Supporting Information

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SI Methods

Cholera Model. Putting the formulations described in *Methods* together gives the following system of differential equations describing the cholera model:

$$\frac{dS}{dt} = \mu N - \beta_{e} S \frac{B}{\kappa + B} - \beta_{h} S I - \mu S,$$

$$\frac{dI}{dt} = \beta_{e} S \frac{B}{\kappa + B} + \beta_{h} S I - (\gamma + \mu) I,$$

$$\frac{dR}{dt} = \gamma I - \mu R,$$

$$\frac{dB}{dt} = \xi I - \delta B.$$
[S1]

Parameter Values. Table S1 shows cholera model parameters and values and Table S2 shows estimated values of β_e and β_h and 95 % confidence intervals.

Basic Reproductive Number and Stability. *Stability of the disease-free equilibrium.* The disease-free equilibrium for the cholera model is given by

$$\varepsilon_0 = (N, 0, 0, 0).$$
 [S2]

We compute the basic reproductive number for the cholera model using the method in van den Driessche and Watmough (3). Here, the associated next generation matrices are given by

$$F = \begin{pmatrix} N\beta_{\rm h} & \frac{N\beta_{\rm e}}{\kappa} \\ 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} \gamma + \mu & 0 \\ -\xi & \delta \end{pmatrix}.$$

The expression of the basic reproductive number is given by

$$\mathcal{R}_{0} = \frac{N}{\delta\kappa(\gamma + \mu)} [\xi\beta_{e} + \delta\kappa\beta_{h}] = \mathcal{R}_{e} + \mathcal{R}_{h}, \qquad [S3]$$

where $\mathcal{R}_e = \xi \beta_e N / \delta \kappa (\gamma + \mu)$ and $\mathcal{R}_h = \beta_h N / (\gamma + \mu)$ are partial reproductive numbers due to environment-to-human transmission and human-to-human transmission, respectively. We note that for $\beta_e = 0$, $\mathcal{R}_0 = \mathcal{R}_h$ and when $\beta_h = 0$, $\mathcal{R}_0 = \mathcal{R}_e$, suggesting that the two modes of cholera transmission can independently or jointly start an epidemic depending on conditions. Thus, precisely speaking \mathcal{R}_0 measures the number of secondary cholera infections generated in a wholly susceptible community when a sufficient concentration of vibrios contaminates the aquatic environment and/or when a cholera-infected individual is introduced into the community. In $\mathcal{R}_e,~1/(\gamma+\mu)$ is the expected time humans will be infected, $\xi/(\gamma+\mu)$ is the average amount of V. cholerae shed per infected individual, $1/\delta$ is the lifetime of the vibrios in the environment, and β_e/κ is the number of new cases generated in terms of vibrios per unit time, measured by the ID₅₀ concentration. In $\mathcal{R}_h, \beta_h/(\gamma + \mu)$ is the average amount of hyperinfectious V. cholerae ingested by an infected individual.

It follows from theorem 2 in ref. 3 that the disease-free equilibrium is locally asymptotically stable, when $\mathcal{R}_0 < 1$. We establish the global stability of the disease-free equilibrium using Theorem 1.

Theorem 1. (*Castillo-Chavez et al.*, *ref.* 4) *If a model system can* be written in the form

$$\frac{dX}{dt} = F(X, Z),$$

$$\frac{dZ}{dt} = G(X, Z), G(X, 0) = 0,$$
[S4]

where $X \in \mathbb{R}^m$ denotes (its components) the number of uninfected individuals and $Z \in \mathbb{R}^n$ denotes (its components) the number of infected individuals including latent, infectious, etc. $\mathbf{U}_0 = (X^*, 0)$ denotes the disease-free equilibrium of the system. And assume that (i) For $dX/dt = F(X, 0), X^*$ is globally asymptotically stable and (ii) $G(X, Z) = AZ - \widehat{G}(X, Z), \widehat{G}(X, Z) \ge 0$ for $(X, Z) \in \Omega$, where $A = D_Z G(X^*, 0)$ is an M-matrix (the off diagonal elements of A are nonnegative) and Ω is the region where the model makes biological sense. Then the fixed point $U_0 = (X^*, 0)$ is a globally asymptotic stable equilibrium of cholera model system Eq. S1 provided that $\mathcal{R}_0 < 1$.

