Supporting Information

Characterizing the reproduction number of epidemics with early sub-exponential growth dynamics[1]

Gerardo Chowell[1,2] , Cécile Viboud[2], Lone Simonsen[3,4], Seyed M. Moghadas[5]

[1] School of Public Health, Georgia State University, Atlanta, GA, USA

[2] Division of International Epidemiology and Population Studies, Fogarty International Center, National Institutes of Health, Bethesda, MD, USA

[3] Department of Public health, University of Copenhagen, Copenhagen, Denmark

[4] Department of Global Health, School of Public Health and Health Services, George Washington University, Washington DC, USA

[5] Agent Based Modelling Laboratory, York University, Toronto, Canada.

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Alternative formulation of the generalized-growth model (GGM)

Here we derive an alternative formulation of the generalized-growth model where the biological factor acts on the growth rate r rather than C. The original generalized-growth model is given by [1]:

$$C' = rC^{p} \qquad (2.1)$$

where $C'(t)$ describes the incidence curve over time t, the solution $C(t)$ describes the cumulative number of cases at time t, r is a positive parameter denoting the growth rate (with the units of $(\text{people})^{1-p}$ per time), and $p \in [0,1]$ is a 'deceleration of growth' parameter (dimensionless).

We first apply a change of variable $u = \log(C)$ so that $C = e^{u}$. Then the model becomes:

$$u' = re^{u(p-1)}$$

The solution of this model is given by:

$$u(t) = \begin{cases} rt & p = 1 \\ \dfrac{1}{1-p}\log\left(r(1-p)t + e^{u_0(1-p)}\right) & 0 \le p < 1 \end{cases}$$

where $u_0 = \log(C_0)$. The rate of change of the growth rate in the original generalized-growth model (Equation 1) is given by:

$$u'(t) = \begin{cases} r & p = 1 \\ \dfrac{r}{r(1-p)t + e^{u_0(1-p)}} & 0 \le p < 1 \end{cases}$$

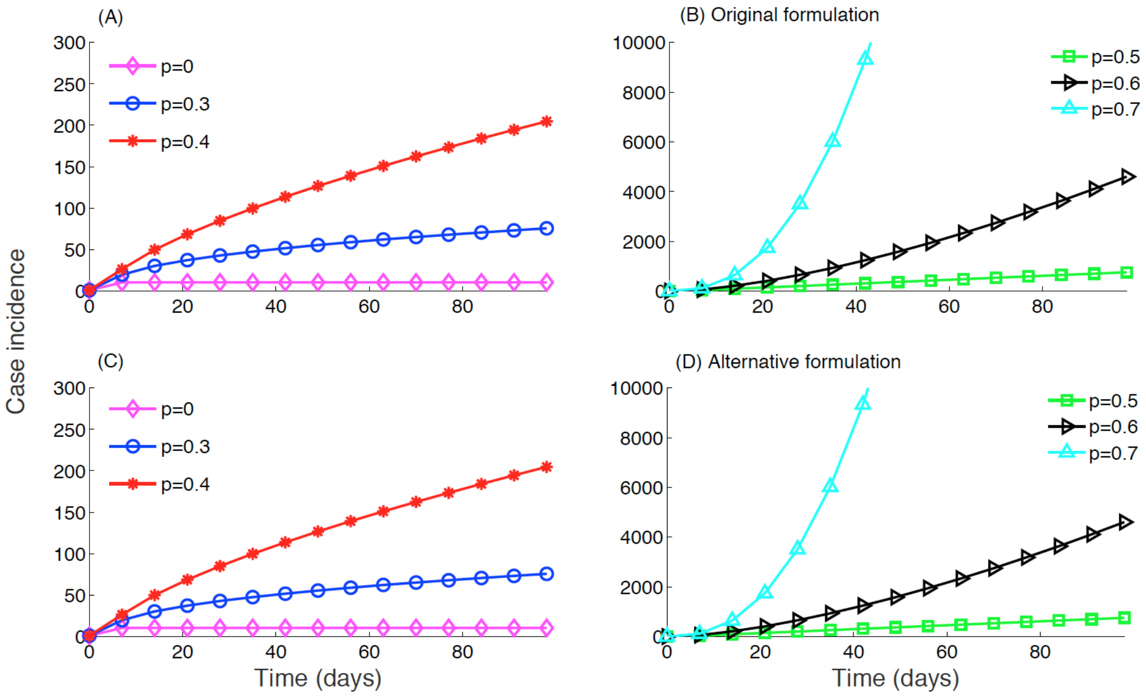
Hence, the alternative formulation of the generalized-growth model is given by:

$$C'(t) = u'(t)C(t)$$

where $u'(t) = \begin{cases} \dfrac{r}{r(1-p)t + e^{\log(C_0)(1-p)}} & 0 \le p < 1 \\ r & p = 1 \end{cases}$

The same numerical results are obtained from both formulations of the generalized growth model as shown in Figure S1.

Figure S1. Comparison of the numerical results derived from both formulations of the generalized-growth model for different values of p when $r = 1.5$ and $C_0 = 1$.



