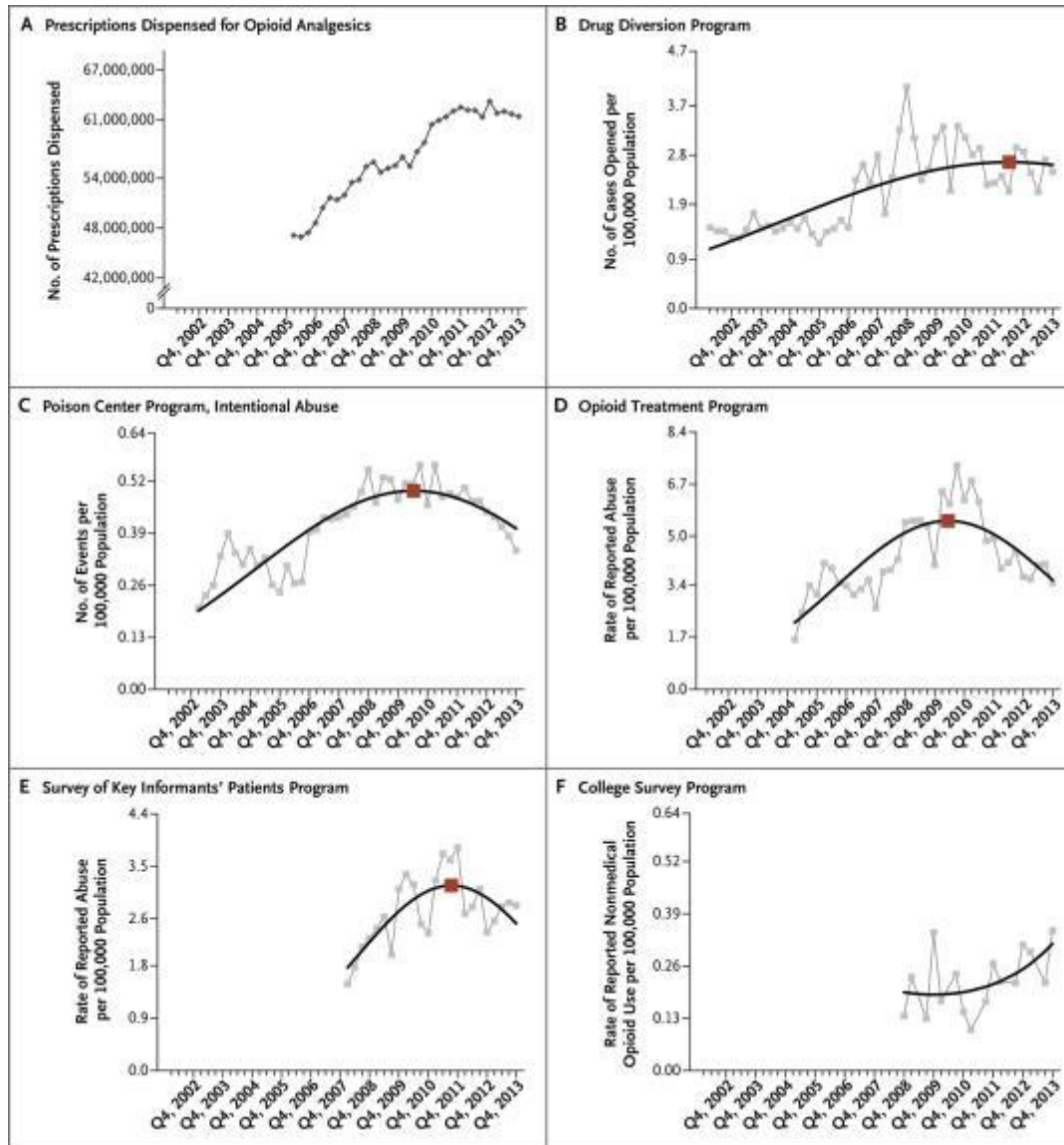


# Anticipated Effects: Reduced Opioid Abuse

# + Abuse-Deterrent OxyContin<sup>®</sup>



Source: Cicero TJ, Ellis MS, Kasper ZA. A tale of two ADF: Differences in the effectiveness of abuse deterrent formulations of oxymorphone and oxycodone extended-release drugs. Pain. 2016 June; 157(6):1232-8.

