Performance of One- versus Two-Dose Oral Cholera Vaccine Campaigns in Response to Outbreaks
S1 Text: Overview of Transmission Models

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We built a set of Susceptible Exposed Infectious Recovered (SEIR) models to encompass different aspects of cholera transmission and ways in which OCV may protect individuals. The most general model is the 'two-path' model which allows for both person-to-person and environmentally mediated transmission and other models include only a single transmission pathway. Parameters shared by all models are displayed in Table S1-1 and additional parameters are shown in the subsections below. In the deterministic versions used in the main text, the transmission parameter β was fit (through minimization of the squared residuals) to the observed daily case reports from a 2008/9 epidemic in Bissau City, Guinea Bissau.[1]

Table S1-1: Core parameters used in deterministic transmission models

Parameter	Desc.	Value	Source
$1\backslash\sigma$	Mean latent period (assumed equal to incubation period)	$1.41\ days$	[2]
$1\backslash\gamma$	Mean duration of infectiousness	$2.0\ days$	[3]
ρ_1	Vaccination rate for first dose	varied	[4]
ρ_2	Vaccination rate for first dose	varied	[4]
β	Transmission parameter	$0.654\ days^{-1}$	calibrated
θ_1	1-dose vaccine efficacy	varied	meta-analysis
θ_2	2-dose vaccine efficacy	varied	meta-analysis

All-or-Nothing Vaccination Model

With all-or-nothing vaccination θ_1 (i.e. VE) of the individuals vaccinated with dose 1 are expected to be 100% protected from infection. In this two-dose all-or-nothing model, we create states for unvaccinated (subscript 0), single-dose vaccinated (subscript 1), two-dose vaccinated (subscript 2). Only those individuals who have received a first dose are at risk of receiving a second dose. With the second vaccination, $\frac{1-\theta_2}{1-\theta_1}$ of those unprotected from the first dose (S_1) remain unprotected moving to S_2. The additional individuals protected per second dose given to an unprotected first dose recipient is:

$$\text{additional protected with second dose} = \overbrace{\frac{\theta_2}{1-\theta_1}}^{\text{total protected after 2-doses}} - \underbrace{\frac{\theta_1}{1-\theta_1}}_{\text{total protected after 1-dose}} \tag{1}$$

$$= \frac{\theta_2 - \theta_1}{(1-\theta_1)} \tag{2}$$

This model can be described by the following system of differential equations:

$$N_i = S_i + E_i + I_i + R_i \qquad i \in (0,1,2) \tag{3}$$

$$\lambda = \frac{\beta\,(I_0 + I_1 + I_2)}{\sum_{i\in(0,1,2)} N_i} \tag{4}$$

$$\frac{dS_0}{dt} = -\lambda S_0 - \rho_1(t)\frac{S_0}{N_0} \tag{5}$$

$$\frac{dS_1}{dt} = -\lambda S_1 + (1-\theta_1)\rho_1(t)\frac{S_0}{N_0} - \rho_2(t)\frac{S_1}{N_1} \tag{6}$$

$$\frac{dS_2}{dt} = -\lambda S_2 + \frac{1-\theta_2}{1-\theta_1}\rho_2(t)\frac{S_1}{N_1} \tag{7}$$

$$\frac{dE_0}{dt} = \lambda S_0 - \sigma E_0 - \rho_1(t)\frac{E_0}{N_0} \tag{8}$$

$$\frac{dE_1}{dt} = \lambda S_1 - \sigma E_1 - \rho_2\frac{E_1}{N_1} + \rho_1(t)\frac{E_0}{N_0} \tag{9}$$

$$\frac{dE_2}{dt} = \lambda S_2 - \sigma E_2 + \rho_2(t)\frac{E_1}{N_1} \tag{10}$$

$$\frac{dI_0}{dt} = \sigma E_0 - \rho_1(t)\frac{I_0}{N_0} - \gamma I_0 \tag{11}$$

