Estimated Drug Overdose Deaths Averted by North America’s First Medically-Supervised Safer Injection Facility

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Abstract

Background: Illicit drug overdose remains a leading cause of premature mortality in urban settings worldwide. We sought to estimate the number of deaths potentially averted by the implementation of a medically supervised safer injection facility (SIF) in Vancouver, Canada.

Methodology/Principal Findings: The number of potentially averted deaths was calculated using an estimate of the local ratio of non-fatal to fatal overdoses. Inputs were derived from counts of overdose deaths by the British Columbia Vital Statistics Agency and non-fatal overdose rates from published estimates. Potentially-fatal overdoses were defined as events within the SIF that required the provision of naloxone, a 911 call or an ambulance. Point estimates and 95% Confidence Intervals (95% CI) were calculated using a Monte Carlo simulation. Between March 1, 2004 and July 1, 2008 there were 1004 overdose events in the SIF of which 453 events matched our definition of potentially fatal. In 2004, 2005 and 2006 there were 32, 37 and 38 drug-induced deaths in the SIF’s neighbourhood. Owing to the wide range of non-fatal overdose rates reported in the literature (between 5% and 30% per year) we performed sensitivity analyses using non-fatal overdose rates of 50, 200 and 300 per 1,000 person years. Using these model inputs, the number of averted deaths were, respectively: 50.9 (95% CI: 23.6–78.1); 12.6 (95% CI: 9.6–15.7); 8.4 (95% CI: 6.5–10.4) during the study period, equal to 1.9 to 11.7 averted deaths per annum.

Conclusions/Significance: Based on a conservative estimate of the local ratio of non-fatal to fatal overdoses, the potentially fatal overdoses in the SIF during the study period could have resulted in between 8 and 51 deaths had they occurred outside the facility, or from 6% to 37% of the total overdose mortality burden in the neighborhood during the study period. These data should inform the ongoing debates over the future of the pilot project.
Discussion

Using data from North America’s first SIF and published estimates of the rate of non-fatal overdose among active IDU, we derived an estimate of the number of fatal overdoses averted by a supervised injecting facility. Following a Monte Carlo simulation and a three-part sensitivity analysis, the estimates of the number of prevented deaths ranged from eight to 51 from March 1, 2004 to July 1, 2008.

The estimate of the number of deaths prevented is equal to a substantial proportion of the total burden of overdose mortality in the area during the study period. Despite the pilot facility only hosting, by design, approximately five per cent of the daily injections in the DTES, the estimated number of averted deaths was equal to between 6.1 and 37.0 per cent of the total overdose burden in the area during the study period. It is impossible to declare with certainty if the SIF prevented these fatalities as it is not possible to know if overdoses occurring in the SIF would have occurred elsewhere. However, despite charges to the contrary [19], a longitudinal analysis of overdose patterns in a representative sample of SIF clients did not demonstrate that individuals took greater risks—i.e., in drug choice, mode of administration or dose—within the apparent safety of an SIF [14].

Our analysis has several limitations, chiefly the reliance on estimates to inform several model parameters, specifically the number of IDU in the DTES and the incidence of non-fatal overdose in the community. For the former, we relied on two previous capture-recapture studies [29, 30] and included a wide confidence interval in the Monte Carlo simulation. For the latter,
we completed a sensitivity analysis to account for the wide range of non-fatal overdose rates reported in the literature. Model outputs such as the DTES fatal overdose rate and non-fatal to fatal overdose ratio are not substantially different from previous observations in other settings [31], lending credence to the estimate of averted deaths. Furthermore, in every case, we endeavoured to use conservative estimates, for example restricting the definition of a potential on-site overdose death to those characterised by a 911 call, provision of naloxone and/or an ambulance. Finally, there may be effects of the SIF that go beyond their impact on those actively using

| Table 1. SIF overdose events by year, substances used, characteristics and interventions |
|----------------------------------------------------------------------------------------------------------------------------------|
| **2004** | **2005** | **2006** | **2007** | **2008** | **ALL** |
| OD events | 189 | 246 | 230 | 201 | 138 | 1004 |
| ODs/day | 0.62 | 0.68 | 0.63 | 0.55 | 0.76 | 0.63 |
| Injections | 136,971 | 178,787 | 178,847 | 183,989 | 87,892 | 766,486 |
| ODs/injection | 1.38 | 1.38 | 1.29 | 1.09 | 1.57 | 1.31 |

