Modeling Vaccination Strategies to Control White-Nose Syndrome in Little Brown Bat Colonies

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Abstract

Since 2006, the North American bat population has been in rapid decline due to a disease, known as white-nose syndrome (WNS), caused by an invasive fungus (*Pseudogymnoascus destructans*). The little brown bat (*Myotis lucifugus*) is the species most affected by this emerging disease in North America. We consider how best to prevent local extinctions of this species using mathematical models. A new vaccine against WNS has been under development since 2017 and thus, we analyze the effects of implementing vaccination as a control measure. We create a Susceptible-Exposed-Infectious-Vaccinated hybrid ordinary differential equation and difference equation model informed by the phenology of little brown bats. We analyze various vaccination strategies to determine how to maximize bat survival with regard to realistic restrictions. Next, we perform a sensitivity analysis to determine the robustness of our results. Finally, we consider other possible control measures in union with vaccination to determine the optimal control strategy. We find that if the vaccine offers lifelong immunity, then it will be the most effective control measure considered thus far.

Keywords: little brown bat, white-nose syndrome, mathematical model, vaccine, disease model, invasive species

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1 Introduction

Over the past decade, the North American bat population has suffered devastating losses due to a rapidly spreading fungal disease. This epizootic was first discovered in 2006 by a group of spelunkers in a cave system outside of Albany, New York. They encountered a colony of hibernating bats and noticed what appeared to be white powder on their noses and wings. Not knowing what this was, they took photographs of the bats and then left. The following year, biologists entered a nearby cave for a routine bat population count and found thousands of dead bats covering the cave floor. Researchers soon realized the white powder was the cause of what has become the first sustained bat epizootic in recorded history. The spelunkers in 2006 had captured the first known photographs of what is now known as white-nose syndrome (WNS) [8]. In the years since, WNS has spread to 31 states and five Canadian provinces, claiming the lives of over six million bats in its wake [21]. Forecasts predict that little brown bats may be regionally extinct in eastern North America as early as 2026 [7].

North American bats play pivotal roles in their ecosystems as well as in various industries. Bats provide a critical service to the forestry industry by facilitating recolonization of native vegetation on degraded sites [24]. Bats also save the United States' agricultural industry approximately $3.7 billion each year in pest control and pollination costs [3]. Beyond the benefits that bats provide for society, they also possess a unique immune system compared to other mammals [15]. Bats have a distinct asymptomatic maintenance of viral infection that suggests an ancient coexistence of bats and diseases [25]. Despite their noteworthy immune system, bats are succumbing to WNS [22].

White-nose syndrome is caused by the invasive, psychrophilic fungus, *Pseudogymnoascus destructans* (*Pd*), which affects bats primarily during hibernation [8]. While hibernating, bats have significantly reduced immune function and body temperature [2], making them susceptible to infection. The fungus causes irritation and

dehydration, leading infected bats to become aroused from torpor significantly more frequently than healthy bats [4]. These frequent bouts of arousal in turn cause rapid depletion of fat stores and lead to starvation [13].

In response to the disease, there have been numerous studies conducted. Past research has focused on the little brown bat (*Myotis lucifugus*), the species suffering the most severe losses from the disease. This species has been studied for a variety of reasons, primarily due to the amount of data available and the severity of their situation. We also conduct our study on little brown bats. Researchers have used metapopulation models to investigate the effects of culling infected bats as a possible control measure for WNS. While targeted culling was found to be effective over a short period of time, it was not found to be an effective long-term solution [9]. Others provided insight regarding the dynamics of the fungus using a Susceptible-Infected-Susceptible model to determine the relative importance of bat-to-bat transmission and environment-to-bat tranmission in the spread of WNS [18]. Recently, a Susceptible-Exposed-Infected model was built around the phenology of little brown bats. It was used to compare five potential methods of control against WNS: thermal refugia, targeted culling, fungicide application, reduced reservoir size, and generalized culling. The results of this study suggested the most promising method of control was a combination of targeted culling and reducing the reservoir size of the fungus [17].

Our research relies and builds upon past work. Specifically it serves as a continuation of this most recent work by Meyer et al., by assessing a new promising method of control, vaccination. Research is currently underway to develop a vaccine that could offer bats protection from the fungal disease [19]. To our knowledge, there has been no attempt to mathematically model the implications of a white-nose syndrome vaccine. In this paper, we will make such an attempt.

This paper is organized as follows: In Section 2, we will provide details of our deterministic model, as well as discuss the implementation of vaccination into the model. In Section 3, we create a stochastic analog of the deterministic model.

In Section 4, we discuss the results of our models and vaccination strategies. We conclude in Section 5 with a discussion of the results and suggestions for future work.

2 Deterministic Model

We created our Susceptible-Exposed-Infectious-Vaccinated hybrid ordinary differential equation and difference equation model following what was previously created by Meyer et al.. We used their model as a basis from which we made modifications to take into account vaccination as a control measure. In this system, susceptible bats (S) become infected with the fungus, moving them into the exposed class (E). Exposed bats become infectious with the disease, which moves them into the infectious class (I). Furthermore, WNS induced mortality only occurs for bats in the infectious class at a rate consistent with field observations. Our model accounts for bats from all three of these classes becoming vaccinated bats (V) at a certain proportion on a single day in the model; this is referred to as the vaccination pulse. While these dynamics are happening within the bat population, the model also takes into account the growth of *Pd* within the hibernaculum (P).

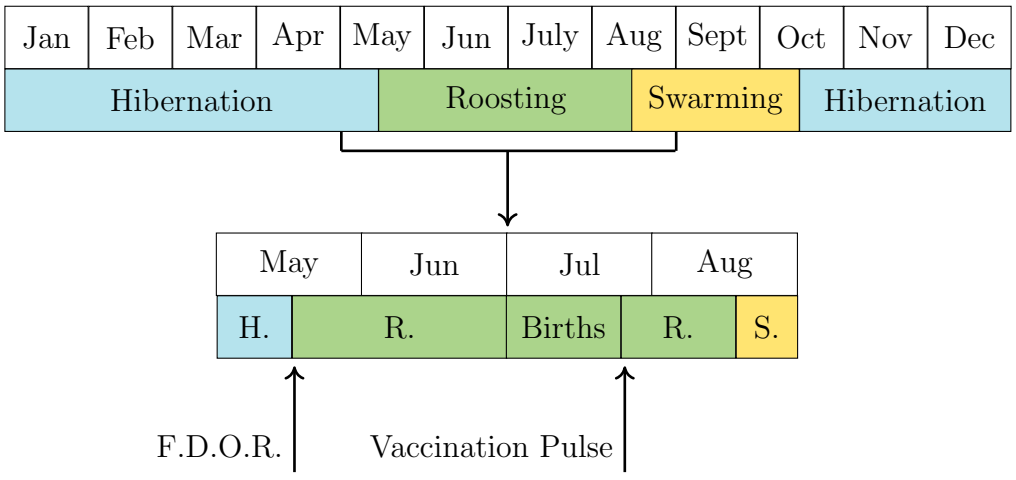


Figure 1: The phenology of little brown bats which informs our model.

The structure of the model is informed by the phenology of little brown bats (see Figure 1) [17]. As a result, our model has three distinct phases: swarming, hibernation, and roosting. The duration of each phase can be seen in Table 1. In order to more realistically represent a bat colony during roosting, we incorporated one subphase and two pulses within the roosting phase portion of the model. We created a total of six compartment models, each with a corresponding set of differential or difference equations.

Phase	Begins	Ends	Total Days
Swarming	1	61	61
Hibernation	62	273	212
First Day of Roosting Pulse	274	274	1
Daily Roosting	275	319	45
Birth Subphase	320	340	21
Vaccination Pulse	341	341	1
Daily Roosting continued	342	365	24

Table 1: Phases of the model.

Our model operates assuming the bat colony begins at a total initial population of N_0. In each portion of the model, natural death is taken into account for each class based on the rate μ. The model considers two disease transmission routes: bat-to-bat and environment-to-bat. These are represented, respectively, by the rates β and ϕ. However, it is important to note that these rates vary based on the phase in which they are used. Our model was created specifically to analyze the effect of vaccination as a control measure. With the vaccine still being in development, it is not known what length of immunity the vaccine will offer; it could last one year, or it could last a lifetime. Our model analyzes the outcomes of various immunity loss rates, a rate which is represented by λ.

2.1 Compartment Models

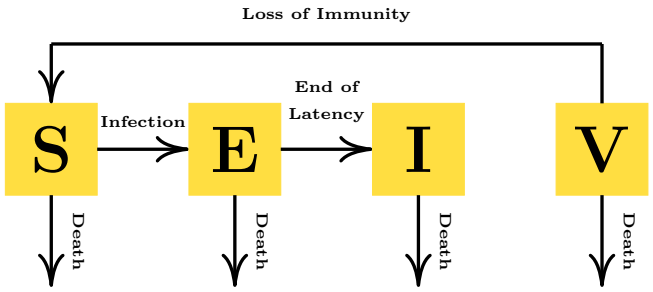


Figure 2: Flow chart of the swarming phase model.

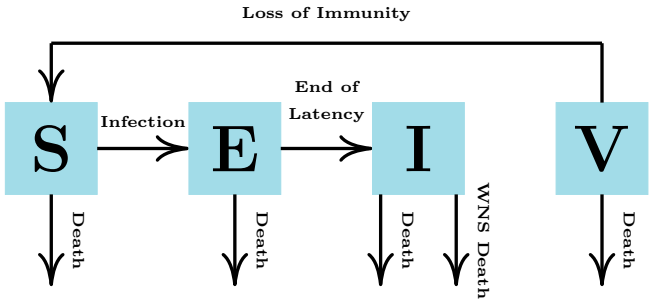


Figure 3: Flow chart of the hibernation phase model.

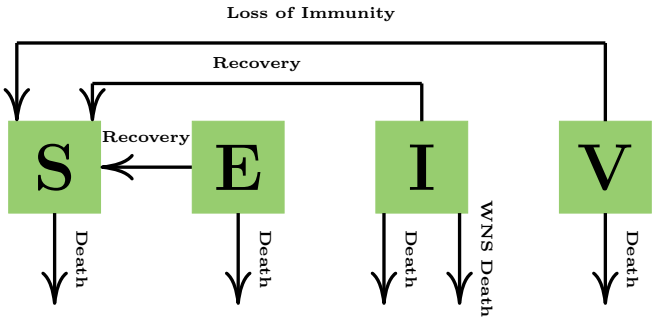


Figure 4: Flow chart of the first day of roosting pulse model.

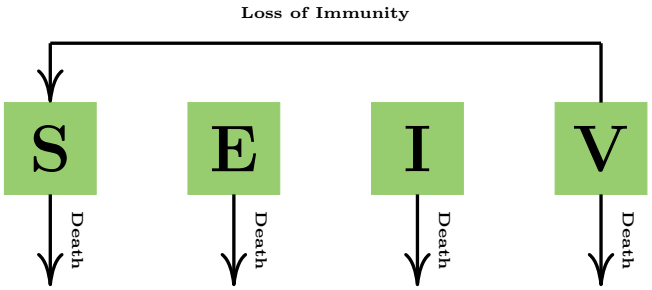


Figure 5: Flow chart of the regular roosting model.

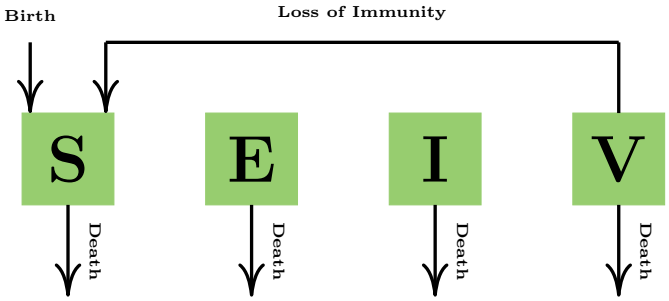


Figure 6: Flow chart of the birth subphase model.

