Supplementary Information S1

A Detailed Discussion of our Mathematical Model

We describe the spread of dengue viruses in a population using a model that classifies humans as Susceptible, Infected, Cross-protected or Recovered (SICR) and mosquito vectors as susceptible or infected (SI). The human population is divided into $A = 12$ age classes. The model accounts for secondary heterogenous infections and assumes that: (i) the birth and death rates in both the human and vector populations are balanced so that each total population is constant in time; (ii) infections do not result in increased death rates; (iii) the recovery periods are the same across all serotypes and independent of vaccine counts; (iv) secondary infections, regardless of their vaccination status, contribute to the force of infection as a multiplicative factor of primary infections allowing for the potential inclusion of Antibody Dependent Enhancement (ADE) of transmissibility of cases with pre-existing immunity; (v) after a primary infection, there is a period of cross-protection against heterologous serotypes [**?**, **?**, **?**]. However, this cross-protection may be imperfect since we allow for a fraction (may be zero) of the people in this class to be susceptible to secondary infections. The model accounts for secondary heterogenous infections; however, tertiary and quaternary infections are not considered since the epidemiological data shows them to be quite rare [**?**].

Our model accounts for multiple formulations of vaccines in terms of serotype specific efficacy and dosing characteristics. We focus on the dengue vaccine being developed by *Sanofi-Pasteur* that requires three doses for maximal protection. The timing of each vaccine dose in relation to previous exposure is an important factor and hence we are careful in distinguishing three cases: 1) before primary infection, 2) between primary and secondary infections and 3) after secondary infection. In the model, the rate at which individuals are vaccinated depends, in general, on their age group, the dose number (assuming some losses from one dose to the next), and on time. Each of these factors depends on the specific vaccine program simulated. Vaccination affects transmission of dengue by the following assumptions (i) for each serotype, the transmission of dengue virus from mosquito to vaccinated individuals occurs at a rate that is reduced by an amount that depends on the vaccine efficacy for the corresponding serotype and on the number of doses received (i.e. the vaccine reduces susceptibility against infection); (ii) conversely, the transmission of dengue virus from vaccinated individuals undergoing primary infection to mosquitoes may be enhanced. This accounts for potential ADE of infectiousness by vaccine derived immunity to a subset of serotypes. Thus, in summary, transmission enhancement can occur from individuals experiencing their second infection (item iv in the paragraph above) and from vaccinees during primary infections.

A number of parameters appear in our deterministic mathematical model of dengue transmission. The parameter values/ranges shown in Table **??** were obtained from the dengue modeling literature, with the exception of the ag-

ing rate $\alpha[a]$, which is determined from the duration of the corresponding age compartment. In our model, the human population is divided into $A = 12$ age classes. Rayong, Thailand, represents a hyper-endemic setting and thus primary infections occur at a fairly young age while secondary infections generally occur before or during the teenage years. For this reason, we selected the duration of our age compartments so as to have a higher resolution in the early years, when most infections occur. Our age compartments span the following age intervals: from birth to 6 months, 6 months to 1 year, 1 to 2 years, 2 to 5, 5 to 10, 10 to 15, 15 to 20, 20 to 25, 25 to 35, 35 to 50, 50 to 65 and finally 65 and over.

Parameter	Description	Value	Source
N_h	Total human population.	616,844	[**?**]
r_{mh}	Ratio of total mosquito population to total human population.	10.0	
$\alpha[a]$	Human a-th aging rate.	$1/\ell[a]$	–
$\ell[a]$	Duration of a-th age compartment.	†	–
μ_m	Mosquito death rate.	15.0	[**?**, **?**]
ϕ_i	ADE factor for serotype i.	1.0 – 2.0	
σ	Recovery rate for both primary and secondary infections.	100.0	[**?**]
ρ	Proportion of cross-immune individuals that may contract secondary infections.	0.3	[**?**]
γ	Cross-immunity loss rate.	1.0	[**?**]

Table S1.1: Model parameters taken from the literature.
† See text.

Table **??** lists all the parameters whose values were obtained by calibrating our model to the population demography and dengue transmission in Rayong. The same table also lists: (*i*) the birth rate, whose value was chosen to maintain a constant human population throughout time; and (*ii*) the vaccination rates for different model compartments, whose values were chosen to reflect the frequency and asymptotic coverage of vaccination campaings in realistic settings. See appendix **??** for more details on the calibration.

Our compartmental age model has an SI (susceptible, infected) structure for the vector and an SICR (susceptible, infected, cross-immune and recovered) structure for the human population; see the schematic representations of the transmission processes in Figs. **??** and **??**. The variables used are listed in Table **??**. The h or m subindex on each symbol indicates whether the variable corresponds to the human or to the mosquito population, respectively. The compartmental model variables have a series of discrete indices. The index $a(= 1 \dots A)$ labels the age of the corresponding human group. We use three indices to label the number of vaccine doses received by a particular human compartment: (*i*) v_1 indicates the number of vaccine doses received before the primary infection in the group; (*ii*) v_2 indicates the number of vaccine doses received between the primary and secondary infections; (*iii*) similarly, v_3 indicates the number of vaccine doses received after the secondary (and final) infection. All three indices v_k, $k = 1 \dots 3$, range from 0 to v_{max}. The indices i and j are used to label different dengue serotypes throughout and range from 1 to 4.

