# Effects of Reformulating OxyContin on Opioid Abuse in 6 National US Abuse Surveillance Systems

P. Coplan, H. Chilcoat

Purdue Pharma L.P., Stamford, CT

## INTRODUCTION

- Opioid analgesics are an important treatment option for patients with pain.
- Abuse of opioid analgesics is a source of morbidity and mortality in the United States (US).
- Prescription opioids are often abused through non-oral routes of administration (ROA) that require tampering with the intact product, including inhalation ("snorting"), injection, and smoking.
- Prescription opioids may be abused by oral routes (eg, swallowing intact tablets whole, chewing and swallowing, or drinking) or non-oral routes. Abuse through non-oral routes can increase the desirability of opioids because of the resulting rapid availability of the opioid and higher rewarding effects.
- While opioid abuse via any ROA remains a significant public health problem, health risks associated with non-oral ROAs are also of particular concern.
- Opioid formulations with abuse deterrent properties have been proposed as an approach to reduce abuse of opioid products via routes that require tampering.
  - OxyContin is an extended-release oxycodone product that was originally approved by the FDA in 1995 and reformulated with abuse deterrent properties including physico-chemical barriers to crushing and dissolving.
  - Reformulated OxyContin was approved in April 2010 and shipments for OxyContin were replaced with the reformulated product starting in Aug 2010.
- Laboratory and clinical studies demonstrated reduced reformulated OxyContin and OC with original OxyContin extractability, likeability, and psychoactive effects relative to OC and placebo after crushing (Harris et al., 2014; Perrino et al., 2013; Sellers et al., 2013) and FDA approved labeling with abuse-deterrent language in April 2013.

## OBJECTIVES

- To assess changes in abuse rates of OxyContin from one year before to three years after reformulation of OxyContin with abuse-deterrent properties.
- To compare changes in abuse for OxyContin with changes in abuse of other opioid analgesics, to differentiate between general trends affecting opioid analgesic abuse (eg, prescription monitoring programs, pill mill shutdown, REMS) and OxyContin-specific trends in abuse.

## METHODS

- Rates of abuse and drug diversion events were compared for the one-year period before reformulation of OxyContin to the three-year period after reformulation using data from 3 national surveillance systems in the US
  - Intentional abuse exposures reported to poison centers
    - Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS)® System Poison Center Program
    - National Poison Data System (NPDS)
  - Reports of abuse among individuals assessed in substance abuse treatment centers
    - National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO)
  - Drug diversion events reported by drug diversion officers
    - RADARS Drug Diversion Program
- Time periods
  - Pre-reformulation period: Year prior to introduction of reformulated OxyContin (July 2009 to June 2010)
  - Transition period: Two-quarter period in which original and reformulated OxyContin were widely available (July 2010 to December 2010)
  - Post-reformulation period: Three-year period following reformulation of OxyContin excluding transition period (January 2011 to December 2013)
- Analysis
  - Means analysis: Comparison of the mean rate per quarter in the post- versus pre-reformulation period
  - Quarterly analysis: Change in the rate for each quarter in the post-reformulation period relative to the mean rate per quarter in the pre-reformulation period
- Adjusting for Study Population Size or Number of Prescription Changes
  - Primary method: Population-adjusted (adjusted for US population in census tract areas covered by the surveillance system). Measures overall public health impact.
  - Number of prescriptions. Sensitivity analysis that accounts for prescription changes.
- Comparators
  - Other opioid products used as comparators to assess whether observed changes are specific to OxyContin and not due to secular trends

## RESULTS

**Figure 1. OxyContin Prescriptions per Quarter between 3Q2009 and 4Q2013 as assessed by retail pharmacy dispensing in IMS National Prescription Audit database**

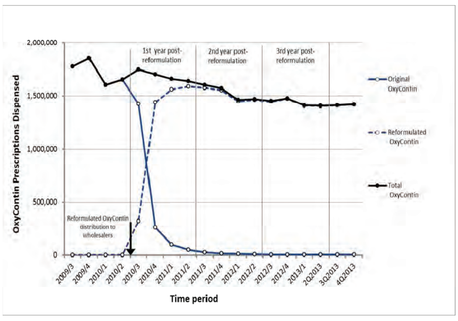
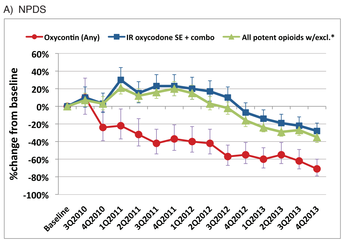
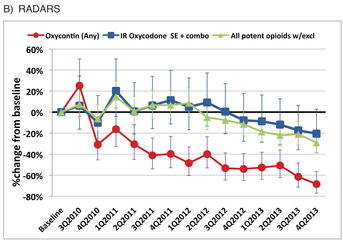



