

# Waning Modeling Methods and Results

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*September 12, 2018*

## Model and parameters

We used a simple, unstructured, susceptible-infectious-removed (=SIR) model to simulate the influenza transmission in a large population. The following parameters were chosen:

Parameter	Symbol	Value
Total Pop.	$N$	$2.0e + 06$
Beginning vaccination uptake	$p_v$	0.47
vaccination uptake rate	$\nu$	0
Removal rate	$\gamma$	0.25
Basic reprod. No.	$R_0$	1.6
Transmission coeff., unvacc.	$\beta = R_0 \gamma$	0.4
Transmission coeff., vacc.	$\beta = R_0 \gamma (1 - \phi)$	0.2
VE	$\phi$	0.2, 0.3, 0.4, 0.5
Pre-existing immunity	$\epsilon$	0

The following initial values were used:

Parameter	Symbol	Value
No. susceptible, vacc.	$x_v$	$9.4e + 05$
No. susceptible, unvacc.	$x_{nv}$	$1.1e + 06$
No. infectious, vacc.	$y_v = \frac{p_v \phi}{p_v \phi + 1 - \phi}$	0.15, 0.21, 0.26, 0.31
No. infectious, unvacc.	$y_{nv}$	0.69
No. removed, vacc.	$z_v$	0
No. removed, unvacc.	$z_{nv}$	0

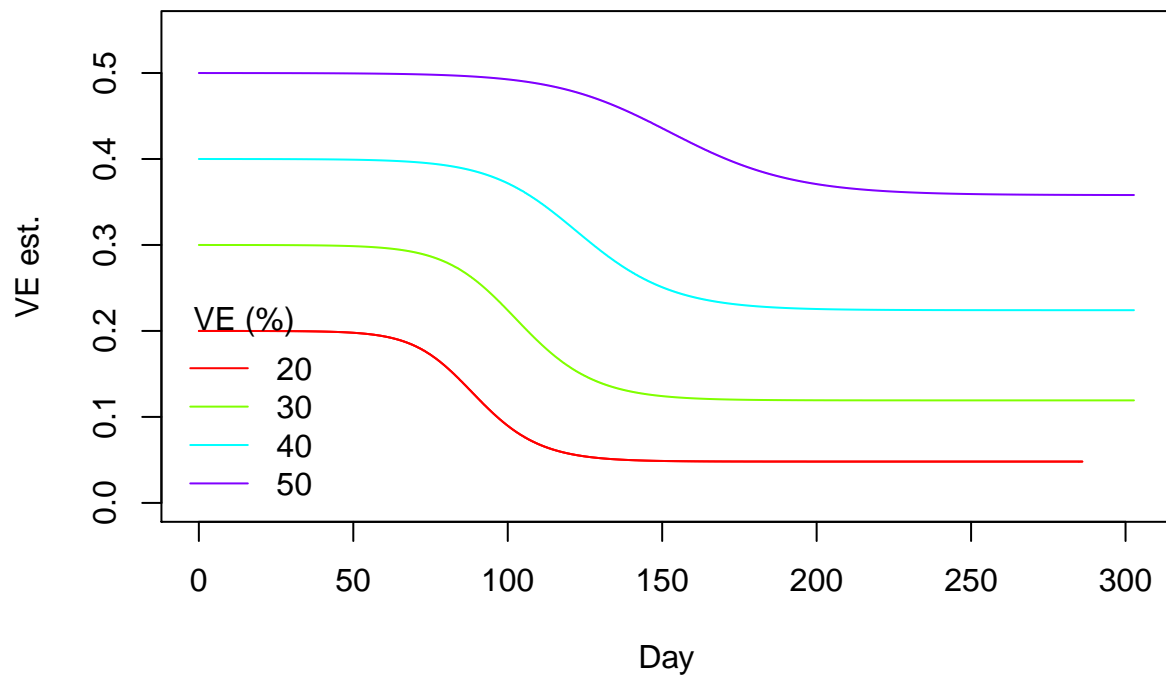
The model used is given by the following system or differential equations:

$$\begin{aligned}
 \frac{x_v}{dt} &= -\beta (1 - \phi) x_v \frac{y_v + y_{nv}}{N} + \nu x_{nv} \\
 \frac{x_{nv}}{dt} &= -\beta x_{nv} \frac{y_v + y_{nv}}{N} - \nu x_{nv} \\
 \frac{y_v}{dt} &= \beta (1 - \phi) x_v \frac{y_v + y_{nv}}{N} - y_v \gamma \\
 \frac{y_{nv}}{dt} &= \beta x_{nv} - y_{nv} \gamma \\
 \frac{z_v}{dt} &= y_v \gamma \\
 \frac{z_{nv}}{dt} &= y_{nv} \gamma
 \end{aligned}$$

The system is numerically solved using the ode function from the deSolve R package. Test-negative design (TND) studies are simulated by keeping track of the incidence of vaccinated and unvaccinated “cases”, i.e. new *infecteds*. The observed VE was calculated based on the ratio of the vaccination odds in the cases to the vaccination odds in the population.