$$\frac{dI_1}{dt} = \sigma E_1 - \rho_2(t)\frac{I_1}{N_1} - \gamma I_1 + \rho_1(t)\frac{I_0}{N_0} \tag{12}$$

$$\frac{dI_2}{dt} = \sigma E_2 + \rho_2(t)\frac{I_1}{N_1} - \gamma I_2 \tag{13}$$

$$\frac{dR_0}{dt} = \gamma I_0 - \rho_1(t)\frac{R_0}{N_0} \tag{14}$$

$$\frac{dR_1}{dt} = \gamma I_1 + \theta_1\rho_1(t)\frac{S_0}{N_0} + \rho_1(t)\frac{R_0}{N_0} - \rho_2(t)\frac{R_1}{N_1} \tag{15}$$

$$\frac{dR_2}{dt} = \gamma I_2 + \frac{\theta_2-\theta_1}{1-\theta_1}\rho_2(t)\frac{S_1}{N_1} + \rho_2(t)\frac{R_1}{N_1} \tag{16}$$

Susceptibility-Reducing Vaccine Model (VE_S)

Our first leaky vaccine model (VE_S) reduces the risk of infection by $\theta.$ in all vaccinees. Figure S1-1 illustrates the model structure and flows between states; with circles representing states and edges representing rates of transition from one state to another.

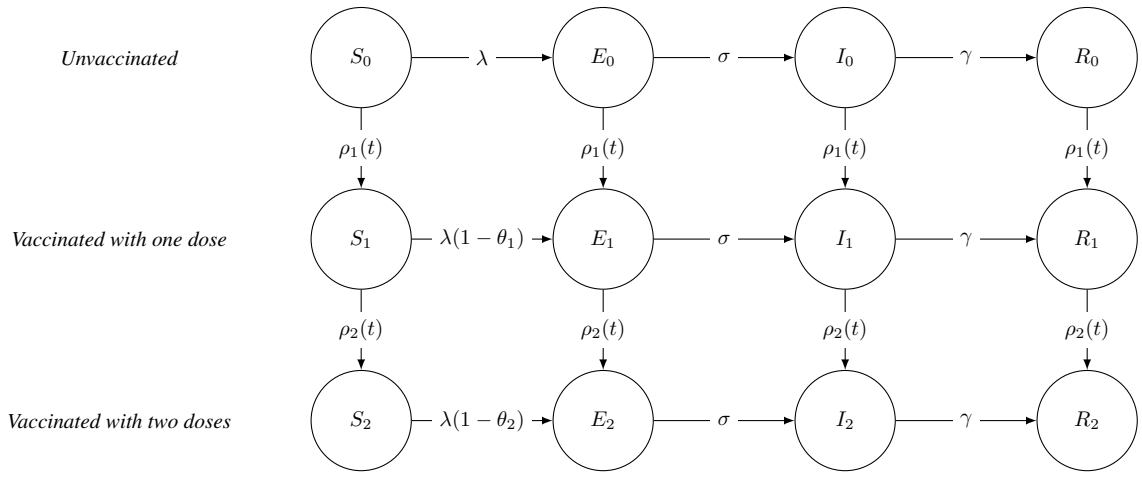

Figure S1-1: Flow diagram of susceptibility-reducing vaccine model VE_S Model

The following system of equations describes the VE_S vaccine model:

$$N_i = S_i + E_i + I_i + R_i \qquad i \in (0,1,2) \tag{17}$$

$$\lambda = \frac{\beta}{\sum_{i=0,1,2} N} (I_0 + I_1 + I_2) \tag{18}$$

$$\frac{dS_0}{dt} = -\lambda S_0 - \rho_1(t)\frac{S_0}{N_0} \tag{19}$$

$$\frac{dS_1}{dt} = -\lambda(1-\theta_1)S_1 + \rho_1(t)\frac{S_0}{N_0} - \rho_2(t)\frac{S_1}{N_1} \tag{20}$$

