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CONTROLLING IMPORTED MALARIA CASES IN THE UNITED STATES OF AMERICA

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Abstract. We extend the mathematical malaria epidemic model framework of Dembele *et al.* and use it to "capture" the 2013 Centers for Disease Control and Prevention (CDC) reported data on the 2011 number of imported malaria cases in the USA. Furthermore, we use our "fitted" malaria models for the top 20 countries of malaria acquisition by USA residents to study the impact of protecting USA residents from malaria infection when they travel to malaria endemic areas, the impact of protecting residents of malaria endemic regions from mosquito bites and the impact of killing mosquitoes in those endemic areas on the CDC number of imported malaria cases in USA. To significantly reduce the number of imported malaria cases in USA, for each top 20 country of malaria acquisition by USA travelers, we compute the optimal proportion of USA international travelers that must be protected against malaria infection and the optimal proportion of mosquitoes that must be killed.

1. **Introduction.** Malaria is a mosquito borne disease that is caused by *plasmodium* parasites [7]. In December 2013, the World Health Organization reported that 207 million cases of malaria occurred in 2012 with 627,000 deaths in the same year worldwide. Most of these deaths occurred in Africa where a child dies every minute from malaria [5, 6, 13, 20, 21].

The majority of malaria infections in the United States of America (USA) occur among USA residents (including both civilian and USA military personnel, regardless of legal citizenship) who have traveled to malaria endemic regions with ongoing malaria transmission. However, in USA the malaria disease is also *occasionally* acquired by USA residents who have not traveled out of the country, through exposure to infected blood products, congenital transmission, laboratory exposure, or local mosquito-borne transmission. Since 1970, USA military personnel, USA civilians, foreign residents and some other people whose immigration status have not been recorded [20, 21] have been importing malaria into the USA. From 1970 to 1972, USA military personnel imported the majority of malaria into USA. During this time interval, USA military personnel produced 7,525 cases of malaria against 516 for all the three other groups. However, this trend was significantly reversed from 1973 to 2011 (1,393 malaria cases for USA military personnel against 42,830

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malaria cases for the other groups). A plausible explanation to this significant reduction of malaria incidence in the USA military group is probably due to good malaria control and prevention policies (e.g. protecting USA military personnel from malaria infection with antimalarial drugs) that were adopted by the USA military agency [20, 21].

In a 2013 Centers for Disease Control and Prevention (CDC) report, malaria surveillance data shows that 1,925 cases of the malaria disease were diagnosed and treated in the USA in 2011. A significant 1,920 of these reported malaria cases in USA were acquired overseas in regions with malaria transmission [21]. This is the largest number reported since 1971. In Table 2, we list the top 20 countries of malaria acquisition by USA travelers in 2011. From the 2011 CDC data that was reported in 2013, information on regions of malaria acquisition by USA residents were missing for 265 (14%) cases. Of the 1,655 imported cases for which the regions of acquisition were known, 1,144 (69%) were acquired in Africa, 363 (22%) were acquired in Asia, 140 (8%) in the Americas, 7 (0.4%) in Oceania and only 1 in the Middle East.

Mathematical epidemic models of malaria have been used to study the impact of various malaria control and prevention policies on the incidence of the disease in various malaria endemic regions [1, 2, 4, 9–19]. For example, Dembele *et al.* used a deterministic system of ordinary differential equations malaria model to illustrate that protecting people and killing mosquitoes at the same time can lead to malaria eradication in Missira, a village in Mali [6]. Koella *et al.* used mathematical models to help design rational strategies for the control of drug resistance [8]. In another study, Dembele *et al.* used mathematical models to determine an optimal use of *sulfadoxine-pyrimethamine* as a temporary malaria vaccine [5]. Others have studied the effect of malaria control interventions on vector and parasite populations, acquired immunity, and burden of the disease in highly malaria endemic regions [13, 19].

In this paper, we extend the mathematical malaria model framework of Dembele *et al.* [5,6] and use it to "capture" the 2013 CDC reported data on the number of imported malaria cases in USA. Furthermore, we use the "fitted" malaria models for the top 20 countries with high malaria acquisition by USA residents to study the impact of the following four malaria control and prevention policies on the number of imported malaria cases into the USA.

- Policy 1: Protecting USA residents traveling to malaria transmission regions from malaria infection (for example by administering drugs for malaria prophylaxis).
- Policy 2: Protecting residents of malaria endemic countries from mosquito bites (for example by offering mosquito bed nets).
- Policy 3: Killing mosquitoes (for example by killing mosquitoes with insecticides) in the malaria endemic countries USA residents usually visit.
- Policy 4: Protecting USA residents traveling to malaria transmission regions from malaria infection while killing mosquitoes in endemic countries.

The paper is organized as follows: In Section 2, we introduce a mathematical model that describes the dynamics of the malaria disease in high malaria transmission countries and the USA. Under our malaria control and prevention policies, in Section 3, we establish the existence of optimal control strategies that would lead to minimal numbers of imported malaria cases in USA. In Sections 4 and 5, we "fit" our deterministic mathematical malaria model to the CDC imported malaria

data of 2011 from the top 20 malaria endemic countries [21]. In Section 6, we introduce four malaria control and prevention policies. We compute, in Sections 6 and 7, the optimal proportion of USA international travelers that must be protected against malaria infection, the optimal proportion of residents of malaria endemic regions that must be protected from mosquito bites and the optimal proportion of mosquitoes that must be killed under each of our four policies in order to significantly reduce the number of imported malaria cases in USA. We summarize our results in Section 8.

2. **Malaria model: Overseas malaria infection and USA imported malaria.** In this section, we introduce an extension of the classical mathematical malaria model framework and use it to study the impact of protecting USA residents from importation of malaria infection when they travel to malaria endemic countries [21]. In addition, we use the model to study the effects of local malaria eradication efforts in these countries on the number of reported imported malaria cases in the USA. The model parameters and descriptions are listed in Table 1.

TABLE 1. Model Parameters and Descriptions.

