Everything you think you know about COVID-19 is probably wrong, but some of it is useful

Pamela Pelizzari, MPH
Stoddard Davenport, MPH
Carol Bazell, MD, MPH

As COVID-19 has spread around the globe, scientists, mathematicians, economists, health professionals, and thinkers of all stripes have worked within their fields of study to try to quickly understand, analyze, and explain the impacts of the global pandemic.

Time-sensitive and important questions that these individuals have raised and explored include:

- How many people will be infected or die?
- How much will all of this cost (to governments, private companies, insurers, healthcare providers, and others)?
- How effective are physical distancing and other countermeasures?
- How can an individual patient’s disease severity be predicted?

These questions, as well as dozens of others, are being posed and answered through the popular media, scientific journal articles (some with peer review and some without, or pre-peer review), and countless other avenues on a daily basis. With the abundance of pandemic-related articles and discussions, it can be difficult to cut through the noise and figure out what sources of information can be trusted, what analysis might not stand up to scrutiny, and how to reconcile apparently conflicting findings.

This article explores the challenge of interpreting data, reports, and media coverage surrounding the COVID-19 pandemic. We provide some examples of challenges researchers face when working to answer key questions related to COVID-19, illustrate the ways that a variety of seemingly reasonable assumptions can lead to widely divergent conclusions, and present key constructs for those invested in becoming more informed and critical consumers of COVID-19 research.

The scope of the problem

Every week since early February, there have been hundreds, or even thousands, of new scientific articles released weekly on COVID-19. Coverage in the popular media likely exceeds this by an order of magnitude or more. Given the sweeping and rapid impact of the COVID-19 pandemic, even sources that normally would have rigorous prepublication review requirements are publishing papers that have not been subjected to what are typically extensive peer-review processes. While this approach to rapid publishing may benefit readers in terms of speed-to-publication, it requires that they become more sophisticated in their own interpretations of what is good, defensible research and what is not. Understanding the effects of assumptions and methodological limitations of an analysis is more important than ever, as the timely release of emerging information is prioritized over the rigor that often accompanies more data and less reliance on assumptions.

This situation has created a need for consumers and researchers alike to exercise greater caution in how they interpret sources they would normally assume have been rigorously vetted prior to publication. Take for example a recent fast-track scientific journal article. This article aimed to estimate the U.S. healthcare cost of COVID-19. The authors used various scenarios of overall population infection rate, from 20% to 80% of the population (reflecting uncertainty regarding how COVID-19 will spread throughout the population and how the spread is driven by human behavior). Among infected individuals, the authors drew an estimate of the percentage that would be entirely asymptomatic from a study of passengers on the Diamond Princess cruise ship. This estimated rate of asymptomatic infection (18% of all infections) had been developed in a closed environment, where study subjects were older than the average U.S. population and may have had a higher likelihood of repeated or high-intensity exposure to the virus. However, in the fast-track journal article the estimate was applied to the entire U.S. population. Although

---

many other studies in other settings have come to widely different conclusions, the authors of the fast-track journal article did not apply a range for this assumption. For example:

- Updated testing data from the Diamond Princess cruise ship through March showed a higher 46.5% of infections were asymptomatic at the time of testing. 4
- A letter in the New England Journal of Medicine reports that, among pregnant women presenting to labor and delivery at one hospital in New York, 88% of infected women were asymptomatic. 5
- A population-based study from China published in BMJ reports that about 80% of infections were asymptomatic. 6
- A population-based study in one Italian village published in BMJ reports that 50% to 75% of infections were asymptomatic. 7
- A population-based study in Iceland, at a time when 5% of the population had been tested, found that 50% of infections were asymptomatic. 8

Given the wide range of literature on asymptomatic infections and the clear bias in the sample of the Diamond Princess passengers, assuming a rate of only 18% asymptomatic infections in the entire U.S. population will result in what may be unreasonably high estimates of symptomatic individuals requiring treatment and, thus, a higher estimate of cost to the U.S. healthcare system.

Example: How soon will our hospitals run out of space?

As another example, consider a recent model developed by a well-known team of academic researchers. 9 This model was built with the purpose of estimating how quickly hospital bed capacity would be reached in various locations across the country. The research team made a comprehensive list of sources available, 10 and this allows readers to investigate how they have lined up various sources in constructing this model and the impacts that these assumptions may have. Specifically, their assumptions of the proportions of people infected with COVID-19 (20%, 40%, and 60% scenarios are presented) are stated in terms of true infection rates—the proportion of people in society who are infected, inclusive of those who are entirely asymptomatic. However, their assumptions of the likelihood of hospitalizations are based on a study from China 11 that only measured hospital utilization in cases that were either confirmed via testing, or symptomatic and suspected (but not confirmed because of a lack of testing capacity).

