## **Full title:**

Opioid losses in terms of dosage and cost: a retrospective analysis of Health Canada data

#### Authors

Mark Fan, BASc, MHSca, Dorothy Tscheng, BScPhm, CGPb, Michael Hamilton, MD, MPHb, Patricia Trbovich, PhDa,c

## **Author Affiliations**

<sup>a</sup>HumanEra, Office of Research and Innovation, North York General Hospital, 4001 Leslie Street, LE-140, Toronto, ON, Canada, M2K 1E1

<sup>b</sup>Institute for Safe Medication Practices Canada, 4711 Yonge Street, Suite 501, Toronto, ON, Canada, M2N 6K8

<sup>c</sup>Institute of Health Policy, Management and Evaluation, University of Toronto, Health Sciences Building, 155 College Street, Suite 425, Toronto, ON, Canada, M5T 3M6

#### Author Email Addresses

Dorothy Tscheng (dorothy.tscheng@ismpcanada.ca) Michael Hamilton (michael.hamilton@ismpcanada.ca) Patricia Trbovich (patricia.trbovich@utoronto.ca)

## **Corresponding Author**

Mark Fan (mark.fan@nygh.on.ca) Office of Research and Innovation North York General Hospital 4001 Leslie Street, LE-140 Toronto, ON Canada M2K 1E1

Phone: 416-756-6000 x3075

## **Disclosure and Funding Statement**

This work was supported by Becton Dickinson (BD) Canada Inc. [grant #ROR2017-04260]H-NYGH]. BD Canada had no involvement in study design; in the collection, analysis or interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Mark Fan and Patricia Trbovich have received honoraria from BD Canada for presenting preliminary study findings at BD sponsored events. All other co-authors have no disclosures to report.

## **Contributor's Statement**

All authors contributed substantially to the conception, design, and analysis of the study, and all drafted and revised the article and give final approval for publication. All authors agree to act as guarantors of the work to ensure questions related to the work are appropriately investigated and resolved.

## Title:

Opioid losses in terms of dosage and cost: a retrospective analysis of Health Canada data

## **Abstract**

Background: Despite increasing opioid-related mortality, there has been no analysis of opioids lost from healthcare facilities (i.e., community pharmacies, companies, and hospitals). We analyzed opioid losses reported to Health Canada (HC) to identify the amount missing, the distribution of losses between types of facilities, and the direct costs of the lost opioids. Additionally, we compared losses as measured in milligrams, 'dosage units', or 'incidents', to identify how they may lead to different trends and interpretations.

**Methods:** We calculated milligrams of drug lost from 5.75 years of HC data, restricting our analysis to codeine, fentanyl, hydromorphone, morphine and oxycodone. We converted the lost milligrams into oral morphine equivalents, daily defined doses, approximate wholesale value, and approximate street value.

**Results:** Over 112 kilograms of opioids were lost, an estimated \$8.7 million in wholesale cost or \$136 million in street value. Unexplained losses were common, but each facility type had other dominant loss categories: armed robberies and break and enter (community pharmacies), losses in transit (companies), and pilferage (hospitals). Loss trends over 5.75 years varied by reporting unit and facility type: community pharmacy losses increased (dosage units, incidents) or remained stable (milligrams); hospital losses increased (milligrams) or showed no

clear trend (dosage units, incidents); companies showed no clear loss trend from any reporting metric.

**Interpretation:** Large quantities of opioids are going missing and cost healthcare facilities millions of dollars. Controlled drug losses should be reported in milligrams instead of 'dosage units' so that differences in drug strength are accounted for when assessing trends.

## Introduction

In recent years, there has been an increasing recognition of drug theft or loss from hospitals<sup>1–5</sup> and community pharmacies.<sup>6,7</sup> Healthcare facilities bear the cost of medications diverted from their stock. For example, in 2018, hospitals were fined in excess of \$4 million to address inadequate safeguards.<sup>8</sup> Drug thefts cost healthcare facilities in investigations, care for affected patients, and reputation-related damages.<sup>9,10</sup> Furthermore, losses from healthcare facilities may have the potential to increase illegal supply of opioids via trafficking. While data from the US Drug Enforcement Agency (DEA) has reported on opioid losses from healthcare institutions (e.g., community pharmacies, hospitals),<sup>11,12</sup> we are unaware of any similar peer-reviewed or government-sponsored analyses based on Health Canada data.

Health Canada (HC) maintains a database of lost opioids from Canadian facilities that are mandated to report opioid losses to HC within 10 days. <sup>13</sup> Several news outlets have used HC data to report the losses as measured in 'dosage units' or as measured in 'incidents of loss', <sup>16</sup> both of which have important limitations that may not be widely understood. Dosage units indiscriminately count

tablets, vials, and packages as if the losses were equivalent. For example, a 'dosage unit' could refer to the loss of 1 tablet or the loss of 1 bottle containing 500 tablets. 'Incidents of loss' refers to the number of line items in the HC data and could be impacted based on reporting frequency. For example, hospital A may discover an opioid that has been lost several times in the last 2 weeks and generate a single report, whereas hospital B might notice these losses regularly and report after each occurrence. As a result, hospital B would have more 'incidents of lost opioid' even though their total losses of the drug might be smaller. Therefore, losses as measured in 'dosage units' or 'incidents' do not support comparative analyses (e.g., differences year to year or between institutions).

Reporting opioid losses in 'dosage units' is a phenomenon that extends beyond Canada. In the US, losses of opioids from healthcare facilities are captured in the DEA's Drug Theft and Loss database. A 2018 DEA report identifies 97.5 million dosage units of lost opioids between 2010 to 2017. Given that both Canadian and US reports of opioid losses are based on 'dosage units', policy makers have not yet had reliable data to accurately assess or compare losses year to year, nor can they accurately estimate costs of the lost drug based on dosage units alone.

To rectify this situation, we analyzed HC data to 1) estimate actual milligram losses for five common opioids, and used this to estimate the approximate wholesale and street value of lost opioids in Canada, 2) compare losses, and reason for loss, by facility type, and 3) compare opioid loss trends as measured by milligrams, dosage units, and incidents of loss to determine whether they suggest

different interpretations, and to select the metric that best represents quantity and cost of lost opioids.

## Methods

## **Data Source**

HC data on controlled drug losses is currently only accessible on request via Access to Information (ATI) legislation, a process which has been criticized for lack of timeliness. In June 2018, CBC News published HC data from an ATI request for all controlled drug losses between January 1, 2012 to September 30, 2017. Is, is the largest release we are aware of and is therefore valuable for assessing trends in Canadian healthcare sources. Pilot work by the authors suggests that HC data represents the best source of data on the incidence of Canadian drug losses (see Appendix).

## **Inclusion Criteria and Constraints**

We limited our analysis to the most commonly dispensed opioids in Canada based on data from the Canadian Institutes of Health Information<sup>20</sup>: codeine, fentanyl, hydromorphone, morphine, and oxycodone. Tramadol is among the 6 most dispensed opioids in Canada,<sup>20</sup> but is not yet classified as a controlled substance,<sup>21</sup> so no loss reports were captured for this drug.

## Data Analysis

HC data states a numeric 'quantity' lost for each line item, but the 'unit code' (e.g., millilitres, tablets, patches) for each report varies. We used this information to manually calculate the milligrams lost for every reported drug loss. We then used

the milligrams lost to calculate oral morphine equivalents (OMEQ) and daily defined doses (DDD) (see Appendix for conversion factors).

We deliberately used the lowest estimate of loss for ambiguous reports. For example, one report lists the loss of 728 'packages' of Hydromorphone HP 50mg/mL. From the dataset, it is unclear whether these containers were 1mL, 5mL, 10mL, or 50 mL (each coming in boxes of various sizes). In this case, the smallest available package per the drug product monographs found on Health Canada's Drug Product Database<sup>22</sup> is a box of 10, 1mL vials.

## Wholesale and Street Drug Costing

Approximate wholesale costs were calculated from the Ontario Drug Benefit (ODB) database for the entire dataset because Ontario lost the most OMEQs of all provinces. If the cost was not available from ODB, other provincial formularies were searched (see Supplemental file for wholesale pricing information). While street value fluctuates<sup>23,24</sup> depending on cycles of supply and demand, geography, and drug strength, we used a single point-in-time street value based on information from the Ontario Provincial Police and literature (see Appendix).

## Results

An analysis of all 64,964 loss reports determined that the cumulative loss of codeine, fentanyl, hydromorphone, morphine and oxycodone in the timeframe of January 2012 to September 2017 was over 112 kilograms (Table 1). This equates to approximately \$8.7 million in wholesale costs and \$136 million if all lost drugs were resold on the street.

<Table 1>

Community pharmacies, companies, and hospitals are responsible for nearly all losses, comprising 76.8%, 17.1% and 6% of lost OMEQs, respectively (Table 2).

As a result, we focused all subsequent analyses on these three facility types.

<Table 2>

The dominant reasons for loss (in milligrams) varies by facility type (Table 3). Community pharmacy losses are primarily from armed robberies (31.1%), break and entry (28.1%), unexplained losses (17.6%), and pilferage (15.5%). Company losses are primarily from unexplained losses (55.8%) and losses in transit (30.7%). Hospitals are primarily affected by pilferage (57.4%) and unexplained losses (33.4%). More detailed breakdowns of loss trends by province or territory for community pharmacies and hospitals show that British Columbia (BC) has made significant reductions in community pharmacy losses over time, whereas Ontario hospitals report an increasing amount of pilferage losses in recent years (see Appendix sections 5 and 6).

