

## Appendix 1 (as supplied by the authors): Supplemental material

The appendix is composed of ten sections.

1. **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 (DDD). 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. **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. **Definitions of loss descriptions:** These definitions are drawn from Health Canada.
9. **Health Canada Loss or Theft Reporting Form:** The January 2019 version is shown.
10. **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.

### Rationale

The database scan was conducted to assess what database provides the most comprehensive data on opioid losses, such that analyses are conducted on the best data available.

### 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 (Supplemental Table S1).

**Supplemental Table S1****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 Supplemental Table S2, along with the data obtained.

## Supplemental Table S2

## 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: <ul style="list-style-type: none"> <li>• Ontario: 556 reports</li> <li>• Alberta: 190 reports</li> <li>• Quebec: 101 reports</li> <li>• British Columbia: 58 reports</li> <li>• Saskatchewan: 39 reports</li> <li>• Manitoba: 29 reports</li> <li>• Newfoundland: 6 reports</li> <li>• Nova Scotia: 5 reports</li> <li>• New Brunswick: 4 reports</li> <li>• Northwest Territories: 3 reports</li> </ul>	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.

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.

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>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.

<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](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>1,2</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>3</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 64,963 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.

Authors (MF, DT) and 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).

These calculations were performed in an iterative manner on a single version of the worksheet, adding the relevant information one step at a time over a period of several months (i.e., calculations were not performed independently or in parallel). For example, the excel worksheet could be filtered for specific generic drug names (e.g., Morphine), and this filtered list could be sub-divided further based on drug name (e.g., Statex 5mg Tab). As a result, the milligrams per unit of quantity and drug route could be copied and pasted for each 'batch' of filtered list (e.g., each Statex 5mg tab has 5mg of morphine, and the drug route for all entries with this name would be set to 'oral').

Each analyst reviewed the worksheet for accuracy and flagged potential concerns for discussion with either MF or DT for resolution. For unresolved anomalous reports, MF and DT met with author MH for a discussion to come to final consensus on how to address them.

We encountered 567 rows (0.87% of the dataset) 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).

Supplemental Table S3 summarizes the anomalous reports we encountered, and how we addressed them.

### Supplemental Table S3. Strategy for Anomalous Reports

Description of Anomalous Report	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 at: <https://github.com/HumanEra/Health-Canada-Drug-Loss-and-Theft-Data-Analysis>. 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.

The milligram losses from the 567 anomalous rows total 12,007,168mg, which is approximately 10.67% of the total milligram losses in the dataset. Supplemental Table S4 further summarizes the anomalous reports by each of the five opioids analyzed in the dataset.

**Supplemental Table S4. Summary of the Number of Anomalous Reports and Corresponding Milligram Losses**

Drug	Total Number of reports	Total Milligram loss	Number of non-anomalous reports	Non-anomalous Milligram loss	Number of Anomalous reports (% of total reports in dataset)	Anomalous Milligram loss (conservative) (% of total milligrams in dataset)
<b>Codeine</b>	20,786	47,304,765	20,749	47,005,756	37 (0.18%)	299,009 (0.63%)

<b>Fentanyl</b>	3,189	264,193	3,037	184,931	152 (4.77%)	79,262 (30.0%)
<b>Hydromorphone</b>	15,182	12,723,946	14,987	9,372,740	195 (1.28%)	3,351,206 (26.34%)
<b>Morphine</b>	9,880	15,687,907	9,739	15,389,434	141 (1.43%)	298,473 (1.9%)
<b>Oxycodone</b>	15,926	36,546,878	15,884	285,65,419	42 (2.64%)	7,981,459 (21.84%)
<b>Total</b>	64,963	112,525,448	64397	100,518,280	567 (8.71%)	12,009,409 (10.67%)

Our current approach to estimating the milligram losses of anomalous reports is to use a conservative approach and use the lowest reasonable loss based on the information available (see the resolution column in Supplemental Table S3, rows 2, 5 and 6). However, it is important to assess how our conservative approach may have impacted our estimate of milligram losses, as well as drug costs.

As a result, we repeated our calculations with a non-conservative approach to estimate the impact on our findings. Due to resource limitations, we did not repeat our calculations for all anomalous reports, but instead selected a subset of the anomalous reports for analysis. The subset was based on several criteria.

