COVID-19 and malaria co-infection: do stigmatization and self-medication matter? A mathematical modelling study for Nigeria

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Abstract

Self-medication and the use of complementary medicine are common among people in the Global South for social, economic, and psychological reasons. Governments in these countries are generally faced with several challenges, including limited resources and poor infrastructure and patient health literacy. For COVID-19, this is fueled by the rapid spread of rumours in favour of these modalities on social media. Also common in the Global South is the stigmatization of people with COVID-19. Because of the stigma attached to having COVID-19, most COVID-19 patients prefer to test instead for malaria, since malaria (which is very common in the Global South) and COVID-19 share several symptoms leading to misdiagnosis. Thus, to efficiently predict the dynamics of COVID-19 in the Global South, the role of the self-medicated population, the dynamics of malaria and the impact of stigmatization need to be taken into account.

In this paper, we formulate and analyze a mathematical model for the co-dynamics of COVID-19 and malaria in Nigeria. The model is represented by a system of compartmental ODEs that take into account the self-medicated population and the impact of COVID-19 stigmatization. Our findings reveal that COVID-19 stigmatization and misdiagnosis contribute to self-medication, which, in turn, increases the prevalence of COVID-19. The basic and invasion reproduction numbers for these diseases and quantification of model parameters uncertainties and sensitivities are presented.

Keywords: Epidemiology, COVID-19, Malaria, Self-medication

1 Introduction

Malaria is caused by parasites transmission from the infected bites of the female Anopheles mosquitoes to people. Even though it is preventable and curable, its potency at incapacitating victims and occasionally eventual death is alarming. This is reflected in the statistics: in 2020, an estimated 241 million cases of malaria worldwide were recorded of which an estimated number of 627000 resulted in deaths [1]. The World Health Organization [1] 2020 reports indicate that the African region disproportionately accounts for the global burden of the disease—95% of malaria cases and 96% of malaria deaths. Sub-Saharan Africa accounts for an estimated 93% of the disease-induced deaths globally: over 50% of deaths were from Nigeria (31.9%), the Democratic Republic of the Congo (13.2%), United Republic of Tanzania (4.1%) and Mozambique (3.8%) [1].

The insurgence of coronavirus (COVID-19), the disease caused by the SARS-CoV-2 virus, has had enormous pressure on health facilities across the globe. Even with the introduction of vaccination programs, it seems the fight against the spread of the disease is far from over. To make matters worse, the disease shares some symptoms of other existing diseases, notably malaria and influenza which could lead to misdiagnosis of the these diseases, in particular, where there is a high dependency of diagnostic on symptoms. The common symptoms malaria and COVID-19 share include, but are not limited to, fever, breathing difficulties, tiredness and acute onset headache, and that of influenza and COVID-19 among others fever, cough, shortness of breath, fatigue, sore throat, runny or stuffy nose and others. Evidently, these diseases have co-circulated since the inception of COVID-19 ([1, 2]), where influenza and COVID-19 co-circulation is more pronounced in Europe and the North America, and Malaria and COVID-19 co-circulation pronounced in Africa [1]. It is imperative to investigate their joint impacts on health.

Since the inception of COVID-19, the disease prevalence or spread is characterized by self-medication—the use of substances or plants without medical advice by individual's own initiative or on the advice of another person devoid

of consultation from certified professional for such a purpose [3]. A situation partly due to inadequate effective treatment of the disease, especially, in developing countries—see [4–6]. In particular, [7] gives a comprehensive systematic review of studies aimed at assessing the prevalence and characteristics of self-medication in the attempt to curb the burden of the disease, where it is established that the most used medications are antibiotics, chloroquine or hydroxychloroquine, acetaminophen, vitamins or supplements, ivermectin, and ibuprofen. Included in these substances used for self-medication is the use of traditional medicines or herbal drugs [5, 8, 9].

Evidence of self-medication as a form of treating malaria, especially in Africa, is ubiquitous (examples, [6, 10] and references therein). An alarming state of affairs, as indicated in the proceeding paragraph, is that malaria and COVID-19 exhibit similar symptoms. It is, therefore, imperative that the impact of such a practice on COVID-19 prevalence or infection is assessed.

Additionally, stigmatization characterizes COVID-19 prevalence, where we define stigmatization as the discrimination or social exclusion of individuals suspected of contracting the disease. As noted in [11], this serves as a potential source of threat to the effective social living in the community; a situation which is crippling the efforts by health authorities in curbing the spread of the disease—individuals do not avail themselves for testing or treatment [12].

These complexities beckon the question: what are the health burden of COVID-19 and malaria co-infection induced by COVID-19 stigma and COVID-19 and malaria-associated self-medications, a question to the best of our knowledge not yet addressed in the literature. We address this question by first addressing the following questions: (1) What is the impact of COVID-19 stigmatization on malaria infections and related deaths? (2) What is the impact of malaria infection via self-medication on COVID-19 infections and related deaths? For question (2), even though an attempt is made by [8] (used Cameroon as a case study) in characterizing the prevalence of COVID-19 within the context of self-medication, where it is established that self-medication is a risk factor for increasing the disease prevalence, the study framework did not look at the interplay and effect of both diseases on their respective prevalence or infections.

This paper addresses the above questions using a hybrid mathematical epidemiological model on COVID-19 and malaria co-dynamics, a case study of Nigeria; and a choice motivated by the ubiquitous knowledge of the heavy dependency of her populace on self-medication, which also has high malaria prevalence [13]. The rest of the paper is organized as follows: Section 3 describes the model formulation, where the necessary model assumptions and parameter descriptions and definitions are presented. Section 4 discusses the quantitative analysis of the model, basic and invasion reproduction numbers are derived and discussed. Estimated model parameters are presented, and used to conduct numerical analysis in section 5. This section also discusses the model parameter uncertainty and sensitivity analysis. Section 6 concludes our study.

2 Model formulation

We commence the modelling process by dividing the vector (female mosquitoes) population into two compartments: susceptible S_v and infected I_v (i.e., mosquitoes that have ingested malaria parasites from infectious humans during blood feeding, are capable of transmitting sporozoites into the next human through bites); we assume direct transitioning from S_v to I_v. Susceptible vectors become infected at the rate λ_v. We partition the human population N_h into fifteen compartments, where we note that susceptible humans comprise of individuals susceptible to both malaria and COVID-19 infections. Susceptible humans to malaria lose susceptibility at a rate of λ_{hm}: a number $\lambda_{hm}S_h$ directly enters the malaria human infected compartment I_{hm} per unit time. The expression governing λ_{hm} is formulated as

$$\lambda_{hm} = b\beta_{hm}\frac{I_v}{N_h}. \tag{1}$$

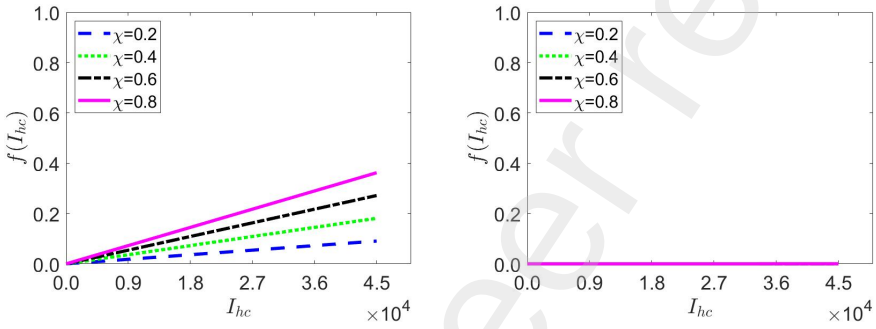
The parameters b and β_{hm} are the numbers of mosquito bites per unit time and the transmission probability of the malaria parasite from a mosquito to a human per mosquito bite. The rate at which individuals in I_{hm} receive treatment is denoted as α. This treatment can either be attributed to self-medication or medication from health care units (e.g., hospitals, clinics, or any recognized treatment agency). We define self-medication as those treatments using home remedies, for example, herbal medicines or concoctions, inhalation of medicated steams, over the counter malaria drugs, or any treatment from an unrecognized source. Let T_{hm} represent the compartment for individuals undergoing formal treatment and U_{hm} as those undergoing unrecognized treatment (self-medication).

Let p be the proportion of people seeking formal treatment for malaria, then formal treatment and self-medication rates are αp and $\alpha(1-p)$ per capita per unit time, respectively. Thus, $\alpha p I_{hm}$ number of individuals enters T_{hm} and $\alpha(1-p)I_{hm}$ number individuals enters U_{hm} per unit time. The proposed model considers the impact of stigmatization of COVID-19 on the dynamics of malaria, which we capture by introducing a barrier function $f(I_{hc})$, where I_{hc} is the number of COVID-19 infected humans. This function dampens the influx of individuals into the formal treatment compartment of the malaria-infected humans $T_{hm}\cdot$ $f(I_{hc})$ defined as an increasing function of infected COVID-19 humans determines the proportion of individuals who will seek formal malaria treatment or self medicate. We therefore have the modified rate of people migrating from I_{hm} to T_{hm} and U_{hm} as $\alpha p(1-f(I_{hc}))$ and $\alpha[1-p(1-f(I_{hc}))]$ respectively. For the purpose of this study, the stigmatization factor $f(I_{hc})$ is defined as

$$f(I_{hc}) = \chi\frac{I_{hc}}{N_h}, \tag{2}$$

where, $0 \leq \chi \leq 1$ is a policy parameter in the sense that policy makers can intervene to reduce stigmatization by putting forth measures to destigmatize

stigmas associated with COVID-19 infections. Thus, increasing values of χ imply decreasing levels of stigmatization and vice-versa, decreasing values of χ imply high levels of stigmatization. Note that the degree of impact of χ is determined by the relative size of the disease cases and population size. This is illustrated in Figure 1, where we observe that for small population size but high disease prevalence χ's impact is severe on the level of stigmatization in the representative jurisdiction or country (see Figure 1a and Figure 1b; we use population sizes 99426 and 206100000, which respectively corresponding to Seychelles and Nigeria [14]).