<Table 3>

Reporting milligrams of lost opioids shows different trends than when reporting dosage units, or number of 'incidents of loss' (Table 4). Specifically, the incidents of loss and dosage units lost from community pharmacies have steadily increased since 2012, but milligram losses have not. Conversely, hospitals show increased milligram losses in recent years, whereas line items and dosage units do not show the same trend. There is no clear trend discernable from any of these metrics for companies. See Appendix section 7 for a visual depiction of trends.

<Table 4>

## **Interpretation**

We found Canadian facilities lost an annual average of 19.6 kilograms of five common opioids; this equates to an annual value of approximately \$23.7 million in street value. Community pharmacies were the largest contributor to the losses, followed by companies and hospitals. Unexplained losses were a major category of loss in all facility types, but each facility type was also particularly susceptible to certain types of loss: community pharmacies were most susceptible to armed robbery and break and enter, hospitals faced a high rate of pilferage, and companies experienced a high proportion of drug losses in transit. Our analysis also showed that community pharmacy losses remained stable over time as measured by dose (i.e., milligrams), but loss rates appeared to be increasing when measured by dosage units or incidents of loss. Opioid losses from hospitals are increasing when measured in dose, but a clear trend is not visible when measured by dosage units or incidents of loss. Based on this data, we suggest that losses as measured by dosage units or incidents of loss can mischaracterize the severity of the opioid loss; a dose based metric (e.g., milligrams, OMEQs) provides a more accurate means of assessing loss trends over time within and between facility types or provinces.

Our analysis suggests that differences in inspection practices across community pharmacies and hospitals may have contributed to differences in how opioid losses are reported. For example, Health Canada began a community pharmacy inspection program (CPIP) in 2015.<sup>25</sup> Our analysis shows a clear upward trend in the number of line items and dosage units of opioid lost after this program

began, but there has been no substantial increase in milligrams lost. It appears the CPIP may have triggered a higher frequency of reporting from community pharmacies, but each report now describes smaller losses on average. In contrast, starting in 2016, Ontario hospitals reported a dramatic increase in milligrams lost to pilferage (Appendix section 6). One hypothesis is that this is the result of the Ontario College of Pharmacists' (OCP's) new mandate to inspect and accredit all hospital pharmacies for the first time, which began in 2016.<sup>26</sup> Perhaps OCP inspections led hospital pharmacies to enhance their record-keeping and subsequently led to a greater detection of lost or stolen opioids. Although the reasons for this change are unclear, we note that OCP inspects every hospital pharmacy, while CPIP only conducts inspections on a random subset of community pharmacies. Perhaps if a greater number of community pharmacies were inspected, there would be a stronger regulatory pressure to ensure strong controlled drug management processes and by extension, community pharmacies would detect and report a higher number of losses in response to the CPIP. Given the potential impact of inspection programs on the detection and reporting of opioid losses, further research is required to investigate whether expanded inspection programs for community pharmacies, companies, and hospitals may be helpful in all Canadian provinces and territories.

Fortunately, our analysis also suggests productive next steps for some areas. For example, British Columbia demonstrates a remarkable reduction in community pharmacy losses from armed robberies and break and enter incidents (see Appendix Table A7), possibly due to the implementation of time-delay safes.<sup>27,28</sup>

Sharing of best practices between provinces may therefore help reduce opioid losses in the future. Similarly, if other provinces were to adopt a hospital accreditation process like the OCP, it is possible that a similar increase in the detection or reporting of opioid losses from other provinces' hospitals could occur.

Our data also suggests areas where more attention is needed. For example, community pharmacies, companies and hospitals all cite 'unexplained losses' as a major category of loss. Across these facility types, approximately 24.4 kilograms opioids were lost without an explanation. Canadian facilities either lack sufficient guidance on how to track and account for controlled drugs, or are unable to implement known best practices; further work is urgently needed to amend this issue. While a recent scoping review outlines the literature on this topic for hospital settings, we are not aware of literature for community pharmacies or companies. Notably companies lost 17.1% of the OMEQs in our dataset, and 'losses in transit' are responsible for 30% of company losses. Further oversight of commercial entities may be an important priority for policy-makers and regulators moving forward.

We suspect that the true quantities of loss are even higher than what our analysis suggests. This is because previous literature highlights challenges with respect to detecting or reporting losses for both controlled and non-controlled drugs (e.g., propofol). For example, hospitals have previously been fined for insufficient record-keeping and failing to report drug losses. <sup>29–31</sup> One endoscopy clinic found over \$10,000 of propofol was unaccounted for in only a 4 week period. <sup>32</sup> These examples suggest that poor traceability obscures detection and reporting of drug losses. In addition, there are other controlled substances that are

reported to HC that we did not analyze, but may be prone to misuse and diversion (e.g., benzodiazepines). Inclusion of non-opioids in future studies would increase the total doses lost, and the subsequent costs of lost drug.

Moving forward, we suggest that Health Canada (HC), like the DEA, <sup>12</sup> publish a freely accessible report describing controlled substance losses, preferably on an annual basis. This report would facilitate a more accurate and regular assessment of controlled substance losses. However, we recommend the report describes dose (i.e., milligrams, OMEQs) losses by province and territory for use by policy makers and the public. As described previously, our findings show that milligram losses provide a more accurate representation of opioid loss trends than either dosage units or incidents of loss. Therefore, the HC loss and reporting form should capture the number of milligrams lost per drug, and the dosage format of the loss. The current HC form is ambiguous as the reported quantity could refer to the dosage form (e.g., patch, ampoule), or the unit (e.g., micrograms, millilitres). We believe such an annual report of dose losses will promote discussion and sharing of best practices, possibly accelerating uptake of safeguards across the country.

## **Limitations**

Our analysis has several limitations. First, HC data may be subject to reporting bias. Jurisdictions with high reported losses may not be undergoing a higher true loss rate, but may only be more diligent at reporting the losses they do experience. Second, not all drugs reported lost are due to diversion, and diverted drugs may be used personally rather than resold on the street market. Our analysis is not intended to estimate actual revenue from street sales of lost drug, but to

contextualize the potential losses and highlight the differences between wholesale costs and street value. Third, our estimates of wholesale costs and street value are simplified, as we applied single point-in-time estimates from select provincial formularies or police services to the whole dataset.

## Conclusion

The drug losses we have conservatively estimated are large and suggest the need for further research given the other indirect costs of drug diversion. For example, drugs diverted from the healthcare system can be resold, channelling taxpayer dollars directly into the hands of drug traffickers, while increasing the supply and harms of illicit opioids to surrounding communities and burdening patients and prescribers who require opioids for legitimate medical use. Ensuring that reports of controlled drug loss unambiguously capture the dose (e.g., milligrams) of the loss, as well as transparent and standardized methods of making this data available, will further the understanding and causes of opioid losses from Canadian facilities.

## **Acknowledgements**

We thank Chris Auger (Ontario Provincial Police) for providing estimates of street value per milligram. We also thank Danny Liu, Lauren Datema, Emily Brown, Kiera Robinson (Doctor of Pharmacy Students), for collecting wholesale drug pricing information and parsing the Health Canada dataset. We thank Iveta Lewis (Information Scientist) for searching the literature on drug street prices. Our thanks to Tara Carman and CBC News for publishing the Health Canada dataset that was

the basis for this article.

## References

- Berge KH, Dillon KR, Sikkink KM, Taylor TK, Lanier WL. Diversion of Drugs
   Within Health Care Facilities, a Multiple-Victim Crime: Patterns of Diversion,
   Scope, Consequences, Detection, and Prevention. Mayo Clin Proc [Internet].
   2012;87(7):674–82. Available from:
   http://dx.doi.org/10.1016/j.mayocp.2012.03.013
- 2. Brummond PW, Chen DF, Churchill WW, Clark JS, Dillon KR, Dumitru D, et al.

  ASHP Guidelines on Preventing Diversion of Controlled Substances. Am J Heal

  Pharm [Internet]. 2017 Mar 1;74(5):325–48. Available from:

  https://academic.oup.com/ajhp/article/74/5/325/5103352
- 3. Canadian Society of Hospital Pharmacists. Controlled Drugs and Substances in Hospitals and Healthcare Facilities: Guidelines on Secure Management and Diversion Prevention [Internet]. 2019. Available from:

  https://www.cshp.ca/sites/default/files/files/publications/Official
  Publications/Guidelines/Controlled Drugs and Substances in Hospitals and Healthcare Facilities\_2019\_02-28.pdf
- 4. Schaefer MK, Perz JF. Outbreaks of Infections Associated With Drug Diversion by US Health Care Personnel. Mayo Clin Proc [Internet]. 2014;89(7):878–87.