Parameter	Description
B	Human birth rate.
$\mu_h[a]$	Human death rate at age a.
$\beta_{hm1}[a, v_1, i]$	Primary-infected human to mosquito transmission rate for humans at age a, vaccine count v_1 and serotype i.
$\beta_{hm2}[a, v_1, v_2, i]$	Secondary-infected human to mosquito transmission rate for humans at age a, vaccine counts v_1 and v_2, and serotype i.
$\beta_{mh}[a, v_1, v_2, i]$	Mosquito to human transmission rate for humans at age a, vaccine counts v_1 and v_2, and serotype i.
$V[a, v_1, v_2, v_3]$	Vaccination rate for humans at age a and vaccine indices v_1, v_2 and v_3.

Table S1.2: Model parameters whose values were either calibrated with demographic and dengue incidence data or selected based on other conditions and constraints.

The compartments for the mosquito population evolve according to the ordinary differential equations

$$\frac{dS_m}{dt} = r_{mh} N_h \mu_m - S_m \sum_{i=1}^{4} \lambda_{mi} - \mu_m S_m, \tag{1a}$$

$$\frac{dI_{mi}}{dt} = S_m \lambda_{mi} - \mu_m I_{mi}, \tag{1b}$$

While the equations that govern the time evolution of the different compart-

System variable	Description
S_m	Susceptible mosquitoes.
I_{mi}	Mosquitoes infected with serotype i.
$S_h[a, v_1]$	Susceptible humans of age a and vaccine index v_1.
$I_{hi}[a, v_1]$	Primary infected humans with serotype i of age a and vaccine index v_1.
$C_{hi}[a, v_1, v_2]$	Cross-immune humans with serotype i of age a and vaccine indices v_1 and v_2.
$R_{hi}[a, v_1, v_2]$	Humans recovered from a primary infection with serotype i, of age a, and vaccine indices v_1 and v_2.
$I_{hij}[a, v_1, v_2]$	Secondary infected humans with serotype j, that had a primary infection with serotype i ($i \neq j$), of age a and vaccine indices v_1 and v_2.
$R_{h**}[a, v_1, v_2, v_3]$	Permanently recovered humans of age a and vaccine indices v_1, v_2 and v_3.

Table S1.3: Model variables. All quantities denote numbers of individuals.

ments in the human population are:

$$\begin{aligned}\frac{dS_h[a,v_1]}{dt} =& B\delta_{a,1}\delta_{v_1,1} - S_h[a,v_1]\sum_{i=1}^{4}\lambda_{hi} - (\alpha[a]+\mu_h[a])S_h[a,v_1] \\ & - V[a,v_1+1,0,0]S_h[a,v_1] + \alpha[a-1]S_h[a-1,v_1] \\ & + V[a,v_1,0,0]S_h[a,v_1-1], \end{aligned} \tag{2a}$$

$$\frac{dI_{hi}[a,v_1]}{dt} = S_h[a,v_1]\lambda_{hi} - (\sigma+\alpha[a]+\mu_h[a])I_{hi}[a,v_1] + \alpha[a-1]I_{hi}[a-1,v_1], \tag{2b}$$

$$\begin{aligned}\frac{dC_{hi}[a,v_1,v_2]}{dt} =& -\rho C_{hi}[a,v_1,v_2]\sum_{\substack{j=1\\j\neq i}}^{4}\lambda_{hj} - (\gamma+\alpha[a]+\mu_h[a])C_{hi}[a,v_1,v_2] \\ & - V[a,v_1,v_2+1,0]C_{hi}[a,v_1,v_2] \\ & + \sigma I_{hi}[a,v_1]\delta_{v_2,0} + \alpha[a-1]C_{hi}[a-1,v_1,v_2] \\ & + V[a,v_1,v_2,0]C_{hi}[a,v_1,v_2-1], \end{aligned} \tag{2c}$$

$$\begin{aligned}\frac{dR_{hi}[a,v_1,v_2]}{dt} =& \gamma C_{hi}[a,v_1,v_2] - R_{hi}[a,v_1,v_2]\sum_{\substack{j=1\\j\neq i}}^{4}\lambda_{hj} - (\alpha[a]+\mu_h[a])R_{hi}[a,v_1,v_2] \\ & - V[a,v_1,v_2+1,0]R_{hi}[a,v_1,v_2] \\ & + \alpha[a-1]R_{hi}[a-1,v_1,v_2] + V[a,v_1,v_2,0]R_{hi}[a,v_1,v_2-1], \end{aligned} \tag{2d}$$

$$\begin{aligned}\frac{dI_{hij}[a,v_1,v_2]}{dt} =& (\rho C_{hi}[a,v_1,v_2] + R_{hi}[a,v_1,v_2])\lambda_{hj} - (\sigma+\alpha[a]+\mu_h[a])I_{hij}[a,v_1,v_2] \\ & + \alpha[a-1]I_{hij}[a-1,v_1,v_2], \end{aligned} \tag{2e}$$

$$\begin{aligned}\frac{dR_{h**}[a,v_1,v_2,v_3]}{dt} =& \sum_{\substack{i,j=1\\j\neq i}}^{4}\sigma I_{hij}[a,v_1,v_2]\delta_{v_3,0} - (\alpha[a]+\mu_h[a])R_{h**}[a,v_1,v_2,v_3] \\ & - V[a,v_1,v_2,v_3+1]R_{h**}[a,v_1,v_2,v_3] \\ & + \alpha[a-1]R_{h**}[a-1,v_1,v_2,v_3] + V[a,v_1,v_2,v_3]R_{h**}[a,v_1,v_2,v_3-1]. \end{aligned} \tag{2f}$$

