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Critical Vaccination Level for Dengue Fever Disease Transmission

Asep K. Supriatna
Department of Mathematics, Universitas Padjadjaran
Km 21 Jatinangor, Bandung 45363 – INDONESIA
asupriat@unpad.ac.id

Edy Soewono
Department of Mathematics & Center of Mathematics, ITB
Ganesha 10, Bandung 40132 - INDONESIA

Abstract

In this paper we discuss a critical vaccination level in the transmission of dengue fever disease. We assume that the vaccination is administrated constantly, either to some proportion of the whole susceptible human population or to some proportion of newborns. We also assume that the effect of vaccination is perfect, that is it prevents the vaccinated susceptible individual from catching the disease caused by all type of dengue viruses. The critical vaccination level then is obtained as a function of the basic reproductive ratio, R_0, which is consistent with the rule for the simple SIR model. Above this prescribed critical level, vaccination will make the disease die out. Conversely, below this prescribed critical level, the disease will persist. The model suggests that vaccinating general susceptible human population is significantly more effective than vaccinating newborn human population.

Keywords : *Mathematical model, Dengue Fever, Vaccination*

1 Introduction

Dengue fever disease has been known as a dangerous disease since 1779 [1]. The spread of the disease is now increasingly becoming an important public health problem in many tropical and subtropical countries, including Indonesia. One among the reasons is because until recently there is no known vaccine to prevent one from this disease. Standard program used by the Indonesian government to control the spread of the disease is the eradication of the main disease vector, that is the eradication of the *Aedes aegypti* mosquitoes. However, many studies show that this program was not fully effective. Many cases of dengue and dengue haemorrhagic fever still occur almost periodically in many urban areas. Fortunately, with the advancement of science and technology, the invention of vaccine for the dengue disease is now getting closer and closer [2].

There are only few researchers who have investigated the effects of vaccination on the transmission of infectious diseases, among them are [3,4,5,6]. In [3] the authors showed that a pulse vaccination strategy is effective to some extent to eradicate an epidemic. The researchers in [4] discussed the role of the vaccination failure to induce the development of the immune response in a disease outbreak. All of the researchers mentioned above work on a direct-transmitted disease. The effect of vaccination on an indirect-transmitted disease or on a vector-borne disease, such as dengue fever disease, has received little attention. The main objective of the present paper is to determine the level of vaccination effort required for eradicating the dengue disease, once a perfect vaccine is available. The vaccine is perfect if it is completely successful and can avoid the vaccinated individual from catching the dengue disease caused by all known types of virus. To address this issue we will develop a mathematical model similar to our previous work with the inclusion of vaccination [6].

2 Host-Vector Model in the Absence of Vaccination

Our model is closely related to the model in [7]. We review the Host-Vector model in [7] for the transmission of dengue fever as follows. The model is based on the assumption that the host population N_H is constant, *i.e.* the death rate and birth rate are equal to μ_H. The vector population N_V, which is in general very difficult to estimate, is governed by a monotonic model

$$N_V^{'} = A - \mu_V N_V . \tag{1}$$

Here μ_N is the mortality rate of the vector, and A is the recruitment rate. This mosquito model can be explained from the fact that only a small portion of a large supply of eggs survives to the adult stage [8]. Hence, A is independent from the adult population. The dynamics of the vector approaches to the equilibria A/μ_V as $t \to \infty$.

In [1] the majority of the host population eventually becomes immune. The host population is subdivided into the susceptible S_H, the infective I_H and the recovered, assumed immune, R_H. The vector population, due to a short life period, is subdivided into the susceptible S_V and the infective I_V. The interaction model for the dengue transmission is given as follows

$$
\begin{aligned}
\frac{d}{dt}S_H &= \mu_H N_H - \frac{\beta_H b}{N_H} S_H I_V - \mu_H S_H \\
\frac{d}{dt}I_H &= \frac{\beta_H b}{N_H} S_H I_V - (\mu_H + \gamma_H) I_H \\
\frac{d}{dt}R_H &= \gamma_H I_H - \mu_H R_H \\
\frac{d}{dt}S_V &= A - \frac{\beta_V b}{N_H} S_V I_H - \mu_V S_V \\
\frac{d}{dt}I_V &= \frac{\beta_V b}{N_H} S_V I_H - \mu_V I_V
\end{aligned}
\tag{2}
$$