First, we limited our non-conservative analysis to the two types of anomalous reports affected by our assumptions. These are:

- reports where the loss was reported as a “package”, and
- reports where no drug concentration was provided.

This reduced our sample for analysis from 567 to 440 reports.

Second, we removed any anomalous reports from this subset where the unit of loss was grams, milligrams, or micrograms, as these reports do not require any assumptions on our part. This reduced our sample for analysis from 440 to 358 reports.

Further, to conduct the analysis within our resource constraints, we sampled roughly 40% of the reports for each drug. To avoid bias, we first organized the reports from largest to smallest milligram loss, and selected the top milligram losses for analysis using a non-conservative approach. The change in milligram losses, wholesale cost, and street value, is summarized in Supplemental Table S5.

#### **Supplemental Table S5. Change in Milligram Loss when Anomalous Reports Analyzed Conservatively Versus Non-Conservatively**

<b>Drug</b>	<b>Number of Sampled Anomalous Reports / Total Subset of Anomalous Reports</b>	<b>Milligram Loss (Conservative)</b>	<b>Wholesale Cost (CAD) (Conservative)</b>	<b>Street Value (CAD) (Conservative)</b>	<b>Milligram Loss (Non-Conservative) (% increase from conservative approach)</b>	<b>Wholesale Cost (CAD) (Non-Conservative) (% increase from conservative approach)</b>	<b>Street Value (CAD) (Non-Conservative) (% increase from conservative approach)</b>
<b>Codeine</b>	10/23	18,824	\$525	\$21,648	179,675 (854%)	\$5,020 (856%)	\$206,626 (854%)

<b>Fentanyl</b>	32/80	231	\$6,335	\$305	544 (135%)	\$11,301 (78%)	\$1,957 (541%)
<b>Hydromorphone</b>	52/132	443,330	\$147,732	\$664,994	2,238,464 (405%)	\$728,842 (393%)	\$3,357,696 (405%)
<b>Morphine</b>	42/105	93,935	\$57,107	\$77,966	347,800 (270%)	\$163,352 (186%)	\$288,674 (270%)
<b>Oxycodone</b>	8/18	352,280	\$12,657	\$440,350	5,636,480 (1500%)	\$202,511 (1500%)	\$7,045,600 (1500%)
<b>Total</b>	144/358	908,599	\$224,356	\$1,205,263	8,402,963 (825%)	\$1,111,026 (395%)	\$10,900,553 (804%)

### 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.

**The conversion factors provided in this Appendix are not for clinical use.** 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>4</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).

#### Supplemental Table S6

##### Oral Morphine Equivalent (OMEQ) Conversion Factors

Drug and Route <sup>a</sup> (assuming drug in question is being converted from milligrams)	OMEQ Conversion Factor	Notes and References
<b>Codeine</b>		
Oral	0.15	Based on conversion factors published by CIHI and Busse et al. <sup>4,5</sup>
Injectable	0.25	Based on conversion factors published by Nielsen et al. <sup>6</sup>
<b>Fentanyl</b>		
Oral (sublingual)	130	Based on conversion factors published by CDC. <sup>7</sup>
Injectable	100	Based on conversion factors published by CDC. <sup>7</sup>

Patch	100	Based on conversion factors published by CDC. <sup>7</sup> 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).
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### Hydromorphone

Oral	5	Based on conversion factors published by CIHI and Busse et al. <sup>4,5</sup>
Injectable	17.5	Based on conversion factors published by Nielsen et al. <sup>6</sup>
Rectal (suppository)	6	There are no widely accepted conversion factors for 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>8</sup>

Bruera et al. (1995) shows that morphine equivalence between rectal and subcutaneous (injectable) morphine is 2.5 to 1,<sup>9</sup> and Nielsen et al. (2016) states that injectable morphine is 3 times stronger than oral morphine.<sup>6</sup> Therefore, we estimate that 1 mg of rectal morphine is equal to 1.2mg (3/2.5) of oral morphine.

