

Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study



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Summary

Background Overdose from illicit drugs is a leading cause of premature mortality in North America. Internationally, more than 65 supervised injecting facilities (SIFs), where drug users can inject pre-obtained illicit drugs, have been opened as part of various strategies to reduce the harms associated with drug use. We sought to determine whether the opening of an SIF in Vancouver, BC, Canada, was associated with a reduction in overdose mortality.

Methods We examined population-based overdose mortality rates for the period before (Jan 1, 2001, to Sept 20, 2003) and after (Sept 21, 2003, to Dec 31, 2005) the opening of the Vancouver SIF. The location of death was determined from provincial coroner records. We compared overdose fatality rates within an a priori specified 500 m radius of the SIF and for the rest of the city.

Findings Of 290 decedents, 229 (79.0%) were male, and the median age at death was 40 years (IQR 32–48 years). A third (89, 30.7%) of deaths occurred in city blocks within 500 m of the SIF. The fatal overdose rate in this area decreased by 35.0% after the opening of the SIF, from 253.8 to 165.1 deaths per 100 000 person-years ($p=0.048$). By contrast, during the same period, the fatal overdose rate in the rest of the city decreased by only 9.3%, from 7.6 to 6.9 deaths per 100 000 person-years ($p=0.490$). There was a significant interaction of rate differences across strata ($p=0.049$).

Interpretation SIFs should be considered where injection drug use is prevalent, particularly in areas with high densities of overdose.

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Introduction

Injecting drug users (IDUs) have a much higher risk of morbidity and mortality than does the general population.¹ Accidental drug overdose is a leading cause of death in IDUs, and contributes substantially to mortality in communities in which injection drug use is prevalent.² In some North American cities, overdose has overtaken homicide as the leading cause of premature mortality.³ In 2007, the rate of unintentional drug overdose death in the USA (nine deaths per 100 000 person-years) was about five times higher than in 1990.⁴ Overdose mortality rates are highest in ethnic minorities: in the USA, overdose deaths are more common in African American and Hispanic individuals,⁵ whereas in Canada, First Nations individuals are more likely than individuals from the general population to die from an overdose.⁶

The primary mechanism of death attributable to opioid overdose is respiratory depression and resultant hypoxia.⁷ Seizures, cardiac arrhythmias, stroke, and hyperthermia have been implicated in deaths related to cocaine overdose.^{8,9} Risk factors for fatal overdose include both individual and environmental factors. Polydrug use (notably the concomitant consumption of opioids and alcohol),¹⁰ public drug use,¹¹ release from prison,¹² and warmer weather¹³ have all been associated

with an increased risk of fatal overdose. Although the risk factors for fatal overdose have been well described, there are few evidence-based strategies to reduce the risk of overdose mortality that have proved effective in population-based studies.

In Vancouver, BC, Canada, high rates of overdose mortality in the 1990s¹⁴ led to the establishment of North America's first medically supervised safer injecting facility (SIF) in the city's Downtown Eastside, a community known for its large open drug market and well described HIV epidemic.¹⁵ The local drug use context is characterised by high rates of polysubstance use, including heroin, cocaine, and metamfetamine injection in addition to crack cocaine smoking.¹⁶ The neighbourhood is also characterised by a concentration of low-cost housing (eg, single room occupancy hotels), large numbers of homeless people, and high levels of drug-related disorder, including public drug injecting.¹⁷ The SIF is located centrally in this neighbourhood, with the aims of reducing public drug injection, decreasing overdose and risk of infectious disease (eg, HIV) transmission, and improving access to health-care services.¹⁸ The local police department supported the opening of the SIF, and throughout the study period officers have actively referred individuals found injecting

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in public to the facility.¹⁹ Similar to the about 65 SIFs that exist around the world,²⁰ IDUs consume pre-obtained illicit drugs under the supervision of health-care professionals, who provide sterile syringes and referrals to primary health services, as well as emergency care in the event of overdose (eg, oxygen and naloxone administration).²¹ Staff are instructed to call an ambulance in the event of a serious overdose; to date, no deaths within the facility have been recorded.²² Although heroin has been reported as the most frequently injected drug in the facility (about 40% of all injections), powder cocaine (about 30%) and metamfetamines (5%) are common.²³ In earlier analyses,²⁴ the SIF has been shown to attract IDUs who are at an increased risk of blood-borne disease acquisition and overdose.²⁵ Use of the SIF has also been associated with reductions in HIV risk behaviour, including syringe sharing,²⁶ an increased uptake of addiction services,²⁷ and improved access to health and social services.²⁸

Although SIFs have been associated with public health and community benefits in several international settings,²⁰ they remain controversial.²⁹ For example, in Canada, although the facility has garnered broad public and local support,³⁰ it continues to be opposed by the federal government.³¹ Some have argued that objective outcomes, as opposed to self-reported behavioural data, are required to definitively establish the true effectiveness of SIFs, and it is worth noting that there is an absence of rigorous assessments of their effect on overdose mortality.³² To address these concerns, we undertook a population-based examination of drug-related overdose mortality rates before and after the establishment of North America's first SIF.

Methods

Procedures

Data for these analyses were derived from a review of files obtained from a central registry maintained by British Columbia Coroners Service (BCCS). Because the BCCS is responsible for investigating and documenting all unnatural, unexpected, unexplained, or unattended deaths,³³ the registry is highly accurate, and therefore serves as the best available census of deaths caused by an illicit drug overdose in the province. Coroners of the agency are required to determine the identity of the deceased, and record the manner, location, and cause of death. The file for each decedent contains: a form detailing the name and demographic information of the deceased; police reports relevant to the death, including witness statements; the results of toxicological and other medical examinations; and a summary of the location and circumstances of death. After each investigation, which includes a comprehensive review of relevant information, the coroner makes an official finding of the cause of death. All deaths deemed by the attending coroner to be caused by an accidental (ie, recreational or otherwise unintentionally fatal) illicit drug overdose were

eligible for inclusion in this analysis. The criteria used to define an accidental overdose—that the proximate and primary medical cause of death resulted from the self-administration of a psychoactive substance that is illegal or diverted from accepted use—remained consistent throughout the study. This study was approved by the University of British Columbia and Providence Health Care Research Ethics Board.

