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A Comparison of Parametric Methods for Modeling Mosquito Survival Using Temperature and Age-Dependent Survival Data

Research Report in Mathematics, Number 11, 2018

Nyatuga Gideon Nyakundi

August 2018

Submitted to the School of Mathematics in partial fulfilment for a degree in Master of Science in Biometry

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Abstract

It is estimated that Malaria affects over 200million people every year, and accounts for about 750,000 deaths during the same period. The adult female Anopheles mosquito accounts for all transmissions of the human malaria pathogen, Plasmodium. The disease control measures often include interventions aimed at reducing the survival of the adult female Anopheles mosquitoes. Various factors such as temperature and age have been found to be associated with vector mortality. Whereas much effort has been paid to evaluate the effects on the vector survival, little research has been done on how temperature and time affect the vector adult life-history parameters.

The objective of the present study is to compare the performance of four parametric models, namely, Gompertz, gamma, Weibull, and exponential models to determine the best model for analyzing the survival of the female Anopheles mosquito. Using experimental data from a mosquito survival experiment, the present study compares the performance of the models in fitting mosquito mortality.

The results show that temperature and age are significant predictors of vector mortality. In addition, the Gompertz model fits the data on the adult *A. gambiae* and *A. stephensi* better than the Weibull, Gamma, and the Exponential model. This implies that the mosquito data survival in the laboratory is age-dependent. The findings of the present study are also useful in parameterizing reliable mathematical models that examine the potential impact of temperature as well as global warming on the transmission of malaria.

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Declaration and Approval

I the undersigned declare that this dissertation is my original work and to the best of my knowledge, it has not been submitted in support of an award of a degree in any other university or institution of learning.

Signature Date

NYATUGA GIDEON NYAKUNDI
Reg No. I56/82003/2015

In my capacity as a supervisor of the candidate's dissertation, I certify that this dissertation has my approval for submission.

Signature Date

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Dedication

This project is dedicated to my parents Elizaphan Nyakundi, and Joyce Nyarusa for the support they offered throughout my academic Journey.

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Nyatuga Gideon Nyakundi

Nairobi, 2018.

1 Introduction

1.1 Background

The adult female adult female Anopheles mosquito (*Anopheles gambiae sensu stricto*)plays a significant role in the transmission of vector diseases in Africa (Muriu et al., 2013). They are the sole vectors for the transmission of the human malaria pathogen, *Plasmodium*. Malaria is among the most significant infectious diseases globally, which is estimated to affect over 200 million people annually, and causes about 750,000 deaths annually (World Health Organization, 2010). The World Health Organization's 2017 Malaria report shows that in 2016, malaria cases increased to 216 million, while deaths reduced to 445,000. Significant research attention has been focused on how malaria can be reduced or eliminated. In this regard, the research focus has been on the interventions of the *Plasmodium* parasite in humans, as well as those designed to interrupt the transmission of the parasite by mosquitoes. The vector control measures have included interventions aimed at reducing the survival of the adult female Anopheles mosquitoes.

The survival of the adult female Anopheles mosquitoes is one of the most significant components of their ability to transmit vector-borne pathogens such as plasmodium virus (Patz et al., 2008). A high survival rate of the arthropod vectors allows the vectors to produce more offspring, which in turn increase their chances of becoming infected, spread over greater distances; survive for longer as well as improving their chances of delivering effective bites throughout their lifetime (Brady et al., 2013). According to Brady et al. (2013), small changes in the survival rates of the vectors often results in large pathogen transmission changes. In addition, the survival rate differences often influence the vector's geographical distribution as well as their seasonality.

An adult female *Anopheles gambiae sensu strict (Anopheles gambiae)* and *Anopheles stephensi* are the principal vector for the transmission of Malaria, a globally important infectious disease. Research interests in quantifying factors affecting the vector's survival rates and how the vector affects disease transmission have been considerable (Costantini et al., 1996; Okech et al., 2003). With the emergence of climate change and global warming as significant human health threats, particularly by increasing vector-borne diseases and water-borne diseases, it is logical that we observe temperature consistently as a key factor influencing the vector survival (Christiansen-Jucht et al., 2015). Studies on the survival of the vector have shown that mosquito survival depends on temperature, rainfall, and humidity, and other factors such as mosquito density, genetic diversity, as well as its ability to find blood (Gilles et al., 2011; Christiansen-Jucht et al., 2015; Muriu et al., 2013).

Brady et al. (2013) also noted other factors such as photoperiod as well as humidity are important, but the effects of temperature is the most rigorously quantified limiting factor for vector survival.

1.2 Mathematical Modeling

Mathematical modeling has proved to be an important tool for understanding disease epidemiology as well as the transmission dynamics associated with infectious diseases. Modeling efforts often help in targeting elimination efforts as well as predicting the outcome of the efforts through allowing an integration of the vector's complex biological mechanisms (Christiansen-Jucht et al., 2015). In studies investigating mosquito-borne diseases, mathematical modeling of the mosquito stages has helped in the researchers' efforts to assess the impact of interventions implemented at the vector's larvae and pupae stages, or helped in ascertaining the effects of external effects on the stages of the vector development.

Given the wide acceptance of climate change and global warming as key component affecting the spread of vector-borne diseases through their influences on the vector ecology, the most recent studies have sought to define the extent to which the life-history parameters of the vector, as well as the vectors' capacity to transmit diseases, depend on climatic variables. Other studies have even incorporated the role of climatic factors in modeling vector populations (Christiansen-Jucht et al., 2015).

1.3 Problem Statement

The vector population dynamics are particularly sensitive to the climatic and environmental factors such as temperature. While data exists on the survival and the effect of the larva environmental temperature on the survival of the adult Anopheles mosquitoes, little research has been done on how temperature and time affect the adult life-history parameters (Christiansen-Jucht et al., 2014). Observations from the few studies on age and temperature-dependent survival modeling have resulted in a range of parametric functions that are suitable for modeling age and temperature dependent mortality for various species. For Anopheles gambiae, the functions include the Gompertz and Logistic functions (Styer et al., 2007). However, there are limited studies comparing the efficacies of the parametric models. The study by Christiansen-Jucht et al. (2014) fitted the mosquito survivorship data using the Gompertz, gamma, Weibull, and exponential distribution functions using a longitudinal dataset of mosquito abundance obtained over a period of 36 months. Whereas Christiansen-Jucht et al. (2014) attempted to compare the efficacy of various parametric models in fitting mosquito survival data, the study is limited in the sense that it focuses on a single species (Anopheles gambiae s.s.). The present study overcomes this limitation by using data drawn from two species of mosquitoes, namely; *Anopheles gambiae*, and *Anopheles stephensi*.

