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**Cover Page Footnote**
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# Modeling the Effects of Water Treatment & Removal in Controlling Yellow Fever

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**Abstract**

In 1878, thousands in Memphis were killed during an outbreak of yellow fever, a viral hemorrhagic fever transmitted by the *Aedes aegypti* mosquito, which has affected regions including North and South America, Europe, Africa, and the Caribbean. This disease still affects individuals in Africa and Central and South America. We have developed a mathematical model consisting of nine ordinary differential equations which describe the dynamics of the human and mosquito populations during a yellow fever epidemic. Our model investigates the effects that treatment and removal of standing water have on a mosquito population and consequently a yellow fever epidemic. We have examined the stability of the disease-free equilibrium and the conditions under which the disease-free equilibrium is stable.

**Keywords:** SEIR model, *Aedes aegypti*, pest eradication, Yellow Fever, water treatment and removal

## 1 Introduction

In the late 1800s, Memphis acquired the reputation of being the center of disease and death. One factor that heavily contributed to this reputation was the poor sanitation conditions in the city [10]. The World Health Organization (WHO) refers to sanitation as the procurement of facilities and services for safe disposal of human urine, feces, and wastewater [28]. During the 1800s, Memphis, like many other urban cities, did not have proper or adequate wastewater disposal. This caused a deficit of fresh water and led to the accumulation of standing water. Consequently, diseases spread rampantly through Memphis. Memphis experienced outbreaks of yellow fever and Asiatic cholera that caused thousands of deaths from 1830–1880 [10]. The most notable outbreak was the yellow fever epidemic in 1878. The first death due to yellow fever during the 1878 epidemic occurred in mid-July, and shortly there after individuals who were capable of leaving escaped the epidemic before it gripped the region [7]. Of the initial population of 47,000, around 25,000 fled and approximately 22,000 remained; approximately 20% of the population that remained in Memphis died [16]. At the time, scientists and residents of Memphis did not understand that yellow fever was transmitted by the *Aedes aegypti* mosquito.

Currently, the transmission of yellow fever by *Aedes aegypti* mosquitoes remains a public health concern with sporadic outbreaks occurring in populations where resources are constrained and vaccines are limited or unavailable [13]. *Aedes aegypti* mosquitoes are ubiquitous in populated areas of the subtropics and tropics with warm and humid climates. They can be found in settings ranging from small rural villages to megacities. In both rural villages and megacities, there exists a wide range of natural and artificial water-holding containers, both in and around human dwellings, that are used as sites for oviposition of eggs and development of immature mosquitoes [18]. The lack of wastewater disposal in Memphis in 1878 allowed for many pools of standing water that served as breeding sites for *Aedes aegypti*. Mosquito eggs are laid in clusters on the surface of water and can hatch into larvae within 48 hours [8]. The larval stage occurs in aquatic environments where the larvae moves from the subsurface of its aquatic environment and filter feeds on microorganisms [23]. The larvae prefer shallow water containers such as water tanks, tires, vases, and roof gutters in order to mature to adult mosquitoes [23]. Because standing water plays a critical role in the growth and development of mosquito larvae and eggs, one efficient and effective way to control the mosquito population is to reduce the amount of standing water, thus diminishing the breeding sites used by female mosquitoes and resulting in a decline in the total population of mosquitoes.

The treatment of standing water involves the application of insecticides into mosquitoes' breeding sites, however these insecticides have limitations. For example, temephos is an organophosphate insecticide that is extremely effective against mosquito larvae, but has lead to insecticide resistance in many populations where yellow

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fever and dengue fever remain endemic [19]. Additionally, *Bacillus thuringiensis israelensis* (*Bti*) is a microbial insecticide that produces protein toxins which are highly toxic to mosquito larvae after ingestion, but are not as effective from the late larval stage onwards, as adult mosquitoes are not exposed to large quantities of *Bti* [17].

Within a mosquito population, only the females consume blood meals. When a female mosquito consumes a blood meal, she inserts her proboscis into the host's skin. If the female mosquito is infectious with yellow fever, the host may contract yellow fever through the infectious proboscis's residue [7]. During the intrinsic incubation period, the virus is present in human blood, and the human host is asymptomatic and non-infectious; this period ranges from 2.3 to 8.6 days [15]. A female mosquito can become infected with yellow fever by consuming a blood meal from an infected host. The extrinsic incubation period is the length of time that the virus is present in mosquitoes before it can be transmitted to a susceptible human; this period ranges from 2 to 37 days [15].

