

Evaluation of the Potential Impact of Expanding Regulated Opioid Access in Seattle Washington

Adam Palayew

A dissertation

submitted in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

University of Washington

2024

Reading Committee:

Stephen J. Mooney, Chair

Sara N. Glick

Caleb J. Banta-Green

Program Authorized to Offer Degree:

Epidemiology

© Copyright 2024

Adam Palayew

University of Washington

Abstract

Evaluation of the Potential Impact of Expanding Regulated Opioid Access in Seattle,
Washington

Adam Palayew

Chair of the Supervisory Committee:

Stephen J. Mooney

Department of Epidemiology

The opioid overdose crisis has resulted in over a million deaths in the US since the turn of the millennia. Deaths continue to rise despite concerted efforts to address the opioid crisis through the expansion of treatment options and harm reduction services like naloxone distribution. A primary factor contributing to the rise in death is the volatility of the unregulated drug supply. Since the drug market is unregulated people who use drugs don't have a way to ensure the potency and quality of their drugs that come from unregulated markets putting them at increased risk of overdose.

In the ensuing dissertation, I try to address existing gaps in potential harm reduction strategies, focusing specifically on the implementation of safe supply interventions in Seattle, Washington.

Through comprehensive research methodologies, I aim to: 1) determine the population size of people who inject drugs in Seattle, 2) elucidate the preferences and perspectives of people who use opioids, both injection and non-injection, regarding various modalities of accessing opioids, and 3) model the potential impact of implementing certain safe supply scenarios on opioid-related mortality among PWID in Seattle, Washington.

Chapter 2 of my dissertation employs several population estimation techniques to ascertain the prevalence of injection drug use in Seattle, Washington. In **Chapter 3**, I conducted a survey of people who use opioids in Seattle to discern their preferences regarding the procurement of opioids and the perceived impact of different access models on their behaviors and patterns of use. In **Chapter 4**, I employ microsimulation modeling techniques to forecast the potential outcomes of implementing distinct safe supply programs among people who inject opioids in Seattle.

In **Chapter 2** of this dissertation, I found a decline in the number of people who inject drugs in Seattle. Respondents in **Chapter 3** expressed strong interest in diverse safe supply models, foreseeing substantial improvements in their quality of life, irrespective of potential modifications to their substance use behaviors. Furthermore, **Chapter 4** underscored the potential of implementing broadly accessible safe supply interventions in mitigating overdose fatalities among people who inject opioids in Seattle, Washington.

The conclusions drawn from this dissertation suggest that implementing safe supply interventions offers a potential promising avenue for reducing overdose fatalities in Seattle. By

legalizing and regulating the opioid supply, individuals can access substances in a controlled way with quality assured while potentially promoting healthier use.

TABLE OF CONTENTS

ABSTRACT	3
ACKNOWLEDGEMENTS	8
DEDICATION	9
LIST OF TABLES	10
LIST OF FIGURES	12
CHAPTER 1. INTRODUCTION	14
CHAPTER 2. ESTIMATING THE NUMBER OF PEOPLE WHO INJECT DRUGS IN SEATTLE, WASHINGTON WITH MULTIPLE APPROACHES	17
ABSTRACT	18
INTRODUCTION	20
METHODS	23
RESULTS	29
DISCUSSION	31
REFERENCES	36
APPENDIX	42
CHAPTER 3. PREFERENCES AND ANTICIPATED BEHAVIOUR CHANGES FOR DIFFERENT MODELS OF SAFE SUPPLY AMONG PEOPLE WHO USE OPIOIDS IN SEATTLE, WASHINGTON	43
ABSTRACT	45
INTRODUCTION	47
METHODS	49
RESULTS	53

DISCUSSION	63
REFERENCES	69
APPENDIX	74
CHAPTER 4. A MICROSIMULATION MODEL OF THE POTENTIAL IMPACT OF THE IMPLEMENTATION OF DIFFERENT MODELS OF OPIOID REGULATION IN SEATTLE WASHINGTON	76
ABSTRACT	77
INTRODUCTION	79
METHODS	81
RESULTS	86
DISCUSSION	89
REFERENCES	93
APPENDIX	98
CHAPTER 5. CONCLUSION	99

ACKNOWLEDGEMENTS

I have a lot of people to be thankful to who made this dissertation possible. I did not do this alone and have a lot of people to thank on this journey. First and foremost, I am thankful to the community of people who use drugs in Seattle who without them this dissertation would not be possible. I am also thankful for their participation in the research, guidance, and friendship. I am also thankful to numerous community organizations (especially VOCAL-WA and PHRA) who helped with recruitment of this study; however, more importantly helped foster my intellectual and personal development. I am very thankful to my dissertation committee and the mentorship that they provided me throughout my dissertation. Their support was critical to my academic and professional success and helped me during hard times. I am also thankful to many other mentors who were not on my dissertation committee, but provided me with critical mentorship and guidance throughout my PhD. I am thankful to the many places where I was able to conduct academic research while at the University of Washington, including the International Clinical Research Center, the Harm Reduction Technical Assistance Center, and the Center for Community-Engaged Drug Education, Epidemiology and Research. I am thankful to the HERU team at SFU who provided intellectual support and is my future home for my postdoc. I am thankful to my amazing peers and cohort at the University of Washington who I could not have completed this dissertation and journey without. Lastly, I am thankful to my friends and family who have provided me with every kind of support throughout my PhD and my life. To everyone who has helped me on this journey and in my life, I am eternally grateful and thank you for your support. I have purposely not named people in this acknowledgment section, but if IYKYK.

DEDICATION

To Dave you were and would have been so proud.

LIST OF TABLES

Table 2.1. Information on the two surveys from, which the analytical samples for population size estimation are derived from	24
Table 2.2. The demographics characteristics of the NHBS-PWID-2022 sample that was collected from June 2022-December 2022 and the UW-PWID-2023 sample that was collected from May 2023-August 2023	30
Supplemental table 2.1. Population size estimates for the different methods displayed with data sources. Presented are the population median as well as the 95% confidence intervals constructed using the bootstrap approach from the empirical distribution	42
Table 3.1. Demographics of the injecting and smoking samples. Data collected May 2023 to August 2023 for the injecting sample and from August 2023 to September 2023 for the smoking sample, Seattle Washington	54
Table 3.2. Drug use behavior and treatment history table injecting and smoking samples. Data collected May 2023 to August 2023 for the injecting sample and from August 2023 to September 2023 for the smoking sample, Seattle Washington	55
Table 3.3 Distribution of demographic factors stratified by top model of interest for first choice. University of Washington respondent driven sample, 2023 (N = 375)	61
Supplemental Table 3.1. Ranking of the different safe supply models. Data collected from May 2023 to September 2023 in Seattle, Washington	74
Supplemental Table 3.2. Ranking of the different models of regulated opioids and expanded treatment. Data collected from May 2023 to September 2023 in Seattle, Washington	75
Table 4.1. Model processes and parameter for the microsimulation model simulation overdose risk in a virtual population	82

Table 4.2. Overall statistics comparing different scenarios for the microsimulation model of overdose deaths. 95% uncertainty intervals are reported based off the 2.5% 97.5% percentiles from 1000 bootstrap replicates of the model	86
--	-----------

LIST OF FIGURES

Figure 2.1. Anchored multiplier and other population size estimate. Blue squares show the mean prevalence estimate for each estimate and the grey bands show the 95% confidence intervals. Along the left side of the graph are identifiers for the different population size estimation methods	31
Figure 3.1. Interest in expanded MOUD treatment and safe supply models with whether accessing the program was anticipated to change their likelihood of overdose compared to their current opioid supply	58
Figure 3.2. Proportions of responses to Likert questions on crime (n for those who reported engaging in illegal activity), frequency of use (n is everyone interested in safe supply), likelihood of starting MOUD treatment (n is for everyone interested in safe supply and not on MOUD), and staying on MOUD treatment (n is for everyone interested in safe supply and on MOUD). Data collected from May 2023 to September 2023 in Seattle, Washington	60
Supplemental figure 3.1. Histogram of age for the participants in the injecting and smoking sample. Data collected from May 2023 to September 2023 in Seattle, Washington	74
Figure 4.1. Pathways for agent transition across dynamic states in the model, status quo is base case	81
Figure 4.2. The mean overdose deaths for the different scenarios for the main analysis over 15 simulated years for 1000 bootstrap replicates. The line represents the median and the predictive intervals represent the 95%th percentile of simulations	87
Figure 4.3. The impact of different levels of access on the population level impact on mean overdose death per time step of the different models	88

Figure 4.4. Threshold analysis of increasing the initiation rate of new people who inject drugs to reverse the effects of implementing safe supply89

CHAPTER 1. INTRODUCTION

The opioid crisis in Seattle has reached a historic number of deaths as fentanyl has become a main component of the unregulated opioid supply. As opioid overdose fatalities continue to increase year on year in Seattle, urgent interventions are needed to lower the number of people dying of opioid-related overdoses. Among the array of potential strategies, the concept of safe supply has emerged as a possible avenue for mitigating harm and saving lives. Safe supply was first coined by the Canadian Association of People Who use Drugs. Since the formalization of safe supply, several jurisdictions in Canada have implemented medicalized versions of safe supply that have been successful in reducing overdose death. The United States could potentially benefit from implementing a similar strategy to reduce the risk of opioid overdose. However, the successful implementation of safe supply initiatives hinges upon robust evidence substantiating its feasibility and efficacy. Importantly, we need to understand the level of interest among individuals who use opioids and gauge their perceptions regarding the potential effectiveness of safe supply interventions. Without such evidence, the first step in establishing viability and impact of safe supply programs remain uncertain, underscoring the necessity for research to inform whether safe supply programs are worth pursuing. To implement safe supply successfully several pieces of information would be helpful including, the size of the potential target population, interest in the intervention among those who the program would be offered to, and the modelled impact of a theoretical program.

There is a need to understand the population size of people who inject drugs in Seattle. This dissertation aimed to use multiple different methods to estimate the prevalence of PWID in Seattle Washington. I also used a synthesis method to have a single estimate that can be used for

public health planning. Population size estimation is an important step in understanding the number of people who could benefit from safe supply policies.

It is important to understand the interest of people who would access safe supply and their interest and what they think the benefit from accessing safe supply would be. Interest in safe supply is important as we need to know if people in Seattle would want safe supply programs if they were offered. Previously published work has found interest in safe supply among people who inject opioids, but the previous study did not have granular data on acceptability of interest for the different models of safe supply under consideration. Moreover, we expand on previous work by also sampling people who primarily smoke opioids and do not inject.

Modelling the potential impact of safe supply programs among people who would access them is a vital policy piece that is needed if safe supply interventions are to be implemented in Seattle. Microsimulation modelling can be used to understand the potential population impact of different interventions. Microsimulation modelling allowed us to evaluate different scenarios of safe supply and compare them to a baseline status quo scenario. The modelling allowed us to explore alternative scenarios with changing the level of access as well as scenarios where there is a large increase in the number of people initiating injection drug use.

This dissertation aimed to fill gaps in knowledge around potential interest and impact around regulated opioids in Seattle, Washington. The hope is that pieces of this dissertation will be used for public health planning. Data were collected for this dissertation from June 2022 to December

2022 and May 2023 to September 2023 which helped inform the results from chapters 2, 3, and 4.

CHAPTER 2. ESTIMATING THE NUMBER OF PEOPLE WHO INJECT DRUGS IN SEATTLE, WASHINGTON WITH MULTIPLE APPROACHES.

Authors: Adam Palayew^{1,2}, Samyukta Singh^{2,3}, Courtney Moreno⁴, Paul Wesson⁵, Tyler H. McCormick^{6,7}, Steven M. Goodreau^{1,8}, Stephen J. Mooney¹, Caleb J. Banta-Green^{1,2,3*}, Sara N. Glick^{1,4,9*}

*Co-senior author

Affiliations:

1. Department of Epidemiology, University of Washington, Seattle, WA, USA.
2. Addictions, Drug & Alcohol Institute, Seattle, WA, USA.
3. Department of Health Systems and Population Health, University of Washington, Seattle, WA, USA.
4. Public Health – Seattle & King County, Seattle, WA, USA.
5. Department of Epidemiology and Biostatistics, School of Medicine, University of California, San Francisco, CA, USA.
6. Department of Statistics, University of Washington, Seattle, WA, USA.
7. Department of Sociology, University of Washington, Seattle, WA, USA.
8. Department of Anthropology, University of Washington, Seattle, WA, USA.
9. Department of Medicine, University of Washington, Seattle, WA, USA.

Abstract:

Background: For planning of public health services, decision makers benefit from knowing the prevalence of people who inject drugs (PWID). Seattle is a city where injection drug use has historically been prevalent; however, local surveys and information from stakeholders have pointed to a potential decrease in the prevalence of PWID. We aim to estimate the prevalence of PWID in Seattle using several methods and data sources.

Methods: Our estimates were derived from two samples of PWID. The first was the National HIV Behavioral Surveillance PWID 2022 (NHBS-PWID-2022) survey, collected from June 2022 to December 2022. The second sample was a University of Washington PWID 2023 (UW-PWID-2023) survey, collected from May 2023 to August 2023. Both samples had similar sampling and inclusion criteria. In total we calculated five direct and two indirect estimates of the prevalence of PWID. We used a capture-recapture (CRC) to generate an estimate with data from both samples and a network scale-up method (NSUM) to generate estimates from each sample. We used a service multiplier method with information from two local services and the NHBS-PWID-2022 sample to generate two unique estimates. We applied the anchored multiplier, a synthesis approach, to combine the direct estimates.

Results: The NHBS-PWID-2022 surveyed 362 individuals and the UW-PWID-2023 had 351 individuals. The CRC estimated a PWID prevalence of 0.66% (95% confidence interval [CI]: 0.52, 0.87). The NHBS-PWID-2022 NSUM estimated a PWID prevalence of 0.49% (95% CI: 0.32, 0.67), while the UW-PWID-2023 NSUM estimated a PWID prevalence of 0.88% (95% CI: 0.56, 1.31). The service multiplier approach produced estimates of 0.026% (95% CI: 0.022,

0.031) for one service and 0.16% (95% CI: 0.13, 0.21) for the other service. The anchored multiplier estimated a PWID prevalence of 0.33% (95%CI: 0.27, 0.39), the variance-adjusted anchored multiplier estimated a PWID prevalence of 0.68% (95% CI:0.51,0.88). These PWID prevalence estimates are all smaller than the 2019 national estimate of 1.5% and although not directly comparable geographically it is lower than the 2014 King County estimate of 1.1%.

Conclusion: Our findings suggest a decrease in the prevalence of PWID in Seattle and King County relative to estimates from a decade ago. The three direct estimates from CRC and NSUM methods were all similar, while the two service multiplier estimates were much lower than the three other direct estimates. Reasons for the apparent decrease in the number of PWID in Seattle should be investigated in future research.

Introduction:

People who inject drugs (PWID) have higher comorbidities and mortality compared to people who use drugs who do not inject and the general population (1). Public health efforts targeted at improving the health of PWID include activities like HIV testing, syringe access, and naloxone distribution, have been shown to decrease morbidity and mortality among PWID (2). Knowing how many PWID are in a population allows decision makers to offer public health and social services at adequate levels.

Seattle, Washington has never had a dedicated estimate for the number of PWID. The most approximate measure is a 2014 estimate from the local health department and is of the number of PWID in King County, Seattle's county. The 2014 estimate was based on national estimates at the time (3) as well as information from a local CDC-funded survey (4). The 2014 estimate was 23,000 PWID in King County, representing a 1.1% population prevalence of PWID in King County (5). However, local surveys as well as information from service providers who serve PWID suggest that the number of PWID has decreased (6,7). Additionally, data from other West Coast cities have indicated a decrease in the prevalence of PWID who have had similar shifts in their drug market since 2020 (8,9). Amidst all this uncertainty, an estimate of the number of PWID for Seattle is needed to help inform public health activity and organizing efforts.

Several techniques are used in public health to calculate population size estimates (PSE) to measure the size of specific populations. PSE can help facilitate the efficient allocation of public health resources by establishing a denominator for interventions and services (10). However, achieving accurate PSE for PWID demands significant energy, effort, and resources (11).

Researchers have applied several methods to estimate the size of populations of PWID, each differing in complexity, required effort, assumptions, and viability in different settings (12). Therefore if possible it is ideal to be able to compare PSE from different techniques to compare estimates to one another (13).

Amidst this array of techniques, the capture-recapture (CRC) method has emerged as a technique that is viewed favorably (14). The CRC is considered to be accurate when assumptions are met. However, CRC is generally considered to be resource intensive and is not a gold standard (15). CRC PSE can be estimated using data from two samples. The two-sample CRC PSE is based on the size of the samples and the number of people who are in both samples (16). The accuracy of the CRC PSE is reliant on how well four assumptions are met: 1) there is no change to the population during the investigation (closed population), 2) there is no loss of tags (individuals can be matched from capture to recapture), 3) for each sample, each individual has the same chance of being included in the sample, and 4) the samples are independent of each other (17). It is common for these assumptions to not be met in practice with different levels of impact of bias on the estimates depending on how well the assumptions are met (16).

Another method for PSE is the network scale up method (NSUM). The NSUM only requires one sample (18) and uses the average network size of individuals (i.e., how many people does a person know who are part of the population of interest?) for a target population to make inferences about the total size of the target population (19). The NSUM relies on two assumptions: that people are accurately reporting their network size (not over or under reporting), and that the network sizes of the people in the sample are representative of the

underlying network sizes in the target population. The second assumption is that the networks sampled are representative of the underlying networks of individuals in the target population. This is also known as non-random mixing i.e. inherent heterogeneity in reported network size among members of the target population (20).

The service multiplier method is a third approach for PSE and has been used for PWID previously. This method requires two data sources, an external reference service and an independent sample of the target population (15,21,22). The service multiplier estimator divides the number of people in the target population who attended the external reference service during a given period by the proportion of people in the independent sample who have attended the reference external service during the same period. The multiplier method requires two key assumptions 1) surveyed individuals are a representative sample of the target population and 2) inclusion in the survey is independent of accessing the external reference service (23).