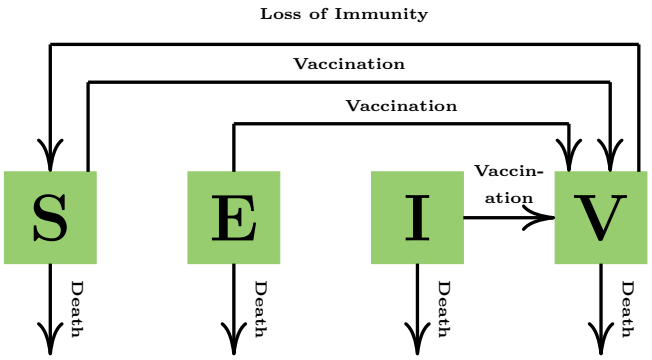


Figure 7: Flow chart of the vaccination pulse model.

2.2 Parameters

Table 2 summarizes the parameters used throughout the model. Our model is designed to confirm results found from Meyer et al., develop them further, and

implement vaccination as a new control method. As a result, many parameters are the same as previous works [17]. The majority of parameters are biologically determined values, or well-estimated. Four transmission parameters ϕ_s, ϕ_h, β_s, and β_h are exceptions to this. Model analyses have shown the amount of bat-to-bat transmission during swarming is negligible compared to transmission in hibernation [17]. Furthermore, disease induced mortality is limited to only the hibernation phase. The primary reasons for these assumptions are pathogen and host physiologies [12]. This allows for the simplifying assumption that $R_0^B = R_0^h$ and that $R_0^s = 0$. By the derivation of the basic reproductive number for the i^{th} phase

$$R_o^i = \frac{\beta_i N_0 \tau_i}{(\mu + \delta)(\tau_i + \mu)} \qquad (\delta = 0 \text{ if } i = s) \tag{1}$$

it can be inferred that $\beta_s = 0$ [17]. In regards to ϕ_s and ϕ_h, we elected to consider a set of parameters that models high bat-to-bat transmission during hibernation ($R_0^B = 4.15$) and greater environment-to-bat transmission during hibernation than swarming ($\phi_h = 2.0 \cdot 10^{-13}$,$\phi_h = 1.75 \cdot 10^{-13}$ [12]). Model analyses considered multiple combinations of these parameters, finding similar results. We selected this combination to compare our results to previous work as well as doing so under the suggestion of Langwig et al..

Parameter	Units	Definition	Default Value [Source]	Latin Hypercube Sampling Ranges [Source]
N_0	Bats	Initial local bat population	15, 000 [5]	Not varied
μ	d^{-1}	Natural mortality rate	$1/(8.5 \cdot 365)$ [6]	$1/(6 \cdot 365)$ - $1/(10 \cdot 365)$
T_s	d	Number of days in the swarming phase	61 [17]	Not varied
T_h	d	Number of days in the hibernation phase	212 [17]	Not varied
T_r	d	Number of days in the roosting phase	92 [17]	Not varied
T_b	d	Number of days in the birth subphase	21	Not varied
K_{Ml}	Bats	Calibrated bat carrying capacity	20,148	Not varied
τ_s	d^{-1}	Transition rate from exposed to infectious (swarming phase)	1/120 [14]	1/110 - 1/130
τ_h	d^{-1}	Transition rate from exposed to infectious (hibernation phase)	1/83 [14]	1/77 - 1/88
δ	d^{-1}	Rate of WNS-induced mortality	1/60 [14]	1/55 - 1/65
β_s	$Bats^{-1}$	Bat-to-bat transmission rate (swarming phase)	0 [12]	Not varied
β_h	$Bats^{-1}$	Bat-to-bat transmission rate (hibernation phase)	$4.826 \cdot 10^{-6}$ [17]	Not varied
ϕ_s	$Bats^{-1}CFUs^{-1}\ d^{-1}$	Environment-to-bat transmission rate (swarming phase)	$1.75 \cdot 10^{-13}$ [12]	0 - $4 \cdot 10^{-13}$
ϕ_h	$Bats^{-1}CFUs^{-1}\ d^{-1}$	Environment-to-bat transmission rate (hibernation phase)	$2.0 \cdot 10^{-13}$ [12]	0 - $4 \cdot 10^{-13}$
a_1	Unitless	Probability of FDOR recovery for an exposed bat	0.75 [17]	0.65 - 0.85
a_2	Unitless	Probability of FDOR recovery for a viable infectious bat	0.75 [17]	0.65 - 0.85
ε	Unitless	Probability of FDOR viability for an infectious bat	1/11 [17]	Not varied
s	d	Scaling parameter for function $\varepsilon(\delta)$	600 [17]	400 - 800
K_{Pd}	$CFUs$	Hibernaculum Pd carrying capacity	10^{10} [18]	Not varied
η	d^{-1}	Natural mortality rate of Pd	0.5 [18]	0.4 - 0.6
ω	$CFUs\ Bats^{-1}d^{-1}$	Rate of Pd shedding from infectious bats	50 [18]	45 - 55
G	d	3 week birth window	21 [6]	Not varied
R_0^B	Unitless	Basic Reproduction Number (hibernation phase)	4.15 [12]	Not varied
R_0^S	Unitless	Basic Reproduction Number (swarming phase)	0 [17]	Not varied
λ	d^{-1}	Rate of immunity loss	1/365	Not varied
ν	Unitless	Proportion of population vaccinated	$0.1 - 0.9$	Not varied
N_{10}	Bats	Local bat population 10 years after infection	N.A.	N.A.
γ	d^{-1}	Rate of birth during birth subphase	0.0194	N.A.
h	Years	The difference between vaccination and infection to maximize	0	N.A

Table 2: Parameter Values

2.3 Swarming

Our model begins during the swarming phase. The swarming phase occurs during autumn, generally from mid-August through mid-October [17]. the swarming phase lasts 61 days in our model (see Table 1). During this time of the year, bats are mating and accumulating fat stores in preparation for hibernation [10]. Our model assumes little brown bats do not die due to WNS during this phase and the bat-to-bat transmission, β_S, of the disease is negligible [12]. However due to environment-to-bat transmission, we assume bats are still transitioning from the susceptible class into the exposed class, as well as from the exposed class into the infectious class [17]. Here, and throughout the model, natural death is occurring out of all four classes (see Figure 2).

The swarming phase is modeled by the system of ordinary differential equations

$$\frac{dS}{dt} = -(\beta_s I + \phi_s P)S + \lambda V - \mu S \tag{2a}$$
$$\frac{dE}{dt} = (\beta_s I + \phi_s P)S - (\tau_s + \mu)E \tag{2b}$$
$$\frac{dI}{dt} = \tau_s E - \mu I \tag{2c}$$
$$\frac{dV}{dt} = -\lambda V - \mu V \tag{2d}$$

where the rate at which the fungus is being transferred from bat-to-bat is represented by β_s. The rate at which the disease is being transferred from the environment-to-bat is represented by ϕ_s. The rate at which bats leave the exposed class and enter the infectious class is represented by τ_s. During the swarming phase, Pd growth is modeled by the following:

$$\frac{dP}{dt} = (\omega I + \eta P)\Big(1 - \frac{P}{K_{Pd}}\Big) \tag{3}$$

where ω is the rate of Pd shedding from infectious bats, η is the natural mortality rate of Pd, and K_{Pd} is the carrying capacity of Pd.

2.4 Hibernation

After swarming, bats enter into the hibernation phase. This is the longest phase, beginning in mid-October and lasting until mid-May [17]. In our model, the hibernation phase lasts 212 days (see Table 1). It is during this phase that bats are most susceptible to the disease. Unlike other fungal pathogens which cause superficial damage, Pd can digest and erode the skin of bats [4]. Due to the irritation and dehydration caused by the growth of the fungus, the bats are more frequently aroused during their torpor, causing their fat stores to be depleted too quickly. This loss of energy, coupled with the lack of insects to consume in the winter, leads to bats dying of starvation [13].

During this time, bats are still moving from the susceptible class into the exposed class, and also from the exposed class to the infectious class (see Figure 3). The hibernation phase is modeled with equations which are structurally the same as the swarming phase. This phase is modeled with the system of equations

$$\frac{dS}{dt} = -(\beta_h I + \phi_h P)S + \lambda V - \mu S \tag{4a}$$
$$\frac{dE}{dt} = (\beta_h I + \phi_h P)S - (\tau_h + \mu)E \tag{4b}$$
$$\frac{dI}{dt} = \tau_h E - (\delta + \mu)I \tag{4c}$$
$$\frac{dV}{dt} = -\lambda V - \mu V \tag{4d}$$

where different values are used for the rates of disease transmission from bat-to-bat and environment-to-bat as indicated, respectively, by β_h and ϕ_h. Also, the rate at which bats are moving from the exposed class to the infectious class is indicated by τ_h.

In this system we include one new parameter, δ, to represent the rate at which bats are dying specifically due to white-nose syndrome. During the hibernation phase, Pd growth is modeled by the following:

$$\frac{dP}{dt} = (\omega I + \eta P)\Big(1 - \frac{P}{K_{Pd}}\Big) \tag{5}$$

where ω is the rate of Pd shedding from infectious bats, η is the natural mortality rate of Pd, and K_{Pd} is the carrying capacity of Pd.

2.5 Roosting

Once the bats awake from hibernation, the roosting phase begins. It is during this phase that female little brown bats are giving birth to and rearing young. Generally, females give birth to only one pup per year [6]. The roosting phase begins in mid-May and lasts until mid-August [17]. This phase lasts 92 days (see Table 1). However, to more realistically represent what is happening within a bat population during this time, our model divides this phase into four separate compartment models with two pulses and two subphases. Also, it is during this phase on a single day that our model assumes the vaccine is administered to a proportion of a bat colony.

When differential equations are used in this phase, Pd is growing according to the following differential equation:

$$\frac{dP}{dt} = \eta P\Big(1 - \frac{P}{K_{Pd}}\Big). \tag{6}$$

During the two pulses within this phase, Pd is assumed to have reached carrying capacity and is treated as a constant on these days.

2.5.1 First Day of Roosting Pulse

The roosting phase begins with a pulse occurring on the first day. The first day of roosting pulse (F.D.O.R) represents the complex transfers between classes that occur at the end of hibernation. At this time, there is a proportion of exposed and infectious bats moving back into the susceptible class. This is done to take into account bats who, though exposed or infectious, are still healthy enough to survive through the remainder of the year (see Figure 4).

To more easily model this singular day, we use a system of difference equations. On the first day,

$$S_t = [S_{t-1} + a_1 E_{t-1} + \varepsilon a_2 I_{t-1} + V(1 - e^{-\lambda})]e^{-\mu} \tag{7a}$$

$$E_t = (1 - a_1)E_{t-1}e^{-\mu} \tag{7b}$$

$$I_t = \varepsilon(1 - a_2)I_{t-1}e^{-\mu} \tag{7c}$$

$$V_t = V_{t-1}e^{-\lambda}e^{-\mu} \tag{7d}$$

where the parameter values used in this system of equations include a_1 and a_2 which, respectively, are the proportion of bats who move from the exposed and infectious classes into the susceptible class. The ε parameter value represents the probability of a bat becoming infectious late enough in the hibernation phase to be healthy enough to fly from the hibernaculum after hibernation and survive through the remainder of the year.

2.5.2 Regular Roosting Subphase

After the first day, a new compartment model is needed to represent what happens on an ordinary day during this phase. Here we create the system of differential

equations

$$\frac{dS}{dt} = \lambda V - \mu S \tag{8a}$$
$$\frac{dE}{dt} = -\mu E \tag{8b}$$
$$\frac{dI}{dt} = -\mu I \tag{8c}$$
$$\frac{dV}{dt} = -\lambda V - \mu V \tag{8d}$$

to represent this period of time within the model.

2.5.3 Birth Subphase

Since female little brown bats typically give birth to a single pup within a three week period during the middle of the roosting phase [6], we convert the single-day, logistic birth pulse from Meyer et al. into a three-week birth subphase. Our birth subphase begins halfway through the roosting phase and lasts for three weeks.

We assume the population grows at a relative rate, γ, throughout the birth subphase. We assume that the susceptible class will grow logistically such that

$$\frac{dS}{dt} = \gamma N \left(1 - \frac{N}{K_{Ml}}\right) + \lambda V - \mu S$$

occurs throughout the three week period. In order to determine the birth rate and the calibrated carrying capacity, γ and K_{Ml}, respectively, we fit our model in two respects. The first condition was that only 25% of a colony's initial population will survive two years after the disease arrives [1]. The second condition was that in a disease-free simulation, the population should return to its initial population size, N_0, each year. To determine the values of γ and K_{Ml} necessary to fulfill these conditions, we utilized MATLAB's `fminsearch` optimization method (MathWorks, Natick, MA,

USA) to minimize the cost functional

$$J(\theta) = 10\left(\frac{N_0}{4} - N(2(365); \theta_{df})\right)^2 + \sum_{i=1}^{10}(N_0 - N(365i; \theta_{ed}))^2 \tag{9}$$

where N is the total bat population at t days under the parameter vector θ_{df} for the disease-free scenario and θ_{ed} for the endemic scenario. This yielded a calibrated carrying capacity K_{Ml} of 20,148 bats and relative birth rate γ of 0.0194 d^{-1}. The results of meeting these conditions are found in Figure 8 and Figure 9.