Parameter	**Description**
α_{hm}	Human infectivity rate
α_{mh}	Mosquito infectivity rate
b_m	Mosquito biting rate
λ_h	Human birth rate
λ_m	Mosquito birth rate
β_h	Human loss of immunity rate
α_h	Human recovery rate
μ_d	Malaria induced death rate
μ_h, μ_m	Human, mosquito death rates
θ_m	Mosquito loss of incubation rate
c_h	Proportion of humans using bed net
c_m	Proportion of mosquitoes killed
c_u	Proportion of USA travellers to endemic countries
$\gamma = \frac{\alpha_{hm} b_m N_m}{N_h}$	Infection rate of humans in endemic countries
γ_u	Infection rate of USA travellers to endemic countries

Next, we introduce our malaria model variables. In malaria endemic countries, susceptible humans, S_h, are those individuals who are not infected with malaria but can get infected through bites from malaria infected mosquitoes. Infected individuals, I_h, are those humans who received bites from infected mosquitoes and show symptoms of the malaria disease. Recovered individuals, R_h, are those who received successful malaria treatment and show no more symptoms of the disease.

In malaria endemic countries, susceptible mosquitoes, S_m, are mosquitoes that do not carry any malaria parasite in their salivary glands. Usually it takes about 10 days for mosquitoes to become infectious after biting an infected individual [5, 6]. Exposed mosquitoes, E_m, are mosquitoes that carry some malaria parasites in their guts but are not yet able to infect humans with malaria. Infected mosquitoes, I_m, are mosquitoes with multitude of malaria parasites in their salivary glands and

are able to infect humans. In our model, we assume that the man-biting rate of mosquitoes in the malaria endemic countries is 1 *bite per day*.

In the USA, malaria susceptible human individuals, S_u, are those USA residents who are not infected with malaria but can get infected with malaria through bites from malaria infected mosquitoes while they are on travel in malaria endemic regions. Malaria infected individuals, I_u, are those humans who were bitten by malaria infected mosquitoes while they were on travel in malaria endemic regions outside of the USA. When the disease is detected in an individual in USA, he or she receives successful treatment. Therefore, after treatment in the USA the individual is no longer susceptible to malaria until he or she travels again to a malaria endemic country. Consequently, in our USA model we only consider the first episodes of imported malaria that occur in USA. Also, in the USA population, there is a non-susceptible group, NS_u. People in this group are USA residents who do not travel to malaria endemic regions outside of the USA.

Following Dembele *et al.*, we use the following first set of system of differential equations to describe the dynamics of the malaria disease in human and mosquito populations of malaria endemic countries [5,6].

$$\left.\begin{array}{rcl}
\frac{dS_h}{dt} &=& \lambda_h N_h + \beta_h R_h - \mu_h S_h - (1-c_h)\,\frac{\alpha_{mh} b_m I_m S_h}{N_h},\\
\frac{dI_h}{dt} &=& (1-c_h)\,\frac{\alpha_{mh} b_m I_m S_h}{N_h} - (\mu_h + \alpha_h + \mu_d)\, I_h,\\
\frac{dR_h}{dt} &=& \alpha_h I_h - (\mu_h + \beta_h)\, R_h,\\
\frac{dS_m}{dt} &=& \lambda_m(t) N_m - \mu_m S_m - (1-c_m)\,\frac{\alpha_{hm} b_m I_h S_m}{N_h},\\
\frac{dE_m}{dt} &=& (1-c_m)\left(\frac{\alpha_{hm} b_m I_h S_m}{N_h} - \theta_m E_m\right) - \mu_m E_m,\\
\frac{dI_m}{dt} &=& (1-c_m)\,\theta_m E_m - \mu_m I_m,
\end{array}\right\} \quad (1)$$

where the total human population is

$$N_h = S_h + I_h + R_h,$$

and the total mosquito population is

$$N_m = S_m + E_m + I_m.$$

Consequently, in malaria endemic countries, the total populations of human and mosquitoes are respectively governed by the following equations.

$$\begin{array}{rcl}
\frac{dN_h}{dt} &=& (\lambda_h - \mu_h)\, N_h - \mu_d I_h,\\
\frac{dN_m}{dt} &=& (\lambda_m(t) - \mu_m)\, N_m.
\end{array}$$

Next, we introduce the following model for the malaria disease in USA resident population that travels to malaria endemic regions.

$$\left.\begin{array}{rcl}
\frac{dS_u}{dt} &=& -(1-c_u)\,\frac{\alpha_{mh} b_m I_m S_u}{N_u},\\
\frac{dI_u}{dt} &=& (1-c_u)\,\frac{\alpha_{mh} b_m I_m S_u}{N_u}.
\end{array}\right\} \quad (2)$$

where the total US population is

$$N_u = S_u + I_u + NS_u.$$

The parameters of Models (1) and (2) are defined in Table 1. In Models (1) and (2), all the model parameters are non-negative and bounded. It is known that there is no population explosion in Model (1) [5, 6]. Consequently, there is no population explosion in Model (2). Furthermore, solutions of Models (1) and (2) are non-negative whenever the initial population sizes are non-negative.

2.1. **Rescaled endemic countries and USA malaria models.** Following Dembele *et al*., we make the following change of variables in Models (1) and (2) [5, 6].

$$s_h = \frac{S_h}{N_h},\ i_h = \frac{I_h}{N_h},\ r_h = \frac{R_h}{N_h},\ s_m = \frac{S_m}{N_m},\ e_m = \frac{E_m}{N_m},\ i_m = \frac{S_m}{N_m},\ s_u = \frac{S_u}{N_u},$$

and $i_u = \frac{I_u}{N_u}$.

