

LETTERS IN BIOMATHEMATICS An International Journal



RESEARCH ARTICLE

∂ OPEN ACCESS

A Mathematical Approach to the Analysis of Harm Reduction Efforts in the Opioid Crisis

Hala K. King^a, Mira Terdiman^b, Ami Radunskaya^b

^aSchool of Mathematical and Natural Sciences, Arizona State University, AZ; ^bDepartment of Mathematics and Statistics, Pomona College, Claremont, CA

ABSTRACT

Opioid addiction in the United States is a national crisis. Various harm reduction strategies have been proposed, including safe injection sites, whose goals are to reduce deaths and improve the health of addicts. Many of these proposed strategies are controversial because their impact is unknown. In this paper we present a discrete time Markov model that captures essential probabilities in the description of the U.S. opioid epidemic, while remaining tractable to analysis. We use the model to analyze the impact of an overdose prevention site and other harm reduction strategies on the number of fatal overdoses and recovery rates, and make quantitative predictions about the consequences of implementing specific policies.

ARTICLE HISTORY

Received June 30, 2023 Accepted September 22, 2023

KEYWORDS

Markov chain, mathematical model, opioid epidemic, optimal resource allocation

1 Introduction

Opioid addiction has become a global pandemic and a national crisis that affects both rural and densely populated areas, tangled with social and political issues that have affected its conception and unsettling growth. The opioid crisis has also resulted in a huge health care expense, criminal justice costs, and income losses. It has been estimated that 4 out of 5 new heroin users have abused painkiller prescriptions: the ease of getting opioid prescriptions and the misconceptions about their addictive nature make this pandemic an extremely difficult one to tackle (Jones, 2013). The available literature suggests that about 90% of those entering treatment relapse during the first year in recovery and close to 70% of recovering heroin addicts relapse one month after treatment ends (Smyth et al., 2010). In response to this public health emergency, several opioid related policies have been implemented by state and federal agencies in the United States to curb prescription drug abuse. On the one hand, making prescriptions of opioids more difficult to obtain should decrease the rate of new users of both prescribed and illicit opioids. On the other hand, proposed reforms in the criminal justice system such as making treatments like take-home naloxone kits (THN) available for everyone, and not only those who can afford it, can reduce the harm done to individuals who are already using opioids. Finally, providing social services such as housing and employment can increase positive outcomes and recovery.

Opioid addiction and overdose rates are reaching unprecedented levels in the United States. Data from the Center for Disease Control (CDC) National Center for Health Statistics indicate there were an estimated 107,622 drug overdose deaths in the United States during 2021, an increase of nearly 15% from the 93,655 deaths estimated in 2020. Data show overdose deaths involving opioids increased from an estimated 70,029 in 2020 to 80,816 in 2021. Provisional data shows there were 105,452 drug overdose deaths in 2022 with the biggest percentage increase in overdose deaths occurring in Washington and Wyoming where deaths were up 22%.

Mathematical models of opioid use include epidemiological models that describe the pandemic as a compartment model with a susceptible population that can be infected, and then either die or recover (see, for example, White and Comisky, 2007; Battista et al., 2019). The conclusions from these models are that the disease-free equilibrium (the state where there are no more opioid users) is unstable: a small number of users will cause the epidemic to grow. This means that, at least in the current state of the world, opioid use is inevitable. The goal of the current study is to quantitatively explore the effect of harm reduction policies on outcomes. In particular, we look at the controversial proposal to create safer places for users to take drugs.

Research has shown that supervised drug consumption sites or Overdose Prevention Sites (OPS) in Canada, Australia and some European countries have saved lives and resulted in people seeking recovery through treatment. Instead of marginalizing these individuals and criminalizing their drug use, such sites provide a safe clean environment in which users bring their own

drugs to use in the presence of trained professionals. These sites have faced solid opposition in the US. For example, in October 2021 the US Supreme Court let stand a lower court ruling that a planned Philadelphia safe site was illegal under a federal law against running a venue for illicit drug use. There are a couple of supervised drug consumption sites in New York and recently Rhode Island has legalized their use. The governor of California, a state with roughly 2.7 million users addicted to opioids, has vetoed a bill that would have allowed some California cities to operate such sites. In an article in The American Journal of Preventive Medicine, the authors reviewed 22 studies (16 focused on one safe injection site in Vancouver, Canada) and concluded that "for people who use drugs, supervised injection facilities might reduce the risk of overdose morbidity and mortality and improve access to care while not increasing crime or public nuisance to surrounding community" (Levengood et al., 1973).