Methods that triangulate several PSE can be useful to incorporate information from several sources. (24). The anchored multiplier is a method that uses a Bayesian model to synthesize multiple different PSE with prior information to create an estimate that borrows information from all available data and prior information (25). The anchored multiplier is not a direct PSE, but rather is a model that synthesizes multiple estimates into a single consensus estimate.

In this study we report seven estimates of the prevalence of the population of PWID in Seattle using four different methods: one CRC estimate, two NSUM estimates from different data sets,

two multiplier estimates from different external reference services, and two consensus estimates using the five previous estimates synthesized with the anchored multiplier method.

Methods:

Setting and data sources:

The study was conducted in Washington State in the Pacific Northwest region of the United States. Data for this study were obtained from two primary samples that were collected from distinct surveys (Table 1). Inclusion criteria for the UW-PWID-2023 was almost identical to the NHBS-PWID-2022 criteria except the UW-PWID-2023 differed geographically in scope and language surveyed.

Both samples were collected using respondent driven sampling (RDS). RDS is a peer referral-based data collection process where people who are members of the target population recruit each other into the sample (26). RDS requires starting individuals called “seeds” who are recruited in collaboration between the research team and different community services and organizations (27). For both surveys individuals needed to come to a fixed site. The fixed site for the NHBS-PWID-2022 was near Pioneer Square Seattle whereas the fixed site for the UW-PWID-2023 was close to the main UW campus (approximately 4 miles apart, but on opposite sides of the body of water that divides Seattle into North and South). Both surveys were incentivized in a similar structure. First, each participant received an incentive for completing the survey. Both surveys also provided coupons to participants who completed the survey. Participants were instructed to give the coupons to other members of the target population. Anyone who met the inclusion criteria and had a coupon could come to the fixed site with the

coupon and participate in the study. For each coupon linked to a completed survey, the original person who distributed the coupon received an incentive for recruiting another participant who completed an interview.

Table 1. Information on the two surveys from, which the analytical samples for population size estimation are derived from.

Survey Name	National HIV Behavioral Surveillance	University of Washington Survey
Abbreviation	NHBS-PWID-2022	UW-PWID-2023
Geographic reach	King and Snohomish County	City of Seattle
Eligibility Criteria	Any injection drug use in the last year, successfully described how to prepare and inject drugs to the satisfaction of the screener, were over the age of 18, could take the survey <i>in English or Spanish</i> , lived in <i>King or Snohomish County</i> , and had a valid study referral coupon.	Any injection drug use in the last year, successfully described how to prepare and inject drugs to the satisfaction of the screener, were over the age of 18, could take the survey <i>in English</i> , lived in <i>Seattle</i> , and had a valid study referral coupon.
Data Collection	June 2022 to December 2022	May 2023 August 2023
Incentive	\$50 Visa gift card (initial survey) \$20 Visa gift card (for each referral)	\$20 cash (initial survey) \$10 cash (for each referral)
Survey content	Demographics, risk behaviors, testing history, and access to preventive services among populations at increased risk of acquiring HIV.	Demographics, risk behaviors, network characteristics of PWID in Seattle, interest in drug user services.
Questions that were used for population size estimates	Network question (NSUM PWID 2022). Additional survey question (Multiplier method community-organization). Additional survey question (Multiplier method municipal sexual health clinic).	Participation in NHBS-PWID-2022 (CRC). Network question (NSUM PWID 2023).

Demographics questions and network size questions were identical between the two surveys. The UW-PWID-2023 survey had an additional question about whether someone participated in the NHBS-PWID-2022 survey. Zip code for individuals experiencing homelessness was based on a

response to a question about what zip code did the participant spend the most time in. The NHBS-PWID-2022 survey also included two unique local questions about whether 1) someone had utilized case management at a local community-based organization that focuses on case management in the last year, and 2) whether someone had utilized a specific municipal sexual health clinic in the last year. Responses to each of these questions were used for PSE.

Data analysis:

Descriptive analysis:

Our descriptive analysis explored the demographics of the two samples including age, gender, race, housing in the last year, current housing status, and employment status. We examined differences between the NHBS-PWID-2022 and UW-PWID-2023 samples demographic variables using a chi-squared test for categorical variables (gender, race, housing in the last year, current housing status, and employment status), and a t-test for continuous variables (age). For the CRC the NHBS-PWID-2022 sample was limited to people who lived in Seattle according to whether their reported zip code fell within the City of Seattle. For the NSUM and the two multiplier methods the NHBS-PWID-2022 sample included everyone in King County.

Population size estimation methods:

Capture recapture (CRC):

The CRC method used both samples. Individuals in the UW-PWID-2023 sample were asked if they participated in the NHBS-PWID-2022 sample. The overlap between the two samples was analyzed to derive the CRC PSE. We used the Lincoln-Pearson estimator (equation 1) to calculate the point estimate and used a bootstrap approach to generate the 95% confidence

intervals from the empirical distribution (15). In the estimator, the estimated population size (n_t) is the product of the two samples (n_1 and n_2), which is divided by the number of people who are in both samples (n_{1and2}).

$$n_t = (n_1 * n_2) / (n_{1and2})$$

Equation 1: Lincoln-Pearson estimator

Network scale-up method:

The NSUM is a PSE method that leverages information on the reported size of a respondent's network. In the NHBS-PWID-2022 survey we determined the reported network size by asking participants how many people in *King County* they knew who injected and who they had seen in the past 30 days whereas in the UW-PWID-2023 survey we asked how many people in *Seattle* they knew who injected and who they had seen in the past 30 days. The distinction here is important as the NHBS-PWID-2022 NSUM PSE is estimated using the population size of King County whereas the UW-PWID-2023 NSUM PSE is estimated using the population size of the city of Seattle. We used the Killworth et al. (28) NSUM estimator (equation 2), wherein n_t is the size of the target population, N is the size of the total population and x_i is the reported network size of individual I . (29). The estimator was calculated using the total population of Seattle in 2022 as the numerator for all estimates except for the NHBS-PWID-2022 NSUM, which used the total population of King County in 2022. We estimated the 95% confidence intervals from the empirical distribution using a bootstrap approach.

$$n_t = \frac{N}{\left(\frac{1}{n}\right) \sum_1^n x_i}$$

Equation 2: NSUM estimator

Multiplier method:

The service multiplier is a PSE that is recommended as a tool by the CDC for NHBS sites to use to estimate their local population size of PWID (30). The Seattle NHBS site attempted to do this with the NHBS-PWID-2022. As previously mentioned, NHBS-PWID-2022 included local questions about whether people utilized case management services at a community-based organization, and whether people attended a specific municipal sexual health clinic during the previous calendar year. In collaboration with those organizations, NHBS staff at Public Health – Seattle & King County also identified the number of PWID who attended those services during the previous calendar year. The service multiplier estimator for the number of PWID (n_t) is equal to the total number of PWID attending a reference service in the last year (M) divided by the proportion of people in the sample who attended that reference service in the last year (p) (21,23,31).

$$n_t = \frac{M}{p}$$

Equation 3: Multiplier method estimator

Anchored multiplier:

The anchored multiplier combines multiple PSE to generate a single consensus estimate. The five PSE integrated into our anchored multiplier estimate were: the CRC estimate (using both NHBS-PWID-2022 and UW-PWID-2023), the NSUM using NHBS-PWID-2022, the NSUM using UW-PWID-2023, and the two service multipliers using NHBS-PWID-2022. The anchored multiplier combined these individual PSE to yield a weighted population size estimate, with each PSE contributing based on the width of the confidence intervals. An online anchored multiplier tool that was published by Wesson et al. (32) was used to estimate the point estimate and 95% confidence intervals for the anchored multiplier approach. The anchored multiplier was estimated using the online anchored multiplier tool (<http://anchoredmultiplier.ucsf.edu/>). The prior for the anchored multiplier was taken from the national estimates from Bradley et al. 2022 (33). We used the point prevalence estimate 1.46% with a lower bound of 0.74% and an upper bound of 2.87%. The online tool calculates a variance and non-variance adjusted estimate.

Calculation of prevalences:

The PWID prevalence estimate for all estimates were calculated by dividing the estimate from the above approach by the corresponding reference population. The population for the city of Seattle for 2022 was the denominator for the CRC, NSUM UW-PWID-2023, the service multipliers, and the anchored multiplier estimates. The prevalence for the NSUM NHBS-PWID-2022 was calculated by dividing by the adult population of King County for 2022.

Graphing of the estimates:

We graphed the point estimates and estimates of uncertainty for all the PSE. For comparison purposes, we added lines indicating the 2014 King County PWID population size estimate (5), as well as the point estimate for the national estimate that was used as a prior (33).

Analyses were conducted and graphics were made using R (Version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria) (34) and the online anchored multiplier tool (<http://anchoredmultiplier.ucsf.edu/>). Data cleaning for the NHBS sample was done in SAS [VERSION 9.4] (35). The Seattle area NHBS-PWID survey was determined by the Washington State IRB to be a surveillance project and does not require ongoing IRB review. The secondary analysis of NHBS data for this study was deemed to be exempt from human subjects' ethics review by the division of human subjects' research at the University of Washington (STUDY00017706). The data collection and data analysis related to the UW-PWID-2023 study was determined exempt from human subjects' review (STUDY00017705).

Results:

The NHBS-PWID-2022 sample had 500 individuals of whom 362 met the eligibility criteria for this analysis based on zip code inclusion. The UW-PWID-2023 sample had 351 individuals. Table 1 shows the demographics of the two samples. The NHBS-PWID-2022 sample was older than the UW-PWID-2023 sample. Additionally, the UW-PWID-2023 sample had more male participants, 73% compared to 62% in the NHBS-PWID-2022 sample. The race demographics were similar between the two samples (Table 2). There were more people who had experienced homelessness in the last year and who were currently homeless in the UW-NHBS-2023 compared to the NHBS-PWID-2022.

Table 2. The demographics characteristics of the NHBS-PWID-2022 sample that was collected from June 2022-December 2022 and the UW-PWID-2023 sample that was collected from May 2023-August 2023.

	NHBS-2022	UW-2023	p-values
N	362	351	-
Age (median (IQR))	46 (38-56)	39 (25-53)	<0.001
Gender			<0.001
Male	221 (62%)	254 (73%)	
Female	138 (37%)	82 (23%)	
Trans or Other	-	14 (4%)	
Race*			0.21
American Indian/Alaska Native	62 (15%)	62 (15%)	
Asian	8 (2%)	9 (2%)	
Black	90 (21%)	67 (16%)	
Native Hawaiian or other Pacific Islander	21 (5%)	11 (3%)	
White	244 (57%)	250 (60%)	
Other	-	20 (5%)	
Housing last year			<0.001
Unhoused at some point	220 (61%)	302 (86%)	
Housed	142 (39%)	49 (14%)	
Currently Homeless			<0.001
Yes	158 (44%)	234 (67%)	
No	204 (56%)	114 (33%)	
Employment			0.51
Employed	23 (7%)	29 (8%)	
Unemployed	319 (93%)	319 (92%)	

*Individuals could select more than one race

Figure 1 shows estimated population size of PWID in the city of Seattle. The CRC estimated a prevalence of 0.66% (95%CI: 0.52,0.87), UW-PWID-2023 NSUM estimated a prevalence of 0.88 (95%CI: 0.56,1.31), the NHBS-PWID-2022 NSUM estimated a prevalence of 0.49% (95%CI: 0.32, 0.67). The estimated prevalence for the anchored multiplier was 0.33% (95%CI: 0.27, 0.39). The variance adjusted anchored multiplier estimated a prevalence of 0.68% (95%CI: 0.51, 0.88). The national estimate from Bradley et al 2022 of, a prevalence of injection drug use of 1.5%, is represented with a dashed line. The 2014 Public Health – Seattle & King County

estimate for the prevalence of PWID for King County (1.1%) is represented by another dashed line.

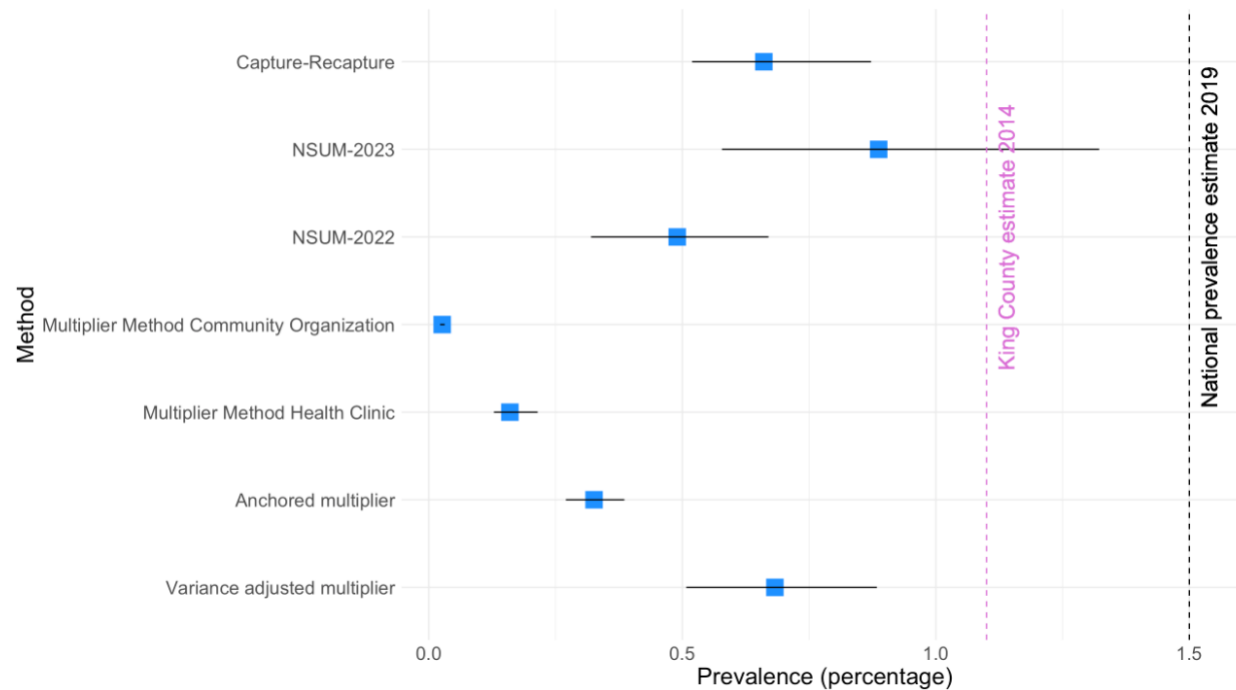


Figure 1. Anchored multiplier and other population size estimate. Blue squares show the mean prevalence estimate for each estimate and the grey bands show the 95% confidence intervals. Along the left side of the graph are identifiers for the different population size estimation methods.

Supplemental Table 1 has population size estimates as derived by each of the methods and respective data sources.

Discussion:

Our study estimated a prevalence of 0.68% (95%CI: 0.51, 0.88) PWID in Seattle, Washington, approximately 5000 individuals. This is the first concerted effort of the prevalence of PWID for Seattle and the first multi-data source effort to estimate the prevalence of PWID in the region since 2014. The PSE for the NSUM and the capture-recapture were all in a similar range and would represent a large decrease in the number of PWID in Seattle and King County compared

to 2014 (5). The service multiplier method had much lower estimates, with one estimate not being plausible as the population estimated was smaller than the number of sampled individuals.

A recent PSE for PWID in the United States found a national prevalence of 1.5%, which is higher than the 0.68% in our study for Seattle (33). Several potential mechanisms could explain a decline in the number of PWID. The drug supply in Seattle has shifted dramatically since 2014. In 2014, the primary unregulated opioid was heroin, which has been displaced by fentanyl since 2019. With the introduction of fentanyl there has been data that people who use opioids have shifted from injecting to smoking (36,37). A study in San Francisco found that people shifted from injecting heroin to smoking fentanyl for a variety of reasons; these include moderating the risk of overdose in response to the shift in the drug supply from heroin to fentanyl and the comparative increased potency and decreased duration of the effects of fentanyl (9). Moreover, a cohort study in San Diego has documented a shift from injecting heroin to smoking fentanyl (8). The decline in PWID on the West Coast contrasts with other areas where the number of PWID have remained stable or increased, emphasizing the uniqueness of different drug markets such as the East Coast (38). The observed decline in the population of PWID could also be a function of the substantial and increasing overdose mortality rate over recent years (39). It should also be noted that the prevalence of the UW-PWID-2023 NSUM had a higher point prevalence than the NHBS-PWID-2022 NSUM indicating a potential increase in the number of PWID from 2022 to 2023. We should be careful comparing these two estimates as they are estimating the prevalence for different geographic areas. Additionally, with the large overlap in confidence interval and only two time points it is impossible to conclude that there is a trend.

Among all the direct PSE the CRC estimate was the most similar to the variance-adjusted estimate. However, we should comment that the CRC estimate of the number of PWID could be an underestimate if there was positive dependence between the two samples (participants in NHBS were more likely to also be in the UW RDS study). There is a possibility of list dependence due to overlap in the organizations from which seeds were recruited. This would mean the true number of PWID in Seattle is greater than estimated from the CRC method. We also could have underestimated the size of the number of PWID for the NSUM methods as NSUM is traditionally done with a random sample of the population and not RDS. The random sample for NSUM is important as the random sample helps meet the NSUM assumption that the network size of the people who are sampled are representative of the underlying population. In RDS people are selected into the sample based on their networks, and therefore people with larger network sizes are more likely to be in an RDS sample than they are to be in a random sample. Therefore, the NSUM assumption that the people in the sample have networks that represent the underlying population is likely to not be met in RDS due to the nature of study recruitment. The overestimation of network size for the group would result in a lower NSUM estimate. However, as mentioned previously since we believe that we have had sufficient waves of recruitment we can treat the RDS sample as an independent sample and thus the NSUM would not be biased.

