Singapore Management University

Institutional Knowledge at Singapore Management University

Research Collection Lee Kong Chian School Of Business

Lee Kong Chian School of Business

3-2022

On the test accuracy and effective control of the COVID-19 pandemic: A case study in Singapore

Guang CHENG National University of Singapore

Sarah Yini GAO Singapore Management University, yngao@smu.edu.sg

Yancheng YUAN Hong Kong Polytechnic University

Chenxiao ZHANG

Zhichao ZHENG Singapore Management University, DANIELZHENG@smu.edu.sg

Follow this and additional works at: https://ink.library.smu.edu.sg/lkcsb_research

Part of the Asian Studies Commons, Operations and Supply Chain Management Commons, and the Public Health Commons

Citation

CHENG, Guang; GAO, Sarah Yini; YUAN, Yancheng; ZHANG, Chenxiao; and ZHENG, Zhichao. On the test accuracy and effective control of the COVID-19 pandemic: A case study in Singapore. (2022). *INFORMS Journal on Applied Analytics*. 1-15.

Available at: https://ink.library.smu.edu.sg/lkcsb_research/6985

This Journal Article is brought to you for free and open access by the Lee Kong Chian School of Business at Institutional Knowledge at Singapore Management University. It has been accepted for inclusion in Research Collection Lee Kong Chian School Of Business by an authorized administrator of Institutional Knowledge at Singapore Management University. For more information, please email cherylds@smu.edu.sg.

On the Test Accuracy and Effective Control of the COVID-19 Pandemic: A Case Study in Singapore

Guang Cheng,^a Sarah Yini Gao,^{b,*} Yancheng Yuan,^c Chenxiao Zhang,^b Zhichao Zheng ^b

^aInstitute of Operations Research and Analytics, National University of Singapore, Singapore 117602; ^bLee Kong Chian School of Business, Singapore Management University, Singapore 178899; ^cDepartment of Applied Mathematics, The Hong Kong Polytechnic University, Hong Kong *Corresponding author contact: yngao@smu.edu.sg

Published in INFORMS JOURNAL ON APPLIED ANALYTICS https://doi.org/10.1287/inte.2022.1117

Abstract. This study examines the impact of coronavirus disease 2019 (COVID-19) test accuracy (i.e., sensitivity and specificity) on the progression of the pandemic under two scenarios of limited and unlimited test capacity. We extend the classic susceptible–exposed–infectious–recovered model to incorporate test accuracy and compare the progression of the pandemic under various sensitivities and specificities. We find that high-sensitivity tests effectively reduce the total number of infections only with sufficient testing capacity. Nevertheless, with limited test capacity and a relatively high cross-infection rate, the total number of infected cases may increase when sensitivity is above a certain threshold. Despite the potential for higher sensitivity tests to identify more infected individuals, more false positive cases occur, which wastes limited testing capacity, slowing down the detection of infected cases. Our findings reveal that improving test sensitivity alone does not always lead to effective pandemic control, indicating that policymakers should balance the trade-off between high sensitivity and high false positive rates when designing containment measures for infectious diseases, such as COVID-19, particularly when navigating limited test capacity.

Keywords: COVID-19, test sensitivity, test specificity, infections

Introduction

Coronavirus disease 2019 (COVID-19) broke out in late2019 and spread globally within weeks with more than 99.7 million confirmed cases and 2.1 million deaths worldwide as of January 26, 2021. One of the major challenges of pandemic containment is effective and efficient detection of infected individuals. Currently, various tests are used to detect COVID-19, and the real-time reverse transcription-polymerase chain reaction (RT-PCR) assay is one of the most widely adopted (Sidiq et al.2020). As with all medical tests, test accuracy is a crucial determinant of effective COVID-19detection (Winichakoon et al.2020). Two key measures of test accuracy, sensitivity and specificity, are defined by the probabilities of infected and noninfected individuals being correctly classified. Ideally, tests with both high sensitivity and specificity are preferred. However, sensitivity is typically inversely associated with specificity. That is, a high-sensitivity test may adversely lead to more noninfected individuals mis-classified as positive (i.e., false positives). By contrast, ahigh-specificity test can result in more infected individuals being undetected (i.e., false negatives). In the context of COVID-19, false

negatives are highly undesirable as they lead to undetected cases. High-sensitivity tests are, thus, acclaimed as one of the approaches toward effective control of the pandemic. Since the outbreak of COVID-19, substantial efforts have been made to improve test sensitivity (Han et al.2020, Wyllie et al.2020). However, the downside of high sensitivity would be more false positives that cause unnecessary quarantine and contact tracing and result in a waste of limited public resources, preventing those in need from receiving essential healthcare services. Furthermore, false positive individuals are then exposed to crossinfection risk in centralized quarantine facilities (Jing and Li2020, Kirk-Bayley et al. 2020, Wangetal.2020), leading to additional infections in healthy individuals. Unnecessary quarantine also causes psychological and economic burdens. Nonetheless, limited research is developed to understand and balance the trade-offs between sensitivity and specificity for disease control. The analysis of the trade-offs is further complicated by different characteristics of the disease at different stages of transmission, government control policies, and the availability of healthcare resources.

This study aims to examine the impact of COVID-19 test sensitivity and specificity on various outcomes (e.g., total detected cases and total infected patients) and transmission patterns. We develop an epidemic model based on the classic susceptible–exposed–infectious–recovered (SEIR) model (Hethcote 2000) to capture underlying transmission dynamics and estimate COVID-19 progression. Our results provide a thorough understanding and important insights on the impact of test sensitivity and specificity on infectious disease control, particularly when societies gradually open up with large-scale testing.

In the remainder of this paper, we first introduce the study methods—in particular, the study materials and our modified SEIR model as well as the parameters estimation approach. In what follows, we show the results on performance of the model and the impact of test sensitivity under various scenarios. Finally, we discuss the findings and provide our conclusions regarding the implications of the findings of the study.

Research Methodology and SEIR Model

Our study is based on the progression of COVID-19 in Singapore. Pandemic data were collected from the daily case reports published by the Ministry of Health (MOH), Singapore.

Background and Study Population

As the main transportation hub and one of the most popular travel destinations in Southeast Asia, Singapore identified more than 59,000 cases as of January 26, 2021. On February 17, 2020, Singapore implemented a stay home notice (SHN) of 14 days for residents and long-term pass holders returning to Singapore from mainland China, which was extended to all world travelers on March 21, 2020. Individuals were barred from leaving their residences during the SHN and were required to be tested before the end of the SHN. On April 3, 2020, a nationwide partial blockade called circuit breaker (CB) was announced to curb the spread of COVID-19 in Singapore, compelling the closure of nonessential workplaces from April 7, 2020. On May 19, 2020, the Multi-Ministry Taskforce announced that Singapore would exit CB by June 1 and resume its activities safely following a three-phase plan-namely, safe reopening (phase 1), safe transition (phase 2), and safe nation (phase 3). The first phase began on June 2, 2020. Economic activities that did not pose a high risk of transmission were gradually reopened, whereas social, economic, and recreational activities of higher risk remained closed. The second stage began on June 19, 2020, allowing social gatherings of up to five people. Phase 3 was initiated on December 28, 2020, after which the limit on group size for the social gathering was increased to eight.

