Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.
**eTable 1. Outcome Measure: Fatal and Nonfatal Overdose Case Definitions**

| NON-FATAL OVERDOSE                                                                 |                                                                 |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------------|
| **BC Emergency Health Services:** Patient Care Information System                 | Naloxone administered by paramedics OR Impression code: Recreational Drug OD AND CARD in (9,23,26,31)*, OR Impression code: Cardiac arrested: treated and CARD 23 |
| **BC Emergency Health Services:** Siren                                            | Naloxone administered OR Impression code: ‘Opioid-related’, ‘opioid-related/OD’, OR Impression code: Cardiac arrest and CARD 23* |
| **Drug and Poison Information Centre**                                            | Any call with a code related to drug overdose/poisoning          |
| **Enhanced Emergency Department**                                                 | Case-based reports by Emergency Departments by participating health authority |
| **Medical Services Plan,** **Discharge Abstract Database,** **National Ambulatory Care Reporting System** | Case defined by ICD version 9 and 10 (e.g., 965.0-poisoning by opiates and related narcotics; E850.0-accidental poisoning by opiates and related narcotics) OR *CARD 9: Cardiac or respiratory arrest/death; CARD 23: Overdose/poisoning (ingestion); CARD 26: Sick; CARD 31: Unconscious |

| FATAL OVERDOSE                                                                   |                                                                 |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------------|
| **BC Coroner Service**                                                           | Open investigations (toxicology pending) and closed drug overdose deaths |
| **Vital Statistics Deaths**                                                      | Case defined by ICD version 9 and 10 (e.g., 965.0-poisoning by opiates and related narcotics; E850.0-accidental poisoning by opiates and related narcotics) OR *CARD 9: Cardiac or respiratory arrest/death; CARD 23: Overdose/poisoning (ingestion); CARD 26: Sick; CARD 31: Unconscious |
| **Drug-related overdose algorithm**                                              | If death date from other administrative databases (e.g., client roster) lies between the start date and end date of an overdose episode, then this overdose episode is defined as a fatal overdose. In these cases, please use the overdose episode start date as the date of the fatal overdose |
**eTable 2.** Exposure: Type of Substance Use Disorder Diagnosis

| Diagnosis              | ICD9 codes       | ICD10 codes | Algorithm                                           |
|------------------------|------------------|-------------|----------------------------------------------------|
| **Substance use disorder** |                  |             |                                                    |
| Stimulant use disorder | 3042, 3052, 3044, 3057 | F14, F15    | Either: 2 family physician visits or 1 hospitalization in 1 year |
| Opioid use disorder    | 3040, 3047, 3055 | F11         | Either: 2 family physician visits or 1 hospitalization in 1 year |
### eTable 3. Comorbidities: ICD-10 codes used in Elixhauser comorbidity categories

