



AAMC Coronavirus Update

March 4, 2022

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.

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. For resources on COVID-19 medical research, [read more here](#).

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Today's Numbers

- World: 442,248,874 confirmed cases (5,982,821 total deaths)
- United States: 79,196,394 confirmed cases (956,262 total deaths)
 - 388,027 new cases this week (new daily reported cases fell 28% in the past week)
 - 11,826 deaths this week (new daily reported deaths fell 12% in the past week)
 - COVID-19-related hospitalizations fell 21% in the past week
- U.S. Hot Spots
 - California: 7,555 average daily new cases in the last 7 days (-20% change in daily cases in the last 7 days)
 - Texas: 4,006 (-34)
 - North Carolina: 2,421 (-30%)
 - Florida: 2,128 (-46%)
 - Kentucky: 2,057 (-31%)
- U.S. COVID-19 Vaccine Distribution and Administration
 - Total doses delivered: 691,748,065
 - Total doses administered: 554,168,735
 - People fully vaccinated: 215,892,470 (65%)
 - People received a booster dose: 94,770,180 (43.9%)

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 AAMC staff who have been writing the AAMC Coronavirus Update newsletter since March 2020 are very optimistic that we are past the worst of this pandemic, at least in the United States. The virus may come back, but it's looking like we're on the cusp of a relatively quieter period with fewer cases. As a consequence, we're going to call it a day and put this newsletter to bed. Thank you to everyone who has worked hard in its production, particularly Julia Omotade, PhD; Amanda Field, PhD; Anurupa Dev, PhD; Philip Alberti, PhD; Sarah Piepenbrink; Steve Heinig; Heather Pierce, JD; Brooke Bergen; Michelle Zajac; Elena Marinaccio; and Mike Randazzo. And thanks to you, the readers, who gave us regular feedback and shared this newsletter with your friends, as we intended. Now for a nice, healthy, and — let me say it — normal spring and summer!
— Ross McKinney, MD, newsletter editor

Clinical and Treatment News

A long-standing COVID-19-related question has been the length of time that someone should quarantine after a positive test. The Yukon-Kuskokwim Health Corporation (YKHC), a tribal organization that delivers health care in rural southwest Alaska, and the Centers for Disease Control and Prevention (CDC) designed a study to answer the question using rapid antigen tests. The results were [published in the CDC Morbidity and Mortality Weekly Report](#). The original recommendation from both organizations was for ten days of isolation after a positive PCR or antigen test. However, isolation could end between 5-9 days if symptoms were resolving or absent, fever was absent for 24 hours without use of a fever-reducing medication, and an Abbot antigen test (BinaxNOW) was negative. Follow-up antigen test results were assessed for 3,502 SARS-CoV-2 positive cases reported to the YKHC between Jan. 1 and Feb. 9. During 5-9 days after the initial test, 396 out of 729 samples (54.3%) were positive. Day 5-9 antigen tests were more likely to be positive after a symptomatic infection (64% versus 21.2%) and less likely to be positive if someone had had a previous SARS-CoV-2 infection [adjusted odds ratio (aOR) of 0.30], receipt of a primary vaccine series (aOR of 0.60), or after a combination of past infection and vaccine series (aOR of 0.17). [Editor's comment: This was a nicely done community-based study. The underlying assumption is that antigen positivity reflects the presence of contagious virus, and while that may not always be true, it is probably a reasonable surrogate for infectivity. Given that more than half of people are still antigen positive after five days, particularly those who had symptomatic infection, the CDC's recommendation to wear a well-fitting mask until day 10 makes excellent sense.]

Over the past week there have been two important studies regarding the effectiveness of the Pfizer-BioNTech vaccine for 5-11-year-olds, one from [the CDC \(in the MMWR\)](#) and

