

Opioid Use and Overdose: What We've Learned in Ontario

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Abstract

The dramatic rise in prescription opioid use in the past two decades across Canada and the United States has been accompanied by increased rates of adverse events, including premature death and neonatal abstinence syndrome. In Ontario, policies and programs designed to address inappropriate prescribing have been implemented with varying degrees of success. Emerging issues that require ongoing attention include the introduction of abuse-deterrent formulations of opioids and generic versions of long-acting oxycodone. As issues related to opioid misuse, abuse and premature overdose death continue to evolve, it is clear that they can only be addressed by more cautious prescribing practices and the provision of support to those already suffering from addiction.

The Issue

The past 20 years have witnessed a major increase in the prescribing of opioids for chronic pain across North America. This change was rooted in several factors, including the toxicities and limited effectiveness of other analgesics. A key driver, however, was the aggressive lobbying of physicians to prescribe opioids more liberally, under the pretext that the drugs were effective for many patients and the risk of addiction was low. Although these claims were not supported by well-designed studies (Chou et al. 2015; Dhalla et al. 2011), physicians were successfully induced to prescribe opioids as never before.

The dramatic rise in the prescribing of opioids was paralleled by an unfortunate rise in opioid-related harms, including dependence, addiction and death. Since 1997, the U.S. Centers for Disease Control and Prevention estimate that more than 175,000 Americans have died of opioid-related causes (Warner et al. 2014). These deaths represent the “tip of the iceberg,” with

millions of others misusing opioids, seeking care for addiction or suffering from a litany of other opioid-related problems.

This is an issue for policy makers in part because they share a measure of responsibility for the epidemic. In the United States, an Institute of Medicine report on the prevalence of chronic pain exaggerated the scope of the problem and may have been influenced by conflicts of interest (Fauber 2014). In 2000, the Joint Commission – the organization responsible for accreditation of U.S. hospitals – implemented the requirement that hospitals treat pain as a vital sign (Hanks 2008), something it is not, leading to a marked increase in the prescribing of opioids (Mehendale et al. 2013). In Canada, long-acting opioids were added to public formularies because they reduced pain scores to a greater extent than placebo in short-term studies of 12- to 16-week duration, not because they represented safe and effective long-term therapies or because they represented good value for money (Dhalla et al. 2009). Moreover, policy makers must now address the growing legacy of addiction spawned by the widespread use of opioids (Vowles et al. 2015). In short, this problem is not going away.

Trends in Opioid Use and Adverse Events

The use of prescription opioids in Ontario has increased considerably over the past two decades (Dhalla et al. 2009). In 2010, these rates exceeded 600 prescriptions per 1,000 population (unpublished). These rates are even higher among public drug beneficiaries, for whom the rate of prescribing of opioids increased from 1,848 to 2,148 prescriptions per 1,000 population between 2003 and 2008 (Gomes et al. 2011a). These rises have been mirrored by increased rates of adverse events, including neonatal abstinence syndrome (NAS) and death from opioid overdose. In fact, the rate of infants born with NAS increased

almost 15-fold between 1992 and 2011, with the majority of this rise occurring since 2007 (Turner et al. 2015). By 2011, the rate of NAS reached more than four cases per 1,000 live births, and more than 70% of mothers of babies born with NAS who were eligible for public drug coverage received prescriptions for opioids before and during pregnancy (Turner et al. 2015).

Similarly, overdose deaths involving opioids have increased by nearly 250% over the past two decades in Ontario, reaching nearly 42 deaths per million (or 550 deaths) annually by 2010 (Gomes et al. 2014a). Most of these deaths were accidental or of undetermined cause (79.7%) and involved at least one other central nervous system depressant such as alcohol (41.4%), benzodiazepines (50.5%) or multiple opioids (35.7%) (Gomes et al. 2014b). Because many of these deaths involve young people (median age 42 years), the toll on public health is enormous (Gomes et al. 2014a). The years of potential life lost (YLLs) due to premature opioid-related death increased more than three-fold from 1992 (7,006 YLLs) to 2010 (21,927 YLLs), and now surpass the toll from alcohol use disorders (18,465 YLLs) and pneumonia (18,987 YLLs) (Gomes et al. 2014a). In 2010, among Ontarians aged 25–34 years, one in eight deaths was opioid-related (Gomes et al. 2014a).

