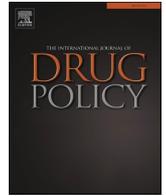




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Research Paper

Reduced risk of overdose among clients of a safer opioid supply program in Southwestern Ontario: A pre-post observational cohort study

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ABSTRACT

Introduction: North America faces an ongoing overdose crisis driven by a volatile and toxic drug supply comprised primarily of fentanyl, fentanyl analogues and other adulterants. Safer opioid supply (SOS) programs prescribe pharmaceutical opioids to individuals at high risk of overdose mortality. This study evaluated changes in non-fatal overdose prevalence in the 6 months after SOS program initiation among SOS participants in Kitchener-Waterloo, Canada.

Methods: We analyzed data from a pre-post observational cohort of clients enrolled in a SOS program between July 2021 and October 2023. Baseline surveys were completed upon program entry, with follow-up surveys after 6 months. We compared non-fatal overdose prevalence between baseline and follow-up using McNemar's test and calculated adjusted odds ratios (aOR) using generalized estimating equation (GEE) models, controlling for potential confounders including homelessness, hospitalization, daily fentanyl use, and incarceration.

Results: Among 100 participants completing follow-up (out of 162 who completed a baseline survey), overdose prevalence decreased significantly from 60 % (95 % Confidence Interval (CI): 50–69) at baseline to 15 % (95 % CI: 9–23) at follow-up ($p < 0.001$). Overdose incidence rates declined from 48.5 to 3.3 per 100 person-months. After adjusting for confounders, participants had 83 % lower odds of overdose during follow-up (aOR 0.17, 95 % CI: 0.08–0.38).

Discussion: Participants in a SOS program experienced significant reductions in non-fatal overdose during the 6 months following program initiation. SOS clients are a high-risk population with elevated overdose rates at baseline; these results support expanding safer supply programs as part of a comprehensive set of strategies to address the overdose crisis.

Introduction

North America continues to face a crisis of overdose-related deaths fueled by an increasingly volatile and toxic unregulated drug supply characterized by the proliferation of fentanyl, fentanyl analogues, and non-opioid adulterants, including unregulated benzodiazepines and xylazine (Federal, provincial, and territorial Special Advisory Committee on Toxic Drug Poisonings, 2025). In Canada, over 50,000 opioid-related deaths were recorded between January 2016 and

September 2024, a trend driven primarily by illicitly manufactured fentanyl. While it is difficult to estimate the number of non-fatal overdoses as many are treated in the community with naloxone and without calling paramedics, between March 2017 and May 2025, there were 65,977 overdoses reversed within supervised consumption sites across Canada (out of 5394,643 total visits) (Health Canada, 2025). In Ontario, Canada's most populous province, 84 % of opioid-related deaths now involve unregulated fentanyl and its analogues (Federal, provincial, and territorial Special Advisory Committee on Toxic Drug Poisonings, 2025;

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Ledlie et al., 2025). In response, a multi-layered public health strategy has been implemented, including overdose education, naloxone distribution, opioid agonist treatment (OAT), and expanded access to harm reduction services.

Among these interventions, prescribed safer opioid supply (SOS) programs – also known as prescribed alternatives – were introduced to reduce exposure to the toxic drug supply and thereby prevent overdose (Fajber et al., 2025; Gomes et al., 2022; Kolla et al., 2025; Ledlie et al., 2024; Nafeh et al., 2023; Schmidt et al., 2024). In these programs, individuals at high risk of overdose are prescribed pharmaceutical opioids – typically including daily-dispensed, immediate-release hydromorphone tablets, often paired with long-acting opioid medications, such as slow-release oral morphine or methadone – to reduce their reliance on unregulated drugs and mitigate opioid-related overdose risk (Gomes et al., 2022; Kolla et al., 2025; Xu et al., 2025). Prescribed SOS programs take an explicitly harm reduction approach in that they do not require abstinence from drug use as a goal of program participation; additionally, they differ from OAT programs as they expand on the medication options available (including hydromorphone tablets in Ontario, and oxycodone and fentanyl formulations in BC) and allow for take-home doses of some safer supply medications for unobserved administration by program participants (Ivins et al., 2025; Kolla et al., 2024, 2025; Norton et al., 2024; Schmidt et al., 2024). In Ontario, many SOS programs were integrated into primary-care and community health settings, where wraparound supports, including medical and social services, were also provided to support clients' complex health and social needs (Fajber et al., 2025; Haines & O'Byrne, 2023b; Schmidt et al., 2023, 2024). And while many SOS programs in Ontario were located in large urban centres of Toronto and Ottawa, SOS programs were also scaled-up in smaller and mid-sized cities across the province, including in the mid-sized city of Kitchener (estimated population in 2021 of 250,000) (Glegg et al., 2022; Perri, Fajber et al., 2023; Schmidt et al., 2024). This provides an opportunity to examine the impacts of SOS programs outside of large urban areas, where research on interventions to address the overdose crisis are often lacking (Bardwell & Lappalainen, 2021).