where $a = 1 \ldots A$, $v_1, v_2, v_3 = 0 \ldots v_{max}$ and $i, j = 1 \ldots 4$. Also, $\delta_{u,v}$ denotes the Kronecker delta, i.e., $\delta_{u,v} = 1$ if $u = v$ and $\delta_{u,v} = 0$ if $u \neq v$. In the above equations, any variable with an age index of zero is taken to be zero also, since the age index starts at 1. Similarly $V[a,0,0,0] = 0$, since this symbol does not correspond to any physically meaningful quantity; also $\alpha[0] = \alpha[A] = 0$. Since we assume that a primary infection with serotype i confers lifelong immunity to that serotype, the variables I_{hij} are restricted so that $i \neq j$.

In Eqs. (**??**) and (**??**), the mosquito and human forces of infection, λ_m and

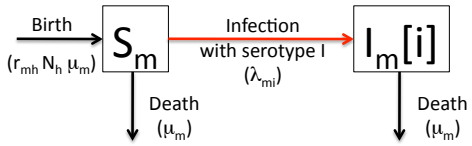

Figure S1.1: Schematic representation of the mosquito dengue transmission process.

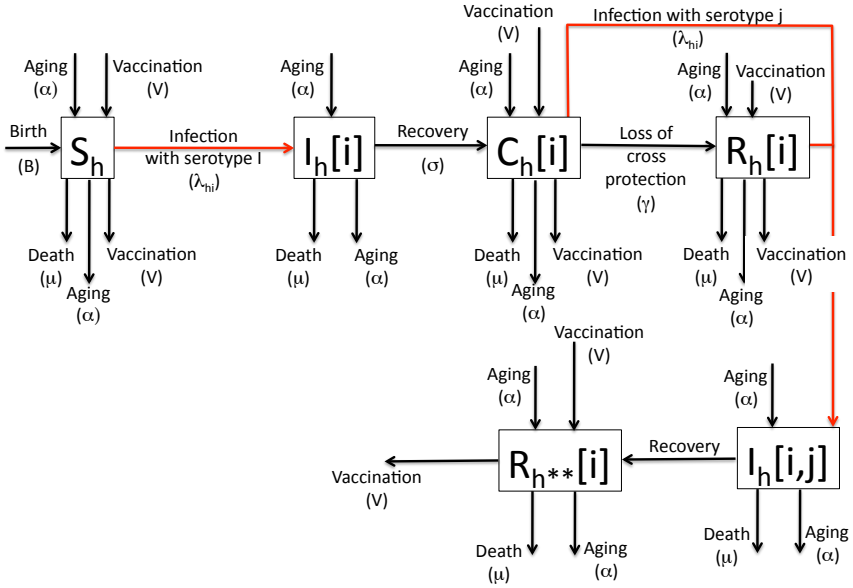

Figure S1.2: Schematic representation of the human dengue transmission process. The discrete indeces i and j label the different serotypes and range from 1 to 4. The full list of the variables' subindeces are omitted for the sake of simplicity.

λ_h, respectively, and the birth rate[1] B are given by:

$$\lambda_{hi} = \frac{\beta_{mh}[a, v_1, v_2, i]}{N_h} I_{mi}, \tag{3a}$$

$$\lambda_{mi} = \frac{1}{N_h} \sum_{a=1}^{A} \left(\sum_{v_1=0}^{v_{max}} \beta_{hm1}[a, v_1 i] I_{hi}[a, v_1] + \phi_i \sum_{\substack{j=1 \\ j \neq i}}^{4} \sum_{v_1, v_2=0}^{v_{max}} \beta_{hm2}[a, v_1, v_2, i] I_{hji}[a, v_1, v_2] \right), \tag{3b}$$

$$B = \sum_{a=1}^{A} \mu_h[a] \left(\sum_{v_1=0}^{v_{max}} S_h[a, v_1] + \sum_{v_1=0}^{v_{max}} \sum_{i=1}^{4} I_{hi}[a, v_1] + \sum_{v_1, v_2=0}^{v_{max}} \sum_{i=1}^{4} \left\{ C_{hi}[a, v_1, v_2] + R_{hi}[a, v_1, v_2] \right\}, + \sum_{v_1, v_2=0}^{v_{max}} \sum_{\substack{i,j=1 \\ j \neq i}}^{4} I_{hij}[a, v_1, v_2] + \sum_{v_1, v_2, v_3=0}^{v_{max}} R_{h**}[a, v_1, v_2, v_3] \right). \tag{3c}$$

The effects of vaccination on transmission

We assume that the application of vaccines on human subjects has an effect on dengue transmission by reducing the susceptibility of vaccinated humans and that protection does not wane over time. We also allow for vaccine induced enhancement in transmissibility due to ADE.

Specifically, for the virus transmission rate from the vector to vaccinated humans, we assume

$$\beta_{mh}[a, v1, v2, i] = \beta_{mh}[a, 0, 0, i](1 - V_e[i])^{v1+v2}, \tag{4}$$

where $V_e[i]$ is the vaccine efficacy against serotype i. That is, the transmission rate is reduced with respect to the base rate by the factor $(1-V_e[i])^{v1+v2}$ which equals the probability that none of the $v_1 + v_2$ vaccine doses were efficacious against serotype i.