  Available from: http://dx.doi.org/10.1016/j.mayocp.2014.04.007
- 5. Fan M, Tscheng D, Hamilton M, Hyland B, Reding R, Trbovich P. Diversion of Controlled Drugs in Hospitals: A Scoping Review of Contributors and Safeguards. J Hosp Med [Internet]. 2019;15(7):419–28. Available from:

- https://www.journalofhospitalmedicine.com/jhospmed/article/202732/hospital-medicine/diversion-controlled-drugs-hospitals-scoping-review
- 6. Carman T, Adhopia V. More than 9 million prescription drugs have gone missing from pharmacies since 2012 [Internet]. CBC News. 2018. Available from: https://www.cbc.ca/news/canada/missing-drugs-pharmacies-part1-1.4708041
- 7. LaVigne N, Wartell J. Robbery of Pharacies [Internet]. Washington, D.C.; 2015.
  Available from:
  https://www.popcenter.org/sites/default/files/problems/PDFs/robbery\_of\_pharmacies.pdf
- 8. Stanton C. 18.7M pills lost due to healthcare employee misuse and theft

  [Internet]. Protentus. 2018. Available from:

  https://blog.protenus.com/18.7m-pills-lost-due-to-healthcare-employee-misuse-and-theft
- 9. Berge KH, Lanier WL. Bloodstream infection outbreaks related to opioid-diverting health care workers: A cost-benefit analysis of prevention and detection programs. Mayo Clin Proc [Internet]. 2014;89(7):866–8. Available from: https://www.scopus.com/inward/record.uri?eid=2-s2.0-84904717730&doi=10.1016%2Fj.mayocp.2014.04.010&partnerID=40&md5=3d47cd0f14c1097da465917935f6831d
- 10. New K. Investigating Institutional Drug Diversion. J Leg Nurse Consult [Internet]. 2015;26(4):15–8. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=113626

- 679&site=ehost-live
- 11. Joranson DE, Gilson AM. Drug crime is a source of abused pain medications in the United States. J Pain Symptom Manag [Internet]. 2005;30(4):299–301.
  Available from: http://dx.doi.org/10.1016/j.jpainsymman.2005.09.001
- 12. Drug Enforcement Administration. 2018 National Drug Threat Assessment [Internet]. 2018. Available from: https://www.dea.gov/sites/default/files/2018-11/DIR-032-18 2018 NDTA final low resolution.pdf
- 13. Health Canada. Reporting of loss or theft of controlled substances, precursors and cannabis Canada.ca [Internet]. 2018. Available from:

  https://www.canada.ca/en/health-canada/services/publications/healthy-living/loss-theft-controlled-substances-precursors.html
- 14. Carman T, Adhopia V. More than half a million prescription drugs are stolen each year and most are opioids [Internet]. CBC News; 2018. Available from: https://www.cbc.ca/news/canada/missing-drugs-pharmacies-part1-1.4708041
- Tromp S. Prescription drug losses, thefts on the rise at smaller B.C. hospitals.
  The Globe and Mail [Internet]. 2016; Available from:
  https://www.theglobeandmail.com/news/british-columbia/prescription-drug-losses-thefts-on-the-rise-at-smaller-bc-hospitals/article28826576/
- 16. Howorun C. "Unexplained losses" of opioids on the rise in Canadian hospitals

  [Internet]. 2017. Available from:

  http://www.macleans.ca/society/health/unexplained-losses-of-opioids-on-

- the-rise-in-canadian-hospitals/
- 17. Pagliaro J. How the freedom of information system often results in secrecy instead of transparency. The Toronto Star [Internet]. 2019 May 7; Available from: https://www.thestar.com/news/city\_hall/2019/04/18/how-the-freedom-of-information-system-often-results-in-secrecy-instead-of-transparency.html
- 18. Carman T. Analysis of Health Canada missing controlled substances and precursors data, Jan. 1, 2012 Sept. 30, 2017 [dataset] [Internet]. 2018. Available from: https://github.com/taracarman/drug\_losses
- 19. Carman T. When prescription opioids run out, users look for the supply on the streets [Internet]. 2018. Available from:
  https://www.cbc.ca/news/canada/when-prescription-opioids-run-out-users-look-for-the-supply-on-the-streets-1.4720952
- 20. Canadian Institute for Health Information. Pan-Canadian Trends in the Prescribing of Opioids and Benzodiazepines, 2012 to 2017 — Data Tables [Internet]. 2018. Available from: https://www.cihi.ca/sites/default/files/document/pan-canadian-prescribed-opioid-benzo-data-tables-june18-en-web.xlsx
- 21. Government of Canada. Forward Regulatory Plan 2019-2021: Regulations amending Schedule I to the Controlled Drugs and Substances Act and the Schedule to the Narcotic Control Regulations to add tramadol and related substances [Internet]. 2019 [cited 2019 May 14]. Available from: https://www.canada.ca/en/health-canada/corporate/about-health-

- canada/legislation-guidelines/acts-regulations/forward-regulatory-plan/plan/tramadol.html
- 22. Health Canada. Drug Product Database online query [Internet]. 2019 [cited 2018 Oct 5]. Available from: https://health-products.canada.ca/dpd-bdpp/index-eng.jsp
- 23. Lebin JA, Murphy DL, Severtson SG, Bau GE, Dasgupta N, Dart RC. Scoring the best deal: Quantity discounts and street price variation of diverted oxycodone and oxymorphone. Pharmacoepidemiol Drug Saf [Internet]. 2019;28(1):25–30. Available from: http://dx.doi.org/10.1002/pds.4558
- 24. Dasgupta N, Freifeld C, Brownstein JS, Menone CM, Surratt HL, Poppish L, et al. Crowdsourcing black market prices for prescription opioids. J Med Internet Res [Internet]. 2013;15(8):e178. Available from: http://dx.doi.org/10.2196/jmir.2810
- 25. Health Canada. Community Pharmacy Inspection Program Annual Report,
  Fiscal Year 2015-2016 [Internet]. 2017 [cited 2019 Apr 18]. Available from:
  https://www.canada.ca/en/health-canada/services/drugs-healthproducts/reports-publications/compliance-enforcement/communitypharmacy-inspection-program-annual-report-fiscal-year-2015-2016.html
- 26. Foxman S. Baseline Assessments Reveal Opportunities for Hospital
  Pharmacies. Pharm Connect [Internet]. 2016;23(1):8–33. Available from:
  http://www.ocpinfo.com/library/practicerelated/download/BaselineAssessmentsWinter2016.pdf
- 27. Lindsay B. Time-delay safes linked to steep drop in robberies from B.C.

- pharmacies [Internet]. CBC News. 2018. Available from: https://www.cbc.ca/news/canada/british-columbia/time-delay-safes-linked-to-steep-drop-in-robberies-from-b-c-pharmacies-1.4725455
- 28. College of Pharmacists of British Columbia. Pharmacy Security Requirements:
  What's in Effect Today? [Internet]. 2017 [cited 2019 Apr 18]. Available from:
  https://www.bcpharmacists.org/readlinks/pharmacy-securityrequirements-what's-effect-today
- 29. Department of Justice-U S Attorney's Office District of Massachusetts. MGH to Pay \$2.3 Million to Resolve Drug Diversion Allegations [Internet]. 2015.

  Available from: https://www.justice.gov/usao-ma/pr/mgh-pay-23-million-resolve-drug-diversion-allegations
- 30. United States Department of Justice. Southern District Of Georgia Announces

  Largest Hospital Drug Diversion Civil Penalty Settlement in U.S. History

  [Internet]. 2018. Available from: https://www.justice.gov/usaosdga/pr/southern-district-georgia-announces-largest-hospital-drugdiversion-civil-penalty
- 31. Drug Enforcement Administration. Record settlement reached in University of Michigan hospital drug diversion civil penalty case [Internet]. 2018. Available from: https://www.dea.gov/press-releases/2018/08/30/record-settlement-reached-university-michigan-hospital-drug-diversion
- 32. Horvath C. Implementation of a new method to track propofol in an endoscopy unit. Int J Evid Based Healthc. 2017;15(3):102–10.

Table 1

Table 1									
Analysis of o	Analysis of opioid losses reported to Health Canada (Jan 2012 to Sept 2017)								
	Route	Milligrams	Oral	Daily	Estimated	Estimated			
		lost	Morphine	Defined	Wholesale	Street Value			
		(rounded)	Milligram	Dose	Value				
			Equivalent	(DDD)					
			(OMEQ)						
Codeine	Oral	47,072,328	7,060,849	196,135	\$1,313,140	\$52,956,369			
	Injectable	3,720	930	58	\$514	\$4,185			
	Indetermi	228,717	34,308	953	\$6,369	\$257,306			
	nate								
Fentanyl	Oral	66,828	8,687,588	111,379	\$3,212,163	\$26,731			
	Injectable	10,642	1,064,527	66,513	\$302,036	\$4,257			
	Patch	184,032	18,403,190	153,360	\$199,936	\$5,111,997			
	Indetermi	2,691	349,819	4,486	\$129,346	\$1,077			
	nate								
Hydro-	Oral	12,157,649	60,788,244	607,882	\$1,446,912	\$18,236,474			
morphone									
	Injectable	544,387	9,526,775	136,097	\$199,890	\$816,581			
	Rectal	468	2808	117	\$593	\$702			
	Indetermi	19,202	96,008	960	\$2,288	\$28,803			
	nate								
Morphine	Oral	15,154,599	15,154,599	151,546	\$353,846	\$12,578,317			
	Injectable	325,571	976,713	10,852	\$205,417	\$270,224			
	Rectal	73,045	87,654	2,435	\$11,318	\$60,627			
	Indetermi	134,692	134,692	1,347	\$3,151	\$111,794			
	nate								
Oxycodone	Oral	36,537,298	54,805,947	487,164	\$1,312,734	\$45,671,623			
	Rectal	9,580	17,244	319	\$3,229	\$11,975			
Total		112,525,448	177,191,636	1,931,603	\$8,702,882	\$136,149,042			

**Notes:** Oral refers to tablets, capsules, sublingual and oral solutions (e.g., syrups). Injectable includes intravenous and subcutaneous formats. Fentanyl is typically dosed in micrograms, but for consistency with other drugs we report in milligrams. Indeterminate refers to line items in the dataset where the route or format of the drug was ambiguous. See Appendix for details on how OMEQ, DDD, wholesale and street value were calculated.

