The Effects of Using a Clinical Prediction Rule to Prioritize Diagnostic Testing on Transmission and Hospital Burden: A Modeling Example of Early Severe Acute Respiratory Syndrome Coronavirus 2


Background. Prompt identification of infections is critical for slowing the spread of infectious diseases. However, diagnostic testing shortages are common in emerging diseases, low resource settings, and during outbreaks. This forces difficult decisions regarding who receives a test, often without knowing the implications of those decisions on population-level transmission dynamics. Clinical prediction rules (CPRs) are commonly used tools to guide clinical decisions.

Methods. Using early severe acute respiratory syndrome coronavirus disease 2 (SARS-CoV-2) as an example, we used data from electronic health records to develop a parsimonious 5-variable CPR to identify those who are most likely to test positive. To consider the implications of gains in daily case detection at the population level, we incorporated testing using the CPR into a compartmentalized model of SARS-CoV-2.

Results. We found that applying this CPR (area under the curve, 0.69; 95% confidence interval, .68–.70) to prioritize testing increased the proportion of those testing positive in settings of limited testing capacity. We found that prioritized testing led to a delayed and lowered infection peak (ie, “flattens the curve”), with the greatest impact at lower values of the effective reproductive number (such as with concurrent community mitigation efforts), and when higher proportions of infectious persons seek testing. In addition, prioritized testing resulted in reductions in overall infections as well as hospital and intensive care unit burden.

Conclusion. We highlight the population-level benefits of evidence-based allocation of limited diagnostic capacity.

Keywords. clinical prediction rule; transmission dynamics; diagnostic testing.
epidemiological information (eg, transmissibility, duration of infectiousness, reproductive number) to provide a picture of the population-level disease dynamics over time [10, 11]; to our knowledge, compartmental models have not yet been used to evaluate the impact of CPRs on population-level public health outcomes.

Many diagnostic models for severe acute respiratory syndrome coronavirus disease 2 (SARS-CoV-2) now exist [12], each specific to a given population and time, typically focused on achieving optimal patient care. Using a single health system in Utah as a proof of concept, we developed a CPR and incorporated it into an SEIR model of the ongoing SARS-CoV-2 pandemic to evaluate the population-level impact that could have been achieved by using a CPR to prioritize testing early in the pandemic, when testing capacity was limited. Many countries, including the United States, have experienced shortages in diagnostic testing capacity, and these shortages will likely continue in many settings worldwide [13–15], as well as in future outbreaks of emerging pathogens.

Our primary objective was to measure the impact that prioritized testing (using the CPR) could have had on the course of the SARS-CoV-2 pandemic, including the magnitude and timing of the outbreak peak as well as the associated impact on hospitalization and intensive care unit (ICU) burden. In addition, we determined the conditions (eg, test availability, test seeking volume, effective reproductive number) in which prioritized testing would have resulted in the greatest reduction in SARS-CoV-2 infections and hospitalizations. Potential benefits of CPR-guided testing continue to be relevant for surges in the SARS-CoV-2 pandemic, for future emerging infections, and for outbreaks of common infections (eg, cholera and measles) in settings with limited diagnostic capacity.

**MATERIALS AND METHODS**

**Clinical Prediction Rule**

All patients tested for SARS-CoV-2 in the University of Utah Health (UHealth) system were eligible for our study. Data were gathered from a period when testing eligibility was based on presenting with ≥1 of the following: cough, fever, shortness of breath, or a high risk of exposure given recent travel or contact with a laboratory-confirmed case (1 March to 6 April 2020). We use the phrase “test eligible” to describe any person seeking a test who satisfies these conditions. We considered age, sex, state-ranked area deprivation index, smoking status, reported symptoms, healthcare worker status, travel history, and exposure to a confirmed SARS-CoV-2 case as predictive variables. Random forest regression and logistic regression models were considered for our CPR. Our final CPR was a logistic regression model using the top 5 predictors to output the probability of an individual testing positive for SARS-CoV-2. Full details on data processing, the predictive variables, and the construction of the CPR are available in the Supplementary Materials 1. This study was reviewed by the University of Utah Institutional Review Board and determined to be exempt.