## Results

The trajectories are only shown for the periods of time when there was substantial transmission (more than 10 infectious) and aligned at their “start times”.



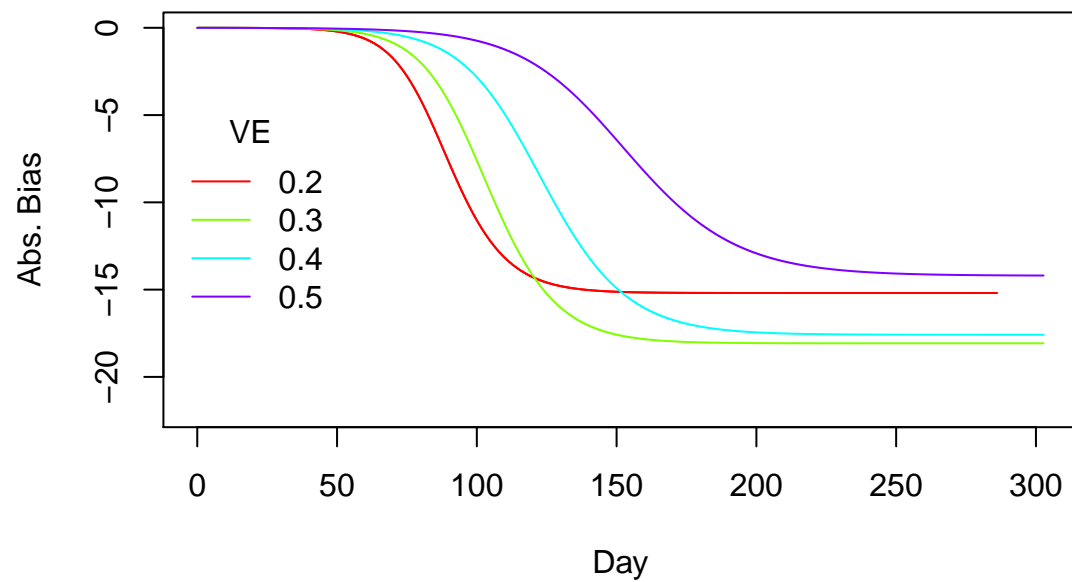


Figure 1: Expected Bias in VE estimates over time, by VE.

As Figure ?? shows, the observed VE always declined, The absolute decline was largest with intermediate VE (VE=30%), while the relative decline was most pronounced for low VE (VE=20%)

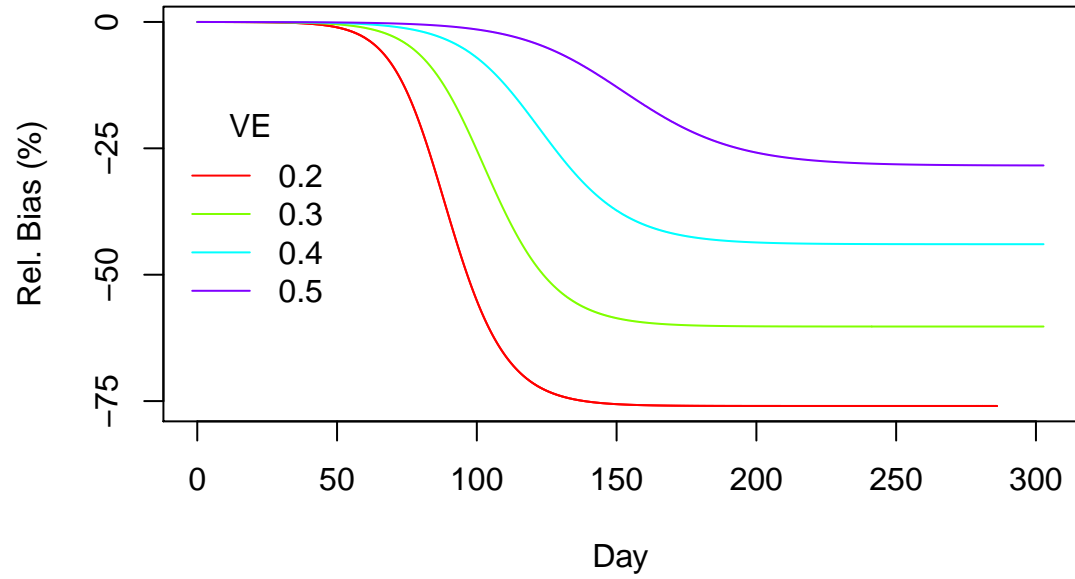


Figure 2: Expected Bias in VE estimates over time, by VE.

