Performance of One- versus Two-Dose Oral Cholera Vaccine Campaigns in Response to Outbreaks: A Modeling Study

S2 Text: Introduction to Minimum Relative Single-Dose Efficacy (MSRE)

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We express the main results in terms of the minimum relative single-dose efficacy, which is equal to the single-dose efficacy needed for a single-dose campaign to avert as many cases as a two-dose campaign with the same total number of doses divided by the two-dose vaccine efficacy (δ_2). Relative vaccine efficacy below this threshold will lead to fewer cases when a single-dose campaign is employed compared to a two-dose campaign with a fixed number of doses. Figure S2-1 illustrates that the MRSE depends on the two-dose vaccine effectiveness and the quantity of vaccine. We can see from Figure S2-1 (purple points) that the highest two-dose effectiveness considered ($0{\cdot}88$, the upper limit of the 95% CI from the meta-analysis) bounds all the other MRSE estimates (i.e., the simulations with 1,000 and 500,000 doses of a vaccine with a single-dose efficacy of 0.88 bound all of the other estimates consistent with the data). Therefore, in order to capture uncertainty in the two-dose efficacy estimates, in the main text we conservatively present results from simulations using a two-dose effectiveness of $0{\cdot}88$ unless otherwise mentioned.

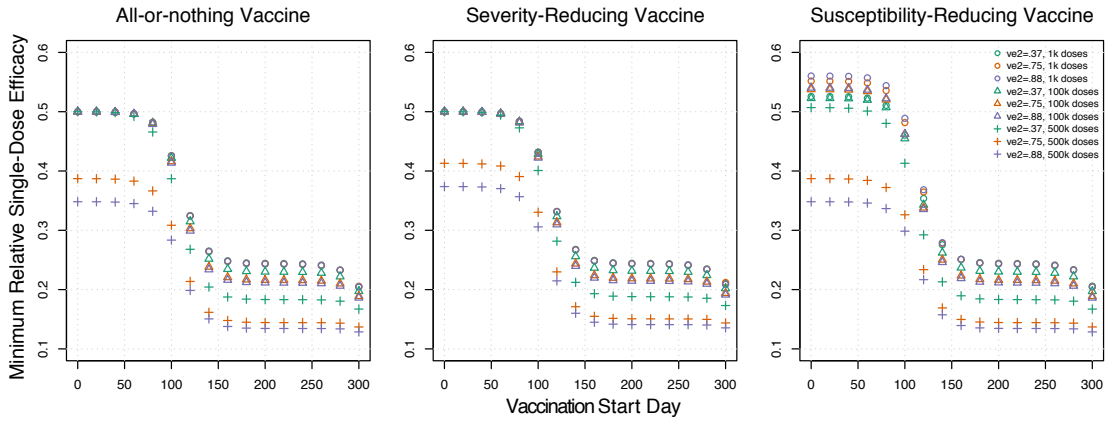

Figure S2-1: Illustration of MRSE for varying two-dose vaccine efficacies and vaccine coverage. Two-dose vaccine efficacies spanning the limits of the 95% confidence intervals from the random effects model, and doses varied between enough for $0{\cdot}2\%$ to 100% of the population in a single-dose campaign.

In a simple proactive vaccination setting where a vaccine acts by removing individuals from Susceptible to Removed ('all-or-nothing vaccine',[1]), the $MRSE$ can be derived using an adaptation of the final size equations described by Longini et al. in 1978.[2] The system below represents the final size for one ($Z_1(\infty, v_1, \delta_1)$) and two-dose $Z_2(\infty, v_2, \delta_2)$) campaigns.

$$Z_1(\infty, v_1, \delta_1) = (S_1(0) - \delta_1 v_1)\left(1 - \exp\left(-\frac{\mathcal{R}_0 Z_1(\infty, v_1, \delta_1)}{N_1}\right)\right) \tag{1}$$

$$Z_2(\infty, v_2, \delta_2) = (S_2(0) - \delta_2 v_2)\left(1 - \exp\left(-\frac{\mathcal{R}_0 Z_2(\infty, v_2, \delta_2)}{N_2}\right)\right), \tag{2}$$

where v_1 represent the number of individuals vaccinated in a single dose campaign and v_2 (individuals vaccinated in a two dose campaign) is assumed to be $v_1/2$. To estimate the MRSE, we can set $N_1 = N_2$ and $S_1 = S_2$ since they are the same population and then set $Z_1 = Z_2$ and solve for $\frac{\delta_1}{\delta_2}$ as follows:

$$(S_1(0) - \delta_2 \frac{v_1}{2})\left(1 - \exp\left(-\frac{\mathcal{R}_0 Z_1}{N_1}\right)\right) = (S_1(0) - \delta_1 v_1)\left(1 - \exp\left(-\frac{\mathcal{R}_0 Z_1}{N_1}\right)\right) \tag{3}$$

$$(S_1(0) - \delta_2 \frac{v_1}{2}) = (S_1(0) - \delta_1 v_1) \tag{4}$$

$$\frac{\delta_1}{\delta_2} = \frac{1}{2} \tag{5}$$

Thus in a simple all-or-nothing proactive vaccination setting, a single dose must be at least half as efficacious as two doses to avert at least as many cases over the course of the epidemic.

References

[1] Halloran ME, Struchiner CJ, Longini IM. Design and Analysis of Vaccine Studies. Springer Verlag; 2009.

[2] Longini IM, Ackerman E, Elveback LR. An optimization model for influenza A epidemics. Mathematical biosciences. 1978 Jan;38(1-2):141–157.