Table 2

Oral Morphii	ne Equivalei	nts (Milligram	s) Lost by Facility T	ype (Jan 2012	to Sept 2017)	
	Codeine	Fentanyl	Hydromorphone	Morphine	Oxycodone	Total (% of column total)
Community Pharmacy	6,222,350	16,983,007	46,535,105	14,255,156	52,112,872	136,108,490 (76.8)
Companies	815,047	10,041,648	15,730,665	1,432,737	2,298,522	30,318,620 (17.1)
Hospital	42,530	1,468,245	8,143,350	647,885	395,222	10,697,232 (6.0)
Long term care facility	11,733	1,999	3,170	930	15,473	33,304 (0)
Nurse station*	3,653	2,000	420	8,580	578	15,230 (0)
Canadian Forces Base	774	7,250	1,100	1,200	525	10,849 (0)
Ambulatory Services <sup>%</sup>	-	1,975	25	7,170	-	9,170 (0)
Total	7096.1	28,506.1	70,413.8	16,353.7	54,823.2	177,192.9

<sup>\*</sup> Nurse stations are found in small rural and isolated communities where access to health care is otherwise limited; they are staffed by registered nurses or nurse practitioners typically providing primary care, and have limited on-site availability of a physician partner.

<sup>&</sup>lt;sup>%</sup> Ambulatory Services are typically clinics affiliated with an institution/hospital and provide procedures or services on an outpatient basis or are stand-alone clinics providing similar services.

Table 3

Tubic 5									
Milligrams Lost by Loss Description and Facility Type (Jan 2012 to Sept 2017)									
		% of		% of		% of			
	Community	column		column		column			
	Pharmacy	total	Companies	total	Hospitals	total			
Armed Robbery	30,935,204	31.1	10,948	0.1	16	0.0			
Break and Entry	27,978,876	28.1	147,467	1.3	64,105	4.5			
Breakage – In Transit	275,596	0.3	58,570	0.5	345	0.0			
Breakage – On Site	5,898	0.0	=	0.0	595	0.0			
Grab Theft	1,381,305	1.4	790,586	6.9	34,337	2.4			
Impersonation	74,438	0.1	-	0.0	-	0.0			
Loss in Transit	159,177	0.2	3,538,645	30.7	15,186	1.1			
Loss Unexplained	17,481,035	17.6	6,429,180	55.8	475,411	33.4			
Manufacturer's Defects									
(Ampoules)	20	0.0	100	0.0	15	0.0			
Manufacturer's									
Shortage (Sealed Bottles)	28,642	0.0	34,543	0.3	1,066	0.1			
•									
Other	5,659,021	5.7	248,294	2.2	14,289	1.0			
Over shipment (picking	422		2.000	0.0		0.0			
error)	433	0.0	2,800	0.0	-	0.0			
Pilferage	15,459,032	15.5	260,175	2.3	817,574	57.4			
Spillage	6,062	0.0	-	0.0	242	0.0			
Under shipment	4,050	0.0	389	0.0	-	0.0			

Table 4

Comparison of Incidents of Loss, Dosage Units Lost, and Milligrams Lost by Facility Type (Jan 2012 to Sept 2017)								
<b></b>	2012	2013	2014	2015	2016	2017 (up to Sept. only)	R <sup>2</sup> Value	
Community Pharmacies								
Incidents of Loss	4587	3948	5879	7768	13743	22517	0.809	
Dosage units lost	736,886	596,185	947,010	978,053	1,152,808	1,425,626	0.870	
Milligrams lost	17,090,993	10,904,398	16,870,555	18,286,108	17,425,604	18,871,131	0.308	
Companies								
Incidents of Loss	338	412	524	568	407	252	0.034	
Dosage units lost	90,562	136,032	173,273	111,022	53,296	24,053	0.399	
Milligrams lost	1,355,671	1,974,753	2,144,427	1,585,595	3,680,476	780,775	0.008	
Hospitals								
Incidents of Loss	650	673	649	625	707	576	0.124	
Dosage units lost	29,692	17,820	47,679	18,379	45,929	16441	0.002	
Milligrams lost	128,593	155,630	88,264	213,066	318,768	518,859	0.738	

## **Appendix**

The appendix is composed of eight sections.

- Database scan: This section describes the methods and results of a pilot study the authors
  conducted to determine what databases containing controlled drug loss reports were available
  in Canada. Health Canada's controlled drug loss database proved to have the largest volume of
  data for analysis.
- 2. **Milligram calculation procedure:** This section outlines the steps the authors undertook to extract the milligram losses from the Health Canada dataset, including assumptions we made for rows that were ambiguous in nature.
- 3. **Conversion factors:** This section outlines the conversion factors used to convert the milligrams lost into Oral Morphine Equivalents (OMEQs) and Daily Defined Doses (DDDs). It includes the references and reasoning we used to select the conversion factors. \*\*These conversion factors should not be used for clinical purposes\*\*
- 4. Street pricing estimates: This section describes our strategy for estimating street pricing.
- 5. **Opioid milligram losses for community pharmacies:** This section provides an extended table showing the milligram losses for community pharmacies from each province and territory. The only loss types shown are armed robbery, break and entry, unexplained losses and pilferage, as these are the major categories of loss for pharmacies (see Table 3 in the main article).
- 6. **Opioid milligram losses for hospitals:** This section provides an extended table showing the milligram losses for hospitals from each province and territory. The only loss types shown are unexplained losses and pilferage, as these are the major categories of loss for hospitals (see Table 3 in the main article).
- 7. Line graphs depicting loss trends for community pharmacies, companies, and hospitals: Loss trends differ when measured in milligrams, dosage units, and incidents of loss (e.g., line items in Health Canada data).
- 8. Reference list for Appendix

## 1. Database Scan

## Scope

As part of a pilot project to understand how hospitals were affected by diversion, data were requested from select national databases and from known Ontario databases. The detailed scan was undertaken in Ontario to assess the feasibility of a comprehensive review of all Canadian databases. Ontario is the most populous province in Canada, and its databases were deemed the most likely to return data if hospital diversion is a rarely reported phenomenon.

## **Database identification**

The database scan was approved by the North York General Hospital Research Ethics Board (#17-0024). Members of the research team associated with the Institute for Safe Medication Practices Canada (ISMP Canada), through relationships with other health care data-holding organizations, identified a series of databases that might hold incident records or information related to diversion of controlled drugs. Clinical members of the research team identified regulatory college databases related to clinical practice in the various health disciplines expected to have contact with controlled drugs. During discussion with database custodians, researchers asked about any additional or alternative databases that might hold relevant data. For instance, one custodian of a regulatory database suggested review of an insurance database.

## **Database search methodology**

Requests for data were made to organizations hosting potentially relevant diversion incidents between July 6, 2017, and November 2, 2017. Database requests were administered via 4 mechanisms (Table A1).

Table A1

Mechanisms of database requests

Mechanism	Description
Freedom of information or access to information requests	Written requests for data held by provincial and federal public sector agencies (e.g., law enforcement agencies)
Direct queries	Searches performed by the research team, whereby XXX had direct interface with the database holdings
Manual review of public data	Individual manual review of publicly available disciplinary records (e.g., disciplinary reports from a regulatory body's website) by members of the research team
Direct inquiries	Requests to database administrators for specific information from the databases of interest, whereby the research team did not have direct access to the databases

Source: Authors' description of methodological approach to database scan.

These search strategies were individualized to reflect variations in data storage constraints, taxonomy and classification systems among the databases. In cases of direct inquiries, database custodians were given the theme of the research and the general request (e.g., "Reports [e.g., investigative, disciplinary, incident, analysis, incident, loss or other] of controlled-drug diversion or theft by health care workers"). For non-health care organizations (e.g., law enforcement agencies), additional qualifiers (e.g., "opioids") were added to the request, to help ensure that all relevant reports were considered for retrieval. The databases used different classification systems and keywords; in most cases, discussion with the database custodian resulted in more refined search strategies that allowed capture of appropriate incidents or case examples. For example "diversion" did not exist as a concept in the law enforcement databases; therefore, only "theft" was used as a search term.

In some cases, data holders did not maintain the data in a format that was easily accessible for review, filtering and/or searching. For example, certain data holders, such as regulatory colleges, held and published case incidents and findings for the purposes of disciplinary hearings or for public disclosure, but not necessarily for research or subsequent analysis. As such, search capability was not always available, and a manual review of public data (e.g. published disciplinary cases) was performed in some instances.

## Database eligibility criteria

Database holdings that were not related to hospital settings (e.g., community pharmacy reports) were excluded, as they were outside the study scope.

The search timeframes ranged from a minimum of 1 year to no time restrictions; the particular timeframe for each database was determined in consultation with database custodians, to adequately capture the types of information held in the database without retrieving an excessive number of reports. For databases that were expected to hold a smaller number of incidents, the timeframe was typically from database initiation to the present. For databases with no or limited search functionality, manual review was required, and time limits were applied, based on the volume of reports encountered and the availability of past reports.

## Results

Data held by 35 Canadian organizations were considered for the database scan. Databases were excluded if they contained only clinical or patient outcome data, drug cost data or non-drug theft data; if the custodian did not

respond; or if the host organizations had acted as bargaining, advocacy or union organizations. Responses were available from 15 organizations about the incidence of controlled drug diversion in their records, but not all shared data. These databases are described in Table A2, along with the data obtained.



