ADOLESCENT VAPING BEHAVIORS:

EXPLORING THE DYNAMICS OF A SOCIAL CONTAGION MODEL

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Abstract

Vaping, or the use of electronic cigarettes (e-cigarettes), is an ongoing issue for public health. The rapid increase in e-cigarette usage, particularly among adolescents, has often been referred to as an epidemic. Drawing upon this epidemiological analogy between vaping and infectious diseases as a theoretical framework, we aim to study this issue through mathematical modeling to better understand the underlying dynamics. In this thesis, we present a deterministic compartmental model of adolescent e-cigarette smoking which accounts for social influences on initiation, relapse, and cessation behaviors. We use results from a sensitivity analysis of the model's parameters on various response variables to identify key influences on system dynamics and simplify the model into one that can be analyzed more thoroughly. Through steady state and stability analyses and simulations of the model, we conclude that (1) social influences from and on temporary quitters are not important in overall model dynamics and (2) social influences from permanent quitters can have a significant impact on long-term system dynamics, including the reduction of the smokers' equilibrium and emergence of multiple smoking waves.

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Abbreviations

APA	American Psychological Association
EVALI	E-cigarette/Vaping Product Use-Associated Lung Injury
LHS	Latin Hypercube Sampling
NGM	Next-Generation Matrix
ODE	Ordinary Differential Equation
PDF	Probability Distribution Function
PRCC	Partial Rank Correlation Coefficient
SFE	Smoking-Free Equilibrium
SIR	Susceptible-Infected-Recovered
SPE	Smoking-Present Equilibrium/Equilibria

Chapter 1

Introduction

1.1 E-cigarettes & Vaping Risks

Vaping, or the use of electronic cigarettes (e-cigarettes), is an ongoing issue for public health. Introduced to the public around 2007 and marketed as a safer alternative to traditional cigarettes, vaping rapidly gained popularity, particularly among adolescents [23]. According to the 2019 Canadian Health Survey of Children and Youth administered by Statistics Canada, nearly one in four adolescents between the ages of 12 and 17 reported vaping daily or almost daily [32]. An e-cigarette is a small, often pen-sized product that is made up of a cartridge, heating element, and battery [21]. This cartridge contains a solution that is heated in order to produce an odorless vapor, which is then inhaled orally by the user. Cartridge solutions are selected according to the user's taste and are easily refillable and/or replaceable. Oftentimes, these cartridges contain nicotine in high doses, which is already known to be an addictive substance [23].

Pods can contain numerous other harmful substances, including, but not limited to, diacetyl, heavy metals, propylene glycol, and glycerin [21, 23]. Due to the aerosolization of the chemicals in the pod at a high temperature, they are able to be inhaled deep into the lungs. These chemicals serve

as pulmonary irritants and can potentially have carcinogenic effects. Although the long term effects of vaping are still unknown due to their novelty, short term effects have included hospitalization due to EVALI, nicotine dependence, and an increased risk for initiating cigarette use [1, 7, 23, 29].

The use of e-cigarettes poses potential health risks for users of any age, however adolescents are particularly vulnerable to becoming users and experiencing these adverse effects due to the marketing of vaping products [38]. During their introduction to the market, e-cigarette companies advertised vaping as a "safer" alternative to traditional tobacco cigarettes. They argued that because there was no combustion taking place, e-cigarettes could be used as a tool for smokers to quit smoking without the exposure to harmful chemicals in cigarettes, such as tar [21]. Despite the presence of numerous harmful chemicals and high levels of nicotine in e-cigarette pods, as well as their associated adverse effects, the messaging as vaping being "safe" still stood. Thus, adolescents have a minimized perception of the risks of e-cigarette usage [16, 21]. Moreover, the lack of odor produced and small size of the device means that vaping can go relatively undetected compared to traditional cigarettes [21].

A common marketing technique used by e-cigarette companies is the use of flavor and customizability, which appeals to adolescents [21]. Vaping cartridges come in a wide selection, with flavor and nicotine content left as a choice to the user. There are hundreds of e-cigarette brands on the market, and several thousands of choices of unique flavors among them [21]. This demonstrates the large scale of production and the efforts taken to make e-cigarettes appeal to the broader market. The variety of flavors available makes experimenting with vaping particularly enticing to adolescents. For example, a 2016 study done at the University of North Carolina found that if adolescents were offered an e-cigarette by a friend, they were more likely to accept if the flavor was menthol, candy, or fruit as opposed to e-cigarettes with tobacco or alcohol flavorings. Adolescents also perceive their preferred flavors as less of a risk to their health [28]. These marketing strategies

have been highly effective. Not only did the proportion of adolescents vaping increase rapidly, but exposure to advertising has also been found to increase curiosity in those who have never vaped, thus predisposing them to the behavior [38].

Over the years, the growth in adolescent-aged users has become an alarming trend. Importantly, e-cigarettes do not have the same level of regulation as other tobacco products, making them of particular concern for public health. For example, in Canada, flavored cigarettes have been banned, while there has been no such legislation passed for e-cigarettes on the federal level [8, 9]. As such, it is important to determine the trajectory of the number of adolescent e-cigarette users and to understand the underlying dynamics of the usage. Equipped with this type of information, public health efforts can be better and more quickly implemented in order to address the concern.

1.2 Scope & Methodology

In this thesis, we aim to study the issue of adolescent vaping using the tools of mathematical modeling. In particular, we will address the following research questions:

- How can research from the social sciences be better incorporated in modeling how an adolescent's social environment impacts their usage of e-cigarettes?
- What types of social influences are most important in adolescent e-cigarette smoking behaviors?

In Chapter 2, background on addiction modeling more broadly will be provided in order to situate the research questions within the larger body of literature. The approach to be taken in the modeling process will also be outlined. In Chapter 3, the main model of study will be formulated and presented. The basic reproduction number will be derived and explained in context and the model's equilibrium solutions will be studied. A sensitivity analysis will be performed

in Chapter 4 in order to identify which model parameters are most influential on various chosen response variables. The results from the sensitivity analysis motivates a reduced model, which will be analyzed in Chapter 5. This analysis will include the derivation of the reduced model's basic reproduction number, investigation of its equilibrium solutions and their local stabilities, followed by a sensitivity analysis. In Chapter 6, numerical simulations will be used to visualize the model's solutions and identify any additional effects of parameters on system dynamics. Finally, key findings from the thesis will be discussed in Chapter 7, along with implications of the model and potential avenues for future research.

Chapter 2

Modeling Background

2.1 Addiction Modeling

Broadly speaking, mathematical models of addiction fall into two categories: neuro-psychological theory-based models and social models [37]. In the former, the focus is on modeling the neuro-psychological processes occurring within the individual that leads to cravings, addiction, and the increase of tolerance thresholds. Models in this category may consider mechanisms such as reinforcement learning and behavioral economics [37]. Social models attempt to describe the way in which environmental factors impact the initiation and usage of addictive substances on a population level. For example, White and Comiskey proposed one of the first unstructured ODE models for the spread of opioid usage and social influences on initiation and relapse [39]. Others have proposed more structured models that take the impact of specific environments into account, as was done by Muyabi et al. for pro-drinking environments in the context of college alcohol consumption [27]. There are, however, some major gaps in both of these approaches. Neuro-psychological models often ignore social context, while a lack of a robust understanding of social contagion makes social modeling difficult. There is also a lack of a unified framework under which to bring both approaches

together. Overall, there is much work to be done in addiction modeling. This thesis will focus on advancing the understanding of social contagion in social models by aiming to better incorporate research from the social sciences to more accurately model how one's social environment impacts their usage of addictive substances.

One question which naturally arises here is that of the difference between modeling nicotine consumption versus the usage of other substances, namely opioids, marijuana, and alcohol, in the adolescent population. Historically, the opioid crisis has been fueled largely by prescription drugs and the influence of the pharmaceutical industry [12]. Therefore, models on opioid usage may wish to consider factors outside of social influence in the initiation of use. Additionally, the risk for addiction to illicit substances is not as prevalent for the adolescent population, despite the substances themselves being more addictive. It has been found that the onset of substance use for illicit drugs tends to occur slightly later in life [40]. While the legality of marijuana differs depending on state or provincial regulations, it has also been found that the proportion of adolescents initiating cannabis use is substantially lower than for nicotine. Of those who do use, a lower proportion make the transition to becoming cannabis-dependent when compared to nicotine users [40]. This transition also occurs more slowly in cannabis users [31]. Collectively, this indicates that the approach used in modeling nicotine consumption versus opioid and cannabis usage in adolescents would be different.

In comparing nicotine and alcohol consumption in adolescents, a key difference lies in the relative addictiveness of the substances. As was the case with marijuana, nicotine has a shorter length of time before the onset of dependence than alcohol [31]. Moreover, a higher proportion of nicotine users make the transition from first and regular use to dependence than is seen in alcohol consumers [40]. Given alcohol was found to be more widely consumed than nicotine, this indicates that people remain more casual consumers of alcohol and are less likely to become dependent [40].

As a result, a risk structure, as employed by Muyabi et al., may more appropriately address a concern of heavy use and binge drinking patterns in alcohol consumption [27].

An important distinction ought to be made in comparing e-cigarette modeling to models of traditional cigarettes, as they are both forms of nicotine delivery. The addictiveness of the nicotine is comparable regardless of delivery device [24]. This suggests that the differences between the choice to use e-cigarettes versus regular cigarettes comes down to the preferences and perceptions of the individual user, rather than a nicotine dependence. As discussed in Chapter 1, a concerning portion of adolescents perceive e-cigarettes to be a safer alternative to cigarettes. Furthermore, they view e-cigarettes as being a more socially acceptable to use than regular cigarettes [16]. This explains the increased popularity seen in adolescent e-cigarette usage, and why social influences may be all the more important than when compared to the context of cigarettes. The popularity and perceived safety of e-cigarettes differentiates it from traditional cigarette smoking from a modeling perspective as well. For example, cigarette smoking models may wish to consider the influences from educational campaigns that were implemented on a population level [13]. In the e-cigarette context, these population level interventions are not yet present.

2.2 The Social Contagion Perspective

The use of a social modeling framework requires evidence grounding it in psychological and sociological concepts, which can often be overlooked in these types of models [2, 3, 34, 39]. Given the epidemic analogy commonly made, the problem will be studied through the lens of social contagion, which the APA defines as "the spread of behaviors, attitudes, and affect through crowds and other types of social aggregates from one member to another." [6] Importantly, social contagion can occur with or without the presence of pressures to conform or the desire to imitate. It can be the result of what the APA describes as "mundane interpersonal processes," meaning that the behavior can

be subtle, but still result in the spread of that behavior [6].

It is fairly well established in the psychological literature that adolescents are prone to risk contagion when among their peers [14]. Further, many studies show that an adolescent's close connections can have a significant impact on their choice to begin using e-cigarettes. In particular, survey-based studies have found that among adolescents who vaped, friends were the most commonly cited source of the e-cigarette product [17, 38]. Additionally, it is common to initiate the behavior while around other adolescents. The majority of youth e-cigarette users initiated vaping while "hanging out with friends."[17] It is also common for more experienced e-cigarette users to guide those who are experimenting and even assist them in obtaining their own e-cigarette product [17]. This highlights the important role of community and socialization in the uptake of vaping behaviors.

The presence of peers who engage in vaping behaviors also serves to normalize the use of e-cigarettes in the population. A cohort study using nationally representative data from the United States collected between 2016 and 2019 found that having friends who vape increases one's curiosity about the behavior. The study also found that non-vaping adolescents who had friends who vaped were at a higher risk to begin using e-cigarettes in the future [38]. It is apparent that an adolescent's social connections, interactions, and environment are key factors in their decision of whether or not to begin smoking e-cigarettes. Therefore, it is justified to view the issue through the lens of social contagion. By doing so, new interventions targeting peer influences on the increasing levels of vaping adolescents can begin to be considered, as is currently being recommended by researchers in the field [17, 38].

2.3 Models of Smoking-Type Behaviors

Past efforts to deterministically model smoking-type behaviors rely on an SIR-type disease model framework with an analogy to smoking. In their paper, Castillo-Garsow et al. first extend the reinterpreted SIR-type model within the context of cigarette smoking to include demography [10]. Assuming a constant population size $N = S + D + R$ and μ as the birth and death rate, the initial model is composed of the following system:

$$\frac{dS}{dt} = \mu N - \beta S\frac{D}{N} - \mu S, \tag{2.1}$$

$$\frac{dD}{dt} = \beta S\frac{D}{N} - \gamma D + \delta R - \mu D, \tag{2.2}$$

$$\frac{dR}{dt} = \gamma D - \delta R - \mu R, \tag{2.3}$$

where S is the class of individuals susceptible to becoming regular cigarette smokers, D is the class of regular cigarette users, and R is the class of those who are in treatment or who have recovered from regular cigarette use. It is assumed that individuals can only begin smoking due to social influence. As such, they define $\beta = \phi pc$, where c is the per capita visit rate to social gatherings per unit time, p is the probability that social influence results in the initiation of cigarette smoking, and ϕ is the proportion of individuals who become habitual cigarette smokers after casual use. Once individuals become smokers, they quit independently of social context at a given rate γ. After quitting, recovered individuals relapse at a given rate δ, independently from social pressures.

Castillo-Garsow et al. extend this model further to account for possible social mechanisms involved in the process of relapse [10]. They now assume that recovered individuals can only re-initiate smoking due to interactions with current smokers. The nonlinear relapse model has the

following equations:

$$\frac{dS}{dt} = \mu N - \beta S\frac{D}{N} - \mu S, \tag{2.4}$$

$$\frac{dD}{dt} = \beta S\frac{D}{N} - \gamma D + \beta' R\frac{D}{N} - \mu D, \tag{2.5}$$

$$\frac{dR}{dt} = \gamma D - \beta' R\frac{D}{N}, \tag{2.6}$$

where β' is defined analogously to the description of β, but modified to the context of relapse.

The work of Sharomi and Gumel sought to better incorporate the dynamics of quitting [34]. They modify the initial model of Castillo-Garsow et al. to account for a state of temporary quitting [10]. Potential smokers (P) become smokers (S) at a rate $\beta = cq$, where c is the average number of contacts per unit time and q is the probability that the contact with a smoker results in the initiation of cigarette smoking. Once smokers attempt to quit at a rate γ, a proportion $1-\sigma$ of them become temporary quitters (Q_t), who can then relapse are a rate α. The remaining proportion σ become permanent quitters (Q_p), who are considered to be in a recovered state where they can no longer relapse. The birth/death rate is defined as μ, and the population is assumed to be constant such that $P + S + Q_t + Q_p = N$. The model's equations are as follows:

$$\frac{dP}{dt} = \mu N - \beta P\frac{S}{N} - \mu P, \tag{2.7}$$

$$\frac{dS}{dt} = \beta P\frac{S}{N} + \alpha Q_t - (\mu + \gamma)S, \tag{2.8}$$

$$\frac{dQ_t}{dt} = \gamma(1-\sigma)S - (\alpha + \mu)Q_t, \tag{2.9}$$

$$\frac{dQ_p}{dt} = \sigma\gamma S - \mu Q_p. \tag{2.10}$$

Researchers Alkhudhari et al. have produced several papers building off of the model proposed by Sharomi and Gumel and modify it in various ways. The most relevant modification for our

purposes is the incorporation of a nonlinear relapse rate, as suggested by Castillo-Garsow et al., into the model presented in equations 2.7-10 [3, 10]. First, they let $\alpha = \alpha S$ such that relapse can only occur due to influence from smokers, and not as an individual process. They also re-scale the population to be of size 1. Note that the parameters β and α were also re-scaled accordingly. The model has the following equations:

$$\frac{dP}{dt} = \mu - \beta PS - \mu P, \tag{2.11}$$

$$\frac{dS}{dt} = \beta PS + \alpha Q_t S - (\mu + \gamma)S, \tag{2.12}$$

$$\frac{dQ_t}{dt} = \gamma(1 - \sigma)S - (\alpha S + \mu)Q_t, \tag{2.13}$$

$$\frac{dQ_p}{dt} = \sigma\gamma S - \mu Q_p. \tag{2.14}$$

In subsequent studies, Alkhudari et al. look at the effects of temporary quitters choosing to become permanent quitters, and compartments representing smoking frequency (ie. light/occasional and heavy smokers) on overall system dynamics [2, 4, 5].

