Mathematical Model of West Nile Virus Dynamics: Study of Passive Immunity and Vertical Transmission

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Abstract

*In this project, a mathematical model is proposed to better understand the transmission dynamics of West Nile Virus (*WNV*) in an entwined nexus of mosquito-bird-human-horse. These dynamics primarily rely on spreading through a cycle involving birds and mosquitoes, with mosquitoes transmitting the virus to people and horses through bites. Additionally, the virus can pass from infected female mosquitoes to their offspring (vertical transmission) and recovered birds can pass immunity to their offspring (passive immunity). The model studied is a Susceptible-Exposed-Infected-Recovered (*SEIR*) scheme of explicit type which depicts a system of first order nonlinear ordinary differential equations with twenty-four unknowns. Simulations are carried out to determine the effect of vertical transmission and passive immunity in the containment of* WNV *outbreak.*

Introduction

The West Nile virus (WNV) is a mosquito-borne arbovirus belonging to the Flavivirus genus [1]. The WNV is an enveloped virion containing a single-stranded, positive-sense RNA genome [2]. The virus is transmitted primarily by mosquitoes, mostly Culex species. In nature, WNV cycles between mosquitoes (Culex) and birds [3], although the different Culex species responsible for transmission vary greatly by region [4]. The US Centers for Disease Control (CDC) has found WNV in 326 species of birds [5]. Some infected birds can develop high levels of the virus in their bloodstream and mosquitoes can become infected by biting these infected birds [6]. Infected mosquitoes can pass the virus to more birds when they bite. Mosquitoes with WNV also bite and infect humans, horses, and other mammals. However, mammals do not produce enough viral particles in their blood to transmit WNV to mosquitoes, so they are considered dead-end hosts [7].

The WNV is a seasonal fluctuations, with peak transmission occurring during warm weather, when mosquito populations are most active. Geographic distribution varies, and regions with previous cases of WNV are at higher risk for subsequent outbreaks. Identification of the human disease was first made in 1937 in Uganda and most dramatic outbreak of the virus in North America occurred during the summer of 2002 [8]. Over the 20-year existence of WNV in the US (between 1999 and 2019), a total of 51,702 human cases of WNV have been reported to CDC's ArboNET, including 25,227 (48.8%) West Nile Neuroinvasive disease (WNND) and 2,376 (4.6%) deaths [9]. The economic burden of West Nile Virus was significant; the cost of treating and providing aftercare to patients with WNV disease have accumulated to around $778 million in health care expenditures and lost productivity [10].

Mathematical models are suitable tools to investigate disease dynamics and their transmission mechanisms such as WNV. Numerous studies of mathematical models for this epidemic can be found everywhere [11]. One of the most commonly used mathematical algorithms to describe an epidemic disease is the SEIR model [12]. The SEIR model can be useful to assess the effectiveness of various measures, such as lock-down, since the infectious disease outbreak [13]. They are helpful in the recognition and observation of necessary data so as to show trends, estimations and also helps in the approximation of uncertainty in these predictions [14]. Typically, more complex models are considered to be more realistic.

Model

In nature, WNV is maintained in a cycle between mosquitoes and animal hosts (reservoir), with the predominant and preferred reservoir being bird species [15, 16, 17, 18]. Different mosquito species can acquire and transmit WNV, but it is highly variable between each species. However, species of mosquitoes that transmit WNV are mainly the *Culex* species of mosquito. The main vectors in the U.S. are *Culex pipiens*, *Culex tarsalis*, and *Culex quinquefasciatus* [19]. Some of the studies [20, 21, 22] suggest that there exist a few species which are capable of both infection and transmission of WNV. Mosquitoes being the vectors, are considered as key players of WNV transmission. The WNV transmission cycle begins when a susceptible mosquito bites infected birds.

A typical mosquito bite begins with the female mosquito lands and probes with the labella (sensory probes that helps to locate a good spot to bite) to find a spot. When female mosquito finds the right place to bite, fascicle (pierces the host tissue) penetrates into the skin while the hypopharynx (transfers saliva to the host tissue through salivary canal) pumps out saliva. The labrum (search for a blood vessel beneath the skin) begins probing for a blood vessel. Once a blood vessel is found, the hypopharynx lays on the labrum, creating a tube that pulls in blood and fills the mosquito's abdomen. As the mosquito takes a blood meal from the infected birds, the virus enters the mosquito's midgut where it accumulates with the mosquito's salivary glands, resulting in a high level of viremia in the mosquito's saliva, from where it can then be transmitted to humans, equines (horse), and other mammalian hosts. In this way, when a susceptible mosquito bites the infected bird, it gets exposed to WNV. This exposed mosquito is not yet infectious but eventually transforms into an infected mosquito which are able to transmit WNV to susceptible birds, humans, and equines (horses).

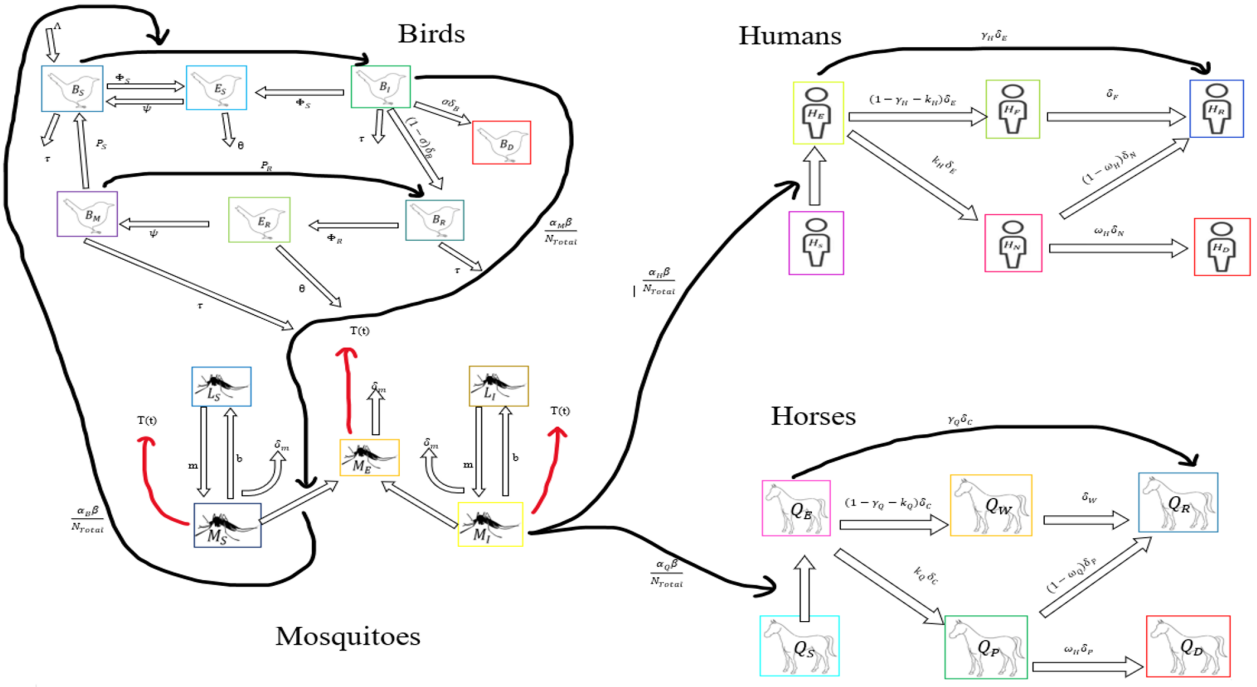


Figure 1: *A schematic of mosquito-bird-human-horse model featuring all 24 populations subdivided into four categories: mosquitoes, birds, humans, horses are represented by their respected morphology. The bold lines showcase the interactions between species while the solid empty lines showcase interactions between within the same species. Note: The cycle of vertical transmission occurs in the mosquito category and passive immunity in bird category.*

Vertical Transmission

Both susceptible and infected mosquitoes are capable of laying eggs. The mosquito life cycle begins as susceptible female mosquitoes lay an susceptible eggs inside containers holding water. These eggs then attaches to the inner, wet walls of container with water, above the waterline. These susceptible eggs must have water to complete development of the egg stage. After completing the egg stage, susceptible larvae emerge from eggs. Susceptible larvae feed on microorganisms in the water. After molting three times, a susceptible larva becomes a susceptible pupa. Susceptible pupae will develop until the body of the newly formed adult flying mosquito emerges from the pupal skin and leaves the water, thus becoming an susceptible mosquito. The egg laying process for infected mosquito are identical to susceptible mosquito however, these infected mosquito are capable of transmitting WNV to its eggs, thus infected mosquito lay eggs that are infected with WNV. Eventually these infected eggs grow into a infected mosquito, in turn spreads more WNV in a given area. This process is known as *vertical transmission* in vectors. Vertical transmission, highlighted by the mosquito population, is a naturally occurring process that plays an important role in vector-borne diseases, such as WNV.

Arboviruses (infections caused by a group of viruses spread to people by the bite of infected arthropods such as mosquitoes and ticks) employ natural vertical transmission as an ecological strategy to secure their survival within mosquito vectors. Under favorable conditions, such as climate change where the average temperature increases, mosquito activity and overall population also increase, resulting in more vertical transmission if mosquitoes are infected. This situation can be dangerous, especially considering the fact that there is no available vaccine against WNV. Consequently, monitoring the WNV in mosquito's population is essential for early detection and effective prevention of widespread outbreaks.

Passive Immunity

As mentioned, WNV is maintained in a cycle involving infected birds and mosquitoes. While infected birds can circulate WNV in their blood for several days, not all infected birds show symptoms. These symptoms are an neurological signs, such as loss of coordination, head tilt, tremors, and weakness are commonly observed in birds with WNV. Certain bird species, particularly corvids (crows, blue jays, and ravens) and raptors, are highly susceptible to WNV. However, the symptoms and disease severity vary among different bird species. While some birds may succumb to the disease, most are capable of recovering and developing immunity against WNV. Some bird species display no signs of disease and serve as asymptomatic carriers. As the infected birds recovers from WNV, it develops antibodies to WNV with long-lasting protection over multiple WNV seasons [23]. Furthermore, when female bird lay eggs, this immunity can be transferred to its young, also known as *passive immunity* - a phenomenon exclusive to the bird's population. This inherited passive immunity provides a rapid protection from virus infection.

