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The Role of HIV Positive Immigrants and Dual Protection in a Co-Infection of Malaria and HIV/AIDS

B. Nannyonga, J. Y. T. Mugisha and L. S. Luboobi

Department of Mathematics
Makerere University
P.O. Box 7062 Kampala, Uganda
bnk@math.mak.ac.ug

Abstract

A deterministic model for the dynamics of malaria and HIV co-infection with protective measures is developed. We extend the model to incorporate HIV positive immigrants into the community. The model is analysed and threshold values determined. Results from the model show that there is no disease-free point. Instead, an initial infection state governed by the infective immigration rate ϵ exists. A small perturbation around this point approaches global stability if there is reduced susceptibility to HIV by malaria infected individuals. Similarly, if HIV infectives are protected against malaria, the system attains global stability. It is shown that both diseases co-exist if the prevalence of one disease is low and the other high. From the results it is concluded that individuals protect themselves against malaria more when prevalence is high. The major finding of this study is that contrary to the malaria case, HIV positive individuals tend not to use protection when there is increased risk of disease transmission. This implies that as the transmission rate increases, protection against HIV/AIDS reduces. Results further conclude that infective immigrants increase the number of secondary infections as well as the influx of co-infections.

Keywords: HIV/AIDS positive immigrants, Malaria Co-infection, Dual Protection

1 Introduction

Malaria is an ancient disease that has influenced human evolution and history, and poses an enormous public health burden in Africa [26]. There are no relapses in malaria, making

it one of the world's greatest threats to life and human performance [22]. Simultaneously, since its emergence in the 1980s, the HIV/AIDS pandemic accounts for 30-46 million infections resulting in over 20 million deaths globally. It continues to fuel the spread of malaria by taking advantage of compromised immunity due to prolonged malaria exposure [1]. The co-infection of malaria with HIV/AIDS is a double blow to Sub-Saharan Africa, where malaria is a leading killer. This co-infection aggravates morbidity to levels that were previously unexpected due to increased risk of complicated and severe malaria [9]. There is thus need to develop strategies aimed at controlling the co-infection without prioritizing on pathogen over the other.

Malaria control in Africa is principally based on the presumptive treatment of fever cases using anti-malarial drugs. Despite unprecedented efforts on malaria vaccine research, there is no approved vaccine for malaria. Although therapeutic treatment strategies appear promising for retarding the progression of HIV related diseases, prevention remains the most effective strategy against the HIV/AIDS epidemic. The use of condoms as preventive strategy has been studied by numerous studies [21]. It has been rigorously tested at population level but the results have been mixed [24]. In addition, the search for effective HIV/AIDS vaccine has not been successful [14]. Therefore, effective programs to reduce HIV transmission are still needed [23]. The enormous public health inflicted by malaria and HIV/AIDS necessitates the use of mathematical modelling to gain insights into their transmission dynamics and to evaluate the control measures in place.

Numerous mathematical models have been developed to explore theoretical aspects of malaria and HIV/AIDS dynamics at population and cellular level. Most of these models ignore the fact that re-emerging malaria poses further significant public health challenges in a population where it co-exists with HIV/AIDS. Such challenges arise not only from the drain of resources on HIV/AIDS, but on the effects of malaria on the dynamics of HIV/AIDS. The need to develop in depth mathematical models to study the effect of the co-infection is further expressed in the synergistic tendency of the interaction between these two diseases when they are co-habiting within one host [1, 20]. It is paramount that we determine and evaluate the best control strategies that target to suppress the co-infection. In this paper, a deterministic model for the co-infection of HIV/AIDS and malaria with protection against both diseases is designed. The model assumes that HIV/AIDS can only be acquired through sexual intercourse with an infected individual. The density of the new recruits is structured by their HIV status and protection against malaria. The primary disease is HIV/AIDS, a slowly progressing disease. Hosts that are already infected with HIV/AIDS become co-infected with malaria. Other researchers, such as [1] and [20] have studied this co-infection. The major differences between their work

and the study proposed in this paper is that both researchers do not consider HIV/AIDS immigrants into the population although it is an important aspect of the disease. Further, they do not consider protection against either disease. The mode of protection considered in HIV/AIDS is by use of condoms while protection against malaria is by the use of mosquito nets, and or other mosquito repellants. The general approach to this article is as follows. The model is formulated and analysed in Section 2. A discussion of results is given in Section 3. At this stage, not enough details or parameter values are known about how often an individual protects against either disease. However, a general analysis of the effects of protective intervention on both diseases is a first step to a better understanding of the importance of the malaria-HIV co-infection.

2 Formulation of the Model

We start by defining the variables of the human population. Let the proportion of individuals at risk of acquiring HIV and malaria be $S(t)$. Define $P(t)$ as the proportion that migrate into the population while protected against malaria and can acquire HIV upon contact with an infected individual. Let $E_m(t)$ be the individuals exposed to malaria and develop clinical symptoms to become $I_m(t)$. For HIV positive individuals, we Let $I_h(t)$ be those infected with HIV but displaying no AIDS symptoms. Upon exposure to malaria, they become $E_{mh}(t)$ and then progress to $I_{mh}(t)$ after they display clinical symptoms of malaria. As in the case for HIV, the AIDS individuals denoted by $I_a(t)$ can be exposed to malaria and become $E_{ma}(t)$. After displaying clinical symptoms of malaria, they progress to the $I_{ma}(t)$ class. Finally, we define $R(t)$ as those individuals that have gained temporary immunity to malaria. Therefore, the total human population at any time t as $N(t) = S(t)+P(t)+E_m(t)+I_m(t)+I_h(t)+E_{mh}(t)+I_{mh}(t)+I_a(t)+E_{ma}(t)+I_{ma}(t)+R(t)$.

Next, we define our parameters. Let μ be the per capita natural death rate for the human host, and Λ be the per capita constant recruitment rate into the human population. A fraction ϵ of these are HIV positive while ρ are protected against malaria. Thus, the total recruitment into the susceptible class is $(1-\epsilon-\rho)\Lambda$. Susceptible individuals become infected with HIV at a rate

$$\alpha_h = \frac{\beta c[I_h + \xi_{mh}(E_{mh} + \zeta_{mh} I_{mh}) + \xi_a(I_a + \xi_{mh}(E_{ma} + \zeta_{mh} I_{ma}))]}{N}$$

where β is the probability that a susceptible individual acquires HIV upon contact with an infected individual and c is the rate at which an individual changes sexual partners. The prevalence of HIV/AIDS is given by $\frac{[I_h+\xi_{mh}(E_{mh}+\zeta_{mh}I_{mh})+\xi_a(I_a+\xi_{mh}(E_{ma}+\zeta_{mh}I_{ma}))]}{N}$. Assuming that an individual infected with HIV and exposed to malaria is more infectious of HIV than one infected with only HIV. We use parameter ξ_{mh} to account for the relative infectiousness

of HIV individuals exposed to malaria as compared to those infected with HIV-only. This implies that the infection rate of an individual with HIV and exposed to malaria is $\beta c\xi_{mh}$. The same assumption is made for an individual dually infected with HIV and malaria to give $\beta c\xi_{mh}\zeta_{mh}$. Similar definitions are made for AIDS individuals. Therefore parameter ξ_a accounts for the fact that AIDS individuals are more infectious than HIV individuals due to a correlation between HIV viral load and infectiousness. Hence, the rates at which $I_a,\ E_{ma}$ and I_{ma} individuals transmit HIV are $\beta c\xi_a,\ \beta c\xi_a\xi_{mh}$ and $\beta c\xi_a\xi_{mh}\zeta_{mh}$ respectively.

Malaria is transmitted horizontally with the transmission modelled by standard incidence function
(Hethcote, 2000). Therefore, individuals at risk of acquiring malaria do so at a rate $\alpha_m = \frac{\sigma a I_v}{N}$ where a is the transmission probability of malaria in the mosquito and σ is the mosquito biting rate. When a mosquito bites a human, they become exposed to malaria. Malaria then develops within the human at a rate τ_m and the individual displays clinical symptoms. The individual dies from the infection at a rate ν_m or recover at a rate γ_m. If an individual is infected with HIV or AIDS, there is increased rates of death ξ and θ respectively. Similarly, HIV/AIDS individuals infected with malaria recover at slower rates γ_{mh} and γ_{ma} respectively. When HIV/AIDS individuals acquire malaria, there is an increase in progression of either disease [1]. We therefore use parameters ω and π to denote the increased rate due to dual infection with malaria and HIV. Similarly, we use η to denote the relative increase in susceptibility to HIV by a malaria infected individual. Further, let δ and υ be the increased susceptibility to malaria by HIV and AIDS infected individuals respectively. Individuals that are infected with malaria-only recover and join the susceptible class or gain temporary immunity. Let p be the fraction of individuals who recover from malaria that gain temporary immunity. The other fraction $(1-p)$ join the susceptible class immediately. Immune individuals lose their immunity at a rate ε to become susceptibles again.

Recent study [1] has concluded that infection with HIV increases susceptibility to malaria and HIV/AIDS viral load. Our model uses a parameter q to represent the fraction of the dually infected malaria and HIV individuals that develop AIDS in the course of infection with malaria. The other fraction $(1-q)$ is assumed to have HIV after recovery from malaria.

