CONTROL OF WEST NILE VIRUS BY INSECTICIDE IN THE PRESENCE OF AN AVIAN RESERVOIR

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The first cases of West Nile virus (WNV) in North America appeared in New York City in the summer of 1999. By 2002, the disease had spread across the continent, resulting in thousands of infections and deaths. WNV is still easily spread from mosquitoes to humans in densely populated areas and since it can be fatal, WNV continues to attract significant public attention. Although this disease has been acknowledged for some time, there are still no recognized effective treatments and public efforts have focused primarily on preventing transmission of the virus. This paper compares the reliability of several distinct mathematical models in predicting the transmission and population dynamics of the virus in mosquito vectors and avian reservoirs. The most robust model is extended to include humans. Numerical experiments are conducted to establish the most effective quantity and timing of chemical insecticide spray needed to prevent a human epidemic of West Nile virus in large urban areas. This study concludes that early insecticide spraying is essential in preventing an epidemic and that the quantity of insecticide sprayed is less important than the timing. The model suggests that a low concentration of insecticide sprayed at the emergence of human cases is an effective strategy for reducing the level of a human epidemic.

1. Introduction

In the summer of 1999, the first reported cases of West Nile virus (WNV) in North America presented in New York City. The virus, which had previously been confined to Africa, the Middle East, western Asia, and some areas of Europe, immediately attracted public attention in the United States as a result of its ease of transmission from infected mosquitoes to humans and its potentially fatal neurological effects. West Nile virus is an arbovirus and a single stranded RNA virus of the genus Flavivirus and the family Fla-

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viviridae [1]. Approximately 80% of people infected with West Nile virus are asymptomatic. Approximately 20% report fever, headache, fatigue, and/or rash as their primary symptoms. However, around 1% of people that contract WNV develop a more severe and potentially fatal form of the disease. Symptoms for severe West Nile virus include meningitis, encephalitis, high fever, ataxia, seizures, and death. An uncharacteristically high number of people infected with West Nile in North America have developed severe symptoms, suggesting the presence of a particularly virulent strain and the relative absence of immunity to the disease in the U. S. By the end of 1999, the Center for Disease Control (CDC) reported 59 confirmed WNV infections and 7 deaths in New York State. No standard preventative measures were implemented and by late 2002, a highly virulent strain of the virus had spread across the continent. The yearly CDC West Nile report confirmed that in the U. S. in 2002 alone, over 4,156 people in 40 states had been infected with the virus, and 284 had died. The virus was becoming an epidemic in North America and there were no known effective treatments.

West Nile virus can take several forms of transmission. The disease exploits birds (140 infected species have been found in North America) and equines as reservoirs for surviving throughout and in between outbreaks although the virus has been recorded in several other mammal species throughout the United States. The West Nile virus, transmitted mainly by Culex mosquito vectors from numerous bird reservoirs, has a complex life cycle. Ultimately, humans are used as a secondary carrier, with human infection occurring through vector-human contact. However, humans usually do not produce enough viremia to be able to infect a healthy vector that bites them.

In their paper comparing the effects of biological assumptions on transmission terms and disease predictions, Wonham *et al*, [2], present five models that were constructed following the 1999 New York City outbreak. Each of these epidemiological models takes a different approach to modeling the disease through varying assumptions, and consequently varying transmission terms, although all are based on the standard susceptible-infected (S-I) model. A core model was constructed with three variations on the form taken by the disease transmission terms. In all cases the reproductive number associated to the system is density dependent. The median, high and low values of each parameter were used to construct distributions as a source for a Monte Carlo simulation. The paper reports mean and variance in the reproductive number for low, medium and high populations of reservoirs and vectors. Substantial variation in the reproductive number results from

choosing different forms for the transmission term. Their paper, [2], serves as a warning that the choice of reservoir model will have serious consequences for human epidemiology when coupled with equations representing human populations. Changing the form of the model varies more than just the reproductive number, however. Transmission to humans involves not only this measure of virulence, but also the density of the infected mosquito population.

Bowman *et al*, [1], has a full epidemiological model including vector, reservoir, and human host. The vector-reservoir submodel in [1] is one of those mentioned in [2]. However, our analysis will show that it is not the best choice for a model that is consistent across bird species with respect to reproductive number and infected vector density. The authors use their full model to study the effects of outbreak control via adulticide and larvicide of the vector. Their model assumes continuous proportional death of either or both forms of the vector. In this paper we apply this strategy using an improved vector-reservoir model and compare its effectiveness for different starting times and mortality rates.

We will look at the consequences of four of the models studied in [2] across six species of North American birds. In Section 2 we introduce models by Thomas and Urena, [3], Wonham *et al*, [4], Bowman *et al*, [1], and Cruz-Pacheco *et al*, [5]. In Section 3 we describe the range of parameters for the model, including the specific death and recovery rates for the various species of birds. In Section 4 we give mean and standard variation in reproductive number and maximum density of infected vector across these six bird species. We also note qualitative differences in output from these models. On the basis of this discussion we choose the model with least variability across bird species. In Section 5 we couple this vector-reservoir model with the human population, following [1] for the human epidemiology submodel. In Section 6 we show the results of attempting to control West Nile virus with American Crow bird reservoir by continuous applications of insecticide (adulticide) introduced at varying times and with varying effectiveness. In Section 7 we discuss our results. All numerical integrations were performed using BGODEM software (Reid, copyright 2008).