2.4 Summary

In this chapter, the main research questions were situated within the larger body of literature on addiction modelling. In particular, the approach taken to modelling adolescent e-cigarette usage behaviors will utilize a modeling framework grounded in a social contagion perspective informed by the social sciences. By reviewing models of smoking-type behaviors, it was identified that the main behavioral factors considered in literature are those impacting initiation of cigarette use, as well as relapse of those who are temporary quitters. Notably, little attention has been given to the role of cessation. In the next chapter, the relevance of cessation in the psychological literature will

be discussed and incorporated into a social contagion model.

Chapter 3

An Improved Social Contagion Model

3.1 Rationale

The deterministic models of smoking-type behaviors reviewed in the previous chapter attempt to incorporate mechanisms of social influence into system dynamics. Notably, they only consider social contagion in the processes of initiation and relapse. To the best of our knowledge, there are no deterministic models which explore the impact of social influences and shifting social norms on cessation of smoking-type behaviors. Social influence on cessation of smoking-type behaviors is not a well-studied or understood topic. However, there is a small body of literature which suggests that social connections can influence quitting behaviors, albeit perhaps not as strongly as they influence initiation [18]. A 2008 network analysis study on longitudinal data found that the decrease in cigarette smoking prevalence in American adults over the last 30 years may be in part due to smokers quitting together [11]. It has also been suggested that among adolescents who smoke cigarettes, having peers who quit smoking is positively associated with cessation [35]. While this literature is not exactly within the context of adolescent vaping, it will be used as a proxy given the lack of literature on adolescent e-cigarette cessation and still indicates that social influences on

cessation are worthwhile to consider.

To model the usage of e-cigarettes in the adolescent population, the models previously presented by Sharomi and Gumel and Alkhudari et al. are combined and extended [3, 34]. In particular, we aim to explore the effects of (1) socially-driven initiation and relapse, (2) relapse due to nicotine dependency and other non-socially related factors, (3) socially-influenced cessation, and (4) cessation of one's own volition as they pertain to overall system dynamics.

3.2 Description

We consider the adolescent population to be comprised of the following four separate compartments: potential e-cigarette smokers (P), e-cigarette smokers (S), temporary quitters (Q_t), and permanent quitters (Q_p). The model assumptions made are as follows:

- Initiation of vaping behaviors only occurs as a result of social contagion from current e-cigarette smokers.
- All individuals age into adolescence as potential e-cigarette smokers.
- The size of the adolescent population remains constant over time, meaning adolescents age into and out of the population at the same rate.
- The adolescent population is well-mixed, although this mixing does not strictly require close physical proximity.

Adolescents who are potential e-cigarette smokers (P) only begin vaping due to social contagion from e-cigarette smoking peers (S) at a rate $\beta > 0$. Once an adolescent is vaping, they quit of their own volition at a rate $\gamma_1 > 0$, quit due to social influences from temporary quitters (Q_t) at a rate $\gamma_2 > 0$, or quit due to social influences from permanent quitters (Q_p) at a rate $\gamma_3 > 0$. Of

those who quit, a proportion $\sigma \in (0, 1)$ of them will become permanent quitters. The remaining proportion $(1 - \sigma)$ will become temporary quitters. Those who become temporary quitters relapse and become e-cigarette smokers again either from nicotine dependency and other non-social factors at a rate $\alpha_1 > 0$ or due to social contagion from other e-cigarette smokers at a rate $\alpha_2 > 0$. Further, individuals age into and out of adolescence at a rate $\mu > 0$. As was done by Alkhudari et al., a normalized population size is used such that $P + S + Q_t + Q_p = 1$, where P, S, Q_t, and $Q_p \geq 0$ represent proportions of the adolescent population [3]. Descriptions of model variables and parameters can be found in Table 3.1. The flow diagram for the improved social contagion model is illustrated in Figure 3.1.

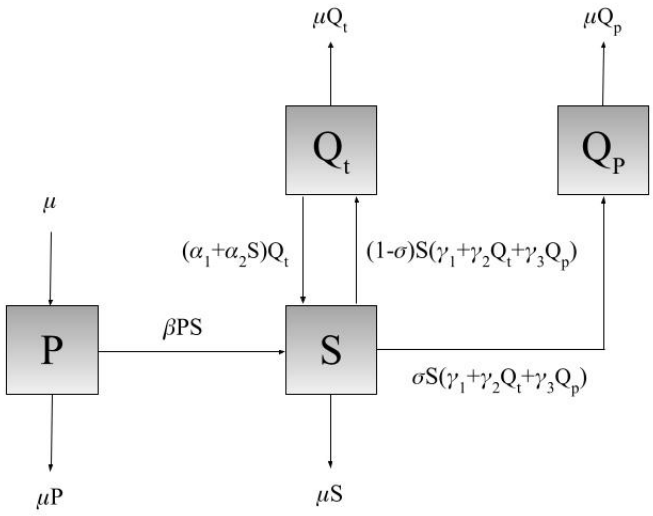

Figure 3.1: Improved social contagion model flow diagram

The resultant system of ODEs for the improved social contagion model is

$$\frac{dP}{dt} = \mu - \beta PS - \mu P \tag{3.1}$$

$$\frac{dS}{dt} = \beta PS + (\alpha_1 + \alpha_2 S)Q_t - (\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p + \mu)S \tag{3.2}$$

$$\frac{dQ_t}{dt} = (1-\sigma)(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p)S - (\alpha_1 + \alpha_2 S + \mu)Q_t \tag{3.3}$$

$$\frac{dQ_p}{dt} = \sigma(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p)S - \mu Q_p \tag{3.4}$$

Importantly, the inherent assumption that adolescents can only initiate vaping behaviors as a consequence of social contagion and interaction with e-cigarette smokers means it is additionally required that $S(0) > 0$ in order for there to be an initial uptake in the behavior. The value of $S(0) > 0$ can be considered to be the result of some stochastic effect, where all those adolescents who initiated the behavior regardless of social influence have already done so by $t = 0$.

Variable	**Definition**	**Unit**
t	Time	Years
P	Potential adolescent e-cigarette smokers	-
S	Adolescent e-cigarette smokers	-
Q_t	Temporary quitters	-
Q_p	Permanent quitters	-
Parameter		
μ	Mean rate at which individuals age in and out of adolescence	$(\text{Years})^{-1}$
β	Mean social contagion initiation rate	$(\text{Years})^{-1}$
α_1	Mean non-social relapse rate	$(\text{Years})^{-1}$
α_2	Mean social relapse rate	$(\text{Years})^{-1}$
γ_1	Mean non-social cessation rate	$(\text{Years})^{-1}$
γ_2	Mean Q_t-influenced cessation rate	$(\text{Years})^{-1}$
γ_3	Mean Q_p-influenced cessation rate	$(\text{Years})^{-1}$
σ	Proportion of quitters who quit permanently	-

Table 3.1: Variable and Parameter Descriptions

3.3 Basic Reproduction Number

In the context of disease outbreaks, the basic reproduction number $\mathcal{R}_0$ is typically defined as the average number of infections produced by a single infectious individual in a fully susceptible population during their entire infectious period [20]. In this context, the definition is adapted such that $\mathcal{R}_0$ can be interpreted as the expected number of secondary e-cigarette users arising

from a single e-cigarette user during their entire smoking period in a population of only e-cigarette non-users. This population of only e-cigarette non-users is represented by the model's SFE of $(P^*, S^*, Q_t^*, Q_p^*) = (1, 0, 0, 0)$.

In order to derive the expression for $\mathcal{R}_0$, the NGM method is employed, as described by van den Driessche and Watmough [36]. An alternative derivation of $\mathcal{R}_0$ using the eigenvalues of the model's Jacobian matrix can be found in Appendix A.1. Accordingly, the "smoke-present" compartments are identified, which are S and Q_t. The differential equations for these compartments can be written as

$$\begin{aligned}\begin{bmatrix} \frac{dS(t)}{dt} \\ \frac{dQ_t(t)}{dt} \end{bmatrix} &= \begin{bmatrix} \beta PS \\ 0 \end{bmatrix} - \begin{bmatrix} -(\alpha_1 + \alpha_2 S)Q_t + (\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p + \mu)S \\ -(1-\sigma)(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p)S + (\alpha_1 + \alpha_2 S + \mu)Q_t \end{bmatrix} \\ &= \mathcal{F} - \mathcal{V}, \end{aligned} \tag{3.5}$$

where $\mathcal{F}$ is the vector of terms that produce new smokers in a compartment, and $\mathcal{V}$ is the vector of terms that represent the transfer of individuals in and out of the compartments by other means. The Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ are F and V, respectively, where

$$F = \begin{bmatrix} \beta P & 0 \\ 0 & 0 \end{bmatrix}, \; V = \begin{bmatrix} -\alpha_2 Q_t + \gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p + \mu & -(\alpha_1 + \alpha_2 S) + \gamma_2 S \\ -(1-\sigma)(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p) + \alpha_2 Q_t & -(1-\sigma)\gamma_2 S + \alpha_1 + \alpha_2 S + \mu \end{bmatrix} \tag{3.6}$$

The Jacobian matrices evaluated at the SFE are

$$F|_{SFE} = \begin{bmatrix} \beta & 0 \\ 0 & 0 \end{bmatrix}, \; V|_{SFE} = \begin{bmatrix} \gamma_1 + \mu & -\alpha_1 \\ -(1-\sigma)\gamma_1 & \alpha_1 + \mu \end{bmatrix} \tag{3.7}$$

From here, it can be determined that the spectral radius $\rho(FV^{-1}) = \mathcal{R}_0$, where

$$\begin{aligned}\mathcal{R}_0 &= \frac{\beta(\alpha_1+\mu)}{(\alpha_1+\mu)(\gamma_1+\mu)-\alpha_1\gamma_1(1-\sigma)} \\ &= \frac{\beta}{(\gamma_1+\mu)\left(1-\frac{\alpha_1}{\alpha_1+\mu}\cdot\frac{\gamma_1}{\gamma_1+\mu}(1-\sigma)\right)} \\ &= \frac{\beta}{(\gamma_1+\mu)\cdot(1-\psi)}\end{aligned} \tag{3.8}$$

In particular, $\mathcal{R}_0$ behaves similarly to reproduction numbers of disease models. The $\beta/(\gamma_1+\mu)$ term represents the spread of behaviors from one vaping individual into a fully non-vaping population over the course of their smoking period when relapse is ignored. However, the relapse function $(1-\psi) \in (0,1)$ serves to increase $\mathcal{R}_0$ due to the relapse of temporary quitters. Specifically, $\gamma_1/(\gamma_1+\mu)$ is the proportion of smokers who actually quit, making $\gamma_1(1-\sigma)/(\gamma_1+\mu)$ the proportion of smokers who make it to the temporary quitting phase. Further, $\alpha_1/(\alpha_1+\mu)$ is the proportion of temporary quitters who revert and become e-cigarette smokers once more. Collectively, this makes ψ the proportion of smokers who quit temporarily and revert back to smoking. Ultimately, increasing ψ would increase one's average smoking period, and thus increases $\mathcal{R}_0$. Notice that social influences on relapse (α_2) and cessation (γ_2, γ_3) do not appear in $\mathcal{R}_0$, indicating they are not influences in the growth phase of the spread of vaping behaviors. This is to be expected given the definition of $\mathcal{R}_0$.

3.4 Equilibria

By setting the left hand side of the system (3.1-4) to zero, equilibrium solutions can be obtained. One equilibrium previously mentioned is the SFE of $(P^*, S^*, Q_t^*, Q_p^*) = (1, 0, 0, 0)$. Note that the local stability of the SFE can be expressed by conditions on $\mathcal{R}_0$. The SFE of the model is locally asymptotically stable if $\mathcal{R}_0 < 1$, but unstable if $\mathcal{R}_0 > 1$ [36]. In practical terms, $\mathcal{R}_0$ can indicate

whether or not one can expect the behavior to reach "epidemic" levels. For $\mathcal{R}_0 > 1$, it is expected that the behavior will spread throughout the population. For $\mathcal{R}_0 < 1$ it is expected that the behavior will die out.

The SPE have the form $(P^{**}, S^{**}, Q_t^{**}, Q_p^{**})$, where

$$P^{**} = \frac{\mu}{\beta S^{**} + \mu}, \tag{3.9}$$

$$Q_t^{**} = \frac{\mu(1-\sigma)S^{**}(\beta(1-S^{**}) - \mu)}{((\alpha_2 S^{**} + \alpha_1)\sigma + \mu))(\beta S^{**} + \mu)}, \tag{3.10}$$

$$Q_p^{**} = \frac{A}{((\alpha_2 S^{**} + \alpha_1)\sigma + \mu)(\beta S^{**} + \mu)\gamma_3}, \tag{3.11}$$

with

$$A = S^{**}(\mu(1-S^{**})(\gamma_2(\mu-\beta)+\beta\alpha_2) - \alpha_2(\sigma\gamma_1(\beta S^{**}+\mu) - \mu^2)) - \beta S^{**}K + \mu(\beta(\alpha_1+\mu) - K), \tag{3.12}$$

$$K = (\alpha_1 + \mu)(\gamma_1 + \mu) - \alpha_1\gamma_1(1-\sigma), \tag{3.13}$$

and S^{**} is a solution of the cubic polynomial

$$\beta\sigma\alpha_2\gamma_3 S^{**3} + BS^{**2} + CS^{**} + D, \tag{3.14}$$

where

$$B = -\alpha_2 * B_1 + B_2, \tag{3.15}$$

$$C = \alpha_2\mu(\beta - \mu - \sigma\gamma_1) - \gamma_2\mu(\beta-\mu)(1-\sigma) - \sigma C_1 - \mu C_2, \tag{3.16}$$

$$D = (R_0 - 1)\mu K, \tag{3.17}$$

such that

$$B_1 = \gamma_3\sigma(\beta - \mu) + \beta(\gamma_1\sigma + \mu), \tag{3.18}$$

$$B_2 = \beta(\gamma_2\mu(1 - \sigma) + \gamma_3\sigma(\alpha_1 + \mu)), \tag{3.19}$$

$$C_1 = (\beta - \mu)\gamma_3(\mu + \alpha_1) + \alpha_1\beta\gamma_1, \tag{3.20}$$

$$C_2 = \beta(\alpha_1 + \gamma_1 + \mu). \tag{3.21}$$

It is always true that $\beta\sigma\alpha_2\gamma_3 > 0$. Note that $D > 0$ if and only if $\mathcal{R}_0 > 1$, which must occur for an outbreak of the behavior to take place. As a result, there are the following four possibilities that arise for the signs of the coefficients of the cubic polynomial for $\mathcal{R}_0 > 1$:

- $B > 0$, $C > 0$
- $B < 0$, $C < 0$
- $B < 0$, $C > 0$
- $B > 0$, $C < 0$

In the first case, Descartes' Rule of Signs implies that there are no positive roots because no sign changes occur. In the remaining cases, the Rule of Signs implies that there are either two or no positive roots due to two sign changes occurring. It can be shown (see Appendix A.2) that the first scenario is not possible for $\mathcal{R}_0 > 1$. So, the polynomial must have two sign changes and has either two or zero positive roots. It remains to be shown in general that the latter is not the case here.