**OVERDOSE: SUBSTANCES USED**

| Substance | 2004 | 2005 | 2006 | 2007 | 2008 | ALL |
|-----------|------|------|------|------|------|-----|
| Cocaine | 39 (20.6) | 48 (19.5) | 44 (19.1) | 24 (11.9) | 14 (10.1) | 169 (16.8) |
| Crack cocaine | 4 (2.1) | 1 (0.4) | 1 (0.4) | 5 (2.5) | 2 (1.4) | 13 (1.3) |
| Dilaudid | 5 (2.6) | 5 (2.0) | 4 (1.7) | 2 (1.0) | 3 (2.2) | 19 (1.9) |
| Heroin | 132 (69.8) | 164 (66.7) | 140 (60.9) | 144 (71.6) | 103 (74.6) | 683 (68.0) |
| Methadone | 2 (1.1) | 1 (0.4) | 1 (0.4) | 4 (2.0) | 0 (0.0) | 8 (0.8) |
| Crystal meth | 1 (0.5) | 0 (0.0) | 2 (0.9) | 5 (2.5) | 1 (0.7) | 9 (0.9) |
| Morphine | 3 (1.6) | 5 (2.0) | 3 (1.3) | 8 (4.0) | 2 (1.4) | 21 (2.1) |
| Speedball | 11 (5.8) | 30 (12.2) | 22 (9.6) | 15 (7.5) | 10 (7.2) | 88 (8.8) |
| Talwin & Ritalin | 0 (0.0) | 1 (0.4) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (0.1) |

**OVERDOSE: CHARACTERISTICS**

| Characteristic | 2004 | 2005 | 2006 | 2007 | 2008 | ALL |
|----------------|------|------|------|------|------|-----|
| Unable to speak | 9 (48) | 44 (17.9) | 48 (20.9) | 60 (29.9) | 51 (37.0) | 212 (21.1) |
| Passed out | 8 (42) | 37 (15.0) | 28 (12.2) | 27 (13.4) | 24 (17.4) | 124 (12.4) |
| Limp | 78 (41.3) | 120 (48.8) | 118 (51.3) | 109 (54.2) | 78 (56.5) | 503 (53.1) |
| Face blue/pale | 71 (37.6) | 123 (50.0) | 120 (52.2) | 119 (59.2) | 45 (32.6) | 478 (47.6) |
| Breath slow | 106 (56.1) | 145 (58.9) | 125 (54.3) | 117 (58.2) | 72 (52.2) | 565 (56.3) |
| Breath stopped | 24 (12.7) | 52 (21.1) | 38 (16.5) | 51 (25.4) | 23 (16.7) | 188 (18.7) |
| Chest tightness | 4 (2.1) | 6 (2.4) | 3 (1.3) | 6 (3.0) | 1 (0.7) | 20 (2.0) |
| Seizure | 18 (9.5) | 15 (6.1) | 45 (19.6) | 30 (14.9) | 8 (5.8) | 116 (11.6) |
| Vomiting | 1 (0.5) | 1 (0.4) | 3 (1.3) | 5 (2.5) | 2 (1.4) | 12 (1.2) |
| Choking | 1 (0.5) | 5 (2.0) | 3 (1.3) | 3 (1.5) | 3 (2.2) | 15 (1.5) |
| Sweaty/hot skin | 16 (8.5) | 31 (12.6) | 24 (10.4) | 42 (20.9) | 28 (20.3) | 141 (14.0) |
| Cold skin | 33 (17.5) | 37 (15.0) | 43 (18.7) | 43 (21.4) | 28 (20.3) | 184 (18.3) |
| Other | 24 (12.7) | 12 (4.9) | 21 (9.1) | 24 (11.9) | 13 (9.4) | 94 (9.4) |
| No response to verbal stimulus | 22 (11.6) | 83 (33.7) | 84 (36.5) | 71 (35.3) | 61 (44.2) | 321 (32.0) |
| No response to pain stimulus | 33 (17.5) | 110 (44.7) | 87 (37.8) | 69 (34.3) | 58 (42.0) | 357 (35.6) |