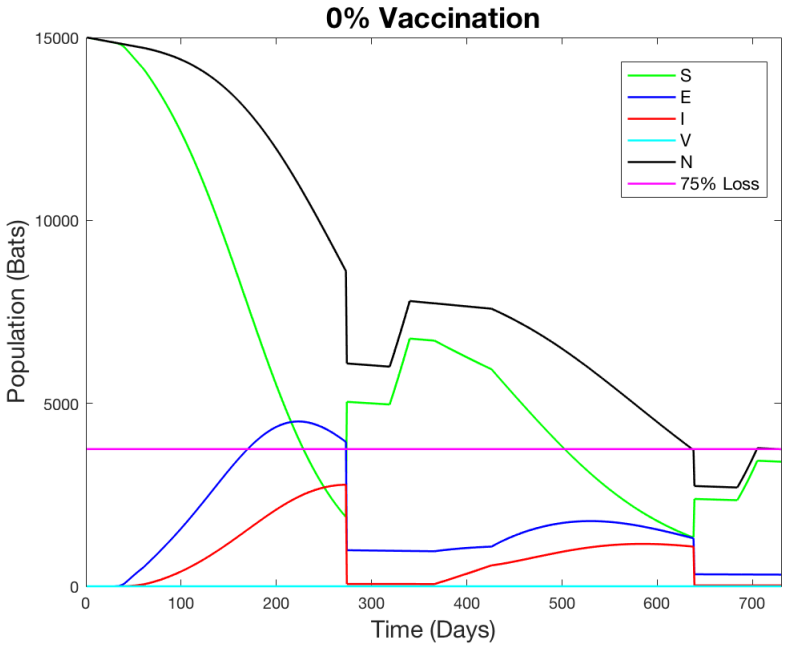


Figure 8: Dynamics over two years of a population with no vaccination. The total population reaches 25% of its initial population size at the end of year 2.

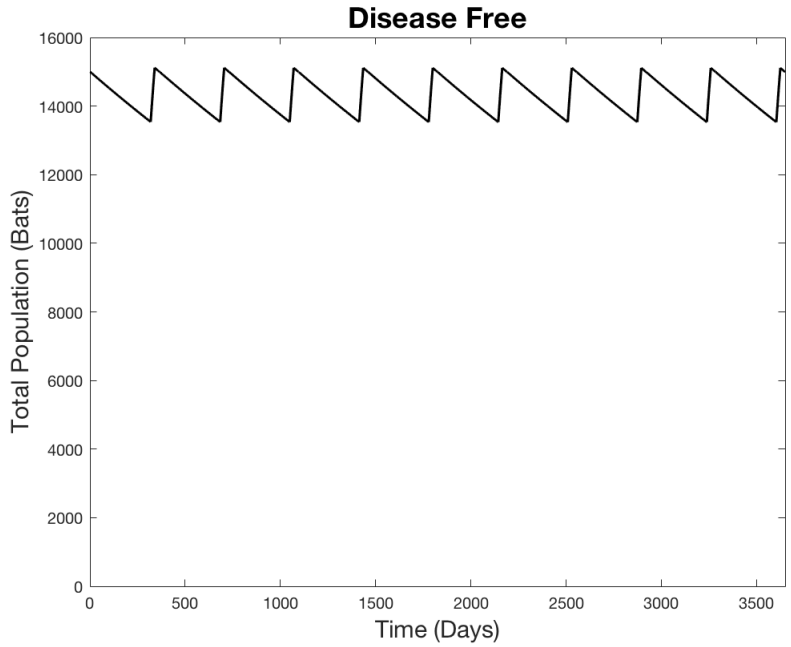


Figure 9: The dynamics over ten years of the total little brown bats in a disease-free population. The total population returns to its initial population size of 15,000 bats by the start of each swarming phase.

Bats with WNS are unlikely to be infectious during the spring and summer due to the psychrophilic nature of *Pd*, therefore vertical transmission of *Pd* from mother to pup is improbable [23]. Hence, we assume that new bats are exclusively added to the susceptible class. The birth subphase is modeled by the system

$$\frac{dS}{dt} = \gamma N\left(1 - \frac{N}{K_{Ml}}\right) + \lambda V - \mu S \tag{10a}$$

$$\frac{dE}{dt} = -\mu E \tag{10b}$$

$$\frac{dI}{dt} = -\mu I \tag{10c}$$

$$\frac{dV}{dt} = -\lambda V - \mu V. \tag{10d}$$

Allowing for this three week period of births, rather than a birth pulse, is one of the major modifications to the model not considered in previous work.

2.5.4 Vaccination Pulse

Our model assumes the vaccine will be administered on a single day, specifically the day following the conclusion of the birth subphase. The vaccine we model is still under development, however the idea is to create it in the form of an edible gel. This gel could then be sprayed onto a proportion of a bat population. The vaccine would take advantage of bats' natural tendency to groom themselves and each other [6]. During grooming, bats would ingest the gel vaccine and it would create antibodies within them that would enable their bodies to fight the fungus [19].

We chose to implement vaccination during this phase for several reasons. It does not make sense to vaccinate the population during hibernation because it would disturb the bats in the midst of their torpor, which is what the disease itself does. Roosting is the optimal time to locate bat populations compared to swarming, as specifically females are easier to find during this time of the year [11]. Also, by vaccinating on this day, the vaccine would reach the most number of bats within a population and also protect young bats before they have a chance of becoming infected.

For this portion of roosting, we once again use a system of difference equations because vaccination administration is assumed to occur on a single day. The day of vaccination is modeled as

$$S_t = [(1-\nu)S_{t-1} + (1-e^{-\lambda})(\nu(S_{t-1}+E_{t-1}+I_{t-1}) + V_{t-1})]e^{-\mu} \tag{11a}$$

$$E_t = (1-\nu)E_{t-1}e^{-\mu} \tag{11b}$$

$$I_t = (1-\nu)I_{t-1}e^{-\mu} \tag{11c}$$

$$V_t = [\nu(S_{t-1}+E_{t-1}+I_{t-1}) + V_{t-1}]e^{-\lambda}e^{-\mu} \tag{11d}$$

with the parameter ν representing the proportion of the bat population that gains immunity from the vaccine.

2.6 Vaccination Strategies

We wanted to analyze our model with regard to realistic restrictions. A restriction our model considers is loss of immunity at various rates, λ. We analyze the consequences of these varying rates of immunity loss. Also, we consider the frequency of vaccine dispersal into a bat population through various vaccination strategies. We analyzed the outcomes of vaccinating a population annually, biennially, or once. For the annual and biennial strategies, we assumed a constant vaccination rate each time the vaccine was implemented. For one time vaccination, we considered various years in which the vaccine can be administered.

2.7 Sensitivity Analysis

We performed a sensitivity analysis of our model using a Latin hypercube sampling (LHS) [16]. By doing so we are able to determine qualitatively if our model is extremely sensitive or not. The LHS operates under the assumption that $\lambda = 0$. We assume that the qualitative results from the LHS when $\lambda = 0$ has similar behavior to when $\lambda \neq 0$. To complete the LHS we varied 12 parameters according to ranges found from literature, or estimated. At each vaccination proportion stepping by 10%, 100 combinations of these 12 parameters were used to calculate a total of 1000 samples of N_{10}, the surviving population ten years after infection. These varied parameters and their respective ranges can be found in Table 2. Note that ε is dependent upon s in the following way:

$$\varepsilon = \frac{1}{s\delta + 1} \tag{12}$$

thus varying s in the LHS directly varies epsilon as well. Additionally, K_{Ml} is updated depending on the value the LHS generates for N_0. The proportion that N_0 is of K_{Ml} was determined by analyzing the disease-free model at different N_0 and K_{Ml} values so that annually the bat population reaches the corresponding N_0. The following

relation between K_{Ml} and N_0 was determined by

$$K_{Ml} = 1.3432N_0. \tag{13}$$

2.7.1 Loss of Immunity

Our results and discussion consider two situations. The first considers lifelong immunity, $\lambda = 0$, and the second considers loss of immunity, $\lambda \neq 0$. This consideration is important as loss of immunity alters the effectiveness of vaccination strategies.

2.7.2 Lag Period

Another restriction we considered was various timing scenarios. We analyzed the effects of implementing the vaccine before and after a colony included infected bats. The timing before and after infection is referred to as the lag, and is denoted as h. The calculation of h is the difference between the year of infection and vaccination implementation. Negative values of h correspond to vaccinating before infection begins, and positive values of h correspond to vaccinating after infection begins. For consistency, the simulation was run for 10 years after the first year of infection regardless of the lag.

2.8 Other Methods of Control

Previous work considered multiple control strategies and highlighted the combination of two control strategies, reduced reservoir size of Pd and targeted culling, as the most effective measures of control for WNS [17]. At the time the research was conducted, vaccination was not explored primarily due to the fact that a vaccine had not been announced. We explored both of these control measures by themselves as well as in union with vaccination.

2.8.1 Reduced Reservoir

Reduced reservoir is a method of control that operates by lowering the carrying capacity Pd. To do this, a proportion of K_{Pd}, ρ, will be removed. It is assumed that this removal only occurs in the year of infection. The effect of this changes the differential equations modeling P. Hibernation and swarming is now modeled by

$$\frac{dP}{dt} = (\omega I + \eta P)\left(1 - \frac{P}{(1-\rho)K_{Pd}}\right) \tag{14}$$

and roosting is now modeled by

$$\frac{dP}{dt} = \eta P\left(1 - \frac{P}{(1-\rho)K_{Pd}}\right). \tag{15}$$

2.8.2 Targeted Culling

Targeted culling is a method of control that operates by removing a proportion of the exposed and infectious bats in hopes of preventing spread of the disease to susceptible bats. It is assumed that this removal of bats occurs twice during the hibernation phase by an equal proportion ζ. The respective time line for when these removals occur is listed below in Table 3. With this method of control there are two new pulses, for each round of culling, and both are implemented using difference equations

$$S_t = S_{t-1}e^{-\mu} \tag{16a}$$

$$E_t = (1-\zeta)E_{t-1}e^{-\mu} \tag{16b}$$

$$I_t = (1-\zeta)I_{t-1}e^{-\mu} \tag{16c}$$

$$V_t = V_{t-1}e^{-\mu} \tag{16d}$$

Phase	Begins	Ends	Total Days
Swarming	1	61	61
Hibernation Part 1	62	131	70
Targeted Culling Part 1	132	132	1
Hibernation Part 2	134	202	69
Targeted Culling Part 2	203	203	1
Hibernation Part 3	204	274	71
First Day of Roosting Pulse	274	274	1
Daily Roosting	275	319	45
Birth Subphase	320	340	21
Vaccination Pulse	341	341	1
Daily Roosting continued	342	365	24

Table 3: Phases of the model considering targeted culling.

3 Stochastic Model

3.1 Purpose

Previous work ignored stochastic effects and suggested that it may be important to consider in two respects. First, stochastic effects may affect how a population heads towards extinction at small population sizes. Second, population recovery and the respective control methods may be influenced by stochastic effects [17]. Our stochastic analog is derived in two parts. First, a Continuous-Time Markov Chain (CTMC) replaces our phases in which differential equations are utilized (hibernation, swarming, regular roosting, and the birth subphase). Second, binomial distributions replace our pulses in which difference equations are utilized (first day of roosting pulse and vaccination pulse). In this way, our model considers each bat as discrete, implementing demographic stochasticity, which is a more accurate depiction of a

population. The stochastic analog operates under the assumption that $\lambda = 0$. We assume that if the stochastic analog is qualitatively similar to the deterministic model when $\lambda = 0$, it is assumed that similar behavior will also be observed when $\lambda \neq 0$. Furthermore, the transition corresponding to the event of Pd growth is fitted to reflect the qualitative behavior of the deterministic model. This is done due to the fact that the bat population and population of CFUs are on different orders of magnitude by the end of the first swarming phase.

