BC Centre for Disease Control
Provincial Health Services Authority

KNOWLEDGE UPDATE

Neurological Injury† Following Overdose: Preliminary Descriptive Results from the Provincial Overdose Cohort

Date: January 3, 2020 **Data Source:** Provincial Overdose Cohort

- Historical highs in overdose deaths and non-fatal events have persisted since the April 2016 declaration of the British Columbia (BC) Public Health Emergency. Concern regarding the unmeasured burden of neurological injury related to overdose has been expressed by many stakeholders in BC, ranging from the medical and public health community to local organizations providing services and supports.[1]

- Questions commonly asked by stakeholders include:
  - Is the prevalence of long-term neurological impairment increasing in BC?
  - What proportion of neurological injury in BC is overdose-related?
  - How does the diagnostic and treatment journey among persons who have an overdose-related neurological injury differ from traumatic brain injury?
  - Will available medical and community services be able to adequately meet the needs of British Columbians with neurological impairment?

- These concerns have prompted this preliminary assessment in the BC Provincial Overdose Cohort (ODC). Measuring neurological injury using administrative health data has limitations and likely only captures the most severe cases.

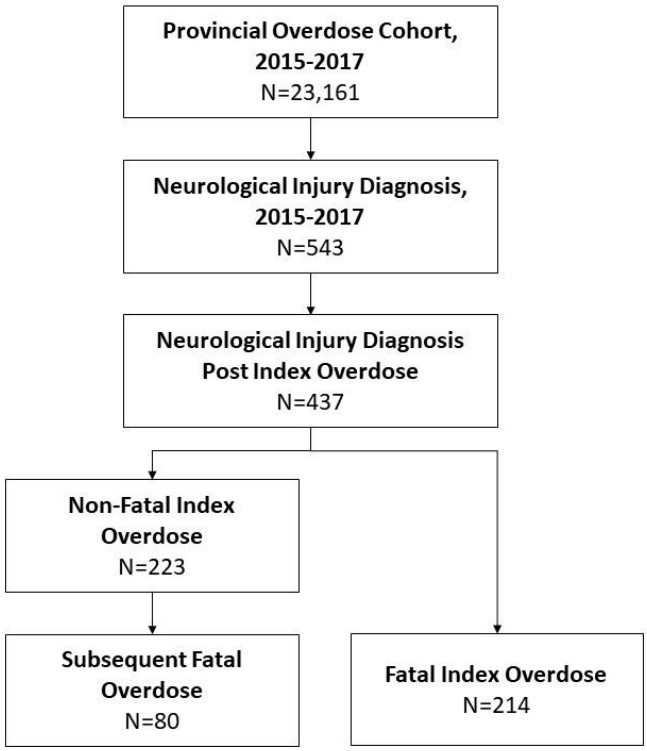
- This summary provides an initial assessment of neurological injury and overdose to inform program and service development, and highlights opportunities for further research.

† In this document, **Neurological Injury** refers to a limited subset of neurocognitive injury or impairment that can be identified from administrative data based on diagnostic codes and is not specific to overdose as a mechanism of injury.

Brain injury can have wide-ranging physical and psychological effects which may include changes in sensory, motor, cognitive, or executive functioning, as well as communication, social, and/or behavioural changes. Effects can range from mild to moderate to severe and can include delayed onset of degenerative changes.

Study Design and Methods:

- We examined data on 23,161 people in the ODC who had one or more overdose events between January 1st, 2015 and December 31st, 2017.
- Neurological injury was identified in the same period based on three diagnostic codes outlined in Morrow et al. (2019).[2]
    - These codes were for:
        - anoxic brain injury
        - toxic encephalopathy; and
        - encephalopathy, unspecified
    - Diagnostic codes were identified from the following data sources:
        - Hospital - Discharge Abstract Database (DAD)
        - National Ambulatory Care Reporting System (NACRS)
        - Physician billing - Medical Services Plan (MSP)
- We first identified all people with a diagnosis of neurological injury in the ODC and in a 20% random sample of the general BC population.
- People were included in further descriptive analysis if they were in the ODC and had a record of a neurological injury at any time after their **first recorded overdose (Index Overdose)**. Descriptive analyses examined basic characteristics of age, sex, geography, and recorded overdose events.



Background literature on neurological injury after a non-fatal overdose:

Literature examining neurological injury following overdose largely focuses on mortality rather than long-term outcomes in survivors. Neurological injuries can be classified as hypoxic, traumatic, or toxic, but there are no standardized ways to distinguish specific mechanisms of injury by clinical or radiologic patterns.