Mercadante et al. (2005) shows 1mg of rectal tramadol is roughly equivalent to 1.5mg of oral tramadol.<sup>10</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. <sup>4,5</sup>
Injectable	3	Based on conversion factors published by Nielsen et al. <sup>6</sup>
Rectal (suppository)	1.2	Bruera treated rectal to subcutaneous (injectable) morphine at 2.5:1. <sup>9</sup> Nielsen does injectable to oral

morphine at 3 to 1.<sup>6</sup> Therefore we consider the conversion factor for rectal to oral is  $3/2.5 = 1.2$

<b>Oxycodone</b>		
Oral	1.5	Based on conversion factors published by CIHI and Busse et al. <sup>4,5</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>a</sup>Reports where the dosage format was unknown were treated as 'oral' for the purposes of the OMEQ conversion.

### Supplemental Table S7

<b>Daily Defined Dose (DDD) Conversion Factors</b>		
Drug and Dosage Format <sup>a</sup>	DDD	Notes and References
<b>Codeine</b>		
Oral	240mg	International narcotics control board has defined the DDD for analgesic use of codeine at 240mg. <sup>11</sup> This value has also been used by CIHI. <sup>4</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 $240\text{mg}/3.75 = 64\text{mg}$ .
<b>Fentanyl</b>		
Oral (sublingual)	0.6mg	DDD defined by WHO. <sup>12</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 $0.6\text{mg}/3.75 = 0.16\text{mg}$ .
Transdermal	1.2mg	DDD defined by WHO. <sup>12</sup>
<b>Hydromorphone</b>		
Oral	20mg	DDD defined by WHO. <sup>12</sup>
Injectable	4mg	DDD defined by WHO. <sup>12</sup>
Rectal (suppository)	4mg	DDD defined by WHO. <sup>12</sup>

<b>Morphine</b>		
Oral	100mg	DDD defined by WHO. <sup>12</sup>
Injectable	30mg	DDD defined by WHO. <sup>12</sup>
Rectal (suppository)	30mg	DDD defined by WHO. <sup>12</sup>
<b>Oxycodone</b>		
Oral	75mg	DDD defined by WHO. <sup>12</sup>
Injectable	30mg	DDD defined by WHO. <sup>12</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>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>13</sup> However, literature suggests that street pricing accurately reflects equianalgesic potency,<sup>13,14</sup> which supports our contention that reporting losses in terms of dose (e.g., milligrams) or potency (e.g., oral morphine equivalents) is a useful addition to complement existing measures (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 (Supplemental Table S6). This price is a national average over 2012 to 2017, recognizing that at any given time, and in different locations across the country, the actual price may vary. 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 Supplemental Table S6 shows different pricing for these formats.

Previous Canadian literature on street pricing is outdated,<sup>15</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).

### Supplemental Table S8

#### Estimates of Street Pricing

Drug	Price range (CAD) estimated by Ontario Provincial Police	Additional Notes and References
Codeine	\$1 to 1.25 per milligram (average \$1.125/mg)	Street price not reported in literature.
Fentanyl (oral, injectable)	\$0.3 to 0.5 per milligram (average \$0.4/mg)	The values provided by the Ontario Provincial Police are 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>16</sup> Therefore, the actual dose in counterfeit pills could be valued between \$5.5 to \$13.3 USD per milligram. <b>This is ten to thirty times higher than the conservative estimate we have used.</b>
Fentanyl (transdermal)	\$1 to 3 per microgram per hour (average \$2 per mcg/hr)	Fentanyl patch street pricing has been estimated at USD \$1/mcg/hr. <sup>17</sup>

Hydromorphone	\$1 to 2 per milligram (average \$1.5/mg)	Crowdsourced street pricing ranges from \$3.55 to 4.47 USD per milligram. <sup>14</sup>
Morphine	\$0.66 to 1 per milligram (average \$0.83/mg)	Crowdsourced street pricing ranges from \$0.42 to 0.67 USD per milligram. <sup>14</sup>
Oxycodone	\$0.50 to 2 per milligram (average \$1.25/mg)	Crowdsourced street pricing ranges from \$0.86 to 0.99 USD per milligram. <sup>14</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.<sup>18</sup> Saskatchewan and Manitoba have seen increasing amounts of unexplained losses in 2016 and 2017.