Appendix for "Opioid losses in terms of dosage and cost: a retrospective analysis of Health Canada data" Authors: Fan, Tscheng, Hamilton, Trbovich

Table A2

Quantitative findings of database scan

Manner of request	Organization Name and Database Name (if applicable)	Organization Type	Expected holdings	Search terms or request	Time limits	Quantitative data	Comments
Freedom of information or access to information request	Health Canada	Regulator	Loss report forms submitted to Health Canada's Office of Controlled drugs	Reports of diversion or loss or misuse of controlled drugs (including narcotics) in Canada	January 2016 to December 2016	Total number of records reported from hospitals: 991  840 out of the 991 reports were categorized as "Loss Unexplained"  By province:  Ontario: 556 reports Alberta: 190 reports Quebec: 101 reports British Columbia: 58 reports Saskatchewan: 39 reports Manitoba: 29 reports Newfoundland: 6 reports Nova Scotia: 5 reports New Brunswick: 4 reports Northwest Territories: 3 reports	Some data available in the loss/theft report forms submitted to Health Canada (including specific drugs and dosages lost, countermeasures taken) were not released by Health Canada, for security reasons.
	York Regional Police	Law enforcement	Investigation reports	"Drug theft from hospitals in York Region investigated by York Regional Police"	January 2012 to December 2016	20 reports, of which 18 (describing 15 separate incidents) were eligible	After discussion with the database custodian, original search timeframe was expanded, to increase the volume of reports available for review.
	Royal Canadian Mounted Police	Law enforcement	Investigation reports	Investigative reports of theft or loss of controlled drugs (opioids, narcotics, stimulants or other controlled drugs) from hospitals in Ontario	January 2015 to December 2016	Response received, but no records found	

Manner of request	Organization Name and Database Name (if applicable)	Organization Type	Expected holdings	Search terms or request	Time limits	Quantitative data	Comments
	Ontario Provincial Police	Law enforcement	Investigation reports	Investigative reports of theft or loss of controlled drugs (opioids, narcotics, stimulants or other controlled drugs) from hospitals in Northwestern Ontario detachments	January 2015 to June 2017	2 loss reports	On advice from database custodian, scope was reduced from the entire province to a single region; Northwestern region was selected on the recommendation of a project informant.
Direct query	Canadian Medication Incident Reporting Program (CMIRPS): - Individual Practitioner Reporting (IPR), - Consumer reporting program (consumer), - Community Pharmacy Incident Reporting Program (CPhIR)	Error reporting system	Medication incident reports	abuse, misuse, addict*, diver* (for divert, diversion, diverting), steal* (for steal, stealing), stole* (for stole, stolen), hid* (for hide, hidden), cheek*, workaround, access, illicit, forge, theft	Database initiation to June 30, 2017  Initiation date of each database: IPR, August 2000  Consumer, March 2010  CPhIR, April 2010	350 reports reviewed (217 from IPR, 15 from consumer program, 118 from CPhIR)  18 eligible reports of opportunity, tampering, suspected diversion or diversion from IPR  No eligible data from consumer or CPhIR reports	Most data in CMIRPS is reported voluntarily; as such, it likely under-represents actual cases of diversion.  Search was not limited to controlled drugs because of limitations with database search functionality; reports unrelated to controlled drugs were manually excluded after the search was run.
Manual review of discipline cases	College of Nurses of Ontario	Professional practice regulator	Disciplinary records	Manual review of cases relating to controlled-drug theft or diversion	2005 to 2017	244 disciplinary records, of which 10 were eligible (6 describing diversion from a hospital, 4 describing diversion from unknown facility type, possibly a hospital)	Data collection was limited to 2005 onward to 1) limit the scope of time-consuming manual review and 2) match the timeframe of the scoping review.

Appendix for "Opioid losses in terms of dosage and cost: a retrospective analysis of Health Canada data" Authors: Fan, Tscheng, Hamilton, Trbovich

Manner of request	Organization Name and Database Name (if applicable)	Organization Type	Expected holdings	Search terms or request	Time limits	Quantitative data	Comments
	College of Physicians and Surgeons of Ontario (CPSO)	Professional practice regulator	Disciplinary records	Manual review of cases relating to controlled-drug theft or diversion	2013 to 2017	176 disciplinary records reviewed, of which 5 cases were eligible	At the time of the manual review, disciplinary reports mentioned in CPSO news releases were available for 2013 onward.
	Royal College of Dental Surgeons of Ontario	Professional practice regulator	Disciplinary records	Manual review of cases relating to controlled-drug theft or diversion	2004 to 2017	120 disciplinary records reviewed; no relevant cases found	
	College of Dental Hygienists of Ontario	Professional practice regulator	Disciplinary records	Internal review of disciplinary records relating to controlled-drug theft or diversion	No restriction	54 disciplinary records reviewed; no relevant cases found	
Direct inquiry	Ontario College of Pharmacists (OCP)	Professional practice regulator	Disciplinary records	Internal review of disciplinary records relating to controlled- drug theft or diversion	No restriction	Response received, but no records pertained to hospital settings <sup>a</sup>	All pharmacists and community pharmacies are regulated by the OCP; however, hospital pharmacies have only recently (in 2016) fallen under its jurisdiction.
	College of Respiratory Therapists of Ontario	Professional practice regulator	Disciplinary records	Internal review of disciplinary records relating to controlled- drug theft or diversion	No restriction	2 disciplinary records; no relevant cases found	
	Canadian Institute for Health Information: National System for Incident Reporting	Error reporting system	Medication incident report forms	abuse, misuse, addict*, diver* (for divert, diversion, diverting), steal* (for steal, stealing), stole* (for stole, stolen), hid* (for hide, hidden), cheek*, workaround, access, illicit, forge, theft	April 2010 to June 2017	94 reports received, of which 7 were eligible	Search was not limited to controlled drugs because of limitations with the database search functionality; Reports unrelated to controlled drugs were manually excluded after the search was run.

## Appendix for "Opioid losses in terms of dosage and cost: a retrospective analysis of Health Canada data" Authors: Fan, Tscheng, Hamilton, Trbovich

Manner of request	Organization Name and Database Name (if applicable)	Organization Type	Expected holdings	Search terms or request	Time limits	Quantitative data	Comments
	Canadian Association of Physician Assistants	Association <sup>b</sup>	Disciplinary records	Internal review of disciplinary records relating to controlled- drug theft or diversion	No restriction	Response received, but indicated there was no evidence of diversion in their records	
	Hospital #1	Teaching hospital	Incident reports and/or loss reports	Incident reports and/or loss reports related to controlled-drug diversion or theft	No restriction	Response received, but organization declined to release data	
	Hospital #2	Community hospital	Incident reports and/or loss reports	Incident reports and/or loss reports related to controlled-drug diversion or theft	No restriction	Response received, but organization declined to release data	

**Source:** Authors' analysis of data from multiple Canadian organizations as described above.

<sup>&</sup>lt;sup>a</sup>Reports were available from community pharmacies, but the Ontario College of Pharmacists have only recently begun the process of accrediting hospital pharmacies in 2016; no hospital reports were found during our search. 19eh

<sup>&</sup>lt;sup>b</sup>No regulatory college for this profession exists in Ontario

Health Canada's mandatory theft or loss report forms represented the largest repository of data regarding controlled-drug diversion from hospital settings. The Freedom of Information request to Health Canada for 2016 data generated more records than any other database source, revealing 556 reports of controlled-drug loss or theft (some involving multiple products) in Ontario alone. This large number contrasts starkly with the number of reports collected from health professionals' regulatory colleges, law enforcement agencies and other national insurance organizations, even with multi-year searches. Regulatory colleges for health professionals often pointed to publicly available disciplinary records on their websites, but in some cases, the regulatory college internally searched its own records and provided results. Other organizational databases did not contain a substantial number of reports related to controlled-drug diversion in hospital settings.

## Limitations

Manual review of some database reports may not have captured all relevant cases; in addition, it is possible that the same incident was reported in multiple databases, and such duplication might not have been recognized from the report details available to reviewers.

## 2. Milligram Calculation Procedure used on Health Canada Dataset

This section describes the process used to calculate the quantity of controlled drugs lost from Canadian healthcare sources. We report this quantity in milligrams, oral morphine equivalents, and daily defined doses.

The original dataset is hosted on a web-based service, GitHub: https://github.com/taracarman/drug losses

The dataset was uploaded by Tara Carman, who also authored a CBC News article on June 28, 2018,<sup>2,3</sup> where we first became aware of the dataset.

This dataset was acquired from Health Canada following an Access to Information Request, and describes losses of controlled drugs from January 1, 2012 to September 30, 2017.<sup>4</sup>

The original dataset is comprised of 142,421 rows, and 8 columns. The columns include:

- Date of loss (e.g., 12-01-01)
- Province where loss is reported (e.g., Alberta)
- Drug name (e.g., Hydromorph Contin 24mg Cap)
- Generic drug name (e.g., Hydromorphone)
- Quantity of loss (e.g., 2)
- Unit of loss (e.g., Capsule)
- Loss Description (e.g., Loss Unexplained)
- Facility Type (e.g., Hospital)

For the purposes of our analysis, we filtered the 'Generic drug name' column to focus on five common opioids:

- Codeine or 'Codeine & Butalbital' or 'Codeine & Phenobarbital'
- Fentanyl
- Hydromorphone or Hydromorphine
- Morphine or 'Morphine Sulfate'
- Oxycodone

This reduced the dataset to 64,693 rows.

In the bullets above, we provided an example of a loss from January 1, 2012, where 2 capsules of Hydromorphone Contin were lost from a hospital in Alberta. The following section continues to use this example to show the additional calculations we performed.

One pharmacist (DT), four pharmacy students (DL, LD, EB, and KR worked collaboratively to add several columns to the spreadsheet to further analyze these reports:

- 1. The year of the loss (as opposed to the full date) (i.e., 2012)
- 2. The drug route (e.g., oral, oral solution, injectable, patch, suppository, unknown)
- 3. The quantity of milligrams per 'unit' of quantity (i.e., 2mg per capsule lost)
- 4. The total milligrams lost in that row (quantity column times the milligrams per unit quantity) (i.e., 2 capsules times 2 mg/capsule = 4 milligrams lost in total)
- 5. The oral morphine equivalent (OMEQ) of the total milligram loss (i.e., the conversion factor from oral hydromorphone to oral morphine is 5, so 4mg times 5 = 20 oral morphine equivalents lost)
- 6. The daily defined dose (DDD) equivalent of the total milligram loss (i.e., the World Health Organization (WHO) defines 1 daily defined dose of oral hydromorphone as 20mg, so in this case, 1 DDD was lost)
- 7. A notes column to describe how the row was altered if the original data was ambiguous and required editing. (i.e., in this case, no anomalies were encountered so no note would be written).

