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Estimating the Parameters of a Disease Model from Clinical Data

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Authors' contributions

This work was carried out in collaboration between all authors. Author GTAT designed the study, performed the analysis, wrote the protocol and it was supervised by authors FTO and GAO. All authors read and approved the final manuscript.

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Abstract

Estimation of parameters (rate constants) in infectious disease models can be done either through literature or from clinical data. This article presents parameter estimation of a disease model from clinical data using the numerical integration followed by minimization of the error function. The error function is the overall sum of squared distances between the model-fitted points and the corresponding clinical data points at certain time points. Numerical integration was done using written Mat lab code using ode15s solver because of stiff nature of the disease models. Minimization of the error function was also done through a written Mat lab code using Mat lab routine "fmincon".

Keywords: Clinical data; parameter estimation; numerical integration; ordinary differential equation (ODE); error function; Mat lab code; minimization; MATLAB routine; fmincon.

1 Introduction

Once a mathematical model for a disease has been built, one of the key areas of the model worth considering is the determination of the model parameter values from a clinical data which is known as parameter

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estimation problem. Different strategies have been proposed for dealing with the parameter estimation problem in ODEs given a set of noisy data. However, in this article a numerical method will be used to determine parameters in a system of nonlinear equations by minimizing the distance between the clinical data points and the computed model –fitted points [1].

2 Model

The mode to be considered in this article is an age-structured malaria disease model with three infectious compartments; that is, infectious infants, infectious adults and infectious pregnant women. The model consists humans and adult female Anopheles mosquitoes and has a system of 6 nonlinear differential equations which is written below. In this model, infectious individuals between 0 to 5yearsold is known as infectious Infants and above 5yearsold who are not pregnant are termed infectious Adults. Infectious pregnant women are infectious women carrying fertilized eggs in their bodies. It is period from conception to birth. The model is based on the susceptible-infectives (SIS) models of infectious disease epidemiology. Therefore, the human population is partitioned into four compartments: susceptible (S_H), infectious infants (I_I), infectious adults (I_A) and infectious pregnant women (I_P) since the data for these compartments are always available at the health directorates of the various malaria endemic countries. The mosquito populace is also divided into two compartments namely: susceptible (S_M) and infectious (I_M). Detailed description of the model (1) is given in Table 1 and Table 2. Table 1 consists of state variables and Table 2 comprises the parameters (rate constants) to be determined from the clinical data. State variables are the set of variables that are used to describe the mathematical "state" of a disease model and the parameters are constants or coefficients of the state variables that have to be determined from the clinical data. State variables are used to represent compartments in the disease models. Therefore, the number of state variables is equal to the number of compartments.

Most of the current malaria models we have now, have used literatures values for their simulations. Therefore, estimating the parameters in this model will assist mathematical researchers in malaria modelling to have true values from clinical data for their simulations. It will also give true parameters to malaria researchers and policy makers so that precise control strategies can be formed to eliminate or control the malaria disease.

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= \psi_H N_H + \Lambda_I I_I + \Lambda_A I_A + \Lambda_P I_P - \frac{(\Phi_I + \Phi_A + \Phi_P)\theta_{MH} I_M S_H}{N_H} - \mu_H S_H \\
\frac{dI_I}{dt} &= \frac{\Phi_I \theta_{MH} I_M S_H}{N_H} - (\mu_H + \pi_I + \Lambda_I + \phi) I_I \\
\frac{dI_A}{dt} &= \frac{\Phi_A \theta_{MH} I_M S_H}{N_H} + \phi I_I - (\mu_H + \pi_A + \Lambda_A + \Omega) I_A \\
\frac{dI_P}{dt} &= \frac{\Phi_P \theta_{MH} I_M S_H}{N_H} + \Omega I_A - (\mu_H + \pi_P + \Lambda_P) I_P \\
\frac{dS_M}{dt} &= \psi_M N_M - \frac{(\Phi_I I_I + \Phi_A I_A + \Phi_P I_P)\theta_{HM} S_M}{N_H} - \mu_M S_M \\
\frac{dI_M}{dt} &= \frac{(\Phi_I I_I + \Phi_A I_A + \Phi_P I_P)\theta_{HM} S_M}{N_H} - \mu_M I_M
\end{aligned}\right\} \quad (1)$$

where the initial values are $S_H(0) = 15$, $I_I(0) = 1.3$, $I_A(0) = 2$, $I_P(0) = 0.1$, $S_M(0) = 20$ and $I_M(0) = 10$.