In this paper we develop a novel ordinary differential equation model simulating the use of water treatment and removal as means of control of a mosquito population and thus limiting the cumulative infections and deaths of a potential outbreak of yellow fever. We first present a simple model of the females of a mosquito population as they mature from eggs to larvae to adults. We then expand this model to include the transmission dynamics of yellow fever between the females of a mosquito population and a human population. Using data from the Memphis 1878 yellow fever epidemic, we determine transmission rates to parameterize the epidemic model. We derive stability conditions for the disease-free equilibrium of the epidemic model to infer the conditions under which mosquito control through water treatment and removal will result in a stable disease-free steady state. Lastly, we use uncertainty analysis to determine the range of possible outbreak control through varying levels of water treatment and removal.

# 2 Mathematical Model

In epidemiology, mathematical models are used to model the dynamics of the transmission of infectious diseases. The most basic models divide a population into those susceptible to the disease and those infected with the disease and model the rates at which individuals move between theses states. In a $SEIR$ model, a population is divided into four states: susceptible, $S$; exposed but not yet infectious, $E$; infectious and symptomatic, $I$; and recovered, $R$, in which an individual has either been vaccinated or developed an immunity to the disease after being infected.

We modify the *SEIR* model to include both human and mosquito populations. The human population is divided in to four states: susceptible, $S_H$; exposed but not yet infectious, $E_H$; infectious and symptomatic, $I_H$; and recovered and immune, $R_H$. The adult female mosquito population is divided into three states: susceptible, $S_M$; exposed but not yet infectious, $E_M$; and infectious and symptomatic, $I_M$. It is important to note that mosquitoes in the exposed state have come into contact with the virus via human blood, but are not able to spread the disease. After the incubation period, mosquitoes enter the infectious state and are able to spread the virus to humans. There is no recovered state since female mosquitoes remain infected with the virus for the duration of their lives. Since the treatment and removal of standing water can reduce a mosquito population by impacting the egg and larval stages as well as the adult stage, we include two additional female mosquito states: unhatched eggs, $U_M$; and larvae, $L_M$. See [25] for a study which constructs a similar model to simulate a chikunguya outbreak in rural Cambodia.

## 2.1 Mosquito Model

Before examining the the full model, we consider a model of the female mosquito population in the absence of yellow fever; we refer to this as the "mosquito model". Female mosquitoes are the only mosquitoes included in the model, as they are the only ones who consume blood meals. The mosquito model simulates the female mosquito egg ($U_M$), larvae ($L_M$), and adult ($S_M$) populations. Since this model does not include an epidemic, the exposed and infectious adult states are not included. A flow diagram of this model can be seen in Figure 1a. The mosquito model is given by the equations

$$U_M' = \tau(1-\omega)(1-\eta)S_M - \gamma U_M \tag{1.1}$$
$$L_M' = (1-\phi)(1-\omega)\gamma\rho_U U_M - \alpha L_M \tag{1.2}$$
$$S_M' = (1-\theta)(1-\omega)\alpha\rho_L L_M - \mu_M S_M, \tag{1.3}$$

where $\tau$ is a density dependent birth rate of female mosquitoes, $\rho_U$ is the proportion of female eggs that naturally survive to become larvae, $\rho_L$ is the proportion of female larvae that naturally survive to become adults, $\gamma$ is the rate of maturation from egg to larvae, $\alpha$ is the rate of maturation from larvae to adult, and $\mu_M$ is the natural death rate of female adult mosquitoes. The parameters $\eta$, $\theta$, and $\phi$ represent the treatment of standing water. The parameter $\eta$ represents the number of eggs that cannot be laid due to the treatment of water. The parameter $\phi$ represents the number of eggs that die once they are laid due to the treatment of water. The parameter $\theta$ represents the number of larvae that do not mature to adults due to the treatment of water. The parameter $\omega$ represents the proportion of standing water that is removed

and therefore the proportion of eggs, larvae, and adults that die due to inviable breeding sites. See Table 1 for full descriptions and parameter values.

