COVID-19: Should We Test Everyone?

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Abstract

Since the beginning of 2020, the coronavirus disease 2019 (COVID-19) has spread rapidly in the city of Wuhan, P.R. China, and subsequently, across the world. The swift spread of the virus is largely attributed to its stealth transmissions in which infected patients may be asymptomatic or exhibit only flu-like symptoms in the early stage. Undetected transmissions present a remarkable challenge for the containment of the virus and pose an appalling threat to the public. An urgent question that has been asked by the public is “Should I be tested for COVID-19 if I am sick?”. While different regions established their own criteria for screening to identify infected cases, the screening criteria have been modified based on new evidence and understanding of the virus as well as the availability of resources. The shortage of test kits and medical personnel has considerably limited our ability to do as many tests as possible. Public health officials and clinicians are facing a dilemma of balancing the limited resources and unlimited demands. On one hand, they are striving to achieve the best outcome by optimizing the usage of the scant resources. On the other hand, they are challenged by the patients’ frustrations and anxieties, stemming from the concerns of not being tested for COVID-19 for not meeting the definition of PUI (person under investigation). In this paper, we evaluate the situation from the statistical viewpoint by factoring into the considerations of the uncertainty and inaccuracy of the test, an issue that is often

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overlooked by the general public. We aim to shed light on the tough situation by providing evidence-based reasoning from the statistical angle, and we expect this examination will help the general public understand and assess the situation rationally. Most importantly, the development offers recommendations for physicians to make sensible evaluations to optimally use the limited resources for the best medical outcome.

**Key Words**: COVID-19, false negative, false positive, pandemic, repeatedly testing.
1 Introduction

The first case of the coronavirus disease 2019 (COVID-19) was found in December of 2019 in Wuhan city, Hubei providence, P. R. China. On December 31, 2019, China informed the World Health Organization (WHO) of a case of novel viral pneumonia in Wuhan (Wong et al. 2020). Since the diagnosis of the first case, this virus has spread with astonishing speed and has caused many infections and a good number of deaths. The origin of the virus, however, remains unclear. An abrupt announcement was made on January 23, 2020 that the city of Wuhan was locked down to control the spread of the virus. Subsequently, almost all areas in China have begun to take serious public health measures to contain the virus (Xiao and Torok 2020).

On January 30, 2020, WHO declared COVID-19 as a public health emergency of international concern. By March 2, 2020, China had confirmed 80,174 infected cases and 2915 deaths. From February 27 to March 11, 2020, the number of cases of COVID-19 outside China has increased 10-fold and the number of affected countries has increased to be 113. As of March 11, 2020, there have 118,429 confirmed cases and 4,292 deaths (WHO, Situation Reports 2020). The number of cases, the number of deaths, and the number of affected countries are expected to climb in the coming days and weeks. On March 11, 2020, WHO declared COVID-19 to be a pandemic.

COVID-19 has been found to be caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); certain epidemiological and clinical characteristics of patients with COVID-19 have been reported. However, comprehensive knowledge of COVID-19 still remains incomplete. For instance, the risk factors for mortality and the clinical course of the illness have not been well understood (Zhou et al. 2020). The early presentation of COVID-19 infection is typically nonspecific. Some infected cases may be asymptomatic, while many infected individuals often show flu-like symptoms such as dry cough, sore throat, low-grade fever, or malaise in the first few days (Wong et al. 2020). The seeming-flu symptoms have created difficulties in differentiating COVID-19 from the common cold and seasonal influenza.
The mystery of the virus and the lack of effective treatment for COVID-19 have presented a striking threat to the public. In contrast to the rapid transmission of the COVID-19 pandemic, news on COVID-19 has traveled swiftly and broadly through internet, radio, newspaper, television, social media, and so on. The wave of fear has escalated in the public. Though it has been reported that people with medical complications are at a greater risk of suffering from COVID-19, the general public also has the fear of contracting the virus.

Clinicians have been under tremendous pressure to triage the high volume of patients for COVID-19 testing. To receive medical care as early as possible, an urgent question that has been asked by patients with flu-like symptoms is “Can I be tested for COVID-19?” More broadly, the public may be puzzled by the concern, “To achieve an effective containment of the virus, why does the government not take a proactive action to test everyone for COVID-19 to identify all infected individuals in a timely manner?”