Table 1. The state variables for the model 1

State variables	Description
$S_H(t)$	Number of susceptible humans at time t.
$I_I(t)$	Number of infectious infants at time t.
$I_A(t)$	Number of infectious adults at time t.
$I_P(t)$	Number of infectious Pregnant women at time t.
$S_M(t)$	Number of susceptible mosquitoes at time t.
$I_M(t)$	Number of infectious mosquitoes at time t.
$N_H(t)$	Total human population at time t.
$N_M(t)$	Total adult female Anopheles mosquito population at time t.

Table 2. The parameters for the model 1

ψ_H	Rate of increase for the human population. Dimension: Humans × Time^{-1}
ψ_M	Per capita birth rate for mosquitoes. Dimensions: Time^{-1}
μ_H	Density-dependent natural mortality rate for humans. Dimensions: Time^{-1}
μ_M	Density-dependent natural mortality rate for adult female Anopheles mosquitoes. Dimensions: Time^{-1}
π_I	Per capita disease-induced mortality rate for infants. Dimensions: Time^{-1}
π_A	Per capita disease-induced mortality rate for adults Dimensions: Time^{-1}
π_P	Per capita disease-induced mortality rate for pregnant women Dimensions: Time^{-1}
Λ_I	Clinical recovery rate for the infants. Dimensions: Time^{-1}
Λ_A	Clinical recovery rate for the adults. Dimensions: Time^{-1}
Λ_P	Clinical recovery rate for the pregnant women. Dimensions: Time^{-1}
Φ_I	Number of bites on infant per female mosquito per unit time. Dimensions: Time^{-1}
Φ_A	Number of bites on adult per female mosquito per unit time. Dimensions: Time^{-1}
Φ_P	Number of bites on pregnant women per female mosquito per unit time. Dimensions: Time^{-1}
θ_{MH}	Fraction of bites that successfully infect humans
θ_{HM}	Fraction of bites that successfully infect mosquitoes.
ϕ	Rate of progression from I_I to I_A compartment. Dimensions: Humans × Time^{-1}
Ω	Rate of progression from I_I to I_A compartment. Dimensions: Humans × Time^{-1}

3 Estimation of the Model Parameters

The model is assumed solvable and differentiable with respect to the state variables and the parameters to be estimated on the whole domain [1]. To be able to solve the model uniquely and to get derivatives in an efficient and numerically stable way, the regularity of the model is also assumed. The numerical solution of the model is achieved in two steps. First the model is solved by odel5s solver using Mat lab code to get model function values [2,3,1].

A fitting criterion depending on the state variables and the independent optimization parameters is formulated subsequently. The resulting data are then inserted into a standard parameter-estimation code to compute the least-squares fit. Upper and lower bounds for the parameters to be estimated should be taken into account.

The two parameters ψ_H and μ_H can be determined from the demography of a country.

For the example Ghana's population growth rate is 2.19% (2014 est.) by 2015 IndexMundi.

$$\text{Hence } \psi_H = \frac{2.19}{100} = 0.0219 \text{ per year}$$

Life expectancy for an individual in Ghana is 62.4 years in 2015 by World Health Organization in 3rd November, 2016.