In Singapore, infected cases are classified into three groups: imported cases, migrant workers residing in dormitories, and community cases. Imported cases refer to infected individuals who enter Singapore regardless of nationality. Given the entry policies mentioned in the previous paragraph, most imported cases did not affect local transmission. Migrant workers live in purpose-built or factory-converted dormitories that are located far from local residences and rather isolated from the community. Thus, the transmission pattern in this cohort differs from that of community cases. In addition, as dormitory cohorts are predominantly young and have no major comorbidities, their risk of serious complications and death is lower than that of the general population (David 2020). By January 24, 2021, none of the 29 death cases in Singapore are from dormitories. Hence, in this paper, we specifically focus on analyzing the disease transmission in the community in Singapore.

Data

The COVID-19–related statistics are publicly reported by MOH on a daily basis, including the number of daily detected cases and deaths. Because we only consider community transmission, data from March 29, 2020 (when MOH started to report dormitory and community cases separately) to January 24, 2021, are included. Data in the last two weeks are used for the out-of-sample test, and the rest are used as the training data to estimate model parameters. The projection error is characterized by mean absolute percentage error (MAPE).

SEIR Model

We extend the classic SEIR model (Hethcote 2000) to capture the impact of test sensitivity and specificity on the evolution of the COVID-19 pandemic. Figure 1 presents the main structure of the proposed model. The compartments in our model are listed as follows:

• *Susceptible* (S): The general populace that is susceptible to the disease and has not been infected.

• *Exposed* (E): Individuals who are infected and within the incubation period (asymptomatic).

• *Infected* (I): Individuals who are infected and have developed symptoms.

• *Recovered* (R): Individuals who have recovered from the disease, including those in the late stage of the disease who are not infectious.

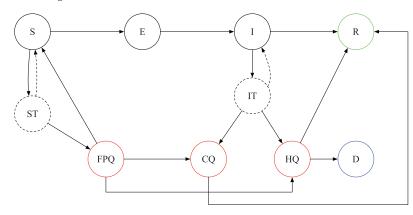
• *Death* (D): Individuals who died from the disease.

• *Susceptible in test* (ST)/*Infected in test* (IT): Susceptible/infected individuals who seek COVID-19 tests.

• *Community quarantined* (CQ)/*Hospital quarantined* (HQ): Individuals who are infected and quarantined in community/hospital units.

• *False positive and quarantined* (FPQ): Individuals who are not infected but are identified as positive and quarantined in the community.

Figure 1. (Color online) Flow Diagram



The FPQ compartment is included to capture the negative effect of false positive test outcomes. We also introduce two pseudocompartments, ST and IT, to capture the effect of COVID-19 tests at different disease stages. These components allow us to model all the possible outcomes of the tests—namely, true negatives, false positives, true positives, and false negatives. The CQ and HQ compartments are added to capture the paths of detected patients. Before elaborating on the dynamics of the model, we first discuss the assumptions of the model.

1. The entire population that has not been infected is susceptible to the virus. Currently, there is no evidence showing that any subgroup of people is immune to the virus. This assumption is also made in other studies modeling the pandemic (Giordano et al. 2020, Kucharski et al. 2020, Li et al. 2020, Zou et al. 2020).

2. All infected individuals are contagious, including those who are in the incubation period. Various reports confirm that patients in the incubation period can transmit the virus to others (Liu et al. 2020a, Rothe et al. 2020). Hence, we consider both compartments E and I as sources of transmission in our model.

3. It is well-recognized that some infected patients can recover without any treatment (Das 2020, Xu et al. 2020).

4. Only patients admitted to hospitals may die because of the infection. Patients with severe symptoms are quarantined in hospitals and receive supportive treatment. This assumption is consistent with the circumstances in Singapore, wherein all deaths in community cases are from hospitalized cases. However, the model can easily be extended to allow patients in other compartments to move to the death compartment to fit the situations in other countries or regions.

5. Recovered patients are immune to the virus. As of the writing of this paper, there are very few reinfected cases. This assumption is also commonly assumed in the literature to avoid overfitting (Giordano et al. 2020, Kucharski et al. 2020, Zou et al. 2020). 6. Patients who are mistakenly identified as having COVID-19 infection are initially quarantined in the community. Because, in reality, such individuals are not infected, they typically do not exhibit severe symptoms. Given the scarcity of healthcare resources, they would not be quarantined in hospitals. Such policies are observed in Singapore and many other countries and regions.

7. Patients quarantined in the community would not be transferred to hospitals. That is, infected patients with mild symptoms do not develop severe deterioration. Recent research suggests that patients who develop severe COVID-19 symptoms have a different interferon response (Hadjadj et al. 2020, Lee and Shin 2020), which is a component of innate immunity. Thus, mild infections rarely deteriorate to severe cases. A similar assumption is also made in the literature (Li et al. 2020).

The dynamics of our model are next discussed in detail. The susceptible cohort can contact exposed and/ or infected individuals, thus becoming exposed. On the other hand, susceptible individuals might develop COVID-19-like symptoms and seek a COVID-19 test, thus entering the ST compartment. Because the test is not perfectly accurate, some non-COVID-19 cases might be misidentified as infected (i.e., false positives) and would subsequently be subject to community quarantine. To differentiate this cohort from true positives, false positive individuals enter the FPQ compartment instead of CQ. In quarantine facilities, false positive cases can be infected from exposure to infected patients; thus, some of them could become true infections and might enter compartments CQ or HQ if their health conditions deteriorate. The rest of the uninfected individuals who are correctly identified return to the susceptible compartment. Exposed individuals gradually pass the incubation period and enter the infected compartment. A proportion of infected patients might seek COVID-19 tests (compartment IT in Figure 1). Similarly, they might be mistakenly identified as uninfected (i.e.,