**OVERDOSE: RESPONSES**

| Response | 2004 | 2005 | 2006 | 2007 | 2008 | ALL |
|-----------|------|------|------|------|------|-----|
| 911 call | 54 (28.6) | 123 (50.0) | 95 (41.3) | 93 (46.3) | 58 (42.0) | 423 (42.1) |
| CPR | 1 (0.5) | 4 (1.6) | 1 (0.4) | 0 (0.0) | 0 (0.0) | 6 (0.6) |
| Oxygen | 152 (80.4) | 202 (82.1) | 188 (81.7) | 176 (87.6) | 92 (66.7) | 810 (80.7) |
| Artificial respiration | 18 (9.5) | 54 (22.0) | 45 (19.6) | 45 (22.4) | 19 (13.8) | 181 (18.0) |
| Ambulance | 14 (7.4) | 27 (11.0) | 32 (13.9) | 33 (16.4) | 22 (15.9) | 128 (12.7) |
| Naloxone 0.4 mg | 35 (18.5) | 89 (36.2) | 59 (25.7) | 56 (27.9) | 46 (33.3) | 285 (28.4) |
| Naloxone 0.4 mg x2 | 23 (12.2) | 44 (17.9) | 25 (10.9) | 25 (12.4) | 24 (17.4) | 141 (14.0) |
| Airway inserted | 7 (3.7) | 50 (20.3) | 50 (21.7) | 46 (22.9) | 26 (18.8) | 179 (17.8) |

\*March 1, 2004 to December 31, 2004/January 1, 2008 to July 1, 2008/OD events per 1,000 injections

doi:10.1371/journal.pone.0003351.t001
the facility. For instance, individuals can receive nurse-delivered education in safer injection practices which may reduce risk behaviours for overdose outside the facility. Over one-third of individuals report receiving this training in a representative cohort of SIF clients [32]. Although this issue requires further study, IDU who experience supervision of a nurse within the SIF may subsequently be more cautious when injecting in environments which are not supervised by trained emergency personnel [33].

In conclusion, we observed that non-fatal overdose was a common occurrence at Vancouver’s SIF and, using a modelling technique based on evidence-based parameter values, we estimated that the facility prevented between eight and 51 deaths over the study period. This is equal to between 37.0 per cent and 6.1 per cent of overdose fatalities in the DTES over the same time or two to 12 averted deaths per annum over the study period. These findings are consistent with analogous evaluations and support the conclusion of the facility’s positive impact on public health in Vancouver’s Downtown Eastside [10].

**Materials and Methods**

In this analysis, we sought to estimate the number of overdose deaths averted by a supervised injection facility using methods described previously [16,31,34,35]. This estimate was calculated by determining how many overdose events in the SIF would have been fatal had they happened outside the facility [16]. Specifically, the number of averted deaths is the product of the number of on-site overdoses multiplied by the ratio of fatal to non-fatal overdoses in the DTES [31], or:

\[
\text{fOD}_{\text{Averted}} = \frac{\text{nfOD}_{\text{SIF}} \times \text{fOD}_{\text{DTES}}}{\text{nfOD}_{\text{DTES}}}
\]

For each term in the equation, we used evidence-based estimates.

**Table 2. Observations and model parameters for Monte Carlo simulation**

| Observations | 2004 | 2005 | 2006 | 2007 | 2008 | ALL |
|--------------|------|------|------|------|------|-----|
| DTES OD deaths | 20.1 | 27.8 | 28.5 | 28.7 | 14.4 | 137.7 |
| SIF OD events | 71   | 126  | 99   | 95   | 62   | 453 |

**Model Parameters**

- IDU in DTES: N (4700, 500)
- Non-fatal OD rate:
  - Scenario 1: N (0.05, 0.01)
  - Scenario 2: N (0.2, 0.01)
  - Scenario 3: N (0.3, 0.01)