$$\text{Therefore } \mu_H = \frac{1}{62.4} = 0.016 \text{ per year}$$

Therefore the model (1) becomes

$$\left.\begin{aligned}
\frac{dS_H}{dt} &= 0.0219N_H + \Lambda_I I_I + \Lambda_A I_A + \Lambda_P I_P - \frac{(\Phi_I + \Phi_A + \Phi_P)\theta_{MH} I_M S_H}{N_H} - 0.016 S_H \\
\frac{dI_I}{dt} &= \frac{\Phi_I \theta_{MH} I_M S_H}{N_H} - (0.016 + \pi_I + \Lambda_I + \phi) I_I \\
\frac{dI_A}{dt} &= \frac{\Phi_A \theta_{MH} I_M S_H}{N_H} + \phi I_I - (0.016 + \pi_A + \Lambda_A + \Omega) I_A \\
\frac{dI_P}{dt} &= \frac{\Phi_P \theta_{MH} I_M S_H}{N_H} + \Omega I_A - (0.016 + \pi_P + \Lambda_P) I_P \\
\frac{dS_M}{dt} &= \psi_M N_M - \frac{(\Phi_I I_I + \Phi_A I_A + \Phi_P I_P)\theta_{HM} S_M}{N_H} - \mu_M S_M \\
\frac{dI_M}{dt} &= \frac{(\Phi_I I_I + \Phi_A I_A + \Phi_P I_P)\theta_{HM} S_M}{N_H} - \mu_M I_M
\end{aligned}\right\} \quad (2)$$

There are 15 parameters left to be estimated from clinical data. In the model (2) above, there are two populations, humans and female Anopheles mosquitoes. For the human population, the exact values of S_H , I_I , I_A and I_P can be calculated from the clinical data. However, the exact values of S_M and I_M cannot be determined, therefore assumed values are used to the variables S_M and I_M . To balance the effect of overestimation or underestimation of the values of the variables S_M and I_M on the model, two coefficient parameters $p16$ and $p17$ are placed on S_M and I_M respectively. So that if the assumed population sizes are greater than the actual values, $p16$ and $p17$ can reduce them to the actual values and the vice versa if assumed population sizes are less than the actual values.

The clinical data in Table 3 will be used for the parameter estimation.

Table 3. Clinical malaria data

Years	S_H	I_I	I_A	I_P	S_M	I_M
2000	15,475,505	1,303,685	2,045,843	102,834	20,714,172	10,357,086
2001	16,248,546	1,316,724	1,728,120	100,036	18,869,280	9,434,640
2002	16,645,417	966,923	2,173,970	103,192	19,464,510	9,732,255
2003	16,748,794	1,421,148	2,131,748	105,055	21,947,706	10,973,853
2004	17,419,477	1,289,874	2,126,159	101,008	21,102,246	10,551,123
2005	17,584,872	900,000	3,175,705	112,337	25,128,252	12,564,126
2006	18,086,432	946,946	2,914,402	126,862	23,929,260	11,946,630
2007	18,086,432	1,239,374	4,145,311	122,068	33,040,518	16,520,259

Years	S_H	I_I	I_A	I_P	S_M	I_M
2008	17,784,946	1,363,920	3,845,506	121,548	31,985,844	15,992,922
2009	16,629,384	1,875,338	5,067,370	141,068	42,502,656	21,251,328
2010	16,172,616	2,223,194	5,768,026	153,894	48,870,684	24,435,342
2011	15,210,099	2,747,162	6,774,978	196,261	58,310,406	29,155,203
2012	14,904,333	3,095,178	7,342,778	202,271	63,841,362	31,920,681
2013	15,107,273	3,311,214	7,528,239	217,704	66,342,942	33,171,471
2014	19,609,450	2,454,620	4,562,437	160,093	43,062,900	21,531,450
2015	23,549,481	1,244,974	2,501,649	112,898	23,157,126	11,578,568
2016	23, 464,661	1,463,608	2,947,607	134,403	27,273,708	13,636,854

In order to have easy computation, each data for the two populations is divided by 1000000 and rounded to the best possible decimal to make it little bit linear. This results in Table 4.

