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COMMENTARY

Prescription opioids, abuse and public health in Canada: is fentanyl the new centre of the opioid crisis?

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For most of the present century, prescription opioid (PO) misuse and related morbidity (e.g. emergency room and substance use treatment admissions), as well as mortality (e.g. fatal poisonings), have formed a major and unique public health crisis in North America.[1,2] In both the USA and Canada, a large proportion of these PO-related harms had been associated with extended-release formulations of oxycodone (e.g. mainly Oxycontin).[2–4] In Canada, specifically, Oxycontin's inclusion in the province of Ontario's public drug benefit formulary was found to be associated with a significant increase in opioid-related deaths in the period 1991–2004.[5] Approximately one-third of POs dispensed (in defined daily doses (DDD))—and up to half or more of opioid-related poisoning deaths—in Canada were Oxycontin-related until 2012, when the majority of Canadian provinces de-listed the drug from its formularies in order to reduce the PO-related public health toll; subsequent to this intervention, both oxycodone formulation dispensing levels and related poisoning mortality—for example in Ontario—substantially declined.[6,7]

While these oxycodone-focused intervention measures have led to reductions in oxycodone-specific use and harm levels, recent data suggest that improvements on this specific front may have been replaced by increases in harms related to other PO formulations—specifically including fentanyl. Fentanyl is a distinct PO formulation product in that it is a highly potent synthetic opioid designed for chronic pain treatment; in recent years—for supposed benefits of increased tamper resistance—it has been marketed largely in formulations for transdermal, intranasal and transmucosal administration.[8,9] Consumption levels of fentanyl have more than doubled in Canada in the past decade (from 4428 DDDs in 2003–2005 to 11 007 DDDs in 2011–2013) and currently make up >35% of overall PO consumption (in DDDs); Canadian fentanyl consumption rates are the highest in the world except for a few European countries, yet surpassing the USA where fentanyl prescriptions have also increased by >500% in the period 1997–2007.[1,10]

Notably, fentanyl is one of two strong PO formulations (besides hydromorphone) registering with persistently increasing dispensing levels in Canada following the delisting of Oxycontin in 2012, and which hence—to an overall substantial extent—have substituted for the reductions in consumption of oxycodone formulations.[6,11] Specifically, while oxycodone dispensing levels (in DDDs) in Canada in 2013—after peaking in 2010/11—have returned to 2007/08 levels, fentanyl dispensing levels have continuously increased by about 50% during that period.[11] Yet markedly more important from a public health perspective is that fentanyl-related poisoning deaths have rapidly increased in jurisdictions across Canada. In Ontario, the annual number of fentanyl-related poisoning deaths more than doubled—from 45 in 2008 to 110 in 2013—and thus counteracted about half the reductions in oxycodone-related deaths observed in 2010–2013.[12] In British Columbia, fentanyl-related deaths more than tripled from 15 in 2012, to 51 in 2013 and 84 in 2014[13]; in Alberta, fentanyl-related poisoning deaths increased from 12 in

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2011 to 150 in 2014.[14] Other Canadian provinces—for example New Brunswick and Saskatchewan—have also reported marked increases in fentanyl-related fatalities; a total number of 655 fentanyl-related poisoning deaths have been estimated for Canada for the period 2009–2014 (but may include underestimations).[15] Moreover, other national jurisdictions (including the USA, Nordic countries, Estonia and Australia) on several continents have reported substantial increases in fentanyl-related mortality over the past decade, largely in the context of parallel increases in the medical availability of fentanyl.[16–19]

The circumstances of fentanyl-related overdose deaths have varied by substance (with either fentanyl alone or combined with other opioid/non-opioid drugs) and by route of administration (including intravenous injection).[8,20,21] Fentanyl mortality rates arose unexpectedly despite the drug's supposed 'tamper-resistant' design (including the transdermal matrix formulation) introduced several years ago. It became quickly evident, however, that the supposed abuse barriers could easily be circumvented and that fentanyl formulations—related to a combination of factors involving their distinct physical design, pharmacological characteristics and high psychoactive utility appeal among abusers—carried an amplified high-risk profile for morbidity and/or mortality outcomes.[9,22,23] Specifically, as fentanyl is a highly potent opioid, transdermal patches provide a high-dose load sufficient for several days of therapeutic use, and even previously used or discarded patches still contain sufficient opioid drug amounts to produce substantial euphorigenic effects, or to contribute to opioid poisoning, and the opioid quantity extracted from patches by tampering is likely to be highly variable and unpredictable.[24] An added distinct feature of recent fentanyl-related mortality incidents in Canada is that they have involved both legitimate fentanyl pharmaceutical products as well as illicitly produced fentanyl products from (domestic and international, mainly suspected in China) clandestine sources; the latter have commonly been mixed into and sold as Oxycontin tablets or heroin by street dealers, presumably trying to capitalize on the limited availability but continued high market appeal of these specific opioid types.[25–27] This constitutes a watershed development in the sourcing pathways for PO misuse in Canada, which previously was dominated by diversion from medical sources but now includes a substantial illicit production and distribution element.

While both public health and law enforcement officials in different Canadian jurisdictions are—in ways closely resembling efforts to the then unfolding 'Oxycontin epidemic' just a few years prior—in the process of developing ad hoc counter-strategies for the emerging fentanyl crisis, this case study reinforces several essential lessons and experiences for public health and policy making in the area of PO misuse and harms. The first is that a series of studies have consistently shown that levels of PO-related morbidity and mortality are strongly correlated with levels of PO-drug availability in the population. The described recent increases in fentanyl dispensing in Canada, combined with the high-risk characteristics of the drug, and subsequent rising mortality rates provide another real-life confirmation of these dynamics.[28–30] Second, there is solid evidence in reference to both legal and illegal psycho-pharmaceutical drug markets that reductions of availability in specific opioid drug commodities (e.g. Oxycontin) without corresponding reductions in demand will likely lead to existing similar drugs (e.g. fentanyl) to increasingly being available and (mis-)used as substitutes for the restricted drug.[7,31] Comparable 'substitution effect' phenomena have been observed in, for example the USA (where recent restrictions on POs have been associated with increases in heroin abuse and harms) and Australia (where a 'heroin drought' has been associated with marked shifts to other, e.g. stimulant, drugs in the early 2000s) in the context of reduced availability of or 'shortages' for specific opioid classes.[32–34]

With persistently high PO availability and demand in Canada, PO-related problems like abuse and/or mortality are unlikely to be effectively addressed by only limited focus or interventions targeting one specific drug type (e.g. whether Oxycontin yesterday or fentanyl today) or ad hoc 'emergency response'-type measures. Existing evidence indicates that these kinds of specific interventions mainly result in displacements or shifts of PO-related problems from one drug type to another. These outcomes are undesirable and ambivalent in their public health benefits and mainly constitute a sort of 'Pyrrhic victory' in efforts of improved PO control. Instead, effective and sustained interventions to reduce PO-related harms are required to comprehensively address the known fundamental determinants and drivers of PO abuse and mortality, which primarily ought to include—but not to be limited to—sensible reductions of the extremely high PO dispensing levels in the Canadian population.[30,35]

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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KEY POINTS

- Extensive spikes in fentanyl abuse and related fatal poisonings have occurred in Canada.
- These increases are following recent reductions in oxycodone-related availability and harms.
- Substitution effects between opioid classes may be at work; a more comprehensive intervention and policy approach is needed.

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