1.4 Objectives

1.4.1 Main Objective

To compare the performance of four parametric models, namely, Gompertz, gamma, Weibull, and exponential models to determine the best model for analyzing the survival of the female Anopheles mosquito.

1.4.2 Specific Objectives

• To determine the contribution of temperature and age in determining the survival of the adult female Anopheles mosquito,

• To determine whether age-dependent models better fit mosquito survival data than the age-independent models.

1.5 Significance of the Study

The models investigated incorporated the effects of age-dependent mortality in predicting vector survival under varying temperature regimes. The study contributes to the understanding of the adult female Anopheles mosquito mortality by presenting a statistical solution to studies investigating the vector's age and temperature dependent survival. The findings from the current study will enhance the current Malaria vector transmission models and improve predictions guiding mosquito control, identification of areas prone to malaria transmission and help in designing early warning systems (Brady et al., 2013).

2 Literature Review

2.1 Malaria Disease

Malaria is a mosquito-borne infectious disease of humans that is caused by a parasitic protozoan of the genus Plasmodium (Rayner, 2015). The disease is commonly transmitted through bites of infected female mosquitoes, whereby the organisms are introduced into a person's blood circulatory system through the saliva of the infected mosquito. Research shows that after the infected mosquito bites a human, the parasite goes to the liver of the person, where it matures before beginning to reproduce (Rayner, 2015). After maturity, the parasites emerge from the liver and start infecting the human red blood cells. The parasites multiply after every 2 to 3 days, resulting in the death of the red blood cells and causing a range of many other complications.

Malaria is among the most significant health global health burdens associated with multi-organ dysfunction, socio-economic burden, as well as long-term incapacitation. It is estimated that over 3 billion people live in areas considered to be at high risk for malaria. With over 200 million malaria cases every year and 750,000 deaths annually (World Health Organization, 2010), the impact of the disease in Sub-Saharan Africa cannot be underestimated. The transmission of the disease is largely dependent on the life-history parameters and population dynamics of the mosquitoes. The survival of adult Anopheles mosquitoes is among the most significant determinants of malaria transmission.

2.2 Mosquito Survival Factors

Many environmental factors interact to influence the organismal development and survival of adult mosquitoes. These include temperature, larval diet and mosquito density (Couret, Dotson, and Benedict, 2014), rainfall and humidity (Rydzanicz, Kącki, and Jawień, 2011), the genetic diversity of the mosquitoes (Hoffman and Sgro, 2011), and their age (Dawes et al., 2009).

2.3 Factors Considered in Models Used in Research

The factors affecting the development and survival of adult mosquitoes have been examined using various statistical analysis methods. Some of the methods considered include simple random models (Costantini et al., 1996), ordinary differential equation models (Abiodun et al., 2016), generalized linear models (Gilles et al., 2011), generalized additive models (Brady et al., 2013), Cox regression model (Dawes et al., 2009).

2.3.1 Costantini et al. (1996)

the study by Costantini et al. (1996) focused on the survival, dispersal and density of the *Anopheles gambiae* species of mosquitoes found in a West African Sudan savanna village (Costantini et al., 1996). Simple random models of dispersal were applied to estimate the vectors' absolute population densities, dispersal parameters and daily survival rates. The models were simulated and the parameters of the models determined through the least squared fit between simulated and observed distributions (Costantini et al., 1996). The study established that the models are oversimplified and include rough guesses and estimates. As such, there was a need for detailed differences as well as the role of the factors in the vector survival.

2.3.2 Yang et al. (2008)

This study used a generalized additive model to examine the effect of temperature on the incidence rates of *Aedes aegypti* mosquito in temperature-controlled experiments (Yang et al., 2008). The model yielded a basic offspring number by obtaining the mortality, transition, and oviposition rates for the vector at different stages of the life cycle (Yang et al., 2008). The offspring number obtained increased up to 29°C and then decreases quickly. However, the model was not compared with other existing models, and it would not be possible to establish how the model compares with other models in modeling the fitting mosquito data.

2.3.3 Dawes et al. (2009)

This study examined the factors of age and *Plasmodium* density and argued that the survival of mosquitoes is dependent on both age and infection intensity dependent (Dawes et al., 2009). Using a Cox regression model, and the authors demonstrated that mosquitoes initially experience high mortality rates, which is associated with feeding. However, the mortality rate declines to a minimum before increasing with the mosquitoes' age. The mosquito survivorship was explored using the Weibull function, Gompertz function, and the constant death rate (Exponential function). Dawes et al. (2009) determined that each of the models applied singly were not adequate to describe the mortality rates experienced by mosquitoes in the experiments presented (Dawes et al., 2009).

2.3.4 Gilles et al. (2011)

Gilles et al. (2011) examined the effect of mosquito density, and diet effects on mosquito survival. The authors analyzed the differences in developmental time and survival using a generalized linear model (GLM), with diet and larval density as the fixed factors and the experiment as the random factor (Gilles et al., 2011). The findings of the study indicated a negative density dependence of survival as a function of increased larval density (Gilles et al., 2011).

2.3.5 Abiodun et al. (2016)

The study examined how temperature and rainfall affected the population dynamics of mosquitoes (Abiodun et al., 2016). The authors developed a climate-based ordinary differential equation model, which they used to analyze how temperature and water availability influence the mosquito population size (Abiodun et al., 2016). The model produced a curve similar to the observed larvae populations. However, the authors indicated that the model needed further development to incorporate other processes, among them, malaria infection.

2.3.6 Brady et al. (2013)

Brady et al. (2013) also modeled the survival of the adult *Aedes albopiticus* and *Aedes aegypti* mosquitoes at different temperature in both field and laboratory settings. They applied generalized additive models to data from 351 published adult *Aedes aegypti* and *Aedes albopiticus* experiments in laboratory settings to create models, which were adjusted to estimate mosquito survival at different temperatures in the field (Brady et al., 2013). Additionally, the study tested the suitability of four parametric models, namely the log-logistic model, Gompertz model, Exponential model, and Weibull model, and established that no single model was consistently most suitable across a range of temperatures tested ((Brady et al., 2013). The study indicated that the GAM captured the survival variation between various experiments better than the conventional parametric models (Brady et al., 2013).

