# An Age-Structured Mathematical Model of Malaria with Heterogenous Mosquito Biting Pattern

Ruijun Zhao*, Sho Kawakami
Department of Mathematics and Statistics, Minnesota State University, Mankato, MN 56001 USA.

* Corresponding author. Tel.: (1)507-389-2719; email: ruijun.zhao@mnsu.edu
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**Abstract:** Human at different age-group is susceptible to mosquito bites at different level due to their age-specific activity behavior when infected-treated bed-nets are used to prevent human from infection f malaria. In this paper, an age-structured mathematical model of malaria with heterogeneous mosquito biting pattern is proposed. The force of infection is formulated by a Bayesian formula by introducing biting probability of a mosquito bite different among different age groups. The resulting mathematical model is a system of mixed age-structured model and ordinary differential equations. An efficient numerical scheme is derived. Numerical simulation was done to simulate the malaria transmission in Nigeria.

**Key words:** Age-structure, heterogenous mosquito biting, Bayesian formula.

## 1. Introduction

Malaria, a mosquito-borne disease, still remains a major public health problem worldwide. According to World Health Organization (WHO), an estimated 228 million cases of malaria occurred worldwide with an estimated 405 thousand deaths in 2018 [1]. The existing WHO-recommended interventions for malaria include: Long Lasting Insecticide Nets (LLINs), Indoor Residual Spraying (IRS), Preventive Treatment for Infants and during Pregnancy, and Prompt Diagnostic Testing and Treatment with Anti-malaria Medicines. In 2014, the first and only vaccine RTS, S/AS01 against malaria finished the Phase III trial. The Phase III trial showed that the vaccine has partial protection against malaria with different efficacy among young children. Through a WHO-coordinated pilot program, three highly malaria endemic countries in Africa introduced the malaria vaccine in selected areas in 2019.

It is well-known that the mosquito biting patterns will be different with existing interventions. For example, it is reasonable to assume that infants are less likely bitten by mosquitoes than active young children. There are some research works in studying vaccine strategy in controlling malaria [2], [3]. But most of these works are based on homogeneous assumptions in either mosquito biting or vaccination strategies. In this paper, an age-structured mathematical model is proposed to study the efficacy of the vaccine in control of malaria transmission. The model incorporates different biting preferences/accesses of mosquitoes to different age group of humans. In modeling mosquito-borne diseases, one has to follow a conservation law between the bites placed by mosquitoes and the bites that the hosts received. A Bayesian formula is derived to model this mosquito biting pattern. An efficient numerical method is derived to simulate the model. Numerical simulation was done to simulate the malaria transmission in Nigeria. The simulation also suggests that the new formulation is more appropriate than the age-independent mosquito

biting pattern in terms of numerical stability.

## 2. Model

Assume that mosquitos have different preference/access in successfully biting human population with different ages. For example, it is less likely for a mosquito to bite a newly-born baby than an active teenager. Let $p(a)$ be the probability of a mosquito bite placed on an individual with age $a$. Let $s_h(t,a), i_h(t,a), r_h(t,a), v_h(t,a)$ be the density of susceptible, infected, recovered and vaccinated human population at age $a$ at time $t$, respectively. Let $S_v(t)$ and $I_v(t)$ be the population of susceptible and infected mosquitos at time $t$ respectively. An age-structured mathematical model of malaria with heterogeneous mosquito biting is given below:

