Mindset and Opioid Use Disorder Treatment: A Mathematical Model

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Introduction

The United States Department of Health and Human Services declared a public health emergency against opioid addiction and misuse on October 26, 2017 [22]. In parallel to national efforts, West Virginia continues to struggle suppressing the opioid epidemic within its borders [17]. In fact, the state is often considered the epicenter of the crisis in the United States and ranks among the highest in rates of opioid abuse and deaths in the nation, regardless of whether it is natural, semi-synthetic, or synthetic drugs being discussed [23]. West Virginia has one of the highest rates of opioid prescription, a leading cause of new addiction [28]. This high prescription rate could be associated with the state's high levels of heavy manual labor jobs, which inherently possess a high risk of serious injury.

Our literature review has not revealed many references of mathematical-model applications to the opioid crisis. To our knowledge, White and Comiskey [27] were some of the first to model the cycle of initial opioid use, habituation, treatment, relapse, and eventual recovery. They used the existing principles in foundational epidemiological compartmental models, such as the Kermack-McKendrick model [14], and applied them to analyze heroin addiction in Ireland. Similarly, Njagarah and Nyabadza [18] present a compartmental model that analyzes the effect of individuals moving from light use to heavy use on the opioid epidemic. Wang et. al [24] provides a review of other mathematical models that use Susceptible-Infective-Recovered (SIR) compartments to study drug addiction. Focusing on opioid addiction rooted in the legal opioid prescriptions in the United States [26], Battista et al. [1] extends the White and Comiskey [27] heroin epidemic model to a four compartment-model with susceptible, prescribed user, addicted, and recovered classes. Their work has significantly contributed to the understanding of prescription drugs, and consequently influences future legislation regulating them. There are many individual, interpersonal, communal, and societal factors that contribute to the opioid crisis. The development of effective intervention strategies will require a detailed analysis of those factors.

Many drug rehabilitation centers such as Cliffside Malibu [7] and Windmill Wellness Ranch[29] define a passive approach to treatment as one in which an individual holds a negative mindset regarding the reality of their ability to manage their substance use disorder. An individual with a passive mindset may go through the physical steps of treatment but ultimately does not take active involvement in the process. Alternatively, an active response to one's addiction means the drug user takes a prominent role in their treatment; they are an active participant and receive help from others readily. Clearly, these categories are distinct by qualitative means. Our model uses HELP4WV call center data to quantitatively distinguish the effect of an "active response"

DOI: 10.55880/furj4.1.05

versus a "passive response" to substance misuse treatment and recovery.

The aim of our work is to develop a deeper understanding of the opioid crisis in the United States, with a particular focus on the impact of helplines in influencing the mindset of individuals with an opioid use disorder. We anticipate that such models can help policymakers explore different treatment and prevention options to help alleviate the burdens of the crisis. Section 1.1 provides a brief overview of HELP4WV, a 24-hour helpline providing help for West Virginia residents who struggle with addiction and mental health issues. Section 2 introduces the compartmental model that sets the foundation for our work. Additionally, equilibrium solutions and R_0 are discussed. The summary of our results is outlined in Section 3.

HELP4WV

In 2010, a comprehensive needs assessment revealed that a large proportion of West Virginians struggling with substance abuse lacked access to necessary healthcare due to uncertainty about whom to contact [17]. In response, HELP4WV was created as a central hub of resources; the 24/7 helpline was launched in 2015 and now answers thousands of calls per year [13]. It is funded by the Department of Health and Human Services and provides access to specialists and recovery coaches for those battling addiction or mental health problems in West Virginia.

The call center streamlines recovery aid for people seeking help by directing drug users to resources such as "self-help groups, out-patient counseling, medication-assisted treatment, psychiatric care, emergency care, and residential treatment" [13]. The HELP4WV staff reach out to callers after the initial call to offer further assistance; this is a core element of the center's model. The call center initiates follow-up calls with individuals at the 48-hour, 1-week, and 1-month checkpoints to ensure that recovery efforts remain on track.

