

## **Reformulation of OxyContin and Pharmacy Dispensing Patterns Near the US-Canada Border**

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Tara Gomes conceived the project, worked on finalizing the methodology, conducted the data analysis, interpreted the findings, and drafted and edited the manuscript. Michael Paterson helped design the study, worked on finalizing the methodology, interpreted the findings, and contributed in editing and reviewing manuscript drafts. David Juurlink helped design the study, interpreted the findings, and contributed in editing and reviewing manuscript drafts. All authors approved the final version of the manuscript. Irfan Dhalla helped design the study, interpreted the findings, and contributed in editing and reviewing manuscript drafts. Muhammad Mamdani helped design the study, interpreted the findings, and contributed in editing and reviewing manuscript drafts.

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## **ABSTRACT**

### **Background**

In August 2010, a tamper-resistant formulation of controlled-release oxycodone (OxyContin-OP) was introduced in the United States (US) but not in Canada. Our objective was to determine whether introduction of OxyContin-OP in the US influenced prescription volumes for the original OxyContin formulation at Canadian pharmacies near the international border.

### **Methods**

We conducted a population-based, serial cross-sectional study among pharmacies in the 3 cities with the highest volume of US-Canada border crossings in Ontario: Niagara Falls, Windsor and Sarnia. We analyzed data on all outpatient prescriptions for OxyContin from pharmacies near each border crossing between April 1, 2010 and February 29, 2012. Monthly prescription rates adjusted per 1000 population, stratified by tablet strength were calculated.

### **Results**

The number of tablets dispensed near four separate border crossings remained stable over the study period. However, the rate of OxyContin dispensing at pharmacies near the Detroit-Windsor Tunnel increased roughly threefold between August 2010 and February 2011, from 685 to 1,969 tablets per 1000 population. By April 2011, following warnings to prescribers and pharmacies regarding drug-seeking behavior, dispensing rates declined to 1,683 tablets per 1000 population. By November 2011, the rates had returned to levels observed in early 2010. These analyses suggest that 242,075 excess OxyContin tablets were dispensed near the Detroit-Windsor Tunnel between August 2010 and October 2011.

## **Conclusions**

OxyContin prescribing rose substantially near a major international border crossing following the introduction of a tamper-resistant formulation in the US. Our findings highlight the potential impact of cross-border differences in medication availability on drug-seeking behavior.

## Introduction

In the United States (US), sales of opioid analgesics have risen by 300% since 1999. While these drugs are generally taken for pain, almost 5% of the population used an opioid analgesic for nonmedical reasons in 2010, and annual opioid overdose death rates neared 15,000 by 2008.[1,2] Of particular concern is the abuse of controlled-release oxycodone (OxyContin), which for more than a decade was subject to misuse by crushing of tablets to allow for inhalation or injection.[3] In April 2010, the United States Food and Drug Administration (FDA) approved a new formulation of OxyContin (OxyContin-OP), that was described by the manufacturer as more difficult to manipulate for the intention of misuse or abuse.[4] In August of that year, US production of the original formulation of OxyContin ceased and all US pharmacies were thereafter supplied with the new, tamper-resistant formulation.

Because the original OxyContin formulation remained available in Canada in 2010, concerns arose that Canada might serve as a *de facto* reservoir for the original formulation of OxyContin. As a result of these concerns, in March 2011 the College of Physicians and Surgeons of Ontario (CPSO) sent a notice to Windsor-area physicians warning of potential drug-seeking behavior, and in April 2011 the Ontario College of Pharmacists (OCP) posted a similar alert on their website.

We examined the impact of the formulation change of OxyContin in the US and the warnings issued by local bodies in Canada on prescriptions for the original formulation of OxyContin at Ontario pharmacies near US-Canada border crossings. We speculated that dispensing of OxyContin in areas of Canada close to border crossings would rise following the introduction of OxyContin-OP in the US, followed by a subsequent drop after the dissemination of warnings to prescribers and pharmacists.

## Methods

We conducted a population-based serial cross-sectional study of all opioids dispensed by pharmacies in Ontario, Canada between April 1, 2010 and February 29, 2012. We restricted our analyses to the three cities in Ontario with the highest volume of private and commercial border crossings in 2011: Niagara Falls (bordering Niagara Falls, New York), Windsor (bordering Detroit, Michigan), and Sarnia (bordering Port Huron, Michigan).[5] Six border crossings were identified in these cities (Table 1), and each was considered separately in the analysis, with the exception of Rainbow and Whirlpool Rapids Bridges, which were combined due to their close proximity. The prescribing region surrounding each border crossing was defined using the largest unit of aggregation for Canadian Postal Codes, and all retail pharmacies operating within each prescribing region were included in the study.

