AAMC Coronavirus Update
March 10, 2021

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

This newsletter will be published once per week on Wednesdays.

Opt-in to receive future updates.

Contact AAMC Lead Science Policy Specialist Anu Dev, 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.

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Today's Numbers

- **World**: 117,717,343 confirmed cases (2,613,747 deaths)
  - 2,385,777 new cases this week (2,717,719 cases last week)
- **United States**: 29,109,695 confirmed cases (527,950 deaths)
  - 402,049 new cases this week (459,666 cases last week)
  - 11,541 deaths this week (13,768 last week)
  - 367,015,805 total tests
- **U.S. Hot Spots**
  - Missouri: 84,397 new cases in the last 7 days (11% change in daily cases)
  - New York: 49,633 (-5%)
  - Texas: 39,134 (-21%)
  - Florida: 33,472 (-13%)
  - California: 28,715 (-3%)
- **U.S. COVID-19 Vaccine Distribution and Administration**
  - Total Doses Delivered: 123,232,775
  - Total Doses Administered: 93,692,598
  - Number of People Receiving One or More Doses: 61,088,527
  - Number of People Receiving Two Doses: 32,102,061

For the most up-to-date data, refer to the Johns Hopkins COVID-19 Map. Details of other U.S. hot spots can be found at the Washington Post's coronavirus data webpage. Overall U.S. COVID-19 vaccine distribution and administration data can be found at the Centers for Disease Control and Prevention (CDC) COVID Data Tracker.
The Institute for Health Metrics and Evaluation at the University of Washington Medicine is [projecting hospital resource use in the United States](https://www.healthmanagement.org) based on COVID-19 deaths.

### Lead News

It’s unusual for this newsletter, but a [tweet chain written by Monica Gandhi, MD, MPH](https://twitter.com/MonicaGandhiMD/status/1370504189740273664), of the University of California, San Francisco, School of Medicine, has nicely gathered together a list of studies addressing whether vaccines decrease the number of people asymptomatically infected with SARS-CoV-2. This is a critical question for many reasons — most significantly, it speaks to the importance of general mask-wearing in a post-vaccine era. There has been concern that vaccinated people might still become infected by and cryptically spread SARS-CoV-2 to people who are not yet vaccinated, which would imply that masks will continue to be necessary in the future. The results from seven studies are consistent: The vaccines reduce the rate of asymptomatic infection just as they have with symptomatic infection, often by more than 90%. Different strategies were used to detect subsequent asymptomatic infections — either prospective polymerase chain reaction (PCR) sampling or detecting antibodies to the nucleocapsid of the virus. The nucleocapsid is a protein seen in the wild type virus that isn’t present in the vaccine, so the presence of anti-nucleocapsid antibodies is a valid indicator of SARS-CoV-2 infection after vaccination. Both strategies found the same result: a significant drop in the asymptomatic infection rate. In addition, viral loads were lower in those who did get infected post-vaccine, indicating lower transmissibility. [Editor’s comment: We shouldn’t rush, but there is real reason to believe we can get back to what many of us recall as normal: restaurants, bars, dinners with friends. We need to be patient, and only when community spread is down to negligible levels should we unmask and resume “normal” life. To rush is to risk pandemic relapse, which we hope is not demonstrated by those states that are acting as real-world trials of early unmasking.]

### Treatment News

The National Institutes of Health (NIH) has been sponsoring a multi-arm controlled clinical trial (ACTIV-3) to evaluate treatments for COVID-19. The trial is designed so that multiple arms studying different options can be underway at the same time. While this is efficient, the NIH announced this week that two arms were closed by the data safety monitoring board because of therapeutic futility. The first arm was evaluating a therapeutic monoclonal antibody treatment, VIR-7831, in adults hospitalized with COVID-19, while the second substudy was evaluating a combination of two monoclonal antibodies, BRII-196 and BRII-198. VIR-7831 was produced by GlaxoSmithKline and Vir Biotechnology, while BRII-196 and BRII-198 were produced by Brii Biosciences. All patients also received remdesivir. The endpoint is the clinical status after five days. After 150 patients enrolled in the study arm and another 150 enrolled in the placebo arm, there was a preplanned safety and efficacy review. In this case, the VIR-7831 arm and control arm enrolled 344 volunteers, and the BRII study enrolled 343 volunteers. The NIH noted there are two other related studies underway: another arm of ACTIV-3 testing AZD7442, a long-acting monoclonal antibody combination in hospitalized patients, and ACTIV-2, which is evaluating BRII-196 and BRII-198 in patients with mild to moderate COVID 19 who have not required hospitalization. [Editor’s comment: Monoclonal antibody treatments in advanced disease don’t seem to have much promise. They may have some benefit early in disease, when patients haven’t yet synthesized their own antibodies. But there’s the additional rub that some of the recent SARS-CoV-2 variants are resistant to]
current monoclonals. At this point, the monoclonals’ niche seems to be early in the disease course for patients at high risk of consequences due to conditions like old age, immune compromise, or perhaps obesity.]