one from New York State (a [non-peer reviewed preprint in MedRxiv](#)). The CDC study looked at the effectiveness of the vaccine in non-immunocompromised children and adolescents between April 2021 and January 2022. The endpoints were emergency department and urgent care encounters and hospitalizations in the VISION Network, of which there were 39,217 and 1,699 with COVID-19-like illnesses, respectively. The study used a case-negative design (patients were classified as infected or not infected on the basis of a diagnostic test). Among children ages 5-11, the vaccine efficacy (VE) during the period of Omicron predominance was 51%. However, children aged 5-11 were only vaccinated from November on, so most of the children had been relatively recently immunized. The VE regarding hospitalization was 74%. In contrast, a study from New York State examined VE in 365,502 vaccinated children aged 5-11 years old between Dec. 13, 2021 and Jan. 30, 2022 — a period of Omicron predominance. During the period of study, the efficacy fell from 68% to 12% by 28-34 days after the second dose. Efficacy for protection from hospitalization fell from 100% to 48%. The authors noted that efficacy for 11-year-olds was 11%, while for 12-year-olds it was 67%, leading them to speculate that the dosage difference between younger children (10 mcg) and older children (30 mcg) might be highly significant. [Editor's comment: These two studies are hard to reconcile. The populations are similar, but the results are not. The one piece of good news was that protection against serious disease was reasonable in both studies. I suspect more attention will need to be paid to the ramifications of the dosage sizes in order to optimize the benefits of vaccination.]

The CDC evaluated the rate of Omicron transmission to household contacts. [Results were published in the MMWR](#). Investigations were performed in four different locations between November 2021 and February 2022. Persons with sequence-confirmed Omicron and their household contacts were interviewed. They evaluated 183 households with 431 household contacts. Omicron transmission occurred in 67.8% of the households, and 52.7% of household contacts were infected. Transmission rates were lower when the index case was vaccinated and boosted (42.7%) or vaccinated with a primary series within five months (43.6%). If the index case was unvaccinated, the transmission rate was 63.9%. The transmission rate was affected by whether the index case was isolated (41.2% versus 67.5%) and by whether the index case ever wore a mask at home during a contagious period (39.5% versus 68.9%). Household attack rates were higher if the index case was a young child (72% for children age 4 and younger and 47.5% for 5-11-year-olds). [Editor's comment: Omicron is very transmissible within households, and children under the age of 5, who can't be vaccinated, can become vectors in their house. In two-thirds of the households studied there was a transmission event. The best you can do? Be vaccinated, isolate at home if you're infected, and the index case should wear a mask if at all possible.]

Careful studies of the antibody responses to the mRNA vaccines against multiple variants are being completed. They are a reminder that Omicron was only recognized a few months ago (in November 2021 in Africa), so the effects of Omicron infection on antibody titers can only be known in the short term for now. A cadre of National Institutes of Health (NIH) investigators evaluated neutralizing antibody titers against both the Pfizer and Moderna vaccines and [published their results in Science](#). They studied neutralization of

D614G, Alpha, Beta, Delta, and Omicron using samples obtained from vaccinated health care workers. Serum samples were obtained pre-vaccine, three weeks after the first dose, one month after the second dose, and six months post-second dose. The second vaccine dose was administered in January or February 2021. Neutralizing antibodies against all the variants other than Omicron declined significantly over the six months post-vaccination, although titers were boosted when individuals had breakthrough infections. In contrast, there were only minimal neutralizing antibody titers detected against Omicron at any time point, including after breakthrough infection with the viruses circulating during the study (mostly D614G and Alpha). In general, titers produced by the Moderna vaccine were twice as high as titers from Pfizer's. [Editor's comment: It's pretty clear that protection against Omicron requires three doses of mRNA vaccine. This particular study did not examine booster doses, although it did consider the effect of breakthrough infections. As the giant wave of Omicron cases and the large number of Omicron breakthrough cases in vaccinees indicated, using the mRNA vaccines to protect against Omicron infection is a marginal proposition. Boosted vaccines are, however, very protective against serious disease and hospitalization.]

In a study quite complementary to the one above, investigators used real-world data from the Kaiser Permanente system to evaluate the effectiveness of the Moderna vaccine against Omicron and Delta variants. [The paper was published in *Nature Medicine*](#). The investigators used a test-negative, case-control design to evaluate protection against infection and hospitalization with Omicron or Delta. 26,683 test-positive cases were included. Two-dose VE against Omicron infection was never good: 44% 14-90 days after vaccination followed by a rapid decline. The three-dose VE for Omicron was much better: 71.6% at 14-60 days and 47.4% at 60 days. Three-dose VE for Delta infection was 93.9% at 14-60 days and 86% after 60 days. The best news? VE to prevent hospitalization for the three-dose regimen was more than 99% for both Delta and Omicron. [Editor's comment: While preventing Omicron infection is a challenge, three-dose regimens are very effective protection against severe COVID-19 and hospitalization. Studies like this, with real-world data, are very reassuring.]