We reviewed the case files for all illicit drug overdose deaths that occurred in the City of Vancouver between Jan 1, 2001, and Dec 31, 2005. As a result of lengthy investigations by the coroner into deaths involving unnatural causes, complete case data are often not available locally until several years after the date of death. Consequently, the complete dataset for the period of interest was not obtained until 2009. Sociodemographic data were extracted, including date of birth and date of death, sex, and ancestry (dichotomised as First Nations *vs* other). The term First Nations refers to members of Canadian indigenous groups who are neither Inuit (originally residing in Arctic or sub-Arctic regions) nor Métis (descendants of marriages between indigenous individuals and European settlers).⁶ We noted the specific illicit drugs determined by the coroner to be contributory to the cause of death. We also obtained information about the location of death, including six-digit postal codes, addresses, or other descriptive geographic identifiers. For cases in which the coroner was unable to assign a postal code, we identified the closest building and attributed the corresponding postal code to that file. The Statistics Canada Postal Code Conversion File³⁴ was used to obtain the latitude and longitude coordinates that best approximated the location of each six-digit postal code. Urban postal codes in Canada are accurate proxies for geographic location,³⁵ and in densely populated areas are equal to or less than one side of a city block.³⁴

Statistical analysis

To obtain the person-years at risk for the overdose mortality rate calculation, we obtained population data from the 2001 and 2006 Canadian Census, aggregated at the level of dissemination blocks. Dissemination blocks represent areas bounded on all sides by roads or boundaries of standard geographic areas, and are the smallest geographic unit for which population and dwelling count data are available from Statistics Canada. We applied a linear interpolation to estimate the population denominators for the intervening years by calculating the average per year increase or decrease for each dissemination block. For example, the population in 2002 was estimated according to the equation:

$$pop_{2002} = \frac{pop_{2006} - pop_{2001}}{5} + pop_{2001}$$

These values were used to estimate the person-years at risk during the pre-SIF (Jan 1, 2001, to Sept 20, 2003) and post-SIF (Sept 21, 2003, to Dec 31, 2005) periods. For example:

$$\text{person years at risk}_{\text{pre}} = \text{pop}_{2001} + \text{pop}_{2002} + \left(\frac{263}{365 \cdot 25}\right) \text{pop}_{2003}$$

because Sept 20 is the 263rd day of the year. This method assumes that all individuals are at a constant risk of the outcome, and does not fully account for the fact that some individuals at risk might not be counted.

To visualise and manage these data, the dissemination block boundary files and population counts were loaded into a geographical information system (ArcGIS 9.3). This software was used to determine the number of overdoses occurring in each dissemination block, and to calculate the mortality rate during the two periods of interest.

To identify the set of city blocks in the Downtown Eastside area within which most visitors to the SIF resided, we examined usage data from the Scientific Evaluation of Supervised Injecting (SEOSI) study.¹⁸ This prospective cohort is derived from a random sample of SIF users, and has been described in detail previously.^{18,24} These data indicated that over 70% of daily SIF users live within four blocks (ie, 500 m) of the facility. Therefore, we proposed that these city blocks represent the area in which the SIF probably had the greatest effect on overdose mortality, and defined the “immediate vicinity of the SIF” as all

dissemination blocks with a centroid within 500 m of the facility. We calculated the rate difference in overdose mortality between the pre-SIF and post-SIF periods within this area, and compared that with the rate difference in the rest of the city over the same period. The Breslow-Day test for interaction across strata³⁶ was used to examine heterogeneity in overdose rate differences between these two geographic areas.

We recognised that the estimation of rate differences from census data is sensitive to fluctuations in population size that might not necessarily represent changes in the number of individuals at risk of fatal overdose. Therefore, we undertook a series of non-parametric analyses that are less sensitive to changes in the population denominators. Specifically, the Wilcoxon signed-rank test was used to compare the overdose mortality rates in each city block before and after the opening of the SIF. We first estimated the block-level changes in rates using 2001 and 2006 census data. We also did a second test assuming the population was fixed at the 2001 census estimate. The null hypothesis was that the median of the distribution of rate differences was zero (ie, there were about equal numbers of increases and decreases in block-level overdose mortality rates).

We also did a sensitivity analysis consisting of data aggregated to the census tract level to investigate whether geographic differences in overdose mortality were dependent on the area unit of analysis. Census tracts are stable geographic units containing populations of 2500

	Overdoses occurring in blocks within 500 m of the SIF			Overdoses occurring in blocks farther than 500 m of the SIF		
	Pre-SIF (n=56)	Post-SIF (n=33)	p	Pre-SIF (n=113)	Post-SIF (n=88)	p
Median age (years) at death (IQR)	39 (32–44)	44 (36–50)	0.050	39 (31–47)	40 (30–49)	0.504
Sex						
Female	12 (21%)	6 (18%)	0.713	16 (14%)	27 (31%)	0.005
Male	44 (79%)	27 (82%)	..	97 (86%)	61 (69%)	..
First Nations*						
Yes	17 (30%)	8 (24%)	0.535	6 (5%)	12 (14%)	0.040
No	39 (70%)	25 (76%)	..	107 (95%)	76 (86%)	..
Opioids						
Yes	27 (48%)	18 (55%)	0.333	68 (60%)	43 (49%)	0.110
No	29 (52%)	15 (45%)	..	45 (40%)	45 (51%)	..
Cocaine						
Yes	34 (61%)	20 (61%)	0.992	67 (59%)	54 (61%)	0.766
No	22 (39%)	13 (39%)	..	46 (41%)	34 (39%)	..
Alcohol						
Yes	6 (11%)	3 (9%)	0.806	8 (7%)	5 (6%)	0.689
No	50 (89%)	30 (91%)	..	105 (93%)	83 (94%)	..
Multiple contributory drugs						
Yes	18 (32%)	12 (36%)	0.684	44 (39%)	28 (32%)	0.296
No	38 (68%)	21 (64%)	..	69 (61%)	60 (68%)	..

All data are n (%) unless stated otherwise. SIF=supervised injecting facility. Pre-SIF period=Jan 1, 2001, to Sept 20, 2003. Post-SIF period=Sept 21, 2003, to Dec 31, 2005.
*First Nations ancestry refers to indigenous individuals who are neither Inuit nor Métis.