**Table 3. DTES fatal overdose rate, non-fatal to fatal overdose ratio and SIF averted deaths from model**

| Year | DTES Fatal OD Rate | NON-FATAL TO FATAL OVERDOSE RATIO | NON-FATAL OVERDOSES IN DTES | SIF Averted Overdose Deaths | SIF Averted Overdose Deaths (Proportion of DTES OD Deaths) | SIF Averted Overdose Deaths (Per Year) |
|------|--------------------|----------------------------------|-----------------------------|-----------------------------|----------------------------------------------------------|-------------------------------------|
| 2004 | 5.1 (4.0–6.2)      | 9.7 (5.4–14.0)                  | 195.4 (1087.8–282.1)       | 7.3 (3.4–11.3)              | Scenario 1: 3.4 (6.8–101.8)                              | 11.7 (5.4–18.0)                     |
|      | (4.6–7.2)          | (4.6–12.1)                      | (232.1 (127.8–336.5)       | (15.1 (1.9–28.3)            | Scenario 2: 6.8 (9.6–15.7)                              | 1.17 (1.5–2.4)                      |
|      |                    |                                  | (232.9 (127.7–338.2)       | (12.1 (5.6–18.7)            | Scenario 3: 7.6 (5.3–9.7)                               | 0.9 (0.6–1.2)                       |
|      |                    |                                  | (232.3 (126.4–338.1)       | (10.1 (4.3–15.9)            |                                                          |                                     |
|      |                    |                                  | (116.7 (63.9–169.6)        | (6.6 (3.0–10.2)             |                                                          |                                     |
|      |                    |                                  | (1010.7 (557.5–1463.9)     | (50.9 (23.6–78.1)           |                                                          |                                     |
|      |                    |                                  | (2004)                      | (2005)                      |                                                          |                                     |

1 March 1, 2004 to December 31, 2004
2 January 1, 2008 to February 6, 2008
3Expressed as deaths per 1,000 person years
4Scenario 1: Non-fatal overdose incidence is 50 per 1,000 person years or 5% per person per year
5Scenario 2: Non-fatal overdose incidence is 200 per 1,000 person years or 20% per person per year
6Scenario 3: Non-fatal overdose incidence is 300 per 1,000 person years or 30% per person per year

doi:10.1371/journal.pone.0003351.t002

Table 3. DTES fatal overdose rate, non-fatal to fatal overdose ratio and SIF averted deaths from model
or direct observations. The number of overdose events in the SIF (nfODSIF) was compiled from the facility’s comprehensive on-site surveillance database. This system was the source of data for an earlier analysis of SIF overdose patterns and has already been described in detail [15]. Briefly, all new clients must register at the SIF using a pseudonymous identifier and basic information (i.e., gender and age). All activities in the SIF, including the type and amount of substances injected, the characteristics of overdose events and the interventions taken in response, are entered into the database and associated with the client’s identifier.

For this analysis, we accessed a dataset from the SIF with all pseudonymous identifiers stripped. In order to limit our analysis to on-site overdose events that might conceivably resulted in a death, we restricted our definition of a potentially-fatal overdose event as any that required the provision of naloxone, a 911 call and/or an ambulance.

The ratio of fatal to non-fatal overdoses in the DTES was estimated using data from various official or peer-reviewed sources. The incidence of fatal overdose (nfODDTES) was calculated using counts of drug-induced deaths in the Downtown Eastside published annually by the British Columbia Vital Statistics Agency [36-44]. As these totals included deaths from drug overdose as well as suicide by drug poisoning and adverse events from medications, we multiplied the counts by 75%, the approximate proportion of deaths from drug overdoses [44]. The number of person-years at risk was calculated using estimates of the size of the IDU population in the DTES in two recent capture-recapture studies [29,30]. The local incidence of non-fatal overdose (nfODDTES) was estimated from a review of cross-sectional and longitudinal surveys of active IDU in both domestic and international settings [3,5,14,23,24,31,45–52]. Both rates were expressed per 1,000 person years.

A small amount of data was missing and its value was imputed. Counts of drug-induced deaths in the DTES were unavailable for 2007 and 2008. Thus, the median number of fatal overdoses per annum between 1997 and 2006 was used for both 2007 and 2008. For 2008, we multiplied this number by the proportion of the year included in our study period.