For the multiplier method neither of the estimates were credible. This was particularly true with the case management sample since the estimated population size of PWID was smaller than the number of PWID who were surveyed for NHBS-PWID-2022 survey. The assumption of the multiplier method that participation in services and the survey are accurately captured was not

met. There were 24 people who the service reported injected drugs in the last year with 36 people in the NHBS-PWID-2022 survey saying they attend case management services at the community-based organization. There is measurement error either on the side of the community-based organization or the survey in either or both the number of clients who report drugs, or the number of participants who attended services. The CDC recommends the use of the service multiplier for NHBS sites to estimate the size of their local target populations (4). However, given the performance of the service multiplier in this study having other PSE would be beneficial to NHBS and the CDC. The NSUM is one option that could be explored as an additional PSE. The NSUM can be calculated using existing NHBS data and does not need an external service that reliably collects data on the target population and is willing to collaborate making it less resource intensive compared to the service multiplier. The anchored multiplier approach mitigates some of the concerns around biases in individual PSE by combining multiple PSEs, the anchored multiplier cannot eliminate the bias that is already inherent in each individual estimate, which all have some threat of bias as previously discussed. Therefore, the anchored multiplier could also be underestimating the number of PWID in the city of Seattle if the PSEs that are synthesized also systematically underestimate the population of PWID.

There are several limitations to this study. First, the two primary samples may not represent the entire population of PWID in Seattle, possibly omitting hidden or marginalized subgroups or subgroups that are less attracted to our studies, including PWID with high socioeconomic status and PWID who are marginalized and do not trust research, government, or academic institutions. The exclusion of high socioeconomic PWID is likely true as over 90% of people in both samples were unemployed. Second, both studies used RDS to collect data and therefore were more likely

to sample people with high network connectivity and people who were similar to the initial seeds. However, we believe that we met the RDS assumption that with enough waves of recruitment that the final sample is independent of the seeds. Third, the samples were collected one year apart, and we are assuming that there was no significant change in the population (in terms of individuals entering or exiting) during this period. This assumption presents a potential threat to the study design; however, we believe any significant decrease in the population likely occurred prior to the study period, around 2019-2020 and that the shift happened relatively quickly (within a year). This belief is based off local news reports as well as information from local surveys (37,40). Finally, there are issues in comparing our estimates to the 2014 King County estimates for several reasons: the estimates cover different geographical areas, they use different estimation methods for the population, and the 2014 estimate was never peer-reviewed.

Given the potential large decrease in PWID, it is important to continue to monitor and investigate factors contributing to the perceived decline in PWID and whether this is an ongoing trend or one that has stabilized. The reduction in the number of PWID in Seattle has profound implications for services as well as public health and harm reduction messaging. Ultimately, the findings underscore the importance of continuous monitoring and adaptable public health strategies.

References:

1. Bluthenthal Ricky N, Lorvick J, Kral Alex H, Erringer Elizabeth A, Kahn James G. Collateral damage in the war on drugs: HIV risk behaviors among injection drug users. *Int J Drug Policy*. 1999 Feb 1;10(1):25–38.
2. Crépault JF, Russell C, Watson TM, Strike C, Bonato S, Rehm J. What is a public health approach to substance use? A qualitative systematic review and thematic synthesis. *Int J Drug Policy*. 2023 Feb 1;112:103958.
3. Tempalski B, Pouget ER, Cleland CM, Brady JE, Cooper HLF, Hall HI, et al. Trends in the Population Prevalence of People Who Inject Drugs in US Metropolitan Areas 1992–2007. *PLOS ONE*. 2013 Jun 5;8(6):e64789.
4. CDC. Persons who inject drugs (NHBS-PWID) | Populations/Projects | NHBS | Surveillance Systems | Statistics Center | HIV | CDC [Internet]. 2022 [cited 2022 May 25]. Available from: <https://www.cdc.gov/hiv/statistics/systems/nhbs/populations-projects/pwid.html>
5. HIV/AIDS annual reports - King County [Internet]. [cited 2021 Jun 6]. Available from: <https://kingcounty.gov/depts/health/communicable-diseases/hiv-std/patients/epidemiology/annual-reports.aspx>
6. WA State Syringe Exchange Health Survey, 2019 Results [Internet]. The Alcohol & Drug Abuse Institute. [cited 2021 Feb 20]. Available from: <https://adai.uw.edu/wa-state-syringe-exchange-health-survey-2019-results/>
7. Reid MC, Oliphant-Wells T, Moreno C, Ketchum J, Fitzpatrick T, McMahan VM, et al. High levels of interest in access to free safer smoking equipment to reduce injection frequency among people who inject drugs in Seattle, Washington. *Drug Alcohol Depend Rep*. 2023 Jun 1;7:100163.

8. Eger WH, Abramovitz D, Bazzi AR, Bórquez A, Vera CF, Harvey-Vera A, et al. Changes in injecting versus smoking heroin, fentanyl, and methamphetamine among people who inject drugs in San Diego, California, 2020–2023. *Drug Alcohol Depend.* 2024 Jun 1;259:111318.
9. Kral AH, Lambdin BH, Browne EN, Wenger LD, Bluthenthal RN, Zibbell JE, et al. Transition from injecting opioids to smoking fentanyl in San Francisco, California. *Drug Alcohol Depend.* 2021 Oct 1;227:109003.
10. Viswasam N, Lyons CE, MacAllister J, Millett G, Sherwood J, Rao A, et al. The uptake of population size estimation studies for key populations in guiding HIV responses on the African continent. *PLOS ONE.* 2020 Feb 26;15(2):e0228634.
11. Purcell DW, Hall HI, Bernstein KL, Gift TL, McCray E, Mermin J. The Importance of Population Denominators for High-Impact Public Health for Marginalized Populations. *JMIR Public Health Surveill.* 2016 May 17;2(1):e5883.
12. Neal JJ, Prybylski D, Sanchez T, Hladik W. Population Size Estimation Methods: Searching for the Holy Grail. *JMIR Public Health Surveill.* 2020 Dec 3;6(4):e25076.
13. Wesson P, Jewell NP, McFarland W, Glymour MM. Evaluating tools for capture-recapture model selection to estimate the size of hidden populations: it works in practice, but does it work in theory? *Ann Epidemiol.* 2023 Jan 1;77:24–30.
14. International Working Group for Disease Monitoring and Forecasting. Capture-Recapture and Multiple-Record Systems Estimation I: History and Theoretical Development. *Am J Epidemiol.* 1995 Nov 15;142(10):1047–58.

15. Hickman M, Taylor C, Chatterjee A, Degenhardt L, Frisher M, Hay G, et al. Estimating the prevalence of problematic drug use: A review of methods and their application. *Bull Narc.* 2002 Feb 5;54:15–32.
16. International Working Group for Disease Monitoring and Forecasting. Capture-Recapture and Multiple-Record Systems Estimation II: Applications in Human Diseases. *Am J Epidemiol.* 1995 Nov 15;142(10):1059–68.
17. International Working Group for Disease Monitoring and Forecasting. Capture-recapture and multiple-record systems estimation I: History and theoretical development. *International Working Group for Disease Monitoring and Forecasting. Am J Epidemiol.* 1995 Nov 15;142(10):1047–58.
18. Maltiel R, Raftery AE, McCormick TH, Baraff AJ. Estimating Population Size Using the Network Scale Up Method. *Ann Appl Stat.* 2015 Sep;9(3):1247–77.
19. McCormick TH. *The Oxford Handbook of Social Networks.* 2021 [cited 2022 May 25]. The Network Scale-Up Method. Available from: <https://www.oxfordhandbooks.com/view/10.1093/oxfordhb/9780190251765.001.0001/oxfordhb-9780190251765-e-14>
20. McCormick TH, Salganik MJ, Zheng T. How many people do you know?: Efficiently estimating personal network size. *J Am Stat Assoc.* 2010 Mar 1;105(489):59–70.
21. Jacka B, Larney S, Degenhardt L, Janjua N, Høj S, Kraiden M, et al. Prevalence of Injecting Drug Use and Coverage of Interventions to Prevent HIV and Hepatitis C Virus Infection Among People Who Inject Drugs in Canada. *Am J Public Health.* 2019 Nov 14;110(1):45–50.

22. Plettinckx E, Crawford FW, Antoine J, Gremeaux L, Van Baelen L. Estimates of people who injected drugs within the last 12 months in Belgium based on a capture-recapture and multiplier method. *Drug Alcohol Depend.* 2021 Feb 1;219:108436.
23. Abdul-Quader AS, Baughman AL, Hladik W. Estimating the size of key populations: current status and future possibilities. *Curr Opin HIV AIDS.* 2014 Mar;9(2):107–14.
24. Morrison CN, Rundle AG, Branas CC, Chihuri S, Mehranbod C, Li G. The unknown denominator problem in population studies of disease frequency. *Spat Spatio-Temporal Epidemiol.* 2020 Nov;35:100361.
25. Wesson PD, Mirzazadeh A, McFarland W. A Bayesian approach to synthesize estimates of the size of hidden populations: the Anchored Multiplier. *Int J Epidemiol.* 2018 Oct 1;47(5):1636–44.
26. Heckathorn DD. Respondent-Driven Sampling: A New Approach to the Study of Hidden Populations. *Soc Probl.* 1997;44(2):174–99.
27. Gile KJ, Handcock MS. Respondent-Driven Sampling: An Assessment of Current Methodology. *Sociol Methodol.* 2010 Aug;40(1):285–327.
28. Killworth PD, Johnsen EC, McCarty C, Shelley GA, Bernard HR. A social network approach to estimating seroprevalence in the United States. *Soc Netw.* 1998 Jan;20(1):23–50.
29. Feehan DM, Salganik MJ. Generalizing the Network Scale-Up Method: A New Estimator for the Size of Hidden Populations. *Sociol Methodol.* 2016 Aug;46(1):153–86.
30. Methods and Questionnaires [Internet]. 2023 [cited 2024 May 5]. Available from: <https://www.cdc.gov/hiv/statistics/systems/nhbs/methods-questionnaires.html>
31. Johnston LG, Prybylski D, Raymond HF, Mirzazadeh A, Manopaiboon C, McFarland W. Incorporating the service multiplier method in respondent-driven sampling surveys to estimate

the size of hidden and hard-to-reach populations: case studies from around the world. *Sex Transm Dis*. 2013 Apr;40(4):304–10.

32. Wesson PD, McFarland W, Qin CC, Mirzazadeh A. Software Application Profile: The Anchored Multiplier calculator—a Bayesian tool to synthesize population size estimates. *Int J Epidemiol*. 2019 Dec 1;48(6):1744–9.

33. Bradley H, Hall E, Asher A, Furukawa N, Jones CM, Shealey J, et al. Estimated number of people who inject drugs in the United States. *Clin Infect Dis*. 2022 Jul 6;ciac543.

34. R: A language and environment for statistical computing [Internet]. [cited 2021 Sep 26]. Available from:

https://scholar.google.com/citations?view_op=view_citation&hl=en&user=yvS1QUEAAAAJ&citation_for_view=yvS1QUEAAAAJ:t6usbXjVLHcC

35. SAS Viya – AI, Analytics and Data Management on a Cloud Native Platform [Internet]. [cited 2024 May 5]. Available from: https://www.sas.com/en_us/software/viya.html

36. Walters K. Twin crises forced harm reduction services to adapt [Internet]. 2023 [cited 2024 May 5]. Available from: <https://www.kuow.org/stories/from-needles-to-pipes-seattle-outreach-adapts-to-morphing-drug-crisis>

37. Results from the 2021 WA State Syringe Service Program Health Survey [Internet]. Addictions, Drug & Alcohol Institute. [cited 2024 May 5]. Available from: <https://adai.uw.edu/syringe-survey-2021/>

38. Shover CL, Falasinnu TO, Dwyer CL, Santos NB, Cunningham NJ, Freedman RB, et al. Steep increases in fentanyl-related mortality west of the Mississippi River: Recent evidence from county and state surveillance. *Drug Alcohol Depend*. 2020 Nov 1;216:108314.

39. Laced & Lethal | Step Up Against Fentanyl [Internet]. [cited 2021 Nov 3]. Available from: <https://www.lacedandlethal.com/>
40. Results from the 2023 WA State Syringe Services Program Health Survey [Internet]. Addictions, Drug & Alcohol Institute. [cited 2024 Jun 10]. Available from: <https://adai.uw.edu/syringe-survey-2023/>

Appendix:

Supplemental table 1. Population size estimates for the different methods displayed with data sources. Presented are the population median as well as the 95% confidence intervals constructed using the bootstrap approach from the empirical distribution.

Estimate name (sample used)	Population median	Lower 95%CI	Upper 95%CI
Capture Recapture (NHBS-2022; UW-2023)	4850	3811	6402
NSUM 2023 (UW-2023)	6512	4243	9704
NSUM 2022 (NHBS-2022)*	11253	7354	15312
Multiplier method case management at a community-based organization (NHBS-2022)	194	164	230
Multiplier method municipal sexual health clinic (NHBS-2023)	1188	943	1586
Anchored multiplier	2392	1984	2831
Anchored Multiplier – variance adjusted	5010	3727	6486

*Number arises from a different denominator estimate of people who inject drugs in King County not Seattle, given the geographic scope specified in the question to determine network size. Note: The main parameters for calculating the capture-recapture were the thirty-three people who were in both samples, the sample size of the NHBS-PWID-2022 sample (n=362), and the sample size of the UW-PWID-2023 sample (n=351). For the network scale up methods the mean value of the network size that is used in the estimator was 67 and 120 for the NHBS-PWID-2022 and UW-PWID-2023 samples, respectively. The main parameters for the community-based organization case management multiplier methods were 24 people who had accessed case management in the last year and 10.2% or 36 individuals who were in the sample who said they had case management at the community-based organization in the last year. The main parameters for the municipal sexual health clinic were 134 PWID who accessed the clinic and 10.3% percent of the sample who had accessed services at the municipal sexual health clinic in the last year.

CHAPTER 3. PREFERENCES AND ANTICIPATED BEHAVIOUR CHANGES FOR DIFFERENT MODELS OF SAFE SUPPLY AMONG PEOPLE WHO USE OPIOIDS IN SEATTLE, WASHINGTON

Authors: Adam Palayew^{1,2}, Samyukta Singh^{2,3}, Christina Harris^{2,4}, Raleigh Haavig², Saul Petersky^{2,4}, Mads Eggerding^{2,4}, Laura Wirkman⁵, TJ Gascho⁵, Malika Lamont^{6,7}, DeAunte Damper⁷, Joe Tinsley⁸, Trevor Evans⁸, Jeremy Hoog⁹, Peter Cleary¹⁰, Steven M. Goodreau^{1,11}, Stephen J. Mooney¹, Sara N. Glick^{1,8,12}, Caleb J. Banta-Green^{1,2,3}

Affiliations:

1. Department of Epidemiology, University of Washington, Seattle, Washington
2. Addictions, Drug & Alcohol Institute, Seattle, Department of Psychiatry, Behavioural Sciences, School of Medicine, Washington
3. Department of Health Systems and Population Health, University of Washington, Seattle, Washington
4. School of Social Work, University of Washington, Seattle, Washington
5. The People's Harm Reduction Alliance
6. Purpose Dignity and Action
7. VOCAL-Washington
8. Public Health - Seattle & King County, Seattle, Washington
9. Downtown Emergency Service Center, Seattle, Washington
10. LGBTQ+ Center, Seattle, Washington
11. Department of Anthropology, University of Washington

12. Department of Medicine, University of Washington

Abstract:

Background: Pragmatic solutions are needed to reduce opioid involved overdose deaths. A regulated supply of opioids is one proposed solution. We gauged the interest of people who use opioids in four different models of regulated opioid access and expanded versions of the long-standing treatment options of methadone and buprenorphine.

Methods: From May to September 2023, we interviewed people who injected or smoked opioids and lived in Seattle, Washington. We asked about interest in six different models of regulated access to opioids. Two of the models were treatment medication focused: expanded methadone and expanded buprenorphine, while four were presented as safe supply: prescribed supervised, prescribed unsupervised, community-based, and dispensary-based. We assessed participants' perceptions of potential personal impacts of different models of opioid access, including change in overdose risk and change in criminal activity.

Results: Respondents included 269 people who injected opioids in the last year and 106 people who smoked opioids but did not inject them in the last year ($n = 375$). Overall, 91% of people reported that they wanted some form of regulated opioid access, of whom 74% preferred a safe supply model as their first choice over an expanded medication treatment model. Interest varied across the six models with prescribed unsupervised being the most popular (83%) and expanded buprenorphine being the least popular (42%). Of those who expressed interest in any regulated opioids, 76% thought accessing a regulated supply would reduce their risk of overdose. Of respondents who self-reported engaging in illegal activity to support their drug use, more than

74% said accessing safe supply would reduce their engagement in criminal activity; this was also true for the expanded treatment models.

Conclusion: There is strong interest in and high expected benefit from access to regulated opioids among people who use opioids in Seattle. Such programs may benefit not only individuals accessing them but also the broader public.

Introduction:

Opioid overdose is a pressing public health emergency in the United States (US) (1). Historically, opioids such as heroin and oxycodone were the primary opioids involved in overdose deaths. As drug markets have shifted in recent years, unregulated fentanyl and its analogs are the most commonly identified primary opioid involved in overdose deaths (2). Use of unregulated fentanyl has become more common in much of the western US since 2020, causing an unprecedented increase in the number of fatal opioid overdoses on the West Coast (3,4).

Unregulated fentanyl causes more overdoses due to its increased potency compared to traditional recreational opioids like heroin and oxycodone (5). People who use drugs often do not know the amount of active ingredient in unregulated drugs. This lack of knowledge increases the risk of overdose when potent opioids like fentanyl are present in varying concentrations (6). The increase in opioid related overdose deaths underscores an urgent need to re-evaluate and develop innovative strategies to deal with the increasingly toxic and potent drug supply. One proposed solution is to increase access to medication for opioid use disorder (MOUD) such as methadone and buprenorphine (7). However, modelling has shown that even though access to MOUD is important, a MOUD-only strategy is insufficient and other strategies combined with MOUD are needed to further reduce overdose mortality (8).

