

Original Report

Abuse Rates and Routes of Administration of Reformulated Extended-Release Oxycodone: Initial Findings From a Sentinel Surveillance Sample of Individuals Assessed for Substance Abuse Treatment

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Abstract: Oxycodone hydrochloride controlled-release, also known as extended-release oxycodone (ER oxycodone), was reformulated with physicochemical barriers to crushing and dissolving intended to reduce abuse through nonoral routes of administration (ROAs) that require tampering (eg, injecting and snorting). Manufacturer shipments of original ER oxycodone (OC) stopped on August 5, 2010, and reformulated ER oxycodone (ORF) shipments started August 9, 2010. A sentinel surveillance sample of 140,496 individuals assessed for substance abuse treatment at 357 U.S. centers between June 1, 2009, and March 31, 2012, was examined for prevalence and prescription-adjusted prevalence rates of past-30-day abuse via any route, as well as abuse through oral, nonoral, and specific ROAs for ER oxycodone and comparators (ER morphine and ER oxymorphone) before and after ORF introduction. Significant reductions occurred for 8 outcome measures of ORF versus OC historically. Abuse of ORF was 41% lower (95% CI: -44 to -37) than historical abuse for OC, with oral abuse 17% lower (95% CI: -23 to -10) and nonoral abuse 66% lower (95% CI: -69 to -63). Significant reductions were not observed for comparators. Observations were consistent with the goals of a tamper resistant formulation for an opioid. Further research is needed to determine the persistence and generalizability of these findings.

Perspective: This article presents preliminary findings indicating that 8 outcome measures of abuse of a reformulated ER oxycodone were lower than that for original ER oxycodone historically, particularly through nonoral ROAs that require tampering (ie, injection, snorting, smoking), in a sentinel sample of individuals assessed for substance use problems for treatment planning.

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Key words: Tamper resistant formulation, abuse resistant formulation, extended-release oxycodone, ER oxycodone, prescription opioid abuse.

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Abuse of opioid analgesics is a growing source of morbidity and mortality in the United States.²³ From 1999 to 2006, poisoning deaths involving any opioid analgesic more than tripled.²¹ Dependence on and abuse of pain relievers rose 27% from 2005 to 2010, and there were about 2 million people initiating nonmedical use in 2010.²⁹

Some prescription opioid abuse involves modifying the original formulation of the product, or "tampering." Tampering renders the intact product into a powder, liquid, or vapor, making it suitable for use through alternative routes of administration (ROAs), including inhalation ("snorting"), injection, and smoking. The intention of

tampering is to achieve rapid release of the drug and higher rewarding effects via these routes.^{15,22,26} For extended-release (ER) analgesics, tampering disables the ER mechanism, accelerating the release of the opioid via ingestion (including oral ingestion), injection, snorting, and smoking.¹⁵ Alternative ROAs, especially snorting and injection, are associated with longer duration of abuse.^{3,12,15} Whereas opioid abuse via any ROA remains a significant public health problem, health risks associated with nonoral ROAs are also of particular concern. Unintentional pharmaceutical overdose fatalities are associated with nonmedical ROAs,⁸ and injection and snorting increase health risks.^{11,14,27,28,31} In addition, abuse of prescription opioids often starts via oral ingestion and evolves to snorting and injecting as the abuse progresses over time.¹³ As a response to such concerns, the concept of “abuse deterrent formulations” (commonly referred to as “tamper resistant formulations” or TRFs) emerged as a pharmaceutical approach to minimizing abusers’ ability to defeat ER mechanisms and to abuse by alternative ROAs, perhaps also reducing abuse rates.^{1,17,18}

OxyContin (Purdue Pharma LP, Stamford, CT) is an ER formulation of oxycodone hydrochloride that was originally approved by the Food and Drug Administration (FDA) in 1995. Abuse of original ER oxycodone (OC) by nonoral ROAs (ie, snorting, injecting, and smoking) became common among abusers.^{2,5,6,15,16,25}