 Table 1. Model Parameters

Parameter	Explanation	Default value
α	Basic infection rate	
β	Cross-infection rate in quarantine facilities	
$\gamma(t)$	Government response factor	
$p_d(t)$	Mortality risk	
$p_i(t)$	The probability that a susceptible individual contacts an infected patient	
$p_{ci}(t)$	The risk of cross-infection in community quarantine facilities	
r _a	Rate of governmental action	
ta	Median days of governmental action	
m _i	Magnitude of resurgence	
t_i	Peak time of resurgence	
σ_i	Rate of resurgence	
p_{d0}	Initial mortality risk	
r _{dde}	Rate of decay in mortality risk	
r_t	Rate of test	$\log 2/2$
r _b	Rate of false positive patients passing the test	$\log 2/(3/(1-p_{fp}))$
r _i	Rate of infections leaving incubation phrase	$\log 2/5$
r _{ri}	Rate of recovery out of hospital	$\log 2/10$
r _{rh}	Rate of recovery in hospital	$\log 2/15$
r _d	Rate of death	
p _{fp}	False positive rate (1 – specificity)	0.024
p_{tp}	True positive rate (sensitivity)	0.843
p _{ts}	Proportion of individuals in S being tested	
p _{ti}	Proportion of symptomatic individuals in I being tested	
p_h	Proportion of detected cases being quarantined in hospital	0.15

false negatives) and, consequently, return to the community. True positives would be quarantined in either community facilities or hospitals, depending on their health conditions, thus entering compartments CQ or HQ. All of the patients in CQ would gradually recover following our assumption tailored to the Singapore context. A proportion of HQ individuals with severe conditions might die from the infection, whereas the rest will eventually recover.

Table 1 summarizes the parameters in our model. Particularly, two parameters vary with time *t*. The parameter $\gamma(t)$ measures the impact of the government response to disease transmission. When the government implements intervention policies, such as social distancing, the infection rate is controlled to a lower level than the basic infection rate. When the epidemic is controlled at an acceptable level, the government gradually lifts the imposed restrictions, and the infection rate increases again. We model this factor as an arctangent function along with an exponential correction introduced by Li et al. (2020):

$$\gamma(t) = \frac{2}{\pi} \arctan\left[-\frac{r_a(t-t_a)}{20}\right] + 1 + m_j \exp\left[-\frac{(t-t_j)^2}{2\sigma_j^2}\right],$$

where r_a is the rate of action that measures the strength of the governmental policies and t_a captures the median days of action. The last term of this equation models the jump resulting from lifting restrictions, in which m_i represents the magnitude of the jump, t_i indicates the time of the peak, and σ_j controls the rate of the resurgence.

We use $p_d(t)$ to characterize the mortality risk. Because of the increasing test capacity over time, more mild cases could be identified. Along with improved quality of medical care, the mortality risk decreases over time. We specify $p_d(t)$ as follows:

$$p_d(t) = p_{d0} \left[\frac{2}{\pi} \arctan\left(-\frac{t \cdot r_{dde}}{20} \right) + 1 \right]$$

where p_{d0} represents the initial mortality risk and r_{dde} captures the rate of decay in COVID-19–related mortality risk. Note that the lower bound of the mortality function is zero, indicating that the mortality risk could decrease close to zero as better treatment and a vaccine become available.

The system dynamics are characterized by the following differential equations:

$$\begin{split} & \left(\frac{dS(t)}{dt} = r_b [1 - p_{ci}(t)] FPQ(t) - \alpha \gamma(t) p_i(t) S(t) - r_t p_{ts} p_{fp} [1 - p_i(t)] S(t), \\ & \frac{dE(t)}{dt} = \alpha \gamma(t) p_i(t) S(t) - r_i E(t), \\ & \frac{dI(t)}{dt} = r_i E(t) - r_t p_{ti} p_{tp} I(t) - r_{ri}(1 - p_{ti} p_{tp}) I(t), \\ & \frac{dFPQ(t)}{dt} = r_t p_{ts} p_{fp} [1 - p_i(t)] S(t) - \beta p_{ci}(t) FPQ(t) - r_b [1 - p_{ci}(t)] FPQ(t), \\ & \frac{dCQ(t)}{dt} = \beta p_{ci}(t) (1 - p_h) FPQ(t) + r_t p_{ti} p_{tp} (1 - p_h) I(t) - r_{ri} CQ(t), \\ & \frac{dHQ(t)}{dt} = \beta p_{ci} p_h FPQ(t) + r_t p_{ti} p_{tp} p_h I(t) - r_{rh} [1 - p_d(t)] HQ(t) - r_d p_d(t) HQ(t), \\ & \frac{dRt}{dt} = r_i (1 - p_{ti} p_{tp}) I(t) + r_{ri} CQ(t) + r_{rh} [1 - p_d(t)] HQ(t), \\ & \frac{dD(t)}{dt} = r_d p_d(t) HQ(t), \end{split}$$

where

$$p_{ci}(t) = \frac{CQ(t)}{FPQ(t) + CQ(t)},$$
$$p_i(t) = \frac{E(t) + I(t)}{N(t)},$$

and

$$N(t) = S(t) + E(t) + I(t) + R(t).$$

Parameter Calibration and Estimation

We calibrate our model parameters using both the data collected in Singapore and the following validated values from the literature:

• r_t is defined as $\log 2/T_t$, where T_t is the median duration of the test, and we set $T_t = 2$ days in accordance with Li et al. (2020).

• r_i is defined as $\log 2/T_i$, where T_i is the median duration of the incubation phase, and we set $T_i = 5$ days in accordance with Lauer et al. (2020).

• r_{ri} is defined as $\log 2/T_{ri}$, where T_{ri} is the median time of recovery without hospital care, and we set $T_{ri} = 10$ days in accordance with Li et al. (2020).

• r_{rh} is defined as $\log 2/T_{rh}$, where T_{rh} is the median time of recovery in the hospital, and we set $T_{rh} = 15$ days in accordance with Liu et al. (2020b) and Cao et al. (2020).

• p_{fp} and p_{tp} were set as 0.024 and 0.843, following the meta-analysis by Bastos et al. (2020).

• We set $p_h = 15\%$ in accordance with Li et al. (2020).

Other parameters are estimated by minimizing the following MAPE of daily detected cases and mortality using the training data set:

$$l(\theta) = \sum_{t=1}^{T} w_t [\log (\hat{AC}_t + c) - \log (AC_t + c)]^2 + \lambda \sum_{t=1}^{T} w_t [\log (\hat{D}_t + c) - \log (D_t + c)]^2,$$

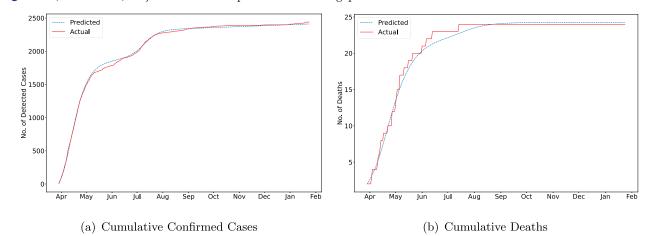
where \hat{AC}_t and AC^t represent predicted and actual cumulative detected cases, excluding deaths, respectively. We use θ to denote all the unknown parameters we need to learn from data. We add a constant c to ensure numerical stability, and w^t is the weight on the observation at time t. Because errors in recent epochs have a more significant impact on future evolution than errors in the early stage, w^t is increasing in t. In the work by Li et al. (2020), w^t is set as t. However, for any linear weight function w^t , the data at early days would have little impact on the parameter fitting when the time window is large as in our case. Therefore, in our study, we set $w_t = \log(t+1)$. We also test the case that $w^t = t$, and the results are consistent with what we report in the paper. The parameter λ is the weight of the deaths in the objective function. Given the initial states, AC_t and \hat{D}_t can be characterized as functions of the parameter θ . Note that some of the initial states, E_0 , I_0 , R_0 , are also unobservable. They are included in the parameter set θ . The estimation problem is solved by the trust region method.