This type of naturally-attained immunity provide immediate but short-term protection against specific pathogens. Natural passive immunity in birds occurs when antibodies are transferred from the female birds to the offspring. During egg formation, antibodies are transferred from the female birds to the egg yolk and provide passive immunity for the developing embryo [24]. This transfer of maternal antibodies provides its young with temporary protection against diseases that the female bird has encountered, helping to protect its young until its own immunity (immune system) is fully developed. However, it is worth noting that while passive immunity provides immediate protection, it does not stimulate the bird's own immune system to produce memory cells. As a result, the bird does not develop long-term immunity or the effective immune response upon exposure to the same disease (pathogen). Thus, as a bird grows, the passive immunity slowly decreases until adult stages, where that bird become susceptible again. Once again, the life cycle of susceptible bird is same as with infected bird, but only difference is that susceptible bird are not capable of passing their passive immunity against WNV. Also, susceptible bird can become exposed to the virus, which over time moves on to become infected bird. A mathematical model which renders insight to the importance of passive immunity in birds in WNV disease dynamics is studied in [25].

The Role of Mammalian Species in the Transmission Cycle

Humans as well as equines (horses), and other mammalian species are considered as “dead end" species in this cycle. This is due to the level of viraemia (the presence of viruses in the blood) being too low to infect mosquitoes which in turn infect humans, horses, and other mammalian species (hosts). The mammalian species does not participate in sustaining the cycle after being infected, thus ending the cycle. Between 2005 and 2009, the CDC received reports of 12,975 cases, which includes 496 deaths. Moreover, approximately 35% of the reported cases corresponded to the more severe variants of neuroinvasive diseases, such as encephalitis [26]. Most WNV cases in humans are predominantly sub-clinical, but those who are infected may develop fever like symptoms such as headache, diarrhea, body aches, skin rash, swollen lymph glands. Ultimately most people recover from the disease. However for about 1% of human population, WNV infection develops into serious cases where the overall mortality rate increases. These severe infections are mostly neurological in nature such as West Nile Encephalitis or Meningitis, coma, muscle weakness, vision lose, numbness, and paralysis.

For human, the virus is transmitted when an infected mosquito feeds and passes infected saliva to the host. The virus then enters the host’s dermal dendritic cells and keratinocytes for initial replication. Next, it migrates to regional lymph nodes, and from there, it spreads systemically to visceral organs like the kidney and spleen for a second round of replication [27, 28]. There is a 1 in 150 chance of WNV virus passes a host’s blood-brain barrier (a tightly locked layer of cells that defend the brain from harmful substances, germs and other things that could cause damage) which causes the invasion of the central nervous system in the form of encephalitis, meningitis, coma, etc. However, the process by which an infection leads to disease which is known as pathogenic mechanism, is not well-studied due to the susceptibility. As mentioned before, most people with WNV will recover from the virus. Although, it is generally believed that, a person infected/exposed withWNV develops a natural immunity to future infection, but this immunity may decrease over time. There is no specific treatment (vaccine) for WNV.

Substantial studies have been done in an effort to develop a vaccine against WNV virus. There is still no human WNV vaccination, and no candidate is even close to approval. The lack of a human vaccine can be attributed to several factors, including scientific challenges, safety concerns, difficulties in clinical study design, and other related issues. Which is why, albeit immunization remains the most sustainable and lasting approach to protecting humans from WNV-related diseases, the majority of current preventative efforts rely on mosquito population controls and personal protective measures to reduce exposure.

The horses are a "dead end" species similar to humans. Most of equines and humans are only mildly affected by the diseases or asymptomatic. The rate of asymptomatic and symptomatic (natural infection) is 90% and 10% respectively [29, 30]. The WNV mildly affects the horse without an vaccination and it generally recovers in 2 to 7 days. Common clinical signs include fever, ataxia (stumbling and staggering), inability to stand, multiple limb paralysis, teeth grinding. In severe cases, horses may develop neurological disease with 30% fatality, and some may recover from the neurological disease but with neurological deficits.

One study suggest that the identification of WNV cases in horses is important due to the fact that the clinical manifestation of WNV-related neurological disease is similar to other neurological disease such as rabies, eastern equine encephalitis (EEE) etc. Correct identification of WNV cases in horses is important since the presence of a pathogen and its vector increases the risk of infection to other equines and humans [31] in the geographic area. Currently, there is no specific treatment for WNV in horses. Some supportive cares such as intravenous fluid, anti-inflammatory medications, and nursing care help increasing the recovery rate for infected horse. Aside from supportive care and therapy, horses must recover on their own. Vaccination plays a critical role in preventing WNV in horses as well. The effectiveness of vaccines have been shown to reduce the WNV cases in horses [32, 33]. Nevertheless, even though these vaccines have shown their effectiveness, these is still a limitations. The vaccination requires an annual boosters, due to the short duration of immunity.

The objective of our work is to study how two aforementioned phenomena, vertical transmission and passive immunity, impact the overall transmission dynamics which moves forward through the interplay between its players - birds, mosquitoes, humans and horses. In order to capture the interplay, we have developed a SEIR model which consists of 24 nonlinear ordinary differential equations. This model represents the susceptible population, exposed population, infected population, and removed (recovered) population. The SEIR model can be used for predicting things such as to what extent a disease can spread, or the total number infected, or the duration

of an epidemic, and to estimate various epidemiological parameters [34]. Every population interacts with one another category in order to properly simulate the spread of WNV. This SEIR model assumes that once recovered, individuals will no longer be susceptible to WNV, each individual has the same chance of susceptibility, exposed, infection, and recovered. The analysis and simulation of the model is done by using MATLAB software.

The Parameter Estimation of SEIR Model

When a susceptible mosquito M_S bites an infected bird B_I at the rate of β, it exposes the mosquito to the virus. This changes susceptible mosquitoes M_S to exposed mosquitoes M_E at the rate of α_M. The exposed mosquitoes change to infected mosquitoes at the rate of η and have ability to transmit virus to other mammals such as susceptible birds, humans, and horses. Both infected and susceptible mosquitoes lay eggs at the rate of b, which become susceptible and infected larvae respectively. Both categories of mosquitoes mature at same growth rate of m to grow into susceptible and infected mosquitoes. Also, susceptible and infected mosquitoes die at the rate of δ_M, and similarly susceptible and infected larvae also die at the rate of δ_L. The rate at which infected mosquitoes pass their WNV to their eggs is represented by the model.

The infected mosquitoes are able to bite susceptible birds and change them into infected birds at rate of α_B. The rate at which the fractions of infected birds die from the diseases is represented by $\sigma\delta_B$. The infected birds have chance to recover from the virus as the rate of $(1-\sigma)\delta_B$, which changes them into recovered birds. The egg laying rate for both susceptible and recovered birds are represented by $\mu\phi_S$ and $\mu\phi_R$, respectively. Susceptible and recovered birds lay egg with the rate of ϕ_S and ϕ_R, respectively. Recovered birds pass their immunity down to their young at the rate of μ. Sometimes, there is a chance that bird's young does not receive the passive immunity from its mother, which is simulated by $(1-\mu)\phi_R$. These eggs would be recovered eggs. Those who have successfully received the passive immunity from its mother is represented by $\mu\phi_R$, these eggs would be immune eggs. Both susceptible and immune eggs would have a same maturation rate (ψ). There is a chance that egg may not hatch, which results in a death (θ), also the natural death rate for birds is (τ). As the immune egg grows into adult birds, it losses it immunity over time, which changes them into a susceptible birds again (p_S) and there is a chance that immune birds that keeps their immunity, which changes them to the recovered bird (p_R).

When infected mosquitoes bite susceptible human at the rate of α_H, the susceptible human becomes expose to the WNV. After going through the incubation period (δ_E), the human fails to display any noticeable symptoms and seems like he has immediately recovered from WNV despite of being infected with a disease. This modelis known as asymptomatic model ($\gamma\delta_E$). However, some may suffer mild form of WNV, which is known as West Nile Fever at a rate of $(1-\gamma_H-\kappa_H)\delta_E$. Most people recover from West Nile Fever at a rate of δ_F. While some may develop a severe form of WNV, which is known as neuroinvasive disease such as West Nile encephalitis. Those who got infected with neuroinvasive disease, can recover at a rate of $(1-\omega_H)\delta_N$ or they may pass away at a rate of $\omega_H\delta_N$. As it mentioned before there is no vaccine available to people, thus when people got infected with WNV, they have to recover using their own immunity.

Like humans, WNV similarly affects horses. The probability of transmission from mosquitoes to horse is represented by α_Q. After being exposed, the incubation period (δ_C) ensues after which exposed horses change to infected horses. Some infection in horses can be asymptomatic when horses recover immediately at a rate of $\gamma_Q\delta_C$. However, some infected horses show signs of symptoms such as fever, limb paralysis, and neurological diseases etc. The fraction of infected horse that develop a fever-like infection is represented by $(1-\gamma_Q-\kappa_Q)\delta_C$, and most horses recover from the fever-like symptoms at the rate of δ_P. The infected horse that develops a neuroinvasive disease is simulated by $\kappa_Q\delta_C$. Some infected horses that have neuroinvasive disease may recover from disease at a rate of $(1-\omega_Q)\delta_W$ or die at a rate of $\omega_Q\delta_W$. There is a vaccine available to horses, which makes horse less susceptible to WNV, however there is still a chance that vaccinated horse may get infected with WNV.

Lastly, to quantify the importance of controlling the mosquito population, a function, $T(t)$, is introduced which is a measure to the effectiveness of the adulticide.

$$T_t = s\left(1-\frac{\mathrm{mod(t,7)}}{7}\right)$$

$T(t)$ can be thought of as a function of t(in days) $\in [0, 50]$ which simulates spraying at certain intervals, say in every seven days. In this current form, the spraying process is more realistic because the initial amount of adulticides, s keeps reducing between days $0 - 6$ and gets replenished on every seventh days.

The parameter values are listed in Table (1). While considering the SEIR model, we have made the following assumptions:

- For both mosquitoes and birds, the rates of maturation for susceptible and infected are same.
- The death rate for humans and horses are not included.
- The death rate for mosquitoes and birds are included despite of short lifespan.
- Once infected humans and horses recover, they become immune to the disease.
- This model does not take into account the impact of temperature.