One proposed solution that could work in tandem with expanded MOUD is implementing access to a regulated supply of opioids, known as “safe supply” (9). People who use drugs first proposed the concept of safe supply and defined safe supply as providing people who use drugs

access to a regulated and quality-assured source of the substances they would otherwise obtain through the illegal market (10). The fundamental objectives of safe supply are to minimize the harms associated with drug use and return autonomy to people who use drugs (11). Medicalized versions of safe supply in Canada, known as “safer supply” or “prescribed alternatives to the unregulated supply,” have been implemented in a few provinces including British Columbia (BC), Ontario, Quebec, and Nova Scotia (12). Robust population-based studies have been conducted independently for BC and Ontario using administrative health data (13,14). The results of both studies showed a large benefit for the individuals who were accessing the program in reducing all-cause mortality and opioid overdose-specific mortality. Additionally, in Vancouver, BC, an unsanctioned compassion club model that operated for over a year was found to be effective in reducing the occurrence of drug overdose among participants of the program (15).

In Seattle and Washington state, the conversation around safe supply has begun (16). In 2022 an advisory panel recommended the formation of a working group to study safe supply that was funded by the Washington state legislature for two years (17,18). Additionally, a previous study among people who inject opioids in King County found that there was a high interest in four different models of safe supply with those interested almost unanimously saying that safe supply would be less risky or the same amount of risk as their current supply (19). The current study builds on this previous work in four main ways. First, this study explores the interest of people who smoke opioids as well as people who inject opioid in contrast to the previous study, which only sampled PWID. Secondly, this study asks about six models of opioid regulation instead of four from the previous study. The six models included in this study are the four safe supply

models from the previous study as well as two expanded MOUD options. Third, the current study captures more detailed data about interest in each safe supply models compared to the previous study, which only asked about outcomes related to the participants most preferred model. Fourth, for all models we also explore additional outcomes that were not asked about in the previous study like expected impact on criminal activity and drug use related behaviour.

Methods:

Setting and recruitment process:

We conducted two surveys using respondent-driven sampling (RDS). We conducted two RDS surveys to ensure comprehensive representation of the two target populations 1) PWID in the last year (injecting sample) and 2) people who smoke opioids and had not injected in the last year (smoking sample). The initial RDS sample focused on people who had injected at least once in the last year (May 2023 to August 2023), while the subsequent RDS sample was dedicated to individuals who primarily smoked opioids and had not injected in the last 12 months (August 2023 to September 2023). Both samples were started by distributing seed coupons to local community organizations that serve people who use drugs. Individuals with referral coupons were instructed to come to a physical location in North Seattle near transit that served as the interview location. People who arrived at the physical location with a coupon and were interested and eligible could complete the interview on the premises. If eligible participants were verbally consented into the study and provided with study information. Once the interview was concluded, individuals were remunerated \$20 cash for their participation and were given study coupons to recruit other participants. People were remunerated \$10 cash for each distributed coupon that resulted in another participant's completed interview.

Study population:

Our two samples aimed to sample from mutually exclusive populations. The injection sample was restricted to people who were 18 or older, had injected drugs in the last 12 months, and lived in the city of Seattle. People could have injected any drug for non-prescribed reasons including non-pharmaceutical forms of opioids, methamphetamine, and cocaine and could have smoked any drugs. Answers to all eligibility questions needed to be satisfactory at the discretion of a trained interviewer for the participant to be eligible; people were asked when they last injected drugs, how they prepared their drugs, and how they injected their drugs. The smoking sample was also restricted to people who were 18 or older and who lived in the city of Seattle, but was limited to people who reported smoking opioids and not injecting drugs in the last 12 months. Participants in the injection sample were not eligible to participate in the smoking sample.

Survey instrument:

The survey consisted of questions about demographics, drug use, and interest in different models of drug regulation, and expanded methadone and buprenorphine. Demographics questions included age, gender, race, homelessness in the last year, current housing status, employment, and engagement in crime — defined to participants as “stealing or boosting goods to trade for drugs or sell for money to provide for their drug use”. In the injection sample drug use questions assessed how often drugs were used alone, drugs injected over the lifetime and in the last 12 months, drugs that have been injected in the lifetime that have been used in other ways in the last 12 months, lifetime and 12-month history of drug treatment, and current MOUD status. For the smoking sample drug use questions assessed how often drugs were used alone, drugs used over

the lifetime and last 12 months, mode of consumption of how drugs were consumed in the last 12 months, lifetime and 12-month history of drug treatment, and current MOUD status.

The study assessed interest in six models of regulated opioids, including two MOUD treatment medication models and four safe supply models.

The expanded MOUD treatment models were:

- 1) *Expanded methadone* described as, receiving methadone in a clinical setting where methadone could be started on the same day and you would get an adequate dose.
- 2) *Expanded buprenorphine* described as, receiving buprenorphine in a clinical setting where buprenorphine could be started on the same day and you would get an adequate dose.

The MOUD treatment models are inspired by efforts to make MOUD treatment more accessible in the US. The US has moved to liberalize methadone with new federal regulations (20).

However, these new regulations fall short of the demands of patients on methadone (21). The question is to explore interest in one version of methadone liberation that is clinic based. The expanded buprenorphine model is based off low-barrier buprenorphine models, which exist and have shown to increase access to care (22).

The safe supply models were described as:

- 1) *Prescribed supervised*, where your drug of choice is prescribed to you by a medical provider and must be consumed onsite.
- 2) *Prescribed unsupervised*, where your drug of choice is prescribed to you by a medical provider, and you can take the drugs home with you.
- 3) *Community-based model*, where you drugs can be accessed in a community-based setting and no prescription is required (e.g., a compassion club model).
- 4) *Dispensary-based model*, where drugs can be accessed at a storefront dispensary and no prescription is required

The safe supply models were based on Canadian work (10,23) and to mirror a previous survey in King County asking about these four safe supply models (19). Participants were asked about their interest in each model and how they anticipated it would impact their overdose risk, engagement in criminal activity, frequency of use, likelihood of either starting buprenorphine and methadone or continuing on these treatment medications. Participants were asked to rank the options that they expressed interest in. We asked participants to rank the safe supply models from most preferred to least preferred. Subsequently we asked participants to rank the safe supply models and expanded MOUD treatment options from most preferred to least preferred.

Data were recorded and managed using REDCap (24), a secure web-based application designed explicitly for the collection and management of research data. The full survey for the injection and smoking samples can be found in appendix 1.

Data analysis:

The data were analyzed descriptively, quantitatively, and visually and only included participants in the study population. We explored demographics of each sample and quantified interest in different models of opioid access. We visually compared proportions endorsing interest in models, using coloring to display responses to questions about expected changes in: risk of overdose, involvement in crime, frequency of use, and likelihood of starting or staying on MOUD treatment. We examined the distribution of choice rankings for both the safe supply models and the safe supply models plus the two expanded MOUD treatment options. We compared demographic variables stratified by the top choice of preferences of individuals. The variables examined were RDS sample, age, gender, race, homelessness in the last year, current housing status, employment status, engagement in criminal activity to provide for drug use, overdosed ever, use drugs alone, and currently on MOUD. Overall model preference was determined by aggregating points assigned to each model based on participant rankings. When participants selected "not interested" for a model, that model received zero points in the total calculation. For models that participants preferred, points were assigned incrementally. For example, the least preferred model received one point, while the most preferred model received points equal to the total number of ranks minus one. The total points for each model were then summed across all participants to establish the overall ranking.

All analyses were conducted in R version 4.3.1 (25). This study was deemed to be exempt from human subjects review by the University of Washington (STUDY00017705).

Results:

Demographics and drug use behavior:

The demographics for the injection sample, the smoking sample, and pooled samples are presented in Table 1. The median and interquartile range of age in both samples were similar; however, the histogram of ages for the injecting sample showed a skewed sample with an older population where the smoking sample ages showed a bimodal shape with a group of younger individuals and another group of older individuals (supplemental figure 1). In the pooled sample 72% were male, 24% female, and 4% reported trans or other gender. White was the most common race in both samples. The injecting sample had a lower proportion of people who identified as American Indian or Alaska Native than the smoking sample. In the injecting and smoking samples there were a similar proportion of people who had experienced homelessness in the last year. Few participants were employed in either sample. Most of the individuals in both samples (65%, overall) reported engaging in theft related activities to provide for their drug use. Moreover, overall people (87%) reported using alone at least some time with 10% using alone all the time and 36% using alone most of the time.

Table 1. Demographics of the injecting and smoking samples. Data collected May 2023 to August 2023 for the injecting sample and from August 2023 to September 2023 for the smoking sample, Seattle Washington. *

	Injecting sample	Smoking sample	Pooled sample
Collection dates	May 2023-August 2023	August 2023-September 2023	
N	269	106	375
Age (median (IQR))	39 (25-53)	37(22-52)	38 (24-52)
Gender			
Male	192 (71%)	79 (75%)	271 (72%)
Female	68 (25%)	20 (19%)	88 (24%)
Trans/Other	9 (3%)	6 (5%)	15 (4%)
Race**			
American Indian/Alaska Native	38 (12%)	27 (21%)	65 (15%)
Asian	6 (2%)	4 (3%)	10 (2%)
Black	48 (15%)	21 (16%)	69 (15%)
Native Hawaiian or other Pacific Islander	8 (3%)	8 (6%)	16 (4%)
White	206 (65%)	61 (47%)	267 (59%)
Other	13 (4%)	9 (7%)	22 (5%)
Unhoused in the last year			

Yes	231 (86%)	96 (91%)	327 (87%)
Currently Homeless			
Yes	179 (67%)	83 (78%)	262 (70%)
Employed			
Yes	24 (9%)	11 (11%)	35 (9%)
Theft activities for drug use			
Yes	179 (70%)	54 (53%)	233 (65%)
Using alone			
Never	37 (14%)	10 (10%)	47 (13%)
Some of the time	110 (41%)	44 (42%)	154 (41%)
Most of the time	96 (36%)	37 (35%)	133 (36%)
Always	24 (9%)	14 (13%)	38 (10%)

*Don't know and missing are excluded from the table and denominators

**Participants could report multiple races.

Participants reported a broad range of drug use and treatment histories (Table 2). In the last 12 months, 83% of the injecting sample had injected methamphetamine, 83% heroin, 59% fentanyl powder, and 52% goofballs (heroin and methamphetamine combined). Most of the injecting sample had tried detox, outpatient, inpatient, 1:1 counselling, 12-step support groups, methadone, and buprenorphine at least once in their lifetime. Only 10% of the sample reported never trying any modality of treatment/support groups in their lifetime. People in the smoking sample had a similar profile of treatment history except the proportion of people who had tried methadone was much lower (27% in the smoking sample vs. 55% in the injecting sample). This was also reflected in treatment in the last 12 months where methadone was less likely to be reported among the smoking sample than the injecting sample. Moreover, 14% of people in the injecting sample reported being currently on methadone compared to 5% of the smoking sample.

Table 2. Drug use behavior and treatment history table of injecting and smoking samples. Data collected May 2023 to August 2023 for the injecting sample and from August 2023 to September 2023 for the smoking sample, Seattle Washington*

	Injecting sample (n = 269)	Smoking sample (n = 106)
Drug injected/used last 12 months		
Fentanyl blue pill	74 (28%)	96 (91%)
Fentanyl powder	158 (59%)	84 (79%)
Heroin	224 (83%)	49 (46%)

Prescription-type opioids	53 (20%)	36 (34%)
Powdered cocaine	86 (32%)	45 (42%)
Crack cocaine	49 (18%)	43 (41%)
Methamphetamine	222 (83%)	98 (92%)
Goofball (fentanyl + meth)	91 (34%)	26 (25%)
Goofball (heroin + meth)	139 (52%)	17 (16%)
Speedball (fentanyl + cocaine)	34 (13%)	17 (16%)
Speedball (heroin + cocaine)	67 (25%)	11 (10%)
Treatment/Support group ever		
Detox	150 (56%)	51 (48%)
Outpatient	158 (59%)	66 (62%)
Inpatient	170 (63%)	60 (57%)
1:1 Counselling	143 (53%)	52 (49%)
12-step support group	150 (56%)	50 (47%)
Group Counselling	117 (43%)	44 (42%)
Methadone	148 (55%)	29 (27%)
Buprenorphine	148 (55%)	48 (45%)
Long acting-naltrexone	21 (8%)	4 (4%)
Other	10 (4%)	1 (1%)
Never	27 (10%)	16 (15%)
Treatment/Support group last 12 months		
Detox	27 (10%)	14 (13%)
Outpatient	19 (7%)	8 (8%)
Inpatient	19 (7%)	11 (10%)
1:1 Counselling	39 (14%)	11 (10%)
12-step support group	13 (5%)	8 (8%)
Group Counselling	18 (7%)	10 (9%)
Methadone	83 (31%)	14 (13%)
Buprenorphine	62 (23%)	24 (23%)
Long acting-naltrexone	5 (2%)	1 (1%)
Other	3 (1%)	0 (0%)
No in the last 12 months	115 (43%)	64 (60%)
Currently on MOUD		
Methadone	46 (14%)	5 (5%)
Buprenorphine	15 (5%)	7 (7%)
Long acting-naltrexone	0 (0%)	0 (0%)
None	263 (81%)	93 (87%)

*For the injecting sample, drugs injected in the last 12 months is presented and defined as if the respondent reported injecting that drug in the last 12 months. For the smoking sample, drugs used in the last 12 months is presented and defined as if the respondent reported using that drug in the last 12 months. Drugs used in the last 12 months was not collected for the injecting sample due to an error in survey design.

Safe supply interests and anticipated behaviors:

Overall, both people who injected opioids and those who smoked opioids displayed interest in safe supply interventions and less interest in expanded MOUD treatment models. Among PWID, interest ranged from 39% to 80%, with the highest interest observed in the prescribed unsupervised (80%) model and the dispensary framework (77%). PWID had the lowest interest in expanded buprenorphine at 39%. Among people who smoked opioids, interest ranged from 44% (expanded buprenorphine) to 87%, with the highest interest observed in the dispensary-based model (87%) and prescribed unsupervised (83%) (Figure 1).

Among PWID interested in safe supply models, most anticipated a decrease (a lot or a little) in overdose risk compared to their current supply. The expanded buprenorphine had the highest proportion of individuals (85%) who thought if accessing expanded buprenorphine their risk of overdose would be lower compared to their current supply, followed by: expanded methadone (82%), prescribed supervised (82%), prescribed unsupervised (71%), community-based model (75%), and dispensary-based model (71%). Individuals in the smoking sample interested in safe supply models and expanded MOUD treatment also expected similar changes in overdose risk as the injecting sample: expanded methadone (81%), expanded buprenorphine (81%), prescribed supervised (73%), prescribed unsupervised (59% less risk), community-based model (65%), and dispensary-based model (58%). A portion of participants in both samples anticipated either no change or a slight increase in risk, but were less than the portion of people that reported less risk.

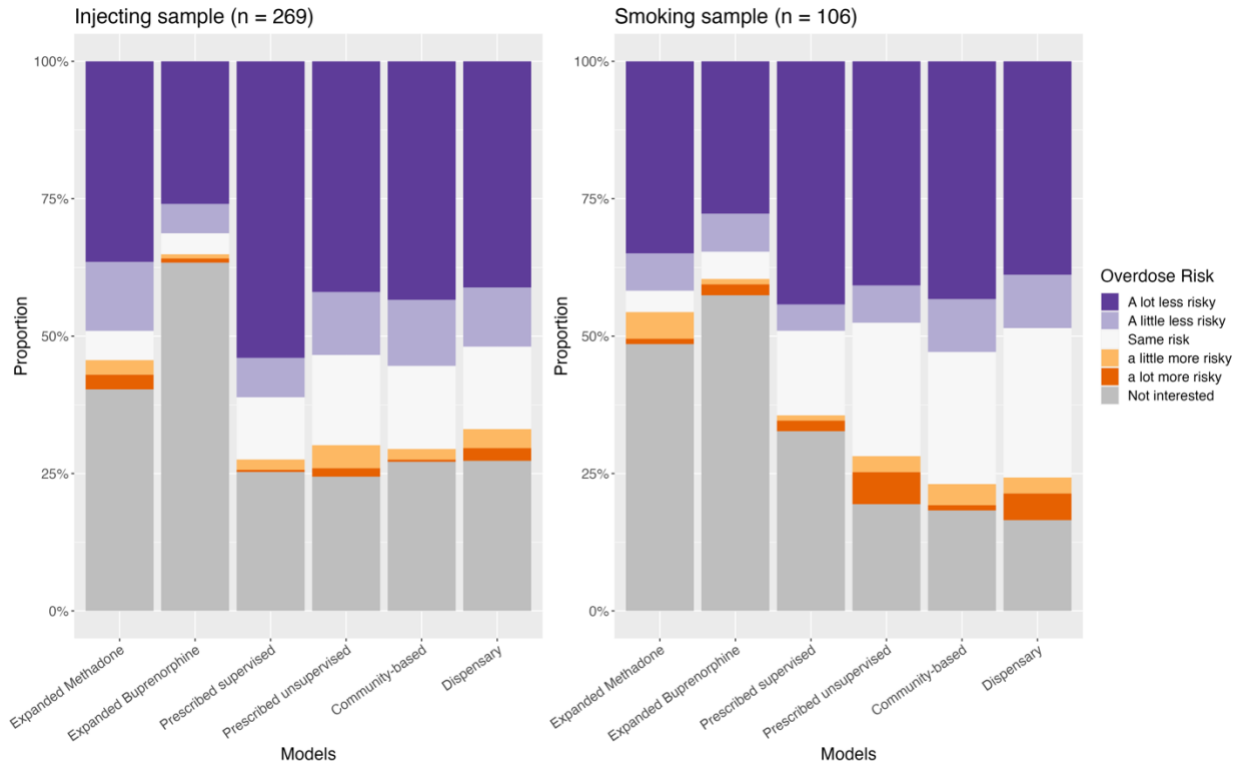


Figure 1. Interest in expanded MOUD treatment and safe supply models with whether accessing the program was anticipated to change their likelihood of overdose compared to their current opioid supply.