Mathematical proof for $R_g^{sub\exp} \to e^{rT_g}$ as $p \to 1^-$

Using methods of limit, one can easily show that the reproduction number $R_g^{sub\exp}$ according to disease generations converges to e^{rT_g} as $p \to 1^-$ as follows:

$$R_g^{sub\exp} = \left[1 + \frac{r(1-p)T_g}{r(1-p)gT_g + C_0^{1-p}}\right]^{\frac{p}{1-p}} \qquad (2.6)$$

If $p \to 1^-$ then $R_g^{sub\exp} \approx 1^{\infty}$

Taking the logarithm on both sides we obtain (when $C_0 \neq 0$):

$$\ln(R_g^{sub\exp}) = \frac{p}{1-p}\ln\left[1 + \frac{r(1-p)T_g}{r(1-p)gT_g + C_0^{1-p}}\right] \approx \frac{0}{0} \text{ when } p \to 1^-$$

Applying L'Hospital's Rule, we obtain:

$$y = \frac{1\left[\dfrac{-rT_g[1] - \dfrac{0}{1^2}}{1+0}\right]^0}{-1} = \frac{-rT_g}{-1} = rT_g$$

as $p \to 1^-$. Then $\lim_{p \to 1^-} R_g^{sub\exp} = e^{rT_g}$

Putting everything together, we have:

$$R_g^{sub\exp} = \begin{cases} 1 & \text{If } g \to \infty \text{ and } p < 1 \\ e^{rT_g} & \text{If p} \to 1^- \end{cases}$$

Figure S2. Simulated profiles of the effective reproduction number during the first 5 generation intervals derived from case incidence curves of the generalized-growth model with different values of the growth rate (r) and the deceleration of growth parameter (p). The initial number of cases is set to C(0)=1. Estimates of the effective reproduction number are generated assuming a fixed generation interval at 3 days.

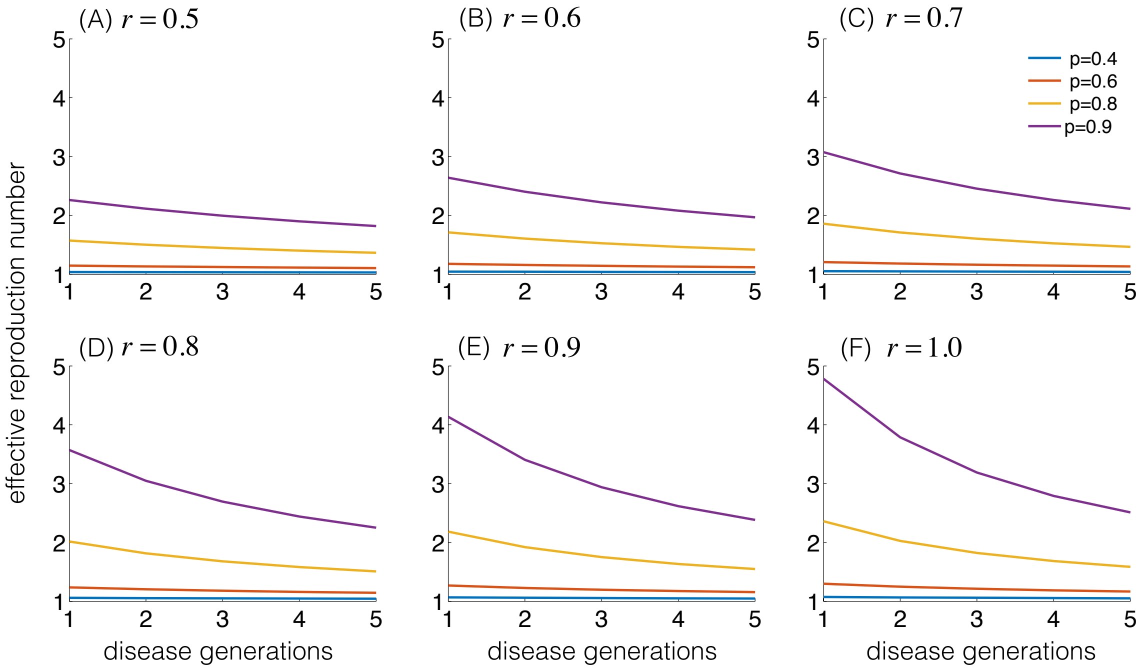


Figure S3. Simulations of the early epidemic growth phase derived from the SIR model described by Equations (2.10) for different values of the power-law scaling parameter α, $\gamma = \frac{1}{5}$, and (A) $\beta_0 = 0.4$, (B) $\beta_0 = 0.48$, (C) $\beta_0 = 0.56$, and (D) $\beta_0 = 0.6$ with a large population size N set at 10^8. The epidemic simulations start with one infectious individual. In semi-logarithmic scale, exponential growth is evident if a straight line fits well several consecutive disease generations of the epidemic curve, whereas a strong downward curvature in semi-logarithmic scale is indicative of sub-exponential growth. Our simulations show that case incidence curves display early sub-exponential growth dynamics even for values of α slightly below 1.0.