In the department of wishful thinking, the anti-parasite drug ivermectin began to be used widely based on some tenuous in vitro data, achieving approval in several countries’ treatment guidelines. A controlled clinical trial of ivermectin in Colombia, published in JAMA, demonstrated that it has no significant effect on the duration of symptoms. 476 adults with mild disease and symptoms for seven days or fewer were enrolled. There were small and neither clinically nor statistically meaningful differences in the treatment and placebo groups. It was therefore recommended that ivermectin not be used as treatment for COVID-19. [Editor’s comment: The main lesson is that mild in vitro benefits often do not result in corresponding clinical improvements. Drugs may affect isolated cells and tissues in different ways than they affect the same tissues in an intact organism.]

Merck and Ridgeback Biotherapeutics have announced preliminary findings on their joint project, molnupiravir (EIDD-2801/MK-4482), for the treatment of COVID-19. The drug was originally conceived as an oral agent for influenza by the Emory Institute for Drug Development, but when SARS-CoV-2 began to spread last year, it was discovered that it also had potential as a coronavirus drug. The most recent announcement was regarding a Phase 2a study in adults infected with SARS-CoV-2. The protocol evaluated nasopharyngeal PCR positivity in 202 symptomatic COVID-19 patients and found that the drug reduced the number of days of infectivity. The study is ongoing, so the results presented at the 2021 Conference on Retroviruses and Opportunistic Infections were limited. At day five after enrollment, zero of 47 patients treated with molnupiravir were still PCR positive versus six of 25 who were placebo treated. [Editor’s comment: It’s early, but promise remains for molnupiravir. And perhaps it will also serve its original purpose and treat influenza as well].

Age has been an important consideration in the response to COVID-19 vaccines, given the differential in susceptibility to COVID-19 clinically. Investigators in Germany compared the responses to the Pfizer vaccine developed in partnership with BioNTech (BNT162b2) in those younger than 60 and those older than 80, and they published their results as a non-peer reviewed preprint in medRxiv. Not surprisingly, younger people had a stronger immune response. 17 days after the second vaccine dose, 31.3% of the elderly had no detectable neutralizing antibody response, as opposed to 2.2% of the volunteers younger than 60. The mean titers were also significantly lower in the elderly cohort. The authors suggest earlier revaccination in the elderly may be necessary to maintain protection.

Clinical News

A group of physicians in Boston described delayed large local reactions to the first dose of the Moderna (mRNA-1273) vaccine in a short communication with the New England Journal of Medicine. The reactions in 12 patients occurred primarily at the injection site at a median of eight days after vaccination, with a range of four to 11 days. The appearances were quite varied (photographs are provided in the communication), but most involved erythema and swelling. Some of the patients had concomitant systemic symptoms like headache, fever, and fatigue. All the patients were given a second dose of the vaccine. Three patients had recurrences that were similar to the first dose reaction, three had similar but milder reactions, and six had no recurrence. The recurrences occurred more rapidly than the first reactions at an average of two days after injection, with a range of one to three days.
CDC: Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in the United States

Policy News

The CDC released a set of public health recommendations for individuals who are fully vaccinated against the SARS-CoV-2 virus. This update includes recommendations on how fully vaccinated people can safely visit with vaccinated or unvaccinated individuals in private settings, as well as recommendations for isolation, testing, and quarantine. Evidence substantiating the CDC’s recommendations are available in the new Science Brief.


Coronavirus and Health Equity

A new report from the Human Rights Campaign found that while members of the LGBTQ+ community are generally more willing to get vaccinated than their heterosexual peers, variation within the community exists. Specifically, while transgender people are the most likely to want to get vaccinated, bisexual women are significantly less likely to report such an intention. Black members of the LGBTQ+ community are also less likely than their White peers to say they will get vaccinated. The two largest barriers to vaccination reported by the LGBTQ+ community were concerns about the vaccine’s affordability and its potential side effects.