A BC study followed 2,433 patients admitted to hospital between 2006 and 2015 and found that 3% of accidental opioid overdose admissions included encephalopathy.[2] An Australian study followed a small sample of patients through rehabilitation after hypoxic injury following heroin overdose, noting significant gains in both motor and global function, though some problem-solving and social deficits remained.[3] Another recent Australian study compared hospital discharges between patients who had an overdose and controls, identifying more frequent deficits in visual motor skills, executive function, working memory, impulsivity, and decision-making.[4]

Diagnosis of neurological injury is complex as clinical presentations vary, delayed onset post-hypoxic syndromes are possible, and there is rarely any objective measure of pre-existing neurological function.[5] There is also a lack of validated approaches to measuring neurological impairment in population-level data. The ability to assess and monitor neurological injury at a population level is hampered by a lack of global, post-overdose neurological screening tools.

A recent Canadian meta-analysis reported high lifetime prevalence of traumatic brain injury among homeless and marginally housed people.[6] A series of studies in marginally housed BC residents have found high rates of substance dependence, mental health conditions, and multi-morbidity, including HIV, hepatitis C, and brain injury.[7-9] A critical gap is the lack of effectiveness of current treatment approaches for people with complex multi-morbidity. [6-9]

Prior to 2015, fentanyl prevalence in the drug supply in BC, while not negligible, was low. There has been an increase in the proportion of deaths in which fentanyl was detected and the presence of fentanyl in community drug and urine testing.[10] The risk of overdose varies by time and place across the province, impacting interpretations of overdose risk factors and trends from the ODC.

To adequately understand the issue of neurological injury, we must identify ways to measure the magnitude of the condition and its drivers while considering the compounding effects of other co-morbid health conditions.[11] A syndemic framework examining the health consequences of disease interactions and the social, environmental, or economic factors that contribute may be a helpful approach for this complex issue.[12]

Key Descriptive Findings:

Neurological injury diagnosis in the ODC as compared to a 20% random sample of the BC population:

From 2015 to 2017, 543 (2.3%) of persons in the ODC were diagnosed with neurological injury compared to 636 (0.06%) of persons from the 20% random population sample. (Table 1)

90% of neurological injury diagnostic codes were obtained from hospitalization data sources (DAD or NACRS) and 10% were from physician billing data (MSP). (Table 2)

People diagnosed in the ODC after the **Index Overdose** (n=437):

While there were 543 persons diagnosed in the ODC (N=23,161), 437(1.9%) of these were diagnosed after the Index Overdose.

Of the 437 people who were diagnosed following Index Overdose, 214(49%) died within the Index Overdose episode (i.e. died during the hospital admission related to the Index Overdose). The high proportion of people dying may reflect that the analysis captures the most severe cases. Further work is needed to elucidate causes of death (e.g. organ failure, infection, neurological injury)

The distribution of age and sex among people with a neurological injury after the Index Overdose was slightly different than the distribution of all persons who have had an overdose in BC but did not have a diagnosis. People with a neurological injury tended to be older and there was a higher proportion of men. Further work is needed to determine if these differences are of meaningful significance. (Table 3 and 7)

Among people whose **Index Overdose** was non-fatal (n=223):

Of the 223 non-fatal index overdose cases, 48% had a single overdose event on record, while 52% had two or more recorded overdoses. This differs from the overall ODC (N=23,161), in which 70% of people had a single overdose event and 30% had two or more overdoses.

Of the 223 people, 36% died from a subsequent overdose before the end of 2017 (Table 4)

Of the 223 people, 28% were diagnosed within 48hrs of the Index Overdose (Table 5). Further work is needed to understand the duration of time after an overdose event in which a diagnosis can occur. This was not attempted here due to the ambiguity in attributing the neurological injury diagnosis to an index event the further out in time the diagnosis is from the event as well as the need to consider all intervening events and varying follow up time of individuals in the ODC.

Summary:

High occurrence of neurological injury in the Provincial Overdose Cohort

- Between 2015 and 2017, 23,161 people were identified in the ODC as having a recorded non-fatal or fatal overdose.
    - 543 persons in the ODC had diagnostic codes for a neurological injury between 2015 and 2017
    - Of the 543 people, 437 people were diagnosed following their first recorded overdose event (**Index Overdose**).
    - The frequency of this diagnosis in the ODC is similar to published studies that used samples of persons hospitalized for overdose and is much higher than in the general population of BC.
    - Further work is required to quantify the BC population prevalence and incidence of neurological injury following overdose, including mild to moderate injury.