In Section 2, we review previous mathematical models of the opioid epidemic. These models have been proposed to analyze the dynamics of the opioid crisis and to propose strategies to help control it. The majority of these models are continuous in time, i.e. a system of differential equations with fixed parameters, representing the average behavior in a population.

In Section 3, we modify the model from Wares et al. (2021) to formulate a discrete time Markov model that captures essential probabilities in the description of the opioid epidemic. With this model we can analyze the impact of an OPS and other harm reduction strategies on the number of fatal overdoses and recovery rates. We suggest that this type of model, which can be readily calibrated to specific geographic and demographic data, can be useful in supporting the implementation of Harm Reduction policies. We present some analysis of the model in Section 4 and conclude with a discussion of possible implications.

2 Background

Sharareh et al. (2019) conducted a broad review of 472 papers published after 2000 describing mathematical models of the opioid epidemic, and ended up with 14 articles appropriate for inclusion in their study, "five of which used system dynamics modeling, three used mathematical modeling, five used conceptual modeling and one used agent-based modeling." Most articles focus on overdoses from prescription opioids or heroin separately, without including the transition from prescription opioids to heroin, a transition that has a significant impact on the epidemic. One of the authors' key findings is that prevention of opioid initiation is much easier than treating opioid addiction.

Differential equations similar to those in the SIR model for the spread of infectious diseases were used by White and Comisky (2007) to describe the heroin pandemic mathematically. The authors' conclusion was that preventing people from becoming opioid users is more effective than focusing on treatment strategies as there is always a relapse in treatment. Battista et al. (2019) formulated and analyzed an SIR-inspired model based on that of White and Comisky (2007) who investigated broad trends in prescription opioid addiction. The authors set up four continuous differential equations relating 4 groups: those who are not using opioids or actively recovering from addiction (S), those who are prescribed opioids but are not addicted to them (P), those who are addicted opioid users (A), and those who are in treatment for their addiction (R). The model assumes a constant population. The authors show that, according to the model, over-prescribing is the primary cause for opioid addiction and indicate that increasing the motivation for drug addicts to start treatment will help combat the epidemic. Befekadu and Zhu (2019) consider optimal control of an SIR compartmental model for opioid dynamics where a random perturbation enters through the dynamics of the susceptible group. Rafiq et al. (2019) describe a stochastic version of the SIR heroin epidemic model and present a numerical analysis of this model, including specific schemes for its solution. They conclude that, under some parameter sets, these numerical schemes lead to an explicit solution of the stochastic model.

Markov chains have also been used to study opioid addiction. For example, Irvine et al. (2019) constructed a Markov model including opioid-related deaths, fentanyl-related deaths, ambulance-attended overdoses and uses of take-home naloxone (THN) kits in British Columbia. The model was calibrated in a Bayesian framework, and the authors sought to estimate the impact of THN in terms of numbers of avoided deaths. Three states were considered: those at risk of overdose, those not at risk of overdose, and those who recently relapsed into illicit drug use and thus are at increased risk from both fentanyl and non-fentanyl overdose. The number of people in each category was fixed, the effect of the weather on the probability of death following an overdose was included, and the proportion of opioid users exposed monthly to a substantial amount of fentanyl in the illegal drug supply was modeled appropriately. The authors concluded that a combination of THN, treatment, and harm reduction approaches might reduce the number of overdoses and deaths.

A somewhat different approach was used by Pitt et al. (2018) who constructed an exhaustive compartmental model by dividing the population of people in the US 12 years or older into 12 compartments according to pain status, opioid use status, and addiction status. Individuals were allowed to flow from one compartment to the other according to parameters describing the dynamics of opioid prescriptions and addiction. The authors considered 11 interventions aiming to limit opioid addiction and overdose deaths and evaluated the 5- and 10-year interventions on each outcome measure. Increasing the availability of naloxone resulted in the largest reduction in addiction deaths among the 11 interventions, with a 4 percent reduction.