$$\frac{dS_2}{dt} = -\lambda(1-\theta_2)S_2 + \rho_2(t)\frac{S_1}{N_1} \tag{21}$$

$$\frac{dE_0}{dt} = \lambda S_0 - \rho_1(t)\frac{E_0}{N_0} - \sigma E_0 \tag{22}$$

$$\frac{dE_1}{dt} = \lambda S_1(1-\theta_1) + \rho_1(t)\frac{E_0}{N_0} - \rho_2(t)\frac{E_1}{N_1} - \sigma E_1 \tag{23}$$

$$\frac{dE_2}{dt} = \lambda S_2(1-\theta_2) + \rho_2(t)\frac{E_1}{N_1} - \sigma E_2 \tag{24}$$

$$\frac{dI_0}{dt} = \sigma E_0 - \rho_1\frac{I_0}{N_0} - \gamma I_0 \tag{25}$$

$$\frac{dI_1}{dt} = \sigma E_1 + \rho_1\frac{I}{N_0} - \rho_2(t)\frac{I_1}{N_1} - \gamma I_1 \tag{26}$$

$$\frac{dI_2}{dt} = \sigma E_2 + \rho_2(t)\frac{I_1}{N_1} - \gamma I_2 \tag{27}$$

$$\frac{dR_0}{dt} = \gamma I_0 - \rho_1(t)\frac{R_0}{N_0} \tag{28}$$

$$\frac{dR_1}{dt} = \gamma I_1 + \rho_1\frac{R}{N_0} - \rho_2(t)\frac{I_1}{N_1} \tag{29}$$

$$\frac{dR_2}{dt} = \gamma I_2 + \rho_2(t)\frac{R_1}{N_1} \tag{30}$$

Severity-Reducing Vaccine Model (VE_{SP})

The second leaky model considered reduces the probability $(1-\theta.)$ of an individual progressing to severe symptomatic disease required the addition of a mildly-symptomatic/asymptomatic class (A). This model is described by the system of ordinary differential equations below and additional parameters are shown in Table S1-2.

Table S1-2: Additional parameters for VE_{SP} model

Parameter	Desc.	Value	Source
θ_0	Probability of asymptomatic infection without OCV	0	assumed
κ	Reduced infectiousness for asymptomatic/mildly symptomatic	0.9	assumed

The following system of equations describes the leaky severity-reducing vaccine model:

$$N_i = S_i + E_i + I_i + A_i + R_i \qquad i \in (0,1,2) \tag{31}$$

$$\lambda = \frac{\beta}{\sum_{i=0,1,2} N}\left(I + I_1 + I_2 + (1-\kappa)(A_1 + A_2)\right) \tag{32}$$

$$\frac{dS_0}{dt} = -\lambda S_0 - \rho_1(t)\frac{S_0}{N_0} \tag{33}$$

$$\frac{dS_1}{dt} = -\lambda S_1 + \rho_1(t)\frac{S_0}{N_0} - \rho_2(t)\frac{S_1}{N_1} \tag{34}$$

$$\frac{dS_2}{dt} = -\lambda S_2 + \rho_2(t)\frac{S_1}{N_1} \tag{35}$$

$$\frac{dE_0}{dt} = \lambda S_0 - \rho_1(t)\frac{E_0}{N_0} - \sigma E_0 \tag{36}$$

$$\frac{dE_1}{dt} = \lambda S_1 + \rho_1(t)\frac{E_0}{N_0} - \rho_2(t)\frac{E_1}{N_1} - \sigma E_1 \tag{37}$$

$$\frac{dE_2}{dt} = \lambda S_2 + \rho_2(t)\frac{E_1}{N_1} - \sigma E_2 \tag{38}$$

$$\frac{dI_0}{dt} = (1-\theta_0)\sigma E_0 - \rho_1(t)\frac{I_0}{N_0} - \gamma I_0 \tag{39}$$