3.1.1 Continuous-Time Markov Chain Derivation

The CTMC is constructed by creating a table for each phase which utilizes a differential equation. The table considers the events that may happen in that phase, the respective transition, as well as the respective rate. The total rate, T, is calculated by summing all of the rates within the phase. Each event is assigned a proportional non-overlapping interval depending on the proportion of the respective rate to the total rate, between $(0, T)$. This means that the interval $(0, T)$ will be subdivided proportionally into a number of intervals equal to the number of events. The process of determining the amount of time between events and which event occurs is outlined below.

1. The number of days until an event occurs is calculated. This is determined by a random number generated from the exponential distribution, $Exp(1/T)$.
2. The number of days calculated in Step 1 is added to the total number of days.
3. Now that an event has occurred it must be classified into which event occurred. A random number is generated from the uniform distribution $U(0, T)$.
4. The number generated in Step 3 falls into an interval belonging to an event. That event is said to occur. The respective transition occurs.
5. Step 1 through Step 4 is repeated until the number of days in a phase is completed.

CTMC tables with event, transition, and rate information for swarming, hibernation, roosting, and the birth subphase are found in Tables 4, 5, 7, and 8 respectively.

3.1.2 Binomial Distributions Derivation

The binomial distribution requires two inputs, the number of trials, n, and the probability of success for a given trial, p. Within our model binomial distributions are applied at two different pulses, and within each pulse, there is a binomial distribution used on each class of bats (S, E, I and V). The corresponding inputs are provided in the Tables 6 and 9.

We considered implementing the Poisson distribution, an approximation of the binomial distribution. The n value would represent the total number of bats alive in a given class, and the p value would represent our definition of success, which varies. The general rule for Poisson distributions calls for its use when n is larger than 20 and p is less than or equal to 0.05 [20]. Our definition of success made p greater than 0.05 for the parameters used in the first day of roosting pulse and the vaccination pulse. The reasoning for the choice to use a binomial distribution rather than a Poisson distribution is outlined as follows.

For the first day of roosting pulse, the natural death the success probability p was determined by $e^{-\mu}$ which equals 0.9997. We evaluated the parameter value ε and found it to equal a 0.09 probability. For the probabilities of infectious and exposed bats moving to the susceptible class we defined success to be when a bat did not leave the infectious or exposed class. These probabilities $1-a_1$ and $1-a_2$ which both equal 0.25 (see Table 6).

For the vaccination pulse, the success definition for natural death was the same and did not meet the standard rule for the Poisson distribution. We defined success to mean bats remained in their class and did not move into the vaccinated class, $1-\nu$. For our model in general, we consider vaccination proportions greater than 0.1 and

less than 0.9. This means the probability of bats staying in their class during this time is at minimum 0.1 (see Table 9).

3.2 Swarming

Event	Transition	Rate
Susceptible Death	$S \to S - 1$	μS
Exposed Death	$E \to E - 1$	μE
Infectious Death	$I \to I - 1$	μI
Vaccinated Death	$V \to V - 1$	μV
Infection	$S \to S - 1$	$(\beta_S I + \phi_S P)S$
	$E \to E + 1$	
End of latency	$E \to E - 1$	$\tau_S E$
	$I \to I + 1$	
Pd Growth	$P \to P * 10^{0.001}$	$(\omega I + \eta P)\left(1 - \frac{P}{K_{Pd}}\right)$

Table 4: Rates of the swarming phase.

3.3 Hibernation

Event	Transition	Rate
Susceptible Death	$S \to S-1$	μS
Exposed Death	$E \to E-1$	μE
Infectious Death	$I \to I-1$	$(\mu+\delta)\, I$
Vaccinated Death	$V \to V-1$	μV
Infection	$S \to S-1$	$(\beta_H I + \phi_H P)\, S$
	$E \to E+1$	
End of latency	$E \to E-1$	$\tau_H E$
	$I \to I+1$	
Pd Growth	$P \to P * 10^{0.001}$	$(\omega I + \eta P)\left(1 - \frac{P}{K_{Pd}}\right)$

Table 5: Rates of the hibernation phase.

3.4 Roosting

3.4.1 First Day of Roosting

Calculation/Success Definition	Success Probability
Infectious bats survive F.D.O.R	$e^{-\mu}$
Viable infectious bats after hibernation	ε
Recovered Infectious bats	$(1-a_2)$
Exposed bats survive F.D.O.R	$e^{-\mu}$
Recovered exposed bats	$(1-a_1)$
Susceptible bats survive F.D.O.R	$e^{-\mu}$
Vaccinated bats survive F.D.O.R	$e^{-\mu}$

Table 6: Binomial distributions for the F.D.O.R.

3.4.2 Regular Roosting Subphase

Event	Transition	Rate
Susceptible Death	$S \to S - 1$	μS
Exposed Death	$E \to E - 1$	μE
Infectious Death	$I \to I - 1$	μI
Vaccinated Death	$V \to V - 1$	μV
Pd Growth	$P \to P * 10^{0.001}$	$\eta P \left(1 - \frac{P}{K_{Pd}}\right)$

Table 7: Rates of the regular roosting subphase.

3.4.3 Birth Subphase

Event	Transition	Rate
Susceptible Death	$S \to S - 1$	μS
Exposed Death	$E \to E - 1$	μE
Infectious Death	$I \to I - 1$	μI
Vaccinated Death	$V \to V - 1$	μV
Birth	$S \to S + 1$	$\gamma N \left(1 - \frac{N}{K_{Ml}}\right)$
Pd Growth	$P \to P * 10^{0.001}$	$\eta P \left(1 - \frac{P}{K_{Pd}}\right)$

Table 8: Rates of the birth subphase.

3.5 Vaccination Pulse

Calculation/Success Definition	Success Probability
Infectious bats survive VP	$e^{-\mu}$
Infectious bats vaccinated	$(1-\nu)$
Exposed bats survive VP	$e^{-\mu}$
Exposed bats vaccinated	$(1-\nu)$
Susceptible bats survive VP	$e^{-\mu}$
Susceptible bats vaccinated	$(1-\nu)$
Vaccinated bats survive VP	$e^{-\mu}$

Table 9: Binomial distributions for the vaccination pulse.

4 Results

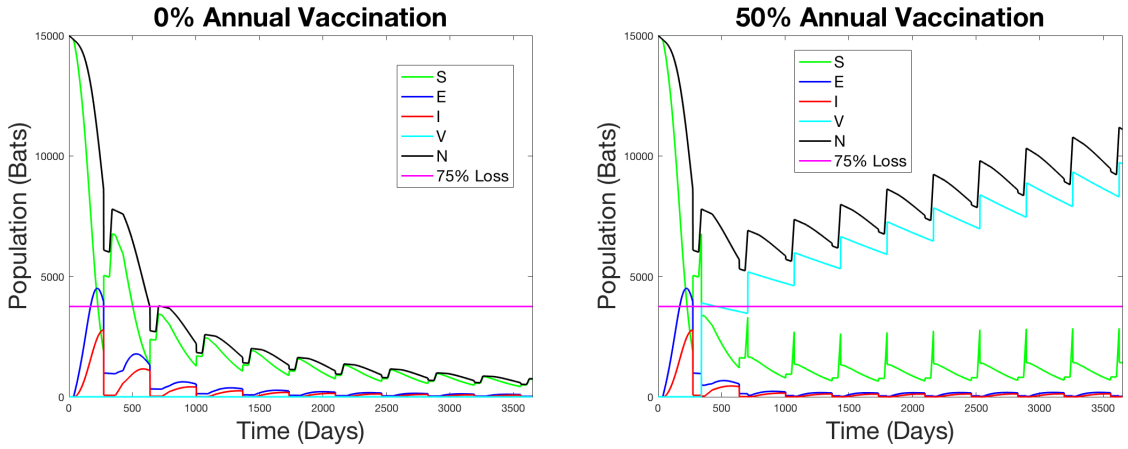
In our research, we attempted to answer five questions. First, we wanted to know if implementing a birth subphase would yield similar results as previous researchers found using a birth pulse (1). Second, we sought to discover if a vaccine could save local bat populations from extinction (2). Third, we compared different implementations of the vaccine under various realistic restrictions (3). This allowed us to make recommendations about how to administer the vaccine in order to maximize its effectiveness. Fourth, we wanted to know how vaccination compared to other control methods (4). Fifth, we wanted to answer the question posed by Meyer et al. regarding whether or not implementing stochastic processes would affect the success of control measures [17] (5).

4.1 Deterministic Model

To answer question (1), we rebuilt the previous model created by Meyer et al.. We confirmed similar dynamics, as well as a loss of 75% of the initial bat population after two years (see Figure 10a), which corresponds to data collected on infected bat populations [1]. After we confirmed these dynamics, we adjusted the model to include a birth subphase in place of a birth pulse. Our model accounts for an influx of bat pups into the population over a three week period, instead of using the simplification of births all occurring on a single day. With this addition, our model had a similar quantitative and qualitative nature to previous research (see Figure 10a).

4.1.1 Various Vaccination Proportions

To answer question (2) in regard to the effectiveness of the vaccine in preventing the local extinction of bat populations, we began by determining the outcome of annual vaccination with lifelong immunity at $\nu = 0.5$. We observed that the total population is retreating away from extinction. By the second year, the vaccinated class has become the dominant class, and in doing so protects the population from suffering severe losses (see Figure 10b). Then, we compared these results to no method of control, where the total population approaches extinction (see Figure 10a). Next, we explored various vaccination proportion values, ν (see Figure 11). We saw that even at small values of ν, such as 0.1, stabilization was possible. We also learned that a high value of ν, such as 0.9, was not significantly more effective than more moderate values of ν, such as 0.5.



(a) The dynamics of the bat population with no control measure implemented.

(b) The dynamics of the bat population with vaccination implemented at $\nu = 0.5$ assuming lifelong immunity and annual vaccination.

Figure 10: The dynamics of the deterministic model.

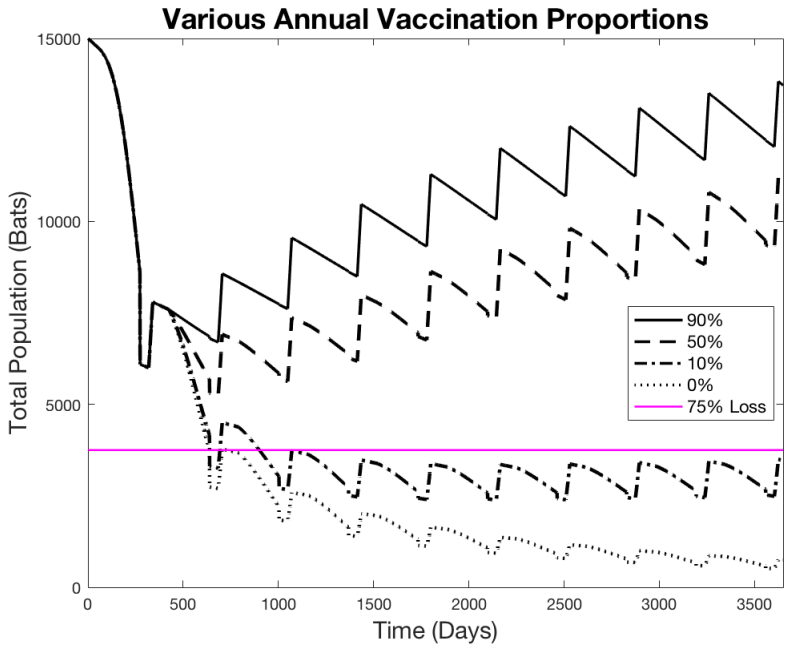


Figure 11: Total population over ten years at four different annual vaccination proportions: 0%, 10%, 50%, and 90%. This plot assumes the vaccine offers lifelong immunity against WNS.

This prompted us to determine the total population alive ten years after infection, N_{10}, for 100 different values of ν ranging from 0% to 100%, as well as the the derivative of this curve (see Figure 12). The derivative suggests that incrementing the vaccination proportion at small values of ν leads to a bigger change in N_{10} in comparison to incrementing at large values of ν.

