

# AAMC Coronavirus Update

June 4, 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 twice a month on alternating Fridays.

**[Opt-in to receive future updates.](#)**

Contact AAMC Senior Science Policy Specialist [Julia Omotade](#), PhD, with any other questions or requests.

To access the latest AAMC updates and resources on COVID-19, visit [aamc.org/coronavirus](https://aamc.org/coronavirus). For resources on COVID-19 medical research, [read more here](#).

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## Today's Numbers

- World: 172,016,873 confirmed cases (3,698,371 deaths)
  - 3,255,390 new cases this week (4,543,419 cases 16 days ago)
- United States: 33,326,054 confirmed cases (596,401 total deaths)
  - 113,666 new cases this week (220,369 cases 16 days ago)
  - 3,188 deaths this week (4,287 deaths 16 days ago)
  - 454,120,086 total tests
- U.S. Hot Spots
  - Florida: 1,627 average daily new cases in the last 7 days (-29% change in daily cases in the last 7 days)
  - Texas: 1,094 (-35%)
  - Washington: 787 (-24%)
  - California: 765 (-36%)
  - Pennsylvania: 652 (-43%)
- U.S. COVID-19 Vaccine Distribution and Administration
  - Total doses delivered: 368,375,195
  - Total doses administered: 297,720,928

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](#) based on COVID-19 deaths.

## Lead News

The world is counting on SARS-CoV-2 vaccines to allow life to return to normal. [In the May 28 edition of the \*Morbidity and Mortality Weekly Report \(MMWR\)\*](#), the CDC reported on breakthrough infections in vaccinated people between Jan. 1 and April 30, 2021. “Breakthrough infections” were defined as detecting virus by polymerase chain reaction (PCR) or antigen detection two weeks or more after the last prescribed dose of one of the three authorized vaccines. 10,262 breakthrough infections were reported to the CDC. Of these, 63% were in females, and the median age was 58 years. 2,725 infections were asymptomatic. 160 patients died. 995 people (10%) were hospitalized, but of those, 29% were asymptomatic or admitted for some reason other than COVID-19. The median age of patients who died was 82 years. 20% of the people who died were asymptomatic or died of something other than COVID-19. Sequence data was available for only 5% of cases, 64% of which were variants of concern. Most common were B.1.1.7 (199; 56%) and B.1.429 (88; 25%). As background, 101 million people in the United States had been fully vaccinated by April 30. [Editor’s comment: It was only a moment in time, but of the 101 million people vaccinated by April 30, only 0.01% became infected (1 in 10,000). To put this in perspective, among all citizens, there were 355,000 COVID-19 cases reported nationally in just the week of April 24-30, 2021. Even though the 10,000 cases are almost certainly an undercount, no one reasonable should doubt that these are remarkably effective vaccines.]

Virology labs at the University of Washington genetically sequenced 20 breakthrough cases of COVID-19 that occurred in vaccinated individuals. [The manuscript was published as a non-peer reviewed preprint in \*medRxiv\*](#). All 20 cases involved one of the CDC’s variants of concern. Eight cases were caused by B.1.1.7 (40%), eight cases by B.1.429 (40%), two cases by B.1.427 (10%), and one case each by B.1.351 and P.1 (5% each). The investigators compared these rates to the sequence data they had from nonbreakthrough cases. 68% of the nonbreakthrough cases were variants of concern: B.1.1.7 (31%), B.1.429 (27%), B.1.427 (3%), B.1.351 (1%), and P.1 (7%). The authors concluded that variants of concern were more likely to produce a breakthrough infection. The breakthrough cases also had higher viral load than in previous reports on breakthroughs. [Editor’s comment: As the authors pointed out, data like this will be useful in designing future vaccines. Though the number of breakthrough cases was not large, it hints that variants of concern may be a problem as immunity wanes over time.]

## Clinical and Treatment News

The variant first identified in India, B.1.617.2, has caused disease in fully vaccinated individuals. B.1.617.2 has now spread to the United Kingdom, and investigators there are evaluating whether the two vaccines predominantly in use — Pfizer’s BNT162b2 and AstraZeneca’s ChAdOx1 — are effective against it. They [published the results as a non-peer reviewed preprint](#). The study design was a “negative case control” where patients who report for care with symptoms and test negative for SARS-CoV-2 are compared to those who test positive. Vaccination status is assessed in both instances. Vaccination status was also compared to the relative proportions of the B.1.1.7 and B.1.617.2 strains. The assumption is that if the vaccines are equally effective against both strains, their isolation in the vaccinated population will be proportional to their isolation in the unvaccinated population. 12,675 sequenced cases were identified: 11,221 were B.1.1.7 and 1,054 were B.1.617.2. The case ratio (B.1.617.2 to B.1.1.7) in unvaccinated individuals was 0.084. With BNT162b2, the ratio was 0.094, while it was 0.142 with ChAdOx1. The authors translated the effectiveness against B.1.617.2 after two doses at 88% for BNT162b2 and 60% for ChAdOx1. [Editor’s comment: The study design is extremely complicated, but it appears that both vaccines are effective against B.1.617.2,

which is important given its worldwide spread.]