Due to the limited availability of trained personnel, testing kits, and PPE (personal protective equipment), it is impossible to test everyone with flu-like symptoms for COVID-19, let alone to test every individual. While these reasons can easily be perceived by the public, the underlying scientific reasonings do not seem to be considered. More importantly, due to the limited availability of resources, the protocol of screening patients for testing COVID-19 can be stringent to prevent a collapse in medical facilities. Based on the evolving global situation, the screening process is constantly being updated and differs from country to country. Initially, the U.S. Centers for Disease Control and Prevention (CDC) recommended testing only people with respiratory symptoms such as fever, dry cough, shortness of breath, and those who had potentially been exposed to the virus. With the evidence for community transmissions, the CDC updated its recommendations on March 4, 2020 to allow anyone with respiratory symptoms to be tested as long as the request is approved by a doctor, though the CDC is encouraging physicians to minimize unnecessary testing by considering patients’ exposure risks (Ferran 2020).
From the medical perspective, testing for COVID-19 has crucial implications and importance. It is impossible to fight the virus blindly without knowing the target population. The early diagnosis of infected patients is essential to manage the situation. Infected people must be isolated to control the virus spread; potentially infected individuals should be quarantined to minimize the possibility of infecting healthy people; and vulnerable people such as the elderly and patients with chronic health issues need to be secluded to prevent infection. Necessary medical attention must be focused on patients at high risk who require immediate medical intervention to prevent mortality. In a broader spectrum of learning and dealing with the virus, acquiring accurate data of infection and transmission is critical for researchers to unveil the correct profile of COVID-19 to implement more effective clinical management.

In response to the increasing need for testing for COVID-19, the U.S. Food and Drug Administration (FDA) announced on February 29, 2020, a new policy that made it easier for commercial and academic laboratories to develop their own tests and allowed other certified labs to test patient samples. Companies, hospitals and institutions are now racing to develop more tests to diagnose COVID-19. On March 10, 2020, Alex Azar, secretary of Health and Human Services, announced that 2.1 million testing kits were available and more than 1 million have shipped to certified labs for testing (Ferran 2020).

With the urgency of identifying infected cases and increase in available test kits, screening criteria for testing COVID-19 have become less restrictive than at the initial stage. It now seems quite tempting to take aggressive action to administer COVID-19 tests to as many patients as possible. However, an important yet overlooked issue is on the imperfectness of test procedures. It is imperative to enhance our understanding of testing for COVID-19 by factoring in the assessment of the uncertainty, randomness and imperfectness associated with the test procedures; otherwise, misleading and erroneous outcomes can be produced.

In this article, we examine the concerns of testing COVID-19 from the statistical standpoint. Our explorations are purely based on accounting for the uncertainty and randomness
associated with medical test procedures. We will look at the uncertainty induced from the
test procedures and assess the degree of the resulting false results. Our explorations are
intended to shed light on the question “Should everyone be tested for COVID-19?”, which
would assist general people to assess situations with rational and evidence-based thinking.
Ultimately, as advocated by Sharkawy (2020), the public should face the challenge of COVID-
19 with educated reasoning and compassion for others. Everyone should seek truth and facts,
as opposed to conjecture and speculation; we all must work together to battle COVID-19.

This article provides a dynamic framework to present the evolving features of COVID-19.
We examine test procedures in terms of their sensitivity and specificity, and quantify the
degrees of false test results under various scenarios. Most importantly, we make sensible
recommendations for physicians to balance the usage of limited test kits and the accuracy
of the test outcome. We offer the assessment as to how likely we may miss identifying
COVID-19 carriers based on consecutive negative results and how many times we should
test a suspected COVID-19 patient to reduce the chance of errors. Our discussion provides
the guidelines for discharging patients who are treated as COVID-19 carriers.

2 Notations and Framework

For generality, we use the term population to describe the group of subjects of our interest.
In the following discussion, population may represent the collection of all people in a coun-
try, a city, or a region; it may also refer to a cohort of individuals, a ward of patients, or a
community of people. We first introduce abstract symbols to represent the quantities of our
interest. To facilitate the dynamic feature of COVID-19, we include the dependence on time
in the notations.

On day $t$ with $t = 1, 2, \ldots$, suppose our target population has $N(t)$ people in total in which
$N_h(t)$ people have no COVID-19 and $N_s(t)$ people have COVID-19. Let $P(t) = N_s(t)/N(t)$
be the prevalence on day $t$. Before patient zero (i.e., the first person who has COVID-19)
appears, no one in the population has the virus. So we assume that when $t = 0, N_s(t) = 0$, and when $t = 1, 2, \ldots, N_s(t) \geq 1$. That is, $P(t) = 0$ for $t = 0$ and $0 < P(t) \leq 1$ for $t = 1, 2, \ldots$. Due to the dynamic feature and the spread of the virus, the relative size of $N_h(t)$ and $N_s(t)$ varies with time $t$. Initially, $N_s(t)$ is negligible and $N_s(t) \ll N_h(t)$ for $t$ in a certain interval, say $[1, T_1]$, i.e., $P(t)$ is near 0. As outbreaks occur and the pandemic is declared, it is possible that $N_s(t) \approx N_h(t)$ for $t$ in a certain interval $[T_1, T_2]$, say, yielding $P(t) \approx 1/2$. In the worst scenario, $N_s(t) \gg N_h(t)$ for $t$ in a certain time period $[T_2, T_3]$, say, leading to $P(t) \approx 1$. Eventually, we hope that the state of coming back to $N_s(t) \approx 0$ or $P(t) \approx 0$ for $t$ in the interval $[T_3, \infty)$ will be reached with $T_3$ being as small as possible.