(a) Seychelles: population size $N_h = 99426$ (b) Nigeria: population size $N_h = 206100000$

Figure 1: Graph of stigmatization function $f(I_{hc})$: χ serves as the policy parameter modulating the severity of COVID-19 associated stigma. For illustration purpose, we considered the population sizes of Seychelles (99426) and Nigeria (206100000) [14]

Those under formal malaria treatment recover at rate γ. We assumed a negligible death rate in this compartment since we assume that individuals in this class undergo proper treatment, and it is know that if malaria is diagnosed and treated properly and quickly most people will fully recover [1, 15, 16]. The self-medicated humans either die or recover at the respective rate of γ_m and δ_m. Let R_{hm} be the recovered compartment for malaria recovered humans, and D_{hm} be for the death compartments for malaria-induced death. Malaria infected individuals are infected by COVID-19 at the rate of λ_{hc} (same as the force of infection for COVID-19), thus a total number of $\lambda_{hc} I_{hm}$ enters the compartment I_{hmc}, which comprises individuals with malaria-COVID-19 co-infections.

Exposed individuals with COVID-19 progress into infectious stage at rate ν_c, meanwhile both exposed and infectious COVID-19 individuals are susceptible to malaria. Let θ_1, θ_2, and θ_3 be the parameters capturing the respective rates at which COVID-19 infected individuals enter H_{hc} (i.e., seek formal treatment), COVID-19 infected individuals who self medicate as a result of

COVID-19 infection, and those who take self-medication for malaria infection even though they have COVID-19. Thus, the quantity $\theta_2 + \theta_3$ is the total rate of infected individuals who self-medicate as a result of COVID-19 infection (θ_2) and those who self-medicate due to malaria even though sick of COVID-19 (θ_3). θ_2 comprises of those treatment based on believes or faith, as well as any herbal medications or concoctions or over the counter drugs. We denote the compartment for self-medication as U_{hc}. U_{hc} can be considered as the compartment constituting undiagnosed COVID-19 infected individuals. We define the force of infection of COVID-19 as

$$\lambda_{hc} = c\beta_{hc}\frac{I_{hc} + U_{hc} + I_{hmc}}{N_h}, \tag{3}$$

where c and β_{hc} are the number of contacts made per individual per unit time and COVID-19 transmission probability per contact. We assume that the rate of spread of the disease is by infected individuals is the same across I_{hc}, U_{hc}, and I_{hmc}, even though we agree that self-medicated individuals U_{hc} are super spreaders of the disease. Co-infected individuals recover at the rate γ_{mc} and die at the rate δ_{mc}. We define γ_{hc} and δ_{hc} as the rates of individuals who recover or die from COVID-19 in H_{hc}; likewise, γ_c and δ_c are the respective rates of individuals in U_{hc} who recover and die from COVID-19. We denote COVID-19 recovery compartments as R_{hc} and that of the death-induced counterpart as D_{hc}. Observe that, in the interest of model simplicity, the modelling framework does not consider self-medication and treatment compartments for co-infections; and it is also partly due to the fact that the magnitude of impact of these two compartments on the model's dynamic is negligible.

Since malaria-infected and recovered humans can carry the malaria parasite [17, 18], we assume this mechanism as a factor affecting the transmission rate of the malaria parasite; same is assumed of the humans infected by malaria and those infected by both malaria and COVID-19. We therefore model the force of infection of the malaria parasite for susceptible vectors as

$$\lambda_v = b\beta_v\frac{I_{hm} + \sigma_T T_{hm} + \sigma_U U_{hm} + \sigma_R R_{hm} + \sigma_R R_{hmc} + I_{hmc}}{N_h}, \tag{4}$$

where b is the number of bites per unit time and β_v is the transmission probability of the malaria parasite from a human to a mosquito per mosquito bite. The parameters σ_T, σ_U, and σ_R capture the reduced infectiousness of individuals undergoing formal treatment, self-medicating, and have recovered from the disease, respectively. In our analysis, we assume that $\sigma_R < \sigma_T < \sigma_U$ in that malaria recovered individuals are likely to carry less of the malaria parasites. We assume recruitment rate Π_v and death rate μ_v for the mosquitoes population. For tractability of our model, we did not consider formal and self-treatment for co-infected individuals. Table 1 summarizes the model variables and parameters. Against this background, Figure 2 depicts the schematic description of the proposed model.

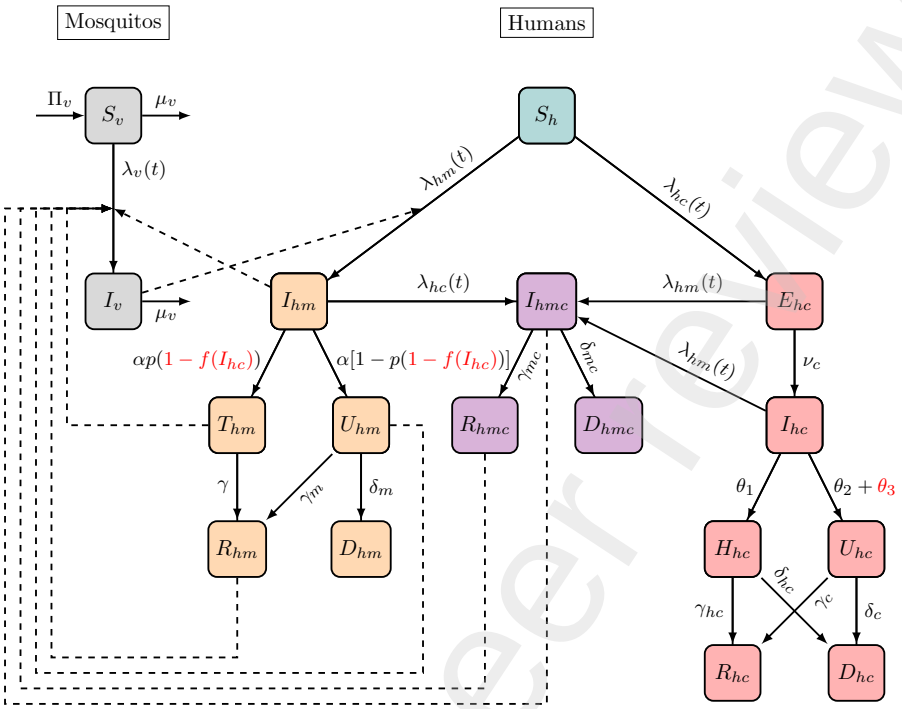


Figure 2: Flow diagram showing the epidemiological process for malaria and COVID-19 co-dynamics. Parameters in red are the ones related to stigmatization.

Additionally, we consider only a short period of time, and therefore we do not take into account the gradual waning of infection-acquired immunity. In the interest of mathematical simplicity, the model does not consider transitioning of individuals from R_{hc} to I_{hm} and R_{hm} to E_{hc}. Furthermore, we assume that individuals in U_{hm} and U_{hc} are conscious of their health status, and as such protective of it; thus we did not consider transitioning from U_{hc} and U_{hm} to I_{hmc}. Hence, the mathematical model for the malaria and COVID-19 co-dynamics we will study in this paper is given by the following system of

differential equations:

$$
\begin{cases}
\frac{dS_h}{dt} &= -\lambda_{hc}S_h - \lambda_{hm}S_h \\
\frac{dE_{hc}}{dt} &= \lambda_{hc}S_h - \lambda_{hm}E_{hc} - \nu_c E_{hc} \\
\frac{dI_{hc}}{dt} &= \nu_c E_{hc} - (\theta_1 + \theta_2 + \theta_3 + \lambda_{hm})I_{hc} \\
\frac{dH_{hc}}{dt} &= \theta_1 I_{hc} - (\gamma_{hc} + \delta_{hc})H_{hc} \\
\frac{dU_{hc}}{dt} &= (\theta_2 + \theta_3)I_{hc} - (\gamma_c + \delta_c)U_{hc} \\
\frac{dR_{hc}}{dt} &= \gamma_{hc}H_{hc} + \gamma_c U_{hc} \\
\frac{dD_{hc}}{dt} &= \delta_c U_{hc} + \delta_{hc}H_{hc} \\
\frac{dI_{hm}}{dt} &= \lambda_{hm}S_h - \alpha I_{hm} - \lambda_{hc}I_{hm} \\
\frac{dT_{hm}}{dt} &= \alpha p\left[1 - f(I_{hc})\right] I_{hm} - \gamma T_{hm} \\
\frac{dU_{hm}}{dt} &= \alpha\left[1 - p\left[1 - f(I_{hc})\right]\right] I_{hm} - (\gamma_m + \delta_m)U_{hm} \\
\frac{dR_{hm}}{dt} &= \gamma T_{hm} + \gamma_m U_{hm} \\
\frac{dD_{hm}}{dt} &= \delta_m U_{hm} \\
\frac{dI_{hmc}}{dt} &= \lambda_{hc}I_{hm} + \lambda_{hm}E_{hc} + \lambda_{hm}I_{hc} - \gamma_{mc}I_{hmc} - \delta_{mc}I_{hmc} \\
\frac{dR_{hmc}}{dt} &= \gamma_{mc}I_{hmc} \\
\frac{dD_{hmc}}{dt} &= \delta_{mc}I_{hmc} \\
\frac{dS_v}{dt} &= \Pi_v - \lambda_v S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= \lambda_v S_v - \mu_v I_v,
\end{cases}
\tag{5}
$$

Adding all equations for human compartments, we have $\frac{dN_h}{dt} = 0$. So the total human population $N_h(t) \equiv N_h$ remains constant at any time $t \geq 0$. We assume that this constant is a non-zero positive constant, in which case the right-hand side of System (5) is well-defined mathematically, and also in the epidemiological sense when a disease is introduced there will be a transmission.

3 Numerical Results and Discussion

This section discusses the estimation of model parameters, uncertainty and sensitivity analysis of model parameters on reproduction numbers, and the sensitive analysis of selected model parameters on the model outputs for the purpose of policy implication and directions.

3.1 Parameter values estimation

The estimation scheme employed is the Delay Rejection Adaptive Metropolis Markov Chain Monte Carlo (MCMC) documented in [19] with the associated

Table 1: Description of symbols for variables and parameters.