2.3.7 Christiansen-Jucht et al. (2014)

The study by Christiansen-Jucht et al. (2014) examined the impact of the constantly fluctuating temperature on the survival of the adult Anopheles gambiae s.s. mosquito. The mosquito larvae and adult experimental data were analyzed using exponential, gamma, Weibull, and Gompertz models. The Gompertz model emerged as a better model since it fitted the data better than the other parametric models in 10 of the 16 scenarios of temperature considered, and was not significantly worse compared to the model of best fit in two other cases (Christiansen-Jucht et al., 2014).

2.3.8 Brand, Rock, and Keeling (2016)

Brand et al. (2016) successfully used the exponential model to examine the relationship between the vector life history and its survival in vector-borne disease transmission and control. The study is based on the classical McDonald theory, which assumes that times between vector blood meals are exponentially distributed. Based on the predictions of the model, the study established a strong dependence between the variations in vector per-capita mortality and details of vector life-cycle.

2.3.9 Styer et al. (2007)

Styer et al. (2007) examined the effect of age on the survivorship of vectors. The acceptance of the operational assumption often perpetuated that the vector mortality is independent of age may result in erroneous conclusions that the age of the mosquitoes is not important, which may result in misleading predictions about disease reductions after the implementation of control measures, as well as repress the study of other aspects of the mosquito biology. The ability to accurately predict vectorial capacity based on the large-scale mortality study was assessed for the exponential model, the Gompertz model, and the logistic model. The findings indicated that the three models differed as the exponential model caused the total vectorial capacity to be overestimated by 29-44 percent. The Gompertz model performed better than the exponential model with possible vectorial capacity overestimation of between 5 and 7 percent, while the logistic model performed the best, producing an error rate of less than 1 percent.

2.3.10 Summary

From the literature above, it emerges that prior studies on the factors influencing mosquito population dynamics have largely relied on non-parametric methods and semi-parametric regression models. While data exists on parametric survival models, little research has been done on how temperature and age affect the adult life-history parameters. Whereas Christiansen-Jucht et al. (2014) attempted to compare the efficacy of various parametric models in fitting mosquito survival data, the study is limited in the sense that it focuses on a single species (Anopheles gambiae s.s.). The present study overcomes this limitation by using data drawn from two species of mosquitoes, namely; *Anopheles gambiae*, and *Anopheles stephensi*.

Table 1. Summary of Literature

Source	Factors Considered	Models Used
Costantini et al. (1996)	Survival rates, Population densities and Dispersal	simple random models of dispersal
Yang et al. (2008)	Temperature, and Mosquito mortality rates	Generalized additive model
Dawes et al. (2009)	Age, Plasmodium density and mosquito mortality rates	Weibull, Gompertz, and Exponential
Gilles et al. (2011)	Mosquito density, diet, and survival rates	Generalized linear model
Abiodun et al. (2016)	Temperature, rainfall and mosquito mortality	Ordinary differential equation model
Brady et al. (2013)	Temperature and mosquito survival	GAM, log-logistic, Gompertz, exponential, and Weibull
Christiansen-Jucht et al. (2014)	Temperature, age and mosquito mortality	Gompertz, exponential, gamma, and the Weibull models
Brand et al. (2016)	Vector life history and its survival	Exponential model
Styer et al. (2007)	Age and mosquito survivorship	The exponential, Gompertz, and logistic model

2.3.11 Survival Analysis and Data

Cox (2003) defines survival analysis is as a set of methods applied to data analysis where the response variable is the time until an event of interest occurs. Here, the time taken until an event of interest occurs is often referred to as survival time. Survival data often includes survival time, vector characteristics related to the response as well as response to a given intervention, and survival. Studies using survival data often seek to predict the probability of the response variable, the survival of animals or organisms of interest, or their mean lifetime, compare survival distributions of various experimental subjects, and identifying the risk factors related to response variable, survival chances or disease development (Lee and Wang, 2003).

The data used in the present study includes the daily mortality for the associated infection experiments. The number of mosquitoes alive is recorded against those that have died or censored. Also, the blood-fed group and the uninfected control group were followed to determine if the diurnal temperature ranges had a different impact on the daily probability of mosquito survival for Plasmodium falciparum-infected mosquitoes. The midguts and salivary glands were dissected on the 7th day, and the 15th-day post-infection for each Plasmodium falciparum exposed to the treatment group. This was aimed at quantifing the effects of mean temmperature variation, diurnal temperature ranges, as well as the treatment measures of the competence of the mosquitoes (Murdock, Sternberg, and Thomas, 2016). The censored mosquitoes were those that were dissected midgets and salivary glands to assess parasite infections (Murdock et al., 2016).

2.3.12 Survival Models

The survival analysis strategies have found wide applications in various fields, including medicine, epidemiology, and biology. Regression models are commonly applied when testing the relationship between an outcome variable with one or more predictor variables. More specifically, the parametric methods for regression models have become popular in the modeling of survival data for various vectors (Christiansen-Jucht, 2014). For instance, parametric models have been used to analyze the Anopheles gambiae mosquito species survival (Christiansen-Jucht, 2014). Brand et al. (2016) successfully used the exponential model to examine the relationship between the vector life history and its survival in vector-borne disease transmission and control, and Styer et al. (2007) assessed the ability to accurately predict vectorial capacity based on the large-scale mortality study for the exponential model, Gompertz model, and the logistic model.

3 Materials and Methods

This section focuses on the description of data, the parametric methods for regression model used to analyze the data, and the criterion used to select the best-fit model for the vector survivorship.

3.1 Data Sources

The current investigation uses data from the Malaria transmission experiment, which was collected from the Dryad Digital Repository. The data consists of 2279 mosquitoes with 8 variables (Murdock et al., 2016). The data was collected from a lab experiment where *Anopheles gambiae* and *Anopheles stephensi* were reared under standard insectary conditions at 27 ± 0.5°C, 80 percent humidity, 12 hours light:12-hour dark photoperiod, and on a 10 percent glucose diet. After emerging, three-day-old female adult mosquitoes were randomly distributed into the 18 x 18 x 18 cm cages. There were a total of 150 cages representing one of the 18 treatment groups consisting of three mean temperatures (27°C, 30°C, and 33°C), two infection treatments (P. falciparum-infected, and blood-fed controls), and three Diurnal Temperature Ranges (DTR 0°C ± 0°C; DTR 6°C ± 3°C, and DTR 9°C ± 4.5°C) (Murdock et al., 2016).