**Figure 2. Change in population-adjusted abuse rates for OxyContin and comparator opioids for each quarter in the post-reformulation period relative to the rate in the year before introduction of reformulated OxyContin in the NPDS, RADARS Poison Centers and NAVIPPRO Systems**

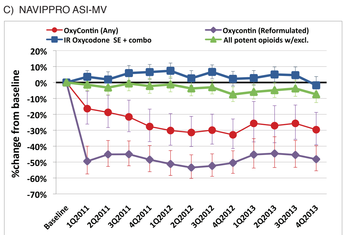
A) NPDS




B) RADARS




C) NAVIPPRO ASI-MV




SE = single-entity oxycodone, combo = oxycodone-acetaminophen combination (eg, percoset)
95% confidence intervals shown.
All potent opioids category includes ER morphine, ER oxymorphone, ER hydromorphone, IR oxycodone, IR hydrocodone and excludes OxyContin, methadone and transdermal patches.

## RESULTS (CONT.)

**Figure 3. Percent change in population- and prescription-adjusted rates of abuse from the pre- to post-reformulation periods of OxyContin and comparator opioids**

A) OxyContin Population adjusted

B) All other Schedule 2 opioid pills excluding methadone – Population adjusted

C) OxyContin Prescription adjusted

D) All other Schedule 2 opioid pills excluding methadone – Prescription adjusted

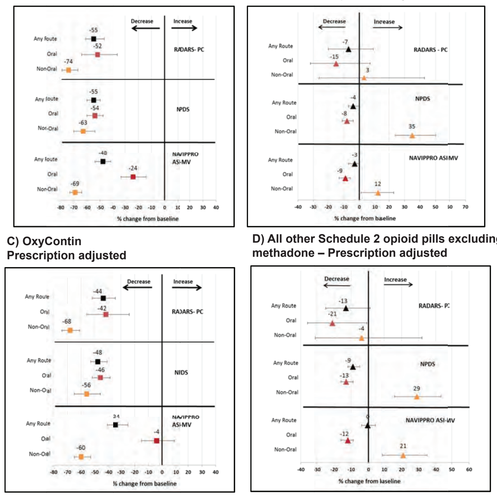



**Figure 4. Fatalities reported to manufacturer associated with OxyContin or ER oxycodone with date of death specified between 3Q2006 and 4Q2014**

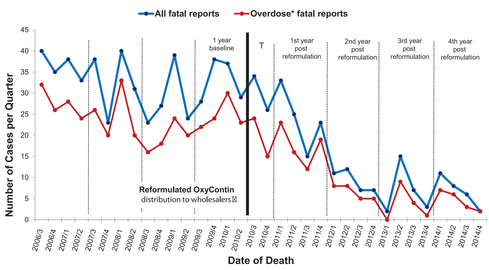
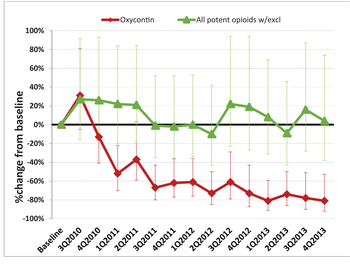



**Figure 5. Change from one-year baseline in drug diversion rates for OxyContin and comparator opioids after introduction of reformulated in the RADARS Drug Diversion program – population-adjusted rates shown**




## SUMMARY

- National Poison Data System
  - 55% reduction (p<0.001) in OxyContin abuse, significantly decreased versus other opioids
  - 54% reduction in oral, 63% reduction in non-oral OxyContin abuse
- RADARS Poison Centers
  - 55% reduction (p<0.001) in OxyContin abuse, significantly decreased versus other opioids
  - 52% reduction in oral, 74% reduction in non-oral OxyContin abuse
- NAVIPPRO Substance Abuse Treatment Centers
  - 48% reduction (p<0.001) in OxyContin abuse, significantly decreased versus other opioids
  - 24% reduction in oral, 55% reduction in non-oral OxyContin abuse
- RADARS Drug Diversion Program
  - Law enforcement events decreased 75% by the end of the three-year post-reformulation period (p<0.001) for OxyContin, significantly less than other opioids