For any individual in the population, we are interested in the COVID-19 status for this individual. Let $Y$ be the binary variable showing the true status for an individual to have COVID-19, with $Y = 1$ if having COVID-19 and 0 otherwise. In reality, the true value of $Y$ is unknown for any individual, and we can only apply proper medical tests to find out an individual’s disease status. To feature this, let $Y^*$ represent the test result for an individual who is tested; $Y^* = 1$, if the test result is positive; and $Y^* = 0$, if the test result is negative.

However, no medical test is 100% accurate in practice. There is a chance that a medical test can give us an incorrect result. To describe the accuracy of a test, we use two useful measures, called the sensitivity and the specificity, which are respectively defined as

$$p_{sen} = P(Y^* = 1|Y = 1) \quad \text{and} \quad p_{spe} = P(Y^* = 0|Y = 0).$$

Basically, the sensitivity $p_{sen}$ is a measure to show how sensitive the test is to testing diseased subjects. It reports the probability that a test successfully confirms the true status for an individual having the disease. In other words, the value of $p_{sen}$ indicates the success rate of the test when applied to the subpopulation of diseased people, so the sensitivity $p_{sen}$ is also called the true positive rate. An accurate test is expected to have a value near 1.

Paying attention to the sensitivity $p_{sen}$ only is, however, not enough to characterize the goodness of a test. A good test should also be accurate in terms of correctly showing the
result for people who do not have the disease. To this end, the specificity $p_{spe}$ comes into the play. It measures the probability that the test successfully reveals the disease-free status for any individual who has no disease. The value of $p_{spe}$ indicates the proportion of the time for obtaining the correct result when the test is applied to the subpopulation of healthy people. Consequently, the specificity $p_{spe}$ is also called the true negative rate. A good test is also expected to have $p_{spe}$ close to 1 to keep the number of misdiagnosed cases small.

Corresponding to the true positive rate and the true negative rate, the complement probabilities $1 - p_{sen} = P(Y^* = 0|Y = 1)$ and $1 - p_{spe} = P(Y^* = 1|Y = 0)$ are also useful to describe the test outcomes. These two measures are called the false negative rate and the false positive rate, respectively.

Because medical tests are not always accurate in testing diseased or non-diseased individuals, it is important to take into account the uncertainty and randomness when interpreting a test result. To make a sensible decision, it is necessary to understand how to evaluate the risk of receiving a false result when applying a test. Ultimately, our goal is to make an educational and evidence-based decision for the health care. Specifically, we are interested in evaluating two numbers of concern,

$$\#_{fp}(t) = \text{the number of false positive on day } t \text{ if everyone in the population is tested},$$

and

$$\#_{fn}(t) = \text{the number of false negative on day } t \text{ if everyone in the population is tested}.$$ 

It is easily seen that those numbers are determined by the size of the diseased subpopulation and the size of the non-diseased subpopulation as well as the sensitivity and the specificity of the test. That is,

$$\#_{fp}(t) = N_h(t) \times (1 - p_{spe}) \quad \text{and} \quad \#_{fn}(t) = N_s(t) \times (1 - p_{sen}). \quad (1)$$
3 Should Everyone Be Tested?

To understand how medical tests with different sensitivities and specificities may perform, we consider the scenario where the population has possibly different prevalence for different days. We make recommendations by examining how the number of false negative \( \#_{fn}(t) \) and the number of false positive \( \#_{fp}(t) \) are determined by the sensitivity and specificity of the test procedure as well as the prevalence of the disease.

3.1 Tracking Patient Zero

To visualize the relationship between the false negative number \( \#_{fn}(t) \) and the sensitivity of the tests, we start with an example with \( N(t) = 10,000 \) for a given day \( t \) and apply a sequence of tests with different sensitivities to everyone in the population. We show the results in Figure 1 for a range of prevalence. As expected, the false negative number drops as the sensitivity of the test becomes higher, and the drop rate is higher for the population with a bigger prevalence than that with a smaller prevalence. When the prevalence is very small, say, \( P(t) = 10^{-4} \), or equivalently, \( P(t) = 1/N(t) \) here (i.e., when patient zero just presents in the population), the false negative number is below 1 no matter what the sensitivity of a test is. In this case, testing everyone for COVID-19 would not virtually yield any false negative result.

In general, in the very beginning of the presence of patient zero (i.e., at time \( t = 1 \)), the population has \( N_s(1) \) to be 1 or nearly 1. If everyone is tested for COVID-19, then

\[
\#_{fn}(1) = N_s(1) \times (1 - p_{sen}) < 1
\]

regardless of the accuracy of test procedures. To track the origin of COVID-19 for a population, we recommend to test everyone in a group of presumptive patients who may potentially include patient zero; this is the only way to identify patient zero, yet it is unnecessary to worry about obtaining false negative results, no matter how inaccurate the test procedure could be.

In reality, it is often difficult to immediately identify the presence time of patient zero in a cohort based on the confirmation of infected cases. The discussion here offers a possible
way to track *patient zero* retrospectively by examining the samples of suspected patients. Checking the sample of *every* suspected patient by the reverse time order is needed to identify *patient zero* in the cohort.