As a result,

$$s_h + i_h + r_h = 1,\ s_m + e_m + i_m = 1,\ and\ s_u + i_u + ns_u = 1.$$

That is,

$$r_h = 1 - s_h - i_h,\ s_m = 1 - i_m - e_m,\ and\ ns_u = 1 - i_u - s_u.$$

In the new variables, Models (1) and (2) respectively reduce to the following systems of equations.

$$\left.\begin{array}{rcl} \frac{ds_h}{dt} &=& (\lambda_h + \beta_h)(1 - s_h) - \beta_h i_h - (1 - c_h)\gamma(t) s_h i_m + \mu_d i_h s_h, \\ \frac{di_h}{dt} &=& (1 - c_h)\gamma(t) s_h i_m - (\lambda_h + \alpha_h + \mu_d) i_h + \mu_d i_h^2, \\ \frac{de_m}{dt} &=& (1 - c_m)(\alpha_{hm} b_m i_h (1 - i_m - e_m) - \theta_m e_m) - \lambda_m(t) e_m, \\ \frac{di_m}{dt} &=& (1 - c_m)\theta_m e_m - \lambda_m(t) i_m, \end{array}\right\} \quad (3)$$

and

$$\left.\begin{array}{rcl} \frac{ds_u}{dt} &=& -(1 - c_u)\gamma_u(t) s_u i_m - s_u f(s_u, i_u, ns_u), \\ \frac{di_u}{dt} &=& (1 - c_u)\gamma_u(t) s_u i_m - i_u f(s_u, i_u, ns_u). \end{array}\right\} \quad (4)$$

where

$$\gamma_u(t) = \alpha_{mh}(t) b_m \frac{N_m}{N_u}$$

and

$$f(s_u, i_u, ns_u) = \frac{1}{N_u}\frac{dN_u}{dt}.$$

In the rest of the paper, we use Models (3) and (4) to study the impact of protecting USA travelers to malaria endemic countries from malaria infection, protecting residents of malaria endemic countries from mosquito bites and killing of mosquitoes in malaria endemic countries on the number imported malaria cases in the USA.

3. **Minimizing USA imported malaria cases.** In this section, we introduce an objective function that we use to seek the minimum number of imported malaria cases in USA travelers, the associated proportion of USA travelers to endemic malaria countries that we must protect from malaria infection, the associated proportion of humans in the malaria endemic countries to protect from malaria, and the associated proportion of mosquitoes to destroy in these malaria endemic countries visited by USA residents. Following [13], we consider the following objective function.

$$J(c_h, c_m, c_u) = \int_0^{t_f} (Ai_u(t) + Bc_h(t) + Dc_m(t) + Ec_u(t))\, dt$$

subject to Models (3) and (4). In the objective function, Ai_u is associated with a number I_u of USA imported malaria cases, Bc_h is associated with proportion of residents of endemic region protected from mosquito bites, Dc_m is associated with proportion of mosquitoes killed and Ec_u is associated with USA travelers to endemic regions protected from malaria infection, where t_f is the time period of the intervention. As in [13], we choose a linear function for the infection i_u and the controls c_h, c_m and c_u.

We seek an optimal control $\mathbf{c}^* = (c_h^*, c_m^*, c_u^*) \in U$ such that

$$J(c_h^*, c_m^*, c_u^*) = \min_{c_h, c_m, c_u \in U} J(c_h, c_m, c_u),$$

where the control set is

$$U = \{(c_h, c_m, c_u) \in [0,1]^3 | c_h, c_m, c_u \text{ are bounded Lebesgue integrable functions and } t \in [0, t_f]\},$$

and where A, B, D and E are constant. Proceeding exactly as in [13], the following result is immediate.

Theorem 3.1. *In Models (3) and (4), there exists*

$$\mathbf{c}^* = (c_h^*, c_m^*, c_u^*) \in U$$

such that

$$J(c_h^*, c_m^*, c_u^*) = \min J(c_h, c_m, c_u).$$

That is, there exists an optimal use of mosquito bed nets, insecticides, and anti-malaria drugs that will minimize the number of imported malaria cases in the United States of America.

Proof. In Models (3) and (4), all the coefficients are bounded. Hence, the set of all controls and corresponding state variables is nonempty. The control set U is convex and closed. Since the system is linear in c_h, c_m and c_u, the right hand side of the system is bounded by a linear function in the state and control variables. Moreover, the integrand of the objective function is convex in c_h, c_m and c_u. Hence, we obtain the existence of c_h^*, c_m^* and c_u^* that minimizes J. □

4. **CDC data on 2011 malaria acquisition regions.** The CDC malaria surveillance data, reported in 2013, shows that 1,925 cases of malaria were diagnosed and treated in USA in 2011. 1,920 of these reported malaria cases in USA were acquired overseas in regions with malaria transmission. This is the largest number reported since 1971. Most of the imported malaria cases were in USA residents who had been to sub-Saharan Africa. West Africa countries accounted for 721 (63%) of cases of malaria acquired in Africa by the USA residents. For example, the 2011 CDC data reported 213 and 156 malaria acquisitions from Nigeria and Ghana, respectively. In Table 2, we list the top 20 countries from the 2011 CDC data with the largest numbers of malaria acquisition by USA residents who had been to these regions. For the first time, India, a non-African country, is the individual country from which the most cases were imported into USA (see Table 2). In Table 2, we group all the other countries in the 2011 CDC data with less than 17 reported malaria acquisitions under the group name "other". There were 540 reported malaria acquisitions in this "other" group of countries.

5. **Model fit to CDC data on USA imported malaria.** In this section, we "fit" our models, Models (3) and (4), to the 2011 CDC USA imported malaria data summarized in Table 2. Following Dembele *et al.*, we choose specific positive and bounded mosquito infection rates γ and γ_u so that Models (3) and (4), fit the 2011 CDC data of Table 1. In particular, for $t \geq 0$, we assume that

$$\frac{N_m}{N_h} = \frac{10t}{5000 + t^2} + 10,$$

TABLE 2. 2011 CDC Data: Number of Imported Malaria Cases and Country Of Acquisition.