3 Model Description

Our model is a discrete Markov chain, a modification of a model built to study the impact of safe-injection sites in Philadelphia, Pennsylvania (Wares et al., 2021). That study developed a discrete, stochastic model to understand the impact of a safe-injection facility on overdoses, fatalities, and treatment/recovery. The model takes into account the effects of proximity to the facility by dividing the city of Philadelphia into twelve regions, depending on their distance to the proposed site. Since users in each region could be in six possible compartments, this resulted in a model with 72 discrete states. Another aspect of the model described by Wares et al. (2021) is that the probability of visiting the overdose prevention site depends on how many people are currently using it, and so the model is not given as a Markov chain. In this paper, we modify the model of Wares et al. (2021) in two ways. To make it Markovian, we use the expected number of users at the site in calculating the probability of visiting it. In addition, since our goal is to build a more general, analytically tractable model, we consider only one geographic region.

We propose a model of opioid use that is an absorbing Markov chain on six states, where an opioid user can be in any one of the states. In what follows we use OPS to designate the state of being in an "Overdose Prevention Site." Note that some literature uses the term "Safe Injection Facility" (SIF)—these are the same type of harm reduction strategy. An OPS or a SIF is a location where an individual can use drugs in a clean, safe environment, with personnel on hand to administer life-saving interventions in the case of an overdose. In terms of the model, the OPS might also provide drug screening, counseling, or other support. Our goal is to quantify the effects of these harm reduction strategies in order to provide data to inform policy decisions.

Model Assumptions: We assume that the probability of a fatal overdose while in the OPS is zero, which is consistent with data gathered from existing sites (Ng et al., 2017). We also assume that individuals are willing to use an OPS if one is relatively close and has available spots, that all individuals have equal access to the OPS, and that individuals using opioids can exist in only one of the six states, described below, in any given time step (Behrends et al., 2019). In the current implementation, a time step is one half hour, which is an estimate of the amount of time someone would spend in the OPS (Kral and Davidson, 2017).

Description of the states and possible transitions between the six states: The following six states and the possible transitions are illustrated in Figure 1.

- State 1: "User" Users not currently using drugs. In each time step, users can decide to stay in "currently not using" state, or to use drugs at the next time step. If they decide to use drugs, they may choose to do so in the OPS (State 3) or not in the OPS (State 2). They may also choose to go to recovery (State 4).
- State 2: "Using" Using drugs outside the OPS. Outside of the OPS, a person using drugs might overdose fatally (State 6) or non fatally (State 5). If they don't overdose they can transition to recovery (State 4) or to being a user not currently using drugs (State 1). We assume that a user waits at least one half hour between drug uses, so they cannot go from State 2 back to State 2.
- State 3:"OPS" Using drugs in the OPS. Since we assume that no fatal overdoses occur in the OPS, users in the OPS can transition to the non -fatal overdose state (State 5), the recovery state (State 4) or back to being a "user currently not using drugs" (State 1).
- State 4: "Rec" Recovery. The Recovery state represents those users undergoing treatment, and not currently using drugs. A person in the recovery state can stay in the recovery state (State 4) or decide to use opioids again and move to user state (State 1). We assume that it takes a least a half hour to actually use drugs once this decision is made, so we do not allow a transition from State 4 (Recovery) to States 2 or 3 (Using in or outside the OPS).
- State 5: "OD-nonfatal" Non-fatal overdose. Users in this state do not die from an overdose, and can thus can go back to being a user (State 1) or decide to go to recovery (State 4).
- State 6: "OD-fatal" Fatal overdose. Users in this state stay in this state. This is the only absorbing state in the Markov chain.

Our Markov Chain model is then defined by its transition probabilities between these six states, where the probability of a transition from one state to another depends only on the current state. We use probabilities based on estimates for the model described by Wares et al. (2021), as well as probabilities taken from the literature. Estimates of yearly transition probabilities were converted to half-hour transition probabilities under the assumption that the choice of moving from one state to another is independent of previous choices. For example, the probability of moving from the "using" state to the "recovery" state in a given half-hour is independent of how long the individual has been in that state. This assumption is probably not realistic, but we use it as a starting point to understand average behavior over a population, and over a relatively long period of time. The advantage of using a Markov Chain model is that we can analyze long term behavior easily by iterating the Markov model. This

167

is discussed in Section 4. In Table 1 we summarize our estimates of the transition probabilities, along with the sources of the data used to compute these probabilities.