ER oxycodone was reformulated with the intention of making the tablets tamper resistant through physiochemical barriers to crushing and dissolving. Reformulated ER oxycodone (ORF) was approved in April 2010. Laboratory studies conducted prior to approval and clinical studies carried out postapproval demonstrated reduced ORF extractability, likability, and psychoactive effects relative to OC and placebo after crushing. As a condition of approval, the FDA required a postmarketing epidemiology program for ORF to assess whether it is less abused and misused than OC, particularly through nonoral ROAs.⁹

This study provides initial results from one of the postmarketing studies conducted under the epidemiology program, based on data from a sentinel surveillance population of individuals assessed for substance use problems for treatment planning.^{2,5} The aims of this study were to assess 1) whether prevalence and prescription-adjusted prevalence rates of abuse of ER oxycodone declined following introduction of ORF compared to historical abuse estimates of OC and compared with changes in comparator opioid analgesics over the same time period; and 2) whether ORF is less likely to be abused through ROAs that require tampering (snorting, injecting, and smoking) compared to OC and comparator opioid analgesics.

Methods

Study Sample

The sample included 140,496 individuals assessed for substance use problems from 357 centers located within the United States and part of the NAVIPRO surveillance

Abuse Rates and Routes of Reformulated ER Oxycodone system.⁵ Data were collected over a 34-month period (approximately 11 quarters) from June 1, 2009, through March 31, 2012, using the Addiction Severity Index-Multimedia Version (ASI-MV). Sites within the ASI-MV network upload data to a central server in near real time. Included sites were those that collected data for OC and ORF in both the pre- and post-ORF periods.

Study Design

An observational design compared the prevalence, prescription-adjusted prevalence rates, and ROA patterns of past-30-day abuse of ORF in the period after its introduction to that of OC before ORF introduction. Shipments of OC ceased on August 5, 2010, and ORF shipments started on August 9, 2010. Historical prevalence of abuse and ROAs of OC were measured over a 14-month period preceding launch of ORF (June 1, 2009, through August 8, 2010) and compared with ORF experience during approximately 20 months following release of ORF (August 9, 2010, through March 31, 2012). The start of the pre-ORF period was selected as June 1, 2009, because historical data on ROA and the program’s ability to differentiate all of the ER opioid products began to be collected on that date. The post-ORF period was from ORF introduction through the first quarter of 2012.

Abuse patterns for 2 comparator opioid compounds (ER morphine and ER oxymorphone) were assessed during the same pre- and post-ORF periods. The primary route of nonoral abuse of ER oxymorphone is by snorting and of ER morphine is by injecting,² thus providing relevant controls for route-specific comparisons. A sensitivity analysis was conducted to account for number of prescriptions dispensed using data from the Vector One National database.³⁰

Outcome Measurement

Measures examined included the following: 1) prevalence of past-30-day abuse among all respondents evaluated or within the subset of individuals reporting past-30-day abuse of any prescription opioid; 2) prescription-adjusted prevalence rates of abuse (defined as prevalence of past-30-day abuse per 10,000 prescriptions dispensed per month); 3) prevalence of abuse via oral and nonoral ROAs for ORF, OC, and comparator opioids; and 4) frequency of abuse. Changes in ROA were measured as the percent of abuse of the product via a specific ROA among those reporting abuse of that product. Frequency of abuse for each drug was the average number of days of reported abuse within the past 30 days prior to assessment among individuals who reported abuse of that drug.

Abuse and ROA patterns were captured via self-report during the ASI-MV interview, a self-administered, computerized, standard clinical assessment for substance abuse treatment with demonstrated reliability and validity.^{4,19,20} The ASI-MV contains product-specific questions about abuse, routes, and sources. Specific medications are identified by presenting images, text, and audio including medication names and slang/street names. To minimize misidentification of OC and ORF, the ASI-MV screen

images include indicia. An alert window reminds respondents to review the images/indicia prior to selection.

