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A modeling study of the opioid epidemic for vulnerable communities in Knoxville, Tennessee.

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Abstract

Background: Over the past three decades, the opioid epidemic has emerged as one of the most pressing public health crises in the United States, disproportionately affecting vulnerable communities and minority populations. Mathematical modeling, widely applied in the study of infectious diseases, offers a rigorous framework to investigate the dynamics of opioid use disorder.
Methods: We present a compartmental model to examine two primary risk factors for opioid misuse: opioid availability and access to preventive resources. The framework consists of two interacting systems of equations, one representing the general population and the other a subset community of interest. The general

population model was calibrated using 2016-2019 data from the Knoxville, Tennessee Metropolitan Statistical Area, a region heavily impacted by the epidemic. Sensitivity analyses were conducted to quantify the influence of model inputs on outcomes.

Results: Embedded within a data-calibrated general population, simulations of hypothetical communities were conducted under varying levels of treatment accessibility, recovery retention, and fatal overdose rates. We found that variations in recovery retention and fatal overdose risk exerted the strongest influence on total overdoses. Notably, increasing treatment access alone—without simultaneously addressing other factors such as relapse reduction—was associated with higher overdose rates, as individuals almost exclusively relapsed using fentanyl or heroin, rather than prescription opioids, all of which carry elevated fatal overdose risk.

Conclusions: For Knoxville during 2016–2019, increasing resources aimed at preventing the initial development of opioid use disorder would likely have had minimal effect on the overall prevalence of opioid use disorder. Our analysis highlights the importance of model scope, as a related study, which was fitted to a broader geographic area and a longer time span, produced findings that differed from ours. While our conclusions are specific to this location and period, the modeling framework we created is readily adaptable to other regions and populations, provided appropriate data is available, and offers a valuable tool for studying vulnerable groups.

Keywords: Opioid use disorder, Substance use disorder, Opioid epidemic, Public health, Compartment model, Epidemiological model

1 Background

Over the past three decades, the opioid epidemic has become one of the most significant public health crises in the United States. The dramatic increases in the misuse of both prescription and non-prescription opioids have led to a staggering rise in deaths from opioid-related overdoses (ODs), with the number of people who died from a drug OD in 2022 being approximately six times larger than in 1999, with almost 76% of these deaths involving an opioid [1].

The opioid epidemic began in the 1990s, when heightened concerns about undertreated pain led physicians to increase opioid prescribing dramatically [2, 3]. The resulting surge fueled a rise in prescription opioid use disorder (POUD) [4]. Unlike many other illicit substances, misused prescription opioids were most often obtained

from leftover pills shared by friends or family, rather than directly from prescriptions or dealers [5]. Between 1999 and 2017, fatal ODs involving prescription opioids rose sharply from 3,442 to 17,029 [6], defining the first wave of ODs of the crisis.

Efforts to curb prescription opioid misuse—through updated prescribing guidelines [7, 8] and the development of abuse-deterrent formulations [9, 10]—were accompanied by a surge in heroin use, fueled by its greater availability and lower cost. Many who turned to heroin had first misused prescription opioids [11]. Between 2010 and 2012, heroin OD deaths more than doubled across 28 states [12], marking the beginning of the crisis's second wave.

The third, and still ongoing, wave of the crisis began in 2013 with the emergence of illicit fentanyl, a synthetic opioid 50 to 100 times more potent than morphine [13]. Frequently mixed into other drugs without the user's knowledge, fentanyl has fueled a steep rise in fatal ODs. By 2022, the death rate from synthetic opioids was nearly 25 times higher than in 2010 [14].

The opioid epidemic has not affected all populations equally, however. Many communities and minority groups have been disproportionately impacted, with certain populations facing heightened vulnerability to developing opioid use disorder (OUD) [15], significant barriers to accessing and receiving treatment [16], and increased risk of fatal OD [17, 18]. For example, Black individuals are less likely than their white peers to be prescribed medications for OUD [19], and people living in poverty or without health insurance face a substantially greater risk of dying from an opioid OD [20]. However, some groups have access to specialized resources that can help mitigate these risks. For instance, although military personnel may be at elevated risk for developing an OUD, they benefit from targeted programs and support services that are often unavailable to the general public [21, 22].

Geographic disparities are also pronounced. The Appalachian Region, for example, has experienced opioid OD rates more than twice the national average [23]. A historical

reliance on injury-prone industries made this region an early target for the aggressive marketing of prescription opioids [24].

