Long-Term Effects of Reducing the Rate of Malaria Infections

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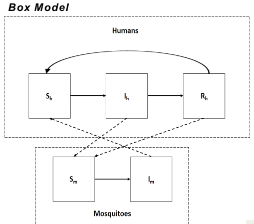
Introduction

Malaria is a mosquito-borne parasitic disease that can infect over 200 million individuals annually (CDC). Mosquitoes act as a vector, transmitting the disease between humans without being harmed by the parasites themselves. This occurs when mosquitoes ingest parasite gametocytes after taking a blood meal from an infected individual, within the mosquito these gametocytes then undergo sporogenesis to produce sporozoites which are then injected into the next human host during a blood meal (CDC). Once within the human host, the parasite infects the liver, where it further matures before eventually being released into the blood and fully infecting the host (CDC). Left untreated, malaria can lead to severe health complications and even death, however, with proper treatment, death is generally preventable. The majority of malaria deaths occur in young children in sub-Saharan Africa where high rates of malaria transmission and lack of access to proper treatment combine to make malaria a dangerous and often deadly disease (CDC). Preventative malaria treatment includes the use of anti-malaria bed nets which can significantly lower susceptible individuals from being infected (Nevill et al., 1996). Anti-malaria bed nets have been shown to reduce malaria incidence rates in high-risk areas by approximately 24%, this improves to a 50% incidence reduction when the bed nets are pre-treated with insecticides (Teutsch et al., 1995). Understanding how malaria is transmitted between humans is an essential step toward the ultimate goal of eradicating malaria. This study attempts to mathematically model malaria transmission by adapting the model proposed by Dudley et al. (2016) which models the rates of susceptibility, infection, and recovery in an untreated population. They studied the relative effectiveness of different intervention strategies through modeling. Success with malaria elimination can change transmission dynamics, and modeling will help determine the best intervention strategies where transmission dynamics are changing as malaria is being eliminated. In our paper, we look at changing h_u, which is the force of infection. We hypothesis that changing the force of infection will allow us to compare how transmission rates change when anti-malaria bed nets are used. We can see how over time, the changing of this force of infection as a result of better treatment coverage, the incidence of malaria can decrease, perhaps to the point of complete elimination, and how long this would take.

Model Development

Box Model



Differential Equations

$$\frac{dS_u}{dt} = \delta(1-q) - (\delta + h_u)S_u + \rho_u R_u$$
$$\frac{dI_u}{dt} = h_u S_u - (\delta + \gamma_u)I_u$$
$$\frac{dR_u}{dt} = \gamma_u I_u - (\delta + \rho_u)R_u$$

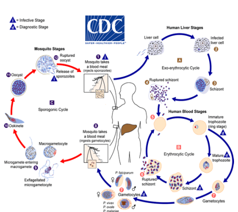


Table of Parameters

Symbol	Description	Value
A_u	Number of bites per mosquito per untreated human per day	0.25
b_u	Transmission probability from infected mosquito to susceptible, untreated human	0.022
C	Transmission probability from infected human to susceptible mosquito	0.36
δ	Daily birth and death rate	4.7895×10^{-5}
γ_u	Recovery rate for untreated people	1/180
m_u	Mosquito density (number of mosquitoes per untreated human)	20
h_u	Force of infection	0.005 (calculated)
μ	Mosquito mortality rate	0.095/days
ω	Duration of immunity without reinfection	274 days
q	Treatment coverage	60%, 40%, or 20%
τ	Incubation period in the mosquito	10 days
ρ_u	Rate of immunity loss for recovered, untreated humans	1/182.5

State Variables

S_u (S_t) is the proportion of the population that is susceptible and untreated (resp., treated).
I_u (I_t) is the proportion of the population that is symptomatic, infectious, and untreated (resp., treated).
R_u (R_t) is the proportion of the population that is recovered with acquired immunity and untreated (resp., treated).

Methods

Our model was a simplification of the SIR models in the paper because we wanted to only focus on the untreated population. We varied the hu, the force of the infection, to mimic intervention methods of no intervention, intervention through bed nets, and intervention through insecticide treated bed nets. hu was determined by an equation that represents the force of an infection in a generic SIR model. With an initial population of 100 susceptible individuals, the number of new infections that was predicted to be 90 assuming that the disease runs its course and infects everyone in a population, and the time spent outside and exposed to the mosquitos was approximately half a year (daytime/time spent not under bed nets), then the force of the infection will be in the range of 0.005-0.01. In disease that can be transmitted via respiratory droplets such as MERs the force of the infection will be higher, but since malaria is a disease that requires a vector to transmit, the average duration of exposure and mosquito vector competence (the ability of the mosquitos to acquire, maintain, and transmit microbial agents) plays a factor in the transmission of the disease.

$$\lambda = \frac{\text{number of new infections}}{\text{number of susceptible persons exposed} \times \text{average duration of exposure}}$$

To test our model, we inputted our model on big green and found that it can predict the course of the infection in 365 days in a village of 500 people, with 10 people infected initially. After 365 days, the model becomes inaccurate because of isolation of the biological population, the disease runs its course and soon there is no longer newly infected individuals as everyone will have been infected and will have recovered.