Mathematical Methods

System of Equations and Model Diagram

Our model utilizes an epidemiological approach to examine the impact of response disposition to treatment among individuals who call the HELP4WV call-line for opioid misuse or addiction. We extend the White and Comiskey heroin addiction model[27] to a five-compartment model, with susceptible, using, active respondents, passive respondents, and recovered ($SUAPR$). Individuals in the susceptible population, S, are the ones who are aged 24-65 and currently not using opioids. Susceptible individuals might enter into the opioid user population, U, if they develop an OUD due to interaction with a current drug user with an OUD. The HELP4WV staff reach out three times within one month of every initial call [13]. It is assumed that after placing an initial call to HELP4WV, individuals enter treatment. The treatment group can be separated into two new categories: individuals who show active responses to treatment and individuals with passive responses to treatment. Those who respond assertively, A, represent individuals who are in treatment and share updates on their progress by answering all three follow-up calls by HELP4WV. Those who respond passively, P, represent individuals who fail to answer one or more of the calls. In the model, the hesitation to stay connected with help indicates that they are

using a passive mindset.

This model assumes that those responding passively can relapse due to interactions with individuals in the U category while those responding actively cannot. Individuals in the recovery group, R, are those who remain sober for 90 consecutive days since completing a treatment. It is assumed that they do not experience any relapses. Individuals at any stage in the model can die and leave the system entirely.

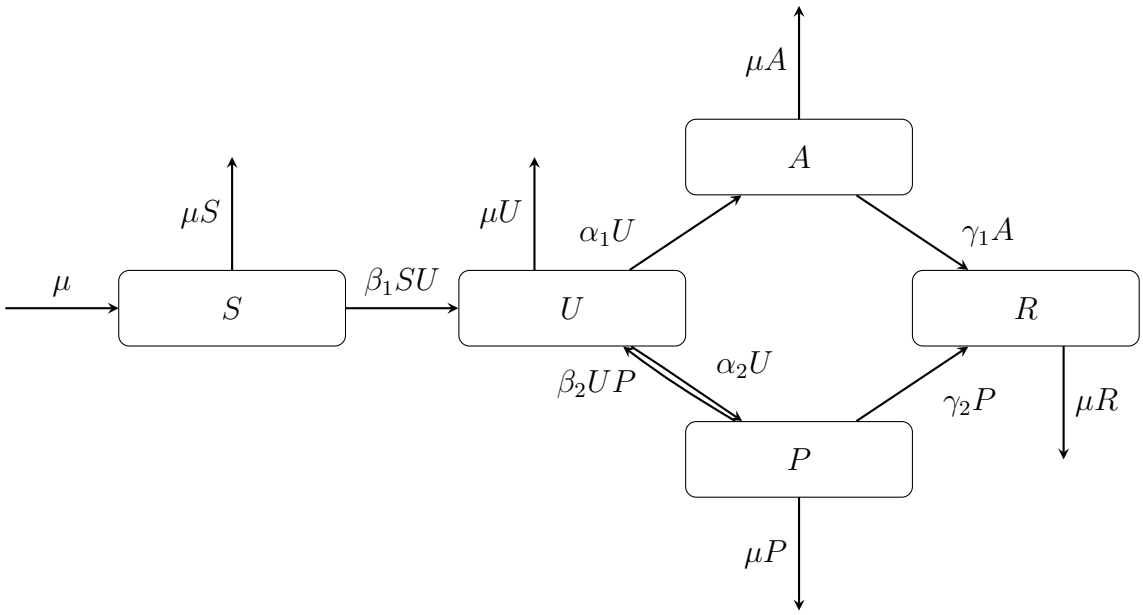

Figure 1: A Schematic Diagram of the $SUAPR$ Model

The systems of differential equations are illustrated in Figure 1 and represented as follows,