Table 4. Data for the curve fitting

Years	S_H	I_I	I_A	I_P	S_M	I_M
2000	15	1.3	2	0.1	20	10
2001	16	1.3	1.7	0.1	18	9
2002	17	1	2.2	0.1	20	10
2003	17	1.4	2.1	0.1	22	11
2004	17	1.3	2.1	0.1	21	11
2005	18	0.9	3.2	0.11	25	13
2006	18	0.9	2.9	0.13	24	12
2007	18	1.2	4.1	0.12	33	17
2008	18	1.4	3.8	0.12	32	16
2009	17	1.9	5.1	0.14	43	21
2010	16	2.2	5.8	0.15	49	24
2011	15	2.7	6.8	0.2	58	29
2012	15	3.1	7.3	0.2	64	32
2013	15	3.3	7.5	0.22	66	33
2014	20	2.5	4.6	0.16	43	22
2015	24	1.2	2.5	0.11	23	12
2016	23	1.5	2.9	0.13	27	14

Now let us present the 15 parameters by Ps and the state variables by Xs in the Table 5.

Table 5. Parameters and state variables

$\psi_M = p1$	$\theta_{MH} = p9$	$p17$
$\mu_M = p2$	$\theta_{HM} = p10$	
$\pi_I = p3$	$\Phi_I = p11$	$S_H(t) = x1$
$\pi_A = p4$	$\Phi_A = p12$	$I_I(t) = x2$
$\pi_P = p5$	$\Phi_P = p13$	$I_A(t) = x3$
$\Lambda_I = p6$	$\phi = p14$	$I_P(t) = x4$
$\Lambda_A = p7$	$\Omega = p15$	$S_M(t) = x5$
$\Lambda_P = p8$	$p16$	$I_M(t) = x6$

The quantities $N_H = x1 + x2 + x3 + x4$ and $N_M = p16x5 + p17x6$

This results in model (3) below

$$\left.\begin{aligned}
\frac{dx1}{dt} &= 0.0219\,(\,x1+x2+x3+x4) + p6x2 + p7x3 + p8x4 \\
&\quad -\frac{(p11+p12+p13)p9p16x6x1}{(\,x1+x2+x3+x4)} - 0.016x1 \\
\frac{dx2}{dt} &= \frac{p11p9p16x6x1}{(\,x1+x2+x3+x4)} - (0.016+p3+p6+p14)x2 \\
\frac{dx3}{dt} &= \frac{p12p9p16x6x1}{(\,x1+x2+x3+x4)} + p14x2 - (0.016+p4+p7+p15)x3 \\
\frac{dx4}{dt} &= \frac{p13p9p16x6x1}{(\,x1+x2+x3+x4)} + p15x3 - (0.016+p5+p8)x4 \\
\frac{dx5}{dt} &= p1(p16x5+p17x6) - \frac{(p11x2+p12x3+p13x4)p10p16x5}{(\,x1+x2+x3+x4)} - p2p16x5 \\
\frac{dx6}{dt} &= \frac{(p11x2+p12x3+p13x4)p10p16x5}{(\,x1+x2+x3+x4)} - p2p17x6
\end{aligned}\right\} \quad (3)$$

with the initial value $x1(0)=15$, $x2(0)=1.3$, $x3(0)=2$, $x4(0)=0.1$, $x5(0)=20$ and $x6(0)=10$.

The equation (3) can be simplified as the system of ODE of the form

$$\frac{d\mathbf{x}}{dt} = \mathrm{f}(\mathbf{x}\ ,\ \mathbf{p}\ ,\ t\ )\ ,\ \boldsymbol{x}(t_0)=\boldsymbol{x}_0 \text{ and } t\in[\,t_0\ ,\ T\,] \quad (4)$$

where $\frac{d\boldsymbol{x}}{dt}=\left(\frac{dx1}{dt},\cdots,\frac{dx6}{dt}\right)$, $\boldsymbol{x}=(x1,\ldots,x6)$ and $\boldsymbol{p}=(p1,\ldots,p17)$.

$\boldsymbol{x}_0$ is the initial values of the state variables.