### Supplemental Table S9

<b>Pharmacy Losses (Per Thousand Milligrams) By Year and by Dominant Loss Description<sup>^</sup> for each Province/Territory in order of Largest to Smallest Milligram Losses (Jan 2012 to Sept 2017)</b>							
	<b>2012</b>	<b>2013</b>	<b>2014</b>	<b>2015</b>	<b>2016</b>	<b>2017 (up to Sept. only)</b>	<b>2017 (up to Sept. only)</b>
<b>Ontario</b>							
Armed Robbery	2,549.0	2,330.9	2,188.0	2,592.4	1,823.1	4,341.3	5,788.4
Break and Entry	1,669.0	942.3	3,038.9	1,291.6	546.2	618.8	825.1
Loss Unexplained	536.4	608.1	409.0	666.4	1,824.1	3,002.3	4,003.1
Pilferage	2,816.6	226.5	2,591.8	2,451.2	1,517.4	532.0	709.4
<b>Alberta</b>							
Armed Robbery	615.4	899.1	1,204.3	619.6	538.8	123.4	164.5
Break and Entry	989.0	460.8	1,158.5	3,471.3	1,505.7	1,089.9	1,453.2
Loss Unexplained	163.7	103.5	329.1	238.7	885.1	1,527.7	2,036.9
Pilferage	177.3	453.1	5.8	43.2	10.5	8.3	11.1
<b>British Columbia</b>							

Armed Robbery	2,501.6	1,476.2	1,159.6	1,305.6	8.6	~0	~0
Break and Entry	752.3	1,236.5	1,200.9	350.5	28.3	14.4	19.2
Loss Unexplained	159.7	83.6	184.1	110.9	2,141.8	1,073.6	1,432.4
Pilferage	-	24.3	12.8	4.2	12.6	19.6	26.2
<b>Newfoundland and Labrador</b>							
Armed Robbery	1352	68.1	168.5	62.2	838.0	256.6	342.1
Break and Entry	44.6	221.8	262.1	936.1	216.2	206.2	274.9
Loss Unexplained	119.6	.9	6.9	14.6	50.6	47.9	63.8
Pilferage	-	1.0	-	82.9	2,276.8	-	-
<b>Quebec</b>							
Armed Robbery	363.6	113.8	296.9	82.2	91.3	12.7	16.9
Break and Entry	97.4	98.7	297.1	153.5	192.3	48.4	64.5
Loss Unexplained	38.7	48.2	70.2	194.6	133.1	153.0	204.0
Pilferage	323.4	164.2	26.8	656.7	426.3	124.6	166.1
<b>Saskatchewan</b>							
Armed Robbery	19.1	172.8	20.7	179.9	106.8	205.9	274.6
Break and Entry	725.7	319.5	361.4	440.2	299.3	338.0	450.7
Loss Unexplained	67.6	83.2	20.5	113.1	204.2	224.1	298.9
Pilferage	0.5	-	2.0	282.8	1.2	2.4	3.2
<b>Manitoba</b>							
Armed Robbery	79.8	142.4	93.9	462.0	245.0	91.7	122.2
Break and Entry	45.5	29.0	165.2	283.4	248.7	98.9	131.9
Loss Unexplained	21.1	11.7	20.0	207.1	115.7	353.5	471.4
Pilferage	25.5	5.5	14.2	-	32.5	15.0	20.0
<b>Nova Scotia</b>							
Armed Robbery	10.6	3.9	65.5	3.6	1.0	37.6	50.2
Break and Entry	769.2	-	384.9	-	-	-	-
Loss Unexplained	73.6	60.3	84.3	110.3	89.0	172.4	229.9
Pilferage	34.8	-	24.9	-	-	-	-
<b>New Brunswick</b>							
Armed Robbery	15.7	-	132.5	61.9	0.9	15.5	20.6
Break and Entry	-	60.2	-	66.6	1.7	6.0	8.1
Loss Unexplained	30.6	4.5	17.1	15.3	160.4	150.7	201.0
Pilferage	-	21.6	3.4	-	-	-	-
<b>Yukon Territories</b>							
Armed Robbery	-	-	-	-	-	0.6	0.7
Break and Entry	-	125.8	-	-	-	-	-
Loss Unexplained	-	0.3	~0	-	29.6	69.0	92.0
Pilferage	-	-	-	-	-	-	-
<b>Prince Edward Island</b>							

Armed Robbery	-	-	-	-	-	-	-
Break and Entry	-	-	69.8	0.5	-	-	-
Loss Unexplained	-	5.4	2.2	2.1	4.1	1.9	20.8
Pilferage	-	~0	-	-	-	-	-
<b>Nunavut</b>							
Armed Robbery	-	-	-	-	-	-	-
Break and Entry	-	-	-	-	-	-	-
Loss Unexplained	-	0.3	6.3	0.3	8.9	-	-
Pilferage	-	-	2.9	-	-	-	-
<b>Northwest Territories</b>							
Armed Robbery	-	-	-	-	-	-	-
Break and Entry	-	-	-	-	-	-	-
Loss Unexplained	0.1	3.6	8.3	0.6	0.7	0.8	1.1
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.