In the mosquito population, we denote $S_v(t)$ as the susceptible vector, $E_v(t)$ as the exposed vector, and $I_v(t)$ the infected vector. Therefore, the total mosquito population at time t, $N_v(t) = S_v(t) + E_v(t) + I_v(t)$. Let Λ_v be the constant recruitment rate into the susceptible mosquito population, and μ_v be the per capita natural mortality. We define the force of

infection of a susceptible mosquito by an infected human as

$$\alpha_v = \frac{\sigma b(I_m + \xi_v(I_{mh} + \zeta_v I_{ma}))}{N}$$

where b is the transmission probability of malaria in the mosquito vector. Like in the human case, we use ξ_v and ζ_v to model the relative increase in infectivity of malaria by a dually infected HIV/malaria and AIDS/malaria individual as compared to an individual infected with malaria-only. Hence, the rate at which a mosquito is infected from an individual with HIV and malaria is $\sigma b\xi_v$, and one with AIDS and malaria is $\sigma b\xi_v\zeta_v$. In this case, $\sigma b\xi_v\zeta_v > \sigma b\xi_v > \sigma b$.

Our major interest of the study is the effect of protection in a population with infective immigrants. We therefore introduce parameters ω_m and ω_h to denote the probability of success in protection against malaria and HIV/AIDS respectively. The modified forces of infection α_h and α_m then become

$$\alpha_h = \frac{\beta c(1-\omega_h)[I_h + \xi_{mh}(E_{mh} + \zeta_{mh}I_{mh}) + \xi_a(I_a + \xi_{mh}(E_{ma} + \zeta_{mh}I_{ma}))]}{N}$$

and

$$\alpha_m = \frac{\sigma a(1-\omega_m)I_v}{N}.$$

We assume no simultaneous infection. Thus, to be dually infected, an individual must be infected first with malaria, or HIV, and then with HIV or malaria respectively. With the above definitions and assumptions, we have the following system of coupled differential equations:

$$\begin{aligned}
\dot{S} &= (1-\epsilon-\rho)\Lambda - \alpha_m S - \alpha_h S - \mu S + \varepsilon R + (1-p)\gamma_m I_m + \lambda P \\
\dot{P} &= \rho\Lambda - \mu P - \lambda P - \alpha_h P \\
\dot{E_m} &= \alpha_m S - \alpha_h E_m - \mu E_m - \tau_m E_m \\
\dot{I_m} &= \tau_m E_m - \eta\alpha_h I_m - \mu I_m - \nu_m I_m - \gamma_m I_m \\
\dot{I_h} &= \epsilon\Lambda + \alpha_h S + \alpha_h P + \alpha_h R - \delta\alpha_m I_h - \mu I_h - \tau_h I_h + (1-q)\gamma_{mh} I_{mh} \\
\dot{E_{mh}} &= \delta\alpha_m I_h + \alpha_h E_m - \mu E_{mh} - \tau_h E_{mh} - \omega\tau_m E_{mh} \\
\dot{I_{mh}} &= \omega\tau_m E_{mh} + \eta\alpha_h I_m - \mu I_{mh} - \gamma_{mh} I_{mh} - \xi\nu_m I_{mh} - \pi\tau_h I_{mh} \\
\dot{I_a} &= \tau_h I_h - \upsilon\alpha_m I_a - \mu I_a - \nu_h I_a + \gamma_{ma} I_{ma} \\
\dot{E_{ma}} &= \upsilon\alpha_m I_a - \mu E_{ma} - \nu_h E_{ma} - \omega\tau_m E_{ma} + \tau_h E_{mh} \\
\dot{I_{ma}} &= \omega\tau_m E_{ma} + \pi\tau_h I_{mh} + q\gamma_{mh} I_{mh} - \mu I_{ma} - \theta\nu_h I_{ma} - \gamma_{ma} I_{ma} - \xi\nu_m I_{ma} \\
\dot{R} &= p\gamma_m I_m - \alpha_h R - \mu R - \varepsilon R \\
\dot{S_v} &= \Lambda_v - \alpha_v S_v - \mu_v S_v \\
\dot{E_v} &= \alpha_v S_v - \mu_v E_v - \tau_v E_v \\
\dot{I_v} &= \tau_v E_v - \mu_v I_v
\end{aligned} \tag{1}$$

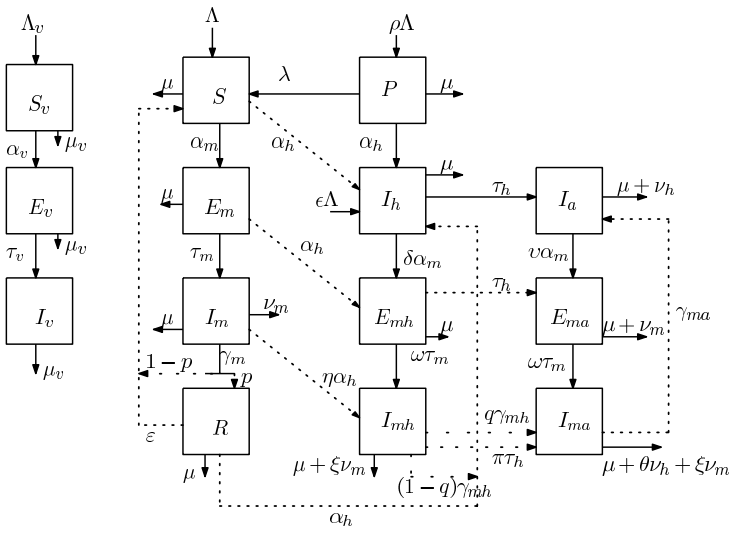

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Figure 1: Compartmentalized model for malaria and HIV/AIDS co-infection

and

$$\begin{array}{ll} \frac{dN}{dt} & = \Lambda - \mu N - \nu_m I_m - \xi\nu_m I_{mh} - \nu_h I_a - \nu_h E_{ma} - \theta\nu_h I_{ma} - \xi\nu_m I_{ma} \\ \frac{dN_v}{dt} & = \Lambda_v - \mu_v N_v \end{array} \tag{2}$$

2.1 Analysis of the model

First, we highlight the role of HIV positive immigrants in the community. Later, we analyse the model and determine the stationary states and the conditions under which

both diseases will prevail. We look at the situation when the imigrants include those that are protected against malaria and some that are HIV positive. Comparison is then done between a situation with no HIV positive imports and when $\epsilon \ll 1$. Finally, we allow protection against either or both diseases and a stability analysis is done.

We note from Equation 2, that since $\frac{dN}{dt} < 0$ for $N > \frac{\Lambda}{\mu}$, all solutions of the system with non-negative initial data approach, enter, or stay inside the subset Ω defined by $0 \leq S + P + E_m + I_m + I_h + E_{mh} + I_{mh} + I_a + E_{ma} + I_{ma} + R \leq \frac{\Lambda}{\mu}$. Hence, we can only consider solutions of the system in Ω. If there is no disease-induced death rate, we have $N^* \to \frac{\Lambda}{\mu}$ as $t \to \infty$. Similarly, $N_v^* \to \frac{\Lambda_v}{\mu_v}$ as $t \to \infty$. In this case, our populations have reached their limiting values [25]. Hence, the feasible region $\Omega = \{(S, P, E_m, I_m, I_h, E_{mh}, I_{mh}, I_a, E_{mh}, I_{ma}, R, S_v, E_v, I_v)$
$: S, P, E_m, I_m, I_h, E_{mh}, I_{mh}, I_a, E_{mh}, I_{ma}, R, S_v, E_v, I_v \geq 0; N \leq \frac{\Lambda}{\mu}; N_v \leq \frac{\Lambda_v}{\mu_v}\}$ is a positively invariant set and the model is well posed and biologically meaningful.

When the infective imports just moved into the population, we assume that there is no interaction with the susceptible population. We call this the initial infection state. This point is given by

$$\begin{aligned} E^0 &= (S^0, P^0, E_m^0, I_m^0, I_h^0, E_{mh}^0, I_{mh}^0, I_a^0, E_{ma}^0, I_{ma}^0, R_0, S_v^0, E_v^0, I_v^0) \\ &= \left(\tfrac{\Lambda[(\mu+\lambda)(1-\epsilon)-\mu\rho]}{\mu(\mu+\lambda)}, \tfrac{\rho\Lambda}{\mu+\lambda}, 0, 0, \epsilon\Lambda, 0, 0, 0, 0, 0, 0, \tfrac{\Lambda_v}{\mu_v}, 0, 0\right) \end{aligned} \tag{3}$$

Note that we can obtain a disease-free state if $\epsilon = 0$. When $0 < \epsilon \ll 1$, there is a small perturbation in the system. We therefore analyse this point to determine if this perturbation causes the system to explode or can be contained. The conditions necessary to control the infection are determined and analysed.