Malaria Acquisition Country	**2011 CDC Data**
Afghanistan	60
Cameroon	62
Cote D'Ivoire	28
Ethiopia	55
Ghana	156
Guinea	40
Guyana	19
Haiti	72
Honduras	21
India	223
Kenya	37
Liberia	90
Nigeria	213
Pakistan	39
Sierra Leone	116
Sudan	32
Uganda	61
Senegal	17
Eritrea	18
Gambia	21
Other	540

Then, $N_m(0) = 10N_h(0)$ and

$$\gamma(t) = \left(\frac{10t}{5000+t^2} + 10\right)\alpha_{hm}b_m.$$

Using the equation $\frac{N_m}{N_h} = \frac{10t}{5000+t^2} + 10$, the equations of the total human and mosquito populations,

$$\frac{dN_h}{dt} = (\lambda_h - \mu_h)N_h - \mu_d I_h$$

and

$$\frac{dN_m}{dt} = (\lambda_m(t) - \mu_m)N_m$$

we obtain that

$$\lambda_m(t) = \frac{5000 - t^2}{(5000+t^2)(t^2+t+5000)} + \lambda_h - \mu_h - \mu_d i_h + \mu_m.$$

Following Dembele *et al.*, we choose

$$\gamma_u(t) = \frac{ut}{34,000+t^2}, \quad 1 \le t \le 365$$

and u is a country dependent positive parameter to be determined from the 2011 CDC data (Table 3).

Typically, it takes 12 days to develop symptoms of malaria after receiving bites from infected mosquitoes. We make the following assumptions for USA residents who contracted malaria overseas**.** When USA residents exhibit malaria symptoms while on travel overseas in malaria endemic regions, then typically they must have spent at least 12 days in the malaria transmission region. Those who exhibit malaria symptoms on arrival in USA, were typically bitten by infected mosquitoes at most 12

days before returning to USA. Since we are only interested in first imported malaria episode cases that occurred in USA, Models (3) and (4) respectively become Models (5) and Model (6); stated below.

$$\left.\begin{array}{rcl} \frac{ds_h}{dt} & = & (\lambda_h+\beta_h)(1-s_h)-\beta_h i_h-(1-c_h)\left(\frac{10t}{5000+t^2}+10\right)\alpha_{hm}b_m s_h i_m \\ & & +\mu_d i_h s_h, \\ \frac{di_h}{dt} & = & (1-c_h)\left(\frac{10t}{5000+t^2}+10\right)\alpha_{hm}b_m s_h i_m-(\lambda_h+\alpha_h+\mu_d)i_h+\mu_d i_h^2, \\ \frac{de_m}{dt} & = & (1-c_m)(\alpha_{hm}b_m i_h(1-i_m-e_m)-\theta_m e_m)-\lambda_m(t)e_m, \\ \frac{di_m}{dt} & = & (1-c_m)\theta_m e_m-\lambda_m(t)i_m, \end{array}\right\} \quad (5)$$

where

$$\lambda_m(t)=\frac{5000-t^2}{(5000+t^2)(t^2+t+5000)}+\lambda_h-\mu_h-\mu_d i_h+\mu_m,$$

and

$$\left.\begin{array}{rcl} \frac{ds_u}{dt} & = & -(1-c_u)\gamma_u(t)s_u i_m, \\ \frac{di_u}{dt} & = & (1-c_u)\gamma_u(t)s_u i_m, \end{array}\right\} \quad (6)$$

where an estimate of each model parameter for each highly malaria acquisition country by USA residents, listed in Table 2, is given in Table 3.

TABLE 3. Estimates of Model Parameters Per Day.

Country	α_{mh}	α_{hm}	**u**	λ_h	β_h	α_h	μ_h	μ_m	θ_m	μ_d
Afghanistan	0.014	0.014	0.020845	0.000124	0.03	0.25	0.0000219	0.033	0.1	$3.1144*10^{-9}$
Cameroon	0.096	0.096	0.0043860	0.000094	0.03	0.25	0.0000329	0.033	0.1	$6.9372*10^{-7}$
Cote D'Ivoire	0.088	0.088	0.002231	0.00009	0.03	0.25	0.0000411	0.033	0.1	$2.3603*10^{-6}$
Ethiopia	0.037	0.037	0.010205	0.000098	0.03	0.25	0.0000219	0.033	0.1	$3.7081*10^{-8}$
Ghana	0.080	0.080	0.013519	0.00008	0.03	0.25	0.0000247	0.033	0.1	$3.8825*10^{-7}$
Guinea	0.081	0.081	0.00343	0.000102	0.03	0.25	0.0000329	0.033	0.1	$1.5945*10^{-7}$
Guyana	0.018	0.018	0.005986	0.000045	0.03	0.25	0.0000192	0.033	0.1	$3.01337*10^{-7}$
Haiti	0.005	0.005	0.02941	0.000071	0.03	0.25	0.0000247	0.033	0.1	$2.4658*10^{-7}$
Honduras	0.001	0.001	0.008831	0.000075	0.03	0.25	0.000037	0.033	0.1	$3.6696*10^{-10}$
India	0.001	0.001	0.09373	0.00006	0.03	0.25	0.0000219	0.033	0.1	$2.5911*10^{-9}$
Kenya	0.204	0.204	0.001605	0.000099	0.03	0.25	0.0000247	0.033	0.1	$1.8904*10^{-6}$
Liberia	0.220	0.220	0.0037256	0.000099	0.03	0.25	0.0000247	0.033	0.1	$1.1818*10^{-6}$
Nigeria	0.028	0.028	0.0506	0.0001	0.03	0.25	0.0000384	0.033	0.1	$1.3319*10^{-7}$
Pakistan	0.023	0.023	0.010676	0.000075	0.03	0.25	0.0000192	0.033	0.1	$1.5343*10^{-6}$
Sierra Leone	0.114	0.114	0.0074855	0.0001	0.03	0.25	0.0000493	0.033	0.1	$8.3397*10^{-7}$
Sudan	0.064	0.064	0.0034228	0.000089	0.03	0.25	0.0000247	0.033	0.1	$9.05*10^{-8}$
Uganda	0.3	0.3	0.0021354	0.000121	0.03	0.25	0.0000193	0.033	0.1	$5.2734*10^{-7}$
Senegal	0.01773	0.01773	0.005383	0.0001	0.03	0.25	0.0000219	0.033	0.1	$1.2547*10^{-7}$
Eritrea	0.0042	0.0042	0.007413	0.000092	0.03	0.25	0.0000192	0.033	0.1	$1.2421*10^{-8}$
Gambia	0.28	0.28	0.0007616	0.000094	0.03	0.25	0.0000274	0.033	0.1	$3.86*10^{-7}$
Other	0.005	0.005	0.220536	0.00009	0.03	0.25	0.00006	0.033	0.1	$1.4227*10^{-5}$

Using the initial population size

$$(s_h(0), i_h(0), e_m(0), i_m(0), s_u(0), i_u(0)) = (0.8, 0.1, 0.2, 0.1, 0.0012, 0),$$

in Models (5) and (6), with the parameter values in Tables 2 and 3, we "fit" the model to the 2011 CDC data on the imported malaria cases in USA. In Table 4, we list our model results for the imported malaria cases and the actual CDC data of Table 2. Using a Pearson's Chi square test, we obtain a chi-square value of 0.00078. The chi-square value with $\alpha = 0.05$ shows that there is no "significant" difference between the CDC malaria surveillance data of Table 2 and our mathematical model results of Table 4 [3].