Symbol	Description
S_v, I_v	Number of susceptible, infected mosquitoes
N_h	Total human population size
S_h	Number of human susceptible to both malaria and COVID-19
E_{hc}	Number of human exposed to COVID-19
I_{hm}, I_{hc}, I_{hmc}	Number of human infected with malaria, COVID-19 or both
T_{hm}, H_{hc}	Number of human undergoing formal treatment for malaria, COVID-19
U_{hm}, U_{hc}	Number of human undergoing self-medication for malaria, COVID-19
R_{hm}, R_{hc}, R_{hmc}	Number of human recovered from malaria, COVID-19 or co-infection
D_{hm}, D_{hc}, D_{hmc}	Number of human died from malaria, COVID-19 or co-infection
$\lambda_v, \lambda_{hm}, \lambda_{hc}$	Force of infection for mosquitoes, human malaria or COVID-19
Π_v	Recruitment rate of mosquitoes
μ_v	Per capita death rate for mosquitoes
b	Number of bites one mosquito can give per unit time
c	Number of contacts one individual can make per unit time
β_v, β_{hm}	Transmission probability from human to mosquitoes, mosquitoes to human per mosquito bite
$\sigma_R < \sigma_T < \sigma_U$	Reduced infectiousness of individuals recovered from malaria, undergoing formal treatment or self-medication
ν_c	COVID-19 progression rate from being exposed to infectiousness for human
$\gamma_m, \gamma_c, \gamma_{hc}, \gamma_{mc}$	Recovery rate for human from self-medication for malaria, COVID-19, from formal treatment for COVID or for co-infection
$\delta_m, \delta_c, \delta_{hc}, \delta_{mc}$	Per capita death rate for human from self-medication for malaria, COVID, from formal treatment for COVID or for co-infection
$\theta_1, \theta_2, \theta_3$	Formal treatment rate, self-medication seeking rate and additional self-medication seeking rate due to misdiagnosis of malaria for human
α	Malaria overall treatment rate for human
p	Proportion of people seeking formal treatment among all treatment for malaria
$f(I_{hc})$	Stigmatization factor for malaria due to COVID-19

MATLAB package in [20]. We assume the daily observed infectious states have the normal distribution likelihood function. The prior distribution of model parameters to be estimated follows uniform distributions. In addition, we estimate the initial values of the state variables, individuals exposed to COVID-19 E_{hc0}, malaria-infected individuals I_{hm0}, susceptible mosquito (vector) population S_{v0}, and infected mosquito (vector) population I_{v0}; all are assumed to have normal prior distributions. We assessed the accuracy of the estimated model using the Normalized Means Square Error (NMSE).

We provide ranges and baseline values for the parameters described in Table 2. For several of the parameters occurring in the malaria model, we take from references in [17, 21], where they estimate some parameter values from published studies and country-wide data. For parameters concerning mosquito population demography, we estimate from its lifespan. For the parameters related to malaria, we assume high transmission occurs in parts of Sub-Saharan Africa such as Nigeria; our case study is based on Nigeria.

The daily average number of contacts one individual makes in Nigeria was calculated using the contact matrix for Nigeria over all locations in [22] and the corresponding Nigeria age structure, so it is a population size weighted average of the aforementioned contact matrix. The resultant number is $c = 15.27$ contacts per day per one typical person. A mean incubation period of 5.1 days

was assumed for COVID-19 [23] and hospitalization, recovery and death rates were found from the literature [24–26]. The transmission probability β_{hc} was estimated.

The data source is from Our World in Data [14]. We considered a time period of March 16, 2020 to June 29, 2020. Table 2 summarizes the values of the estimated parameters. Figure 3 shows the graph of the fitted model for the COVID-19 infected population to that of the observed.

The estimated proportion of COVID-19 infected individuals who self-medicate constitute 12.22% ($\frac{\theta_2+\theta_3}{\theta_1+\theta_2+\theta_3}$) and those who self medicate because they thought the infection is a malaria infection due to the similarity between COVID-19 and malaria symptoms constitute 45% ($\frac{\theta_3}{\theta_2+\theta_3}$). The proportion of malaria-infected individuals seeking self-medication and not as a result of stigmatization due to COVID-19 infection is 65.96% $(1-p)$; indicative that more malaria-infected individuals resort to self-medication in comparison to COVID-19 infected individuals; and more than those who self-medicate as a result of misdiagnoses (those believe to be infected with malaria instead of COVID-19).

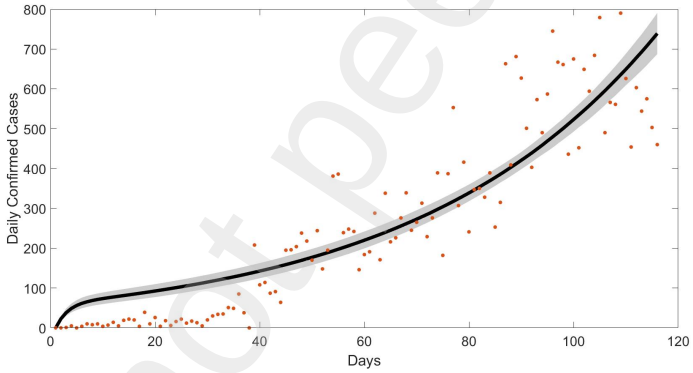


Figure 3: Fitted Model: Daily confirmed Nigeria COVID-19 cases from March 16, 2020 to June 29, 2020. Initial state values are presented in Table 2.

3.2 Numerical results and discussion

3.2.1 Uncertainty and sensitivity analysis of reproduction numbers

The basic reproduction number gives the expected number of secondary infections caused by one infectious individual (human) during his or her entire infectious period in a population completely susceptible to one pathogen (both humans and mosquitoes) and without the other. It is a crucial threshold quantity used to determine the capability of a disease to invade a population: if the value is greater than one, there will be an outbreak; if less than one, the

Table 2: Parameter values used in the model.

Symbol	Value	Range	Source
ν_c	$1/5.1$ day^{-1}		[23]
c	15.27 day^{-1}		[22]
γ_{hc}	$1/14$ day^{-1}		[24, 25]
δ_{hc}	0.151 day^{-1}	[0.151, 0.238]	[26]
γ_c	$1/7$ day^{-1}		[24, 25]
δ_c	0.288 day^{-1}	[0.243, 0.291]	[26]
θ_1	0.154 day^{-1}	[0.069, 0.183]	[26]
b	4.3 day^{-1}	[0.1, 50]	[17]
β_v	0.48	[0, 1]	[17, 21]
δ_m	9×10^{-5} day^{-1}	$[0, 4.1 \times 10^{-4}]$	[17]
γ_m	0.0035 day^{-1}	[0.0014, 0.017]	[17]
γ	0.07143 day^{-1}	[0.0357, 0.333]	[27]
μ_v	0.033 day^{-1}	[0.001, 0.01]	[17]
Π_v	1000 day^{-1}		[28]
β_{hc}	0.014671 day^{-1}	[0, 1]	Fitted
β_{hm}	0.2194 day^{-1}	[0, 1]	Fitted
γ_{mc}	0.51915 day^{-1}		Fitted
δ_{mc}	0.5246		Fitted
θ_2	0.027036 day^{-1}		Fitted
θ_3	0.022122 day^{-1}		Fitted
α	0.0023992 day^{-1}		Fitted
p	0.34036		Fitted
σ_T	0.39458	[0,1]	Fitted
σ_U	0.55241	[0,1]	Fitted
σ_R	0.24885	[0,1]	Fitted
χ	0.45194		Fitted
E_{hc0}	142.8		Fitted
I_{hm0}	390.29		Fitted
S_{v0}	423.87		Fitted
I_{v0}	374.97		Fitted

disease would die out. Here, we calculated the basic production numbers for both COVID-19 and malaria, denoted by $\mathcal{R}_0^C$ and $\mathcal{R}_0^M$ respectively. Note that the basic reproduction number with *chi* is the control reproduction number. In this study we use the basic and control reproduction interchangeably. Their expressions are given in (6)-(7), and the detailed derivation can be found in subsection A.1 and subsection A.2.

$$\mathcal{R}_0^C = c\beta_{hc}\left[\frac{1}{\theta_1+\theta_2+\theta_3} + \frac{\theta_2+\theta_3}{(\theta_1+\theta_2+\theta_3)(\gamma_c+\delta_c)}\right], \tag{6}$$

$$\mathcal{R}_0^M = \sqrt{K_{hv}^0 K_{vh}^0}, \tag{7}$$

with

$$K_{hv}^0 = b\beta_v \frac{1}{N_h}\left[\frac{1}{\alpha} + \frac{\sigma_T p}{\gamma} + \frac{\sigma_U(1-p)}{\gamma_m+\delta_m} + \sigma_R\left(p + \frac{(1-p)\gamma_m}{\gamma_m+\delta_m}\right)\right]\frac{\Pi_v}{\mu_v}, \tag{8}$$

$$K_{vh}^0 = b\beta_{hm}\frac{1}{\mu_v}. \tag{9}$$

K_{hv}^0 is the average number of infected mosquitoes one infectious human can produce during his/her entire infectious period and K_{vh}^0 is the average number of infected humans one infectious mosquito can generate during its whole period of infectiousness. $\mathcal{R}_0^M$ is the geometric average of the two.