Parameter estimation of the model (4) requires numerical integration of the model (4) followed by minimization of the error function. The error function is the overall sum of squared distances between the model-fitted points and the corresponding clinical data points at certain time points. The error function can be termed the total error of the model. The aim of the error function is to measure the fit to the data. A smaller error function value indicates a good fit of the model by the clinical data values. Hence the error function can be written using the least squares error [4,5,6,7,1,8,9].

$$E(\mathbf{p}) = \begin{bmatrix} \sum_{i=}^{n}[x_2(\text{Predicted model data}) - x_2(\text{Actual clinical data})]_i^2 + \\ \sum_{i=}^{n}[x_3(\text{Predicted model data}) - x_3(\text{Actual clinical data})]_i^2 + \\ \sum_{i=}^{n}[x_4(\text{Predicted model data}) - x_4(\text{Actual clinical data})]_i^2 \end{bmatrix} \quad (5)$$

The next target is to minimize the error function to obtain the parameter estimates

$$\min_{\mathbf{p}} E(\mathbf{p}) \quad (6)$$

subject to equation (4)

Parameter estimation algorithm [10]:

1. Guess initial parameter values.
2. Using an appropriate ODE solver, solve the model given the current parameter values. Compute the solution of the model.
3. Evaluate E using equation (5).
4. Update parameter values to minimize E . This step and the next are usually controlled by an optimization package.
5. Check convergence criteria. If not converged, change guess initial parameter values of $\mathbf{p}$ and go to (2).

The minimization of the model (5) is done by the Mat lab routine "fmincon" which reacquires that the initial guess values of $\mathbf{p}$ should have upper and lower bounds defined on them, that is, $\boldsymbol{a} \leq \mathbf{p} \leq \mathbf{b}$. $\boldsymbol{a}$ and $\mathbf{b}$ are vectors. A written Mat lab code with initial state values was used to simulate model(4) After which another Mat lab code which import the malaria data from Excel was used to calculate and minimize the error function ($E(\mathbf{p})$), and plot the model values and the malaria data. ..The second code containing "fmincon" stops when it achieves the minimum total error and displays the parameter values and minimum total error [4].

Description of Mat lab routine "fmincon"

fmincon attempts to find a constrained minimum of a scalar function of several variables starting at an initial estimate. This is generally referred to as constrained nonlinear optimization or nonlinear programming [11].

Syntax

[p, fval] =fmincon(fun , p0, A, b, Aeq, beq, lb, ub) starts at p0 and attempts to find a minimizer p of the function described in fun subject to the inequalities $A * p \leq b$. p0 can be a scalar, vector, or matrix.

It also minimizes fun subject to the linear equalities $Aeq * p = beq$ and $A * p \leq b$. If no inequalities exist, set $A = [\ ]$ and $b = [\ ]$.

It defines a set of lower and upper bounds on the design variables in p , so that the solution is always in the range $lb \leq p \leq ub$. If no equalities exist, set $Aeq = [\ ]$ and $beq = [\ ]$. If p(i) is unbounded below, set $lb(i) = -Inf$ and p(i) is unbounded above, set $ub(i) = Inf$.

If the specified input bounds for a problem are inconsistent, the output p is p0 and the output fval is [ ] .

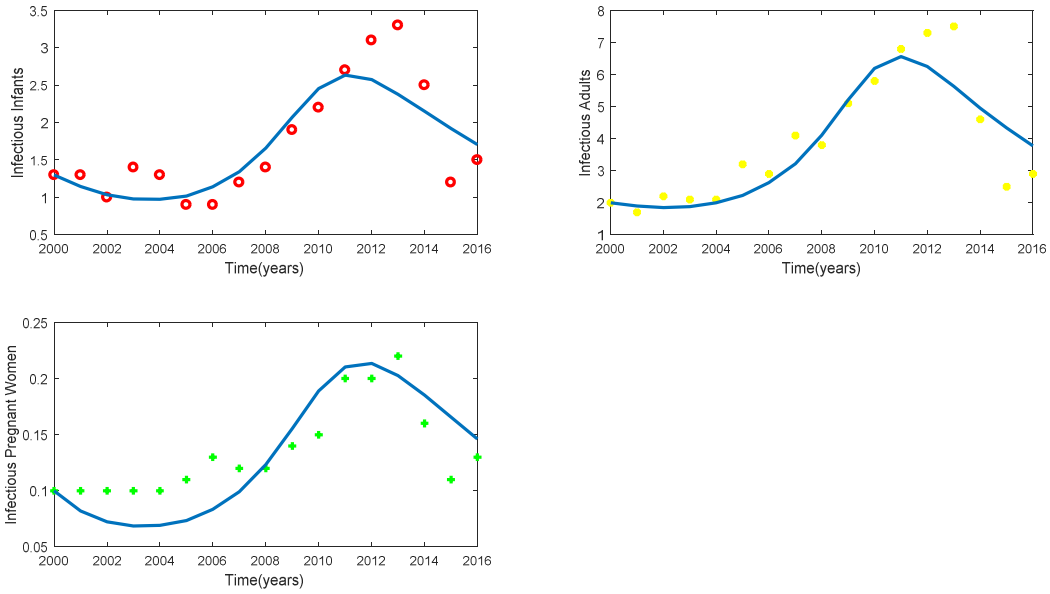
Components of p0 that violate the bounds $lb \leq p \leq ub$ are reset to the interior of the box defined by the bounds. Components that respect the bounds are not changed. There are other several syntaxes for fmincon, but the above directly relates to parameter estimation in infectious disease models [4,11]. The results in Table 6 were obtained for the parameters in model (1).