Past-30-day abuse was defined as any nonmedical use of a prescription opioid product. Positive responses to a series of questions regarding use via alternative ROAs, source of the product, and use not as prescribed for pain established the patient as having engaged in non-medical use and were considered to indicate abuse.^{2,5}

Data Analysis

Data analysis was carried out in 3 stages. The first stage involved estimating 1) the quarterly unadjusted percentages of past-30-day abuse of OC (during the entire study period), ORF (after the introduction of ORF), and any ER oxycodone (OC or ORF after the introduction of ORF); and 2) the pre- to post-ORF changes in unadjusted and prescription volume-adjusted percentages of past-30-day abuse for ER oxycodone (OC in pre versus ORF in post) and comparator products. Prescription volume was calculated as the monthly average number of prescriptions dispensed per compound during the pre-ORF period and during the post-ORF period. The second stage involved estimating pre- to post-ORF changes in percentages of abuse via specific routes of administration (oral, nonoral, injecting, snorting, and smoking) for ER oxycodone (OC in pre versus ORF in post) and comparator products. The third and final stage involved estimating pre- to post-ORF changes in the mean number of days (over the 30-day period prior to the assessment) for ER oxycodone (OC in pre versus ORF in post) and comparator products.

Generalized estimating equation (GEE) log-binary regression models were employed when estimating pre- and post-ORF period percentages and relative percent change from the pre- to post-ORF period. A GEE log-binomial (number of events/total number of trials) regression model was used to estimate the pre- and post-ORF period mean number of days of abuse (multiplied by 30 to convert the proportions into days) and

relative percent change in the mean number of days of abuse from the pre- to post-ORF period. GEE logistic regression models were used to estimate quarterly percentages of abuse. In order to calculate quarterly percentages of abuse, the inverse logit link function was employed.

GEE-type regression models were used to account for within-subject correlation due to multiple observations per ASI-MV respondent; that is, each respondent is provided the opportunity to indicate each compound abused and, if endorsed, the route(s) in which the compound was abused. Moreover, some individuals were administered the ASI-MV multiple times. Notably, the residual covariance matrix (the component of the model that accounts for within-subject correlation) was blocked by calendar quarters. This covariance structure allowed for responses distant in time made by the same ASI-MV respondent to be treated as independent. All analyses were performed using the GLIMMIX procedure in SAS v.9.3 (SAS Institute, Cary, NC).

Results

Sample Characteristics

Among the total sample, 18.8% reported abuse of any prescription opioid. Of those, most were male (55.6%) and white (66.2%). The majority of prescription opioid abusers (53.9%) were between 21 and 34 years old, 32.6% were 35 to 54 years old, 9.9% were under 21, and 3.7% were over 55. During the pre-ORF period, 2,894 individuals (24.0% of prescription opioid abusers) reported past-30-day ER oxycodone abuse, while 1,705 (12.1% of prescription opioid abusers) reported ORF abuse (post-ORF).

Change in Rates of Abuse

The trend of ER oxycodone abuse (OC and ORF) via any ROA over the study period showed a decline in the

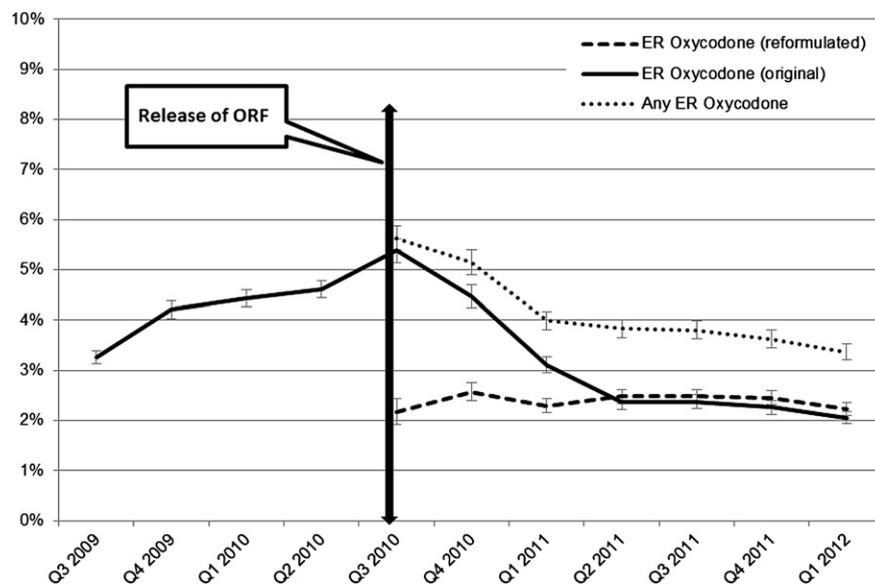


Figure 1. Quarterly prevalence of past-30-day abuse for original ER oxycodone, reformulated ER oxycodone (ORF), or any ER oxycodone (OC or ORF) among individuals assessed for substance abuse treatment.

