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Supplementary Material for

Which interventions work best in a pandemic?

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Which Interventions Work Best in a Pandemic? Supplementary Materials*

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Measurement requirements for identifying SIR model parameters

In this section, we outline how a discrete-time SIR model can be used to answer a number of policy questions after the randomized tightening or loosening of interventions in some locations but not others. We intentionally keep the exposition stylized for the sake of simplicity; the approach can be extended to accommodate variation in transmission through time and by age, latent periods, and loss of immunity.

Assume that a treatment is deployed in a randomly chosen subset of locations at time t, and remains in place until time $t+1$. We refer to these areas as "treatment" areas (T). A second randomly chosen subset of locations serves as the control areas (C). This is the simplest and most intuitive case; alternative approaches might test two treatments relative to each other without controls, or might test multiple treatments against each other and/or against the control.

The rate of recovery from infection is given by γ, which we normalize to 1 without loss of generality. As a result, the duration of a period can be thought of as the duration of recovery, $\frac{1}{\gamma}$. This normalization simplifies the expressions below because individuals infected in period t, I_t, are no longer infected in period $t+1$.We assume that γ is unaffected by the intervention.

We can then express the transmission process as $I_{t+1} = \beta I_t S_t$, where β is the transmission rate; I_t and I_{t+1} refer to the number of infected individuals (I) in periods t and $t+1$, respectively; and S_t is the number of susceptible individuals in period t. This expression makes use of the normalization of the recovery rate to 1, as explained above. We can rearrange this expression to obtain the transmission rate: $\beta = \frac{I_{t+1}}{I_t S_t}$. We denote the transmission rate under the treatment regime (T) in the absence of spillovers as β_T, and that under the control regime (C) as β_C. With these definitions in hand, we can specify the measurement requirements to answer different policy questions.

1. **How effective are two treatments relative to each other (e.g. a treatment relative to a control condition, or two treatment**

conditions relative to each other)?

The following ratio defines the relative transmission rate in the treatment relative to the control condition:

$$\frac{\beta_T}{\beta_C} = \frac{\frac{I_{t+1,T}}{I_{t,T}S_{t,T}}}{\frac{I_{t+1,C}}{I_{t,C}S_{t,C}}}$$

We rearrange by taking logs:

$$\begin{aligned}\ln\left(\frac{\beta_T}{\beta_C}\right) &= \ln \frac{\frac{I_{t+1,T}}{I_{t,T}S_{t,T}}}{\frac{I_{t+1,C}}{I_{t,C}S_{t,C}}} \\ &= \ln \frac{I_{t+1,T}}{I_{t+1,C}} - \ln I_{t,T} - \ln S_{t,T} + \ln I_{t,C} + \ln S_{t,C}\end{aligned}$$

Random assignment implies that before the intervention, the number of infected and susceptible individuals in treatment and control areas is the same in expectation: $E[I_{t,C}] = E[I_{t,T}]$ and $E[S_{t,C}] = E[S_{t,T}]$. We can therefore take expectations and simplify the relative transmission rate as follows:

$$E\left[\ln\left(\frac{\beta_T}{\beta_C}\right)\right] = \ln \frac{I_{t+1,T}}{I_{t+1,C}}$$

Thus, the relative transmission rate can be measured using the number of infected individuals in treatment and control areas *at a single point in time* after the intervention has been deployed.[1] As pointed out above, this approach can also be used to estimate which of several interventions reduces transmission the most.

Note that a sufficient number of treatment and control areas is required to obtain a precise estimate. Moreover, if additional information about

[1] Alternatively, we can write $E\left[\frac{\beta_T}{\beta_C}\right] \approx \frac{E[\beta_T]}{E[\beta_C]} \approx \frac{\frac{E[I_{t+1,T}]}{E[I_{t,T}S_{t,T}]}}{\frac{E[I_{t+1,C}]}{E[I_{t,C}S_{t,C}]}} = \frac{E[I_{t+1,T}]}{E[I_{t+1,C}]}$. To obtain this result, we use (twice) the fact that the expectation of a ratio of two random variables can be approximated by the ratio of the expectations using a first-order Taylor expansion, i.e. $E\left[\frac{X}{Y}\right] \approx \frac{E[X]}{E[Y]}$; and that randomization ensures that $E[I_{t,T}S_{t,T}] = E[I_{t,C}S_{t,C}]$. We thank Clement de Chaisemartin and David Strömberg for help with these derivations, and also gratefully acknowledge lecture notes by Howard Seltman.

these areas is available, such as the number of infected individuals at other timepoints, or demographic information, these estimates can be included in the analysis to increase precision further.