where

N_H = *the host population*
S_H = *the number of susceptibles in the host population*
I_H = *the number of infectives in the host population*
R_H = *the number of immunes in the host population*
N_V = *the vector population*
S_V = *the number of susceptibles in the vector population*
I_V = *the number of infectives in the vector population*
μ_H = *the birth/death rate in the host population*
μ_V = *the death rate in the vector population*
β_H = *the transmission probability from vector to host*
β_V = *the transmission probability from host to vector*
γ_H = *the recovery rate in the host population*
b = *the biting rate of vector*.

Note that we remove the alternative blood resource from [7] due to the fact that practically there is no other blood resource other than human in urban areas.

Further reduction of (2) to a three-dimensional dynamics is obtained from a restriction to an invariant subset defined by

$$
S_H + I_H + R_H = N_H \text{ and } S_V + I_V = \frac{A}{\mu_V}. \tag{3}
$$

The resulting dynamics, expressed in proportions

$$
x = \frac{S_H}{N_H}, y = \frac{I_H}{N_H}, \text{ and } z = \frac{I_V}{A/\mu_V}, \tag{4}
$$

is given by

$$
\begin{aligned}
\frac{d}{dt}x &= \mu_H (1-x) - \alpha\, x\, z \\
\frac{d}{dt}y &= \alpha\, x\, z - \beta\, y \\
\frac{d}{dt}z &= \gamma(1-z)y - \delta\, z
\end{aligned}
\tag{5}
$$

where

$$
\alpha = \frac{b\beta_H A}{\mu_V N_H},\ \beta = \gamma_H + \mu_H, \gamma = b\beta_V, \delta = \mu_V. \tag{6}
$$

Two possible fixed points of the system are

$$
F_1 = (1,0,0) \text{ and } F_2 = (x_0, y_0, z_0), \tag{7}
$$

with

$$
x_0 = \frac{\mu_H \gamma + \beta\delta}{\gamma(\mu_H + \alpha)},\ y_0 = \frac{\mu_H(\alpha\gamma - \beta\delta)}{\beta\gamma(\mu_H + \alpha)} \text{ and } z_0 = \frac{\mu_H(\alpha\gamma - \beta\delta)}{\alpha(\mu_H \gamma + \beta\delta)} \tag{8}
$$

Note that the second fixed point exists in the region of biological interest, *i.e.* $0 < x, y, z < 1$, only if the threshold parameter $R^\bullet = \frac{\alpha\gamma}{\delta\beta} > 1$. The number $R_0 = \sqrt{R^\bullet}$ represents the *basic reproductive ratio.* It has been proven in [7], that if $R^\bullet \le 1$, the fixed point F_1 is globally asymptotically stable in the region of interest $\Omega = \{(x, y, z) : 0 < x, y, z < 1\}$ and if $R^\bullet > 1$, $F_{1\text{ is}}$ unstable and the endemic fixed point F_2 is globally asymptotically stable in the interior of Ω. In the next section we will determine the levels of vaccination that able to change the globally asymptotically stable fixed point F_2 to a fixed point where the components y_0 and z_0 vanish.

3 Host-Vector Model with the Inclusion of Vaccination

In this section we consider two types of vaccination programs, one is applied just to newborns and the other one is applied to general population.

3.1 Vaccination for newborns

We assume p proportion, $(0 \le p \le 1)$, of a newly born infant is vaccinated with a perfect vaccine. The vaccine is perfect if it is completely successful and can avoid the vaccinated individual from catching the dengue disease caused by all known types of dengue virus. With this assumption, the governing equations as in (2) except the dynamics of the human susceptible is given by

$$\frac{d}{dt}S_H = (1-p)\mu_H N_H - \frac{\beta_H b}{N_H} S_H I_V - \mu_H S_H . \tag{9}$$