There were two replicates of *Anopheles gambiae*, and 3 replicates of *Anopheles stephensi* experiments and the mosquitoes in each experiment were deprived of sugar solution for 12 hours prior to being introduced to either the uninfected blood meal or Plasmodium falciparum culture to minimize inter-culture variations and ensure similar dosages (Murdock et al., 2016). Directly after the blood feeds, the mosquitoes were introduced into the appropriate temperature treatments and maintained on a 10 percent sugar solution daily. The average temperatures and the diurnal temperature ranges were selected based on the microclimate data collected from the various housing types throughout the transmission season in Tanzania, India, and Chennai.

The midguts and salivary glands were dissected on the 7th-day, and the 15th-day post-infection for each P. falciparum exposed to the treatment group to quantify the effects of variation in mean temperature, diurnal temperature ranges, and treatment measures of the vector competence. The number of dead mosquitoes was counted in each cage throughout the experiment to quantify the effects of temperature fluctuation on the daily mortality (Murdock et al., 2016). Figure 1 below gives the head of the dataset used in the study.

ID	Block	Days_PI	Species	Treatment	Temperature	DTR	Status	Num_Mosqs
1	1	1	1	0	0	0	1	
2	1	1	1	1	0	0	1	
3	1	1	2	0	0	0	1	
4	1	1	1	1	0	1	1	
5	1	1	2	1	0	1	1	
6	1	1	1	0	0	2	1	

Figure 1. Screenshot of the dataset used in the study (Source: Murdock et al., 2016)

3.2 Parametric Methods of Regression

The parametric methods for regression modeling considered in the present study were the exponential, Weibull, gamma, and the Gompertz models.

3.2.1 Exponential Distribution

The exponential distribution is an important distribution in survival studies, which researchers often choose to describe life patterns. It is often referred to as a purely random failure pattern, and famous for its lack of memory, which requires that the age of a person, animal, or organism does not affect failure survival (Lee, and Wang, 2003). Whereas the distribution does not adequately describe many survival data, its understanding facilitates the treatment of more general situations. The distribution is characterized by a constant hazard rate, whereby a high hazard rate value is an indication of high risk and short survival, and a low hazard rate value is an indication of low risk and long survival.

The exponential distribution can be parameterized by its *mean* α with the probability density function

$$f(t) = \frac{1}{\alpha} e^{-t/\alpha} \qquad t > 0,$$

for $\alpha > 0$.

The variable T can also be parameterized using its *rate* λ with the following probability density function

$$f(t) = \lambda e^{-\lambda t} \qquad t > 0,$$

for $\lambda > 0$.

Using the mean parameterization, the cumulative distribution function of the variable T would be given as follows:

$$F(t) = P(T \leq t) = 1 - e^{-t/\alpha} \qquad t > 0.$$

The survivor function of T would be given by:

$$S(t) = P(t \geq t) = e^{-t/\alpha} \qquad t > 0.$$

The hazard function of T would be given by:

$$h(t) = \frac{f(t)}{S(t)} = \frac{1}{\alpha} \qquad t > 0.$$

The cumulative hazard function of T would be given by:

$$H(t) = -\ln S(t) = \frac{t}{\alpha} \qquad t > 0.$$

The exponential distribution has been successfully used by researchers to model the mosquito vector mortality rates accounting for the effects of seasonal variations in the vector recruitment recruitment (Briet, 2002). A recent study by Brand, Rock, and Keeling (2016) successfully used the model for the survival in vector-borne disease transmission and control.

3.2.2 Weibull Distribution

The Weibull distribution, which was developed by Weibull (1951), is a generalized exponential distribution with a shape distribution equal to one. It has found wide application in studies examining the reliability as well as the human disease mortality since it allows the survival distribution for populations whose risk is either decreasing, increasing, or constant (Cowles, 2004). The main contrast between the Weibull and the Exponential distribution is that the Weibull distribution is not based on the assumption of a constant hazard rate, hence has a wider application as compared to the exponential distribution.

The shorthand $T \sim \text{Weibull}(\alpha, \beta)$ indicates that the random variable T is Weibully with scale parameter $\alpha > 0$ and shape parameter $\beta > 0$. The variable T has probability density function

$$f(t) = \frac{\beta}{\alpha} t^{\beta-1} e^{-(1/\alpha)t^{\beta}} \qquad t > 0.$$

The cumulative distribution function of T is given by:

$$F(t) = P(T \leq t) = 1 - e^{-(1/\alpha)t^{\beta}} \qquad t > 0.$$

The survivor function of T is given by:

$$S(t) = P(T \geq t) = e^{-(1/\alpha)t^{\beta}} \qquad t > 0.$$

The hazard function of T is given by:

$$h(t) = \frac{f(t)}{S(t)} = \frac{\beta}{\alpha} t^{\beta - 1} \qquad t > 0.$$

The cumulative hazard function of T is given by:

$$H(t) = -\ln S(t) = \frac{1}{\alpha} t^{\beta} \qquad t > 0.$$

The Weibull distribution has been successfully used to model for survival time in various vector development and survival studies. For instance, Degallier et al. (2012) successfully applied the model in examining how the local environment affected the aging and mortality of mosquitoes in Fortaleza, Brazil (Degallier et al., 2012). In comparison with other parametric models, the Weibull model provided a better fit for mosquito survival data as compared to other models. Stone et al. (2012) also applied the Weibull model to assess how plant community composition influenced the vectorial capacity and fitness of the *Anopheles gambiae* mosquito.

3.2.3 Gamma Distribution

The gamma distribution encompasses two distributions: the exponential distribution and the chi-square distribution. The distribution was used by Phelan and Roitberg (2013) to assess how food, temperature, and water depth influenced the diving activity of mosquitoes.

The shorthand $T \sim \text{gamma}(\alpha, \beta)$ indicates that the random variable T has a gamma distribution. A gamma random variable T with positive scale parameter α and positive shape parameter β has probability density function

$$f(t) = \frac{t^{\beta - 1} \mathrm{e}^{-t/\alpha}}{\alpha^{\beta} \Gamma(\beta)} \qquad t > 0.$$

The cumulative distribution function of T is given by:

$$F(t) = P(T \leq t) = \frac{\Gamma(\beta, t/\alpha)}{\Gamma(\beta)} \qquad x > 0,$$

where

$$\Gamma(s,t) = \int_0^t t^{s-1} e^{-t} dt$$

for $s > 0$ and $t > 0$ is an incomplete gamma function and

$$\Gamma(s) = \int_0^{\infty} t^{s-1} e^{-t} dt$$

for $s > 0$ is the gamma function. The survivor function of T is given by:

$$S(t) = P(T \geq t) = 1 - \frac{\Gamma(\beta, t/\alpha)}{\Gamma(\beta)} \qquad t > 0.$$

The hazard function of T is given by:

$$h(t) = \frac{f(t)}{S(t)} = \frac{t^{\beta-1} e^{-t/\alpha}}{\left(\Gamma(\beta) - \Gamma(\beta, t/\alpha)\right) \alpha^{\beta} \Gamma(\beta)} \qquad t > 0.$$

The cumulative hazard function of T is given by:

$$H(t) = -\ln S(t) = -\ln\left(1 - \frac{\Gamma(\beta, t/\alpha)}{\Gamma(\beta)}\right) \qquad t > 0.$$

The hazard function of the distribution gives rise to a variety of forms depending on the value of the gamma parameter.