2. Vector-Reservoir Transmission Models

We preserve the notation of [2], referring to the models in this section as WN2-WN5. We refer the reader to Table 1 of [2], which summarizes the basic features of each model, giving here only the equations for each. A

more complete description of the final model chosen is in section 5. The differential equations for the various models include the population dynamics of L_V (larval vectors), S_V (susceptible vectors), E_V (exposed vectors, accounting for incubation time of the virus), I_V (infected vectors), S_R (susceptible reservoirs), I_R (infected reservoirs), and R_R (recovered reservoirs). Reproduction numbers are as stated in [2]. The quantities N_V^* and N_R^* are the disease free equilibrium values for vector and reservoir populations respectively. All models are assumed to be valid only for a single season.

2.1. *WN2 (Thomas and Urena, [3])*

This model uses a mass action disease transmission term, which assumes biting rates, the main factor in disease transmission, are limited by both vector and reservoir densities. It does not model the larval vector population, nor does it take into account the species specific disease mortality.

$$\frac{dS_V}{dt} = b_V[S_V + (1-\rho_V)(E_V + I_V)] - \beta_R I_R S_V - d_V S_V \tag{1}$$

$$\frac{dE_V}{dt} = b_V \rho_V (E_V + I_V) + \beta_R I_R S_V - (d_V + \kappa_V) E_V \tag{2}$$

$$\frac{dI_V}{dt} = \kappa_V E_V - d_V I_V \tag{3}$$

$$\frac{dS_R}{dt} = b_R N_R - \beta_R^* S_R I_V - d_R S_R \tag{4}$$

$$\frac{dI_R}{dt} = \beta_R^* S_R I_V - (d_R + \gamma_R) I_R \tag{5}$$

The reproduction number associated to WN2 is (equation here).

$$R_0 = \frac{\rho_V}{2} + \sqrt{(\frac{\rho_V}{2})^2 + \frac{\phi_V \beta_R^{*2} N_V^* N_R^*}{d_V(d_R + \gamma_R)}} \tag{6}$$

2.2. *WN3 (Wonham et al, [4])*

This model uses a reservoir frequency dependent transmission term, which assumes the vector biting rate is saturated and doesnt depend on reservoir densities. This model includes all populations, accounting for all constants.

$$\frac{dL_V}{dt} = b_L N_V - (m_L + d_L)L_V \tag{7}$$

$$\frac{dS_V}{dt} = -\alpha_V \beta_R \frac{I_R}{N_R} S_V + m_L L_V - d_V S_V \tag{8}$$

$$\frac{dE_V}{dt} = \alpha_V \beta_R \frac{I_R}{N_R} S_V - (\kappa_V + d_V)E_V \tag{9}$$

$$\frac{dI_V}{dt} = \kappa_V E_V - d_V I_V \tag{10}$$

$$\frac{dS_R}{dt} = -\alpha_R \beta_R \frac{S_R}{N_R} I_V \tag{11}$$

$$\frac{dI_R}{dt} = \alpha_R \beta_R \frac{S_R}{N_R} I_V - (\delta_R + \gamma_R)I_R \tag{12}$$

$$\frac{dR_R}{dt} = \gamma_R I_R \tag{13}$$

The reproduction number associated to WN3 is

$$R_0 = \sqrt{\frac{\phi_V \beta_R^2 \alpha_R \alpha_V N_V^*}{d_V(\delta_R + \gamma_R)N_R^*}} \tag{14}$$

2.3. *WN4 (Bowman et al, [1])*

This model uses a reservoir frequency dependent transmission term, which assumes the vector biting rate is saturated and doesnt depend on reservoir densities. This model does not include larval or exposed vector populations, does not account for recovery rate of reservoirs, nor incubation time, and uses a recruitment rate in place of birth and death rates.

$$\frac{dS_V}{dt} = a_V - \alpha_V \beta_R \frac{I_R}{N_R} S_V - d_V S_V \tag{15}$$

$$\frac{dI_V}{dt} = \alpha_V \beta_R \frac{I_R}{N_R} S_V - a_V I_V \tag{16}$$

$$\frac{dS_R}{dt} = a_R - \alpha_R \beta_R \frac{S_R}{N_R} I_V - d_R S_R \tag{17}$$

$$\frac{dI_R}{dt} = \alpha_R \beta_R \frac{S_R}{N_R} I_V - (\delta_R + d_R) I_R \tag{18}$$

The reproduction number associated to WN4 is

$$R_0 = \sqrt{\frac{\beta_R^2 \alpha_R \alpha_V N_V^*}{d_V (\delta_R + d_R) N_R^*}} \tag{19}$$