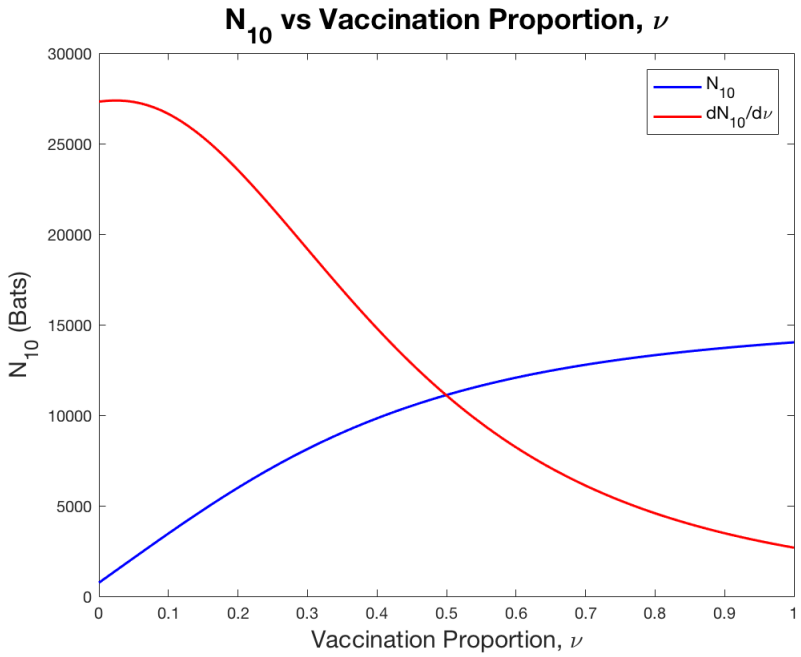


Figure 12: The blue curve represents the relationship between the vaccination proportion, ν, and the resulting total population after ten years, N_{10}. The red line is the derivative of the blue curve, visualizing where the most increase occurs between ν values. This plot assumes annual vaccination with lifelong immunity.

4.1.2 Sensitivity Analysis

We performed a sensitivity analysis on the results of Figure 12 using Latin hypercube sampling (see Figure 13). Our results show that our model is somewhat sensitive to variations in parameter values, however the model consistently follows the same qualitative behavior. The mean at each value of ν of the LHS simulations

follows a similar pattern to the simulations with default values, with a slightly less optimistic outlook.

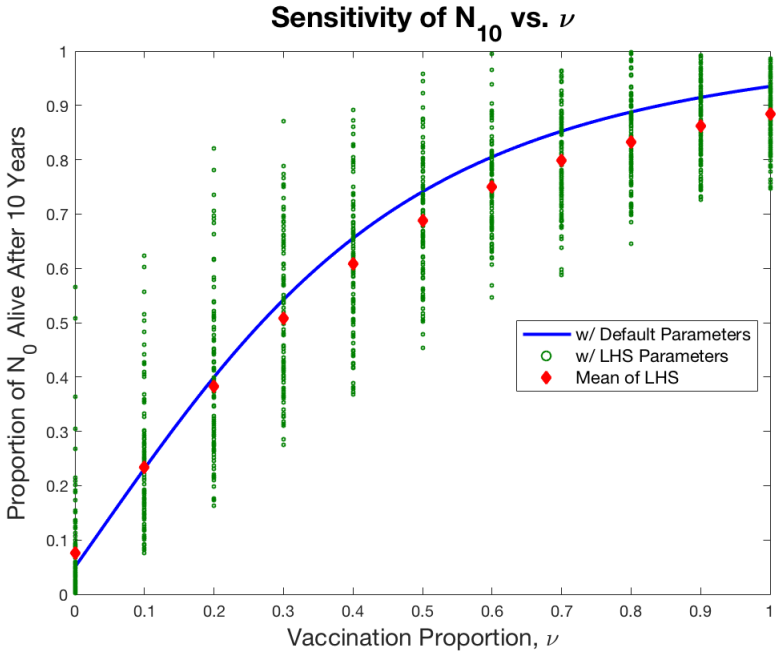


Figure 13: Latin hypercube sampling varying twelve parameter values within our model. For each value of ν the twelve parameters were varied 100 times, represented by the green dots. The mean of the realizations are represented by the red diamonds. The blue curve is the result of using the default values in our model.

4.1.3 Loss of Immunity

In order to answer question (3) we consider some restrictions that could realistically occur when implementing vaccination as a control measure for WNS. We created a new parameter, λ, which allows us to control the rate at which bats lose immunity to the disease after becoming vaccinated. We considered a situation in which immunity only lasts one year, $\lambda = 1/365$, and vaccination occurred annually. Under these assumptions, vaccination by itself was not as effective of a control measure over ten years (see Figure 14). We considered ν at the proportions 0%, 10%, 50%, and

90% to evaluate the effect of one year immunity on these various ν values (see Figure 15).

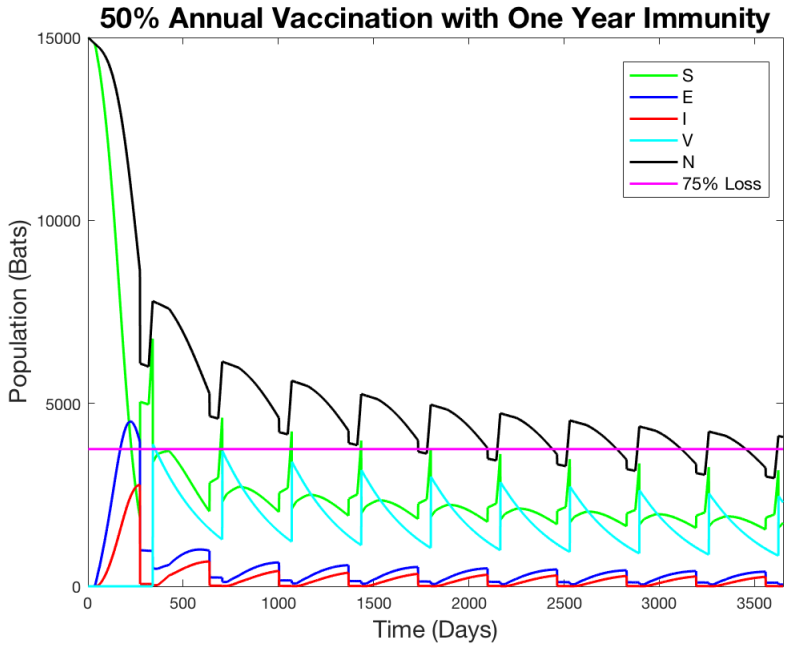


Figure 14: The dynamics of the bat population with vaccination implemented at $\nu = 0.5$ assuming lifelong immunity and annual vaccination.

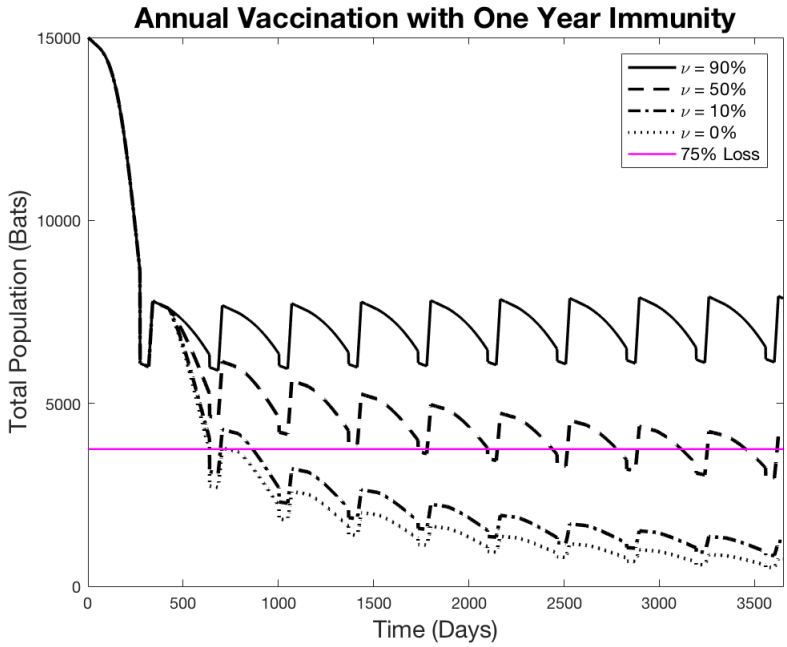


Figure 15: Total population over ten years at four different annual vaccination proportions: 0%, 10%, 50%, and 90%. This plot assumes loss of immunity occurs, on average, one year after vaccination.

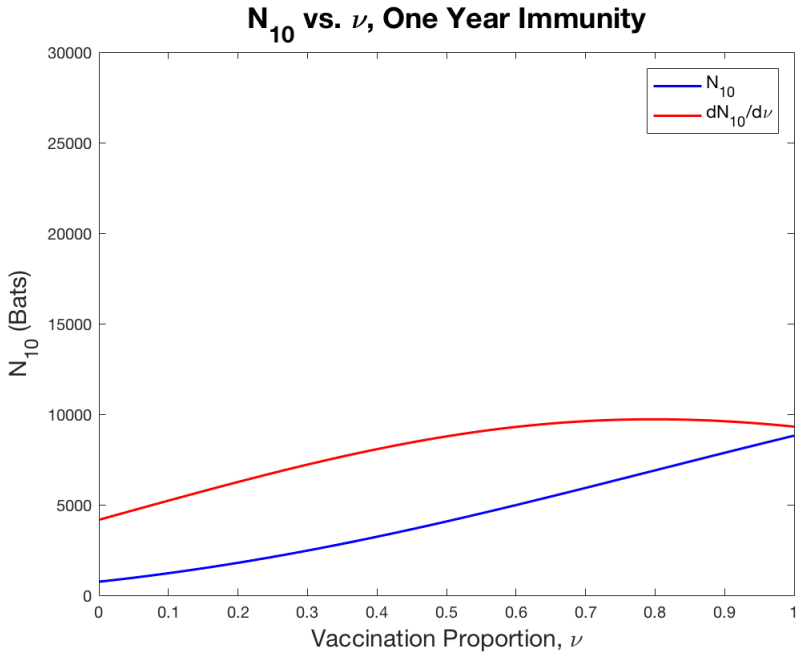


Figure 16: The blue curve represents the relationship between the annual vaccination proportion, ν, and the resulting total population after ten years, N_{10}. The red curve is the derivative of the blue curve, visualizing where the most increase occurs between ν values. This plot assumes that loss of immunity occurs, on average, one year after vaccination.

We determined the total the total population alive ten years after infection, N_{10}, for 100 different values of ν ranging from 0% to 100%, with immunity lasting one year, $\lambda = 1/365$. Next, we plotted the derivative of this curve. The derivative tells us that incrementing the vaccination proportion at large values of ν leads to a bigger change in N_{10} in comparison to incrementing at small values of ν (see Figure 16).

4.1.4 Multiple Realistic Restrictions

We also considered various timing strategies for the vaccine. The difference between the year of infection and the year of vaccination. This lag is represented

on the horizontal axis as seen in Figures 17, 18, and 19. The negative numbers represent vaccination occurring before infection, zero represents the same year, and positive numbers represent vaccination occurring after infection. In these figures we also consider three different implementation options: annual, biennial, and once. We do this for lifelong immunity, the black curves, as well as one year immunity, the red curves.

From these plots we are able to identify several trends. For annual and biennial vaccination with lifelong immunity, the total population is always higher after ten years if vaccination occurs before infection. These two strategies offer comparable outcomes after ten years. Also for lifelong immunity, if the vaccine can only be administered once, there is consistently a spike in the N_{10} value at the year before infection. By analyzing the behavior of populations with one year immunity after vaccination, we find similar results for the annual and biennial strategies. Generally it is best to implement the vaccine before infection for these situations (see Figures 17, 18, and 19).