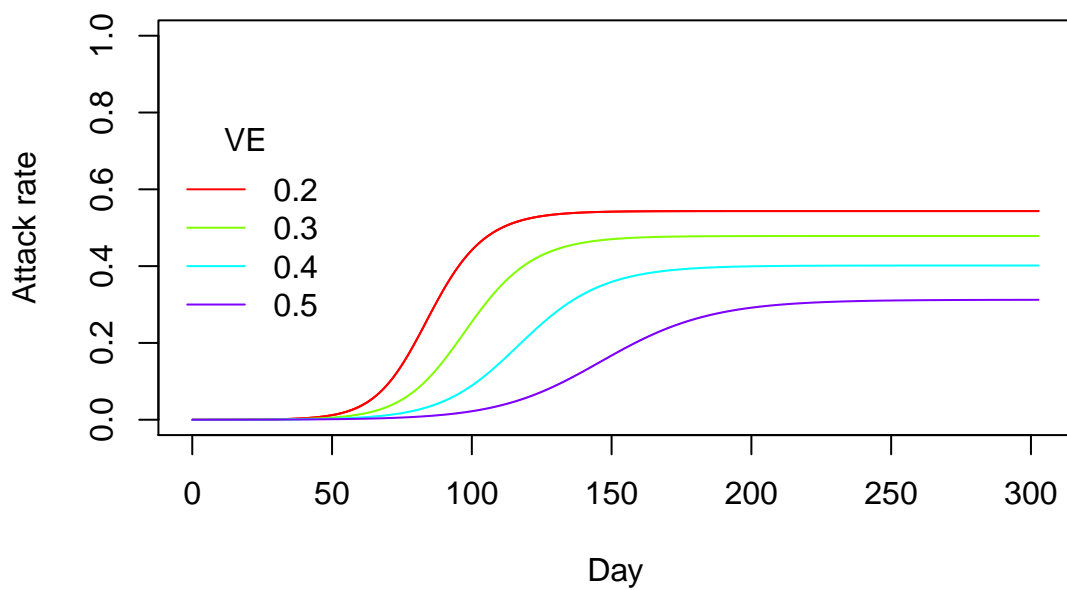
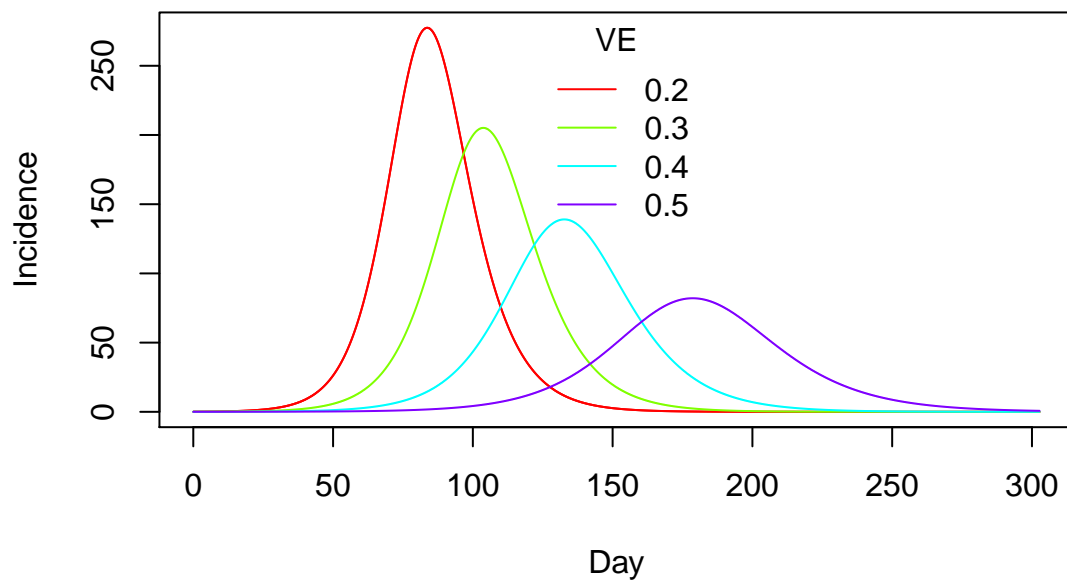


Figure 3: Epi curve (top) and cumulative attack rates (bottom) over time, by VE.