Prescription Stimulants SEIR Model

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1 Introduction

Adderall, Vyvanse, Ritalin, and other prescription stimulants are used to help treat Attention Deficit Hyperactivity Disorder (ADHD). They increase the levels of dopamine and norepinephrine released in the brain, which are integral to attention and focus[10]. Stimulants are highly effective at treating ADHD when used safely, but their notoriety as a study drug causes many college/university students to abuse Adderall and other stimulants in order to achieve academic success, rather than use them for their intended purpose [3, 4, 9, 7].

Although the most common motivation behind abusing stimulants is academic, current research suggests a number of different motivations and factors that influence a student's susceptibility to stimulant addiction. Students have reported taking stimulants to lose weight, to feel euphoric, or due to social pressure in addition to using the drug to study [1, 5]. Numerous studies suggest a link between abuse of other substances, such as alcohol, marijuana, nicotine, and cocaine; and stimulant addiction (sources). Additionally, various research indicates that being in a sorority or fraternity and having a low-grade point average are correlated with abusing Adderall[8].

Furthermore, Adderall is a Schedule II controlled substance and is thus seen as highly addictive by the United States government. Further research on the specific factors that put students at risk of becoming addicted to stimulants is essential to maintaining the health and well-being of university students in the U.S. and globally. Researching college/university students specifically is crucial considering these students often have readily available access to Adderall and other stimulants. Many students with prescriptions choose to sell off some of these pills on campus, though students may acquire stimulants in other ways, such as online stores, mutual friends, or dealers selling at social events.

2 Abstract

Stimulant abuse on college campuses is a generally under-researched topic. We aim to represent stimulant use and abuse on college campuses using a mathematical model that

looks specifically at how stimulants spread among the population. We designed a system of differential equations. In phase II we will collect data and fit the data to our model. Using these results, we hope to continue to gain a better understanding of stimulant use/abuse on college campuses and hope to propose policies for prevention.

3 Model

3.1 Assumptions

In order to create our model, we will make various assumptions about the population and the movement of stimulants among college students. First, we will assume that all college students are equally susceptible to becoming addicted to stimulants. This allows us to examine a broader population, including students who will never use or abuse stimulants.

Movement from susceptible to exposed will happen based on interactions with members of the exposed or infected group. These groups may entice non-users to use stimulants, which can eventually lead to addiction. We will focus only on these movements, and not on any other interactions or scenarios that may cause susceptible people to use stimulants. We assume that there is homogeneous interaction between all populations.

We will assume that those who recover from addiction will either relapse or remain in recovery, rather than going back to being susceptible. Although there may be some former addicts who can go back to medical use or non-frequent use of stimulants, we will assume that the majority either remain sober or skip the S and E stages and become addicted again with any use of stimulants. That is, individuals who are recovered cannot return to becoming susceptible but can relapse and return to being infected.

3.2 Our Model

We separate our general population of students who have been in an Undergraduate program within the last three years into five classes: S (susceptible), S_p (susceptible, prescribed), E (exposed), I (infected), and R (recovered), with operational semantics as follows: a given person within the studied population typically starts in either S or S_p, based on whether or not they have a prescription for stimulant medication. They may then move to E on stimulant abuse. We model this as a facet of interaction with somebody who is misusing stimulants: either E or I. From E, one can either stop abusing (re-entering S or S_p), or get addicted (entering I). Eventually, people in I can

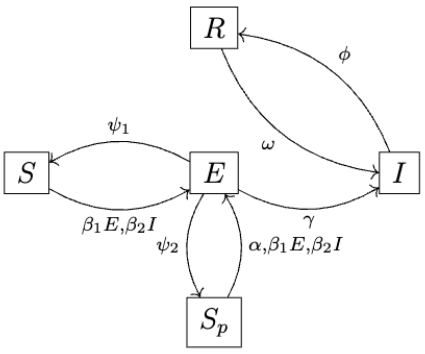


Figure 1: Our Model

recover (move to R), and then potentially relapse (re-entering I).