The Systems of Governing Equations

$$
\begin{aligned}
\frac{dE_S}{dt} &= \phi_S(B_S + B_I) + (1-\mu)\phi_R B_R - \theta E_S - \psi E_S \\
\frac{dE_R}{dt} &= \mu\phi_R B_R - \theta E_R - \psi E_R \\
\frac{dB_S}{dt} &= \Lambda - \frac{\alpha_B \beta M_I B_S}{N_{Total}} + p_S B_M + \psi E_S - \tau B_S \\
\frac{dB_I}{dt} &= \frac{\alpha_B \beta M_I B_S}{N_{Total}} - \delta_B B_I - \tau B_I \\
\frac{dB_R}{dt} &= (1-\sigma)\delta_B B_I + p_R B_M - \tau B_R \\
\frac{dB_M}{dt} &= \psi E_R - (p_S + p_R) B_M - \tau B_M \\
\frac{dB_D}{dt} &= \sigma\delta_B B_I \\
\frac{dL_S}{dt} &= b(M_S + M_E) - mL_S - \delta_L L_S \\
\frac{dL_I}{dt} &= bM_I - mL_I - \delta_L L_I \\
\frac{dM_S}{dt} &= mL_S - \frac{\alpha_M \beta M_S B_I}{N_Total} - \delta_M M_S - T(t) M_S \\
\frac{dM_E}{dt} &= \frac{\alpha_M \beta M_S B_I}{N_{Total}} - \eta M_E - \delta_M M_E - T(t) M_E \\
\frac{dM_I}{dt} &= mL_I + \eta M_E - \delta_M M_I - T(t) M_I
\end{aligned}
$$

$$
\begin{aligned}
\frac{dH_S}{dt} &= -\frac{\alpha_H \beta M_I H_S}{N_{Total}} \\
\frac{dH_E}{dt} &= \frac{\alpha_H \beta M_I H_S}{N_{Total}} - \delta_E H_E \\
\frac{dH_F}{dt} &= (1 - \gamma_H - \kappa_H)\delta_E H_E - \delta_F H_F \\
\frac{dH_N}{dt} &= \kappa_H \delta_E H_E - \delta_N H_N \\
\frac{dH_R}{dt} &= \delta_F H_F + (1-\omega_H)\delta_N H_N + \gamma_H \delta_E H_E \\
\frac{dH_D}{dt} &= \omega_H \delta_N H_N \\
\frac{dQ_S}{dt} &= -\frac{\alpha_Q \beta M_I Q_S}{N_{Total}} \\
\frac{dQ_E}{dt} &= \frac{\alpha_Q \beta M_I Q_S}{N_{Total}} - \delta_C Q_E \\
\frac{dQ_W}{dt} &= (1 - \gamma_Q - \kappa_Q)\delta_C Q_E - \delta_W Q_W \\
\frac{dQ_P}{dt} &= \kappa_Q \delta_C Q_E - \delta_P Q_P \\
\frac{dQ_R}{dt} &= \delta_W Q_W + (1-\omega_Q)\delta_P Q_P + \gamma_Q \delta_C Q_E \\
\frac{dQ_D}{dt} &= \omega_Q \delta_P Q_W
\end{aligned}
$$

where the total blood supply is denoted by

$$N_{Total} = B_S + B_I + B_R + B_M + H_S + H_E + H_F + H_N + H_R + Q_S + Q_E + Q_W + Q_P + Q_R$$

The absence of birth and natural death rates for humans and horses, as noted in the model, reflects a simplification made for the simulation. In this context, the simulation focuses on a relatively short time frame of 50 day, during which the impact of birth and natural death rates for humans and horses is considered negligible. In realistic scenarios, the birth and death rates becomes essential for more comprehensive models, especially when extending

Parameter	Value	Description	Unit	Sources
b	0.045	Mosquito Birth Rate	Larvae/(Day·Adults)	[35]
m	0.07	Mosquito Maturation Rate	Adults/(Larvae · Day)	[36, 37]
δ_L	0.027	Natural Larval Death Rate	Day^{-1}	[38]
α_M	0.23	Probability of Transmission form Birds to Mosquitoes	–	[39]
β	2.5	Bite Rate	Day^{-1}	[35]
δ_M	0.031	Natural Mosquito Death Rate	Day^{-1}	[38]
T_t	varies	$T_t = s$; Success rate of Adulticides	Day^{-1}	[35]
η	0.1	Virus Incubation Rate in Mosquitoes	Day^{-1}	[40]
ϕ_S	varies	Egg Laying Rate for Susceptible Birds	Day^{-1}	[41, 42, 43]
μ	varies	Percent of Eggs Receiving Passive Immunity	–	[41, 42, 43]
ϕ_R	varies	Egg Laying Rate for Recovered Birds	Day^{-1}	[41, 42, 43]
θ	0.45	Natural Death Rate of Bird Eggs	Day^{-1}	[41, 42, 43]
ψ	varies	Maturation Rate of Bird Eggs	Day^{-1}	[41, 42, 43]
Λ	varies	Recruitment Rate of Birds	Birds/Day	[35]
α_B	0.27	Probability of Transmission from Mosquitoes to Birds	–	[39]
τ	varies	Natural Bird Death Rate	Day^{-1}	[44]
δ_B	$1/(4.5)$	Rate of Recovery in Birds	Day^{-1}	[45]
σ	0.72	Fraction of WNV Infected Birds Dying from the Disease	Day^{-1}	[45]
α_H	0.06	Probability of Transmission from Mosquitoes to Humans	–	[46]
δ_E	$1/4$	Incubation Period in Humans	Day^{-1}	[35]
γ_H	0.80	Fraction of Human Population that is Asymptomatic	Day^{-1}	[47]
κ_H	0.01	Fraction of Human Population that can Develop Neuroinvasive disease	Day^{-1}	[47]
δ_F	$1/14$	Rate of Recovery for WNV Fever in Humans	Day^{-1}	[46]
δ_N	$1/(37.5)$	Rate of Recovery for Neuroinvasive Disease in Humans	Day^{-1}	[48]
ω_H	0.1	Fraction of Humans Dying from the Neuroinvasive Disease	Day^{-1}	[47]
p_S	varies	Percent of Immune Birds that Lose their Immunity	–	[41, 42, 43, 49]
p_R	varies	Percent of Immune Birds that Keep their Immunity	–	[41, 42, 43, 49]
α_Q	0.33	Probability of Transmission from Mosquitoes to Horse	Day^{-1}	[31, 50]
δ_C	varies	Incubation Period in Horse	Day^{-1}	[51, 52]
δ_W	varies	Rate of Recovery for Neuroinvasive Disease in Horse	Day^{-1}	[53, 31]
δ_P	varies	Rate of Recovery for WNV Fever in Horse	Day^{-1}	[31]
γ_Q	0.8	Fraction of Horse Population that is Asymptomatic	Day^{-1}	[53]
κ_Q	$1/11$	Fraction of Horse Population that Can Develop Neuroinvasive Disease	Day^{-1}	[53, 54]
ω_Q	0.4	Fraction of Horse Dying from Neuroinvasive Disease	Day^{-1}	[53, 54]

Table 1: *Parameters and their units, values, and sources for the system of ordinary differential equations that models the disease dynamics. All parameters were estimated from literature.*

the simulation over longer duration. Birth rates would contribute to the increase in the susceptible population, while natural death rates would affect the overall population dynamics. However, in the this simulation, these factors are deemed negligible, simplifying the model for the sake of clarity and efficiency. It's essential to recognize that model simplifications are common in epidemiological simulations, allowing for a balance between accuracy and computational efficiency. The other parameter values, as mentioned in Table 1, likely play crucial roles in shaping the outcomes of the simulation, and their values should be considered in the interpretation of the results.

Vinodh, please review up to this point.

Results and Discussion

you may review the content below, but I am still fine-tuning it.

Bird

The simulation focuses on the interplay between growth rates or maturation rates (denoted as ψ) and passive immunity (μ), with respect to various treatment effectiveness rates. The susceptibility of the bird population is directly influenced by the prevalence of infected mosquito populations. In regions characterized by high population density of mosquitoes carrying the infection, the likelihood of susceptible birds contracting the disease or virus significantly increases. To address this issue, treatments such as insecticides, which includes adulticides targeting mature mosquitoes and larvicides targeting mosquito larvae, were implemented to manage the mosquito population. Also in this simulation, the insecticides were given weekly treatments with varying effectiveness rates (20% control, 40%, 60%, and 80%) was implemented. These treatments are designed to affect the entire mosquito population, including susceptible, infected, and exposed mosquitoes. The increased use of such treatments proves effective in reducing the overall mosquito population, thereby mitigating the risk of disease transmission among susceptible birds, humans, and horses. Passive immunity, vertical transmission, and treatment effectiveness provides valuable insights into the dynamics of disease transmission and the potential impact of interventions. Fine-tuning these parameters and optimizing treatment strategies based on the simulation results can contribute to more effective and targeted disease control measures.

The graph of the infected bird population, as depicted in Fig. 2, reveals compelling insights. When the treatment effectiveness is set at 20%, a notable exponential increase in the number of infected birds occurs from day 0 to day 15. This surge is further intensify by a higher maturation rate among birds, amplifying the prevalence of the disease within the specified area. However, between day 20 and 25, a gradual decline in the number of infected birds is observed. Remarkably, higher maturation rates contribute to a more rapid reduction in the infected bird count during this phase. The decrease in line is due to, some birds recover from the disease, acquiring immunity to the WNV, while others may succumb to the illness.

As the simulation progresses, by the end of day 50, a persistent presence of WNV-infected birds is evident in the area. Yet, a noticeable positive trend emerges with increased effectiveness in treatment measures. Notably, at 80% treatment effectiveness, a substantial decrease in the number of infected birds can observed by the conclusion of day 50. This correlation implies a direct proportionality between the number of infected birds and the number of birds developing immunity. In simpler terms, a reduction in the infected bird population signifies a diminished number of birds recovering and acquired immunity. Consequently, there is a notable decline in instances of birds succumbing to the disease, indicating a positive trajectory in our collective efforts to combat WNV. The dynamics of the recovered bird population are intricately linked to the population of infected birds, as previously discussed. Notably, the effect of treatment plays a pivotal role in shaping these dynamics, with less effective treatment correlating to a higher population of infected birds. The Fig 3 show, as treatment effectiveness increases, there is a noticeable reduction in the number of infected birds that recover, which also indicates a decrease in the rate of bird mortality. This graph shows an inverse relationship between the susceptible and recovered bird populations. With a decline in the number of susceptible birds succumbing to infection, there is a significant decrease in the population of recovered birds.