Table 1: Sociodemographic characteristics and contributory drug(s) of overdose deaths (n=290) in the city of Vancouver between Jan 1, 2001, and Dec 31, 2005

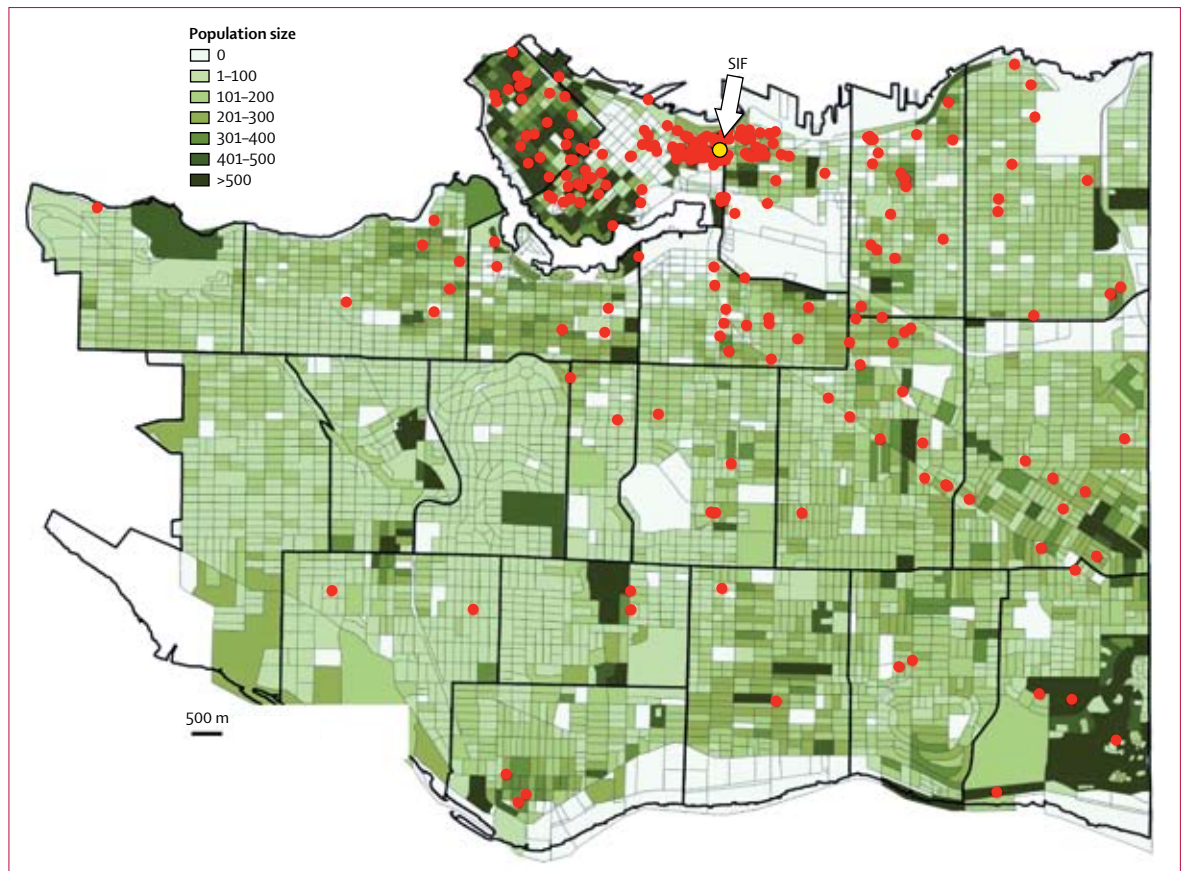


Figure 1: Fatal overdoses in Vancouver between Jan 1, 2001, and Dec 31, 2005

The location of the city's supervised injecting facility (SIF) is shown in yellow. The locations of deaths are shown in red. Population sizes for each dissemination block as shown were derived from the 2006 Canadian Census. The six-digit postal code attributed to each overdose was used to estimate the precise location of death from the postal code conversion file available from Statistics Canada.³⁴

to 8000 people in urban areas. We calculated the rate difference in overdose mortality between the pre-SIF and post-SIF periods for each census tract, and used ArcGIS to obtain the Euclidean shortest path distance between the centroid of each census tract and the SIF.³⁷ The relations between overdose rate differences and distance to the SIF were then investigated with non-linear regression, with an exponential best fit,

$$\text{Rate difference}(x) = a + be^{-cx}$$

where x is the distance to the SIF.

Finally, we recognised that a co-occurring differential expansion in access to methadone maintenance therapy in close proximity to the SIF relative to the rest of the city could confound any relations between overdose mortality and the opening of the facility. To assess whether trends in participation in the maintenance programme varied between the two geographic areas, we analysed area of residence and programme data from the random sample of SIF users. Participants were stratified on the basis of their reported area of residence (ie, within four blocks of

the SIF vs elsewhere). Then, the proportions who reported being enrolled in a methadone maintenance programme at baseline (ie, Sept, 2003, to May, 2004) and at three consecutive 6-month follow-ups were determined. Trends in participation in the programme between the two areas were compared with the Cochran-Armitage test for trend. All analyses were done with ArcGIS 9.3.1, SAS 9.1.3, and OpenEpi 2.2, and all p values are two-sided and significant at the $\alpha=0.05$ level.

Role of the funding source

The sponsors of the study had no role in the design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Between Jan 1, 2001, and Dec 31, 2005, 290 accidental illicit drug overdoses occurred within the city boundaries of Vancouver—an average of 1.1 per week. Men accounted for 229 (79.0%) deaths, and the median age at death was 40 years (IQR 32–48). We did not detect evidence of

seasonality in the rates of overdose; an ANOVA analysis showed that the mean number of overdoses did not vary significantly when the study period was divided into 3-month periods ($F=0.365$, $p=0.780$). The crude mortality rate over the study period was 10.4 per 100 000 person-years (95% CI 9.2–11.6 per 100 000 person-years). Table 1 shows the characteristics of the decedents, stratified by proximity to the SIF and whether the death occurred in the pre-SIF or post-SIF period. Decedents in city blocks greater than 500 m from the facility were more likely to be female ($p=0.005$) and of First Nations ancestry ($p=0.040$) in the post-SIF period. No other significant differences were noted in either stratum, including in the types of drugs implicated in the cause of death. The locations of death were heavily concentrated in the Downtown Eastside area (figure 1): a third (89, 30.7%) occurred in city blocks located within 500 m of the SIF.

Table 2 shows overdose mortality rates stratified by proximity to the SIF during the pre-SIF and post-SIF periods. In city blocks within 500 m of the facility, the overdose rate decreased by 35.0% in the post-SIF period, from 253.8 per 100 000 person-years (95%CI 187.3–320.3 per 100 000 person-years) to 165.1 per 100 000 person-years (108.8–221.4 per 100 000 person-years). The rate

difference (RD=88.7 per 100 000 person-years) between these two periods was significant (1.6–175.8 per 100 000 person-years, $p=0.048$). By contrast, the fatal overdose rate in the rest of the city decreased by 9.3% from 7.6 per 100 000 person-years (6.2–9.0 per 100 000 person-years) to 6.9 per 100 000 person-years (5.5–8.4 per 100 000 person-years) during the same period. The rate difference was not significant (RD=0.7 per 100 000 person-years, 95% CI –1.3 to 2.7 per 100 000 person-years, $p=0.490$). The Breslow-Day test for interaction of rate differences indicated that heterogeneity might be present between these two strata ($p=0.049$). The overdose rates (per 100 000 person-years) for each city block located within the immediate vicinity of the SIF before and after the opening of the SIF are shown in figure 2.

