

## S1 File. Supplemental Appendix

### Direct transmission via households informs models of disease and intervention dynamics in cholera

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Below we describe a set of additional analyses and calculations relevant to content in the main text. These include:

- Calculation of the sum total of cases as a function of direct infection
- An outline of the method for determining the reproductive ratio ( $R_0$ ) for the Cholera household (direct) infection model.
- Discussion of the stability of the system at the disease free equilibrium

#### Model dynamics: sum total values

In S1 Table we present the summed total number of counts for all nine dynamic cases considered in Fig 3. These values can be thought of analogous to the area under each of the nine curves in Fig 3a-c. Of note, given that the three curves in fig 3c are normalized to the maximum amount of Cholera summed across both the high and low infectious reservoirs; the values reported in column 3 of S1 Table are that of the sum total amount of bacteria across both reservoirs for each of the three model runs.

#### Basic reproductive ratio – $R_0$

The numeric value for the basic reproductive ratio  $R_0$  of *V. cholera* referenced in the main text, and used as part of our sensitivity analysis, was derived following the methods of Diekmann et. al. 2009 [1].

	Total infected cases	Total recovered cases	Total bacterial count ( $W_H + W_L$ )
No direct infection $\eta = 0$	$1.55 \cdot 10^7$	$1.04 \cdot 10^7$	$8.99 \cdot 10^{11}$
direct infection $\eta = \text{nominal value}$	$7.74 \cdot 10^7$	$5.24 \cdot 10^7$	$4.53 \cdot 10^{12}$
direct infection & 0.5x water consumption	$3.20 \cdot 10^7$	$2.88 \cdot 10^7$	$2.51 \cdot 10^{12}$

**S1 Table.** In S1 Table we present the summed total number of counts for all nine dynamic cases of this model considered in Fig 3. Of note, the values reported in column 3 of S1 Table are that of the sum total amount of bacteria across both reservoirs for each of the three model runs.

Firstly, we construct the arrays  $t = (t_0, t_1, \dots, t_m)$  and  $\sigma = (\sigma_0, \sigma_1, \dots, \sigma_m)$ . The  $i^{\text{th}}$  element of  $t$ , denoted  $t_i$ , is defined to be the rate term associated with the flow of *new* infection *into* the  $i^{\text{th}}$  compartment. That is, the flow of infection between two infected compartments is not included in  $t$ . The  $i^{\text{th}}$  element of  $\sigma$ , denoted  $\sigma_i$ , is defined to be the sum of all other rate terms associated with flows into or out of the  $i^{\text{th}}$  compartment. That is, the total rate of change of the  $i^{\text{th}}$  compartment is given by  $t_i + \sigma_i$ . In calculating  $R_0$ , it suffices to restrict the index  $i$  in  $t_i$  and  $\sigma_i$  to infected compartments only. In the case of *V. cholerae*, these are the compartments  $I$ ,  $A$ ,  $W_L$ , and  $W_H$ . Below we present the elements of  $t$  and  $\sigma$  at the disease free equilibrium.

$$t = \begin{pmatrix} \frac{\pi(A+I)\eta N(1-p)(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)} + \frac{\pi\alpha N(1-p)W_H(\mu+\epsilon)}{\mu\kappa_H(\mu+\tau+\epsilon)} + \frac{\pi\alpha N(1-p)W_L(\mu+\epsilon)}{\mu\kappa_L(\mu+\tau+\epsilon)} \\ \frac{\pi\eta Np(A+I)(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)} + \frac{\pi\alpha NpW_H(\mu+\epsilon)}{\mu\kappa_H(\mu+\tau+\epsilon)} + \frac{\pi\alpha NpW_L(\mu+\epsilon)}{\mu\kappa_L(\mu+\tau+\epsilon)} \\ 0 \\ \frac{A\xi_A}{W} + \frac{I(\theta\psi-\theta+1)\xi_S}{W} \end{pmatrix} \quad \sigma = \begin{pmatrix} I(\gamma\theta\lambda + \gamma(1-\theta) + \mu_c + \mu) \\ A(\gamma + \mu) \\ -\chi W_H + \delta W_L \\ \chi W_H \end{pmatrix}$$