**Recommendation 1:** *To identify patient zero, it is recommended to test everyone in a presumptive group which may potentially include patient zero.*

![Graph](image)

**Figure 1:** The false negative number versus the sensitivity of the test for populations of the common size 10,000 but different prevalence

### 3.2 Testing for COVID-19

We now visualize the relationship between the false positive number $\#fp(t)$ and the specificity of the test. Figure 2 shows the results for populations with a common size $N(t) = 10,000$ but with different prevalence. The false positive number becomes smaller when the specificity of the test becomes higher. Interestingly, the decreasing rate appears fairly stable regardless of the prevalence value, though those drop rates are not identical. For a given test, the false positive number is bigger for a population with a smaller prevalence, and the difference between two populations with different prevalence tends to be negligible, especially for those tests with a high specificity. In a population with 10,000 people, the false positive number...
can be as high as 6,000 if a test of the specificity around 40% is applied to everyone in the population; the false positive number can be lowered to about 1,000 if everyone in the population is tested with a procedure having a high specificity (such as 95%). Given that even for the best scenario the false positive number is still around 1,000 for a population of size 10,000, we conclude that it is not sensible to test everyone in the population for a disease without discretion (even if it is affordable in terms of availability of resources and the cost).

**Recommendation 2:** *Do not test everyone for COVID-19 without discretion.*

To further illustrate this, we consider two examples. The accuracy of the current COVID-19 tests is not precisely known. Based on the test performance in China and the performance of the influenza tests, Hutchison (2020) suggested that the sensitivity and specificity of COVID-19 tests were estimated to be 60% and 90%, respectively.

![Figure 2: The false positive number versus the specificity of a test for populations with the common size 10,000 but different prevalence](image)

**Example 1:** As of March 16, 2020, there were 8 confirmed cases in Waterloo Region,
Ontario, Canada (CBC News 2020), whose population size is about 601,220 (Region of Waterloo 2019). That is, \( P(t) \approx 0.00099797\% \) for \( t \) representing the day March 16, 2020. If we would test everyone in Waterloo for COVID-19, then we would expect

\[
\#_{fp}(t) = (601,220 - 8) \times (1 - 90\%) = 60,121.2
\]

and

\[
\#_{fn}(t) = 8 \times (1 - 60\%) = 3.2.
\]

That is, three infected person would be missed, and 60,121 healthy people (i.e., near 10% of the population in Waterloo Region) would be misdiagnosed as infected with COVID-19. This clearly demonstrates the blunder of testing everyone in a sizable population for COVID-19 without discretion.

**Example 2:** This example examines an opposite situation where the population is defined to be a cohort of a small size. In the period of March 11-16, 2020, among those in-person assessments and virtual visits in the clinic of Dr. Yu (the last co-author), 18 patients had flu-like symptoms and they all expressed interest to be tested for COVID-19.

Assume that this small cohort has the same prevalence as that of the Waterloo Region. If all those patients were to be tested for COVID-19, we would then expect

\[
\#_{fp}(t) = 18 \times (1 - 0.00099797\%) \times (1 - 90\%) = 1.78
\]

and

\[
\#_{fn}(t) = 18 \times 0.00099797\% \times (1 - 60\%) \approx 0,
\]

where \( t \) represents the short time interval March 11-16, 2020. That is, almost no infected patients would be mis-identified but about 1 or 2 healthy people would be misdiagnosed as infected cases, if all 18 patients are tested for COVID-19 without being screened.

In fact, for those 18 patients with flu-like symptoms, only one patient was offered testing based on the public health definition of PUI. If we perceive that this cohort should have a
higher prevalence than that of the general population in the Waterloo Region and assume that $P(t) = 1/18$, then we would expect

$$\#_{fp}(t) = 18 \times (1 - 1/18) \times (1 - 90\%) = 1.70$$

and

$$\#_{fn}(t) = 18 \times (1/18) \times (1 - 60\%) = 0.4$$

if everyone in this cohort would be tested for COVID-19.

4 Am I Infected with COVID-19 if I have a Positive Result after Several Consecutive Negative Results?

Since no medical tests can produce 100% accurate results, both false negative and false positive results are possible when testing suspected patients. We are interested in whether repeating the test can help improve the accuracy of the diagnosis. In particular, we evaluate the chance that a tested subject is an infected case, given that the first $(k - 1)$ consecutive tests are negative but the $k$th test is positive, where $k \geq 1$. We hope to study whether it is necessary to continuously repeat the test, if consecutive negative results have been obtained after certain repetitions. When should we stop testing in order to not miss infected cases?

To this end, let $Y^*_k$ represent the $k$th test result of applying the test to an individual, where $k$ is a positive integer. This binary random variable has the same distribution as that of $Y$. We want to find the value of $k$ so that the conditional probability $P(Y = 1|Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 1)$ is smaller than a tolerance value, where $k = 1, 2, \ldots$.