The CDC evaluated safety reports for adolescents receiving a booster dose of the Pfizer vaccine between Dec. 9, 2021, and Feb. 20, 2022. [Their analysis was published in the *MMWR*](#). Data from two reporting systems, v-safe and the Vaccine Adverse Event Reporting System (VAERS), were included. Overall, 2.8 million adolescents received a booster dose. V-safe is a voluntary, prospective phone app-based system. 3,418 individuals who had received a booster dose logged their experiences into v-safe. The side effects were mostly mild to moderate: injection site pain (80%), fatigue (58.5%), headache (55.9%), and myalgia (46.2%) with most side effects reported the day after the booster dose. VAERS is a passive system used to report adverse events after vaccination. There were 914 reports. 91.6% were non-serious, while 77 (8.4%) were classified as serious. There were 64 cases of myocarditis, 47 of which were considered serious. 32 cases were confirmed by discussion with a physician or by medical record review, and all cases were male. 27 were hospitalized (84.4%), but by Feb. 20, all had been discharged. The myocarditis rate was 11.4 cases per 1 million booster doses. [Editor's comment: These results seem consistent with expectations. Myocarditis, usually

transient, is an uncommon but real adverse reaction in adolescent males. Fortunately, there were no myocarditis-related deaths.]

[medRxiv: Occurrence and Significance of Omicron BA.1 Infection Followed by BA.2 Reinfection](#)

This study from Denmark shows that Omicron BA.2 infections can occur in people who had already had an Omicron BA.1 infection, but the instances are rare and seem to be mild.

[medRxiv: Protection of Omicron Sub-lineage Infection Against Reinfection With Another Omicron Sub-lineage](#)

Omicron BA.1 infection results in considerable, but not complete, protection against Omicron BA.2 infection in this study from Qatar.

[NEJM: Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults With Covid-19](#)

Pfizer's oral antiviral nirmatrelvir produced an 89% reduction in the risk of hospitalization due to COVID-19 in high-risk adults.

[Cell: SARS-CoV-2 Vaccination Washes Away Original Antigenic Sin](#)

[medRxiv: Post-acute Symptoms, New Onset Diagnoses and Health Problems 6 to 12 Months After SARS-CoV-2 Infection: A Nationwide Questionnaire Study in the Adult Danish Population](#)

A large population survey in Denmark demonstrated the high frequency of post-acute symptoms after COVID-19, even in people who had not been hospitalized. More than half of test-positive individuals reported at least one of the following: concentration difficulties, memory issues, sleep problems, and exhaustion, compared to 11.5% of the test negative subjects.

[Cell: Antibody Responses Following Third mRNA COVID-19 Vaccination in Patients With Cancer and Potential Timing of a Fourth Vaccination](#)

[JAMA: Risk of Second Allergic Reaction to SARS-Cov-2 Vaccines](#)

[Cell: Efficacy of a Third SARS-Cov-2 mRNA Vaccine Dose Among Hematopoietic Cell Transplantation, CAR T Cell, and BiTE Recipients](#)

[Lancet: Durability Of Omicron-Neutralizing Serum Activity After mRNA Booster Immunization in Older Adults](#)

[NEJM: Population Immunity and Covid-19 Severity With Omicron Variant in South Africa](#)

Coronavirus and Health Equity

This Feb. 22 [analysis from Kaiser Family Foundation](#) used CDC data to examine how racial and ethnic COVID-19 case and death-rate inequities changed over the course of the

pandemic, including the most recent Omicron wave. The study found that while inequities have widened and narrowed at points across the last two years, Black, Hispanic, and American Indian/Alaska Native people have been most impacted by inequities in cases, hospitalizations, and deaths during surges, especially when data are adjusted for age.