2. **Has transmission has been sufficiently reduced that the outbreak is shrinking (effective reproductive number $R_{eff} < 1$)?**
   A further question of interest may be whether an intervention has reduced transmission sufficiently to bring the effective reproductive number, R_{eff}, below 1, the point beyond which the outbreak shrinks, as one infected individual gives rise to less than one new infection. The effective reproductive number in treatment areas after the deployment of the intervention is defined as

$$R_{\text{eff}_{t,T}} = R_{0_T} S_{t,T}$$

   where $R_{0_T} = \frac{\beta_T}{\gamma} = \beta_T$ (the last equality here uses the normalization of the recovery rate γ to 1). This simplifies to

$$R_{\text{eff}_{t,T}} = \frac{I_{t+1,T}}{I_{t,T}}$$

   Thus, the effective reproductive number in the treatment condition can be estimated if we add a single measurement of the number of infected individuals, $I_{t,T}$, before the intervention.

3. **What is the final size of the pandemic in a treatment relative to a control condition?**
   In addition to learning how much an intervention changes the transmission rate, policymakers may also want to know how an intervention affects the "final size" of the pandemic; i.e., what share of the population would have been infected in total when the pandemic has died down, if the same intervention had been in place over the full time-course of the outbreak. Using the same normalization of γ as above, final size is given

by the standard final size equation (e.g. as derived in Miller, 2012):

$$R_\infty = 1 - \exp(-\beta R_\infty)$$

We can therefore estimate final size by measuring the transmission rate β. Because $\beta = \frac{I_{t+1}}{I_t S_t}$, this amounts to adding a single measurement at one timepoint to those described above, namely the number of susceptibles, S_t. If measurement of susceptibles before the intervention is not feasible, the fact that $S_t = S_{t+1} + I_{t+1}$ can be used to replace it with measurement after the intervention. Note that this will not reflect the final size if the interventions have been tightened or loosened at different time-points, but rather what would have been obtained had the same magnitude of transmission been experienced over the full time-course of the outbreak. If the time-variation of β is known, final size can be obtained numerically (see inset, Figure 1, main text).

4. **What would the effect of an intervention be if it was deployed at a different point in the outbreak?**
   Policymakers may only have an opportunity to test an intervention at a certain time during an outbreak, but may nevertheless want to know what the effect of the intervention would be if it was deployed at a different time—e.g., in a future outbreak. The above illustration of how absolute transmission rates can be computed immediately answers this question: because the transmission rate governs the time course of the entire outbreak, once it has been estimated based on an intervention tested at a specific timepoint, it can be used to make predictions about the remainder of the outbreak (assuming that transmission varies only minimally over time).

5. **What is the relative effectiveness of interventions that were deployed at different timepoints during the outbreak?**
   Policymakers may want to compare interventions that were tested at different times during an outbreak: for example, elementary school closures

may have been tested late in an outbreak, and high school closures early. The above discussion illustrates that estimation of the transmission rates is independent of the timepoint at which it occurs, and is therefore sufficient to compare different interventions to each other, even if they were never tested at the same time.