**Note:** Figures are reported per thousand milligrams, and rounded per 100 milligrams. The 2017 prorated data is based on unrounded values, and may therefore appear differently than readers expect.

^ Definitions of loss descriptions can be found in Supplemental Table S11.

## 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.

**Supplemental Table S10**

<b>Hospital Losses (Per Thousand Milligrams) By Year and by Dominant Loss Description<sup>^</sup> for each Province/Territory in order of Largest to Smallest Milligram Losses (Jan 2012 to Sept 2017)</b>							
	<b>2012</b>	<b>2013</b>	<b>2014</b>	<b>2015</b>	<b>2016</b>	<b>2017 (up to Sept. only)</b>	<b>2017 (prorated)</b>
<b>Ontario</b>							
Loss Unexplained	10.4	36.7	19.2	26.7	27.6	7.8	10.5
Pilferage	24.2	29.0	21.6	12.7	120.6	415.9	554.5
<b>Quebec</b>							
Loss Unexplained	38.3	14.8	6.8	10.2	7.5	4.9	6.6
Pilferage	2.3	2.7	1.5	0.4	70.3	27.2	36.2
<b>Manitoba</b>							
Loss Unexplained	1.7	0.2	0.1	121.5	0.5	3.2	4.2
Pilferage	1.4	32.5	2.2	-	13.2	0.1	0.1
<b>British Columbia</b>							
Loss Unexplained	4.9	1.1	2.9	12.3	2.8	5.9	7.8
Pilferage	3.3	16.5	12.3	1.1	1.7	2.1	2.8
<b>Alberta</b>							
Loss Unexplained	4.4	9.9	6.4	9.2	3.0	4.6	6.1
Pilferage	0.4	~0	-	0.1	0.2	-	-
<b>Newfoundland and Labrador</b>							
Loss Unexplained	2.9	0.4	0.6	0.2	0.1	25.0	33.4
Pilferage	-	-	-	-	-	-	-
<b>Saskatchewan</b>							
Loss Unexplained	0.3	0.4	4.1	32	19.1	0.2	0.3
Pilferage	0.2	~0	1.2	~0	-	-	-
<b>Nova Scotia</b>							
Loss Unexplained	2.7	1.0	~0	0.3	~0	4.1	5.4
Pilferage	-	0.1	-	-	-	-	-
<b>Nunavut</b>							
Loss Unexplained	-	~0	~0	2.8	-	-	-

Pilferage	-	-	-	-	-	-	-
<b>New Brunswick</b>							
Loss Unexplained	0.2	0.6	~0	~0	~0	1.1	1.5
Pilferage	-	~0	-	0.2	-	~0	0.1
<b>Northwest Territories</b>							
Loss Unexplained	-	-	~0	~0	~0	~0	~0
Pilferage	-	-	-	-	-	-	-
<b>Yukon Territories</b>							
Loss Unexplained	0.1	-	-	-	-	-	-
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.

**Note:** Figures are reported per thousand milligrams, and rounded per 100 milligrams. The 2017 prorated data is based on unrounded values, and may therefore appear differently than readers expect.