Projection Results and Impact Analysis

In this section, we first present the pandemic projection from our model as a validation of the proposed model. We then conduct counterfactual analyses to investigate the impact of COVID-19 test accuracy on different outcomes by varying the two accuracy parameters p_{tp} and p_{fp} .

Model Validation

The parameters are estimated using data from March 29, 2020, to January 10, 2021, containing 288 successive observations. The data in the following two weeks are used for the out-of-sample test. Figure 2 presents the projected number of cumulative detected cases and deaths in our model against the actual values. By incorporating detected cases and deaths separately in the objective function, our model exhibits a nice fit



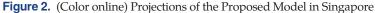


Table 2. MAPE of the Projections

Sample	Detected cases	Deaths
In sample, %	1.53	3.09
Out of sample, %	1.08	1.84
Total, %	1.51	3.03

with relatively small MAPEs. The in- and out-of-sample MAPEs are summarized in Table 2.

Impact of Test Sensitivity and Specificity

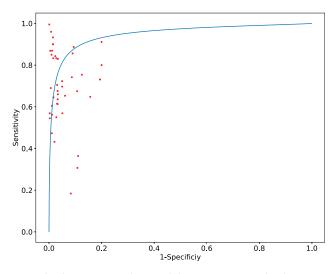
In the counterfactual analyses, we simulate the disease progression using our model with previously estimated parameters under varying levels of sensitivity and specificity. We consider two key outcomes: the total numbers of infected and detected cases. The number of infected cases represents the scale of the pandemic. The number of detected cases, including both true and false positives, reflects the burden on public healthcare resources as all the detected cases should be quarantined. While containing the spread of the pandemic, unnecessary waste should be reduced, and overutilization of healthcare resources should be avoided, which might also lead to negative outcomes and create barriers for patients in need of healthcare resources. Besides these two key factors, other outcome measurements in specific scenarios are also monitored. For example, we report the total number of hospitalization days (i.e., the number of days that all hospitalized patients stay in hospitals) to capture consumption of hospital resources.

Varying Sensitivity and Specificity. There is a wide range of reported values for sensitivity and specificity of the RT-PCR test in the literature. We adopt the commonly used method introduced by Littenberg and Moses (1993) to characterize the inverse relationship between sensitivity and specificity from reported numbers:

Sensitivity =
$$\frac{1}{1 + \frac{1}{e^{b/(1-a)} \cdot \left(\frac{\text{Specificity}}{1 - \text{Specificity}}\right)^{(1+a)/(1-a)}},$$

where *a* and *b* are parameters associated with the test. As shown by Littenberg and Moses (1993), the parameters can be estimated from empirical data via linear regression. We use pairwise values of sensitivity and specificity of the RT-PCR test summarized in (Bastos et al. 2020) to learn *a* and *b*, which are estimated as a = -0.15 and b = 4.18. Figure 3 shows the estimated summary receiver operating characteristic curve from which we generate a set of sensitivity–specificity pairs and investigate their impact on the pandemic.

Figure 3. (Color online) Receiver Operating Characteristic Curve Fitted from Data

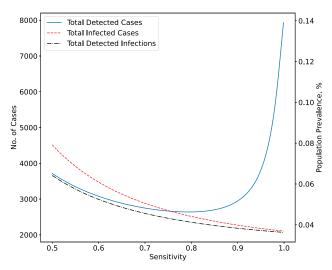


Note. The dots represent the actual data points reported in literature, and the line is the fitted receiver operating characteristic curve.

Scenario with Unlimited Test Capacity. We first examine the impact of test sensitivity (and specificity) on pandemic control and resource consumption in the case of unlimited test capacity. We run our model simulation from March 29, 2020, to January 24, 2021—302 days in total. Figure 4 presents the total numbers of infected cases, detected cases, and detected infections (true positives) with sensitivity varying from 0.5 to 0.99.

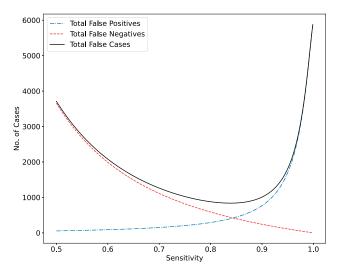
We observe that the total number of infected cases decreases as sensitivity increases. Because a high-sensitivity test detects more infected patients, subsequently, fewer

Figure 4. (Color online) The Impact of Test Accuracy on Total Cases



Notes. The solid line corresponds to the total number of detected cases, the dashed line to the total number of truly infected cases, and the dash-dot line to the total number of detected infections being identified. The right *y*-axis represents the population prevalence corresponding to the left *y*-axis.

Figure 5. (Color online) The Impact of Test Accuracy on Total Errors



Note. The dashed line corresponds to the total number of false negatives, the dash-dot line to the total number of false positives, and the solid line to the total number of falsely identified cases.

susceptible individuals are exposed to and infected by the virus. The total number of hospitalizations and the total number of deaths exhibit trends similar to those of the total number of infected cases for the same reason. These results are shown in Figures A.1 and A.2. We also observe that the total number of detected infections decreases as sensitivity increases. In this case, although increasing sensitivity detects a larger proportion of infected patients, the decreasing effect on the number of infected cases dominates.

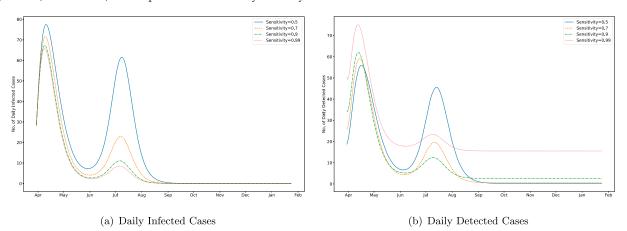
The total number of detected cases first decreases as sensitivity increases. When sensitivity is higher than a certain level (approximately 0.85), the total number of detected cases begins to rise as sensitivity further increases. As discussed in the previous paragraph, a test with higher sensitivity can help control the spread of the disease and reduce the total number of infections, whereas higher sensitivity produces lower specificity, resulting in additional false positive cases being quarantined. When sensitivity is too high (i.e., approximately 0.85), the increase in false positives dominates the reduction in the number of infected cases, leading to an increase in the number of the total detected cases. This is further confirmed by the trends in the total numbers of false positives and negatives under different sensitivity levels in Figure 5. Increasing sensitivity leads to more infected cases being detected (fewer false negatives) and also more uninfected people being quarantined (more false positives). The total number of falsely identified cases results in a U-shaped curve against sensitivity.