We begin by showing condition *i* as

$$F(X,0) = \begin{pmatrix} \mu N - \mu S \\ - \mu R \end{pmatrix},$$

and solving these two ordinary differential equations gives

$$R(t) = R(0)e^{-\mu t}$$
 and $S(t) = N - (N - S(0))e^{-\mu t}$

Thus, $R(t) \to 0$ and $S(t) \to N$ as $t \to \infty$, regardless of the values of R(0) and S(0). Thus, ε_0 is globally asymptotically stable.

Next, applying Theorem 1 to cholera model system Eq. S1 gives

$$G(X,Z) = \left(\frac{\beta_{\rm e}SB}{\kappa + B} + \beta_{\rm h}SI - (\gamma + \mu)I \atop \xi I - \delta B\right),$$

and

$$A = \begin{pmatrix} \beta_{\rm h} N - (\gamma + \mu) & \frac{\beta_{\rm e} N}{\kappa} \\ \xi & -\delta \end{pmatrix},$$

which is clearly an M-matrix. Meanwhile, we find

$$\widehat{G}(X,Z) = \begin{pmatrix} \beta_{\rm h}(N-S) \ I + \frac{\beta_{\rm e}NB}{\kappa} - \frac{\beta_{\rm e}SB}{\kappa+B} \\ 0 \end{pmatrix},$$

Because $0 \le S \le N$, it follows that $\widehat{G}(X, Z) \ge 0$. We summarize the result in Lemma 1.

Lemma 1. The disease-free equilibrium of the model system, given by ε_0 , is globally asymptotically stable whenever $\mathcal{R}_0 < 1$. Local stability of the endemic equilibrium. The endemic equilibrium of the cholera model is given by $\varepsilon^* = (S^*, I^*, R^*, B^*)$, where

$$S^* = N - \frac{(\gamma + \mu)I^*}{\mu},$$
[S5]

$$I^* = \frac{\beta_c S^*}{\gamma + \mu - \beta_h S^*} - \frac{\delta \kappa}{\xi},$$
 [S6]

$$R^* = \frac{\gamma I^*}{\mu},$$
 [S7]

$$B^* = \frac{\xi I^*}{\delta}.$$
 [S8]

We establish the following theorem. Lemma 2. If $\mathcal{R}_0 > 1$, a unique endemic equilibrium exists and is locally asymptotically stable.

Proof. By solving Eqs. S5–S8, we obtain

$$I^*(AI^{*2} + BI^* + C) = 0,$$
 [S9]

where

$$\begin{split} A &= -p_{\rm h} (\gamma + \mu)\varsigma, \\ B &= \beta_{\rm h} N \mu \xi - (\gamma + \mu) (\beta_{\rm e} \xi + \beta_{\rm h} \delta \kappa + \mu \xi), \\ C &= \beta_{\rm e} \xi \mu N - (\gamma + \mu) \mu \delta \kappa + \beta_{\rm h} N \mu \delta \kappa. \end{split}$$

From Eq. **S9**, we have $I^* = 0$, which corresponds to the disease-free equilibrium and a quadratic equation given by

$$AI^{*2} + BI^* + C = 0.$$
 [S10]

The roots of this quadratic equation must satisfy

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$$I_1^* I_2^* = \frac{C}{A}$$
 [S11]

and

$$I_1^* + I_2^* = -\frac{B}{A}.$$
 [S12]