2.4. *WN5 (Cruz-Pacheco et al, [5])*

This model uses a reservoir frequency dependent transmission term, which assumes the vector biting rate is saturated and doesnt depend on reservoir densities. It does not model larval or exposed vector populations, and thus ignores incubation time, although it does account for all constants.

$$\frac{dS_V}{dt} = b_V [S_V + (1 - \rho_V)(E_V + I_V)] - \beta_R I_R S_V - d_V S_V \tag{20}$$

$$\frac{dI_V}{dt} = b_V \rho_V I_V + \alpha_V \beta_R \frac{I_R}{N_R} S_V - d_V I_V \tag{21}$$

$$\frac{dS_R}{dt} = a_R - \alpha_R \beta_R \frac{S_R}{N_R} I_V - d_R S_R \tag{22}$$

$$\frac{dI_R}{dt} = \alpha_R \beta_R \frac{S_R}{N_R} I_V - (\delta_R + d_R + \gamma_R) I_R \tag{23}$$

$$\frac{dI_R}{dt} = \gamma_R I_R - d_R R_R \tag{24}$$

The reproduction number associated to WN5 is

$$R_0 = \frac{\rho_V}{2} + \sqrt{(\frac{\rho_V}{2})^2 + \frac{\alpha_R \alpha_V \beta_R^2 N_V^*}{d_V(d_R + \delta_R + \gamma_R)}} \tag{25}$$

3. Parameter ranges for all models

Wonham *et al* [2] gives values for all parameters in models WN2-WN5 based on quantities reported in the literature or calculated from simple assumptions. We have used these values with the exceptions of parameters a_V, a_R, δ_R and γ_R , which are explained below. We also summarize the notation and values from Wonham *et al* (2006), to which we refer the reader for further information such as ranges and bibliographic sources.

Quantities δ_R and γ_R stand for the disease mortality rate of reservoirs and for the reservoir recovery rate respectively. These two values were the focus of the sensitivity analysis done here and were the only changed values from model to model. Using the values of π_R (survival probability), σ_R (days infectious), and τ_R (days to death) from [2], the values of δ_R and γ_R, (for the six North American species of American Crow, American Robin, Blue Jay, House Sparrow, Northern Mockingbird and Northern Cardinal), were calculated and the resulting rates are given in Table 1.

Table 1. Reservoir Species Specific Parameter Values

Species	survival probability π_R	days infectious σ_R	days to death τ_R	death rate δ_R	recovery rate γ_R
American Crow	0	3.25	5.10	0.20	0
American Robin	1.00	3.00	n.a.	0.00	0.33
Blue Jay	0.25	3.75	4.70	0.29	0.08
House Sparrow	0.47	3.00	4.70	0.16	0.21
Northern Mockingbird	1.00	1.25	n.a.	0.00	.80
Cardinal	0.78	1.50	4.00	0.06	0.89

Parameters a_V and a_R are both titled recruitment rates and are specific to the vectors and reservoirs of WN4. The recruitment rate a_R was set to zero, reflecting the assumption that the model is for only one season. These values take the place of a typical birth rate. The value for a_V was taken from [1]. The reported range of 5000-22000 mosquitoes born per day was

averaged to a constant value of 13500 mosquitoes born/day.

The value of m_L is 0.07 mosquitoes per day and this value accounts for the maturation rate of the mosquitos. The values of d_V, d_L, and d_R, are 0.03 mosquitoes/day, 0.02 larvae/day, 0.0015 birds/day respectively, accounting for natural death of vectors, larvae, and reservoirs respectively. The birth rates for these particular models (b_V, b_L, and b_R) are equal to their respective death rates (0.03 mosquitoes/day, 0.02 larvae/day, 0.0015 birds/day). The value of ρ_V is 0.001 mosquitoes/day and this value is accounting for the number of mosquitoes born that are already infected with West Nile virus. 0.69 is the probability in a single day that the virus will be transmitted to a vector, and this value is represented by the variable α_k. κ_V is used in several of the models to account for the incubation rate of the virus and is measured as .10 mosquitoes per day. ϕ_V is an account of the proportion of vectors that survive the incubation period, and here it is calculated using the supplied equation as 0.77 mosquitoes/day.

The quantity β_R is the saturated reservoir frequency dependent bite rate measured as a constant 0.44 bites/mosquito/day and can be thought of as maximum possible number of bites per day made by a single mosquito. This term drives the reservoir frequency dependent disease transmission term. β_R^* is measured in bites per day per unit density bird at disease-free equilibrium values, and this ratio was taken into account as a moving variable in the graphical input programs by using the equation supplied in [2]. This term drives the mass action disease transmission term and varies depending on the density of reservoirs. The constant m_R is the maturation rate of reservoirs and is again set to 0 and not used in the equations due to the single season nature of the models. For models with reservoir frequency dependent transmission terms, 0.74 is the probability in a single day that the virus will be transmitted to a reservoir, and this value is represented by the parameter α_R.