A non-parametric sensitivity analysis was then done to assess the robustness of the findings. As shown in figure 2, of the 22 blocks in the area of interest within which overdoses were recorded, most (15, 68.2%) showed decreases. The Wilcoxon signed-rank test indicated that the median of the distribution of rate differences was significantly less than 0 ($p=0.039$), which suggests that overall block-level overdose mortality decreased after the

	ODs occurring in blocks within 500 m of the SIF*		ODs occurring in blocks farther than 500 m of the SIF*	
	Pre-SIF	Post-SIF	Pre-SIF	Post-SIF
Number of overdoses	56	33	113	88
Person-years at risk	22 066	19 991	1 479 792	1 271 246
Overdose rate (95% CI)*	253.8 (187.3–320.3)	165.1 (108.8–221.4)	7.6 (6.2–9.0)	6.9 (5.5–8.4)
Rate difference (95% CI)*	88.7 (1.6–175.8); $p=0.048$..	0.7 (-1.3–2.7); $p=0.490$..
Percentage reduction (95% CI)	35.0% (0.0%–57.7%)	..	9.3% (-19.8% to 31.4%)	..

SIF=supervised injection facility. Pre-SIF period=Jan 1, 2001, to Sept 20, 2003. Post-SIF period=Sept 21, 2003, to Dec 31, 2005. *Expressed in units of per 100 000 person-years.

Table 2: Overdose mortality rate in Vancouver between Jan 1, 2001, and Dec 31, 2005 (n=290), stratified by proximity to the SIF

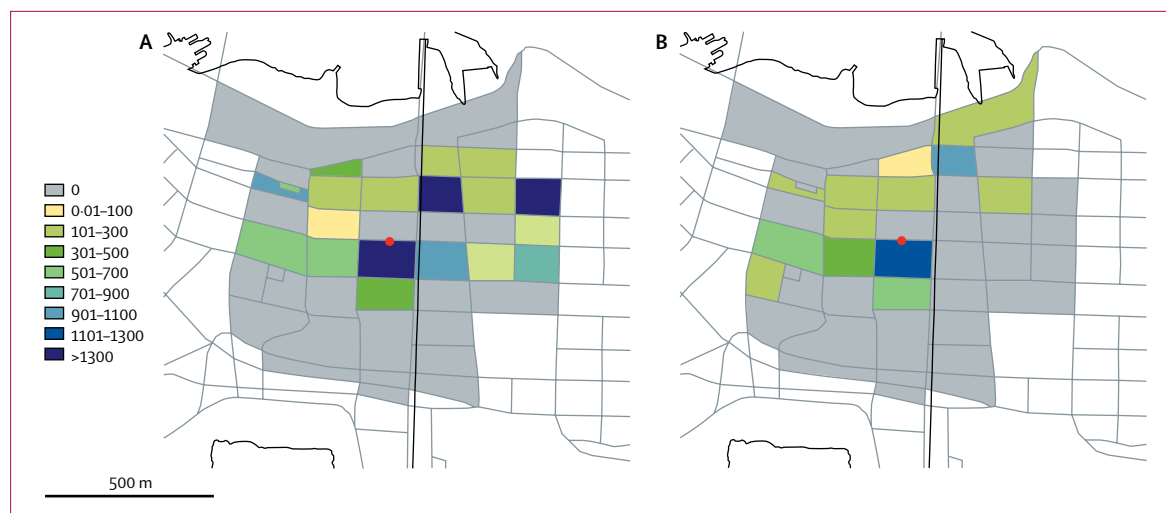


Figure 2: Fatal overdose rates before (A) and after (B) the opening of Vancouver's SIF (shown in red) in city blocks located within 500 m of the facility Rates are given in units of 100 000 person-years and were calculated by aggregating the locations of death to the dissemination block level as shown.

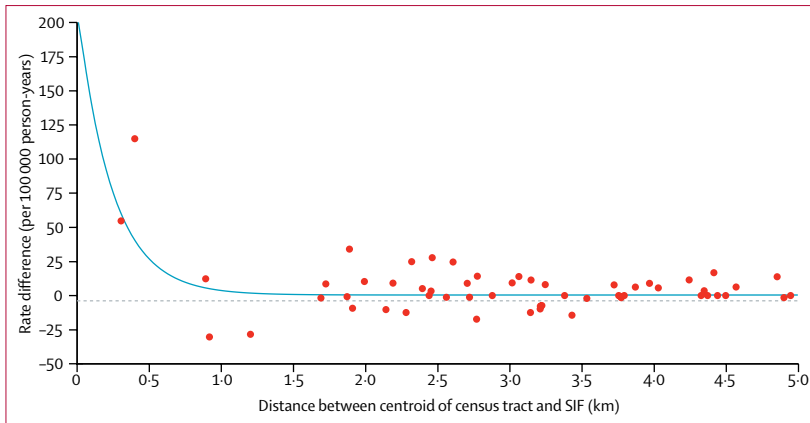


Figure 3: Reduction in fatal overdose rates following the opening of Vancouver's supervised injection facility (SIF) by census tract, Jan, 2001, to Dec, 2005

Rate Difference (RD) represents the absolute change in fatal overdose rate ($\text{Rate}_{\text{pre-SIF}} - \text{Rate}_{\text{post-SIF}}$) before and after the opening of the SIF on Sept 21, 2003. Thus, values greater than one indicate a reduction in the rate during the post-SIF period. Distance was measured as the Euclidean shortest path between the centroid of each census tract and the location of the SIF. A non-linear exponential regression weighted by the total number of overdoses in each census tract was done. The best fit (shown in blue) was $\text{RD}(x) = 0.40 + 212.4e^{-4.57x}$. The r^2 goodness of fit statistic was 0.58, which represents the proportionate reduction in uncertainty due to the inclusion of the distance covariate x .⁵⁷

opening of the facility. A second sensitivity analysis assuming that the block-level population remained constant at the 2001 census level over the study period produced a similar result ($p=0.039$).

In another sensitivity analysis consisting of data aggregated to the census tract level, we noted greater reductions in overdose mortality within census tracts close to the SIF (figure 3). A non-linear regression with an exponential best fit explained 58% of the variance in the data ($r^2=0.58$), and suggested that the observed effect was minimal in census tracts further than about 500 m from the facility, and negligible beyond 1 km.

As a final subanalysis, we examined trends in methadone maintenance therapy participation in a random sample of SIF users to determine whether a differential expansion of these programmes in close proximity to the SIF compared with other areas might have partly explained the findings. Of 1084 participants enrolled in the SEOSI cohort, 93 (23.4%) of 398 participants living within 500 m of the SIF and 118 (23.9%) of 493 participants living elsewhere were enrolled in an MMT programme at baseline ($p=0.843$). The Cochran-Armitage test indicated that the trends in the proportion of participants enrolled in a methadone maintenance therapy programme did not vary significantly between the two areas over time ($p=0.833$).