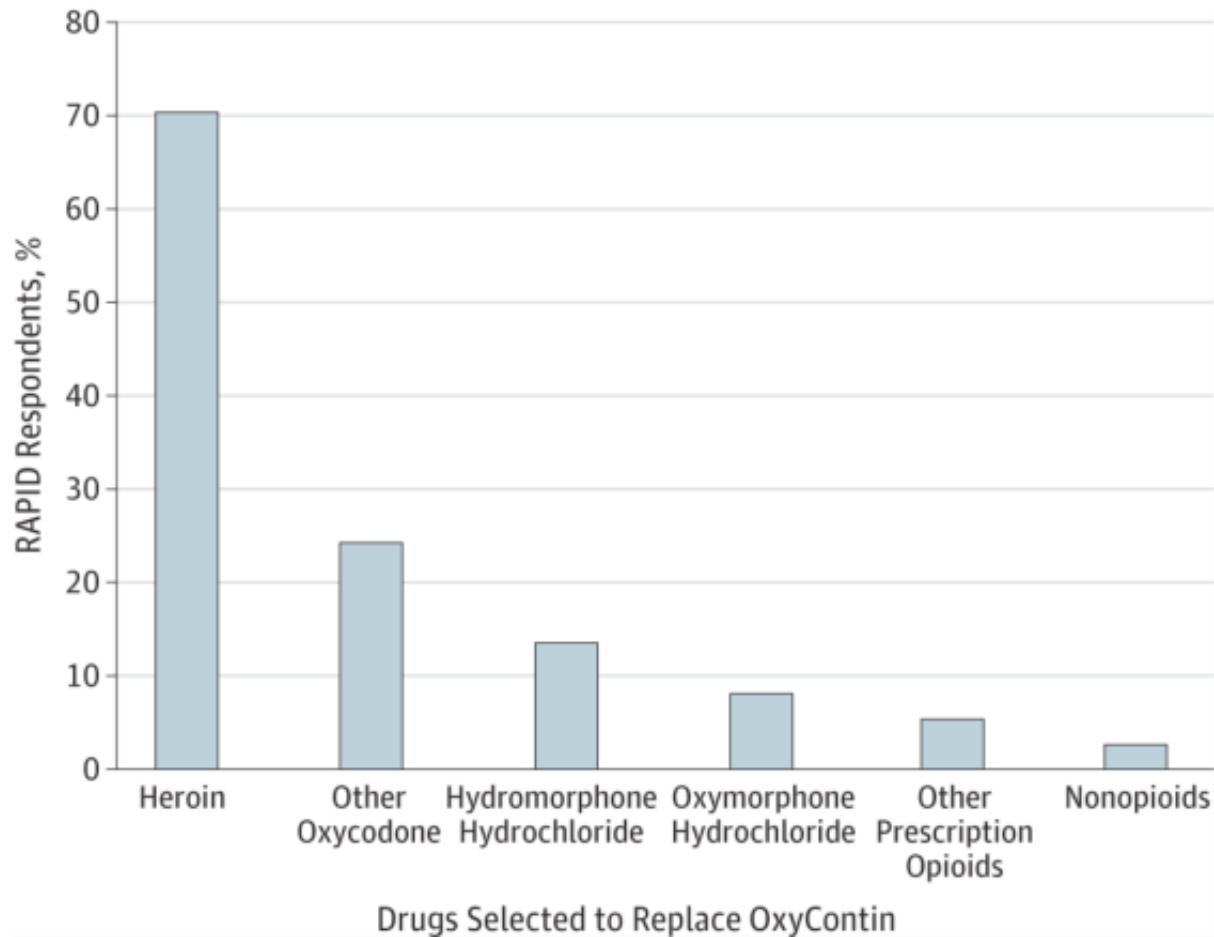


Source: Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, Green JL. Trends in opioid analgesic abuse and mortality in the United States *N Engl J Med.* 2015 Jan 15.