To investigate the impact of test accuracy on the transmission pattern, we plot daily cases (e.g., daily detected and infected cases) under different values of sensitivity in Figure 6. Note that a second-wave transmission began in early June, which corresponds to phase 3 reopening in Singapore. As is discussed later, different sensitivity levels exhibit different impacts on the two waves.

In terms of daily infected cases (Figure 6(a)), a high-sensitivity test effectively controls the disease transmission in the first wave. With such early containment, the second wave is significantly mild. Notably, for daily detected cases (Figure 6(b)), the impact of sensitivity on the two waves of disease spread differs. In the first wave, the number of daily detected cases at the beginning of the pandemic is high with a high-sensitivity test because of more individuals testing positive. Although this results in high demand on quarantine facilities in the first wave, most infected patients are identified and guarantined, and the pandemic can be effectively controlled. However, as sensitivity becomes too high (e.g., 0.99), the number of daily detected cases in the second wave would increase because of more false positives.

We further analyze the workload of quarantine and hospital facilities under different levels of sensitivity.

Figure 6. (Color online) The Impact of Test Accuracy on Daily Cases





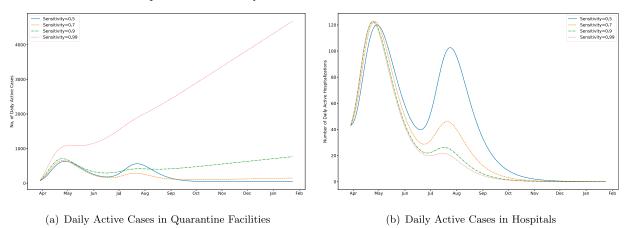
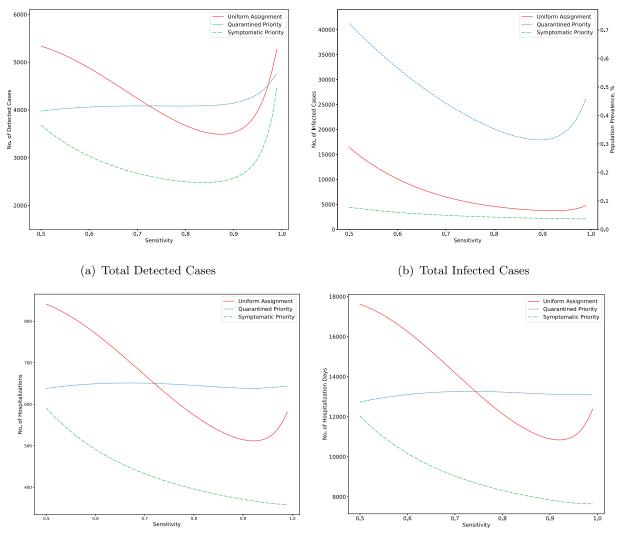


Figure 8. (Color online) The Impact of Test Accuracy on the Pandemic Under a Test Capacity Constraint with a Daily Test Capacity of 400



(c) Total Hospitalized Cases

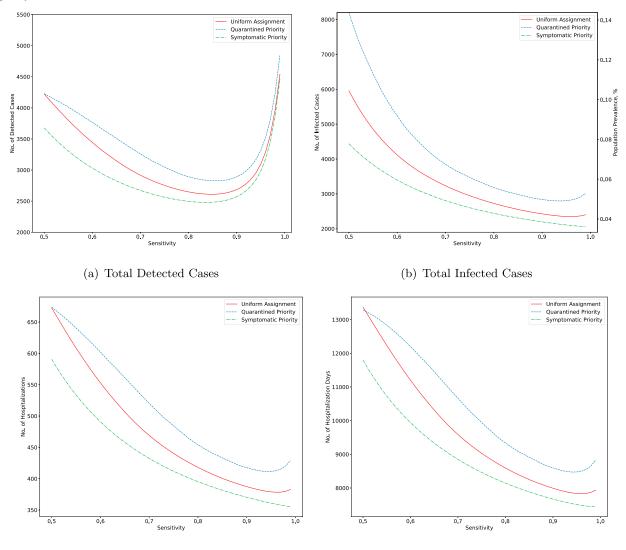
(d) Total Hospitalization Days

Notably, increasing test sensitivity results in different implications on the workloads of quarantine and hospital facilities. In Figure 7, the workload of quarantine facilities might substantially increase because of a large number of false positives if the test sensitivity is too high. In terms of daily active hospitalizations, sensitivity level does not affect much initially. However, after reopening, lower sensitivity would generally result in more active cases because of less effective containment during the first wave, leading to increasing infected cases and hospitalizations in the second wave.

Scenario with Limited Test Capacity. Our base model assumes that enough test kits are available to handle daily test demand. This is the case in Singapore, wherein sufficient test kits are in place as of May 2020. However, in most situations, particularly during the early stage of

the pandemic, testing capacity is limited. Hence, it is crucial to analyze the transmission pattern under different capacity constraints to provide broader implications. We extend our model by imposing a daily test capacity constraint. If the number of individuals demanding a test exceeds capacity, the excess demand is delayed to the next day and so on. In this case, the guarantined cohort also requires daily tests to enable healthcare workers to decide whether an infected patient has recovered and can be discharged from a quarantine facility. Those who recover from the disease as well as those with false positive cases can be blocked in quarantine facilities if there is no access to test kits. The test kits are assigned in accordance with three policies: symptomatic priority (SP), quarantined priority (QP), and uniform assignment (UA). The SP policy prioritizes tests for symptomatic patients (i.e., among patients in ST and IT compartments),

Figure 9. (Color online) The Impact of Test Accuracy on the Pandemic Under a Test Capacity Constraint with a Daily Test Capacity of 600