| Category | ICD-10 codes |
|----------|--------------|
| 1. Congestive heart failure | I099, I110, I130, I193, I255, I420, I425, I426, I427, I428, I429, I43, I50, P290 |
| 2. Cardiac arrhythmia | I441, I442, I443, I456, I459, I47, I48, I49, R000, R001, R008, T821, Z450, Z950 |
| 3. Valvular disease | A520, I05, I06, I07, I08, I091, I098, I34, I35, I36, I37, I38, I39, Q231, Q232, Q233, Z952, Z953, Z954 |
| 4. Pulmonary circulation disorders | I26, I27, I280, I288, I289 |
| 5. Peripheral vascular disorders | I70, I71, I731, I738, I739, I771, I790, I792, K551, K558, K559, Z958, Z959 |
| 6. Hypertension uncomplicated | I10 |
| 7. Hypertension complicated | I11, I12, I13, I15 |
| 8. Paralysis | G041, G114, G801, G802, G81, G82, G830, G831, G832, G833, G834, G839 |
| 9. Other neurological disorders | G10, G11, G12, G13, G20, G21, G22, G254, G255, G312, G318, G319, G32, G35, G36, G37, G40, G41, G931, G934, R470, R56 |
| 10. Chronic pulmonary disease | I278, I279, J40, J41, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, J684, J701, J703 |
| 11. Diabetes uncomplicated | E100, E101, E109, E110, E111, E119, E120, E121, E129, E130, E131, E139, E140, E141, E149 |
| 12. Diabetes complicated | E10-E0E108, E112-E118, E122-E128, E132-E138, E14-E148 |
| 13. Hypothyroidism | E00-E03, E890 |
| 14. Renal Failure | I120, I131, N18, N19, N250, Z490, Z491, Z492, Z940, Z992 |
| 15. Liver disease | B18, I85, I865, I982, K70, K711, K713, K714, K715, K717, K72, K73, K74, K760, K762-K769, Z94 |
| 16. Peptic ulcer excluding bleeding | K257, K259, K267, K269, K277, K279, K287, K289 |
| 17. HIV/AIDS | B20, B21, B22, B24 |
| 18. Lymphoma | C81-C85, C88, C96, C900, C902 |
| 19. Metastatic cancer | C77-C80 |
| 20. Solid tumor without metastasis | C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C76, C97 |
| 21. Rheumatoid arthritis/collagen | L940, L941, L943, M05, M06, M08, M120, M123, M30, M310, M311, M312, M313, M32, M33, M34, M35, M45, M461, M468, M469 |
| 22. Coagulopathy | D65, D66, D67, D68, D691, D693, D694, D695, D696 |
| 23. Obesity | E66 |
| 24. Weight loss | E40-E46, R634, R64 |
| 25. Fluid and electrolyte disorders | E222, E86, E87 |
| 26. Blood loss anemia | D500 |
| 27. Deficiency anemia | D508, D509, D51, D52, D53 |

Based on ICD-10 codes categorised by Quan et al.

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1 Quan, H., Sundararajan, V., Halfon, P., Fong, A., Burnand, B., Luthi, J. C., ... & Ghali, W. A. (2005). Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Medical care*, 1130-1139
**eTable 4. Mental Illness Algorithm**

| Diagnosis                      | ICD9 codes       | ICD10 codes | Algorithm                                                                 |
|-------------------------------|------------------|-------------|---------------------------------------------------------------------------|
| **Mental illness**            |                  |             |                                                                           |
| Depression                    | 300.4            | F32         | Either: 2 family physician visits or 1 hospitalization in 1 year         |
|                               | 311              | F33         |                                                                           |
|                               | 50B (also requires another code to qualify) | F34.1       |                                                                           |
| Anxiety                       | 300 (excluding 300.4) | F40         | Either: 2 family physician visits or 1 hospitalization in 1 year         |
|                               | 50B (also requires another code to qualify) | F41         |                                                                           |
| Stress and adjustment disorder | 308              | F43         | Either: 2 family physician visits or 1 hospitalization in 1 year         |
|                               | 309              |             |                                                                           |
| Schizophrenia                 | 295              | F20         | Either: 2 family physician visits or 1 hospitalization in 1 year         |
|                               | 297              | F21         |                                                                           |
|                               | 298              | F22         |                                                                           |
|                               |                  | F23         |                                                                           |
|                               |                  | F24         |                                                                           |
|                               |                  | F25         |                                                                           |
|                               |                  | F28         |                                                                           |
|                               |                  | F29         |                                                                           |
| Bipolar disorder              | 296              | F30         | Either: 2 family physician visits or 1 hospitalization in 1 year         |
|                               |                  | F31         |                                                                           |
|                               |                  | F34 (excluding F34.1) |                                               |
|                               |                  | F38         |                                                                           |
|                               |                  | F39         |                                                                           |
Table 5. Hazard ratios for fatal overdose in relation to each characteristic of interest based on the Cox proportional-hazards model