To increase the efficiency of approval, most SARS-CoV-2 vaccine studies used the same vaccine for the prime and boost doses, and most used the shortest possible reasonable interval (three or four weeks) between doses. Those intervals may not be the ideal timing, and it may be more effective to use a heterologous boost with a different vaccine than the one used for the prime. [An article in Nature](#) described a study from Spain, CombivacS, that enrolled 663 people in a trial where the AstraZeneca ChAdOx1 vaccine was administered first. Two-thirds of participants were given BNT162b2 at least eight weeks after the first dose. One-third have not yet been boosted. The investigators stated that the neutralizing antibody titers after the heterologous prime-boost were better than had been seen with previous studies of two doses of ChAdOx1. A similar U.K. study is in progress, where patients are first given ChAdOx1 and then are boosted at two dosing intervals (28 and 84 days) with either ChAdOx1 or BNT162b2, but the [immunological results are pending](#). [Editor's comment: The comparison of the results of the Spanish study against historical controls is suboptimal and not that useful. However, the notion of heterologous boosting remains tenable. It will be particularly important in the future if variants become a problem and require vaccines that are built around the variant sequences.]

[The FDA has issued an emergency use authorization \(EUA\)](#) for another monoclonal antibody, sotrovimab, that can be used to treat patients with mild-to-moderate COVID-19 who have not yet been hospitalized. The drug is produced by GlaxoSmithKline and Vir Biotechnology. It is not authorized for those who have been hospitalized, nor for people with an oxygen requirement. The basis for the approval was a study that enrolled 583 nonhospitalized adults. The primary endpoint was COVID-19 progression (hospitalization for COVID-19 symptoms or death). The endpoint occurred in three sotrovimab recipients (1%) compared to 21 placebo recipients (7%) — an 85% reduction.

There are reports of myocarditis and pericarditis following vaccination with the two mRNA SARS-CoV-2 vaccines. The reports have come from several sources: [The Connecticut Department of Health/Yale New Haven Health](#), [the CDC](#), and [Israel](#). The typical symptom has been chest pain. The condition occurs most often in young males, 16-24 years old in Israel, within a few weeks of vaccination, most often after the second dose. The reaction appears to be self-limited and treatment is with anti-inflammatory drugs. [The incidence rate was reportedly 1 in 50,000 doses overall](#), although it may be higher in young males. [Editor's comment: This adverse event, which appears to be linked to administration of both the Pfizer and Moderna vaccines, adds to concerns about any signal that might increase vaccine reluctance. All indications are that the side effect is rare and more inconvenient than consequential, but evaluations continue.]

The Chinese company, Sinopharm, has been developing inactivated SARS-CoV-2 vaccines. The results of their placebo-controlled clinical trial of two products, SARS-CoV-2 WIV04 and SARS-CoV-2 HB02, [were published in JAMA](#). The trial enrolled 40,382 adult participants in Bahrain and the United Arab Emirates. 13,459 received WIV04, 13,465 received HB02, and 13,458 received placebo. Because of the location of the study, 84.4% of participants were men. Median follow-up was 77 days after the second dose (with a range of one to 121 days), and in that time period, there were 26 symptomatic COVID-19 cases in the WIV04 cohort, 21 cases in the HB02 cohort, and 95 in the alum-only control group (placebo group). This translated into vaccine efficacy of 72.8% for WIV04 and 78.1% for HB02. [Editor's comment: The gender distribution was striking, but the study does appear to demonstrate that Sinopharm's inactivated vaccines are safe and reasonably effective.]

Full results of a placebo-controlled clinical trial of Pfizer's BNT162b2 vaccine in 12- to 15-year-old adolescents was [published in the New England Journal of Medicine \(NEJM\)](#). 2,260 participants enrolled — 1,131 received BNT162b2 and 1,129 received placebo. The

adverse event profile was similar to past studies. The geometric mean antibody titer ratio in the 12- to 15-year-olds was 1.76 times that of the pool average compared to antibody titers in 16- to 25-year-olds. There were no cases of SARS-CoV-2 detected seven or more days after the second dose in the BNT162b2 cohort, while there were 16 cases in the placebo group (an efficacy rate of 100%).