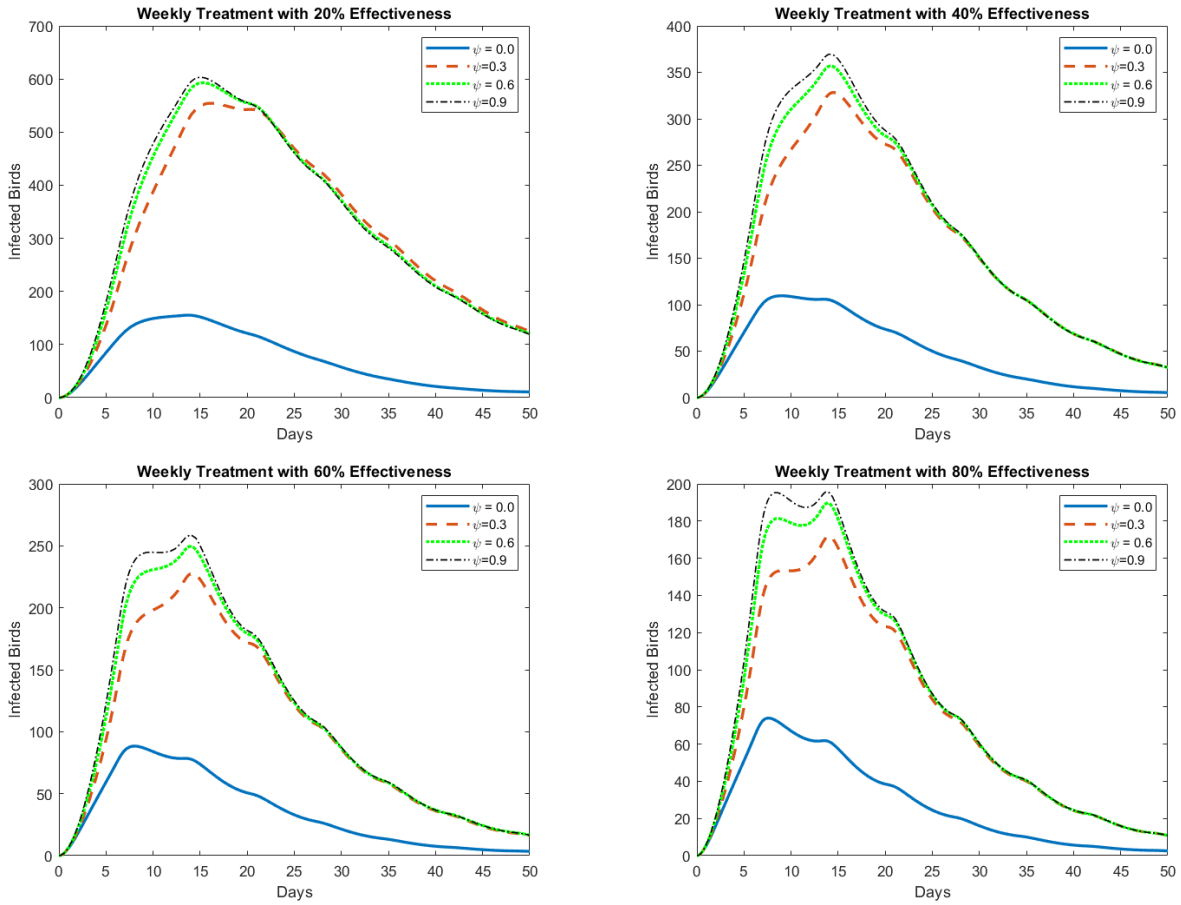


Figure 2: *Infected bird population as affected by different ψ-values (0.0, 0.3, 0.6, 0.9) with treatment frequency being weekly. The parameter ψ is the maturation rate from eggs to birds. The treatment effectiveness increases left to right at 20% increments. we can see that as ψ increases, so does the overall bird populations since more birds are in the population. Also, as treatment increases, both the infected and immune bird populations decrease because fewer birds are becoming infected since the infected mosquitoes are being eliminated.*

This points to a crucial implication—that the number of eggs acquiring immunity to the WNV through passive immunity diminishes and this also tells us that the number of recovered bird population is inversely proportional to the effectiveness of the treatment. In essence, controlling the mosquito population, particularly through the use of adulticides, results in a cascading effect. This effect manifests as a decrease in the number of birds recovering from the disease and a reduction in the number of birds developing immunity to WNV. Consequently, there is a likelihood of their offspring receiving passive immunity diminished or decreases. In short a decrease in the number of susceptible birds that recovers from the virus, lowers the number of birds that develops immunity to WNV. The population of immune birds, as depicted in Fig 4, is influenced by the number of recovered birds. In the initial phase, from day 0 to day 5, there is a noticeable upward trend in the population of immune birds, signifying an accumulation of immune birds over time. This trend also implies an increase in the number of susceptible eggs, as fewer birds in the population are becoming infected with the virus during this period. By day 10, as evident in Fig 4, the population of immune birds experiences a more pronounced accumulation, influenced by the growing number of birds recovering from the disease. This connection is particularly significant because when a bird recovers from the virus, it gains immunity. Consequently, eggs laid by immune birds inherit passive immunity. The parameter p_S becomes crucial in this context, representing the percentage of immune birds losing their passive immunity throughout their life cycle. Once an immune bird becomes an adult, it becomes susceptible to the virus and loses passive immunity entirely. The observed dynamics suggest that when a percentage of birds lose their immunity, there is a subsequent increase in the number of birds transitioning from immune to susceptible after their brief period of immune status. In summary, an increase in treatment effectiveness is associated with a decrease in the population of immune birds. Simultaneously, an increase in the value of p_S correlates with a rise

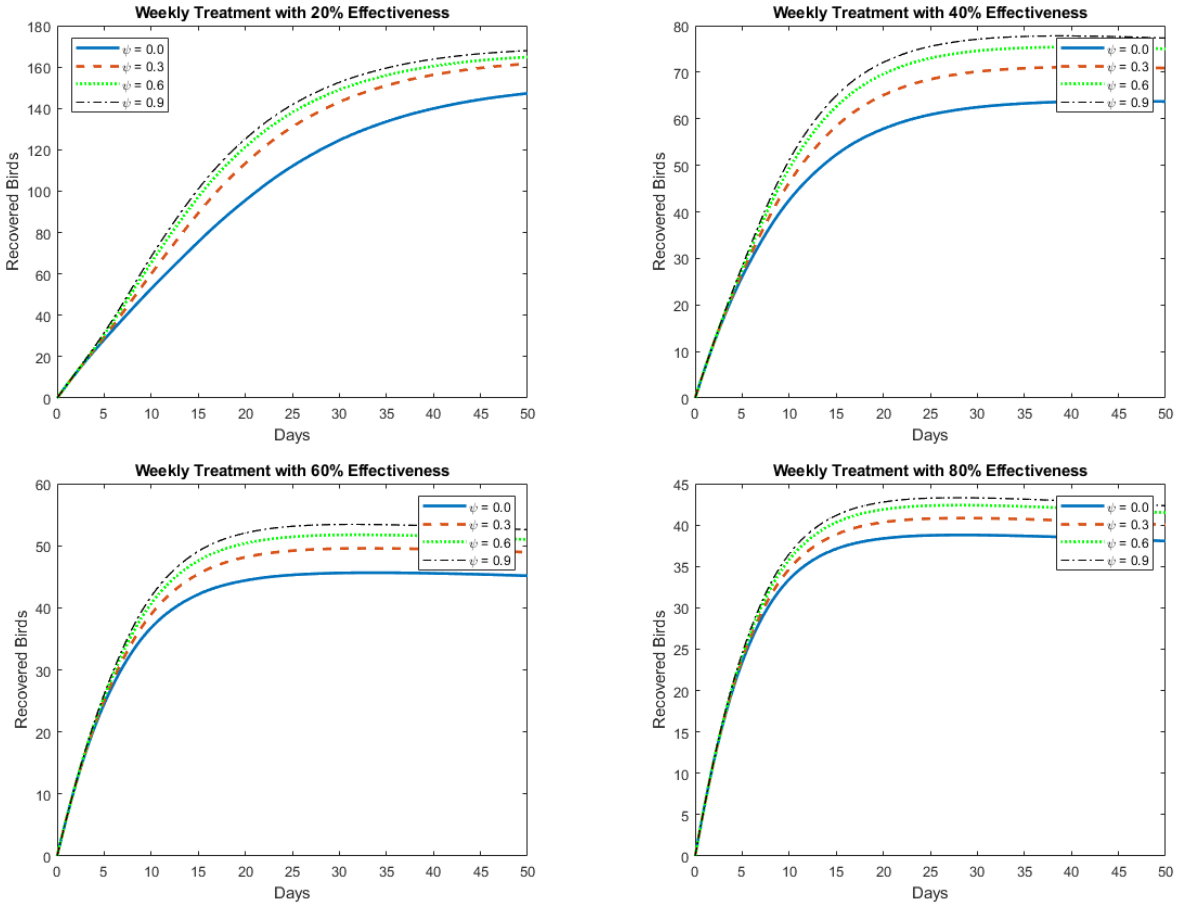


Figure 3: *Recovered bird population as affected by different ψ-values (0.0, 0.3, 0.6, 0.9) with treatment frequency being weekly.The parameter ψ is the maturation rate from eggs to birds. The treatment effectiveness increases left to right at 20% increments.*

in the number of susceptible bird populations. These findings shows the complex interplay between treatment efficacy, immune bird dynamics, and the critical role of passive immunity in shaping the susceptibility of bird populations to the West Nile Virus.

Mosquito

The susceptible mosquito population is profoundly influenced by the uses of insecticides, which utilize/employ/uses both adulticides and larvicides. As demonstrated in Fig 5, the trajectory of the susceptible mosquito population is characterized by a decreasing curve over time, reflecting the increasing exposure of mosquitoes to the virus. The relationship between treatment effectiveness and the susceptible mosquito population is inversely proportional, with higher treatment effectiveness leading to a drastic reduction in mosquito populations. Examining Fig 5 at 20% effectiveness, each graph begins with an initial population of susceptible mosquitoes at day 0.

As time progresses, the number of mosquitoes population decreases, following a typical exponential decay curve. Conversely, at 80% effectiveness, a remarkable observation is made between day 0 and day 5, where almost the entire susceptible mosquito population is eradicated by the treatment. This significant reduction suggests that with fewer susceptible mosquitoes population are being exposed to the virus. Consequently, this decrease in exposure contributes to a drastic reduction in the number of infected birds, as well as a decrease in the risk of infection for humans and horses. It's important to note that not all susceptible mosquitoes become exposed to the virus. Some portion of the population naturally dies off at the rate of the natural death rate. This shows that treatment such as adulticides and larvicides are pivotal in shaping effective strategies for controlling and