# Unanticipated Consequences

# + Abuse-Deterrent OxyContin<sup>®</sup>



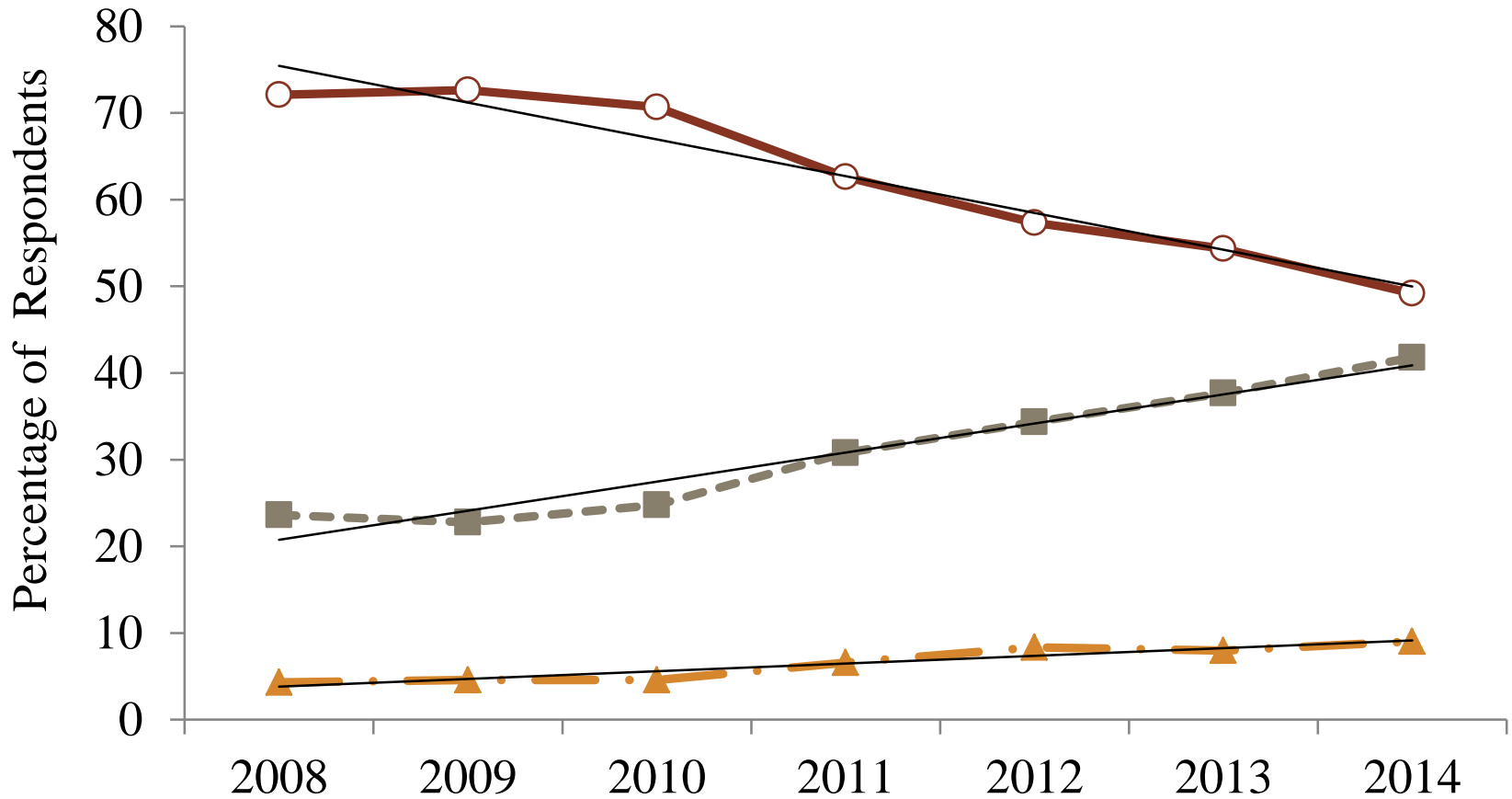
**Source:** Cicero TJ, Ellis MS. Abuse deterrent formulations and the prescription opioid abuse epidemic in the United States: lessons learned from OxyContin. *JAMA Psychiatry*. 2015 Mar 11.



# Shifts in Opioid Abuse Patterns



○ Prescription Opioids Only   ■ Heroin+Prescription Opioids   ▲ Heroin Only



## + Reduced Stigma of Heroin

“...The 2 dealers and the people around them are middle class white kids, not even kids we were all in the age range of 25-41. It just became easy, and we weren't really looked at as being addicts because everyone thinks heroin addicts are all homeless, shady looking, dirty junkies.”





# + Reduced Stigma of Heroin



“I knew I liked it above all else, and once I had a drug dealer it became almost too easy to get.

I had access to money because I’m an upper middle class family and I also became close to my dealers, driving them around so I could get paid in drugs and just becoming super close, even if it meant sexually, so I could get the drug.....”



# Understanding the DEMAND



# Getting 'High'



“I loved the [feeling] of euphoria. I finally felt comfortable in my own skin. I could talk to anyone I felt what I thought I was supposed to fill like. Extremely happy. I knew I found the secret to my happiness. “



Is getting 'high'  
the sole motivation?



# How do opioids make you feel?



Source: Cicero TJ, Ellis MS, Kasper ZA. Understanding the demand side of the prescription opioid epidemic: does the initial source of opioids matter? Drug and Alcohol Dependence. Accepted. In Press.



“I did not have any tools for coping with uncomfortable situations.

Which made using drugs my go to coping skill for anything from handling emotional abuse to taking a shower.”



“They made me feel like I could talk to people and not be scared or embarrassed to walk around and just talk and be part of society.”





“Mask inside emotions/traumas, feelings of fear, self-esteem, self-pity, anger and avoiding the growing stress and responsibility of life”



“It made me feel happy and gave me the energy and want to do daily activities such as working that otherwise wouldn’t have been possible due to the debilitating depression at that time in my life.”

# + Treatment-Seeking Opioid Abusers

- 75% self-report they used opioids to self-medicate psychiatric related issues.
- 85% self-report the use of opioids to “escape from life”.
- No difference between those who started using from a doctor’s prescription and those who experimented.



# Conclusions



# Implications for Treatment/Prevention



- Old adage: 25% get better, 50% remain unchanged, 25% get worse.
- Relapse likely unless you solve the base problem.
  - Understanding the 'why' of persistent drug use.
- Must address the motivations for abusing opioids for either treatment and prevention efforts to be successful.

# + Conclusions

- Post-marketing surveillance is effective in identifying risk
  - STRENGTH: Better than passive studies
  - **WEAKNESS: Not useful for dealing with the problem.**
- Supply side efforts cannot exist alone.
- Understanding the demand for these drugs is essential to developing effective treatment and prevention strategies.
- Physician education should include understanding motivations for misuse/abuse and recognizing these individualized risk factors.