**Effects of Reformulating OxyContin on Opioid Abuse**

**in 6 National US Abuse Surveillance Systems**

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**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 physicochemical

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 prereformulation

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**

1. NPDS table
2. RADARS table
3. NAVIPPRO ASI-MV table

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.

**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 table**

**B) All other Schedule 2 opioid pills excluding**

**methadone – Population adjusted table**

**C) OxyContin**

**Prescription adjusted table**

**D) All other Schedule 2 opioid pills excluding**

**methadone – Prescription adjusted table**

**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 postreformulation

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.

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