AAMC Novel Coronavirus Update
December 16, 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 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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Note: The AAMC Coronavirus Update will take a break for the remainder of December and return on Wednesday, Jan. 6.

Today's Numbers

- World: 73,773,321 confirmed cases (1,641,578 deaths)
  - 5,182,900 new cases this week (4,341,991 new cases last week)
- United States: 16,769,765 (304,841)
  - 1,485,506 new cases this week (1,443,337 new cases last week)
  - 17,704 deaths this week (15,594 deaths last week)
  - 220,869,970 total tests
- U.S. Hot Spots
  - California: 227,663 new cases in last 7 days (38% change in daily cases)
  - Texas: 95,884 (-11%)
  - Pennsylvania: 74,052 (6%)
  - New York: 72,093 (7%)
  - Florida: 70,024 (7%)

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.

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.
In what appears to be a tight flight path parallel to the Pfizer/BioNTech BNT-162b2 vaccine, Moderna’s COVID-19 vaccine, mRNA-1273, will be evaluated by the Center for Biologics Evaluation and Research’s Vaccines and Related Biological Products Advisory Committee (VRBPAC) of the Food and Drug Administration (FDA) on Thursday, Dec. 17. Based on the FDA staff’s briefing document, the vaccine should have little trouble en route to an emergency use authorization (EUA). In a final analysis of primary endpoints, the vaccine was 94.1% effective at preventing symptomatic COVID-19 14 days or more after the second vaccine dose. There were 185 COVID-19 cases in the placebo group and 11 in the vaccine cohort. In a planned secondary analysis, there were 30 severe COVID-19 cases in the placebo group and none in the vaccine arm. In an analysis of the subgroups, individuals age 18-64 had efficacy of 95.6%, while individuals age 65 and older had efficacy of 86.4%. Otherwise, subgroups had little variability from the overall outcomes. The most frequent adverse events were pain at injection site (91.6%), fatigue (68.5%), headache (63%), muscle pain (59.6%), joint pain (44.8%), and chills (43.4%). All adverse events were more common after the second dose. Adverse events were somewhat more common in the 18-64 age group. As with BNT-162b2, the rate of COVID-19 cases began to diverge between vaccine and placebo roughly 10-14 days after the first dose of vaccine. [Editor’s comment: The results from Moderna could hardly look more similar, and heartwarming, to the results from the Pfizer-BioNTech vaccine. Both vaccines will be distributed as widely as possible given limited availability as manufacturing ramps up.]

**Treatment News**

As expected after a very positive briefing document and a 17-4 vote by the VRBPAC, the FDA issued an EUA for the Pfizer/BioNTech BNT-162b2 COVID-19 vaccine. The EUA is valid for individuals age 16 and older with no known allergy to a component of the vaccine. The results of the 43,548-volunteer clinical trial that resulted in the EUA were published in the New England Journal of Medicine (NEJM) and confirmed that the vaccine efficacy is 95%. [Editor’s comment: Given the high level of efficacy of the two mRNA vaccines (BNT-162b2 and mRNA-1273), we should all have reasons for hope that we can do more than dream about returning to a less restricted way of life by next fall. Time, vaccine production, and public acceptance of vaccination will all be critical elements.]

One of the six vaccine products on which Operation Warp Speed has been betting ran into a major obstacle, Sanofi Pasteur’s SARS-CoV-2 spike protein-based vaccine did not produce a sufficient antibody response when tested in people over 60 years old. The vaccine, which used a GlaxoSmithKline (GSK) adjuvant as an immunological booster, will be reformulated, and the company will continue early phase testing instead of switching to a large Phase 3 efficacy trial as they had anticipated. The company’s timeline was pushed back to at least late 2021 for completion of a Phase 3 trial, provided the reformulation achieves the desired effect. [Editor’s comment: It is fortunate that several vaccines and vaccine strategies are being tried simultaneously. Setbacks happen, and the urgency of the epidemic makes the good news from Pfizer/BioNTech and Moderna all the more significant. For Sanofi Pasteur/GSK, having other authorized vaccines already in use may make completing Phase 3 clinical trials difficult.]