Moderna presented the results of their placebo-controlled clinical trial in 12- to 17-year-olds in a [press release](#). 3,732 participants enrolled and were randomized at a 2-1 ratio to the company's mRNA-1273 vaccine. The adverse event profile looked similar to adult data. Using the adult standard of symptomatic COVID-19, there were no cases among vaccinated individuals and four cases among placebo recipients. Using a milder standard (any COVID-19-related symptom and a positive PCR test for SARS-CoV-2), vaccine efficacy was 93% after the first dose. The company stated they planned to request an extension to their EUA for individuals 12 to 17 years old.

[BMJ: Covid-19: Pfizer-BioNTech vaccine is "likely" responsible for deaths of some elderly patients. Norwegian review finds](#)

## Policy News

On May 31, the World Health Organization (WHO) announced that they will use the Greek alphabet to assign ["simple, easy-to-say labels for SARS-CoV-2 Variants of Interest and Concern."](#) These labels are now [posted to the WHO website](#). The WHO noted that these new labels do not replace existing scientific names, which convey important scientific information and will continue to be used in research. The impetus behind these changes was clearly stated: "while they have their advantages, these scientific names can be difficult to say and recall, and are prone to misreporting. As a result, people often resort to calling variants by the places where they are detected, which is stigmatizing and discriminatory. To avoid this and to simplify public communications, the WHO encourages national authorities, media outlets and others to adopt these new labels." Popular media outlets such as [NPR](#) and the [Washington Post](#) have commented on these changes.

## Coronavirus and Health Equity

A [new CDC report](#) found that between December 2020 and May 2021, disparities "in county-level vaccination coverage by social vulnerability have increased as vaccine eligibility has expanded." Specifically, as measured by the [Social Vulnerability Index](#) (SVI), adult vaccination differences in counties with the highest versus lowest SVI were between 8% and 17%, depending on the size and urbanicity of the counties. Further, and counter to other recent analyses, analysis of the race/ethnicity-related "SVI theme" found that coverage was *higher* in counties with larger proportions of racial and ethnic minority residents (57% versus 45%). The opposite was true for the themes of socioeconomic status and disability/housing composition.

[Health Security: Covid-19 Mental Health Disparities](#)

[New York Times: The U.S. Vaccination Story Varies Widely Across Regions](#)

[BMJ: Covid-19 Vaccination Hesitancy](#)

## Research News

Followers of primary research articles relating to SARS-CoV-2 and immunity will be familiar with the ongoing efforts to characterize the longevity of anti-SARS-CoV-2 serum antibodies after infection. [A recent paper in Nature](#) investigated 77 patients who experienced mild SARS-CoV-2 infection and found that “serum anti-SARS-CoV-2 spike (S) antibodies decline rapidly in the first 4 months after infection and then more gradually over the following 7 months, remaining detectable at least 11 months after infection.” This is consistent with previous reports. The investigators also examined whether SARS-CoV-2 infection “induces long-lived antigen-specific human bone marrow plasma cells (BMPCs),” which are “a persistent and essential source of protective antibodies.” The results from this study indicated that SARS-CoV-2 infection not only generates a transient “wave of serum antibodies that decline relatively quickly” but also elicits “more stably maintained serum antibody levels that are supported by long-lived BMPCs.” An [accompanying news piece in Nature](#), “Had COVID? You’ll probably make antibodies for a lifetime,” summarized the implications of these findings: “People who recover from mild COVID-19 have bone-marrow cells that can churn out antibodies for decades, although viral variants could dampen some of the protection they offer.” [Editor’s comment: Though there are limitations of this study, this work sheds light on the complexity of the immune system.. To their knowledge, the authors noted that “the current study provides the first direct evidence for induction of antigen specific BMPCs after a viral infection in humans.” Researchers have thus far made seminal contributions to our understanding of how we stay healthy, yet the immunological orchestra that keeps us healthy and wards off pathogens and subsequent diseases is being recognized — more and more — as a “whole body” endeavor. A [recent comment article in Nature](#) exposed how “the pandemic has revealed major gaps in our understanding of the human immune system.” Author Donna Farber, PhD, stressed that our understanding of immunity must not solely focus on the blood. “One of the biggest [immune responses] is the reactions in tissues — at sites of infection and where disease manifests. ... To fully grasp the immune system, researchers need to understand respiratory, gut and skin immunity, and how each interacts with nearby lymph nodes,” she said. This comment article explored the author’s view on “how to make such research happen and what can be learnt.”]