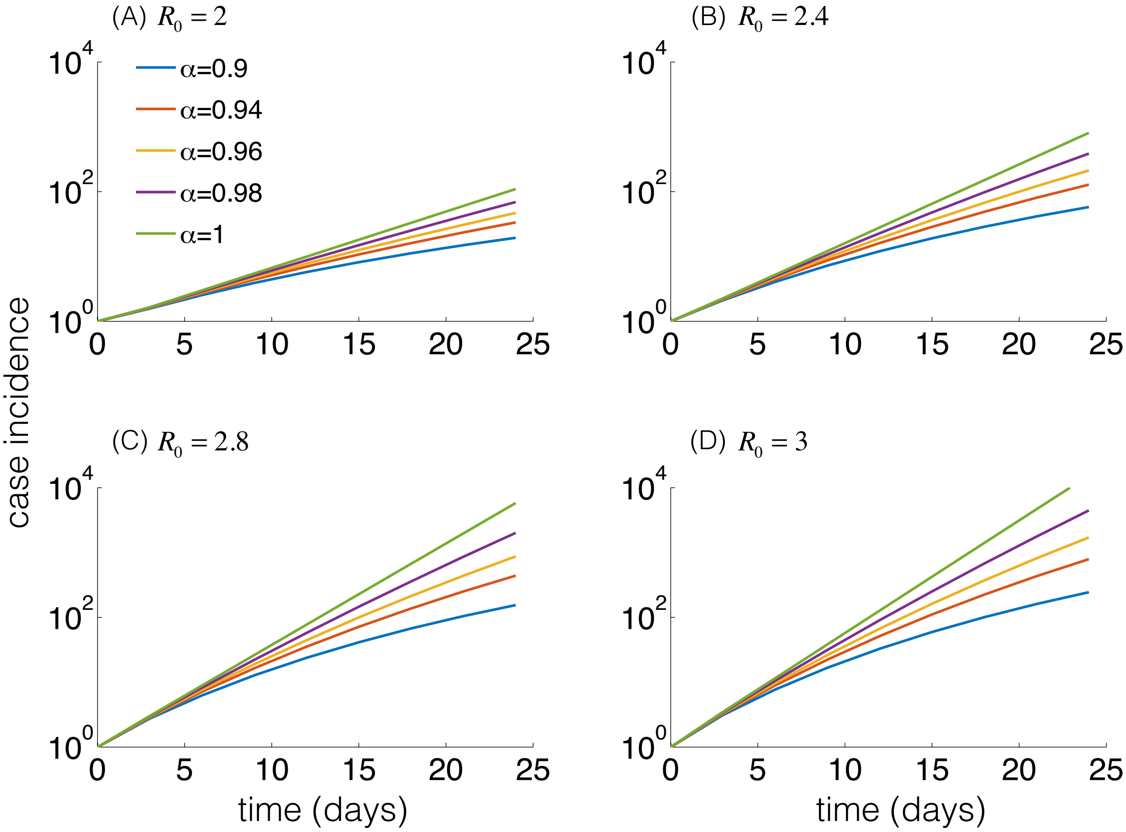


Figure S4. Examples of the fits provided by the exponential and generalized-growth models to three infectious disease outbreaks (pandemic influenza in San Francisco in 1918, HIV/AIDS epidemic in Japan, and Ebola epidemic in Western Urban, Sierra Leone in 2014).