To find how the performance of the test comes into play, we express the conditional probability $P(Y = 1|Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 1)$ using the sensitivity and specificity of the test as well as the prevalence. Assuming that the test is independently applied to an
individual $k$ times, Using the Bayesian theorem gives that

$$
P(Y = 1|Y_1^* = 0, \ldots, Y_{k-1}^* = 0, Y_k^* = 1) = \sum_{r=0,1} P(Y_1^* = 0, \ldots, Y_{k-1}^* = 0, Y_k^* = 1|Y = r)P(Y = r)$$

$$= \frac{(1 - p_{sen})^{k-1}p_{sen}P(t) + p_{spe}(1 - p_{spe})(1 - P(t))}{(1 - p_{sen})^{k-1}p_{sen}P(t) + p_{spe}(1 - p_{spe})(1 - P(t))}$$

(2)

for $k = 1, 2, \ldots$.

For any test with the specificity higher than the false negative rate, (2) shows that a larger value $k$ suggests a smaller chance for an individual to be infected if the first positive test result appears at the $k$th test, no matter what the sensitivity of the test and the population prevalence are. However, for a smaller number of $k$, the sensitivity of the test and the population prevalence do matter for quantifying the probability.

In Figure 3, we report the conditional probability $P(Y = 1|Y_1^* = 0, \ldots, Y_{k-1}^* = 0, Y_k^* = 1)$ versus the sensitivity and specificity of the test for populations with different prevalence. In the top panel of Figure 3, we display the results for $k = 1$. As long as the test has a high specificity, applying the test to an individual from the population with a high prevalence can be very informative. If the test result is positive, then it is highly likely that this individual is infected with the disease; this is true, even if the test does not have a high sensitivity. However, for a population with a low prevalence (e.g., 1%), even if the test has both a high specificity and sensitivity, the probability of correctly confirming an infected case is very low if the test is applied only once. This finding further suggests that it is unwise to apply a test to everyone from the population with a low prevalence. It is advised that prior measures should be taken to identify a suspected subpopulation (or a group of presumptive cases) so that the resulting prevalence becomes high. Then applying the test to individuals in this subpopulation can increase accuracy to identify infected cases.
The bottom panel of Figure 3 shows the results for $k = 3$. For a test with a low sensitivity, there is a high chance that a patient is infected even when the first positive result appears at the third test, if we test individuals from the population with a high prevalence (such as 85%). However, if the population has a small prevalence (such as 1%), it is unlikely that the patient with the first positive result occurring at the third try is infected.

**Recommendation 3:** With a given test, when interpreting a positive result after consecutive negative results, caution should be taken for patients coming from different cohorts with different prevalence.

To further visualize how the cohort prevalence affects the probability of identifying an infected case, given consecutive negative results followed by a positive result, we examine the COVID-19 test described by Hutchison (2020) as opposed to the COVID-19 IgM/IgG
Rapid Test, a test newly released by the ISO13485 registered company BioMedomics. On March 8, 2020, the company announced that it has received CE Mark-IVD certification for its new test to help diagnose novel COVID-19. This test, available only for research use at this stage, takes 15 minutes to obtain the result and can be used for rapid screening of COVID-19 carriers who are symptomatic or asymptomatic. The sensitivity and specificity of the test were estimated to be 88.66% and 90.63%, respectively, based on the test results for 525 infected cases and 128 non-SARS-CoV-2 infection patients (BioMedomics 2020).

We graph the results in Figure 4. There is a high chance that the tested person contracts COVID-19 if the result of applying the COVID-19 IgM/IgG Rapid Test is positive at the first test, unless the population prevalence is very small; the chance is higher for testing patients coming from a cohort with a higher prevalence. For the COVID-19 IgM/IgG Rapid Test, if the positive result occurs only at the 4th test, then the chance of the tested subject is infected is very slim unless the patient comes from a cohort with a high prevalence (such as 60% or higher); if the first positive result occurs at the 6th test, the chance of the tested subject is infected is almost 0 no matter which cohort this patient comes from. However, for the COVID-19 test described by Hutchison (2020), even the first five test results are negative, there is still a good chance that the tested subject is infected with COVID-19.

**Recommendation 4:** With the same cohort of patients, different interpretations should be given for the positive result after the same number of consecutive negative results that are obtained from different tests with different sensitivities and specificities.
Figure 4: The probability of identifying an infected case after \( k - 1 \) consecutive negative results followed by a positive result: the plots of the probability versus the prevalence for \( k = 1, \ldots, 6 \); The left panel is for the COVID-19 IgM/IgG Rapid Test and the right panel is for the COVID-19 test described by Hutchison (2020).

5 Can I Get COVID-19 Twice?

As of March 13, 2020, in mainland China, there have been more than 100 reported cases of cured patients released from hospitals, who later tested positive for COVID-19 a second time. In China’s Guangdong province, 14% of people who recovered in the province were later retested to be positive. Similar cases have been reported in Japan and South Korea (Guzman 2020). This prompts the question “Can I get COVID-19 twice?” Put in other words, we want to know whether we can differentiate the two scenarios: (1) patients who contracted COVID-19 again after they were cured, and (2) patients who have never really been cured and their discharge was due to the false negative test results.

Researchers perceive that reinfection is an unlikely explanation for patients who test positive a second time. Testing errors and releasing patients from hospitals prematurely
are very likely the reason for reports of patients who retest positive. Although it has not been proved that people who have contracted COVID-19 are immune, this is very likely the case, as noted by Anthony Fauci, Director of the National Institute of Allergy and Infectious Disease (Guzman 2020).