Since basic reproduction numbers provide information about only one pathogen, and that we want to study co-circulation and co-infection of both COVID-19 and malaria, invasion reproduction numbers are also investigated additionally. Invasion reproduction numbers give the average number of secondary infections produced by one infectious individual in a population that is completely susceptible to one pathogen, given the presence of the other. The expressions are presented in (10)-(11) with derivations in subsection A.3 and subsection A.4.

$$\begin{aligned}\mathcal{R}_V^C =& c\beta_{hc}\frac{S_h^*}{N_h}\left[\frac{\nu_c}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)} + \frac{\nu_c(\theta_2+\theta_3)}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)(\gamma_c+\delta_c)}\right.\\ &\left. + \frac{\lambda_{hm}^*}{(\lambda_{hm}^*+\nu_c)(\gamma_{mc}+\delta_{mc})} + \frac{\lambda_{hm}^*\nu_c}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)(\gamma_{mc}+\delta_{mc})}\right]\\ &+ c\beta_{hc}\frac{I_{hm}^*}{N_h}\frac{1}{\gamma_{mc}+\delta_{mc}},\end{aligned} \tag{10}$$

$$\begin{aligned}\mathcal{R}_V^M =& \left[b\beta_{hm}\frac{S_h^*}{N_h}\frac{1}{\mu_v}\left(b\beta_v\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{1}{\alpha+\lambda_{hc}^*} + b\beta_v\sigma_T\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\alpha p(1-f(I_{hc}^*))}{(\alpha+\lambda_{hc}^*)\gamma}\right.\right.\\ &+b\beta_v\sigma_U\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\alpha(1-p(1-f(I_{hc}^*)))}{(\alpha+\lambda_{hc}^*)(\gamma_m+\delta_m)} + b\beta_v\sigma_R\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\lambda_{hc}^*\gamma_{mc}}{(\alpha+\lambda_{hc}^*)(\gamma_{mc}+\delta_{mc})}\\ &+b\beta_v\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\lambda_{hc}^*}{(\alpha+\lambda_{hc}^*)(\gamma_{mc}+\delta_{mc})}\\ &\left.+b\beta_v\sigma_R\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\left[\frac{\alpha p(1-f(I_{hc}^*))}{\alpha+\lambda_{hc}^*} + \frac{\alpha(1-p(1-f(I_{hc}^*)))\gamma_m}{(\alpha+\lambda_{hc}^*)(\gamma_m+\delta_m)}\right]\right)\\ &\left.+b\beta_{hm}\frac{E_{hc}^*+I_{hc}^*}{N_h}\frac{1}{\mu_v}b\beta_v\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{1}{\gamma_{mc}+\delta_{mc}}\right]^{\frac{1}{2}},\end{aligned} \tag{11}$$

where

$$\lambda_{hm}^* = b\beta_{hm}\frac{I_v^*}{N_h}, \quad \lambda_{hc}^* = c\beta_{hc}\frac{I_{hc}^*+U_{hc}^*}{N_h}.$$

Variables superscripted by * are the values at endemic equilibrium.

Because human vital dynamics are ignored, i.e., birth and death, this model simulated epidemic rather than the endemic situation of the co-circulation, which means asymptotically either disease would stabilize at an endemic level. So when computing the invasion reproduction numbers, instead of using endemic equilibrium of the present disease, values at one year after running the simulation with COVID-19 only and values at five years after simulating with malaria only were used.

Based on expressions (6)-(11), we conducted uncertainty analysis and sensitivity analysis on these reproduction numbers to analyze how sensitive our

choices of model parameter values are to them. For each parameter, Latin Hypercube Sampling [29, 30] was adopted to generate parameter values with assumed ranges and distributions as specified in Table 3. 3000 sets of parameter values were generated for the analysis.

Table 3: Parameter ranges and distributions for sensitivity analysis.

Parameter	Lower Bound	Upper Bound	Distribution
θ_1	0.069	0.183	T
θ_2	0	0.05	T
θ_3	0	0.05	T
α	0	0.005	T
p	0	1	T
χ	0	1	U

U indicates uniform distribution and T indicates triangular distribution with its peak value from Table 2.

The first column of Figure 4 shows the distributions of $\mathcal{R}_0^C$ and $\mathcal{R}_0^M$ with the generated 3000 sets of parameter values. The distribution mean was annotated by a red point with mean $\mathcal{R}_0^C$ equal to 1.38 and mean $\mathcal{R}_0^M$ being 2.26, consistent with the literature [31]. The first column of Figure 5 depicts distributions for invasion ones. Both mean $\mathcal{R}_V^C$ (1.38) and mean $\mathcal{R}_V^M$ (1.91) are greater than one, implying a successful invasion of each pathogen while the other has already been established.

In addition, using generated sets of parameter values, partial rank correlation coefficients (PRCC) were calculated to determine the impact of varying each parameter on the reproduction numbers, while preserving possible interactions among them [32]. The PRCC indices range between -1 and 1, with positive (negative) values indicating a positive (negative) relationship, and magnitudes indicating the relative level of impact on the quantity of interest (relative to other varying parameters and their ranges), with a magnitude of 0 having almost no impact and 1 having the most impact.

The PRCC indices of selected parameters are shown in the second columns of Figure 4 and Figure 5. In Figure 4, for $\mathcal{R}_0^C$, only θ_1, θ_2 and θ_3 were included due to the irrelevance of α, p and χ. Intuitively, θ_1 has a negative impact on $\mathcal{R}_0^C$: as more people are going for formal treatment or at a faster rate, the mean infectious period of COVID-19 in infected population is reduced, and moreover hospitalized individuals are excluded from pathogen transmission, therefore, lowering the possible number of secondary infections. However counter-intuitively, θ_2 and θ_3 also impact negatively on $\mathcal{R}_0^C$. From the formula for $\mathcal{R}_0^C$ in (6), the reason is revealed mathematically: although the increased rate of self-medication or stigmatization due to misdiagnosis of malaria would still put the infected individual at a risk of contracting the disease in a mass population, it, on the other hand, helps diminish the mean time of stay in the infected stage (I_{hc}), which is much longer than the mean time spent in

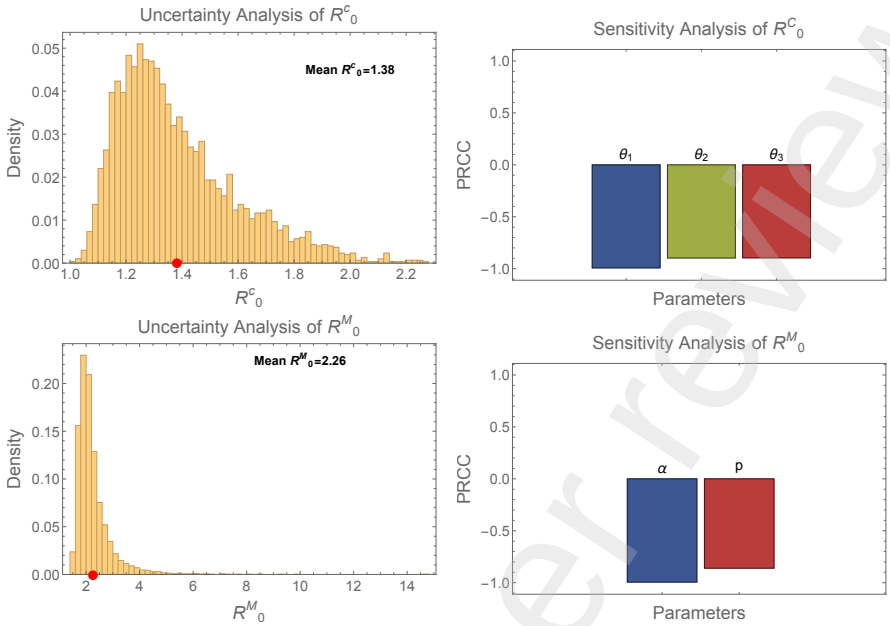


Figure 4: Densities of the basic reproduction number $\mathcal{R}_0^C$ for COVID-19 (top left) and $\mathcal{R}_0^M$ for malaria (bottom left) obtained from Latin Hypercube parameter ranges. The red point indicates the mean of the distribution. Partial rank correlation coefficients (PRCC) of selected parameters calculated using parameter ranges from Latin Hypercube Sampling with respect to the basic reproduction numbers $\mathcal{R}_0^C$ (top right) and $\mathcal{R}_0^M$ (bottom right).

self-treatment stage (U_{hc}), so collectively raising self-medicating rates helps downgrade the basic reproduction number of COVID-19. But in terms of the level of influence, θ_1 outcompetes the other two, suggesting formal treatment rate is still the most influential among all kinds of treatment rates.

As for $\mathcal{R}_0^M$, only α and p were selected as $\theta_1, \theta_2, \theta_3$ and χ are not involved in the composition of $\mathcal{R}_0^M$ (7). The overall treatment rate α and formal treatment proportion p are both negatively related with $\mathcal{R}_0^M$ as expected because people undergoing either medication are less infectious compared to those receiving no medication at all ($\sigma_T, \sigma_U < 1$), with α having more impact. This implies that the importance of getting some treatment outweighs the importance of getting the "right" treatment for malaria.

In terms of invasion reproduction numbers, the PRCC indices of all considered parameters are shown in the second column of Figure 5. The effect of θ_1, θ_2 and θ_3 on $\mathcal{R}_V^C$ is similar to that on $\mathcal{R}_0^C$. The malaria-related parameters α, p and χ exhibit positive influence though almost negligible. The positive relation results from the fact that having less malaria in the population would save more naive susceptibles for COVID-19 and hence make it more likely to

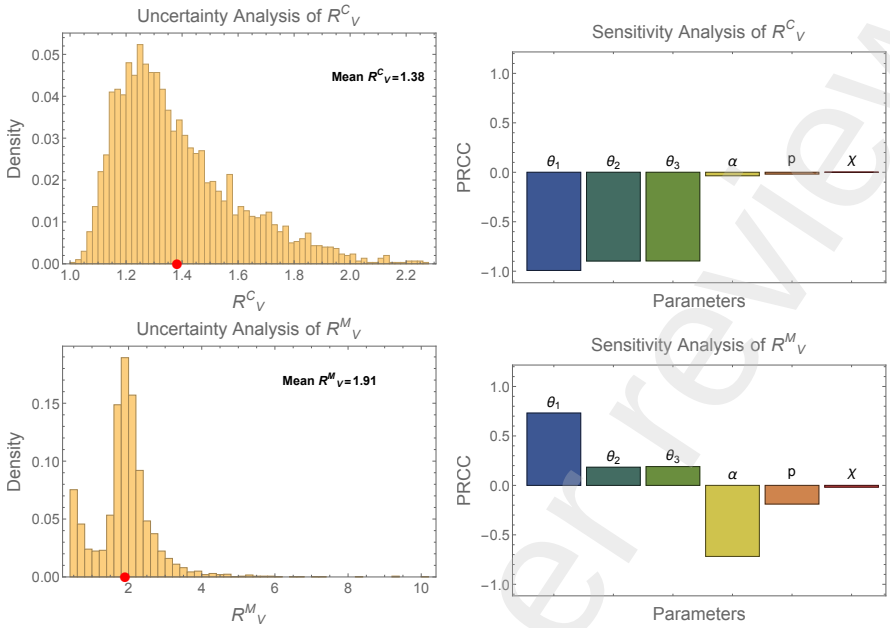


Figure 5: Densities of the invasion reproduction number $\mathcal{R}_V^C$ for COVID-19 (top left) and $\mathcal{R}_V^M$ for malaria (bottom left) obtained from Latin Hypercube parameter ranges. The red point indicates the mean of the distribution. Partial rank correlation coefficients (PRCC) of selected parameters calculated using parameter ranges from Latin Hypercube Sampling with respect to the invasion reproduction numbers $\mathcal{R}_V^C$ (top right) and $\mathcal{R}_V^M$ (bottom right).