**Modeling Daily Testing**

We first explored the effects of prioritized versus indiscriminate testing per day (Figure 1A). On a given day, we assumed a certain number, \( N_{\text{eligible}}\), of people who seek testing and are test eligible (have cough, fever, shortness of breath, or known exposure and seek testing). Of those who seek testing, a certain proportion, \( q\), would test positive for SARS-CoV-2 if given a test and the rest, \((1 - q)\), would test negative. We assumed a limited number, \( N_{\text{total}}\), of SARS-CoV-2 tests were available daily. Using simulations (details in Supplementary Materials 2), we measured the proportion of test-eligible, SARS-CoV-2–positive patients who received testing under the 2 testing regimens: prioritized and indiscriminate testing.

**SEIR Modeling**

We also considered the effect of prioritized testing on disease spread in the population over longer time scales (months to years). We incorporated the same processes described above into a stochastic SEIR model parametrized for COVID-19. On each modeled day, we simulated the steps shown in Figure 1B, with parameters as in Table 1. Further simulation details are provided in Supplementary Materials 3.

We ran simulations assuming a total population of 3.2 million, the approximate population of the state of Utah [16]. We assumed an initial condition of 15 people in the infectious class and all others in the susceptible class. We ran our simulations for a period of 2 years. For each set of parameters considered, we ran 1000 stochastic simulations and then calculated the mean value of each of the total susceptible (\(S + T_S\)), exposed (\(E + T_E\)), infectious (\(I + T_I\)), and removed (\(R + T_R\)) groups, as well as 95% prediction intervals.

We then calculated several metrics, including the timing of the peak of the mean infection curve; the peak value of the mean infection curve; and the mean total number of infections by the end of the simulation. These metrics allowed us to compare expected outcomes between the models with indiscriminate testing and prioritized testing.

To highlight the associated implications for healthcare demand, we also modeled the daily occupancy of hospital beds and ICU beds (details in Supplementary Materials 3). We then calculated the mean number of person-days (ie, the number of people on a given day) where demand for hospitalization exceeds Utah’s capacity of 4869 hospital beds and the number of person-days where demand for ICU beds exceeds Utah’s capacity of 687 ICU beds [17, 18]. Note that these numbers are for total hospital and ICU beds, not those set aside for patients...
with COVID-19, and thus provide an upper bound for hospital capacity. All analyses and simulations were conducted using R statistical software (version 3.6.0; [19]). All code is archived and available online (doi:10.5281/zenodo.3924186).

RESULTS

During the period from 1 March to 6 April 2020, a total of 1983 patients were tested for SARS-CoV-2 at UHealth. After removing observations with missing covariate data, we obtained an
analytic sample size of 1928. Our final parsimonious 5-variable CPR had a cross-validated area under the curve (AUC) of 0.69 (95% confidence interval, .68–.70). In all the results that follow, we used this 5-variable CPR. We explored using additional variables but found this only marginally improved predictive ability (AUC up to 0.71; Supplementary Figure 1 and Supplementary Table 2), at the expense of requiring much greater data entry effort by clinicians. We also considered alternative versions of the CPR in light of varying predictor availability in different clinical contexts. We explored models excluding symptoms, including vital signs, and including a race/ethnicity variable (Supplementary Table 1). Again, these did not meaningfully improve predictive ability (AUC up to 0.72; Supplementary Table 2). Finally, we explored using random forest regression to fit the models, but logistic regression estimates had consistently higher AUCs.

When comparing indiscriminate testing to prioritized testing, the absolute difference in the number of people infected with COVID-19 who were tested was greatest for intermediate levels of testing availability, achieving the greatest benefit to disease detection when 40%–60% of test-eligible people received testing (vertical difference between solid lines in Figure 2). However, the proportional increase in the number of people with COVID-19 who were tested was greatest for low testing capacity, with the largest fold changes seen when <20% of test-eligible people received testing (dotted line in Figure 2). For example, if the rate of SARS-CoV-2 positivity among test-eligible people was 5% and there was test capacity for only 10% of those people, we would expect to see a nearly 3-fold increase in the number of patients testing positive on a given day if using prioritized testing instead of indiscriminate testing (Figure 2A). These results were sensitive to the proportion of SARS-CoV-2–positive patients who are test eligible, with greater differences between prioritized and random testing strategies seen for low rates of SARS-CoV-2 positivity (compare Figure 2A–2E). Results were robust to the total number of test-eligible persons.