While these examples highlight differences in how the epidemic affects specific populations—particularly minorities and other vulnerable groups—the surrounding population still plays a critical role in shaping outcomes. Previous modeling studies have examined the opioid epidemic from various perspectives [25–48], but, to our knowledge, none have specifically investigated how a vulnerable subcommunity may be affected by the broader population surrounding it. More details on previous modeling studies can be found in the online supplementary material.

To address this gap, we have developed a model examining two major risk factors for opioid misuse—availability of opioids (including prescription opioids, fentanyl, and heroin) and access to essential preventative resources (such as therapy, physical rehabilitation, and medical care)—within a community of interest. Our approach uses two interacting systems of ordinary differential equations (ODEs): one representing the general population and the other representing a subset community of interest. Our analysis focuses on the Knoxville Metropolitan Statistical Area (MSA) in Tennessee, U.S., located within the Appalachian region, for the period 2016–2019. This model is easily adaptable to other locations and time periods, provided the necessary data are available.

The time span for our study is the years 2016 to 2019 for two reasons: (1) between 2015 and 2016, OD deaths from synthetic opioids (such as fentanyl) surpassed those from heroin and prescription opioids nationally, a trend that has continued since [1], and (2) we conclude in 2019 due to disruptions caused by the COVID-19 pandemic [49]. More information on these disruptions can be found in the supplementary material. After calibrating the model to Knoxville MSA data, we explore several hypothetical communities to assess how they would be affected by the opioid epidemic under similar conditions. We propose a simple yet robust modeling framework that captures how

different communities are uniquely impacted over time, while remaining adaptable for application to other locations and communities.

2 Methods

2.1 Model

The terminology related to OUD can be ambiguous—often used interchangeably with terms such as abuse, addiction, dependence, or misuse. For clarity, we adopt the definition of substance use disorder as outlined in the DSM–5 [50]. In this context, we categorize opioid addiction as a specific manifestation of OUD; a more detailed description is available in the supplementary material.

At its root, OUD is a disease; thus, we use a compartment modeling method popular in disease epidemiology to study its dynamics. We developed two interacting, deterministic, compartmental models of OUD among individuals aged 12 and older for the Knoxville MSA: one representing the general population and another for a specific community of interest, which is a subset of the general population. The compartments represent the proportions of the general population and the proportions of the community for the respective models. Table 1 provides a detailed description of each compartment.

Figure 1 and Figure 2 depict the compartmental structures of the general population and community models, respectively. By having these two interacting models, we can examine the effects of the availability of opioids in the general population surrounding the community. Additionally, we stratify the susceptible community into susceptibles without and with chronic pain, denoted S_C and S_H, to determine the effects of access to preventative resources, such as physical therapy. Full model details and assumptions are available in the supplementary material.

In the community model, susceptible individuals without chronic pain (S_C) may develop chronic pain, moving them to the susceptible individuals with chronic pain

Table 1 Description of compartments in the general population model and community model

State	Indicator	Description
General population susceptibles	S_G	Proportion of the general population who are not using prescribed opioids, fentanyl, or heroin.
Community susceptibles without chronic pain	S_C	Proportion of the community who are not using prescribed opioids, fentanyl, or heroin and who do not have chronic pain.
Community susceptibles with chronic pain	S_H	Proportion of the community who are not using prescribed opioids, fentanyl, or heroin and who have chronic pain.
General population/community prescription opioid users	$P_{G/C}$	Proportion of the general population/community who are prescribed opioids by a health care provider and take them in a manner not constituting an opioid use disorder (some misuse is possible, as long as it is in a manner such that potential for immediate harm is negligible).
General population/community prescription opioid use disorders	$A_{G/C}$	Proportion of the general population/community who have a POUD but are not using fentanyl or heroin. They may be actively in treatment for opioid use disorder and are still considered in this class for one month after being discharged from treatment, regardless of current use.
General population/community fentanyl or heroin use disorders	$F_{G/C}$	Proportion of the general population/community who have a fentanyl or heroin use disorder (FHUD) or are actively in treatment for opioid use disorder, including fentanyl/heroin. Individuals remain in this class for at least one month after being discharged from treatment, regardless of current use.
General population/community stably recovered individuals	$R_{G/C}$	Proportion of the general population/community who have completed treatment for OUD and do not relapse within one month after treatment is over. In cases where treatment is not a well-defined, discrete event (e.g., ongoing counseling, group support, solo attempts at recovery), one month without relapse alone characterizes inclusion in $R_{G/C}$ versus $A_{G/C}$ or $F_{G/C}$.

class (S_H). Once in this class, individuals may move back to the susceptible individuals without chronic pain (S_C), either through the route of being prescribed opioids or may move directly there. While this direct route could happen naturally over time, it is also subject to the availability of certain non-opioid resources, like physical therapy. In both models, all susceptible individuals may be prescribed opioids, though individuals with and without chronic pain are prescribed at differing rates.