Conversely, the virus transmission rate from primary infected, vaccinated humans takes the form

$$\begin{aligned}\beta_{hm1}[a, v1, i] =& \beta_{hm1}[a, 0, i] \prod_{\substack{j=1 \\ j\neq i}}^{4} (1 - V_e[j])^{v1} \\ &+ \beta_{hm1}[a, 0, i]\phi_i \left(1 - \prod_{\substack{j=1 \\ j\neq i}}^{4} (1 - V_e[j])^{v1} \right).\end{aligned} \tag{5}$$

The first term represents the transmission of viruses of serotype i, occurring at the base rate, by humans with no vaccine-induced heterologous protection (hence behaving as primary infections). The second term represents the transmission of viruses of serotype i, occurring at a rate enhanced by the factor ϕ_i, by humans with some vaccine-induced heterologous protection (hence behaving as secondary infections for which ADE has an effect).

In addition, we assume that secondary infected individuals contribute to the force of infection in the same manner, regardless of their vaccination status. That is:

$$\beta_{hm2}[a, v1, v2, i] = \beta_{hm2}[a, 0, 0, i]. \tag{6}$$

Estimating the number of clinically apparent infections

Finally, we make some assumptions on the likelihood that infected individuals develop clinically apparent disease i) We assume that secondary infections are 4 times more likely to result in clinically apparent disease than primary infections.[**?**] ii) We make the assumption that immunity acquired through vaccination will play the same role as immunity from natural infection with regards to the development of symptoms when imperfectly-covered. Thus, we assume that the vaccinated individuals undergoing primary natural infection will only

behave as a primary infection if they fail to develop immunity against any of the heterologous serotypes (i.e, with probability $1-\prod_{j=1\,j\neq i}^{4}(1-V_e[j])^{v1}$). Similarly, vaccinated individuals undergoing primary natural infection will behave as a secondary infection if through vaccination they have developed immunity to any of the heterologous serotypes (i.e., with probability $\prod_{j=1\,j\neq i}^{4}(1-V_e[j])^{v1}$)

B Parameter Calibration of our Mathematical Model

The fitting of model parameters was done using nonlinear optimization methods in `R`[**?**] and was carried out in two stages. In the first stage we calibrated the mortality rates for the different age compartments ($\mu[a]$) in order to obtain a population with an age structure matching the data of the 2010 census of Rayong province.

In the second stage we calibrated the disease transmission parameters. For this we used age-specific incidence data from the Thai Ministry of Public Health in addition to age-stratified serological data from a seroprevalence study conducted among school-age children in 2010[**?**]. The transmission rates were assumed to be increasing, sigmoidal functions of age that reach their saturating values in the late teen years. This assumption is commonly made with vector-borne diseases and accounts for the way in which individuals with larger body surface areas are bitten by mosquitoes at a higher rate and thus contribute more strongly to the transmission cycle.[**?**]

C Transmission Scenarios Explored with our Mathematical Model

In our computational studies, we explored three scenarios of serotype heterogeneity that could potentially lead to an increase in clinical cases, upon mass-vaccination with vaccines effective only against 3 out of 4 circulating serotypes. The three scenarios can be described as.

1. Heterogeneity in clinical expression rates. In this scenario we consider that the vaccine has a lower efficacy against the serotype with the highest probability of clinically apparent disease. This scenario is motivated by the fact that the factors that are involved in the development of symptoms in an individual infected with a dengue virus still remain poorly understood. Hence, the vaccine efficacy against clinically apparent infection quantified in vaccination trials does not immediately yield the efficacy against infection. If the conditions in this scenario are met, it is a concern that mass-vaccination campaigns might suppress clinical infections with three of the serotypes but those with the remaining serotype could become more frequent, particularly if the vaccination status plays a role in exacerbating the development of clinical symptoms.

2. Heterogeneity in transmission intensity. Here, we consider that the vaccine has a lower efficacy against the serotype with the highest transmission intensity. This scenario reflects a concern with the possibility that large numbers of individuals might obtain protection against all but one of the serotypes and that, due to a higher transmission rate, cases with the remaining serotype would become more frequent. Furthermore, it is a good possibility that these cases would present the characteristics of clinically-riskier secondary infections, due to the seroconverting effect of the vaccine. Finally, thus far dengue models have not explored serotypical asymmetries in detail and their dynamic consequences are not well understood.

3. Interaction between serotypes. Finally, in this scenario we consider that the vaccine has a lower efficacy against the serotype with highest immune enhancement coefficient. This scenario is concerned with the possibility that the serotype that is poorly protected against may exploit immune-enhancement to infect a large portion of the pool of individuals that seroconverted against the other three serotypes through vaccination. As in the previous scenario, these cases would likely present the characteristics of clinically-riskier secondary infections.