(c) Total Hospitalized Cases

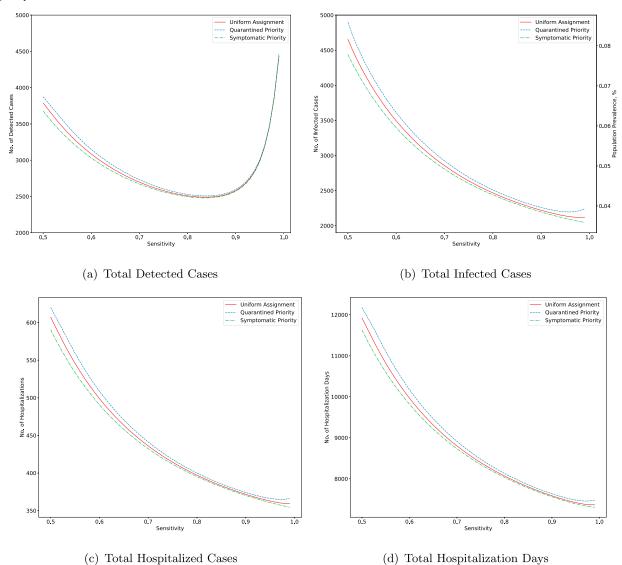
(d) Total Hospitalization Days

subsequently assigning the remaining capacity to quarantined patients (i.e., patients in FPQ, CQ, and HQ compartments). The QP policy inversely prioritizes test kits compared with the SP policy. As a benchmark, the UA policy allocates test kits to all demands with equal probability. We examine the results under three levels of daily test capacities: 400, 600, and 800. We simulate disease transmission for a one-year period and stop the simulation whenever the number of exposed and infected patients falls to 10 or fewer. The main results are presented in Figures 8–10.

We find that, if test capacity is low, the impact of sensitivity on the total number of infected cases is no longer monotone under UA and QP policies (subfigures (b) in Figures 8–10). When sensitivity exceeds 0.9, the number of infected cases gradually increases as sensitivity increases. This simulation study reveals that a high-sensitivity test might lead to an inferior disease control under UA or QP policies under limited test capacity. We also notice that, under the SP policy, the number of infected cases remains a decreasing trend, and this policy dominates the other two in all the other metrics (subfigures (a), (c), and (d) in Figures 8–10). Therefore, our results illustrate a promising policy that government should consider adopting: using high-sensitivity test kits and prioritizing individuals with symptoms.

Scenario with a High Cross-Infection Rate. The cross-infection rate estimated in our model is very small ($\beta = 0.001$). Nonetheless, cross-infection is one of the main concerns regarding the pandemic in other countries (Gan et al. 2020, Zheng et al. 2020, Zhou et al. 2020).

Figure 10. (Color online) The Impact of Test Accuracy on the Pandemic Under a Test Capacity Constraint with a Daily Test Capacity of 800



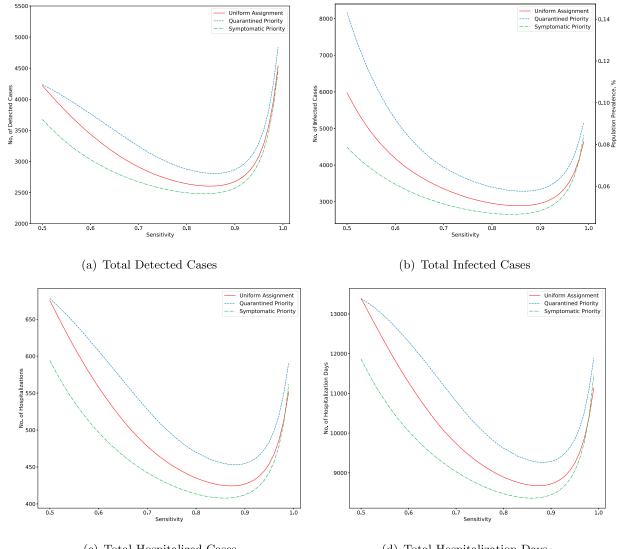


Figure 11. (Color online) The Impact of Test Accuracy on the Pandemic Under a Medium Test Capacity Constraint and a Higher Cross-Infection Rate

(c) Total Hospitalized Cases

(d) Total Hospitalization Days

Thus, we further investigate the impact of test sensitivity with limited test capacity under a relatively higher cross-infection rate. Particularly, we set the cross-infection rate $\beta = 0.1$ and repeat the previous analysis.

As shown in Figure 11, we find that, even under the SP policy, the total number of infected cases no longer decreases as sensitivity increases. More healthy individuals are quarantined and cross-infected in the quarantine facilities because of the high false positive rate associated with high sensitivity. High sensitivity coupled with a high cross-infection rate may fail to control the pandemic, resulting in more infected cases. Moreover, the SP policy does not dominate the UA policy in terms of the total infected cases when test sensitivity is extremely high (i.e., above 0.98). This is

due to delays in identifying and releasing false positives from quarantine facilities, which leads to more crossinfections. As shown in Figure 11, we also observe that a sensitivity of approximately 0.85 is nearly optimal under all three prioritized policies.

Conclusion and Discussion

COVID-19 tests have an essential role in the containment of the pandemic. A stream of research is devoted to improving sensitivity (Han et al. 2020, Wyllie et al. 2020). However, there remains insufficient analysis regarding whether higher test sensitivity could lead to more effective and efficient control of the disease. The impact of test sensitivity on the evolution of the pandemic remains largely understudied. In this study, we investigate the impact of sensitivity on the progression of the pandemic, discovering that improving test sensitivity is not always beneficial even in total infected cases when quarantine facilities cannot effectively isolate individuals.

We first develop a transmission model that captures both test sensitivity and specificity. The dynamics of false positive and negative cases are included in the proposed model. The model parameters are estimated using historical data from Singapore. Projection results validate that the proposed model captures the reality well. Based on the model, we conduct counterfactual simulation analyses to examine the impact of sensitivity in different scenarios.

Under the scenario of unlimited test capacity, the number of infected cases decreases as sensitivity increases. This is intuitive as most infected patients can be identified at the beginning of the pandemic, which could effectively control the disease. Nevertheless, the number of detected cases increases as sensitivity increases above 0.8. Particularly, it grows exponentially when sensitivity is beyond 0.9, whereas the number of infected cases decreases marginally. Having such high test sensitivity would cause unnecessary stress for the government to quarantine a large number of detected cases, which can potentially act as a barrier for infected patients' accommodation in quarantine facilities.

We further examine the scenario of limited test capacity. We consider three assignment policies: UA, QP, and SP. Under UA and QP policies, the number of infected cases no longer monotonically decreases as sensitivity increases. Increasing sensitivity leads to lower specificity, which implies more false positive cases that sequentially require a large number of test kits for retesting and confirmation. Such a large number of false positive cases can be a barrier to timely testing for those who are truly infected, consequently causing more individuals to become infected. Under the SP policy, the trade-off is not as straightforward. The SP policy could potentially lead to more false positives with high sensitivity by testing more symptomatic cases, whereas by prioritizing test kits for symptomatic cases, infected patients could be detected with shortened testing delay. In the Singapore context, with an extremely low crossinfection rate, the benefit of timely testing for symptomatic cases dominates the drawback of increased false positives. Thus, the results under the SP policy are consistent with the unlimited test capacity scenario: increasing sensitivity helps control the pandemic by reducing the number of infected cases. Our findings suggest that policymakers should consider assigning the highest priority of testing for symptomatic individuals.