$$\begin{aligned}
\frac{dS}{dt} &= \mu - \beta_1 SU - \mu S \\
\frac{dU}{dt} &= \beta_1 SU - \alpha_1 U - \alpha_2 U + \beta_2 PU - \mu U \\
\frac{dA}{dt} &= \alpha_1 U - \gamma_1 A - \mu A \\
\frac{dP}{dt} &= \alpha_2 U - \beta_2 PU - \gamma_2 P - \mu P \\
\frac{dR}{dt} &= \gamma_1 A + \gamma_2 P - \mu R
\end{aligned}$$

In our model, we assume the normalization, $S + U + P + A + R = 1$.

Individuals in treatment are not infectious in the sense that they cannot recruit new drug users to the system regardless of whether they exhibit a passive or an assertive response. For mathematical simplicity, we assume that the death rate m does not change for individuals in treatment groups.

Model Parameters

The parameters utilized in our model are defined in Table 1. Whenever possible, these values are taken from statistics or specific studies. Additionally, except α_1 and α_2 value estimations, each parameter reflects the estimated national average values and are not specific to West Virginia.

Parameter	Description	Est. Value	References
μ	Natural death rate	0.0073	CDC[5, 6]
β_1	Transition rate of S due to U	0.0095	Estimated
β_2	Relapse rate of P due to interaction with A	0.65	Broers et al. [2]
α_1	Rate of U callers entering into treatment with an assertive mindset	0.0001	HELP4WV[13], CDC[5, 6],NSDUH[19] [20]
α_2	Rate of U callers entering into treatment with a passive mindset	0.0018	HELP4WV data, CDC[5, 6], NSDUH[19], [20]
γ_1	Rate of recovery from assertive group	0.5	NSDUH[19], Batista et al. [1]
γ_2	Rate of recovery from passive group	0.2	NSDUH[19], Batista et al. [1]

Table 1: Table of estimated parameters for $\mathcal{SUAPR}$

The proportion of callers who answer all three follow-up calls after initially contacting the center for OUD issues is used to estimate an assertive mindset and is represented by α_1. On the other hand, individuals who initially call the center for OUD help, but miss at least one of the follow-up calls are classified as those who choose to be in treatment without actively engaging in the process, i.e individuals with passive mindsets, and the rate is represented by α_2. Both α_1 and α_2 were found using an amalgamation of national data and HELP4WV data. Among individuals who called HELP4WV, we estimated that the rate of entering OUD treatment with an active mindset and a passive mindset are $\alpha_1 = 0.0001$ and $\alpha_2 = 0.0018$, respectively.

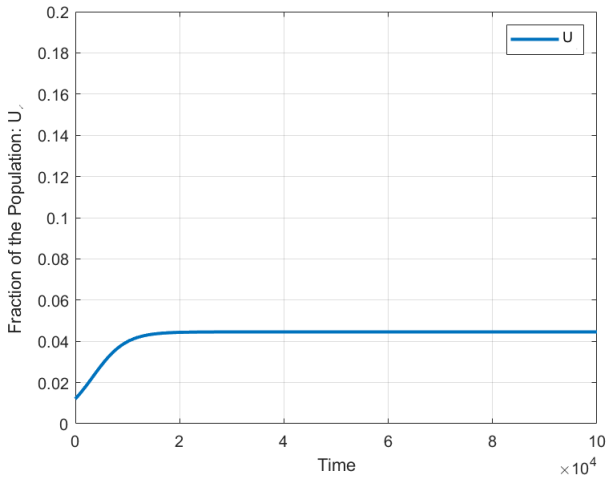

Figure 2: U over time with $\mu = .0073, \beta_1 = .0095, \alpha_1 = .0001, \alpha_2 = .0018, \gamma_1 = 0.5, \beta_2 = .6500, \gamma_2 = .2$

Given the parametric values in Table 1, these graphs show an endemic equilibrium with the OUD population staying around 4% in the long run. Even in our conservative scenario where relapse is designated only for passive respondents and "immunity" is secured by all recovered individuals, there exists an endemic equilibrium. However, it is anticipated that the endemic state in reality is lower than 4% of all WV residents. In our model, we assumed that calling HELP4WV is the only way for an individual to enter treatment, whereas in actuality individuals with OUDs have many other resources and mechanisms to help them ascertain treatment.