With

$$\mathcal{R}_0 = \frac{N(\xi\beta_e + \delta\kappa\beta_h)}{\delta\kappa(\gamma + \mu)} \text{ and defining } S_c = \frac{\delta\kappa(\gamma + \mu)}{\xi\beta_e + \delta\kappa\beta_h}$$

gives $N > S_c$ when $\mathcal{R}_0 > 1$. It follows that A < 0 and C > 0, and the right-hand side of Eq. S11 is <0. Thus, the quadratic Eq. S10 has a unique positive root I^* . On the other hand, if $\mathcal{R}_0 < 1$, which yields $N < S_c$, we can obtain C < 0 so that the right-hand side of Eq. S11 >0, and the right-hand side of Eq. S12 <0 if B < 0. In fact, we have $(\gamma + \mu) > N\beta_h$ for $N < S_c$, and thus we obtain $(\gamma + \mu)\mu\xi > N\beta_h\mu\xi$, which gives B < 0. In this case, Eq. S10 has two negative roots and the positive endemic equilibrium does not exist. Hence it is not biologically feasible.

To deduce the local stability of the endemic equilibrium, we use the Jacobian of cholera model system Eq. **S1**. For simplicity we set

 $P = \beta_e B^* / (\kappa + B^*) + \beta_h I^*, Q = \beta_e S^* \kappa / (\kappa + B^*)^2$, and the Jacobian matrix becomes

$$J_B^* = \begin{bmatrix} -P - \mu & -\beta_h S & 0 & -Q \\ P & \beta_h S - (\gamma + \mu) & 0 & Q \\ 0 & \gamma & -\mu & 0 \\ 0 & \xi & 0 & \delta \end{bmatrix}.$$

The characteristic equation of the matrix J_B^* is given by

$$Det (\lambda I - J_B^*) = (\lambda + \mu)[(\lambda + \mu)(\lambda - \beta_h S^* + \gamma + \mu)(\lambda + \delta) + P(\lambda + \gamma + \mu)(\lambda + \delta) - Q\xi(\lambda + \mu)] = 0.$$
 [S13]

Clearly, Eq. 13 has a negative root $\lambda = -\mu$. Expanding Eq. 13 gives $(\lambda + \mu)(\lambda - \beta_h S^* + \gamma + \mu)(\lambda + \delta) + P(\lambda + \gamma + \mu)(\lambda + \delta) - Q\xi(\lambda + \mu)$, which we write as

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0,$$
 [S14]

where

 $\begin{array}{l} a_0 = 1, \\ a_1 = P + \delta + \gamma + 2\mu - \beta_h S^*, \\ a_2 = \mu^2 + P\delta + P\gamma + P\mu - Q\xi + \delta\gamma + 2\delta\mu + \gamma\mu - \beta_h S^*\delta - \beta_h S^*\mu, \\ a_3 = \delta\mu^2 + P\delta\gamma + P\delta\mu - Q\mu\xi + \delta\gamma\mu - S^*\beta_h\delta\mu. \end{array}$

Routh's stability criterion (5) requires

$$a_1 > 0, a_2 > 0, a_3 > 0$$
 and $a_1a_2 - a_0a_3 > 0$

as the necessary and sufficient conditions for stability.

From Eq. S6, we have the expression of $(\gamma + \mu)$ at the positive endemic equilibrium,

$$\gamma + \mu = \frac{S^* \beta_e \xi \delta \kappa + S^* \beta_e \xi^2 I^*}{\left(\delta \kappa + \xi I^*\right)^2} + \beta_h S^*.$$

Note that $Q\xi = \delta^2 \beta_e S^* \kappa \xi / (\kappa \delta + \xi I^*)^2$, and we have two conditions that we use to prove the necessary and sufficient conditions, which are

$$\gamma + \mu > \beta_h S^*$$
 [S15]

and

$$\delta(\gamma + \mu) > Q\xi + \beta_{\rm h} S^* \delta.$$
 [S16]

First, we prove that $a_1 > 0$ using condition Eq. **S15** and P > 0. We have

$$a_1 = P + \delta + \mu + (\gamma + \mu) - \beta_h S^* > 0.$$
 [S17]

