

Changes in Diagnosed Addiction Rates in Patients Prescribed OxyContin or Other Opioids after Introduction of Reformulated OxyContin

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BACKGROUND

- Opioid analgesics are an important option for the treatment of moderate to severe chronic pain, but their potential for abuse presents a significant risk
- OxyContin® (oxycodone HCl controlled release) is an extended-release (ER) oxycodone analgesic that was reformulated in August 2010 with physicochemical barriers to breaking, crushing, or dissolving, intended to deter abuse by injecting and snorting
- Post-marketing studies have reported reductions in abuse of reformulated OxyContin in substance abuse treatment centers¹, poison centers^{2,3}, and abuser cohorts⁴, as well as reductions in overdose fatalities⁵ and in doctor-shopping⁶
- This study assessed changes in the rates of diagnosed addiction/dependence among individuals dispensed OxyContin or other opioid analgesics before and after introduction of reformulated OxyContin
- The research done on validating ICD-9 codes for opioid abuse and addiction/dependence show that these codes capture the intended events. Palmer, et al. in a study at Group Health Cooperative found that 59.4% of patient who had ICD-9 codes for opioid abuse, addiction/dependence diagnoses also had diagnosed opioid abuse or addiction/dependence based on medical chart review.⁵ The number could be higher than 59.4% if cases of addiction did not have this noted in their medical charts

AIMS

- We evaluated changes in the rates of diagnosed addiction among patients prescribed OxyContin after its reformulation. Comparator opioids were used to distinguish OxyContin-specific changes from general opioid changes.
- The analysis focused on experience using a single opioid, rather than multiple opioids concomitantly, so the effect of the single opioid could be studied without the influence of other opioids.

METHODS

- Study Design:** retrospective cohort study
- Dataset:** MarketScan commercial database, August 2009-October 2013
- Population**
 - patients 18-64 years of age
 - incident or prevalent users of OxyContin or 4 comparator opioids
 - separate cohorts were included for each drug.
- Study period:** divided in three times around introduction of reformulated OxyContin
 - 1 year before (August 2009 – July 2010)
 - 3 months transition period (August 2010 – October 2010)
 - 3 years after (November 2010 – October 2013).
- Opioid use:**
 - Duration of continuous use defined by ≤15 days between prescriptions plus 15 days end of last prescription
- Person time of opioid use:**
 - Addition of another opioid during an episode of continuous use of the primary opioid was taken into consideration
 - Person time was divided into two categories: opioid monotherapy and concomitant multiple opioid use
 - Person time in each category was summed for all individuals
 - Person time accumulation began at the date of initial dispensing of opioid and ended at the occurrence of an event or at the end of a dispensed medication use episode, whichever came first
- Diagnosed event of interest:**
 - Based on ICD-9 CM diagnostic codes of 304.0x and 304.7x codes
- Classification of cases:**
 - Cases classified by opioid based on medications used on day of diagnosed event or within 29 days prior to the event

