

Topic: Prescription history and toxicology findings among people who died of an illicit drug overdose in BC, 2015-2017

Data: October 18th, 2019 **Data Source:** B.C. Provincial Overdose Cohort

Key Findings:

- Among people who died from illicit*drug toxicity in BC, 7% had been prescribed opioids found to be relevant to death. As expected, few illicit drug toxicity deaths involved prescription opioids; these results show that the combination of prescribed and illicit opioids is also uncommon.
- Methadone (an opioid agonist) was relevant to death in a low proportion of cases (6%); 3.7% of people had a methadone prescription at the time of death. Methadone was found to be relevant to death more commonly than buprenorphine (130 cases vs 2 cases). Of those with an active prescription for methadone on the day of overdose, >50% received a low dose of 60mg or less. 39% of cases with methadone detected had no record of a community pharmacy dispensation for the medication in the 60 days prior to the overdose.
- Other classes of medications relevant to death varied in the proportions prescribed versus illicit. Essentially all stimulants deemed relevant to death were non-prescribed. More than half (63%) of benzodiazepines relevant to death were non-prescribed.

*Please note that the terms illicit and illicit drug toxicity death are used to be consistent with the BC Coroners Service terminology and case definitions (https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug.pdf). Some drugs can be both prescribed and obtained in the unregulated drug market while others appear in only the regulated or unregulated supply. In this short report, the term non-prescribed is used interchangeably with illicit or illegal.

Background:

- The B.C. Provincial Overdose Cohort is a set of linked datasets related to overdose
 events, including death, ambulance, emergency room, hospital, physician, and
 prescription records. The datasets were brought together to better understand factors
 associated with overdose in order to target provincial, regional, and local response
 activities.
- This analysis uses cases of illicit drug toxicity deaths, as identified by the BC Coroner's Service (N=2,872). Cases were restricted to those where the investigation was closed and post-mortem toxicology results were available (N=1,789). Prescription history is based on PharmaNet data.
- In a previous <u>Knowledge Update</u> (21 February 2018), prescription drug histories among people who overdosed from illegal drugs were described. It showed that among persons who overdosed, active prescriptions for opioids for pain at the time of overdose or in the past five years were not common.



 The focus of this update is to assess the correspondence between substances found relevant on decedent toxicology and the substances prescribed to the person in question.

Study Design and Methods:

- Cases were linked to their PharmaNet prescribing histories. We assessed for the presence of an active prescription within 60 days before overdose (with the period of active prescription defined as the day of medication dispensation until the supply end date as estimated by the pharmacist).
- Toxicology results were available to the Provincial Overdose Cohort only for those substances determined by the Coroner to have been relevant to the death (i.e. not incidentally detected). It is common for decedent toxicology to identify multiple substances of different classes as relevant to death. Substances were considered prescribed if there was an exact match between prescription and toxicology (e.g. hydromorphone on prescription and toxicology) or a correspondence between a prescription and a metabolite on toxicology (e.g. fentanyl on prescription and norfentanyl on toxicology).
- The following classes of medication were assessed: opioids, benzodiazepines/z-drugs, stimulants, gabapentinoids, antidepressants, and antipsychotics. A full list of the medications included in these classes is available in Smolina et al. (2018).

Findings & Interpretation:

Prescribed and Non-Prescribed Opioids

Of the people who the BC Coroners Service determined to have died from an illicit drug overdose¹ and for whom post-mortem toxicology was available, few (7%) had any opioids relevant to death that were prescribed to them; very few (0.2%) had only prescribed opioids and no non-prescribed opioids (Table 1 below). Of cases with one or more non-prescribed opioids relevant to death, most (92%) were found to have consumed fentanyl, a fentanyl analogue, and/or heroin. Fentanyl and fentanyl analogues were found in more than twice as many of these cases as heroin (79% vs. 33%) (Table 2).

As expected, few illicit drug toxicity deaths involved solely prescription opioids; these results confirm that the combination of prescribed and illegal opioids is also uncommon. Physicians should prescribe opioids in compliance with the updated CPSBC standards, which support tapering and discontinuation of opioids for chronic pain only with patient consent.

¹ I.e. at least one illegal or diverted substance was detected based on the Coroner's investigation.