Suppose that μ is small (i.e., $\mu << 1$), which is likely to be the case in a real-world setting. Here, perturbation methods can be used to analyze the roots of the cubic polynomial. S^{**} can be

expressed as a power series in μ, such that

$$S^{**} = \sum_{j=0}^{\infty} \mu^j s_j = s_0 + \mu s_1 + ... \tag{3.22}$$

Substituting the power series, up to order μ, into the cubic polynomial, we obtain the following equation to solve:

$$\beta\sigma\alpha_2\gamma_3(s_0 + \mu s_1)^3 + B(s_0 + \mu s_1)^2 + C(s_0 + \mu s_1) + D = 0. \tag{3.23}$$

After expanding the polynomial and collecting powers of μ to order μ, we have

$$s_0\beta\sigma(s_0\alpha_2 + \alpha_1)(s_0\gamma_3 - \gamma_1 - \gamma_3) + \mu(m_0 s_0^2 s_1 + m_1 s_0 s_1 + m_2 s_0^2 - m_3 s_1 + m_4 s_0 - m_5) = 0, \tag{3.24}$$

where

$$m_0 = 3\beta\sigma\alpha_2\gamma_3, \tag{3.25}$$

$$m_1 = 2\beta\sigma(\alpha_1\gamma_3 - \alpha_2\gamma_1 - \alpha_2\gamma_3), \tag{3.26}$$

$$m_2 = \beta\gamma_2(1 - \sigma) + \beta\sigma\gamma_3 + \sigma\alpha_2\gamma_3 - \beta\alpha_2, \tag{3.27}$$

$$m_3 = \beta\sigma\alpha_1(\gamma_1 + \gamma_3), \tag{3.28}$$

$$m_4 = \beta\sigma\gamma_2 - \beta\sigma\gamma_3 + \sigma\alpha_1\gamma_3 - \sigma\alpha_2\gamma_1 - \beta\alpha_1 + \beta\alpha_2 - \beta\gamma_1 - \beta\gamma_2, \tag{3.29}$$

$$m_5 = \alpha_1(\sigma\gamma_1 + \beta). \tag{3.30}$$

Due to the linear independence of the terms in the power series, solving the equation is equiv-

alent to finding s_0, s_1 such that the coefficients of the expanded polynomial are zero. So,

$$s_0\beta\sigma(s_0\alpha_2+\alpha_1)(s_0\gamma_3-\gamma_1-\gamma_3)=0 \tag{3.31}$$

$$\implies s_0^{(1)}=0 \tag{3.32}$$

$$\implies s_0^{(2)}=-\alpha_1/\alpha_2 \tag{3.33}$$

$$\implies s_0^{(3)}=(\gamma_3+\gamma_1)/\gamma_3 \tag{3.34}$$

Substituting these results into the coefficient of μ and solving for s_1 yields

$$s_1^{(1)}=\frac{\alpha_1(\sigma\gamma_1-\beta)}{-\beta\sigma\alpha_1(\gamma_1+\gamma_3)}, \tag{3.35}$$

$$s_1^{(2)}=\frac{-((1-\sigma)\gamma_2(\alpha_1+\alpha_2)+\sigma\gamma_3(\alpha_1+\alpha_2)+\alpha_2\gamma_1)}{\sigma((\gamma_3+\gamma_1)\alpha_2+\alpha_2\gamma_1}, \tag{3.36}$$

$$s_1^{(3)}=\frac{((1-\sigma)\gamma_3+\sigma\gamma_2+\alpha_2)\beta\gamma_1^2+\gamma_1\gamma_3(((1-\sigma)\beta-\sigma\alpha_2)\gamma_3+\beta(\sigma\gamma_2+\alpha_1+\alpha_2-\gamma_2))-\sigma(\alpha_1+\alpha_2)\gamma_3^3}{\beta((\alpha_1+\alpha_2)\gamma_3+\alpha_2\gamma_1)\sigma\gamma_3(\gamma_3+\gamma_1)}. \tag{3.37}$$

Therefore, the solutions of the cubic take the following forms:

$$S_1^{**}\approx s_0^{(1)}+s_1^{(1)}\mu=0+s_1^{(1)}\mu, \tag{3.38}$$

$$S_2^{**}\approx s_0^{(2)}+s_1^{(2)}\mu=\frac{-\alpha_1}{\alpha_2}+s_1^{(2)}\mu, \tag{3.39}$$

$$S_3^{**}\approx s_0^{(3)}+s_1^{(3)}\mu=\frac{\gamma_1+\gamma_3}{\gamma_3}+s_1^{(3)}\mu. \tag{3.40}$$

The sign of S_1^{**} depends on the sign of $s_1^{(1)}$. When $\mathcal{R}_0\sim\beta/\gamma_1\sigma>1$, which must be the case for the spread of the behavior to occur, then $\beta>\gamma_1\sigma$ for $\mu<<1$. (For a discussion on $\mathcal{R}_0$ in this μ limit, see Appendix A.3.) This implies that $s_1^{(1)}>0$, so $S_1^{**}>0$ is small and is one feasible SPE.

The leading terms of S_2^{**} and S_3^{**} are not feasible, as they do not satisfy the model's assumptions. As $s_1^{(2)} < 0$, any small deviation will cause S_2^{**} to remain negative. The sign of $s_1^{(3)}$ remains unclear, so small deviations from $(\gamma_1 + \gamma_3)/\gamma_3 > 1$ may or may not lead to a feasible value for S_3^{**}. If $s_1^{(3)} > 0$, then S_3^{**} will not satisfy the model's assumptions. If $s_1^{(3)} < 0$ and $(\gamma_1 + \gamma_3)/\gamma_3 \sim 1$, then it is possible for a second potential SPE could arise depending on the magnitude of $s_1^{(3)}$. It is worth noting that even if S_3^{**} is viable, this does not necessarily mean the corresponding Q_t^{**} and/or Q_p^{**} will be.

3.5 Summary

In this chapter, the rationale behind considering social influences on cessation of e-cigarette smoking was outlined. Specifically, the possibility of social contagion mechanisms in cessation and the relative uncertainty surrounding the strength of its influence served as motivators for exploring its effects mathematically. As a result, an improved social contagion model was proposed in order to capture these additional behavioral influences. Analysis of the model included the derivation of its basic reproduction number along with the computation of its equilibrium solutions. However, the number of SPE still remains unclear due to the complexity of the analysis. Further, any additional analysis, such as steady state stability, would prove difficult. Given these complications, a sensitivity analysis will be conducted in the next chapter to aid in reducing the model.

Chapter 4

Sensitivity Analysis

Given that e-cigarette smoking is a recent and currently understudied phenomenon, there is no literature available that provides the information needed to guide us in the selection of precise model parameters. As such, a sensitivity analysis will prove useful in identifying important parameters and helping to simplify the model into one that captures the key dynamics of adolescent vaping behavior. With a simpler model, a more robust analysis can be performed. In this chapter, the sensitivity of various key response variables to changes in the parameters will be studied numerically. First, the methods of LHS and PRCC will be outlined and any assumptions being placed on the parameter ranges will be explained. After, a sensitivity analysis will be carried out on key metrics of the behavioral spread.

4.1 Methods

The methods of LHS and PRCC will be employed, as described by Marino et al., to perform our global sensitivity analysis on the model [26]. LHS is a common sampling method used to randomly select values from a parameter's PDF. LHS is designed such that it ensures samples are taken from the entire spectrum of the PDF, which avoids the potential biases of other sampling methods,

and allows the span of the parameter space to be studied. These samples are taken and stored in an LHS matrix. PRCC first requires the use of the LHS matrix to compute a chosen response variable over a variety of sampled parameter combinations, which is stored in a vector. Note that a monotonic relationship between the parameters and the response variable is required in order to successfully use the method. From here, the entries of this vector and the LHS matrix are rank-transformed. Finally, multiple linear regression is applied and the PRCCs are computed for each parameter, which measures the linearity of the relationship between each model parameter and the chosen response variable. PRCCs are measured between -1 and +1, where results near ± 1 indicate that changes in the parameter are highly correlated with changes in the response variable. The sign of the PRCC indicates whether this correlation is positive or negative. A PRCC of 0 indicates that changes in the parameter are uncorrelated with changes in the response variable. Statistical significance of each PRCC can also be calculated, where a p-value of < 0.05 indicates a statistically significant result.

For our purposes, only uniform distributions will be sampled from, given that the PDFs are unknown. A summary of the parameter assumptions is given in Table 4.1. Adolescence can be defined as the period of transition between childhood and adulthood, which is roughly from 11 to 19 years old [33]. Therefore, the fixed value $\mu = 1/8$ years^{-1} is assumed. Through survival analysis, it has been found that nicotine users who are able to quit for at least a year are unlikely to return to using [15]. With similar reasoning, it is assumed that if a never-smoker has not been influenced after a year of contact with a smoker, then they are unlikely to be influenced at all as they are not as predisposed as temporary quitters. Thus, the lower bound of β is assumed to be 1 year^{-1}. An upper bound of 4 years^{-1} (or three months) is assumed. Given that the relationship between initiation rates and quitting rates is unknown, we avoid making assumptions on the relationship and assume the ranges for γ_1, γ_2, and γ_3 to be the same. Relapse curves for nicotine usage show

that relapse mostly occurs within days to two weeks after the cessation attempt for regular users [15, 22]. In our model, we allow the S compartment to be made up of any type of user, including light users, and so we shift the range and assume relapse occurs between roughly 8 to 20 days, which gives the range of 18 to 45 years^{-1} for α_1 and α_2. Again, we avoid making assumptions regarding the relationship between these parameters. Finally, it is assumed that the proportion of cessation attempts which are successful (σ) is low [30]. An LHS sample size of 3000 was used, with initial conditions of $P(0) = 0.92$ and $S(0) = 0.08$ [19].

Parameter	**Value or Range of Uniform PDF**
μ	1/8 years^{-1}
β	[1, 4] years^{-1}
α_1	[18, 45] years^{-1}
α_2	[18, 45] years^{-1}
γ_1	[1, 4] years^{-1}
γ_2	[1, 4] years^{-1}
γ_3	[1, 4] years^{-1}
σ	[0.01, 0.2]

Table 4.1: Sensitivity Analysis Parameter Assumptions

In our analyses, the sensitivities of several response variables that are most important for the purposes of public health interventions and serve as key behavioral measures will be tested. In order to understand the sensitivity of the initial spread of vaping behaviors to model parameters, $\mathcal{R}_0$ will be studied. The peak value of smokers and the time at which this value occurs is also chosen as a measure of the potential severity of the issue. The smokers' equilibrium and final size of the "outbreak" of vaping behaviors (taken to be the total population proportion who has ever smoked e-cigarettes) provide insight into the long term trajectory of adolescent e-cigarette usage. They indicate the level of smoking one can expect to persist in the population as time goes on, as well as the how widespread the behavior can become.

4.2 Results

The results of the sensitivity analysis can be found in Figure 4.1. In this discussion, all of the PRCC values without a p-value less than 0.05 will not be considered, as they are not statistically significant. Parameters associated with producing smokers $(\beta, \alpha_1, \alpha_2)$ were found to be positively correlated with the response variables of $\mathcal{R}_0$, peak value, smokers' equilibrium, and final size. This was to be expected, as these response values are measures of how quickly smoking spreads, how intense the issue is, and vaping as a long-term problem. However, the correlations of α_1 and α_2 prove to be insignificant, indicating that relapse is not an important factor in the metrics for the parameter ranges tested. This seems to be due to relapse occurring quite quickly, where the residence time of an individual in the temporary smoker compartment is so short that they are effectively leaving the smoking compartment and re-entering almost immediately. The results also indicate that β is the most significant factor in the severity of e-cigarette smoking in the population, with a PRCC value of > 0.8 with respect to $\mathcal{R}_0$, peak value, and final size. For the smokers' equilibrium, the PRCC value for β was approximately 0.4987, which is close to the widely accepted significance threshold of 0.5 for positive correlations. The smoking producing associated parameters were, however, negatively correlated with peak time, with β being the most contributing factor.

Parameters associated with smoking cessation $(\gamma_1, \gamma_2, \gamma_3, \sigma)$ were found to be negatively correlated with all response variables. Across all response variables, σ was found to be the most significant parameter of all the cessation associated parameters. As the proportion of quitters who are able to quit permanently decreases, the more they are able to re-initiate smoking and increase the average smoking lifetime. As a result, they are able to also ensure that vaping becomes more widespread. For these reasons, it is unsurprising that σ carries the observed significance, with PRCC values of > 0.9 for 5 out of the 6 response variables. The effect of temporary quitters on e-cigarette smoking cessation, captured in γ_2, was found to be insignificant overall. Again, this seems

to be due to the proportion of the population in the temporary quitter compartment remaining relatively small in the simulations. The non-social cessation rate of γ_1 was found to be significant in relation to 5 out of the 6 response variables.

The most interesting finding arising from the sensitivity analysis is the significance of γ_3 on the smokers' equilibrium and final size values. Analytically, it is known that the parameter has no effect on $\mathcal{R}_0$. Additionally, the PRCC values of < 0.5 for peak value and peak time indicate that γ_3 is also not an influential parameter for those response variables. Collectively, this suggests that γ_3 is not influential in the growth phase of the spread of vaping. While it is not important early on, it is a significant factor in the long-term trajectory of e-cigarette usage in the population. The PRCC values for γ_3 are approximately -0.6643 and -0.5345 for smokers' equilibrium and final size, respectively. It appears that as time goes on, the proportion of the population in the permanent quitter compartment increases to a level that allows permanent quitters to have a significant effect. This effect is twofold, where (1) the more permanent quitters increase the number of quitting attempts, the more that smokers are likely to become permanent quitters and (2) the permanent quitters assist in decreasing the average smoking period of smokers later in the timeline and so less potential smokers are recruited into the smoking compartment. Thus, the smokers' equilibrium and final size decreases as γ_3 increases.