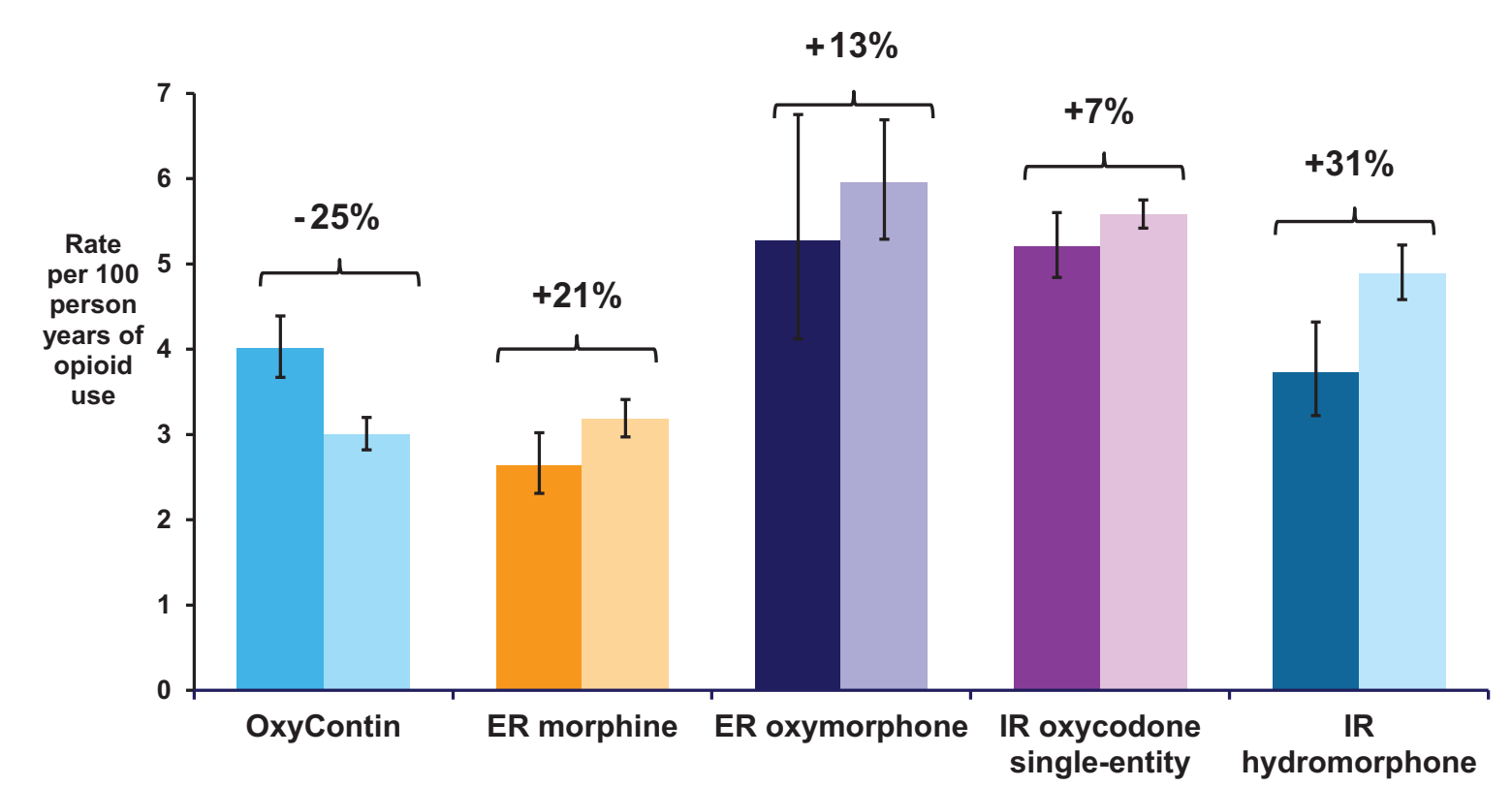
METHODS (CONT.)

- Rates of diagnosed events:**
 - Rates per 100 person years were calculated among patients prescribed OxyContin and comparator opioids
 - Change in rate one year before vs. three years after OxyContin reformulation assessed using Poisson regression
 - The 3-month transition period was excluded when calculating changes from the one year before to the three years after reformulation
 - Difference in change for comparator opioid groups versus OxyContin was calculated