### 2.2 Epidemic Model

In the epidemic model, the dynamics of the yellow fever virus are modeled by considering both host (human) and vector (mosquito) populations as shown in Figure 1b. In the epidemic model, we denote the human population size by $N_H$. The human population consists of four states: susceptible, $S_H$; exposed but not infectious or symptomatic, $E_H$; infectious and symptomatic, $I_H$; and recovered, $R_H$. The recovered state, $R_H$, denotes individuals that have recovered from the disease and are immune to infection, but does not include deceased. Due to the fact that only adult female mosquitoes consume blood meals from humans, the male mosquito population is not considered in this model. The total female mosquito population is denoted by $N_M$. Susceptible individuals can only become infected by an infectious female mosquito. The adult female mosquito population is divided into susceptible, $S_M$; exposed but not infectious, $E_M$; and infectious, $I_M$. During the exposed stage, a female mosquito cannot transmit the virus. The differential equations for the epidemic model are given by

$$S_H' = -\beta_H S_H I_M \tag{2.1}$$
$$E_H' = \beta_H S_H I_M - \kappa_H E_H \tag{2.2}$$
$$I_H' = \kappa_H E_H - \nu I_H \tag{2.3}$$
$$R_H' = (1-\delta)\nu I_H \tag{2.4}$$
$$U_M' = \tau(1-\omega)(1-\eta)(S_M + E_M + I_M) - \gamma U_M \tag{2.5}$$
$$L_M' = (1-\phi)(1-\omega)\gamma\rho_U U_M - \alpha L_M \tag{2.6}$$
$$S_M' = (1-\theta)(1-\omega)\alpha\rho_L L_M - (\beta_M I_H - \mu_M)S_M \tag{2.7}$$
$$E_M' = \beta_M S_M I_H - \kappa_M E_M - \mu_M E_M \tag{2.8}$$
$$I_M' = \kappa_M E_M - \mu_M I_M, \tag{2.9}$$

where all parameters from System (1) are the same, $\beta_H$ and $\beta_M$ are the transmission rates between mosquitoes and humans, $\kappa_H$ and $\kappa_M$ are the intrinsic and extrinsic incubation periods, respectively, $\nu$ is the recovery rate (in humans), and $\delta$ is the proportion of infectious humans who die due to yellow fever. Since the time frame for a yellow fever outbreak is relatively small when compared to the typical life span of a human, the natural birth and death rates of the human population are negligible and thus not included in this model. See Table 1 for full descriptions and parameter values.

## 3 Parameter Estimation

Most of the parameters describing the dynamics of how humans and mosquitoes transition between states were taken from scientific literature (see Table 1 for sources). To find the rates of transmission of the yellow fever virus between humans and mosquitoes we used known data from the Memphis 1878 epidemic [16] to estimate the values of $\beta_H$ and $\beta_M$. Using the same method for parameter estimation as described in [4], we used Latin Hypercube Sampling (LHS) to sample $\beta_H$ and $\beta_M$ over a range of values generating 1,000 unique parameter combinations without replacement. We then simulated the epidemic model, System (2), for each parameter set using known parameter values, assuming no mosquito control measures were used (i.e., $\eta = \phi = \theta = \omega = 0$), and using initial conditions $S_H(0) = 17{,}000$, $E_H(0) = 0$, $I_H(0) = 2$, $R_H(0) = 5{,}000$, $U_M(0) = 200{,}000$, $L_M(0) = 200{,}000$, $S_M(0) = 950{,}000$, $E_M(0) = 0$, and $I_M(0) = 0$. The model solution for each of the 1,000 parameter sets was used to calculate the number of deaths due to yellow fever that occurred on each day of the epidemic. We selected the parameter combination $(\beta_H, \beta_M)$ that minimized the square root of the residual sum of squares per data point [1]

$$\text{error} = \frac{1}{n}\sqrt{\sum_{t\in\mathbf{T}}\left(D_t - \hat{D}_t\right)^2}, \tag{3}$$

where $D_t$ is the number of deaths on day $t$ of the epidemic as predicted by System (2), $\hat{D}_t$ is the number of deaths on day $t$ of the epidemic given by Memphis 1878 epidemic death records published in [16], $\mathbf{T}$ is the set of days for which data exists, and $n$ is the total number of data points.

The values of $\beta_H$ and $\beta_M$ that minimize the error defined by Equation (3) are given in Table 1. Here, only the parameter estimates are reported, and the confidence intervals are not included. Note, this method does not guarantee a unique minimum. The daily death count due to yellow fever generated by the solution to System (2) using the values of $\beta_H$ and $\beta_M$ given in Table 1 is shown in Figure 2.