Using (3), (4) and (6) we end up to a complete dimensionless equations for the dynamics of the dengue disease transmission with vaccination, *i.e.*

$$\begin{aligned} \frac{d}{dt}x &= \mu_H[(1-p)-x)] - \alpha\, x\, z \\ \frac{d}{dt}y &= \alpha\, x\, z - \beta\, y \\ \frac{d}{dt}z &= \gamma(1-z)y - \delta\, z \end{aligned} \tag{10}$$

Appendix 1 shows that if $R^\bullet = \frac{\alpha\gamma}{\delta\beta}$, the dengue disease transmission with the inclusion of constant vaccination has equlibrium points

$$F_1{}^p = (1-p,0,0) \text{ and } F_2{}^p = (x_0^p, y_0^p, z_0^p), \tag{11}$$

with

$$\begin{aligned} x_0^p &= \frac{\mu_H\gamma(1-p)+\beta\delta}{\gamma(\mu_H+\alpha)}, \\ y_0^p &= \frac{\mu_H(\alpha\gamma(1-p)-\beta\delta)}{\beta\gamma(\mu_H+\alpha)} = \frac{\mu_H(R^\bullet(1-p)-1)\beta\delta}{\beta\gamma(\mu_H+\alpha)}, \\ z_0^p &= \frac{\mu_H(\alpha\gamma(1-p)-\beta\delta)}{\alpha(\mu_H\gamma(1-p)+\beta\delta)} = \frac{\mu_H(R^\bullet(1-p)-1)\beta\delta}{\alpha(\mu_H\gamma(1-p)+\beta\delta)}. \end{aligned} \tag{12}$$

Since $0 \le p \le 1$ then the proportion of susceptible, x_0^p, is always positive. Furthermore if $p \ge 1-\frac{1}{R^\bullet}$, or equivalently $R^\bullet(1-p) \le 1$, both y_0^p and z_0^p disappear. It means that if we vaccinate p proportion of newborns with $p \ge 1-\frac{1}{R^\bullet}$ then it will ensure that

eventually the disease will fade away. While conversely, if only p proportion of newborns with $p < 1-\frac{1}{R^\bullet}$ then the disease will persist. The number

$$p_c = 1-\frac{1}{R^\bullet} \tag{13}$$

is a *critical vaccination level*. This *critical vaccination level* is different from the one for the direct-transmission disease.

In [3] it has been shown that the *critical vaccination level* for the direct-transmission disease is exactly the same as one minus the inverse of the *basic reproductive ratio, i.e.* $p_c = 1-\frac{1}{R_0}$. It is assumed in [3] that the growth of susceptible in the absence of the disease is linear. In [5] the same result is also established for the logistic growth of the susceptible. In ours the *critical vaccination level* for the indirect-transmission disease is exactly the same as one minus the inverse of the square of the *basic reproductive ratio*[1]. Appendix 2 shows that, compared to the system without vaccination, the basic reproductive ratio R_0 does not change,

3.2 Vaccination for general population

We consider the system in which q proportion of susceptible host is vaccinated. Then we have

$$\begin{aligned} \frac{d}{dt}S_H &= \mu_H N_H - \frac{\beta_H b}{N_H}(1-q)S_H I_V - \mu_H S_H \\ \frac{d}{dt}I_H &= \frac{\beta_H b}{N_H}(1-q)S_H I_V - (\mu_H+\gamma_H)I_H \end{aligned} \tag{14}$$

The dynamic of I remains the same as in (2). Appendix 1 shows that the fixed poits for the system are:

$$F_1{}^q = (1,0,0) \text{ and } F_2{}^q = (x_0^q, y_0^q, z_0^q), \tag{15}$$

with

$$x_0^q = \frac{\gamma\mu_H+\beta\delta}{\gamma(\mu_H+(1-q)\alpha)}, \quad y_0^q = \frac{\mu_H((1-q)R^\bullet-1)\beta\delta}{\gamma\beta((1-q)\alpha+\mu_H)} \text{ and } \quad z_0^q = \frac{\mu_H((1-q)R^\bullet-1)\beta\delta}{(1-q)\alpha(\mu_H\gamma+\beta\delta)} \tag{16}$$

[1] In [9] R_0 is defined as the spectral radius of the next generation matrix. Appendix 2 derives R_0 directly for our host-vector transmission with vaccination.