- Half of people diagnosed with a neurological injury after the **Index Overdose** died during the hospitalization from the **Index Overdose**.
    - Of people whose Index Overdose was non-fatal, 36% died from a subsequent overdose before the end of 2017.
    - This analysis approach likely identifies severe cases with very high mortality.

- Diagnosis of neurological injury is complex and may occur after the overdose event. There is uncertainty in attributing a neurological diagnosis to a particular overdose event as it may be related to a different and/or uncaptured event.

Interpretation:

In the ODC, there is high occurrence of neurological injury diagnosis compared to the general BC population. In addition, there is high fatality among persons with an overdose admission and a neurological injury diagnosis. Assessing neurological injury using diagnostic codes in administrative health data is biased towards more severe cases and likely underestimates mild to moderate injuries. Of people whose first recorded overdose was non-fatal and later had a diagnosis of neurological injury, 36% died from a subsequent overdose between 2015 and 2017. While the toxicity of the drug supply in BC has increased during this period, this finding suggests increased risk of mortality among people who have experienced an overdose and a neurological injury.

Diagnosis of neurological injury and long-term impairment is complex; thus it is challenging to measure and examine the burden of disease attributable to overdose. A validated case definition shared across disciplines could assist clinicians in recording these events and allow population health assessment, addressing the current issues of conceptual ambiguity. There is also a need to improve and validate methods for measuring this condition in administrative health data along with other approaches such as standardized prospective data collection and qualitative and community-based inquiry. A critical gap identified in the literature is lack of effective treatment approaches for people with complex multi-morbidity who use drugs. Finally, future health services research could fill in gaps in our understanding of whether services and support are accessible and adequate for people with complex multi-morbidity, including neurological impairment.

Next Steps:

Further work is needed to better distinguish newly acquired neurological injuries from pre-existing/prevalent neurological impairment in order to report *incidence* (rate of newly acquired neurological injury in a population) and *prevalence* (number of people living with neurological impairment in a population).

Additional analyses are required to understand the impact of multiple overdoses on severity and presentation of neurological diagnoses.

Beyond descriptive analyses, survival analyses and other approaches that consider multiple predictors and confounders while assessing relative risk are planned for the ODC with data refreshed to the end of 2019.

Limitations:

- This analysis used administrative health data to identify people who had a neurological injury following Index Overdose. Administrative data do not capture all diagnoses, particularly mild to moderate diagnoses. Additionally, there are no validation studies which examine the reliability of these diagnostic codes for identifying neurological outcomes.

- Due to the cross-sectional and descriptive nature of this analysis, we cannot confirm that all diagnoses were as a result of overdose. Historical data covering the lifespan was not available, such that some prior diagnoses or contributing events may have been be missed. For cases where the diagnosis was distal from the overdose event, it is challenging to attribute diagnosis to an overdose event.

- The ODC only captures overdose cases where people accessed health care for an overdose. People who had a non-fatal overdose in the community but did not seek medical care may be excluded, or may be included for some events while other events may be missing. These data do not capture all overdoses people are experiencing or all people who have had a non-fatal overdose event in BC. Unrecorded overdose events (e.g. overdose events responded to by bystanders) may mean we are not capturing the closest overdose event to the diagnosis.

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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. Neurological injury diagnosis in the ODC and 20% Random Population Sample, 2015 – 2017

	ODC		20% Random Sample of the BC Population
	Any Diagnosis	Diagnosis After Index Overdose	Any Diagnosis
Neurological Injury	543	437	636
Population Denominator	23,161	23,161	1,048,647
Proportion (%) with Neurological Injury	2.3%	1.9%	0.06%

Table 2. Data source of neurological injury diagnosis following Index Overdose (n=437)

Diagnosis Source	**Diagnosed after Index Overdose (n=437)**		**Non-Fatal (n=223)**		**Fatal (n=214)**	
	N	**%**	**N**	**%**	**N**	**%**
Discharge Abstract Database (DAD)	387	88.56	182	81.61	205	95.79
Medical Services Plan (MSP)	43	9.84	34	15.25	9	4.21
National Ambulatory Care Reporting System	7	1.60	7	3.14	0	0.00

Table 3. Demographic characteristics of people with neurological injury diagnosis following Index Overdose