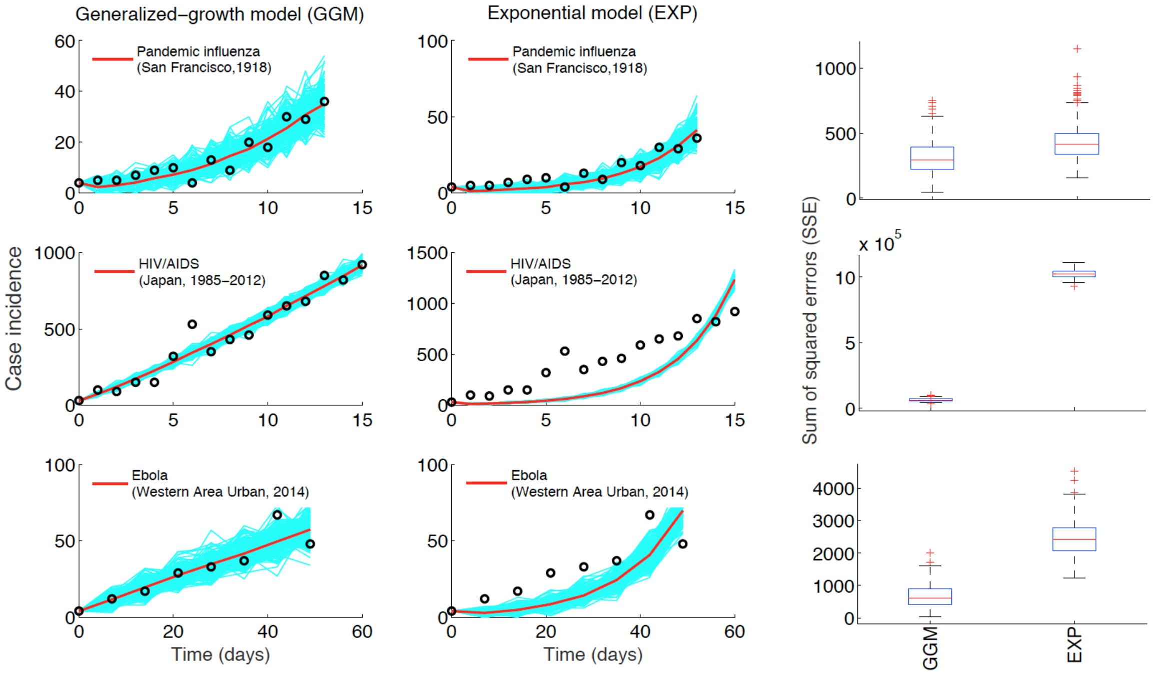


Figure S5. Comparison of the goodness of fit provided by the exponential and the generalized-growth models across all of the 21 infectious disease outbreaks (see Table 1).

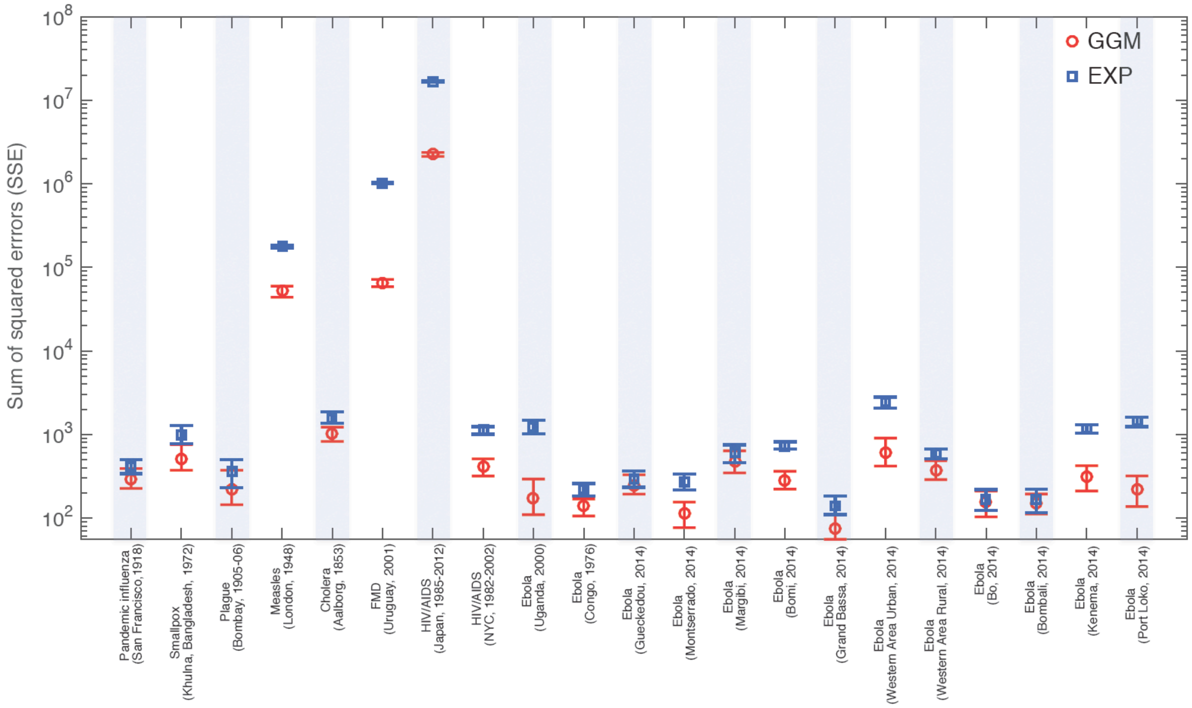


Figure S6. Mean estimates of the effective reproduction number and the deceleration of growth parameter *p* derived from our sample of infectious disease datasets (Table 1) were significantly correlated for three estimation periods with an initial phase length comprising 3 to 5 generation intervals.