$$\frac{dI_1}{dt} = (1-\theta_1)\sigma E_1 + \rho_1(t)\frac{I_0}{N_0} - \rho_2(t)\frac{I_1}{N_1} - \gamma I_1 \tag{40}$$

$$\frac{dI_2}{dt} = (1-\theta_2)\sigma E_2 + \rho_2(t)\frac{I_1}{N_1} - \gamma I_2 \tag{41}$$

$$\frac{dA_0}{dt} = \theta_0\sigma E_0 - \rho_1(t)\frac{A_0}{N_0} - \gamma A_0 \tag{42}$$

$$\frac{dA_1}{dt} = \theta_1\sigma E_1 + \rho_1(t)\frac{A_0}{N_0} - \rho_2(t)\frac{A_1}{N_1} - \gamma A_1 \tag{43}$$

$$\frac{dA_2}{dt} = \theta_2\sigma E_2 + \rho_2(t)\frac{A_1}{N_1} - \gamma A_2 \tag{44}$$

$$\frac{dR_0}{dt} = \gamma(I_0 + A_0) - \rho_1(t)\frac{R_0}{N_0} \tag{45}$$

$$\frac{dR_1}{dt} = \gamma(I_1 + A_1) + \rho_1(t)\frac{R_0}{N_0} - \rho_2(t)\frac{R_1}{N_1} \tag{46}$$

$$\frac{dR_2}{dt} = \gamma(I_2 + A_2) + \rho_2(t)\frac{R_1}{N_1} \tag{47}$$

Two-path Transmission Model

Cholera is thought to spread via two modes of transmission, a 'fast' route dominated by person-to-person transmission, and a 'slow' route where transmission is mediated through the environment.[5] The mix of these two modes help dictate the time course of the epidemic by modifying the generation time distribution (i.e. distribution of time between infector-infected pairs). In the primary analyses we consider a subset of this model where transmission is 100% fast. Here we also consider this full two-path model to explore the impact of varying contributions of environmentally mediated (slow) transmission. The slow path is conceptualized as a series of infectious compartments which leads to a gamma (Erlang) distributed infectious period (Figure S1-2). Vaccine is implemented within this model as a leaky vaccine that reduces vaccinees susceptibility to infection (VE_S).