The transition matrix, then, is given by P, where P_{ij} is the probability of transitioning from state *i* to state *j* in a given halfhour. Probabilities not listed in Table 1 can be filled in using the fact that the entries in each row must sum to one. In order to examine the effect of varying the transition probabilities via interventions, or the dependence of probabilities on location or demographics, we write the transition matrix symbolically:

			User	Using	OD-nonfatal	OPS	Rec	OD-fatal	
		User	1 - (u + s)	u - x	0	x	S	0	
		Using	1 - (n + s + f)	0	п	0	S	f	
Р	=	OD-nonfatal	1-r	0	0	0	r	0	(1)
		OPS	1 - (y + n)	0	п	0	у	0	
		Rec	v	0	0	0	1 - v	0	
		OD-fatal	0	0	0	0	0	1	

where the variables are defined as follows (and in Table 1):

$u = \text{User} \mapsto \text{Using}$ (assuming no OPS),	$x = \text{User} \mapsto \text{OPS},$
$n = \text{Using or OPS} \mapsto \text{Nonfatal overdose},$	$f = \text{Using} \mapsto \text{Fatal overdose (OD-fatal)},$
$r = \text{Nonfatal overdose (OD-nonfatal)} \mapsto \text{Recovery,}$	$s = $ User or Using \mapsto Recovery,
$y = OPS \mapsto Recovery,$	$v = $ Recovery \mapsto User.

The parameters *x* and *y* are those that are most related to health outcomes which are affected by the availability of the OPS. The parameter *x*, the probability of a user entering the OPS, is a function of both the users' willingness to go and the capacity of the OPS. We assume that a user is more likely to go to the OPS if it is close by and welcoming. Our estimate of the probability that a user will head to the OPS (0.168), comes from data from Behrends et al. (2019), but is a rough approximation that would, in reality, depend on many local factors. For example, in a survey of drug users in San Francisco, 85 percent of people interviewed said that they would use an OPS (Gordon, 2018), so this probability could vary a great deal.

Once a user decides to go to the OPS, their likelihood of getting in depends on the capacity and the expected number of other users that are trying to get in. So, for example, having multiple overdose prevention sites in a city would increase both the willingness of a user to go to one, because there would be one nearby, and it would also increase the probability that there would be space available.

We calculate x, the probability of a transition from the "User" state to the "OPS" state as the product of three probabilities:

- the probability of using in that time step, either in or out of an OPS, given by the variable *u*;
- the probability that a user, once they have decided to use drugs, will want to go the OPS;
- the probability that a user who has decided to go to the OPS actually gets into the OPS (i.e. the probability that the OPS is not full).

Thus

 $x = Prob using per time-step \times Prob user wants to go to OPS \times \frac{Capacity}{Exp number of users at OPS}$

where Capacity \leq Exp number of users at OPS. We note that the expected number of users is a constant over the simulation time. It is calculated as the total number of users, multiplied by the probability that a user who is using drugs is willing to go to the OPS.

Transition Probabilities – Capacity Equal to Demand As an example, we use the values in Table 1 and assume that everyone who is willing to go to an OPS is able to get in (i.e., the capacity is equal to the expected number of users). This gives the transition matrix below:

			User	Using	OD-nonfatal	OPS	Rec	OD-fatal
		User	9.1666×10^{-1}	6.933×10^{-2}	0	1.4×10^{-2}	9.28×10^{-6}	0
		Using	9.98261×10^{-1}	0	1.3×10^{-3}	0	9.28×10^{-6}	4.3×10^{-4}
P	=	OD-nonfatal	$9.9999399 imes 10^{-1}$	0	0	0	6.01×10^{-6}	0
		OPS	$9.986648 imes 10^{-1}$	0	1.3×10^{-2}	0	3.52×10^{-5}	0
		Rec	3.96×10^{-5}	0	0	0	9.9996×10^{-1}	0
		OD-fatal	0	0	0	0	0	1

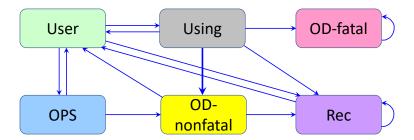


Figure 1: Diagram indicating the possible transitions between the six states. The state "User" indicates a user who is not currently using drugs; the state "OPS" stands for users at the overdose prevention site; the states "OD-fatal" and "OD-nonfatal" represents fatal and non-fatal overdoses, respectively; the state "Rec" indicates users who are in treatment or recovery, and so they are not using drugs.