D Estimating vaccine effects

Since our model tracks the number of vaccines received for all age-groups and disease states, we were able to estimate specific vaccine effects at the population level. We estimated the *overall*, *direct* and *indirect* vaccine effects as proposed by Halloran, Longini and Struchiner.[**?**]:

- *overall*: Compares the cumulative incidence (CI) in the population where the vaccine is introduced to the cumulative incidence over the same period of time in the counterfactual population (same population had the vaccine not been introduced):

$$1 - \frac{\text{CI in vaccinated population}}{\text{CI in counterfactual population}}$$

- *direct*: Compares the cumulative incidence in vaccinated individuals from the population where the vaccine is introduced to the cumulative incidence in unvaccinated individuals of the same population.

$$1 - \frac{\text{CI in vaccinees of vaccinated population}}{\text{CI in non-vaccinees of vaccinated population}}$$

- *indirect*: Compares the cumulative incidence in unvaccinated individuals of the population where the vaccine is introduced to the cumulative incidence in the counterfactual population.

$$1 - \frac{\text{CI in non-vaccinees of vaccinated population}}{\text{CI in counterfactual population}}$$

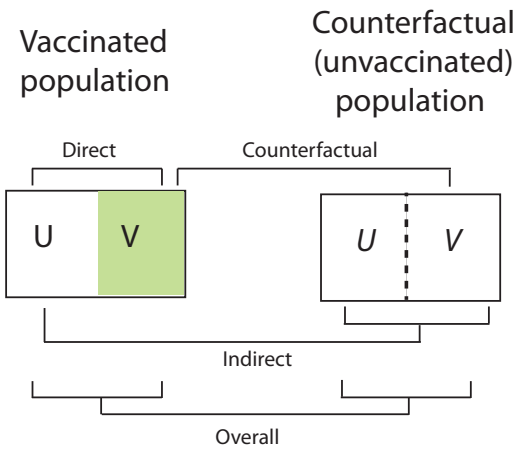

Figure S1.3: Modified from Halloran, Longini and Struchiner [**?**]. Figure illustrating the different vaccine effects calculated. V = Vaccinated. U = Unvaccinated. Vaccinated/Unvaccinated groups in the counterfactual population are formed by segregating individuals with an identical population makeup as the vaccinated/unvaccinated groups in the actual population. See text for description.

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In addition, we defined the *counterfactual* vaccine effect as follows

- *Counterfactual*: Compares the cumulative incidence in vaccinated individuals of the population where the vaccine is introduced to the cumulative incidence in individuals that would have been vaccinated of the counterfactual population.

$$1 - \frac{\text{CI in vaccinees of vaccinated population}}{\text{CI in ``vaccinees'' (i.e placebo recipients) of counterfactual population}}$$

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Supplementary Information S2

Supplementary figures

Age structure of the population

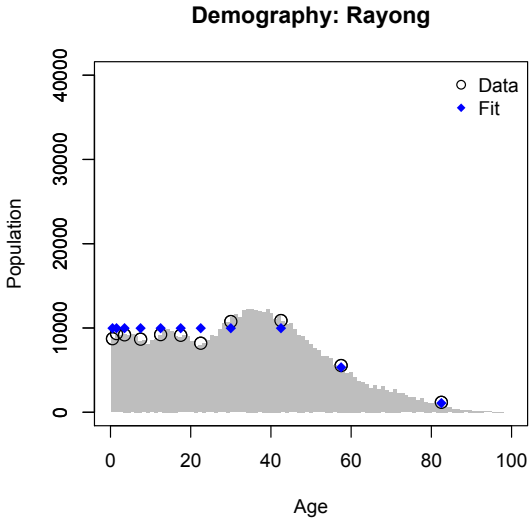

Figure S2.1: Structure of the population of Rayong, Thailand in 2010 and structure of the simulated population.

Simulated incidence of clinical cases of dengue

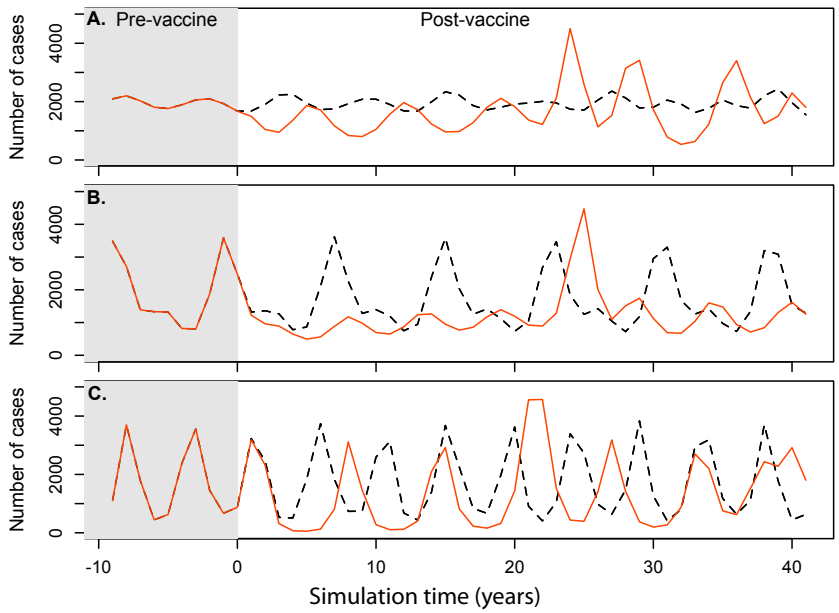

Figure S2.2: Figure showing example output (incidence of clinical cases of dengue across all serotypes) of the model under the three scenarios explored. A: Risk of developing clinical disease after DENV-2 infection is 1.5 times greater than after infection by any other serotype. B: Transmission intensity of DENV-2 is 1.5 times higher than the transmission intensity of any other serotype. C: Secondary infection by DENV-2 results in infectiousness enhancement by a factor of 1.5. In all cases, the vaccine efficacy against dengue 1, 3, and 4 was assumed to be 0.8. For these examples, we assumed that the vaccine efficacy against DENV-2 was 0.3. Colored line shows number of clinical cases, across all serotypes, before and after vaccination. Black line shows the number of clinical cases, had the vaccine not been introduced.