Ancillary outcomes around criminal activity, drug use, and MOUD treatment effects

The majority of participants who reported engaging in criminal activity to provide for their drug use in both samples expressed they would decrease (a lot or a little) criminal activity if they were to access any of the interventions. The proportion of PWID who were interested in various models and anticipated reductions in criminal behavior ranged from 73% to 90%. Most participants expected they would engage in less criminal activity, with the prescribed unsupervised model having the highest proportion of respondents indicating less criminal activity. Similarly, among the smoking sample, a majority expected reductions in criminal activity across all safe supply models, with the proportion of respondents expecting a reduction in their criminal activity ranging from 73% to 87% of the sample (Figure 2).

For all models, the proportion of participants that expected a decrease in drug use with safe supply interventions was much greater than the proportion of participants who expected it would increase their use. People interested in expanded methadone and buprenorphine had the highest proportion of responses indicating that accessing those models would reduce their use, with 86% of PWID and 81% people who smoke opioids reporting they would use less frequently.. The safe supply scenarios ranged from 35% to 49% of respondents reporting they would reduce their frequency of use. The majority of people not on MOUD in both samples expressed no change in their likelihood of starting MOUD across all models of safe supply. More participants not on MOUD who wanted safe supply reported they thought accessing safe supply would make them more likely to start MOUD than the proportion of people who said accessing safe supply would make them less likely to start MOUD. For participants already on MOUD most people said accessing safe supply would have no impact on them staying on MOUD (Figure 2). There were more people on MOUD treatment who said they thought accessing safe supply would increase their likelihood of staying on MOUD than people who said it would make them less like to stay on their current MOUD.



Figure 2. Proportions of responses to Likert questions on crime (n for those who reported engaging in illegal activity), frequency of use (n is everyone interested in safe supply), likelihood of starting MOUD treatment (n is for everyone interested in safe supply and not on MOUD), and staying on MOUD treatment (n is for everyone interested in safe supply and on MOUD). Data collected from May 2023 to September 2023 in Seattle, Washington.

Model preferences and ranking:

There were 343 people (91%) who had a preferred opioid regulation model when asked to rank the six available choices. The most popular choice was the prescribed unsupervised 21% (n = 80), followed by dispensary-based 18% (n = 69), expanded methadone 18% (n = 68), community-based 15% (n = 58), 13% prescribed supervised (n = 47), and expanded buprenorphine 6% (n = 21) (Table 3). Generally, people who were younger appeared to prefer models that required less oversight whereas older people tended to prefer more MOUD treatment based and fixed site models. Whether someone was currently on methadone was indicative of someone selecting expanded methadone as the first option. Whether someone was currently on buprenorphine was not indicative of selecting buprenorphine as their first option.

Table 3. Distribution of demographic factors stratified by top model of interest for first choice. University of Washington respondent driven sample, 2023 (N = 375)

	Preferred Opioid Regulation Model						Any model (sum columns 1 to 6)	No Interest	Total*
	Prescribed supervised	Prescribed unsupervised	Communit y-based	Dispensary based	Expanded Methadone	Expanded Buprenorphine			
N	47 (13%)	80 (21%)	58 (15%)	69 (18%)	68 (18%)	21 (6%)	343 (91%)	32 (9%)	375
RDS Sample									
Injecting	34 (13%)	59 (22%)	36 (13%)	45 (17%)	56 (21%)	16 (6%)	246 (91%)	23 (9%)	269 (72%)
Smoking	13 (12%)	21 (20%)	22 (21%)	24 (23%)	12 (11%)	5 (5%)	97 (92%)	9 (8%)	106 (28%)
Age (median (IQR))	42 (14)	39 (12)	37 (15)	35 (14)	40 (16)	42 (11)	39 (14)	40 (14)	38 (15)
Gender									
Male	37 (14%)	58 (21%)	43 (16%)	48 (18%)	48 (18%)	13 (5%)	247 (91%)	24 (9%)	271 (72%)
Female	8 (9%)	18 (21%)	11 (13%)	18 (21%)	20 (23%)	8 (9%)	83 (94%)	5 (6%)	88 (24%)
Trans and Other	2 (13%)	4 (27%)	4 (27%)	3 (20%)	0	0	13 (87%)	2 (13%)	15 (4%)
Race**									
American Indian/Alaska Native	9 (14%)	11 (17%)	9 (14%)	14 (22%)	11 (17%)	4 (6%)	58 (89%)	7 (11%)	65 (15%)
Asian	2 (20%)	2 (20%)	1 (10%)	3 (30%)	2 (20%)	0 (0%)	10 (100%)	0 (0%)	10 (2%)
Black	13 (19%)	12 (17%)	6 (9%)	15 (22%)	6 (9%)	5 (7%)	57 (83%)	12 (17%)	69 (15%)

Native Hawaiian or other Pacific Islander	2 (13%)	2 (13%)	2 (13%)	4 (25%)	1 (6%)	0	11 (69%)	5 (31%)	16 (4%)
White	30 (11%)	64 (24%)	42 (16%)	47 (18%)	54 (20%)	13 (5%)	250 (94%)	17 (6%)	267 (59%)
Other	1 (5%)	2 (9%)	4 (18%)	5 (23%)	2 (9%)	2 (9%)	16 (73%)	6 (27%)	22 (5%)
Housing last year									
Unhoused at some point	43 (13%)	74 (23%)	51 (16%)	57 (17%)	56 (17%)	20 (6%)	301 (92%)	26 (8%)	327 (87%)
Housed	4 (8%)	6 (12%)	7 (15%)	12 (25%)	12 (25%)	1 (2%)	42 (88%)	6 (12%)	48 (13%)
Housing status									
Unhoused	33 (12%)	55 (21%)	43 (16%)	49 (19%)	45 (17%)	15 (6%)	240 (92%)	22 (8%)	262 (70%)
Housed	12 (11%)	25 (23%)	15 (14%)	20 (18%)	23 (21%)	5 (5%)	100 (91%)	10 (9%)	110 (30%)
Employment									
Employed	2 (6%)	6 (17%)	4 (11%)	8 (23%)	9 (26%)	2 (6%)	31 (89%)	4 (11%)	35 (9%)
Unemployed	45 (13%)	74 (22%)	54 (16%)	61 (18%)	58 (17%)	18 (5%)	310 (92%)	26 (8%)	336 (91%)
Crime for drug use									
Yes	23 (10%)	60 (26%)	38 (16%)	43 (18%)	42 (18%)	9 (4%)	215 (92%)	18 (8%)	233 (65%)
No	22 (18%)	19 (15%)	14 (11%)	21 (17%)	25 (20%)	11 (9%)	112 (90%)	13 (10%)	125 (35%)
Overdose ever									
Yes	27 (12%)	49 (22%)	29 (13%)	34 (15%)	52 (24%)	13 (6%)	204 (93%)	16 (7%)	220 (59%)
No	20 (13%)	30 (20%)	28 (18%)	35 (23%)	16 (11%)	8 (5%)	137 (90%)	15 (10%)	152 (41%)
Use drugs alone									
Never	4 (9%)	8 (17%)	6 (13%)	12 (26%)	10 (21%)	4 (9%)	44 (94%)	3 (6%)	47 (13%)
Some of the time	20 (13%)	34 (22%)	24 (16%)	30 (19%)	24 (16%)	10 (6%)	142 (92%)	12 (9%)	154 (41%)
Most of the time	19 (14%)	30 (23%)	23 (17%)	18 (14%)	25 (19%)	6 (5%)	121 (91%)	12 (9%)	133 (36%)
Always	4 (11%)	8 (21%)	4 (11%)	9 (24%)	8 (21%)	1 (3%)	34 (89%)	4 (11%)	38 (10%)
Currently on MOUD									
Methadone	9 (18%)	5 (10%)	5 (10%)	2 (4%)	29 (57%)	0 (0%)	50 (98%)	1 (2%)	51 (14%)
Buprenorphine	6 (27%)	5 (27%)	2 (9%)	5 (27%)	0 (0%)	3 (14%)	21 (95%)	1 (5%)	22 (6%)
Naltrexone	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
None	32 (11%)	70 (23%)	50 (17%)	62 (21%)	38 (13%)	17 (7%)	269 (90%)	30 (10%)	299 (80%)

*all row percentages except for the overall column to the far right (column percent).

**People could select more than one race

Among PWID, we found that the most preferred model of regulated opioids in terms of ranking was the prescribed unsupervised model, followed by the community-based model, a dispensary-based model, and then the prescribed supervised model (Supplemental Table 1). Results were similar for the smoking sample except the prescribed supervised model was less popular among people who smoked drugs compared to PWID. When asked to rank the four safe supply models with the two expanded MOUD treatment scenarios, participants rated the safe supply models in

the same order and the MOUD treatment scenarios methadone and buprenorphine were ranked fifth and sixth respectively (Supplemental Table 2). Methadone had a strong bimodal distribution with 18% (n =68) people ranking it as their first choice. In both samples buprenorphine was the least popular of all the options with most people not being interested. When people were interested in the expanded buprenorphine model, people consistently ranked it as the last choice when ranked against other models.

Discussion:

We surveyed people who used opioids in Seattle, Washington, in 2023. People in our sample were socially marginalized, with a high proportion of people experiencing homelessness and using drugs alone. The majority had tried MOUD treatment and/or abstinence-based treatment modalities in their lifetime. We found that most people were interested in most models of regulated opioids. More respondents indicated interest in safe supply models compared to the expanded MOUD treatment options. Respondents indicated that they believed that safe supply models as well as expanded MOUD options would curtail their risk of overdose compared to their current supply of unregulated opioid. People who reported engaging in crime to supplement their drug use indicated that getting access to regulated opioids either safe supply or MOUD would greatly diminish their engagement in criminal activity. Participants expressed a range of preferences for different models of opioid regulation. The prescribed unsupervised model appeared to be the most preferred by both samples. Both samples favored safe supply options over any of the expanded MOUD treatment options. Additionally, they preferred expanded methadone more than expanded buprenorphine.

A smaller study found similar interest in safe supply among people who inject opioids in King County (19). This same study also found a high proportion of people thought accessing safe supply would reduce their risk of overdose. The current study replicated these findings, strengthening the evidence base that PWID want safe supply and think it would significantly reduce their overdose risk. These findings show similar interest in safe supply among people who smoke opioids, an important finding given data showing that smoking has become more common among people who use opioids in Washington State who attend syringe service programs (26). The consistent finding that access to safe supply models, where reductions or cessation in use is not the focus, reduces perceived overdose risk aligns with other studies showing that participants accessing prescribed alternatives to the toxic drug supply were less likely to die compared to matched controls who did not access these programs (12,15). We found that those interested in expanded methadone and buprenorphine believed that accessing these opioids would reduce their risk of overdose and significantly decrease their frequency of use. This is consistent with findings from meta-analyses, which have shown that methadone and buprenorphine as MOUD to be highly effective for those who initiate and stay engaged in care (27,28). The reported potential reduction in criminal activity found in this study is congruent with results from participants in safer supply programs who said that they reduced the amount of crime related to their drug use compared to the time period before they accessed the program (29,30). Participants also reported expected reduction in crime for the expanded MOUD models which is consistent with existing evidence that accessing MOUD reduces engagement in criminal activity (31).

The results from the questions related to frequency of drug use demonstrated an important distinction between the two MOUD treatment options and the four safe supply models. We found that those who were interested in the two MOUD treatment options overwhelmingly said that it would reduce their use. In contrast, for the safe supply models, most people said it would not impact the frequency at which they use drugs. More individuals anticipated that safe supply would reduce their frequency of use than the number of individuals who anticipated that safe supply would increase their frequency of use. This aligns with other descriptions of safe supply, which aims to reduce unregulated drug use but not stop drug use. This contrasts generally with the goal of most current models utilizing MOUD, which is to stop drug use (32). However, as some providers and systems move towards a focus of staying engaged on MOUD, safe supply could be an overlapping model of services, as MOUD and safe supply are not mutually exclusive.

In this study more people who were not on MOUD expected that accessing safe supply would make them more likely to access MOUD than less likely to access MOUD. Among those who were on MOUD, most said accessing safe supply would have no impact on whether they stayed on MOUD or make them more likely to stay on MOUD. This is consistent with findings from BC that found that those accessing safe supply were more likely to stay on MOUD (33,34). In our survey 57% of people on methadone wanted a more liberated clinic-based version of their treatment instead of any of the safe supply models. However, 28% of methadone patients also wanted some prescribed version of safe supply as their first choice of regulation model over expanded methadone. These findings further highlight the demand for both expanded methadone treatment and safe supply. A study from BC, Canada, found varied preferences of safer supply

programs. Some participants described wanting more autonomy in their models while others preferred closer contact with care to help with other health needs (35). In our study we found similar results including, PWID preferring the prescribed supervised option more than those who smoked (36).

There are several limitations to our study. The RDS sampling method may introduce selection bias and limit generalizability (37). However, RDS diagnostics suggested that our sample met the RDS assumptions. We asked about safe supply, an intervention that most participants had not heard of before; therefore, people may have not fully understood what the interventions would look like in practice. There are also limitations comparing safe supply, an intervention no one in the sample has experienced, with MOUD which has known barriers and challenges that participants have experienced. Therefore, safe supply acceptability could be a lot lower in practice if implemented and individuals have direct experience with a safe supply program. For example, a study from New York found that among PWID who were interested in receiving injectable hydromorphone in a supervised setting had a 55% acceptability, which is lower than what we found for our prescribed supervised model (which did not specify a particular type of opioid) (38). Additional limitations of this study are that costs of the various models and the types of opioids provided were not specified. The unregulated drug market has certain costs. Providing a safe supply at no cost to participants would not just provide a reduced likelihood of health concerns but also remove financial burden on participants. In future studies adding details about who pays for safe supply could change the number of people interested as well as how it would be anticipated to change the behaviours of participants. Respondents' preferences for short versus long-acting opioids as well as preference for euphorigenic versus withdrawal

alleviating effects warrant further investigation. We also incentivized the survey and thus some people may have tried to enter the study for the compensation and provided data that was not accurate. This is a problem that is hard to mitigate in the context of a marginalized population that intersects with poverty and an incentivized survey.

One could argue the biggest limitation of this study is that safe supply is not likely to happen any time soon in the US. In the US there are serious regulatory barriers that preclude all of the models of safe supply discussed. There are federal and state regulations that block the prescription of medications by medical providers to maintain a person's substance use and the non-medical models, all currently illegal and in the eyes of the law, are tantamount to drug dealing (39). Despite these barriers, gauging the interest in these interventions and showing that there is acceptability is important as we explore pragmatic solutions to reduce fatal opioid overdoses. We should note that the expanded methadone and buprenorphine scenarios described in the survey do not match the reality of most care delivery systems in the US. However, in 2024, new rules in the US made substantial changes to improve access to methadone, increased dosages, decreased in person dosing frequency, and removed counseling mandates making the models asked about in this survey potentially implementable in reality (20). This is welcomed as expanded MOUD including non-clinic-based options are urgently needed as one part of a solution to addressing the number of overdose deaths in the US.

The strong interest in safe supply models by our respondents underscores the desire for such programs by a population of people that would use these services. From a public health perspective implementing safe supply could be a substantial step towards reducing overdose

fatalities. The findings suggest a pathway to reduce the burden on emergency services and medical facilities dealing with overdoses. Socially, the potential reduction in drug-related crimes can foster safer communities, while also paving the way for people who use drugs to have more stability and autonomy in their lives without living under the fear of criminalization.

References:

1. Drug Overdose Deaths | Drug Overdose | CDC Injury Center [Internet]. 2021 [cited 2021 Nov 3]. Available from: <https://www.cdc.gov/drugoverdose/deaths/index.html>
2. Jalal H, Burke DS. Carfentanil and the rise and fall of overdose deaths in the United States. *Addiction*. 2021;116(6):1593–9.
3. Overdose deaths - King County [Internet]. [cited 2021 Nov 3]. Available from: <https://kingcounty.gov/depts/health/examiner/services/reports-data/overdose.aspx>
4. Shover CL, Falasinnu TO, Dwyer CL, Santos NB, Cunningham NJ, Freedman RB, et al. Steep increases in fentanyl-related mortality west of the Mississippi River: Recent evidence from county and state surveillance. *Drug Alcohol Depend*. 2020 Nov 1;216:108314.
5. Volkow ND, Jones EB, Einstein EB, Wargo EM. Prevention and Treatment of Opioid Misuse and Addiction: A Review. *JAMA Psychiatry*. 2019 Feb 1;76(2):208–16.
6. Tobias S, Grant CJ, Laing R, Arredondo J, Lysyshyn M, Buxton J, et al. Time-Series Analysis of Fentanyl Concentration in the Unregulated Opioid Drug Supply in a Canadian Setting. *Am J Epidemiol*. 2022 Jan 24;191(2):241–7.
7. Humphreys K, Shover CL, Andrews CM, Bohnert ASB, Brandeau ML, Caulkins JP, et al. Responding to the opioid crisis in North America and beyond: recommendations of the Stanford–Lancet Commission. *The Lancet*. 2022 Feb 5;399(10324):555–604.
8. Pitt AL, Humphreys K, Brandeau ML. Modeling Health Benefits and Harms of Public Policy Responses to the US Opioid Epidemic. *Am J Public Health*. 2018 Oct;108(10):1394–400.
9. Ivsins A, Boyd J, Beletsky L, McNeil R. Tackling the overdose crisis: The role of safe supply. *Int J Drug Policy*. 2020 Jun 1;80:102769.