Calculating the Basic Reproduction Number

The basic reproduction number, R_0, is the average number of secondary cases that arise from the introduction of one person with an OUD into a fully susceptible population. This value plays an important role in the analysis of outbreak situations where on average each person infects at least one more individual during the period of their infectiousness. We use the next generation method [8, 9], with U treated as the only "infected" compartment as follows

$$\mathcal{F} = [\beta_1 SU + \beta_2 PU]$$
$$\mathcal{V} = [\alpha_1 U + \alpha_2 U + \mu U],$$

where $\mathcal{F}$ represents the $1x1$ matrix of newly infected individuals and $\mathcal{V}$ represents a $1x1$ matrix for any other transfers related to the infectious compartment. Those in A and P are not considered infectious to the population in our model. Here, we consider both new cases of OUD as well as cases of OUD caused by relapse from passive recovery to be "new infections." This assumption follows from Driessche & Watmough's [10, 11] example of a disease treatment model that includes reinfection in the Castillo-Chavez & Feng model for tuberculosis [3],[4]. The disease-free equilibrium (DFE) exists for the $SUAPR$ model. Below, the partial derivatives of $\mathcal{F}$ and $\mathcal{V}$ are taken with respect to the infectious compartment U and evaluated at the DFE.

$$F = [\ \beta_1]$$
$$V = [\ \alpha_1 + \alpha_2 + \mu]$$

The next generation $1x1$ matrix is then given by

$$K = FV^{-1} = [\frac{\beta_1}{\alpha_1 + \alpha_2 + \mu}] \tag{1}$$

whose singular entry is also the spectral radius of the matrix. The basic reproduction number of our model is the probability of developing an opioid use disorder due to interacting with a current drug user divided by the sum of the proportion of callers who answer all three follow-up calls, the proportion of callers who initially call HELP4WV but fail to answer follow-up calls, and the natural death rate. Hence, the basic reproduction number can be written as

$$R_0 = \frac{\beta_1}{\alpha_1 + \alpha_2 + \mu}$$

Stability of the Disease-Free Equilibrium when $\mathbf{R_0 < 1}$

Now, the stability of the disease-free equilibrium such that, $(S^*, U^*, A^*, P^*, R^*) = (1, 0, 0, 0, 0)$, is analyzed. The general Jacobian Matrix is as follows

$J(S, U, A, P, R) =$

$$\begin{pmatrix} -\beta_1 U - \mu & -\beta_1 S & 0 & 0 & 0 \\ \beta_1 U & \beta_1 S - \mu - \alpha_1 - \alpha_2 + \beta_2 P & 0 & \beta_2 U & 0 \\ 0 & \alpha_1 & -\mu - \gamma_1 & 0 & 0 \\ 0 & \alpha_2 - \beta_2 P & 0 & -\mu - \gamma_2 - \beta_2 U & 0 \\ 0 & 0 & \gamma_1 & \gamma_2 & -\mu \end{pmatrix}$$

We then substituted the disease-free equilibrium, which yields

$$J^*(1, 0, 0, 0, 0) = \begin{pmatrix} -\mu & -\beta_1 & 0 & 0 & 0 \\ 0 & \beta_1 - \alpha_1 - \alpha_2 - \mu & 0 & 0 & 0 \\ 0 & \alpha_1 & -\gamma_1 - \mu & 0 & 0 \\ 0 & \alpha_2 & 0 & -\mu - \gamma_2 & 0 \\ 0 & 0 & \gamma_1 & \gamma_2 & -\mu \end{pmatrix}$$