The *critical vaccination level* is given by $q_c = 1 - \frac{1}{R^\bullet}$, which is the same threshold as in the case of vaccination for the newborn (13). Above this threshold, vaccination convert both y_0^p and z_0^p to zero, which ensures that the disease fade away. We also found that the square of the basic reproductive ratio is

$$R_q^\bullet = \frac{b^2 \beta_H \beta_V A / \mu_V (1-q)}{(\gamma_H + \mu_H)\mu_V N_H}. \qquad (18)$$

4 Concluding Remarks

In this paper we present *the critical vaccination level* for indirect transmission disease and consider two vaccination strategies, newborn vaccination and general vaccination. We found that *the critical vaccination level*s for both strategies are consistent in form to the one in the direct-transmission model.

Different from the case of newborn vaccination, in which $R^\bullet = R_p^\bullet$, we note that general vaccination alters the square of the basic reproductive ratio from $R^\bullet$ to $R_q^\bullet = R^\bullet(1-q)$. This is not surprising since the basic reproductive ratio measures the strength of the disease in the early stage; hence the effect of the newborn vaccination has not been observed yet. This also suggests that general vaccination is more effective than newborn vaccination as far as time needed concern. However, in long term, both strategies are able to eliminate the disease provided they are above the critical vaccination level, as indicated by the shifting of endemic equilibrium into the stable disease-free equilibrium [see (12), (16) and Appendix 3].

A numerical example (Figure 1.c) shows that, if we apply the newborn vaccination then there is still a single outbreak followed by exponential decay cases going toward the disease-free equilibrium. Hence, the effect of vaccination is to replace multiple outbreaks with a single outbreak. However, if we apply the general vaccination there is almost no outbreak occurs and the cases exponentially decay approaching the disease-free equilibrium (Figure 1.d). Future research can be done by taking into account more realistic complexities, such as strain-specific vaccination, decreasing immunity effect of vaccination and adding return path from recover to susceptible. We also investigate the effect of the diversion in the implementation of the vaccine elsewhere [10].

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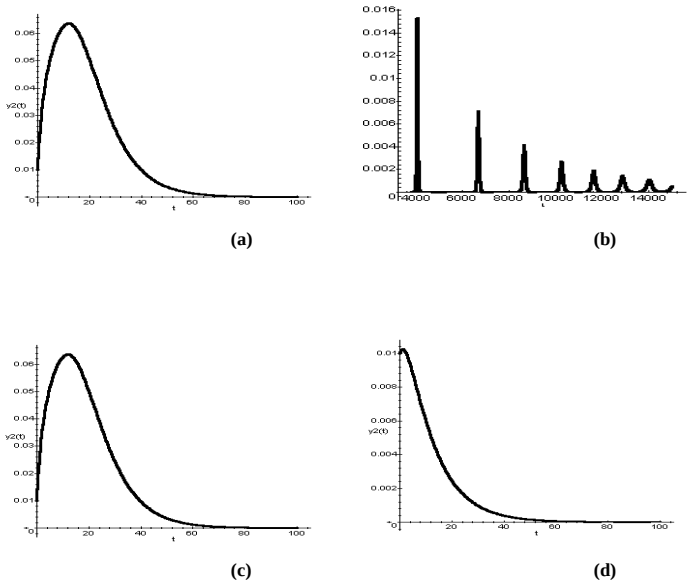

Figure 1: Figure (a) and (b) show the proportion of the infective human population without vaccination. First outbreak occurs at approximately *t*=12 (a). Second outbreak and onwards begin from *t*=4000 (b). Figure (c) and (d) show the proportion of the infective human population if, respectively, newborn vaccination and general susceptible vaccination is being applied. If the newborn vaccination is applied, Figure (c) shows that still one outbreak occurs followed by exponential decay cases (c). However, if the general susceptible vaccination is applied, Figure (d) shows that there is almost no outbreak and the number of subsequent cases exponentially decay. This suggests that vaccinating general susceptible human population is significantly more effective than vaccinating newborn human population. The parameters used to produce the figures are as in [6] with *p* and *q* are above the threshold.