Table 6. Estimated parameters

$\psi_M = \text{Par}(1) = 0.05883$	$\theta_{HM} = \text{Par}(10) = 0.00535$
$\mu_M = \text{Par}(2) = 0.05882$	$\Phi_I = \text{Par}(11) = 0.32437$
$\pi_I = \text{Par}(3) = 0.01924$	$\Phi_A = \text{Par}(12) = 0.96144$
$\pi_A = \text{Par}(4) = 0.19821$	$\Phi_P = \text{Par}(13) = 0.01405$
$\pi_P = \text{Par}(5) = 0.5337$	$\phi = \text{Par}(14) = 0.10349$
$\Lambda_I = \text{Par}(6) = 0.13908$	$\Omega = \text{Par}(15) = 0.01957$
$\Lambda_A = \text{Par}(7) = 0.16157$	$A = \text{Par}(16) = 11501$
$\Lambda_P = \text{Par}(8) = 0.16244$	$B = \text{Par}(17) = 142000$
$\theta_{MH} = \text{Par}(9) = 0.00016$	

4 Graphs of the Infectious Human Compartments

The graphs below are the curve fitting for the three infectious human compartments.



After the parameter estimation, Table 3 becomes Table 7 below:

Table 7. Clinical malaria data after parameter estimation

Years	S_H	I_I	I_A	I_P	S_M	I_M
2000	15,475,505	1,303,685	2,045,843	102,834	238,233,692,200	1,470,706,212,000
2001	16,248,546	1,316,724	1,728,120	100,036	217,015,589,300	1,339,718,880,000
2002	16,645,417	966,923	2,173,970	103,192	223,861,329,500	1,381,980,210,000
2003	16,748,794	1,421,148	2,131,748	105,055	252,420,566,700	1,558,287,126,000
2004	17,419,477	1,289,874	2,126,159	101,008	242,696,931,200	1,498,259,466,000
2005	17,584,872	900,000	3,175,705	112,337	289,000,026,300	1,784,105,892,000
2006	18,086,432	946,946	2,914,402	126,862	275,210,419,300	1,696,421,460,000
2007	18,086,432	1,239,374	4,145,311	122,068	379,998,997,500	2,345,876,778,000
2008	17,784,946	1,363,920	3,845,506	121,548	367,869,191,800	2,271,004,864,000
2009	16,629,384	1,875,338	5,067,370	141,068	488,823,046,700	3,017,688,576,000

Years	S_H	I_I	I_A	I_P	S_M	I_M
2010	16,172,616	2,223,194	5,768,026	153,894	562,061,736,700	3,469,818,564,000
2011	15,210,099	2,747,162	6,774,978	196,261	670,627,979,400	4,140,038,826,000
2012	14,904,333	3,095,178	7,342,778	202,271	734,239,504,400	4,532,736,702,000
2013	15,107,273	3,311,214	7,528,239	217,704	763,010,175,900	4,710,348,882,000
2014	19,609,450	2,454,620	4,562,437	160,093	495,266,412,900	3,057,465,900,000
2015	23,549,481	1,244,974	2,501,649	112,898	266,330,106,100	1,644,156,656,000
2016	23, 464,661	1,463,608	2,947,607	134,403	313,674,915,700	1,936,433,268,000

Susceptible mosquito (S_M) and infectious mosquito (I_M) populations for each year have been estimated through the parameter estimation. Next, we consider the interpretation of the parameters in the model (I).