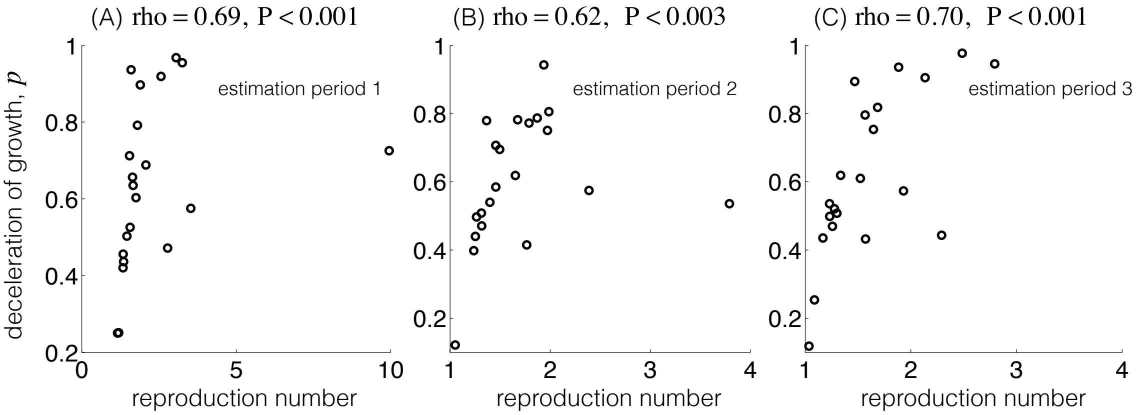


Figure S7. The 1918 influenza pandemic in San Francisco. Estimates and 95% confidence intervals of the effective reproduction number derived from fitting the generalized-growth model to an increasing length of the early epidemic phase comprising of approximately 3-5 disease generation intervals. The generation interval is assumed to be gamma distributed with the mean of 3 days and standard deviation of 1 day. Estimates and 95% confidence intervals for parameters r and p are also shown.

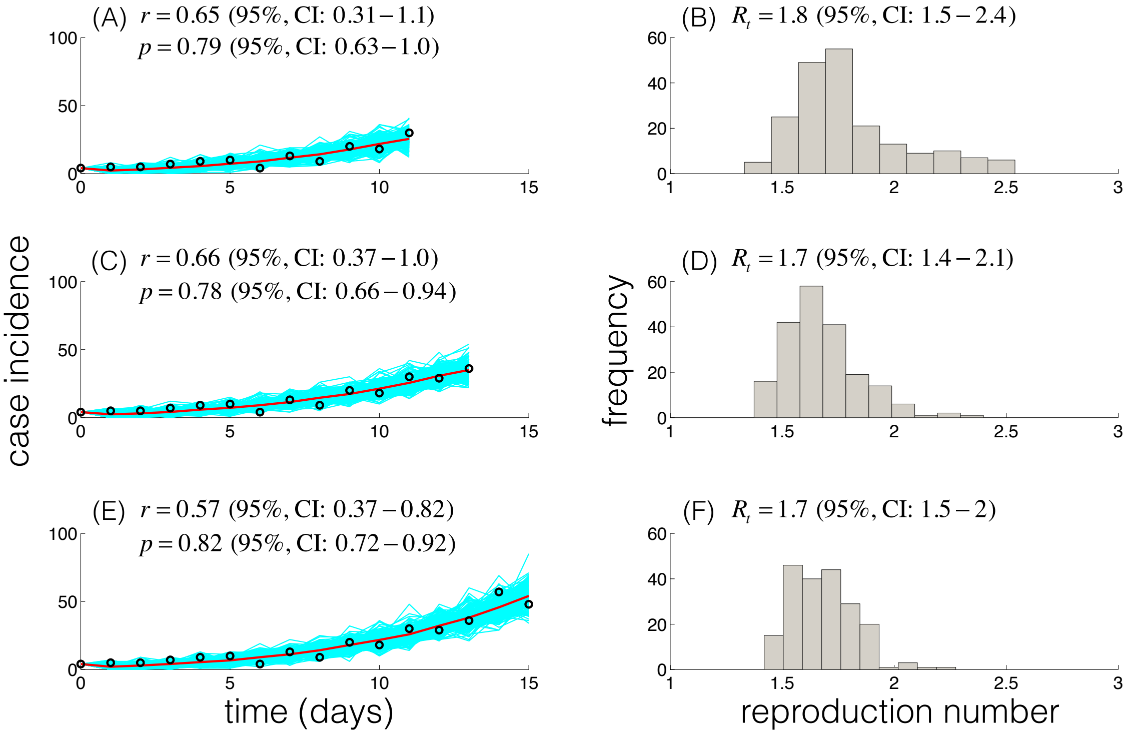
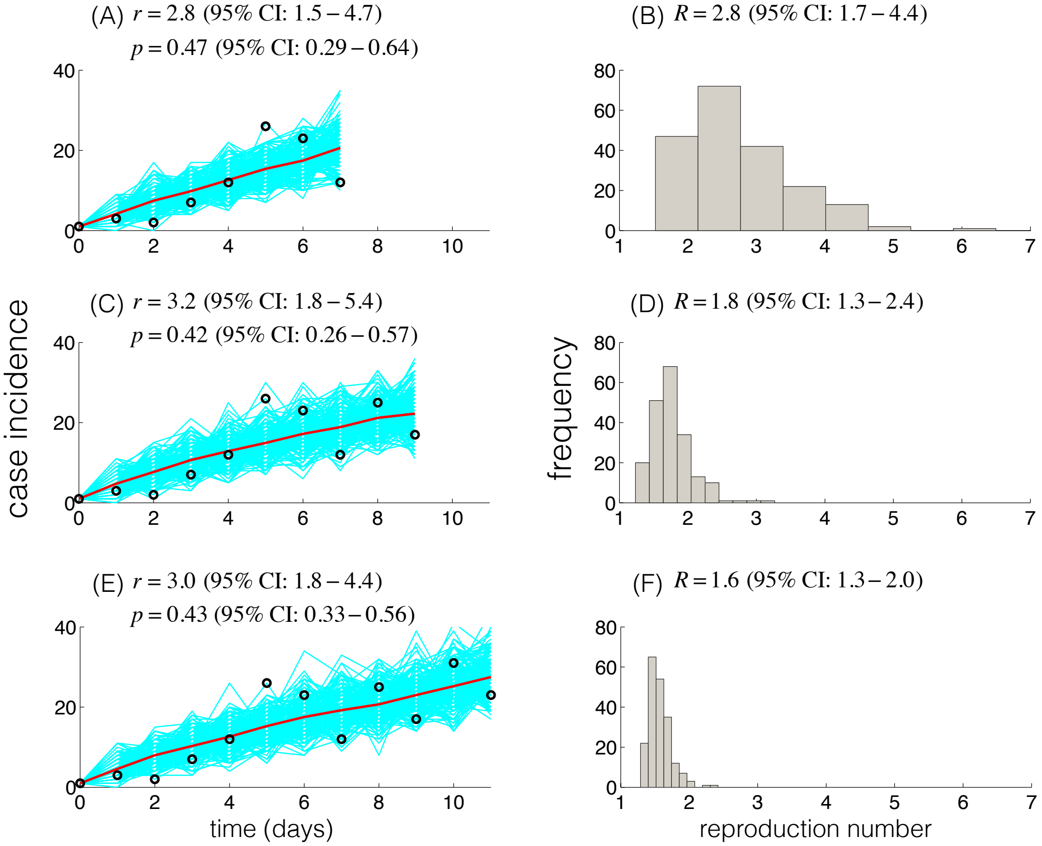