The primary goal of SOS is to reduce fatal and non-fatal overdoses related to continued use of the toxic drug supply (Hales et al., 2019). Emerging evidence suggests programs are achieving this goal. For example, a robust quasi-experimental analysis of administrative data in British Columbia found that receiving a safer supply prescription was associated with immediate, significant reductions in overdose-related mortality and all-cause mortality compared to matched controls (Slaunwhite et al., 2024). Similarly, quasi-experimental research in Ontario using administrative health data found significant reductions in opioid toxicity, emergency department visits, hospitalization and incident infections among SOS recipients at both the program and provincial level (Gomes, Kolla et al., 2022; Gomes et al., 2025). This quasi-experimental evidence corroborates findings from cohort studies where clients self-report reductions in overdose frequency following program engagement (Haines & O'Byrne, 2023a; Kalicum et al., 2024; Kolla et al., 2021, 2024; Nafeh et al., 2023; Schmidt et al., 2023). However, research relying on administrative health data captures only those overdoses resulting in a healthcare encounter or death. This approach may underestimate the true effect of SOS on overdose reduction, as many overdose events are reversed in community settings with naloxone and go unrecorded. Our aim was to use self-reported survey data to examine changes in the prevalence and incidence of non-fatal overdose during the first 6 months of enrollment in a safer supply program in Kitchener-Waterloo, a city in Southwestern Ontario, Canada.

Methods

Study setting

This observational cohort study uses data collected by Sanguen Health Centre - a not-for-profit, community-based health care agency

working primarily with people living with or at risk for Hepatitis C virus (HCV) - as part of their internal program monitoring and quality improvement activities. The prescribed safer opioid supply program at Sanguen Health began in 2021 as a partnership between several local organizations offering a range of health and social services using a low-barrier, person-centred model of care, and was funded through time-limited federal pilot program funding from the Substance Use and Addictions Program (SUAP) at Health Canada (Perri, Fajber et al., 2023a; Perri, Fajber et al., 2023b)

In partnership with external evaluators as part of their internal program monitoring activities, Sanguen Health Centre designed a short survey that was completed by clients upon entry into the program (baseline) and again after 6-months in the program to assess program impacts and support quality improvement. Inclusion criteria was all clients who were admitted to the safer supply program between July 2021 and October 2023, and who received at least one prescription for safer supply medications. Staff from Sanguen Health Centre conducted baseline surveys with 162 clients when they entered the program, and follow-up outcome surveys were completed with clients after they had been in the program for at least 6 months (and within 2 weeks of reaching 6 months in the program).

Survey data were collected between July 2021 and October 2023. Clients were asked questions about their substance use, health, and overall social well-being. Survey data were collected internally by SOS program staff who were not involved in clinical service delivery. Data were stored using unique identifiers, with the program maintaining a separate record linking those identifiers to client names; survey data was not linked to any clinical or electronic medical data, and the evaluation team had no access to identifiable data. During program enrollment, all clients were asked for consent to have their survey data used in research and evaluation activities. All clients have provided verbal, informed consent for use of survey data for research and evaluation. The survey instrument is available on request from the investigators. Approval for the secondary data analysis presented here was received from the University of Toronto Research Ethics Board.