Probability	Value	Variable	Source & Notes			
User → Using (assuming no OPS)	8.333×10^{-2}	и	Recovery in Tune, 2023; Ross et al., 2002 This assumes on average four uses a day. Opioid use varies quite a bit between individuals and over time: we consider an average of 4 uses per day a conservative estimate.			
$User \mapsto OPS$	0 to 1.4×10^{-2}	x	Behrends et al., 2019 Depends on the OPS capacity: further explained in text.			
$User \mapsto Rec$	9.28×10^{-6}	S	Addiction Center, 2023; Larochelle, 2018 We assume that 15% of users seek treatment per year.			
Using → OD-nonfatal	1.331×10^{-3}	п	Kerr et al., 2006 We assume an average of 1.33 overdoses per 1000 injections.			
Using \mapsto Rec	9.28×10^{-6}	S	Addiction Center, 2023; Larochelle, 2018 We assume that 15% of users seek treatment per year.			
Using → OD-fatal	4.3×10^{-4}	f	Florida Department of Health, 2023 We assume that one fourth of overdoses, on average, are fatal without intervention.			
OD-nonfatal ↔ Rec	6.01×10^{-6}	r	Alta Mira, 2023; Wares et al., 2021 We assume that per year 10% of users who overdose, but don't die, decide to seek treatment.			
$OPS \mapsto Rec$	3.52×10^{-5}	у	Alta Mira, 2023; Wares et al., 2021 We assume that per year 46% of users who enter an OPS seek treatment.			
OPS → OD-nonfatal 1.331 × 10 ⁻		n	Kerr et al., 2006 Assuming the same overdose rate in and out of the OPS, but that no fatal overdoses occur in the OPS. The overdose rate may, in fact, be smaller since drugs might be screened.			
$\operatorname{Rec} \mapsto \operatorname{User}$	3.96×10^{-5}	v	Alta Mira, 2023 We assume a yearly relapse rate of 50%.			

Table 1: Transition probabilities and their sources.

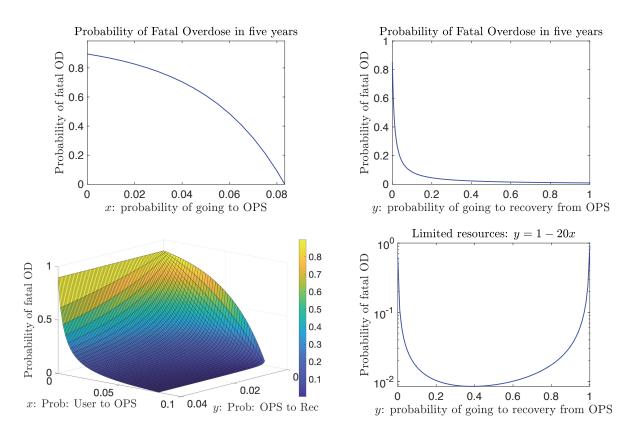


Figure 2: The probability of a fatal overdose in five years as a function of *x* (the probability of going to the OPS) and *y* (the probability of entering the recovery state from the OPS). Upper left panel: $y = 3.5 \times 10^{-5}$; upper right panel: x = 0.014: maximum capacity. We see that fatal overdoses are a decreasing function of both *x* and *y*, with the most dramatic effects occurring when both are increased. This indicates that education efforts at the OPS will have the most positive effects on reducing fatal overdoses when the OPS is operating at high capacity. In the lower right panel we see that, with limited resources, spending on both *x* and *y* in moderate amounts results in the lowest probability of overdose.

4 Analysis and Results

What are the implications of this model? If we consider the five-year transition probabilities, which corresponds to 87,600 iterations of the model, we obtain the transition matrix $P^{87,600}$ shown below. This shows that, with the assumption of one OPS with capacity 30, and an estimated 55,000 users (a conservative estimate for Philadelphia), the probability of a typical user fatally overdosing in five years is close to 90 percent (see last column in Equation (2), emphasized in red). Since opioid use decreases life expectancy by 45 to 50 years (World Health Organization, 2023; Shoreline Recovery Center, 2023), this estimate highlights the urgent need for harm reduction strategies.

$$P_{5 \text{ yr}} = P^{87600} = \begin{array}{cccccc} User & Using & OD-nonfatal & OPS & Rec & OD-fatal \\ User & Using & 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00004 & 0.035 & 0.894 \\ 0.066 & 0.005 & 0.00001 & 0.00001 & 0.082 & 0.770 \\ 0D-fatal & 0 & 0 & 0 & 0 & 1 \end{array}$$

We can quantitatively explore the effect of the two harm-reduction parameters, x (probability of a user entering an OPS) and y (probability of a user at the OPS entering recovery) by plotting the probability of a fatal overdose in five years against these two variables. This is shown in Figure 2. To generate this figure, we set the values of u, f, r, n, s and v as in Table 1, and vary x and y. For each value of x and y, we estimate the probability of fatally overdosing as the (1, 6) entry in $P^{87,600}$.