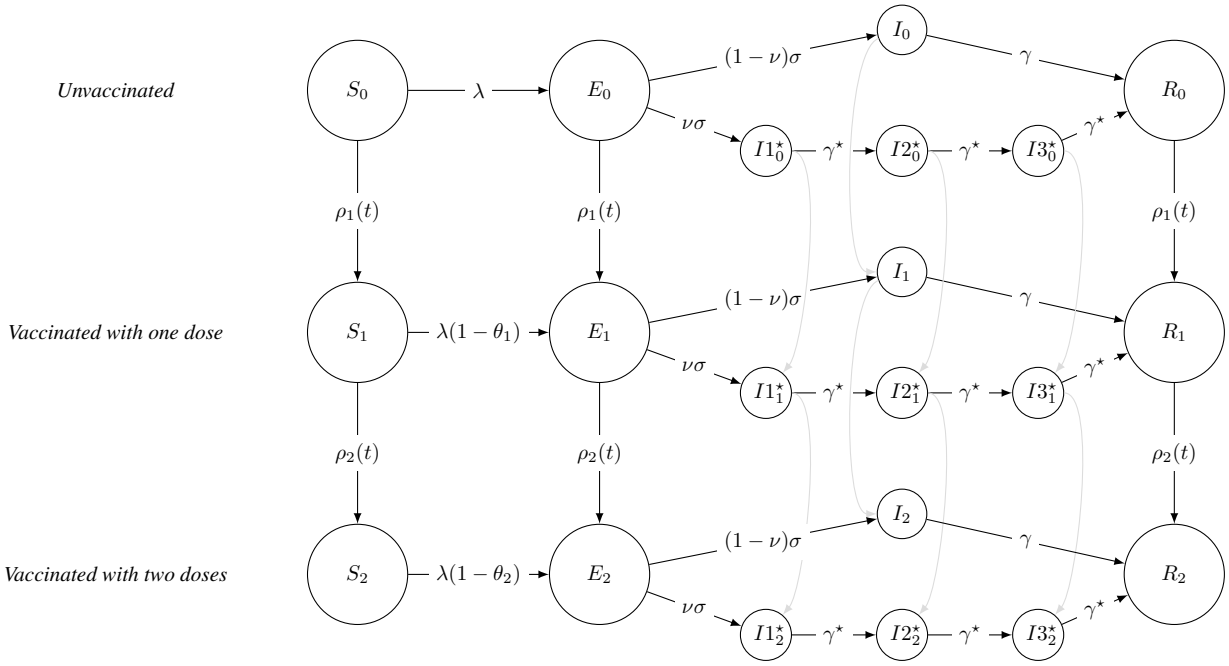

Figure S1-2: Flow diagram of two-path model. Rates from infectious compartments shown as grey edges for visualization purposes.

The infectious period distribution was fit to empirical data on the survival of *Vibrio cholerae* (Figures S1-3 and S1-4) by minimizing the squared difference between the observations and the survival function of a gamma distribution.[6] We found the best fit to include three compartments ($n_{slow} = 3$, see section Supplemental Text S4) each with a mean residence time of 7.5 days ($\gamma^\star = \frac{1}{7.5}$ See Supplemental Text S4).

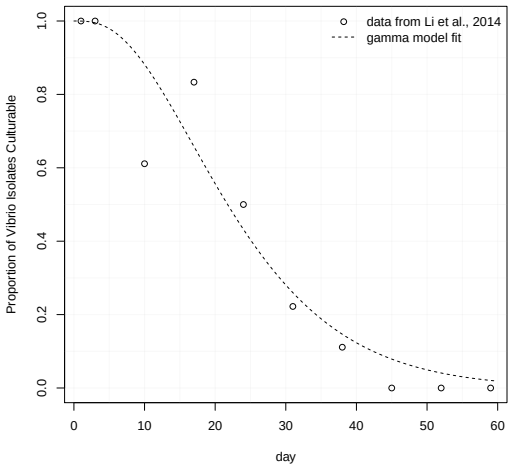

Figure S1-3: Proportion of *Vibrio cholerae* isolates surviving at different time points (from[6]) along with best fit gamma distributed survival curve.

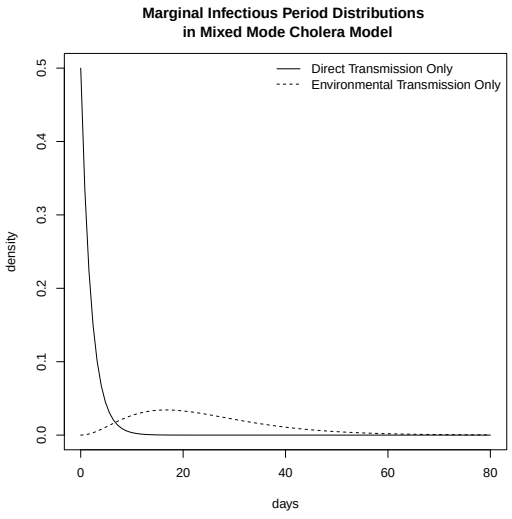

Figure S1-4: Distributions of the infectious period for the fast (person-to-person) and the slow (environmentally-mediated transmission) pathways.

References

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[6] Li XQ, Wang M, Deng ZA, Shen JC, Zhang XQ, Liu YF, et al. Survivability and molecular variation in Vibrio cholerae from epidemic sites in China. Epidemiology and Infection. 2014 Mar;p. 1–10.