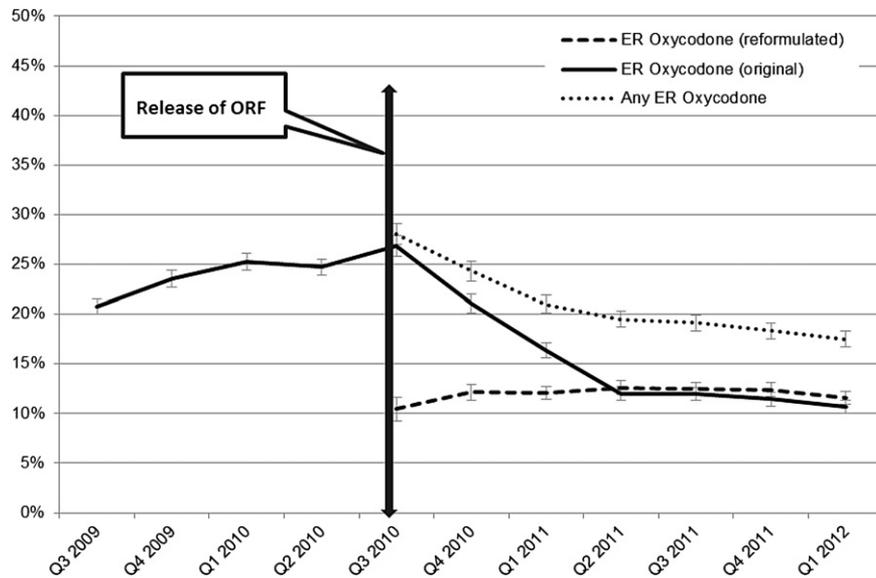


Figure 2. Quarterly prevalence of past-30-day abuse for original ER oxycodone, reformulated ER oxycodone (ORF), or any ER oxycodone (OC or ORF) among individuals who reported abuse of any prescription opioid.

quarterly prevalence of past-30-day abuse following introduction of ORF as a proportion of all assessments (Fig 1) and among prescription opioid abusers (Fig 2). Prior to ORF introduction, past-30-day OC abuse increased significantly from approximately 3.3 cases per 100 assessed in Q3 2009 to 5.4 cases per 100 assessed in Q3 2010. Quarterly prevalence of past-30-day abuse of ORF rapidly achieved a steady level of approximately 2.4 cases per 100 assessed. Following introduction of ORF, reports of OC abuse declined precipitously until sometime in Q2 2011, at which point reported abuse levels stabilized at about the same level as that seen for ORF. Secondary analyses examined any ER oxycodone abuse (OC and/or ORF) during the post-ORF period. While the pre-post comparison of any ER oxycodone did not reach significance ($P = .06$), exclusion of the “transition” period (8/9/10 to 12/31/10) during which both original and reformulated ER oxycodone were widely available in pharmacies as pharmacies’ supplies were used up yielded a significant pre-post difference (ie, 9.7% reduction of any ER oxycodone from the pre- to post-ORF period excluding “transition” period, $P = .0003$).

Comparisons of abuse estimates across the pre- and post-ORF periods revealed a 41% reduction in prevalence of past-30-day abuse of ORF via any ROA compared to OC (Table 1), while a nonsignificant increase (+2%) was noted for ER morphine, and a significant increase (+246%) was noted in ER oxymorphone abuse (Table 1: Rows 1a, 1b, and 1c). A similar pattern of findings was observed among respondents reporting abuse of any prescription opioid (Table 1), where a 49% reduction in ORF abuse compared with abuse of OC was observed (Table 1: Rows 3a, 3b, and 3c).