There is general consensus in the literature that a large percentage of infections are entirely asymptomatic. When the academic researchers applied assumptions for the proportion of symptomatic or testing-confirmed positive cases that would be hospitalized to an overall population infection rate that includes asymptomatic individuals, they would naturally come to a conclusion of astronomical hospital bed utilization. This approach does not reflect the fact that a large proportion of the 20%, 40%, or 60% of the population that is infected may never use any healthcare resources to treat COVID-19, and the hospitalization rate assumption they have selected should more likely be applied to only a subset of the population assumed to be symptomatic or testing-confirmed. Without reviewing the sources of information used in the study, the casual reader would not be able to identify this key assumption that drastically impacts the outcome.

Sample calculation: How many COVID-19 hospitalizations will there be in a given population?

The challenge with developing and aligning appropriate assumptions, as demonstrated in our examples above, is present for complicated questions and for those that may seem much more straightforward. For example, let’s try to answer this simple question: In a given population, how many COVID-19 hospitalizations do we expect to see? This is a question that might be relevant to a hospital planning for how many beds it needs available, a government planning for what kind of resources to put in place to expand local healthcare system capacity, or a healthcare payer determining how much the treatment of COVID-19 might cost in its population.

---

10 Sources: COVID-19 Model. Retrieved May 27, 2020, from https://docs.google.com/spreadsheets/d/1Z0WnrKbZ1_yb2J9J7s6uU0iF3J0Jn8UwLebqO9M/edit#gid=0.
We make several simplifying assumptions here but, at a general level, in order to come up with an answer to this question, a researcher will need to identify sources for the following:

- How big is the population, what is the age/gender mix, and what risk factors may make some people more susceptible to COVID-19?
- Within the population, what percentage of people will become infected with COVID-19?
- Among those people with an infection, what percentage will be symptomatic?
- Among those symptomatic infections, how many people will be hospitalized, and for how long?

Let’s assume that, in this example, we have a known population size and age/gender mix, so that these factors do not incorporate any explicit uncertainty in the outcome of the calculation. Further, let’s assume that we are reasonably adjusting the rates of infected and symptomatic individuals and hospitalizations within age bands (it is widely believed that older individuals are more likely to have an infection and to have symptoms or require medical care related to COVID-19). Here are some examples of high-end and low-end estimates that could reasonably be used for the other needed assumptions:

- **Percentage of individuals infected:** An influential study from Imperial College London researchers predicted that, in a state of unmitigated spread, as many as 80% of individuals in the United States and Great Britain could be infected by COVID-19.\(^\text{12}\) Based on early information detailing how infectious COVID-19 has been, epidemiologists estimate that approximately 70% of the population will need to be immune to offer some herd protection, which controls the spread of disease by providing indirect protection to those who are not immune.\(^\text{13}\) More recently, antibody testing in New York state has indicated that approximately 15% of New York state residents and approximately 25% of New York City residents tested positive for COVID-19 antibodies, meaning they had already likely been exposed to the virus.\(^\text{14}\) In the table in Figure 1, we use 20% and 80% as low-end and high-end estimates for infection rates in our sample population.

- **Percentage of infected individuals who are symptomatic:** Per the discussion above, we have seen estimates in the literature of what percentage of infected individuals show symptoms of disease that are as high as 82% (in the Diamond Princess cruise ship study) and as low as 12% (in a sample of pregnant women presenting at New York City hospitals). These estimates are applied as the high and low ranges in Figure 1.

### Percentage of symptomatic individuals who are hospitalized:

For this assumption, we look to the U.S. Centers for Disease Control and Prevention (CDC). A recent CDC study identified a range of hospitalization rates among confirmed infections between 20% and 31%.\(^\text{15}\) These rates are applied as the high and low ranges in Figure 1.

As demonstrated in Figure 1, these relatively reasonable assumptions—all based on published studies—can lead to a wide range of hospitalization rate estimates, from 4,800 to over 200,000. This level of variability demonstrates that it is imperative for informed readers to consider not just the results but also the underlying assumptions used in studies.

---


\(^\text{15}\) CDC (March 27, 2020). Severe Outcomes Among Patients With Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020, Figure 2. Retrieved May 27, 2020, from https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm?s_cid=mm6912e2_w#F2_down.
Example: How does COVID-19 testing (or lack thereof) impact research outcomes?