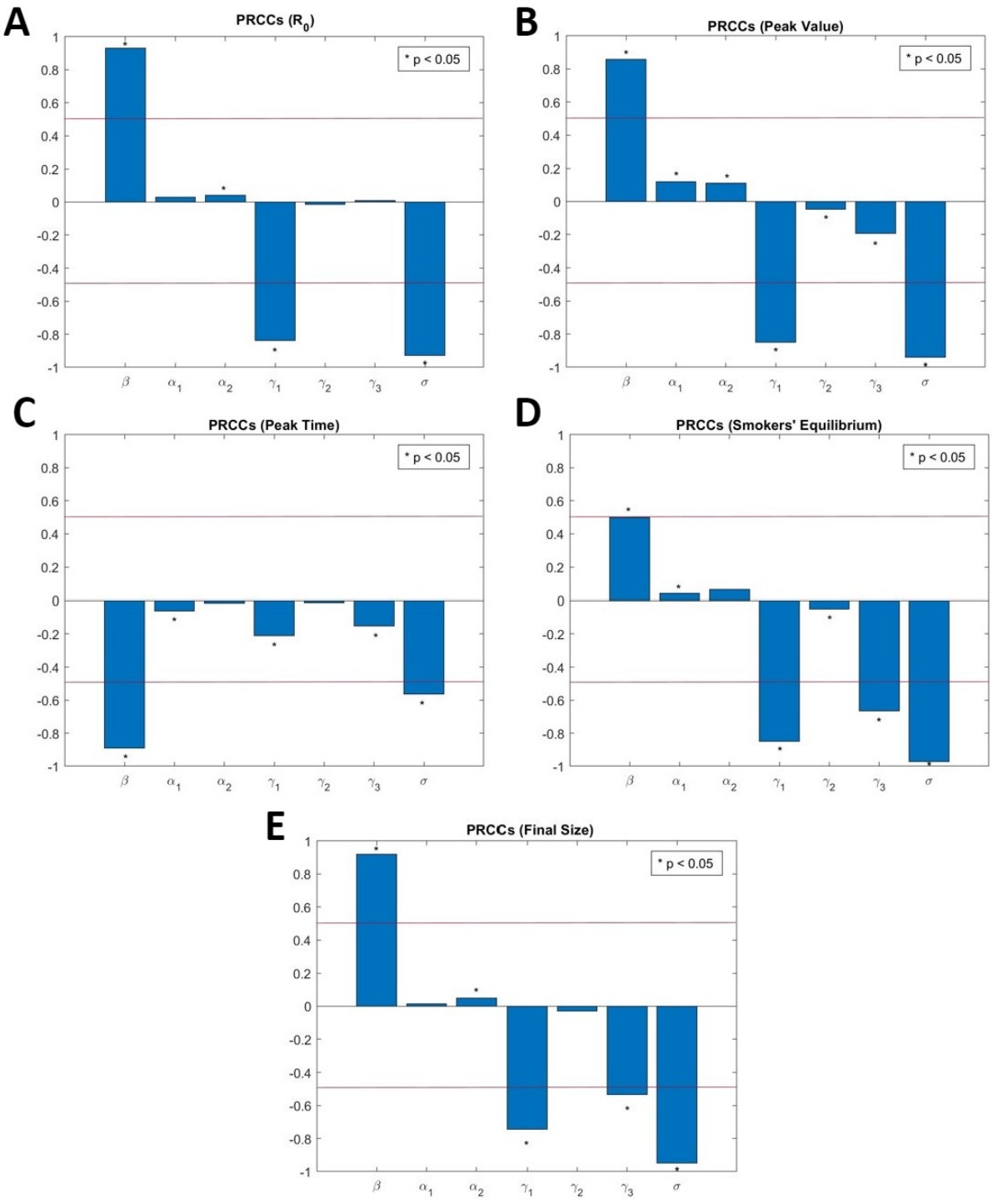

Figure 4.1: PRCC analyses for the improved social contagion model using 3000 LHS samples for the parameter ranges in Table 4.1, where the red horizontal lines at ± 0.5 indicate the threshold for significance and * denotes a statistically significant result (p-value < 0.05).

4.3 Summary

The sensitivity analysis performed uncovered key underlying mechanisms of the proposed model as it pertains to the chosen response variables. As expected, the social initiation rate, non-social cessation rate, and proportion of quitters who quit permanently were the main contributors to system dynamics. The findings also suggested that when relapse occurs quickly, as is not unusual with addictive substances, the effect of temporary quitters is negligible in the overall trajectory of the spread of vaping behaviors throughout the population. Mathematically, this is due to short residence times in Q_t. Socially, an interpretation is that temporary quitters are not as determined to maintain their quitting status [15]. As such, they are not effective in deterring smokers from their vaping habits. If relapse rates were slower, then relapse may have a more significant role in system dynamics (See Appendix A.4). Most interestingly, γ_3 was found to play a significant role in the long term dynamics of vaping behaviors in the adolescent population. Over time, this indicates that the change in social norms in a population can prove important in shaping the trajectory of the spread of vaping behaviors. The higher the proportion of individuals in the Q_p compartment, the less adolescents view vaping as being a popular activity and so they may be more inclined to attempt quitting. Equipped with this new insight, the model can now be reduced into one that captures key dynamics, but is simpler to analyze.

Chapter 5

Reduced Model Analysis

5.1 The Reduced Model

The results of the sensitivity analysis only identified four parameters as being significant as it pertains to the chosen response variables. As such, a reduced model that involves only terms with $\beta, \gamma_1, \gamma_3$, and σ will now be considered. In doing so, unnecessary complexity is removed and a more in-depth analysis of the model can be conducted to deepen the understanding of how the sensitive parameters affect the model interpretations. Model reduction can also prove beneficial later on to simplify analysis if additional extensions to the model are made. While parameters relating to relapse were not found to be significant, terms with α_1 will be included.[1] In doing so, the relapse structure and basic reproduction number remain preserved. Note that if terms with parameters α_1 and α_2 were all removed, then temporary quitters would effectively become permanent quitters. Thus, the model's structure is sensitive to relapse. Intuitively, choosing α_1 assumes that relapse due to nicotine dependence and cravings is a more prevalent factor than socially-influenced relapse [25]. The flow diagram for the model is illustrated in Figure 5.1.

[1] The emergence of α_1 as the only additional significant parameter under the slower relapse assumptions in Appendix A also supports the choice to retain it in the reduced model structure, and suggests that the reduced model may be applicable to a wider range of parameters than is assumed here.

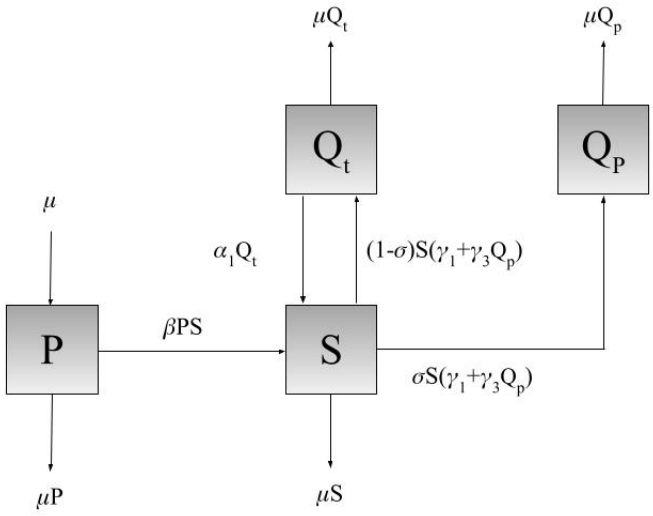

Figure 5.1: Reduced model flow diagram

The resultant system of ODEs for the reduced model is

$$\frac{dP}{dt} = \mu - \beta PS - \mu P, \tag{5.1}$$

$$\frac{dS}{dt} = \beta PS + \alpha_1 Q_t - (\gamma_1 + \gamma_3 Q_p + \mu)S, \tag{5.2}$$

$$\frac{dQ_t}{dt} = (1-\sigma)(\gamma_1 + \gamma_3 Q_p)S - (\alpha_1 + \mu)Q_t, \tag{5.3}$$

$$\frac{dQ_p}{dt} = \sigma(\gamma_1 + \gamma_3 Q_p)S - \mu Q_p. \tag{5.4}$$

This reduced model carries the same assumptions as the full model, however socially-influenced relapse and cessation influences by temporary quitters are no longer considered.

5.2 Basic Reproduction Number

The NGM method is again employed to derive $\mathcal{R}_{sub}$, or the basic reproduction number of the reduced model.[2] Recall that the "smoke-present" compartments are S and Q_t. The differential equations for these compartments can be written as

$$\begin{aligned}\begin{bmatrix} \frac{dS(t)}{dt} \\ \frac{dQ_t(t)}{dt} \end{bmatrix} &= \begin{bmatrix} \beta PS \\ 0 \end{bmatrix} - \begin{bmatrix} -\alpha_1 Q_t + (\gamma_1 + \gamma_3 Q_p + \mu)S \\ -(1-\sigma)(\gamma_1 + \gamma_3 Q_p)S + (\alpha_1 + \mu)Q_t \end{bmatrix} \\ &= \mathcal{F}_{sub} - \mathcal{V}_{sub},\end{aligned} \tag{5.5}$$

where $\mathcal{F}_{sub}$ is the vector of terms that produce new smokers in a compartment, and $\mathcal{V}_{sub}$ is the vector of terms that represent the transfer of individuals in and out of the compartments by other means. The Jacobian matrices of $\mathcal{F}_{sub}$ and $\mathcal{V}_{sub}$ are F_{sub} and V_{sub}, respectively, where

$$F_{sub} = \begin{bmatrix} \beta P & 0 \\ 0 & 0 \end{bmatrix}, \; V_{sub} = \begin{bmatrix} -\alpha_2 Q_t + \gamma_1 + \gamma_3 Q_p + \mu & -\alpha_1 \\ -(1-\sigma)(\gamma_1 + \gamma_3 Q_p) & \alpha_1 + \mu \end{bmatrix}. \tag{5.6}$$

The SFE of the model is $(P^*, S^*, Q_t^*, Q_p^*) = (1, 0, 0, 0)$. The Jacobian matrices evaluated at the SFE are

$$F_{sub} = \begin{bmatrix} \beta & 0 \\ 0 & 0 \end{bmatrix}, \; V_{sub} = \begin{bmatrix} \gamma_1 + \mu & -\alpha_1 \\ -(1-\sigma)\gamma_1 & \alpha_1 + \mu \end{bmatrix}. \tag{5.7}$$

Observe that $F_{sub} = F$ and $V_{sub} = V$, and so we obtain $\mathcal{R}_{sub} = \mathcal{R}_0$. This makes sense despite the modifications, as the basic reproduction number describes the initial spread of vaping behaviors into a fully non-smoking population. As such, social influences on relapse and quitting do not yet apply in this early phase.

[2]Note that the alternate derivation for $\mathcal{R}_{sub}$ is equivalent to deriving $\mathcal{R}_0$ for the full model (see Appendix A.1) due to their Jacobian matrices being equal when evaluated at the SPE.

5.3 Equilibria

By setting the left hand side of the system (5.1-4) to zero, equilibrium solutions can be obtained. One equilibrium previously mentioned is the SFE of $(P^*, S^*, Q_t^*, Q_p^*) = (1, 0, 0, 0)$. The smoking-present equilibrium is found to be $(P^{**}, S^{**}, Q_t^{**}, Q_p^{**})$, where

$$P^{**} = \frac{\mu}{\beta S^{**} + \mu}, \tag{5.8}$$

$$Q_t^{**} = \frac{(1-\sigma)\gamma_1 \mu S^{**}}{(\mu + \alpha_1)(\mu - S^{**}\sigma\gamma_3)}, \tag{5.9}$$

$$Q_p^{**} = \frac{\sigma\gamma_1 S^{**}}{(\mu - S^{**}\sigma\gamma_3)}, \tag{5.10}$$

and S^{**} is a root of the quadratic polynomial

$$AS^{**2} - BS^{**} + C, \tag{5.11}$$

where the coefficients are defined as

$$A = \beta\gamma_3\sigma(\alpha_1 + \mu), \tag{5.12}$$

$$B = \beta((\alpha_1 + \mu)(\gamma_1 + \mu) - \gamma_1\alpha_1(1-\sigma)) + \gamma_3\sigma(\alpha_1 + \mu)(\beta - \mu), \tag{5.13}$$

$$C = \mu((\alpha_1 + \mu)(\beta - \mu - \gamma_1) + \alpha_1\gamma_1(1-\sigma)). \tag{5.14}$$

In particular, the solutions to the polynomial have the form

$$S_{1,2}^{**} = \frac{1}{2A}(B \pm \sqrt{B^2 - 4AC}) \tag{5.15}$$

However, this does not indicate which roots are feasible in the model's context. By assuming $\mu << 1$, and expanding S^{**} such that

$$S^{**} = \sum_{j=0}^{\infty} \mu^j S_j = S_0 + \mu S_1 + ... \tag{5.16}$$

we obtain the following polynomial, to order μ, to solve:

$$\beta\sigma\alpha_1 S_0(S_0\gamma_3 - (\gamma_1 + \gamma_3)) + \mu[\beta\gamma_3\sigma S_0^2 + 2\beta\sigma\alpha_1\gamma_3 S_0 S_1 - \beta\sigma\alpha_1(\gamma_1 + \gamma_3)S_1 \\ - (\beta(\gamma_3\sigma + \alpha_1 + \gamma_1) - \gamma_3\sigma\alpha_1)S_0 + \alpha_1(\beta - \gamma_1\sigma))] = 0. \tag{5.17}$$

Solving for the leading order terms, we obtain

$$\beta\sigma\alpha_1 S_0(S_0\gamma_3 - (\gamma_1 + \gamma_3)) = 0 \tag{5.18}$$

$$\implies S_0^{(1)} = 0 \tag{5.19}$$

$$\implies S_0^{(2)} = (\gamma_3 + \gamma_1)/\gamma_3 \tag{5.20}$$

Substituting these results into the coefficient of μ and solving for S_1 yields

$$S_1^{(1)} = \frac{\beta - \sigma\gamma_1}{\beta\sigma(\gamma_1 + \gamma_3)}, \tag{5.21}$$

$$S_1^{(2)} = \frac{\beta(1-\sigma)\gamma_1^2 + \beta\gamma_1((1-\sigma)\gamma_3 + \alpha_1) - \gamma_3^2\sigma\alpha_1}{\sigma\beta\alpha_1\gamma_3(\gamma_1 + \gamma_3)}. \tag{5.22}$$

Therefore, the solutions of the quadratic take the following forms:

$$S_1^{**} \approx S_0^{(1)} + S_1^{(1)}\mu = 0 + S_1^{(1)}\mu, \tag{5.23}$$

$$S_2^{**} \approx S_0^{(2)} + S_1^{(2)}\mu = \frac{\gamma_1 + \gamma_3}{\gamma_3} + S_1^{(2)}\mu. \tag{5.24}$$

The sign of S_1^{**} depends on the sign of $S_1^{(1)}$. When $\mathcal{R}_0 > 1$, which must be the case for the spread of the behavior to occur, then $\beta > \gamma_1\sigma$ for $\mu << 1$. This implies that $S_1^{(1)} > 0$, so $S_1^{**} > 0$ is small and is one SPE. Looking at S_2^{**}, if $S_1^{(2)} > 0$, then it cannot be a feasible SPE. If $S_1^{(2)} < 0$ and $S_2^{**} \approx 1$, then $\mu << 1$ means that $Q_p^{**} \sim -\gamma_1/\gamma_3 < 0$, so S_2^{**} is not a feasible SPE. In summary, if $\mathcal{R}_0 > 1$, then the only feasible smoking equilibrium is $S_1^{**} \approx S_1^{(1)}\mu$. Otherwise, the SFE is the only feasible equilibrium.

In reducing the model, it was shown that the root which vanishes from the full model's polynomial in S^{**} was negative and therefore, infeasible in the model's context regardless. It was also shown that the larger SPE of the reduced model is always infeasible. However, it remains unclear whether this is due to the model reduction, or if the larger SPE is also infeasible in the full model. In order to demonstrate that the structure of the model is preserved, it remains to be shown that the potential second, larger SPE will not arise in this parameter space for the full model. Using 3000 LHS samples for the assumed parameter ranges and initial conditions from Chapter 4, the smaller, positive analytical SPE for both the full and reduced model was computed numerically. For each parameter set, the SPE reached in the numerical simulation of the model was also found. Note that the same LHS samples were used for the full and reduced model parameters, excluding γ_2 and α_2.

Figure 5.2 shows the analytical and simulated SPE plotted for both the full and reduced models. In the plot for the full model, it can be observed that the SPE computed in the simulations converges to the smaller analytical SPE across all of the samples. This suggests that within the assumed parameter space, only the smaller SPE is stable. The lack of an emergence of a larger stable SPE in the full model, together with infeasibility of a larger SPE after model reduction, conjectures that the existence of a larger feasible SPE is not a concern in this region. Additionally, comparing the analytical SPE for the full and reduced models (see Figure 5.3) reveals that the difference between

the two is negligible. This confirms that within the assumed parameter ranges, the reduced model is able to structurally represent the full model.