Susceptibles and prescription opioid users may develop POUD through one of three pathways: (1) progression from their own prescription use, (2) interactions with individuals who have POUD (including illicit purchases), or (3) use of leftover or stolen prescription opioids—modeled as interactions with individuals who have prescriptions.

Additionally, susceptibles, prescription opioid users, and individuals with POUD can develop a fentanyl or heroin use disorder (FHUD) through interactions with people who have FHUD.

Due to the challenges of OUD recovery and high relapse rates [51], individuals with POUD or FHUD do not enter the stably recovered compartment until they have completed treatment and remained relapse-free for one month. In cases where treatment is not a well-defined, discrete event (e.g., ongoing counseling, group support, solo attempts at recovery), one month without relapse alone characterizes inclusion into the stably recovered compartment versus the POUD or FHUD compartments. Individuals in the stably recovered compartment may relapse into either the POUD or FHUD compartments.

All compartments include a natural mortality rate. Those in the POUD and FHUD compartments have an additional mortality rate due to their increased chance of fatal ODs.

Lastly, all of the model parameters are continuous values except for α_G, α_C, and α_H, which are linear terms based on time such that $\alpha_X = \tilde{m}_X t + \tilde{b}_X$, where $X \in \{G, C, H\}$.

2.2 Parameter Estimation

Using the weighted least squares method, we fit the general population model to publicly available data for the Knoxville MSA covering the years 2016 to 2019. More details on the data and the parameter estimation are available in the supplementary material.

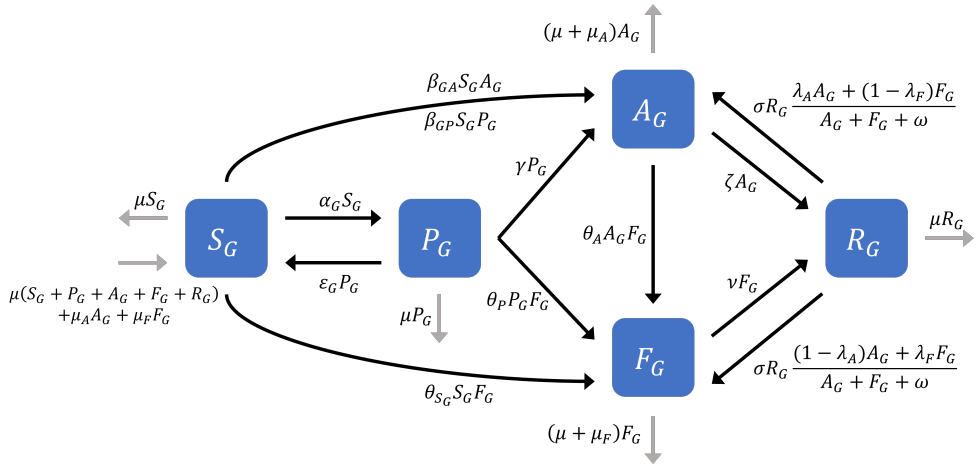


Fig. 1 Connection diagram of the general population model for the various compartments, where the arrows represent the direction of movement of individuals from one to the other

2.3 Sensitivity Analysis

To identify and quantify the influence of model inputs — parameters and initial conditions — on model outputs, defined as the class values at the final time point, we performed a Sobol sensitivity analysis (SA). The Sobol method partitions the model's output variance into fractions attributed to the model inputs or combinations of interacting inputs; these fractions serve as a measure of sensitivity [52]. A detailed description of our use of the Sobol SA method, along with the model input ranges used, is available in the supplementary material.

3 Results

3.1 Parameter Estimation

Table 2 presents the estimated parameter values for the general population model. Figure 3 compares the general population model simulation outputs to observed data, including yearly and quarterly prescription opioid users without a POUD, yearly POUD and FHUD prevalence, and yearly fatal OD counts for both POUD and FHUD.