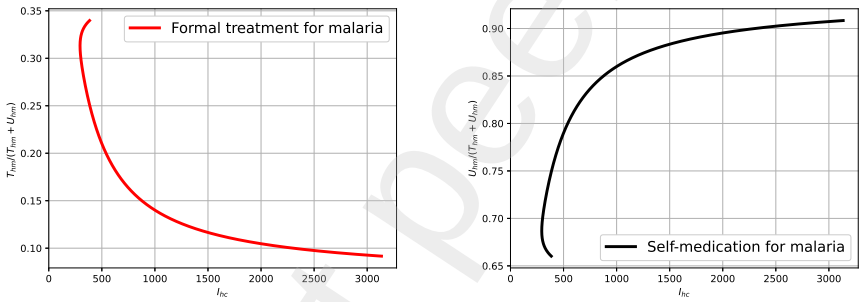
invade. The reverse is also true: θ_1, θ_2 and θ_3 impact positively on $\mathcal{R}_V^M$. However, in neither case does the stigmatization control factor χ play a significant role in affecting the reproduction numbers for malaria, whereas for COVID-19, its stigmatization rate θ_3 is being influential.

3.3 Sensitivity analysis of trajectories (outputs solution) of the model

In this section, we investigate how the model solution (outputs of the model) are sensitive to varying one or more of the inputs (parameters) of the model. We considered March 16 to June 29, 2020 as the time period for all our simulations, a 120 days period. We used initial conditions, $N_h(0) = N_h = 206100000$, which is the total population size of Nigeria on $t_0 =$ March 16, 2020, $E_{hc}(0), I_{hm}(0)$, $S_v(0), I_v(0$ fitted values given in Table 2, and initial values of the remaining variables are set to zero. The simulation results are graphically presented in Figure 6–Figure 10.

Figure 6 plots the fraction of malaria-infected individuals undergoing formal treatment, $\frac{T_{hm}}{T_{hm}+U_{hm}}$ against I_{hc}, and those undergoing self-medication

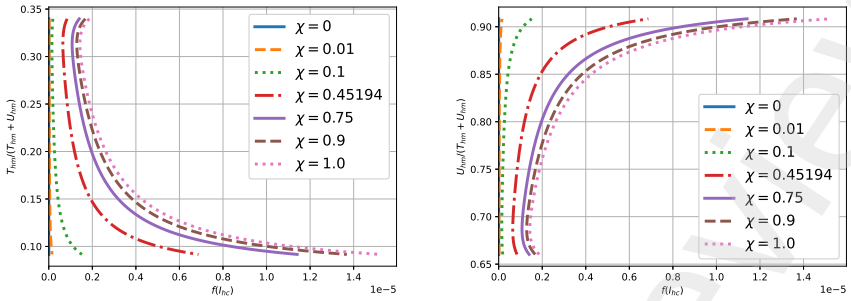
$\frac{U_{hm}}{T_{hm}+U_{hm}}$ against I_{hc} (this accounts for the presence of COVID-19 stigmatization). For the purpose of our discussion, recall that per definition of the stigmatization function $f(I_{hc})$, we assumed a positive dependency between the two quantities, thus as COVID-19 cases increase so is the stigmatization factor, and vice-versa, and decreasing COVID-19 cases implies decreasing level of stigmatization within the population. With that in mind, the inverse relationship between the proportion of individuals undergoing formal treatment and COVID-19 cases implies that increasing level of stigmatization leads to decreasing level of the number of individuals seeking formal treatment (Figure 6a). The converse holds for the proportion of those resorting to self-medication, we see a positive relationship (Figure 6b). Summarizing, the fear factor associated with COVID-19 stigmatization is mitigating against malaria-infected individuals in seeking appropriate treatments; and this may be the contributing factor to the number of malaria deaths recorded during the COVID-19 pandemic.



(a) $\frac{T_{hm}}{T_{hm}+U_{hm}}$ plotted vs I_{hc}. (b) $\frac{T_{hm}}{T_{hm}+U_{hm}}$ plotted vs I_{hc}.

Figure 6: Proportion of malaria infected humans undergoing formal malaria treatment, and self-medication for malaria as as function of I_{hc} for a fixed value of χ as given in Table 2.

Figure 7 presents the graphs of the respective proportions of malaria-infected individuals who resort to formal treatments and those resorting to self-medication as a function of $f(I_{hc})$ for different values of the policy parameter, χ. Observe that as the policy parameter increases, we have a bodily shift of the curves from left to right. In the case of the proportion of those seeking treatment, the increasing value of the policy parameter increases this proportion and the converse holds for the proportion of individuals seeking self-treatment, a decreased number of such a group of individuals. This indicates, as a policy direction, resources tailored to campaigns against COVID-19 stigma will impact in reducing the burden associated with malaria infection and its related deaths.



(a) Effect of varying χ on $\frac{T_{hm}}{T_{hm}U_{hm}}$, plotted vs $f(I_{hc})$

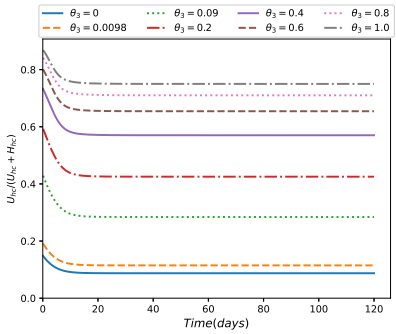
(b) Effect of varying χ on $\frac{U_{hm}}{T_{hm}U_{hm}}$, plotted vs $f(I_{hc})$

Figure 7: Impact of the parameter value χ on the proportion of humans undergoing formal treatment or self-medication for malaria, plotted vs $f(I_{hc})$ for 120 days.

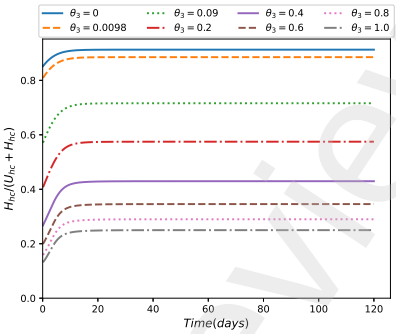
Figure 8 exhibits the effect of self-medication due to COVID-19 θ_3 and self-medication due to COVID-19 and misdiagnoses of malaria $\theta_2+\theta_3$. In particular, Figure 8b show that as self-medication due to COVID infection increases the proportion of individuals who hospitalize decreases as θ_3—Observe the bodily shift of the curves in the figures, a downward shift of the curve for the proportion of the hospitalized COVID-19 infected (Figure 8b) as θ_3 increases. Figure 8c and Figure 8d show the impact of the sum effect of self-medication due to COVID-19 and COVID-19 misdiagnosing on the proportion of COVID-19 infected individuals who resort to self-medication and those who resort to hospital treatment. We see an increase in those seeking hospital treatment increase as the sum of self-medication and misdiagnosing decreases as expected. Implying that, attention should be paid to COVID-19 misdiagnoses as a health policy direction.

Figure 9 shows the number of infectious humans by COVID-19 only, by malaria only, and by co-infection from COVID-19 and malaria for the time period from March 16 to June 29, 2020, in Nigeria. However, Figure 10 depicts the number of humans who died of COVID-19 induced complications, malaria-induced deaths and deaths caused by the co-infection from COVID-19 and malaria. We used the parameter values and initial conditions provided in Table 2.

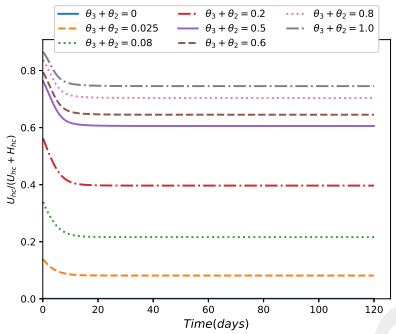
Figure 11 shows the sensitivity of the cumulative number of cases of each disease and co-infection to our selected parameters in Nigeria from March 16 to June 29, 2020. COVID-19 cumulative incidence is most sensitive to COVID-related parameters θ_1, θ_2 and θ_3. The result is similar to that for the COVID-19 invasion reproduction number in Figure 5. The sensitivity of malaria cases is also similar to that of the malaria invasion reproduction number. As for



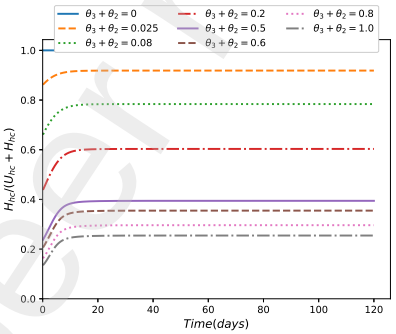
(a) Evolution of $\frac{U_{hc}}{U_{hc}+H_{hc}}$ vs t



(b) Evolution of $\frac{H_{hm}}{U_{hc}+H_{hc}}$ vs t

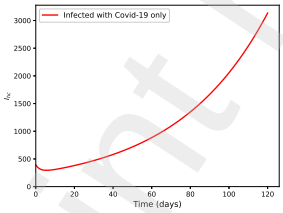


(c) Evolution of $\frac{U_{hc}}{U_{hc}+H_{hc}}$ vs t

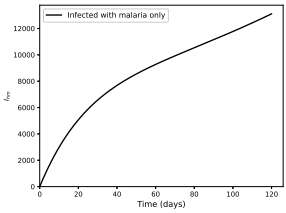


(d) Evolution of $\frac{H_{hm}}{U_{hc}+H_{hc}}$ vs t

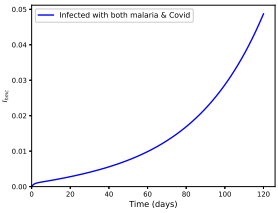
Figure 8: COVID-19 infected: proportion of individuals undergoing self-medication (Figure 8a and Figure 8c) and formal hospitalization (Figure 8b and Figure 8d for different levels of self-medication θ_3 and self-medication and COVID-19 misdiagnoses $\theta_2 + \theta_3$.