$$\begin{aligned}
\frac{\partial s_h}{\partial t}+\frac{\partial s_h}{\partial a} &= -\lambda_{vh}(t,a)s_h(t,a)+\gamma_h(a)r_h(t,a)+\eta_h(a)v_h(t,a)-\xi_h(t,a)s_h(t,a)-\ \mu_h(a,N_h)s_h(t,a)\\
\frac{\partial i_h}{\partial t}+\frac{\partial i_h}{\partial a} &= \lambda_{vh}(t,a)s_h(t,a)-\zeta_h(a)i_h(t,a)-\delta_h(a)i_h(t,a)-\ \mu_h(a,N_h)i_h(t,a),\\
\frac{\partial r_h}{\partial t}+\frac{\partial r_h}{\partial a} &= \zeta_h(a)i_h(t,a)-\gamma_h(a)r_h(t,a)-\ \mu_h(a,N_h)r_h(t,a),\\
\frac{\partial v_h}{\partial t}+\frac{\partial v_h}{\partial a} &= \xi_h(t,a)s_h(t,a)-\ \eta_h(a)v_h(t,a)-\mu_h(a,N_h)v_h(t,a),\\
\frac{dS_v}{dt} &= \Lambda_v-\lambda_{hv}(t)S_v(t)-\ \mu_vS_v(t),\\
\frac{dI_v}{dt} &= \lambda_{hv}(t)S_v(t)-\ \mu_vI_v(t)
\end{aligned} \tag{1}$$

where the forces of infection are defined

$$\lambda_{vh}(t,a)=p_1\beta I_v p(a)/\int_0^A p(a)n_h(t,a)da,\ \lambda_{hv}(t)=p_2\beta\int_0^A p(a)i_h(t,a)da\ /\int_0^A p(a)n_h(t,a)da, \tag{2}$$

And $n_h(t,a)=s_h(t,a)+i_h(t,a)+r_h(t,a)+v_h(t,a)$. It is worth to point out that the force of infection has a Bayesian form. The model is completed with initial and boundary conditions

$$s_h(0,a)=s_{h0}(a), i_h(0,a)=i_{h0}(a), r_h(0,a)=r_{h0}(a), v_h(0,a)=v_{h0}(a), S_v(0)=S_{v0}, I_v(0)=I_{v0} \tag{3}$$

And

$$s_h(t,0)=\int_0^A b_h(a)n_h(t,a)da,\ i_h(t,0)=0, r_h(t,0)=0, v_h(t,0)=0. \tag{4}$$

All parameter descriptions and values are listed in Table 1. Most of parameter values can be found in [4].

Table 1. Parameter Descriptions and Values

| Parameter | Description | Baseline values and range |
|---|---|---|
| A | Maximum age of humans | 90 years |
| $b_h$ | Birth rate of humans | |
| $\mu_h$ | Death rate of humans | |
| $\delta_h$ | Additional death rate of humans due to malaria | |
| $\zeta_h$ | Treatment rate of infected humans | $1 \in [1/2, 6]$ |
| $\gamma_h$ | Rate of loss of immunity of recovered humans per year | $2 \in [1/50, 4]$ |
| $\xi_h$ | Vaccination rate of humans | |
| $\eta_h$ | Rate of loss of immunity of vaccinated humans per year | $¼ \in [1/5, 1]$ |
| $\Lambda_v$ | Recruitment rate of mosquitos per year | $10^{12}$ |
| $\mu_v$ | Natural death rate of mosquitoes per year | $365/21 \in [365/28, 365/14]$ |
| $\beta$ | Mosquito biting rate per year | 18 |
| $p_1$ | Probability of humans being infected by one bite | 1/2 |
| $p_2$ | Probability of mosquitos being infected by one bite | 2/45 |

## 3. Fitting of Parameters

The maximum age was chosen as 90 from the population data available. The recruitment rate for the mosquito population was chosen so that it is significantly larger than the human population. For our case, we looked at Nigeria, which has a population around $10^8$, so the mosquito recruitment rate per year was set as $10^{12}$.