2.1.1 Threshold values for the model

We define an important quantity for our model, the basic reproduction number R_{mh}. It measures the average number of new infections generated by a single infectious individual in a population where there are HIV positive imports and protective measures. The conditions under which the disease will prevail or be controlled is determined by this parameter at the point (3). As shown in Appendix A,

$$\begin{aligned} R_{mh} &= \max\{R_m, R_h\} \\ &= \max\left\{\sqrt{\tfrac{(1-\omega_m)\sigma^2 ab\tau_m\tau_v\mu\Lambda_v[(\mu+\lambda)(1-\epsilon)-\mu\rho]}{\mu_v^2\Lambda(\mu+\lambda)(\mu+\tau_m)(\mu+\nu_m+\gamma_m)(\mu_v+\tau_v)}}, \tfrac{\beta c(1-\omega_h)(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)}\right\} \end{aligned} \tag{4}$$

$R_{mh} < 1$ implies that a small perturbation by the infective imports does not explode to an endemic state. Thus, our initial infection state is stable if $R_{mh} < 1$ and unstable if

$R_{mh} > 1$. In the absence protection $\omega_m = \omega_h = 0$, and

$$\begin{aligned} R^0_{mh} = & \max\{R_{m0}, R_{h0}\} \\ & = \max\left\{\sqrt{\frac{\sigma^2 ab\tau_m\tau_v\mu\Lambda_v[(\mu+\lambda)(1-\epsilon)+\mu\rho]}{\mu_v^2\Lambda(\mu+\lambda)(\mu+\tau_m)(\mu+\nu_m+\gamma_m)(\mu_v+\tau_v)}}, \frac{\beta c(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)}\right\} \end{aligned} \tag{5}$$

It can be noted that $R_{mh} < R^0_{mh}$. This implies that protective interventions can significantly reduce the burden of disease.

As in other co-infections, the largest of these two values is the reproduction number for the co-infection [27]. If malaria has a higher endemic state than HIV, then

$$R_{mh} = R_m = \sqrt{R_{human}R_{vector}} = \sqrt{\frac{(1-\omega_m)\sigma a\tau_m\mu[(\mu+\lambda)(1-\epsilon)-\mu\rho]}{\Lambda(\mu+\lambda)(\mu+\tau_m)(\mu+\nu_m+\gamma_m)}\frac{\sigma b\tau_v\Lambda_v}{\mu_v^2(\mu_v+\tau_v)}} \tag{6}$$

R_m is the product of the basic reproduction number in the human, R_{human}, and in the vector, R_{vector}. Both R_{human} and R_{vector} must be great than 1 for R_m to be greater than 1. The value of R_m depends on the contact rates σa and σb. If $\sigma b\tau_v\Lambda_v > \mu_v^2(\mu_v+\tau_v)$ then $R_{vector} > 1$ and malaria is endemic in the vector population. Using the parameters in Table 1, we show that at the point when $R_{vector} = 1$, $b = 21.85\%$. Therefore, $b = 21.85\%$ is the critical value of b below which malaria will not develop in the mosquito. Similarly, if $(1-\omega_m) > \frac{\Lambda(\mu+\tau_m)(\mu+\nu_m+\gamma_m)}{\sigma a\mu\tau_m}$ then $R_{human} > 1$ and malaria persists in the human population. This gives $\omega_m = 33.01\%$ as the threshold value of protection against malaria. When the protection rate is below this value, malaria develops to endemic levels in the human population. If R_{vector}, $R_{human} < 1$, both populations remain free from malaria invasion. If however $R_{human} < 1$ and $R_{vector} > 1$, malaria will have a large impact in the mosquito population and less impact in the human. Similarly, whenever $R_{human} > 1$ and $R_{vector} < 1$ malaria has a higher impact in the human population and less impact in the mosquito population. In both cases when one of the reproduction numbers is less than 1, $R_m < 1$ and malaria does not develop. The fraction $\frac{(\mu+\lambda)(1-\epsilon)-\mu\rho}{\mu+\lambda}$ gives the proportion of individuals that lose protection against malaria. The larger this value is, the higher the value of R_m.

As in the case for malaria, when HIV has a higher endemic state,

$$R_{mh} = R_h = \frac{\beta c(1-\omega_h)(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)} \tag{7}$$

The term $\frac{\beta c(\mu+\nu_h+\xi_a\tau_h)(1-\epsilon)}{(\mu+\nu_h)}$, represents the average number of susceptible individuals infected by one infectious individual during their effective infectious period in the presence of infective immigrants. $\frac{1-\omega_h}{\mu+\tau_h}$ is the fraction of individuals that lose protection against

HIV/AIDS in the course of disease progression. Let us assume that $\xi_a = 2$, $\epsilon = 0.01$ and $\beta c = 0.0011$. When $R_h = 1$, $\omega_h = 89.67\%$. This implies that atleast 89.67% of the population would need to protect against HIV/AIDS for effective control. It is noted from the expressions for R_m and R_h that as ω_m and ω_h decrease, R_m and R_h respectively increase. This would give rise to an increase in disease prevalence. Figure 2 (A) and (B).

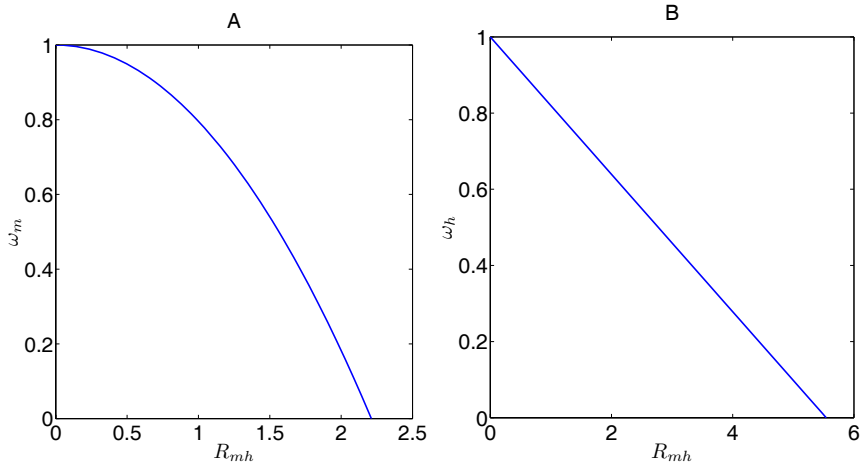

Figure 2: Plots showing variation of R_{mh} with protection. (A) shows change in R_{mh} with protection against malaria ω_m, while (B) shows change in R_{mh} with protection against HIV/AIDS ω_h. $\beta c = 0.0011$, $b = 0.50$, other parameters are as in Table 1.

Malaria and HIV coinfections aggravate morbidity to levels that were previously unexpected [1, 9]. In the general sense, for any protective measures to work, individuals must be willing to try and successfully apply them. The question that remains is when would individuals adopt to protective interventions. In trying to answer this question, we derive general expressions that give the adoptive criterion. We start by assuming that malaria has a higher endemic state than HIV. Then, $R_{mh} = R_m = \sqrt{\frac{(1-\omega_m)\sigma^2 ab\tau_m\tau_v\mu\Lambda_v[(\mu+\lambda)(1-\epsilon)+\mu\rho]}{\mu_v^2\Lambda(\mu+\lambda)(\mu+\tau_m)(\mu+\nu_m+\gamma_m)(\mu_v+\tau_v)}}$. This gives $1-\omega_m = \frac{R_{mh}^2}{bk}$ where $k = \frac{\sigma^2 a\tau_m\tau_v\mu\Lambda_v[(\mu+\lambda)(1-(\epsilon+\rho))+\rho\lambda]}{\mu_v^2\Lambda(\mu+\lambda)(\mu+\tau_m)(\mu+\nu_m+\gamma_m)(\mu_v+\tau_v)}$ and b is the transmission probability of malaria in the mosquito vector. Therefore, $\omega_m = 1 - \frac{R_{mh}^2}{bk}$. It can be noted that as b, increases ω_m increases. This concludes that as endemicity increases, individuals tend to protect more, Figure 3 (A).

When HIV has a higher prevalence rate, it implies that $R_{mh} = R_h = \frac{\beta c(1-\omega_h)(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)}$. Let $q = \frac{(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)}$ then $\omega_h = 1 - \frac{R_{mh}}{q\beta c}$. Contrary to the case for malaria, the rate at which individuals protect against HIV/AIDS decreases as the transmission probability increases. This would imply that individuals would less likely use protection if they sus-

pect transmitting the disease. These results as depicted in Figure 3 (B). The higher the probability of transmission βc, the less likely individuals will protect against HIV/AIDS.

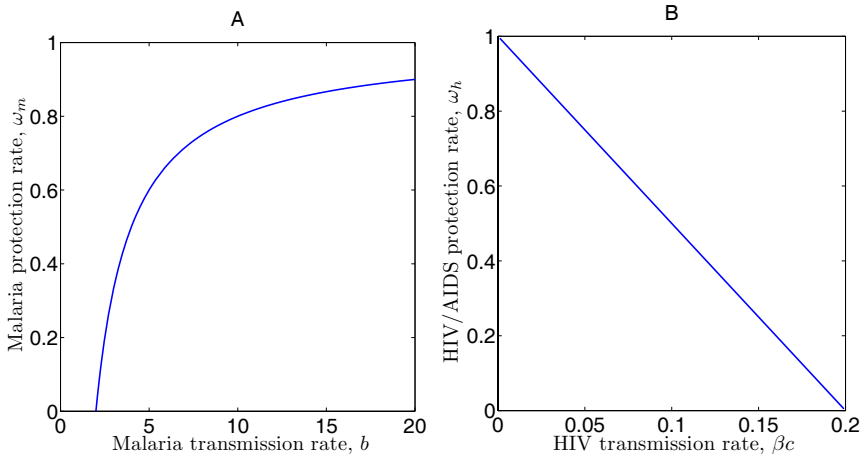

Figure 3: Plots showing variations in probability of transmission of malaria from human to mosquito, b with protection ω_m, and variation of transmission of HIV/AIDS βc, with ω_h. In both cases we have set the basic reproduction number $R_{mh} = 2$. Parameters defined in Table 1.