TABLE 4. 2011 CDC Data Versus Model Results: Number of Imported Malaria Cases and Country Of Acquisition.

Malaria Country	**CDC Data**	**Model Result**
Afghanistan	60	60.02
Cameroon	62	62.04
Cote D'Ivoire	28	28.02
Ethiopia	55	55.01
Ghana	156	156.06
Guinea	40	40.04
Guyana	19	19.06
Haiti	72	72.04
Honduras	21	21.02
India	223	223.03
Kenya	37	37.09
Liberia	90	90.04
Nigeria	213	213.03
Pakistan	39	39.02
Sierra Leone	116	116.05
Sudan	32	32.06
Uganda	61	61.01
Senegal	17	17.02
Eritrea	18	18.01
Gambia	21	21.02
Other	540	540.03

To compute the optimal control $\mathbf{c}^* = (c_h^*, c_m^*, c_u^*) \in U$, we first define the Hamiltonian, H, as

$$H = Ai_u + Bc_h + Dc_m + Ec_u + \lambda_1 \frac{ds_h}{dt} + \lambda_2 \frac{di_h}{dt} + \lambda_3 \frac{de_m}{dt} + \lambda_4 \frac{di_m}{dt} + \lambda_5 \frac{ds_u}{dt} + \lambda_6 \frac{di_u}{dt},$$

where for each $i \in \{1, 2, 3, 4, 5, 6\}$, λ_i is the adjoint. Let $(x_1, x_2, x_3, x_4, x_5, x_6) = (s_h, i_h, e_m, i_m, s_u, i_u)$. Using the equation $\frac{\partial \lambda_i}{\partial t} = -\frac{\partial H}{\partial x_i}$, we obtain the following adjoint equations.

$$\left.\begin{array}{rcl}
\frac{d\lambda_1}{dt} &=& -[-(\lambda_h + \beta_h)\lambda_1 - (1 - c_h)\left(\frac{10t}{5000+t^2} + 10\right)\alpha_{hm} b_m (\lambda_1 - \lambda_2) i_m \\
& & +\mu_d i_h \lambda_1], \\
\frac{d\lambda_2}{dt} &=& -[(-\beta_h + \mu_d s_h)\lambda_1 - (\lambda_h + \alpha_h + \mu_d - 2\mu_d i_h)\lambda_2 \\
& & +(\alpha_{hm} b_m (1 - c_m)(1 - e_m - i_m) + \mu_d e_m)\lambda_3 + \mu_d i_m \lambda_4], \\
\frac{d\lambda_3}{dt} &=& -\left[((1 - c_m)(\alpha_{hm} b_m i_h - \theta_m) - \lambda_m(t))\lambda_3 + (1 - c_m)\theta_m \lambda_4\right], \\
\frac{d\lambda_4}{dt} &=& -[-\alpha_{hm} b_m (1 - c_h)\left(\frac{10t}{5000+t^2} + 10\right)(\lambda_1 - \lambda_2) s_h \\
& & -(1 - c_m)\alpha_{hm} b_m i_h \lambda_3 - \lambda_m(t)\lambda_4 - (1 - c_u)\gamma_u(t) s_u (\lambda_5 - \lambda_6)], \\
\frac{d\lambda_5}{dt} &=& -\left[-(1 - c_u)\gamma_u(t) i_m (\lambda_5 - \lambda_6)\right], \\
\frac{d\lambda_6}{dt} &=& -A.
\end{array}\right\} \quad (7)$$

Now, we let $t_1 = \frac{\partial H}{\partial c_h}$, $t_2 = \frac{\partial H}{\partial c_m}$, and $t_3 = \frac{\partial H}{\partial c_u}$. Then

$$\begin{aligned}
t_1 &= 0.05 + \alpha_{hm} b_m \left(\frac{10t}{5000+t^2} + 10\right) s_h i_m (\lambda_1 - \lambda_2), \\
t_2 &= 0.05 + (\theta_m e_m - \alpha_{hm} b_m (1 - i_m - e_m))\lambda_3 - \theta_m e_m \lambda_4, \\
t_3 &= 0.05 + \left(\frac{ut}{34{,}000+t^2}\right) s_u i_m (\lambda_5 - \lambda_6).
\end{aligned}$$

Using these, for each country we obtain the following corresponding functional values.

$$c_h^*(t_1) = \begin{cases} 0 & if \quad t_1 < 0 \\ c_1 & if \quad t_1 > 0 \end{cases}$$

$$c_m^*(t_2) = \begin{cases} 0 & if \quad t_2 < 0 \\ c_2 & if \quad t_2 > 0 \end{cases}$$

and

$$c_u^*(t_3) = \begin{cases} 0 & if \quad t_3 < 0 \\ c_3 & if \quad t_3 > 0 \end{cases}$$

where for each $i \in \{1, 2, 3\}$, $c_i \in \{0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9\}$.

To compute the number of malaria acquisition by USA residents when they travel to endemic countries, we assume that 365,776 USA residents travel to the malaria countries. Let $s_u(0)$ denote the initial proportion of the USA population who traveled to malaria endemic areas. Then, the number of malaria acquisition by USA residents when they travel to malaria endemic country u is $\frac{(s_u(0)-s_u(t_f))*365{,}776}{s_u(0)}$.