### 3.1. Birth Rate of Humans $b_h(a)$

We model the birth and death rates for Nigeria with data obtained from the United Nations [5] and the World Health Organizations [6] for the year of 2015. For the birth rate, we first find the shape of the birth rate function then calculate the magnitude based on estimates from the age distribution of the population. The age specific fertility rate was obtained from the United Nations [5] and we fit the following curve using least squares suggested in [7]. The parameters $\beta_1$, $\beta_2$, $\beta_3$, $\beta_4$ determine the shape of the curve:

$$B_h(a) = \beta_1 \exp\{-\beta_2(a-\beta_3) - \exp[-\beta_4(a-\beta_3)]\}. \quad (5)$$

We obtain the least square estimate

$$\hat{\beta}_1 = 0.0001218, \hat{\beta}_2 = 0.3022, \hat{\beta}_3 = 78.38, \hat{\beta}_4 = 0.04006.$$

Fig. 1 shows the fitted birth rate curve and the data. The birth function we will use in our model will have the form

$$b_h(a) = cB_h(a)$$

where $c = n_h(0,0)/\int_0^A B_h(a)n_h(a,0)da$. The value of $c$ will make sure that $b_h(a)$ has the correct magnitude and also that any solution achieved is continuous. We cannot use c = 1 since the data collected is for females in Nigeria but $b_h(a)$ is the birth rate over the entire population. For our model we can obtain the numerator $(n_h(0,0))$ with estimates of newborns per year and the denominator $(\int_0^A B_h(a)n_h(a,0)da)$ by using a rough estimate of the population age distribution obtained from the UN [5]. In this paper, $c$ = 0.4496. Note that the value of $c$ only depends on the shape of the distribution over age and not the magnitude of the values.

### 3.2. Death Rate of Humans $\mu_h(a, N_h)$

The death rate will take the density dependent form

$$\mu_h(a, N_h) = \mu_{h0}(a) + \mu_{h1}N_h \quad (6)$$

We model death rate in a similar fashion as the age dependent birth rate. The only difference will be that there is no need to adjust the magnitude of the values. Life table data is obtained from the World Health Organization for 2015 [6]. The death rate is assumed to follow the distribution suggested in [7]

$$\mu_{h0}(a) = \mu_c(a) + \mu_m(a) + \mu_o(a) \quad (7)$$

where $\mu_c(a) = \alpha_c \exp(-\beta_c a)$, $\mu_m(a) = \alpha_m \exp\{-\beta_m(a-\gamma_m) - \exp[\delta_m(a-\gamma_m)]$, $\mu_o(a) = \alpha_o/(A-a)$. We obtained the least square estimates

$$\hat{\alpha}_c = 0.9959, \hat{\beta}_c = 0.6776, \hat{\alpha}_m = 0.1277, \hat{\beta}_m = -0.09171, \hat{\delta}_m = -0.0006743, \hat{\gamma}_m = 66.78, \hat{\alpha}_o = 0.05859$$

Fig. 1 shows the fitted death rate curve to the data.

The death rate does not need their magnitudes adjusted because the values fitted were the death rates for the entire population. For the value of $\mu_{h1}$, we choose it to be constant and set it equal to $1.6 \times 10^{-10}$. We can change the value depending on what we wish the maximum population size to be. The expected lifetime can be computed from the death rate by $\int_0^A \exp(-\mu_{h0}(a)a)da = 50.49$ years.

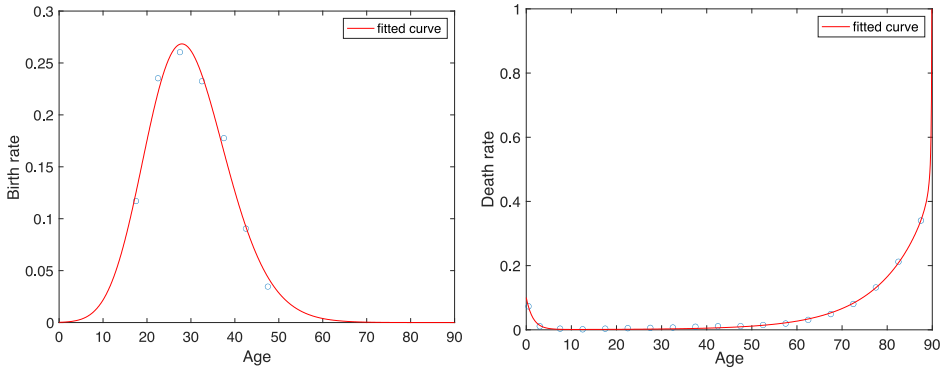


Fig. 1. Left: Birth rate function shape. Right: Death rate estimate. The open circles are data retrieved from the United Nation website.