2015 – 2017	**Diagnosed after Index Overdose (n=437)**		**Non-Fatal (n=223)**		**Fatal (n=214)**	
	N	**%**	**N**	**%**	**N**	**%**
Age[a]						
<15 years	0	0.00	0	0.00	0	0.00
15 - 19 years	12	2.75	s	s	s	s
20 - 24 years	27	6.18	14	6.28	13	6.07
25 - 29 years	54	12.36	34	15.25	20	9.35
30 - 34 years	53	12.13	24	10.76	29	13.55
35 - 39 years	58	13.27	30	13.45	28	13.08
40 - 44 years	38	8.70	15	6.73	23	10.75
45 - 49 years	61	13.96	39	17.49	22	10.28
50 - 54 years	40	9.15	16	7.17	24	11.21
55 - 59 years	38	8.70	16	7.17	22	10.28
60 - 64 years	32	7.32	20	8.97	12	5.61
65 years +	24	5.49	12	5.38	12	5.61
Sex						
Male	324	74.14	161	72.20	163	76.17
Female	113	24.86	62	27.80	51	23.83

s- counts between 1 and 4 have been suppressed. Additionally counts equal to zero or greater than four were also suppressed in some instances to avoid identification of another single cell suppressed in the same category.

Table 3. Continued - Demographic characteristics of people with neurological injury diagnosis following Index Overdose

Health Authority[b]	Diagnosed after Index Overdose (n=437)		Non-Fatal (n=223)		Fatal (n=214)	
	N	%	N	%	N	%
Interior Health	58	13.27	27	12.11	31	14.49
Fraser Health	175	40.05	81	36.32	94	43.93
Northern Health	19	4.35	10	4.48	9	4.21
Vancouver Island Health	61	13.96	34	15.25	27	12.62
Vancouver Coastal	120	27.46	69	30.94	51	23.83

[a] Age in 2017 or at time of death; [b] Health Authority of residence in 2015

Table 4. Overdose characteristics among people with neurological injury diagnosis following Index Overdose

	Diagnosed after Index Overdose (n=437)		Non-Fatal (n=223)		Fatal (n=214)	
	N	%	N	%	N	%
First Recorded Overdose, 2015-2017						
2015	129	29.52	87	39.01	42	19.63
2016	152	34.78	79	35.43	73	34.11
2017	156	35.70	57	25.56	99	46.26
Number of Overdoses[c]						
1 overdose	319	73.00	105	47.09		
2 overdoses	55	12.59	55	24.66		
3 overdoses	29	6.64	29	13.00		
4 or more overdoses	34	7.78	34	15.25		
Yes	294	67.28	80	35.87		
No	143	32.72	143	64.13		

[c] Number of overdoses between 2015-2017 for persons who were diagnosed with a brain injury post-overdose

Table 5. Time to Diagnosis Following Index Overdose

	Diagnosed after Index Overdose (n=437)		Non-Fatal (n=223)		Fatal (n=214)	
	N	%	N	%	N	%
Less than 48h	266	60.87	62	27.8	204	95.33
48h or more	171	39.13	161	72.19	10	4.67

Table 6. Diagnostic Codes[d] - International Classification of Diseases (ICD) 10th and 9th edition

Diagnosis Source	ICD-10	ICD-9	Description
DAD	G93.1 G92 G93.4		Encephalopathy, including anoxic brain damage, toxic encephalopathy, or unspecified encephalopathy
MSP		348.1 323.71 323.72 349.82 348.30	Encephalopathy, including anoxic brain damage, toxic encephalopathy, toxic encephalitis and encephalomyelitis, toxic myelitis, or unspecified encephalopathy
NACRS	G931 G92 G934		Encephalopathy, including anoxic brain damage, toxic encephalopathy or unspecified encephalopathy

[d] Neurological injury was defined following the encephalopathy definition from the study by Morrow et al. 2019, which included ICD-10 codes. To examine neurological injury diagnoses in MSP, we converted the ICD-10 to ICD-9 codes.

Table 7. Age and sex comparison in those diagnosed and not diagnosed after Index Overdose from the Overdose Cohort
(N=23, 161)

	Diagnosed after Index Overdose		Not Diagnosed		
	n=437	%	n=22,724	%	Sig
Age					**p < 0.05**
<15	0	0.0%	81	0.4%	
15 - 19 years	12	2.7%	943	4.1%	
20 - 24 years	27	6.2%	2455	10.8%	
25 - 29 years	54	12.4%	3205	14.1%	
30 - 34 years	53	12.1%	3046	13.4%	
35 - 39 years	58	13.3%	2747	12.1%	
40 - 44 years	38	8.7%	2111	9.3%	
45 - 49 years	61	14.0%	2132	9.4%	
50 - 54 years	40	9.2%	1959	8.6%	
55 - 59 years	38	8.7%	1537	6.8%	
60 - 64 years	32	7.3%	996	4.4%	
65 years +	24	5.5%	1512	6.7%	
Sex					**p < 0.01**
Female	113	25.9%	7430	32.7%	
Male	324	74.1%	15294	67.3%	