Figure S8. The 2001 foot-and-mouth disease epidemic in Uruguay. Estimates and 95% confidence intervals of the effective reproduction number derived from fitting the generalized-growth model to an increasing length of the early epidemic phase comprising of approximately 3-5 disease generation intervals. The generation interval is assumed to be gamma distributed with the mean of 5 days and standard deviation of 1 day. Estimates and 95% confidence intervals for parameters r and p are also shown.



(A) $r = 2.8$ (95% CI: 1.5 – 4.7) $p = 0.47$ (95% CI: 0.29 – 0.64)

(B) $R = 2.8$ (95% CI: 1.7 – 4.4)

(C) $r = 3.2$ (95% CI: 1.8 – 5.4) $p = 0.42$ (95% CI: 0.26 – 0.57)

(D) $R = 1.8$ (95% CI: 1.3 – 2.4)

(E) $r = 3.0$ (95% CI: 1.8 – 4.4) $p = 0.43$ (95% CI: 0.33 – 0.56)

(F) $R = 1.6$ (95% CI: 1.3 – 2.0)

Figure S9. The HIV/AIDS epidemic in Japan (1985-2012).
Estimates and 95% confidence intervals of the effective reproduction number derived from fitting the generalized-growth model to an increasing length of the early epidemic phase comprising of approximately 3-5 disease generation intervals. The generation interval is assumed to be gamma distributed with the mean of 4 years and standard deviation of 1.4 years. Estimates and 95% confidence intervals for parameters r and p are also shown.