Study outcomes

Primary outcome was prevalence of overdose within the last 6 months. This was defined based on the answer to the question "Have you overdosed in the past 6 months" (yes/no); for those responding yes, a follow-up question on the number of overdoses in the past 6 months was asked. Similar questions were asked at baseline and again at the 6-month follow up for a range of outcomes including: emergency department use; hospitalization for at least one night; contact with police or arrest; incarceration for at least one night; experience of homelessness; difficulty finding enough food to eat or to pay for basic needs; engaging in criminalized activities to pay for drugs; and engaging in sex work to pay for drugs. Participants were also asked to give a self-rating of their overall physical and mental health on a 5-point scale.

Data analysis

We summarized the participants' baseline characteristics as frequencies and percentages and compared participants who completed follow-up to those lost to follow-up using these baseline characteristics. We calculated the prevalence of overdose in the past six months for the baseline and follow-up periods, across all levels of independent variables, along with their 95 % confidence intervals (CI). To assess changes in prevalence between baseline and follow-up, we used McNemar's test for paired comparisons.

For incidence rate calculations, we defined the incidence rate as the total number of overdose events during the six-month period, divided by the total person-months at risk, and multiplied by 100. We counted all overdose events reported by participants, allowing multiple events per person to be included in the numerator. Person-time was calculated as

the full 6-month period for all participants, regardless of overdose occurrence, as individuals can experience multiple overdoses during a given timeframe and we were interested in measuring the total burden of overdose events rather than restricting analysis to time-to-first-event. We also reported the frequency of overdoses during follow-up across all independent variables and examined associations between individuals with and without overdoses using Chi-square and Fisher's exact tests, as appropriate.

We used a logistic generalized estimating equation (GEE) regression model to compare baseline and follow-up period overdoses. This model accounted for the correlated nature of the data by employing an exchangeable correlation structure. In the initial unadjusted model, we included only the exposure variable and overdose in the past six months as the dependent variable. We then fitted a second GEE model that included both the exposure variable and potential confounders, selected a priori based on established literature identifying factors associated with both safer supply program engagement and overdose risk (Nafeh et al., 2023), while also being constrained by data availability given that the survey was designed primarily for program quality improvement purposes. Potential confounders included experiencing homelessness for at least one night, hospitalization for one or more nights, daily use (injection and/or non-injection) of street-acquired fentanyl, and incarceration for at least one night in the past six months. We reported adjusted odds ratios (ORs) and 95 % CIs from the multivariable model, with confounders controlled.

We calculated incidence rate ratios (IRRs) using zero-inflated negative binomial mixed models to analyze the number of new overdose events during the six-month follow-up. We selected the zero-inflated approach due to the large number of participants who reported no overdose events. The negative binomial distribution accounted for overdispersion in the data. Similar to the logistic regression models, we included confounders to adjust the IRRs for exposure. To assess the robustness of our findings to potential attrition bias, we conducted a sensitivity analysis under several assumptions regarding overdose outcomes among participants lost to follow-up (Supplement 1). We considered p-values < 0.05 statistically significant. All analyses were conducted using R software (version 4.4.3).

Results

At baseline, 162 participants were enrolled, of whom 100 (62 %) completed a follow-up visit after 6 months post-enrollment, while 62 (38 %) were lost to follow-up or did not complete a follow-up survey. We found no significant differences in baseline characteristics between participants who completed follow-up and those lost to follow-up (Table 1). Among those who completed follow-up, 55 % ($n = 55$) were under 45, most (77 %; $n = 75$) self-identified as White, and 36 % ($n = 36$) were female. At baseline, 73 % ($n = 72$) of the participants had experienced homelessness for at least one night in the past 6 months, and 31 % ($n = 30$) were hospitalized for one or more nights. While 15 % ($n = 15$) had ever been incarcerated in the previous 6 months, 35 % ($n = 35$) had been in contact with police or arrested. Difficulty meeting basic needs was prevalent, with 94 % ($n = 94$) reporting challenges affording their basic needs and 62 % ($n = 62$) reporting food insecurity in the previous 6 months. Lastly, at baseline, only 24 % ($n = 24$) of participants rated their physical health as good, and 21 % ($n = 21$) reported good mental health in the past 6 months (Table 1).