To assess this perception, we evaluate the chance of incorrectly claiming a COVID-19 carrier to be cured after obtaining several consecutive negative results. We are interested in assessing the conditional probability

$$P(Y = 1|Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 0)$$

for $k = 1, 2, \ldots$. Assuming that the test is independently applied to a patient $k$ times, then using the Bayesian theorem, we obtain that

$$P(Y = 1|Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 0) = \frac{P(Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 0|Y = 1)P(Y = 1)}{\sum_{r=0}^{1} P(Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 0|Y = r)P(Y = r)} = \frac{(1 - p_{sens})^k P(t)}{(1 - p_{sens})^k P(t) + p_{spe}^k (1 - P(t))}$$

for $k = 1, 2, \ldots$.

In Figure 5, for populations with different prevalence, 3-dimensional graphs were made to show how the conditional probability for missing an infected case with $k$ consecutive negative results may depend on the sensitivity and specificity of the test, where $k = 1, 3$. It is clearly seen that if the test has a low sensitivity, the chance of missing an infected case is high if the test is done only once for populations with a large prevalence, even if the specificity of the test is high; the larger the prevalence, the higher the chance of missing. For a test with a reasonably large sensitivity, the more we test, the smaller the chance of missing an infected case.

More rigorously, we rewrite the conditional probability [3] as

$$P(Y = 1|Y^*_1 = 0, \ldots, Y^*_{k-1} = 0, Y^*_k = 0) = \frac{1}{1 + \left(\frac{p_{spe}}{1 - p_{sens}}\right)^k \times \left(\frac{1 - P(t)}{P(t)}\right)}$$

for $k = 1, 2, \ldots$. The probability [4] decreases as $k$ increases if and only if

$$\frac{p_{spe}}{1 - p_{sens}} > 1,$$

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which is satisfied by a test with the sensitivity larger than the false positive rate (i.e., $1 - p_{spe}$) or the specificity higher than the false negative rate (i.e., $1 - p_{sen}$). This condition must be met by any test in use, otherwise, there is no point of using a test that is even worse than a random guess. Hence, for any test in use, increasing the test number reduces the chance of mistakenly discharging infected patients.

**Recommendation 5:** To reduce the chance of missing a COVID-19 carrier based on negative test results, it is important to increase the number of tests.

**Figure 5:** The chance of missing a case with $k$ consecutive negative results versus the sensitivity and specificity of the test: $k = 1, 3$ and the prevalence $P(t) = 0.01, 0.25, 0.85$; The color shows the magnitude of the chance.

To see how doctors may implement this recommendation when they need to discharge inpatients with COVID-19-like symptoms, we compare the COVID-19 test described by Hutchison (2020) to the COVID-19 IgM/IgG Rapid Test. Figure 6 displays how the probability of missing an infected case after receiving $k$ consecutive negative test results depends
on the population prevalence of COVID-19 for \( k = 1, 2, \ldots, 6 \). With the COVID-19 IgM/IgG Rapid Test, having two consecutive negative test results ensures a nearly zero chance of missing infected cases if testing patients admitted to the ward with less than 50% COVID-19 carriers; for the inpatient ward with about 80% COVID-19 carriers, obtaining 3 consecutive negative test results warrants a slim chance of missing infected cases; receiving 4 consecutive negative results is enough for discharging any inpatients.

In comparison, the COVID-19 test described by Hutchison (2020) has about 20% smaller sensitivity than the COVID-19 IgM/IgG Rapid Test. It requires more consecutive negative results than the COVID-19 IgM/IgG Rapid Test for retaining a slim chance of missing infected cases, and different numbers of consecutive negative results produced by this test yield more different probabilities of missing infected cases than those obtained from the COVID-19 IgM/IgG Rapid Test. This comparison also illustrates how a high sensitivity of a test can make a difference in reducing the chance of missing infected cases based on consecutive negative results.

**Recommendation 6**: Different numbers of consecutive negative test results are required to discharge inpatients admitted to wards with different prevalence. For the COVID-19 test described by Hutchison (2020), to ensure the chance of mis-discharging to be smaller than 5%, 2, 3, 4, 5, and 6 consecutive negative test results are needed to discharge inpatients in a ward with the prevalence about 20%, 40%, 50%, 70%, and 80%, respectively.
Figure 6: The conditional probability for missing an infected case based on $k$ consecutive negative results: the plots of the conditional probability versus the prevalence for $k = 1, \ldots, 6$; The left panel is for the COVID-19 IgM/IgG Rapid Test and the right panel is for the COVID-19 test described by Hutchison (2020)

6 Analysis of Diamond Princess Data

To illustrate our discussion, we analyze the data of the Diamond Princess cruise for the period of January 19, 2020 (the day before patient zero embarked on the cruise) to February 20, 2020 when all passengers were disembarked (Princess 2020). Diamond Princess was on a 14-day round trip itinerary, departing from Yokohama in Tokyo on January 20, 2020 and returning on February 4, 2020. There were 2,666 guests and 1,045 crew on board. Patient zero traveled for five days on Diamond Princess and disembarked in Hong Kong on January 25. During those five days, patient zero did not report being ill; he was tested positive for COVID-19 on February 1, six days after leaving the ship.