| Characteristic          | Fatal overdose |          |          |
|-------------------------|----------------|---------|---------|
|                         | Unadjusted HR (95% CI) | Adjusted HR (95% CI) |
| SUD diagnosis           |                |         |         |
| Neither                 | Reference (1.00) | Reference (1.00) |
| OUD only                | 2.00 (1.22-3.29) | 1.58 (0.95-2.64) |
| StUD only               | 1.98 (1.28-3.06) | 1.47 (0.93-2.34) |
| OUD & StUD              | 3.46 (2.32-5.16) | 2.37 (1.50-3.75) |
| Age group, years        |                |         |         |
| < 30                    | Reference (1.00) | Reference (1.00) |
| 30 - 39                 | 1.16 (0.86-1.57) | 1.13 (0.84-1.54) |
| ≥ 40                    | 1.10 (0.81-1.49) | 1.15 (0.83-1.57) |
| Sex                     |                |         |         |
| Females                 | Reference (1.00) | Reference (1.00) |
| Males                   | 1.33 (0.88-2.03) | 1.65 (1.07-2.55) |
| Mental illness diagnosis|                |         |         |
| No                      | Reference (1.00) | Reference (1.00) |
| Yes                     | 1.51 (1.17-1.94) | 1.04 (0.79-1.36) |
| Elixhauser comorbidity index |            |         |         |
| None                    | Reference (1.00) | Reference (1.00) |
| 1                       | 1.82 (1.19-2.78) | 1.23 (0.78-1.91) |
| ≥ 2                     | 2.61 (1.63-4.18) | 1.79 (1.09 -2.95) |
| Number of incarceration  |                |         |         |
| 1 - 2                   | Reference (1.00) | Reference (1.00) |
| 3 - 4                   | 1.52 (1.07-2.15) | 1.65 (1.16-2.35) |
| 5 - 7                   | 1.71 (1.18-2.47) | 1.76 (1.21-2.55) |
| ≥ 8                     | 2.25 (1.62-3.11) | 2.02 (1.44-2.83) |
| Region of residence     |                |         |         |
| Interior                | Reference (1.00) | Reference (1.00) |
| Fraser                  | 1.47 (0.93-2.30) | 1.38 (0.88-2.18) |
| Vancouver Coastal       | 1.87 (1.17-2.98) | 1.54 (0.96-2.48) |
| Island                  | 1.69 (1.03-2.78) | 1.64 (1.00-2.70) |
| Characteristic | Fatal overdose |
|---------------|----------------|
|               | Unadjusted HR (95% CI) | Adjusted HR (95% CI)<sup>a</sup> |
| Northern      | 1.16 (0.65-2.08)       | 1.13 (0.63-2.04) |
| Unspecified   | 0.14 (0.05-0.40)       | 0.14 (0.05-0.40) |

CI = confidence interval; HR = hazard ratio; OUD = opioid use disorder; StUD = stimulant use disorder; SUD = substance use disorder.

<sup>a</sup> Adjusted HRs were controlled for all other variables in the table.

<sup>b</sup> Excluding mental illness and substance use categories.

<sup>c</sup> Occurred between 2010 and 2019.
### eTable 6. Hazard Ratios for Drug Overdose in Relation to Each Characteristic of Interest