We accounted for the uncertainty in some model parameters in two ways. First, we performed a Monte Carlo simulation for each year of the study period and the entire study period. By permitting the mean, variability and distribution for each model value to be defined, Monte Carlo simulations enable the calculation of point estimates and 95% Confidence Intervals (95% CI) for model outputs. For each year in the study period we performed 10,000 iterations; for the entire study period, we performed 50,000 iterations. We have previously used the Monte Carlo method to model the impact of antiretroviral medication on mortality from HIV infection in the DTES [35] and the Americas [34]. Second, owing to the wide range of non-fatal overdose rates cited in the literature, we conducted a sensitivity analysis by repeating the Monte Carlo simulation three times, using different plausible values for the local non-fatal overdose rate: 50 per 1,000 person years, reflecting the lowest value observed in a local cohort of IDU [24]; 200 per 1,000 person years, the median value observed in a local cohort of IDU [14]; and 300 per 1,000 person years, the largest external estimate observed [31].

In a subanalysis, we calculated estimates of the number of non-fatal overdoses in the DTES for each year in the study period as well as the entire study period. These estimates are the product of the number of non-fatal overdoses defined in the model multiplied by the non-fatal to fatal overdose ratio. As above, we performed Monte Carlo simulations using three different non-fatal overdose rates to calculate three point estimates with 95% CI.

The evaluation of Vancouver’s SIF has been reviewed and approved by the University of British Columbia/Providence Healthcare Research Ethics Board.

Acknowledgments

The authors wish to thank the participants in SEOSI and the staff of Insite, the Portland Hotel Society, and Vancouver Coastal Health (Chris Buchner, David Marsh, and Heather Hay). We also thank the current and past SEOSI staff. We would specifically like to thank Deborah Graham, Tricia Collingham, Leslie Rae, Caitlin Johnston, Steve Kain, and Calvin Lai for their research and administrative assistance.

Author Contributions

Conceived and designed the experiments: EW. Performed the experiments: MJSM. Analyzed the data: MJSM EW. Contributed reagents/materials/analysis tools: TK MT JM. Wrote the paper: MJSM. Edited the manuscript: EV TK.

References

1. (2007) Unintentional poisoning deaths—United States, 1999–2004. MMWR: Morbidity and mortality weekly report 56: 93–96.
2. Degenhardt L, Roshburgh A, Barker B (2005) Underlying causes of cocaine, amphetamine and opioid related deaths in Australia. Journal of clinical forensic medicine 12: 187–195.
3. Fischer B, Brissette S, Brochu S, Bruneau J, E-Gurbay N, et al. (2004) Determinants of overdose incidents among illicit opioid users in 5 Canadian cities. Canadian Medical Association journal 171: 235–239.
4. Bargagli AM, Hickman M, Davoli M, Perucci CA, Schiffano P, et al. (2006) Drug-related mortality and its impact on adult mortality in eight European countries. European journal of public health 16: 198–202.
5. Darke S, Ross J. Hall W (1996) Overdose among heroin users in Sydney, Australia: I. Prevalence and correlates of non-fatal overdose. Addiction 91: 405–411.
6. Hulse GK, English DR, Milne E, Holman CD (1999) The quantification of mortality resulting from the regular use of illicit opiates. Addiction 94: 221–229.
7. Oppenheimer E, Tobutt C, Taylor C, Andrew T (1994) Death and survival in a cohort of heroin addicts from London clinics: a 22-year follow-up study. Addiction 89: 1299–1308.
8. Fischer B, Popova S, Rehm J, Ioannidis A (2006) Drug-related overdose deaths in British Columbia and Ontario, 1992–2004. Canadian journal of public health 97: 384–387.
9. Wood E, Kerr TH, Lloyd-Smith E, Buchner C, Marsh DC, et al. (2004) Methodology for evaluating Insite: Canada’s first medically supervised injection facility for injected drug users. Harm reduction journal 1: 9.
10. Wood E, Tyndall MW, Montaner JS, Kerr T (2006) Summary of findings from the evaluation of a pilot medically supervised safer injecting facility. Canadian Medical Association journal 175: 1399–1404.
11. Wood E, Tyndall MW, Zhang R, Stodz JA, Lai C, et al. (2006) Attendance at supervised injecting facilities and use of detoxification services. N Engl J Med 354: 2512–2514.
12. Wood E, Kerr T, Small W, Li K, Marsh DC, et al. (2004) Changes in public order after the opening of a medically supervised safer injecting facility for illicit injection drug users. Cmaj 171: 731–734.
13. Kerr T, Tyndall M, Li K, Montaner J, Wood E (2005) Safer injection facility use and syringe sharing in injection drug users. Lancet 366: 316–318.
14. Milloy M-JS, Kerr T, Mathias R, Zhang R, Montaner J, et al. (2008) Non-fatal overdose among a cohort of active injection drug users recruited from a Supervised Injection Facility. American journal of drug and alcohol abuse 34: 499–510.
15. Kerr T, Tyndall MW, Lai C, Montaner JS, Wood E (2006) Drug-related overdoses within a medically supervised safer injecting facility. International Journal of Drug Policy 17: 436–441.
16. (2003) Final report of the evaluation of the Sydney Medically Supervised Injecting Centre. Sydney, Australia: MSIC Evaluation Committee.
17. Poschade S, Hoger R, Schnitzler J (2003) Evaluation der Arbeit der Injecting Centre. Sydney, Australia: MSIC Evaluation Committee.
18. van Beek I, Dakin A, Kimber J, Gilmour S (2004) The Sydney medically supervised injecting centre: Reducing harm associated with heroin overdose. Critical public health 14: 391–406.
19. Selby P, Kahan M, Srivastava A (2007) Safe Injecting Sites (SIS): Need for equipose and evidence of net benefit to illicit drug users. Canadian Medical Association journal eLetters.
20. Andrensen M, Boyd N (2008) A cost-benefit and cost-effectiveness analysis of Vancouver's Safe Injection Facility. Vancouver, British Columbia.