10. Google Docs [Internet]. [cited 2021 Mar 3]. CAPUD safe supply English March 3 2019.pdf. Available from: https://drive.google.com/file/d/1GZ1HkoApYIEcQ8qQGQdAEp-WpU6XX94F/view?usp=sharing&usp=embed_facebook
11. Bonn M, Palayew A, Touesnard N, Brothers TD, Bodkin C. Safe Supply in the Midst of a Crisis of Unregulated Toxic Drug Deaths—A Commentary on Roberts and Humphreys (2023). *J Stud Alcohol Drugs*. 2023 Jul;84(4):648–50.
12. Ledlie S, Garg R, Cheng C, Kolla G, Antoniou T, Bouck Z, et al. Prescribed safer opioid supply: A scoping review of the evidence. *Int J Drug Policy*. 2024 Mar 1;125:104339.
13. Gomes T, Men S, Campbell TJ, Tadrous M, Mamdani MM, Paterson JM, et al. Changing patterns of opioid initiation for pain management in Ontario, Canada: A population-based cross-sectional study. *PLOS ONE*. 2022 Dec 8;17(12):e0278508.
14. Slaunwhite A, Min JE, Palis H, Urbanoski K, Pauly B, Barker B, et al. Effect of Risk Mitigation Guidance opioid and stimulant dispensations on mortality and acute care visits during dual public health emergencies: retrospective cohort study. *BMJ*. 2024 Jan 11;384:e076336.
15. Kalicum J, Nyx E, Kennedy MC, Kerr T. The impact of an unsanctioned compassion club on non-fatal overdose. *Int J Drug Policy*. 2024 Feb 22;104330.
16. The Seattle Times [Internet]. 2022 [cited 2024 May 5]. Substance use is a health issue, not a legal one | Op-Ed. Available from: <https://www.seattletimes.com/opinion/substance-use-is-a-health-issue-not-a-legal-one/>
17. 2021-23 enacted budgets | Office of Financial Management [Internet]. [cited 2024 Jun 25]. Available from: <https://ofm.wa.gov/budget/state-budgets/2021-23-enacted-budgets>
18. Substance Use Recovery Services Advisory Committee (SURSAC) | Washington State Health Care Authority [Internet]. [cited 2024 Jun 25]. Available from:

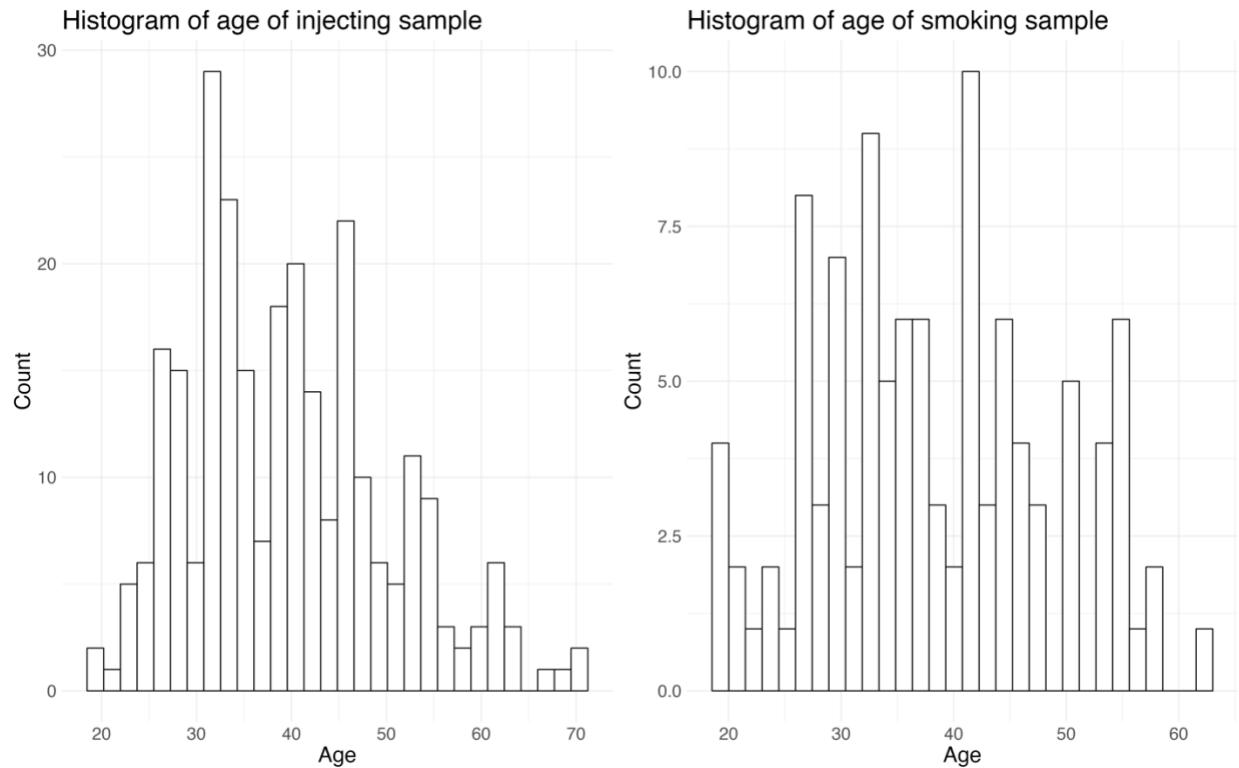
<https://www.hca.wa.gov/about-hca/programs-and-initiatives/behavioral-health-and-recovery/substance-use-recovery-services-advisory-committee-sursac#recommendation-plans>

19. Palayew A, Banta-Green CJ, Lamont M, Damper D, Moreno C, Goodreau SM, et al. Acceptability and anticipated effectiveness of a safe supply of opioids, among people who inject opioids in King County, WA. *Int J Drug Policy*. 2024 May 1;127:104389.
20. The 42 CFR Part 8 Final Rule Table of Changes [Internet]. 2024 [cited 2024 May 28]. Available from: <https://www.samhsa.gov/medications-substance-use-disorders/statutes-regulations-guidelines/42-cfr-part-8/final-rule-table-changes>
21. Simon C, Vincent L, Coulter A, Salazar Z, Voyles N, Roberts L, et al. The Methadone Manifesto: Treatment Experiences and Policy Recommendations From Methadone Patient Activists. *Am J Public Health*. 2022 Apr;112(S2):S117–22.
22. Hood JE, Banta-Green CJ, Duchin JS, Breuner J, Dell W, Finegood B, et al. Engaging an unstably housed population with low-barrier buprenorphine treatment at a syringe services program: Lessons learned from Seattle, Washington. *Subst Abuse*. 2020 Jul 2;41(3):356–64.
23. Foreman-Mackey A, Pauly B, Ivsins A, Urbanoski K, Mansoor M, Bardwell G. Moving towards a continuum of safer supply options for people who use drugs: A qualitative study exploring national perspectives on safer supply among professional stakeholders in Canada. *Subst Abuse Treat Prev Policy*. 2022 Oct 8;17(1):66.
24. REDCap [Internet]. [cited 2023 Jan 18]. Available from: <https://www.project-redcap.org/>
25. R: A language and environment for statistical computing [Internet]. [cited 2021 Sep 26]. Available from: https://scholar.google.com/citations?view_op=view_citation&hl=en&user=yvS1QUEAAAAJ&citation_for_view=yvS1QUEAAAAJ:t6usbXjVLHcC

26. Results from the 2023 WA State Syringe Services Program Health Survey [Internet]. Addictions, Drug & Alcohol Institute. [cited 2024 Jun 10]. Available from: <https://adai.uw.edu/syringe-survey-2023/>
27. Stone AC, Carroll JJ, Rich JD, Green TC. Methadone maintenance treatment among patients exposed to illicit fentanyl in Rhode Island: Safety, dose, retention, and relapse at 6 months. *Drug Alcohol Depend.* 2018 Nov 1;192:94–7.
28. McAnulty C, Bastien G, Eugenia Socias M, Bruneau J, Foll BL, Lim R, et al. Buprenorphine/naloxone and methadone effectiveness for reducing craving in individuals with prescription opioid use disorder: Exploratory results from an open-label, pragmatic randomized controlled trial. *Drug Alcohol Depend.* 2022 Oct 1;239:109604.
29. Bardwell G, Small W, Lavalley J, McNeil R, Kerr T. “People need them or else they’re going to take fentanyl and die”: A qualitative study examining the ‘problem’ of prescription opioid diversion during an overdose epidemic. *Soc Sci Med.* 2021 Jun 1;279:113986.
30. Schmidt RA, Kaminski N, Kryszajtyś DT, Rudzinski K, Perri M, Guta A, et al. ‘I don’t chase drugs as much anymore, and I’m not dead’: Client reported outcomes associated with safer opioid supply programs in Ontario, Canada. *Drug Alcohol Rev.* 2023;42(7):1825–37.
31. Calcaterra SL, Bach P, Chadi A, Chadi N, Kimmel SD, Morford KL, et al. Methadone Matters: What the United States Can Learn from the Global Effort to Treat Opioid Addiction. *J Gen Intern Med.* 2019 Jun 1;34(6):1039–42.
32. Glegg S, McCrae K, Kolla G, Touesnard N, Turnbull J, Brothers TD, et al. “COVID just kind of opened a can of whoop-ass”: The rapid growth of safer supply prescribing during the pandemic documented through an environmental scan of addiction and harm reduction services in Canada. *Int J Drug Policy.* 2022 Aug 1;106:103742.

33. Selfridge M, Card K, Kandler T, Flanagan E, Lerhe E, Heaslip A, et al. Factors associated with 60-day adherence to “safer supply” opioids prescribed under British Columbia’s interim clinical guidance for health care providers to support people who use drugs during COVID-19 and the ongoing overdose emergency. *Int J Drug Policy*. 2022 Jul 1;105:103709.
34. Min JE, Guerra-Alejos BC, Yan R, Palis H, Barker B, Urbanoski K, et al. Opioid Coprescription Through Risk Mitigation Guidance and Opioid Agonist Treatment Receipt. *JAMA Netw Open*. 2024 May 15;7(5):e2411389.
35. Pauly B, McCall J, Cameron F, Stuart H, Hobbs H, Sullivan G, et al. A concept mapping study of service user design of safer supply as an alternative to the illicit drug market. *Int J Drug Policy*. 2022 Dec 1;110:103849.
36. Ferguson M, Parmar A, Papamihali K, Weng A, Lock K, Buxton JA. Investigating opioid preference to inform safe supply services: A cross sectional study. *Int J Drug Policy*. 2022 Mar 1;101:103574.
37. Heckathorn DD. Comment: Snowball versus Respondent-Driven Sampling. *Sociol Methodol*. 2011 Aug 1;41(1):355–66.
38. Ohlendorf E, Perez-Correa A, Riback L, Ghiroli M, Lopez-Castro T, Fox AD. Treatment History and Interest in Injectable Opioid Agonist Treatment With Hydromorphone Among People Who Inject Drugs. *J Addict Med*. :10.1097/ADM.0000000000001093.
39. Kleinman RA, Morris NP. Federal Barriers to Addressing the Opioid Epidemic. *J Gen Intern Med*. 2020 Apr;35(4):1304–6.

Appendix:



Supplemental figure 1: Histogram of age for the participants in the injecting and smoking sample. Data collected from May 2023 to September 2023 in Seattle, Washington.

Supplemental Table 1. Ranking of the different safe supply models. Data collected from May 2023 to September 2023 in Seattle, Washington.

Injecting sample					Points
Model	Choice 1	Choice 2	Choice 3	Choice 4	
Prescribed supervised	80 (30%)	50 (18%)	49 (18%)	91 (33%)	389
Prescribed unsupervised	91 (34%)	70 (26%)	76 (28%)	34 (13%)	489
Community-based model	61 (23%)	93 (35%)	77 (29%)	38 (14%)	446
Dispensary-based model	79 (29%)	72 (27%)	57 (21%)	62 (23%)	438
Smoking sample					
Model	Choice 1	Choice 2	Choice 3	Choice 4	
Prescribed supervised	18 (25%)	12 (17%)	11 (15%)	30 (42%)	89
Prescribed unsupervised	27 (33%)	31 (37%)	21 (25%)	4 (5%)	164
Community-based model	22 (26%)	24 (29%)	30 (36%)	8 (10%)	144

Dispensary-based model	31 (35%)	22 (25%)	20 (23%)	15 (17%)	157
------------------------	----------	----------	----------	----------	-----

Supplemental Table 2. Ranking of the different models of regulated opioids and expanded treatment. Data collected from May 2023 to September 2023 in Seattle, Washington.

Injecting							
Model	Choice 1	Choice 2	Choice 3	Choice 4	Choice 5	Choice 6	points
Prescribed supervised	54 (20%)	52 (20%)	49 (18%)	70 (26%)	24 (9%)	16 (6%)	789
Prescribed unsupervised	70 (26%)	65 (25%)	72 (27%)	44 (17%)	9 (3%)	5 (2%)	923
Community-based model	44 (17%)	84 (32%)	65 (24%)	41 (15%)	24 (9%)	8 (3%)	857
Dispensary-based model	70 (26%)	59 (22%)	48 (18%)	54 (20%)	22 (8%)	13 (5%)	860
Methadone	65 (31%)	18 (8%)	26 (12%)	20 (9%)	46 (21%)	39 (18%)	561
Buprenorphine	17 (11%)	15 (9%)	9 (6%)	12 (7%)	49 (30%)	59 (37%)	245
Smoking							
Model	Choice 1	Choice 2	Choice 3	Choice 4	Choice 5	Choice 6	
Prescribed supervised	13 (18%)	11 (15%)	13 (18%)	25 (35%)	7 (10%)	3 (5%)	205
Prescribed unsupervised	21 (25%)	30 (36%)	18 (22%)	7 (8%)	5 (6%)	2 (2%)	298
Community-based model	22 (26%)	19 (23%)	26 (31%)	9 (11%)	8 (10%)	0 (3%)	290
Dispensary-based model	24 (27%)	19 (22%)	23 (26%)	20 (23%)	1 (1%)	1 (1%)	306
Methadone	12 (26%)	6 (13%)	1 (22%)	5 (11%)	18 (39%)	4 (9%)	115
Buprenorphine	5 (14%)	7 (20%)	3 (9%)	6 (17%)	7 (20%)	7 (20%)	81

CHAPTER 4. THE POTENTIAL IMPACT ON FATAL OVERDOSE AMONG PEOPLE WHO INJECT DRUGS WITH THE IMPLEMENTATION OF DIFFERENT SCENARIOS OF SAFE SUPPLY IN SEATTLE WASHINGTON A MICROSIMULATION MODEL.

Authors: Adam Palayew^{1,2}, Stephen J. Mooney¹, Sara N. Glick^{1,3,4}, Ali Rowhani-Rahbar¹, Malika Lamont⁵, DeAunte Damper⁵, Caleb J. Banta-Green^{1,2,6}, Steven M. Goodreau^{1,7}

Affiliations:

1. Department of Epidemiology, University of Washington, Seattle, Washington
2. Addictions, Drug & Alcohol Institute, Department of Psychiatry, Behavioural Sciences, School of Medicine, Seattle, Washington
3. Public Health – Seattle & King County, Seattle Washington
4. Department of Medicine, University of Washington
5. VOCAL-Washington
6. Department of Health Systems and Population Health, University of Washington, Seattle, Washington
7. Department of Anthropology, University of Washington

Abstract:

Background: Opioid overdose deaths have significantly increased over the last two decades in the United States, particularly among people who inject drugs (PWID). A proposed approach to mitigate this crisis is providing people who use drugs with access to opioids of known potency and purity (“safe supply”), which aims to reduce exposure to the unregulated drug supply. This study used a microsimulation model to explore the potential impact of four different safe supply delivery scenarios on the incidence of fatal overdose among PWID in Seattle.

Methods: We developed a microsimulation model calibrated to the number of opioid overdose deaths and the number of people on medications for opioid use disorder in Seattle, Washington for the period 2019-2023. The four modeled scenarios were: 1) reference (*status-quo*) 2) prescribed supervised, 3) prescribed unsupervised, and 4) community-based model. A sensitivity analysis explored varying levels of access (pilot, some, and full) and a threshold analysis examined the impact of increased new user initiation rates on overdose mortality.

Results: Over 15 simulated years, the reference scenario projected 3612 (95%CI: 3585, 3639) overdose deaths. The prescribed supervised scenario resulted in 1171 (95%CI: 1146, 1193) deaths, prescribed unsupervised scenario in 1803 (95%CI: 1739, 1817) deaths, and community-based model in 2066 (95%CI: 1931, 2095) deaths. Sensitivity analyses indicated that the pilot scenario for safe supply scenarios did not achieve population-level impacts on overdose deaths. The threshold analysis indicated that the new user rate would need to increase by three-fold for the prescribed-unsupervised and community-based model to return to the reference scenario and

would need five-fold increase for the prescribed-supervised scenario to have the same number of deaths as the reference scenario.

Conclusion: Implementing safe supply models could reduce overdose deaths at the population level if sufficient access is achieved.

Introduction:

In the last two decades, the United States has experienced a significant increase in opioid overdose deaths, particularly among people who inject drugs (PWID) (1). In 2022, there were over 80,000 overdose deaths involving opioids, with synthetic opioids such as non-pharmaceutical-fentanyl being the primary driver of the increasing number of opioid-related deaths (2). Fentanyl has contributed to the increase in deaths since fentanyl is more potent than previous opioids. Moreover, the amount of fentanyl in the unregulated drug supply is variable; therefore, people who use opioids do not know the amount of fentanyl in their drugs. Due to this combination people who use drugs are at higher risk of overdose when using unregulated fentanyl. The surge in overdose deaths related to fentanyl and opioids in general has prompted urgent calls for action to reduce the harms associated with opioid use (3). In response, governments have expanded medications for opioid use disorder (MOUD) and, in some jurisdictions, harm reduction services (4).

One additional proposed approach is providing a regulated supply of opioids, also known as a safe supply, which aims to reduce overdose deaths by ensuring that people who use opioids have access to opioids of known potency (dose), and purity (quality) as an alternative to those they would consume from the unregulated market (5). This approach has proven successful in several Canadian contexts (6,7). Medically unsupervised models of safe supply, also known as safer supply or prescribed alternatives to the unregulated drug supply have been found to be effective in reducing all-cause mortality, fatal overdose, and non-fatal overdose in several settings (6). An observational study in British Columbia found that accessing one dose of safer supply reduced all-cause mortality by 61% in the following week compared to matched controls (8).