We obtained data on all outpatient prescriptions for OxyContin from retail pharmacies near each border crossing over our study period using the IMS Brogan Canadian CompuScript Database.[6] This database is collected from a sample drawn from an IMS panel of over 5600 pharmacies in Canada, and stratified by province, size, and pharmacy type, and is used regularly for research purposes.[7-9] Monthly prescription volumes are projected by province, and are representative of all pharmacies in Ontario. During the study period, eight OxyContin tablet strengths were available in Ontario: 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg and 80mg. Population estimates within each prescribing region were obtained from the 2006 Statistics Canada census.[10] All analyses were descriptive in nature. We calculated the total number of tablets dispensed and the number of tablets dispensed per thousand Ontario residents at each of the border crossings each month. Volumes were calculated overall and stratified by formulation strength.

## Results

The details of the border crossings are shown in Table 1. The population size of the prescribing regions ranged between 26,129 people (Detroit-Windsor Tunnel) and 50,300 people (Queenston-Lewiston Bridge), and there were between 7 and 25 retail pharmacies in each area. A total of 3.7 million tablets for OxyContin were dispensed over the 23-month study period by pharmacies in the 5 prescribing regions, equivalent to 5,231 tablets per day.

The number of tablets dispensed near the Blue Water Bridge (monthly range 754 to 1008 tablets per 1000 population), Queenston-Lewiston Bridge (monthly range 405 to 529 tablets per 1000 population), Rainbow Bridge/Whirlpool Rapids Bridge (monthly range 1186 to 1437 tablets per 1000 population), and Ambassador Bridge (monthly range 513 to 638 tablets per 1000 population) remained relatively stable over the study period (Figure 1). However, near the Detroit-Windsor Tunnel, the rate of OxyContin dispensing remained stable for the first 4 months of the study period (monthly range between 490 and 505 tablets per 1000 population), and then steadily increased from 685 to 1,969 tablets per 1000 population between August 2010 and February 2011. This fourfold increase was driven primarily by prescriptions for the 10mg, 20mg, 40mg and 80mg formulations with minimal prescribing of all other strengths (Figure 2).

Although OxyContin dispensing rates near the Detroit-Windsor Tunnel remained above baseline level in March 2011, by April (after which both the physician and pharmacist self-regulatory bodies had released warnings) the rates had declined to 1,683 tablets per 1000 population, and by November 2012, the rates had returned to levels observed in early 2010 (Figure 1).

Under the assumption that dispensing of OxyContin near the Detroit-Windsor Tunnel should have been relatively constant between July 2010 and November 2011, we estimated the number of excess OxyContin tablets dispensed over our study period. A total of 13,205 tablets

were dispensed in July 2010. Therefore, our data suggest that 242,075 excess OxyContin tablets were dispensed in the region near the Detroit-Windsor Tunnel between August 2010 and October 2011.

## **Discussion**

In this population-based study, we found an immediate and substantial rise in dispensing of the original formulation of OxyContin near the Detroit-Windsor Tunnel following the introduction of the tamper-resistant formulation in the US. Furthermore, following notification of prescribers and pharmacies in the Windsor area regarding potential diversion of OxyContin, we saw a rapid drop in the dispensing of these products. Interestingly, no similar increase was observed near the other border crossing in Windsor (Ambassador Bridge), or in the areas surrounding other high-volume border crossings in Ontario.

The observation that increased dispensing of OxyContin was limited to the region around the Detroit-Windsor Tunnel warrants discussion. Although both Michigan and New York are identified as “High Intensity Drug Trafficking Areas” (HIDTAs) by the US Department of Justice[11,12], the epicenter of the Michigan HIDTA is Detroit, serving as the primary distribution center for the region.[11] Conversely, in New York state the regions of high drug trafficking are located closer to New York City, farther from the US-Canada border.[12] It is more difficult to explain the differences in OxyContin dispensing patterns between the areas surrounding the Detroit-Windsor Tunnel and the Ambassador Bridge, which are approximately one mile apart. Both regions are of similar size and population density, have a similar number of pharmacies, and are located close to major thoroughfares in both Canada and the US. Of note, however, the Detroit-Windsor Tunnel does not carry large commercial trucks, and provides direct access to downtown Detroit; while the Ambassador Bridge is the busiest commercial border crossing in



North America, and connects directly to a highway. Therefore, it is possible that our findings are related to drug trafficking and transportation patterns in the Detroit area.

Several limitations to our study merit discussion. First, we do not know what proportion of the OxyContin tablets were dispensed to residents of Ontario as compared to people living in other regions. Secondly, we are unable to study individual pharmacies or physicians, and therefore are cannot determine whether the observed increases in OxyContin prescribing are attributable to only a select group of prescribers or pharmacists. Finally, although we cannot directly attribute the drop in OxyContin dispensing in April 2011 to warnings by the physician and pharmacist self-regulatory authorities, we are unaware of any other regulatory or law enforcement efforts that would have precipitated this change.

These findings have important implications for other jurisdictions in North America, particularly with the potential introduction of new opioid formulations in the future, some of which may be tamper resistant and some of which may not (e.g., generic controlled-release oxycodone). It can be expected that the availability of generic drugs may differ between jurisdictions as differing regulatory and formulary decisions are made. The results of this study highlight the impact that differing availability of opioids may have on trafficking across borders, and also suggests that timely notification of prescribers and dispensers of this drug-seeking behavior may help mitigate the problem.

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