(a) Evolution of I_{hc} vs t

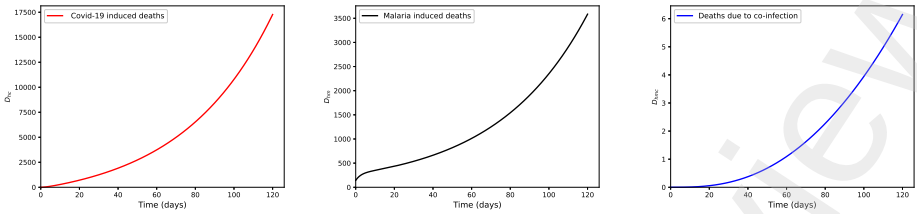


(b) Evolution of I_{hm} vs t



(c) Evolution of I_{hmc} vs t

Figure 9: Number of infectious humans from malaria, COVID-19, and co-infection of COVID-19 and malaria.



(a) Evolution of D_{hc} vs t (b) Evolution of D_{hm} vs t (c) Evolution of D_{hmc} vs t

Figure 10: Number of induced-deaths from malaria only, COVID-19 only, and co-infection of COVID-19 and malaria.

the co-infection, the analysis suggested a higher impact from COVID-19-related parameters than malaria ones, with the stigmatization control policy parameter χ playing a minimal role in curbing single disease or co-infections.

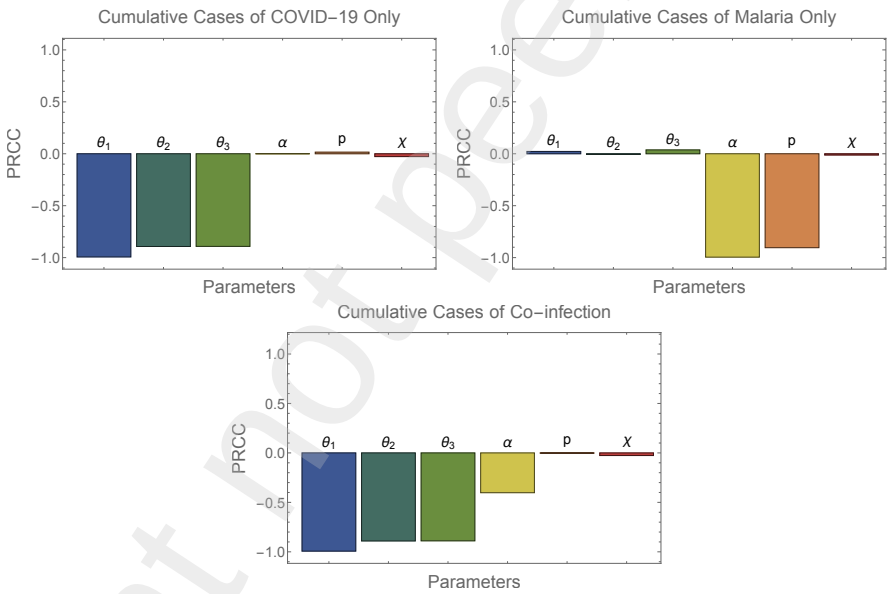


Figure 11: Partial rank correlation coefficients (PRCC) calculated using parameter ranges from Latin Hypercube Sampling with respect to the cumulative number of cases of COVID-19 only (top left), malaria only (top right) and co-infection (bottom) in Nigeria from Mach 16, 2020 to June 29, 2020.

Finally, we quantified the fraction of contribution in the cumulative number of cases for the time period considered of each disease due to self-medication. The fractions were calculated as follows.

$$f_c = \frac{\int_0^T b\beta_{hc} U_{hc} S_h dt}{\int_0^T b\beta_{hc} \left[U_{hc} + I_{hc}\right] S_h dt}, \quad f_m = \frac{\int_0^T b\beta_{hm} I_{vU} S_h dt}{\int_0^T b\beta_{hm} \left[I_{vU} + I_{vT}\right] S_h dt}, \tag{12}$$

where

$$I_{vU} = b\beta_v \frac{\sigma_U U_{hm}}{N_h}, \quad I_{vT} = b\beta_v \frac{\sigma_U U_{hm} + \sigma_T T_{hm}}{N_h}, \tag{13}$$

are the incidences of mosquitoes infected by self-medicated infectious humans and by infectious humans undergoing either self-medication or formal treatment. The uncertainty and sensitivity analysis of these fractions are shown in Figure 12. It was estimated that of all COVID-19 cases from March 16 to June 29, 2020, in Nigeria, a mean of 9.65% are due to self-medication (neglecting the co-infectious people due to the small number of them) and it was shown that this fraction is most sensitive to θ_2 and θ_3 and in almost the same level. For malaria, a mean of 4×10^{-7}% of all cases are contributed to self-medicated individuals among all treated people and the fraction is most influenced by α and p, where the stigmatization control parameters χ's impact is also minimal.

4 Conclusions

We present in this study a hybrid mathematical model on COVID-19 and malaria infections to explore the impact of COVID-19 stigmatization and misdiagnoses on self-medication; and self-medication impact on the dynamics of these two diseases.

As evident in the literature [11], the stigma associated with COVID-19 infection cannot be overlooked when putting forth policy interventions to curb the spread of the disease. We have also had instances where COVID-19 infections are misconstrued as malaria infections as both diseases share to some extent similar symptoms. The proposed model for this study accounted for the above factors in quantifying the disease burden for a season. This implies that the model presented did not account for population demographics. Against this backdrop, the study investigates: (1) the impact of COVID-19 and stigmatization on malaria infection and related deaths, and (2) the impact of malaria infection via self-medication on COVID-19 infections and related death.

We first quantify the uncertainty of the model parameters on the basic and invasion reproduction numbers and then conducted the sensitivity analysis of model properties on the basic and invasion reproduction numbers of both diseases. The mean basic reproduction numbers of COVID-19 and malaria are 1.38 and 2.26 respectively which are consistent with the values in the literature [31].

Also, we observe the danger stigma can be in increasing malaria infection and thus malaria-induced deaths. In particular, if the stigmatization policy factor is pegged at 45.19% (the model implied estimate), the proportion of malaria-infected individuals who self medicate increases with time. This means stigmatization could be a major factor in the increase in malaria-related death

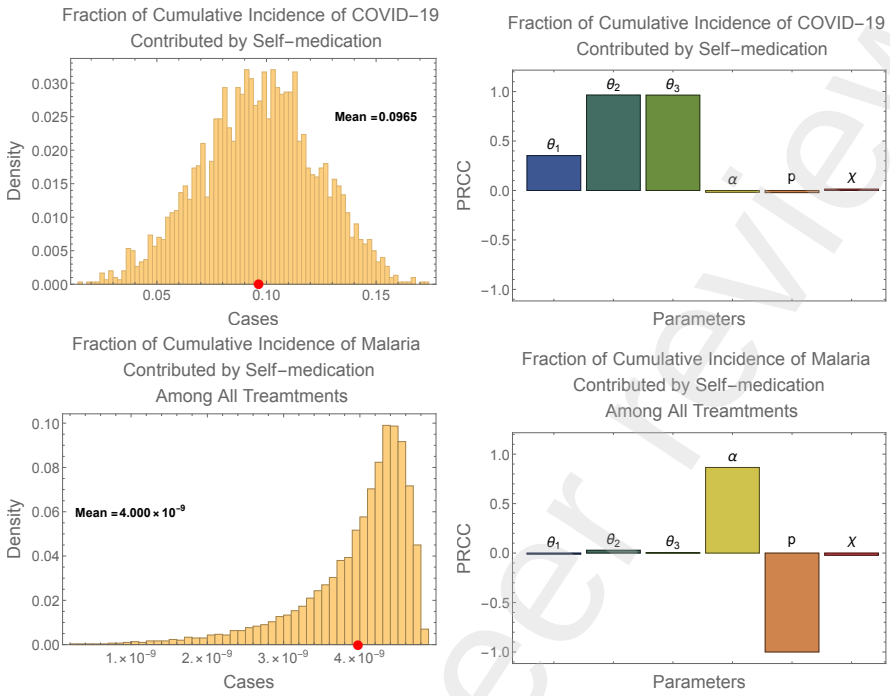


Figure 12: Density of the fraction of cumulative incidence of COVID-19 (top left) and of malaria (bottom left) that is contributed by self-medication among all treatments. The red point indicates the mean of the distribution. Partial rank correlation coefficients (PRCC) of selected parameters calculated using parameter ranges from Latin Hypercube Sampling with respect to this fraction for COVID-19 (top right) and for malaria (bottom right).

during the COVID-19 pandemic. This is an observation that is worth noting in putting forth pubic policy interventions during this crucial moment in the world's history. We noted, however, that this phenomenon is not indefinite; there is a saturation point, where at a particular level of COVID-19 number of infections, the impact of COVID-19-induced stigmatization is negligible. We further demonstrated that the death due to co-infection of the disease can be alarming as time increases. On the other hand, the presence of malaria infection can increase COVID-19 cases due to similarity in symptoms of both diseases, leading to individual misdiagnoses of COVID-19: this is captured in misdiagnostic parameter θ_3 estimated as 45%—the proportion due to self-medication induced by misdiagnoses. Implying, misdiagnoses could contribute to almost half of the population undergoing self-medication for COVID-19.