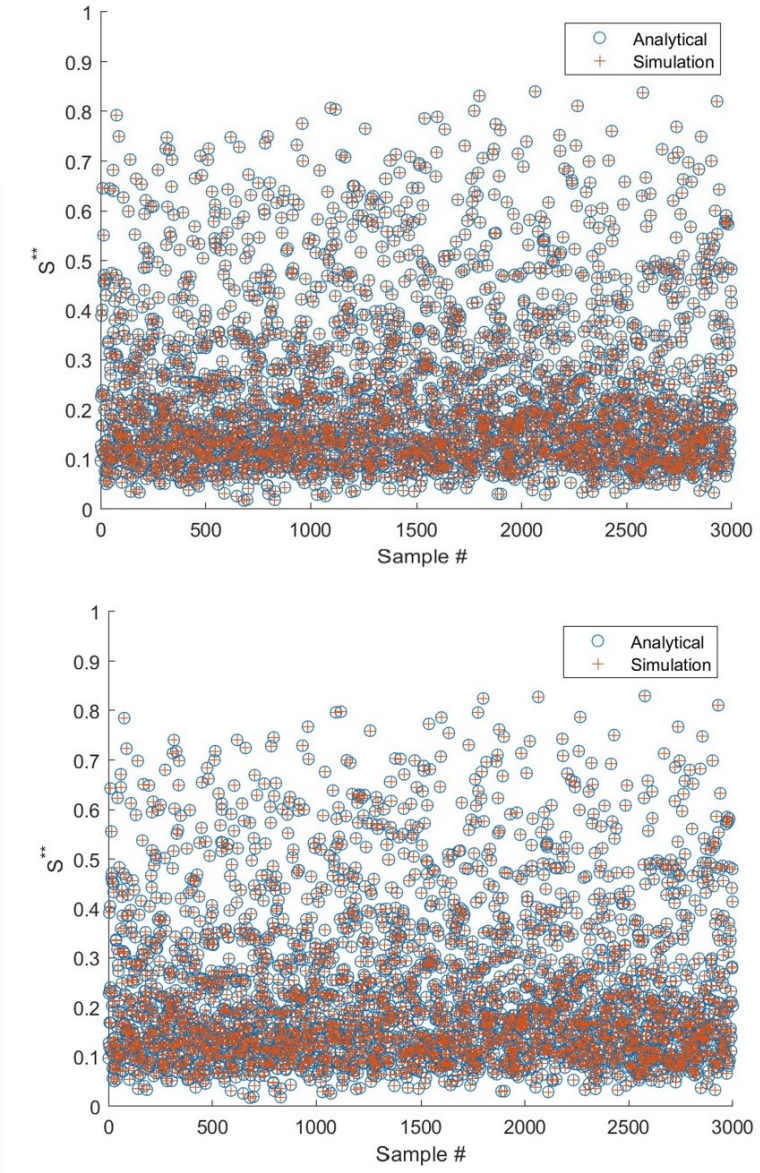

Figure 5.2: Scatter plots showing the smaller, positive analytical SPE versus simulated SPE for 3000 LHS samples from the parameter ranges in Table 4.1 with initial conditions $P(0) = 0.92$ and $S(0) = 0.08$ for (*top*) the full model and (*bottom*) the reduced model.

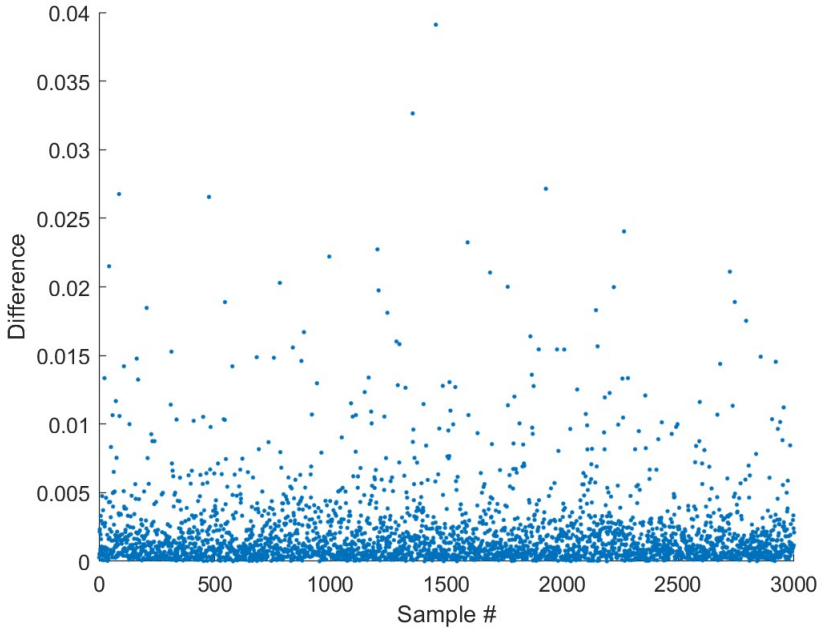

Figure 5.3: Scatter plot showing the absolute value of the difference between the smaller, positive analytical SPE for the full and reduced models for each of the 3000 LHS samples.

5.4 Local Stability

Again, the local stability of the SFE can be expressed by conditions on $\mathcal{R}_{sub}$. The SFE of the model is locally asymptotically stable if $\mathcal{R}_{sub} < 1$, but unstable if $\mathcal{R}_{sub} > 1$ [36].

In order to investigate the local stability of the SPE, the characteristic polynomial of the reduced model's Jacobian matrix will be studied. The Jacobian matrix for the system is

$$J_{sub} = \begin{bmatrix} -\beta S - \mu & -\beta P & 0 & 0 \\ \beta S & \beta P - (\gamma_1 + \gamma_3 Q_p + \mu) & \alpha_1 & -\gamma_3 S \\ 0 & (1-\sigma)(\gamma_1 + \gamma_3 Q_p) & -(\alpha_1 + \mu) & (1-\sigma)\gamma_3 S \\ 0 & \sigma(\gamma_1 + \gamma_3 Q_p) & 0 & \sigma\gamma_3 S - \mu \end{bmatrix}. \tag{5.25}$$

Given the complexity of the characteristic polynomial of J_{sub} and the uncertainty of the signs of its coefficients, perturbation methods will again be used to analyze its roots. Assuming $\mu << 1$,

the SPE can be rewritten as power series in μ. In the previous section, we obtained

$$S^{**} \sim \mu \left(\frac{\beta - \sigma\gamma_1}{\beta\sigma(\gamma_1 + \gamma_3)} \right). \tag{5.26}$$

By substituting this into the expressions for P^{**} and Q_p^{**}, we obtain

$$P^{**} \sim \frac{\sigma(\gamma_1 + \gamma_3)}{\beta + \sigma\gamma_3}, \tag{5.27}$$

$$Q_p^{**} \sim \frac{\beta - \sigma\gamma_1}{\beta + \sigma\gamma_3}. \tag{5.28}$$

Evaluating J_{sub} at this SPE and computing its characteristic polynomial yields

$$\lambda^4 + (A_0 + A_1\mu)\lambda^3 + \mu(B_0 + B_1\mu)\lambda^2 + \mu(C_0 + C_1\mu + C_2\mu^2)\lambda + \mu^2(D_0 + D_1\mu + D_2\mu^2), \tag{5.29}$$

where

$$A_0 = \frac{\beta((1-\sigma)(\gamma_1 + \gamma_3) + \alpha_1) + \sigma\alpha_1\gamma_3}{\sigma\gamma_3 + \beta} > 0, \tag{5.30}$$

$$A_1 = \frac{\beta^2 + 3\beta\sigma(\gamma_1 + \gamma_3) + \gamma_1\gamma_3\sigma^2}{\sigma\beta(\gamma_1 + \gamma_3)} > 0, \tag{5.31}$$

$$B_0 = \frac{k_0\beta^3 - 3\beta^2\sigma((\gamma_1 + \gamma_3)k_1\sigma - \frac{2}{3}k_0(\gamma_1 + \frac{3}{2}\gamma_3)) - \gamma_3\sigma^2\beta(\sigma\gamma_1(\gamma_1 + \gamma_3) - 3\alpha_1k_1) + \sigma^3\alpha_1\gamma_1\gamma_3^2}{(\sigma\gamma_3 + \beta)(\gamma_1 + \gamma_3)\beta\sigma},$$

(5.32)

$$B_1 = \frac{(2\sigma\gamma_3 + 3\beta)\gamma_1^2\sigma + (3\sigma^2\gamma_3^2 + 8\beta\sigma\gamma_3 + 3\beta^2)\gamma_1 + \beta\gamma_1(3\sigma\gamma_3 + 2\beta)}{\sigma\beta(\gamma_1 + \gamma_3)^2}, \tag{5.33}$$

$$C_0 = D_0 = \alpha_1(\beta - \sigma\gamma_1), \tag{5.34}$$

$$C_1 = \frac{\beta^3((2\gamma_3^2 + (\alpha_1 + 4\gamma_1)\gamma_3 + 2\gamma_1(\alpha_1 + \gamma_1)) - \sigma\beta^2k_2 - \gamma_3\sigma^2\beta k_3 + \sigma^3\alpha_1\gamma_1\gamma_3^2(\gamma_1 + 2\gamma_3)}{\beta\sigma(\sigma\gamma_3 + \beta)(\gamma_1 + \gamma_3)^2}, \tag{5.35}$$

$$C_2 = \frac{3\gamma_1(\sigma\gamma_3 + \beta) + \beta\gamma_3 + \sigma\gamma_1^2}{\beta\sigma(\gamma_1 + \gamma_3)^2}, \tag{5.36}$$

$$D_1 = \frac{-\beta\sigma^2\gamma_1^3 + \beta\gamma_1^2(-2\sigma^2\gamma_3 + \beta) + ((\alpha_1 + 2\gamma_3)\beta^2 + (-\sigma^2\gamma_3^2 + \sigma\gamma_3\alpha_1)\beta + \sigma^2\alpha_1\gamma_3^2)\gamma_1 + \beta^2\gamma_3^2}{(\gamma_1 + \gamma_3)^2\beta\sigma}, \tag{5.37}$$

$$D_2 = \frac{\gamma_1(\sigma\gamma_3 + \beta)^2}{(\gamma_1 + \gamma_3)^2\beta\sigma}, \tag{5.38}$$

such that

$$k_0 = \alpha_1 + \gamma_1 + \gamma_3, \tag{5.39}$$

$$k_1 = \gamma_1 + \frac{2}{3}\gamma_3, \tag{5.40}$$

$$k_2 = (\sigma - 3)\gamma_3^3 + (5\sigma\gamma_1 - 2\alpha_1 - 7\gamma_1)\gamma_3^2 + \gamma_1\gamma_3(7\sigma\gamma_1 - 6\alpha_1 - 5\gamma_1) + \gamma_1^2(3\sigma\gamma_1 - \alpha_1 - \gamma_1), \tag{5.41}$$

$$k_3 = (2\sigma\gamma_1 - \alpha_1)\gamma_3^2 + 2\gamma_1\gamma_3(2\sigma\gamma_1 - 3\alpha_1) + 2\gamma_1^2(\sigma\gamma_1 - \alpha_1). \tag{5.42}$$

Expanding $\lambda = \lambda_0 + \mu\lambda_1$ in the characteristic polynomial, we obtain the following polynomial to evaluate, up to order μ^2:

$$(A_0\lambda_0^3 + \lambda_0^4) + \mu\lambda_0\tilde{B}(\lambda_0, \lambda_1) + \mu^2\tilde{C}(\lambda_0, \lambda_1) = 0, \tag{5.43}$$

with coefficients defined as

$$\tilde{B}(\lambda_0, \lambda_1) = (A_1 + 4\lambda_1)\lambda_0^2 + (3A_0\lambda_1 + B_0)\lambda_0 + C_0, \tag{5.44}$$

$$\tilde{C}(\lambda_0, \lambda_1) = (3A_1\lambda_1 + 6\lambda_1^2 + B_1)\lambda_0^2 + 93\lambda_0\lambda_1^2 + 2B_0\lambda_1 + C_1)\lambda_0 + C_0\lambda_1 + D_0. \tag{5.45}$$

Solving for the leading order terms, we obtain

$$A_0\lambda_0^3 + \lambda_0^4 = 0 \tag{5.46}$$

$$\implies \lambda_0^{(1),(2),(3)} = 0 \tag{5.47}$$

$$\implies \lambda_0^{(4)} = -A_0 < 0 \tag{5.48}$$

Substituting $\lambda_0^{(1)}$ into the coefficient of μ yields no results for $\lambda_1^{(1)}$. Therefore, we turn to the order μ^2 to provide insight, where we find

$$\lambda_1^{(1)} = -E_0/C_0 = -1 \tag{5.49}$$

Substituting $\lambda_0^{(4)}$ into the coefficient of μ and solving for λ_1 yields

$$\lambda_1^{(4)} = \frac{A_0B_0 - A_0^2A_1 - C_0}{A_0^2} \tag{5.50}$$

In summary, to leading order, the eigenvalues are

$$\lambda = -A_0, -\mu, -\mu, -\mu < 0, \tag{5.51}$$

which indicates stability for the SPE when $R_{sub} > 1$.

Numerically studying the stability reflects the results of this analysis for the parameter range assumed for the reduced model. 5000 LHS samples were used to obtain the results in Figure 5.4, which shows the relationship between $\mathcal{R}_{sub}$ and the maximum real part of the eigenvalues of the J_{sub} evaluated at the analytically derived SPE for that respective set of parameters. Note that the figure axes were modified for visual clarity. In these simulations, all of the basic reproduction

numbers are greater than 1. In all 5000 simulations, the maximum real part of the eigenvalues of J_{sub} are all negative. This again leads to the conclusion that the SPE is stable, particularly within this parameter region.

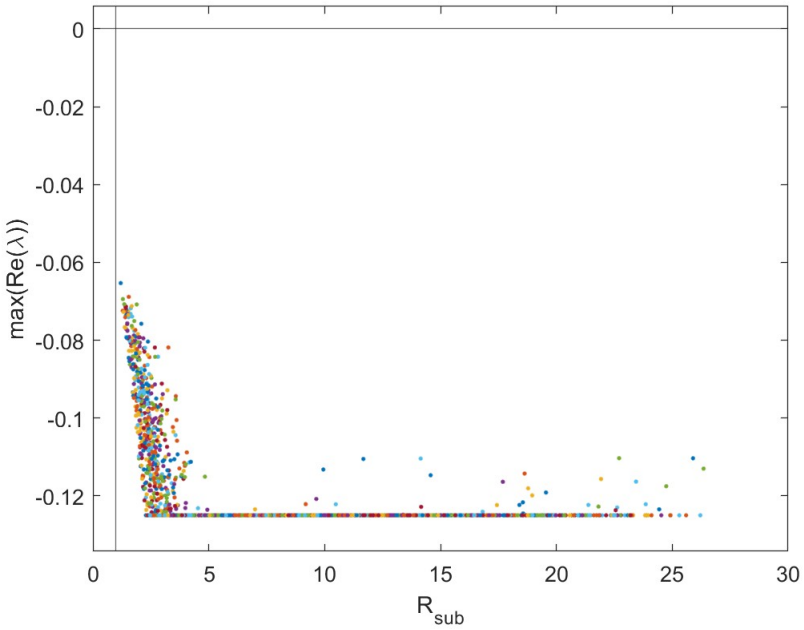

Figure 5.4: Local stability simulations of the SPE using 5000 LHS samples from the parameter ranges in Table 4.1, plotting $\mathcal{R}_{sub}$ vs max(Re(λ)) of J_{sub} for each parameter set, with a vertical line at $\mathcal{R}_{sub} = 1$.

5.5 Sensitivity Analysis

A sensitivity analysis, similar to the one performed on the full model, was performed on the reduced model in order to verify that the same relationships previously observed between the parameters and response variables hold for the chosen parameter ranges. The same LHS matrix from the prior sensitivity analysis was used, but restricted only to the relevant parameters. The PRCC results from the sensitivity analysis are shown in Figure 5.5. Statistically insignificant results were ignored.

