# Appendix S1: The transmission and vaccination model

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## 1. Transmission model description

We adapted clinical cross protection model originally developed by Nagao and Koelle ([33)](https://www.zotero.org/google-docs/?2w6bVj). It comprises four sequential dengue infections. The first infection among dengue naïve people is a homotypic infection, whilst the infection with second, third, and fourth serotypes is called secondary, tertiary, and quaternary heterotypic infections. In dengue, a heterotypic infection can lead to an infection enhancement instead of neutralisation because the existing antibody against one serotype is non-neutralising against the other serotypes. This phenomenon is known as antibody-dependent enhancement (ADE). The detailed of the transmission model was described elsewhere [(33)](https://www.zotero.org/google-docs/?2w6bVj).

However, this we simplified the original model so that only up to two infectious were considered. The model was mathematically represented by the following equation:

Homotypic infection part:

Heterotypic (2 serotypes) infection part:

## 2. Modelling ADE

Several studies attempted to modeI ADE through an increased infectiousness during heterotypic infection. Meanwhile, recent evidence showed a strong correlation between the antibody level at the time of exposure and the disease risk. Those with high pre-existing antibody levels are more protected against subsequent severe infection (14, 36). Then, the protection wanes over time as the antibody titre decreased, causing an increased risk against DHF (36). Therefore, we model ADE on disease outcomes, whereby heterotypic infection poses an increased probability in developing symptomatic infections (VCD) and DHF, rather than increased infectivity and transmission.

## 3. Incorporating age into the model

The model will account for two age groups spanning from 0 to 14 and 15-75+ years old. The cut-off was determined based on the age-specific case distribution of the case-notification data reported in Jakarta’s epidemiology surveillance system. The purpose of the age division was to evaluate the impact if the vaccination was performed only in a selected population as a means of redirecting the resources into a targeted population. In Indonesia, dengue cases mostly occurred in children, thus posing this sub-population to be at the highest risk of DHF. We would be able to evaluate what would be the likely impact on the overall DHF transmission when we vaccinate only the specific group as vaccinating everyone would be impractical.

We repeated the population compartments to account for both age groups. However, the transmission rate would be age specific. We assume that the WAIFW contact matrix to be expressed as follows:

(1)

and:

and . (2)

Therefore,

(3a)

(3b)

Let the probability of being hospitalised due to DHF in age group A from primary and secondary infection are h.dhfi,A and h.dhfij,A, respectively, while for primary and secondary infection in age group B are h.dhfi,B and h.dhfij,B. The hospitalised DHF incidence can be expressed by the following equations:

(4a)

(4b)

Alternatively, it can also be approximated in a more simplified form from the number of people who are recovered from infection by the following equations, which were used in the model:

(5a)

(5b)

## 4. Dengue vaccination model formulation

To account for immune waning from vaccination, the assumption is that vaccination does not confer protection the same as that acquired from natural infection, i.e., vaccination does not give full and life-long protection against any of DENV serotype. We assume that the vaccine immunity wanes in 5 years, and we evaluated vaccination only for a short term, i.e., for 3 years.

Secondly, the VE obtained from the trials was actually VE against VCD, but we assumed that it would work similarly against infection. As a result, we assume that the reported VE in the trials would be modelled to modify the transmission rate . As vaccinated individuals can get infected with any serotype, but they already had some degree of protection, they will experience a reduced susceptibility through the reduction in transmission rate, given by the following equation:

; (6a)

; (6b)

S compartment consists of immunologically naive individuals. For this compartment, VE data from seronegative vaccinees were used, while for the other compartments, SJ, the VE data from seropositive vaccinees were applied:

; (7a)

; (7b)

; (8a)

; (8b)

The assumption of clinical cross-protection and ADE were still held for vaccinated compartments. Under the assumption that the vaccination coverage would be achieved within the time campaign of one year then vaccination rate is estimated as:

(9)

Under scenarios where both Qdenga and Dengvaxia vaccines were used in the population, the vaccination rate of Qdenga and Dengvaxia vaccinations were multiplied by the probability of receiving such vaccine, being for Qdenga and for Dengvaxia, as the following equation:

(10)

(11)

The target vaccination coverage was defined as:

(12)

The basic target immunisation coverage from Indonesia’s Ministry of Health is at 88% (39), while the seropositivity among the targeted population (SPA) is estimated from the model as:

, (13)

where:

(14)

Meanwhile, the objective of screening was to minimise vaccination among naive individuals and maximise vaccination among seropositive DENV serotypes. The false negative and true positive are given by the following equation:

(15a)

(16b)

In circumstances where screening is certainly needed, such as prior to Dengvaxia vaccination, the vaccine can only be given after screening was done. A test with 100% sensitivity and specificity will allocate the vaccines only to seropositive individuals (the targeted population) where its proportion in the population was estimated as SPA. The intended target coverage of 88% was, therefore, the target percentage of children who were screened with such a test. Thus, the actual proportion of those receiving vaccines was given by equation (10), and the total screening performed was defined as:

(17)

The chance of receiving vaccines is proportional to the proportion of a sub-population in a total population, that is given by:

(18a)

(18b)

Meanwhile, the chance of receiving vaccines depend on the diagnostic performance of the test used. This is given by the following equations:

(19a)

(19b)

Using vaccination rate defined in equation (9), thus the vaccination rate in seronegative and seropositive population are:

(20a)

(20b)

The total vaccination allocated to the population is:

(21)

Under scenarios where pre-vaccination screening was not applied, then the probability of seronegative and seropositive individuals in receiving vaccines is akin to probability of receiving screening since it is proportional to the corresponding subpopulation.

In any scenario, the number of vaccines used in a 3-year time frame would be the same. They differ only in how these vaccines were allocated which depends on two factors: first, whether pre-vaccinations were applied, and second, the sensitivity and specificity used for pre-vaccination screening. Under the implementation of pre-vaccination screening, we used diagnostic screening tools with a sensitivity of 95.2% (95%CI 94.2 to 96.2%) and specificity of 93.4% (95%CI 89.6 to 97.2%). Since the number of allocated vaccines depends on the diagnostic performance and the vaccine coverage, to allocate the same number of vaccines throughout the scenario, we adjusted the target coverage as:

(22)

## 5. Integrating age, vaccination, and screening into the model

As the model was structured by two age groups, at this point, the model would have been extended according to the number of the age group. However, as vaccination was applied only to the age group A, therefore:

Let:

. (23)

. (24)

### 5.1. Age group A

Homotypic infection part:

(25)

(26)

(27)

Heterotypic (2 serotypes) infection part:

(28)

(29)

(30)

### 5.2. Age group A: vaccinated

Homotypic infection part:

(31)

(32)

(33)

Heterotypic (2 serotypes) infection part:

(34)

(35)

(36)

### 5.3. Age group B

The inflow to age group B can from aging and immune waning of people in age group B who are under the effect of vaccination.

Homotypic infection part:

(37)

(38)

(39)

Heterotypic (2 serotypes) infection part:

(40)

(41)

(41)

### 5.4. Age group B: under vaccination effect

The are some people in age group B who are in effect of vaccination due to aging of vaccinated people in age group A.

Homotypic infection part:

(41)

(42)

(43)

Heterotypic (2 serotypes) infection part:

(44)

(45)

(46)

Note that the terms marked in red represents immune waning from vaccination, while green represents aging, and blue represents vaccination rate.