One of the most widely reported metrics about COVID-19 is the number of confirmed cases. In general, reports of confirmed cases reflect the total number of tests that are positive for the presence of the virus, but there is considerable variation among communities in the criteria used to determine who should be tested, the types of tests used, and how or with what frequency results are reported. Each of these factors may also change over time, and the variation can be compounded by issues such as whether some individuals are being tested repeatedly and the quality of the tests themselves. Because of these differences, care should be taken when comparing the number of confirmed cases between two locations, or between two points in time.

WHO SHOULD BE TESTED?

The CDC provides guidance for who should be tested, but decisions are ultimately made by state and local health departments and clinicians. At the time of writing, the CDC’s latest guidance suggested prioritizing symptomatic individuals (particularly hospitalized patients, healthcare workers, first responders, and residents of congregate living settings) as well as individuals without symptoms who are prioritized by health departments or clinicians for certain reasons. The criteria were updated five times in March, April, and May, and both state and local adaptations of the CDC guidance have been periodically revised over the course of the pandemic as well. Regardless of the criteria in place at any given time, the availability (or lack of availability) of tests in a given area may substantially impact who actually receives one.

Different testing strategies can lead to differences in the percentage of the population that is tested, and the percentage of all infected individuals who are positively identified. Restrictive testing criteria that result in less testing may lead to a larger difference between the number of confirmed cases and the total number of individuals infected, while less restrictive criteria that result in more testing may lead to a smaller divide. Further, the divide between confirmed cases and the total number of individuals infected can change over time as testing strategies evolve. This becomes a challenge when the number of confirmed cases is used to estimate the prevalence, severity, or mortality of COVID-19, or when making planning decisions for healthcare resources. While stratified reporting of test results could alleviate this problem (e.g., reporting results for healthcare workers separately from symptomatic individuals or those tested in broad testing blitzes), we typically see results reported at aggregate levels in geographic regions.

The table in Figure 2 provides an example of how much estimates for the case fatality rate could vary for two communities with the same number of infections and fatalities, but with different levels of testing.

<table>
<thead>
<tr>
<th># of individuals infected</th>
<th># of fatalities</th>
<th>Testing strategy</th>
<th># of confirmed cases</th>
<th>Case fatality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10,000</td>
<td>50</td>
<td>Less testing</td>
<td>1,000</td>
<td>5%</td>
</tr>
<tr>
<td>10,000</td>
<td>50</td>
<td>More testing</td>
<td>4,000</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

In this example, differences in testing strategy led to a fourfold difference in the estimated case fatality rate. If those differences were not considered, then those in communities with fewer confirmed cases might conclude that they are experiencing a less severe outbreak than those in communities with more confirmed cases, even if the underlying outbreaks were actually of similar size.

One measure that can be helpful for determining how thorough current levels of testing might be in identifying infected individuals is the positivity rate, which is the percentage of all completed tests that returned a positive result. A low positivity rate means that a high proportion of tests are returning negative results, which may indicate that enough tests are being performed to identify a high proportion of all infections. If most tests are returning positive results, a community may not be testing enough to capture all of their infections. The positivity rate can vary significantly, even over short time periods. For example, the CDC reports that, in the week ending May 16, 2020, the positivity rate across the United States had dropped from 10.7% to 8.9% in public health laboratories, 6.4% to 5.8% in clinical laboratories, and 9.9% to 7.9% in commercial laboratories, compared to the prior week. As of the time of writing, the positivity rate varied from as low as 2% to as high as 24% for the states for which data were available.

---


In February, the only tests available in the United States to confirm active COVID-19 infections were produced by the CDC and required processing by qualified laboratories. This process could often require a week or more to produce results, and the first batch of test kits contained manufacturing defects that prevented labs from confirming results. Over time, additional testing options have become available, including tests that produce results faster that can be processed at the point of care, as well as tests that identify infections by different means, such as rapid antigen tests that can generate results faster than the more sensitive but slower polymerase chain reaction tests. However, even as test availability has improved there have been continued issues with the accuracy of some tests. For example, the U.S. Food and Drug Administration (FDA) recently announced publicly some concerns with the Abbott ID NOW point-of-care tests, which may have returned false negative results as recently as May.

