AAMC Novel Coronavirus Update
June 12, 2020

To help filter through the large volume of news about the novel coronavirus, Ross McKinney Jr., MD, AAMC chief scientific officer, with assistance from his team in the Scientific Affairs unit at the AAMC, has initiated a new, science-focused newsletter.

As of June 17, this newsletter will be published once per week on Wednesdays.

If you would like to opt-in to receive future updates, add your name, email, and institution to this survey.

Contact AAMC Senior Science Policy Specialist Amanda Field, PhD, with any other questions or requests.

To access the latest AAMC updates and resources on COVID-19, visit aamc.org/coronavirus. For resources on COVID-19 medical research, read more here.

Please share/forward this newsletter freely.

Today's Numbers

- World: 7,558,687 (422,544 deaths)
  - 1.1 times the number of cases and 1.1 times the number of deaths over the past week
- United States: 2,029,037 (113,924)
  - 1.1 times the number of cases and 1.1 times the number of deaths over the past week
  - 21,933,301 total tests
- States With Most Confirmed Cases:
  - New York: 381,714 (30,580)
  - New Jersey: 165,816 (12,443)
  - California: 143,513 (4,934)
  - Illinois: 130,603 (6,185)
  - Massachusetts: 104,667 (7,492)

For the most up-to-date data, refer to the Johns Hopkins COVID-19 Map.

The Institute for Health Metrics and Evaluation at the University of Washington Medicine is projecting hospital resource use in the United States based on COVID-19 deaths.

Lead News

The most important question for the United States regarding the COVID-19 pandemic is
how the virus will respond to the loosening of the social distancing lockdowns. Recent data show that while the overall number of new COVID-19 cases in the United States may be going down, cases are surging in many regions. Since June 1, 14 states (Alaska, Arizona, Arkansas, California, Florida, Kentucky, New Mexico, North Carolina, Mississippi, Oregon, South Carolina, Tennessee, Texas, and Utah) and Puerto Rico hit their highest seven-day averages of new infections. States reopening may be a factor, as since reopening, Arizona has had to reactivate hospital emergency plans and Texas has reported a record-breaking number of COVID-19 hospitalizations. The uptick could be due to increased Memorial Day activity, and several more states are reporting increased hospitalizations while the "data suggest people in the U.S. are moving around at a level that's up to about two-thirds of what it was before shutdown rules were implemented." Additionally, the World Health Organization (WHO) warned that cases are also increasing globally. [Editor's comment: There are many markers available to measure the state of the epidemic in a region: new cases, total cases, deaths, excess deaths, amount of testing, percentage of tests positive, amount of influenza-like illness, hospitalizations, and intensive care utilization. Here are comments on how to interpret each:

**New Cases:** This is the most accurate marker if it is close to the number of new infections, but many people with COVID-19 only have mild disease and so never appear at a clinical facility that could report them. In addition, not everyone is tested for COVID-19 for many reasons, including limited availability of testing, expense, and the lack of interventions. The case definition is critical — does it require a positive polymerase chain reaction (PCR) test (which indicates the acute illness) or antibody test (taken two weeks or more after the start of symptoms), or are classical symptoms sufficient? Reporting agencies can manipulate the number of new cases by using a broader or narrower definition. False negative PCR tests can also affect the perceived new case rate.

**Total Cases:** This number is often reported by the press (and this newsletter), but cumulative cases are not that useful to monitor what's happening in the present moment.

**Deaths:** Deaths related to SARS-CoV-2 infection would seem to be straightforward, but the same problem that was present in the case definition exists here. Does assignment of death to COVID-19 require a positive ante-mortem PCR test? Most people never have an autopsy, so assignment of cause of death is done with few standards. Someone who truly died of COVID-19 may be labeled as dying of "pneumonia" or an "influenza-like illness." Since most people are not tested prior to death, and since a PCR test may or may not be positive at the time of death in any case (the amount of virus peaks early in the illness), counting deaths may or may not be accurate. Deaths also lag behind the state of the epidemic, since the average time from infection to death is about three weeks.

**Excess Deaths:** One traditional way to monitor the effects of influenza outbreaks is to measure excess deaths — the number of deaths above what normally would be occurring in a given time span. When there is a single cause for the excess mortality, as is currently the case with the pandemic, this is actually a very sound measure. It feels fuzzy, since you cannot specifically attribute the deaths to COVID-19, but in fact, the death rate is constant enough in large enough populations that this marker should be believed. It is, however, not as reliable when there is more than one cause for an increase in death rate, as when influenza and SARS-CoV-2 outbreaks are occurring simultaneously.