Second, using the two inequalities $\delta(\gamma + \mu) > Q\xi + \beta_h S^* \delta$ and $\mu(\gamma + \mu) > \beta_h S^* \mu$, it can be shown that $a_2 > 0$. In addition, it can also be shown that $a_3 > 0$ by using $\delta\mu(\gamma + \mu) > Q\xi\mu + \beta_h S^* \delta\mu$. We show that $a_1a_2 - a_0a_3 > 0$ in the following:

$$\begin{aligned} a_2(\mu+\delta) - a_3 = & (\delta^2\gamma + \delta^2\mu - Q\delta\xi - S^*\beta_h\delta^2) \\ & + (\gamma\mu^2 + \mu^3 + \delta\gamma\mu + \delta\mu^2 - S^*\beta_h\mu^2 - S^*\beta_h\delta\mu) \\ & + P\delta^2 + P\mu^2 + \delta\mu^2 + \delta^2\mu + P\delta\mu + P\gamma\mu. \end{aligned}$$

Using conditions Eqs. S15 and S16, we have

$$\delta^2 \gamma + \delta^2 \mu > Q \delta \xi + S^* \beta_h \delta^2$$

and

$$\label{eq:eq:stars} \begin{split} \gamma \mu^2 + \mu^3 + \delta \gamma \mu + \delta \mu^2 > S^* \beta_h \mu^2 + S^* \beta_h \delta \mu \end{split}$$

Thus, $a_2(\mu + \delta) > a_3$ holds. Because $a_1 > (\mu + \delta)$, on the basis of Eq. **S17**, we obtain $a_1a_2 > a_3$. Thus, we have shown that when $\mathcal{R}_0 > 1$, a unique endemic equilibrium is locally asymptotically stable.

Global stability. By considering the following domain that is a result of a nondimensionalized model system Eq. S1,

$$D = \{ (S, I, B) | S \ge 0, I \ge 0, S + I \le 1, B \ge 0 \},\$$

we construct the Lyapunov function

$$V = w_1 (S - S^*)^2 + w_2 (I - I^*)^2 + w_3 (B - B^*)^2$$
 [S18]

with $w_1 > 0$, $w_2 > 0$, and $w_3 > 0$.

Note that for the endemic equilibrium $\varepsilon^* = (S^*, I^*, B^*)$, we have the following three equations for the nondimensionalized system:

$$\mu - \beta_{\rm e} S^* \frac{B^*}{\kappa + B^*} - \beta_{\rm h} S^* I^* - \mu S^* = 0, \qquad [S19]$$

$$\beta_{\rm e}S^* \frac{B^*}{\kappa + B^*} + \beta_{\rm h}S^*I^* - (\gamma + \mu)I^* = 0,$$
 [S20]

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$$\xi I^* - \delta B^* = 0.$$
 [S21]

From Eqs. S20 and S21, we have

$$(\gamma + \mu)\delta = \beta_{h}S^{*}\delta + \frac{\beta_{e}S^{*}\xi\delta}{\delta\kappa + \xiI^{*}} > \beta_{h}S^{*}\delta + \frac{\beta_{e}S^{*}\kappa\xi}{(\kappa + B^{*})(\kappa + B)}.$$

Using Eqs. S19–S21, we obtain

a positive diagonal matrix W exists such that $WA + A^TW$ is negative definite.

Theorem 2. Let A be a 2×2 matrix (7, 8). Then

$$A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix}$$

is Volterra-Lyapunov stable if and only if $a_{11} < 0$, $a_{22} < 0$, and $a_{11}a_{22} - a_{12}a_{21} > 0$.