The variable *x* depends on both the individual's willingness to go to the OPS and the availability of a spot once they arrive at the facility. Thus, we can increase *x* by making the OPS more attractive in terms of location, lack of stigma and welcoming

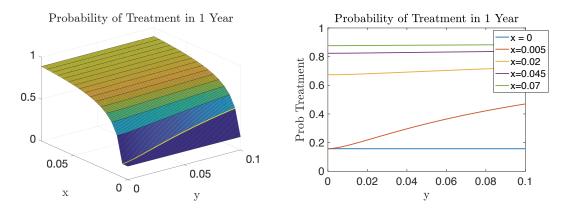


Figure 3: The probability of entering treatment in one year as a function of *x* (the probability of visiting the OPS) and *y* (the probability of entering the recovery state from the OPS). On the left, the cross-section at x = 0.005 is highlighted, showing the most dramatic increase in treatment as a function of *y*, which can be interpreted as education efforts at the OPS.

atmosphere, or we can increase x by increasing the capacity of the OPS. The variable y represents the probability that an individual, once they are at the OPS, enters treatment. We can interpret increasing y as putting more resources into education and communication with individuals who choose to enter the facility. Figure 2 shows that the probability of fatally overdosing decreases as x (probability of going to the OPS) and y (probability of getting treatment in OPS) increase. We see the most dramatic decrease in fatal overdoses when both x and y increase. This makes sense, since interventions at the OPS prevent fatal overdoses and increase the likelihood of treatment. A user in recovery is a user who is not doing drugs.

Any intervention that either increases the probability of going to an OPS or increases the probability of entering treatment requires resources. Since resources are limited, we can also use the model to explore different allocation scenarios. For example, suppose increasing the capacity of OPS sites is twenty times more costly than increasing the the probability of entering treatment from an OPS. We can allocate a fixed amount of resources, which will result in either an increase in *x* or an increase in *y*, with 20x + y = 1. We can vary *x* and *y* under this constraint, and calculate the resulting probability of a user fatally overdosing in one year. This calculation is depicted in Figure 2, lower right panel, which shows that a probability of *y* = .4 and *x* = .03 results in the smallest probability of fatally overdosing.

This analysis shows how two of the consequences of the OPS operate synergistically. To further explore this relationship, we calculate the probability of entering State 5 (Recovery) at some point during one year, as a function of the two harm reduction variables, x and y. The results are shown in Figure 3, and details of the calculation are given in the next paragraph. The results show that efforts to encourage treatment programs have the largest marginal effect when the probability of going to an OPS is low, either due to low capacity, or due to an unwillingness on the part of users to go. In the left panel of Figure 3, the cross-section at x = 0.005 is highlighted. This corresponds to only one half of one percent of drug uses occurring in the OPS. At this level of OPS attendance, the probability of entering Recovery in the first year increases from 18% when y = 0 to nearly 50% when y = .1. If the probability of going to an OPS is relatively high, then Figure 3 shows that increasing the value of y has little effect. The effect of varying y for different fixed values of x is shown in the right panel of the figure. Intuitively, if a user visits the OPS often, they will be exposed many times to any efforts or education to get them into Recovery. Even if these efforts are not that effective, i.e. if the value of y is small, multiple exposures still have a positive effect. However, if a user only goes a few times, then the effectiveness of these educational efforts is very important.

To estimate the probability of entering the Recovery state for the first time in one year, we let Recovery be an absorbing state by setting P(5,5) = 1. This ensures that we do not count multiple returns to State 5. We then find the expected time until the first visit to State 5 from each state b calculating the matrix R_{1yr} :

$$R_{1 \text{ yr}} = \sum_{i=1}^{N} P^{i}, \qquad N = 48 \cdot 365 = \text{number of time steps in one year.}$$

From the matrix $R_{1 \text{ yr}}$ we estimate the *first return probability matrix*

$$H_{1\,\rm yr} = R_{1\,\rm yr} \cdot \left(\rm{diag}(R_{1\,\rm yr}) \right)^{-1}$$

The (k, 5) entry of H_{1yr} gives an estimate of the probability of visiting State 5 (Recovery) in one year. In Figure 3 we plot the values of $H_{1yr}(1, 5)$ for a range of values of x and y, noting that the first four entries in the fifth column of H_{1yr} are nearly identical.