**Numbers of Tests:** The number of PCR tests for COVID-19 should correlate with the number of people who are presenting to clinical facilities with suspicious symptoms. However, factors like the availability of tests, the enforcement of testing guidelines, the expense of testing, and the effectiveness of reporting tests to authorities all affect the number of tests reported. Blended with the percentage of tests positive, the number of tests can be useful, but as a single factor there are too many confounding concerns.

**Percentage of Tests Positive:** The percentage of tests positive can be combined with the number of tests to indicate how many new cases there are. In addition, a higher percentage indicates that more people who have an influenza-like illness actually have
COVID-19 instead of some other cause for their symptoms like fever and cough.

**Influenza-like Illness:** Public health agencies have used rates of influenza-like illness as a marker of influenza's presence, since most people are not formally tested for the flu. Given the rough similarity of COVID-19 symptoms to influenza (although COVID-19 is clearly worse), monitoring levels of influenza-like illness can actually provide a reflection of COVID-19 in the community, particularly when flu is not widely extant. This fall, the utility will diminish since influenza and SARS-CoV-2 are likely to be circulating at the same time.

**Hospitalizations:** Hospitalizations labeled for possible COVID-19 are a very concrete marker. Overall hospital utilization may not be as useful, since many large hospitals used elective procedures to be nearly full most of the time prior to the pandemic. To be useful, hospitalization as an indicator of pandemic activity should only count patients who were admitted for COVID-19 treatment or evaluation or who have a positive PCR test during the hospitalization. Once again, the case definition matters.

**Intensive Care Utilization:** Intensive care unit utilization goes up during COVID-19 outbreaks. Similarly, ventilator and ECMO (extra-corporeal membrane oxygenator) use is measurable and increases during an outbreak. This marker is important since it may reflect the capacity of the health system to respond to the most ill patients.

 Treatment News

The *New York Times* has provided an [excellent summary of the many SARS-CoV-2 vaccines under development](https://www.nytimes.com/).  

*STAT: The Novel Coronavirus Attacks the Lungs. A Biotech Company Sees a Common Enzyme as Key to Protecting Them.*

Clinical News

The multisystem inflammatory syndrome in children (MIS-C) that has been associated with SARS-CoV-2 infection can be confusing to diagnose because of the frequency of gastrointestinal (GI) symptoms — as high as 100% in one case series. A retrospective series from Columbia University found that [GI symptoms were a presenting manifestation in 84% of children, fever in 100%, and rash in 70.5%](https://academic.oup.com/lanj/article/25/5/556/5212468). The disease can mimic inflammatory bowel disease, so it should be considered in the differential diagnosis of children presenting with symptoms that mimic GI infection or inflammatory bowel disease.

The evidence continues to build that surfaces and fomites (contaminated objects) play only a small role in SARS-CoV-2 transmission. A non-peer-reviewed preprint (available publicly online but not yet published in a journal) looked at 21 households with at least one infected person, and while they could find viral RNA on some commonly touched surfaces (3%), [they could not find viable infectious virus](https://www.sciencedirect.com/science/article/pii/S0140260820336943). The investigators found a higher rate of positive RNA in bathroom drains and toilets (15%). [Editor's comment: While fomites still present a low risk for COVID-19 transmission, which means it would be ill-advised to take extreme risks like licking contaminated counters, the consensus is growing that droplets in the air are the major concern for COVID-19 transmission, not grocery bags and countertops.]

The ideal setup for vaccine studies is to vaccinate people who are later exposed to the infection. In a randomized trial, the people who received the real vaccine are protected and the people who received a placebo vaccine (or an alternative vaccine, perhaps a different dose) are not protected from infection. One difficulty is that these ideal challenge
studies require a certain amount of disease in the community, and one concern of SARS-CoV-2 vaccine researchers is that there is not enough COVID-19 disease in the population. If at some point it is demonstrated that a certain level of antibodies in COVID-19 patients reflects protection against infection, measurement of antibody titers might be available as a surrogate endpoint. But we don’t currently have that data, so real-time challenge studies are still important in the vaccine approval process.

A study in the BMJ shows that personal protective equipment (PPE) can be very effective when used correctly. 420 doctors and nurses went to Wuhan, China, from other parts of China to treat COVID-19 patients for six to eight weeks. All were trained in appropriate PPE use and given adequate supplies. By the conclusion of the stint in Wuhan, no one had acquired symptomatic SARS-CoV-2 infection despite many aerosol-generating procedures. All staff were tested by PCR three times on return and were also tested using antibody assays. All tests were negative. PPE, when used appropriately, works.

Regeneron has begun clinical trials of their monoclonal antibody cocktails for COVID-19. The company reports they are using a combination of two monoclonal antibodies because the virus was able to develop resistance to neutralization when only one was used. The initial use for the therapeutic will be for infected patients, but it might also be tested as a preventive measure. If the drug works, one major challenge will be manufacturing it in sufficient quantities.