Typical runs for the system WN3 are shown in Figure 1 for American Crow and Figure 2 for American Robin. It is easy to see that the change in death and recovery rates has a big effect on model predictions. Figure 3 shows how model WN3 varies across all six species in terms of the proportion of mosquitos which are infected, which is the key predictor of infection in human populations.

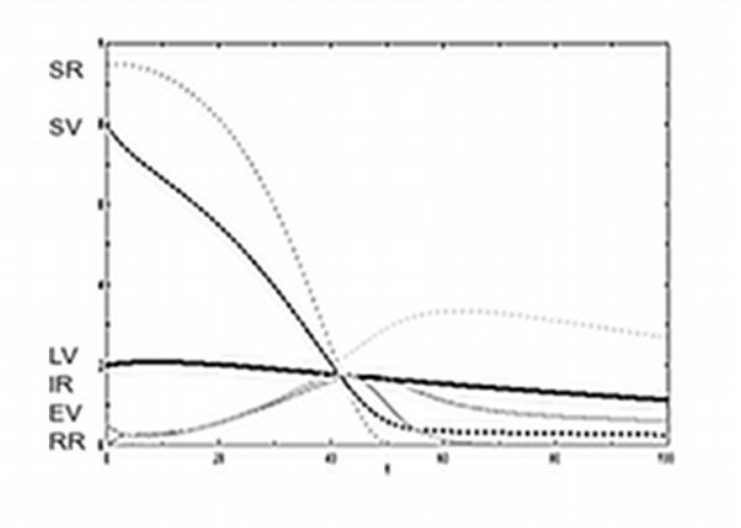

Figure 1. The model WN3 with parameters for American Crow

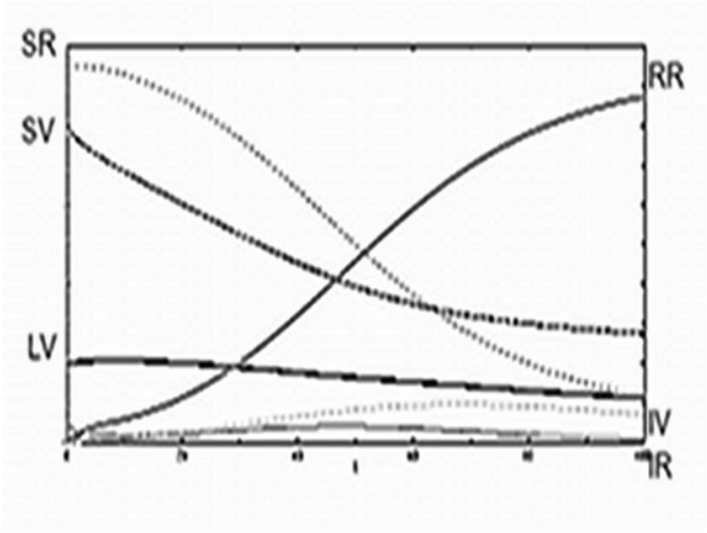

Figure 2. The model WN3 with parameters for American Robin.

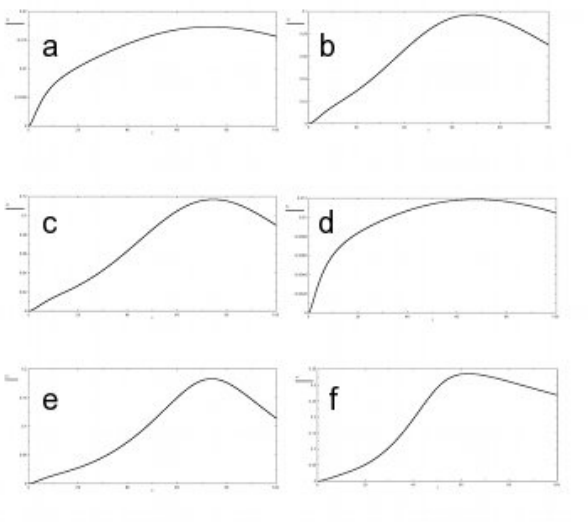

Figure 3. Infected vector populations in model WN3 for all reservoirs considered. a. Northern Mockingbird, b. American Robin, c. House Sparrow, d. Cardinal, e. Blue Jay, f. American Crow