We encountered a variety of rows where a straightforward calculation was not possible, or suspect. We made several assumptions, generally seeking to estimate a reasonable lower limit for the drug lost (i.e., we attempted to be more conservative in our estimates of drug loss).

Table A3 summarizes the anomalous reports we encountered, and how we addressed them.

**Table A3. Strategy for Anomalous Reports** 

<b>Description of Anomalous Report</b>	Resolution
The 'Drug name' conflicted with the 'Unit of loss' (e.g., fentanyl patches were reported with losses of millilitres)	In the majority of cases, we used the drug strength described in the 'Drug name' column to calculate the milligrams lost.
Units of loss were reported in 'packages' (it was unclear what size of package was lost)	We searched Health Canada's Drug Product Database (DPD), reviewed relevant product monographs, selected the smallest package size, and used this to calculate the quantity of milligrams lost per package.
Units of loss are high (e.g., kilograms or litres)	We left these reports as is, assuming they were reported accurately. Exceptions are noted in the 'notes' column.
Quantities of losses exceed what would typically be held by a facility of that type (e.g., 165,997 tablets of 5mg oxycodone were lost from a pharmacy)	It is possible this report was the discovery of losses over a long period of time. As a result, we generally left these reports untouched.
No concentration was reported in the 'Drug name' column (e.g., 'Oxycodone' provides no details on the dosage format or strength)	In these cases, we looked to the unit of loss, where some rows provided clues (e.g., unit of loss is reported in Capsules or Tablets, suggesting an oral route). The pharmacy reviewers sought out the drug strength manually, where possible, using the DPD and relevant product monographs. When unclear, we used a

	1 mg/quantity lost as a conservative measure of loss. Where the pharmacy reviewers felt reasonable, the drug strength was altered and a note is provided in these cases.
Reported concentration in drug name is not available as a drug product	We reduced to the lowest concentration (e.g., Hydromorphone HP 30mg/mL reduced to 10mg/mL).
Quantity of reported loss is zero	Since these rows have no impact on our total, we left them as is.
Unclear what unit of loss is (e.g., MF)	We assumed these rows referred to milligram losses and treated them as such.
Drug route cannot be determined	We treated these rows as oral medications for all analytical purposes (e.g., OMEQ and DDD calculations). They are labelled as 'unknown' in the route column of the dataset, and are referred to as 'indeterminate' in the article.

Source: Authors' description of calculation methodology.

Our analytical dataset is available online as a supplemental file and accompanies this article. Interested readers can open the original dataset from CBC, and find the corresponding row in our analytical dataset to see how we altered the row. We believe this maximizes transparency and should allow for further analyses, reviews, or critiques for those who are interested.

## 3. Conversion Factors for Oral Morphine Equivalents and Daily Defined Doses

We have tabulated conversion factors from existing literature where possible, but please note there are inconsistencies between sources.

<u>The conversion factors provided in this Appendix are not for clinical use</u>. They represent an academic attempt to characterize opioid losses from Canadian facilities and allow policy-makers to approximate and/or benchmark the losses against other values.

We have attempted to use the same conversion factors as the Canadian Institute of Health Information (CIHI) where possible.<sup>5</sup> However, CIHI focuses primarily on oral and transdermal drug formats, and therefore additional sources were used in the analysis of our dataset (see references associated with each factor below).

## **Table A4**

Oral Morphine Equiv	Oral Morphine Equivalent (OMEQ) Conversion Factors							
Drug and Route <sup>a</sup>	OMEQ	Notes and References						
(assuming drug in	Conversion							
question is being	Factor							
converted from								
milligrams)								
Codeine								
Oral	0.15	Based on conversion factors published by CIHI and Busse						
		et al. <sup>5,6</sup>						

Injectable	0.25	Based on conversion factors published by Nielsen et al. <sup>7</sup>
Fentanyl		CIHI or Busse et al. do not describe conversions for non- oral fentanyl formats, so we used the US Centers for Disease Control and Prevention (CDC) as an alternate reference.
Oral (sublingual)	130	Based on conversion factors published by CDC.8
Injectable	100	Based on conversion factors published by CDC.8
Patch	100	Based on conversion factors published by CDC.8 Factor
		of 100 assumes 3 days worth of drug, and uses
		parenteral conversion factor. For example, 100mcg/h *
		72 hours = 7200mcg delivered over 3 days; 7.2 mg x 100
		(conversion factor in row above) = 720mg of OMEQ per
		patch).
Hydromorphone		
Oral	5	Based on conversion factors published by CIHI and Busse
		et al. <sup>5,6</sup>
Injectable	17.5	Based on conversion factors published by Nielsen et al. <sup>7</sup>
Rectal	6	There are no widely accepted conversion factors for
(suppository)		rectal hydromorphone to oral morphine. However, for
		the purposes of this article, we have attempted to
		estimate using studies investigating morphine.
		Both rectal and oral formulations are technically enteral,
		and the few studies investigating show close
		effectiveness in pain relief between oral and rectal
		routes. <sup>9</sup>
		Bruera et al. (1995) shows that morphine equivalence
		between rectal and subcutaneous (injectable) morphine
		is 2.5 to 1, <sup>10</sup> and Nielsen et al. (2016) states that
		injectable morphine is 3 times stronger than oral
		morphine. <sup>7</sup> Therefore, we estimate that 1 mg of rectal
		morphine is equal to 1.2mg (3/2.5) of oral morphine.
		Managed arts at al. (2005) sharing 1 mag of mastel transportal
		Mercadante et al. (2005) shows 1mg of rectal tramadol
		is roughly equivalent to 1.5mg of oral tramadol. <sup>11</sup>
		Therefore, we anticipate that rectal routes are slightly
		more efficient (more powerful) than oral routes.
		• • •
		Using Bruera et al.'s conversion values for morphine as a
		benchmark for our calculations, we estimate that 1mg of
		rectal hydromorphone is equivalent to 1.2 milligrams of
		oral hydromorphone. Therefore, 1mg of rectal

hydromorphone is 6mg (5\*1.2) of oral morphine.

Morphine		
Oral	1	Based on conversion factors published by CIHI and Busse et al. 5,6
Injectable	3	Based on conversion factors published by Nielsen et al. <sup>7</sup>
Rectal	1.2	Bruera treated rectal to subcutaneous (injectable)
(suppository)		morphine at 2.5:1.10 Nielsen does injectable to oral
		morphine at 3 to 1. 7 Therefore we consider the
		conversion factor for rectal to oral is $3/2.5 = 1.2$
Oxycodone		
Oral	1.5	Based on conversion factors published by CIHI and Busse et al. <sup>5,6</sup>
Rectal	1.8	This conversion factor is based on the same rationale for
		rectal hydromorphone. In short, rectal morphine has
		been estimated to be 1.2 times as strong as oral
		morphine; this has been extrapolated to oxycodone (i.e.,
		1.5 * 1.2 = 1.8).

<sup>&</sup>lt;sup>a</sup>Reports where the dosage format was unknown were treated as 'oral' for the purposes of the OMEQ conversion.

Table A5

Daily Defined Dose (D	DDD) Conversion	Factors
Drug and Dosage	DDD	Notes and References
Format <sup>a</sup>		
Codeine		
Oral	240mg	International narcotics control board has defined the
		DDD for analgesic use of codeine at 240mg. 12 This value
		has also been used by CIHI. <sup>5</sup>
Injectable	64mg	NO DDD has been defined by the World Health
		Organization (WHO) for injectable codeine.
		Note that in other injectable DDDs, the DDD is 2.5
		(oxycodone) to 5 (hydromorphone) times lower than the
		oral DDD. As an average between hydromorphone and
		oxycodone, we divided the oral DDD by 3.75 to
		approximate a reasonable DDD. In this case, parenteral
		codeine DDD would be 240mg/3.75 = 64mg.
Fentanyl		
Oral (sublingual)	0.6mg	DDD defined by WHO. <sup>13</sup>
Injectable	0.16mg	NO DDD has been defined by the WHO for injectable
		fentanyl.
		Using the rationale for codeine above, the injectable

		fentanyl DDD would be 0.6mg/3.75 = 0.16mg.
Transdermal	1.2mg	DDD defined by WHO. <sup>13</sup>
Hydromorphone		
Oral	20mg	DDD defined by WHO. <sup>13</sup>
Injectable	4mg	DDD defined by WHO. <sup>13</sup>
Rectal	4mg	DDD defined by WHO. <sup>13</sup>
(suppository)		
Morphine		
Oral	100mg	DDD defined by WHO. <sup>13</sup>
Injectable	30mg	DDD defined by WHO. <sup>13</sup>
Rectal	30mg	DDD defined by WHO. <sup>13</sup>
(suppository)		
Oxycodone		
Oral	75mg	DDD defined by WHO. <sup>13</sup>
Injectable	30mg	DDD defined by WHO. <sup>13</sup>
Rectal	30mg	NO DDD has been defined by the WHO for rectal
		oxycodone. However, WHO has defined a parenteral
		oxycodone DDD of 30mg. Since DDDs for rectal are the
		same as the DDD for parenteral in other instances (see
		morphine and hydromorphone), we have used 30 mg
		here.