A 33% decline was observed in prescription-adjusted past-30-day abuse of ORF compared to OC prior to the reformulation (Table 1: Row 2a). ER oxymorphone showed a significant increase in prescription-adjusted abuse (+111%; Table 1: Row 2b), and ER morphine showed

a nonsignificant increase (+.9%; Table 1: Row 2c). Prescription-adjusted analyses of prescription opioid abusers only yielded similar findings, with a larger effect size for the decrease in ER oxycodone abuse (−42%), a smaller one for the increase in ER oxymorphone abuse (+80%), and a significant decrease for ER morphine (−13%; Table 1: Rows 4a, 4b, and 4c).

Routes of Administration

Among all individuals assessed, nonoral abuse of ORF was 66% lower than observed for OC before ORF (Table 1: Row 1a.2). Oral abuse of ORF was also significantly lower (17%) than oral abuse of OC before ORF (Table 1: Row 1a.1). Analyses of prescription opioid abusers yielded similar findings (Table 1: Rows 3a.1 and 3a.2).

Figs 3 to 5 show the percent who abuse through specific ROAs among those who reported abuse of ER oxycodone (OC versus ORF), ER oxymorphone, or ER morphine before and after introduction of ORF. In contrast to comparator products, significant differences were observed in abuse through each nonoral route for OC versus ORF. Injection of ORF (16%) was significantly lower than injection for OC (36%, $P = .0002$), as was snorting (53% to 25% for OC and ORF, respectively, $P < .0001$) and smoking (6% to 4% for OC and ORF, $P = .0373$). Because analysis was restricted to only those who reported ER oxycodone abuse, the reduction in nonoral route rates observed in this population was accompanied by a corresponding increase in relative rate of oral abuse (55% for OC to 76% for ORF, $P < .0001$), although the decrease in oral abuse of ER oxycodone among all respondents indicates that fewer respondents were abusing the drug orally post-ORF. Figs 4 and 5 illustrate that this pattern of reduced abuse by specific nonoral routes was not observed in the ROA profiles for the comparator opioids.

Table 1. Changes in Abuse Patterns of ER Oxycodone and Comparator Opioids Before and After Introduction of ORF

	BEFORE PERIOD* (%)	AFTER PERIOD† (%)	PRE-POST RELATIVE CHANGE‡	95% CI		P VALUE
Prevalence of product-specific abuse among all individuals assessed by ASI-MV in pre- and post-ORF periods						
1a. ER oxycodone	4.06	2.41	-41	-44	-37	<.0001
1a.1. Oral	2.15	1.79	-17	-23	-10	<.0001
1a.2. Nonoral	3.03	1.02	-66	-69	-63	<.0001
1b. ER oxymorphone	.32	1.11	+246	+199	+301	<.0001
1c. ER morphine	.92	.95	+2	-8	+14	.6634
Prescription-adjusted§ prevalence rate of product-specific abuse among all individuals assessed by ASI-MV						
2a. ER oxycodone	.07	.05	-33	-37	-29	<.0001
2b. ER oxymorphone	.06	.12	+111	+82	+144	<.0001
2c. ER morphine	.02	.02	+9	-10	+12	.8778
Prevalence of abuse among prescription opioid abusers assessed by ASI-MV in pre- and post-ORF periods						
3a. ER oxycodone	23.69	12.12	-49	-52	-46	<.0001
3a.1. Oral	12.44	9.03	-27	-32	-22	<.0001
3a.2. Nonoral	17.83	5.15	-71	-73	-69	<.0001
3b. ER oxymorphone	1.87	5.54	+196	+156	+242	<.0001
3c. ER morphine	5.37	4.7	-12	-21	-2	.0209
Prescription-adjusted§ prevalence rate of abuse among prescription opioid abusers assessed by ASI-MV						
4a. ER oxycodone	.42	.24	-42	-45	-39	<.0001
4b. ER oxymorphone	.33	.60	+80	+56	+109	<.0001
4c. ER morphine	.12	.10	-13	-22	-3	.0094

*Before period = June 2009 through August 8, 2010.

†After period = August 9, 2010, through March 31, 2012. Only ORF (and not OC) is included in this column.

‡Pre-post relative change reflects the percent change in percent abuse from the pre- to post-introduction period.