3.2.4 Gompertz Distribution

The Gompertz distribution is derived from the Gompertz Makeham family of distributions. The model is very closely related to the Weibull distribution in the sense that it represents the log of a Weibull distribution. The model provides a very close fit to adult mortality in contemporary developed nations (Bongaarts, 2005). The Gompertz distribution is based on the assumption that there is a law of mortality that explains the existence of common age patterns of death (Olshansky, 2010).

The shorthand $T \sim \text{Gompertz}(\delta, \kappa)$ indicates that the random variable T has the Gompertz distribution with parameters δ and κ. A Gompertz random variable T with shape parameters δ and κ has probability density function

$$f(t) = \delta \kappa^t e^{-\delta(\kappa^t - 1)/\ln(\kappa)} \qquad t > 0,$$

for all $\delta > 0$ and $\kappa > 1$.

The cumulative distribution function of T is given by:

$$F(t) = P(T \leq t) = 1 - e^{-\delta(\kappa^t - 1)/\ln(\kappa)} \qquad t > 0.$$

The survivor function of T is given by:

$$S(t) = P(T \geq t) = e^{-\delta(\kappa^t - 1)/\ln(\kappa)} \qquad t > 0.$$

The hazard function of T is given by:

$$h(t) = \delta \kappa^{t} \qquad t > 0.$$

The cumulative hazard function of t is given by:

$$H(t) = \frac{\delta\,(\kappa^{t} - 1)}{\ln(\kappa)} \qquad t > 0.$$

The model has been widely used in actuarial and biological applications as well as in demography. Clements and Peterson (1981) used the model to analyze the mortality and survival rates in wild mosquito populations. The model has also been applied in the analysis of the effects of larval food quantities on the capacity of adult mosquitoes to transmit human malaria. Therefore, it would be interesting to see how the model performs in analyzing the effect of temperature and age-dependent survival in mosquitoes.

3.3 Model Selection Criteria

The present study sought to compare the efficacy of the exponential model, the gamma model, the Weibull model, and the Gompertz model in fitting the temperature and age-dependent mosquito survival data. It involves comparing the goodness of fit of the four parametric models in regard to fitting of the observed data. In the context of model selection, the assumptions are that the statistical inference is model-based and that there is only one correct model or best fit model that suffices as the best model for making inferences (Burnham, and Anderson, 2004). The objective of model selection can be achieved by use of Akaike's Information Criterion (AIC), Log-likelihood (-2LL) or the Bayesian Information Criterion (BIC) (Burnham, and Anderson, 2004).

3.3.1 AIC

The AIC is a powerful, multimodal inference that can be used to determine the model that the model that best describes the factors that influence the variable of interest (Snipes and Taylor, 2014). The method was first described by Akaike (1973) as a strategy for comparing various models on a given outcome. For instance, the researcher in the present paper is interested in what variables influence the survival of mosquitoes, and how the variables may influence the survival of mosquitoes. Akaike (1973) demonstrated that the best model is determined by calculating an AIC score as follows:

$$AIC = 2K - 2ln(L)$$

Where k represents the number of parameters and L represents the likelihood function's maximized value. The constant 2 means is used for historical reasons (Snipes and Taylor, 2014). The AIC value is interpreted such that the lower value of AIC indicates a better model.

3.3.2 BIC

The BIC is a popular tool used by researchers for the selection of statistical models. It is preferred by many researchers due to its computational simplicity as well as its good performance in various modelling framworks where where other distributions have proved to be elusive (Neath and Cavanaugh, 2012). Under the assumption that the model errors are independently and identically distributed in accordance to a normal distribution, and that the boundary condition that the derivative of the log likelihood with respect to the true variance is zero, the formula for BIC is given as follows

$$BIC = -nln(\hat{\sigma}_e^2) + kln(n)$$

Where $\hat{\sigma}_e^2$ is the error variance given by $\hat{\sigma}_e^2 = \frac{1}{n}\sum_{i=1}^{n}(x_i - \bar{x})^2$

Under the assumption of normality, a more tractable version is given by

$$BIC = X^2 + k.ln(n)$$

Just like the AIC, the BIC value is interpreted such that the lower value of BIC indicates a better model. The statistical analyses were conducted using the R software. The AIC and BIC values for each model were conducted, and the model with the smallest AIC and BIC selected as the best fit model.

4 Results

This chapter presents the data analysis, presentation, and interpretation of the study findings. The objective of the present study was to compare four parametric methods for regression models to mosquito survival data. In this section, data from Murdock et al. (2016) is analyzed in relation to the topic of study. Models and formulas presented in the materials and methods section will be applied in analyzing the data.

4.1 Data Exploration

The information of the current dataset is given in Table 2 below. It has 2279 observations. The variable of age is considered in terms of days post-infection, and is measured on an interval scale while the temperature is considered in as the average temperature and diurnal temperature range. There are no cases of missing values in the present dataset. Figure 2 below illustrates a Kaplan Mier plot of the data. Out of the 2279 mosquitoes considered, 931 mortalities were recorded in a period of 15 days.