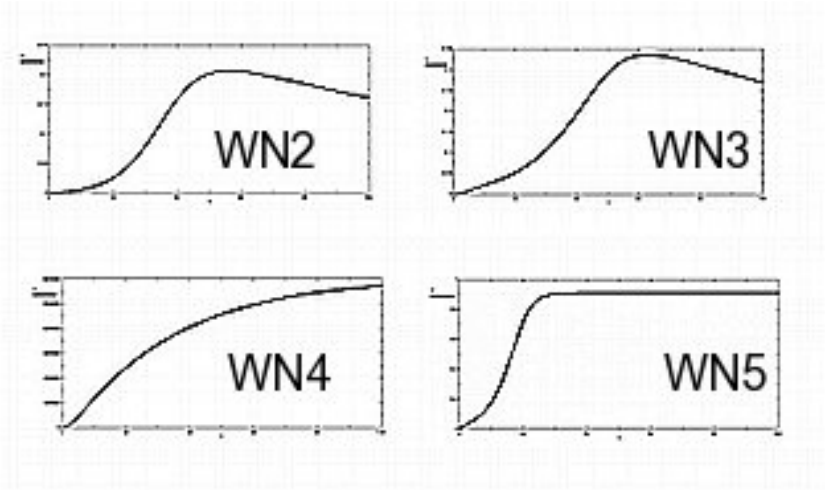

Figure 4. Infected vector populations in models WN2-WN5 with parameters for American Crow.

Similarly, there is a wide range of predictive outputs across the four models we are considering. Figure 4 shows the infected mosquito output for all four models, using the death and recovery rates for American Crow. In the next section we analyze the variation among these models as the parameters range across the six species of bird.

4. Variation in reproductive number and density of infected vector across six reservoir species

The reservoir species specific values for disease reproduction rate, R0, which has a direct correlation with human infection rate, were calculated algebraically from the four R_0 equations listed above and the reported parameters. The average and standard deviation were then calculated to test for species specific sensitivity. The values of N_V^* and N_R^* are the population disease-free equilibrium values at low, medium and high densities of vector and reservoir populations. The values for WN2 were low density for numerical reasons and WN3-WN5 were all medium density models. The results are giving in Table 2.

Table 2. Species Specific R_0 and Standard Deviation

Species	death rate δ_R	recovery rate γ_R	R_0 WN2 $N_v = 1000$ $N_R = 100$	R_0 WN3 $N_v = 10,000$ $N_R = 1000$	R_0 WN4 $N_v = 10,000$ $N_R = 1000$	R_0 WN5 $N_v = 10,000$ $N_R = 1000$
Crow	0.20	0.00	36.40	11.66	12.79	13.243
Robin	0.00	0.33	2.45	9.08	148.21	10.32
Blue Jay	0.29	0.08	4.94	8.58	10.63	9.75
Sparrow	0.16	0.21	3.07	8.58	14.28	9.75
Mockingbird	0.00	0.80	1.58	5.83	22.78	6.08
Cardinal	0.06	0.89	1.49	5.35	22.78	6.09
Average			8.32	8.18	59.48	9.30
STD			13.81	2.32	68.85	2.62

The reservoir species specific values for maximum density of infected vector, I_V, which has a direct correlation with human infection rate as well, were found using outputs from BGODEM (Reid, 2008) which uses a Runge-Kutta algorithm to numerically integrate systems of ordinary differential

equations. The averages and standard deviations were then calculated to test for species specific sensitivity. All values were taken directly from graphical solution proportion values for models WN2, WN3, and WN5. WN4 did not have a population cap and thus did not produce per capita population proportions so the maximum portion of the mosquito population that was infected at any time within the 100 days was calculated through turning the given values of IV and SV, into proportions, ($\frac{I_V}{[I_V+S_V]}$ = the proportion of the mosquito population that is infected), which could then be directly compared to the other graphical outputs. The results are given in Table 3.

Table 3. Species Specific Infected Vector Maximum Values

Species	WN2	WN3	WN4	WN5
American Crow	0.21	0.34	0.093	0.91
American Robin	0.001	0.097	0.093	0.385
Blue Jay	0.17	0.18	0.93	0.63
House Sparrow	0.036	0.117	0.093	0.46
Northern Mockingbird	0.00018	0.017	0.093	0.138
Cardinal	0.00014	0.0119	0.093	0.112
Average	0.0695	0.127	0.093	0.44
STD	0.0948	0.12	0	0.30

In order to determine which model was the most consistent, or in other words, least affected by species specific values while still being biologically viable, both sets of standard deviations as well as general trends will be analyzed. Looking first to model WN2, [3], the standard deviation for the infected vector maximum values was fairly low, at 0.09479, which was larger than the mean value across the six species; however, the graphical outputs were fairly inconsistent in terms of population trends. In addition, the standard deviation for R_0 values at 13.8144 was large, (in fact larger than the mean value), despite the consistency with general trends. This model as previously mentioned also fails to take into account species specific disease mortality, which could certainly cause erroneous outputs as this value ranges from 100 % mortality to 0 % depending on the species.

Examining model WN4, [1], the standard deviation for R_0 values at 68.8504 was extremely high (also larger than the mean), and the trends were inconsistent with those of the other three models. This model, as previously mentioned, fails to take into account any reservoir recovery and

uses a recruitment rate in place of a birth rate, which has been set to zero in these trials. It also does not account for incubation time. The graphical outputs for infected vectors were very similar and produced no noticeable difference at 100 days across the six bird species. It seems likely, that without a nonzero recruitment rate or recovery rate for the reservoir species, those quantities arrive at equilibrium too quickly to have much effect on the overall dynamics of the system. Computer simulations did confirm the authors claim of an endemic equilibrium. This model was eliminated due to the conflict between the high variance of the reproduction number, which did not translate into a corresponding effect on the proportion of infected vectors. If a good estimate of the recruitment rate for bird species became available, then this model might be more realistic.