2.1.2 Global stability analysis

In this subsection, we determine if the population can attain global stability after a small perturbation by the infective immigrants in the presence of protection. We start by assuming that $\lim_{N\uparrow} \frac{\epsilon}{N} \approx 0(\epsilon)$. Then, using an approach applied by Castillo-Chavez *et al.* (2002), we rewrite system (1) in the form

$$\begin{array}{rcll} \frac{dX}{dt} & = & F(\mathbf{x}, Z) & \\ \frac{dZ}{dt} & = & G(X, Z) & G(\mathbf{x}, 0(\epsilon)) = 0(\epsilon) \end{array} \tag{8}$$

where the components of vector $X \in \Re^m$ denotes the number of uninfected individuals and the components of vector $Z \in \Re^n$ denotes the number of infected individuals including the exposed and infectious. $E^o = (x^*, 0(\epsilon))$ is the initial state of infection. The following two conditions must be met to guarantee *global asymptotic stability.*

(1) For $\frac{dX}{dt} = F(X, 0(\epsilon))$, X^* is *globally asymptotically stable (g.a.s)*,

(2) $G(X, Z) = AZ - \hat{G}(X, Z)$, $\hat{G}(X, Z) \geq 0$ for $(X, Z) \in \Omega$, where $A = D_z G(X^*, 0(\epsilon))$ is an M-matrix (the off-diagonal elements of A are nonnegative) and Ω is the region where the model makes biological sense. $\frac{dX}{dt}|_1 = F(X, 0(\epsilon))$ denotes the matrix of

the uninfected classes at the initial infection state. A is defined as the Jacobian matrix for the transfer terms into the respective infected classes of vector Z at the initial state, and $\hat{G}(X,Z)$ denotes the infection terms in the respective classes. If system (1) satisfies the above two conditions then the fixed point $E^o = (x^*, 0(\epsilon))$ is a *globally asymptotic stable (g.a.s.)* equilibrium of (1) provided $R_{mh} < 1$ and assumptions (1) and (2) are satisfied.

For system (1)

$$\begin{aligned} X &= (S, P, R, S_v) \\ Z &= (E_m, I_m, I_h, E_{mh}, I_{mh}, I_a, E_{ma}, I_{ma}, E_v, I_v) \\ F(X, 0(\epsilon)) &= \begin{pmatrix} (1-(\epsilon+\rho)\Lambda - \mu S & \rho\Lambda & 0 & \Lambda_v - \mu_v S_v \end{pmatrix}^T \end{aligned} \tag{9}$$

$$A = \begin{pmatrix} -A_{11} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{(1-\omega_m)}{N}\sigma a \\ \tau_m & -A_{22} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -A_{33} & \Theta\xi_{mh} & Y & \Theta\xi_a & \Theta\xi_a\xi_{mh} & \Theta\xi_a\xi_{mh}\zeta_{mh} & 0 & 0 \\ 0 & 0 & 0 & -A_{44} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & w\tau_m & -A_{55} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau_h & 0 & 0 & -A_{66} & 0 & \gamma_{ma} & 0 & 0 \\ 0 & 0 & 0 & \tau_h & 0 & 0 & -A_{77} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (\pi\tau_h + q\gamma_{mh}) & 0 & w\tau_m & -A_{88} & 0 & 0 \\ 0 & \sigma bp & 0 & 0 & \xi_v\sigma bp & 0 & 0 & \xi_v\zeta_v\sigma bp & -A_{99} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_v & -\mu_v \end{pmatrix} \tag{10}$$

where $A_{11} = (\mu + \tau_m)$, $A_{22} = (\mu + \nu_m + \gamma_m)$, $A_{33} = (\mu + \tau_h) - \Theta$, $\Theta = \frac{(1-\omega_h)\mu\beta c(1-\epsilon)}{\Lambda}$, $A_{44} = (\mu + \tau_h + w\tau_m)$, $A_{55} = (\mu + \gamma_{mh} + \xi\nu_m + \pi\tau_h)$, $A_{66} = (\mu + \nu_h)$, $A_{77} = (\mu + \nu_h + w\tau_m)$, $A_{88} = (\mu + \theta\nu_h + \gamma_{ma} + \xi\nu_m)$, $A_{99} = (\mu_v + \tau_v)$, $p = \frac{\Lambda_v\mu}{\mu_v\Lambda}$, $Y = \Theta\xi_{mh}\zeta_{mh} + (1-q)\gamma_{mh}$.

Since from definition $\omega_m \leq 1$, $\epsilon \leq 1$, and $q \leq 1$, all the off diagonal elements of A are non negative. Matrix $\hat{G}(X,Z)$ is given by

$$\begin{pmatrix} \alpha_m(1-\frac{S}{N}) + \alpha_h E_m & \phi & \alpha_h(1-\frac{(S+P+R)}{N}) + \delta\alpha_m I_h - \epsilon\Lambda & -F & -\phi & \psi & -\psi & 0 & \alpha_v(1-\frac{S_v}{N}) & 0 \end{pmatrix}^T \tag{11}$$

where $F = (\delta\alpha_m I_h + \alpha_h E_m)$, $\phi = \eta\alpha_h I_m$, $\psi = \upsilon\alpha_m I_a$. The global stability of this point is analysed for different conditions as follows:

I. Case of maximum protection against malaria, that is, $\sigma = 0$

First we assume that there are no new malaria infections due to maximum protective interventions. This case is not practical in regions of high disease burden but may be applicable in settings where protection is enforced. This would imply that the daily biting rate of the mosquito, σ, equal to zero. Therefore we analyse (1) under this assumption. The resulting model and matrix are shown in Appendix B. From Section 2.1.1, with $\sigma = 0$, $R_{mh} = R_h = \frac{\beta c(1-\omega_h)(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)}$ which is the HIV basic reproduction number. This is

stable if $R_{mh} < 1$ and unstable if $R_{mh} > 1$.

For global stability, we use matrix A and set $\sigma = 0$ to obtain matrix A_m in Appendix B. Note that since from definition $\omega_h \leq 1$ and $\epsilon \leq 1$, then all the off-diagonal elements of A are non negative. Similarly from (11),

$$\hat{G_m}(X,Z) = \Big(\ \alpha_h E_m \quad \eta\alpha_h I_m \quad \alpha_h(1 - \tfrac{(S+P+R)}{N}) - \epsilon\Lambda \quad -\alpha_h E_m \quad -\eta\alpha_h I_m \quad 0 \quad 0 \quad 0 \quad 0 \quad 0 \ \Big)^T \quad (12)$$

It is observed that the entries in columns four and five of $\hat{G_m}(X,Z)$ are negative. In this case, condition (2) is not satisfied. This implies that there is no global stability. However, we can obtain global stability if $\eta = 0$. This would imply that there is reduced susceptibility to HIV by malaria infected patients. Further, the time from exposure to development of malaria symptoms is very short, (0.08333/day), [8] as compared to the HIV to AIDS cycle (approximately six weeks), [7]. Thus, malaria exposed patients may not play a significant role in the epidemics of the malaria-HIV co-infection. Biologically, the term $\alpha_h E_m$ can be neglected. In addition, since $\epsilon \ll 1$, then $\alpha_h \gg \epsilon$. Under these conditions we can obtain global stability otherwise, the perturbation will cause the disease to blow up.

II. Case of maximum protection against HIV/AIDS, that is $\beta = 0$

Let us now assume that there are no new HIV infections. The resulting model and matrix are shown in Appendix B. We see that when $\beta = 0$ matrix A becomes A_h as shown in Appendix B. Note that all the off diagonal elements of A_h are non negative. Further from (11), matrix $\hat{G_h}(X,Z)$, the matrix without new HIV infections is given by

$$\hat{G_h}(X,Z) \ = \ \Big(\ \alpha_m(1 - \tfrac{S}{N}) \quad 0 \quad \delta\alpha_m I_h - \epsilon\Lambda \quad -\delta\alpha_m I_h \quad 0 \quad \upsilon\alpha_m I_a \quad -\upsilon\alpha_m I_a \quad 0 \quad \alpha_v(1 - \tfrac{S_v}{N}) \quad 0 \ \Big)^T$$

which is negative. However, if we assume that HIV/AIDS patients protect against malaria, then $\delta, \ \upsilon \approx 0$ and $\hat{G_h}(X,Z) > 0$. This leads to global stability. Hence, without new HIV infections, we can attain global stability if HIV positive individuals protect themselves against malaria.

III. The general case when $\sigma, \ \beta > 0$

In real situations, it is impossible to have no new HIV infections. It is equally impractical not to have any mosquito bites in a population. We therefore look at the general case when there is continuing flow of both infections. From Section 2.1.1, there is initial stability if $R_{mh} < 1$. Global stability can be attained if

(i) there is reduced susceptibility to HIV by malaria infected patients. This would imply that there is diminished rate of HIV infection to malaria infectives during malaria episodes,

(ii) HIV/AIDS patients are protected against malaria.