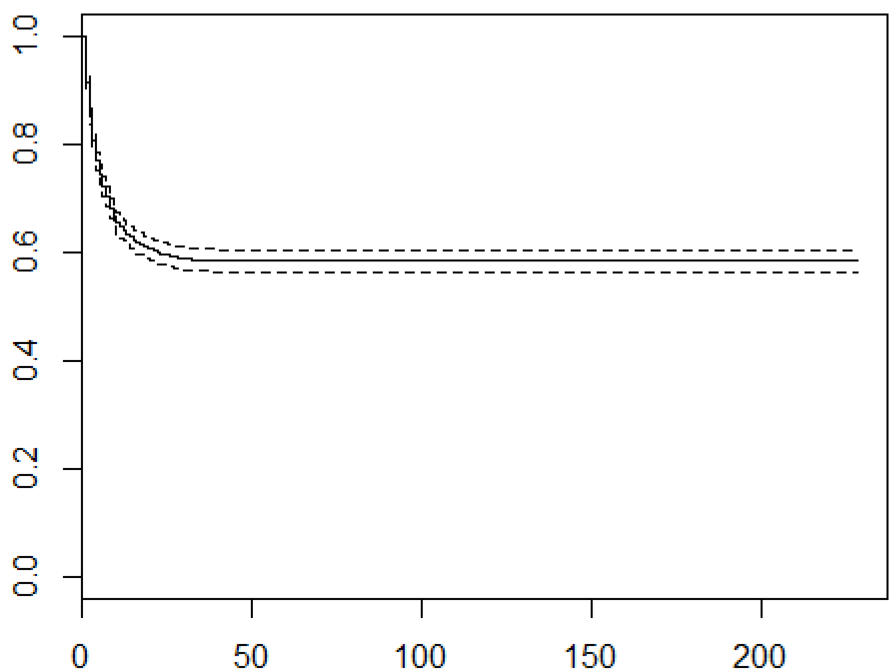

Figure 2. Kaplan Mier Curve

4.2 Model Selection

The goal of the present study is to confirm age and temperature as significant factors affecting the survival of mosquitoes and determine the model that best fits mosquito survival data. As such, model selection forms the center of focus of this data analysis. Using the flexsurfreg() function in R, the mosquito survival data was fitted using four different models: the exponential, gamma, Weibull, and Gompertz model. In the next section, a comparison of the covariates is offered.

4.2.1 Comparison of Covariates

Table 2 below shows that the variables of age and average temperature are significantly associated with the survival time for all the four parametric models considered. Under the exponential model, the coefficients of age and temperature were found to be statistically significant predictors of mosquito survival ($p<0.05$) at 0.05 level of significance. Similarly, the variables were found to be statistically significant under the Weibull (Temperature:

p=0.013, Age: p=0.0004), gamma (Temperature: p<0.05, Age: p=0.05), and Gompertz (Temperature: p<0.05, Age: p=0.05).

Table 2. Comparison of Covariates

Covariates	Exponential	Weibull	Gamma	Gompertz
Age (Est)	0.1701	0.0775	0.0960	0.0046
p-value	<0.05	<0.05	<0.05	<0.05
Temperature (Est)	0.0650	-0.2805	0.3004	0.0567
p-value	<0.05	<0.05	<0.05	<0.05

4.2.2 Model Selection Criteria

Table 3 below shows the values of the log-likelihood (-2LL), Akaike's Information Criterion (AIC) and the Bayesian Information Criterion (BIC) criteria for the fitted models. The log-likelihood results provide strong evidence that the Gompertz model (-2LL=-4138.59) is the best fit model for the mosquito survival data, followed by the Weibull (-2LL=-4764.97), gamma model (-2LL=-4822.81), and the exponential model (-2LL=-5707.03) in that order. The -2LL results were confirmed by the AIC and BIC criteria, which showed the lowest values for the Gompertz model (AIC= 8285.18, BIC= 8308.11), followed by the Weibull (AIC= 9537.95, BIC= 9560.87), Gamma (AIC= 9653.62, BIC= 9676.55), and the Exponential model emerged as the worst model of the four (AIC= 11420.06, BIC= 11437.25).

Table 3. Model Selection

Parametric Distributions	-2LL	AIC	BIC
Exponential	-5707.03	11420.06	11437.25
Weibull	-4764.97	9537.95	9560.87
Gamma	-4822.81	9653.62	9676.55
Gompertz	-4138.59	8285.18	8308.11

4.2.3 Graphical Goodness-of-fit Test

The goodness-of-fit of a model describes how well a model fits a set of observations. Whereas measures of goodness-of-fit above gives a summary of the discrepancy between the observed values and the expected values of the dataset under the four models, fitted line plots of the models given in figures 3, 4, 5, and 6 display the relationship between the variables of age and temperature and the survival of the mosquitoes. In addition, the models display the efficacy of each model in fitting the survival data.

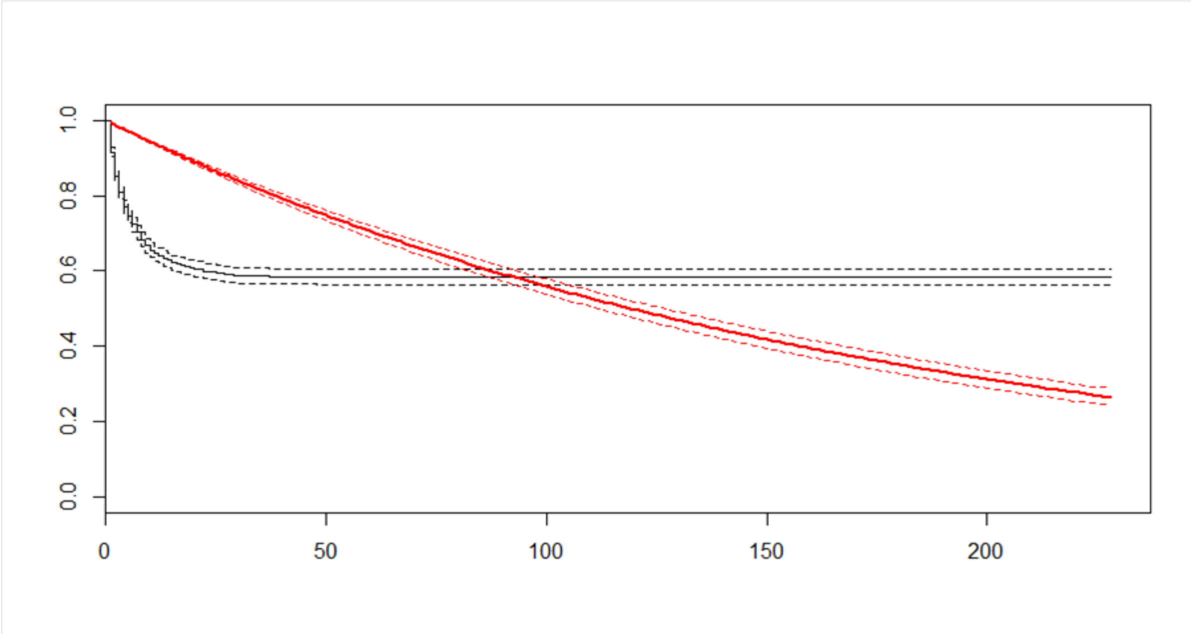

Figure 3. Exponential Model data plot

The data plot under the exponential model shows that the model is a poor fit. The black curve represents the survival curve as estimated by the Kaplan-Meier process, and the black dotted lines represent the 95 percent confidence interval. On the other hand, the red line and the red dotted lines represent the abstract function fitted by the exponential model and the confidence interval respectively. The objective of the model selection process is to achieve a model where the red and black curves to get close to each other. In the exponential model, the red and black curves are far from each other, indicating a poor fit.