The eigenvalues of the Jacobian matrix are

$$\lambda_1 = -\mu$$

$$\lambda_2 = \beta_1 - \alpha_1 - \alpha_2 - \mu$$

$$\lambda_3 = -\gamma_1 - \mu$$

$$\lambda_4 = -\mu - \gamma_2$$

$$\lambda_5 = -\mu$$

Clearly, $\lambda_1, \lambda_3, \lambda_4, \lambda_5$ are real and negative. Since $R_0 < 1$, it follows that λ_2 is negative as well. Thus, we can conclude the DFE is locally asymptotically stable.

Stability of the Disease-Free Equilibrium when $\mathbf{R_0 = 1}$

To study the direction of bifurcation when $R_0 = 1$ following the work of [27, 4], we write our system of differential equations as $dx/dt = f(x, \lambda_1)$. The Jacobian matrix evaluated at DFE is

$$\tilde{J} = \begin{pmatrix} -\mu & -\kappa & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & -\gamma_1 - \mu & 0 & 0 \\ 0 & \alpha_2 & 0 & -\mu - \gamma_2 & 0 \\ 0 & 0 & \gamma_1 & \gamma_2 & -\mu \end{pmatrix}$$

where $\kappa = \alpha_1 + \alpha_2 + \mu$. The eigenvalues of the Jacobian matrix $\tilde{J}$ are

$$\lambda_1 = -\mu$$

$$\lambda_2 = 0$$

$$\lambda_3 = -\gamma_1 - \mu$$

$$\lambda_4 = -\mu - \gamma_2$$

$$\lambda_5 = -\mu$$

One eigenvalue, namely λ_2, is zero, while the others are real and negative. Next, we find the left and right eigenvectors associated with the zero eigenvalue. The left eigenvector is vector L.

$$L = \begin{pmatrix} l_1 \\ l_2 \\ l_3 \\ l_4 \\ l_5 \end{pmatrix}$$

The transpose of matrix L is multiplied by matrix $\tilde{J}$.

$$L^T\tilde{J} = \begin{pmatrix} l_1 & l_2 & l_3 & l_4 & l_5 \end{pmatrix} \begin{pmatrix} -\mu & -\kappa & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & -\gamma_1 - \mu & 0 & 0 \\ 0 & \alpha_2 & 0 & -\mu - \gamma_2 & 0 \\ 0 & 0 & \gamma_1 & \gamma_2 & -\mu \end{pmatrix}$$

To calculate the left matrix, $L^T\tilde{J}$ is set equal to zero.

$$0 = \begin{pmatrix} -\mu l_1 \\ -\kappa l_1 + \alpha_1 l_3 + \alpha_2 l_4 \\ (-\gamma_1 - \mu) l_3 + \gamma_1 l_5 \\ (-\mu - \gamma_2) l_4 + \gamma_2 l_5 \\ -\mu l_5 \end{pmatrix}$$

Since l_2 is a free-variable, the left eigenvector is $(0, 1, 0, 0, 0)$.

The right eigenvector corresponding to the zero eigenvalue is found below by multiplying matrix $\tilde{J}$ by matrix R and setting the sum equal to zero.

$$0 = \begin{pmatrix} -\mu & -\kappa & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha_1 & -\gamma_1 - \mu & 0 & 0 \\ 0 & \alpha_2 & 0 & -\mu - \gamma_2 & 0 \\ 0 & 0 & \gamma_1 & \gamma_2 & -\mu \end{pmatrix} \begin{pmatrix} r_1 \\ r_2 \\ r_3 \\ r_4 \\ r_5 \end{pmatrix}$$