Methadone and Buprenorphine

Methadone was found to be relevant to death more often than buprenorphine (130 cases vs. 2 cases) but was still only relevant in 6% of the illicit drug death cases with toxicology available. Of the cases where methadone was relevant, 39% had no history of it being prescribed within 60 days before overdose (Table 3). Of those with an active prescription on the day of overdose, approximately 50% had doses of <60mg, and only 30% had doses >=80mg.

Use of non-prescribed methadone can be an important way of managing opioid use and reducing harm for people who experience barriers or for other reasons they do not wish to access clinical OAT services (Harris and Rhodes, 2012). These results support the continued emphasis on decreasing barriers to medically-supervised OAT as a key priority for the provincial overdose response, in order to provide a safer alternative to contaminated illegal drugs and diverted methadone. At the same time, acknowledging that structured medical therapy will not be a preferred option for all people using opioids, supporting peer-based organizations and harm reduction agencies may provide an opportunity to help people more safely manage non-medically supervised methadone use.

Benzodiazepines and Z-Drugs

Only 6% of fatal cases had benzodiazepines or z-drugs relevant to death. In the majority (63%) of these cases, benzodiazepines and z-drugs had not been prescribed within 60 days before overdose (Table 4).

Non-prescribed benzodiazepines were more commonly found to be relevant to death among people experiencing fatal overdose than were prescribed benzodiazepines. With decreasing prescription of benzodiazepines in BC and increasing detection of novel illegal benzodiazepines (e.g. etizolam and fluabromazolam), attention should be given to supporting people with benzodiazepine use disorder. Drug checking and surveillance activities to better understand and respond to benzodiazepine contamination of other substances is also essential. Expansion of mental health services to better address untreated anxiety and trauma, which may lead to self-treatment with benzodiazepines, is also important, as is harm reduction messaging specifically around benzodiazepines.

Other Classes of Medication

Other classes of medication that were assessed were stimulants, gabapentinoids, antidepressants, and antipsychotics (Table 5). Among persons with stimulants found relevant in death, very few had prescriptions for this class of medication. Absolute numbers of cases with gabapentinoids, antidepressants, and antipsychotics relevant in death were low; approximately one-fifth of those with each class relevant had no active prescription within 60 days.

Essentially all stimulants identified on toxicology were non-prescribed. This may reflect the low rates of prescribing of stimulants for ADHD in this population, or the reduction in risk of overdose among those who do receive stimulants. Prescription of stimulants for



people with stimulant use disorder is an area being explored within specialist addiction medicine and in research environments. Results about the contribution of stimulant maintenance therapy to the reduction of overdose risk are eagerly awaited, particularly given the limited therapeutic options currently available for stimulant use disorder.

Limitations:

A limitation of this analysis is that we are unable to identify the sources of medications that are consumed but not prescribed. Street methadone, whether diverted or imported, may have contributed to some of the fatal cases where methadone was detected. Diversion or illegal importation is also a potential factor for other classes of medication; other possibilities include provision of samples at physicians' offices; consumption of previously prescribed medication; provision of medication by first responders, in acute care settings, or in prison; or contamination/adulteration of other illegal drugs.

In cases where an opioid was detected on toxicology and associated to a prescription, consumption of an illicit opioid may also be possible as compounds may break down in a similar manner, e.g. prescribed morphine and illicit morphine. This may be captured in the full Coroners investigation but not in the data received by BCCDC. In addition, the case definition for illicit drug toxicity death excludes people who died from prescription drugs only. At the present rate of opioid-associated mortality in BC, the proportion attributable to pharmaceutical opioids exclusively is thought to be low (McLarnon 2017).

For more information on the Prescribing Patterns Working Group or the Provincial Overdose Cohort, please contact Amanda Slaunwhite amanda.slaunwhite@bccdc.ca

All inferences, opinions, and conclusions drawn in this Knowledge Update are those of the authors, and do not reflect the opinions or policies of the Data Steward(s).



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Table 1. Prescribed* and non-prescribed opioids among illicit drug overdose deaths, 2015-2017.