The prevalence of overdose in the past six months at baseline was 60 % (95 % CI: 50–69), which significantly declined to 15 % (95 % CI: 9–23) at follow-up (P -value < 0.001). The total number of overdose events was 291 at baseline and 20 at follow-up, with total person-time of 600 person-months for each period. The incidence rate per 100 person-months also decreased significantly from 48.5 (95 % CI: 42.9–54.1) at baseline to 3.3 (95 % CI: 1.9–4.8) at follow-up (P -value < 0.001). Differences in overdose prevalence between baseline and follow-up were significant across most independent variables (Table 2). Among those

Table 1

Comparison of baseline characteristics between participants beginning a prescribed safer supply program in Kitchener-Waterloo, Ontario from 2021 to 2023 who were those lost to follow-up (Without FU) ($n = 62$) and who completed follow-up (With FU) ($n = 100$).

Variables		Total (N = 162) N (%)	Without FU N = 62 N (%)	With FU N = 100 N (%)	P-value
Age	<45	98 (61)	43 (69)	55 (55)	0.114
	≥45	63 (39)	19 (31)	44 (44)	
Gender	Women	58 (36)	22 (36)	36 (36)	0.580
	Men	100 (62)	37 (61)	63 (63)	
	Non-binary/2-Spirit	3 (2)	2 (3)	1 (1)	
Race	White	122 (77)	47 (76)	75 (77)	0.978
	Other	37 (23)	15 (24)	22 (23)	
Homelessness (Last 6 months)	Yes	115 (72)	43 (71)	72 (73)	0.901
	No	45 (28)	18 (30)	27 (27)	
Hospitalized (Last 6 months)	Yes	44 (28)	14 (23)	30 (31)	0.354
	No	116 (73)	48 (77)	68 (69)	
Daily fentanyl use	Yes	135 (91)	50 (91)	85 (91)	0.999
	No	13 (9)	5 (9)	8 (9)	
Non-prescribed opioid injection (current)	Yes	68 (43)	20 (32)	48 (49)	0.065
	No	92 (58)	42 (68)	50 (51)	
Inject/use stimulants (current)	Yes	140 (87)	51 (82)	89 (90)	0.245
	No	21 (13)	11 (18)	10 (10)	
Incarcerated (Last 6 months)	Yes	25 (16)	10 (17)	15 (15)	0.955
	No	135 (84)	50 (83)	85 (85)	
Police encounter/arrest (Last 6 months)	Yes	65 (40)	30 (48)	35 (35)	0.127
	No	97 (60)	32 (52)	65 (65)	
Difficulty with food access (Last 6 months)	Yes	102 (37)	40 (66)	62 (62)	0.773
	No	59 (63)	21 (34)	38 (38)	
Difficulty with money for basic needs (Last 6 months)	Yes	152 (94)	58 (94)	94 (94)	0.999
	No	10 (6)	4 (7)	6 (6)	
Criminal activity for drugs (Last 6 months)	Yes	129 (80)	46 (75)	83 (83)	0.333
	No	32 (20)	15 (25)	17 (17)	
Sex work for drugs (Last 6 months)	Yes	29 (18)	8 (13)	21 (21)	0.287
	No	129 (82)	52 (87)	77 (77)	
Overall physical health	Good	37 (23)	13 (30)	24 (24)	0.679
	Okay	56 (35)	24 (38)	32 (32)	
	Poor	69 (43)	25 (40)	44 (44)	
Overall mental health	Good	36 (22)	15 (24)	21 (21)	0.234
	Okay	52 (32)	15 (24)	37 (37)	
	Poor	74 (46)	32 (52)	42 (42)	

• 2-Spirit is an umbrella term used by some Indigenous people who identify with another gender identity or whose gender identity does not fit within a male-female gender binary, or for people in some Indigenous communities who embody both male and female energy (Metis Nation of Ontario, 2022); All % are rounded to the nearest whole number. FU = follow-up.

enrolled in the program, there were no differences in overdose prevalence across independent variables, except for history of incarceration in the previous 6 months; when comparing those who had overdosed to those who had not, participants with a history of incarceration were more likely to have overdosed (28 % vs. 7 %; P -value = 0.042) (Table 3).