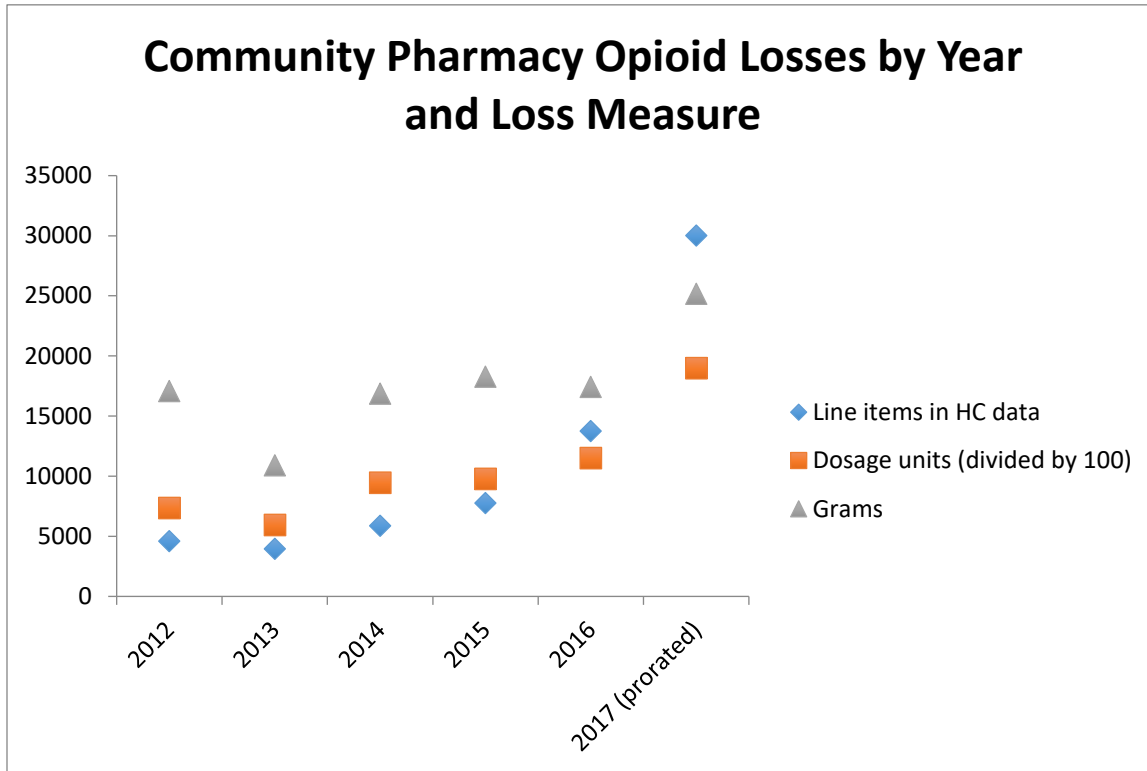
^ Definitions of loss descriptions can be found in the Appendix Table A11.

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

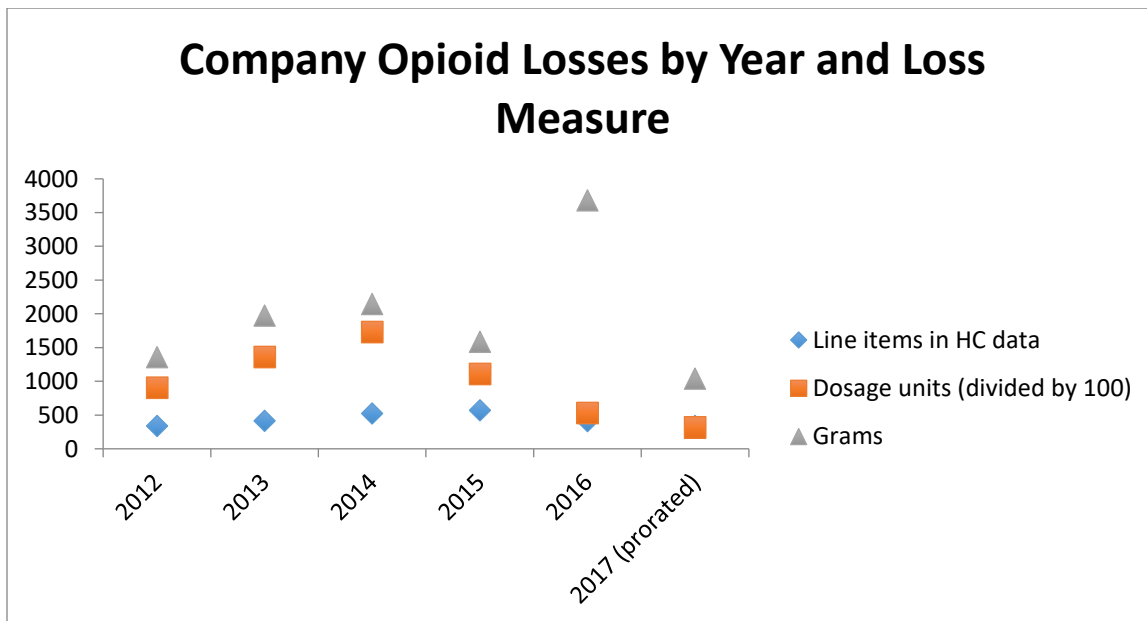
This section complements Table 4 in the article by providing a visual depiction of the loss trends from community pharmacies, companies, and hospitals. Specifically, loss trends appear to vary depending on the unit of measure. In Supplemental Figures S1, S2, and S3 below, we show that depending on which 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.