[Journal of Racial and Ethnic Health Disparities: The Past Is so Present: Understanding COVID-19 Vaccine Hesitancy Among African American Adults Using Qualitative Data](#)

[medRxiv \(preprint\): COVID-19 Mortality and Excess Mortality Among Working-Age Californians, by Occupational Sector: March 2020 Through November 2021](#)

[NIH: People from Racial, Ethnic, And Other Groups Report Frequent COVID-19-Related Discrimination](#)

[Science: Neighborhood Socioeconomic Inequality Based on Everyday Mobility Predicts COVID-19 Infection in San Francisco, Seattle, and Wisconsin](#)

Research News

An Ode to Research

It has been my pleasure digesting, reading, and sharing COVID-19 and SARS-CoV-2 research during this protracted pandemic. As a black female scientist, I am proud to represent not only those at the bench and bedside, but those beyond the bench. Academic medicine is an enterprise. It is more than pipettes and patients. Academic medicine is our community, our funders, and our institutions of learning and higher education. Academic medicine is our societies, associations, and consortiums. It is our leaders — deans, directors, chief medical officers, chairs, and presidents. It is our graduate and postdoc workforce wading through failure and disappointment daily in attempts to reveal the inner workings of cells and systems. Academic medicine is a complex, ever-changing, and integrated enterprise. Beyond the data, academic medicine represents the “who.” It is our scientists, clinicians, doctors, researchers, and postdocs, but also K-12 students, lawyers, public health officials, editors, and writers.

In writing the Research News segment, I have been keenly aware that beyond the publications and excellent science is a research system: a research enterprise that dictates *who* gets to do research and *how* research is done. Data security, anti-racism in science, diversifying clinical trials, open-access, elevating science leaders to cabinet level, the NIH specifically launching the UNITE initiative to combat structural racism — these are just a few examples of the factors that determine which articles we report on every week.

As we transition away from the newsletter and hopefully move towards some semblance of normalcy, I urge you to think about research and academic medicine beyond the canonical “tripartite” mission. Research is gender equity, access to journals, and a diverse workforce. Research is postdocs, undergraduates, and lab techs. More than antibodies,

blots, and primers, research is *how* we investigate our natural world and put forth hypotheses based on data and evidence (not fake news!)

It has been an honor contributing to the AAMC Coronavirus Newsletter. Cheers for reliable, fact-based science communication. Cheers to equity, inclusion, diversity, accessibility, and allyship in academic medicine.

— Julia Omotade, PhD, newsletter co-lead, writer of Research News

Spike's Sugar Strategy

A [manuscript published on March 1 in Science](#) shed more light on spike (S) protein and its sugars, which have been the subject of much scientific investigation. S protein, the main focus of SARS-CoV-2 vaccine development, is heavily glycosylated. In fact, it contains 22 nitrogen- (N-) linked, and at least two oxygen- (O-) linked, glycosylation sites per monomer. Structure is equal to function, and the question is what is the advantage of being heavily modified in sugars?

As well stated in this [in this review](#), “glycans confer two benefits on the virus:

- “First, the mannose residues within these glycans are important moieties to interact with cell surface attachment factors, like glycosaminoglycans and sialic acid-containing oligosaccharides before binding to the high-affinity receptor—in the case of SARS-CoV-2, angiotensin-converting enzyme 2 (ACE2). In the complex of spike-ACE2, extensive glycosylation at the interface of the complex was reported, highlighting roles for glycans in modulating spike-ACE2 interactions.
- “Glycans sterically mask the underlying polypeptide epitopes from recognition of potentially neutralizing antibodies, and thus are sometimes referred to as the ‘glycan shield.’ Viral glycoproteins are the main targets of host antibodies, as these molecules are prominently displayed on the virion surfaces. Different from bacteria, in which glycans are encoded by the bacterial genome and are treated as ‘nonself’ epitopes by corresponding hosts, viruses take advantage of host cell machinery for glycosylation and generally are decorated with the ‘self’-glycans. These ‘self’-glycans are generally thought to be a strategy to escape the host immune response.”

Sugars, it turns out, are key to viral host cell entry, replication, and pathogenicity. In fact, “not a single N-glycosite mutation has been observed in any SARS-CoV-2 [variant of concern] identified so far; this is true even for the Omicron variant, which has more than 30 mutations in the S protein, again highlighting the importance of S protein glycosylation during viral evolution.” As aptly stated by the authors of the manuscript in question, “understanding the glycosylation of S protein can uncover the role in which glycans play and guide rational vaccine design.”