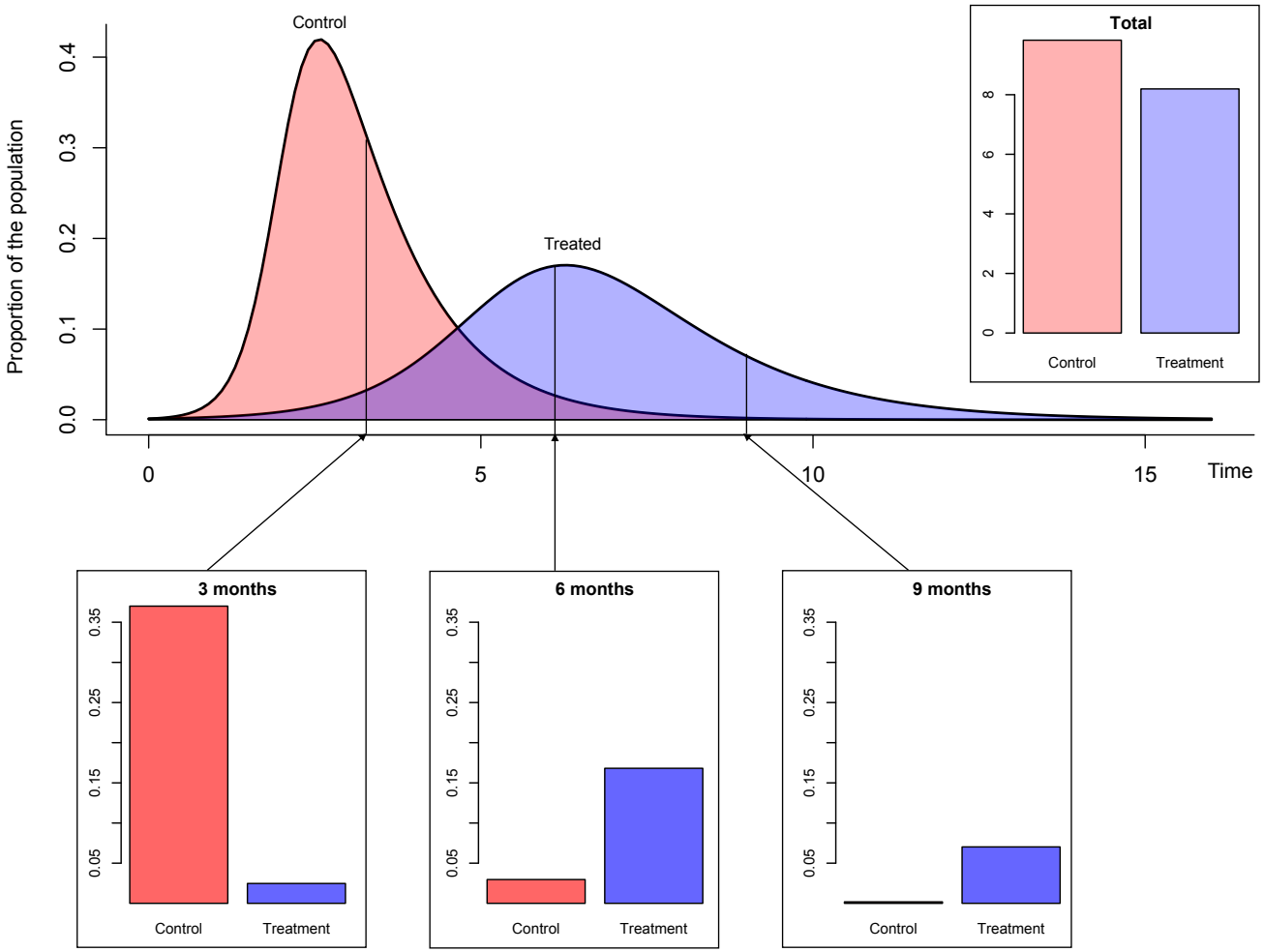
Figure details

All figures were created in R using the 'deSolve' package to numerically integrate the ordinary differential equations of the SIR model. Code is available for download at www.sciencemag.org. We used parameter values that are roughly applicable to the COVID-19 pandemic. To create Figure 1, reflecting "tightening/loosening", we set the initial proportions of "susceptible" (S), "infected" (I), and "removed" (R) individuals to $S = 0.998$, $I = 0.001$, and $R = 0.001$. The parameter γ (rate of recovery from infection) is set to $\gamma = 1$, and the parameter β (transmission rate) to $\beta = 2.25$ for the unconstrained outbreak (red line) and $\beta = 1.5$ for the outbreak where interventions have been implemented (blue line). Loosening of interventions occurs for two weeks at three different time points (3, 10 and 15 weeks after the beginning of the outbreak). During these two weeks, transmission β returns to the unconstrained magnitude of $\beta = 2.25$. Tightening occurs at the same time points, and is captured by setting the transmission rate to $\beta = 1.05$ for two weeks. For the inset showing final sizes, we used the 'rootSolve' package to obtain the equilibria for the full spectrum of possible loosening/tightening times for all scenarios. Colors are from the 'RColorBrewer' package. For Figure S1, initial conditions and γ are as above; and we set $\beta = 3$ for the unconstrained outbreak, and $\beta = 2.1$ for the outbreak where interventions have been implemented.

References

Miller, J. C. (2012). A note on the derivation of epidemic final sizes. *Bulletin of Mathematical Biology*, *74*(9), 2125–2141.

Figure S1: Accounting for time



Notes: Time-course of infection in the absence of an intervention (red) and with a treatment (blue). The total number of cases (area under the time-course curves; right panel) provides an appropriate measure of the impact of the treatment on incidence. In contrast, snapshot measurement of treatment effects 3, 6 or 9 months after the start of the outbreak (lower panels) can be misleading, with the treatment appearing to decrease incidence early on, and increase it later.