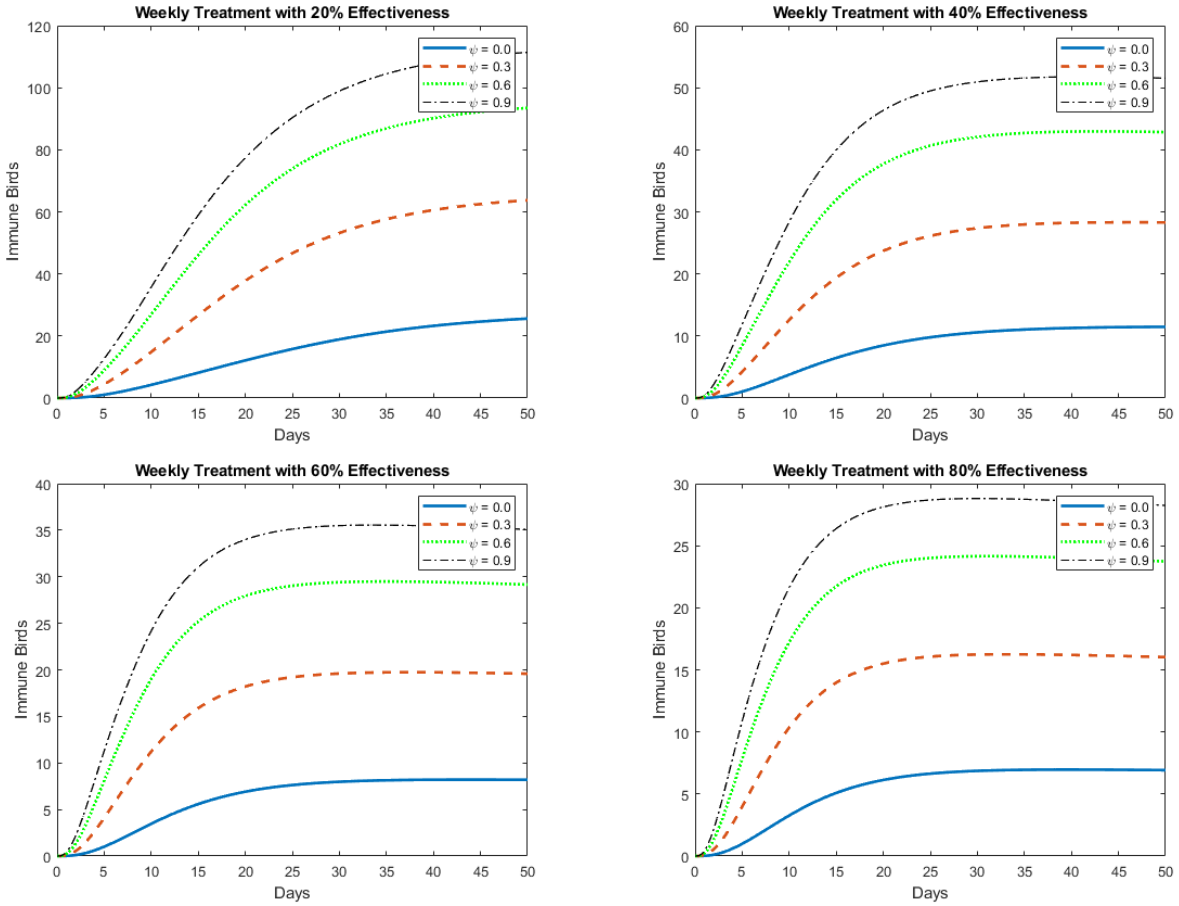


Figure 4: *Immune bird populations as affected by different μ-values (0.2, 0.4, 0.6, 0.8) with treatment frequency being weekly. The parameter μ, p_S represents the percent of eggs receiving passive immunity and percent of immune birds that loss their passive immunity. The treatment effectiveness increases left to right at 20% increments.As the treatment effectiveness increases, number of immune bird populations decreases. Fewer susceptible birds are getting infected with the* WNV*, resulting in fewer birds recovering. As a result, there will be fewer immune birds since there will be fewer recovered birds laying immune eggs.*

monitoring the transmission of the virus within the mosquito population and overall dynamics.

The dynamics of the infected mosquito population, as illustrated in Fig 6, are profoundly linked to the number of susceptible mosquitoes. In Fig 6, on day 0, there is a increase in the infected mosquito population over time. This rise is attributed to a portion of the mosquito population transitioning from the exposed to the infectious category following the incubation period. Between day 5 and day 10, the graph peaks, indicating the highest point in the infected mosquito population. The subsequent valley between day 10 and 15 is a noteworthy, this is due to the uses of adulticides (treatment). The treatment kills a portion of the infected mosquito population, leading to a decrease in the overall population or may die from from the neutral death. Each valley in the graph corresponds to the addition of a new weekly treatment, further diminishing the infected mosquito population.

It's essential to note that not every infected mosquito is impacted by the treatment, potentially allowing for it to lay an eggs, which natural passed to the offspring (egg) via vertical transmission, which the virus is maintain throughout the mosquito population. However, the use of adulticides indirectly controls vertical transmission, minimizes or mitigating its impact. In Fig 6 with 80% effectiveness, a drastic reduction in the number of infected mosquitoes can be seen, although the isolated valleys persist due to the ongoing weekly treatments. It's also, crucial to highlight that the infected mosquito population is influenced by the number of infected birds. However, the reduction in the number of exposed mosquitoes contributes to a decline in West Nile cases in humans and horses, emphasizes the broader implications of managing the mosquito population for public health outcomes.

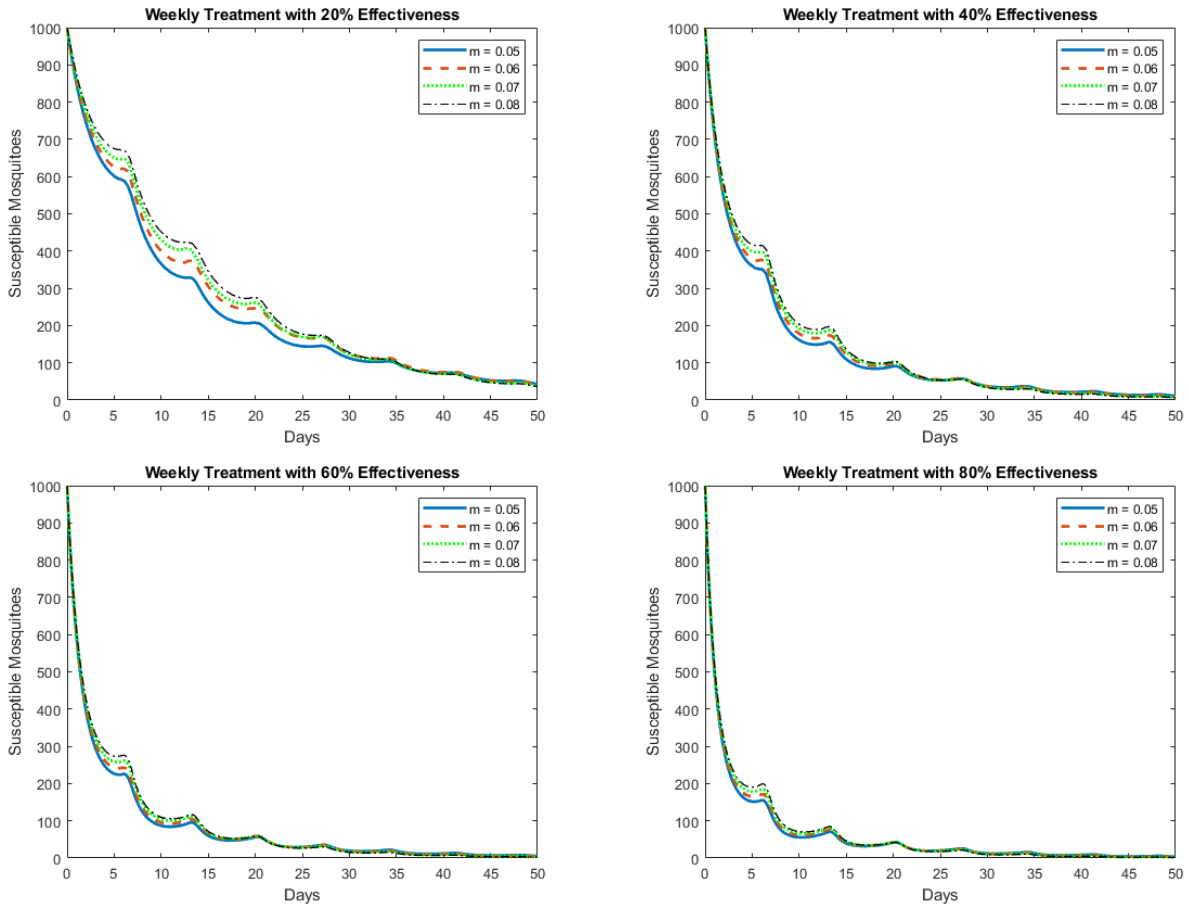


Figure 5: *Susceptible mosquitoes population as affected by different m-values (0.05, 0.06, 0.07, 0.08) with treatment frequency being weekly. The parameter m is the maturation rate from eggs to mosquitoes. The treatment effectiveness increases left to right at 20% increments. As the more uses of insecticides (adulticides or larvicides), the number of population decreases. Less number of mosquitoes decreases the chance of birds, humans, and horse becoming exposed or get infected.*

The population of infected larvae is intricately connected to the number of infected mosquitoes, as shown in Fig 7. The transmission of the West Nile Virus (WNV) to offspring occurs exclusively when an infected mosquito lays eggs, representing vertical transmission. It's important to note that mosquitoes exposed to the virus through biting an infected bird lay susceptible eggs. The initial increase in the infected larvae population is shown in Fig 7, with a peak observed between day 10 and 15 at 20% effectiveness. Notably, as treatment effectiveness increases, the peak is reached more rapidly. At 80% effectiveness, the peak occurs around day 5 to 10, showcasing the accelerated impact of the treatment. Following the peak, the infected larvae population decreases, influenced by various factors such as uses of adulticides and larvicides, as well as the natural death of larvae at the rate of the natural larvae death rate, contribute to this decline. Also in fig 7 tells just that, higher maturation rates result in a comparatively higher death rate of infected larvae. This phenomenon can be attributed to the faster maturation, increasing susceptibility to larvicides targeting the larvae. Although the difference may not be highly significant, the data indicates that higher maturation rates lead to a relatively higher death rate, contributing to a growing population of susceptible larvae over time.