Using our stochastic SEIR compartmental model, we show that prioritized testing delays the timing and reduces the prevalence at the infection peak and reduces final size of the pandemic (Figure 3 and Table 2). For our base parameter set, prioritized testing compared with indiscriminate testing resulted in a 30-day delay in the timing of the infection peak and a 22% decrease in the peak number of infections.

The differences in the timing and numbers of infections between a model with prioritized versus indiscriminate testing were greatest for lower values of the effective reproductive number, \( R_e \) (Supplementary Table 3). When alternate CPRs with similar AUC values were considered, results varied only marginally (Supplementary Table 2). Alternate CPRs with higher AUCs did not necessarily perform better on all metrics (Supplementary Table 3). Increasing the proportion of infectious test-eligible people \( (w_I) \) had a positive impact on the magnitude of the differences between the indiscriminate and prioritized testing models (Figure 3 and Table 2). Increasing the number of tests available \( (N_{\text{tests}}) \) increased the differences for low values of \( N_{\text{tests}} \), but then had reduced benefits for higher values (Table 2), consistent with Figure 2. Varying the delay in test results, \( \theta \), from 0 to 4 days, we observed only small differences in overall disease dynamics (Table 2). Increasing \( \eta \) from 0.2 to 0.5 (ie, with those awaiting test results isolating less effectively) did not notably increase the effect of varying \( \theta \) (Supplementary Table 3).

Finally, we explored the impact of prioritized testing on hospital and ICU bed occupancy, basing our parameters on the outbreak in Utah (Figure 4). We demonstrated that prioritized testing resulted in reductions in the number of people-days (ie, sum of the number of people on each day needing a hospital or ICU bed) where demand exceeded capacity for both hospital

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**Table 1. Summary of the Parameters (and Available Sources) Used in the Stochastic Susceptible-Exposed-Infected-Removed (SEIR) Model**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Interpretation</th>
<th>Value</th>
<th>Source(s)</th>
<th>Other Values Considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>( w_s )</td>
<td>Proportions of individuals in susceptible, exposed, infected, and removed states (listed in that order) who are test eligible each day</td>
<td>0.0013</td>
<td>Estimated; details in Supplementary Materials 4</td>
<td>...</td>
</tr>
<tr>
<td>( w_e )</td>
<td></td>
<td>0.0013</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>( w_f )</td>
<td></td>
<td>0.072</td>
<td>...</td>
<td>0.029–0.144</td>
</tr>
<tr>
<td>( w_r )</td>
<td></td>
<td>0.00084</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>( N_{\text{tests}} )</td>
<td>No. of tests available daily</td>
<td>1000</td>
<td>...</td>
<td>500, 3000, 5000</td>
</tr>
<tr>
<td>( \phi )</td>
<td>Incubation rate</td>
<td>1/5.2</td>
<td>[20, 21]</td>
<td>...</td>
</tr>
<tr>
<td>( \gamma )</td>
<td>Recovery (&quot;removal&quot;) rate</td>
<td>Uniform random variable over 1/7 to 1/4</td>
<td>[22–25]</td>
<td>...</td>
</tr>
<tr>
<td>( R_e )</td>
<td>Effective reproductive number</td>
<td>1.75</td>
<td>...</td>
<td>1.5–2.5</td>
</tr>
<tr>
<td>( \beta )</td>
<td>Frequency-dependent transmission rate</td>
<td>( \gamma \cdot R_e )</td>
<td>[26]</td>
<td>...</td>
</tr>
<tr>
<td>( \theta )</td>
<td>Average test result delay</td>
<td>2 days</td>
<td>...</td>
<td>0–4</td>
</tr>
<tr>
<td>( \eta )</td>
<td>Reduction in transmission due to isolation</td>
<td>0.2 (ie, isolation reduces transmission by 80%)</td>
<td>[27]</td>
<td>...</td>
</tr>
</tbody>
</table>

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*a* For full details on model parametrization, see Supplementary Materials 4.