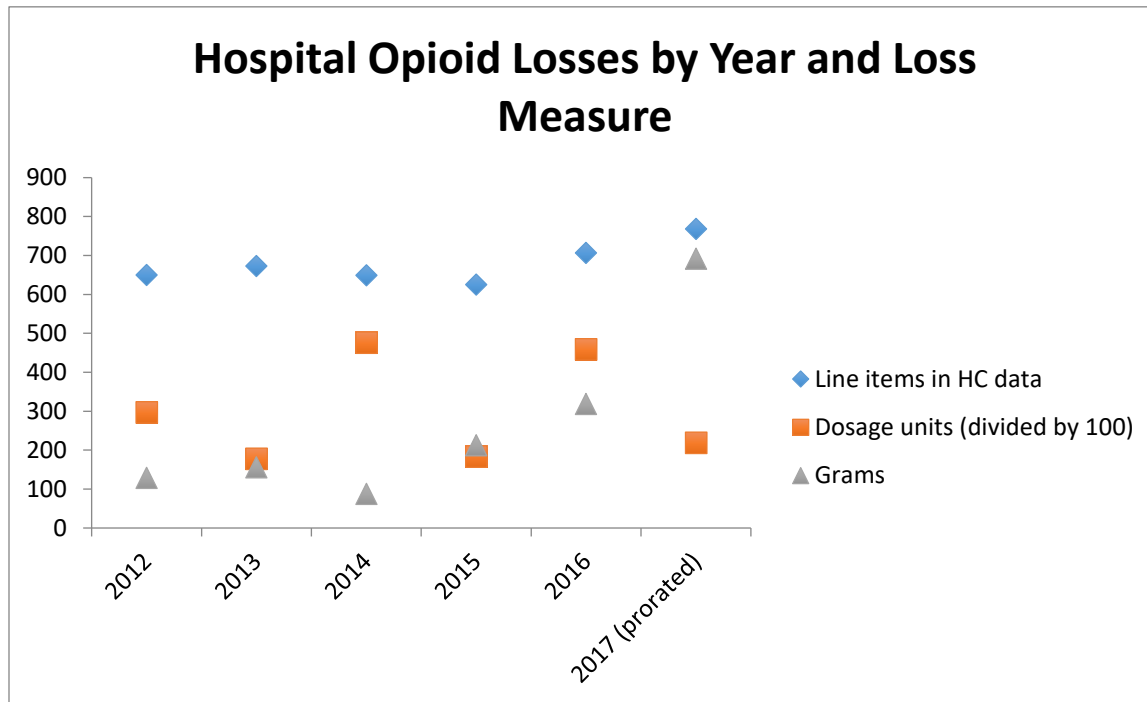
Supplemental Figure S1.



Supplemental Figure S2.



Supplemental Figure S3.



## 8. Definitions of Loss Descriptions

These definitions are copied word for word from Health Canada's guidance document (Appendix B) on reporting the loss or theft of Controlled substances (accessed December 6, 2019).<sup>19</sup>