Again, parameters associated with producing smokers (β, α_1) were found to be positively correlated with the response variables of $\mathcal{R}_0$, peak value, smokers' equilibrium, and final size. The

correlations of α_1 still prove to be insignificant. The results continue to indicate that β is the most significant factor in the severity of e-cigarette smoking in the population. It is also the most significant factor in when the vaping peak would occur, with a strong negative correlation. Parameters associated with smoking cessation $(\gamma_1, \gamma_3, \sigma)$ were found to be negatively correlated with all response variables, with σ remaining the most significant parameter of all the cessation associated parameters. The non-social cessation rate of γ_1 was once again found to be significant in relation to 5 out of the 6 response variables. Importantly, γ_3 was still found to have a significant effect on the smokers' equilibrium and final size values. In comparing these results to those of the sensitivity analysis for the full model, one finds that the results agree.

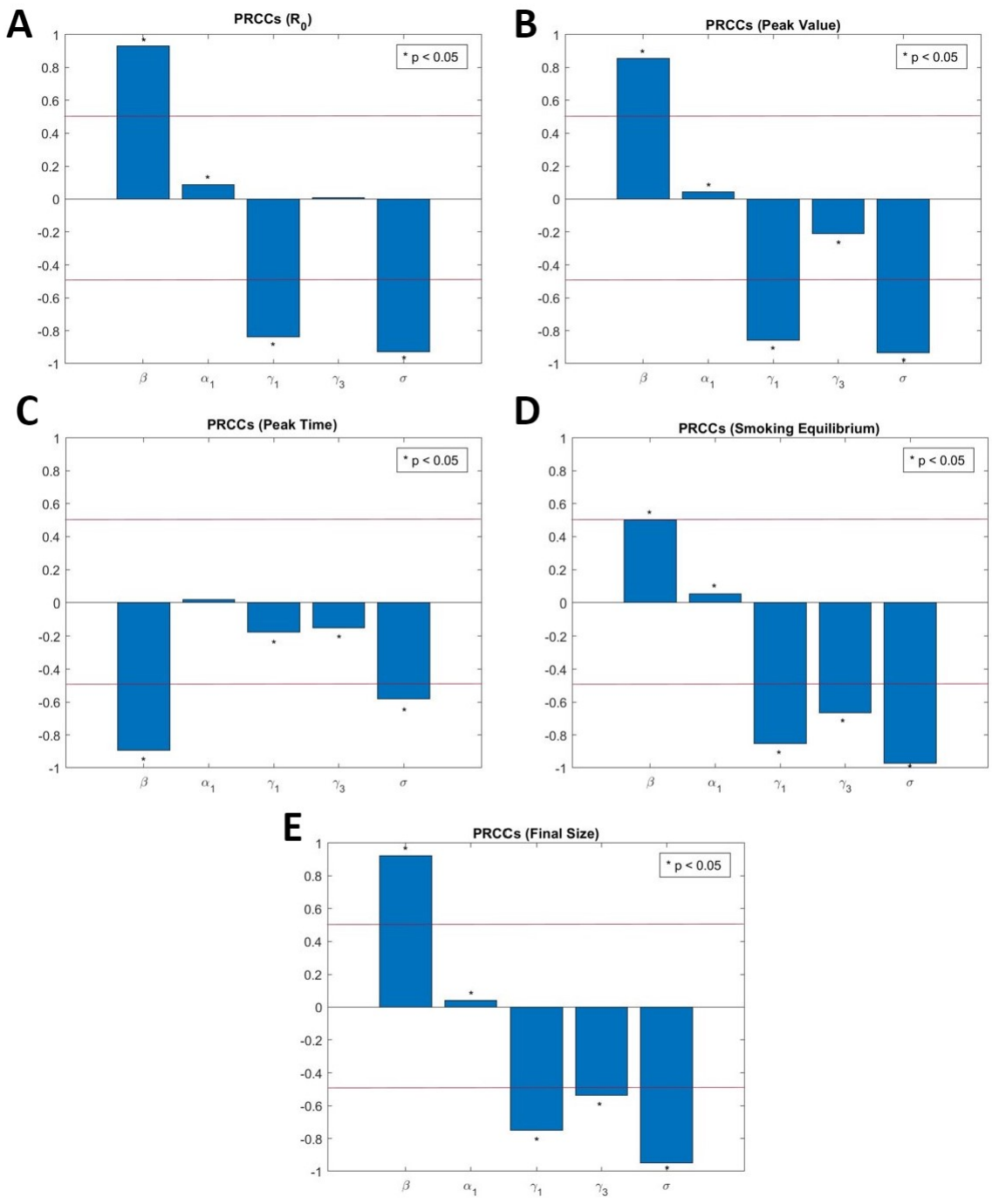

Figure 5.5: PRCC analyses for the reduced model using 3000 LHS samples for the parameter ranges in Table 4.1, where the red horizontal lines at ± 0.5 indicate the threshold for significance and * denotes a statistically significant result (p-value < 0.05).

Chapter 6

Numerical Simulations

In this chapter, the trajectory of the spread of vaping behaviors will be simulated numerically in order to visualize the dynamics of adolescent e-cigarette usage. First, the parameters found to be significant are varied to see how they influence overall system dynamics. Simultaneously, the full and reduced models will be compared. Based on observations from the simulations, potential oscillatory behavior of the models' solutions will be explored.

6.1 Simulations

Simulations of the full and reduced models were conducted in order to explore the effect of varying the sensitive parameters (β, γ_1, γ_3, σ), and ensure that the reduced model is an appropriate approximation of the full model. In Figure 6.1, the baseline parameters were set to be the following, where the value in parentheses reflects the practical interpretation of the average length of time it takes before that given event occurs: $\mu = 1/8$ (8 years), $\beta = 2$ years^{-1} (6 months), $\alpha_1 = 36.5$ years^{-1} (10 days), $\gamma_1 = 1$ year^{-1} (1 year), $\gamma_3 = 1.5$ years^{-1} (8 months), and $\sigma = 0.15$. For the full model, we additionally let $\alpha_2 = 36.5$ years^{-1} (10 days) and $\gamma_2 = 1$ year^{-1} (1 year). In the early phase of the simulation, there is an initial increase in S, which is to be expected as the simulations

have a basic reproduction number greater than one. As time goes on, individuals begin quitting. As suggested in the sensitivity analyses, the simulation confirms that the level of temporary quitters (Q_t) remains quite small over time within the realistic parameter space explored such that it would indeed be ineffective in influencing other populations. As Q_p increases over time, the influence permanent quitters have over the smoking population can be seen by a simultaneous decrease in S. Accordingly, the potential e-cigarette smoker population also recovers to its equilibrium. The differences observed between the full and reduced model simulations are negligible.

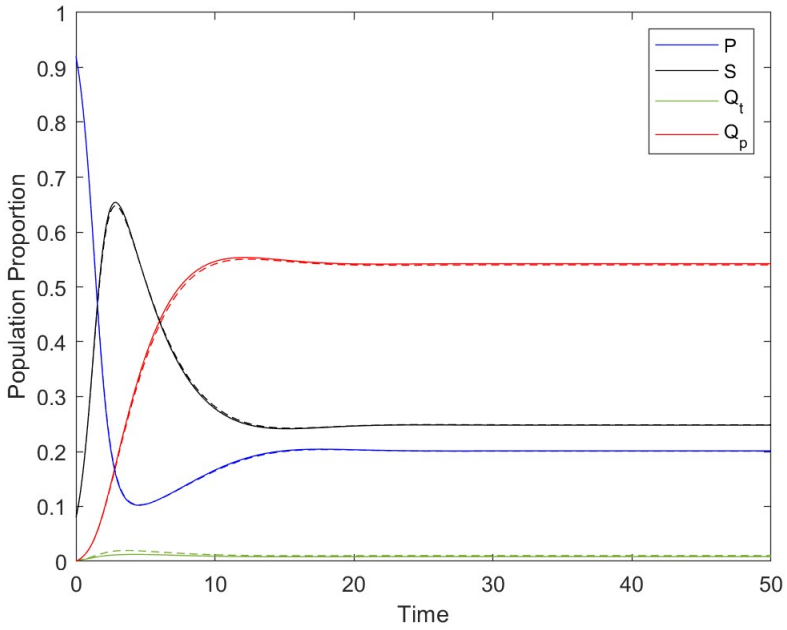

Figure 6.1: Simulation of the full model (solid lines) versus reduced model (dashed lines), with baseline parameters $\mu = 1/8$ years^{-1}, $\beta = 2$ years^{-1}, $\alpha_1 = \alpha_2 = 36.5$ years^{-1}, $\gamma_1 = \gamma_2 = 1$ year^{-1}, $\gamma_3 = 1.5$ years^{-1}, $\sigma = 0.15$ and initial conditions $P(0) = 0.92$, $S(0) = 0.08$, with $\mathcal{R}_0 = 7.20$.

The effects of varying the sensitive parameters (β, γ_1, γ_3, σ) individually on S are shown in Figure 6.2. As was seen in the sensitivity analysis, changes in β have a strong positive correlation with changes in the smoker's peak and peak time. Otherwise, the general shapes of the curves remain consistent, where after the initial peak, there is a decrease in the smoking population, which eventually levels out to the smoker's equilibrium. The non-social cessation rate γ_1 significantly

impacts both the peak value and smoker's equilibrium, while the Q_p-influenced cessation rate γ_3 only significantly impacts the smoker's equilibrium. However, changes in these cessation rates both result in interesting changes to the S curves. As they are increased, a second smoking peak, although much lower than the initial peak, begins to arise before decreasing again and leveling out to the equilibrium value. Lastly, varying σ supports the conclusions from the sensitivity analysis, where simulations show the same monotonic relationship between changes in σ and peak value, peak time, and smoking equilibrium. Again, the differences observed between the full and reduced model simulations are negligible.

6.2 Oscillatory Behavior

Due to the emergence of additional peaks observed in the simulations, a more in-depth investigation will be conducted in order to determine which influences are most important in producing these subsequent smoking waves and to what extent they can be sustained. The parameter sets chosen in this section are not necessarily realistic, but are used to illustrate additional model characteristics not accounted for by the previous analyses.

In the previous section, the cessation parameters γ_1 and γ_3 were identified as being potential contributors to the emergence of additional e-cigarette smoking waves. For the purposes of this investigation, these parameters will be varied to their extremes in order identify the way they impact system dynamics. The baseline parameters from the previous section will be used again, along with the same initial conditions. The simulations plotted in Figure 6.3 demonstrate that while γ_1 is able to induce a very small additional smoking wave, it is not the main driver of the periodic behavior able to be observed in the models. Importantly, continuing to increasing γ_1 will not result in the intensification of these smoking waves, as $\mathcal{R}_0 \longrightarrow 0$ when $\gamma_1 \longrightarrow \infty$. Therefore, the trajectory of the model will eventually tend towards the SFE.

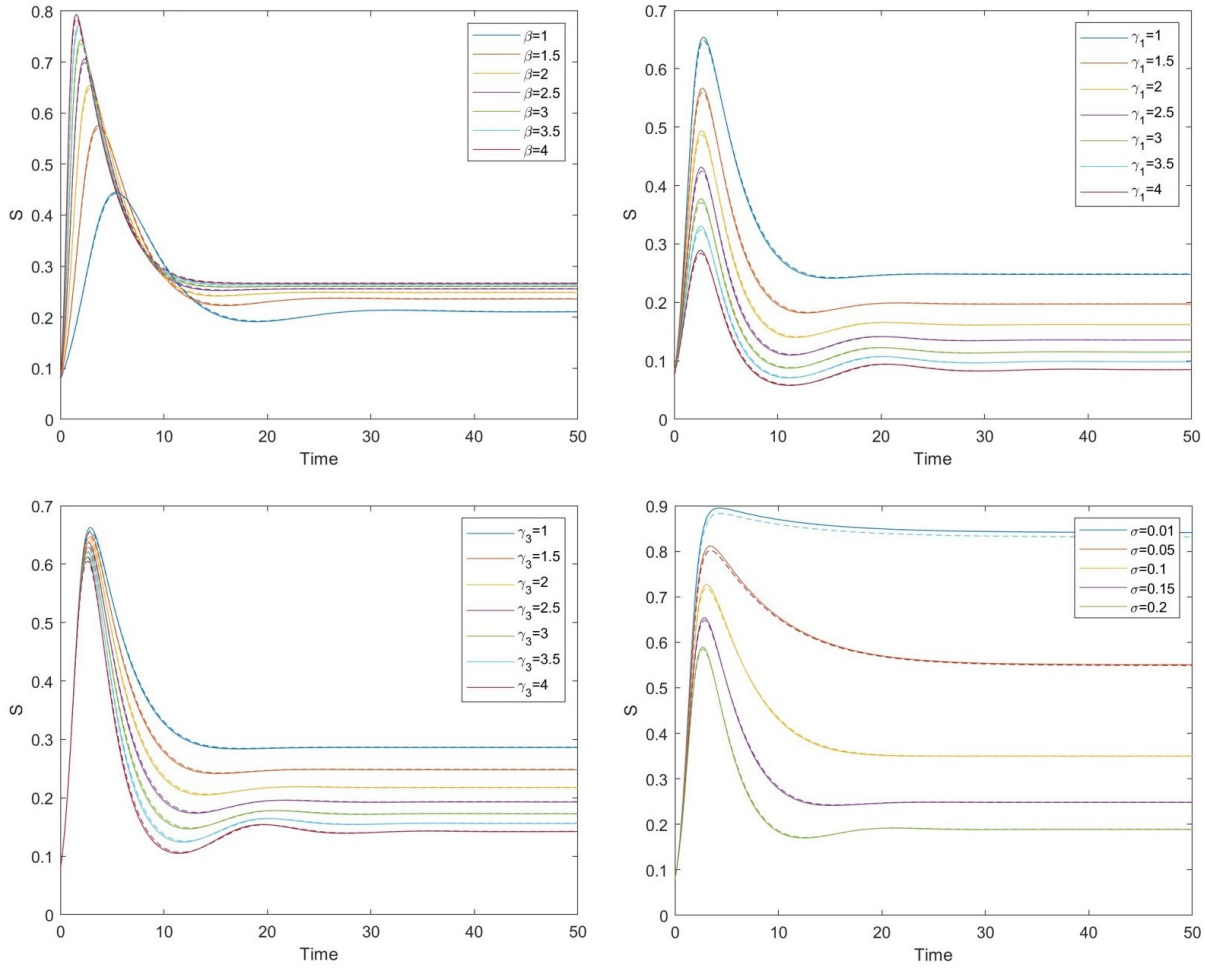

Figure 6.2: Simulations showing the smoker's curves (S) of the full model (solid lines) versus reduced model (dashed lines), varying β, γ_1, γ_3, and σ from the baseline parameters ($\mu = 1/8$ years^{-1}, $\beta = 2$ years^{-1}, $\alpha_1 = \alpha_2 = 36.5$ years^{-1}, $\gamma_1 = \gamma_2 = 1$ year^{-1}, $\gamma_3 = 1.5$ years^{-1}, $\sigma = 0.15$) and initial conditions $P(0) = 0.92$, $S(0) = 0.08$. $\mathcal{R}_0$ increased from 3.60 to 14.39 as β increased, decreased from 7.20 to 2.72 as γ_1 increased, remained 7.20 for all γ_3, and decreased from 14.45 to 6.10 as σ increased.