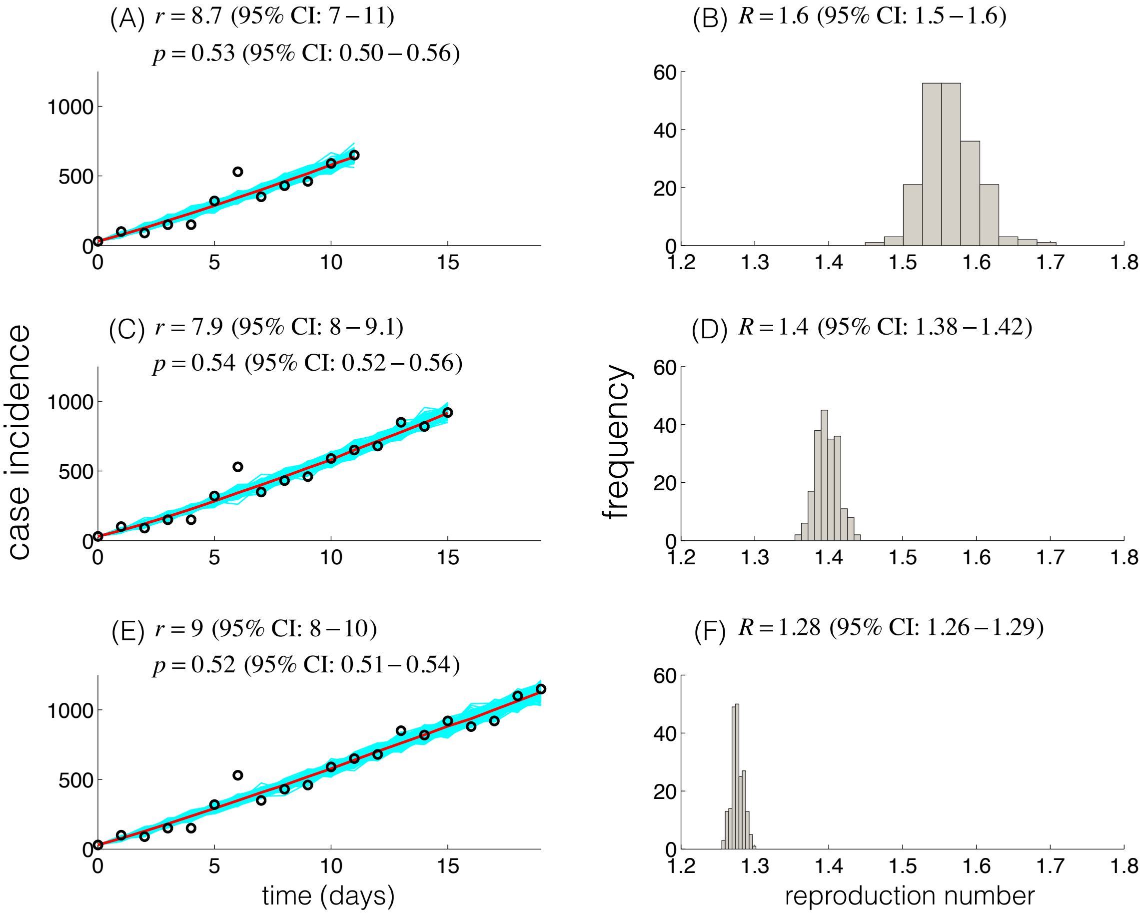


Figure S10. The 2014-15 Ebola epidemic in Gueckedou, Guinea.
Estimates and 95% confidence intervals of the effective reproduction number derived from fitting the generalized-growth model to an increasing length of the early epidemic phase comprising of approximately 3-5 disease generation intervals. The generation interval is assumed to be gamma distributed with the mean of 19 days and standard deviation of 11 days. Estimates and 95% confidence intervals for parameters r and p are also shown.