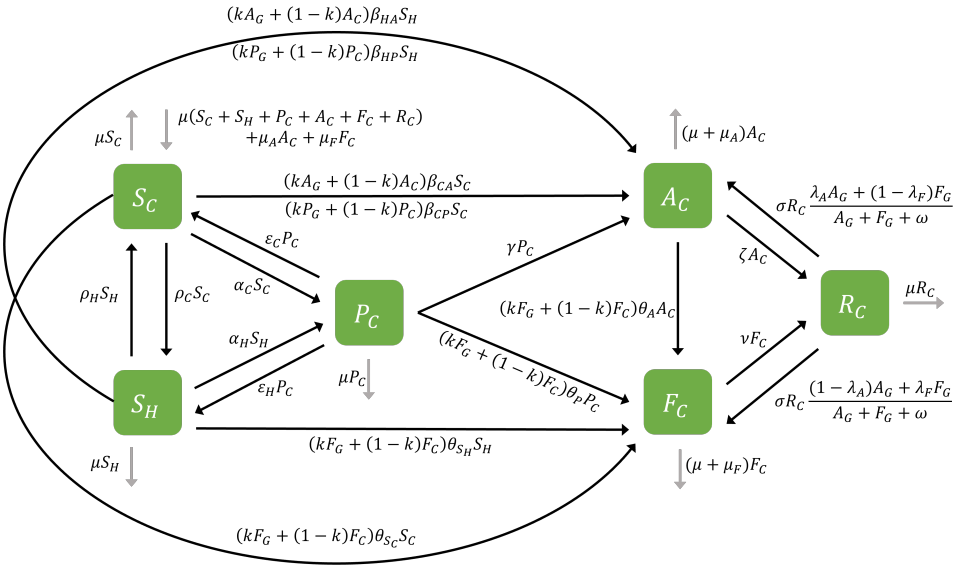


Fig. 2 Connection diagram of the community model for the various compartments, where the arrows represent the direction of movement of individuals from one to the other

3.2 Sensitivity Analysis

The Sobol SA total-order index results, which describe the proportion of the total model output variance that remains when uncertainty is removed from all other inputs except this input, can be seen in Figure 4. The length of the colored bars represents the contribution of that parameter to the variance of that population class at the final time; the longer the colored bars, the higher the effect of that parameter on that class.

The Sobol SA first-order index results are available in the supplementary material. The first-order index and the total-order index results were found to be very similar, suggesting there are no significant interactions between the input parameters.

3.3 Community Scenarios

We now investigate how different hypothetical communities might fare during the study period, given their interactions with the surrounding general population, which is rooted in real-world data. To determine the hypothetical communities, we focus on

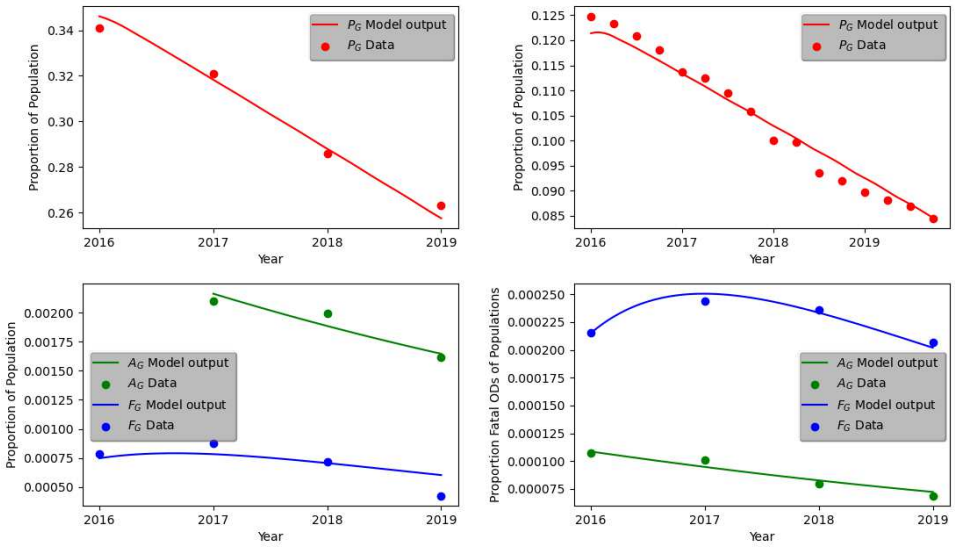


Fig. 3 General population model simulation results fit to data, which includes yearly prescription opioid data, quarterly prescription opioid data, yearly POUD data, yearly FHUD data, yearly POUD fatal OD data, and yearly FHUD fatal OD data.

the parameters identified through the Sobol sensitivity analysis as having the most significant impact on the community OUD classes (A_C and F_C) and stably recovered class (R_C) at the start of 2020, as changes in R_C could also influence fatal ODs. More precisely, we examine how communities fare under differing conditions of treatment accessibility (ζ and ν), recovery retention (σ), and fatal OD risk (μ_A and μ_F).