Since relapse is always possible, and more likely than becoming addicted in the first place, it's impossible to go from R or I to S, S_p, or E.

$$
\begin{aligned}
S' &= -\beta_1 SE - \beta_2 SI + \psi_1 E \\
S_p' &= -\alpha S_p - \beta_1 S_p E - \beta_2 S_p I + \psi_2 E \\
E' &= \beta_1(S + S_p)E + \beta_2(S + S_p)I + \alpha S_p - \psi_1 E - \psi_2 E - \gamma E \\
I' &= \omega R + \gamma E - \phi I \\
R' &= \phi I - \omega R
\end{aligned}
$$

3.3 Parameter Interpretation

Parameter	Interpretation	Units
β_1	transmission from interactions between S and E	per person per day
β_2	transmission from interactions between S and I	per person per day
ψ_1	reciprocal of the number of days someone is misusing a stimulant before stopping	per day
ψ_2	reciprocal of the average number of days someone is misusing their prescription before going back to using as prescribed	per day
ω	proportion who relapse within the first year	unitless
α	reciprocal of the average number of days before someone misuses their prescription	per day
γ	percentage of young adults who become addicted after misusing stimulants	unitless
ϕ	proportion who do not relapse within the first year	unitless

Table 1: The parameters in our model with their interpretations and units.

4 Stability Analysis

We will now derive the basic reproductive number $\mathcal{R}_0$ using the Next Generation Method. We will define our diseased classes to be E and I and derive our system of infected as below [2].

$$\begin{pmatrix} E \\ I \end{pmatrix}' = \mathcal{F} - \mathcal{V}$$

where

$$\mathcal{F} = \begin{pmatrix} \beta_1(S+S_p)E + \beta_2(S+S_p)I + \alpha(S_p) \\ \omega R \end{pmatrix}$$
$$\mathcal{V} = \begin{pmatrix} \psi_1 E + \psi_2 E + \nu E \\ -\nu E + \phi I \end{pmatrix}$$

Here, $\mathcal{F}$ represents the new infections and $\mathcal{V}$ represents the remaining transitions in and out of the diseased classes. The Jacobian matrices corresponding to $\mathcal{F}$ and $\mathcal{V}$ are:

$$F = \begin{pmatrix} \beta_1(S^* + S_p^*) & \beta_2(S^* + S_p^*) \\ 0 & 0 \end{pmatrix}$$
$$V = \begin{pmatrix} \psi_1 + \psi_2 + \nu & 0 \\ -\nu & \phi \end{pmatrix}$$

where S^* and S_p^* are the equilibrium conditions. We can now compute V^{-1} and FV^{-1}:

$$V^{-1} = \begin{pmatrix} \frac{1}{\psi_1+\psi_2+\gamma} & 0 \\ \frac{\gamma}{\phi(\psi_1+\psi_2+\gamma)} & \frac{1}{\phi} \end{pmatrix}$$
$$FV^{-1} = \begin{pmatrix} \frac{\beta_1(S^*+S_p^*)}{\psi_1+\psi_2+\gamma} + \frac{\gamma\beta_2(S^*+S_p^*)}{\phi(\psi_1+\psi_2+\gamma)} & \frac{\beta_2(S^*+S_p^*)}{\phi} \\ 0 & 0 \end{pmatrix}$$

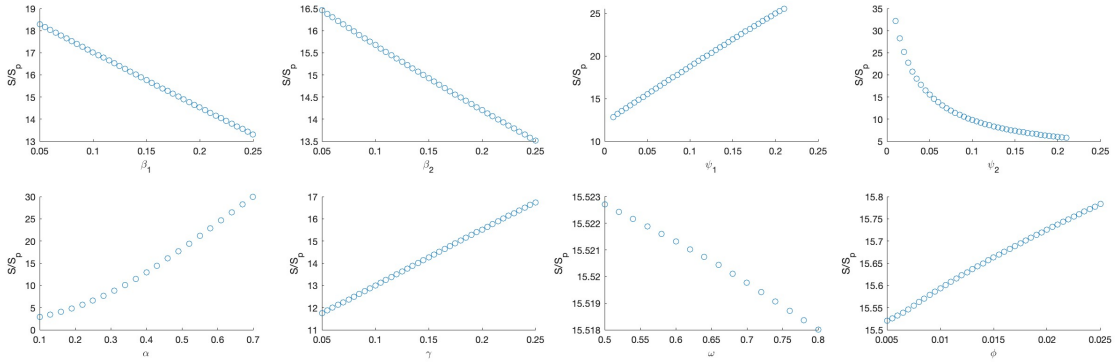
$\mathcal{R}_0$ is equal to the spectral radius of FV^{-1}, which is:

$$\mathcal{R}_0 = \frac{\beta_1}{\psi_1 + \psi_2 + \gamma}(S^* + S_p^*) + \frac{\beta_2\gamma}{\phi(\psi_1 + \psi_2 + \gamma)}(S^* + S_p^*)$$