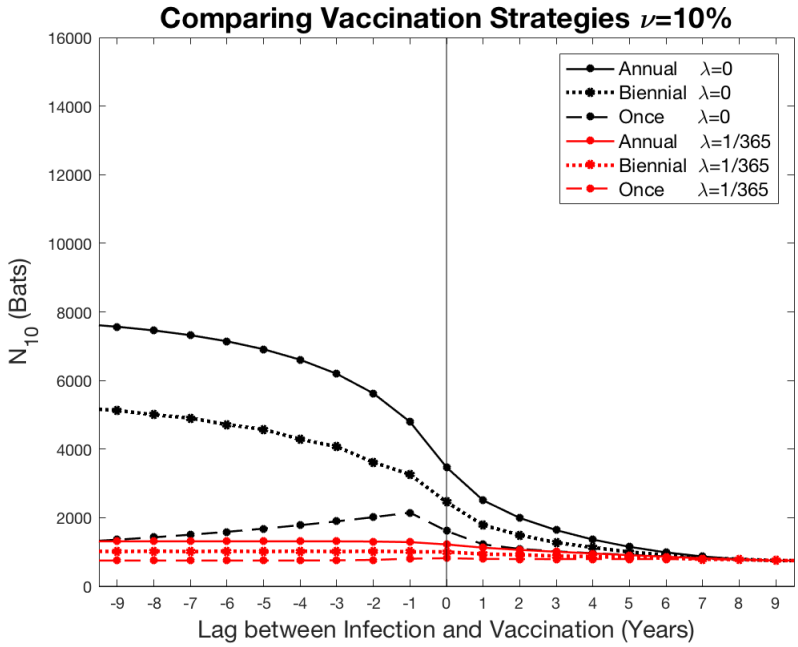


Figure 17: Population remaining ten years after infection, N_{10}, with various vaccination strategies (curve style) and immunity length (color) at 10% vaccination. Each dot represents a single run of the model. Initial population size is 15000 bats.

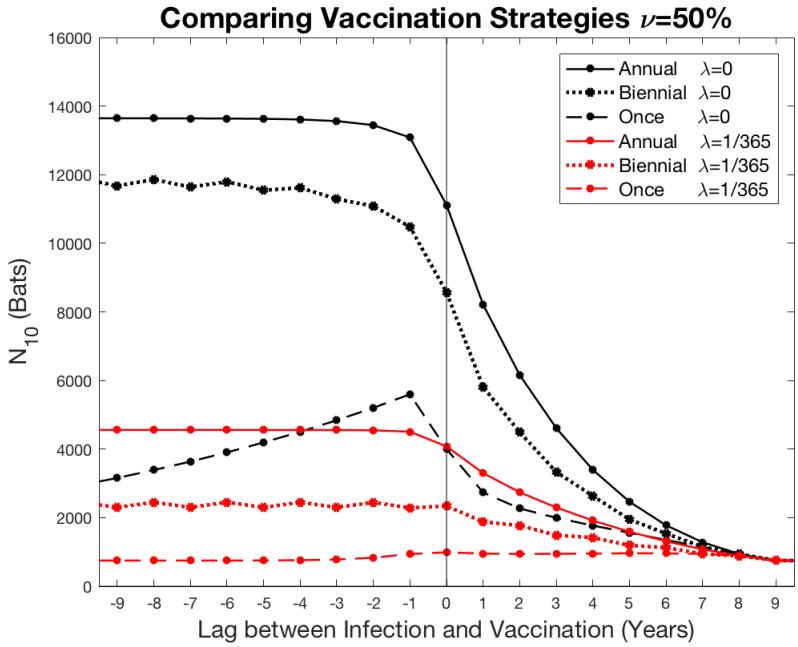


Figure 18: Population remaining ten years after infection, N_{10}, with various vaccination strategies (curve style) and immunity length (color) at 50% vaccination. Each dot represents a single run of the model. Initial population size is 15000 bats.

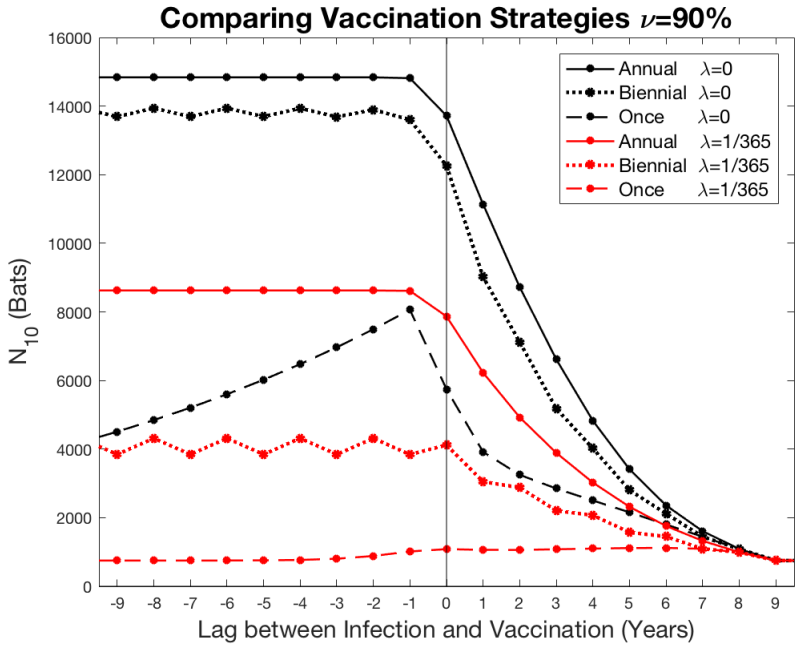


Figure 19: Population remaining ten years after infection, N_{10}, with various vaccination strategies (curve style) and immunity length (color) at 90% vaccination. Each dot represents a single run of the model. Initial population size is 15000 bats.

Next, we performed a sensitivity analysis of N_{10} versus lag between infection and vaccination using Latin hypercube sampling of 12 perturbed parameter values. We plot the LHS results in Figure 20 for the three vaccination strategies (annual, biennial, and once) as well as for three vaccination proportions (10%, 50%, and 90%). We find that the results are somewhat sensitive to variations in parameter values, however it consistently follows the same qualitative behavior as the default parameters.

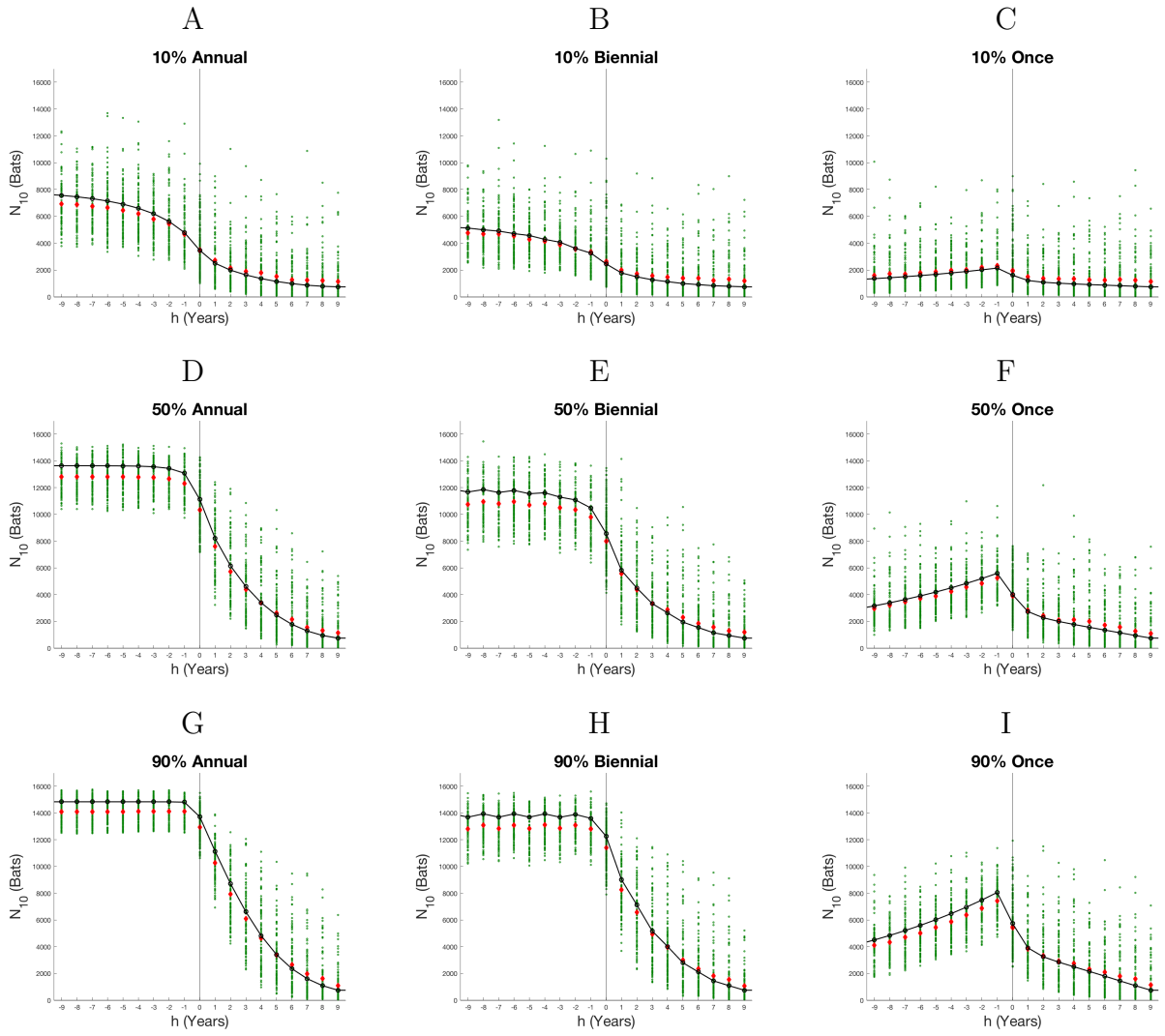


Figure 20: Sensitivity analysis of number of bats surviving ten years after infection, N_{10}, vs. lag between infection and vaccination, h, for three vaccination strategies: annual, biennial, and once. Each green point is a realization of the model using perturbed parameter values from a Latin hypercube sampling. The means of the green points are represented by red diamonds. These plots assume the vaccine offers lifelong immunity ($\lambda = 0$).

In Figure 21 we investigate the dynamics of various vaccination strategies coupled with both lifelong immunity as well as one year immunity. The assumption made

in all plots is that $h = 0$ and $\nu = 0.5$. We see the differences in dynamics, as well as the ten-year-survival, N_{10}, depending on the immunity length, of all vaccination strategies.

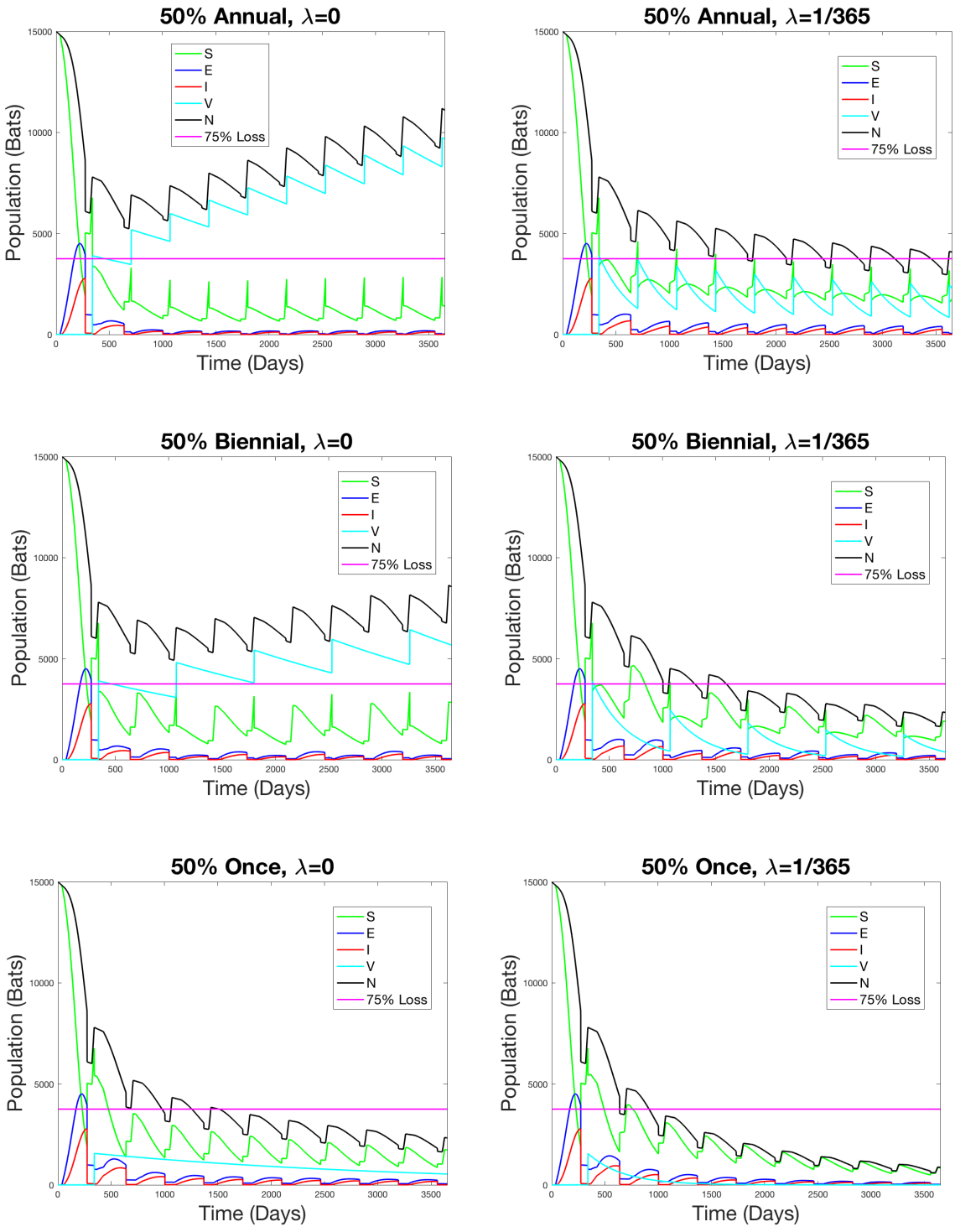


Figure 21: Population dynamics over ten years, with three different vaccination strategies: annual, biennial, and once. Plots on the left assume lifelong immunity and plots on the right assume loss of immunity occurs, on average, one year after vaccination