The resulting equations are as follows:

$$-\mu r_1 - \kappa r_2 = 0$$

$$0 = 0$$

$$\alpha_1 r_2 + (-\gamma_1 - \mu) r_3 = 0$$

$$\alpha_2 x_2 + (-\mu - \gamma_2) r_4 = 0$$

$$\gamma_1 r_3 + \gamma_2 r_4 - \mu r_5 = 0$$

The right eigenvector is $R = \left(\frac{-\kappa}{\mu}, 1, \frac{\alpha_1}{\gamma_1+\mu}, \frac{\alpha_2}{\gamma_2+\mu}, \frac{\gamma_1}{\mu}\left(\frac{\alpha_1}{\gamma_1+\mu}\right) + \frac{\gamma_2}{\mu}\left(\frac{\alpha_2}{\gamma_2+\mu}\right)\right)$.

Following the steps in Appendix A [27], let $x_1 = S$, $x_2 = U$, $x_3 = A$, $x_4 = P$, $x_5 = R$, and f be the model equations with these variables,

$$\begin{aligned}
\frac{dx_1}{dt} &= \mu - \beta_1 x_1 x_2 - \mu x_1 \\
\frac{dx_2}{dt} &= \beta_1 x_1 x_2 - \alpha_1 x_2 - \alpha_2 x_2 + \beta_2 x_4 x_2 - \mu x_2 \\
\frac{dA}{dt} &= \alpha_1 x_2 - \gamma_1 x_3 - \mu x_3 \\
\frac{dP}{dt} &= \alpha_2 x_2 - \beta_2 x_4 x_2 - \gamma_2 x_4 - \mu x_4 \\
\frac{dR}{dt} &= \gamma_1 x_3 + \gamma_2 x_4 - \mu x_5
\end{aligned}$$

where f_k be the kth component of f. We choose β_1 as the bifurcation parameter. To determine the direction of the bifurcation, the following equations must calculated and compared, such that $a, b > 0$ and

$$a = \sum_{k=1}^{n}\sum_{i=1}^{n}\sum_{j=1}^{n} y_k x_i x_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}\Big|_{\text{DFE}}$$

$$b = \sum_{k=1}^{n}\sum_{i=1}^{n} y_k x_i \frac{\partial^2 f_k}{\partial x_i \partial \beta_1}\Big|_{\text{DFE}}$$

The non-zero partial derivatives are the following:

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_2} = \frac{\partial^2 f_2}{\partial x_2 \partial x_1} = \kappa$$

$$\frac{\partial^2 f_2}{\partial x_2 \partial x_4} = \frac{\partial^2 f_2}{\partial x_4 \partial x_2} = \beta_2$$

By applying the summation formula for a, it is found that

$$a = \frac{-2(\kappa)^2}{\mu} + \frac{2\beta_2\alpha_2}{\gamma_2+\mu}$$

So, when $a > 0$, then

$$\frac{\beta_2\alpha_2}{\gamma_2+\mu} > \frac{(\kappa)^2}{\mu} \text{ where } \kappa = \alpha_1 + \alpha_2 + \mu$$

To calculate b, the only non-zero partial derivative evaluated at the DFE is

$$\frac{\partial^2 f_2}{\partial x_2 \partial \beta_1}$$

Thus $b = 1 > 0$.

A backwards bifurcation will occur, allowing a stable endemic equilibrium and a stable disease free equilibrium to coexist when $R_0 < 1$ [12, 27, 4], if it is the case that

$$\frac{\beta_2\alpha_2}{\gamma_2+\mu} > \frac{(\kappa)^2}{\mu}$$

Therefore, lowering $R_0 = \dfrac{\beta_1}{\alpha_1+\alpha_2+\mu}$ to be less than 1 is not sufficient to contain the opioid epidemic. Similar to the results in [27], this finding highlights the difficulty of combating the opioid crisis once it has become established in society.