**Clinical News**

A study published in the Centers for Disease Control and Prevention (CDC) Morbidity and Mortality Weekly Report found that close contact with persons with COVID-19, gatherings with persons outside the household, and lack of consistent mask use in school were all factors associated with SARS-CoV-2 infection. Researchers analyzed data collected from 397 children and adolescents younger than 18 years old in emergency departments and
outpatient health facilities who tested positive for SARS-CoV-2. The findings emphasize the importance of behavioral interventions to reduce exposure and stem viral spread.

Researchers at Premier Applied Sciences, an administrative health care database that serves 592 hospitals, evaluated factors associated with in-hospital mortality related to COVID-19 in April and May and published their results in JAMA Network Open. Their study included 65,471 COVID-19 patients, 35,302 of whom were treated as inpatients. The median age for inpatients was 65, and the in-hospital mortality rate was 20.3%. 19.4% of inpatients were admitted to an intensive care unit (ICU) at some point in their hospitalization. Patients treated with statins, angiotensin-converting enzyme inhibitors, and calcium channel blockers had lower odds of death, while patients treated with hydroxychloroquine and azithromycin had increased odds of death. [Editor's comment: This is a nice retrospective cohort study that reminds us that correlation does not equal causality. However, I suspect medical historians will look back with real skepticism at the misguided attention paid to hydroxychloroquine and azithromycin as treatments for COVID-19 during the early months of the epidemic.]

As this newsletter reported last week, the combination of baricitinib and remdesivir was granted an EUA for hospitalized patients with COVID-19. The results of the National Institutes of Health (NIH)-sponsored ACTT-2 Trial that justified the EUA were published in the NEJM. The study treated adults hospitalized with COVID-19 with remdesivir and either placebo or baricitinib. Baricitinib is a Janus kinase inhibitor and immunomodulator. 1,033 patients enrolled in the study, and the median time to recovery for those treated with remdesivir and baricitinib was seven days, while it was eight days for those treated with remdesivir and placebo. 28-day mortality in the baricitinib cohort was 5.1%, while it was 7.8% for those who received placebo. The mortality difference was not statistically significant. The positive effect of the combination was most striking in patients who were on high-flow oxygen at the time of admission, with a median time of recovery of 10 days for combination therapy and 18 days for the control group. [Editor's comment: The positive results in this study look real but marginal. The NIH COVID-19 treatment guidelines also considered data from the United Kingdom's RECOVERY trial and recommended that the clinical data were insufficient to weigh in for or against the addition of baricitinib in hospitalized patients.]

Policy News

A multinational group of disease-modeling researchers considered the introduction of seven nonpharmacological public health measures — like distancing and masks — and the impact of those interventions on the spread of COVID-19 in 41 countries, including 34 from Europe. The results were published in Science. The investigators used a Bayesian hierarchical model on data from January to May 2020, and they found that closing educational institutions, limiting gatherings to 10 people or less, and closing nonessential face-to-face businesses all had a positive effect on reducing transmission. Other stay-at-home orders had little benefit. [Editor's comment: As the authors note, the study could only look at governmental mandates, not whether the interventions were applied in the community. They also didn't look at mask-wearing. So, the study is far from the last word on the issue of which nonpharmacological interventions a government should choose, but it's an interesting start.]

People with Down syndrome are unusually susceptible to COVID-19, with a fatality rate tenfold that of people who do not have Down syndrome, leading to calls that this class of individuals be vaccinated relatively early.

The CDC's Advisory Committee on Immunization Practices' Interim Recommendation for
Coronavirus and Health Equity

A new report released by the Essie Justice Group explored the impact COVID-19 has had on women whose loved ones are incarcerated. Fifty-two percent of survey respondents reported that their incarcerated loved one has at least one “high-risk” underlying health condition, 33% noted that their loved one’s attorney meetings have been canceled due to the pandemic, and 62% said their loved ones were scared of losing their lives to COVID-19 while incarcerated.

New research published ahead of peer review found significant social gradients in case, death, and positivity rates across U.S. and Canadian cities, providing more evidence that COVID-19-related inequities are in large part created by avoidable social and economic differences between populations.