Our results suggest that global stability is attained when the prevalence of one of the diseases is very low. From this we conclude that the influence of one disease on the other is higher when the independent prevalence of one of them is very high and the other very low. When both prevalences are very high, there is no significant interaction. This means that areas with higher HIV endemicity and low malaria prevalence, and areas with high malaria and low HIV prevalence are the most at risk for the interaction. This is depicted in Figure 4 (A) and (B) below. As seen in both figures, initially the prevalence of malaria

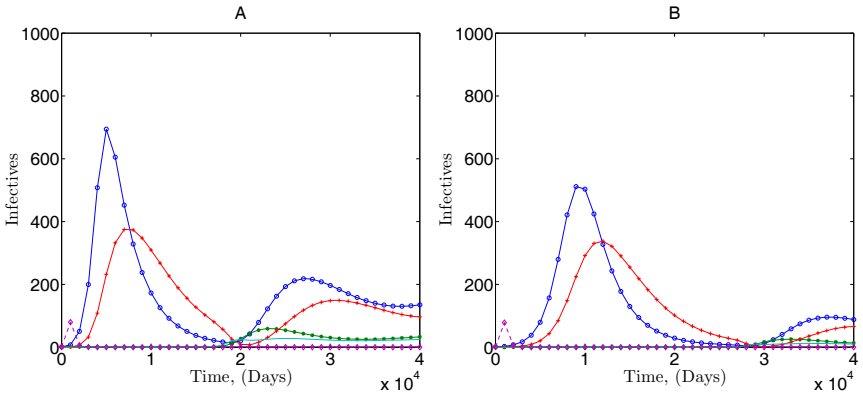

Figure 4: Plots showing variations in the infected with and without protection. In both graphs, the probability of transmission of malaria from human to mosquito $b = 0.9$, HIV transmission rate is $\beta c = 0.0011$ and 40% of immigrants are assumed HIV-positive, that is, $\epsilon = 0.40$. In (A), no protection against both infections, $\omega_m = 0$, $\omega_h = 0$. The diamond line is malaria infected, circled is HIV, star line is malaria/HIV co-infected, crossed line is AIDS, and solid line is malaria/AIDS co-infected. In (B), protection is both at 50%, that is, $\omega_m = 0.5$, $\omega_h = 0.5$. Other parameters as in Table 1.

is high and that of HIV is low. As malaria drops, HIV begins to rise to endemic states. The oscillations observed in the HIV classes correspond to the immigration of HIV/AIDS positive immigrants. The peaks signify high levels of HIV positive flow into the population and prevalence is higher when $\epsilon > 0$ as seen in Figures 4 and 5. In the later, $\epsilon = 0$ and we note that disease prevalence is low.

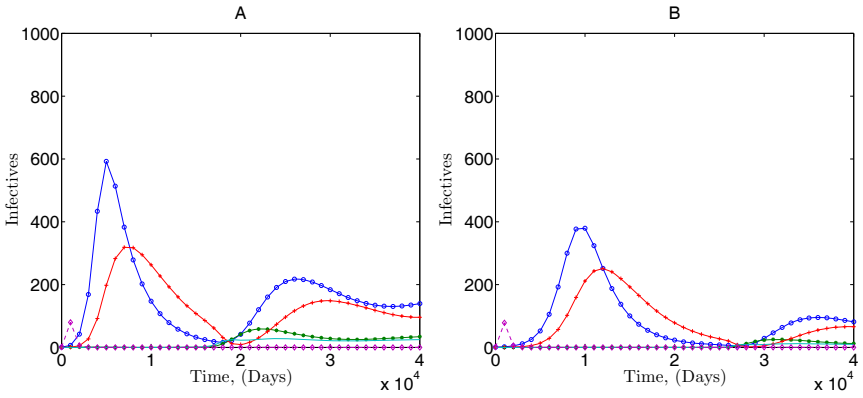

Figure 5: Plots showing variations in the infected when there are no HIV/AIDS immigrants, that is, $\epsilon = 0$. In both graphs, the probability of transmission of malaria from human to mosquito $b = 0.9$ and HIV transmission rate is $\beta c = 0.0011$. In (A), there is no protection $\omega_m = 0$, $\omega_h = 0$. The diamond line is malaria infected, circled is HIV, star line is malaria/HIV co-infected, crossed line is AIDS, and solid line is malaria/AIDS co-infected. In (B) there is 50% protection, $\omega_m = 0.5$, $\omega_h = 0.5$. Other parameters as in Table 1.

Table 1: Table for parameters used in the malaria and HIV/AIDS co-infection

Parameters	Description	Nominal Value	Reference
Λ	Per capita natural birth rate of humans	0.0015875/day	[13]
Λ_v	Per capita natural birth rate of mosquitoes	0.071/day	[13]
μ	Per capita death rate of humans	0.00004	[11]
μ_v	Per capita death rate for mosquitoes	0.05/day	[19]
ϵ	Fraction of new recruits that are HIV positive	Variable	Variable
ρ	Fraction that are protected against malaria	Variable	Variable
βc	Transmission probability for HIV in humans	Variable	Variable
$\omega_m,\ \omega_h$	Respective protection rates	Variable	Variable
p	Fraction that gains immunity after recovery	0.00019/day	[11]
ε	Per capita rate of loss of immunity in human hosts	0.000017/day	[17]
γ_m	Per capita rate of recovery from malaria by human hosts	0.0022/day	[2, 13]
τ_m	Progression rate of malaria in human host	0.08333/day	[8]
τ_v	Progression rate of malaria in vector host	0.0714286/day	[8]
τ_h	Progression rate to AIDS	0.000274	Assumed
q	Fraction of individuals that develop to AIDS due to malaria	0.8	Assumed
$\xi_a, \xi_{mh}, \zeta_{mh}$	Relative infection rate of dually infected	1.009,1.003,1.006	Assumed
$\xi_v \zeta_v$	Relative infection rate of dually infected	1.3,1.4	Assumed
ξ, ω, π, η	Relative progression/removal/recovery rate of dually infected	1.6,1.75,1.7,1.7	Assumed
		1.8,1.8,1.4	Assumed
ν_h	HIV/AIDS induced death rate	0.00023	[10]
ν_m	Malaria induced death rate	0.0003454	[3]
σ	Mosquito biting rate	0.5/day	[18]
a	Transmission rate of malaria in humans	0.8333/day	[8]
b	Transmission rate of malaria in mosquitoes	Variable/day	Variable
λ	Per capita rate of loss of protection to malaria	0.5	Assumed

2.1.3 Stability and bifurcation analysis of the model

Malaria co-infection with HIV models are known to exhibit the phenomenon of backward bifurcation. Our model is analysed to determine if protective intervention will have any effect on the expected backward bifurcation property. The Center Manifold Theorem as in van den Driessche and Watmough (2002) is used to investigate this property. Our model is re-defined by letting $S = x_1,\ P = x_2,\ E_m = x_3,\ I_m = x_4,\ I_h = x_5,\ E_{mh} = x_6,\ I_{mh} = x_7,\ I_a = x_8,\ E_{ma} = x_9,\ I_{ma} = x_{10},\ R = x_{11},\ S_v = x_{12},\ E_v = x_{13},\ I_v = x_{14}$. The forces of infection then become

$$\begin{array}{lll} \alpha_h^* & = & \frac{(1-\omega_h)\beta c(x_5+\xi_{mh}(x_6+\zeta_{mh}x_7)+\xi_a(x_8+\xi_{mh}x_9+\zeta_{mh}x_{10}))}{N^*} \\ \alpha_m^* & = & \frac{(1-\omega_m)\sigma a x_{14}}{N^*} \\ \alpha_v^* & = & \frac{\sigma b(x_4+\xi_v(x_7+\zeta_v x_{10}))}{N^*} \end{array} \tag{13}$$