$$\begin{split} \frac{dV}{dt} &= 2w_1(S-S^*) \left[-\frac{\beta_c}{\kappa+B} SB - \beta_h SI - \mu S + \frac{\beta_c}{\kappa+B^*} S^*B^* + \beta_h S^*I^* + \mu S^* \right] \\ &+ 2w_2(I-I^*) \left[\frac{\beta_c}{\kappa+B} SB + \beta_h SI - (\gamma+\mu)I - \frac{\beta_c}{\kappa+B^*} S^*B^* - \beta_h S^*I + (\gamma+\mu)I^* \right] \\ &+ 2w_3(B-B^*) [\xi I - \delta B - \xi I^* + \delta B^*] \\ &= 2w_1(S-S^*) \left[-\left(\frac{\beta_c}{\kappa+B} SB - \frac{\beta_c}{\kappa+B} S^*B + \frac{\beta_c}{\kappa+B} S^*B - \frac{\beta_c}{\kappa+B^*} S^*B^* \right) \\ &- \beta_h (SI - S^*I + S^*I - S^*I^*) \right] - 2w_1(S-S^*)^2 \mu \\ &+ 2w_2(I-I^*) [(\frac{\beta_c}{\kappa+B} SB - \frac{\beta_c}{\kappa+B} S^*B + \frac{\beta_c}{\kappa+B} S^*B - \frac{\beta_c}{\kappa+B^*} S^*B^*) \\ &+ \beta_h (SI - S^*I + S^*I - S^*I^*) \right] - 2w_2(\gamma+\mu)(I-I^*)^2 \\ &+ 2w_3(B-B^*) [\xi(I-I^*) - \delta(B-B^*)] \\ &= -2w_1(\frac{\beta_c}{\kappa+B} B + \beta_h I + \mu)(S-S^*)^2 - 2w_1\beta_h S^*(S-S^*)(I-I^*) \\ &- 2w_1 \frac{\beta_c S^* \kappa}{(\kappa+B^*) + (\kappa+B)} (S-S^*) + 2w_2[\beta_h S^* - (\gamma+\mu)](I-I^*)^2 \\ &+ 2w_2(\frac{\beta_c S^* \kappa}{(\kappa+B^*) + (\kappa+B)} (I-I^*)(B-B^*) \\ &+ 2w_3\xi(B-B^*)(I-I^*) - 2w_3\delta(B-B^*)^2 \\ &= Y(WA + A^TW)Y^T, \end{split}$$

where $Y = [S - S^*, I - I^*, B - B^*]$, $W = \text{diag}(w_1, w_2, w_3)$, and

$$A = \begin{bmatrix} -\frac{\beta_{\rm e}B}{\kappa+B} - \beta_{\rm h}I - \mu & -\beta_{\rm h}S^* & -\frac{\beta_{\rm e}S^*\kappa}{(\kappa+B^*)(\kappa+B)} \\ \frac{\beta_{\rm e}B}{\kappa+B} + \beta_{\rm h}I & \beta_{\rm h}S^* - (\gamma+\mu) & \frac{\beta_{\rm e}S^*\kappa}{(\kappa+B^*)(\kappa+B)} \\ 0 & \xi & -\delta \end{bmatrix}.$$
[S24]

Theorem 3. Let A be a nonsingular $n \times n$ matrix, where $n \ge 2$, with inverse $A^{-1} = B$ and W a positive diagonal $n \times n$ matrix (6). Let A^* , B^* , and W^* denote the $(n - 1) \times (n - 1)$ matrices obtained from A, B, and W, respectively, by deleting the last row and column. Then (i) if $WA + (WA)^T > 0$, we must have $a_{nn} > 0$, $W^*A^* + (W^*A^*)^T > 0$, and $W^*B^* + (W^*B^*)^T > 0$; and (ii) if $a_{nn} > 0$, $W^*A^* + (W^*A^*)^T > 0$, and $W^*B^* + (W^*B^*)^T > 0$, it is possible to choose $w_n > 0$ such that $WA + (WA)^T > 0$.

The global stability of ε^* will be established if we can show the matrix A defined in Eq. S24 is Volterra–Lyapunov stable (6); i.e.,