Human and Horse

The simulation results for both susceptible humans and horses, depicted in Fig 8, show an similar patterns. At day 0, the susceptible populations for both humans and horses decrease over time, reaching a plateau around

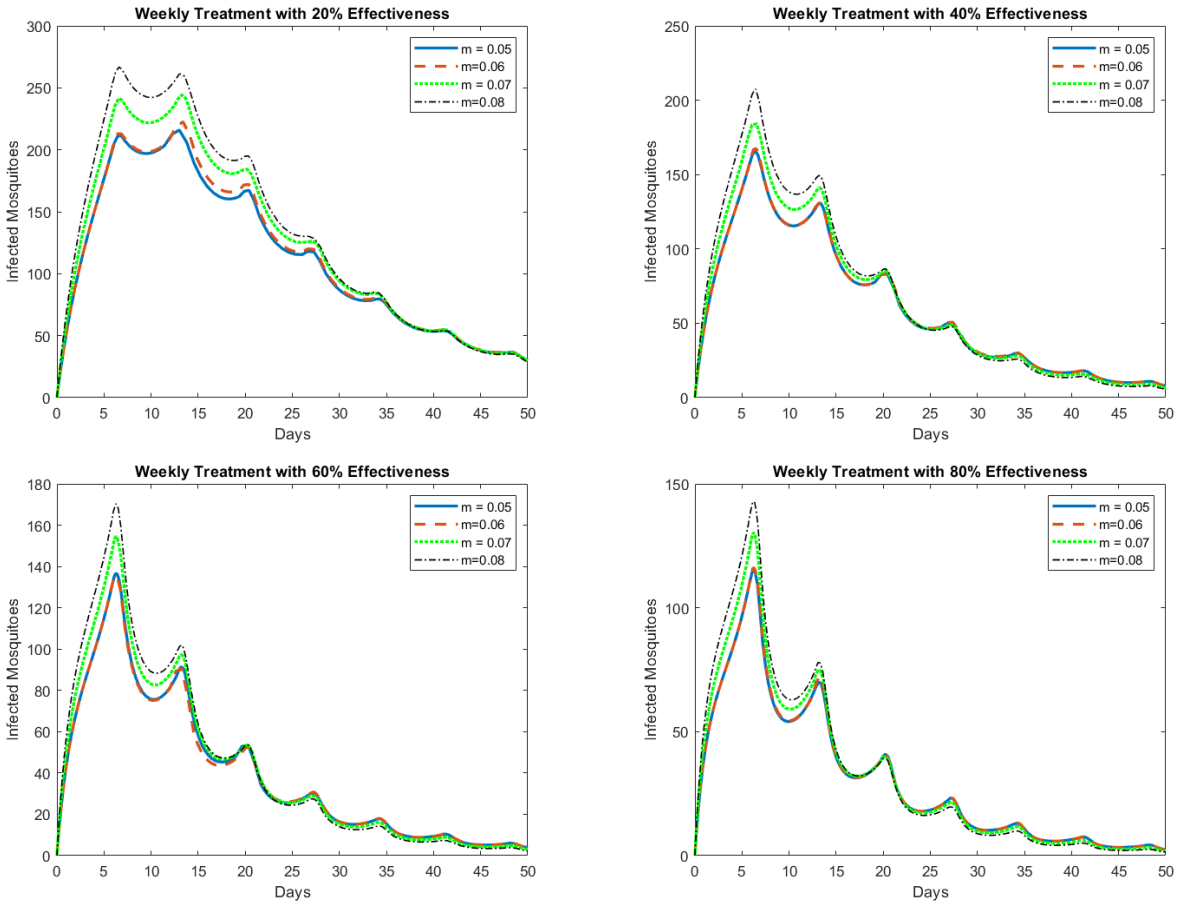


Figure 6: *Infected mosquito population as affected by different m-values (0.05, 0.06, 0.07, 0.08) with treatment frequency being weekly. The parameter m is the maturation rate from eggs to mosquitoes. The treatment effectiveness increases left to right at 20% increments. As the treatment effectiveness increases, the number of infected mosquito populations decreases. As the infected mosquito population decreases, the infected larvae population decreases. Overall, with more effective the treatment, fewer humans and horses that become infected with the disease.*

day 10. The plateau in the graph signifies that the rate of new infections has significantly slowed down, and the number of susceptible individuals is no longer decreasing rapidly. Also, it implies that substantial portion of the population has either been exposed to the infectious agent and moved to the Exposed (E) compartment or has entered the Recovered (R) compartment due to recovering from the infection. As a result, the remaining susceptible individuals are encountering fewer infectious individuals, leading to a slower rate of new infections. It's crucial to note that the specific shape and timing of the plateau are influenced by various factors, including the nature of the infectious agent, population dynamics, and the effectiveness of public health interventions. The simulation results suggest that the spread of the disease is being controlled to some extent. Regarding treatment effectiveness, although there isn't a significant difference between each effectiveness level (20%, 40%, 60%, and 80%), Fig 8 indicates that an increase in the use of adulticides is associated with an increase in the total number of susceptible individuals.

West Nile Virus (WNV) is one of the most common viruses transmitted by mosquitoes in the United States. In WNV dynamics, it's important to note that many people infected with these viruses may not show any symptoms, and those who do may experience mild symptoms such as fever, headache, nausea, sore throat, vomiting, and diarrhea. However, in some cases, especially among individuals with weakened immune systems or older adults, the diseases can lead to more severe complications like severe neurological diseases (encephalitis). However, even if the individual who survives the encephalitis are left with permanent neurological problems such as disabling fatigue, weakness, difficulty walking and memory loss. Some of the best way to prevent WNV infection other

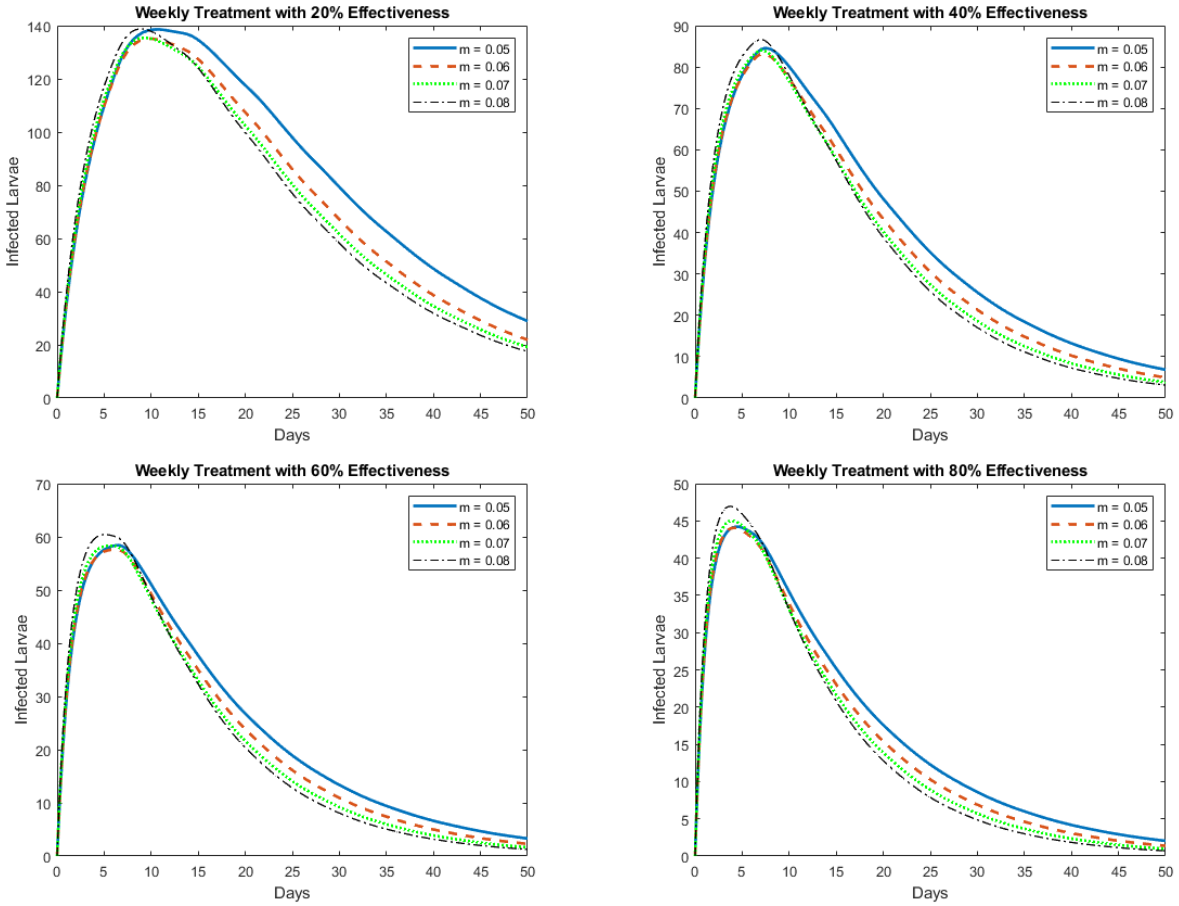
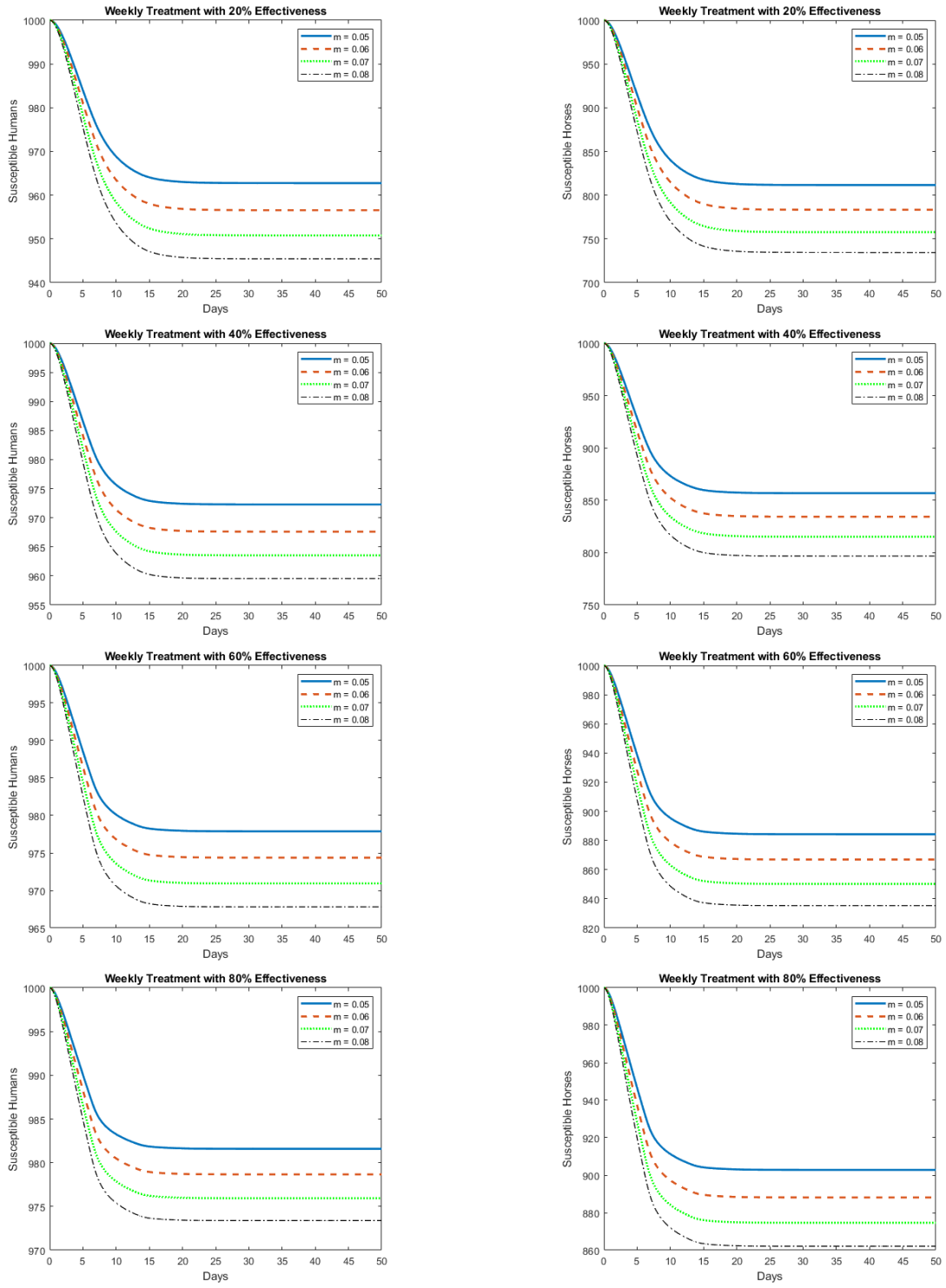