In Summary, we have exhibited that the stigma associated with COVID-19 and the issue of self-medication can be inimical to reducing COVID-19 and malaria infections, and their burdens, and that a policy measure against this

is civic education centring on stigma and self-medication and their dangers to thwarting effort by health authorities in the fight against these diseases.

It is worth noting that this study considered the period between March and June 2020, close to the outset of COVID-19; as such human population demographics and vaccination are not considered in the model formulation. As a future work, a mathematical model accounting for vital dynamics will be handy in studying the endemicity of these diseases. Furthermore, the impact of vaccination and immune response could be investigated. Even though this study is based on Nigeria it can be extended to other countries with similar population characteristics.

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Ethics and consent: All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.
Competing Interest Statement: The authors declare no conflict of interest.

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Appendix A Derivation of the basic and invasion reproduction numbers.

A.1 Derivation of $\mathcal{R}_0^C$

When there is only COVID-19 in the population, we consider the sub-system of (5) with only COVID-19:

$$\text{COVID-19 sub-system:} \begin{cases} \frac{dS_h}{dt} &= -\tilde{\lambda}_{hc} S_h, \\ \frac{dE_{hc}}{dt} &= \tilde{\lambda}_{hc} S_h - \nu_c E_{hc}, \\ \frac{dI_{hc}}{dt} &= \nu_c E_{hc} - (\theta_1 + \theta_2 + \theta_3) I_{hc}, \\ \frac{dH_{hc}}{dt} &= \theta_1 I_{hc} - (\gamma_{hc} + \delta_{hc}) H_{hc}, \\ \frac{dU_{hc}}{dt} &= (\theta_2 + \theta_3) I_{hc} - (\gamma_c + \delta_c) U_{hc}, \\ \frac{dR_{hc}}{dt} &= \gamma_{hc} H_{hc} + \gamma_h U_{hc}, \\ \frac{dD_{hc}}{dt} &= \delta_c U_{hc} + \delta_{hc} H_{hc}, \end{cases} \tag{A1}$$

with $\tilde{\lambda}_{hc} = c\beta_{hc}\frac{I_{hc}+U_{hc}}{N_h}$. We find the basic reproduction number for COVID-19 using the approach of the next-generation matrix [33]. We construct matrix $\mathcal{F}$, which describes new infections to the system, and matrix $\mathcal{V}$, which describes all other transitions within the system. The infected compartments are E_{hc}, I_{hc}, H_{hc} and U_{hc}.

$$\mathcal{F} = \begin{bmatrix} \tilde{\lambda}_{hc}S_h \\ 0 \\ 0 \\ 0 \end{bmatrix}, \quad \mathcal{V} = \begin{bmatrix} \nu_c E_{hc} \\ -\nu_c E_{hc} + (\theta_1+\theta_2+\theta_3)I_{hc} \\ -\theta_1 I_{hc} + \gamma_{hc}H_{hc} + \delta_{hc}H_{hc} \\ -(\theta_2+\theta_3)I_{hc} + (\gamma_c+\delta_c)U_{hc} \end{bmatrix}.$$

Note that at the disease-free equilibrium (DFE), $S_h^0 = N_h$. Then, taking partial derivatives and then evaluating them at the DFE yields

$$F = \begin{bmatrix} 0 & c\beta_{hc} & 0 & c\beta_{hc} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \nu_c & 0 & 0 & 0 \\ -\nu_c & \theta_1+\theta_2+\theta_3 & 0 & 0 \\ 0 & -\theta_1 & \gamma_{hc}+\delta_{hc} & 0 \\ 0 & -\theta_2-\theta_3 & 0 & \gamma_c+\delta_c \end{bmatrix},$$

and

$$FV^{-1} = \begin{bmatrix} c\beta_{hc}\left[\frac{1}{\theta_1+\theta_2+\theta_3} + \frac{\theta_2+\theta_3}{(\theta_1+\theta_2+\theta_3)(\gamma_c+\delta_c)}\right] & * & 0 & * \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

Therefore, the basic reproduction number for COVID-19 is given by

$$\mathcal{R}_0^C = c\beta_{hc}\left[\frac{1}{\theta_1+\theta_2+\theta_3} + \frac{\theta_2+\theta_3}{(\theta_1+\theta_2+\theta_3)(\gamma_c+\delta_c)}\right]. \tag{A2}$$

A.2 Derivation of $\mathcal{R}_0^M$

When there is only malaria in the population, we consider the sub-system of (5) with only malaria:

$$\text{Malaria sub-system:} \begin{cases} \frac{dS_h}{dt} &= -\lambda_{hm}S_h, \\ \frac{dI_{hm}}{dt} &= \lambda_{hm}S_h - \alpha I_{hm}, \\ \frac{dT_{hm}}{dt} &= \alpha p I_{hm} - \gamma T_{hm}, \\ \frac{dU_{hm}}{dt} &= \alpha(1-p)I_{hm} - (\gamma_m+\delta_m)U_{hm}, \\ \frac{dR_{hm}}{dt} &= \gamma T_{hm} + \gamma_m U_{hm}, \\ \frac{dD_{hm}}{dt} &= \delta_m U_{hm}, \\ \frac{dS_v}{dt} &= \Pi_v - \tilde{\lambda}_v S_v - \mu_v S_v, \\ \frac{dI_v}{dt} &= \tilde{\lambda}_v S_v - \mu_v I_v, \end{cases} \tag{A3}$$

with $\tilde{\lambda}_v = b\beta_v\frac{I_{hm}+\sigma_T T_{hm}+\sigma_U U_{hm}+\sigma_R R_{hm}}{N_h}$. Similarly, we derive the basic reproduction number for malaria. The infected compartments are $I_{hm}, T_{hm}, U_{hm}, R_{hm}$ and I_v.

$$\mathcal{F} = \begin{bmatrix} \lambda_{hm} S_h \\ 0 \\ 0 \\ 0 \\ \tilde{\lambda}_v S_v \end{bmatrix}, \quad \mathcal{V} = \begin{bmatrix} \alpha I_{hm} \\ -\alpha p I_{hm} + \gamma T_{hm} \\ -\alpha(1-p) I_{hm} + (\gamma_m + \delta_m) U_{hm} \\ -\gamma T_{hm} - \gamma_m U_{hm} \\ \mu_v I_v \end{bmatrix}.$$

At the DFE, $S_h^0 = N_h, S_v^0 = \frac{\Pi_v}{\mu_v}$. Then, taking partial derivatives and evaluating at the DFE gives

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & b\beta_{hm} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ b\beta_v \frac{\Pi_v}{\mu_v} \frac{1}{N_h} & b\beta_v \sigma_T \frac{\Pi_v}{\mu_v} \frac{1}{N_h} & b\beta_v \sigma_U \frac{\Pi_v}{\mu_v} \frac{1}{N_h} & b\beta_v \sigma_R \frac{\Pi_v}{\mu_v} \frac{1}{N_h} & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \alpha & 0 & 0 & 0 & 0 \\ -\alpha p & \gamma & 0 & 0 & 0 \\ -\alpha(1-p) & 0 & \gamma_m + \delta_m & 0 & 0 \\ 0 & -\gamma & -\gamma_m & 0 & 0 \\ 0 & 0 & 0 & 0 & \mu_v \end{bmatrix},$$

and

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 & \frac{b\beta_{hm}}{\mu_v} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ b\beta_v \frac{\Pi_v}{\mu_v N_h} \frac{1}{\alpha} + b\beta_v \sigma_T \frac{\Pi_v}{\mu_v N_h} \frac{p}{\gamma} + b\beta_v \sigma_U \frac{\Pi_v}{\mu_v N_h} \frac{1-p}{\gamma_m + \delta_m} + b\beta_v \sigma_R \frac{\Pi_v}{\mu_v N_h} \left[p + \frac{(1-p)\gamma_m}{\gamma_m + \delta_m} \right] & b\beta_v \sigma_T \frac{\Pi_v}{\mu_v N_h} \frac{1}{\gamma} + b\beta_v \sigma_U \frac{\Pi_v}{\mu_v N_h} \frac{1}{\gamma_m + \delta_m} + b\beta_v \sigma_R \frac{\Pi_v}{\mu_v N_h} \frac{\gamma_m}{\gamma_m + \delta_m} & b\beta_v \sigma_R \frac{\Pi_v}{\mu_v} \frac{1}{N_h} & 0 \end{bmatrix}.$$

The basic reproduction number for malaria is the spectral radius of FV^{-1}:

$$\mathcal{R}_0^M = \sqrt{b\beta_v \frac{1}{N_h} \left[\frac{1}{\alpha} + \frac{\sigma_T p}{\gamma} + \frac{\sigma_U (1-p)}{\gamma_m + \delta_m} + \sigma_R \left(p + \frac{(1-p)\gamma_m}{\gamma_m + \delta_m} \right) \right] \frac{\Pi_v}{\mu_v} \times b\beta_{hm} \frac{1}{\mu_v}}. \tag{A4}$$

A.3 Derivation of $\mathcal{R}_V^C$

We now derive the invasion reproduction number $\mathcal{R}_V^C$ around the malaria endemic equilibrium $(S_h^*, 0, 0, 0, 0, 0, 0, I_{hm}^*, T_{hm}^*, U_{hm}^*, R_{hm}^*, D_{hm}^*, 0, 0, 0, S_v^*, I_v^*)$ by the same next-generation matrix approach [33]. The infected compartments considered here are $E_{hc}, I_{hc}, H_{hc}, U_{hc}$ and I_{hmc}.

$$\mathcal{F} = \begin{bmatrix} \lambda_{hc} S_h \\ 0 \\ 0 \\ 0 \\ \lambda_{hc} I_{hm} \end{bmatrix}, \quad \mathcal{V} = \begin{bmatrix} \lambda_{hm} E_{hc} + \nu_c E_{hc} \\ -\nu_c E_{hc} + (\theta_1 + \theta_2 + \theta_3 + \lambda_{hm}) I_{hc} \\ -\theta_1 I_{hc} + \gamma_{hc} H_{hc} + \delta_{hc} H_{hc} \\ -(\theta_2 + \theta_3) I_{hc} + (\gamma_c + \delta_c) U_{hc} \\ -\lambda_{hm} E_{hc} - \lambda_{hm} I_{hc} + \gamma_{mc} I_{hmc} + \delta_{mc} I_{hmc} \end{bmatrix}.$$