Next, we wanted to further analyze the relationship between the vaccination proportion, ν, and the length of immunity, λ, to be able to determine the best year to distribute the vaccine within a bat population assuming vaccination occurs one time. Based on the results in Figure 22, we were able to divide the graph into four sections. Each section corresponds to the vaccination year, h, that will yield the best outcome after ten years. Our model found that the four best years to vaccinate, if it can only be done once, are one year before, the year of, five years after, and six years after infection.

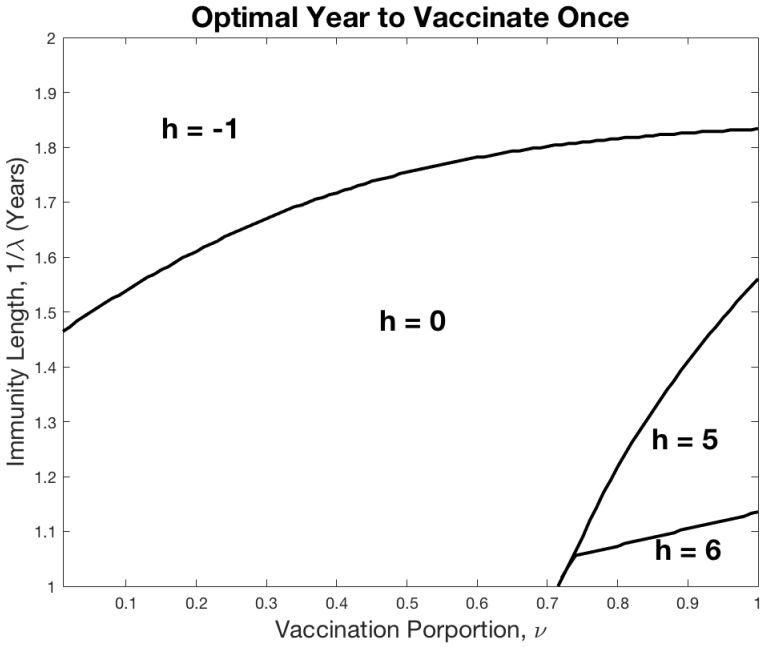


Figure 22: Each region defines a lag, h, which describes the optimal lag in the one time vaccination strategy, given a vaccination proportion and average duration of immunity.

Ultimately we wanted to be able to provide insight into how many bats would be alive after 10 years, N_{10}, depending on the vaccination strategy chosen, the length of immunity the vaccine provides, as well as optimistic lag situations. Figure 23 shows four various situations, with either vaccinating the year before, or the year of

infection, with either biennial or annual vaccination. Given this information, the 10 year survival is given by the corresponding color.

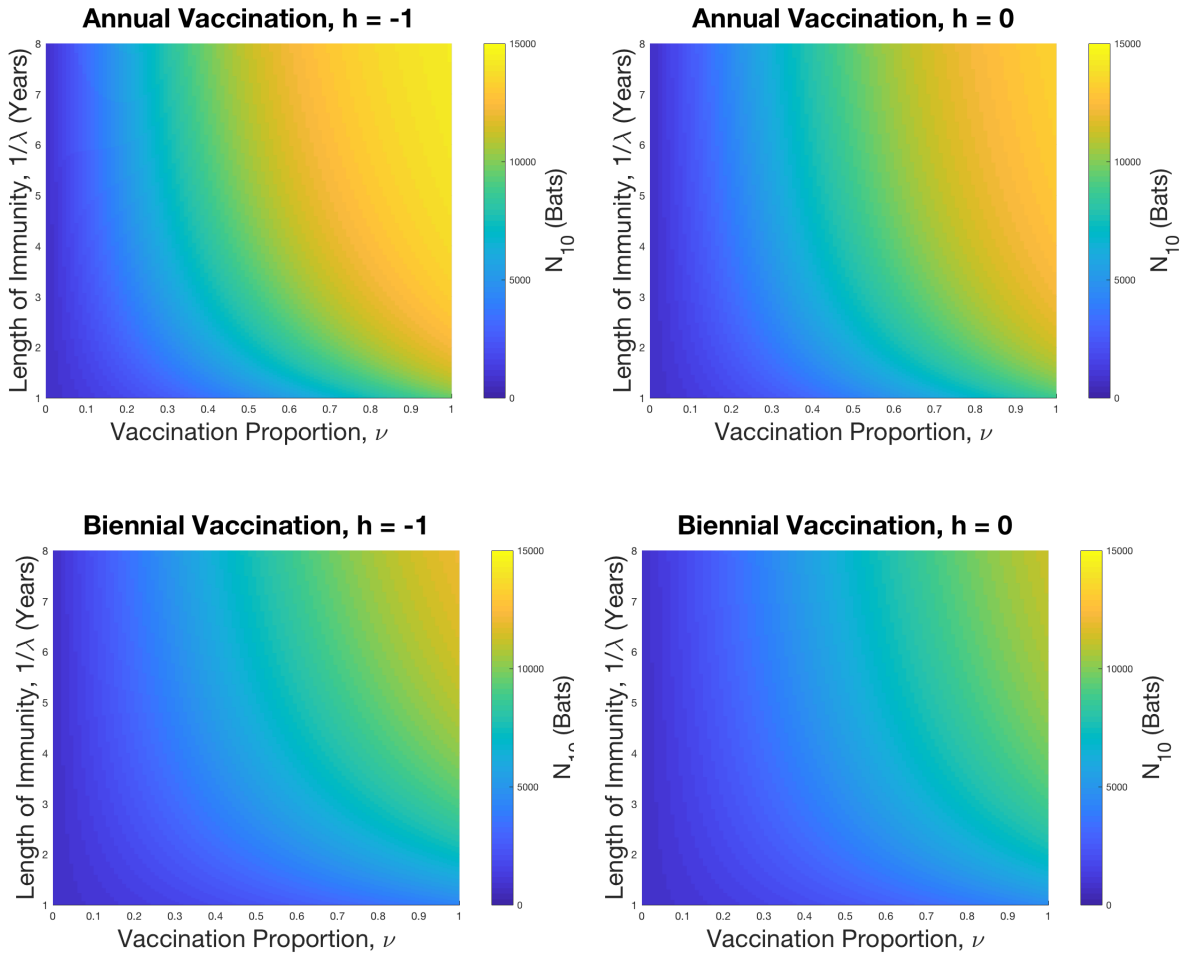


Figure 23: Comparing effectiveness of vaccination strategies with regard to length of immunity, $\frac{1}{\lambda}$, and vaccination proportion, ν. Color corresponds to number of bats surviving ten years after infection, N_{10}.

4.2 Multiple Methods of Control

To answer question (4) regarding the vaccine's effects compared to other control measures, we analyzed two of the controls proposed by Meyer et al.. Meyer et al.

suggested that, based on their study, the combination of targeted culling and reducing the reservoir size of *Pd* offered the most promising results [17]. We analyzed the effects of all three control measures, and their combinations, after 10 years. We began by assuming lifelong immunity, $\lambda = 0$, and annual vaccination. Under these assumptions, vaccination was the most effective control measure over ten years when comparing the individual performance. Vaccination in union with reducing the reservoir size of *Pd*, ρ, was the most effective combination of controls (see Figure 24).

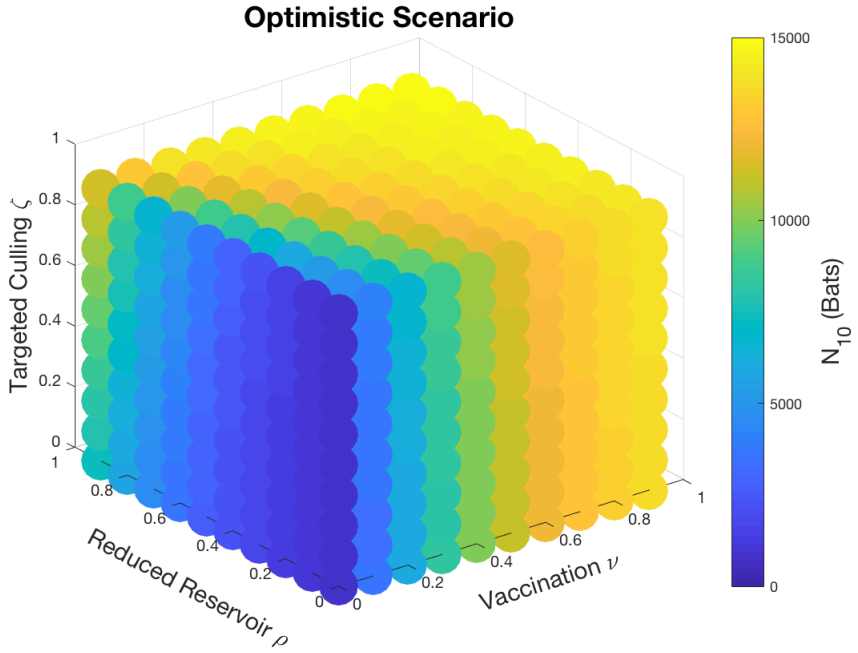


Figure 24: Comparing control methods of targeted culling (ζ), reduced reservoir (ρ), and vaccination (ν). Each sphere represents a combination of these three methods of control. Lifelong immunity and annual vaccination is assumed.

However it is not definitively known that the vaccine will offer lifelong immunity, nor is it known that implementing the vaccine annually will be feasible. Therefore, next we considered the results of immunity lasting one year, $\lambda = 1/365$, and vaccination occurring once. The results of these assumptions dramatically change the outcome after ten years. Vaccination by itself with these conditions offers bleak results

of very low bat populations after ten years (see Figure 25).