In the bivariable GEE logistic regression, we observed an OR of 0.15 (95 % CI: 0.07–0.32) for follow-up compared to baseline. After adjusting for confounders in the multivariable GEE model, the aOR was 0.17 (95 % CI: 0.08–0.38), indicating an 83 % reduction in the odds of overdose (Table 4). Findings from our sensitivity analysis suggested that even in the most conservative scenario, which assumed that all participants lost to follow-up continued to experience overdose at their baseline rate, the protective effect of the intervention persisted (aOR 0.55; 95 % CI: 0.40–0.75)(Supplement 1).

Table 2
Prevalence of overdose in the last 6 months at baseline and follow-up among participants in a prescribed safer supply program in Kitchener-Waterloo, Ontario from 2021–2023 (n = 100).

Variables	Prevalence of overdose in the last 6 months (95 % CI)		
	Baseline	Follow-up	P-value
Overall	60 (50–69)	15 (9–23)	<0.001
Age	<45 (52–76)	12 (6–24)	<0.001
	≥45 (38–66)	17 (9–30)	<0.001
Gender	Women (35–66)	14 (6–29)	0.003
	Men (52–75)	15 (8–25)	<0.001
Race	White (47–69)	15 (9–24)	<0.001
	Other (43–80)	16 (6–38)	0.005
Homelessness (Last 6 months)	Yes (50–72)	14 (7–27)	<0.001
	No (34–69)	16 (8–28)	0.002
Hospitalized (Last 6 months)	Yes (70–95)	24 (10–47)	<0.001
	No (35–58)	13 (8–22)	<0.001
Daily fentanyl use	Yes (50–70)	16.4 (9–28)	<0.001
	No (22–79)	16.7 (3–56)	0.301
Non-prescribed opioid injection (current)	Yes (54–80)	33 (6–79)	0.546
	No (37–63)	15 (9–23)	<0.001
Inject/use stimulants (current)	Yes (51–71)	16 (9–25)	<0.001
	No (24–76)	17 (5–45)	0.172
Incarcerated (Last 6 months)	Yes (36–80)	40 (17–69)	0.428
	No (49–69)	12 (7–21)	<0.001
Police encounter/arrest (Last 6 months)	Yes (44–75)	19 (9–38)	0.003
	No (47–71)	14 (8–23)	<0.001
Difficulty with food access (Last 6 months)	Yes (56–79)	14 (7–25)	<0.001
	No (30–60)	17 (9–30)	0.011
Difficulty with money for basic needs (Last 6 months)	Yes (51–71)	14 (8–23)	<0.001
	No (10–70)	21 (9–43)	0.606
Criminal activity for drugs (Last 6 months)	Yes (51–72)	18 (11–30)	<0.001
	No (26–69)	10 (4–24)	0.006
Sex work for drugs (Last 6 months)	Yes (50–86)	29 (8–64)	0.076
	No (44–66)	12 (7–21)	<0.001
Overall physical health	Good (31–69)	10 (4–26)	0.003
	Okay (41–74)	20 (10–34)	0.002
	Poor (51–78)	14 (6–31)	<0.001
Overall mental health	Good (28–68)	15 (6–33)	0.031
	Okay (48–78)	14 (7–28)	<0.001
	Poor (47–75)	16 (7–33)	<0.001

CI = Confidence Interval *All prevalences are rounded to the nearest whole number.

Table 3
Characteristics of individuals with and without overdose at 6-month follow-up after beginning in a prescribed safer supply program in Kitchener-Waterloo, Ontario from 2021–2023 across all variables.