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Appendix 1: Equilibrium Points

Consider the system

$$\frac{d}{dt}x = \mu_H[(1-p)-x)] - (1-q)\alpha\, x\, z \qquad \text{A1}$$

$$\frac{d}{dt}y = (1-q)\alpha\, x\, z - \beta\, y \qquad \text{A2}$$

$$\frac{d}{dt}z = \gamma(1-z)y - \delta\, z \qquad \text{A3}$$

with $\frac{dx}{dt} = \frac{dy}{dt} = \frac{dz}{dt} = 0$. The case of newborns vaccination is represented by q=0 and the case of general population vaccination is represented by p=0. Solving x, y and z, respectively in A1, A3 and A2, and by recalling that $R^* = \frac{\alpha\gamma}{\delta\beta}$, gives $x_0 = \frac{\mu_H(1-p)}{\mu_H + (1-q)\alpha z}$,

$y_0 = \frac{\delta z}{\gamma(1-z)}$ and $z_0 = \frac{\mu_H\left((1-q)R^*(1-p)-1\right)\beta\delta}{(1-q)\alpha\left(\mu_H\gamma(1-p)+\beta\delta\right)}$. Substitute z_0 into x_0 and y_0 to produce $x_0 = \frac{\gamma\mu_H(1-p)+\beta\delta}{\gamma(\mu_H+(1-q)\alpha)}$ and $y_0 = \frac{\mu_H\left((1-q)R^*(1-p)-1\right)\beta\delta}{\gamma\beta\left((1-q)\alpha+\mu_H\right)}$.

Appendix 2: The Basic Reproductive Ratio

Consider the system where both vaccinations are applied. The number of vectors infected by one infectious host is the force of infection times the proportion of susceptible vectors times sojourn time of the infectious host, which is, $R_{H\to V} = \left(\frac{b\beta_V}{N_H}\right)\left(\frac{A}{\mu_V}\right)\left(\frac{1}{(\mu_H+\gamma_H)}\right)$. The number of hosts infected by one infectious vector is the force of infection times the proportion of susceptible hosts times sojourn time of the infectious vector, which is, $R_{V\to H} = (b\beta_H)(1-q)\left(\frac{1}{\mu_V}\right)$. Then $R^* = \frac{b^2\beta_H\beta_V A/\mu_V(1-q)}{(\gamma_H+\mu_H)\mu_V N_H}$ is the square of the basic reproductive ratio.

Appendix 3: Stability Analysis

In order to reduce the number of parameters in the system, we re-scale the time variable by $\alpha, \tau = \alpha t$. Using the same notations, the system (10) can be written in a simpler form by replacing $\alpha = 1$. Further, starting from this point, we assume that $\alpha = 1$. We can investigate the behavior of the endemic equilibrium in (11) by noting the characteristic polynomial of the second fixed point, $A_3\lambda^3 + A_2\lambda^2 + A_1\lambda + A_0 = 0$

where

$$A_0 = \beta\mu(\mu+1)[\gamma(1-p)-\beta\delta][\mu\gamma(1-p)+\beta\delta]$$

$$A_1 = \beta^2\mu(\mu+1)^2[\gamma(1-p)-\beta\delta] + \mu[\mu\gamma(1-p)+\beta\delta]^2 + \mu^2[\gamma(1-p)-\beta\delta]^2$$
$$+ \beta^3\mu\delta(\mu+1)^2 + \beta\mu[\gamma(1-p)-\beta\delta][\mu\gamma(1-p)+\beta\delta] + \beta\delta\mu(\mu+1)[\gamma(1-p)-\beta\delta]$$

$$A_2 = [\mu\gamma(1-p)+\beta\delta]^2 + \beta(\mu+1)[\mu^2\gamma(1-p)+\beta\mu\gamma(1-p)+\mu\gamma(1-p)+\beta^2\delta]$$

$$A_3 = \beta(\mu+1)[\mu\gamma(1-p)+\beta\delta].$$

All coefficients of the characteristic equation are non-negative for $p \geq 1 - \frac{1}{R^*}$. Direct calculation shows that $A_1A_2 \geq A_0A_3$, which implies that the second fixed point is locally stable. More precisely, in this case the endemic equilibrium changes into the stable disease-free equilibrium. The stability analysis for the endemic equilibrium in (15) can be done similarly.