Figure 7: *Infected Larvae population as affected by different m-values (0.05, 0.06, 0.07, 0.08) with treatment frequency being weekly. The parameter m is the maturation rate from eggs to mosquitoes. The treatment effectiveness increases left to right at 20% increments.*

than insecticides is to avoid mosquito bites, which includes using insect repellent, wearing long sleeves and pants, using screens on windows and doors, and eliminating standing water around homes where mosquitoes can breed. As for the treatment, There is no specific treatment for West Nile virus in humans. Supportive care is provided to reduce symptoms, and severe cases may require hospitalization. Taking preventive measures, such as using mosquito repellent and controlling mosquito populations, is essential for areas where WNV is prevalent. As illustrated in Fig 9, similar results can be observed for both infected humans and horses. With an increasing use of treatment, the peak of the infectious curve decreases, indicating a potential reduction in the number of individuals infected. Notably, in the graph with 80% effectiveness, it is evident that there are more infected horses compared to infected humans. This observation aligns with information from the American Association of Equine Practitioners (AAEP) and the U.C. Davis Center for Equine Health, which highlight that horses represent a significant majority (96.9%) of all reported non-human mammalian cases of WNV disease. We speculate that their larger size may expose them to a greater number of mosquito bites compare to humans, contributing to the higher cases of WNV infection in the equine population. However, further studies are needed as to why some mammals are more susceptible to WNV. Also in Fig 9, we can observe that higher values of the maturation rate (m-values) which represents the speed at which mosquitoes progress through their life stages, and higher values suggest a faster maturation process. For both infected mosquitoes lead to an increasing number of infected humans and horses over the day 0 to 10 periods. Simply put, a higher maturation rate results in a more rapid increase in the adult mosquito population and can lead to a greater WNV cases of humans and horses. Which tells us the importance of controlling the overall mosquitoes population.

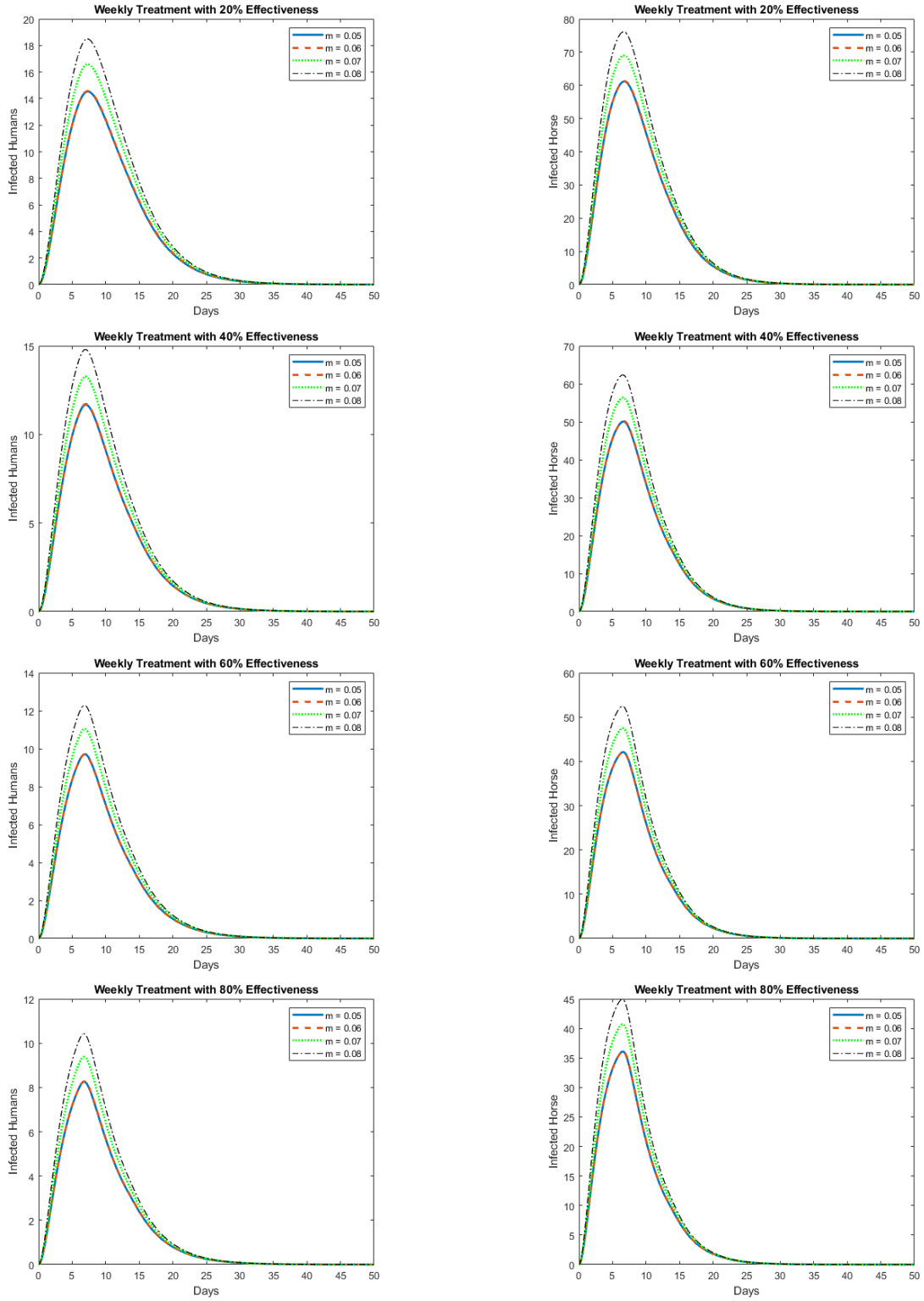
In this simulation horses are particularly susceptible to WNV, and the infection can cause a range of symptoms. Importantly, not all horses infected with the virus will manifest/show signs of symptoms and in some cases, horses



(a) Susceptible Humans (b) Susceptible Horses

Figure 8: *Susceptible humans (a) and horses (b) populations, Both of the populations are affected by different m-values (0.05, 0.06, 0.07, 0.08) with treatment frequency being weekly. The treatment effeteness increase top to bottom at 20% increments.*

can succumb to the illness without any apparent symptoms. Some of the mild symptoms includes: indications of discomfort or anxiety, lameness, a mild fever, or a general sense of malaise. As the disease progresses, neurological



(a) Infected Humans (b) Infected Horses

Figure 9: *Infected humans (a) and horses (b) populations, Both of the populations are affected by different m-values (0.05, 0.06, 0.07, 0.08) with treatment frequency being weekly. The treatment effeteness increase top to bottom at 20% increments.*

symptoms can manifest, presenting a range of abnormalities such as muzzle twitching, impaired vision, aimless wandering, head pressing, circling, difficulty swallowing, an irregular gait, trembling, lack of coordination, muscle weakness, contractions, paralysis, convulsions, and, ultimately, death. Treatment for infected horses is also largely supportive. Severely affected horses may require intensive veterinary care, and the treatment and diagnosis can vary depending on the severity of the symptoms. As it discussed previously, it is crucial to monitor and control mosquito population. It is important for horse owners to be aware of the risk of WNV in their region, taking preventive measures, and veterinary attention if symptoms are observed. Vaccination is also available for horses to help protect them from the virus.

Conclusion

The SEIR model provides a valuable framework for predicting the dynamics of infectious diseases, it is essential to acknowledge its simplifications regarding population dynamics. The model allows us the ability to make informed predictions about disease spread and if the prediction of early prediction comes with better actuary, it becomes more importance to explore further. Nevertheless, it is crucial to bear in mind that no model can be perfect in foreseeing the future. Embracing uncertainty and refining our understanding through continuous research and data uses remains critical in navigating the complexities of infectious disease dynamics. Our model explores the passive immunity and vertical transmission and how these two natural phenomena affects and shapes the overall disease dynamics. In future work, the author would like to explore the stability of the model. This ensures the consistent and reliable across various conditions and scenarios. Also, stability analysis can help identify key factors influencing the model's behavior and provide insights into its long-term dynamics. Additionally, incorporating temperature into the model is relevant consideration. Temperature plays a fundamental role in the life cycles and behaviors of mosquitoes and birds. Variations in temperature can affect mosquito biting rates, the rate at which mosquitoes lay eggs, and the movement patterns of birds in and out of the community.

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References

[1] John S Mackenzie, Duane J Gubler, and Lyle R Petersen. "Emerging flaviviruses: the spread and resurgence of Japanese encephalitis, West Nile and dengue viruses". In: *Nature medicine* 10.Suppl 12 (2004), S98–S109. DOI: 10.1038/nm1144.

[2] Tonya Colpitts et al. "West Nile Virus: Biology, Transmission, and Human Infection". In: *Clinical microbiology reviews* 25 (Oct. 2012), pp. 635–48. DOI: 10.1128/CMR.00045-12.

[3] CDC. *Transmission, West Nile virus*. URL: https://www.cdc.gov/westnile/transmission/index.html. (accessed: 02.17.2023).

[4] Louis D Bergsman, James M Hyman, and Carrie A Manore. "A mathematical model for the spread of West Nile virus in migratory and resident birds". In: *Mathematical Biosciences & Engineering* 13.2 (2016), p. 401.

[5] CDC. *West Nile Virus & Dead Birds*. URL: https://www.cdc.gov/westnile/dead-birds/index.html. (accessed: 02.17.2023).

[6] CDC. *St. Louis Encephalitis Virus | Transmission*. URL: https://www.cdc.gov/sle/transmission/index.html. (accessed: 02.17.2023).

[7] Wildlife Futures Team. *West Nile Virus*. URL: https://www.vet.upenn.edu/research/centers-laboratories/research-initiatives/wildlife-futures-program/our-research/fact-sheet-detail/west-nile-virus. (accessed: 02.18.2023).