Discussion

In this population-based analysis, we showed that overdose mortality was reduced after the opening of a SIF. Reductions in overdose rates were most evident within the close vicinity of the facility—a 35% reduction in mortality was noted within 500 m of the facility after its opening. By contrast, overdose deaths in other areas

of the city during the same period declined by only 9%. Consistent with earlier evidence showing that SIFs are not associated with increased drug injecting (panel),^{38,39} these findings indicate that such facilities are safe and effective public-health interventions, and should therefore be considered in settings with a high burden of overdose related to injection drug use.

In both the primary and sensitivity analyses, we saw no significant reductions in overdose mortality further than 500 m from the SIF. This finding is not surprising, since over 70% of frequent SIF users reported living within four blocks of the facility. Although the facility operates at capacity with over 500 supervised injections per day on average,²³ it is a pilot programme with only 12 injection seats in a neighbourhood with about 5000 injection drug users.⁴⁰ Therefore, and since previous studies have shown that waiting times and travel distance to the facility are barriers to SIF use,⁴¹ larger reductions in community overdose mortality would probably require an expansion of SIF coverage.

Our findings are consistent with the time-series analyses of drug-related deaths occurring after the opening of SIFs in Germany⁴² and Australia.⁴³ However, the German study did not assess the relation between proximity to a facility and overdose mortality within the surrounding environs. Furthermore, an abrupt reduction in heroin supply that occurred during the same period as the Australian facility's opening limited the conclusions that could be drawn from this assessment. By contrast, we have no evidence that significant changes in drug supply or purity occurred during the study period. We noted no differences in the types of drugs implicated in deaths between the two periods within either area of interest. Further, data from a prospective cohort study of IDUs done in the same neighbourhood suggest that drug-use patterns remained largely constant from 2001 to 2005.⁴⁴ For example, the proportion of IDUs who reported injecting heroin daily was 24% in 2001 and 25% in 2005, whereas daily cocaine injecting was 17% in 2001 and 15% in 2005. Although the scale-up of other interventions, such as methadone maintenance therapy, could have explained the reduction in overdose mortality, it is notable that rates of methadone use and other known addiction treatment interventions remained stable during the study period.⁴⁴ Furthermore, in a subanalysis of a large random sample of SIF users, we found no evidence of a differential expansion of methadone maintenance therapy programmes within 500 m of the SIF relative to other areas in the city.

The large proportion of cocaine-related overdoses in this study is not surprising considering the high prevalence of cocaine and other stimulant use previously noted in this setting.^{23,45} We note that most evidence-based overdose prevention interventions (eg, methadone maintenance therapy, naloxone distribution) are not effective at reducing the risk of overdose associated with stimulant consumption; therefore, it is encouraging that

the SIF has been highly accepted by cocaine users.⁴⁶ The rise in the proportion of female and First Nations deaths in areas further than 500 m from the facility is concerning, especially in view of previous evidence showing increased drug-related vulnerability in these subpopulations.^{47,48} Because the SIF is well received by women and First Nations individuals,^{23,49} efforts should be made to expand services to reach vulnerable IDUs who reside outside of the Downtown Eastside. Furthermore, the fact that a third of fatal overdoses were attributed to multiple combinations of drugs suggests that a range of innovative public health responses that addresses the risks of polydrug use is required. The development and implementation of these interventions should proceed in tandem with improved access to methadone maintenance therapy and other opioid substitution therapies, in view of their proven effectiveness at reducing the risk of overdose mortality in opioid users.⁵⁰

This study has limitations that should be noted. Although we recognise that IDUs may go through periods of higher or lower injecting intensity,⁵¹ our method using population data from the 2001 and 2006 Canadian Census assumes that all individuals are at a constant risk of the outcome (death from overdose). Furthermore, this method does not fully account for the fact that some individuals at risk might not be counted (eg, missed by the census or removed from the population due to incarceration). However, extensive efforts are made to ensure that the population estimates account for under-coverage error (including four separate studies that are independent of the census itself).⁵² Therefore, although under-counting of marginalised populations is an issue, Statistics Canada undertakes great efforts to obtain accurate estimates.

Although, as indicated above, detailed data for community drug use patterns and other interventions show no apparent changes during the study period, we cannot exclude the possibility that the reduction in overdose mortality was confounded by unmeasured factors that affected overdose rates. We attempted to address this difficulty by including a quasi-control consisting of overdoses that occurred in other areas of the city. We feel this approach is conservative, since any IDUs residing in the city can use the programme, thereby potentially reducing overdose mortality in areas outside the immediate vicinity of the SIF. Additionally, because Statistics Canada suppresses characteristic information at the geographical level needed to do this analysis, we were unable to do adjusted analyses and therefore control for potential neighbourhood-level changes. However, the study period was short, and was not associated with notable neighbourhood-level changes that might explain the reduction.⁵³ Migration of IDUs out of the study area could also theoretically explain the decrease in overdose mortality rates. However, a previous analysis of Vancouver IDUs showed that migration rates were stable and low throughout the study period, and that active injectors and

Panel: Research in context

Systematic review

We searched PubMed and ISI Web of Knowledge databases (from inception to Dec 31, 2009) for empirical studies assessing the effect of supervised injecting facilities (SIFs) on drug-related overdose mortality. MeSH terms used to identify studies included “supervised injecting centers”, “supervised injecting facilities”, as well as “mortality” or “overdose”. We also identified grey literature using keywords such as “drug consumption room”, “safer injecting facilities”, and “drug poisoning” or “drug-related death”. We identified no peer-reviewed studies that have assessed the real world effect of SIFs on drug-related overdose mortality rates. Two grey literature reports described analyses showing a reduction in overdose deaths associated with the implementation of SIFs.