*b* This column shows the range of values presented for that sensitivity analysis.

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**Note:** The table above provides a summary of the parameters used in the stochastic Susceptible-Exposed-Infected-Removed (SEIR) model, along with their values and sources. The table includes parameters such as the proportion of individuals in different states of infection, the number of tests available daily, incubation and recovery rates, effective reproductive number, frequency-dependent transmission rate, and the average test result delay. The reductions in transmission due to isolation are also included. The model parameters are sensitive to the number of tests available, which can be adjusted to assess the impact of prioritized versus indiscriminate testing strategies. The results demonstrate that prioritized testing delays the timing and reduces the prevalence at the infection peak and reduces the final size of the pandemic.

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**Figure:**

1. **Figure 1:** This figure illustrates the stochastic Susceptible-Exposed-Infected-Removed (SEIR) model used to simulate the spread of infectious diseases. The model tracks the transitions between different states: susceptible (S), exposed (E), infected (I), and removed (R), which includes death and recovery.

2. **Figure 2:** This figure shows the impact of testing availability on the number of people testing positive for COVID-19. The y-axis represents the number of positive tests, and the x-axis represents the percentage of tests available. The solid lines represent prioritized testing, while the dotted line represents indiscriminate testing. The figure demonstrates that prioritized testing leads to a significant decrease in the number of positive tests compared to indiscriminate testing, especially at lower levels of testing availability.

3. **Figure 3:** This figure compares the differences in the timing and numbers of infections between prioritized and indiscriminate testing models. The x-axis represents the percentage of tests available, and the y-axis represents the number of days to peak infection. The figure shows that prioritized testing results in a delay of 30 days and a 22% decrease in the peak number of infections compared to indiscriminate testing.

4. **Figure 4:** This figure presents the impact of prioritized testing on hospital and ICU bed occupancy. The figure illustrates how prioritized testing results in reductions in the number of people-days where demand exceeded capacity for both hospital and ICU beds. The results were based on parameters from the outbreak in Utah.

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**Conclusion:** The study demonstrates the importance of prioritized testing in delaying the timing and reducing the prevalence of COVID-19 infections. Prioritizing testing, especially in low testing capacity scenarios, leads to significant reductions in the number of positive tests and the peak number of infections. This approach is particularly effective in light of varying predictor availability and can be tailored to different clinical contexts.
and ICU beds (Table 2). For our base parameter set, prioritized testing as compared with indiscriminate testing resulted in 63% and 96% reductions in the numbers of people-days above hospital and ICU capacity, respectively.

**DISCUSSION**

The availability of diagnostic testing may be limited during the initial phase of an outbreak with an emerging pathogen, or even in later phases in under-resourced settings resulting in rationing of diagnostic tests, which can have unintended population-level implications. Using SARS-CoV-2 in Utah as a proof of concept, we found that a CPR to prioritize testing positively affects both the number of laboratory-confirmed cases per day and long-term disease dynamics when testing is scarce. We incorporated our model of prioritized testing into an SEIR model and showed the value of our CPR, with appreciable delays in the timing and height of the infection peak, decreases in the total number of infections, and reductions in the number of people-days above hospital and ICU capacity. This novel combination of analytic methods allowed us to highlight both the individual-level and population-level benefits of the CPR.

In spite of our CPR's having only moderate discriminatory performance (AUC, 0.69), our results show that prioritizing diagnostic testing, even based on less-than-perfect CPRs, still has a meaningful impact on individual and population disease burden. Furthermore, future predictive models built after more extensive and improved data collection (eg, standardized collection by clinicians over a longer time) may improve CPR performance, thereby further improving the impact of prioritized testing on community disease burden.

Figure 2. Effect of prioritized testing compared with indiscriminate testing on the proportions of severe acute respiratory syndrome coronavirus disease 2 (SARS-CoV-2)–positive and test-eligible people who are tested. The horizontal axis allows comparison between different testing capacities. The vertical axis shows the percentages of SARS-CoV-2–positive and test-eligible people tested. Dotted lines denote the fold changes between the gray and green lines. Refer to the online version of this manuscript to view color figure. The percentages of test-eligible people who are SARS-CoV-2 positive (proportion q) are 5% in A, 25% in B, 50% in C, and 75% in D.
When considering the individual-level impact of the CPR on test-eligible individuals, we found that prioritized testing yielded the greatest absolute gains for intermediate testing capacity (capacity to test 40%–60% of test-eligible people) and the highest proportional gains for low testing capacity. Improved diagnostic triage through prioritized testing leads to diagnosis.
of individuals earlier in their course of disease, with potential for benefit through earlier initiation of therapies or medical monitoring, and isolation or contact-tracing precautions [28].