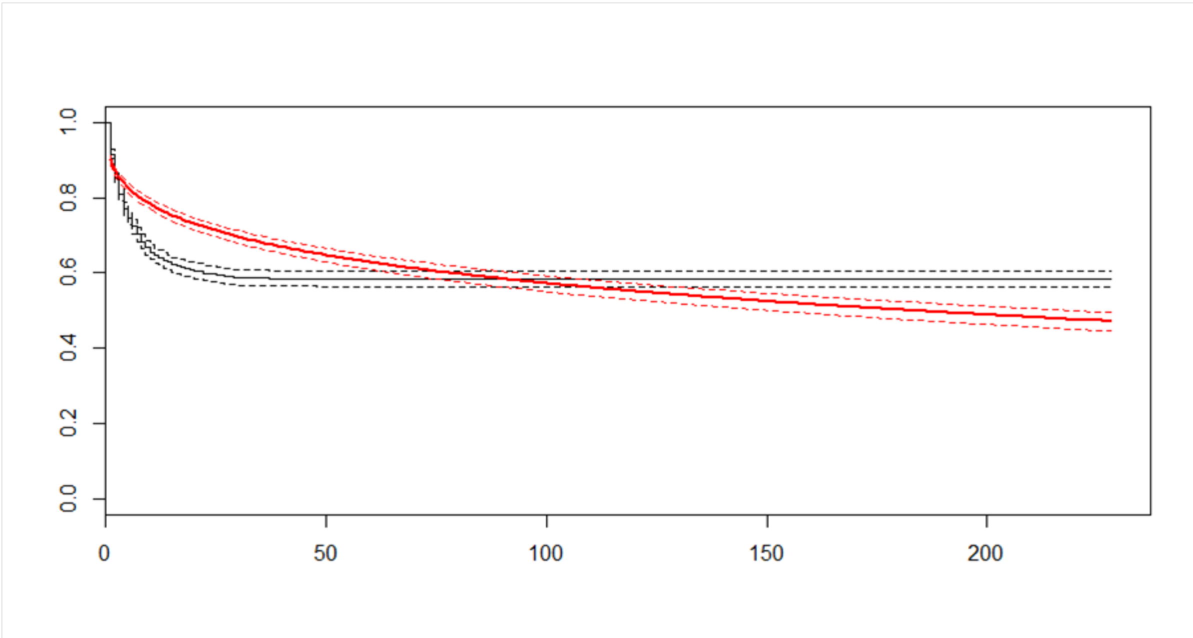

Figure 4. Gamma Model data plot

Figure 4 displays how the gamma model fits the mosquito survival data. As compared to the exponential model, the gamma model curve is closer to the Kaplan Meier curve but not as close as the Weibull and the Gompertz model curves.

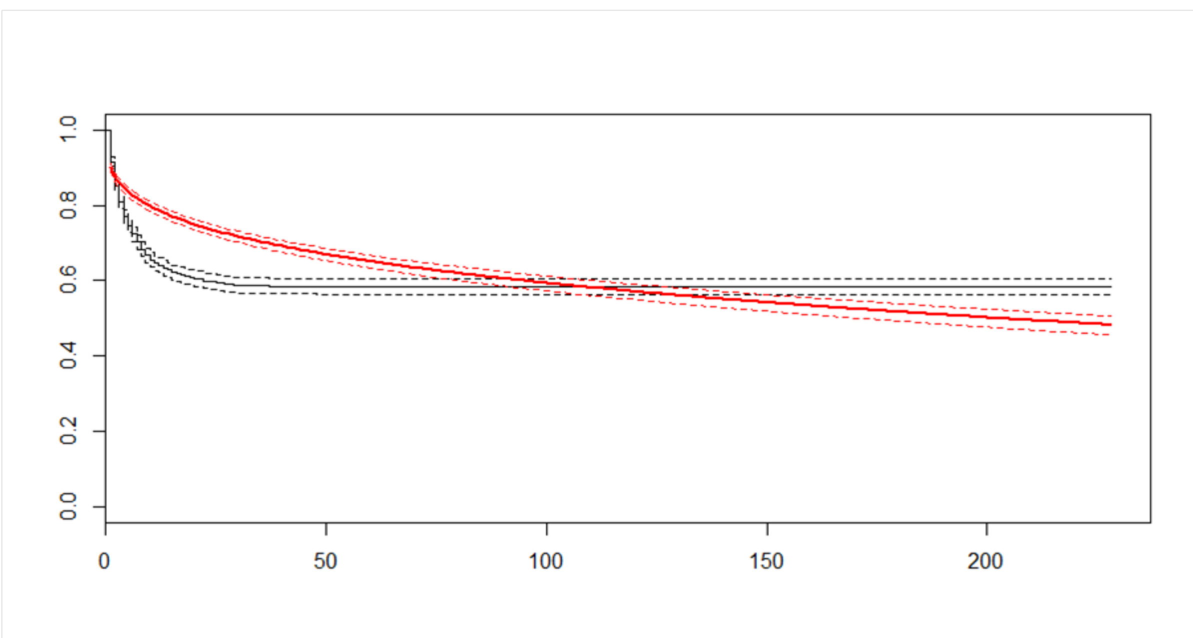

Figure 5. Weibull Model data plot

Figure 5 is a Weibull model curve of the data compared to the Kaplan Meier curve. Evidently, the Weibull curve is closer to the Gamma model curve but does not provide the best fit for the data.