The results under the scenarios with a high crossinfection rate confirm our previous analysis. When the cross-infection rate becomes relatively higher, which could be the case in countries or regions with inadequate resources, the number of infected cases also exhibit a U-shaped relationship with sensitivity under the SP policy. The negative impact of increasing false positives gradually dominates the benefit of timely detection owing to more cross-infections in quarantine facilities crowded with both false and true positive cases. In this case, further increasing sensitivity leads to ineffective control of the pandemic. Our results suggest that a median level of sensitivity (i.e., 0.8–0.85), coupled with SP policy, can effectively and efficiently help control the disease spread.

It is worth highlighting several inherent limitations of the SEIR model and their implications on our results. First, the SEIR framework assumes a homogeneous population. Therefore, the parameter values we used or estimated in the model represent the population average. It might not be able to capture the heterogeneous factors, such as population-specific infection rates. Therefore, the results and insights in our paper are relevant to the population-based public policy design and may not be applicable to derive insights for specific subgroups. To address this limitation, we can extend the SEIR framework to a multilayer SEIR compartmental model in which each layer of SEIR compartments corresponds to one subgroup. Links can be present across multiple layers to capture the interactions among different subgroups. Despite its advantage in capturing heterogeneous factors, it leads to a complex model that requires more parameters to be estimated. The model potentially suffers from overfitting or identifiability issues. Similarly, it is also assumed that the individual contact is spatially homogeneous; that is, each individual can contact one another with an equal probability. In the context of Singapore, being a city-state with a dense population, this assumption could be well-justified. One might also adopt the multilayer SEIR compartmental model if the spatial heterogeneity is significant and partition the population into subgroups by different contact rates. Second, the SEIR model assumes a closed population. Given that our current analysis focuses on community cases and the data used in this study cover Singapore's lockdown period, there is little impact from migration because of limited interaction between the local population and foreign visitors. Nevertheless, one should be careful applying the SEIR model and extend it to capture the interaction with external populations when the countries gradually open up. Third, our current approach models the country-wide time-varying features, such as the dynamics of government policy and the progression of mortality risk at the population level. We do not incorporate individual-level time-varying factors, such as the infectivity profiles. This limitation can be addressed by adding more compartments that trace more granular partitions of individuals at different states of infectivity. However, such an extension would also lead to a complex model with a large number of parameters to estimate. Fourth, our paper studies the containment of COVID-19 during the early stage, during which new variants were not observed. One can further extend our model to capture new variants if corresponding data are more available. The idea of multilayer SEIR can be adopted to model the presence of more than one variant with each layer being a sub-SEIR model corresponding to one variant. By constructing the interlinks among different layers, one can model more involved cases, such as a recovered individual from one variant being infected by another. Fifth, because of viral shedding, infected individuals may still test positive, but they are not infectious (He et al. 2020, Young et al. 2020). In this paper, we focus on analyzing the impact of test accuracy on pandemic control in the early stage, when there are insufficient test kits to support large-scale testing. Most individuals who initiate a test would have developed some COVID-19 symptoms and are largely infectious. Therefore, the false positives we estimate from our data are mostly a result of test accuracy, not viral shedding. In addition, for those individuals that are not infectious in the later stage of the disease, including both detected and undetected cases, we capture them in the recovered compartment. The recovered compartment is an absorbing state of the model, and individuals in this compartment are not subject to testing. Therefore, ignoring viral shedding for these individuals may potentially underestimate the demand for community quarantine because, in practice, individuals in the recovered compartment may test positive and be required to quarantine in the community (as they are asymptomatic). With more knowledge on the virus transmission and more technologies to

confirm whether individuals are infectious, we can reduce such community quarantine cases. The model can also be extended to capture additional testing to confirm the transmissibility of individuals. Finally, the parameters in the SEIR model are point estimates, which do not account for potential uncertainty in the parameters. As pointed out by Tolles and Luong (2020), one can use more complicated estimation methods that use distributions for each parameter instead of a point estimate (i.e., Bayesian SEIR model in De Oliveira et al. 2020, Lai et al. 2021) to tackle this issue. However, this is beyond the scope of the current paper, and we leave it to future research.

Appendix. Additional Figures

Figure A.1. (Color online) The Impact of Test Accuracy on Total Cases

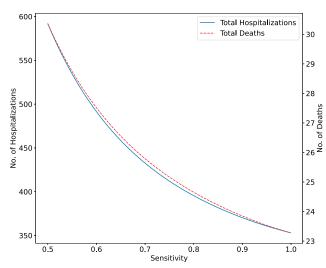
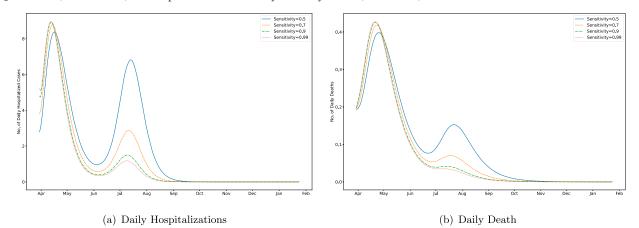


Figure A.2. (Color online) The Impact of Test Accuracy on Daily Cases (Continued)