As one can imagine, there has been no shortage of studies and articles testing and reporting on the efficacy of the various circulating vaccines. As the proportion of vaccinated individuals continues to climb, the contributors of this newsletter frequently report on “real world” studies — which capture the dynamics of infection, morbidity, and mortality in an array of global populations. Such data address critical questions and gaps in our knowledge and has major implications for public health, such as vaccine rollout strategies. Three recent studies (all preprints published in *medRxiv*) that add to our “real world” knowledge of vaccines are summarized below:

1. Results from a [medRxiv preprint](#) published on May 29 “investigated the association between daily mortality due to COVID-19 and vaccination coverage.” Of note, this study took factors into account such as the proportions of SARS-CoV-2 variants, demographics, health, and mobility across Europe and Israel. According to the authors, the results suggest that vaccination effectiveness is 72%, which is “lower effectiveness against death than reported efficacy against severe or critical disease course in clinical trials of vaccines (84-100%).” [Editor’s comment: The authors noted that the lower-than-expected effectiveness (72%) “might be explained by the difference in considered populations: clinical trials included restrictive populations and our study covers general populations, irrespective of age, concomitant therapies, condition and general condition.” Studies such as these highlight the utility of using real-world data to track the impact and effectiveness of COVID-19 vaccinations in time and space.]
2. Given that the global population is not fully vaccinated, studying the dynamics of



transmission between vaccinated and unvaccinated individuals is key. A May 29 [medRxiv preprint](#) “studied the direct and indirect effectiveness of Covid-19 vaccines among vaccinated healthcare workers and their unvaccinated adult household members in a mass vaccine program in Finland.” The authors’ results “suggest that mRNA-based vaccines do not only prevent SARS-CoV-2 infections among vaccinated individuals but lead to a substantial reduction in infections among unvaccinated household members.” As the authors point out, these results are “consistent with the notion that mRNA-based vaccines affect susceptibility in vaccinated individuals and prevent transmission from vaccinated to unvaccinated individuals.”

3. Investigators “evaluated SARS-CoV-2 specific antibody responses following a single-dose of BNT162b2 (Pfizer-BioNTech) mRNA vaccine in 155 previously SARS-CoV-2-infected individuals participating in a population-based prospective cohort study of COVID-19 patients.” [They reported that](#) “within one week of vaccination, IgG antibody levels to virus spike and RBD proteins increased 27 to 29-fold and neutralizing antibody titers increased 12-fold, exceeding titers of fully vaccinated SARS-CoV-2-naïve controls.” Moreover, “COVID-19 severity, the presence of comorbidities and the time interval between infection and vaccination had no discernible impact on vaccine response.” The authors concluded that “a single dose of BNT162b2 mRNA vaccine up to 15 months after SARS-CoV-2 infection provides neutralizing titers exceeding two vaccine doses in previously uninfected individuals.” Because various regions are dealing with limited vaccine availability, this data indicates that single-dosing vaccination of individuals who have had previous SARS-CoV-2 infection might be a feasible pathway for dose-sparing strategies.

In the ever-evolving quest to identify and characterize SARS-CoV-2 variants, [a recent Nature review](#) “summarizes the literature on mutations of the SARS-CoV-2 spike protein, the primary antigen, focusing on their impacts on antigenicity and contextualizing them in the protein structure, and discuss them in the context of observed mutation frequencies in global sequence datasets.”

[CDC MMWR: Mask Use and Ventilation Improvements to Reduce COVID-19 Incidence in Elementary Schools — Georgia, November 16–December 11, 2020](#)

[medRxiv: UV-A and UV-B Can Neutralize SARS-CoV-2 Infectivity](#)

[bioRxiv: Correlation of Vaccine-Elicited Antibody Levels and Neutralizing Activities Against SARS-CoV-2 and its Variants](#)

[Nature: The Mini Lungs and Other Organoids Helping to Beat COVID](#)

## Other COVID-19 News

[Nature: After COVID-19 Successes, Researchers Push to Develop mRNA Vaccines for Other Diseases](#)

[BMJ: Covid-19: Variants Are Spreading in Countries With Low Vaccination Rates](#)

[medRxiv: Out-of-Pocket Spending for COVID-19 Hospitalizations in 2020](#)

[Nature: Count the Cost of Disability Caused By COVID-19](#)

[Science: Blind Spots Thwart Global Coronavirus Tracking](#)

[NEJM: Incentives for Immunity — Strategies for Increasing Covid-19 Vaccine Uptake](#)

For questions, contact [Julia Omotade](#), PhD, AAMC lead science policy specialist.



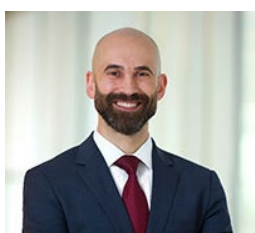
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