Interpretation

Our results suggest that SIFs are an effective intervention to reduce community overdose mortality in Canada and in other cities internationally, and should be considered for assessment particularly in communities with high levels of injection drug use.

those at greater risk of overdose tend to remain entrenched in the Downtown Eastside neighbourhood.⁵⁴ Additionally, we know of no changes in policing policy that could have confounded our results. A clustering or spike in deaths (eg, from an unusually pure batch of drugs) might also have had an effect on our results. However, we identified only one report of a spike in deaths from stolen powdered methadone in mid-August, 2005.⁵⁵ In the 15-day period between Aug 15 and Aug 30, 2005, ten overdoses were noted (4.7 per week), four of which occurred within 500 m of the SIF. Since the spike in deaths occurred after the SIF’s opening, this effect only serves to diminish the estimated reduction in overdose mortality. Regarding the potential for the ecological fallacy (ie, the primary unit of analysis was an aggregated measure as opposed to an individual-level estimate of risk), we emphasise that the nature of our results requires caution in interpretation. Finally, our calculation of rate differences between periods depended on an estimate of the population at risk, and it is noteworthy that Statistics Canada recorded a 14% increase in population in city blocks within 500 m of the SIF between 2001 and 2005. If one assumes that the population at risk remained stable at the 2001 level throughout the study period, the percentage decrease in overdose mortality is still 30% in the post-SIF period, although this change was not significant. However, we feel that accounting for the changing population at risk is justified, since Statistics Canada makes extensive efforts to account for traditionally hard-to-reach (eg, homeless and drug-using) individuals in the census.⁵¹ Further, a net growth in the population is consistent with an increase in supportive housing for individuals living with

addictions in the neighbourhood.⁵⁶ We also note in subanalyses that considered block-level overdose rates and assumed a constant 2001 population over time, the decline in overdose remained significant. Finally, although other techniques can be used to estimate the size of drug-using populations (eg, capture–recapture approaches), such data are not available in our setting.

In conclusion, with our findings and the other public health and community benefits of SIFs,^{20,24} these programmes should be considered for assessment where injection drug use is prevalent, particularly in areas with high densities of overdose.

Contributors

TK, BDLM, and MJM designed the study and wrote the analytical protocol. TK was responsible for acquiring the data, and BDLM did the analysis. BDLM managed the literature review and wrote the manuscript. All authors contributed to the interpretation of the findings and the critical revision of the manuscript for intellectual content.

Conflicts of interest

JSGM has received educational grants from, serves as an ad hoc adviser to, or speaks at various events sponsored by Abbott Laboratories, Agouron Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals, Boreon Pharma AS, Bristol-Myers Squibb, DuPont Pharma, Gilead Sciences, GlaxoSmithKline, Hoffmann-La Roche, Immune Response Corporation, Incyte, Janssen-Ortho Inc, Kucera Pharmaceutical Company, Merck Frosst Laboratories, Pfizer Canada, Sanofi Pasteur, Shire Biochem, Tibotec Pharmaceuticals, and Trimeris. No other authors declared any conflicts of interest.

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References

- Hulse GK, English DR, Milne E, Holman CD. The quantification of mortality resulting from the regular use of illicit opiates. *Addiction* 1999; **94**: 221–29.
- Stoové MA, Dietze PM, Aitken CK, Jolley D. Mortality among injecting drug users in Melbourne: a 16-year follow-up of the Victorian Injecting Cohort Study (VICS). *Drug Alcohol Depend* 2008; **96**: 281–85.
- Warner M, Chen LH, Makuc DM. Increase in fatal poisonings involving opioid analgesics in the United States, 1999–2006. NCHS data brief, no 22. Hyattsville, MD, National Center for Health Statistics; 2009.
- Centers for Disease Control and Prevention. Unintentional drug poisoning in the United States. National Center for Injury Prevention and Control, CDC. <http://www.cdc.gov/HomeandRecreationalSafety/pdf/poison-issue-brief.pdf> (accessed Nov 1, 2010).
- Galea S, Ahern J, Tardiff K, et al. Racial/ethnic disparities in overdose mortality trends in New York City, 1990–1998. *J Urban Health* 2003; **80**: 201–11.
- Milloy MJ, Wood E, Reading C, Kane D, Montaner J, Kerr T. Elevated overdose mortality rates among First Nations individuals in a Canadian setting: a population-based analysis. *Addiction* 2010; **105**: 1962–70.
- White JM, Irvine RJ. Mechanisms of fatal opioid overdose. *Addiction* 1999; **94**: 961–72.
- Crandall CG, Vongpatanasin W, Victor RG. Mechanism of cocaine-induced hyperthermia in humans. *Ann Intern Med* 2002; **136**: 785–91.
- Kaye S, Darke S. Non-fatal cocaine overdose among injecting and non-injecting cocaine users in Sydney, Australia. *Addiction* 2004; **99**: 1315–22.
- Darke S, Hall W. Heroin overdose: research and evidence-based intervention. *J Urban Health* 2003; **80**: 189–200.
- Bohnert AS, Tracy M, Galea S. Circumstances and witness characteristics associated with overdose fatality. *Ann Emerg Med* 2009; **54**: 618–24.
- Binswanger IA, Stern MF, Deyo RA, et al. Release from prison—a high risk of death for former inmates. *N Engl J Med* 2007; **356**: 157–65.
- Bohnert AS, Prescott MR, Vlahov D, Tardiff KJ, Galea S. Ambient temperature and risk of death from accidental drug overdose in New York City, 1990–2006. *Addiction* 2010; **105**: 1049–54.
- Fischer B, Popova S, Rehm J, Ivsins A. Drug-related overdose deaths in British Columbia and Ontario, 1992–2004. *Can J Public Health* 2006; **97**: 384–87.
- Strathdee SA, Patrick DM, Currie SL, et al. Needle exchange is not enough: lessons from the Vancouver injecting drug use study. *AIDS* 1997; **11**: F59–F65.
- Werb D, Debeck K, Kerr T, Li K, Montaner J, Wood E. Modelling crack cocaine use trends over 10 years in a Canadian setting. *Drug Alcohol Rev* 2010; **29**: 271–77.
- Small W, Rhodes T, Wood E, Kerr T. Public injection settings in Vancouver: physical environment, social context and risk. *Int J Drug Policy* 2007; **18**: 27–36.
- Wood E, Kerr T, Lloyd-Smith E, et al. Methodology for evaluating Insite: Canada's first medically supervised safer injection facility for injection drug users. *Harm Reduct J* 2004; **1**: 9.
- DeBeck K, Wood E, Zhang R, Tyndall M, Montaner J, Kerr T. Police and public health partnerships: evidence from the evaluation of Vancouver's supervised injection facility. *Subst Abuse Treat Prev Policy* 2008; **3**: 11.
- Kimber J, Dolan K, van Beek I, Hedrich D, Zurhold H. Drug consumption facilities: an update since 2000. *Drug Alcohol Rev* 2003; **22**: 227–33.
- Wood E, Kerr T, Montaner JS, et al. Rationale for evaluating North America's first medically supervised safer-injecting facility. *Lancet Infect Dis* 2004; **4**: 301–306.
- Kerr T, Tyndall MW, Lai C, Montaner JSG, Wood E. Drug-related overdoses within a medically supervised safer injection facility. *Int J Drug Policy* 2006; **17**: 436–41.
- Tyndall MW, Kerr T, Zhang R, King E, Montaner JG, Wood E. Attendance, drug use patterns, and referrals made from North America's first supervised injection facility. *Drug Alcohol Depend* 2006; **83**: 193–98.
- Wood E, Tyndall MW, Montaner JS, Kerr T. Summary of findings from the evaluation of a pilot medically supervised safer injecting facility. *Can Med Assoc J* 2006; **175**: 1399–404.
- Wood E, Tyndall MW, Li K, et al. Do supervised injecting facilities attract higher-risk injection drug users? *Am J Prev Med* 2005; **29**: 126–30.
- Kerr T, Tyndall M, Li K, Montaner J, Wood E. Safer injection facility use and syringe sharing in injection drug users. *Lancet* 2005; **366**: 316–18.
- Wood E, Tyndall MW, Zhang R, et al. Attendance at supervised injecting facilities and use of detoxification services. *N Engl J Med* 2006; **354**: 2512–14.
- Small W, Wood E, Lloyd-Smith E, Tyndall M, Kerr T. Accessing care for injection-related infections through a medically supervised injecting facility: a qualitative study. *Drug Alcohol Depend* 2008; **98**: 159–62.
- Kerr T, Montaner J, Wood E. Supervised injecting facilities: time for scale-up? *Lancet* 2008; **372**: 354–55.
- Angus Reid. Canadians are supportive of Insite and oppose moves to shut it down. Angus Reid Public Opinion. http://www.angus-reid.com/polls/39366/canadians_want_to_keep_safe_injection_site (accessed Nov 1, 2010).