To establish a baseline for the community-specific parameters, we select parameter values and initial conditions that closely reproduce the overall output of the general population model. Additional details on the baseline parameterization are provided in the supplementary materials.

Our initial modeling objective was to maintain simplicity—minimizing the number of parameters—to ensure it is adaptable to various contexts. However, since the parameters we are interested in varying (ζ, ν, σ, μ_A, and μ_F) are shared between the general population and community models, we distinguish them to explore community-specific effects. For instance, when assessing the influence of varying σ, we replace it in the

Table 2 Estimated parameter values for the general population model

Input	**Estimated Value**	**Units**
$\tilde{m}_G$	-0.0288	$\frac{1}{\text{year}}$
$\tilde{b}_G$	0.332	$\frac{1}{\text{year}}$
β_{GA}	0.001	$\frac{1}{\text{year}}$
β_{GP}	0.0001	$\frac{1}{\text{year}}$
θ_{S_G}	0.00111	$\frac{1}{\text{year}}$
θ_P	0.0101	$\frac{1}{\text{year}}$
θ_A	48.9	$\frac{1}{\text{year}}$
ε_G	7.0	$\frac{1}{\text{year}}$
γ	1.16×10^{-5}	$\frac{1}{\text{year}}$
ζ	0.0536	$\frac{1}{\text{year}}$
ν	0.00319	$\frac{1}{\text{year}}$
σ	0.97	$\frac{1}{\text{year}}$
λ_A	0.00633	$\frac{1}{\text{year}}$
λ_F	1.0	$\frac{1}{\text{year}}$
μ_A	0.0471	$\frac{1}{\text{year}}$
μ_F	0.471	$\frac{1}{\text{year}}$
P_{G_0}	0.0432	dimensionless
A_{G_0}	0.00246	dimensionless
F_{G_0}	0.000339	dimensionless
R_{G_0}	0.000508	dimensionless

community model with σ_C to allow independent variation of the community-specific parameter, σ_C, while not affecting the general population model.

For each hypothetical community scenario, we vary the parameter of interest by $\pm 25\%$ and $\pm 50\%$ from its baseline value and rerun the model over our study period. We then evaluate how these changes affect the community OUD classes (A_C and F_C) and stably recovered class (R_C) at the final time point, as well as the resulting impact on fatal ODs.

3.3.1 Accessibility to Treatment

We aim to investigate how changes in ζ, the rate at which individuals with POUD stably recover, affect the community. To isolate this effect, we introduce a new parameter, ζ_C, which replaces ζ in the community ODEs. This modification allows us to assess the impact of changes in recovery rates specifically within the community context. An

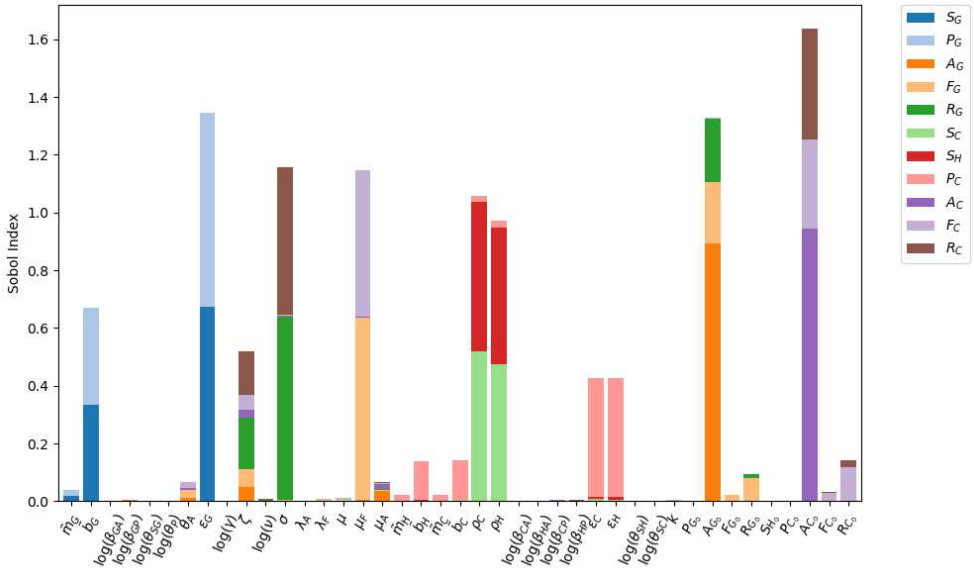


Fig. 4 Sobol sensitivity results for the size of each class at the beginning of 2020 run over four years with 2,752,512 samples for the total-order indices.

increase in ζ_C may represent expanded access to treatment for individuals with POUD in the community, while a decrease could reflect diminished treatment availability.