The simulations where γ_3 was varied show that as γ_3 increases, periodic behavior begins to be observed in the smoking population in the form of distinct smoking waves with distinct smoking peaks. These waves intensify as γ_3 increases, and are able to be sustained for a longer period of time before dampening to an SPE. It was established that γ_3 has no impact on $\mathcal{R}_0$, and so as long as $\mathcal{R}_0 > 1$, these increases will not induce a change in stability of the SPE as was the case with γ_1. It can also be seen that the full and reduced models continue to agree in these simulations, even as

the two parameters are varied outside of their assumed ranges.

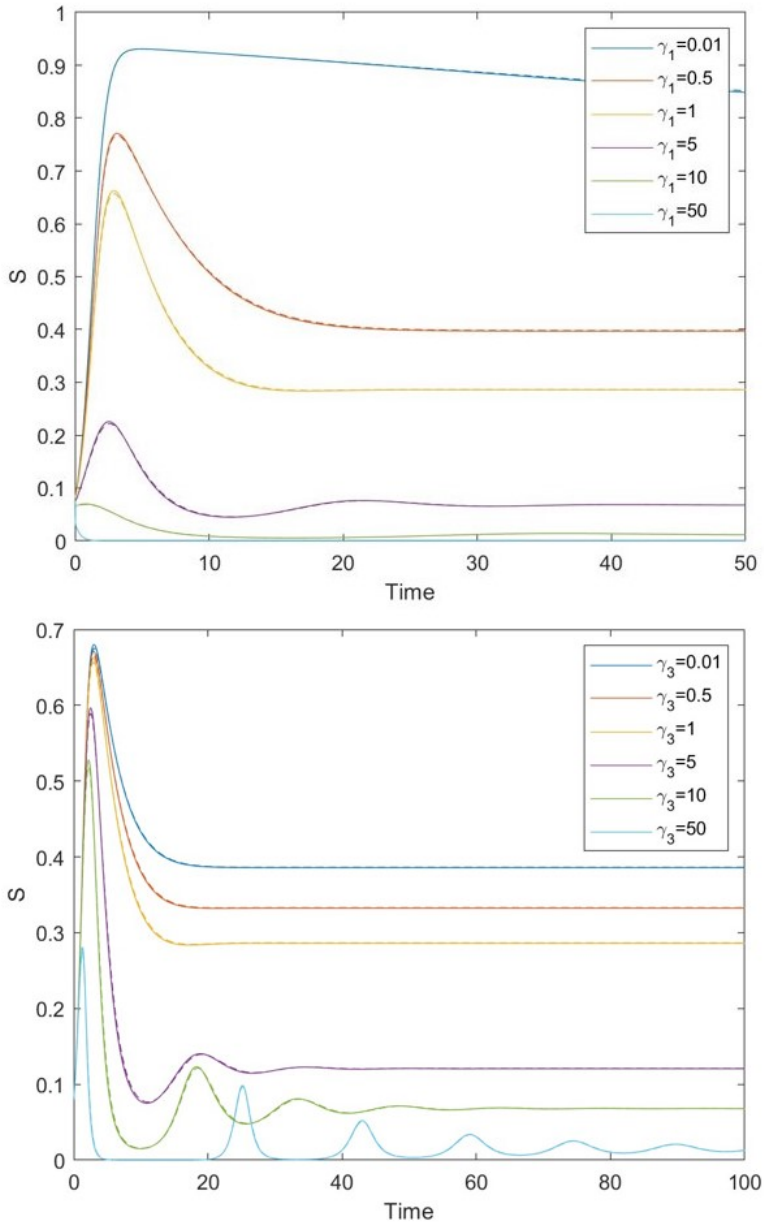

Figure 6.3: Simulations showing oscillatory behavior of the smoker's curves (S) of the full model (solid lines) and reduced model (dashed lines), varying γ_1 and γ_3 from the baseline parameters ($\mu = 1/8$ years^{-1}, $\beta = 2$ years^{-1}, $\alpha_1 = \alpha_2 = 36.5$ years^{-1}, $\gamma_1 = \gamma_2 = 1$ year^{-1}, $\gamma_3 = 1.5$ years^{-1}, $\sigma = 0.15$) and initial conditions $P(0) = 0.92$, $S(0) = 0.08$. $\mathcal{R}_0$ increased from 0.26 to 15.81 as γ_1 increased, while $\mathcal{R}_0 = 7.20$ for all γ_3.

By looking at the simulation for all compartments of the models for $\gamma_3 = 50$ years^{-1} (Figure 6.4), it can be observed that the solutions show clear waves in the spread of vaping behaviors with multiple, but decreasing, peaks. After the initial spread of vaping behaviors where S increases to its peak and P decreases to its minimum value, an increase in the population of quitters is seen. In turn, this increase in quitters begins to have an impact on the smoking population. Additionally, each time a peak occurs in S, a trough in P occurs simultaneously. Similarly, each time a peak in Q_p occurs, a trough in S is observed. The size of Q_t remains relatively small throughout the entirety of the simulation, but also has some oscillatory behavior. Over time with the replenishment of the population, these oscillations begin to dampen and tend towards a smoking-present equilibrium.

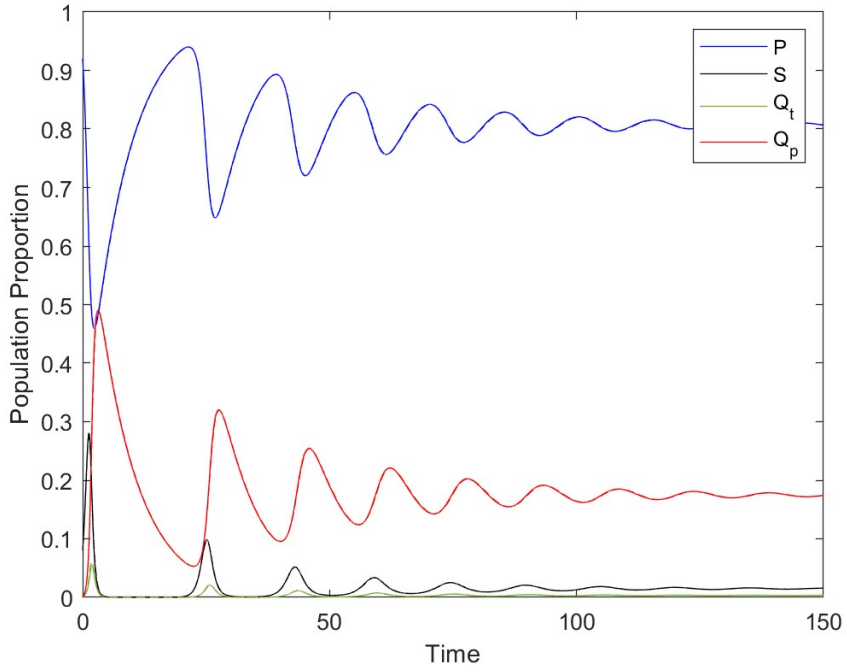

Figure 6.4: Simulations showing oscillatory behavior of the full model (solid lines) and reduced model (dashed lines), with baseline parameters ($\mu = 1/8$ years^{-1}, $\beta = 2$ years^{-1}, $\alpha_1 = \alpha_2 = 36.5$ years^{-1}, $\gamma_1 = \gamma_2 = 1$ year^{-1}, $\sigma = 0.15$), $\gamma_3 = 50$ years^{-1}, and initial conditions $P(0) = 0.92$, $S(0) = 0.08$, with $\mathcal{R}_0 = 7.20$.

6.3 Summary

This case study demonstrated that the proposed models are capable of producing solutions with oscillatory behavior and some sort of periodicity, with the reduced model continuing to capture the key dynamics of the full model. Further adjustments to the parameters found to drive the oscillatory dynamics (γ_1, γ_3) show that the periodicity can be sustained over relatively long periods of time before dampening to a SPE. It is important to note that the oscillations observed here are mainly fueled by socially-influenced cessation caused by permanent quitters (γ_3). These waves can be interpreted as a change in social norms. As the number of quitters increases, their influence causes e-cigarette smokers to quit. As the population is replenished due to aging, this collective memory of the impacts of vaping and the establishment of an anti-vaping sentiment could disappear. Therefore, the number of e-cigarette smokers rises and this cycle persists until it eventually reaches endemicity.

Chapter 7

Discussion & Conclusion

Adolescent e-cigarette usage has emerged as a widespread issue that has garnered public health attention. Despite this, researchers have only recently begun to study which factors influence an adolescent's decision to initiate e-cigarette usage as well as the dangerous health effects vaping can have [1, 7, 16, 17, 28, 38]. Given the harm posed by e-cigarettes to public health, it is important to have an understanding of which factors play a role in e-cigarette smoking dynamics. Equipped with this type of information, research and public health efforts can be better targeted to address the concern. In this thesis, research from the social sciences was used to inform a deterministic model that is able to account for several types of behavioral influences. Through analysis and simulations, we aimed to identify which factors were most important in adolescent vaping dynamics and analyze the ways in which they influenced vaping behaviors.

We first extended existing smoking models to be able to account for the effects of (1) socially-driven initiation and relapse, (2) relapse due to nicotine dependency and other non-socially related factors, (3) socially-influenced cessation, and (4) cessation of one's own volition in the context of adolescent vaping. Importantly, socially influenced cessation has not, to the best of our knowledge, ever been considered in models of this type. It has also seldom been studied in the social sciences

[11, 18, 35]. A calculation of model's reproduction number showed that social influences on relapse and cessation are not important in the initial spread of vaping behaviors. Analysis of the model's equilibria proved difficult, with uncertainty still remaining about the potential number of smoking present equilibria.

Due to the complexity of the full model and limitations in the analysis, a sensitivity analysis was conducted. The results of the sensitivity analysis served to identify the strength of the relationships between the model's parameters and key response variables. The results demonstrated that within parameter ranges informed by literature, behavioral influences from and on temporary quitters were insignificant in overall model dynamics. This reinforces results from behavioral studies that temporary quitters are not as motivated to maintain their quitting status [15]. The influence of smokers on relapse of temporary quitters was also insignificant, suggesting that social factors are not important in decisions to re-initiate vaping [25]. As expected, behavioral influences on initiation, quitting by one's own volition, and the proportion of quitters who quit permanently were all found to be significant parameters. Interestingly, the influence of permanent quitters on cessation, which had not previously been considered in models, emerged as an important factor in the long-term trajectory of e-cigarette usage in the adolescent population. Behaviorally, this suggests permanent quitters can induce a change in social norms within the adolescent population through social contagion. Over time with enough individuals quitting permanently, it is possible that vaping becomes less normalized and curiosity about e-cigarettes decreases, which are factors known to encourage e-cigarette initiation [38].

Using the results of the sensitivity analysis, the model was reduced into one that captured the key dynamics of the full model within the assumed parameter ranges. Through the analysis of the reduced model, we were able to deepen our understanding of model behavior and the role of significant parameters on the model interpretations. Specifically, it was determined that when the

basic reproduction number is greater than one, the unique smoking present equilibrium becomes stable. Simulations of the models uncovered the potential importance of influence from temporary quitters in inducing multiple smoking waves in the trajectory of e-cigarette smoking throughout longer periods of time. Socially, these smoking waves indicate that changes in social norms are dynamic and can shift back and forth over time. This highlights the importance of continuous efforts in maintaining a social environment that is not pro-vaping. Otherwise, the replenishment of the adolescent population as time goes on can result in re-emergent e-cigarette smoking peaks.

7.1 Conclusions & Future Directions

In conclusion, the results of this thesis have important implications for approaches to researching e-cigarette usage in adolescents in the social sciences. When relapse occurs quickly, temporary quitters are not a key demographic in influencing the overall spread of vaping behaviors. Behavioral influence, in this case, is not as important as the strong draw of nicotine dependence [25]. However, social influences from permanent quitters emerged as an important factor in the long-term trajectory of e-cigarette usage. This presents a new potential area of study for additional interventions within in the adolescent population that has yet to be investigated in the social sciences, as far as we are aware.

Conclusions drawn from studies in mathematical modeling are always subject to the model's assumptions. The main limitation of this thesis is that the results of the sensitivity analysis were dependent on the parameter assumptions made. Although efforts were made to use literature to guide the parameter assumptions, the lack of parameter data available within the context of adolescent e-cigarette studies means that some uncertainty in the parameter ranges remains. In order to address some of this uncertainty, a non-dimensional model could also be studied in order to investigate how relative sizes of the parameters influences system dynamics, rather than needing

to select explicit parameter ranges. With this approach, a more comprehensive understanding of behavioral influences on system dynamics could be obtained. Additional future directions could include studying the conditions under which multiple smoking peaks can arise and become relatively sustained, as well as extending the model to incorporate the impact of media and advertising on adolescent vaping behaviors [38].

Appendix A

Supplementary Material

A.1 Alternate Derivation of $\mathcal{R}_0$

An alternate approach to deriving $\mathcal{R}_0$ is to find the threshold condition for stability of the SFE.

The Jacobian matrix of the improved social contagion model is

$$J = \begin{bmatrix} -\beta S - \mu & -\beta P & 0 & 0 \\ \beta S & \beta P + \alpha_2 Q_t - (\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p + \mu) & \alpha_1 + (\alpha_2 - \gamma_2) S & -\gamma_3 S \\ 0 & (1-\sigma)(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p) - \alpha_2 Q_t & -(1-\sigma)\gamma_2 S - (\alpha_1 + \alpha_2 S + \mu) & (1-\sigma)\gamma_3 S \\ 0 & \sigma(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p) & \sigma\gamma_2 S & \sigma\gamma_3 S - \mu \end{bmatrix}. \tag{A.1}$$

Evaluating J at the SFE, we obtain

$$J|_{SFE} = \begin{bmatrix} -\mu & -\beta & 0 & 0 \\ 0 & \beta - (\gamma_1 + \mu) & \alpha_1 & 0 \\ 0 & (1-\sigma)\gamma_1 & -(\alpha_1 + \mu) & 0 \\ 0 & \sigma\gamma_1 & 0 & -\mu \end{bmatrix}. \tag{A.2}$$

The eigenvalues of $J|_{SFE}$ are defined as the roots of its characteristic polynomial $p(\lambda)$, which is defined as

$$p(\lambda) = (\lambda+\mu)^2(\lambda^2 + (\gamma_1+\mu-\beta+\alpha_1+\mu)\lambda + (\gamma_1+\mu-\beta)(\alpha_1+\mu) - \alpha_1\gamma_1(1-\sigma)). \tag{A.3}$$

Therefore, two of the eigenvalues of $J|_{SFE}$ are $\lambda_{1,2} = -\mu < 0$. The remaining eigenvalues are defined by the roots of

$$\lambda^2 + (\gamma_1+\mu-\beta+\alpha_1+\mu)\lambda + (\gamma_1+\mu-\beta)(\alpha_1+\mu) - \alpha_1\gamma_1(1-\sigma). \tag{A.4}$$

The Routh-Hurwitz criterion for stability states that in order to have $\mathrm{Re}(\lambda) < 0$ for a quadratic polynomial, all coefficients must be of the same sign. In this case, this means that it is required for

$$(\gamma_1+\mu-\beta+\alpha_1+\mu) > 0, \tag{A.5}$$

$$(\gamma_1+\mu-\beta)(\alpha_1+\mu) - \alpha_1\gamma_1(1-\sigma) > 0. \tag{A.6}$$

Rearranging the inequalities yields

$$1 > \frac{\beta}{\alpha_1+\gamma_1+2\mu}, \tag{A.7}$$

$$1 > \frac{\beta(\alpha_1+\mu)}{(\gamma_1+\mu)(\alpha_1+\mu) - \alpha_1\gamma_1(1-\sigma)}. \tag{A.8}$$

We note that

$$\frac{\beta(\alpha_1+\mu)}{(\gamma_1+\mu)(\alpha_1+\mu) - \alpha_1\gamma_1(1-\sigma)} > \frac{\beta}{\alpha_1+\gamma_1+2\mu}, \tag{A.9}$$

and so we define

$$\mathcal{R}_0 = \frac{\beta(\alpha_1+\mu)}{(\gamma_1+\mu)(\alpha_1+\mu) - \alpha_1\gamma_1(1-\sigma)}. \tag{A.10}$$

Deriving $\mathcal{R}_0$ based on the stability conditions for the SPE yields the same basic reproduction number as was given by the NGM method. This confirms that no errors were made in the interpretation of which model compartments are "smoking present" compartments and that the expression initially derived is the true basic reproduction number for the full system.