In a highly collaborative study, the authors investigated the differential influences of overall and site-specific glycosylation of the S protein on SARS-CoV-2 infectivity. Expressing S

protein from lung epithelial cells, the authors clearly demonstrate that S glycosylation impacts avidity of ACE2 receptor binding and SARS-CoV-2 infection. A comparison of the N-glycosylation profile of recombinant S protein (expressed in lung epithelial cells) demonstrated that cell type matters: “The glycan profile analysis of S protein revealed a higher abundance of complex-type glycans (78%) and fewer hybrid-type glycans (less than 1%) for S protein produced in the human lung epithelial cell line BEAS-2B as compared to S protein produced in the human kidney epithelial cell line, HEK293T (61% and 23%, respectively).” As compared with other cell types, S produced in lung cells also had increased infectivity. Structural studies also showed a clever evolutionary tactic: Highly conserved epitopes in S protein are largely shielded by glycans. The kicker of the paper comes when the authors report that immunization of S protein with modified N-glycans “elicited a stronger immune response and better protection for human angiotensin converting enzyme 2 (hACE2) transgenic mice against VOCs.” Broadly neutralizing monoclonal antibody were identified from mice immunized with the modified S protein (trimmed glycans) that could neutralize Wild Type SARS-CoV-2 and VOCs with sub-picomolar potency.

[Editor’s comment: though there are limitations of this study, it is nonetheless an exquisitely designed one that uses everything from structure, cell lines, transgenic mice, and mutational analysis to peel back the layers of S protein glycosylation. Sugars are much more than a posttranslational modification — they are an evolutionary strategy that must be taken into account as we design vaccines and therapeutics against some of the world’s most infectious and formidable viruses. As aptly stated by the authors, “together, these results demonstrate that removal of glycan shields to better expose the conserved sequences has the potential to be an effective and simple approach for developing a broadly protective SARS-CoV-2 vaccine.”]

[medRxiv: Neural Dysregulation In Post-Covid Fatigue](#)

[Nature: Omicron's Lasting Mysteries: Four Questions Scientists Are Racing to Answer](#)

[bioRxiv: Highly Divergent White-Tailed Deer SARS-Cov-2 With Potential Deer-to-Human Transmission](#)

[Cell: A Decoy Mutant ACE2 Designed to Reduce COVID-19](#)

[NIH: Scientists Pinpoint Mechanisms Associated With Severe COVID-19 Blood Clotting](#)

[Nature: Fighting the SARS-Cov-2 Pandemic Requires a Global Approach to Understanding the Heterogeneity of Vaccine Responses](#)

[Science: Predicting the Mutational Drivers of Future SARS-Cov-2 Variants of Concern](#)

[medRxiv: Risk of COVID-19 Related Deaths for SARS-Cov-2 Omicron \(B.1.1.529\) Compared With Delta \(B.1.617.2\)](#)

[Science: Why Do People Die From COVID-19?](#)

[Nature: Potential SARS-Cov-2 Kidney Infection and Paths to Injury](#)

Testing News

[Cell: Assessment of the Abbott BinaxNOW SARS-Cov-2 Rapid Antigen Test Against Viral Variants of Concern](#)

[CDC MMWR: Antigen Test Positivity After COVID-19 Isolation — Yukon-Kuskokwim Delta Region, Alaska, January - February 2022](#)

Other COVID-19 News

[Bloomberg: Hong Kong's Covid Death Rate Is Now One of the World's Highest](#)

[Nature: Had Omicron? You're Unlikely to Catch its Rising Variant](#)

[New York Times: How Long Covid Exhausts the Body](#)

[Nature: Wuhan Market Was Epicenter of Pandemic's Start, Studies Suggest](#)

We have continued to receive positive feedback from readers of this newsletter since its first publication in March 2020. We hope our readers continue to find value in this science-focused newsletter, and we encourage you to connect with the AAMC in other ways to stay up to date on important issues in medical research, science, and academic medicine:

- [Follow us on social media](#), including [Ross McKinney, MD](#), AAMC chief scientific officer.
- [Subscribe to AAMCNews](#) for news, features, current trends, and ongoing conversations about topics important to medical schools and teaching hospitals.
- [Subscribe to CFAS News](#) to receive a weekly roundup of the latest news and happenings in academic medicine.
- [Subscribe to Washington Highlights](#) to receive a weekly update on the latest legislative and regulatory activities affecting medical schools and teaching hospitals.
- [Join the AAMC Virtual Communities*](#) to connect and continue the conversation (*for AAMC members only; login required).

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

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