We calculate the corresponding  $T$  and  $\Sigma$  matrices. These are  $m \times m$  matrices (in this case  $m = 4$ ) defined by,

$$T_{ij} = \frac{\partial t_i}{\partial X_j}(x_0)$$

$$\Sigma_{ij} = \frac{\partial \sigma_i}{\partial X_j}(x_0)$$

where  $X_j$  is the  $j^{\text{th}}$  agent, selected from the  $m$  agents associated with  $t$  and  $\sigma$ , and  $x_0$  is the disease-free equilibrium of the model. Calculating these derivatives for the *V. cholera* model one finds,

$$T = \begin{pmatrix} \frac{\pi\eta N(1-p)(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)} & \frac{\pi\eta N(1-p)(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)} & \frac{\pi\alpha N(1-p)(\mu+\epsilon)}{\mu\kappa_L(\mu+\tau+\epsilon)} & \frac{\pi\alpha N(1-p)(\mu+\epsilon)}{\mu\kappa_H(\mu+\tau+\epsilon)} \\ \frac{\pi\eta Np(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)} & \frac{\pi\eta Np(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)} & \frac{\pi\alpha Np(\mu+\epsilon)}{\mu\kappa_L(\mu+\tau+\epsilon)} & \frac{\pi\alpha Np(\mu+\epsilon)}{\mu\kappa_H(\mu+\tau+\epsilon)} \\ 0 & 0 & 0 & 0 \\ \frac{(\theta\psi-\theta+1)\xi_S}{W} & \frac{\xi_A}{W} & 0 & 0 \end{pmatrix}$$

$$\Sigma = \begin{pmatrix} \gamma\theta\lambda + \gamma(1-\theta) + \mu_c + \mu & 0 & 0 & 0 \\ 0 & \gamma + \mu & 0 & 0 \\ 0 & 0 & \delta & -\chi \\ 0 & 0 & 0 & \chi \end{pmatrix}$$

Next we calculate the inverse of the matrix  $\Sigma$ . For our case this turns out to be,

$$\Sigma^{-1} = \begin{pmatrix} \frac{1}{\gamma\theta(1-\lambda) - \mu_c - \gamma - \mu} & 0 & 0 & 0 \\ 0 & \frac{1}{\gamma + \mu} & 0 & 0 \\ 0 & 0 & \frac{1}{\delta} & \frac{1}{\delta} \\ 0 & 0 & 0 & \frac{1}{\chi} \end{pmatrix}$$

We then calculate the matrix product  $-T \cdot \Sigma^{-1}$ .

$$-T \cdot \Sigma^{-1} = \begin{pmatrix} \frac{\pi\eta N(1-p)(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)(\gamma\theta(\lambda-1) + \mu_c + \gamma + \mu)} & \frac{\pi\eta N(1-p)(\mu+\epsilon)}{\mu(\gamma+\mu)(\mu+\tau+\epsilon)} & \frac{\pi\alpha N(1-p)(\mu+\epsilon)}{\delta\mu\kappa_L(\mu+\tau+\epsilon)} & \frac{\pi\alpha N(1-p)(\mu+\epsilon)(\chi\kappa_H + \delta\kappa_L)}{\delta\mu\chi\kappa_H\kappa_L(\mu+\tau+\epsilon)} \\ \frac{\pi\eta Np(\mu+\epsilon)}{\mu(\mu+\tau+\epsilon)(\gamma\theta(\lambda-1) + \mu_c + \gamma + \mu)} & \frac{\pi\eta Np(\mu+\epsilon)}{\mu(\gamma+\mu)(\mu+\tau+\epsilon)} & \frac{\pi\alpha Np(\mu+\epsilon)}{\delta\mu\kappa_L(\mu+\tau+\epsilon)} & \frac{\pi\alpha Np(\mu+\epsilon)(\chi\kappa_H + \delta\kappa_L)}{\delta\mu\kappa_H\kappa_L\mu\chi(\mu+\tau+\epsilon)} \\ 0 & 0 & 0 & 0 \\ \frac{(\theta\psi+1-\theta)\xi_S}{W(\gamma\theta(\lambda-1) + \mu_c + \gamma + \mu)} & \frac{\xi_A}{W(\gamma+\mu)} & 0 & 0 \end{pmatrix}$$

Due to its analytic complexity, an analytic expression for  $R_0$  was not explicitly determined. Instead the characteristic polynomial of  $-T \cdot \Sigma^{-1}$  from which the maximum eigenvalue of this expression, was numerically determined.