An analysis by FamiliesUSA estimated that 1 out of every 3 COVID-19-related deaths — and more than 40% of all infections — nationally can be linked to health insurance inequities.

FiveThirtyEight: The Reason Black Americans Are Getting Vaccinated At A Much Slower Rate Is Not Because They’re Reluctant

CNN: Rural Americans in Pharmacy Deserts Hurting for COVID-19 Vaccines

New York Times: ‘I Really Loved My Job’: Why the Pandemic Has Hit These Workers Harder

New York Times: Pandemic’s Racial Disparities Persist in Vaccine Rollout

Washington Post: As Schools Reopen, Asian American Students Are Missing From Classrooms

Research News
Researchers continue to characterize and investigate the activity of the SARS-CoV-2 variants in circulation. An article in *Nature* characterized the emergence of the now well-recognized variant B.1.351, which originated in South Africa and has eight mutations in the spike protein domain. Genomic analyses have suggested that this lineage is associated with a selection advantage, likely as a result of increased transmissibility or immune escape. To understand whether these variants might be able to "escape" the vaccine, two recent papers also examined their neutralizing activity by serum samples from vaccinated individuals, with one manuscript focused on the variant first detected in the United Kingdom, B.1.1.7, and another testing six variants, including B.1.1.7 and B.1.351. Both studies found that the serum samples effectively neutralized the viruses with variant spikes, although there was some variability in the potency of neutralization. On the clinical side, a study in Denmark noted an increased risk of hospitalization association with B.1.1.7, with an adjusted odds ratio of 1.64 (95% confidence interval [CI]: 1.32-2.04). Finally, a non-peer reviewed preprint looking at the case fatality risk of B.1.1.7, using data from England's open electronic health record system, found that the variant is associated with increased risk of death, with a hazard ratio of 1.67 (95% CI: 1.34–2.09).

Using surveillance data collected at the University of Colorado, Boulder, investigators published a preprint looking at a subset of 1,405 individuals who tested positive for SARS-CoV-2 but were asymptomatic or pre-symptomatic at the time of collection. There was an extremely wide variation in viral load, ranging from 8 virions/mL to 6 trillion virions/mL. In an analysis of how the virus is distributed between individuals within populations, the researchers found that just 2% of individuals harbor 90% of the circulating virions (in both their asymptomatic population as well as published studies of symptomatic individuals), suggesting that these people function as viral “super-carriers” and possibly also superspreaders.

In a recent *JAMA* article, researchers analyzed the changes in mortality of adults hospitalized with COVID-19 at U.S. medical centers between March 1 and Aug. 31, 2020, shedding light on characteristics and outcomes of adults during the initial six-month period of the COVID-19 pandemic. The data revealed high in-hospital mortality (13.6%), with in-hospital mortality increasing with age (particularly in patients age 80 or older). Despite an overall high mortality rate, a significant reduction in mortality was observed between March (22.1%) and August (6.5%), with mortality decreasing each month over the course of the study. Data from this cohort study of patients revealed that the most common comorbidities were hypertension, diabetes, and obesity. Though limitations of this study include factors such as the underdiagnosing of COVID-19 and the possible miscoding and misclassification of data, this study represents “the largest US cohort of hospitalized COVID-19 adults to date.”

Elucidating immune markers correlative with protection against the SARS-CoV-2 virus is essential for driving COVID-19 interventions, yet markers are not currently well defined. A recent study examined the longitudinal evolution of the SARS-CoV-2 antibody repertoire in patients with "mild" versus “acute” COVID-19, revealing differential antibody markers associated with both disease severity and resolution of patients with COVID-19.

*Nature Genetics*: Genome-Wide CRISPR Screening Identifies TMEM106B As a Proviral Host Factor for SARS-CoV-2

**CDC MMWR**: Estimated SARS-CoV-2 Seroprevalence Among Persons Aged <18 Years — Mississippi, May–September 2020

**Testing**
News

FDA Issues Authorization for First Molecular Non-Prescription, At-Home Test

FDA Authorizes Adaptive Biotechnologies T-Detect COVID Test

Other COVID-19 News

AAMCNews: Are the COVID-19 Vaccines Safe During Pregnancy? Experts Weigh In

Nature: Pregnancy and COVID: What the Data Say

Nature: COVID is Amplifying the Inadequacy of Research-Evaluation Processes

Wall Street Journal: Biden Expects U.S. to Have Covid-19 Vaccines for All Adults by End of May

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