On February 4, 10 people were tested positive for COVID-19 among the first batch of tested passengers. In subsequent days, more guests were tested positive. People with positive
test results were transported to local hospitals for medical care. Table 1 displays the number of people whose test results were positive on different days. Using the notation in Section 2, January 19 is taken at $t = 0$ on which $N(0) = N_h(0) = 3711$ and $N_s(0) = 0$; January 20 is taken as $t = 1$ on which $N(1) = N(0)$ and $N_s(1) = 1$; on February 4 (i.e., $t = 17$), $N_s(17) = 10$ and $N(17) = N(0) - 10$. The left panel of Figure 8 displays the day-dependent prevalence, and in the middle panel we report the changing population size using the red curve.

Without discretion, we would use the COVID-19 test described by Hutchison (2020) to test all passengers every day starting $t = 17$, then the daily numbers of false positive and negative results can be worked out by (1). We visually display those numbers in the middle panel (blue dashed curve) and the right panel in Figure 7. Clearly, when $P(t)$ is very small, $\#_{fp}(t)$ is close to $N(t)$ and $\#_{fn}(t)$ is near 0; when $P(t)$ becomes larger, $\#_{fp}(t)$ becomes smaller but $\#_{fn}(t)$ gets larger.

Though having a large value of $\#_{fp}(t)$ would not exacerbate the virus spread, it would waste limited medical resources. Having a nonzero value of $\#_{fn}(t)$ would be harmful because those undetected infected cases would be spreaders of the virus; on the day $t = 30$ of disembarking all the passengers, there could be 300 missed COVID-19 carriers if we test everyone on the ship without carefully screening.

It is sensible to focus on testing suspected patients to reach a balance between the use of limited medical resources and the result accuracy. By (2), the COVID-19 test should be repeated at least three times for a suspected patient, and all three negative results would ensure the chance of missing an infected case to be under 5%.
Table 1: COIVD-19 Data from Diamond Princess Cruise

| Day    | 1-16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33-44 |
|--------|------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|-------|
| # Cases| 0    | 10 | 10 | 41 | 3  | 0  | 6  | 65 | 39 | 0  | 47 | 0  | 134 | 0  | 99 | 88 | 79 | 84    |

Figure 7: Analysis of the Diamond Princess data if everyone would be tested everyday from day 17 to day 44: the left panel records the prevalence versus the date, the right panel shows the false negative number versus the date, and the middle panel displays the false positive number versus the date (in blue) and the population size versus the date (in red).

7 Conclusion and Discussion

In this article we take the statistical standpoint and examine several aspects of COVID-19 testing. We evaluate the uncertainty induced from the imperfectness of COVID-19 tests and make recommendations. In summary, we highlight the following points:

1. Testing everyone without discretion is not recommended. A large number of false negatives is typical for medical tests with a low sensitivity. A large number of false positives is produced from a test with a lower specificity. It is not feasible to test everyone who shows flu-like symptoms. It is important to prioritize the testing of people who need it the most, not only for the economical considerations of the availability of test kits,
but also for the statistical concerns of controlling false positive or negative results.

Even with enough test kits for the entire population, it is advised to identify suitable candidates for the test. It is unwise to test everyone in the population without careful discretion. Medical personnel generally believe that people in the following groups should be prioritized to test for COVID-19 (Ferran 2020): (1) those at high risk such as health care workers who have been in contact with COVID-19 patients, (2) symptomatic people in areas with high infection rates, (3) people 65 years of age and older with chronic health issues, such as heart disease, lung disease, and diabetes, and (4) patients who have immunodeficiency diseases.

2. The accuracy of the COVID-19 test described by Hutchison (2020) is not precisely known. Based on the test performance in China and the performance of the influenza tests, the test is estimated to correctly identify around 60% of the patients with the disease and correctly identify 90% of the patients that are disease-free. The low sensitivity of the current tests for COVID-19 would yield a large number of false negative if we test everyone in a cohort with a low prevalence. That is, a large number of people having the virus would be misdiagnosed as healthy if we attempt to test the entire cohort which has not been carefully scrutinized for COVID-19.

3. The tests should only be applied to presumptive people in order to control false positive and false negative results. With limited resources, targeting the presumptive people and applying the tests repeatedly is the best strategy to make sure the true COVID-19 carriers are not missed and discharged inpatients are truly virus-free.