[8] Ken Madden. "West Nile virus infection and its neurological manifestations". In: *Clinical Medicine & Research* 1.2 (2003), pp. 145–150.

[9] Shannon E Ronca, Jeanne C Ruff, and Kristy O Murray. "A 20-year historical review of West Nile virus since its initial emergence in North America: Has West Nile virus become a neglected tropical disease?" In: *PLOS Neglected Tropical Diseases* 15.5 (2021), e0009190.

[10] J Erin Staples et al. "Initial and long-term costs of patients hospitalized with West Nile virus disease". In: *The American journal of tropical medicine and hygiene* 90.3 (2014), p. 402.

[11] Karthick Kanagarathinam, Ebrahem A Algehyne, and Kavaskar Sekar. "Analysis of 'earlyR'epidemic model and time series model for prediction of COVID-19 registered cases". In: *Materials Today: Proceedings* (2020). DOI: 10.1016/j.matpr.2020.10.086.

[12] José M. Carcione et al. "A Simulation of a COVID-19 Epidemic Based on a Deterministic SEIR Model". In: *Frontiers in Public Health* 8 (2020). ISSN: 2296-2565. DOI: 10.3389/fpubh.2020.00230. URL: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00230.

[13] Alberto Godio, Francesca Pace, and Andrea Vergnano. "SEIR modeling of the Italian epidemic of SARS-CoV-2 using computational swarm intelligence". In: *International journal of environmental research and public health* 17.10 (2020), p. 3535. DOI: 10.3390/ijerph17103535.

[14] Muhammad Asif et al. "Numerical simulation for solution of SEIR models by meshless and finite difference methods". In: *Chaos, Solitons & Fractals* 141 (2020), p. 110340. ISSN: 0960-0779. DOI: https://doi.org/10.1016/j.chaos.2020.110340. URL: https://www.sciencedirect.com/science/article/pii/S0960077920307359.

[15] John F Anderson et al. "Isolation of West Nile virus from mosquitoes, crows, and a Cooper's hawk in Connecticut". In: *Science* 286.5448 (1999), pp. 2331–2333.

[16] Duane J Gubler. "The continuing spread of West Nile virus in the western hemisphere". In: *Clinical infectious diseases* 45.8 (2007), pp. 1039–1046.

[17] Goudarz Molaei et al. "Host feeding patterns of Culex mosquitoes and West Nile virus transmission, northeastern United States". In: *Emerging infectious diseases* 12.3 (2006), p. 468.

[18] John H Rappole, Scott R Derrickson, and Zdenek Hubalek. "Migratory birds and spread of West Nile virus in the Western Hemisphere." In: *Emerging infectious diseases* 6.4 (2000), p. 319.

[19] Vector Disease Control International. *West Nile Virus*. URL: https://www.vdci.net/vector-borne-diseases/west-nile-virus-education-and-mosquito-management-to-protect-public-health/#:~:text=West%20Nile%20virus%20is%20spread,feed%20from%20evening%20to%20morning.. (accessed: 07.8.2023).

[20] Gabriel L Hamer et al. "Culex pipiens (Diptera: Culicidae): a bridge vector of West Nile virus to humans". In: *Journal of medical entomology* 45.1 (2008), pp. 125–128.

[21] William K Reisen, Ying Fang, and Vincent M Martinez. "VECTOR COMPETENCE OF CULISETA INCIDENS AND CULEX THRIAMBUS FOR WEST NILE VIRUS1". In: *Journal of the American Mosquito Control Association* 22.4 (2006), pp. 662–665.

[22] Christopher J Vitek et al. "Arbovirus transmission by Culex nigripalpus in Florida, 2005". In: *Journal of medical entomology* 45.3 (2014), pp. 483–493.

[23] Nicole M Nemeth, Paul T Oesterle, and Richard A Bowen. "Humoral immunity to West Nile virus is long-lasting and protective in the house sparrow (Passer domesticus)". In: *The American journal of tropical medicine and hygiene* 80.5 (2009), p. 864.

[24] Jennifer Kovacs-Nolan and Yoshinori Mine. "Egg yolk antibodies for passive immunity". In: *Annual review of food science and technology* 3 (2012), pp. 163–182.

[25] Noelle West and Vinodh K. Chellamuthu. "Modeling the Effects of Passive Immunity in Birds for the Disease Dynamics of West Nile Virus". In: *Spora: A Journal of Biomathematics* 6.1 (2020), pp. 16–25.

[26] NP Lindsey et al. "West Nile Virus activity-United States, 2006 (Reprinted from MMWR, vol 56, pg 556-559, 2007)". In: *JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION* 298.6 (2007), pp. 619–621.

[27] Schaefer TJ Clark MB. *West Niel Virus*. StatPerarls, 2022. URL: https://www.ncbi.nlm.nih.gov/books/NBK544246/.

[28] SM Lim, P Koraka, and A Osterhaus. *DM E., & Martina, B. EE (2011). West Nile virus: Immunity and pathogenesis*. DOI: 10.3390/v3060811.

[29] Michel L Bunning et al. "Experimental infection of horses with West Nile virus". In: *Emerging infectious diseases* 8.4 (2002), p. 380.

[30] N Komar et al. "West Nile viral encephalitis". In: *Revue Scientifique et Technique-Office International des Epizooties* 19.1 (2000), pp. 166–176.

[31] Julie Paré and Alison Moore. "West Nile virus in horses—What do you need to know to diagnose the disease?" In: *The Canadian Veterinary Journal* 59.10 (2018), p. 1119.

[32] Lyle R Petersen and John T Roehrig. *Flavivirus DNA vaccines—Good science, uncertain future*. 2007.

[33] Ian Gardner et al. "Incidence and effects of West Nile virus infection in vaccinated and unvaccinated horses in California". In: *Veterinary research* 38.1 (2007), pp. 109–116.

[34] Shirin Kordnoori, Mahboobe Sadat Kobari, and Hamidreza Mostafaei. "Predict the spread of COVID-19 in Iran with a SEIR model". In: *IPTEK The Journal for Technology and Science* 32.1 (2021), pp. 31–40.

[35] Kasia A Pawelek et al. "Modeling dynamics of Culex pipiens complex populations and assessing abatement strategies for West Nile virus". In: *PloS one* 9.9 (2014), e108452. DOI: 10.1371/journal.pone.0108452.

[36] John T Roehrig. "West Nile virus in the United States—a historical perspective". In: *Viruses* 5.12 (2013), pp. 3088–3108. DOI: 10.3390/v5123088.

[37] Marjorie J Wonham et al. "Transmission assumptions generate conflicting predictions in host–vector disease models: a case study in West Nile virus". In: *Ecology letters* 9.6 (2006), pp. 706–725. DOI: 10.1111/j.1461-0248.2006.00912.x.

[38] Peter Daszak, Andrew A Cunningham, and Alex D Hyatt. "Emerging infectious diseases of wildlife–threats to biodiversity and human health". In: *science* 287.5452 (2000), pp. 443–449. DOI: 10.1126/science.287.5452.443.

[39] Odo Diekmann and Johan Andre Peter Heesterbeek. *Mathematical epidemiology of infectious diseases: model building, analysis and interpretation*. Vol. 5. John Wiley & Sons, 2000.

[40] T Darensburg and VL Kocic. "On the discrete model of West Nile-like epidemics". In: *Proc Dyn Sys Appl* 4 (2004), pp. 358–366.

[41] DC Hahn et al. "Passive West Nile virus antibody transfer from maternal Eastern screech-owls (Megascops asio) to progeny". In: *Avian Diseases* 50.3 (2006), pp. 454–455.

[42] Nicole M Nemeth and Richard A Bowen. "Dynamics of passive immunity to West Nile virus in domestic chickens (Gallus gallus domesticus)." In: *The American journal of tropical medicine and hygiene* 76.2 (2007), pp. 310–317.

[43] Nicole M Nemeth, Paul T Oesterle, and Richard A Bowen. "Humoral immunity to West Nile virus is long-lasting and protective in the house sparrow (Passer domesticus)". In: *The American journal of tropical medicine and hygiene* 80.5 (2009), pp. 864–869.

[44] Jennifer E Simpson et al. "Vector host-feeding preferences drive transmission of multi-host pathogens: West Nile virus as a model system". In: *Proceedings of the Royal Society B: Biological Sciences* 279.1730 (2012), pp. 925–933. DOI: 10.1098/rspb.2011.1282.

[45] Nicholas Komar et al. "Experimental infection of North American birds with the New York 1999 strain of West Nile virus". In: *Emerging infectious diseases* 9.3 (2003), p. 311. DOI: 10.3201/eid0903.020628.

[46] C Bowman et al. "A mathematical model for assessing control strategies against West Nile virus". In: *Bulletin of mathematical biology* 67.5 (2005), pp. 1107–1133.

[47] CDC. *St. Louis Encephalitis Virus | Transmission*. URL: https://www.cdc.gov/westnile/index.html. (accessed: 02.18.2023).

[48] Edgardo M Flores Anticona et al. "Two case reports of neuroinvasive west nile virus infection in the critical care unit". In: *Case Reports in Infectious Diseases* 2012 (2012). DOI: 10.1155/2012/839458.

[49] Nicole M Nemeth, Paul T Oesterle, and Richard A Bowen. "Passive immunity to West Nile virus provides limited protection in a common passerine species". In: (2008). DOI: 10.4269/ajtmh.2008.79.283.

[50] Antoine Levasseur, Julie Arsenault, and Julie Paré. "Surveillance of West Nile virus in horses in Canada: A retrospective study of cases reported to the Canadian Food Inspection Agency from 2003 to 2019". In: *The Canadian Veterinary Journal* 62.5 (2021), p. 469.

[51] Turner Jason L. *West Nile Virus in Horses*. URL: https://pubs.nmsu.edu/_b/B719/index.html#:~:text=While%20all%20horses%20are%20susceptible,is%20three%20to%2015%20days.. (accessed: 03.21.2023).

[52] Veterinary Health Center Kansas State University. *Equine Internal Medicine West Nile Virus in Horses*. URL: https://www.ksvhc.org/services/equine/internal-medicine/west-nile.html#:~:text=Horses%20become%20ill%203%20to,no%20breed%20or%20gender%20predilection.. (accessed: 03.23.2023).

[53] American Association of Equine Practitioners. *West Nile Virus*. URL: https://aaep.org/guidelines/vaccination-guidelines/core-vaccination-guidelines/west-nile-virus. (accessed: 03.21.2023).

[54] J Scott Weese et al. "West Nile virus encephalomyelitis in horses in Ontario: 28 cases". In: *The Canadian Veterinary Journal* 44.6 (2003), p. 469.