Moving to model WN5, [5], the standard deviation for R_0, despite general consistency with trends, was slightly higher than WN3 at 2.6229, and the maximum I_V output deviation was the highest of any model at 0.30353. In addition, this model fails to consider incubation time of the virus, which we felt was an important feature.

Consequently model WN3, [4], was selected as the optimal predictor of real-world disease transmission for multi-species or unknown avian reservoir analysis. Its trends for modeling infected vector population were graphically consistent and it had the second lowest standard deviation at 0.12059, although this is still quite close to the mean value. Not only was this model consistent with the general trends of highest and lowest disease reproduction rates, but it most importantly also had the smallest standard deviation of R_0 at 2.3154. Its nature as a reservoir frequency dependent model also makes it a more believable model than WN2, [3]. Finally, this model accounts for all populations and all constants, which no other model in the study does.

5. The Human/Vector/Reservoir model

The model we construct here combines the vector-reservoir model of [4] with the human submodel in [1]. This hybrid model incorporates all three animal populations and effectively demonstrates transduction of the disease from bird to mosquito to human. The resulting box model is depicted in Figure 5.

The top section of the model is the transmission of West Nile virus between bird (reservoir) and mosquito (vector) while the bottom section is between mosquito and humans. These two schemes are connected by the

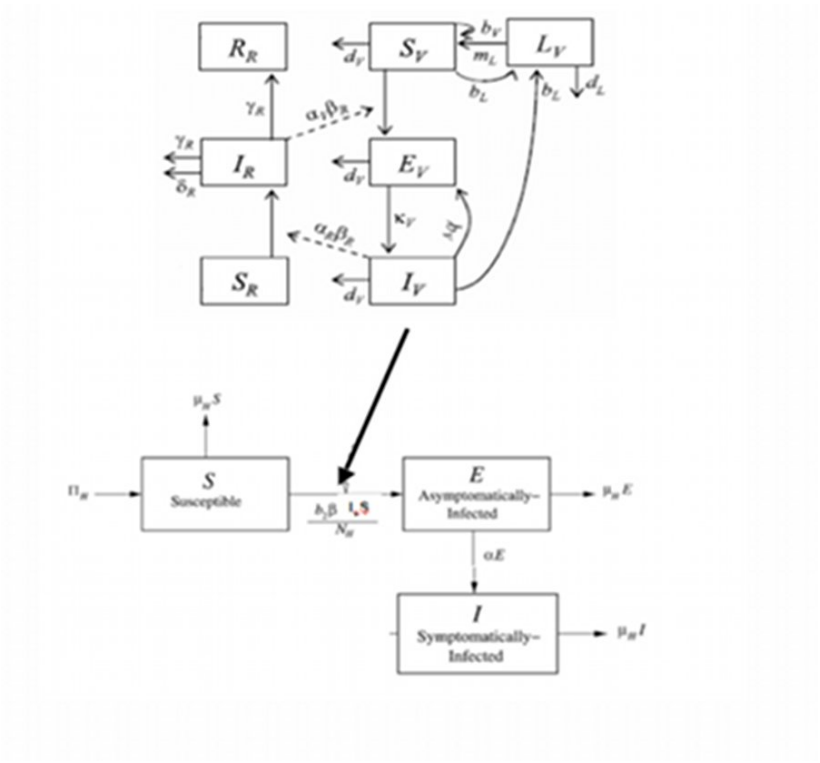

Figure 5. The box model for the full system based on WN3.

population of infected vector, which contracts the virus from the reservoirs and transmits it to humans. Quantities represented in Figure 5 include the populations of larval vector (L_V), susceptible vector (S_V), exposed vector (E_V), infected vector (I_V), susceptible reservoir (S_R), infected reservoir (I_R), recovered reservoir (R_R), susceptible human (S), asymptomatically infected human (E), and symptomatically infected human (I). The resulting system of equations is given here.

Change in larval vector = birth - (death and maturation)

$$\frac{dL_V}{dt} = b_L N_V - (m_L + d_L)L_V \tag{26}$$

Change in susceptible vector = -loss to exposed vectors + maturation - death

$$\frac{dS_V}{dt} = -\alpha_V \beta_R \frac{I_R}{N_R} S_V + m_L L_V - d_V S_V \tag{27}$$

Change in exposed vector =
gain from susceptible - progress to infection - death

$$\frac{dE_V}{dt} = \alpha_V \beta_R \frac{I_R}{N_R} S_V - (\kappa_V + d_V) E_V \tag{28}$$