In an announcement about the frequency of how often asymptomatic patients are infecting others, the WHO created considerable confusion about how SAR-CoV-2 is spread. The confusion occurred because classically, the term "asymptomatic" simply means "without symptoms" and does not distinguish between those who never develop symptoms and those who eventually do. But with SARS-CoV-2, a distinction has been made between "asymptomatic" and "pre-symptomatic" — the former meaning a person who never develops symptoms and the latter meaning a person who will develop symptoms but who has not yet started showing them. Asymptomatic patients have less virus and are probably not very contagious. Pre-symptomatic patients have more viral load and are quite contagious. Is the WHO's distinction useful? Not practically — you can't separate a pre-symptomatic patient from an asymptomatic patient in a prospective way, so the distinction is useless (and confusing) for operational purposes. The WHO did attempt to clarify its statement.

Policy News

Washington Post: CDC Wants States to Count 'Probable' Coronavirus Cases and Deaths, but Most Aren't Doing It

Roll Call: HHS Announces Plan to Send Out COVID-19 Medicaid Payments

Coronavirus and Health Equity

An NPR analysis of COVID-19 case data from Pennsylvania and New York, two states that collect data on patients' disability status, found that "people with intellectual disabilities and autism who contract COVID-19 die at higher rates than the rest of the population." Experts say there are two likely reasons for the inequity for people with developmental disabilities: they are more likely to have preexisting comorbidities and they are more likely to live with roommates or in a group home.
A new study from Dartmouth's Center for Global Health Equity found key strengths in rural northern New England that mitigated the impact of the virus on the region's vulnerable populations. "Our research highlights that vast disparities in health outcomes are not inevitable. Rural regions faced the triple challenge of limited health systems capacity, high percentage of older and sicker populations, and significant social vulnerability. Yet, rural health systems and communities were able to mount an effective pandemic response and protect their most vulnerable populations," explained Anne Sosin, MPH, the center's program director.

COVID-19 continues to hit low-income, marginalized communities hard. But there's an untapped army that can battle deadly health care inequities and inefficiencies. Community health workers understand what patients need — and how to help them get it.

The Government Accountability Office covered "some of the factors that may be contributing to a higher number of infections among American Indians."

**STAT:** "The Direct Result of Racism": COVID-19 Lays Bare How Discrimination Drives Health Disparities Among Black People

### Research News

**National Institutes of Health (NIH) Researchers Identify Key Genomic Features That Could Differentiate SARS-CoV-2 from Other Coronaviruses That Cause Less Severe Disease**

The NIH National Library of Medicine is "preparing to launch a pilot project to test the viability of making preprints resulting from NIH-funded research available via PubMed Central." The goal is to "explore approaches to increasing the discoverability of early NIH research results." The pilot launched this week and will run for at least one year.

A non-peer-reviewed preprint has found another protein, neuropilin-1, that SARS-CoV-2 uses to enter human cells in addition to the ACE2 receptor.

Two recent studies have provided further evidence that people unknowingly spread the coronavirus, reinforcing the need for wearing masks and social distancing. A study in Vietnam did repeated testing of 14,000 people at high risk of infection and determined that of 30 infected people who were monitored, only 13 developed symptoms. A Centers for Disease Control and Prevention (CDC) study of the 1,000 infected service members on the Navy ship USS Theodore Roosevelt found that 1 in 5 had no symptoms and many who did had only mild symptoms.

The NIH Director's Blog discusses how a blood test may be able to predict if a COVID-19 patient will become severely ill by performing a molecular profile of the proteins and metabolites in the sample. Another blog entry features a discussion with the director of the NIH's Heart, Lung, and Blood Institute on possible reasons why COVID-19 "triggers the formation of blood clots that can lead to strokes and other life-threatening complications, even in younger people."

The National Center for Biotechnology Information has provided a webpage to help bench scientists, bioinformaticians, clinicians, and others connect with SARS-CoV-2 DNA and protein sequence information.

**Science:** Aggregating Data From COVID-19 Trials
STAT: 'Flying Blind': Doctors Race to Understand What COVID-19 Means for People With HIV

Nature: Frozen Cells and Empty Cages: Researchers Struggle to Revive Stalled Experiments After the Lockdown

Testing News

Modern Healthcare: CDC Develops Test to Simultaneously Detect COVID-19, Flu

Other COVID-19 News

A non-peer-reviewed preprint examined social distancing practices across people with various vulnerability, race, politics, and employment and found that black people followed social distancing rules more than white people. It also observed more social distancing during weekdays than weekends by early May.

Science Editorial: COVID-19 and Flu, a Perfect Storm

New York Times: When 511 Epidemiologists Expect to Fly, Hug and Do 18 Other Everyday Activities Again

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