Our discussion is carried out exchangeably at the population level and on the basis of an individual. When interpreting the results, caution should be taken for this difference. In the initial stage, COVID-19 was transmitted in an unrecognized way. Limited testing capacity and strict testing criteria delayed the identification of COVID-19 carriers in many
countries (Sullivan 2020). Our discussion here is useful to help make prudent decisions from the administrative standpoint to optimize the usage of limited resources of test kits, healthcare workers, and medical facilities. However, from the perspective of an individual thinking “better safe than sorry”, one might argue that having a false positive result is tolerable but a false negative is troublesome. From a physician’s viewpoint, missing an infected case can be more detrimental than misdiagnosing a COVID-19-free patient as a carrier. Such an error would cause a spread of virus and delay medical care for the COVID-19 infected patients. This article provides the assessment as to how likely we may miss identifying COVID-19 carriers based on consecutive negative results and how many times we should test a suspected COVID-19 patient to reduce the chance of errors. On equal footing, our discussion provides the guidelines for discharging inpatients who are treated for COVID-19.

There are several limitations of our discussion. In the discussion of the Diamond Princess Cruise Data in Section 6, we ignore the fact that the population size $N(t)$ and the prevalence $P(t)$ are error-contaminated. In our discussion, the dynamic number of COVID-19 carriers $N_s(t)$ is taken as the confirmed cases for each day $t$. The true value of $N_s(t)$ is, however, highly likely to be larger than the reported number for day $t$ since some infected passengers were asymptomatic and thus were not being tested on day $t$ for $t = 17, 18, \ldots, 34$.

While we consider a dynamic framework in Section 2 to characterize the change in the population size and the relationship between the number of infected people and the number of healthy people, our discussion on the COVID-19 status for individuals focuses on a static state to highlight the ideas. More specifically, time-dependent status $Y(t)$, instead of $Y$, should be used to reflect the time-dependent status for individuals in the population on day $t$. As our understanding of COVID-19 grows and more accurate test kits become available, our development should be modified and the recommendations can be made by incorporating time windows to reflect influencing factors, including the evolving stage of COVID-19, preventive measures done by the local administration and the government, and the changes in the public social behavior for different periods.
Another notable issue is that our discussion merely investigates testing errors from the statistical angle to quantify the randomness and uncertainty associated with the test inaccuracy. We have not explicitly accommodated in the development the characteristics of patients, such as age, severity of COVID-19-like symptoms, health conditions, and the medical history. This is caused by the lack of information on the sensitivity and specificity of available test kits estimated from different cohorts of patients with varying medical conditions. As a last recommendation, we suggest that rather than reporting an overall sensitivity and specificity for a developed test, developers of COVID-19 tests should evaluate a sequence of the sensitivities and specificities of the test applicable to different cohorts of patients. This will allow physicians and medical personnel to make more precise decisions to accommodate the personalized-features of the patients.

**Recommendation 7:** *Instead of being assessed by an overall sensitivity and specificity, the performance of COVID-19 tests should be evaluated in a more refined measure by reporting their sensitivities and specificities obtained from the stratified population by the patient’s medical conditions.*

In the article, we compare two COVID-19 tests, the COVID-19 test described by Hutchinson (2020) and the COVID-19 IgM-IgG Rapid Test. While the calculations show that the COVID-19 IgM-IgG Rapid Test outperforms the COVID-19 test described by Hutchinson (2020), we are not ready to recommend to replace the latter test by the former one. While the sensitivity and specificity of the COVID-19 IgM-IgG Rapid Test are higher than those of the COVID-19 test described by Hutchinson (2020), these results are obtained from different groups of patients whose conditions may differ considerably and the sizes may not be comparable either.

Having fast and effective test tools is crucial for controlling the rapidly evolving COVID-19 course while emerging research results offer new ways for testing COVID-19. For instance, investigating the temporal changes of COVID-19 pneumonia on CT scans, Shi et al. (2020) found that a CT could be a useful tool to detect COVID-19 pneumonia, even for asym-
omatic individuals. Their findings suggested that CT scans can be considered as a screening tool together with RT-PCR for patients who traveled recently or have had close contact with an infected individual. Furthermore, CT scans may be an important screening tool in the small proportion of patients who have false-negative RT-PCR results (Lee, Ng and Khong 2020). Announced on March 21, 2020, diagnostics company Cepheid received emergency authorization from the U.S. FDA to use its rapid molecular test, SAR-CoV-2 Xpert Xpress, that can detect COVID-19 in 45 minutes for point-of-care patients (Scipioni 2020). A review of the current laboratory methods available for testing COVID-19 was given by Loeffelholz and Tang (2020).

Our discussion here considers repetitions of the same test procedures. With multiple test kits becoming available, we face the decision of choosing suitable test kits to reach a balance among several key factors. This includes but not limited to the time of acquiring results, the associated cost, the test accuracy, and the suitability for patients with different conditions. It is useful to ponder the question: How do we use them effectively? We may apply a fast but less accurate test kit to do screening, and then apply a more accurate but time-consuming and costly test to do further checks. If repeated tests need to be done, we need to decide the number of the tests in order to not miss the infected patients. In addition, in our discussion of repeating the test for COVID-19, we have not looked into the issue of the gap time between two consecutive tests.

Acknowledgements

The research of Yi and He is partially supported by fundings from the Natural Sciences and Engineering Research Council of Canada (NSERC). Yi is Canada Research Chair in Data Science (Tier 1). Her research was undertaken, in part, thanks to funding from the Canada Research Chairs Program.
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