Recognizing that shifts in community treatment access for POUD may also influence individuals with FHUD, we introduce a corresponding parameter, ν_C, representing the stable recovery rate for individuals with FHUD in the community. This parameter replaces ν in the community ODEs to reflect analogous changes in access to care.

We vary both ζ_C and ν_C by $\pm 25\%$ and $\pm 50\%$ from the baseline values of ζ and ν, respectively. The results of these simulations are presented in Table 3.

Interestingly, increasing these recovery rates (ζ_C and ν_C) leads to a decrease in A_C—as one might expect—but leads to an increase in F_C and an increase in fatal ODs from the baseline. This is because, in the model, there is minimal relapse into the POUD class, and the majority of relapses go into the FHUD class because of the estimated values of λ_A and λ_F. Thus, increasing R_C, which would be done by

Table 3 Effect on size of the A_C, F_C, R_C classes at the start of 2020 from altering ζ_C and ν_C by ±25% and ±50% from the baseline value, as well as the effect on the total number of fatal ODs between 2016 and 2019.

Value of ζ_C	Value of ν_C	Change in ζ_C, ν_C	Change in A_C	Change in F_C	Change in R_C	Change in Total ODs
0.026800	0.001596	−50.0%	+11.2%	−16.9%	−41.4%	−4.3%
0.040200	0.002394	−25.0%	+5.46%	−8.24%	−19.9%	−2.11%
0.053600	0.003192	0.0%	—	—	—	—
0.067000	0.003989	+25.0%	−5.17%	+7.81%	+18.3%	+2.05%
0.080400	0.004787	+50.0%	−10.1%	+15.2%	+35.2%	+4.03%

increasing the recovery rates (ζ_C and ν_C), leads to more people relapsing into F_C rather than A_C, answering the question as to why F_C increases.

We also note that increasing accessibility to treatment (increasing ζ_C and ν_C) alone leads to an increase in fatal ODs for the community. This can also be explained by the high relapse rate into the FOUD class, which has a much higher fatal OD rate than the POUD class (an order of magnitude higher). Thus, the fatal ODs coming from the increased F_C outweigh the decrease in fatal ODs coming from A_C.

3.3.2 Retention of Stably Recovered Individuals

We now examine how changes in σ, the relapse rate of stably recovered individuals, influence community dynamics. Specifically, we replace σ in the community ODE with σ_C, varying it by ±25% and ±50% from its baseline value, and simulate the resulting scenarios. A decrease in σ_C corresponds to a lower relapse rate—indicating a higher likelihood of individuals remaining stably recovered—which may reflect enhanced post-treatment monitoring or improved access to medications for opioid use disorder (MOUD). MOUD have been shown to support recovery more effectively than counseling or psychosocial support alone [53]. The results are presented in Table 4.

We observe that varying σ_C had a minimal effect on A_C and F_C at the final time, but it significantly impacted R_C at the final time. This led to a significant change in the total number of ODs over the time period. A community with better retention in

recovery (reducing σ_C by 50%) had the potential to reduce its fatal ODs by nearly 10%, while a community with worse retention in recovery (increasing σ_C by 50%) had the potential to lose nearly 4% more to fatal ODs.

Table 4 Effect on size of the A_C, F_C, R_C classes at the start of 2020 from altering σ_C by ±25% and ±50% from the baseline value, as well as the effect on the total number of fatal ODs between 2016 and 2019.

Value of σ_C	Change in σ_C	Change in A_C	Change in F_C	Change in R_C	Change in Total ODs
0.485000	−50.0%	−0.0307%	−3.71%	+136.0%	−9.78%
0.727500	−25.0%	−0.00948%	+0.025%	+45.2%	−3.67%
0.970000	0.0%	—	—	—	—
1.212500	+25.0%	+0.00462%	−1.0%	−24.7%	+2.34%
1.455000	+50.0%	+0.00713%	−2.1%	−39.6%	+3.91%

3.3.3 Change in Fatal OD Rates

We aim to investigate how changes in the fatal OD death rates, μ_F and μ_A, impact the community. Given the interconnected nature of opioid use patterns, a change in the fatal OD rate among individuals with POUD in the community is likely to influence those with FHUD as well, and vice versa. Therefore, we examine the combined effects of varying these two parameters on the community. To isolate the effects within the community, we introduce new parameters, μ_{F_C} and μ_{A_C}, which replace μ_F and μ_A, respectively, in the community ODEs.