§Prescription-adjusted prevalence defined as prevalence of past-30-day abuse per 10,000 prescriptions dispensed per month.

Specifically, ER morphine products showed virtually no change in ROA profile across the study periods. ER oxymorphone, however, demonstrated significant increases in snorting (62% of ER oxymorphone abusers versus 69%, $P = .0162$) and injection (9% to 16%, $P = .0124$). The proportion of those who reported smoking the product increased, albeit nonsignificantly, from .2 to 1.9%, while oral abuse of ER oxymorphone decreased significantly (38 to 30%, $P = .0056$).

Frequency of Abuse

Frequency of abuse of ER oxycodone decreased 30% following introduction of ORF (Table 2; average of 10.8 days for OC and 7.5 days for ORF). No significant difference was observed for ER morphine. A 52% increase was observed in the frequency of ER oxymorphone abuse from the pre- to post-ORF period.

Discussion

This article reports on initial findings of one of the epidemiology studies conducted under FDA requirements to examine public health impacts of ORF. To our knowledge, this is the first epidemiological study to examine the public health impact of a tamper-resistant formulation of an extended-release opioid analgesic. Results were consistent with the mechanism of action for an opioid analgesic reformulation aimed at lowering abuse by tampering, and a priori hypotheses were confirmed. Specifically, during the first 20 months following ORF introduction, reformulated ER oxycodone was abused significantly less than original ER oxycodone on 8 outcome measures: 1) prevalence of abuse

by any route among all individuals assessed; 2) prevalence of abuse by oral route; 3) prevalence of abuse by nonoral routes; 4) prevalence of abuse among individuals abusing any prescription opioid; 5) prescription-adjusted prevalence rate of abuse among all individuals assessed; 6) prescription-adjusted prevalence rate of abuse among individuals abusing any prescription opioid; 7) prevalence abusing a drug by injecting, snorting, or smoking; and 8) number of days

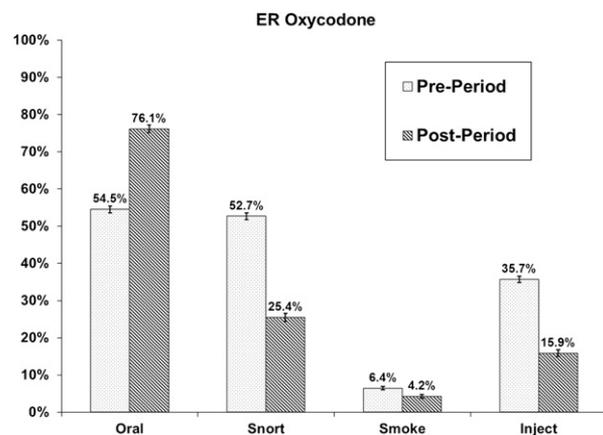


Figure 3. Percent of people abusing ORF and OC historically via specific ROAs* before and after introduction of ORF†. *Percents do not add up to 100% because respondents can report multiple routes of administration. †Pre-period includes only OC while post-period includes only ORF. Because analysis is limited to those reporting abuse of ER oxycodone, a reduction in percent reporting ORF abuse through nonoral routes was accompanied by a corresponding increased percent reporting abuse through oral routes.

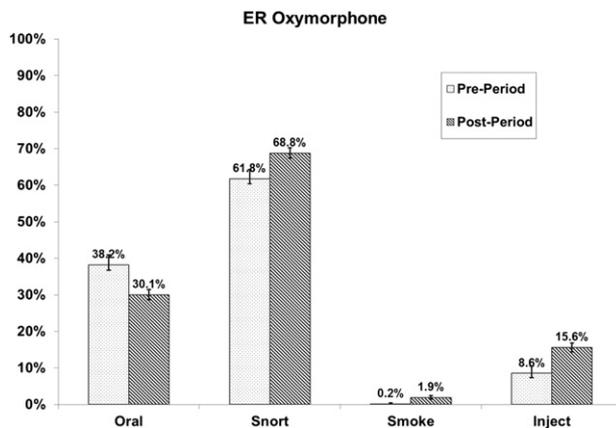


Figure 4. Percent of people abusing ER oxymorphone via specific ROAs* before and after introduction of ORF. *Percents do not add up to 100% because respondents can report multiple routes of administration.

of abuse in the past 30 days. Across all outcomes, effect sizes were large.