- 31 Wood E, Kerr T, Tyndall MW, Montaner JS. The Canadian government's treatment of scientific process and evidence: inside the evaluation of North America's first supervised injecting facility. *Int J Drug Policy* 2008; **19**: 220–25.
- 32 Hall W, Kimber J. Being realistic about benefits of supervised injecting facilities. *Lancet* 2005; **366**: 271–72.
- 33 Legislative Assembly of British Columbia. Coroners Act. Victoria, BC: Queen's Printer; 2007.
- 34 Statistics Canada. Postal Code Conversion File (PCCF), Reference Guide. Ottawa, ON: Statistics Canada; 2007.
- 35 Bow CJ, Waters NM, Faris PD, et al. Accuracy of city postal code coordinates as a proxy for location of residence. *Int J Health Geogr* 2004; **3**: 5.
- 36 Rothman KJ, Greenland S, Lash TL. Modern epidemiology, 3rd edn. Philadelphia, PA: Lippincott Williams and Wilkins; 2008.
- 37 Apparicio P, Abdelmajid M, Riva M, Shearmur R. Comparing alternative approaches to measuring the geographical accessibility of urban health services: Distance types and aggregation-error issues. *Int J Health Geogr* 2008; **7**: 7.
- 38 Kerr T, Stoltz JA, Tyndall M, et al. Impact of a medically supervised safer injection facility on community drug use patterns: a before and after study. *BMJ* 2006; **332**: 220–22.
- 39 Kerr T, Tyndall MW, Zhang R, Lai C, Montaner JS, Wood E. Circumstances of first injection among illicit drug users accessing a medically supervised safer injection facility. *Am J Public Health* 2007; **97**: 1228–30.
- 40 Vancouver Coastal Health. Injection drug use in the DTES. http://www.supervisedinjection.vch.ca/docs/sis_info_sheet.pdf (accessed March 22, 2010).
- 41 Petrar S, Kerr T, Tyndall MW, Zhang R, Montaner JS, Wood E. Injection drug users' perceptions regarding use of a medically supervised safer injecting facility. *Addict Behav* 2007; **32**: 1088–93.
- 42 Hedrich D. European report on drug consumption rooms. European Monitoring Centre for Drugs and Drug Addiction. http://www.emcdda.europa.eu/attachements.cfm/att_2944_EN_consumption_rooms_report.pdf (accessed Mar 4, 2010).
- 43 MSIC Evaluation Committee. Final report of the evaluation of the Sydney Medically Supervised Injecting Centre. http://www.druginfo.nsw.gov.au/_data/page/1229/NDARC_final_evaluation_report4.pdf (accessed March 8, 2010).
- 44 Wood E, Stoltz JA, Li K, Montaner JS, Kerr T. Changes in Canadian heroin supply coinciding with the Australian heroin shortage. *Addiction* 2006; **101**: 689–95.
- 45 Lloyd-Smith E, Wood E, Li K, Montaner JS, Kerr T. Incidence and determinants of initiation into cocaine injection and correlates of frequent cocaine injectors. *Drug Alcohol Depend* 2009; **99**: 176–82.
- 46 Wood E, Tyndall MW, Qui Z, Zhang R, Montaner JS, Kerr T. Service uptake and characteristics of injection drug users utilizing North America's first medically supervised safer injecting facility. *Am J Public Health* 2006; **96**: 770–73.
- 47 Spittal PM, Hogg RS, Li K, et al. Drastic elevations in mortality among female injection drug users in a Canadian setting. *AIDS Care* 2006; **18**: 101–108.
- 48 Wood E, Montaner JS, Li K, et al. Burden of HIV infection among Aboriginal injection drug users in Vancouver, British Columbia. *Am J Public Health* 2008; **98**: 515–19.
- 49 Fairbairn N, Small W, Shannon K, Wood E, Kerr T. Seeking refuge from violence in street-based drug scenes: women's experiences in North America's first supervised injection facility. *Soc Sci Med* 2008; **67**: 817–23.
- 50 Brugal MT, Domingo-Salvany A, Puig R, Barrio G, Garcia de Olalla P, de la Fuente L. Evaluating the impact of methadone maintenance programmes on mortality due to overdose and aids in a cohort of heroin users in Spain. *Addiction* 2005; **100**: 981–89.
- 51 Galai N, Safaiean M, Vlahov D, Bolotin A, Celentano DD. Longitudinal patterns of drug injection behavior in the ALIVE Study cohort, 1988–2000: description and determinants. *Am J Epidemiol* 2003; **158**: 695–704.
- 52 Statistics Canada. Population and family estimation methods at Statistics Canada. Catalogue no 91-528-XIE. Ottawa, ON: Demography Division, Statistics Canada; 2003.
- 53 Buxton JA. Vancouver drug use epidemiology: Vancouver site report for the Canadian Community Epidemiology Network on Drug Use (CCENDU). CCENDU. http://vancouver.ca/fourpillars/pdf/report_vancouver_2005.pdf (accessed March 22, 2010).
- 54 Rachlis BS, Hogg RS, Wood E, Li K, Kerr T. Factors associated with geographic migration among a cohort of injection drug users. *Health Place* 2008; **14**: 536–43.
- 55 Fielden SJ, Marsh DC. It's time for Canadian community early warning systems for illicit drug overdoses. *Harm Reduct J* 2007; **4**: 10.
- 56 City of Vancouver. Downtown Eastside community monitoring report. City of Vancouver. <http://vancouver.ca/commsvcs/planning/dtes/pdf/2006MR.pdf> (accessed Dec 7, 2010).
- 57 Cameron AC, Windmeijer FAG. An R-squared measure of goodness of fit for some common nonlinear regression models. *J Econ* 1997; **77**: 329–42.