Prior exposure to dengue serotypes

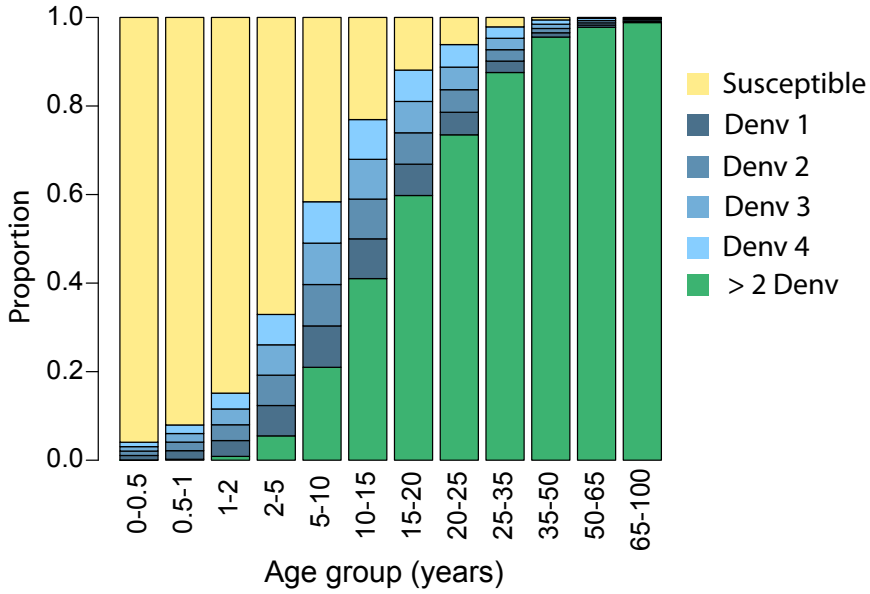

Figure S2.3: Prior exposure to dengue serotypes: Simulated age-specific history to exposure to the four dengue serotypes in the steady state model prior to vaccine introduction

Vaccine coverage

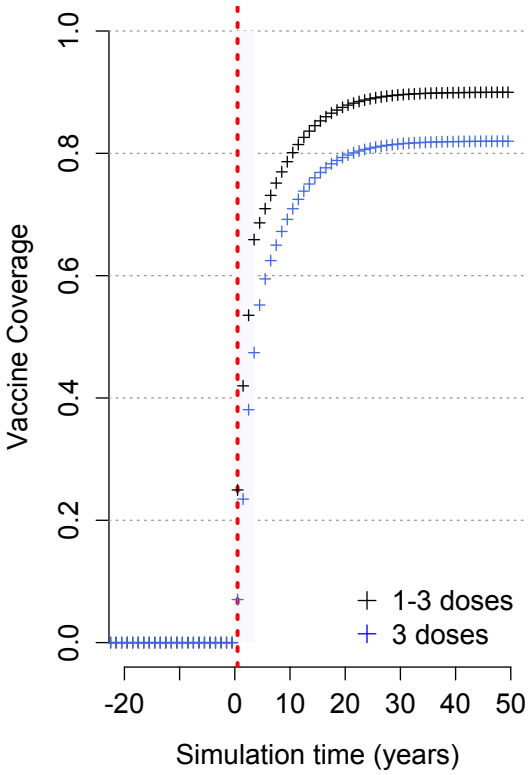

Figure S2.4: Vaccine coverage achieved among 2-15 year olds in the simulations: Figure showing the vaccine coverage achieved in the simulations. Red line indicates the time of vaccine introduction. Shaded area indicates the period of catch-up vaccination, targeting chilldren aged 2-15 years. Regular vaccination targeting children 2-5 years followed the catch-up period.