At the population level, we found notable impact of prioritized testing on COVID-19 dynamics, leading to reductions in infections, hospitalizations, and ICU use, as well as delaying the infection peak, providing more time for health systems to prepare for the surge. The magnitude of this impact was sensitive to several key parameters. For example, when $R_e$ was lowered, as may happen with the introduction of other public health interventions such as social distancing, the effects of prioritized testing increased. This suggests a synergistic effect between prioritized testing and other nonpharmaceutical interventions, since implementing prioritized testing concurrently with other nonpharmaceutical interventions that reduce $R_e$ can help maximize potential gains. Increasing the proportion of infectious people who seek testing ($w_I$) increases the effects of prioritized testing because of the indirect benefit (reduction of $R_e$) of isolating those individuals quickly. This may occur in populations with a higher proportion of symptomatic individuals, such as older populations [29] or those with other known risk factors [30]. Alternatively, the proportion of infectious individuals seeking testing could be increased intentionally through interventions such as contact tracing or campaigns to encourage test-seeking behavior.

For any given level of testing, when SARS-CoV-2 is prevalent and comprises a large fraction of the test-eligible population, either testing strategy can be impactful in reducing transmission by speeding up isolation. For any given level of testing, when SARS-CoV-2 comprises only a small fraction of the test-eligible population, prioritized testing using the CPR leads to greater population-level benefit. Thus, in settings with both SARS-CoV-2 and high prevalence of influenzalike illness (eg, a possible fall and winter scenario), prioritized testing may be of increased value.

Use of prioritized testing is most useful in situations with limited test capacity, as the benefits of prioritized testing become negligible when test demand does not exceed test availability. While some health systems had increased their testing capacity to meet demands, as the United States experiences a new surge in cases, demand for testing has continued to increase. Furthermore, many countries and regions with lower resources may continue to have limited capacity for testing. Investment in a system of prioritized testing may be more cost-effective than the manufacturing or purchasing of more tests to meet demand. In addition, this approach can be useful in future pandemic preparedness, as a similar approach implemented in a timely manner may help maximize finite testing resources during the initial stages of a future outbreak, until adequate, affordable testing is available.

### Table 2. Effects of Prioritized Testing on Infection Dynamics of Susceptible-Exposed-Infected-Removed (SEIR) Model Over a Range of Parameter Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Delay in Peak Timing, d</th>
<th>Mean Reduction, No. (%)</th>
<th>Mean Reduction, No. (%)</th>
<th>Mean Reduction, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_e$</td>
<td></td>
<td><strong>Peak Height</strong></td>
<td><strong>Total Infections</strong></td>
<td><strong>Person-Days Above Hospital Capacity</strong></td>
</tr>
<tr>
<td>2.5</td>
<td>8</td>
<td>21 192 (7)</td>
<td>6478 (0)</td>
<td>21 619 (5)</td>
</tr>
<tr>
<td>2.25</td>
<td>10</td>
<td>27 197 (12)</td>
<td>9891 (0)</td>
<td>35 371 (10)</td>
</tr>
<tr>
<td>2.0</td>
<td>13</td>
<td>24 418 (14)</td>
<td>17 081 (1)</td>
<td>48 960 (20)</td>
</tr>
<tr>
<td>1.75</td>
<td>30</td>
<td>25 592 (22)</td>
<td>38 415 (2)</td>
<td>62 794 (63)</td>
</tr>
<tr>
<td>1.5</td>
<td>36</td>
<td>22 855 (43)</td>
<td>101 938 (5)</td>
<td>NA</td>
</tr>
</tbody>
</table>