To illustrate the application of the model to a particular city, we can estimate the impact of placing overdose prevention sites in a particular city. For example, if San Francisco, with an estimated 25,000 drug users (Coffin et al., 2022) had 10 overdose prevention sites, each with a capacity of 30, then there would be 176 fewer deaths from overdoses per year, and 668 users would be in treatment or recovery after one year. To get these estimates, we used a probability of willingness to go to the OPS as .85, and a probability of fatal overdose of 4×10^{-5} to be consistent with Coffin et al. (2022). Thus, our model gives evidence that an OPS reduces fatal overdoses and encourages users to seek treatment.

5 Discussion and Conclusion

Due to its political and social implications, the opioid epidemic has been extremely difficult to address. In the last 20 years, overdose prevention sites have gained traction in North America as a form of harm reduction during this public health emergency. Staffed with trained officials, sterile supplies, and overdose prevention tools such as naloxone, overdose prevention sites provide a medically supervised environment for people to use illicit drugs with a decreased risk for overdose. However, despite their studied effectiveness, overdose prevention sites have faced many political barriers in the US, portrayed as too expensive and encouraging of drug use. Many of these beliefs are informed by negative generalizations about drug users, as well as an inclination towards criminalization and policing as "solutions" to the opioid crisis. The purpose of overdose prevention sites is to mitigate the harms experienced by drug users, including the potential of fatally overdosing or disease transmission. Harm reduction provides a decriminalized framework for keeping people safe that does not rely on policing and punishment to mitigate drug use, with the goal of reducing the number of drug-related deaths.

In terms of policy decisions, the model can be used to measure the impact of the construction of an OPS in a particular neighborhood or city. The model also highlights the impact of resources available at the OPS. Figure 3 shows that, even when OPS capacity is low, strategies that increase the probability that a user who is at the OPS seeks treatment, such as counseling, employment opportunities, or drug replacement programs, can have a significant impact.

This relatively simple model can be calibrated to a specific city or community by specifying key parameters, such as the population of users, the number of overdoses, the accessibility and capacity of overdose prevention sites, and the availability of treatment. This would allow quantitative predictions of the benefits of harm reduction strategies such as overdose prevention sites, enabling policy makers to make data-driven decisions. By expanding the number of states to describe different city or county districts, information could be obtained on the local impact of various strategies

There are many factors not considered in this model that could also be addressed in future iterations. For example, some critics argue that OPS sites also run the risk of bringing crime to surrounding communities. Others argue the opposite: one study conducted in Vancouver, Canada (where the first sanctioned safe-injection sites in North America opened in 2003) revealed an abrupt and persistent decrease in crime after the opening of an OPS in a particular district (see Samuels et al., 2022, and references therein). A model that includes criminal activity and policing could inform this discussion.

References

- Addiction Center (2023). Addiction statistics. https://www.addictioncenter.com/addiction/addictionstatistics, Last accessed 06/13/2023. 169
- Alta Mira (2023). Opiate addiction recovery statistics. https://www.altamirarecovery.com/opiates/opiateaddiction-recovery-statistics, Last accessed 06/13/2023. 169
- Battista, N., L. Pearcy, and W. Strickland (2019). Modeling the prescription opioid epidemic. Bull. Math. Biol. 81, 2258–2289. 165, 166
- Befekadu, G. and Q. Zhu (2019). Optimal control of diffusion processes pertaining to an opioid epidemic dynamical model with random perturbations. *J. Math. Biol.* 78, 1425–1438. 166
- Behrends, C., D. Paone, M. Nolan, E. Tuazon, S. Murphy, S. Kapadia, P. Jenga, A. Bayoumid, H. Kninsb, and B. Schackmana (2019). Estimated impact of supervised injection facilities on overdose fatalities and healthcare costs in New York City. J Subst Abuse Treat 106, 79–88. 167, 168, 169
- Coffin, P. O., K. Long, and V. McMahan (2022). Substance use trends in San Francisco through 2021. Department of Public Health, City and County of San Francisco. 172
- Florida Department of Health (2023). Substance abuse dashboard. https://www.flhealthcharts.gov/ ChartsDashboards/rdPage.aspx?rdReport=SubstanceUse.Overdose, Last accessed 06/13/2023. 169