Variables	With Overdose N (%)	Without Overdose N (%)	P-value
Overall	15 (100)	85 (100)	
Age	<45 (8 (53))	40 (48)	0.576
	≥45 (7 (47))	43 (52)	
Gender	Women (5 (36))	30 (36)	0.999
	Men (9 (64))	53 (64)	
Race	White (12 (80))	63 (77)	0.999
	Other (3 (20))	19 (23)	
Homelessness (Last 6 months)	Yes (7 (47))	42 (49)	0.999
	No (8 (53))	43 (51)	
Hospitalized (Last 6 months)	Yes (4 (27))	13 (15)	0.279
	No (11 (73))	72 (85)	
Daily fentanyl use	Yes (13 (100.0))	72 (90.0)	0.594
	No (0 (0.0))	8 (10.0)	
Non-prescribed opioid injection (current)	Yes (1 (8))	2 (2)	0.393
	No (14 (93))	82 (98)	
Inject/use stimulants (current)	Yes (13 (87))	70 (88)	0.999
	No (2 (13))	10 (13)	
Incarcerated (Last 6 months)	Yes (4 (27))	6 (7)	0.042
	No (11 (73))	78 (93)	
Police encounter/arrest (Last 6 months)	Yes (5 (33))	21 (25)	0.531
	No (10 (67))	63 (75)	
Difficulty with food access (Last 6 months)	Yes (7 (47))	45 (54)	0.780
	No (8 (53))	39 (46)	
Difficulty with money for basic needs (Last 6 months)	Yes (11 (73))	70 (82)	0.476
	No (4 (27))	15 (18)	
Criminal activity for drugs (Last 6 months)	Yes (11 (73))	49 (58)	0.392
	No (4 (27))	35 (42)	
Sex work for drugs (Last 6 months)	Yes (2 (15))	5 (6)	0.240
	No (11 (85))	78 (94)	
Overall physical health	Good (3 (20))	27 (32)	0.529
	Okay (8 (53))	33 (39)	
	Poor (4 (27))	25 (29)	
Overall mental health	Good (4 (27))	23 (27)	0.976
	Okay (6 (40))	36 (42)	
	Poor (5 (33))	26 (31)	

*All prevalences are rounded to the nearest whole number.

Table 4
Bivariable and multivariable GEE logistic regression analysis of reduction in the odds of overdose at follow-up among participants in a prescribed safer supply program in Kitchener-Waterloo, Ontario.

Intervention	Baseline	Crude OR (95 % CI)	P-value	Adjusted OR (95 % CI)*	P-value
Follow-up	1	0.15 (0.07–0.32)	<0.001	0.17 (0.08–0.38)	<0.001

Adjusted for homelessness, hospitalization, daily fentanyl use, and incarceration in the last 6 months.

Discussion

In this prospective study of individuals enrolled in a SOS program in Southwestern Ontario, we found that receiving a safer supply prescription was associated with reduced non-fatal overdose risk among participants. The 83 % reduction in odds of overdose (aOR 0.17) and the sharp decline in overdose incidence from 48.5 to 3.3 per 100 person-months is consistent with previous quasi-experimental research using health administrative data in two separate provinces among all people in those respective provinces receiving safer supply, and that found an

association between SOS prescribing with reduced opioid toxicity and overdose mortality (Gomes et al., 2025; Slaunwhite et al., 2024). Additionally, the significant reduction in odds of overdose after initiating safer supply is consistent with other observational cohort studies of both prescribed safer supply programs and compassion club models of safer supply (Kalicum et al., 2024; Nafeh et al., 2023), suggesting that the reduction in overdose observed may be due to access to a known dose of known substance, regardless of whether it is in a prescribed safer supply or compassion club model of service delivery.

Analysis of baseline characteristics suggests that the program successfully engaged a population experiencing extreme structural vulnerability, including high prevalence of injection drug use (>50 %) and homelessness (>70 %), as well as inability to afford basic needs at baseline (94 %). This finding is notable as the rate of fatal overdose among people experiencing homelessness increased by 129 % in Ontario during the period of the COVID-19 pandemic (Gomes et al., 2021). That such a significant reduction in overdose was observed in this cohort demonstrates that a low-barrier model integrating SOS with primary care and comprehensive wraparound supports can effectively mitigate overdose risk even among those with the most complex health and social needs. Additionally, a population-level study in Ontario also documented high levels of prior receipt of opioid agonist treatment among people receiving SOS (87.4 % had received OAT in the past year) alongside a significant reduction in opioid toxicity following initiation of SOS (Gomes et al., 2025). Taken together, the findings from this and other studies suggest that SOS programs are reaching and reducing overdose toxicities in a highly vulnerable population who are treatment-experienced. While SOS program scale-up has been limited to Canada as a response to high rates of overdose toxicity, international studies have highlighted challenges with retention to OAT, and SOS prescribing may provide a complementary alternative to existing OAT options in a broad range of settings (Degehardt et al., 2023; German et al., 2025).