Persistence of serotypes 10 years after vaccination

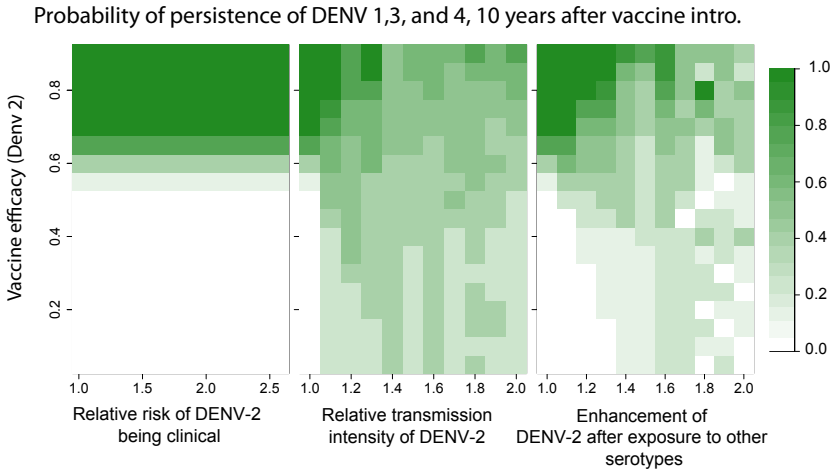

Figure S2.5: Figure summarizing the probability that DENV-1, DENV-3 or DENV-4 persist 10 years after vaccine introduction. We defined persistence as the circulation of at least one infected mosquito, 10 years after vaccine introduction. Each grid cell represents the probability that either DENV-1, DENV-2 or DENV-3 will persist. Since timing of vaccine introduction may impact the short and medium term effects of vaccination, we performed simulations introducing the vaccine at different points in the multiannual dengue cycle. Thus, each grid cell shows the average probability over eight possible introduction years.We performed simulations over a wide range of vaccine efficacies (for DENV-2) and A) relative risk of DENV-2 being clinical, B) relative transmission intensity of DENV-2, C) enhancement/inhibition of transmission intensity of secondary infections by DENV-2 (after prior primary exposure by any of the other serotypes). For all simulations we assumed the efficacy of the vaccine against other circulating serotypes to be 0.8.

Probability of clinical disease

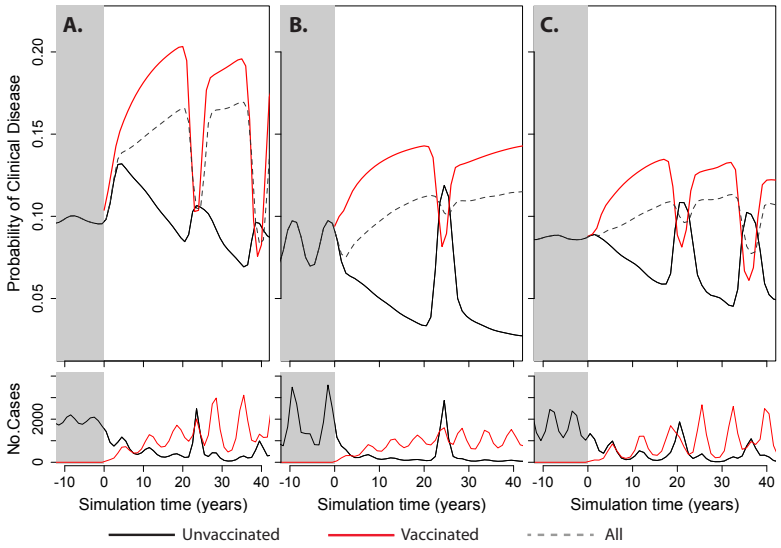

Figure S2.6: Figure exemplifying the effects of vaccination on the probability of clinical disease. Top panels show the effects of vaccination on the probability of developing clinal disease (given infection) experienced by unvaccinated individuals, vaccinated individuals and overall. We present results for three of the scenarios explored. A) Risk of developing clinical disease after dengue 2 infection is 1.5 times greater than after infection by any other serotype. B) Transmission intensity of dengue 2 is 1.5 times higher than the transmission intensity of any other serotype. C) Secondary infection by dengue 2 results in infectiousness enhancement by a factor of 1.5. In all cases, the vaccine efficacy against dengue 1, 3, and 4 was assumed to be 0.8. For these examples, we assumed that the vaccine efficacy against DENV-2 was 0.3. For reference, the bottom panels show the incidence of clinical dengue cases in vaccinated and unvaccinated individuals.

Supplementary Information S3

A Sensitivity analyses

Age dependence of clinical disease

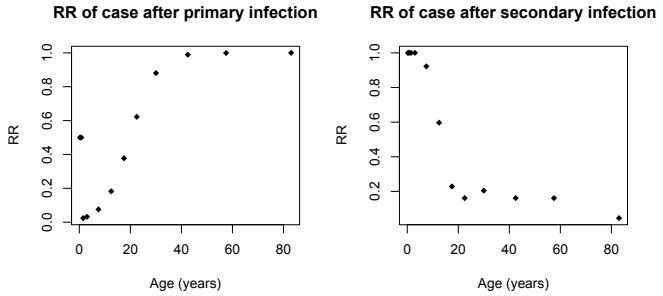

Figure S3.1: Relative risk of being a clinically apparent case by age, as used in the sensitivity analysis.. Primary: Modified from Egger et al. 2007. Secondary: From Guzman et al. 2002

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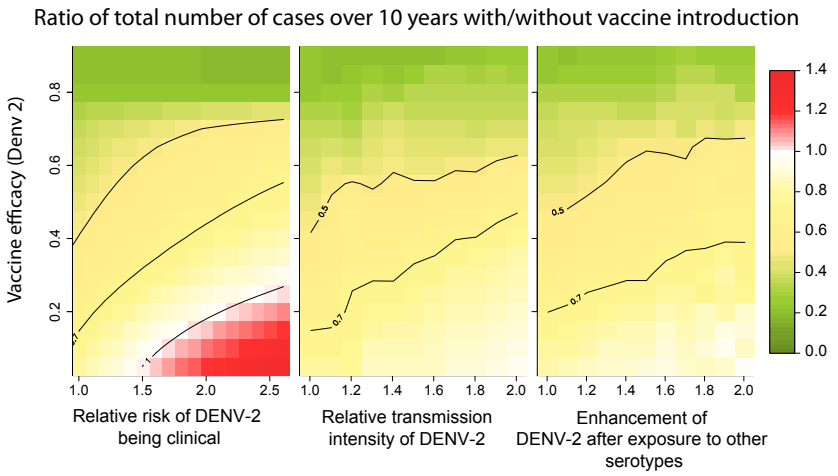