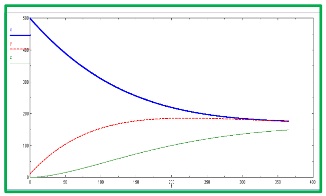


Figure 1. Model of malaria infection without the use of preventative measures

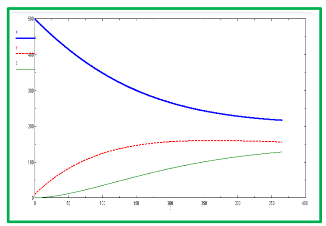


Figure 2. Model of malaria infection with the use of preventative measures, ie. bednets

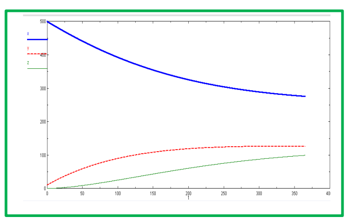


Figure 3. Model of malaria infection with the use of preventative measures, ie. Insecticide-treated bednets

Results

After running the model, we observed that the susceptible population declines as the infected population rises, but both eventually reach an equilibrium at the end of one year (Figure 1). In addition, the recovered population begins to rise as the infected people begin to recover. This population should also reach an equilibrium because there will be a constant flow of infected people into the recovered group, and a constant flow of recovered people back into the susceptible group as they lose their immunity. When we manipulate hu, for example dropping it from 0.005 to 0.0025 due to the use of bednets which has been found to reduce malaria infections by 25%, we find that the rate at which the susceptible population declines slows, and similarly, the rate at which the infected population rises slows (Figure 2). They both also seem to approach an equilibrium after one year, but are further apart than with the higher hu when no preventative treatments were used. This effect is further highlighted when insecticide treated bednets are used, that drops the infection rate 50%, thereby reducing hu from 0.005 to 0.0025. The gap between the susceptible and infected population is even larger, and the slopes are less steep as well, indicating a decrease in infection rates (Figure 3).

Discussion

Our results aligned with our hypothesis that decreasing the force of infection through introduction of preventative treatment methods would lead to a decreased rate in the rise of the infected population, as well as a corresponding decreased rate in the fall of the susceptible population. In addition, the different preventative treatments, bednets or insecticide treated bednets, led to different equilibrium values for the susceptible and infected population. To improve our model, we could investigate why it is not accurate after a year. Our model is accurate for a period of a year. After a year, all three populations start to dip down and eventually hit zero after a long time period of ~50 years. This is likely because our model treats the population as an enclosed population with no introduction of new, uninfected and susceptible people. Thus, as the number of infected people fall and recovered people rise, the population will hit a point at which all the infected people have shifted to the recovered group and there will be no more infected group to spread the disease back to the susceptible group, thereby leading to an eradication of the disease. To circumvent this problem, we could look at introducing a term into our equation that allows for a constant immigration of susceptible people, in addition to the transfer of people from the recovered group back into the susceptible group. A previous paper suggests that controlling malaria can actually lead to an increased efficiency of transmission, likely caused by increase in gametocyte density. They also report that there is likely lower efficiency in transmission in an area of high malaria prevalence, and that the transmission-reducing drugs should be targeted to those areas (Churcher et al, 2015). In regards to our modeling, this could explain why the infected population will hit an equilibrium, rather than declining to the point where there will be no more infected people to spread the diseases, essentially eradicating the disease. This equilibrium represents the balance between treatment and transmission efficiency, which will fluctuate and change when different treatment options are introduced (through changing hu). Our model reveals the importance of malaria control on disease transmission, especially in regards to using bed nets. The models of our paper reveal that bednets significantly reduce the rise of force of infection. Furthermore, the reduction is accompanied by a reduced rate in the decrease of susceptible population. Hence, our model shows that preventive treatment methods slows down the transmission of malaria, which provides time for therapy and lowering the risk of transmission from human to human. Additionally, we show that certain preventive treatments like bednets with insecticide are more effective than other preventive treatments like non-insecticide bednets in reducing the rate of transmission and increasing the susceptible to infected population. Furthermore, by studying a village population, our model is applicable to study rural population affected by malaria where cost-efficiency is more critical. Thus, usage of a mathematical model to precisely predict transmission rates would be extremely useful in planning for prevention and therapy. Though our results favored the usage insecticide treated bednets, one caveat to this solution is that the long term effects of insecticide bed nets usage may have undesirable effects. According to research by Tanya Russell of James Cook University, the usage insecticide-treated bed nets may have shifted the behavior of Anopheles funestus, a species of mosquitoes that are vectors for malaria, so that it feeds more during the daytime (Greenwood et al., 2017). Unnatural selection may occur that selects for mosquitos that are active during the daytime rather than the mosquitos that are active during the night as those are quickly killed off by the insecticide treated bednets. Therefore, there needs to be development of more innovative intervention methods to circumvent this effect; methods that does not aim to kill the mosquitos but rather interfere with the mosquito vector competence factor.

Aknowledgements

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