A reduction in μ_{F_C} and μ_{A_C} may represent increased availability of harm reduction resources in the community, such as Naloxone—a medication that rapidly reverses opioid ODs [54]—or fentanyl test strips, which help individuals detect the presence of fentanyl in other drugs such as heroin. Because fentanyl is extremely potent and frequently mixed into other illicit drugs in unknown quantities [55], access to testing strips can play a critical role in reducing the risk of fatal OD.

We vary μ_{F_C} and μ_{A_C} by $\pm 25\%$ and $\pm 50\%$ from the baseline values of μ_A and μ_F, respectively. The resulting outcomes are presented in Table 5.

Table 5 Effect on size of the A_C, F_C, R_C classes at the start of 2020 from altering μ_{F_C} and μ_{A_C} by $\pm 25\%$ and $\pm 50\%$ from the baseline value, as well as the effect on the total number of fatal ODs between 2016 and 2019.

Value of μ_{F_C}	Value of μ_{A_C}	Change in μ_{F_C}, μ_{A_C}	Change in A_C	Change in F_C	Change in R_C	Change in Total ODs
0.235500	0.023550	-50.0%	$+9.83\%$	$+75.2\%$	$+7.19\%$	-36.4%
0.353250	0.035325	-25.0%	$+4.8\%$	$+31.0\%$	$+3.48\%$	-15.9%
0.471000	0.047100	0.0%	—	—	—	—
0.588750	0.058875	$+25.0\%$	-4.58%	-22.1%	-3.27%	$+12.8\%$
0.706500	0.070650	$+50.0\%$	-8.95%	-38.1%	-6.38%	$+23.4\%$

The changes in A_C, F_C, and R_C are not of particular interest to us in this community case because, as one would expect, if we increase/decrease the rate of fatal ODs, this leads to reductions/additions in the OUD classes and recovery classes. Here, we focus on the changes to the total fatal ODs.

We see that a community with more access to OD-reversing drugs like Naloxone or fentanyl test strips (decreasing μ_{F_C} and μ_{A_C} by 50%) had the potential to decrease its fatal ODs by approximately 36%, while a community with less access (decreasing μ_{F_C} and μ_{A_C} by 50%) had the potential to lose approximately 23% more to fatal ODs.

4 Discussion

4.1 Principal findings

Our analysis revealed that variations in fatal OD rates (μ_A and μ_F) and recovery retention rates (σ) in the hypothetical communities had the greatest impact on total fatal ODs during 2016–2019 in the Knoxville MSA. This suggests that, for this location and time period, the factors most likely to influence outcomes—either positively or

negatively—were access to and education on harm-reduction resources, such as Naloxone and fentanyl test strips, along with the availability of post-treatment monitoring and access to MOUD.

Additional insights gained through our model exploration included finding that relapse predominantly occurred into the FHUD classes rather than the POUD classes. The estimated value for λ_A was near zero, while λ_F was estimated at one (see Table 2). This implies that, regardless of the proportion of the community in the POUD or FHUD classes, individuals who relapse tend almost exclusively to re-enter the FHUD class. This result is consistent with the understanding that part of the draw to heroin and fentanyl over prescription opioids is their availability and lower cost [11]. Consequently, the relatively large relapse rate into the FHUD class, which carries a higher fatal OD risk than the POUD class, helps explain why expanding access to treatment alone (increasing ζ and ν) in the community without simultaneously addressing other factors, such as relapse reduction, could actually increase fatal ODs.

Further analysis indicated that the susceptible and prescribed classes function almost as a separate system from the OUD and stably recovered classes. Several key observations support this conclusion. First, the estimated parameter values for transitions from the susceptible and prescribed classes to the OUD and stably recovered classes were notably low. These parameters—β_{GA}, β_{GP}, γ, θ_P, and θ_{SG}—can be found in Table 2, and most of their estimated values were very close to the lower bounds of the ranges used for the least squares parameter estimation, despite the wide ranges used. Second, the Sobol SA revealed that these same parameters, along with their corresponding community counterparts (β_{CA}, β_{HA}, β_{CP}, β_{CP}, θ_{SC}, and θ_{SH}), did not significantly influence the sizes of the OUD or stably recovered classes at the start of 2020. Finally, parameters linked to transitions between susceptible and prescribed classes ($\tilde{m}_G$, $\tilde{b}_G$, ε_G, $\tilde{m}_C$, $\tilde{b}_C$, ε_C, $\tilde{m}_H$, $\tilde{b}_H$, ε_H, ρ_C, and ρ_H) also showed negligible effects on the OUD and stably recovered class sizes at the 2020, according to the SA.

