The Baseline and Elimination Model Equations, Derivations and Parameter Values

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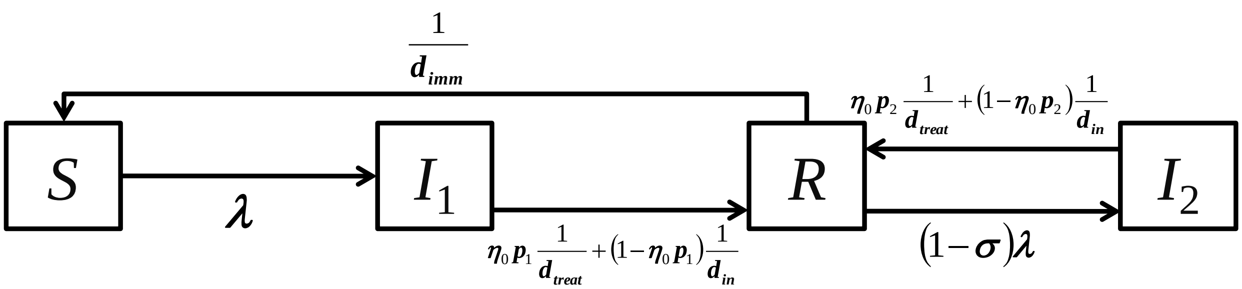
Baseline model

The diagram shows the compartmental structure of the model with time dependent variables: S (uninfected and non-immune); I_1 (infected with no prior immunity); R (uninfected with immunity); I_2 (infected with prior immunity). Model output variables are: C (clinical infections); P (proportion of people receiving treatment or selective pressure); C_c (cumulative clinical infections); P_c (cumulative selective pressure).



The equations below describe this system:

$$S' = \frac{N}{L} - \left(\lambda + \frac{1}{L}\right)S + \frac{1}{d_{imm}}R$$

$$I_1' = \lambda S - \left(\eta_0 p_1 \frac{1}{d_{treat}} + (1-\eta_0 p_1)\frac{1}{d_{in}} + \frac{1}{L}\right)I_1$$

$$I_2' = \lambda R - \left(\eta_0 p_2 \frac{1}{d_{treat}} + (1-\eta_0 p_2)\frac{1}{d_{in}} + \frac{1}{L}\right)I_2$$

$$R' = \left(\eta_0 p_1 \frac{1}{d_{treat}} + (1-\eta_0 p_1)\frac{1}{d_{in}}\right)I_1 + \left(\eta_0 p_2 \frac{1}{d_{treat}} + (1-\eta_0 p_2)\frac{1}{d_{in}}\right)I_2 - \left[\lambda + \frac{1}{d_{imm}} + \frac{1}{L}\right]R$$

$$\lambda = R_0\left(\frac{1}{L} + \frac{1}{d_{treat}}\right)\frac{(I_1 + I_2)}{N}$$

$$C = p_1 I_1 + p_2 I_2$$

$$P = \frac{\eta_0 (p_1 I_1 + p_2 I_2)}{I_1 + I_2}$$

$$C_c' = C$$

$$P_c' = P$$

$$p_{res} = \frac{\frac{1}{d_{treat}} - \frac{1}{d_{treat0}}}{\frac{1}{d_{in}} - \frac{1}{d_{treat0}}}$$

$$\tau' = -kPp_{res}\left(\tau - \frac{1}{d_{in}}\right)$$

$$d_{treat} = \frac{1}{\tau}$$

The initial conditions of the variables S, I_1, I_2 and R are given by the equilibrium solution of the system with $d_{treat} = d_{treat0}$. The initial conditions of C_c and P_c are zero and the initial condition of τ is $(1/d_{treat0})$.