From Eq. S24, we obtain

$$A^{-1} = \frac{1}{\det A} \begin{bmatrix} -\beta_{\rm h} S^* \delta + (\gamma + \mu) \delta - \frac{\beta_{\rm e} S^* \kappa \xi}{(\kappa + B^*)(\kappa + B)} & -\beta_{\rm h} S^* \delta - \frac{\beta_{\rm e} S^* \kappa \xi}{(\kappa + B^*)(\kappa + B)} & -\frac{(\gamma + \mu) \beta_{\rm e} S^* \kappa}{(\kappa + B^*)(\kappa + B)} \\ \beta_{\rm h} I \delta + \frac{\delta \beta_{\rm e} B}{\kappa + B} & \beta_{\rm h} I \delta + \frac{\delta \beta_{\rm e} B}{\kappa + B} + \mu \delta & \frac{\beta_{\rm e} S^* \kappa \mu}{(\kappa + B^*)(\kappa + B)} \\ \beta_{\rm h} I \xi + \frac{\xi \beta_{\rm e} B}{\kappa + B} & \beta_{\rm h} I \xi + \frac{\xi \beta_{\rm e} B}{\kappa + B} + \mu \xi & -\mu \beta_{\rm h} S^* + (\gamma + \mu) (\frac{\beta_{\rm e} B}{\kappa + B} + \beta_{\rm h} I + \mu) \end{bmatrix},$$

where

$$\det A = -\left(\frac{\beta_{e}B}{\kappa + B} + \beta_{h}I + \mu\right)$$
$$\times \left[(\gamma + \mu)\delta - \beta_{h}S^{*}\delta - \frac{\beta_{e}S^{*}\kappa\xi}{(\kappa + B^{*})(\kappa + B)} \right]$$
$$- \left(\beta_{h}I + \frac{\beta_{e}B}{\kappa + B}\right) \left[\beta_{h}S^{*}\delta + \frac{\beta_{e}S^{*}\kappa\xi}{(\kappa + B^{*})(\kappa + B)} \right].$$

It can easily be shown that det A < 0 because $(\gamma + \mu)\delta - \beta_h S^*\delta - \beta_e S^*\kappa\xi/((\kappa + B^*)(\kappa + B)) > 0$ (Eq. S22). On the basis of Theorem 2, it is straightforward to verify that $(A^{-1})^*$ is Volterra–Lyapunov stable. Hence, a 2 × 2 positive diagonal matrix $W^* = \text{diag}(w_1, w_2)$ exists such that $W^*(A^{-1})^* + (W^*(A^{-1})^*)^T < 0$.

After some calculation, we obtain the matrices $W^*M^* + (W^*M^*)^T$ and $W^*(-A)^* + (W^*(-A)^*)^T$, as

$$(-\det A)[W^*M^* + (W^*M^*)^T] \triangleq Q,$$

where

$$Q = \begin{bmatrix} -2w_1 \left[\beta_{\rm h} S^* \delta - (\gamma + \mu) \delta + \frac{\beta_{\rm e} S^* \kappa \xi}{(\kappa + B^*)(\kappa + B)} \right] \\ w_2 \left(\beta_{\rm h} I \delta + \frac{\delta \beta_{\rm e} B}{\kappa + B} \right) - w_1 \left(\delta \beta_{\rm h} S^* + \frac{\beta_{\rm e} S^* \kappa \xi}{(\kappa + B^*)(\kappa + B)} \right) \end{bmatrix}$$

and

$$\begin{split} & W^*(-A)^* + (W^*(-A)^*)^T \\ & = \begin{bmatrix} 2w_1 \left[\beta_{\rm h}I + \mu + \frac{\beta_{\rm e}B}{\kappa + B} \right] w_1 \beta_{\rm h}S^* - w_2 \left(\beta_{\rm h}I + \frac{\beta_{\rm e}B}{\kappa + B} \right) \\ \\ & w_1 \beta_{\rm h}S^* - w_2 \left(\beta_{\rm h}I + \frac{\beta_{\rm e}B}{\kappa + B} \right) & 2w_2(\gamma + \mu - \beta_{\rm h}S^*) \end{bmatrix}. \end{split}$$

We show that $W^*(-A)^* + (W^*(-A)^*)^T > 0$. In fact, because $W^*M^* + (W^*M^*)^T$ is positive definite, and $-\det A > 0$, we have