Figure S3.2: Sensitivity analysis assuming age dependence of risk of clinically apparent disease as specified in supplementary figure S2.2. Figure summarizing the expected 10 year impact of vaccination with a partially effective vaccine under different scenarios. Each grid cell represents the ratio of the cumulative number of dengue cases 10 years after vaccine introduction, vs the cumulative number of cases in the same 10 years, had the vaccine not been introduced We performed simulations over a wide range of vaccine efficacies (for DENV-2) and a) relative risk of DENV-2 being clinical, b) relative transmission intensity of DENV-2, c) enhancement/inhibition of transmission intensity of secondary infections by DENV-2 (after prior primary exposure by any of the other serotypes). For all simulations we assumed the efficacy of the vaccine against other circulating serotypes to be 0.8

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Low-transmission setting

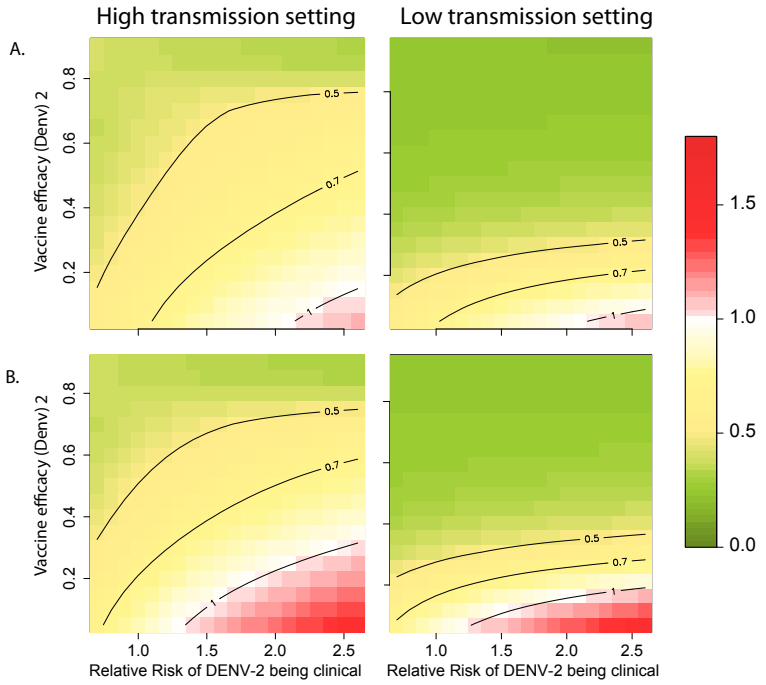

Figure S3.3: Sensitivity analysis comparing results in high (left) vs. low (right) transmission settings. Figure summarizing the expected 10 year impact of vaccination with a partially effective vaccine under the scenario where the relative risk of DENV-2 being clinical is higher than that of other serotypes. Each grid cell represents the ratio of the cumulative number of dengue cases 10 years after vaccine introduction, vs the cumulative number of cases in the same 10 years, had the vaccine not been introduced. For all simulations we assumed the efficacy of the vaccine against other circulating serotypes to be 0.8. Top panels show the results assuming age-independence of clinical disease while bottom panels show results taking age-dependence into account.

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Number of vaccine doses

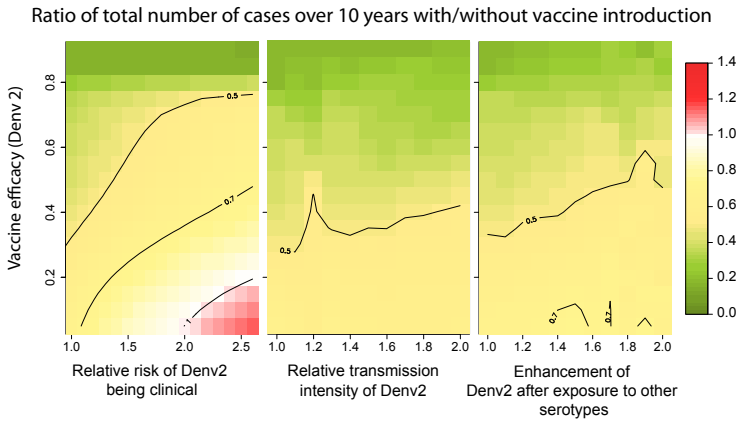

Figure S3.4: Sensitivity analysis summarizing the expected 10 year impact of vaccination with a partially effective vaccine in a scenario where a single vaccine dose has the desired vaccine efficacy (instead of three). Each grid cell represents the ratio of the cumulative number of dengue cases 10 years after vaccine introduction, vs the cumulative number of cases in the same 10 years, had the vaccine not been introduced We performed simulations over a wide range of vaccine efficacies (for DENV-2) and a) relative risk of DENV-2 being clinical, b) relative transmission intensity of DENV-2, c) enhancement/inhibition of transmission intensity of secondary infections by DENV-2 (after prior primary exposure by any of the other serotypes). For all simulations we assumed the efficacy of the vaccine against other circulating serotypes to be 0.8

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