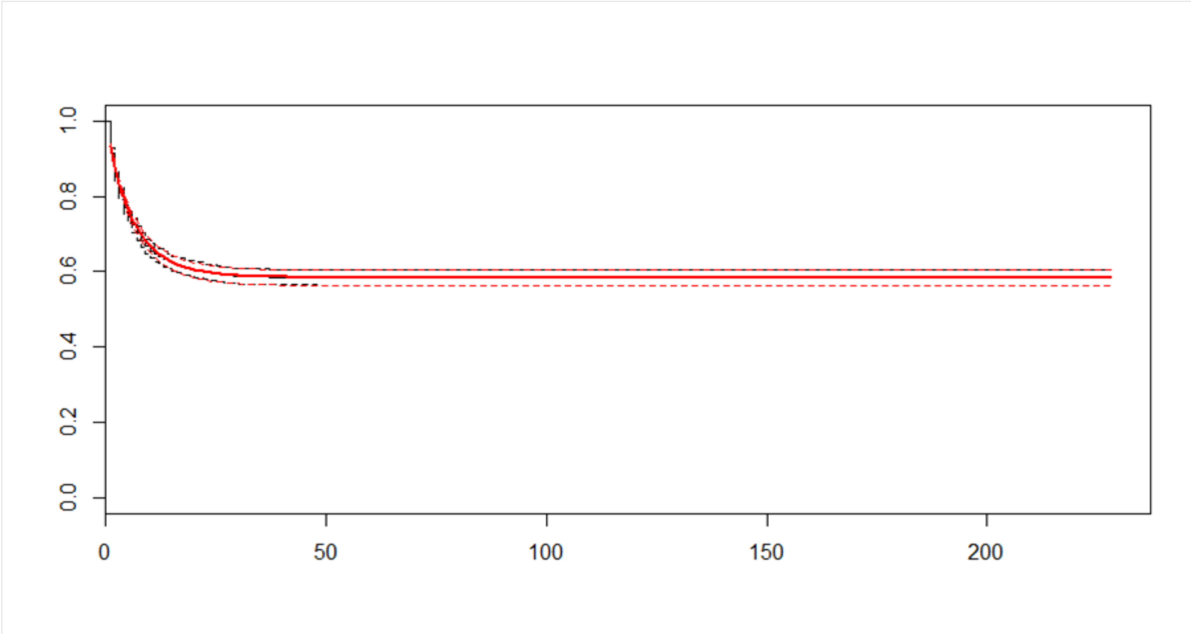

Figure 6. Gompertz Model data plot

The Gompertz model data plot shown in figure 6 above shows a perfect fit of the observed values and the expected values. The Gompertz model curve lies very close to the Kaplan Meier Curve. Based on the visual assessment of the four curves, the Gompertz model provides the perfect fit for the mosquito survival data.

5 Discussion and Conclusion

Section five of this report presents the summary of the study findings and discusses their implications for studies involving survival analysis of vector mortality data. The significance of the parametric survival models in modeling mosquito-vector mortality data is discussed in light of the existing literature, and new insights about the problem explained in consideration to the findings of the present study.

5.1 Summary of Findings

Malaria is one of the most significant infectious diseases globally. It is estimated to affect over 200million people every year and accounts for about 750,000 deaths during the same period. The adult female Anopheles mosquito accounts for all transmissions of the human malaria pathogen, Plasmodium. Research on the interventions and control of the disease has often focused on interrupting the transmission of the parasite by mosquitoes. Scientists have sought to disrupt the survival of mosquitoes using such factors as temperature, and age. To better understand the impacts of the individual factors on the survival of the vectors, many parametric models have been built for measuring their effect. These include the exponential, gamma, Weibull, Gomperts models among others. However, significant variations are usually observed across vector populations by applying a specific model. As such, models have been cross-validated with different cohorts.

Therefore, the aim of the present study was to compare the performance of four parametric models, namely, Gompertz, gamma, Weibull, and exponential models to determine the best model for analyzing the survival of the female Anopheles mosquito. The current investigation attempts to validate a predictive model based on mosquito mortality data by survival analysis.

The present study used data from 2279 *Anopheles gambiae* and *Anopheles stephensi* adult female mosquitoes to construct a temperature and age-dependent survival. The study reaffirms that environmental temperature affects the survival of *Anopheles gambiae* and *Anopheles stephensi* during their lifetime as adults. The results from the present study indicate that changes in the adult temperatures may have a significant impact on the survival of the mosquitoes. There was a statistically significant increase in environmental temperature with every 3°C increase in temperature. These results were consistent with results reported by Christiansen-Jucht et al. (2014) who used the temperature intervals of 4°C.

In general, the Gompertz survivorship function fitted the mosquito survival data reasonably well, confirming the results by Christiansen-Jucht et al. (2014), and confirming the age-dependent mortality in adult female *A. gambiae* and *A. stephensi* species of mosquitoes. Early studies by Dawes et al. (2009) and Christiansen-Jucht et al. (2014) had reported age-dependent mortality in the laboratory adult *A. stephensi* mosquito populations. Some authors have pointed out that vector-borne disease models tend to dismiss evidence supporting the age-dependent mortality for the sake of tractability, and because of the contradictory evidence between the laboratory and field studies (Christiansen-Jucht et al., 2014), but the present study further solidifies the evidence on the age-dependent vector mortality. This is because the age-independent exponential model is a poor fit.

5.2 Implications

The findings of the present study indicate that environmental temperature to which *A. gambiae* and *A. stephensi* are exposed to during their adult stages significantly affect their survival. This has important implications for the A. gambiae and A. stephensi population dynamics, ecology as well as the transmission of the Plasmodium pathogen. The Gompertz model emerges as the best-fit model for fitting data on adult A. gambiae and A. stephensi survival in the laboratory as compared to the other parametric models such as the exponential, gamma and the Weibull models. This implies that the survival of the vector is age-dependent. The results will help in parameterizing reliable mathematical models that examine the potential impact of temperature as well as global warming on the transmission of malaria.

5.3 Conclusion

This paper offers a comparison of the performance of four parametric models to determine the best model for analyzing the survival of the female Anopheles mosquito. The Gompertz, gamma, Weibull, and exponential models were utilized to model the survival of A. gambiae and A. stephensi species of mosquitoes. The four models differed significantly. The exponential model provided a poor fit of the vector survival data, while the Gompertz model provided a better fit compared to the Weibull, Gamma, and the Exponential models. On the other hand, temperature and age were reaffirmed as important predictors of mosquito survival. Overall, the Gompertz model provides a powerful statistical tool for the survival analysis of mosquito vector mortality data.

5.4 Future Research

The present study is based on a laboratory experiment. Other researchers exploring the problem have suggested a potential contradiction between laboratory data and field studies data (Christiansen-Jucht et al., 2014). In addition, the experimental design conducted in the present study did not consider differences in humidity, which would affect mosquito development as well as survival. Therefore, the model needs further confirmation from vector mortality data from the field given its importance in modeling vector population dynamics as well as malaria transmission.

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