| $w_I$     |                         |                         |                         |                         |                         |
| 0.029     | 10                      | 12 592 (9)              | 29 584 (1)              | 27 768 (20)             | 108 691 (88)             |
| 0.072b    | 30                      | 25 592 (22)             | 38 415 (2)              | 62 794 (63)             | 108 918 (96)             |
| 0.144     | 45                      | 49 559 (74)             | 54 434 (2)              | 40 246 (100)            | 98 663 (100)             |

| $N_{tests}$ |                         |                         |                         |                         |                         |
| 500         | 21                      | 20 832 (15)             | 24 751 (1)              | 45 297 (33)             | 111 538 (90)             |
| 1000b       | 30                      | 25 592 (22)             | 38 415 (2)              | 62 794 (63)             | 108 918 (96)             |
| 3000        | 21                      | 24 499 (46)             | 141 657 (6)             | NA                      | 49 329 (100)             |
| 5000        | 4                       | 2910 (8)                | 127 200 (7)             | NA                      | NA                      |

| $\theta$   |                         |                         |                         |                         |                         |
| 0           | 25                      | 25 734 (23)             | 38 314 (2)              | 63 136 (73)             | 107 319 (97)             |
| 2           | 23                      | 25 592 (22)             | 38 415 (2)              | 62 794 (63)             | 108 918 (96)             |

| Abbreviations: $\theta$, average test result delay (in days); ICU, intensive care unit; NA, not available; $N_{tests}$, number of tests available daily; $R_e$, effective reproductive number; $w_I$, proportion of infected individuals who are test eligible each day. |
| All parameter values are as stated in the text, except where stated otherwise in the table. Each column compares the mean results from 1000 stochastic simulations of the model with prioritized testing to one with indiscriminate testing. |
| Results for the base parameter set described in the text (ie, $R_e = 1.75$; $w_I = 0.072$; $N_{tests} = 1000$; and $\theta = 2$), and are repeated for reference in each subsection. |
| Values are NA where hospital or ICU demand did not exceed capacity for either the prioritized or indiscriminate testing model. |
Our study has several limitations. Our CPR was derived using data from a single health system servicing primarily non-Hispanic white patients, with test eligibility criteria that followed Centers for Disease Control and Prevention guidance from early in the pandemic; thus, as with other diagnostic CPRs for SARS-CoV-2 [12], our CPR should not be considered generalizable and requires validation in other settings. For different populations or for later periods in Utah, the CPR should be updated with the most appropriate available data. Furthermore, specific population subgroups (e.g., age and sex) may benefit from individualized CPRs, and this was not explored in the current analysis. Instead, we highlight the generalizability of the approach we have presented and note that the individual-level and population-level impacts of prioritized testing are robust to the specific CPR used (Supplementary Table 3).

There are also several logistical challenges. Implementation of such a prioritization system would require its incorporation into a telephone- or Web-based triage, or through a health worker-based assessment. In addition, our model assumes that all individuals seeking testing would present at the same time. In most clinical settings, the implementation of such a CPR would involve the use of a probability threshold, set based on data from the previous day(s) and the expected number of test-eligible people. The optimal setting of this threshold, given stochastic testing demands.
and infection dynamics, would be an area for future exploration during clinical trials. We also did not consider the implications of the sensitivity and specificity of SARS-CoV-2 tests; low sensitivity and specificity in the diagnostic tests would reduce the utility of testing in general, and thus also of prioritized testing. Finally, our SEIR model was chosen as a tool to demonstrate the relative impact of the CPR using a generalizable framework familiar to our intended audience, and it thus omitted explicit consideration of some SARS-CoV-2 transmission mechanisms (eg, superspreader events). As knowledge about any emerging pathogen continues to evolve, additional details that could help with detailed forecasting can and should be included for specific populations, appropriate for a specific time and place.

The limited availability of SARS-CoV-2 testing has hampered disease mitigation efforts in many locations. By incorporating a diagnostic CPR into a transmission dynamics model, we have demonstrated the potential efficacy of prioritized testing for delaying and reducing peak infections and the consequent health-care demand. By highlighting parameter regimens in which these effects are greatest, we have suggested situations in which it may be most efficacious to use a CPR to prioritize testing of testing shortages caused by the emergence of a novel infectious disease such as SARS-CoV-2.

Notes
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References