<sup>&</sup>lt;sup>a</sup>Reports where the dosage format was unknown were treated as 'oral' for the purposes of the DDD conversion.

## 4. Street Pricing Estimates

The street values of pharmaceutical opioids are subject to significant variability (e.g., potency, formulation, bulk purchasing).<sup>14</sup> However, literature suggests that street pricing accurately reflects equianalgesic potency,<sup>14,15</sup> which supports our contention that reporting losses in terms of dose (e.g., milligrams) or potency (e.g., oral morphine equivalents) is superior to alternative forms of measurement (e.g., dosage units, incidents of loss).

Given the lack of consensus regarding street price per drug per milligram, we used the average price per milligram as provided by a Provincial Policing Service to estimate street value (Table A6). This average price per milligram was used regardless of the dosage format with the exception of fentanyl. The street pricing for fentanyl varied between transdermal and other formats, so Table A6 shows different pricing for these formats.

Previous Canadian literature on street pricing is outdated,<sup>16</sup> and newer articles often describe street pricing in the US (reported in US dollars); it is unclear if street pricing varies considerably between the US and Canada. Pricing is typically reported for oral formats, but it is unclear how accurately this represents other formats (e.g., injectable, transdermal, rectal).

## Table A6

Tubic Au		
Estimates of Street	Pricing	
Drug	Price range estimated by	Additional Notes and References
	Ontario Provincial Police	
Codeine	\$1 to 1.25 per milligram	Street price not reported in literature.
	(average \$1.125/mg)	
Fentanyl (oral,	\$0.3 to 0.5 per milligram	The values provided by the Ontario Provincial Police are
injectable)	(average \$0.4/mg)	for powdered fentanyl, which likely underestimates
		street prices for fentanyl tablets.
		For example, the US Drug Enforcement Administration
		has used 1.5 to 1.8mg as possible doses per counterfeit
		fentanyl tablets, and has provided estimates of sale
		prices ranging from \$10 to \$20 USD per pill. <sup>17</sup> Therefore,
		the actual dose in counterfeit pills could be valued
		between \$5.5 to \$13.3 USD per milligram. This is ten to
		thirty times higher than the conservative estimate we
		have used.
Fentanyl	\$1 to 3 per microgram per	Fentanyl patch street pricing has been estimated at USD
(transdermal)	hour (average \$2 per mcg/hr)	\$1/mcg/hr. <sup>18</sup>
Hydromorphone	\$1 to 2 per milligram	Crowdsourced street pricing ranges from \$3.55 to 4.47
	(average \$1.5/mg)	USD per milligram. <sup>15</sup>
Morphine	\$0.66 to 1 per milligram	Crowdsourced street pricing ranges from \$0.42 to 0.67

(average \$0.83/mg) USD per milligram. <sup>15</sup>
Oxycodone \$0.50 to 2 per milligram Crowdsourced street pricing ranges from \$0.86 to 0.99
(average \$1.25/mg) USD per milligram. <sup>15</sup>

Source: Data provided by Ontario Provincial Police and literature as cited.

## 5. Opioid Milligram Losses for Pharmacies by Canadian Province/Territory (Major Loss Categories only)

This section examines the dominant reasons for loss in pharmacies and hospitals respectively, broken down by province and territory, in descending order of milligrams lost.

Ontario pharmacies show an increasing trend of armed robberies and unexplained losses, but a downward trend in break and enter and pilferage. Alberta pharmacies show a reduction in losses from armed robberies, but a recent upward trend in unexplained losses. BC pharmacies show an astonishing downward trend in losses from armed robbery and break and entry. Newfoundland and Labrador (NL) is ranked fourth in terms of total losses from pharmacies in the dataset, losing over 6kg of the five opioids in our analysis; this is an average of 1.89mg per capita, compared to Ontario, British Columbia and Alberta, which range from 0.5 to 0.7mg per capita. Saskatchewan and Manitoba have seen increasing amounts of unexplained losses in 2016 and 2017.

Table A7

	2012	2013	2014	2015	2016	2017 (up to
Ontario						Sept. only)
Armed Robbery	2,548,985	2,330,881	2,188,001	2,592,363	1,823,099	4,341,288
Break and Entry	1,669,073	942,251	3,038,883	1,291,617	546,219	618,799
Loss Unexplained	536,416	608,142	408,980	666,368	1,824,123	3,002,302
Pilferage	2,816,645	226,533	2,591,775	2,451,156	1,517,376	532,015
Alberta						
Armed Robbery	615,440	899,115	1,204,313	619,595	538,780	123,365
Break and Entry	988,964	460,809	1,158,541	3,471,349	1,505,720	1,089,889
Loss Unexplained	163,664	103,481	329,089	238,729	885,076	1,527,698
Pilferage	177,270	453,095	5,840	43,240	10,467	8,324

Armed Robbery	2,501,598	1,476,241	1,159,592	1,305,586	8600	72
Break and Entry	752,315	1,236,488	1,200,863	350,460	28,341	14,400
Loss	159,674	83,621	184,072	110,938	2,141,798	1,073,561
Unexplained	133,074	03,021	104,072	110,938	2,141,738	1,073,301
Pilferage	-	24,292	12,750	4,150	12,560	19,629
Newfoundland						
and Labrador						
Armed Robbery	135,193	68,055	168,541	62,283	838,005	256,595
Break and Entry	44,550	221,791	262,133	936,148	216,153	206,209
Loss	119,645	861	6,947	14,649	50,592	47,880
Unexplained			3,3			,,,,,,
Pilferage	-	1,010	-	82,860	2,276,750	-
Quebec						
Armed Robbery	363,585	113,785	296,879	82,213	91,300	12,685
Break and Entry	97,367	98,677	297,084	153,512	192,260	48,381
Loss	38,664	48,158	70,229	194,565	133,079	152,992
Unexplained						
Pilferage	323,370	164,231	26,795	656,670	426,301	124,605
Saskatchewan						
Armed Robbery	19,115	172,774	20,690	179,880	106,769	205,917
Break and Entry	725,734	319,453	361,435	440,172	299,346	338,045
Loss	67,647	83,247	20,533	113,097	204,236	224,138
Unexplained		ŕ				
Pilferage	478	-	1,960	282,826	1,209	2,415
Manitoba				<u></u>		
Armed Robbery	15,720	-	132,486	61,910	900	15,458
Break and Entry	-	60,229	-	66,578	1,698	6,040
Loss	30,649	4,510	17,084	15,326	160,383	150,742
Unexplained	-				·	
Pilferage	-	21,600	3,400	_	-	_
Nova Scotia						
Armed Robbery	428	195	578	180	13	685
Break and Entry	11454	-	4720	-	-	-
Loss	490	976	1303	2024	782	1095
Unexplained	426		4200			
Pilferage	426	=	4389	-	-	-
New Brunswick	222		4222	4212		7=0
Armed Robbery	330	-	1398	1218	45	773
Break and Entry	-	687	-	936	22	255
Loss	311	61	628	126	1741	1395
Unexplained		4000	F0			
Pilferage	-	1080	50	-	-	-
Yukon						

т.	rritories	
10	rritories	

rerritories						
Armed Robbery	-	-	=	=	-	560
Break and Entry	-	125,761	-	-	-	-
Loss Unexplained	-	262	5	-	29,591	68,987
Pilferage						560
Prince Edward						
Island						
Armed Robbery	-	-	-	=	-	-
Break and Entry	-	-	69,719	500	-	-
Loss Unexplained	-	5,400	2,180	2,112	4,078	1,856
Pilferage	-	70	-	-	-	-
Nunavut						
Armed Robbery	-	-	-	-	-	-
Break and Entry	-	-	-	-	-	-
Loss Unexplained		270	6,323	300	8,930	
Pilferage			2,888			
Northwest						
Territories						
Armed Robbery	-	-	4	-	-	-
Break and Entry	-	-	· (V)	-	-	-
Loss Unexplained	148	3,619	8,330	600	664	847
Pilferage	-	-	_	<b>3</b>	-	-

**Source:** Authors' analysis of data for Jan. 2012 to Sept. 2017 from reports of Controlled Substances Loss or Theft Reports to Health Canada as published by CBC News in June 2018.

# 6. Opioid Milligram Losses for Hospitals by Canadian Province/Territory (Major Loss Categories only)

This section examines the dominant reasons for hospitals, broken down by province and territory, in descending order of milligrams lost.

Ontario hospitals show a rapid increase in pilferage losses starting in 2016. Other provinces and territories show no clear trends, but Quebec and Manitoba hospitals show peaks in milligram losses in 2016 and 2015, respectively.