### 3.3. Preference Function $p(a)$

A commonly used force of infection for vector-born disease models is a special case for which $p(a)$ takes the following form.

$$p_{unif}(a) = \begin{cases} 1, & 0 \le a < A, \\ 0, & a \ge A. \end{cases}$$

We use an age-dependent function to account for the differences in exposure for different age groups. Newborns are relatively protected from outside factors, having no risk of being bitten at birth, and the opportunity to come in contact with mosquito increases as they gain the ability to walk and become more active. We account for this with the following curve, which has lower values for newborns and drastically increases by the age of 10.

$$p(a) = \begin{cases} \dfrac{1}{1+e^{-(x-4)}} - \dfrac{1}{1+e^{4}}, & 0 \le a < A, \\ 0, & a \ge A. \end{cases}$$

Fig. 2 shows the curve $p(a)$. The value for newborns is consistent with our previous explanation, *p(0) = 0*. Furthermore, for this curve, the preference for humans over 10 is relatively uniform.

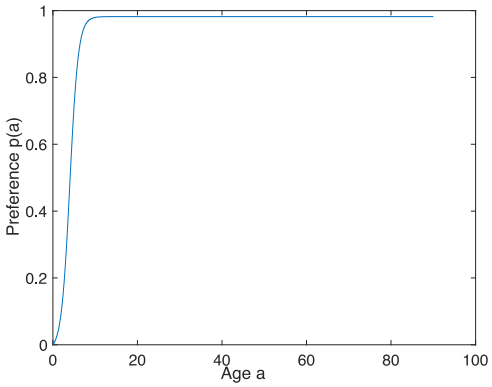


Fig. 2. Preference function $p(a)$ in the function of force of infection.

### 3.4. Disease Induced Death Rate $\delta_h(a)$

Malaria cause high mortality among young age groups, particularly those in age 0-5 years old. We will find a function to model the high death rate within the 0-5 age range and the lower death rate within higher

age groups. The function is also chosen so it is continuous and differentiable. We assume that the additional death rate due to malaria follows the following distribution

$$\delta_h(a) = \begin{cases} c \times \dfrac{1}{1+e^{2a-14}}, & 0 \le a < A \\ 0, & a \ge A \end{cases}$$

The additional death rate will be steady around rate $c$ for age 0 – 5. It will then drop quickly to a value close to 0. We will use data obtained from WHO in 2009 [8] to determine the value of $c$. The shape of the additional death rate allows us to assume for the purpose of finding an appropriate value of c that the additional death rate is constant between ages 0 and 5 at rate c. We use the following relation

(Number of infected individuals) · (Average time spent infected) · (Probability of dying from the disease)

= Average number of deaths due to infection

We restrict to age 0 to 5. The number of infected individuals age 0 to 5 in one year is 34096000 and the number of deaths due to malaria in one year is 219000. The disease induced death rate for 0 to 5 years old is assumed constant at c, so the probability of dying from the disease over a year is $1 - e^{-c}$. Since the natural death rate due to malaria is way smaller than the recovery rate ($\mu_{h0}(a) \ll \zeta_h$) and infection period is short, we can assume that the average infection period is

$$\int_0^A e^{-\zeta_h(a)a} da = \int_0^A e^{-a} da = 1 - e^{-A} \approx 1.$$

Then we have the equation

$$34096000 \times 1 \times (1 - e^{-c}) = 219000.$$

Solving for $c$, we get $c = 0.006444$.