A new commentary in the Lancet delineated a community-engaged, bottom-up approach to vaccine communication that “devolves the power of design and implementation of communication strategies to local actors ... enabling them to mobilise local expertise that can engage with and shift attitudes on vaccines and wider government handling of the COVID-19 pandemic.”


U.S. News and World Report: Study: COVID-19 Mortality Twice as High Among Native Americans

NPR: California May Consider ‘Historical Injustice’ When Allocating Coronavirus Vaccine

NPR: What Inequities In The U.S. Health Care System Are Amplified By The Pandemic?

Vox: Study: Allowing Evictions During COVID-19 Could Have Caused Nearly 11,000 Unnecessary Deaths

Research News

Investigators in Japan found that high nasopharyngeal viral loads around COVID-19 onset may contribute to secondary transmission of the disease. Patients were divided into two groups: those who subsequently transmitted the disease to at least one other patient (index patients), and those who were not the cause of secondary transmission (non-index patients). Nasopharyngeal swabs were collected from the patients from two to 36 days after symptom onset, and a nonlinear regression model showed that the viral load of the index patients at onset was higher than that of the non-index patients, and this trend continued until 10 days after onset. The authors posit that the results could explain why transmission is observed in some instances but not in others, and they may lead to the establishment of a viral load threshold to clarify COVID-19 disease transmission and infectivity.

A recent study investigated whether infection with seasonal human coronaviruses leads to cross-protection against SARS-CoV-2. By using a flow cytometry assay for SARS-CoV-2–
Acquiring antibodies, researchers were able to detect antibodies against the S2 subunit of the SARS-CoV-2 spike proteins in a small proportion of SARS-CoV-2–uninfected individuals, highlighting the potential for preexisting humoral immunity against SARS-CoV-2. Uninfected children and adolescents were found to be positive for these antibodies in much higher numbers than adults, suggesting a possible explanation for the age distribution of COVID-19 susceptibility. By contrast, COVID-19 patients generated IgA, IgG, and IgM antibodies that recognized both the S1 and S2 subunits, providing insight into preexisting versus de novo immune responses against the virus.

A genomewide association study in over 2,200 critically ill COVID-19 patients in ICUs in the United Kingdom identified a number of novel associations — including gene clusters coding for antiviral restriction enzyme activators — near the gene encoding tyrosine kinase 2 (TYK2), within the gene encoding dipeptidyl peptidase 9, and in the interferon receptor gene IFNAR2. The authors found evidence in support of a causal link from low expression of IFNAR2, and high expression of TYK2, to life-threatening disease. Overall, the findings show gene activation relating to both host antiviral as well as inflammatory pathways — findings that could lead to potential targets for existing drugs.

*Nature: Gene Expression Network Analysis Provides Potential Targets Against SARS-CoV-2*

### Testing News

The FDA has authorized the first completely over-the-counter, no prescription required, home COVID-19 diagnostic test. The EUA for the Ellume COVID-19 Home Test, a lateral flow antigen detection assay, notes that the test is less sensitive and specific for SARS-CoV-2 detection than polymerase chain reaction (PCR), but for symptomatic people, the Ellume detected viral antigen in 96% of the PCR-positive samples, and for asymptomatic individuals, antigen was detected in 91% of the PCR-positive samples. The negative predictive value was 100% in the symptomatic sample set and 96% correct for the asymptomatic individuals (compared to PCR). The device’s development was supported by the NIH’s Rapid Acceleration of Diagnostics (RADx) initiative. [Editor’s comment: If performed correctly, the Ellume COVID-19 Home Test looks like a reasonable option for most people, especially at a time when testing centers are often backed up and results are delayed. The test is performed on an analyzer that connects to a smartphone that gives results in less than 20 minutes. The results are automatically reported to public health authorities by zip code and date of birth, with other information optionally entered by the user. The company expects to be able to produce more than three million test kits in January, so it may actually be a useful and convenient addition to the diagnostic armamentarium.]

### Other COVID-19 News

*JAMA: Behaviorally Informed Strategies for a National COVID-19 Vaccine Promotion Program*


*AAMCNews: Doctors Forgo Mental Health Care During Pandemic Over Concerns About Licensing, Stigma*
For questions, contact Anu Dev, PhD, AAMC lead science policy specialist.

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