## 4 Equilibrium Analysis

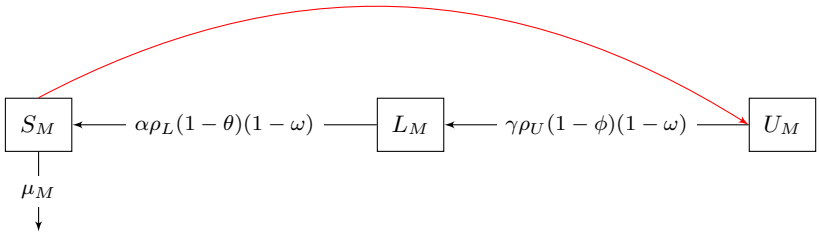
In the absence of yellow fever, the human and mosquito populations are decoupled. Therefore, at the disease-free equilibrium, we will analyze the stability of each population separately.

### 4.1 Mosquitoes

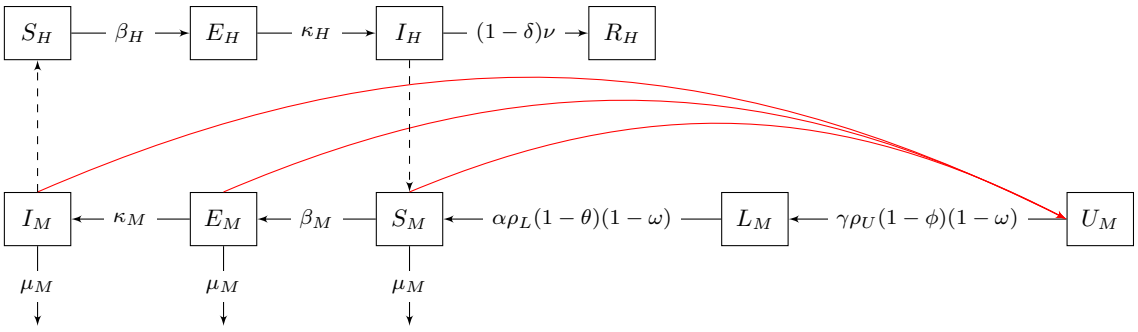
Let $U_M^*$, $L_M^*$, $S_M^*$, $E_M^*$, and $I_M^*$ be the size of the female egg, larvae, susceptible adult, exposed adult, and infectious adult mosquito populations at the disease-free equilibrium. Since the disease-free equilibrium represents the absence of yellow fever in the system, $E_M^* = I_M^* = 0$.

Table 1: Parameters for models given by Systems (1) and (2).

| | Parameter | Units | Value | Source | Definition |
|---|---|---|---|---|---|
| Humans | $\beta_H$ | $1/(\text{mosq} \cdot \text{days})$ | $5.18 \times 10^{-7}$ | Estimated | Transmission rate per infectious human contact |
| | $1/\kappa_H$ | days | 4.3 | [15] | Average time of incubation period in humans |
| | $1/\nu$ | days | 3.875 | [16] | Average time of recovery |
| | $\delta$ | – | 0.303 | [16] | Proportion of humans who die |
| Mosquitoes | $\beta_M$ | $1/(\text{ppl} \cdot \text{days})$ | 0.000075225 | Estimated | Transmission rate per infectious mosquito contact |
| | $1/\kappa_M$ | days | 10 | [15] | Average time of incubation period in mosquitoes |
| | $1/\gamma$ | days | 5.64 | [21] | Average time to maturation from eggs to larvae |
| | $1/\alpha$ | days | 13.54 | [21] | Average time of maturation from larvae to adults |
| | $1/\mu_M$ | days | 33 | [29] | Average life span of adult female mosquitoes |
| | $\rho_U$ | – | 0.195 | [24] | Proportion eggs that naturally survive to larvae |
| | $\rho_L$ | – | 0.861 | [24] | Proportion of larvae that naturally survive to adults |
| | $\tau$ | 1/days | $\frac{\mu_M}{\rho_U \rho_L}$ | | Density dependent birth rate of mosquitoes |
| Mosquito Control | $\eta$ | – | 0–0.70 | | Proportion of eggs made inviable due to the treatment of standing water |
| | $\phi$ | – | 0–0.70 | | Proportion of mosquito eggs that die due to the treatment of standing water |
| | $\theta$ | – | 0–0.70 | | Proportion of mosquito larvae that die due to the treatment of standing water |
| | $\omega$ | – | 0–0.65 | | Proportion of standing water that is removed |




(a) Mosquito Model




(b) Epidemic Model

Figure 1: Flow diagrams for the mosquito and epidemic models, Systems (1) and (2), respectively. Solid lines represent movement from one state to another, while dashed lines represent interactions between populations. The red lines represent the birth rate of the adult mosquito classes, which depend on the presence and condition of water.