Safe injection facilities save lives



Provision of sterile injecting equipment to people who inject drugs has long been a cornerstone of HIV-prevention programmes, with pragmatic public health approaches leading policy development.¹ Cheap, effective, and safe needle-and-syringe exchanges and related approaches to the reduction of drug-related harms have impressive records of success in reducing morbidity and mortality, controlling disease spread, and facilitating access to other health services for people who use drugs.²⁻⁴ But these approaches have proven difficult to implement in multiple settings, largely because of political, legal, and moral objections.¹ Supervised injection facilities have faced similar challenges,⁵ and to see why is not difficult. Such facilities are a logical progression from other harm-reduction measures. By providing people who inject with safe and medically supervised settings in which to use drugs, these facilities aim to address important health issues beyond the provision of equipment: reduction in sharing, safe disposal of used equipment, and, most crucially, the opportunity to reduce drug-overdose fatalities.

Drug overdoses are a major cause of morbidity and mortality in people who inject heroin or other opioids.^{6,7} Overdoses are also seen in people who inject cocaine and those who use mixed or multiple substances. In *The Lancet*, Brandon Marshall and co-workers⁸ report a reduction in overdose mortality rates associated with North America's first safe-injection facility. Results of their population-based assessment are impressive: an overall 35% reduction in overdose fatalities in the affected community. But the political battle about this facility has been intense, and is by no means over.^{5,9} The Conservative Government of Steven Harper has appealed a lower court ruling, which affirmed the facility's right to exist, to Canada's Supreme Court, which will hear the case in May, 2011. Let us hope evidence prevails.

How strong is the evidence for the reduction in mortality reported by Marshall and colleagues? It could be argued that the findings were the result of an observational assessment rather than those from a randomised trial. This point is important, because a randomised trial was deemed to be unethical in this instance.¹⁰ But, in the emerging domain of implementation science, also known as operational research, programme assessments in public health are

increasingly being done and reported with methods other than controlled trials.¹¹ The Vancouver group has much experience of working with those at risk in the city's Downtown Eastside, the high-density area for substance misuse. The group also has an extensive and enviable level of integration with British Columbia's public-sector institutions. Both these factors seem to have been crucial to the success of the assessment. The group's intimate knowledge of context—what we might call deep epidemiology—allowed comparison of this community with other districts of the urban core.

Mortality data came from the provincial coroner's registry of all unnatural or unexplained deaths.⁸ (The median age of overdose death in British Columbia was 40 years, so the years of productive life lost are substantial.) With coroner's data on mortality throughout the observational period, census data, and a careful assessment of distance from the facility based on usage data from another study, Marshall and co-workers constructed a person-years-at-risk analysis of overdose mortality. Although a modest but not statistically significant reduction was noted across the census tracts in the study period in areas that were distant from the supervised injection facility, a statistically significant fall of 35% ($p=0.048$) was observed in those census tracts within 500 m of the facility. For public health interventions for which randomised trials might be unfeasible, unethical, or otherwise unlikely to take place, findings from well-done implementation science are

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arguably the highest attainable standard of research that we might achieve. Furthermore, when mortality is the outcome, as it was in this observational assessment, these results might be sufficient for sound and timely decision making.

This intervention also has a human-rights dimension, as does the legal controversy now surrounding it. A lower-court decision in favour of the supervised injection facility argued that closing the site would undermine Canada's Charter of Rights and Freedoms to life, liberty, and security of the person.⁵ Marshall and colleagues' report adds credence to this argument, because an intervention that reduces preventable deaths from overdose certainly helps to realise the rights to life and to security.

Supervised injection facilities clearly have an important part to play in communities affected by injection drug use. They should be expanded to other affected sites in Canada, on the basis of the life-saving effects identified in Vancouver. Moreover, such facilities should be taken to scale more broadly—wherever drug overdoses are a substantial cause of preventable losses of life. That such a move will be politically fraught in other settings is virtually assured. All the more reason, then, to begin action now.

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- 1 Beyrer C, Malinowska-Sempruch K, Kamarulzaman A, Kazatchkine M, Sidibe M, Strathdee SA. Time to act: a call for comprehensive responses to HIV in people who use drugs. *Lancet* 2010; **376**: 551–63.
- 2 Guinness L, Vickerman P, Quayyum Z, et al. The cost-effectiveness of consistent and early intervention of harm reduction for injecting drug users in Bangladesh. *Addiction* 2010; **105**: 319–28.
- 3 Vickerman P, Kumaranayake L, Balakireva O, et al. The cost-effectiveness of expanding harm reduction activities for injecting drug users in Odessa, Ukraine. *Sex Transm Dis* 2006; **33** (suppl 10): 89–102.
- 4 Palmateer N, Kimber J, Hickman M, et al. Evidence for the effectiveness of sterile injecting equipment provision in preventing hepatitis C and HIV transmission among injecting drug users: a review of reviews. *Addiction* 2010; **105**: 844–59.
- 5 Small D. An appeal to humanity: legal victory in favour of North America's only supervised injection facility: Insite. *Harm Reduct J* 2010, **7**: 23.
- 6 Degenhardt L, Hall W, Warner-Smith M. Using cohort studies to estimate mortality among injecting drug users that is not attributable to AIDS. *Sex Transm Infect* 2006; **82**: 56–63.
- 7 Stoové MA, Dietze PM, Aitken CK, Jolley D. Mortality among injecting drug users in Melbourne: a 16-year follow-up of the Victorian Injecting Cohort Study (VICS). *Drug Alcohol Depend* 2008; **96**: 281–85.
- 8 Marshall B, Milloy M-J, Wood E, Montaner J, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet* 2011; published online April 18. DOI:10.1016/S0140-6736(10)62353-7.
- 9 Hall N. "B.C. court rules Vancouver's Insite safe injection site can stay open." *Vancouver Sun (Vancouver)* Jan 15, 2010. <http://www.vancouversun.com/news/court+rules+Vancouver+Insite+safe+injection+site+stay+open/2446233/story.html> (accessed Feb 7, 2011).
- 10 Christie T, Wood E, Schechter MT, O'Shaughnessy MV. A comparison of the new Federal Guidelines regulating supervised injection site research in Canada and the Tri-Council policy statement on ethical conduct for research involving human subjects. *Int J Drug Pol* 2003; **16**: 56–73.
- 11 Padian N, Holmes C, McCoy S, Lyerla R, Bouey P, Goosby E. Implementation Science for PEPFAR. *J Acquir Immune Defic Syndr* 2011; **56**: 199–203.