## Jacobian ODE system analysis & related values

$$\begin{pmatrix} \frac{-\tau_1(W_{u+p}) + \gamma(I+N)(W_{u+p})(R(\kappa_H+1)S+\alpha)}{(W_{u+p})(I+N)} & -R\theta & -R\theta & \mu_C & \tau & \frac{-W_{u+p}\delta}{(I+N)^2} & \frac{-N\delta}{(I+N)^2} \\ \frac{[(A-1)(-\tau_1(W_{u+p}) + R(W_{u+p})(I+N)(\kappa_H+1)W_{L,S,H}\xi_A + \alpha - \kappa_H(\xi_A-1) + \phi) - \gamma(I+N)]}{(W_{u+p})(I+N)} & R\theta(A-1)(W_{L,S,H}\xi_A + \alpha - \kappa_H(\xi_A-1) + \phi) & R\theta(A-1)(W_{L,S,H}\xi_A + \alpha - \kappa_H(\xi_A-1) + \phi) & 0 & 0 & \frac{-W_{u+p}\delta(A-1)}{(I+N)^2} & \frac{-N\delta(A-1)}{(I+N)^2} \\ \frac{A(\tau_1(W_{u+p}) + R(W_{u+p})(I+N)(\kappa_H+1)W_{L,S,H}\xi_A + \alpha - \kappa_H(\xi_A-1) + \phi)}{(W_{u+p})(I+N)} & AR\theta & AR\theta & 0 & 0 & \frac{-W_{u+p}\delta}{(W_{u+p})^2} & \frac{-N\delta}{(I+N)^2} \\ 0 & \kappa_H(W_{L,S,H}\xi_A - \xi_A + 1) & AR\theta - \alpha - \kappa_H & -\alpha - \mu_C & 0 & 0 & 0 \\ S & 0 & 0 & 0 & -\alpha - \tau & 0 & 0 \\ 0 & \frac{\alpha}{(\xi_A - \xi_A + 1)} & \frac{\alpha}{\tau} & 0 & 0 & -V & 0 \\ 0 & 0 & 0 & 0 & 0 & V & -\delta \end{pmatrix}$$

Here we present both a symbolic and numeric form of the Jacobian Matrix of the *V. cholerae* ODE system, the numeric form being at the disease-free equilibrium. The eigenvalues for the disease-free Jacobian are predominantly non-positive but include 2 positive values.

$$\begin{pmatrix} -0.25004 & -0.35399 & -2.7317 & 0.00342 & 0.00137 & 0.0 & 0.0 \\ 0.0 & 0.08194 & 0.0 & 0.0 & 0.0 & 0.0 & 0.0 \\ 0.0 & 0.0 & 2.53166 & 0.0 & 0.0 & 0.0 & 0.0 \\ 0.0 & 0.226 & 0.2 & -0.00347 & 0.0 & 0.0 & 0.0 \\ 0.25 & 0.0 & 0.0 & 0.0 & -0.00141 & 0.0 & 0.0 \\ 0.0 & 16501.33333 & 17.33333 & 0.0 & 0.0 & -1.0 & 0.0 \\ 0.0 & 0.0 & 0.0 & 0.0 & 0.0 & 1.0 & -0.03333 \end{pmatrix}$$

Above we present the numeric form of the DFE Jacobian Matrix. This was calculated using the nominal model parameters applied throughout the simulation. Below are the eigenvalues corresponding to this matrix.

$$-0.0035, \quad -0.2514, \quad 0.0, \quad -0.0333, \quad -1.0, \quad 2.5317, \quad 0.082$$

As with any set of ordinary differential equations, the Jacobian Matrix represents a linear approximation of the flow of the system in phase space at the selected point. The eigenvectors give the direction of flow and the sign of the associated eigenvalues indicates whether the flow is toward or away from the selected point. Given that the Jacobian Matrix is computed at the disease-free equilibrium and there exists positive eigenvalues, we can say that the DFE is an unstable equilibrium (given the nominal chosen model parameters) and the system tends not to equilibriate to the DFE point in phase space [2, 3]. This is consistent with an  $R_0$  value greater than one.

## References

1. Diekmann O, Heesterbeek JAP, Roberts MG. The construction of next-generation matrices for compartmental epidemic models. *Journal of the Royal Society Interface*. 2010 Nov;7(1):873–885.
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3. Morris H, Stephan S. *Differential Equations, Dynamical Systems, and Linear Algebra*. Academic Press, Inc; 1974.