Parameter values

Symbol	Definition	Value	Source
N	Population size	10^6	
L	Average life expectancy	50 years	
d_{imm}	Average duration of immunity in the absence of re-exposure	1 year	[1]
d_{in}	Average duration of untreated infection	0.5 year	Assumed
d_{treat0}	Average duration of treated sensitive infection	2 wks (figure 5) 4 wks (other figures)	[2] Assumed
p_1	Average proportion of infected individuals without preexisting immunity that have clinical malaria	0.87	[1] & $p_1 = \frac{d_{treat}(d_{in} - 14.12)}{d_{treat} d_{in} - \eta_0}$
p_2	Average proportion of infected individuals that have clinical malaria who have experienced infection previously within a year	0.08	[1] & $p_1 = \frac{d_{treat}(d_{in} - 2.23)}{d_{treat} d_{in} - \eta_0}$
k	coefficient of speed of spread of resistance	0 - 0.1	Assumed
η_0	precentage of individuals with clinical infection that receive treatment	60	Assumed
R_0	Basic reproduction number	2.4 – 63	corresponds to parasite prevalence of 20% to 98%

Given presumptive treatment of clinical cases at a coverage of 60%, k=0.04 indicates that the percentage of resistant infections would increase from 0% to about 50% in 20 to 40 years depending on transmission intensity. k=0.08 indicates that the percentage of resistant infections would increase from 0% to about 50% in 5 to 20 years depending on transmission intensity

Elimination model

This model is produced from two linked copies of the basic model with the presence or absence of the subscript *V* representing individuals who have received or not received effective vaccine respectively. The additional variables *h*, *m* and *x* represent respectively rates of receiving routine treatment, receiving treatment as part of MSAT and vaccination.

$$S' = (1-c_b)\frac{N}{L} - \left(\pi\lambda + \frac{1}{L}\right)S + \frac{1}{d_{imm}}R - x(t)S + yS_V$$

$$I_1{}' = \pi\lambda S - \left(\frac{(\eta p_1 + m)}{d_{treat}} + \frac{(1-\eta p_1 - m)}{d_{in}} + \frac{1}{L} + \frac{m}{d_{treat}}\right)I_1 - x(t)I_1 + yI_{1V} - m(t)I_1$$

$$I_2{}' = \pi\lambda R - \left(\frac{(\eta p_2 + m)}{d_{treat}} + \frac{(1-\eta p_2 - m)}{d_{in}} + \frac{1}{L} + \frac{m}{d_{treat}}\right)I_2 - x(t)I_2 + yI_{2V} - m(t)I_2$$

$$R' = \left(\frac{(\eta p_1 + m)}{d_{treat}} + \frac{(1-\eta p_1 - m)}{d_{in}} + \frac{m}{d_{treat}}\right)I_1 + \left(\frac{(\eta p_2 + m)}{d_{treat}} + \frac{(1-\eta p_2 - m)}{d_{in}} + \frac{m}{d_{treat}}\right)I_2$$
$$-\left[\pi\lambda + \frac{1}{d_{imm}} + \frac{1}{L}\right]R - x(t)R + yR_V$$

$$S_V' = c_b\frac{N}{L} - \left(\rho\pi\lambda + \frac{1}{L}\right)S_V + \frac{1}{d_{imm}}R_V + x(t)S - yS_V$$

$$I_{1V}{}' = \rho\pi\lambda S_V - \left(\frac{(\eta p_1 + m)}{d_{treat}} + \frac{(1-\eta p_1 - m)}{d_{in}} + \frac{1}{L} + \frac{m}{d_{treat}}\right)I_{1V} + x(t)I_1 - yI_{1V}$$

$$I_{2V}{}' = \rho\pi\lambda R_V - \left(\frac{(\eta p_2 + m)}{d_{treat}} + \frac{(1-\eta p_2 - m)}{d_{in}} + \frac{1}{L} + \frac{m}{d_{treat}}\right)I_{2V} + x(t)I_2 - yI_{2V}$$