In the short term, slower testing methods will yield lower counts of confirmed cases on any given day than faster testing methods. For example, if two patients were both tested on the same day, and one was tested using a kit that required a week to process, while the other was tested using a rapid point-of-care kit, then the first individual may not be counted as a confirmed case until a week after the other. The table in Figure 3 shows how the number of confirmed cases might vary between communities using different types of tests.

In this example, it may take a week longer for a community using slow tests to notice an uptick in confirmed cases than a community using fast tests, and even then the number of confirmed cases would appear to be much lower on any given date. In reality, most communities are using a mix of testing methods, and a specific mix may change over time. Considering the long incubation periods observed for COVID-19, additional delays between exposure to and confirmation of infection can make it even more difficult for communities to observe the impact of any changes in their responses to an outbreak. However, faster tests are not without their trade-offs. In some cases, faster tests can be less accurate, which creates challenges as well.

The date to which new test results are attributed can also affect how case counts should be interpreted. In many communities, test results are attributed to the date on which the results were reported. In some communities, however, test results are instead attributed to the date of symptom onset. This can lead to the appearance of significant decreases in case counts in the most recent days or weeks because those with recent onset of illness may not have been tested yet or may still be waiting on results, and will therefore be unaccounted for. Some states report both, allowing for a comparison of how apparent trends might differ depending on the reporting method. For example, Figure 4 shows the total number of new cases reported since May 1 in one state where case counts are provided using both approaches.

---

in the week appearing abnormally high for some communities. These cyclical patterns in reporting may be hard to detect without careful inspection because many public health agencies are still reporting data on weekends, data are often aggregated across multiple reporting agencies, and the exponential nature of infectious disease transmission can make daily developments naturally volatile.

**Tools to use in interpreting data**

Because of the detrimental impact COVID-19 is having on many aspects of society, it is important to cultivate and maintain a free flow of emerging information. New data and research findings may be useful to researchers, clinicians, and others trying to fight the virus and its effects. Nevertheless, it is imperative that readers remain vigilant about the quality and limitations of information being released. Below are some constructs that readers can rely on to avoid misinterpretation or misapplication of COVID-19 analysis:

- **Has the article or study been peer-reviewed?** The peer-review processes that journal articles typically undergo before publication provide an extra layer of expert scrutiny of methodology and findings prior to their reporting.

- **Are the assumptions described or cited?** Do they take into account all existing knowledge and are they appropriate to the methodology? As demonstrated in some of our examples above, reasonable studies and pieces of information can sometimes be combined in ways that render the conclusions unreasonable or extreme. Carefully examine the assumptions used in research, and make sure that those assumptions make sense both in isolation and when combined.

- **What is the range of scenarios examined and results shown?** Given the amount of uncertainty that currently exists surrounding COVID-19, we recommend caution when looking to any study coming to one individual answer (without a range of scenarios or results shown). As a result of the uncertainty in the underlying assumptions for COVID-19 research, there will undoubtedly be uncertainty in the results. Higher-quality studies will typically demonstrate this uncertainty in their results.

- **Are the study limitations described?** Given the uncertainties and challenges discussed, it is reasonable to expect that higher-quality studies will acknowledge and review the limitations inherent in their methodologies and assumptions. Helpful discussions often address issues of the directionals of bias that may result and provide rationale for the selection of one methodology over another.

---

By applying these constructs and remaining attuned to the strengths and limitations of forthcoming studies, researchers and consumers can responsibly wade through the deluge of information about the changing COVID-19 landscape. Those producing research or projections related to COVID-19 prevalence, outcomes, or impacts would do well to clearly and carefully describe any key assumptions or limitations involved with their work. In the end, understanding the limitations and assumptions underlying each study is key to leveraging results to improve our understanding of this pandemic’s impact on our healthcare systems, our economies, and ultimately our lives.

CONTACT
Pamela Pelizzari
pamela.pelizzari@milliman.com
Stoddard Davenport
stoddard.davenport@milliman.com
Carol Bazell
carol.bazell@milliman.com

Milliman is among the world’s largest providers of actuarial and related products and services. The firm has consulting practices in life insurance and financial services, property & casualty insurance, healthcare, and employee benefits. Founded in 1947, Milliman is an independent firm with offices in major cities around the globe.

milliman.com

© 2020 Milliman, Inc. All Rights Reserved. The materials in this document represent the opinion of the authors and are not representative of the views of Milliman, Inc. Milliman does not certify the information, nor does it guarantee the accuracy and completeness of such information. Use of such information is voluntary and should not be relied upon unless an independent review of its accuracy and completeness has been performed. Materials may not be reproduced without the express consent of Milliman.