Change in infected vectors = gain from exposed - death

$$\frac{dI_V}{dt} = \kappa_V E_V - d_V I_V \tag{29}$$

Change in susceptible reservoir = loss due to infection

$$\frac{dS_R}{dt} = -\alpha_R \beta_R \frac{S_R}{N_R} I_V \tag{30}$$

Change in infected reservoir = gain from infection - loss due to recovery or death

$$\frac{dI_R}{dt} = \alpha_R \beta_R \frac{S_R}{N_R} I_V - (\delta_R + \gamma_R) I_R \tag{31}$$

Change in recovered reservoir = gain from recovery of infected individuals

$$\frac{dR_R}{dt} = \gamma_R I_R \tag{32}$$

Change in susceptible humans = -loss due to infection - death

$$\frac{dS}{dt} = -\frac{b_2 \beta_3 I_V S}{N_H} - \mu_H S \tag{33}$$

Change in asymptomatic humans = gain due to infection - death - progression to symptomatic

$$\frac{dE}{dt} = \frac{b_2 \beta_3 I_V S}{N_H} - \mu_H E - \alpha E \tag{34}$$

Change in symptomatic humans = progression to symptomatic - death

$$\frac{dI}{dt} = \alpha E - \mu_H I \tag{35}$$

All of the parameters for vector/reservoir dynamics remain the same as in Section 3. The American Crow was determined to be the most lethal reservoir with the highest transmission rate and constants representing death and recovery for this reservoir were therefore used in our analysis to determine potential human epidemic.

Another set of constants describing the transmission terms between vector and human are reported by Bowman, [1] and are found in Table 4.

Table 4. Constants for vector and human transmission

Parameter	Description	Value
$1/\mu H$ Average human lifespan (days)	70*365	
b_2	Bite rate of humans by mosquitoes per day	0.09
β_3	Probability of mosquito/human transmission per bite	0.88
$1/\alpha$	Incubation period (days)	14
δ	Hospitalization rate (days)	1

A typical output for this system is given in Figure 6.

6. Control of an outbreak through spraying

The analysis was modeled after the New York City outbreak in 1999 in which the disease was carried into the population by bird reservoirs that had migrated to the location. In the model, therefore, the infected reservoir has a small nonzero initial population whereas the infected vectors and infected humans start at zero. The recruitment rate of the susceptible human population was set to zero, reflecting the short time frame of an outbreak. The output allowed a determination of the population curves for all subpopulations and, of interest, the infected reservoir, infected mosquito, and infected human populations.

These trends were then used in the second part of the analysis to determine the effectiveness of prevention techniques. The model focuses on insecticide spraying of adult mosquitoes, which stems from actual treatment used in New York City in 1999 and Sacramento in 2005. These massive sprayings of Pyrethrin, a biodegradable, organic insecticide, were conducted over large masses of urban land and carried out as one-time treatment events

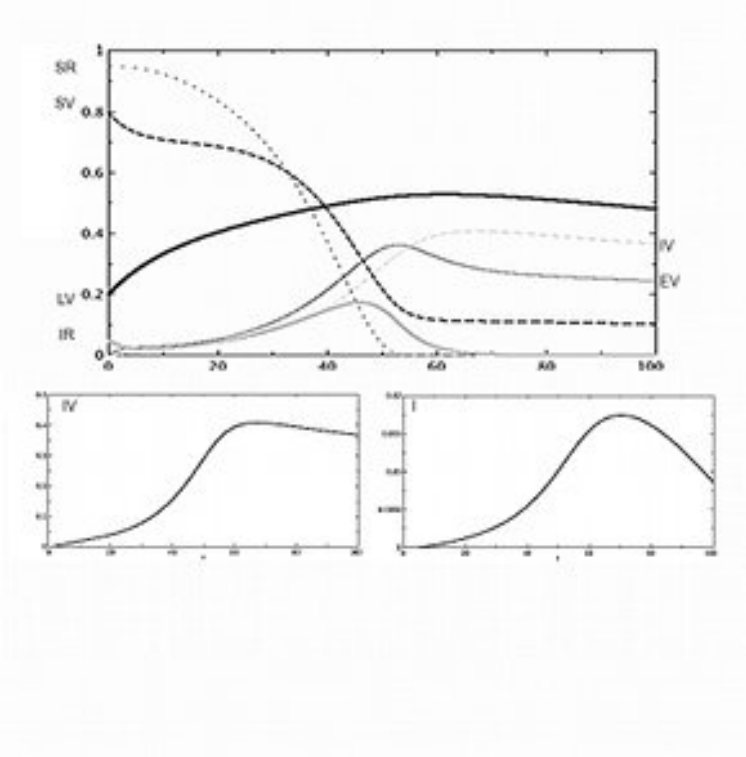

Figure 6. The full vector/reservoir/human model for American Crow parameters. The top graph is the vector/reservoir submodel. The lower left (IV) is the proportion of mosquitoes infected. The lower right (I) is infected humans.

[6]. The effects of insecticide persist for a while after spraying, so in this study we incorporate a continuous proportional mortality rate from spraying, varying the mortality rate and the timing of the start of spraying with reference to the disease cycle.