- 1. WHO (2010) Zimbabwe. Available at http://www.who.int/countries/zwe/en/. Accessed April 5, 2010.
- Hartley DM, Morris JG, Jr., Smith DL (2006) Hyperinfectivity: A critical element in the ability of V. cholerae to cause epidemics? PLoS Med 3:e7.
- van den Driessche P, Watmough J (2002) Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Math Biosci* 180: 29–48.

$$\begin{aligned} \det\left\{(-\det A)\left[W^*M^* + (W^*M^*)^T\right]\right\} \\ &= 4w_1w_2\delta^2[(\gamma+\mu) - \beta_h S^*]\left(\mu + \beta_h I + \frac{\beta_e B}{\kappa + B}\right) \\ &+ 2w_1w_2\beta_h S^*\delta^2\left(\beta_h I + \frac{\beta_e B}{\kappa + B}\right) - w_2^2\delta^2\left(\beta_h I + \frac{\beta_e B}{\kappa + B}\right)^2 \\ &- w_1^2(S^*)^2\beta_h^2\delta^2 - w_1^2\left[\frac{\beta_e S^*\kappa\xi}{(\kappa + B^*) + (\kappa + B)}\right]^2 \\ &- 2w_1\beta_h S^*\delta\frac{\beta_e S^*\kappa\xi}{(\kappa + B^*)(\kappa + B)} - 4w_1w_2\frac{\delta\beta_e S^*\kappa\xi\mu}{(\kappa + B^*) + (\kappa + B)} \\ &- 2w_1w_2\frac{\delta\beta_e S^*\kappa\xi}{(\kappa + B^*)(\kappa + B)}\left(\beta_h I + \frac{\beta_e B}{\kappa + B}\right) > 0. \end{aligned}$$

It can easily be shown that

$$det(W^{*}(-A)^{*} + (W^{*}(-A^{*})^{T}))$$

= $4w_{1}w_{2}[(\gamma + \mu) - \beta_{h}S^{*}] \left(\mu + \beta_{h}I + \frac{\beta_{e}B}{\kappa + B}\right)$
+ $2w_{1}w_{2}\beta_{h}S^{*}\left(\beta_{h}I + \frac{\beta_{e}B}{\kappa + B}\right) - w_{2}^{2}\left(\beta_{h}I + \frac{\beta_{e}B}{\kappa + B}\right)^{2} - w_{1}^{2}(S^{*})^{2}\beta_{h}^{2} > 0$

$$\frac{w_2 \left(\beta_{\rm h} I \delta + \frac{\delta \beta_{\rm e} + B}{\kappa + B}\right) - w_1 \left(\delta \beta_{\rm h} S^* + \frac{\beta_{\rm e} S^* \kappa \xi}{(\kappa + B^*)(\kappa + B)}\right)}{2w_2 \left(\mu \delta + \beta_{\rm h} I \delta + \frac{\delta \beta_{\rm e} B}{\kappa + B}\right)} \right]$$

Hence, the matrix $W^*(-A)^* + (W^*(-A)^*)^T$ is positive definite. On the basis of Theorem 3, $w_3 > 0$ exists such that $W(-A) + (-A)^T W^T > 0$; i.e., $WA + A^T W^T < 0$. We have thus established the following result.

Theorem 4. The endemic equilibrium ε^* is globally asymptotically stable when $\mathcal{R}_0 > 1$.

We illustrate the existence of the unique globally asymptotically stable endemic equilibrium using a phase plane portrait in Fig. S1 based on a set of varying initial conditions and parameter values in Table S1.

Transmission Routes and Model Dynamics. In Fig. S2 we present numerical simulation results illustrating the contribution of the transmission routes in the dynamics of cholera for the following scenarios: (*i*) $\mathcal{R}_0 > 1$, $\mathcal{R}_e < 1 < \mathcal{R}_h$; (*ii*) $\mathcal{R}_0 > 1$, $\mathcal{R}_e > 1 > \mathcal{R}_h$; (*iii*) $\mathcal{R}_0 < 1$, $\mathcal{R}_e > \mathcal{R}_h < 1$; and (*iv*) $\mathcal{R}_0 < 1$, $\mathcal{R}_e > \mathcal{R}_h < 1$.