References

- Bastos ML, Tavaziva G, Abidi SK, Campbell JR, Haraoui LP, Johnston JC, Lan Z, Law S, MacLean E, Trajman A, et al. (2020) Diagnostic accuracy of serological tests for Covid-19: systematic review and meta-analysis. *BMJ* 370:m2516.
- Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, Ruan L, Song B, Cai Y, Wei M, et al. (2020) A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. *New England J. Medicine* 382: 1787–1799.
- Das A (2020) How patients recover from COVID-19. *Times of India Online* (April 17), https://timesofindia.indiatimes.com/india/how-patients-recover-from-covid-19/articleshow/75193901.cms.
- David K (2020) Migrant workers and COVID-19. Occupational Environ. Medicine 77(9):634–636.
- De Oliveira ACS, Morita LHM, Da Silva EB, Zardo LAR, Fontes CJF, Granzotto DCT (2020) Bayesian modeling of COVID-19 cases with a correction to account for under-reported cases. *Infectious Disease Model*. 5:699–713.
- Gan WH, Lim JW, David K (2020) Preventing intra-hospital infection and transmission of COVID-19 in healthcare workers. *Safety Health Work* 11(2):241–243.
- Giordano G, Blanchini F, Bruno R, Colaneri P, Di Filippo A, Di Matteo A, Colaneri M (2020) Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. *Nature Medicine* 26(6):855–860.
- Hadjadj J, Yatim N, Barnabei L, Corneau A, Boussier J, Smith N, Péré H, Charbit B, Bondet V, Chenevier-Gobeaux C, et al. (2020) Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. *Sci.* 369(6504):718–724.
- Han H, Luo Q, Mo F, Long L, Zheng W (2020) SARS-COV-2 RNA more readily detected in induced sputum than in throat swabs of convalescent COVID-19 patients. *Lancet Infectious Diseases* 20(6):655–656.
- He X, Lau EH, Wu P, Deng X, Wang J, Hao X, Lau YC, Wong JY, Guan Y, Tan X, et al. (2020) Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature Medicine* 26(5): 672–675.
- Hethcote HW (2000) The mathematics of infectious diseases. SIAM Rev. 42(4):599–653.
- Jing G, Li J (2020) Expert consensus on preventing nosocomial transmission during respiratory care for critically ill patients infected by 2019 novel coronavirus pneumonia. *Zhonghua Jie He Hu Xi Za Zhi.* 17:E020.
- Kirk-Bayley J, Combes J, Sunkaraneni S, Challacombe S (2020) The use of povidone iodine nasal spray and mouthwash during the current COVID-19 pandemic may reduce cross infection and protect healthcare workers. Preprint, submitted March 30, https://dx.doi.org/10.2139/ssrn.3563092.
- Kucharski AJ, Russell TW, Diamond C, Liu Y, Edmunds J, Funk S, Eggo RM, Sun F, Jit M, Munday JD, et al. (2020) Early dynamics of transmission and control of covid-19: a mathematical modelling study. *Lancet Infectious Diseases* 20(5):553–558.
- Lai CC, Hsu CY, Jen HH, Yen AMF, Chan CC, Chen HH (2021) The Bayesian susceptible-exposed-infected-recovered model for the outbreak of COVID-19 on the Diamond Princess Cruise Ship. *Stochastic Environ. Res. Risk Assessment* 35(7):1319–1333.
- Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, Azman AS, Reich NG, Lessler J (2020) The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann. Internal Medicine* 172(9):577–582.
- Lee JS, Shin EC (2020) The type I interferon response in COVID-19: Implications for treatment. *Nature Rev. Immunology* 20(10):585– 586.
- Li ML, Bouardi HT, Lami OS, Trikalinos TA, Trichakis NK, Bertsimas D (2020) Forecasting COVID-19 and analyzing the effect of

government interventions. Preprint, submitted June 24, https://www.medrxiv.org/content/10.1101/2020.06.23.20138693v1.

- Littenberg B, Moses LE (1993) Estimating diagnostic accuracy from multiple conflicting reports: A new meta-analytic method. *Medical Decision Making* 13(4):313–321.
- Liu Y, Liao CH, Chang CF, Chou CC, Lin YR (2020a) A locally transmitted case of SARS-CoV-2 infection in Taiwan. N. Engl. J. Med. 382(11):1070–1072.
- Liu Y, Sun W, Chen L, Wang Y, Zhang L, Yu L (2020b) Clinical characteristics and progression of 2019 novel coronavirusinfected patients concurrent acute respiratory distress syndrome. Preprint, submitted February 27, https://www.medrxiv. org/content/10.1101/2020.02.17.20024166v3.
- Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, et al. (2020) Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *New England J. Medicine* 382(10): 970–971.
- Sidiq Z, Hanif M, Dwivedi KK, Chopra KK (2020) Benefits and limitations of serological assays in COVID-19 infection. *Indian J. Tuberculosis* 67(4S):S163–S166.
- Tolles J, Luong T (2020) Modeling epidemics with compartmental models. *JAMA* 323(24):2515–2516.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, et al. (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 323(11):1061–1069.
- Winichakoon P, Chaiwarith R, Liwsrisakun C, Salee P, Goonna A, Limsukon A, Kaewpoowat Q (2020) Negative nasopharyngeal and oropharyngeal swabs do not rule out COVID-19. J. Clinical Microbiology 58(5):e00297-20.
- Wyllie AL, Fournier J, Casanovas-Massana A, Campbell M, Tokuyama M, Vijayakumar P, Warren JL, Geng B, Muenker MC, Moore AJ, et al. (2020) Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. New England J. Medicine 383(13):1283–1286.
- Xu H, Huang S, Qiu C, Liu S, Deng J, Jiao B, Tan X, Ai L, Xiao Y, Belliato M, et al. (2020) Monitoring and management of homequarantined patients with COVID-19 using a Wechat-based telemedicine system: Retrospective cohort study. *J. Medical Internet Res.* 22(7):e19514.
- Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, Ng OT, Marimuthu K, Ang LW, Mak TM et al. (2020) Epidemiologic features and clinical course of patients infected with SARS-COV-2 in Singapore. JAMA 323(15):1488–1494.
- Zheng L, Wang X, Zhou C, Liu Q, Li S, Sun Q, Wang M, Zhou Q, Wang W (2020) Analysis of the infection status of the healthcare workers in Wuhan during the COVID-19 outbreak: A cross-sectional study. *Clinical Infectious Diseases* 71(16):2109– 2113.
- Zhou Q, Gao Y, Wang X, Liu R, Du P, Wang X, Zhang X, Lu S, Wang Z, Shi Q et al. (2020) Nosocomial infections among patients with COVID-19, SARS and MERS: A rapid review and meta-analysis. *Ann. Translational Medicine* 8(10):629.
- Zou D, Wang L, Xu P, Chen J, Zhang W, Gu Q (2020) Epidemic model guided machine learning for COVID-19 forecasts in the United States. Preprint, submitted May 25, https://www. medrxiv.org/content/10.1101/2020.05.24.20111989v1.

Guang Cheng is a PhD student at the National University of Singapore. His primary research interests are in datadriven modeling with applications in healthcare operations management and medical decision making.

Sarah Yini Gao is an assistant professor of operations management, Lee Kong Chian Fellow in Lee Kong Chian School of Business, Singapore Management University. Her current research interests lie in applying optimization theory in various domains, including supply chain risk management, healthcare and humanitarian operations, and topics on innovative business models.

Yancheng Yuan is a research assistant professor at The Hong Kong Polytechnic University. His current research interests are numerical optimization, mathematical foundation for machine learning, and big data-driven applications with focus on healthcare. **Chenxiao Zhang** received an MS degree in technopreneurship and innovation from Singapore Nanyang Technology University in 2017. She is currently working as a project management professional (nontech) at Lenovo.

Zhichao Zheng is an associate professor of operations management at the Singapore Management University. His main research interests lie in data analytics and optimization for healthcare operations management and medical decision making. He also applies his research in sharing economics and supply chain risk management, etc.