- Gordon, E. (2018). What's the evidence that supervised drug-injection sites save lives? https://www.npr.org/sections/ health-shots/2018/09/07/645609248/whats-the-evidence-that-supervised-drug-injectionsites-save-lives\protect\@normalcr\relax. 168
- Irvine, M. A., M. Kuo, J. A. Buxton, R. Balshaw, M. Otterstatter, L. Macdougall, M.-J. Milloy, A. Bharmal, B. Henry, M. Tyndall, D. Coombs, and M. Gilbert (2019). Modelling the combined impact of interventions in averting deaths during a synthetic-opioid overdose epidemic. *Addiction 114*(9), 1602–1613. 166
- Jones, C. (2013). Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers-united states. Drug Alcohol Depend 132, 95–100. 165
- Kerr, T., M. W. Tyndall, C. Lai, J. S. Montaner, and E. Wood (2006). Drug-related overdoses within a medically supervised safer injection facility. *International Journal of Drug Policy* 17(5), 436–441. 169
- Kral, A. H. and P. J. Davidson (2017, december). Addressing the nation's opioid epidemic: Lessons from an unsanctioned supervised injection site in the U.S. American Journal of Preventive Medicine 53, 919–922. 167
- Larochelle, M. R. e. a. (2018). Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: A cohort study. *Annals of Internal Medicine 169*, 137–145. 169
- Levengood, R., P. Lowinger, and K. Schooff (1973). Heroin addiction in the suburbs-an epidemiologic study. *American Journal of Public Health 63*(3), 209–214. 166
- Ng, J., C. Sutherland, and M. Kolber (2017, Nov). Does evidence support supervised injection sites? *Can Fam Physician 63*, 866. 167
- Pitt, A., K. Humphreys, and M. Brandeau (2018). Modeling health benefits and harms of public policy responses to the US opioid epidemic. Am. J. Public Health 108, 1394–1400. 166
- Rafiq, M., A. Raza, M. U. Iqbal, Z. Butt, H. A. Naseem, M. A. Akram, M. K. Butt, A. Khaliq, Q. ul Ain, and S. Azam (2019). Numerical treatment of stochastic heroin epidemic model. *Advances in Difference Equations* 434, 1687–1847. 166
- Recovery in Tune (2023). How long does a heroin high last? https://www.recoveryintune.com/how-long-doesa-heroin-high-last/, Last accessed 06/13/2023. 169
- Ross, J., M. Teesson, S. Darke, M. Lynskey, K. Hetherington, K. Mills, A. Williamson, and S. Fairbairn (2002). Characteristics of heroin users entering three treatment modalities in New South Wales: Baseline findings from the Australian treatment outcome study (ATOS). NDARC Technical Report No.139, National Drug and Alcohol Research Centre, University of New South Wales. 169
- Samuels, E. A., D. A. Bailer, and A. Yolken (2022, 07). Overdose prevention centers: An essential strategy to address the overdose crisis. *JAMA Network Open 5*(7), e2222153–e2222153. 172
- Sharareh, N., S. Sabounchi, M. McFarland, and R. Hess (2019). Evidence of modeling impact in development of policies for controlling the opioid epidemic and improving public health: A scoping review. *Substance Abuse 13*, 1–10. 166
- Shoreline Recovery Center (2023). Life expectancy of a heroin addict. https://www.shorelinerecoverycenter.com/ life-expectancy-of-a-heroin-addict/, Last accessed 05/26/2023. 170
- Smyth, B., J. Barry, E. Keenan, and D. K (2010). Lapse and relapse following inpatient treatment of opiate dependence. *Ir Med. J 106*, 176–179. 165
- Wares, J. R., J. Dong, J. L. Gevertz, A. Radunskaya, K. Viner, D. Wiebe, and S. Solomon (2021). Predicting the impact of placing an overdose prevention site in Philadelphia: a mathematical modeling approach. *Harm Reduction Journal 18*(1), 110. 166, 167, 169
- White, E. and C. Comisky (2007). Heroin epidemics, treatment and ODE modelling. *Math Biosciences 208*, 312–324. 165, 166
- World Health Organization (2023). Opioid overdose fact sheets. https://www.who.int/news-room/fact-sheets/ detail/opioid-overdose, Last accessed 05/26/2023. 170