5 Establishing Monotonicity

To determine how different parameters affect our SEIR model, we decide to conduct a sensitivity analysis using LHS (Latin Hypercube Sampling) - PRCC (Partial Rank Correlation Coefficient). Since a partial rank correlation measures the strength of a relationship between two variables while controlling the others, we need to establish a monotonic relationship between each parameter as input and the corresponding output which in our case is $\frac{S}{S_p}$. Each parameter was tested in MATLAB using separately estimated bounds. We leaned on the error of a larger scale such that if the bounds need to be shrunk, the relationship will still be monotonic.

Figure 2: Monotonicity plot for eight parameters



6 Sensitivity Analysis

The first step in our sensitivity analysis is Latin Hypercube Sampling (LHS). We conduct LHS by dividing the distributions of each parameter into sub-groups, assuming a uniform distribution for each parameter, unless another distribution is known. The random section of a randomly chosen parameter is selected until one sub-section of each parameter distribution has been selected. Multiple rounds of selecting random subsections of randomly chosen parameters are done until all sections of each parameter are accounted for. These parameter distribution sub-groups form the LHS matrix, which is then used to simulate different variations of parameter groupings in the following step of our sensitivity analysis, finding the Partial Rank Correlation Coefficient (PRCC).

PRCC analysis determines the statistical relationships between each input parameter and the outcome variable while keeping all other input parameters constant at their expected value. The input matrix obtained from LHS is the input vector for conducting the processes to find the PRCC and corresponding t-value. The input vector is plugged into the PRCC equations and the outputs of the equation(s) are the p values and correlation coefficients for each parameter. Our significance level is .01; any p-value above .01 will be considered insignificant for our purposes.

Correlation Coefficient Equation:

$$r_{x,y} = \frac{Cov(x_j, y)}{\sqrt{Var(x_j, y)Var(y)}} = \frac{\sum_{i=1}^{N}(x_{ij} - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{N}(x_{ij} - \bar{x})^2 \sum_{i=1}^{N}(y_i - \bar{y})^2}}$$

$$j = 1, 2, ..., k$$

We conducted our PRCC calculations using existing MATLAB code created by Dr. Denise Kirschner from the University of Michigan [6].

7 Data Collection and Methodology

The data in our study was obtained from an anonymous survey sent out to various groups including but not limited to U.W. Madison students, Delta Kappa Delta Sorority, Inc., and student connections via social media. We are aiming to include any students who have actively pursued an undergraduate degree within the last five years. The survey will ask individuals to disclose information about their age, year at university, and stimulant use habits; specifically the frequency of use and any timelines associated with stimulant use.

We used data obtained from our survey to assess the number of individuals in our designated susceptible, exposed, infected, and recovered groups respectively, specifically estimating the average amount of time each person spends in the aforementioned groups in order to find the parameters in our model. The model consists of a series of equations corresponding to the rate of change of each of the respective susceptible, infected, exposed, and recovered groups. We have obtained these parameters from our data in order to build our model.

8 Future Works

The survey will be active for about a month to collect responses. After collecting data, we began estimating our parameters. We initially obtained values for ω, γ, and ϕ during the literature review process, but have later decided to obtain all of our parameters from the data. This is because our sensitivity analysis determined that the parameters are too sensitive to obtain from existing literature. We will use a code to stimulate the SEIR model with different values of our parameters and plot the resulting curve for different stages of our model. Since we have already estimated some parameters, we might use the data we already have as input to help estimate other unknown parameters. Finally, we will do parameter fitting and optimal control analyses to determine whether we find the parameters from the curve that fit the data best. And also try to allocate the available resources to maximum effect in the best way.

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