In one treatment, the insecticide concentration killed 30% of the vectors per day while the in the other, it killed 70% of the vectors per day. The two concentrations of insecticide are sprayed at 20 days and at 40 days, when the number of cases is rising as well as at 60 days, the peak of human cases (visible in Figure 6). 20 days represents a scenario in which insectide was immediately sprayed after the first WNV cases were confirmed because the CDC reports that it takes a minimum of 20 days to confirm WNV [7]. Combined, these trials allowed a determination of insecticide concentration

and timing in order to maximize effect in decreasing human transmission of the virus while minimizing the use of insecticide.

The spraying trials were conducted by first running a normal transmission cycle. The populations for all relevant species were then determined at the target time for spraying (20, 40, or 60 days). These populations were taken and used as the initial conditions for the subsequent insecticide prevention trials. The spray was incorporated into the model by adding a term to the adult vector populations (S_V, E_V, and I_V), which either expressed 30% killing ($-0.3I_V$) or 70% killing $-0.7I_V$. The trials were restarted with the additional term and the change in infected vectors and infected humans was noted. Table 5 shows the results of these numerical experiments.

Table 5. Effect of Different Prevention Strategies on Infected Vector and Human Populations

Time of spraying	Kill rate	maximum % infected vector	Time of peak IV	maximum % infected human	Time of peak I
n.a.	none	41%	67 days	1.7 %	70 days
20	30%	4.6%	20 days	.14 %	25 days
20	70%	4.5%	20 days	.13 %	22 days
40	30%	14%	40 days	.58 %	44 days
40	70%	14%	40 days	.56 %	42 days
60	30%	40%	60 days	1.5 %	62 days
60	70%	40%	60 days	1.5 %	61 days

7. Discussion

The first trials tested infected vector and symptomatic humans in a population exposed to infected West Nile reservoirs. As seen in Figure 6, infected vector population reaches 41% of total vectors and then levels off to a predicted equilibrium state. This population of infected vectors is very high and leads to a peak of 1.7% of humans showing West Nile virus symptoms. In NYC, with a population of 10 million, this would signify adverse effects in 170,000 people. The peak of symptomatic humans (70 days) also comes after the peak of infected vectors (67 days) confirming the transmission scheme of reservoirs to vectors to humans. With symptomatic populations reaching epidemic levels, the insecticides were implemented to reduce virus transmission.

To determine the effect of spray concentrations, insecticide quantities

were used that would either kill 30% of existing vectors or 70% of existing vectors at the time of spraying. When comparing 30% and 70% spray concentrations within the same spray time, the infected vectors did indeed decrease at a faster rate with higher concentration of insecticide. However, the effect that this vector death rate had on the symptomatic human population was of little significance. For example, at the 20 day spray time, the 30% insecticide concentration led to a peak of .14% symptomatic humans while the 70% insecticide concentration led to a peak of .13% symptomatic humans. These small differences in human populations between spray concentrations were also seen in the 40 day and 60 day trials. Therefore, the concentration of insecticide does not greatly effect the variation in human epidemic and can thus be reduced to amounts that will not adversely effect the environment.

To determine the effect of the time at which insecticide was sprayed over the course of human infection trends, spraying was started at either 20, 40, or 60 days after introduction of the virus to the population via infected reservoirs. In contrast to the spray concentration results, the time of insecticide spraying had a significant effect on symptomatic human populations. The 20 day trials represent spraying at the first sign of human infection. When sprayed at this time, the insecticide reduced infected vectors to zero within 20 days and reduced symptomatic humans to a peak of .14%, down from 1.7% without spray. The 40 day spray time was chosen as a midway point between the first symptomatic human showing and the peak of symptomatic humans in the no spray trial. While this trial reduced the peak of symptomatic humans from the no spray trial to .58%, it did not reduce the epidemic as much as the 20 day trial. Lastly, the 60 day trial, which occurred at the peak of symptomatic humans in the no spray trial had the least effect in reducing symptomatic human populations. It left a peak of 1.5%, which was almost equivalent to the original symptomatic human population. These results demonstrate that the timing of the spray is critical to its effectiveness in reducing human disease. Although all spray times reduce the infected vector to zero, the earlier the spray the more it prevents virus transmission to the human population. Our results show that the effect of insecticide depends far more on the early application of spray than on the amount of pesticide used. A concentration of insecticide that reduces 30% of adult mosquitoes at 20 days after the first symptomatic humans are identified is sufficient to reduce the maximum number of human infections by over 90%. It takes approximately 20 days for the CDC to confirm West Nile virus. This model suggests that large urban areas begin

preparing to spray as soon as they suspect the first WNV cases, and spray as soon as they are confirmed. During this waiting period, health professionals in the area should be advised to closely monitor the population for West Nile symptoms. Our data shows that this early mosquito reduction is crucial in preventing an epidemic of WNV in humans. We also note that a 30% reduction rather than 70% since 70% reduction does not result in significantly fewer symptomatic humans.

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