| Characteristic                  | Non-fatal overdose | Fatal overdose |
|--------------------------------|--------------------|---------------|
|                                | Unadjusted HR (95% CI) | Adjusted HR (95% CI)<sup>b</sup> | Unadjusted HR (95% CI) | Adjusted HR (95% CI)<sup>b</sup> |
| SUD diagnosis                  |                    |               |                    |                             |
| Neither                        | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| OUD only                       | 3.37 (2.64-4.29)   | 2.03 (1.57-2.62) | 1.99 (1.21-3.27)   | 1.58 (0.93-2.68)            |
| StUD only                      | 2.69 (2.13-3.39)   | 1.52 (1.20-1.92) | 1.96 (1.27-3.01)   | 1.46 (0.92-2.32)            |
| OUD & StUD                     | 5.15 (4.24-6.24)   | 2.45 (1.94-3.11) | 3.45 (2.31-5.14)   | 2.39 (1.48-3.86)            |
| Age group, years               |                    |               |                    |                             |
| < 30                           | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| 30 - 39                        | 0.92 (0.79-1.08)   | 0.91 (0.78-1.06) | 1.15 (0.85-1.56)   | 1.13 (0.84-1.53)            |
| ≥ 40                           | 0.61 (0.51-0.73)   | 0.71 (0.60-0.84) | 1.08 (0.80-1.46)   | 1.12 (0.81-1.54)            |
| Sex                            |                    |               |                    |                             |
| Females                        | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| Males                          | 0.82 (0.69-0.98)   | 1.09 (0.92-1.30) | 1.34 (0.88-2.04)   | 1.65 (1.07-2.54)            |
| Mental illness diagnosis       |                    |               |                    |                             |
| No                              | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| Yes                             | 2.42 (2.10-2.78)   | 1.49 (1.28-1.73) | 1.50 (1.17-1.93)   | 1.04 (0.78-1.37)            |
| Elixhauser comorbidity index<sup>c</sup> |  |  |  |  |
| None                            | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| 1                               | 2.47 (1.98-3.09)   | 1.46 (1.15 - 1.86) | 1.77 (1.16 - 2.71) | 1.20 (0.76 - 1.90)          |
| ≥ 2                             | 1.57 (1.14-2.17)   | 1.03 (0.75 - 1.42) | 2.38 (1.49 - 3.80) | 1.66 (1.01 - 2.73)          |
| Number of incarceration<sup>d</sup> |  |  |  |  |
| 1 - 2                           | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| 3 - 4                           | 1.84 (1.55-2.19)   | 1.92 (1.61-2.28) | 1.52 (1.07-2.15)   | 1.66 (1.17-2.35)            |
| 5 - 7                           | 2.76 (2.32-3.30)   | 2.78 (2.33-3.31) | 1.71 (1.19-2.47)   | 1.75 (1.20-2.54)            |
| ≥ 8                             | 4.72 (4.01-5.56)   | 4.21 (3.57-4.98) | 2.26 (1.64-3.11)   | 2.03 (1.44-2.85)            |
| Region of residence             |                    |               |                    |                             |
| Interior                        | Reference (1.00)    | Reference (1.00) | Reference (1.00)   | Reference (1.00)            |
| Fraser                          | 0.29 (0.23-0.38)   | 0.17 (0.13-0.22) | 1.48 (0.94-2.32)   | 1.39 (0.88-2.19)            |
| Vancouver Coastal               | 1.95 (1.53-2.50)   | 1.35 (1.06-1.73) | 1.88 (1.18-2.99)   | 1.55 (0.97-2.48)            |
| Island                          | 1.54 (1.17-2.02)   | 1.40 (1.08-1.82) | 1.70 (1.03-2.79)   | 1.65 (1.00-2.71)            |
| Northern                        | 1.17 (0.84-1.61)   | 1.07 (0.78-1.46) | 1.16 (0.65-2.09)   | 1.13 (0.63-2.04)            |
| Characteristic | Non-fatal overdose | Fatal overdose |
|---------------|-------------------|----------------|
|               | Unadjusted HR (95% CI) | Adjusted HR (95% CI)<sup>b</sup> | Unadjusted HR (95% CI) | Adjusted HR (95% CI)<sup>b</sup> |
| Unspecified   | 0.08 (0.04-0.14) | 0.08 (0.04-0.14) | 0.14 (0.05-0.41) | 0.14 (0.05-0.40) |

CI = confidence interval; HR = hazard ratio; OUD = opioid use disorder; StUD = stimulant use disorder; SUD = substance use disorder.

<sup>a</sup> The Andersen-Gill model was used for recurrent non-fatal overdose events, and the Fine & Gray competing risk model was used for fatal overdose events.

<sup>b</sup> Adjusted HRs were controlled for all other variables in the table.

<sup>c</sup> Excluding mental illness and substance use categories.

<sup>d</sup> Occurred between 2010 and 2019.