Similar changes were not observed for comparator opioid analgesics, suggesting that the ER oxycodone findings were not the result of secular trends during the study period. Comparator products changed little or not at all (ER morphine) or evidenced an increase of abuse (ER oxymorphone).

Several points should be emphasized. First, these findings reflect the experience in the first approximately one-and-a-half years postintroduction of ORF. It is possible that abusers will adapt to thwart the new formulation over time, so continued monitoring is warranted. Second, while the rate of abuse of ORF via both oral and nonoral routes was lower than that for OC historically, the prevalence of oral abuse among abusers of ORF appeared to increase as the prevalence of nonoral abuse of ORF declined. Because the latter prevalence analyses included only those who reported ORF abuse, a decrease in the prevalence of nonoral routes will be associated with an increase in the prevalence of oral use. Third, discontinuation of shipments of OC and introduc-

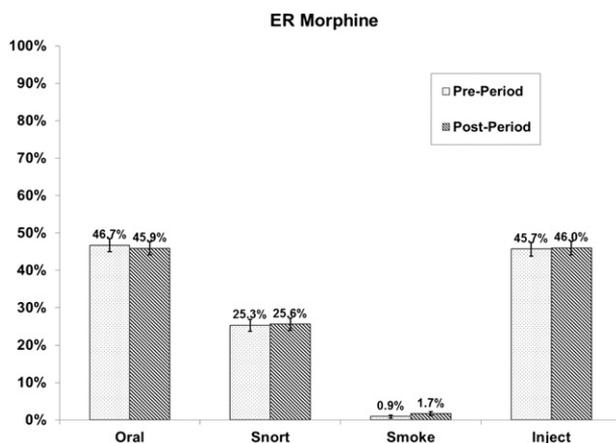


Figure 5. Percent of people abusing ER morphine via specific ROAs* before and after introduction of ORF. *Percents do not add up to 100% because respondents can report multiple routes of administration.

Abuse Rates and Routes of Reformulated ER Oxycodone
 tion of ORF presents challenges to interpreting observed abuse rates, as abuse of a product is related to its level of prescription volume and thus its availability for abuse.^{2,7} While the percentage of respondents who report abusing original ER oxycodone has decreased since introduction of ORF, abuse of the original formulation has remained at a level comparable to that of the reformulated version (Figs 1 and 2). Prescriptions filled at pharmacies for original ER oxycodone constituted 7.4%, 1.8%, and .6% of total ER oxycodone prescriptions in January 2011, June 2011, and December 2011, respectively. The limited supply of original ER oxycodone from prescriptions filled at pharmacies is unlikely to account for the continued levels of abuse of OC reported. However, the time lag from opioid prescriptions filled at pharmacies to the availability to abusers is not known. It is also possible that, despite efforts in the ASI-MV assessment to help respondents differentiate the 2 versions, some degree of misclassification between the original and reformulated versions remains. It is interesting to note, however, that analyses of the ROA profile of original ER oxycodone during the post-ORF period more closely resembles the ROA profile of the original ER oxycodone in the pre-ORF period than ORF in the post-ORF period (eg, injection and snorting of original ER oxycodone after ORF introduction at 31% and 54% of abusers, respectively). Further examination of this issue is planned.

Taken together, the current findings suggest that a formulation of ER oxycodone introduced on a large-scale did impact abuse patterns as reflected in a sentinel surveillance sample of individuals assessed for substance use problems in the first 20 months after introduction. Findings reported here provide postmarketing, "real-world" results that corroborate results from pre-approval pharmacokinetic and abuse liability studies as well as from laboratory extraction studies that demonstrated reduced abuse potential in controlled environments.⁹ This study is part of a series of studies intended to create a mosaic understanding of the broader impact of ORF on abuse and its consequences, including analyses of electronic medical record databases, National Survey on Drug Use and Health data, Internet drug abuse forum monitoring, poison center data, drug diversion surveillance data, and a cohort study of ER oxycodone abusers in Kentucky.⁹ This growing body of work is consistent with the President's plan on addressing prescription drug abuse, which calls for development and testing of abuse-deterrent formulations and for advancing the design and evaluation of epidemiological studies to address changing abuse patterns.²⁴