21. Wood E, Tyndall MW, Qiu Z, Zhang R, Montaner JS, et al. (2006) Service uptake and characteristics of injection drug users utilizing North America's first medically supervised safer injecting facility. American journal of public health 96: 770–773.

22. Wood E, Stoltz JA, Li K, Montaner JS, Kerr T (2006) Changes in Canadian heroin supply coinciding with the Australian heroin shortage. Addiction 101: 689–695.

23. Coffin PO, Tracy M, Buccizzelli A, Ompad D, Vlahov D, et al. (2007) Identifying injection drug users at risk of nonfatal overdose. Academic emergency medicine 14: 616–623.

24. Kerr T, Fairbairn N, Tyndall MW, Marsh D, Li K, et al. (2007) Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. Drug and alcohol dependence 87: 39–45.

25. Darke S, Williamson A, Ross J, Mills KL, Havard A, et al. (2007) Patterns of nonfatal heroin overdose over a 3-year period: findings from the Australian treatment outcome study. J Urban Health 84: 283–293.

26. Binswanger IA, Stern MF, Deyo RA, Heagerty PJ, Cheadle A, et al. (2007) Release from prison—a high risk of death for former inmates. The New England journal of medicine 356: 157–165.

27. (2007) News release: Insite given six-month extension says Minister Clement. In: Evidence from the evaluation of Vancouver's safer injection facility. International Journal of Drug Policy 18: 37–45.

28. (2006) Annual Report 2005. Victoria, British Columbia, Canada: British Columbia Vital Statistics Agency.

29. (2005) Annual Report 2004. Victoria, British Columbia, Canada: British Columbia Vital Statistics Agency.

30. (2004) Annual Report 2003. Victoria, British Columbia, Canada: British Columbia Vital Statistics Agency.

31. (2003) Annual Report 2002. Victoria, British Columbia, Canada: British Columbia Vital Statistics Agency.

32. (2002) Annual Report 2001. Victoria, British Columbia, Canada: British Columbia Vital Statistics Agency.

33. Kerr T, Small W, Moore D, Wood E (2007) A micro-environmental intervention to reduce the harms associated with drug-related overdose: evidence from the evaluation of Vancouver’s safer injection facility. International Journal of Drug Policy 18: 37–45.