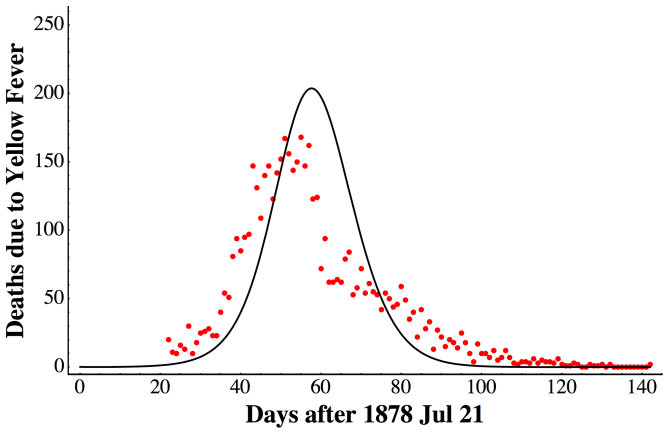



Figure 2: Daily deaths due to yellow fever during the Memphis 1878 epidemic as reported in [16] (points) and predicted by System (2) given the parameter combination $(\beta_H, \beta_M)$ that minimize the error defined in Equation (3) (curve).

The values of $U_M^*$, $L_M^*$, and $S_M^*$ depend on the initial conditions $U_M(0)$, $L_M(0)$, and $S_M(0)$, and thus cannot be expressed solely as functions of parameter values. However, at the disease-free equilibrium, the proportion of each mosquito state with respect to the total mosquito population

$$N_M^* = U_M^* + L_M^* + S_M^* + E_M^* + I_M^*$$

is independent of initial conditions, specifically

$$\frac{U_M^*}{N_M^*} = \frac{\alpha\tau(1-\omega)(1-\eta)}{\alpha\gamma + \tau(1-\omega)(1-\eta)[\alpha + \gamma(1-\phi)(1-\omega)\rho_U]}$$
$$\frac{L_M^*}{N_M^*} = \frac{\gamma\tau(1-\eta)(1-\phi)(1-\omega)^2\rho_U}{\alpha\gamma + \tau(1-\omega)(1-\eta)[\alpha + \gamma(1-\phi)(1-\omega)\rho_U]}$$
$$\frac{S_M^*}{N_M^*} = \frac{\alpha\gamma}{\alpha\gamma + \tau(1-\omega)(1-\eta)[\alpha + \gamma(1-\phi)(1-\omega)\rho_U]}.$$

In the absence of the treatment or removal of standing water (i.e., $\eta = \phi = \theta = \omega = 0$), the disease-free equilibrium has $S_M^*, U_M^*, L_M^* > 0$ (i.e, the mosquito population approaches a positive steady state) when

$$\tau = \frac{\mu_M}{\rho_U \rho_L}. \tag{4}$$

When mosquito control measures are used (specifically, if either $\theta > 0$ or $\phi > 0$ or $\omega > 0$ or $\eta > 0$), then the disease-free equilibrium with $S_M^* = U_M^* = L_M^* = 0$ (i.e., the extinction of the mosquito population) is stable when

$$\tau < \frac{\mu_M}{\rho_U \rho_L (1-\eta)(1-\theta)(1-\phi)(1-\omega)^3}. \tag{5}$$

Note that since $\theta, \phi, \omega, \eta \in [0, 1]$, when comparing Conditions (4) and (5),

$$\frac{\mu_M}{\rho_U \rho_L} \leq \frac{\mu_M}{\rho_U \rho_L (1-\eta)(1-\theta)(1-\phi)(1-\omega)^3}.$$

Thus, when mosquito control measures are used the mosquito extinction equilibrium is stable even when the density dependent birth rate of mosquitoes ($\tau$) is somewhat larger than the mosquito birth rate that makes the positive mosquito steady state stable in the absence of mosquito controls measures, i.e., Equation (4).

### 4.2 Humans

Let $S_H^*$, $E_H^*$, $I_H^*$, and $R_H^*$ be the size of the susceptible, exposed, infectious, and recovered human populations at the disease-free equilibrium, and let

$$N_H^* = S_H^* + E_H^* + I_H^* + R_H^*.$$

Since the disease-free equilibrium represents the absence of yellow fever in the system, $E_H^* = I_H^* = 0$, and thus the population is divided into the susceptible and recovered classes, $S_H^* = qN_H^*$ and $R_H^* = (1-q)N_H^*$, where $q$ is the proportion of the human population that is susceptible.