The limitations and strengths of the present study should be highlighted. As noted, findings are preliminary and abuse patterns may change over time. Use of the ASI-MV sentinel surveillance sample allows examination of abuse trends among a sensitive population at high risk for prescription opioid abuse and likely with a high prevalence of tampering. However, the ASI-MV network is not a probability sample, and results may not be generalizable to the U.S. population of prescription drug abusers. On the other hand, the ASI-MV network has several

Table 2. Changes in Average Number of Days* in the Past 30 Days Reported Abusing ER Oxycodone and Comparator Opioids Before and After Introduction of Reformulated ER Oxycodone

	BEFORE PERIOD† (MEAN DAYS)	AFTER PERIOD‡ (MEAN DAYS)	PRE-POST RELATIVE CHANGE§	95% CI		P VALUE
ER oxycodone	10.75 days	7.48 days	-30.44	-34.90	-25.68	<.0001
ER oxymorphone	5.11 days	7.78 days	+52.23	+23.53	+87.59	<.0001
ER morphine	9.11 days	10.07 days	+10.55	-1.58	+24.19	.0909

NOTE. Time period was 6/1/2009 to 3/31/2012.

*These analyses are limited to cases for which the individual reported at least 1 day of abuse of the opioid.

†Before period = June 2009 through August 8, 2010.

‡After period = August 9, 2010 through March 31, 2012. Only ORF (and not OC) is included in this column.

§Pre-post relative change reflects the percent change in percent abuse from the pre- to post-introduction period.

critical advantages over other national data streams that were recognized by an FDA public Advisory Committee,⁹ including detailed data that differentiate product-specific abuse and ROA in near real-time (compared with lags of 2 years of some national data sources). While selection bias due to the sample of sites cannot be ruled out, it is unlikely that this would account for changes in abuse patterns for ER oxycodone over time, but not for comparator products. The sample size is relatively large and draws from sites across the United States. Although ASI-MV coverage might miss a unique pattern emerging in isolated areas, it is unlikely that a general trend in abuse of these products would be mischaracterized by bias in this sample. To minimize geographic and other covariate confounding, we examined a common subset of assessment sites that provided data during both pre- and post-ORF introduction time periods and included comparator opioids, although similar estimates were obtained when analyses were based on all sites that contributed data during the study period.

The data examined here rely on self-report. This source, however, is the only one that can capture specific products and routes. The assessment is a validated instrument,⁴ and the data were collected as part of a clinical assessment, rather than for purely research purposes, and may therefore be more accurate because reports may influence patients' treatment protocols. The ASI-MV also constitutes a uniform method over time and across sites.⁵ Because both OC and ORF were available for abuse during the post-ORF period, misidentification was reduced by presenting product images, a method shown to reduce reporting bias.¹⁰

The findings presented here reflect observations of ER oxycodone abuse in the first 20 months after ORF introduction in a sentinel surveillance sample of individuals

at high risk for prescription opioid abuse. Consistent with hypotheses, substantially lower rates of abuse of ORF were observed than for OC historically, especially via routes that require tampering, including injection and snorting. While abuse of prescription opioids continues to be a significant public health concern, these findings suggest that this reformulation thus far has been successful in deterring tampering relative to the original formulation. Further research is needed to determine whether these effects persist over time and whether similar effects are observed in other populations that abuse or misuse prescription opioids. Finally, this work serves as a proof of concept that TRFs may help reduce overall abuse and abuse by nonoral ROAs and suggests that TRFs may be a valuable component of the President's plan to employ a multipronged, multi-agency strategy to prevent prescription drug abuse and its consequences.²⁴ At the same time, given the ease with which abusers can currently switch to non-tamper-resistant products, it may be difficult to evaluate the potential public health impact of the new formulations until all prescription opioids include effective tamper-or abuse-resistant properties. This would allow a more definitive national test of the effects of these formulations on the morbidity and mortality associated with prescription opioids.

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