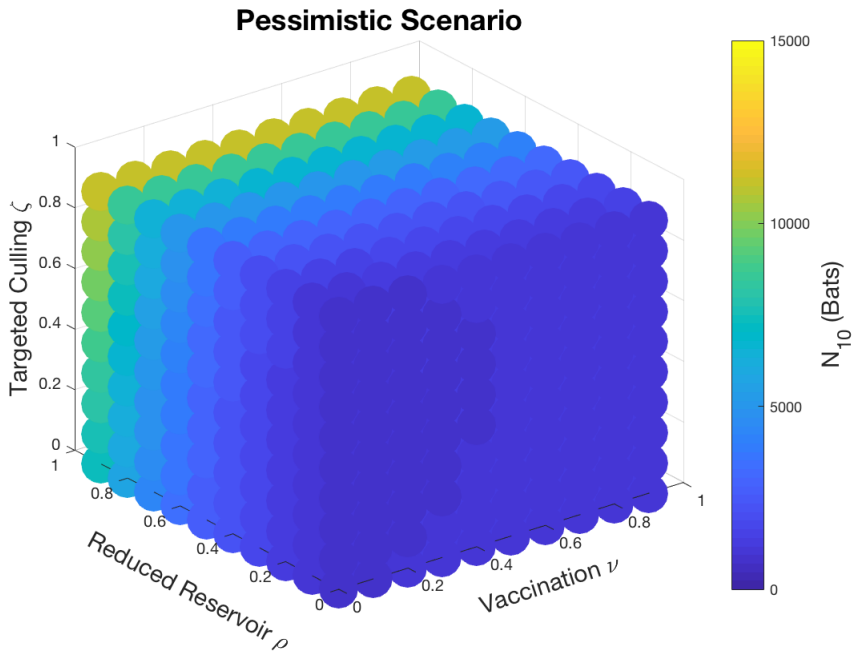


Figure 25: Comparing control methods of targeted culling (ζ), reduced reservoir (ρ), and vaccination (ν). Each sphere represents a combination of these three methods of control. One year immunity and one time vaccination is assumed.

4.3 Stochastic Model

To answer question (5) we created a stochastic analog of our deterministic model. We found it was qualitatively the same over 100 realizations in comparison to the deterministic model (see Figure 26). The average of 100 realizations was also similar to the deterministic model at various values of ν (see Figure 27). The assumption made in both of these figures was that $\lambda = 0$. It is important to note that the deterministic model was slightly more optimistic than the average of the stochastic realizations. With these results we recognized both models would provide us with an equal amount of accuracy. We chose to solely further analyze the deterministic model for this reason.

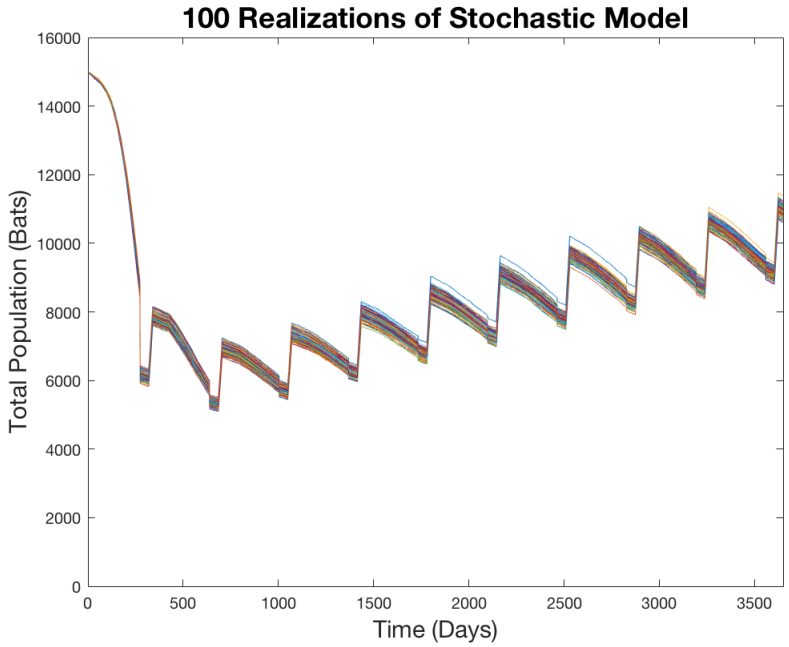


Figure 26: 100 realizations of the stochastic model with 50% annual vaccination. Total population (bats) over ten years.

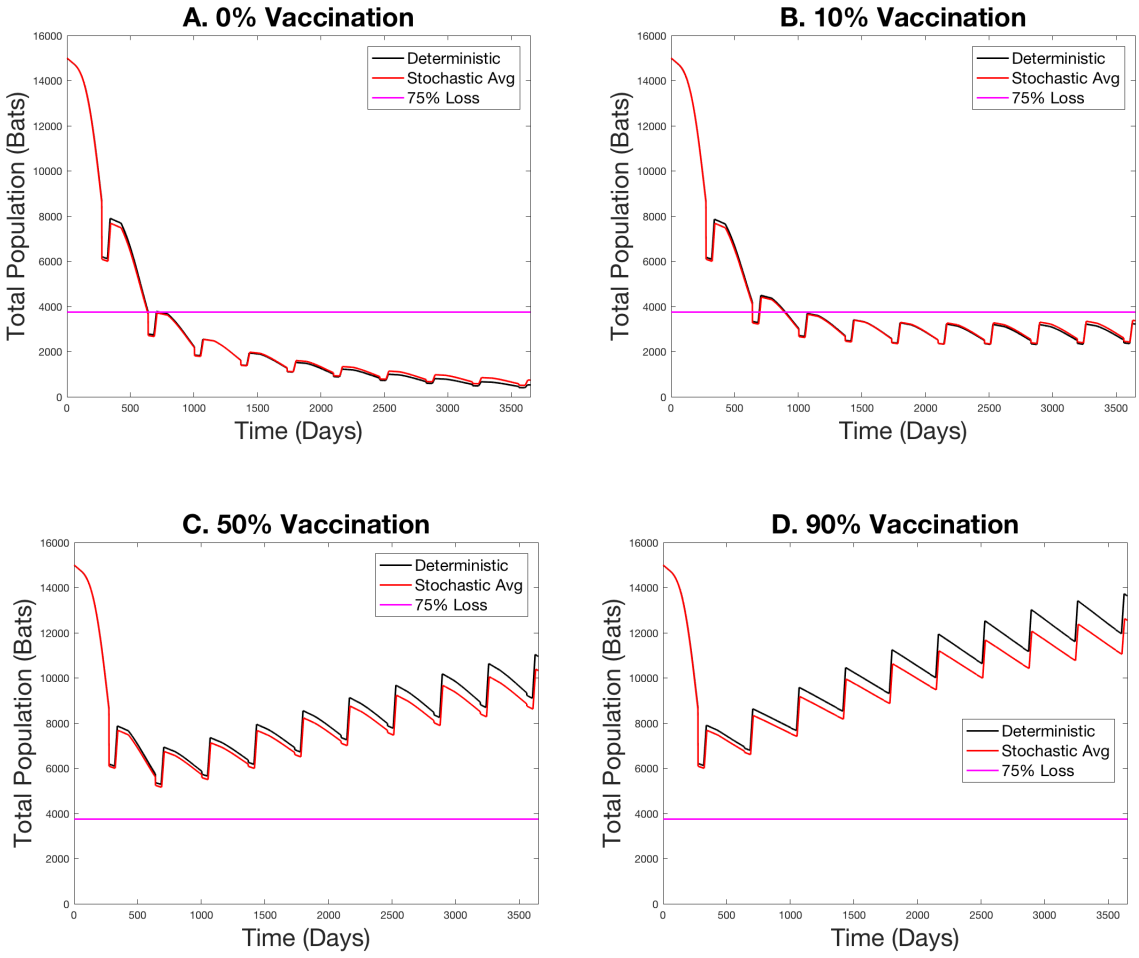


Figure 27: Comparison of the deterministic model (black curve) and the average of 100 realizations of stochastic model (red curve). Total population (bats) over ten years with various vaccination proportions.

5 Discussion

With a white-nose syndrome vaccine still under development, its level of impact is based on numerous assumptions; however, the devastating effects of WNS warrant predicting the success of vaccination. Furthermore, mathematical modeling of this disease allows researchers to analyze the effects of implementing various control methods *in situ* before enacting a plan *in vivo*, thus protecting bat populations from suffering further losses.

We have shown that, if the vaccine provides lifelong immunity, even at a small vaccination proportion (ν), the bat population can be sustained (see Figure 11). We also have shown that the gain in ten-year-survival between high vaccination proportions is not large (see Figure 12). Thus, it appears to be an effective measure of control even if conservationists cannot vaccinate an entire colony.

Our results show that if the vaccine provides lifelong immunity, it will be the most effective control method considered thus far. While targeted culling (ζ) coupled with reduced Pd reservoir size (ρ) has the potential to be effective, vaccination alone saves more bats over ten years than this coupling (see Figure 24). In particular, when $\zeta = \rho = 0.9$, ten-year survival is 75.2% while when $\nu = 0.9$, the ten-year survival is 91.7%. Even though vaccination coupled with reduced Pd reservoir size is the most effective control method in terms of increasing ten-year-survival, it is important to note the difficulty in implementing a reduced reservoir of the fungus. It is known that Pd prefers to grow on specific substrate, so it would be possible to remove such cave sediment; yet, cave systems are fragile and mass removal of sediment could compromise the hibernacula themselves [18]. Furthermore, the impact from targeted culling is sensitive to parameter variation, specifically the transmission route parameters ($\beta_s, \beta_h, \phi_s, \phi_h$). Changes in these values could lead to targeted culling negatively affecting the population rather than helping [17]. Therefore, we conclude that vaccination by itself poses a practical and efficient method of control.

We believe the limiting cost in administering the vaccine is the number of times the colony is vaccinated rather than the number of vaccine doses per visit. This is due to the suggested method of distribution of the vaccine, namely, an edible gel that can be sprayed on a large number of bats. This prompted us to explore different vaccination strategies in order to determine the optimal implementation. For annual and biennial vaccination strategies, vaccinating at least the year before infection provides significant benefits, with either lifelong immunity or only an average immunity period of a year (see Figures 17, 18, and 19). With a vaccine that offers lifelong immunity, the results after ten years are comparable. The similarity of these results are worth consideration when weighing the cost and effort required to vaccinate.

When considering vaccinating only once, the optimal timing of vaccination is dependent on the length of immunity that the vaccine provides, as well as the vaccination proportion. We found that for one-time vaccination, it is never best to vaccinate more than one year before infection, as the number of vaccinated bats decreases over time due to natural death. At low vaccination proportions and high immunity lengths, vaccinating the year before infection provides optimal ten-year-survival. Perhaps surprisingly, at high vaccination proportions and low immunity lengths, vaccinating five or six years after infection provides optimal ten-year-survival (see Figure 22). This is primarily an artifact of our measure of success, ten-year-survival. Since the average lifespan of a little brown bat is about 8.5 years [6], the closer you vaccinate to the ten year mark, the more vaccinated bats would still be alive.

Next, we showed that the continuous time Markov chain stochastic analog model is qualitatively and quantitatively similar to the deterministic model. This allowed us to use the deterministic model for our later analysis, as similar results were expected from the stochastic analog. Note, however, that our models did not include absolute or relative noise, only demographic stochasticicty, so a different noise structure could change this conclusion.

We also saw from our LHS that the qualitative behavior of our results is similar

across parameter ranges. The general trend of each realization, conceptualized as the mean of all realizations, follows the trend of our default parameter assumptions (see Figure 13). Clearly as parameters vary, the quantitative specifics must vary in turn, such as the exact boundaries of the strategy regions in Figure 22, but ultimately these specifics are nuances.

We have also shown the importance of developing a vaccine with a long immunity period as well as the importance of administering that vaccine regularly. With only an average immunity period of a year, in combination with vaccinating only once, vaccination is ineffective. In particular, when $\zeta = \rho = 0.9$, ten-year survival is 75.2%, while when $\nu = 0.9$, the ten-year survival is 7.24% (see Figure 25). Thus, we arrive at a suggestion of vaccinating at least a year before infection, as well as administering the vaccine as frequently as possible. It is important to note that realistic restrictions such as cost may prevent the administration of the vaccine from being deployed frequently. For long immunity periods, this is acceptable, since biennial and annual vaccination strategies produce similar survival rates at high vaccination proportions.

Note that vaccination without vertical transmission of immunity is insufficient to solve this epizootic. Since *Pd* can survive in the environment even in the absence of bats, the epizootic will return after vaccination ends. Furthermore, the ability of *Pd* to propogate in the environment means that it would be impossible for a critical vaccination proportion to be reached where remaining members of the colony obtain herd immunity. Therefore, research into how to remove the fungus is key for a long-term solution. Yet, with regional bat extinction in the Northeastern United States on the horizon, and the lack of possible long-term control methods, vaccination is a promising short-term solution.

We believe that a useful next direction of research would be modeling the spatial spread of this disease between bat colonies. With the ability to predict where the fungus will grow next, coupled with the results of our study, proactive measures could be taken to determine the best time to vaccinate each bat colony. Furthermore,

developing a control method to remove *Pd* from the environment appears to be the most realistic long-term solution.

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