In this case, $N^* = x_1+x_2+x_3+x_4+x_5+x_6+x_7+x_8+x_9+x_{10}+x_{11}$ and $N_v = x_{12}+x_{13}+x_{14}$. The constants $C = \mu+\lambda,\ C_1 = \mu+\tau_m,\ C_2 = \mu+\nu_m+\gamma_m,\ C_3 = \mu+\tau_h,\ C_4 = (1-q)\gamma_{mh},\ C_5 = \mu+\tau_h+\omega\tau_m,$
$C_6 = \mu+\gamma_{mh}+\xi\nu_m+\pi\tau_h,\ C_7 = \mu+\nu_h,\ C_8 = \mu+\nu_h+\omega\tau_m,\ C_9 = \pi\tau_h+q\gamma_{mh},$
$C_{10} = \mu+\theta\nu_h+\gamma_{ma}+\xi\nu_m,\ C_{11} = (1-p)\gamma_m,\ C_{12} = \mu+\varepsilon,\ C_{13} = \mu_v+\tau_v$. Therefore model (1) can be written as

$$\begin{array}{lll} \frac{dx_1}{dt} & = & (1-\epsilon-\rho)\Lambda-\alpha_m^*x_1-\alpha_h^*x_1-\mu x_1+\varepsilon x_{11}+(1-p)\gamma_m x_4+\lambda x_2 := f_1 \\ \frac{dx_2}{dt} & = & \rho\Lambda-Cx_2-\alpha_h^*x_2 := f_2 \\ \frac{dx_3}{dt} & = & \alpha_m^*x_1-\alpha_h^*x_3-C_1x_3 := f_3 \\ \frac{dx_4}{dt} & = & \tau_m x_3-\eta\alpha_h^*x_4-C_2x_4 := f_4 \\ \frac{dx_5}{dt} & = & \epsilon\Lambda+\alpha_h^*x_1+\alpha_h^*x_2+\alpha_h^*x_{11}-\delta\alpha_m^*x_5-C_3x_5+C_4x_7 := f_5 \\ \frac{dx_6}{dt} & = & \delta\alpha_m^*x_5+\alpha_h^*x_3-C_5x_6 := f_6 \\ \frac{dx_7}{dt} & = & \omega\tau_m x_6+\eta\alpha_h^*x_4-C_6x_7 := f_7 \\ \frac{dx_8}{dt} & = & \tau_h x_5-\upsilon\alpha_m^*x_8-C_7x_8+\gamma_{ma}x_{10} := f_8 \\ \frac{dx_9}{dt} & = & \upsilon\alpha_m^*x_8-C_8x_9+\tau_h x_6 := f_9 \\ \frac{dx_{10}}{dt} & = & \omega\tau_m x_9+C_9x_7-C_{10}x_{10} := f_{10} \\ \frac{dx_{11}}{dt} & = & C_{11}x_4-C_{12}x_{11}-\alpha_h^*x_{11} := f_{11} \\ \frac{dx_{12}}{dt} & = & \Lambda_v-\mu_v x_{12}-\alpha_v^*x_{12} := f_{12} \\ \frac{dx_{13}}{dt} & = & \alpha_v^*x_{12}-C_{13}x_{13} := f_{13} \\ \frac{dx_{14}}{dt} & = & \tau_v x_{13}-\mu_v x_{14} := f_{14} \end{array} \tag{14}$$

The Jacobian of the system at the initial state of infection is given by

$$J(E^o) = \left\{ \begin{array}{ccc} J(E^{11}) & J(E^{12}) & J(E^{13}) \\ J(E^{21}) & J(E^{22}) & J(E^{23}) \end{array} \right\}$$

$$\text{where } J(E^{11}) = \begin{Bmatrix} -\mu - A\epsilon\Lambda x_{10} & \lambda & 0 & (1-p)\gamma_m & -A\epsilon\Lambda x_{10} \\ 0 & -C - A\epsilon\Lambda & 0 & 0 & -A\epsilon\Lambda x_{20} \\ 0 & 0 & -C_1 - A\epsilon\Lambda & 0 & 0 \\ 0 & 0 & \tau_m & -C_2 - \eta A\epsilon\Lambda & 0 \\ A\epsilon\Lambda & A\epsilon\Lambda & 0 & 0 & -C_3 + D \\ 0 & 0 & A\epsilon\Lambda & 0 & 0 \\ 0 & 0 & 0 & \eta A\epsilon\Lambda & 0 \end{Bmatrix}$$

with $A = \frac{(1-\omega_h)\beta c}{N^*}$

$$J(E^{21}) = \begin{Bmatrix} 0 & 0 & 0 & 0 & \tau_h \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & C_{11} & 0 \\ 0 & 0 & 0 & -\frac{\sigma b\Lambda_v}{\mu_v N^*} & 0 \\ 0 & 0 & 0 & \frac{\sigma b\Lambda_v}{\mu_v N^*} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{Bmatrix},$$

$$J(E^{12}) = \begin{Bmatrix} -B\xi_{mh} & -B\xi_{mh}\zeta_{mh} & -B\xi_a & -B\xi_a\xi_{mh} & -B\xi_a\xi_{mh}\zeta_{mh} \\ -C\xi_{mh} & -C\xi_{mh}\zeta_{mh} & -C\xi_a & -C\xi_a\xi_{mh} & -C\xi_a\xi_{mh}\zeta_{mh} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ D\xi_{mh} & D\xi_{mh}\zeta_{mh} & D\xi_a & D\xi_a\xi_{mh} & D\xi_a\xi_{mh}\zeta_{mh} \\ -C_5 & 0 & 0 & 0 & 0 \\ \omega\tau_m & -C_6 & 0 & 0 & 0 \end{Bmatrix},$$

where $B = \frac{(1-\omega_h)\beta c X_{10}}{N^*}$, $C = \frac{(1-\omega_h)\beta c X_{20}}{N^*}$ and $D = \frac{\beta c(1-\omega_h)(1-\epsilon)\Lambda}{\mu N^*}$

$$J(E^{22}) = \begin{Bmatrix} 0 & 0 & -C_7 & 0 & \gamma_{ma} \\ \tau_h & 0 & 0 & -C_8 & 0 \\ 0 & C_9 & 0 & \omega\tau_m & -C_{10} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & -\frac{\xi_v\sigma b\Lambda_v}{\mu_v N^*} & 0 & 0 & -\frac{\xi_v\zeta_v\sigma b\Lambda_v}{\mu_v N^*} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\xi_v\sigma b\Lambda_v}{\mu_v N^*} & 0 & 0 & \frac{\xi_v\zeta_v\sigma b\Lambda_v}{\mu_v N^*} \\ 0 & 0 & 0 & 0 & 0 \end{Bmatrix}, \quad J(E^{13}) = \begin{Bmatrix} \varepsilon & 0 & 0 & -\frac{(1-\omega_m)\sigma a x_{10}}{N^*} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{(1-\omega_m)\sigma a x_{10}}{N^*} \\ 0 & 0 & 0 & 0 \\ A\epsilon\Lambda & 0 & 0 & -\frac{\delta\sigma a(1-\omega_m)\epsilon\Lambda}{N^*} \\ 0 & 0 & 0 & \frac{\delta\sigma a(1-\omega_m)\epsilon\Lambda}{N^*} \\ 0 & 0 & 0 & 0 \end{Bmatrix},$$

$$\text{and } J(E^{23}) = \begin{Bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ -C_{12} - A\epsilon\Lambda & 0 & 0 & 0 \\ 0 & -\mu_v & 0 & 0 \\ 0 & 0 & -C_{13} & 0 \\ 0 & 0 & \tau_v & -\mu_v \end{Bmatrix}$$

$R_{mh} = max\{R_m, R_h\}$ as before. Consider the case when $R_{mh} = 1$ and let $\sigma^* = \sigma b$ be the bifurcation parameter. Let $\lim_{N\uparrow} \frac{\epsilon}{N} \approx 0(\epsilon)$. Using a theorem by [6] stated in Appendix C, we can obtain the left and right eigenvectors of J_{E^o} at the bifurcation parameter σ^*. Note that $0(\epsilon)$ is a simple eigenvalue of J_{σ^*} when $R_{mh} = 1$. Therefore, we can apply the theorem to our model. We show from $a = \sum_{k,i,j=1}^{14} v_k w_i w_j \frac{\partial^2 f_k(0,0)}{\partial x_i \partial x_j}$, that the non vanishing partial derivatives are $a = \frac{2\sigma b}{N^*} v_{13} w_{12}(w_4 + \xi_v w_7 + \xi_v \zeta_v w_{10})$ and from $b = \sum_{k,j=1}^{n} v_k w_j \frac{\partial^2 f_k(0,0)}{\partial x_j \partial \beta^*}$ we get $b = \frac{v_{13}\Lambda_v}{\mu_v N^*}(w_4 + \xi_v w_7 + \xi_v \zeta_v w_{10})$. Computation shows that $v_{12} = 0$. If $a < 0$ the initial state of infection is locally asymptotically stable if R_{mh} is slightly less than one. If $R_{mh} > 1$ then the initial state is unstable and there is a locally asymptotically stable positive equilibrium near the initial state. The positivity of the endemic stationary state follows from the positivity of the infected components w_4, w_7 and w_{10} of the right null vector. This vector gives the direction of the invasion when the initial state is unstable. If $a > 0$ then there exists an unstable sub-threshold endemic equilibrium near the initial state. The significance of this unstable equilibrium is not trivial. It implies that although the initial state is locally stable, perturbations above a small threshold can cause the epidemic to explode. Further, if $R_{mh} > 1$, then not only the initial state is unstable, but also there is no nonzero stable equilibrium near the initial state and thus, a small perturbation will grow rapidly to significant proportions even when R_{mh} is near one.

3 Discussion

A model for the co-infection of malaria and HIV/AIDS was considered when there is effect of protection. The model allowed HIV positive immigrants into the population. We have assumed that it takes an average of 10 years for HIV to develop into AIDS. Therefore, the daily progression rate of HIV, $\tau_h = 0.000274$. Modification parameters were used to model the relative infectiousness of dually infected individuals as compared to individuals with one infection. These parameters can take on any value greater than 1. This is so since the chances of acquiring an infection from an individual infected with malaria and HIV or AIDS are greater than if the individual had a single infection. We have further assumed that $\lim_{N\uparrow} \frac{\epsilon}{N} \approx 0(\epsilon)$. Since co-infection with malaria while HIV positive increases

viral load, [1], a value of $q = 0.8$ is assumed to be the fraction that develops AIDS after a malaria episode of HIV positive individuals. The model was then analysed and conditions of stability obtained.