6. **Malaria control and prevention policies in acquisition regions and USA.** To control and prevent the spread of malaria disease in the world, and in particular in USA, humans need to be protected from malaria infection while efforts are underway for the global reduction or eradication of the malaria infected mosquito population. Several integrated malaria prevention and control policies are being adopted to achieve these goals [1, 4]. Dembele *et al.*, used a mathematical model to illustrate that in Mali, a malaria endemic country, complete malaria eradication can be achieved by adopting an integrated policy that consists of reducing the mosquito population and protecting Malians from mosquito bites. Dembele *et al.*, also pointed out that using chemically treated mosquito bed nets alone to protect Malians from mosquito bites will not be sufficient for the effective control of malaria in Mali. In this paper, we study the effect of adopting each of the following three malaria control policies on the number of USA imported malaria cases by USA residents.

Policy 1: *Protecting USA residents traveling to malaria transmission regions from malaria infection (for example by administering drugs for malaria prophylaxis).*

Policy 2: *Protecting residents of malaria endemic countries from mosquito bites (for example by offering mosquito bed nets).*

Policy 3: *Killing mosquitoes (for example by spraying mosquitoes with insecticides) in the malaria endemic countries USA residents usually visit.*

Policy 4: *Protecting USA residents traveling to malaria transmission regions from malaria infection while killing mosquitoes in endemic countries.*

In the next sections, we use Models (5) and (6) with the initial condition

$$(s_h(0), i_h(0), e_m(0), i_m(0), s_u(0), i_u(0)) = (0.8, 0.1, 0.2, 0.1, 0.0012, 0)$$

to study the impact of implementing each of our four malaria control policies on the 2011 CDC data of Tables 2.

6.1. **Policy 1: Protecting USA international travelers from malaria infection.** Under Policy 1, to reduce significantly the number of imported malaria infection cases in USA, we compute the optimal proportion of USA residents that we need to protect from malaria infection when they travel to malaria endemic countries. Thus, in Models (5) and (6), we set $c_h = c_m = 0$, where all the other

parameters are fixed at their values in Tables 2 and 3. Using our initial condition, we obtain an optimal value of c_u, $c_u^* = 90\%$, for each of the malaria endemic region of Table 5.

Under Policy 1, protecting at least 90% of the USA residents who travel to malaria endemic areas leads to the smallest number of imported malaria cases in the USA (see Table 5). Furthermore, under Policy 1, we obtain that the larger the percentage of protected USA travelers to the malaria regions, the smaller the number of USA imported malaria cases from those regions (see Table 5). For example, under Policy 1, protecting 90% of USA residents traveling to India results in only about 22 USA imported malaria cases, while protecting 10% of traveling USA residents to India leads to about 200 USA imported cases (see Table 5).

TABLE 5. Policy 1: Percentage of USA Protection and Optimal Number of Imported Malaria Cases.

Country	**10%**	**20%**	**30%**	**40%**	**50%**	**60%**	**70%**	**80%**	**90%**
Afghanistan	54.03	48.04	42.05	36.03	30.04	24.02	18.02	12.02	6.01
Cameroon	55.84	49.65	43.46	37.25	31.05	24.83	18.62	12.02	6.21
Cote D'Ivoire	25.23	22.43	19.63	16.82	14.02	11.22	8.41	5.61	2.8
Ethiopia	49.52	44.03	38.54	33.03	27.53	22.02	16.51	11.01	5.5
Ghana	140.49	124.91	109.34	93.7	78.11	62.48	46.85	31.25	15.62
Guinea	36.04	32.05	28.05	24.04	20.04	16.03	12.02	8.02	4.01
Guyana	17.16	15.26	13.36	11.45	9.54	7.63	5.72	3.82	1.91
Haiti	64.85	57.66	50.47	43.26	36.06	28.84	21.63	14.42	7.21
Honduras	18.92	16.82	14.73	12.63	10.52	8.41	6.31	4.21	2.1
India	200.78	178.53	156.27	133.92	111.64	89.3	66.96	44.66	22.32
Kenya	33.39	26.69	25.99	22.27	18.57	14.85	11.13	7.43	3.71
Liberia	81.05	72.07	63.08	54.06	45.06	36.04	27.03	18.03	9.01
Nigeria	191.77	170.52	149.26	127.92	106.63	85.29	63.96	42.66	21.32
Pakistan	35.12	31.23	27.34	23.43	19.53	15.62	11.71	7.81	3.9
Sierra Leone	104.47	92.89	81.31	69.68	58.09	46.46	34.84	23.24	11.61
Sudan	28.86	25.66	22.46	19.25	16.04	12.83	9.62	6.42	3.21
Uganda	54.92	48.83	42.74	36.63	30.54	24.42	18.31	12.21	6.1
Senegal	15.32	13.62	11.93	10.22	8.52	6.81	5.11	3.41	1.7
Eritrea	16.21	14.41	12.61	10.81	9.01	7.21	5.4	3.6	1.8
Gambia	18.92	16.82	14.73	12.62	10.52	8.41	6.31	4.21	2.1
Other	486.17	432.30	378.42	324.33	270.38	216.27	162.19	108.18	54.07
Total	1,729.06	1,537.42	1,345.77	1,153.35	961.44	768.99	576.66	384.64	192.22

6.2. **Policy 2: Protecting malaria endemic region residents from mosquito bites.** Under Policy 2, to reduce significantly the number of imported malaria infection cases in USA, we compute the optimal proportion of residents of malaria endemic countries that we need to protect from malaria bites. Thus, in Models (5) and (6), we set $c_u = c_m = 0$, where all the other parameters are fixed at their values in Tables 2 and 3. In this case, we obtain an optimal value of c_h, $c_h^* = 90\%$.

Under Policy 2, using bed nets to protect the residents of malaria endemic countries from mosquito bites does not seem to lead to a significant change in the number of imported malaria cases in the USA (not shown here). However, under Policy 2, we obtain that the larger the percentage of protected residents of malaria endemic countries, the smaller the number of USA imported malaria cases from those regions. For example, under Policy 2, protecting 90% of residents of India results in only about 222 USA imported malaria cases, while protecting 10% of residents of India leads to about 223 USA imported cases.