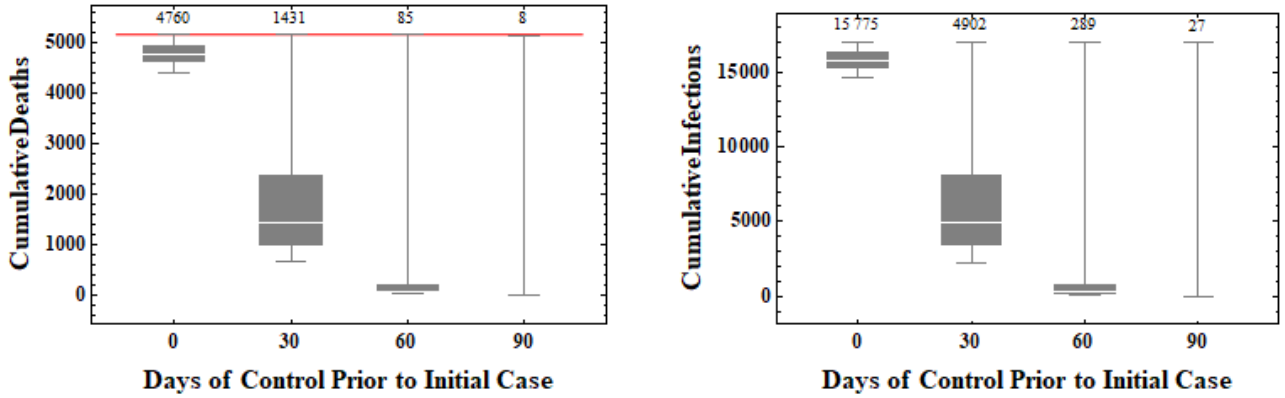
## 5 Methods

To measure the effectiveness of the treatment and removal of standing water in reducing the severity of a yellow fever outbreak, we calculated the cumulative deaths (CD) and cumulative infections (CI) that resulted from an epidemic started 0, 30, 60, and 90 days after the mosquito control measures were implemented where the model parameters otherwise approximated the 1878 Memphis epidemic. The cumulative deaths and infections are calculated as

$$\text{CD} = \int_0^{t_f} \delta\nu I_H dt \tag{6}$$

$$\text{CI} = \int_0^{t_f} \kappa_H E_H dt \tag{7}$$

where $t = 0$ corresponds to the day the first infected humans are introduced to the population, and $t_f = 142$, the length of the 1878 Memphis epidemic. To determine the range of the cumulative deaths and infections due to the variation of the mosquito control parameters ($\eta$, $\phi$, $\theta$, and $\omega$), Latin Hypercube Sampling (LHS) was used to sample the entire mosquito control parameter space generating 1,000 unique parameter combinations of $\eta$, $\phi$, $\theta$, and $\omega$. We sampled each mosquito control parameter from uniform distributions over the ranges given in Table 1. The model was then simulated for each parameter combination (using the values in Table 1 for all other parameters) with mosquito control being implemented for 0, 30, 60, and 90 days before the initial infected humans are introduced into the system; we will refer to these as the four different mosquito control implementation strategies.