RESULTS

- The rate of diagnosed addiction/dependence decreased 25% in the pre- versus post-reformulation period among patients dispensed OxyContin (Figure 1)
- In contrast, the rate of diagnosed addiction/dependence among patients dispensed other opioids changed by:
 - ER morphine increased 21%
 - ER oxymorphone increased 13%
 - IR oxycodone SE increased 7%
 - IR hydromorphone increased 31%
- The difference in change from baseline for OxyContin minus other comparator opioid groups was significantly different (95% CI did not include) 0% change (Figure 2)
- The rates of diagnosed addiction per 100 person-years of opioid use were lower among patients dispensed OxyContin (3 per 100 person-years of OxyContin monotherapy use) than the rates for the four comparator opioids in the 3 years after reformulation (Figure 3)
- The number of diagnosed addiction/dependence cases decreased by 35% (from 481 to 315 per year), while the person-time decreased by 13%, from 1 year before to 3 years after reformulation (Table 1)

Figure 1. Changes in Rates of Diagnosed Addiction/Dependence per 100 Person-Years of Opioid Use in Individuals Dispensed One Opioid Change from 1 year before to 3 years after introduction of reformulated OxyContin



RESULTS (CONT.)

Figure 2. Difference in Change from Baseline for OxyContin minus Other Opioid Analgesics