Existence of Non-Disease Free Equilibrium Solution

Solving the $SUAPR$ model for the non-disease free equilibrium yields

$$\begin{aligned}
S^* &= \frac{\mu}{\beta_1 U^* + \mu} \\
U^* &= U^* \\
A^* &= \frac{\alpha_1 U}{\gamma_1 + \mu} \\
P^* &= -\frac{1}{\beta_2}\left[\beta_1 \cdot \frac{\mu}{\beta_1 U^* + \mu} - (\alpha_1+\alpha_2+\mu)\right] \\
R^* &= \frac{\gamma_1}{\mu}\cdot\frac{\alpha_1 U^*}{\gamma_1+\mu} - \frac{\gamma_2\beta_1}{\mu\beta_2}\cdot\frac{\mu}{\beta_1 U^*+\mu} + \frac{\gamma_2}{\mu\beta_2}(\alpha_1+\alpha_2+\mu)
\end{aligned}$$

We substitute S^*, U^*, A^*, P^*, and R^* into

$$S^* + U^* + A^* + P^* + R^* = 1$$

From algebraic manipulation, we get a quadratic equation, $A(U^*)^2 + BU^* + C = 0$, such that

$$\begin{aligned}
A &= \beta_1\left(\frac{\alpha_1}{\mu}+1\right) \\
B &= \alpha_1+\mu+\beta_1\left(\frac{\gamma_2}{\mu\beta_2}(\alpha_1+\alpha_2+\mu) + \frac{(\alpha_1+\alpha_2+\mu)}{\lambda_2} - 1\right)\mu \\
C &= \left(\frac{\gamma_2+\mu}{\beta_2}\right)(\mu+\alpha_1+\alpha_2)(1-R_0)\mu(M+N)
\end{aligned}$$

The existence of a non-disease free equilibrium solution can be ascertained when $R_0 > 1$ by using the Descartes' Rule of Signs. Consider two cases below, acknowledging the fact that

$$A = \beta_1\left(\frac{\alpha_1}{\mu}+1\right) > 0$$

is always true.

Case 1: $\mathbf{R_0 > 1}$ and $\mathbf{B < 0}$. In this scenario, since $R_0 > 1 \implies C < 0$, there is one real, positive solution for U_1^*. Thus, an endemic equilibrium exists.

Case 2: $\mathbf{R_0 > 1}$ and $\mathbf{B > 0}$. Similar to case 1, this case yields a negative value for C. There is one real, positive solution for U_1^*. Thus, an endemic equilibrium exists.

Conclusion

In this paper, we present an epidemiological model that studies the effectiveness of a helpline in the opioid epidemic by quantitatively differentiating between an active mindset from a passive mindset in drug use. To account for this effect, two separate classes, active respondents and passive respondents, are introduced to the model developed by White and Comiskey [27].

A key result of our model analysis is the basic reproduction number R_0. In the fight against the opioid epidemic, it is important that the rate of developing an OUD due to the interaction of susceptible individuals and opioid users be less than the rate of leaving the U users compartment. Our results support the research findings from White and Comiskey [27] that preventing individuals from developing OUDs is the key method for combating the opioid crisis. However, our results also show that this is not enough by itself. Additionally, we find that expanding the reach and capacity of HELP4WV will increase the rates α_1 and α_2 at which individuals move to some type of treatment and thus decrease R_0. This model shows the importance of encouraging opioid users to utilize helplines by building trust between the using community and the helplines.

The summary of parameter values used for computational examples are provided in Table 1. While some parametric values rely on data specific to the state of West Virginia, others are estimated from national averages or relevant literature. Our model only considers parameter estimation values from 2017 because HELP4WV altered its data collection methods from tracking individual callers to tracking individual calls including repeat calls as new calls in the count.

Further studies focusing on integrating relapses into different treatment groups, changing parametric values over time, and removing the immunity state from the recovered group would contribute to improving our understanding of the opioid epidemic.

Acknowledgement

We thank the Center for Undergraduate Research in Mathematics(CURM) grant program for their support through this project.

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