(a) Cumulative Deaths at $t_f = 142$

(b) Cumulative Infections at $t_f = 142$

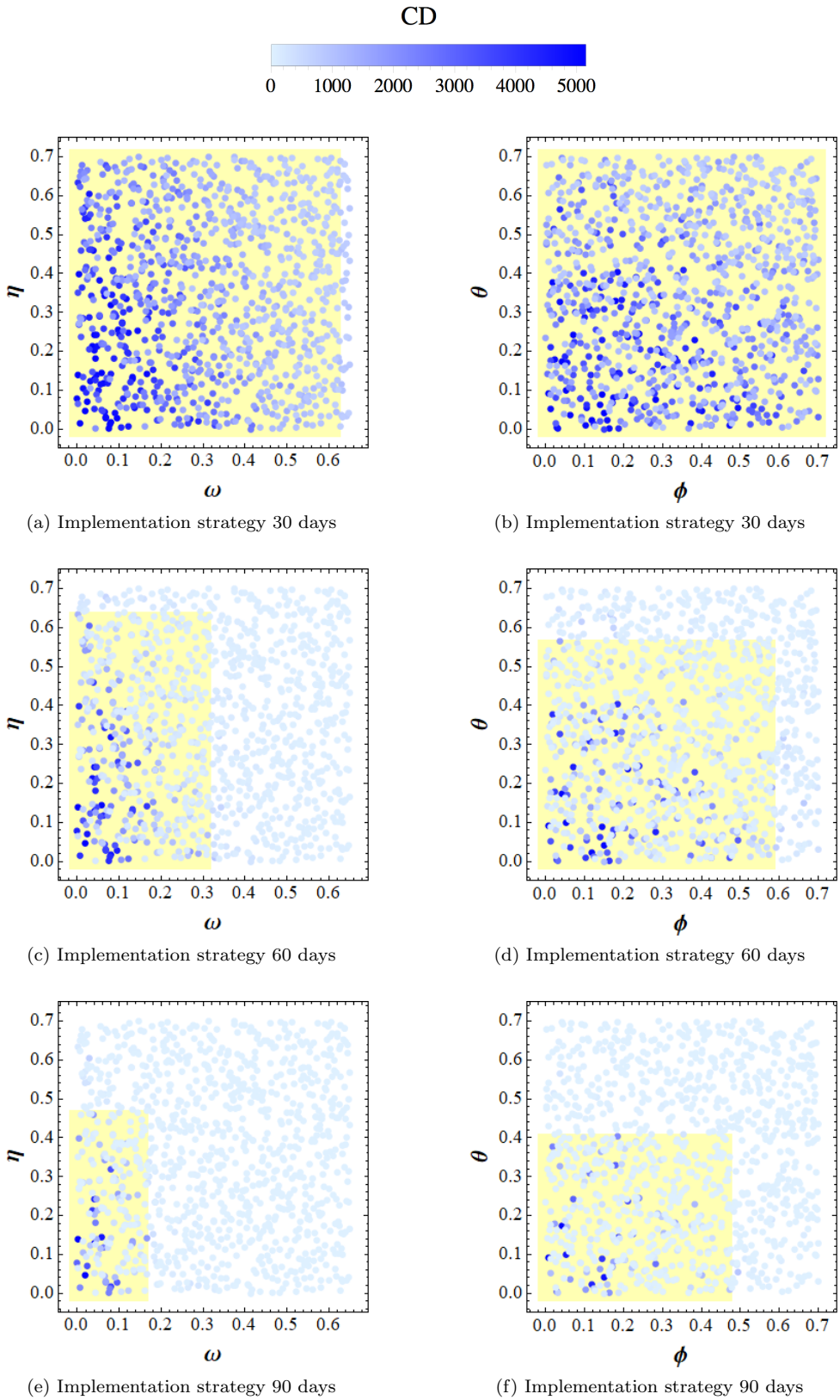
Figure 3: Range of cumulative deaths (a) and infections (b) resulting from varying control parameters $\eta$, $\phi$, $\theta$, and $\omega$ over the ranges given in Table 1 for each mosquito control implementation strategy. Whiskers show the full range, the box showing the interquartile range, and the white line showing the median. The value given at the top of each column show the median value for that column's implementation strategy. The red line in (a) shows the 5,150 deaths that occurred in the 1878 Memphis epidemic.

## 6 Results

The range of values for CD and CI for the 1,000 simulations for each implementation strategy are shown in Figure 3. Each box-and-whisker column shows the range of cumulative deaths (Figure 3a) and cumulative infections (Figure 3b) over all 1,000 simulations for a single mosquito control implementation strategy with the whiskers showing the full range, the box showing the interquartile range, and the white line showing the median. The value given at the top of each column shows the median value for that column's implementation strategy.

When the mosquito control strategy is implemented only at the start of the outbreak (i.e., there are 0 days of control prior to an initial human yellow fever case), the number of cumulative deaths and infections remain close to the values seen when no water treatment or removal is included in the simulation. As the length of time over which the water treatment and removal is allowed to occur prior to an initial case increases, the median number of cumulative deaths and infections drops. When the mosquito control strategies are implemented 90 days prior to the initial human yellow fever case, 50% of the 1,000 simulations resulted in 27 or fewer cumulative infections, and 8 or fewer cumulative deaths. However, even when water treatment and removal occurs for 90 days prior to the initial human yellow fever infection, there are still some mosquito control parameter sets which allow for numbers of cumulative deaths and infections at or near values seen when control is not included in the simulation.