	N	% of total	% of opioid-
	(1789)	cases	related cases
No opioids relevant to death**	259	14.5%	-
Any opioid relevant to death	1530	85.5%	-
Prescribed opioids***	36	0.2%	2.4%
Prescribed and non-prescribed opioids	120	6.7%	7.8%
Non-prescribed opioids	1374	76.8%	89.8%

^{*}Active prescription within 60 days before overdose

Table 2. Presence of fentanyl/analogues and heroin among fatal illicit drug overdose cases who had at least one non-prescribed opioid relevant, 2015-2017.

	N (1494)	Proportion (%)
Fentanyl or analogue (3-Methylfentanyl, acetylfentanyl, carfentanil, furanylfentanyl)	1,173	78.5%
Heroin	494	33.1%
No fentanyl/analogue or heroin	115	7.7%

Table 3. Past 60-day prescriptions of methadone and buprenoprphine among fatal overdose cases with methadone, EDDP (a methadone metabolite), and/or buprenorphine relevant to death, 2015-2017.

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Methadone/EDDP relevant			
	N	% of total illicit drug deaths	% of deaths with methadone/EDDP relevant
Active Rx within 60 days	80	4.5%	61.5%
No active Rx within 60 days	50	1.7%	38.5%
Total with methadone and/or EDDP relevant	130	7.3%	100%
	Bupre	norphine relevant	
	N	% of total illicit drug deaths	% of deaths with buprenorphine relevant
Active Rx within 60 days	<5	0.1%	100%
No active Rx within 60 days	0	0%	0%
Total with buprenorphine relevant	<5	0.1%	100%

^{**} The most common substances found relevant to death among the cases without opioids detected were cocaine, methamphetamine, and alcohol.

^{***} Note that an illicit substance was involved in death in order for the Coroner to categorize the case as an illicit drug toxicity death, e.g. methamphetamine.



Table 4. Prescribed* and non-prescribed benzodiazepines and z-drugs relevant to death among illicit drug overdose deaths, 2015-2017.

	N	% of total	% of benzo/z-drug-
	(1,789)	cases	related cases
No benzo/z-drugs relevant	1,682	94.0%	-
Any benzo/z-drugs relevant	107	6.0%	-
Prescribed benzo/z-drugs	35	2.0%	32.7%
Prescribed and non-prescribed benzo/z-drugs	5	0.3%	4.7%
Non-prescribed benzo/z-drugs	67	3.7%	62.6%

^{*}Active prescription within 60 days before overdose.

Table 5. Prescription status* of other classes of medication relevant to death among illicit drug overdose deaths, 2015-2017.

	N (1,789)	% of total cases	% of class- related cases
Gabapentinoids		1	
No gabapentinoids relevant	1,760	98.4%	-
Any gabapentinoids relevant	29	1.6%	-
Prescribed gabapentinoids	24	82.8%	82.8%
Non-prescribed gabapentinoids	5	17.2%	17.2%
Stimulants			
No stimulants relevant	526	29.4%	-
Any stimulants relevant	1,263	70.6%	-
Prescribed; prescribed and non-prescribed stimulants ^a	12ª	0.67%	1.0%
Non-prescribed stimulants	1,251	69.9%	99.0%
Antidepressants	·		
No antidepressants relevant	1,667	93.2%	-
Any antidepressants relevant	122	6.8%	-
Prescribed antidepressants	82	4.6%	67.2%
Prescribed and non-prescribed antidepressants	13	0.7%	10.7%
Non-prescribed antidepressants	27	1.5%	22.1%
Antipsychotics			
No antipsychotics relevant	1,743	97.4%	-
Any antipsychotics relevant	46	2.6%	-
Prescribed antipsychotics	38	2.2%	82.6%
Non-prescribed antipsychotics	8	0.4%	17.4%

^{*}Active prescription within 60 days before overdose.

^aThe categories "Prescribed only" and "Prescribed and non-prescribed" were collapsed due to small cell size (<5) for the "Prescribed only" category.



References:

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- 3. McLarnon M. Preventing Pharmaceutical Opioid-Associated Mortality in British Columbia: A Review of Prescribed Opioid Deaths, 2009-2013. BC Ministry of Health: 2017. https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/pharmaceutical-opioid-mortality.pdf