Fig. 3 shows a plot for the disease induced death rate.

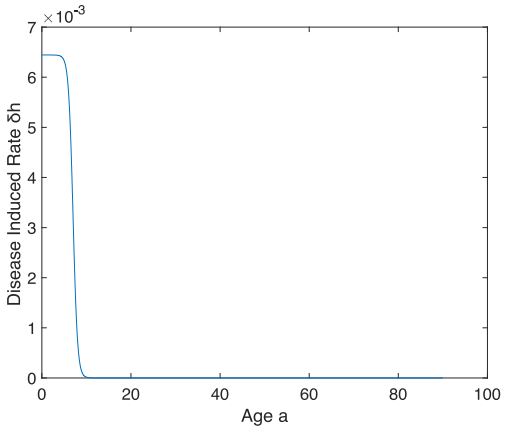


Fig. 3. Disease induced death rate $\delta_h(a)$.

## 4. Numerical Results

For numerical simulation, we use implicit finite difference schemes along the characteristic line. We first run the iterations until population reaches an equilibrium state.

Fig. 4 shows the equilibrium age distribution of the total population plotted against the age profile of the population of Nigeria. The equilibrium distribution closely mirrors the data for the population being modeled.

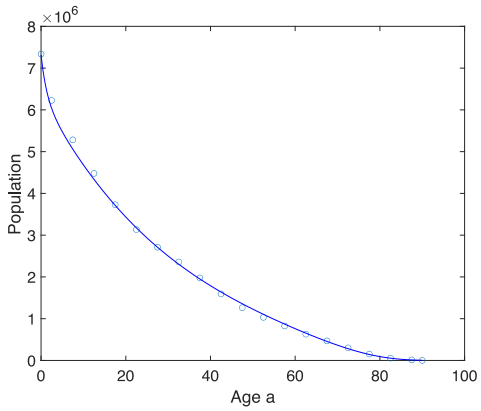


Fig. 4. Age distribution of total population. Solid line represents the numerical simulation results. The open circles represent the survey data by age group from Nigeria.

Fig. 5 shows the age distributions of susceptible, infected and recovered groups at equilibrium under no vaccinations. The disease has reached a steady endemic state. The infected individuals reach the peak around age 5, which can be explained by the choice of biting preference function in the force of infection functions.

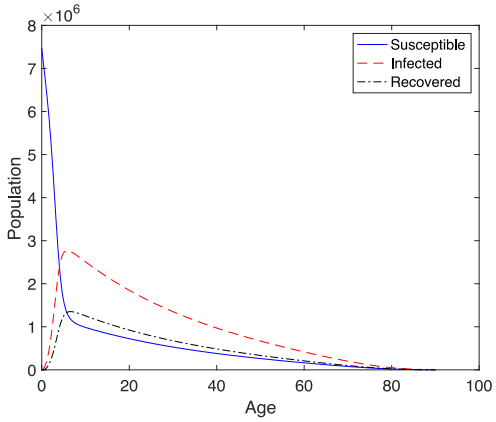


Fig. 5. Age distribution of population at equilibrium under no vaccinations.

Fig. 6 shows the age distribution of population at equilibrium under a constant vaccination rate of .5. The disease has again reached an endemic steady state but the total number of infectives are less than the no vaccination case. For best illustration, we only show the age profile for ages 0-20. Due to the effort of vaccination, less individuals are infected and age of infected group are pushed further.

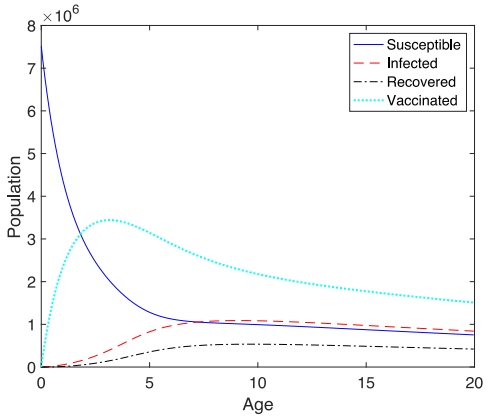


Fig. 6. Age distribution of population at equilibrium with vaccination rate $\xi_h = 0.5$.