Supplemental Table S11. Definitions of Loss Descriptions

Incident Type	Incident Sub-Type	Definition	Report?
Loss	Loss Unexplained	A loss that cannot be attributed to any particular cause or action on the basis of normally accepted business activities.	Yes
	Manufacturer's Shortage	The content of a sealed bottle is less than expected after counting.	Yes, if greater than value listed in FDR C.01.061
	Manufacturer's Shortage	The content of a sealed bottle is less than expected after counting.	No, if smaller than or equal to value listed in FDR C.01.061
	Wrong Dispensing	Documented dispensing the wrong quantity or to the wrong patient.	No
	Breakage, and Spillage	Change in the dosage form, or other known incident preventing dispensing (for example crushed tablet).	No
	Unusual Waste	Waste or destruction of inventory	Yes



		beyond what is expected on the basis of normally accepted business practices. This could arise from unusual yield loss due to broken equipment, etc.	
	Miscounts	Error made in counting during inventory reconciliation or during dispensing.	No, if documented and part of normal business practices. Otherwise report as Loss Unexplained.
	Overages	Quantity found to be in excess of inventory.	No
	Destruction	Denaturation of a controlled substance to an extent that its consumption is rendered impossible or improbable.	No
	Other	Any other type of loss not described above.	Yes
Theft	Filled Forged Prescription	Dispensing a prescription that was found to be fraudulent.	Yes
	Unfilled Forged Prescription	Forged prescription that was not dispensed.	No
	Armed Robbery	Theft accomplished through threats of violence toward personnel at a site.	Yes
	Pilferage (Internal Theft)	Theft from a site by authorized personnel.	Yes
	Grab Theft	Theft from a site during working hours without warning. The person conducting the theft 'grabs' the product and escapes.	Yes
	Break and Entry	Theft from a site by forced entry.	Yes
	Impersonation	An individual impersonating the individual for which the prescription has been dispensed.	Yes
	Other	Any other type of theft not described above.	Yes

## 9. Health Canada Loss or Theft Reporting Form

The January 2019 version is depicted here.<sup>20</sup>



Healthy Environments and Consumer Safety Branch / Cannabis Legalization and Regulations Branch  
 Office of Controlled Substances / Office of Medical Cannabis  
 January 2019

In order to fill out and submit this form, please download and open in a PDF reader.

## Loss or Theft Report Form for Controlled Substances, Precursors and Cannabis

Office of Controlled Substances / Office of Medical Cannabis  
 File No.

1. Name of Establishment <input type="text"/>		Type of Report: <input checked="" type="radio"/> New <input type="radio"/> Amendment		2. Date of Discovery <input type="text"/>	
CRA Business Number <input type="text"/>					
3. Street <input type="text"/>	City <input type="text"/>	Province <input type="text" value="Select Province"/>	Postal code <input type="text"/>	4. Telephone <input type="text"/>	

5. Type of Establishment  
  Authorization/Registration # or Other

6. Type of Loss or Theft  If "Other", specify

7. Has this been reported to the police?  
 Yes  No

Name of Police Service   
 Incident number  Telephone number   
 Date reported to Police :   
 Name of Investigating officer   
 E-mail of Investigating officer

8. For loss in transit  
 Name of transport company  Investigation Report Received ?  Yes  No  
 Report Number

List of controlled substances, precursors and/or cannabis lost or stolen				
9. Trade name and unit strength. If no trade name exists, the generic or other product name and the name of the manufacturer.	10. Dosage form if applicable.	11. Unit of Measurement	12. Quantity	13. DIN/ NPN or Lot #
	<a href="#">Click to see options</a>	<a href="#">Click to see optio</a>		
	<a href="#">Click to see options</a>	<a href="#">Click to see optio</a>		
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	<a href="#">Click to see options</a>	<a href="#">Click to see optio</a>		
	<a href="#">Click to see options</a>	<a href="#">Click to see optio</a>		

\* Please indicate if a separate page is attached –  Yes  No

- Please attach the following as separate pages
- 14. Details of loss or theft discovery (including occurrence date if known)
  - 15. Description of physical security measures in place (for Licensed Dealers, if different than on file with the Authorization Division at the Office of Controlled Substances)
  - 16. Description of security measures put in place to prevent future loss or theft
  - 17. Summary of the report submitted to the Police

18. Name and title of official individual reporting loss or theft (printed):  Licence number:   
 Signature :  Date :  Email Address:



Appendix to: Fan M, Tscheng D, Hamilton M, et al. Opioid losses in terms of dosage and value, January 2012 to September 2017: a retrospective analysis of Health Canada data. *CMAJ Open* 2020. DOI:10.9778/cmajo.20190112. Copyright © 2020 Joule Inc. or its licensors

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