Taking derivatives and evaluating at the DFE yields

$$F = \begin{bmatrix} 0 & c\beta_{hc}\frac{S_h^*}{N_h} & 0 & c\beta_{hc}\frac{S_h^*}{N_h} & c\beta_{hc}\frac{S_h^*}{N_h} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & c\beta_{hc}\frac{I_{hm}^*}{N_h} & 0 & c\beta_{hc}\frac{I_{hm}^*}{N_h} & c\beta_{hc}\frac{I_{hm}^*}{N_h} \end{bmatrix},$$

$$V = \begin{bmatrix} \lambda_{hm}^* + \nu_c & 0 & 0 & 0 & 0 \\ -\nu_c & \theta_1+\theta_2+\theta_3+\lambda_{hm}^* & 0 & 0 & 0 \\ 0 & -\theta_1 & \gamma_{hc}+\delta_{hc} & 0 & 0 \\ 0 & -(\theta_2+\theta_3) & 0 & \gamma_c+\delta_c & 0 \\ -\lambda_{hm}^* & -\lambda_{hm}^* & 0 & 0 & \gamma_{mc}+\delta_{mc} \end{bmatrix},$$

and

$$FV^{-1} = \begin{bmatrix} c\beta_{hc}\frac{S_h^*}{N_h}\left[\frac{\nu_c}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)} + \frac{\nu_c(\theta_2+\theta_3)}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)(\gamma_c+\delta_c)}\right. & * & 0 & * & * \\ \left. + \frac{\lambda_{hm}^*}{(\lambda_{hm}^*+\nu_c)(\gamma_{mc}+\delta_{mc})} + \frac{\lambda_{hm}^*\nu_c}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)(\gamma_{mc}+\delta_{mc})}\right] & & & & \\ 0 & & 0 & 0 & 0 \\ 0 & & 0 & 0 & 0 \\ 0 & & 0 & 0 & 0 \\ * & & * & 0 & * \; c\beta_{hc}\frac{I_{hm}^*}{N_h}\frac{1}{\gamma_{mc}+\delta_{mc}} \end{bmatrix}.$$

From the structure of F, it is easily seen that FV^{-1} is a rank one matrix, and therefore the spectral radius is its trace. Hence the invasion reproduction number of COVID-19 around malaria endemic equilibrium is given by

$$\begin{aligned} \mathcal{R}_V^C =& c\beta_{hc}\frac{S_h^*}{N_h}\left[\frac{\nu_c}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)} + \frac{\nu_c(\theta_2+\theta_3)}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)(\gamma_c+\delta_c)}\right. \\ &\left. + \frac{\lambda_{hm}^*}{(\lambda_{hm}^*+\nu_c)(\gamma_{mc}+\delta_{mc})} + \frac{\lambda_{hm}^*\nu_c}{(\lambda_{hm}^*+\nu_c)(\theta_1+\theta_2+\theta_3+\lambda_{hm}^*)(\gamma_{mc}+\delta_{mc})}\right] \\ &+ c\beta_{hc}\frac{I_{hm}^*}{N_h}\frac{1}{\gamma_{mc}+\delta_{mc}}, \end{aligned}$$

where

$$\lambda_{hm}^* = b\beta_{hm}\frac{I_v^*}{N_h}.$$

A.4 Derivation of $\mathcal{R}_V^M$

Similarly, we derive the invasion reproduction number $\mathcal{R}_V^M$ around the COVID-19 endemic equilibrium $(S_h^*, E_{hc}^*, I_{hc}^*, H_{hc}^*, U_{hc}^*, R_{hc}^*, D_{hc}^*, 0, 0, 0, 0, 0, 0, 0, 0, \frac{\Pi_v}{\mu_v}, 0)$. The infected compartments are $I_{hm}, T_{hm}, U_{hm}, R_{hm}, I_{hmc}, R_{hmc}$ and I_v.

$$\mathcal{F} = \begin{bmatrix} \lambda_{hm} S_h \\ 0 \\ 0 \\ 0 \\ \lambda_{hm} E_{hc} + \lambda_{hm} I_{hc} \\ 0 \\ \lambda_v S_v \end{bmatrix}, \quad \mathcal{V} = \begin{bmatrix} \alpha I_{hm} + \lambda_{hc} I_{hm} \\ -\alpha p(1 - f(I_{hc})) I_{hm} + \gamma T_{hm} \\ -\alpha(1 - p(1 - f(I_{hm}))) I_{hm} + (\gamma_m + \delta_m) U_{hm} \\ -\gamma T_{hm} - \gamma_m U_{hm} \\ -\lambda_{hc} I_{hm} + \gamma_{mc} I_{hmc} + \delta_{mc} I_{hmc} \\ -\gamma_{mc} I_{hmc} \\ \mu_v I_v \end{bmatrix}.$$

Taking derivatives and evaluating at the DFE yields

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & b\beta_{hm} \frac{S_h^*}{N_h} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & b\beta_{hm} \frac{E_{hc}^* + I_{hc}^*}{N_h} \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ b\beta_v \frac{S_v^*}{N_h} & b\beta_v \frac{\sigma_T S_v^*}{N_h} & b\beta_v \frac{\sigma_U S_v^*}{N_h} & b\beta_v \frac{\sigma_R S_v^*}{N_h} & b\beta_v \frac{S_v^*}{N_h} & b\beta_v \frac{\sigma_R S_v^*}{N_h} & 0 \end{bmatrix},$$

$$V = \begin{bmatrix} \alpha + \lambda_{hc}^* & 0 & 0 & 0 & 0 & 0 & 0 \\ -\alpha p(1 - f(I_{hc}^*)) & \gamma & 0 & 0 & 0 & 0 & 0 \\ -\alpha(1 - p(1 - f(I_{hc}^*))) & 0 & \gamma_m + \delta_m & 0 & 0 & 0 & 0 \\ 0 & -\gamma & -\gamma_m & 0 & 0 & 0 & 0 \\ -\lambda_{hc}^* & 0 & 0 & 0 & \gamma_{mc} + \delta_{mc} & 0 & 0 \\ 0 & 0 & 0 & 0 & -\gamma_{mc} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \mu_v \end{bmatrix},$$

and

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & A \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & B \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ C & * & * & * & D & * & 0 \end{bmatrix},$$

where

$$A = b\beta_{hm} \frac{S_h^*}{N_h} \frac{1}{\mu_v}, \quad B = b\beta_{hm} \frac{E_{hc}^* + I_{hc}^*}{N_h} \frac{1}{\mu_v}, \quad D = b\beta_v \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \frac{1}{\gamma_{mc} + \delta_{mc}},$$

$$\begin{aligned} C =& b\beta_v \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \frac{1}{\alpha + \lambda_{hc}^*} + b\beta_v \sigma_T \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \frac{\alpha p(1 - f(I_{hc}^*))}{(\alpha + \lambda_{hc}^*)\gamma} + b\beta_v \sigma_U \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \frac{\alpha(1 - p(1 - f(I_{hc}^*)))}{(\alpha + \lambda_{hc}^*)(\gamma_m + \delta_m)} \\ &+ b\beta_v \sigma_R \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \left[\frac{\alpha p(1 - f(I_{hc}^*))}{\alpha + \lambda_{hc}^*} + \frac{\alpha(1 - p(1 - f(I_{hc}^*)))\gamma_m}{(\alpha + \lambda_{hc}^*)(\gamma_m + \delta_m)} \right] + b\beta_v \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \frac{\lambda_{hc}^*}{(\alpha + \lambda_{hc}^*)(\gamma_{mc} + \delta_{mc})} \\ &+ b\beta_v \sigma_R \frac{\Pi_v}{\mu_v} \frac{1}{N_h} \frac{\lambda_{hc}^* \gamma_{mc}}{(\alpha + \lambda_{hc}^*)(\gamma_{mc} + \delta_{mc})}. \end{aligned}$$

By standard calculation, the spectral radius of FV^{-1} is $\sqrt{AC+BD}$, so the he invasion reproduction number of malaria around COVID-19 endemic equilibrium is given by

$$\begin{aligned}\mathcal{R}_V^M = \Bigg[& b\beta_{hm}\frac{S_h^*}{N_h}\frac{1}{\mu_v}\Bigg(b\beta_v\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{1}{\alpha+\lambda_{hc}^*}+b\beta_v\sigma_T\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\alpha p(1-f(I_{hc}^*))}{(\alpha+\lambda_{hc}^*)\gamma} \\ & +b\beta_v\sigma_U\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\alpha(1-p(1-f(I_{hc}^*)))}{(\alpha+\lambda_{hc}^*)(\gamma_m+\delta_m)}+b\beta_v\sigma_R\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\left[\frac{\alpha p(1-f(I_{hc}^*))}{\alpha+\lambda_{hc}^*}+\frac{\alpha(1-p(1-f(I_{hc}^*)))\gamma_m}{(\alpha+\lambda_{hc}^*)(\gamma_m+\delta_m)}\right] \\ & +b\beta_v\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\lambda_{hc}^*}{(\alpha+\lambda_{hc}^*)(\gamma_{mc}+\delta_{mc})}+b\beta_v\sigma_R\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{\lambda_{hc}^*\gamma_{mc}}{(\alpha+\lambda_{hc}^*)(\gamma_{mc}+\delta_{mc})}\Bigg) \\ & +b\beta_{hm}\frac{E_{hc}^*+I_{hc}^*}{N_h}\frac{1}{\mu_v}b\beta_v\frac{\Pi_v}{\mu_v}\frac{1}{N_h}\frac{1}{\gamma_{mc}+\delta_{mc}}\Bigg]^{\frac{1}{2}},\end{aligned} \tag{A5}$$

where

$$\lambda_{hc}^* = c\beta_{hc}\frac{I_{hc}^*+U_{hc}^*}{N_h}.$$