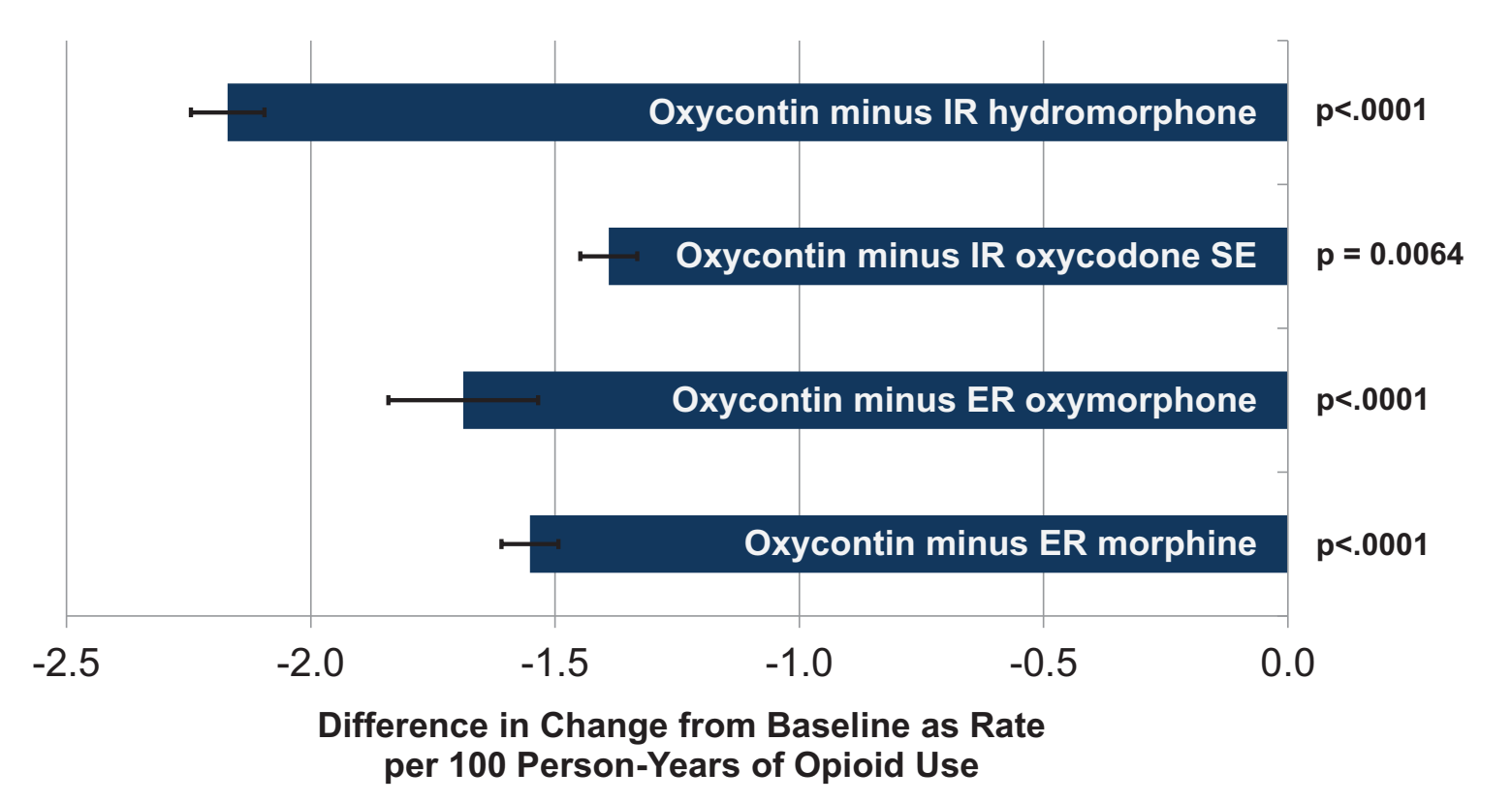


Figure 3. Rates of Diagnosed Addiction/Dependence per 100 Person-Years of Opioid Use in Individuals Dispensed One Opioid, 2011-2013