Taken together, these results suggest that the development of OUD from personal prescriptions or leftover prescriptions from others did not play a significant role in the opioid epidemic during this time period. Granted, this does not suggest that prescribing regulations and the like during this time should have been rolled back, but rather that the ones in place were likely functioning as intended.

As a result of the segregation between the susceptible and prescribed classes from the OUD and stably recovered classes in the community, we see that the parameters associated with access to essential preventative resources, ρ_C and ρ_H, had little effect on the proportion of the community with an OUD. This is evident by the Sobol SA results in Figure 4. This suggests that adding more resources to measures that reduce the number of opioid prescriptions, like access to physical therapy, during this time would not have a strong effect on preventing the development of OUD or preventing OD deaths in the community.

4.2 Strengths and limitations of this study

To our knowledge, this is the first model to explicitly examine the impact of general population dynamics on a specific community of interest. The model is also well-suited to incorporate additional community-level data to refine parameter estimates when such data are available. For example, communities such as veterans—where more detailed data are often collected—present a valuable opportunity to enhance model precision and tailor scenario analyses to specific groups.

All results presented here are specific to the dataset used in our model, i.e., the Knoxville MSA data from 2016 to 2019. This likely explains some of the differences between our findings and those of Phillips et al. (on which our model is based), who analyzed Tennessee state-level data from 2013 to 2019 [46]. Because our dataset is a geographic and temporal subset of theirs, these differences underscore the importance of scope—both location and time—when interpreting model outcomes. Conclusions

drawn from our results should therefore not be assumed to apply directly to other regions or periods.

The modeling framework is flexible and can be adapted by fitting its parameters to data from other locations or time frames. Doing so could produce substantially different results and may reveal that certain structural elements—such as stratifying the susceptible community into those with and without chronic pain—are critical for understanding and controlling the opioid epidemic in a given context.

4.3 Future Research

With data from a specific real-world community, it would be possible to calibrate the community-level parameters in our model and examine in greater detail how the surrounding general population influences outcomes. Depending on the characteristics of the community, it may also be necessary to further stratify the model's classes to refine recommendations. For example, if veterans were the community of interest, compartments could be divided based on the presence or absence of post-traumatic stress disorder (PTSD), since benzodiazepines—commonly prescribed for PTSD—can significantly increase OD risk when combined with opioids [56, 57]. Such refinements would require fitting additional parameters, essentially repeating the initial model for each subgroup. These extensions would not necessarily be more complex, highlighting the value of first establishing a clear understanding of the simpler base model.

As more data becomes available, the model could be extended beyond 2019 to capture the effects of the COVID-19 pandemic on the opioid epidemic. While OUD-specific data during the peak of the pandemic (years 2019 to 2020) does not exist for this area [49], existing records show that fatal opioid ODs in the Knoxville MSA were declining before 2020 but rose again in 2020 and 2021. This pattern suggests a pandemic-related impact, though the full scope may never be completely understood. Importantly, post-COVID data may not be directly comparable to pre-COVID

data, potentially necessitating the development of separate models for each period. If community-specific data from the pandemic years is available, it could provide rare and valuable insights into how OUD trends shifted during this time.

Ultimately, incorporating richer datasets will enable more accurate and tailored management strategies—both at the community level and for individual patients—leading to more precise, evidence-based recommendations for the continued improvement in the management of OUD.

5 Abbreviations

FHUD: fentanyl or heroin use disorder

MOUD: medications for opioid use disorder

MSA: Metropolitan Statistical Area

OD(s): overdose(s)

ODE(s): ordinary differential equation(s)

OUD: opioid use disorder

POUD: prescription opioid use disorder

SA: sensitivity analysis

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data analyzed during this study are included in its supplementary materials. The code used in this study is publicly available at https://github.com/keversma/Opioid_Model_Knoxville_TN.

Competing interests

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Authors' contributions

KE designed the model, built the computational framework, and performed all simulations, analysis, and data visualization under the advisement of WCS with valuable input from AS. RC and LBP assisted in development. AK and JT provided the support necessary to carry out the work. KE drafted the manuscript, and all the authors provided crucial input on several iterations of the manuscript. All authors read and approved the final version of the manuscript.

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Supplementary Files

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