Despite the overall program's success in reducing overdoses among the participants, our finding that participants with a history of recent incarceration had higher odds of overdose during follow-up (27 % vs. 7 %) requires careful consideration. While we do not know the timing between release from custody and enrolment in the program, this finding may reflect the profound disruption to care that occurs during incarceration. Prior research has demonstrated higher rates of overdose immediately after release from prison (Binswanger et al., 2007; Kinner et al., 2021). Previous research has also shown how individuals receiving opioid agonist treatment who are incarcerated can experience a disruption or abrupt cessation of their prescribed medications in addition to difficulties with continuity of care upon release, which may contribute to the increased risk of overdose upon release due to loss of tolerance (Bozinoff et al., 2018; Kouyoumdjian et al., 2018; Russell et al., 2022). Our findings suggest similar patterns may be occurring for individuals receiving SOS, particularly as qualitative research has documented abrupt cessation of SOS medications following incarceration in Ontario (Perri, Fajber et al., 2023a). This suggests that people receiving SOS may face similar issues with continuity of care within correctional facilities and timely re-engagement in care after release as people receiving opioid agonist treatment, a systems-level failure highlighting how the intersection of criminalization and substance use creates additional barriers to achieving optimal health outcomes and reducing rates of overdose. This also underscores the urgent need to implement robust discharge planning that reconnects individuals to community-based care immediately upon release.

Our findings should be interpreted in the context of several limitations. First, attrition was considerable (38 %). However, we found no significant differences in baseline characteristics between participants who completed follow-up and those lost to follow-up, and our primary finding remained robust in a sensitivity analysis that made conservative assumptions about outcomes among those with missing data. Second, reliance on self-reported overdose events may be subject to recall or

social desirability bias; though we tried to mitigate this by using non-clinical staff for data collection. Third, the study's single-arm, pre-post design lacks a concurrent comparison group, meaning we cannot definitively rule out the influence of secular trends on the observed outcomes. While this is an important limitation, it is partially mitigated by provincial surveillance data showing that overall overdose rates were not declining in Ontario during the study period. This context suggests that the dramatic reduction in overdose seen in our cohort is unlikely to be attributable to a general, province-wide improvement and strengthens the case for an intervention-specific effect. Additionally, this study was conducted during the COVID-19 pandemic, which may have disrupted health service delivery and reduced access to wraparound supports that typically accompany safer supply programs. However, any such disruptions would likely bias our findings toward the null, suggesting that the observed reduction in overdose risk may represent a conservative estimate of the intervention's true effectiveness under optimal operating conditions. Finally, as this study was conducted in a single program in Ontario, the findings may not be generalizable to all SOS models or jurisdictions. Despite these limitations, our findings provide important evidence supporting the role of safer supply programs in reducing overdose prevalence and incidence, as part of a comprehensive range of health services and harm reduction strategies.

CRediT authorship contribution statement

Gillian Kolla: Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization. **Jerri-Lyn Lewis:** Writing – review & editing, Writing – original draft. **Adrian Guta:** Writing – review & editing, Funding acquisition, Conceptualization. **Ashley Schaff:** Writing – review & editing, Data curation, Conceptualization. **Megan Boyle:** Writing – review & editing, Conceptualization. **Kourteney King:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Carol Strike:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Mohammad Karamouzian:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Gillian Kolla reports financial support was provided by Health Canada - Substance Use and Addictions Program. Given their role as Associate Editor at the International Journal of Drug Policy, Gillian Kolla had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to another journal editor. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.drugpo.2025.105124](https://doi.org/10.1016/j.drugpo.2025.105124).

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