A.2 Showing B, C cannot both be positive for $\mathcal{R}_0 > 1$

Suppose that $\mathcal{R}_0 > 1$. Then we have the following:

$$\begin{aligned} \mathcal{R}_0 > 1 &\iff \frac{\beta(\alpha_1+\mu)}{(\alpha_1+\mu)(\gamma_1+\mu)-\alpha_1\gamma_1(1-\sigma)} > 1 \\ &\iff \beta > \frac{(\alpha_1+\mu)(\gamma_1+\mu)-\alpha_1\gamma_1(1-\sigma)}{(\alpha_1+\mu)} \\ &\iff \beta > \mu + \gamma_1(1-\frac{\alpha_1(1-\sigma)}{\alpha_1+\mu}) > \mu \end{aligned} \tag{A.11}$$

Returning to the coefficients and looking at C, we note that $-\mu C_2 > 0$ always. Additionally, $-\gamma_2\mu(\beta-\mu)(1-\sigma)$ and $-\sigma C_1$ are both negative because $\beta > \mu$. Extending the argument from (A.11), we have

$$(\beta-\mu-\sigma\gamma_1) > \gamma_1(1-\sigma-\frac{\alpha_1(1-\sigma)}{\alpha_1+\mu}) = (1-\sigma)\gamma_1(1-\frac{\alpha_1}{\alpha_1+\mu}) > 0, \tag{A.12}$$

so $\alpha_2\mu(\beta-\mu-\sigma\gamma_1)$ must be positive for $\mathcal{R}_0 > 1$. The coefficient C is monotonic in α_2, and so the sign of C can be expressed by a condition on α_2. Thus, $C > 0$ for

$$\alpha_2 > \alpha_2^* = \frac{\gamma_2\mu(\beta-\mu)(1-\sigma)+\sigma C_1+\mu C_2}{\mu(\beta-\mu-\sigma\gamma_1)}. \tag{A.13}$$

Similarly, looking at the coefficient B, notice that $B_2 > 0$ always and $B_1 > 0$ for $\beta > \mu$. B is

also monotonic in α_2, and so its sign can be expressed by a condition on α_2. Therefore, $B > 0$ for

$$\alpha_2 < \alpha_2^+ = \frac{B_2}{B_1}. \tag{A.14}$$

In order to show that B and C cannot both be positive, we will first demonstrate that $\alpha_2^+ > \alpha_2^*$. Observe that α_2^* and α_2^+ are both linear in γ_2. Taking their derivatives with respect to γ_2 yields the following:

$$\frac{d\alpha_2^*}{d\gamma_2} = \frac{\mu(\beta-\mu)(1-\sigma)}{\mu(\beta-\mu-\sigma\gamma_1)} > (1-\sigma) > 0 \tag{A.15}$$

and

$$\frac{d\alpha_2^+}{d\gamma_2} = \frac{\beta\mu(1-\sigma)}{\gamma_3\sigma(\beta-\mu)+\beta(\gamma_1\sigma+\mu)} < (1-\sigma) < 1 \tag{A.16}$$

Therefore, $\frac{d\alpha_2^*}{d\gamma_2} > \frac{d\alpha_2^+}{d\gamma_2} > 0$. Further, γ_2 is bounded below by zero. Evaluating α_2^* and α_2^+ at $\gamma_2 = 0$ gives the following:

$$\alpha_2^*|_{\gamma_2=0} = \frac{\sigma C_1 + \mu C_2}{\mu(\beta-\mu-\sigma\gamma_1)} > \frac{C_2}{\beta-\mu-\sigma\gamma_1} > \frac{\beta(\alpha_1+\gamma_1+\mu)}{\beta-\mu} > \frac{\beta(\alpha_1+\mu)}{\beta-\mu}, \tag{A.17}$$

and

$$\alpha_2^+|_{\gamma_2=0} = \frac{\beta\gamma_3\sigma(\alpha_1+\mu)}{\gamma_3\sigma(\beta-\mu)+\beta(\gamma_1\sigma+\mu)} < \frac{\beta(\alpha_1+\mu)}{\beta-\mu}. \tag{A.18}$$

Thus, $\alpha_2^*|_{\gamma_2=0} > \alpha_2^+|_{\gamma_2=0}$ and it can be concluded that $\alpha_2^* > \alpha_2^+$ always. The cases for α_2 are summarized in Figure A.1.

$0 < \alpha_2 < \alpha_2^+$	$\alpha_2^+ < \alpha_2 < \alpha_2^*$	$\alpha_2^* < \alpha_2$
B > 0	B < 0	B < 0
C < 0	C < 0	C > 0

Figure A.1: Signs of B and C by condition on α_2.

The analysis performed has demonstrated that only three cases can arise for the signs of B and C. Importantly, it is not possible for both B and C to be positive simultaneously. This means that when $\mathcal{R}_0 > 1$, the case where the polynomial exclusively has no positive roots cannot occur.

A.3 Discussion on $\mathcal{R}_0$ for $\mu << 1$

Using the NGM method, it can be shown that the small μ limit of the basic reproduction number of the full model is equivalent to the basic reproduction number of the limiting model for small μ. Again, the differential equations for the "smoke-present" compartments, S and Q_t, can be written as

$$\begin{aligned}\begin{bmatrix} \frac{dS(t)}{dt} \\ \frac{dQ_t(t)}{dt} \end{bmatrix} &= \begin{bmatrix} \beta PS \\ 0 \end{bmatrix} - \begin{bmatrix} -(\alpha_1 + \alpha_2 S)Q_t + (\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p)S \\ -(1-\sigma)(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p)S + (\alpha_1 + \alpha_2 S)Q_t \end{bmatrix} \\ &= \mathcal{F} - \mathcal{V}\end{aligned} \tag{A.19}$$

The Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ are F and V, respectively, where

$$F = \begin{bmatrix} \beta P & 0 \\ 0 & 0 \end{bmatrix}, \; V = \begin{bmatrix} -\alpha_2 Q_t + \gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p & -(\alpha_1 + \alpha_2 S) + \gamma_2 S \\ -(1-\sigma)(\gamma_1 + \gamma_2 Q_t + \gamma_3 Q_p) + \alpha_2 Q_t & -(1-\sigma)\gamma_2 S + \alpha_1 + \alpha_2 S \\ . \end{bmatrix} \tag{A.20}$$

The Jacobian matrices evaluated at the SFE are

$$F|_{SFE} = \begin{bmatrix} \beta & 0 \\ 0 & 0 \end{bmatrix}, \; V|_{SFE} = \begin{bmatrix} \gamma_1 & -\alpha_1 \\ -(1-\sigma)\gamma_1 & \alpha_1 \end{bmatrix}. \tag{A.21}$$

From here, it can be determined that the spectral radius $\rho(FV^{-1}) = \mathcal{R}_0$, where

$$\begin{aligned}\mathcal{R}_0 &= \frac{\beta}{\sigma\gamma_1} \\ &= \frac{\beta}{\gamma_1\left(1 - \frac{\alpha_1}{\alpha_1} \cdot \frac{\gamma_1}{\gamma_1}(1-\sigma)\right)} \\ &= \frac{\beta}{\gamma_1\left(1-\psi\right)}\end{aligned} \tag{A.22}$$

One way to interpret the value of $\mathcal{R}_0$ for the limiting system is similar to the interpretation of $\mathcal{R}_0$ for the full system. In this case, the β/γ_1 term represents the spread of behaviors from one vaping individual into a fully non-vaping population over the course of their smoking period when relapse is ignored. The relapse function $(1-\psi) \in (0,1)$ still serves to increase $\mathcal{R}_0$ due to the relapse of temporary quitters. Because μ is negligible, all smokers who attempt to quit and become temporary quitters will relapse without ever aging out of the system first, which is represented in ψ. Increasing ψ would increases one's average smoking period, and thus increases $\mathcal{R}_0$.

The basic reproduction number can also be interpreted in its $\beta/\sigma\gamma_1$ form. The greater the proportion of those who quit permanently (σ) is, the shorter the average smoking period $1/\gamma_1$ becomes. Therefore, $\beta/\sigma\gamma_1$ is the spread of vaping behaviors from one vaping individual into a fully non-vaping population over the course of their smoking period when relapse is accounted for. As the proportion of quitters who quit permanently decreases, or $\sigma \longrightarrow 0$, the basic reproduction number grows infinitely large, or $\mathcal{R}_0 \longrightarrow \infty$. If all individuals were to quit temporarily, the average smoking period becomes infinitely long, as no aging out of the system occurs and smokers become stuck in a loop of quitting temporarily and relapsing. In reality, a fully susceptible population is finite and the basic reproduction number only describes growth in the initial phase of the spread of the behavior. This means $\mathcal{R}_0$ is limited to the size of the population, and that considering an infinitely long smoking period does not align with the assumptions implicit in defining a basic

reproduction number. Therefore, $\mathcal{R}_0$ should be interpreted with caution if σ is arbitrarily close to 0. However, literature suggests this is unlikely to be the case [30].

A.4 Sensitivity Analysis for Slower Relapse Rates

In the sensitivity analysis for the realistic parameter ranges, it was assumed that relapse occurs quickly. With this assumption, parameters α_1 and α_2 remained insignificant in overall system dynamics. Further, the population of temporary quitters remained small and uninfluential over time. It was hypothesized that if relapse rates were slower, then relapse would have more influence over system dynamics. In order to explore this, an additional sensitivity analysis was performed using 3000 LHS samples from the parameter ranges in Table A.1 and initial conditions $P(0) = 0.92$ and $S(0) = 0.08$. The ranges of α_1 and α_2 were modified arbitrarily such that relapse rates are slower. All other parameter assumptions from Table 4.1 remain unchanged.

Parameter	**Value or Range of Uniform PDF**
μ	1/8 years^{-1}
β	[1, 4] years^{-1}
α_1	[2, 12] years^{-1}
α_2	[2, 12] years^{-1}
γ_1	[1, 4] years^{-1}
γ_2	[1, 4] years^{-1}
γ_3	[1, 4] years^{-1}
σ	[0.01, 0.2]

Table A.1: Sensitivity Analysis Parameter Assumptions with Slower Relapse Rates

Results from the sensitivity analysis are shown in Figure A.2. Statistically insignificant results are ignored in this discussion. Adjusting the relapse rates to be slower appears to have no discernible impact on the relationship between β, γ_1, γ_3, and σ and the response variables as was observed in the sensitivity analysis of the realistic parameter set. The only parameter to cross the threshold of significance was α_1 with respect to peak value, which has a PRCC of 0.6402. As α_1 increases, or as

natural relapse rates become faster, the peak value of e-cigarette smokers increases. This supports the idea that if relapse were slower, temporary quitters would be absent from the S compartment long enough to have an impact on mitigating the severity of the outbreak of the behavior. It can also be observed that the significance of α_1 increased across all other response variables. Similarly, the significance of α_2 and γ_2 was found to increase in across all response variables.

While parameters relating to temporary quitters still did not emerge as having any significant PRCC values, the results of the sensitivity analysis suggests that continuing to decrease relapse rates would eventually result in the emergence of temporary quitters as an influential group. Importantly, these results also indicate that the influence of permanent quitters, an influence not previously considered, remains unchanged even if relapse rates are lowered within the range tested.

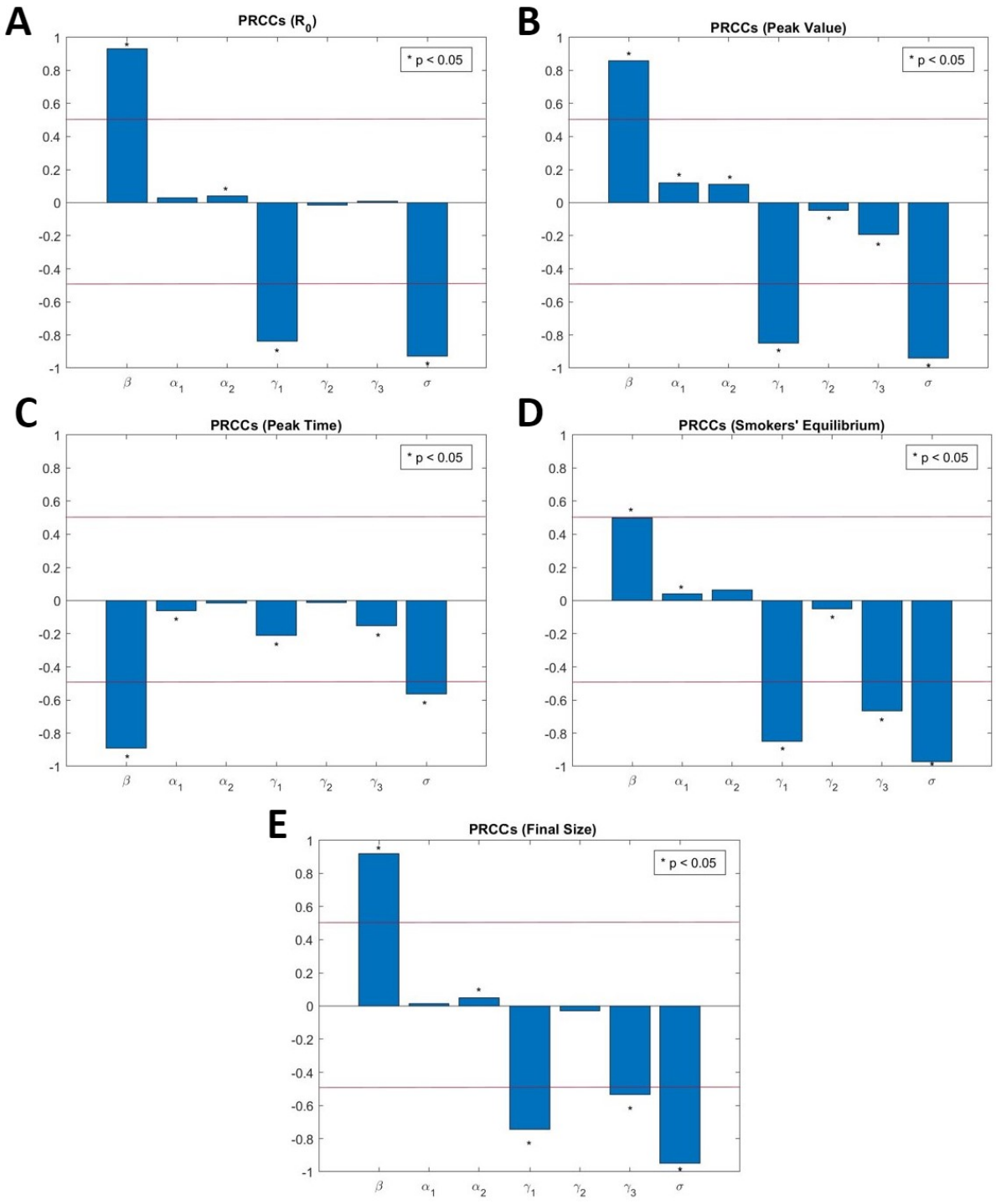

Figure A.2: PRCC analyses for the full model using 3000 LHS samples for the parameter ranges in Table A.1, where the red horizontal lines at ± 0.5 indicate the threshold for significance and * denotes a statistically significant result (p-value < 0.05).

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