Relationship between Opioid Dose and Outcomes

In recent years, debate has evolved regarding the definition of a “high” opioid dose and the extent to which patients treated with opioids for chronic non-cancer pain are surpassing this threshold. Most guidelines suggest maximum doses of between 120 and 200 mg morphine or equivalent (MEQ) per day, with additional caution warranted for higher doses (Chou et al. 2009; National Opioid Use Guideline Group 2010; Washington State Agency Medical Directors’ Group 2007). However, in Ontario, 32.6% of all individuals aged 15–64 years receiving long-acting oxycodone under the public formulary exceeded 200 mg MEQ daily, as did approximately 20% of those treated with other long-acting opioids (Gomes et al. 2011a). Furthermore, although these dose thresholds are based on clinical consensus, several studies conducted in the Ontario population demonstrate an association between increasing opioid dose and adverse outcomes. For example, a nested case-control study among Ontarians aged 15–64 years and eligible for public drug coverage found that individuals prescribed more than 200 mg MEQ had a nearly threefold increased risk of fatal opioid overdose compared to those treated with less than 200 mg MEQ (Gomes et al. 2011b). Even moderate opioid doses (between 50 and 199 mg MEQ) were associated with a doubling in the risk of an overdose death (Gomes et al. 2011b). A similarly designed study found a comparable relationship between increasing opioid dose and risk of injury due to motor vehicle accidents when driving (Gomes et al. 2013).

Impact of Opioid Policies

As concerns about opioid misuse have mounted over the past decade, drug policy makers and healthcare professionals have implemented policies and programmes designed to address inappropriate prescribing, with varying degrees of success. For example, the College of Physicians and Surgeons of Ontario (CPSO) offers a course designed to improve physicians’ opioid prescribing habits. An evaluation of the impact of this course found no significant changes in the prescribing patterns of physicians who completed the course voluntarily (Kahan et al. 2013). In contrast, physicians directed to take the course by the CPSO prescribed fewer opioids, but these reductions occurred *prior* to course enrolment, suggesting that awareness of scrutiny by regulatory bodies can dramatically influence prescribing of opioids (Kahan et al. 2013).

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In November 2011, the Ontario Ministry of Health and Long-Term Care (MOHLTC) implemented the *Narcotics Safety and Awareness Act*, a multifaceted strategy designed to promote appropriate narcotic prescribing and dispensing in the province (Ontario MOHLTC 2012). A key component of this strategy was the introduction of a prescription monitoring program, the Narcotic Monitoring System (NMS), which allows the MOHLTC to identify all prescriptions for controlled substances dispensed in Ontario. An evaluation of the impact of the NMS published in 2014 found that the legislation and prescription monitoring program led to significant reductions in the inappropriate prescribing of opioids and other controlled substances (Gomes et al. 2014c). Specifically, the prevalence of opioid prescriptions that are highly suggestive of misuse fell from 1.6% (12,346 prescriptions) in October 2011 to 1.0% (9,138 prescriptions) by May 2013 (Gomes et al. 2014c).

Finally, two studies have been conducted with the goal of determining whether the asynchronous introduction of a new abuse-deterrent formulation of long-acting oxycodone in Canada and the United States was accompanied by evidence of diversion near the border. One study found a significant rise in dispensing of long-acting oxycodone from Canadian pharmacies close to the Detroit Windsor Tunnel following the introduction of tamper-deterrent, long-acting oxycodone in the United States (Gomes et al. 2012). This activity was ameliorated following warnings issued by healthcare professional organizations, but only after an estimated

250,000 additional long-acting oxycodone prescriptions were dispensed over roughly one year of elevated dispensing (Gomes et al. 2012). Interestingly, a more recent study found no evidence of large-scale trafficking of generic long-acting oxycodone from Canada into the United States despite different regulatory decisions regarding the availability of this product in the two countries (Gomes et al. 2015).

Emerging Issues

Two emerging issues that have recently garnered attention are the development of abuse-deterrent formulations (ADFs) of opioids and the introduction of generic versions of long-acting oxycodone. The original formulation of OxyContin was easily crushed and either injected or insufflated nasally. The product's manufacturer withdrew this formulation in the United States in 2010 and in Canada in 2012, replacing it with an ADF formulation (marketed as OxyNEO in Canada) that does not powderize when crushed. Although some evidence suggests that this change was associated with reductions in opioid-related harm, the move was also associated with a marked increase in heroin use, most likely reflecting the transition of abusers from OxyContin to heroin because of the latter's ready availability and low cost (Cicero et al. 2012).

Generic drug manufacturers concurrently developed formulations of long-acting oxycodone that, like the original, are not tamper-resistant. While these products are less expensive than ADF formulations, many jurisdictions, including Ontario, have declined to add them to the public formulary out of concern that they will be especially prone to abuse. Despite their limited availability, there has been concern about the potential for generic non tamper-resistant formulations to negate any positive impact of ADFs. This has led to the federal government's recent announcement that, in the coming years, all opioids marketed in Canada will require abuse-deterrent formulations (Gonçalves 2015). However, experts have expressed concern that ADFs represent a "gimmick" of primary benefit to the pharmaceutical industry and that undue focus on them may undermine more meaningful measures aimed at reducing the harm associated with opioids (Leece et al. 2015).

Conclusion

Although rooted in well-intentioned medical care, the prescription opioid epidemic has evolved into the largest drug safety threat facing Canadians today. Policy makers should have an awareness of the magnitude of the epidemic. They should also understand that measures such as ADFs, while desirable, are not independent solutions. The epidemic can only be addressed by physicians prescribing opioids far more cautiously, and through the provision of support to those already suffering from addiction. **HQ**

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