5 Interpretation of Parameters Results

Interpretation of the parameters are given in Table 8.

Table 8. Interpretation of results

Parameter	Source	Interpretation
$\psi_H = 0.0219$	Population growth rate per annum: 2.19% (2014 est.). 2015 IndexMundi	Rate of increase for the human population per annum
$\psi_M = 0.05883$	Fitted	Rate of increase for the mosquito population per annum
$\mu_H = \frac{1}{62.4} = 0.016$	Life expectancy for an individual in Ghana is 62.4 years in 2015 by World Health Organization in 3rd November, 2016.	Natural death rate per annum for humans
$\mu_M = 0.05882\text{years} = 0.05882 \times 365.25\text{days} = 21.484\text{days}$	Fitted	Life expectancy for adult female Anopheles Mosquito is approximately 22 days.
$\pi_I = 0.01924$	Fitted	Disease death rate per annum for infants
$\pi_A = 0.19821$	Fitted	Disease death rate per annum for adults
$\pi_P = 0.5337$	Fitted	Disease death rate per annum for pregnant women
$\Lambda_I = 0.13908\text{years} = 0.13908 \times 365.25\text{days} = 50.8\text{ days}$	Fitted	The recovery rate could vary based on the gametocyte, and it may take an average of 50.8 days for the parasite to be cleared from bloodstream after treatment for infants
$\Lambda_A = 0.16157\text{years} = 0.16157 \times 365.25\text{days} = 59.0\text{ days}$	Fitted	The recovery rate could vary based on the gametocyte, and it may take an average of 59 days for the parasite to be cleared from bloodstream after treatment for adults.
$\Lambda_P = 0.16244\text{years} = 0.16244 \times 365.25\text{days} = 59.3\text{ days}$	Fitted	The recovery rate could vary based on the gametocyte, and it may take an average of 59.3 days for the parasite to be cleared from bloodstream after treatment for pregnant women.
$\theta_{MH} = 0.00016$	Fitted	Fraction of bites that successfully infect humans

Parameter	Source	Interpretation
$\theta_{HM} = 0.00535$	Fitted	Fraction of bites that successfully infect mosquitoes.
$\Phi_I = 0.32437$	Fitted	The number of bites on infants per mosquito per day.
$\Phi_A = 0.96144$	Fitted	The number of bites on adults per mosquito per day.
$\Phi_P = 0.01405$	Fitted	The number of bites on pregnant women per mosquito per day.
$\phi = 0.10349$	Fitted	Rate of progression from I_I to I_A compartment
$\Omega = 0.01957$	Fitted	Rate of progression from I_A to I_P compartment .

6 The Mean Squared Error

The Mean Squared Error is a measure of how close a fitted line is to data points. For every data point, you take the distance vertically from the point to the corresponding y value on the curve fit (the error), and square the value. Then you add up all those values for all data points, and divide by number of points minus two. The squaring is done so values do not cancel positive values. The smaller the Mean Squared Error, the closer the fit is to data. The MSE has the units squared of whatever is plotted on the vertical axis [12].

The Mean-Squared Error (MSE) of the curve fitting is

$$\text{RMSE} = \sqrt{\frac{13.592}{49}} = \sqrt{0.2774} = 0.5267$$

7 Conclusion

The estimation of parameters of model (1) was done through the combination numerical integration of the model followed by optimization technique using Mat lab routine " fmincon " . A Mat lab code was written which imports the clinical data from Microsoft Excel, simulates the differential equations, calculates and minimizes the total error, displays the parameter values and plots the model and clinical data values. The researcher hopes the estimated parameters will assist malaria elimination worldwide and also inform policy makers about the key parameters in their planning. The Mean Squared Error(MSE) of the curve fitting is 0.5267.

Competing Interests

Authors have declared that no competing interests exist.

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