6.3. **Policy 3: Killing mosquitoes in malaria endemic regions.** Under Policy 3, to reduce significantly the number of imported malaria infection cases in USA, we compute the optimal proportion of mosquitoes in malaria endemic countries that we need to kill. Thus, in Models (5) and (6), we set $c_u = c_h = 0$, where all the other parameters are fixed at their values in Tables 2 and 3. In Table 6, we obtain an optimal value of c_m, $c_m^* = 90\%$.

Under Policy 3, killing at least 90% of mosquitoes in the malaria endemic countries leads to the smallest number of imported malaria cases in the USA (see Table 6). Furthermore, under Policy 3, as in Policy 1, we obtain that the larger the percentage of mosquitoes killed in the countries of malaria acquisition, the smaller the number of USA imported malaria cases from those regions (see Table 6). For example, under Policy 3, killing 90% of mosquitoes in India results in only about 135 USA imported malaria cases, while killing 10% of mosquitoes in India leads to about 221 USA imported cases (see Table 6).

TABLE 6. Policy 3: Percentage of Mosquitoes Killed in Endemic Regions and Optimal Number of Imported Malaria Cases.

Country	**10%**	**20%**	**30%**	**40%**	**50%**	**60%**	**70%**	**80%**	**90%**
Afghanistan	58.12	56.16	54.14	51.87	49.37	46.42	42.75	37.73	30.16
Cameroon	55.81	49.43	42.91	36.34	29.79	23.42	17.45	12.14	7.66
Cote D'Ivoire	25.18	22.27	19.32	16.36	13.44	10.63	8.01	5.67	3.66
Ethiopia	50.15	45.46	40.95	36.63	32.46	28.41	24.37	20.12	15.22
Ghana	140.02	123.75	107.33	91.00	75.05	59.78	45.64	32.99	21.83
Guinea	35.93	31.75	27.54	23.34	19.24	15.31	11.66	8.41	5.55
Guyana	18.25	17.43	16.60	15.74	14.81	13.78	12.55	10.98	8.71
Haiti	71.15	70.1	68.84	67.26	65.21	62.43	58.44	52.38	42.38
Honduras	20.84	20.61	20.31	19.91	19.37	18.61	17.48	15.71	12.74
India	221.1	218.65	215.49	211.32	205.58	197.49	185.47	166.69	135.18
Kenya	33.91	30.51	26.90	23.70	19.04	14.88	10.67	6.66	3.35
Liberia	82.45	74.33	65.67	56.43	46.67	36.51	26.19	16.28	8.01
Nigeria	198.11	183.65	169.59	155.75	142.02	128.04	113.13	96.19	74.54
Pakistan	36.80	34.62	32.47	30.30	28.07	25.72	23.10	19.92	15.63
Sierra Leone	104.75	93.06	80.98	68.66	56.19	43.87	32.13	21.61	12.96
Sudan	28.71	25.38	22.08	18.86	15.78	12.87	10.17	7.70	5.35
Uganda	56.29	51.16	45.59	39.53	33.00	26.03	18.76	11.55	5.31
Senegal	16.31	15.59	14.86	14.10	13.28	12.36	11.27	9.86	7.83
Eritrea	17.80	17.56	17.26	16.88	16.38	15.7	14.71	13.19	10.68
Gambia	19.36	17.56	15.62	13.52	11.26	8.86	6.38	3.93	1.83
Other	533.34	525.49	516.02	504.20	488.82	468.03	438.16	392.72	317.79
Total	1,824.38	1,724.52	1,620.43	1,511.7	1,394.83	1,269.15	1,128.49	962.43	746.37

7. **Policy 4: Integrated malaria control and prevention policy.** Unlike the single malaria control protocols of Policies 1-3, in this section, we explore the impact of an integrated malaria policy, Policy 4, a combination of Policies 1 and 3.

Under the integrated Policy 4, to reduce significantly the number of imported malaria infection cases in USA, we simultaneously compute the optimal proportion of USA travelers to protect from malaria infection and the optimal proportion of mosquitoes to kill in these countries. Thus, in Models (5) and (6) with $c_u \neq 0$, $c_h = 0$, $c_m \neq 0$, we keep all the other parameters fixed at their values in Tables 2 and 3. In this case, for each malaria endemic country, we seek the optimal values c_u^* and c_m^*, that lead to the smallest number of imported cases from that country. We summarize our results in Table 7.

TABLE 7. Policy 4: Percentage of Protected USA Residents Plus Percentage of Mosquitoes Killed and the Resulting Number of Imported Malaria Cases.

Country	**USA Protected**	**Mosquitoes Killed**	**Malaria cases**
Afghanistan	90%	70%	4.27
Cameroon	90%	70%	1.75
Cote D'Ivoire	90%	70%	0.80
Ethiopia	90%	70%	2.44
Ghana	90%	70%	4.56
Guinea	90%	70%	1.17
Guyana	90%	70%	1.26
Haiti	90%	70%	5.85
Honduras	90%	70%	1.75
India	90%	70%	18.56
Kenya	90%	70%	1.07
Liberia	90%	70%	2.62
Nigeria	90%	70%	11.32
Pakistan	90%	70%	2.31
Sierra Leone	90%	70%	3.21
Sudan	90%	70%	1.02
Uganda	90%	70%	1.88
Senegal	90%	70%	1.13
Eritrea	90%	70%	1.47
Gambia	90%	60%	0.64
Other	90%	70%	43.85

From Table 7, we obtained that an integrated policy of protecting at least 90% of USA travelers from malaria infection while killing 60% to 70% of mosquitoes in the countries of malaria acquisitions can lead to smaller numbers of imported malaria cases than either of the single Policies 1-3 alone. For example, protecting 90% of USA travelers to Gambia while killing 60% of the mosquitoes in that country leads no imported malaria cases from Gambia, a West African country (see Table 7).