## CONCLUSIONS

Reductions in rates of abuse of OxyContin occurred from the one year before to the three years after reformulation of OxyContin in two poison center studies, a substance abuse treatment study, a drug diversion surveillance study, and an analysis of fatalities reported to the manufacturer. These decreases in OxyContin abuse occurred despite relatively small decreases in prescriptions for OxyContin in a national prescription database. Thus both population- and prescription adjusted rates of abuse of OxyContin decreased significantly.

The decreases in OxyContin abuse were consistent with Hill's Criteria:

- Temporality:
  - Reductions in abuse/diversion for OxyContin occur soon after introduction of reformulation, sooner than reductions for comparator opioids
  - Decreases in OxyContin were sustained for the 3 years after reformulation
- Effect size
  - Rates of OxyContin abuse decreased by 48% to 85% in population-adjusted analyses in the surveillance systems in this analysis. Prescription-adjusted rates of OxyContin abuse decreased by 34% to 60%. These are large effect sizes.
- Specificity:
  - Larger reductions in OxyContin abuse occurred for non-oral abuse than oral abuse, as expected given formulation properties
  - Reductions in population-adjusted rates are larger for OxyContin than for comparator opioids
  - Reductions in prescription-adjusted rates larger than for comparator opioids, except for ER morphine (but not all morphine) in the poison center studies
- Consistency:
  - Reductions in rates of OxyContin abuse occurred consistently across the studies and surveillance systems
  - Reductions in rates of OxyContin abuse consistent with results from clinical trials
- Alternative explanations:
  - Several other interventions to reduce opioid abuse were introduced during the 3-year study period (eg, prescription drug monitoring programs, ER/LA opioid analgesic REMS, pill mill shut down), but none occurred soon after reformulation of OxyContin when a big drop in OxyContin abuse occurred. In addition, other interventions focused on all opioid analgesics not OxyContin specifically, and the decrease in OxyContin abuse after introduction of reformulated OxyContin was specific to OxyContin and not other opioid analgesics.

## REFERENCES


- Butler SF, Cassidy TA, Black RA, Chilcoat H, Budman SH, Landau C, Coplan C. Abuse rates and routes of administration of reformulated OxyContin®: initial findings from a sentinel surveillance sample of individuals assessed for substance abuse treatment. Journal of Pain. 2013;14(4):351-358.
- Coplan PM, Kale H, Sandstrom L, Landau C, Chilcoat HD. Changes in oxycodone and heroin exposures in the National Poison Data System after introduction of extended-release oxycodone with abuse-deterrent characteristics. Pharmacoepidemiology & Drug Safety. 2013;22:1274-1282.
- Harris SC, Perrino PJ, Smith I, Shram MJ, Colucci SV, Bartlett C, Sellers EM. Abuse potential, pharmacokinetics, pharmacodynamics, and safety of intranasally administered crushed oxycodone HCl abuse-deterrent controlled-release tablets in recreational opioid users. Journal of Clinical Pharmacology. 2014;54(4):468-77.
- Perrino PJ, Colucci SV, Apseloff G, Harris SC. Pharmacokinetics, tolerability, and safety of intranasal administration of reformulated OxyContin tablets compared with original OxyContin® tablets in healthy adults. Clinical Drug Investigation. 2013;33(6):441-9.
- Severtson SG, Bucher Bartelson B, Davis JN, Muñoz A, Schneider MF, Chilcoat H, Coplan PM, Surratt H, Dart R. Reduced abuse, therapeutic errors, and diversion following reformulation of extended-release Oxycodone in 2010. Journal of Pain. 2013;14(10):1122-1130.
- Sellers EM, Perrino PJ, Colucci SV, Harris SC. Attractiveness of reformulated OxyContin® tablets: assessing comparative preferences and tampering potential. Journal of Psychopharmacology. 2013;27(9):808-16.


## Disclosure Statement

Research funded by Purdue Pharma L.P. H. Chilcoat and P. Coplan are employees of Purdue Pharma L.P.

Presented at the International Society for Pharmacoepidemiology Annual Meeting, Boston, MA, August 23-26, 2015