The analysis shows that protection against both diseases alters the qualitative behavior of solutions. Further more, it is noted that the initial state of infection is stable if $R_{mh} < 1$. If $R_{mh} > 1$, then a small perturbation in the disease-free state by the HIV positive migrants causes the disease to explode to an endemic state. This endemic state can be globally stable if HIV positive individuals are protected against malaria and if malaria infected individuals do not engage in sexual activities during the malaria episode. Further, varying the transmission rate of malaria in mosquito has effect on dynamics of infection and endemicity. The higher this value is, the higher the prevalence of malaria. This results in a high endemic state. At this state, individuals will feel obligated to protect themselves against malaria. Results further show that the higher the transmission rate of HIV, the less individuals use protection. This is a vital result since it would imply that when there is chance of transmission, individuals do not use protection. Further we conclude that even when protection against HIV/AIDS is enforced, continued immigration of HIV positive individuals makes it imppossible to achieve a disease-free state.

Appendix A

Here, we show how the basic reproduction number is obtained. From system (1), using a notation as in van den Driessche and Watmough (2002), the matrices F, the vector of rates of the appearance of new infections in each compartment, and V, the vector of rates of transfer of individuals into the particular compartment are respectively given by

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{(1-\omega_m)\sigma a S_o}{N} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & A & \xi_{mh}A & \xi_{mh}\zeta_m A & \xi_a A & \xi_a\xi_{mh}A & \xi_a\xi_{mh}\zeta_{mh}A & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\sigma b\mu\Lambda_v}{\mu_v\Lambda} & 0 & 0 & \frac{\sigma b\xi_v\mu\Lambda_v}{\mu_v\Lambda} & 0 & 0 & \frac{\sigma b\xi_v\zeta_v\mu\Lambda_v}{\mu_v\Lambda} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

where $A = \frac{(1-\omega_h)\mu\beta c(1-\epsilon)}{\Lambda}$ and

$$V = \begin{pmatrix} \mu+\tau_m & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\tau_m & K & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \mu+\tau_h & 0 & (q-1)\gamma_{mh} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu+\tau_h+\omega\tau_m & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\omega\tau_m & L & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau_h & 0 & 0 & \nu_h+\mu & -\gamma_{ma} & 0 & 0 & 0 \\ 0 & 0 & 0 & -\tau_h & 0 & 0 & M & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\pi\tau_h - q\gamma_{mh} & 0 & -\omega\tau_m & N & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \mu_v+\tau_v & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -\tau_v & \mu_v \end{pmatrix}$$

with $K = \mu + \nu_m + \gamma_m,\ L = \pi\tau_h + \xi\nu_m + \gamma_{mh} + \mu,\ M = \omega\tau_m + \nu_h + \mu,\ N = \xi\nu_m + \gamma_{ma} + \theta\nu_h + \mu.$

The next generation matrix, FV^{-1} has the non zero eigenvalue corresponding to the spectral radius $s(FV^{-1})$ of the matrix FV^{-1}. This represents the control reproductive number of the disease in the presence of protective measures given by

$$\begin{aligned} R_{mh} &= max\{R_m, R_h\} \\ &= max\left\{\sqrt{\frac{(1-\omega_m)\sigma^2 ab\tau_m\tau_v\mu\Lambda_v[(\mu+\lambda)(1-\epsilon)+\mu\rho]}{\mu_v^2\Lambda(\mu+\lambda)(\mu+\tau_m)(\mu+\nu_m+\gamma_m)(\mu_v+\tau_v)}}, \frac{\beta c(1-\omega_h)(1-\epsilon)(\mu+\nu_h+\xi_a\tau_h)}{(\mu+\tau_h)(\mu+\nu_h)}\right\} \end{aligned} \quad (15)$$

Appendix B

The following model is obtained from (1) when $\sigma = 0$.

$$\begin{aligned} \dot{S} &= (1-(\epsilon+\rho))\Lambda - \alpha_h S - \mu S + \varepsilon R + (1-p)\gamma_m I_m + \lambda P \\ \dot{P} &= \rho\Lambda - \mu P - \lambda P - \alpha_h P \\ \dot{E_m} &= -\alpha_h E_m - \mu E_m - \tau_m E_m \\ \dot{I_m} &= \tau_m E_m - \eta\alpha_h I_m - \mu I_m - \nu_m I_m - \gamma_m I_m \\ \dot{I_h} &= \epsilon\Lambda + \alpha_h S + \alpha_h P + \alpha_h R - \mu I_h - \tau_h I_h + (1-q)\gamma_{mh} I_{mh} \\ \dot{E_{mh}} &= \alpha_h E_m - \mu E_{mh} - \tau_h E_{mh} - \omega\tau_m E_{mh} \\ \dot{I_{mh}} &= \omega\tau_m E_{mh} + \eta\alpha_h I_m - \mu I_{mh} - \gamma_{mh} I_{mh} - \xi\nu_m I_{mh} - \pi\tau_h I_{mh} \\ \dot{I_a} &= \tau_h I_h - \mu I_a - \nu_h I_a + \gamma_{ma} I_{ma} \\ \dot{E_{ma}} &= -\mu E_{ma} - \nu_h E_{ma} - \omega\tau_m E_{ma} + \tau_h E_{mh} \\ \dot{I_{ma}} &= \omega\tau_m E_{ma} + \pi\tau_h I_{mh} + q\gamma_{mh} I_{mh} - \mu I_{ma} - \theta\nu_h I_{ma} - \gamma_{ma} I_{ma} - \xi\nu_m I_{ma} \\ \dot{R} &= p\gamma_m I_m - \alpha_h R - \mu R - \varepsilon R \\ \dot{S_v} &= \Lambda_v - \mu_v S_v \\ \dot{E_v} &= -\mu_v E_v - \tau_v E_v \\ \dot{I_v} &= \tau_v E_v - \mu_v I_v \end{aligned} \quad (16)$$

For global stability, we use the method in Section (2.1.2), and from Jacobian (10), for the case of $\sigma = 0$

$$A_m = \begin{pmatrix} -A_{11} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \tau_m & -A_{22} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -A_{33} & \Theta\xi_{mh} & Y & \Theta\xi_a & \Theta\xi_a\xi_{mh} & \Theta\xi_a\xi_{mh}\zeta_{mh} & 0 & 0 \\ 0 & 0 & 0 & -A_{44} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & w\tau_m & -A_{55} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau_h & 0 & 0 & -A_{66} & 0 & \gamma_{ma} & 0 & 0 \\ 0 & 0 & 0 & \tau_h & 0 & 0 & -A_{77} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (\pi\tau_h + q\gamma_{mh}) & 0 & w\tau_m & -A_{88} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -A_{99} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_v & -\mu_v \end{pmatrix}$$

where A_m is the M-matrix for the case of no new malaria infections and $A_{11} = (\mu+\tau_m), A_{22} = (\mu+\nu_m+\gamma_m), A_{33} = (\mu+\tau_h) - \Theta, \Theta = \frac{(1-\omega_h)\mu\beta c(1-\epsilon)}{\Lambda}$,
$A_{44} = (\mu+\tau_h+w\tau_m), A_{55} = (\mu+\gamma_{mh}+\xi\nu_m+\pi\tau_h), A_{66} = (\mu+\nu_h), A_{77} = (\mu+\nu_h+w\tau_m)$,
$A_{88} = (\mu+\theta\nu_h+\gamma_{ma}+\xi\nu_m), A_{99} = (\mu_v+\tau_v), Y = \Theta\xi_{mh}\zeta_{mh} + (1-q)\gamma_{mh}$.

When $\beta = 0$, model (1) is reduced to the following

$$\begin{aligned}
\dot{S} &= (1-(\epsilon+\rho))\Lambda - \alpha_m S - \mu S + \varepsilon R + (1-p)\gamma_m I_m + \lambda P \\
\dot{P} &= \rho\Lambda - \mu P - \lambda P \\
\dot{E_m} &= \alpha_m S - \mu E_m - \tau_m E_m \\
\dot{I_m} &= \tau_m E_m - \mu I_m - \nu_m I_m - \gamma_m I_m \\
\dot{I_h} &= \epsilon\Lambda - \delta\alpha_m I_h - \mu I_h - \tau_h I_h + (1-q)\gamma_{mh} I_{mh} \\
\dot{E_{mh}} &= \delta\alpha_m I_h - \mu E_{mh} - \tau_h E_{mh} - \omega\tau_m E_{mh} \\
\dot{I_{mh}} &= \omega\tau_m E_{mh} - \mu I_{mh} - \gamma_{mh} I_{mh} - \xi\nu_m I_{mh} - \pi\tau_h I_{mh} \\
\dot{I_a} &= \tau_h I_h - \upsilon\alpha_m I_a - \mu I_a - \nu_h I_a + \gamma_{ma} I_{ma} \\
\dot{E_{ma}} &= \upsilon\alpha_m I_a - \mu E_{ma} - \nu_h E_{ma} - \omega\tau_m E_{ma} + \tau_h E_{mh} \\
\dot{I_{ma}} &= \omega\tau_m E_{ma} + \pi\tau_h I_{mh} + q\gamma_{mh} I_{mh} - \mu I_{ma} - \theta\nu_h I_{ma} - \gamma_{ma} I_{ma} - \xi\nu_m I_{ma} \\
\dot{R} &= p\gamma_m I_m - \mu R - \varepsilon R \\
\dot{S_v} &= \Lambda_v - \alpha_v S_v - \mu_v S_v \\
\dot{E_v} &= \alpha_v S_v - \mu_v E_v - \tau_v E_v \\
\dot{I_v} &= \tau_v E_v - \mu_v I_v
\end{aligned} \tag{17}$$