$$R_V' = \left(\frac{(\eta p_1 + m)}{d_{treat}} + \frac{(1-\eta p_1 - m)}{d_{in}} + \frac{1}{L} + \frac{m}{d_{treat}}\right)I_{1V} + \left(\frac{(\eta p_2 + m)}{d_{treat}} + \frac{(1-\eta p_2 - m)}{d_{in}} + \frac{1}{L} + \frac{m}{d_{treat}}\right)I$$
$${}_{2V} - \left[\rho\pi\lambda + \frac{1}{d_{imm}} + \frac{1}{L}\right]R_V + x(t)R - yR_V$$

$$\lambda = \frac{R_0\left(\frac{1}{L} + \frac{1}{d_{treat}}\right)(I_1 + I_2 + I_{1V} + I_{2V})}{N}$$

$$C = p_1(I_1 + I_{1V}) + p_2(I_2 + I_{2v})$$

$$P = \frac{\eta p_1(I_1 + I_{1V}) + \eta p_2(I_1 + I_{1V}) + m(I_1 + I_{1V} + I_2 + I_{2V})}{(I_1 + I_{1V} + I_2 + I_{2V})}$$

$$C_c' = C$$

$$P_c' = P$$

$$\eta(t) = \begin{cases} 0 & \textbf{for } \mathrm{mod}(t,1) \geq \frac{9}{12} \\ \eta_0 & \textbf{for } \mathrm{mod}(t,1) < \frac{9}{12} \end{cases}$$

$$p_{res} = \frac{\frac{1}{d_{treat}} - \frac{1}{d_{treat0}}}{\frac{1}{d_{in}} - \frac{1}{d_{treat0}}}$$

$$x(t) = \begin{cases} -4\ln\left(\frac{100-c}{100}\right) & \textbf{for } \mathrm{mod}(t,1) \geq \frac{9}{12} \\ 0 & \textbf{for } \mathrm{mod}(t,1) < \frac{9}{12} \end{cases}$$

$$\tau' = -k\,P\,p_{res}\left(\tau - \frac{1}{d_{in}}\right)$$

$$m(t) = \begin{cases} 1 - \exp\left(4\ln(1 - \mathrm{m_{sat}})\mathrm{mod}\left(t - \frac{9}{12}\right)\right) & \textbf{for } \mathrm{mod}(t,1) \geq \frac{9}{12} \\ 0 & \textbf{for } \mathrm{mod}(t,1) < \frac{9}{12} \end{cases}$$

$$d_{treat} = \frac{1}{\tau}$$

The initial conditions are as for the baseline model for the non-vaccine variables. The initial conditions for the vaccine variables are all zero. To derive the formula for the rate of vaccination $x(t)$, we consider a population being vaccinated at a constant rate q given an initial condition of 100%. Then the differential equation describing the percentage of vaccinated individuals, n, is given by $\boldsymbol{n}' = \boldsymbol{q}(100-\boldsymbol{n})$ with solution $\boldsymbol{n}(\boldsymbol{t}) = 100 - 100\boldsymbol{e}^{-\boldsymbol{qt}}$. Thus to achieve a coverage, c, in 3 months (i.e. ¼ years) $\boldsymbol{n}\left(\frac{1}{4}\right) = 100 - 100\boldsymbol{e}^{-\frac{\boldsymbol{q}}{4}} = \boldsymbol{c}$, thus $\boldsymbol{q} = -4\ln\left(\frac{100-\boldsymbol{c}}{100}\right)$, which should be the function for $x(t)$ during the period of vaccination each year.

Parameter values

Symbol	Definition	Value	Source
ρ	proportional vaccine efficacy	0 to 1	[3]
π	reduction in force of infection due to increased vector control	0.3	[4]
c	annual vaccine coverage	80 %	
y	rate of loss of vaccine effect	1- 10 $year^{-1}$	[3]
m_{sat}	proportion of infected people treated during MSAT	0.8	[2]

References

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