Furthermore, a community-based model operated by the Drug Users Liberation Front distributed three kilograms of cocaine, heroin, and methamphetamine and reported zero overdoses requiring naloxone among their pilot participants over a full calendar year of operation and found that participants had reduced non-fatal overdose risk by 44% (7). However, there is ongoing criticism about the potential impact of different regulatory approaches on the opioid epidemic, specifically regarding the diversion of drugs from safer supply programs and encouraging new initiation of drug use (9). In the United States, these models are unlikely to be implemented soon (10). There are several legal obstacles, making highly restricted pilots that provide substances like hydromorphone in treatment settings, which some would argue is not safe supply, the most feasible option in the near future (11).

Seattle is experiencing significant impact from the opioid crisis, characterized by high rates of opioid-related mortality, especially among PWID (12). Seattle is representative of many West Coast cities facing similar challenges (13,14). In this paper we decided to evaluate different scenarios of opioid access among PWID in Seattle, Washington despite the likelihood of these models being implemented any time soon not being a reality. We used microsimulation modelling to explore the potential impact of regulatory interventions on fatal opioid overdose (15). By simulating the behavior of individuals within a population over time, microsimulation models can estimate the effects of different policy scenarios on health indicators such as overdose incidence and mortality while accounting for existing MOUD services (16). The rationale for restricting the modelling to PWID is based on the reality from other countries that only people who were experienced with injection drug use were able to access the earliest iterations of the prescribed supervised scenarios when first rolled out. The reason these services

were limited largely to PWID was to help assuage concerns among certain stakeholders that the interventions were only being utilized by individuals who have used drugs for a long time and not those who might be experimenting.

Methods:

We utilized a microsimulation model to predict the impact of three different scenarios of safe supply interventions focused on opioids over a 15-year time horizon. The microsimulation model was based off Macmadu et al. 2021 (17). The model was implemented and run using the R programming language (18). Each individual in the model had a base risk of overdose that was then modified by their demographic characteristics and whether they were accessing MOUD, the intervention, or both. Individuals were able to discontinue MOUD and safe supply in the model. Individuals at every time step had a probability of experiencing opioid-related overdose mortality or leave the model due to deaths from other causes or cessation of drug use (Figure 1).

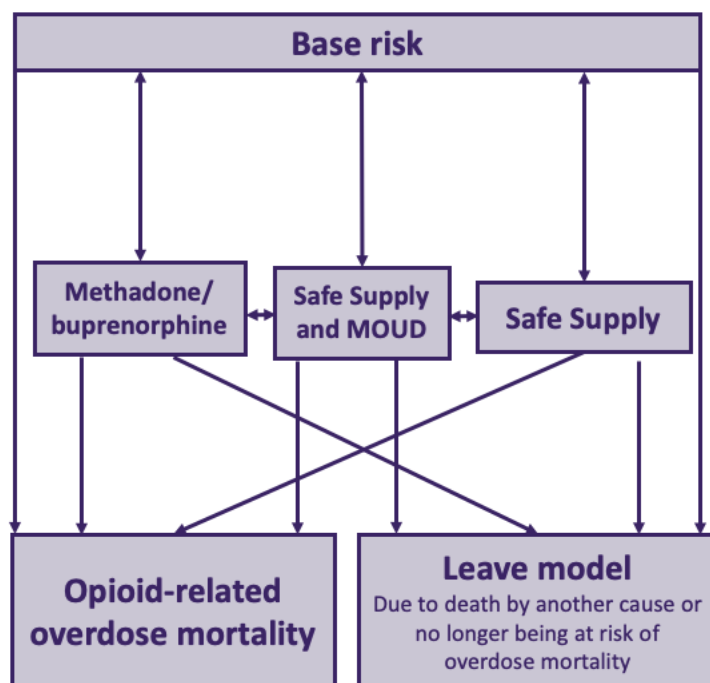


Figure 1. Pathways for individual transition across dynamic states in the model.

We specified the log odds of an overdose as an additive function of age, gender, MOUD status, and access to safe supply. Individuals had decreased log odds of overdose mortality while being enrolled in MOUD or safe supply programs while discontinuation of MOUD or safe supply generated an increased risk of overdose. Log odds were then converted to probabilities. The effect of MOUD on the probability of overdose was estimated based on previous studies from the United States (19).

The log odds of initiating and cessation of MOUD was an additive function of the age, gender, and safe supply status of an individual. Individuals had an increased log odds of initiation MOUD if they were over the age of 30, were male, and were on safe supply. Individuals had a lower log odds of cessation if they were over the age of 30, were male, and were on safe supply. These probabilities were estimated based on data from previous studies of opioid use and MOUD outcomes (20,21). The total number of MOUD was capped at a maximum of 50% of individuals in the model based off data from Palayew *et al. in preparation*.

The log odds of initiation and cessation of safe supply was an additive function of the age, gender and MOUD status of an individuals. Individuals who were over the age of 30, male, and on MOUD were more likely to access safe supply and less likely to stop safe supply. The number of people who were able to access safe supply was capped at the levels of interest from Palayew *et al. in preparation*.

Additionally, the model accounted for the risk of dying from other causes or natural cessation of drug use by applying a fixed probability to each individual for exiting the model at each time

step. We assumed that if someone stopped using opioids that that same individual would not restart using and leave the model permanently. We assumed that the probability of initiating injection opioid use follows a rate derived from NSDUH data (22). The baseline probability of overdose was a calibrated parameter (Table 1).

Table 1. Model processes and parameter for the microsimulation model simulation overdose risk in a virtual population.

Parameter	Description	Sources
Demography		
Population size	Initial size of the initial population.	Palayew <i>et al. in preparation</i>
Age	Distribution of age group.	Washington Syringe Services Survey 2021, 2023 (23,24)
Gender	Distribution of genders of initial population.	Washington Syringe Services Survey 2021, 2023 (23,24)
Proportion on MOUD	The proportion of individuals on MOUD at the start of the simulation	King County data
Rate of new people initiating injection drug use	Rate of new people who inject drugs at each time step.	NSDUH(22)
Probability of death of other causes	The probability of death from other causes at each time step.	Cohort study examining mortality among people who inject drugs (25)
Person overdose characteristics		
Baseline overdose risk	The baseline risk of overdose at each timestep for each individual.	Calibrated
Age overdose risk adjustment	A fixed decrease in overdose risk with increased age.	NSDUH (22)
Gender overdose risk adjustment	A fixed increase in overdose risk for women relative to men.	NSDUH (22)
MOUD protective of overdose effect parameter	The decrease in overdose risk for individuals on MOUD.	Systematic-review.(21)
Safe supply intervention protective of overdose effect parameter (by model)	The decrease in overdose risk for individuals accessing safe supply.	Prescribed supervised, meta-analysis of heroin assisted treatment. (26) Prescribe unsupervised, risk mitigation guideline evaluation. (8) Community-based, Drug User Liberation Front compassion club evaluation. (7)
MOUD		
MOUD initiation for methadone and buprenorphine (by individual)	Probability of initiating methadone or buprenorphine at each timestep.	Calibrated
MOUD cessation for methadone and buprenorphine	Probability of stopping methadone or buprenorphine at each timestep.	Calibrated
MOUD initiation for methadone and buprenorphine (by safe supply scenario)	An increase in likelihood of starting MOUD for people on safe supply.	Risk mitigation guideline evaluation (8)
MOUD cessation for methadone and buprenorphine (by safe supply scenario)	The decrease in likelihood of cessation of MOUD for people on safe supply.	Min et al. 2024. (20)
Maximum proportion of the population who would access MOUD	The maximum proportion of people interested in expanded MOUD.	Palayew <i>et al. in preparation</i>

Safe supply characteristics		
Safe supply initiation rate.	The probability of accessing safe supply at each timestep.	Calibrated
Safe supply initiation adjustment by age	The fixed increase in likelihood of starting safe supply for older individuals.	Risk mitigation guideline evaluation (8)
Safe supply initiation adjustment by gender	A fixed increase in likelihood of men starting safe supply.	Risk mitigation guideline evaluation (8)
Baseline Safe supply cessation	The probability at each timestep of stopping safe supply.	Calibrated
Safe supply cessation	The decreased cessation of safe supply for individuals on MOUD.	Cross-sectional study.(27)
Maximum proportion of the population who would access safe supply	The proportion of people who would want to access a certain model of safe supply.	<i>Palayew et al. in preparation</i>

Population and Data Sources

The population in the model consists of PWID in Seattle. Data on the prevalence of opioid use and injection drug use in Seattle were obtained from Public Health – Seattle & King County and *Palayew et al. in preparation* (12). Demographic and behavioral characteristics of PWID in Seattle were derived from a University of Washington 2023 survey of PWID that collected data from May 2023 to August 2023 (*Palayew et al. in preparation*).

Scenarios of a Safe Supply of Opioids:

We considered four total scenarios including three scenarios of safe supply provision in Seattle. The scenarios were: the reference scenario, which involved no safe supply intervention; the prescribed supervised scenario, where opioids are prescribed and consumed under the supervision of a healthcare professional; the prescribed unsupervised scenario, where opioids are prescribed but can be consumed without supervision; and the community-based scenario, which involved community provision of opioids without a prescription. Each scenario was simulated for 1000 iterations.

Outcomes measured:

The primary outcome of the model was the cumulative number of opioid related deaths over the simulated time period. The main measure was deaths averted comparing each of the simulated scenarios with the corresponding reference scenario. All estimates are presented with 95% predictive intervals (PI) to reflect the stochastic nature of the model. All models were simulated for 1000 iterations.

Calibration:

The model was calibrated to ensure that two simulated outcomes (observed overdose deaths and number on MOUD) matched observed data from Seattle for the years spanning 2019 to 2023. Inputs selected for calibration are presented in supplemental table 1. Input values were generated using Latin hypercube sampling (28). Goodness-of-fit for the model was determined by minimizing the sum of the square differences between the model outputs and the calibration targets (29).

Sensitivity Analyses:

Two additional analyses were conducted. The first sensitivity analysis examined the population-level impact of varying levels of access to a prescribed supervised safe supply program. These levels were pilot project (maximum 5% of the population access), some access (maximum 20% access) to full access (maximum 80% access, same as primary analysis).

The second sensitivity analysis investigated how increases in the number of people initiating injection drug use might reverse the effects of the program on overdose mortality. In this analysis, we adjusted the model in the primary analysis to simulate higher rates of new people

initiating injection drug use and observed the resulting impact on overdose deaths. This allowed us to assess whether the benefits of the safe supply programs would be outweighed by potential increases in people initiating injection drug use, providing insights into the conditions under which the program would remain beneficial.

Results:

The reference scenario consistently showed the most deaths (Table 2). The model with the fewest deaths on average was the prescribed supervised scenario, followed by the prescribed unsupervised, and community-based. Additionally, the safe supply scenarios had a higher number of people on MOUD after 15 years compared to the reference scenario.

Table 2. Overall statistics comparing different scenarios for the microsimulation model of overdose deaths. 95% uncertainty intervals are reported based off the 2.5% 97.5% percentiles from 1000 bootstrap replicates of the model.

Scenario	Median Cumulative Overdose Deaths at Year 15	Number on Safe Supply at Year 15	Number on MOUD at Year 15	Deaths Averted Over 15 years
Reference	3268 (95%CI: 3165, 3232)	-	1223 (95%CI: 1154, 1293)	-
Prescribed supervised	1036 (95%CI: 994, 1113)	4649 (95%CI: 4553, 4786)	1496 (95%CI: 1451, 1521)	3034 (95%CI: 2929, 3138)
Prescribed unsupervised	1647 (95%CI: 1530, 1691)	5319 (95%CI: 5274, 5510)	1431 (95%CI: 1397, 1459)	2479 (95%CI: 2369, 2585)
Community-based	1832 (95%CI: 1758, 1891)	4851 (95%CI: 4738, 4876)	1399 (95%CI: 1365, 1434)	2271 (95%CI: 2156, 2379)

Figure 2 shows the projected mean number of overdose deaths over a 15-year period across different safe supply intervention scenarios, compared to the reference scenario. The reduction in deaths becomes apparent within 12 months as soon as individuals start accessing the safe supply interventions in the model.

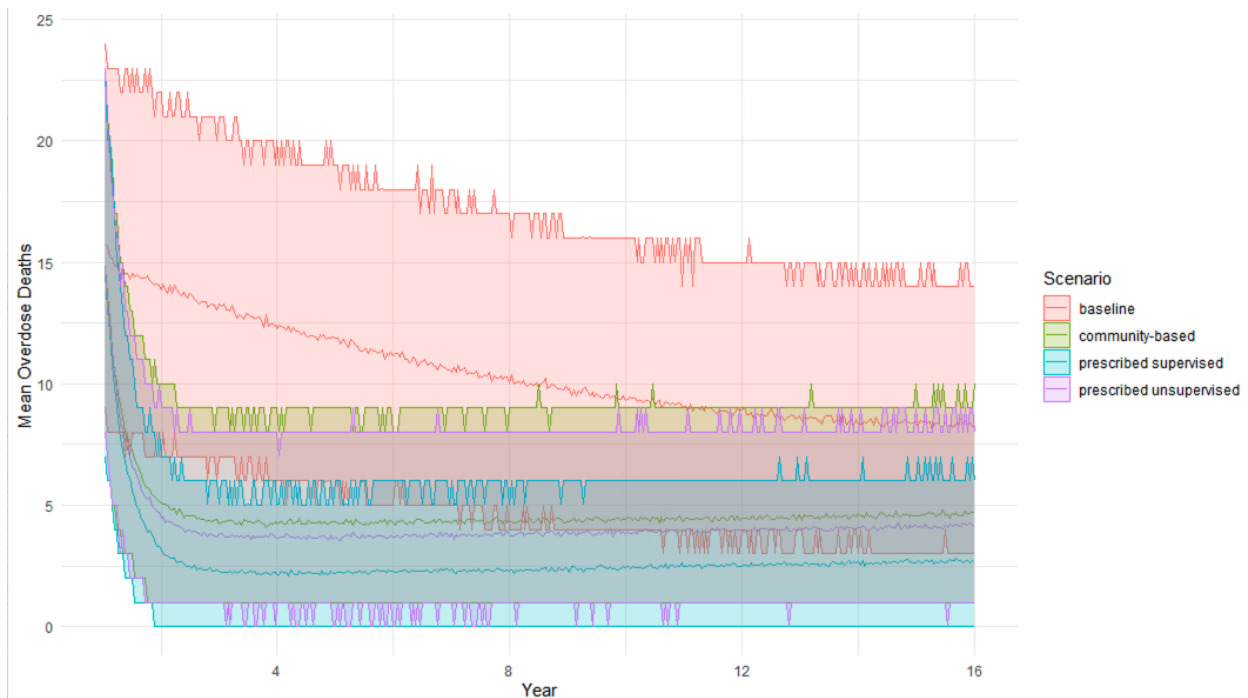


Figure 2. The mean overdose deaths for the different scenarios for the main analysis over 15 simulated years for 1000 bootstrap replicates. The line represents the median and the predictive intervals represent the 95%th percentile of simulations.

Access analysis:

Figure 3 further explores the impact of different levels of access to safe supply interventions on the population-level outcomes for overdose deaths. The reference scenario continues to show the highest number of overdose death. The full access scenario demonstrates a rapid and substantial reduction in overdose deaths, with the mean number of deaths rapidly decreasing within the first few years and remaining low for the rest of the simulation period. The full access scenario also exhibits the most consistent results with the narrowest uncertainty interval. The some access scenarios also result in significant reductions in overdose deaths compared to the reference. The pilot access scenario and the reference scenario were similar. The deaths averted for the pilot project was 164 (95% CI: 41, 289), for the some access 1805 (95% CI: 1696, 1919) deaths were averted, and for the full access 2965 (95% CI: 2859, 3067) deaths averted compared to the reference scenario.

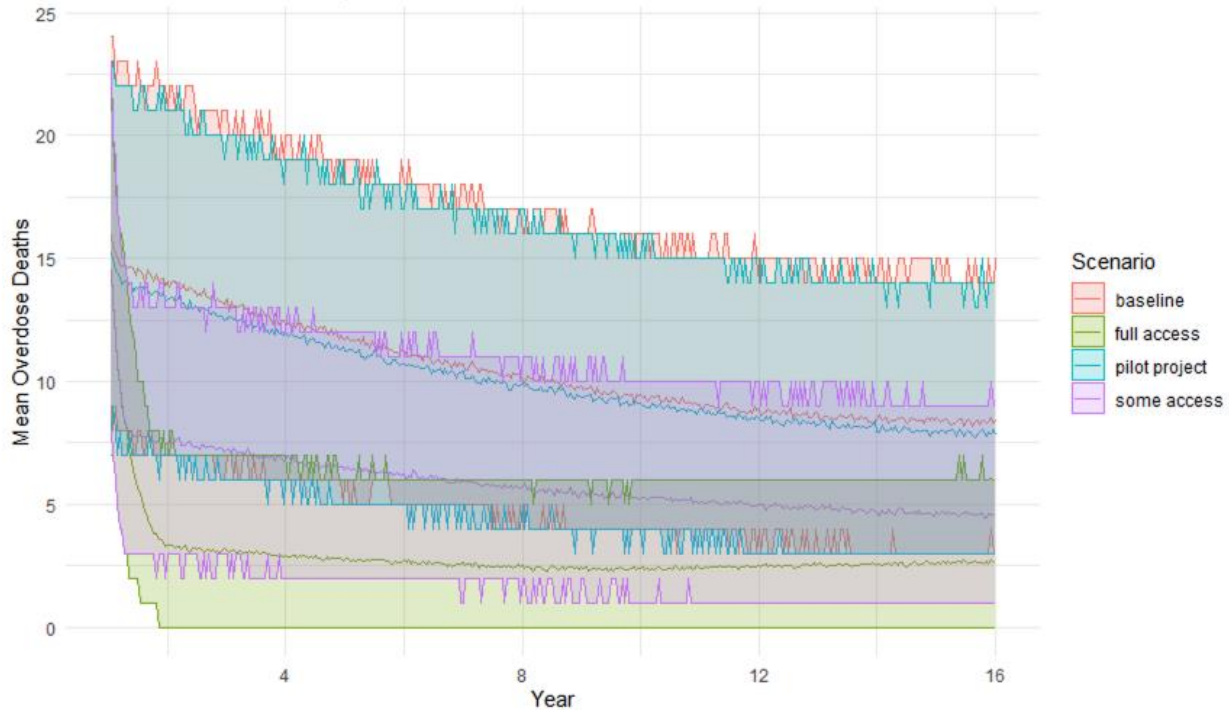


Figure 3. The impact of different levels of access on the population level impact on mean overdose death per time step of the different models.