As in Section 2.1.2, the resulting matrices are given by

$$A_h = \begin{pmatrix} -A_{11} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \frac{(1-\omega_m)}{N}\sigma a \\ \tau_m & -A_{22} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -A_{33} & 0 & (1-q)\gamma_{mh} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -A_{44} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & w\tau_m & -A_{55} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau_h & 0 & 0 & -A_{66} & 0 & \gamma_{ma} & 0 & 0 \\ 0 & 0 & 0 & \tau_h & 0 & 0 & -A_{77} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & (\pi\tau_h + q\gamma_{mh}) & 0 & w\tau_m & -A_{88} & 0 & 0 \\ 0 & \sigma bp & 0 & 0 & \xi_v\sigma bp & 0 & 0 & \xi_v\zeta_v\sigma bp & -A_{99} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \tau_v & -\mu_v \end{pmatrix}$$

Appendix C

The follwing theorem is based on Castillo-Chavez and Song, 2004. We state the theorem and apply it for bifurcation analysis.

Theorem 3.1 *Consider the following general system of ordinary differential equations with a parameter β^*.*

$$\frac{dx}{dt} = f(x, \beta^*), \quad f : R^n \times R \to R^n \text{ and } f \in C^2(R^2 \times R)$$

where 0 is an equilibrium point of the system (that is, $f(0,p) \equiv 0 \ \ \forall \beta^*$) and

(1.) $A = D_x f(0,0) = (\frac{\partial f_x}{\partial x_j}(0,0))$ is the linearization matrix of the system around the equilibrium 0 with β^* evaluated at 0;

(2.) Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;

(3.) Matrix A has a right eigenvector w and a left eigenvector v corresponding to the zero eigenvalue.

Let f_k be the k^{th} component of f and denote

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k(0,0)}{\partial x_i \partial x_j}$$

$$b = \sum_{k,j=1}^{n} v_k w_j \frac{\partial^2 f_k(0,0)}{\partial x_j \partial \beta^*}$$

then the local dynamics of the system around the equilibrium point 0 is totally determined by the signs of a and b. Dushoff et al. (1998) decomposed the center manifold and found out that the sign of a = can be used to determine the direction of the bifurcation, particularly, if $a > 0$ *and* $b > 0$*, then a backward bifurcation occurs at* $\beta^* = 0$*, and if*

(i) $a > 0, b > 0$*, when* $\beta^* < 0$ *with* $|\beta^*| \ll 1$ *then 0 is locally asymptotically stable, and there exists a positive unstable equilibrium; when* $0 < \beta^* \ll 1$*, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium;*

(ii.) $a < 0, b < 0$*, when* $\beta^* < 0$ *with* $|\beta^*| \ll 1$*, then 0 is unstable; when* $0 < \beta^* \ll 1$*, 0 is locally asymptotically stable, and there exists a positive unstable equilibrium;*

(iii.) $a > 0, b < 0$*, when* $\beta^* < 0$*with* $|\beta^*| \ll 1$*, then 0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when* $0 < \beta^* \ll 1$*, 0 is stable, and a positive unstable equilibrium appears;*

(iv.) $a < 0, b > 0$*, when* β^* *changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.*

References

[1] Abu-Raddad, L.J., Patnaik, P. and Kublin, J.G. (2006). Dual infection with HIV and malaria fuels the spread of both diseases in Sub-Saharan Africa. *Science,* **314:** 1603.

[2] Aron, J.L. (1988). Mathematical modelling of immunity to malaria. *Mathematical Biosciences,* **90:** 385-396.

[3] Arriola, L.M. and Hyman, J.M. (2007). Being sensitive to uncertainty. *Science and Engineering,* **9:2**.

[4] Carr, J. (1981). Applications of center manifold theory. Springer-Verlag, New York.

[5] Castillo-Chavez, C. and Song, B. (2004). Dynamical Models of Tuberculosis and their Applications. *Mathematical Biosciences and Engineering,* **1**(2): 361-404.

[6] Castillo-Chavez, C., Feng, Z. and Huang, W. (2002). On the computation of R_o and its role on global stability. In: *Mathematical approaches for emerging and re emerging infectious diseases. An Introduction.* Castillo-Chavez, C., Blower, S., van den Driessche, P., Kirschner, D. and Yakubu, A.-A. (Eds.) Springer-Verlag, New York. 229-250.

[7] Centers for Disease Control and Prevention (CDC) Department of health and human services. Division of parasitic diseases. Accessed *http://www.cdc.gov*. Available May 05 2008.

[8] Chitnis, N., Cushing, J.M. and Hyman, J.M. (2006). Bifurcation analysis of a mathematical model for malaria transmission. *SIAM J. Appl. Math.,* **67(1):** 24-45.

[9] Cohen, C., Karstaedt, A., Frean, J., Thomas, J., Govender, N., Prentice E., Dini, L., Galpin, J. and Crewe-Brown, H. (2005). Increased prevalence of severe malaria in HIV-infected adults in South Africa. *Clin. Infect. Dis.,* **41:** 1631-7.

[10] Corbett, E.L., Steketee, F. K., Latif, A.S., Kamali, A. and Hayes, R.J. (2002). AIDS in Africa III: HIV-1/AIDS and the control of other infectious diseases in Africa. *Lancet,* **359:** 2177-87.

[11] Coutinho, F.A.B., Burrattini, M.N., Lopez, L.F. and Massad, E. (2005). An approximate threshold condition for non-autonomous system: an application to a vector-borne infection. *Mathematics and Computers in Simulation,* **70:** 149-158.

[12] Dushoff, J., Huang, W. and Castillo-Chavez, C. (1998). Backwards bifurcations and catastrophe in simple models of fatal diseases. *J. Math. Biol.,* **36:** 227-248.

[13] Gemperli, A., Vounatsou, P., Sogoba, N. and Smith, T. (2006). Malaria mapping using transmission models: application to survey data. *American Journal of Epidemiology,* **163:** 289-297.

[14] Harrington, M., Huff, B., Camp, R., Jeffreys R., and Swan, T. (2005). What's in the pipeline? New HIV drugs, vaccines, microbicides, HCV and TB treatments in clinical trials. *New York: Treatment Action Group.*

[15] Hethcote, H.W. (2000). The mathematics of infectious diseases. *SIAM REV.,* **42(4):** 599-653.

[16] Huang, W., Cooke, K.L. and Castillo-Chavez, C. (1992). Stability and bifurcation for a multiple-group model for the dynamics of HIV/AIDS transmission. *SIAM J. Appl. Math.,* **52(3):** 835-854.

[17] Ishikawa, H., Ishii, A., Nagai, N., Ohmae, H., Masakazu, H., Suguri, S. and Leafasia, J. (2003). A mathematical model for the transmission of *Plasmodium vivax* malaria. *Parasitology International,* **52:** 81-93.

[18] Laxminarayan, R. (2004). Act now or later? Economics of malaria resistance. *The American Journal of Tropical Medicine and Hygiene,* **71(2):** 187-195.

[19] Macdonald, G. (1957). *The Epidemiology and Control of Malaria*. Oxford: Oxford University Press.

[20] Mukandavire, Z., Gumel, A.B., Garira, W. and Tchuenche, J.M. (2008). Mathematical analysis of a model for HIV-malaria co-infection. *Math. Biosc. and eng.,* **6(2):** 333-362.

[21] Mukandavire, Z. and Garira, W. (2007). Sex-structured HIV/AIDS model to analyse the effects of condom use with application to Zimbabwe. *J. Math. Biol.,* **54(5):** 669-699.

[22] Nannyonga, B. (2000). Mathematical models for single or multi-dose administration of drugs for the treatment of malaria and the role of immunity. *MSC Dissertation. Dept. of Mathematics, Makerere University Kampala, Uganda.*

[23] Salomon, J.A., Hogan, D.R., Stover, J., Stanecki, K.A., and Walker, N. (2005). Integrating HIV prevention and treatment: From slogans to Impact. *PLOS Med.,* **2:** 50-55.

[24] Siegfried, N., Muller, M., Deeks, J., Volmink, J. and Egger, M. (2005) HIV and male circumcision-A systematic review with assessment of the quality of studies. *Lancet Infect. Dis.,* **5:** 165-173.

[25] Thieme, R.H. (1994). Asymptotical autonomous differential equations in the plane, *Rocky Mountain J. Math.,* **24:** 351-380.

[26] Tumwine, J., Mugisha, J.Y.T. and Luboobi, L.S. (2007). A mathematical model for the dynamics of malaria in a human host and mosquito vector with temporary immunity. *Applied Mathematics and Computation,* **189:** 1953-1965.

[27] van den Driessche, P. and Watmough, J. (2002). Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission. *Math. Biosc.,* **180:** 29-48.

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