- Castillo-Chavez C, Feng Z, Huang W (2002) On the computation of R₀ and its role on global stability. Available at math.la.asu.edu/chavez/2002/JB276.pdf. Accessed April 5, 2010.
- Katsuhiko O (1970) Modern Control Engineering (Prentice-Hall, Inc., Englewood Cliffs, NJ), pp 252–258.
- 6. Redheffer R (1985) Volterra multipliers ii. SIAM J Alg Disc Math 6:612-623.
- 7. Cross GW (1978) Three types of matrix stability. Linear Algebra Appl 20:253-263.
- 8. Goh BS (1976) Global stability in two species interactions. J Math Biol 3:313-318.



Fig. S1. The endemic equilibrium point of *I* versus *S* with six different initial conditions and using parameter values in Table S1, with $\beta_e = 0.2668$ and $\beta_h = 5.8991 \times 10^{-5}$.



Fig. 52. An illustration of the contribution of each transmission route for (A) $\mathcal{R}_0 > 1$, $\mathcal{R}_e < 1 < \mathcal{R}_h$; (B) $\mathcal{R}_0 > 1$, $\mathcal{R}_e > 1 > \mathcal{R}_h$; (C) $\mathcal{R}_0 < 1$, $\mathcal{R}_e < \mathcal{R}_h < 1$; and (D) $\mathcal{R}_0 < 1$, $\mathcal{R}_e > \mathcal{R}_h < 1$ using parameter values in Table S1 and choosing β_e and β_h arbitrarily and a suitable population size. The blue line denotes contribution from the environment, the black line denotes human–human transmission, and the red line is a combination of both modes of transmission.



Fig. S3. Cholera model fitting for the cumulative cholera cases where the thick red line represents the model fit and the circles mark the reported data for the cumulative number of cholera for Zimbabwe using parameter values in Table S1 and population size in Table 1.



Fig. S4. Cholera model fitting for the cholera cases. The red line represents the model fit, and the blue dashed line and the circles mark the reported data for cholera cases for Zimbabwe using parameter values in Table S1 and population size in Table 1.



Fig. S5. The relationship between \mathcal{R}_0 and the percentage of symptomatic cholera cases reported using data from Zimbabwe, parameter values from Table S1, and population size from Table 1.

Parameter	Symbol	Value	Source
Natural human birth and death rate	μ	(43.5 y) ⁻¹	(1)
Concentration of V. cholerae in environment (ID ₅₀)	κ	10 ⁶ cells/mL	(2)
Rate of recovery from cholera	γ	(5 d) ⁻¹	(2)
Rate of contribution to V. cholerae in the aquatic environment	ξ	10 cells·mL ⁻¹ ·d ⁻¹ per person	(2)
Death rate of vibrios in the environment	δ	(30 d) ⁻¹	(2)

Table S2. Estimated values of β_e and β_h and 95% confidence intervals

	β_e	β _e 95% Cl	β _h	β _h 95% Cl
Harare	2.1	(1.31–2.88)	0.00043	(0.0004–0.005)
Bulawayo	0.94	(0.46–1.42)	0.0024	(0.0020-0.0027)
Mashonaland Central	0.87	(0.47–1.27)	0.0016	(0.0015–0.0017)
Mashonaland East	1.75	(1.22–2.28)	0.00077	(0.0007–0.0009)
Mashonaland West	1.13	(0.038–2.22)	0.0017	(0.0014–0.0019)
Midlands	0.23	(0.035–0.43)	0.0012	(0.0011–0.0013)
Manicaland	0.55	(0.28–0.82)	0.0016	(0.0014–0.0017)
Matebeleland South	9.62	(4.57–14.8)	0.0026	(0.001–0.0041)
Matebeleland North	0.85	(0.23–1.48)	0.003	(0.0026–0.0033)
Masvingo	0.85	(0.16–1.54)	0.0014	(0.0011–0.0016)
Zimbabwe	0.075	(0.055–0.094)	0.00011	(0.000105–0.000111)