Increasing initiation rate analysis:

Figure 4 presents the threshold analysis, demonstrating the impact of increasing the number of people who initiate injecting opioids, initiation rate, on the overdose mortality rate of different safe supply interventions in reducing overdose deaths. The x-axis represents the initiation rate, while the y-axis shows the corresponding number of overdose deaths. Each line represents a different intervention scenario, with the reference scenario fixed at an initiation rate of 0.001 (meaning on average an additional 130 new PWID per year). The analysis reveals that as the initiation rate increases, the number of overdose deaths for each intervention scenario gradually rises. The initiation rate would need to increase approximately three-fold for the prescribed unsupervised, and community-based models to return to reference. For the prescribed supervised scenario, the initiation rate would need to increase five times to return to the reference scenario.

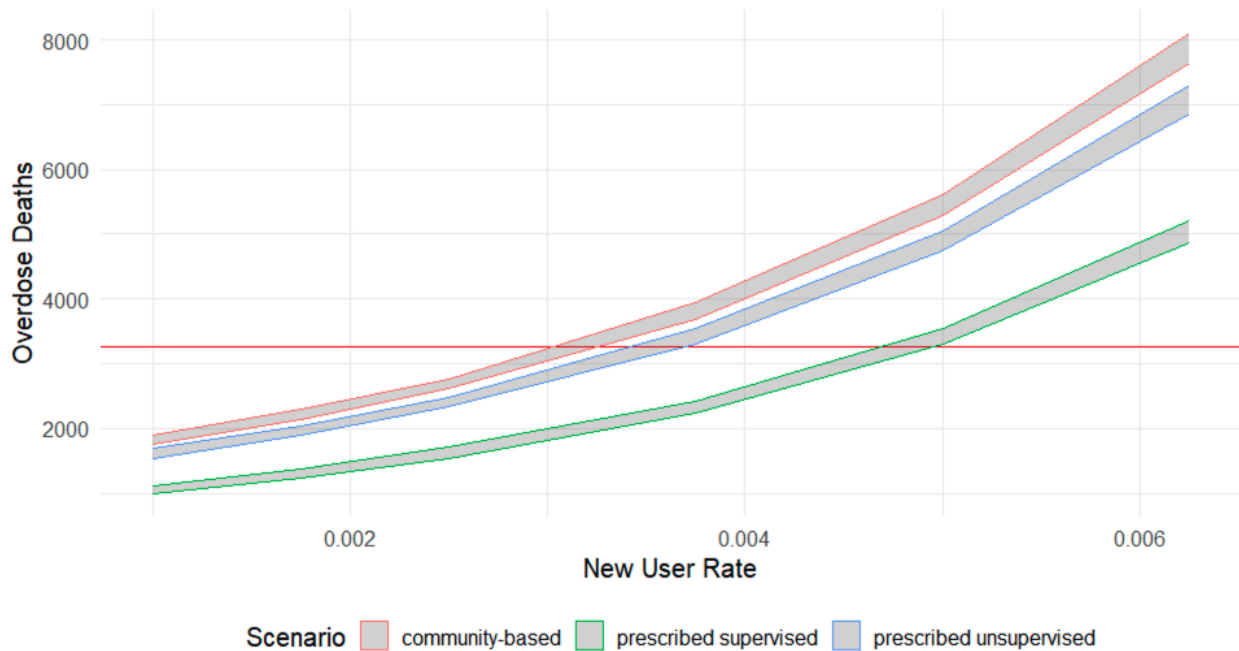


Figure 4. Threshold analysis of increasing the initiation rate of new people who inject drugs to reverse the effects of implementing safe supply.

Discussion:

In this study, we found that implementing safe supply in several modeled scenarios could significantly reduce the number of overdose deaths in Seattle, Washington. Moreover, we found that the number of MOUD initiations would increase in safe supply scenarios compared to the reference scenario including the community-based scenario. The results that the safe supply models resulted in less deaths and more MOUD initiations were to be expected based on how the model was parameterized. The results demonstrate that it is plausible the safe supply interventions could have an impact at a population level if scaled sufficiently.

The results from the model align with previous evidence. The idea that providing people with an alternative to the unregulated drug market can be transformative for individuals accessing the programs is well-supported by the literature (30). There is substantial qualitative evidence indicating that people are much less likely to overdose and experience greater stability in their

lives when provided with regulated substances (31). This increased stability is an important outcome of social interest, although it was not explicitly modeled, we argue that the effect is captured in the measures of safe supply reduction on overdose death from the literature. Figure 3 shows a reduction in overdose deaths over a 15-year period when safe supply is implemented. This scenario, characterized by the provision of safe, regulated substances to people who inject opioids, leads to a significant decrease in mortality rates, highlighting the potential of such interventions to mitigate the ongoing overdose crisis effectively.

We also found that there would be limited impact from a small pilot projects on a population level. While these projects may demonstrate local success and individual benefits, their scale is insufficient to produce noticeable reductions in overall overdose deaths. This finding underscores the necessity of scaling up safe supply interventions to achieve broader public health improvements. The lack of a significant population-level impact from pilot projects aligns with findings from other studies, such as the difference-in-difference analysis conducted in British Columbia (32). Despite critiques of the methodologies (33) in the Nguyen et al. 2024 study (32), the conclusion remains consistent: limited access to safer supply programs cannot significantly alter population-level overdose mortality rates.

One of the critical aspects explored in this study is the potential for diversion of safe supply and the introduction of new people who inject drugs. Diversion, the redirection of prescribed drugs for non-prescribed use, is a significant concern with safe supply models. Critics argue that increased availability of regulated opioids could lead to higher rates of drug misuse and an increase in new people using drugs who would have otherwise never used drugs. Our modeling

considered these potential outcomes, incorporating scenarios where diversion rates and new PWID were higher. Despite these considerations, the models showed a net benefit in terms of reduced overdose deaths, suggesting that the controlled provision of opioids could mitigate more harm than it potentially causes. This finding challenges common arguments that safe supply would lead to higher rates of drug use and associated harms (9). Instead, it reinforces the argument that the benefits of safe supply in reducing overdose deaths outweigh the risks of potential increases in new people using drugs because of the program. Furthermore, researchers have found positive benefits of diversion such as reduced overdose for those who access them; however, these benefits were not modelled in this study and only some negative consequences of diversion were incorporated into the model (34,35). Therefore, the threshold for diversion to be harmful at a population level is likely higher than estimated in this study.

This study has limitations. First, it is based on a sample that may not be representative of everyone who injects opioids, especially those who are affluent and less likely to participate in scientific research as well as marginalized individuals who do not trust scientists. Moreover, we modelled a population of PWID, which is a limitation as most people who use drugs at risk of overdose do not inject their drugs, but the trade-off is that the number of PWID is much better defined than the number at risk of general opioid overdose. However, the mechanism of action of safe supply suggests that the reduction in overdose deaths is potentially generalizable to PWID not included in the study and people who use opioids who do not inject. Another shortcoming of this study is that we did not directly model problematic use of opioids and instead focusing on mortality from opioid overdoses. Future research should be conducted to investigate how the burden of opioid use disorder might change in the population under different modeled scenarios.

Examining the impact on the burden of opioid use disorder would be beneficial to health planners and policy makers. Additionally, modeling work that cross-validates these findings in other systems would help support the robustness of the results and serve as an empirical example for cross-multi-model validation. We assumed fixed rates of baseline overdose risk over the study period, which is likely to not hold as well as fixed rates of several parameters that are dynamic. However, since these parameters are fixed across all scenarios, we can still compare the difference in magnitude between the different scenarios.

Overall, we found that implementing safe supply in numerous scenarios would greatly reduce the number of people dying of opioid overdoses in Seattle. The impact of implementing these models at scale on other health outcomes, social issues, and public safety still needs to be carefully examined. However, the evidence strongly supports the effectiveness of safe supply interventions in reducing overdose deaths and highlights the importance of expanding access to these programs to achieve significant public health benefits.

References:

1. Ciccarone D. The triple wave epidemic: supply and demand drivers of the US opioid overdose crisis. *International Journal of Drug Policy*. 2019 Sep 1;71:183-8.
2. Drug Overdose Deaths | Drug Overdose | CDC Injury Center [Internet]. 2024 [cited 2024 Aug 12]. Available from: <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>
3. Donroe JH, Socias ME, Marshall BDL. The Deepening Opioid Crisis in North America: Historical Context and Current Solutions. *Curr Addict Rep*. 2018 Dec 1;5(4):454–63.
4. Cerdá M, Krawczyk N, Keyes K. The Future of the United States Overdose Crisis: Challenges and Opportunities. *Milbank Q*. 2023 Feb 22;
5. Ivsins A, Boyd J, Beletsky L, McNeil R. Tackling the overdose crisis: The role of safe supply. *Int J Drug Policy*. 2020 Jun 1;80:102769.
6. Ledlie S, Garg R, Cheng C, Kolla G, Antoniou T, Bouck Z, et al. Prescribed safer opioid supply: A scoping review of the evidence. *Int J Drug Policy*. 2024 Mar 1;125:104339.
7. Kalicum J, Nyx E, Kennedy MC, Kerr T. The impact of an unsanctioned compassion club on non-fatal overdose. *Int J Drug Policy*. 2024 Feb 22;104330.
8. Slaunwhite A, Min JE, Palis H, Urbanoski K, Pauly B, Barker B, et al. Effect of Risk Mitigation Guidance opioid and stimulant dispensations on mortality and acute care visits during dual public health emergencies: retrospective cohort study. *BMJ*. 2024 Jan 11;384:e076336.
9. Michaud L, Kolla G, Rudzinski K, Guta A. Mapping a moral panic: News media narratives and medical expertise in public debates on safer supply, diversion, and youth drug use in Canada. *Int J Drug Policy*. 2024 May 1;127:104423.

10. Bonn M, Palayew A, Touesnard N, Brothers TD, Bodkin C. Safe Supply in the Midst of a Crisis of Unregulated Toxic Drug Deaths—A Commentary on Roberts and Humphreys (2023). *J Stud Alcohol Drugs*. 2023 Jul;84(4):648–50.
11. Kleinman RA, Morris NP. Federal Barriers to Addressing the Opioid Epidemic. *J Gen Intern Med*. 2020 Apr;35(4):1304–6.
12. Overdose deaths - King County [Internet]. [cited 2021 Nov 3]. Available from: <https://kingcounty.gov/depts/health/examiner/services/reports-data/overdose.aspx>
13. Eger WH, Abramovitz D, Bazzi AR, Bórquez A, Vera CF, Harvey-Vera A, et al. Changes in injecting versus smoking heroin, fentanyl, and methamphetamine among people who inject drugs in San Diego, California, 2020–2023. *Drug Alcohol Depend*. 2024 Jun 1;259:111318.
14. Kral AH, Lambdin BH, Browne EN, Wenger LD, Bluthenthal RN, Zibbell JE, et al. Transition from injecting opioids to smoking fentanyl in San Francisco, California. *Drug Alcohol Depend*. 2021 Oct 1;227:109003.
15. Lash TL, VanderWeele TJ, Haneause S, Rothman K. *Modern Epidemiology*. Lippincott Williams & Wilkins; 2020. 1340 p.
16. Krijkamp EM, Alarid-Escudero F, Enns EA, Jalal HJ, Hunink MGM, Pechlivanoglou P. Microsimulation modeling for health decision sciences using R: a tutorial. *Med Decis Mak Int J Soc Med Decis Mak*. 2018 Apr;38(3):400–22.
17. Macmadu A, Adams JW, Bessey SE, Brinkley-Rubinstein L, Martin RA, Clarke JG, et al. Optimizing the impact of medications for opioid use disorder at release from prison and jail settings: A microsimulation modeling study. *Int J Drug Policy*. 2021 May;91:102841.

18. R: A language and environment for statistical computing [Internet]. [cited 2021 Sep 26]. Available from:
https://scholar.google.com/citations?view_op=view_citation&hl=en&user=yvS1QUEAAAAJ&citation_for_view=yvS1QUEAAAAJ:t6usbXjVLHcC
19. Klimas J, Hamilton MA, Gorfinkel L, Adam A, Cullen W, Wood E. Retention in opioid agonist treatment: a rapid review and meta-analysis comparing observational studies and randomized controlled trials. *Syst Rev*. 2021 Aug 6;10(1):216.
20. Min JE, Guerra-Alejos BC, Yan R, Palis H, Barker B, Urbanoski K, et al. Opioid Coprescription Through Risk Mitigation Guidance and Opioid Agonist Treatment Receipt. *JAMA Netw Open*. 2024 May 15;7(5):e2411389.
21. Santo T, Clark B, Hickman M, Grebely J, Campbell G, Sordo L, et al. Association of Opioid Agonist Treatment With All-Cause Mortality and Specific Causes of Death Among People With Opioid Dependence: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2021 Sep 1;78(9):979–93.
22. National Survey on Drug Use and Health [Internet]. [cited 2023 Apr 27]. Available from:
<https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health>
23. Results from the 2023 WA State Syringe Services Program Health Survey [Internet]. Addictions, Drug & Alcohol Institute. [cited 2024 Jun 10]. Available from:
<https://adai.uw.edu/syringe-survey-2023/>
24. Results from the 2021 WA State Syringe Service Program Health Survey [Internet]. Addictions, Drug & Alcohol Institute. [cited 2024 May 5]. Available from:
<https://adai.uw.edu/syringe-survey-2021/>

25. Salekešin M, Vorobjov S, Des Jarlais D, Uusküla A. Mortality among people who inject drugs – the interwoven roles of fentanyl and HIV: a community-based cohort study. *Eur J Public Health*. 2023 Dec 1;ckad204.
26. McNair R, Monaghan M, Montgomery P. Heroin assisted treatment for key health outcomes in people with chronic heroin addictions: A context-focused systematic review. *Drug Alcohol Depend*. 2023 Jun 1;247:109869.
27. Selfridge M, Card K, Kandler T, Flanagan E, Lerhe E, Heaslip A, et al. Factors associated with 60-day adherence to “safer supply” opioids prescribed under British Columbia’s interim clinical guidance for health care providers to support people who use drugs during COVID-19 and the ongoing overdose emergency. *Int J Drug Policy*. 2022 Jul 1;105:103709.
28. Helton JC, Davis FJ. Latin hypercube sampling and the propagation of uncertainty in analyses of complex systems. *Reliab Eng Syst Saf*. 2003 Jul 1;81(1):23–69.
29. Oliva R. Model calibration as a testing strategy for system dynamics models. *Eur J Oper Res*. 2003 Dec 16;151(3):552–68.
30. McCall J, Hobbs H, Ranger C, Cameron F, Stuart H, Nelken J, et al. Prescribed safer supply during dual public health emergencies: a qualitative study examining service providers perspectives on early implementation. *Subst Abuse Treat Prev Policy*. 2024 Mar 5;19(1):19.
31. Henderson N, Marris J, Woodend K. “And this is the life jacket, the lifeline they’ve been wanting”: Participant perspectives on navigating challenges and successes of prescribed safer supply. *PLOS ONE*. 2024 Mar 22;19(3):e0299801.
32. Nguyen HV, Mital S, Bugden S, McGinty EE. British Columbia’s Safer Opioid Supply Policy and Opioid Outcomes. *JAMA Intern Med* [Internet]. 2024 Jan 16 [cited 2024 Jan 25]; Available from: <https://doi.org/10.1001/jamainternmed.2023.7570>

33. Nosyk B, Slaunwhite A, Urbanoski K. Examining Safer Opioid Supply Policies. JAMA Intern Med [Internet]. 2024 May 6 [cited 2024 Jun 5]; Available from: <https://doi.org/10.1001/jamainternmed.2024.1211>
34. Socias ME, Grant C, Hayashi K, Bardwell G, Kennedy MC, Milloy MJ, et al. The use of diverted pharmaceutical opioids is associated with reduced risk of fentanyl exposure among people using unregulated drugs in Vancouver, Canada. Drug Alcohol Depend. 2021 Nov 1;228:109109.
35. Bardwell G, Small W, Lavalley J, McNeil R, Kerr T. “People need them or else they’re going to take fentanyl and die”: A qualitative study examining the ‘problem’ of prescription opioid diversion during an overdose epidemic. Soc Sci Med. 2021 Jun 1;279:113986.

Appendix:

Supplemental Table 1. Calibration targets for overdose deaths and number of people on medications for opioid use disorder. Microsimulations parameters were calibrated for the reference scenario to match the following numbers for the first four years of the simulation.

Calibration Target	Overdose Deaths	Number on MOUD
2019	300	1100
2020	450	1100
2021	500	1000
2022	600	1000

CONCLUSION

The work presented in this dissertation provides the opportunity to understand the number of PWID in Seattle, the potential interest in different models of regulated opioids in Seattle and modelling the potential impact of these interventions among PWID.

Key findings include:

- There has likely been a large decrease in the number of PWID in Seattle compared to 10 years ago.
- There is interest in several models of regulated opioids and individuals who were interested in accessing regulated opioids expected that it would greatly reduce their risk of overdose compared to their current supply.
- Microsimulation modelling suggests that implementing safe supply can reduce overdose deaths. However, limited pilot projects or smaller scale implementations of safe supply are not expected to have a population level impact on the overdose mortality rate.

Next Steps:

- Chapter 2 will be submitted for academic publication.
- Chapter 3 will be submitted for academic publication as well as have more detailed information around the assumptions of the RDS.
- Chapter 4 will be submitted for academic publication after careful reframing of the results and narrative of the manuscript in collaboration with co-authors. Changes that will be considered are alternative visualizations of the results, displaying simulations over

time periods that are more relevant to policy makers, and any other potential changes to the manuscript that may be raised by co-authors.