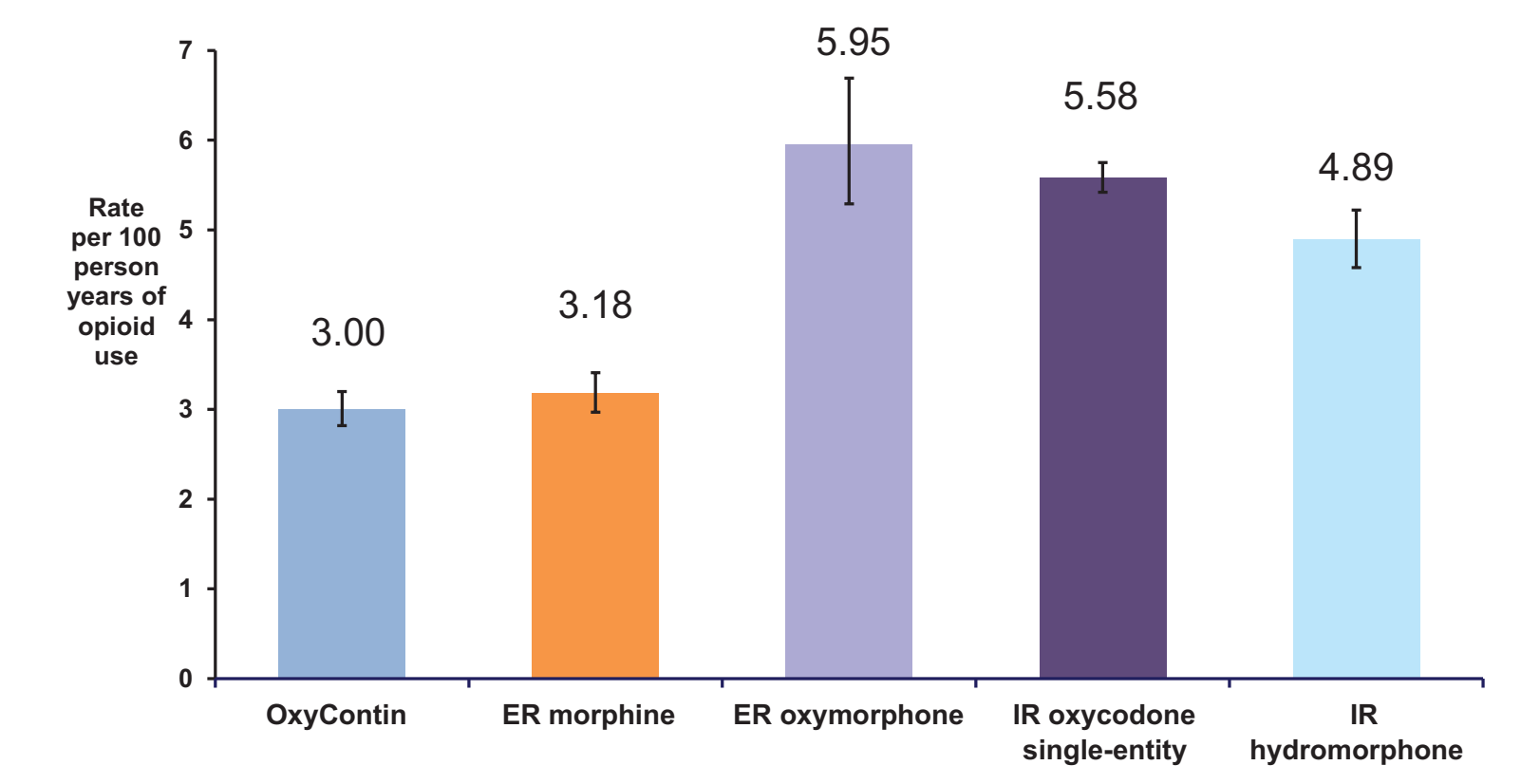


Table 1. Diagnosed Cases, Patients and Person Time for OxyContin and Comparator Opioids before and after Reformulation of OxyContin

	Cases 1 year before	Cases mean of 3 years after	Cases Change	Patients 1 year before	Patients Mean 3 years after	Patient Change	Person-Time 1 year before	Person Time Mean 3 years after	Person-Time Change
OxyContin	481	314	-35%	85,978	87,935	2%	11,987	10,463	-13%
ER morphine	214	267	25%	56,568	62,209	10%	8,102	8,379	3%
ER oxymorphone	63	93	48%	11,644	15,618	34%	1,194	1,562	31%
IR oxycodone SE	726	1,400	93%	135,371	216,566	60%	13,947	25,083	80%
IR hydromorphone	178	301	69%	71,172	86,929	22%	4,777	6,152	29%

ADVANTAGES AND LIMITATIONS OF THE STUDY

- Advantages**
 - Focuses on patients dispensed opioid analgesics
 - A validation study has shown that ICD-9 codes have good positive predictive value
 - Very large sample size
 - Geographically representative of the US
- Limitations**
 - Does not capture Medicare and Medicaid patients
 - Not all events are diagnosed
 - ICD-9 codes assess opioid dependence, a euphemism for addiction, as defined by DSM-IV
 - Not all diagnoses are accurate
 - In patients using multiple opioids cannot identify which opioid associated with addiction

PERSPECTIVE

- Among individuals dispensed OxyContin without other opioids, rates of diagnosed addiction/dependence per 100 person-years of opioid use decreased substantially from one year before to three years after introduction of reformulated OxyContin
- In contrast, rates of diagnosed addiction/dependence increased among individuals dispensed other opioid analgesics in the same time period
- The difference in change from baseline for OxyContin minus comparator opioids was significantly different from 0%
- The results of this study indicate that diagnoses for opioid addiction/dependence decreased among individuals prescribed OxyContin after its reformulation. It is not clear whether diagnoses decreased because abusers stopped using OxyContin or pain patients using OxyContin were less likely to become addicted, or a combination of both
- The findings from this study complement results from studies that assessed the effect of reformulated OxyContin on abuse, misuse, or diversion to provide a more comprehensive assessment of the introduction of reformulated OxyContin on public health

CONCLUSIONS

- Among individuals dispensed OxyContin without other opioids, rates of diagnosed addiction/dependence per 100 person-years of opioid use decreased 25% from one year before to three years after introduction of reformulated OxyContin
- The changes from one-year baseline among patients dispensed OxyContin were significantly different from the changes from baseline for comparator opioid groups
- Abuse of OxyContin is still possible, including by oral use. Appropriately designed and evaluated formulations appear able to improve addiction, however, residual addiction remains. Addiction is a complex problem and a multi-dimensional approach is needed.

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