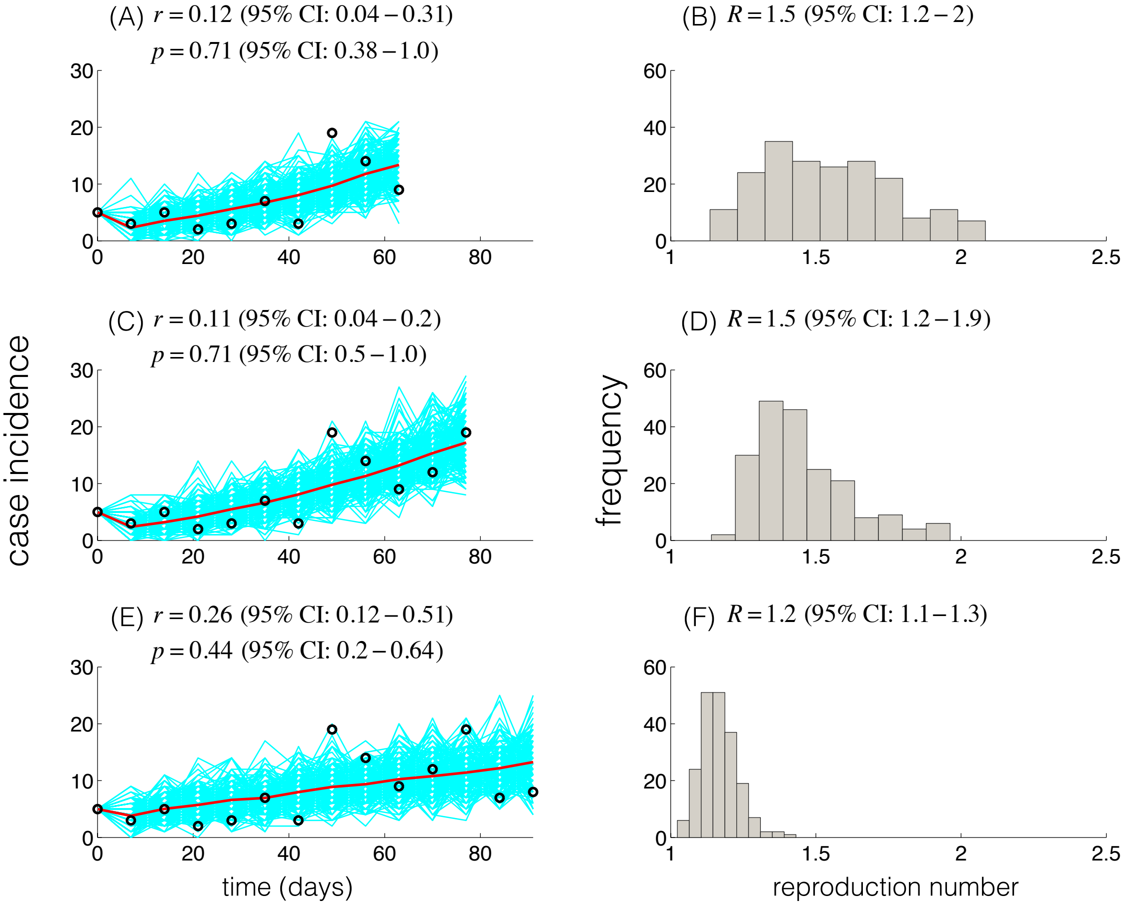
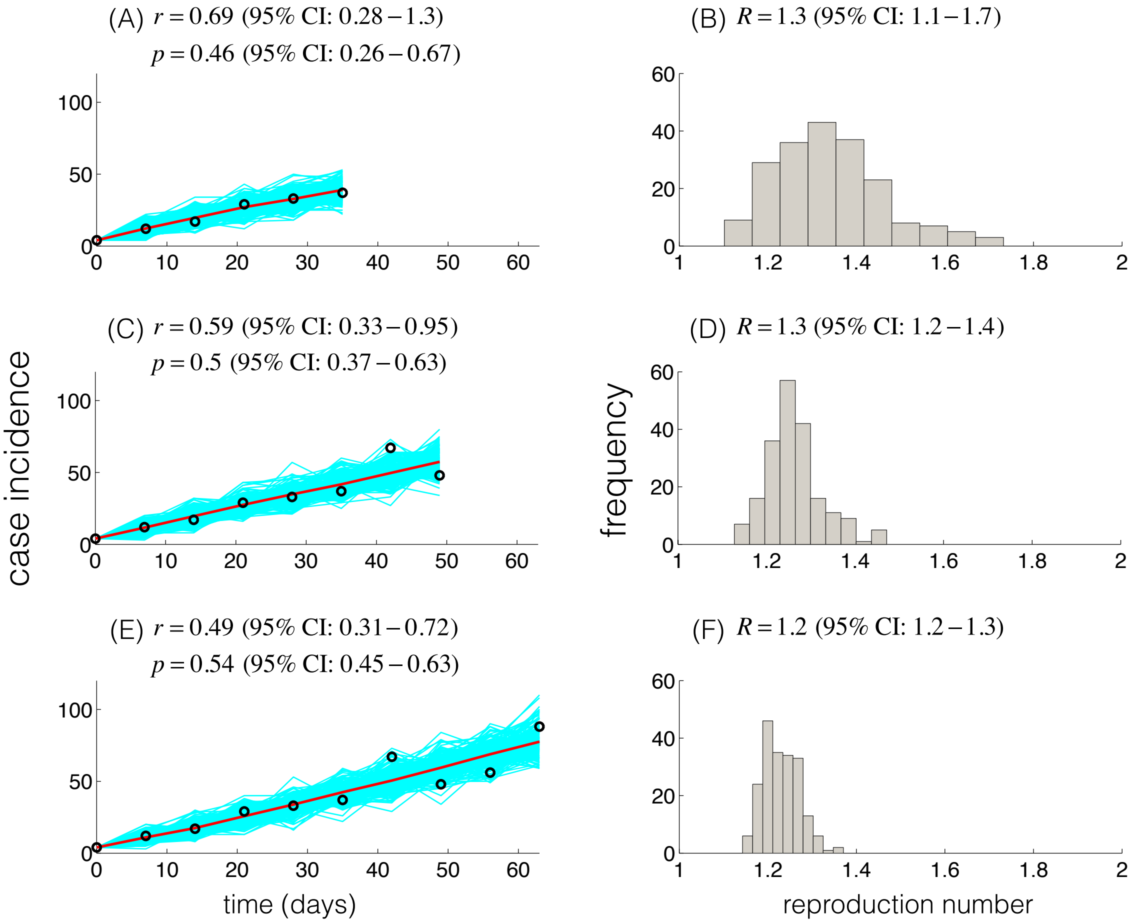


Figure S11. The 2014-15 Ebola epidemic in Western Area Urban, Sierra Leone. Estimates and 95% confidence intervals of the effective reproduction number derived from fitting the generalized-growth model to an increasing length of the early epidemic phase comprising of approximately 3-5 disease generation intervals. The generation interval is assumed to be gamma distributed with the mean of 11.6 days and standard deviation of 5.6 days. Estimates and 95% confidence intervals for parameters r and p are also shown.



(A) $r = 0.69$ (95% CI: $0.28 - 1.3$)
$p = 0.46$ (95% CI: $0.26 - 0.67$)

(B) $R = 1.3$ (95% CI: $1.1 - 1.7$)

(C) $r = 0.59$ (95% CI: $0.33 - 0.95$)
$p = 0.5$ (95% CI: $0.37 - 0.63$)

(D) $R = 1.3$ (95% CI: $1.2 - 1.4$)

(E) $r = 0.49$ (95% CI: $0.31 - 0.72$)
$p = 0.54$ (95% CI: $0.45 - 0.63$)

(F) $R = 1.2$ (95% CI: $1.2 - 1.3$)

References

1. Viboud C, Simonsen L, Chowell G. A generalized-growth model to characterize the early ascending phase of infectious disease outbreaks Epidemics **2016**; 15:27–37.