Fig. 7 shows the age distribution at equilibrium under a constant vaccination rate of 1. The disease vanishes and only the susceptible and vaccinated populations remain, with most of the population being vaccinated.

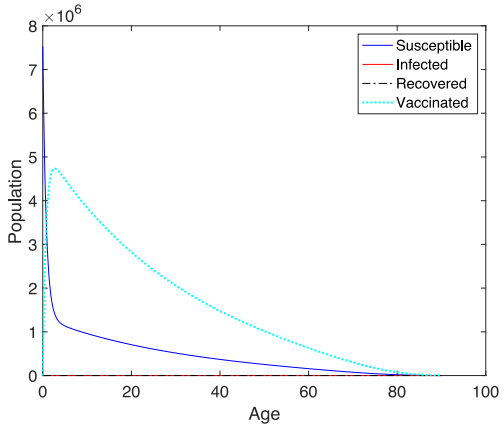


Fig. 7. Age distribution of population at equilibrium with vaccination rate $\xi_h = 1$.

## 5. Conclusion

In this paper, we proposed a new age-structure mathematical model to study the efficacy of vaccine in control of malaria. In particular, a Bayesian formula was used to describe the force of infection. Key age-dependent parameter functions are estimated using public data available online. A numerical simulation was carried out. Numerical simulations suggest that the disease can be controlled if the efficacy of the vaccine is effective and effort of implementation of vaccination is enough.

### Conflict of Interest

The authors declare no conflict of interest.

### Author Contributions

Sho Kawakami is a graduate student of Ruijun Zhao; The work is done by Sho Kawakami under the supervision of Ruijun Zhao; all authors had approved the final version.

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### References

[1] World Health Organization. (2019). Geneva: World malaria report 2019. Licence: CC BY-NC-SA 3.0 IGO.

[2] Mohammed-Awel, J, Zhao, R., Numfor, E., & Lenhart, S. (2017). Management strategies in a malaria model combining human and transmission-blocking vaccines. *Discrete and Continuous Dynamical Systems – Series B*, *22(3)*, 977-1000.

[3] Zhao, R., & Mohammed-Awel, J. (2014). A mathematical model studying mosquito-stage transmission-blocking vaccines. *Mathematical Biosciences and Engineering*, *11(5)*, 247-261.

[4] Chitnis, N., Hyman, J. M., & Cushing, J. M. (2008). Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. *Bulletin of Mathematical Biology*, *70(5)*, 1272.

[5] United Nations. (2019). Undata. Retrieved from http://data.un.org/

[6] World Health Organization. (2019). Global health observatory data repository. Retrieved from

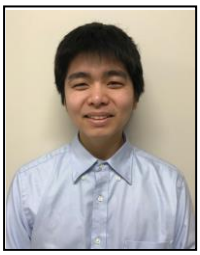
https://www.who.int/gho/en/

[7] Iannelli, M. & Milner, F. (2017). The basic approach to age-structured population dynamics. *Lecture Notes on Mathematical Modelling in the Life Sciences*. Dordrecht: Springer.

[8] World Health Organization. (2008). Nigeria profile. Retrieved from https://www.who.int/malaria/publications/country-profiles/2008/mal2008-nigeria-en.pdf



**Ruijun Zhao** received his PhD in mathematics from Purdue University. He is currently a professor at Minnesota State University, Mankato USA. His research focuses on mathematical modeling of infectious diseases.



**Sho Kawakami** is currently a PhD graduate student at Northwestern University. The work was conducted when he was a graduate student pursuing his Master degree at Minnesota State University. He is interested in both numerical analysis and mathematical modeling.