Table A8

Table As							
Hospital Milligram Losses By Year and by Dominant Loss Description for each Province/Territory in order of Largest to Smallest Milligram Losses (Jan 2012 to Sept 2017)							
Largest to Smalle	2012	2013	2 to Sept 2017 2014	2015	2016	2017 (up to Sept. only)	
Ontario						55p 31 51.17,	
Loss Unexplained	10,408	36,746	19,205	26,657	27,576	7,844	
Pilferage <b>Quebec</b>	24,226	28,952	21,552	12,736	120,645	415,879	
Loss Unexplained	38,265	14,761	6,760	10,176	7,479	4,920	
Pilferage <b>Manitoba</b>	2,342	2,675	1,532	382	70,287	27,169	
Loss Unexplained	1,747	173	144	121,547	508	3,169	
Pilferage <b>British</b>	1,423	32,533	2,165	9-	13,227	100	
Columbia							
Loss Unexplained	4,862	1,077	2,899	12,290	2,849	5,882	
Pilferage <b>Alberta</b>	3,340	16,496	12,318	1,051	1,733	2,112	
Loss Unexplained	4,368	9,934	6,420	9,239	3,027	4,575	
Pilferage	392	20	-	105	205	-	
Newfoundland and Labrador							
Loss Unexplained Pilferage	2,901 -	424 -	573 -	160 -	82 -	25,038 -	
Saskatchewan							

Loss	317	441	4,088	3,208	19,142	217
Unexplained Pilferage	239	19	1,200	3	-	-
Nova Scotia						
Loss	2,675	1071	44	331	32	4,060
Unexplained	2,073	1071	44	331	32	4,000
Pilferage	-	100	-	-	-	-
Nunavut						
Loss		4	50	2,760		_
Unexplained		4	30	2,700		
Pilferage	-	-	-	-	-	-
<b>New Brunswick</b>						
Loss	187	568	55	47	6	1,132
Unexplained	107	308	55	47	U	1,132
Pilferage	-	95	-	242	-	80
Northwest						
Territories						
Loss			94	45	12	15
Unexplained	_	-	34	43	12	13
Pilferage	-	-	<u>-</u>	-	-	-
Yukon						
Territories						
Loss	130					
Unexplained	130	-	-	_	-	-
Pilferage	-	-	-	-	-	-

**Source:** Authors' analysis of data for Jan. 2012 to Sept. 2017 from reports of Controlled Substances Loss or Theft Reports to Health Canada as published by CBC News in June 2018.

# 7. Line Graphs Comparing Opioid Loss Trends as Measured by Milligrams, Dosage Units, and Incidents of Loss

This section complements Table 4 in the article by providing a visual depiction of the loss trends from community pharmacies, companies, and hospitals. Specifically, loss trends appear to vary depending on the unit of measure. In Figures A1, A2, and A3 below, we show that depending on which measure is reported, readers may be inclined to believe that losses are increasing or decreasing when other measures show differing trends.

\*\*Note, the units of measure have been scaled so that the y-axis is comparable between the reporting metrics. Specifically the dosage units lost have been reduced by a factor of 100, and milligrams lost has

been divided by 1000 to provide losses in grams. These figures are primarily to demonstrate differences in trends, rather than a comparison of absolute values between the reporting metrics.

Figure A1.

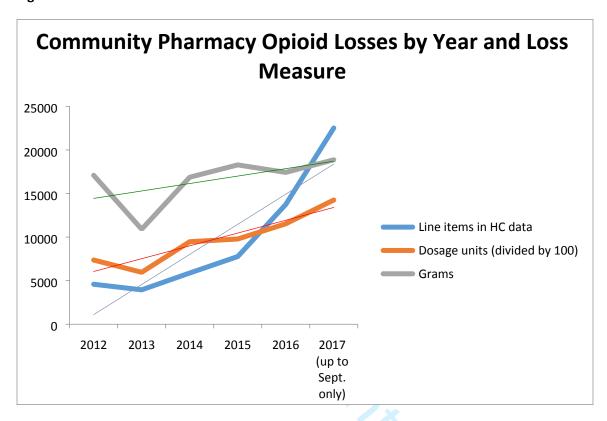
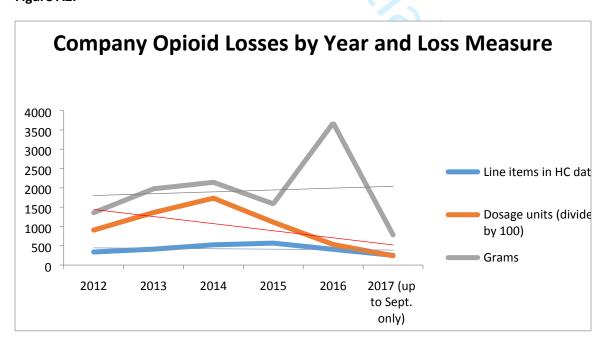
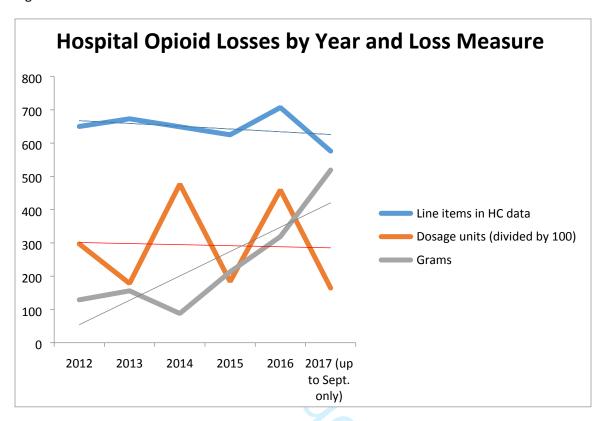


Figure A2.



Appendix for "Opioid losses in terms of dosage and cost: a retrospective analysis of Health Canada data" Authors: Fan, Tscheng, Hamilton, Trbovich

Figure A3.



## 8. References for Appendix

- 1. Foxman S. Baseline Assessments Reveal Opportunities for Hospital Pharmacies. Pharm Connect [Internet]. 2016;23(1):8–33. Available from: http://www.ocpinfo.com/library/practice-related/download/BaselineAssessmentsWinter2016.pdf
- Carman T. When prescription opioids run out, users look for the supply on the streets [Internet].
   2018. Available from: https://www.cbc.ca/news/canada/when-prescription-opioids-run-out-users-look-for-the-supply-on-the-streets-1.4720952
- Carman T, Adhopia V. More than half a million prescription drugs are stolen each year and most are opioids [Internet]. CBC News; 2018. Available from: https://www.cbc.ca/news/canada/missing-drugs-pharmacies-part1-1.4708041
- Carman T. Analysis of Health Canada missing controlled substances and precursors data, Jan. 1, 2012 - Sept. 30, 2017 [dataset] [Internet]. 2018. Available from: https://github.com/taracarman/drug\_losses
- 5. Canadian Institute for Health Information. Pan-Canadian Trends in the Prescribing of Opioids and Benzodiazepines, 2012 to 2017 Data Tables [Internet]. 2018. Available from: https://www.cihi.ca/sites/default/files/document/pan-canadian-prescribed-opioid-benzo-data-tables-june18-en-web.xlsx

- 6. Busse J. Appendix 1 (as supplied by the authors): The 2017 Canadian guideline for opioids for chronic non-cancer pain [Internet]. 2017. Available from: http://nationalpaincentre.mcmaster.ca/documents/Opioid
- 7. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. Pharmacoepidemiol Drug Saf [Internet]. 2016 Jun;25(6):733–7. Available from: http://doi.wiley.com/10.1002/pds.3945
- 8. National Center for Injury Prevention and Control. CDC compilation of benzodiazepines, muscle relaxants, stimulants, zolpidem, and opioid analgesics with oral morphine milligram equivalent conversion factors, 2018 version [dataset] [Internet]. Atlanta, Georgia: Centers for Disease Control and Prevention; 2018. Available from: https://www.cdc.gov/drugoverdose/data-files/CDC Oral Morphine Milligram Equivalents Sept 2018.xlsx
- 9. Wiffen PJ, Wee B, Moore RA. Oral morphine for cancer pain. Cochrane database Syst Rev [Internet]. 2016 Apr 22;4:CD003868. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27105021
- 10. Bruera E, Fainsinger R, Spachynski K, Babul N, Harsanyi Z, Darke AC. Clinical efficacy and safety of a novel controlled-release morphine suppository and subcutaneous morphine in cancer pain: a randomized evaluation. J Clin Oncol [Internet]. 1995 Jun;13(6):1520–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/7751901
- 11. Mercadante S, Arcuri E, Fusco F, Tirelli W, Villari P, Bussolino C, et al. Randomized double-blind, double-dummy crossover clinical trial of oral tramadol versus rectal tramadol administration in opioid-naive cancer patients with pain. Support Care Cancer [Internet]. 2005 Sep;13(9):702–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15645186
- 12. International Narcotics Control Board. Narcotic Drugs 2018 estimated World Requirements for 2019. New York, New York; 2019.
- 13. World Health Organization Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2019 [Internet]. 2018 [cited 2019 May 9]. Available from: https://www.whocc.no/atc\_ddd\_index/
- 14. Lebin JA, Murphy DL, Severtson SG, Bau GE, Dasgupta N, Dart RC. Scoring the best deal: Quantity discounts and street price variation of diverted oxycodone and oxymorphone. Pharmacoepidemiol Drug Saf [Internet]. 2019;28(1):25–30. Available from: http://dx.doi.org/10.1002/pds.4558
- 15. Dasgupta N, Freifeld C, Brownstein JS, Menone CM, Surratt HL, Poppish L, et al. Crowdsourcing black market prices for prescription opioids. J Med Internet Res [Internet]. 2013;15(8):e178. Available from: http://dx.doi.org/10.2196/jmir.2810
- 16. Sajan A, Corneil T, Grzybowski S. The street value of prescription drugs. CMAJ [Internet]. 1998 Jul 28;159(2):139–42. Available from: papers2://publication/uuid/966333E5-EDCA-4618-86CB-01C1BA13F254
- 17. Drug Enforcement Administration; Counterfeit Prescription Pills Containing Fentanyls: A Global Threat. 2016.

- 18. Bonnie RJ, Ford MA, Phillips JK, editors. Pain Management and the Opioid Epidemic [Internet]. Washington, D.C.: National Academies Press; 2017. Available from: https://www.nap.edu/catalog/24781
- 19. Newfoundland & Labrador Statistics Agency. Annual Estimates of Population for Canada, Provinces and Territories, from July 1, 1971 to July 1, 2017 [Internet]. 2017. p. 1. Available from: https://www.stats.gov.nl.ca/statistics/Population/PDF/Annual\_Pop\_Prov.PDF