Using the 1878 epidemic as a basis of comparison, we use uncertainty analysis to determine which parameter sets would correspond to large numbers of cumulative deaths for each mosquito control implementation strategy, we plotted points in the $(\eta, \phi, \theta, \omega)$ parameter space where the shading of each point scales with the value CD where 5,150 is the number of deaths due to yellow fever that occurred in the 1878 Memphis epidemic (see Figure 4). The values are scaled such that darker values are closer to 5,150 and lighter values are closer to zero. There was no simulation of an implementation strategy that resulted in more deaths then the 1878 outbreak. In each graph in Figure 4, lower values of the control parameters correspond to larger numbers of cumulative deaths, which is to be expected. Figures 4a, 4c, and 4e show that increasing $\omega$ is slightly more effective than $\eta$ in reducing the number of cumulative deaths by $t_f = 142$. This is also to be expected since $\omega$ corresponds to the removal of water which impacts all three age classes of the mosquito population: eggs, larvae, and adults. Specifically, when the mosquito control implementation strategy is in place for 90 days prior to the introduction of an infected human, values of $\omega$ above 0.3 always result in less than 125 cumulative deaths (see Figure 4e). In contrast, for the same mosquito control implementation strategy there are parameter combinations with $\eta > 0.5$ resulting in more than 650 cumulative deaths; and parameter combinations with $\phi > 0.5$ or $\theta > 0.5$ resulting in more than 200 cumulative deaths (see Figures 4e and 4f).




(a) Implementation strategy 30 days

(b) Implementation strategy 30 days

(c) Implementation strategy 60 days

(d) Implementation strategy 60 days

(e) Implementation strategy 90 days

(f) Implementation strategy 90 days

Figure 4: The effects of $\eta$, $\omega$, $\phi$, and $\theta$ on cumulative deaths (CD) given mosquito control implementation strategies of 30, 60, and 90 days. CD is the number of cumulative deaths at $t_f = 142$ calculated according to Equation (6).

# 7 Conclusion

From our results, it is evident that the treatment and removal of water has positive effects on reducing the amount of cumulative deaths and infections during a yellow fever epidemic. The longer these control measures are implemented prior to the epidemic, the greater effect they will have. By having the control measures set in place before the epidemic, it reduces the burden of disease by reducing the amount of mosquitoes able spread yellow fever. If you begin the mosquito control measures after the epidemic has begun, they will have minimal effect in controlling the outbreak. These measures are better utilized as preventative and should not be regarded as intervention measures. For best results, the control measures need to be implemented for a prolonged amount of time.

Our results show it would be best to implement the treatment and removal of water 60 days or more before an epidemic starts, since implementing the control measures 90 days before an epidemic only slightly improves the effects seen at 60 days. Furthermore, there is a practical and cost-saving advantage to implementing control measures over a shorter period of time. Since outbreaks are random in nature, our recommendation is to begin removal and treatment of water as temperatures become warmer, allowing the control measures to be in effect before any potential outbreak. This would effectively limit the vector population by reducing and eliminating many early developmental stages of mosquitoes that occur in aquatic environments. By removing and treating standing water, female mosquitoes are unable to lay their eggs and the eggs are unable to mature. This in turn would limit the cumulative deaths and infections caused by yellow fever or any other mosquito born pathogen.

The treatment and removal of water work best when implemented at the same time. However, our results show that even if at least one of the four control parameters is large, a significant reduction is still made on the number of deaths caused by an epidemic. One complication that arises with the treatment of water is that there are a variety of insecticides that can be used. Each insecticide targets a different life stage of the mosquito population. Therefore, choosing the most effective insecticide would require more time and resources due to a need for trial and error. The results of our sensitivity analysis aid in this decision. Our results show that controlling the proportion of eggs that mature to larvae and larvae that mature to adults through the treatment of water is more effective than controlling the proportion of eggs an adult mosquito is able to lay through the treatment of water.

In a case where time or resources are limited, it would be best to focus on the removal of water. This tactic ensures that the vector population is reduced both immediately and in the future, as removal directly impacts the number of existing eggs and larvae, and the number of eggs that can be laid in the future.

Continued investigations into this question might include comparing different parameters in the sensitivity analysis. We could also directly compare different time lines for the introduction of control measures including looking at introducing controls when an epidemic begins and after it has begun. Our next step in investigating the dynamics of a yellow fever epidemic will be to develop an agent-based model (ABM) using geographic information systems (GIS) data from the Memphis 1878 epidemic. This method of modeling allows us to investigate an epidemic with respect to both space and time, instead of being limited to just time as we are in this paper.

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