8. **Conclusion.** The literature is filled with deterministic systems that have been used to study various aspects of the malaria disease dynamics [5, 6, 14]. A CDC malaria surveillance data showed that, in 2011, about 1,920 cases of malaria that were acquired overseas in regions with malaria transmission were diagnosed and treated in the USA. In the first part of this paper, we used an extension of a deterministic system of ordinary differential equations malaria model to "capture" the 2011 CDC reported data on the number of imported malaria cases in USA. In the second part of the paper, we used our "fitted" malaria model to compare the effects of four malaria control and prevention policies on the 1,920 cases of imported malaria cases in USA. In particular, we obtain the following results.

- If at least 90% of USA residents are protected from malaria infection when they travel to malaria endemic countries, then the number of imported malaria cases in the USA would reduce to no more than 192 cases. This would then

reduce the number of overseas acquired malaria in the USA by at least 1,728; about 90% less USA imported malaria cases.

- If at least 90% of mosquitoes are killed in the malaria endemic countries that are usually visited by USA residents, then the number of imported malaria cases in USA would reduce to no more than 746 cases. This would then reduce the number of overseas acquired malaria in the USA by at least 1,174; about 61% less USA imported malaria cases.
- If an "optimal" 90% of USA travelers are protected from malaria infection while $60\% - 90\%$ of mosquitoes are killed in each of the malaria transmission countries visited by USA residents, then the total number of imported malaria cases in USA would be less than 44. The "optimal" percentages depend on the specific countries (see Table 7).

Malaria disease caused by *Plasmodium falciparum* parasite is the most dangerous form of the disease; with the highest rates of complications and mortality [7]. In future work, it would be useful to study the relationship between *Plasmodium falciparum* malaria incidence in malaria transmission countries and the incidence of *Plasmodium falciparum* malaria in USA travelers when they visit malaria endemic regions.

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REFERENCES

[1] P. -L. Alonso, A. Djimde, H. Hughes and S. -A. Ward, A research agenda for malaria eradication: Drugs, DOI: 10.1371/journal.pmed.1000402, January 25, 2011.

[2] P. Carnevale, J. Mouchet, M. Coosemans, J. Julvez, S. Manguin, R. -D. Lenoble and S. Sircoulou, *Biodiversite du Paludisme dans le Monde*, Editions John Libbey Eurotext, Paris, 2004.

[3] R. -P. Cody and J. -K. Smith, *Applied Statistics and the SAS Programming Language*, Pearson Prentice Hall, Fifth Edition, 2006.

[4] K. -A. Cullen and P. -M. Arguin, Malaria Surveillance-United States, *2011 Centers for Diseases Control and Prevention,* (2013), 1–17.

[5] B. Dembele, A. Friedman and A. -A. Yakubu, Mathematical Model for optimal use of sulfadoxine-pyrimethamine as a temporary vaccine, *Bulletin of Mathematical Biology*, **72** (2010), 914–930.

[6] B. Dembele and A. -A. Yakubu, Optimal treated mosquito bed nets and insecticides for eradication of malaria in Missira, *Discrete and Continuous Dynamical Systems Series B*, **17** (2012), 1831–1840.

[7] A. -M. Dondorp, F. Nosten, P. Yi, D. Das and A. -P. Phyo, et al., Artemisinin resistance in Plasmodium falciparum malaria, *N Engl J Med*, **361** (2009), 455–467.

[8] J. -C. Koella and R. Antia, Epidemiological models for the spread of anti-malaria resistance, *Malaria Journal*, 2003, 2–3.

[9] W. -O. Kermack and A. G. McKendrick, Contributions to the mathematical theory of epidemics, *Proc. R. Soc A*, **115** (1927), 700–721.

[10] A. J. Lokta, Contributions to the analysis of malaria epidemiology, *Am. J. Hyg.*, **3** (1923), 11–21.

[11] G. Macdonald, The analysis of infection rate in diseases in which superinfection occurs, *Trop. Dis.*, **47** (1950), 907–915.

[12] C. -A. Mertler and R.-A. Vannatta, *Advanced and Multivariate Statistical Methods: Pratical Application and Interpretation*, Pyrczak Publishing, Fifth Edition, 2013.

[13] K. O. Okosun, R. Ouifki and N. Marcus, Optimal control analysis of a malaria disease transmission model that includes treatment and vaccination with waning immunity, *Biosystems*, **106** (2011), 136–145.
[14] C. Y. -J. Peng, *Data Analysis Using SAS*, Sage, 2009.
[15] R. Ross, *The Prevention of Malaria*, 2^{nd} edition, With Addendum on the Theory of Happenings, Murray, London, 1911.
[16] C. H. Sibley, J. E. Hyde, P. F. G. Sims, C. V. Plowe, J. G. Kublin, E. K. Mberu, A. F. Cowman, P. A. Winstanley, W. M. Watkins and A. M. Nzila, Pyrimethamine-sulfadoxine resistance in Plasmodium falciparum: What next?, *Trends in Parasitology*, **17** (2001), 570–571.
[17] N. Sogoba, S. Doumbia, P. Vounatsou, I. Baber, M. Keita, M. Maiga, S. Toure, G. Dolo, T. Smith and J. M. C. Ribeiro, Monotoring of larval habitats and mosquito densities in the sudan savanna of Mali: Implications of malaria vector control, *Am. J. Trop. Med. Hyg.*, **77** (2007), 82–88.
[18] B. -G. Tabachnick and L. -S. Fidell, *Using Multivariate Statistics*, Pearson, Sixth Edition, 2013.
[19] J. -F. Trape, A. Tall, C. Sokhna, A. -B. Ly, N. Diagne, O. Ndiath, C. Mazenot and V. Richard, The rise and fall of malaria in a West African rural community, Dielmo, Senegal, from 1990 to 2010: A 22 year longitudinal study, *The Lancet Infectious Diseases*, 14 (2014), 476–488.
[20] `http://www.cdc.gov/mmwr/preview/mmwrhtml/ss6205a1.htm`. Accessed 7/2/2016.
[21] World-Health-Organization, Malaria, Available from: `http://www.who.int/mediacentre/factsheets/fs094/en/`. Accessed 7/2/2016.

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