Good morning. As a reminder, the Daily Briefing will not be published on Friday.

Today I start with an editorial I have titled: “Turning the Corner on COVID-19”. Comments are always welcomed.

In COVID-19 News I review two vaccines: Novavax and Astra Zeneca and the news of the confirmation of the variant B.1.1.7 in Colorado.

Under Journal Reviews I selected Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers, and IDSA Guidelines on the Diagnosis of COVID-19: Molecular Diagnostic Testing.

Stay safe-Back in 2021!

Ed

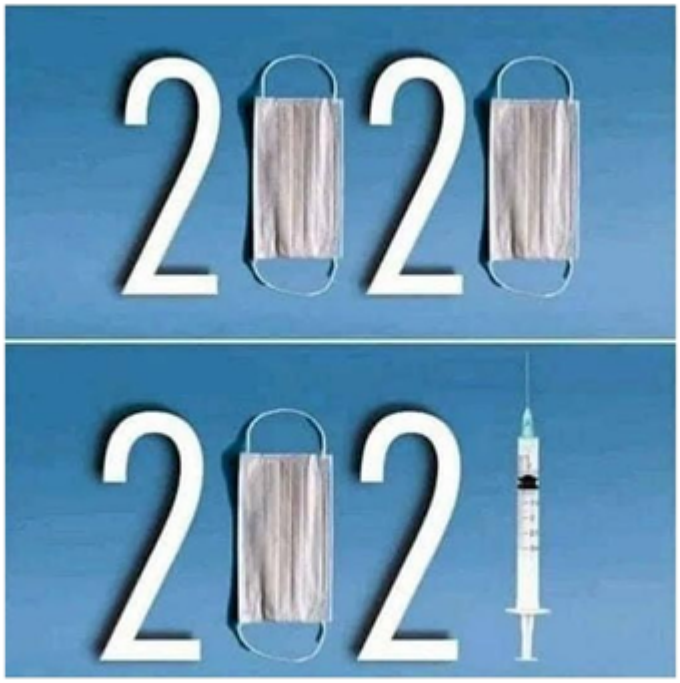
VII: 2021: Turning the Corner on COVID-19

2020 will be in our rear-view mirror soon and 2021 looks better, but we need to get through the next few months. As I reflect on the year, I have thought deeply about what we value. We have all been in the same storm, but not the same boat. Regular people are suffering, and many have lost their lives. Businesses have failed, loved ones have been lost, and the psychological damage may take years to heal and some may never recover from this year’s isolation, fear, and deprivation. The process of recovery will take years — and in some ways, some of us may never recover. We must thank repeatedly those keeping us going, like the garbagemen, truckers, fireman, police, transit workers, the people who stock the shelves, and of course our frontline HCWs.

Next year will still require caution, but fear of COVID-19 should not dominate our lives after the winter recedes. I honestly believe prevalence will significantly decline this spring. The virus may reemerge in the fall, but with immunizations and with improved herd immunity I think it will be manageable. I believe the virus will likely become endemic and will continue to circulate but at a much lower level than the pandemic. If a high percentage of the high-risk populations are vaccinated, that would sharply reduce COVID-19 mortality. The benefits will be even greater if, as hoped, vaccines do not merely reduce the risk of symptomatic disease but also reduce the chance of being infected and thereby by reducing spread to others. I believe the CDC recommendation putting many seniors in phase 1c behind essential workers is flawed. This delay will put many of our most vulnerable at risk at a time when infections are going up in many areas of our country.

What we have learned about COVID-19 will hopefully impact transmission of influenza and other respiratory viruses. It is easy to forget but influenza results in more than 40 million symptomatic illnesses [2009 pandemic over 63 million people were infected in the US] and over 600,000 hospitalizations in an average year. Deaths from influenza related illnesses can range from 20,000 to over 70,000 per year depending on the strain and effectiveness of the vaccine. Coming to work ill will be frowned upon. Testing for influenza and COVID-19 will be widespread including home testing. We will be more aware of ventilation indoors and crowds in confined spaces. Some of us may even wear masks in certain venues, but it will probably not be required.

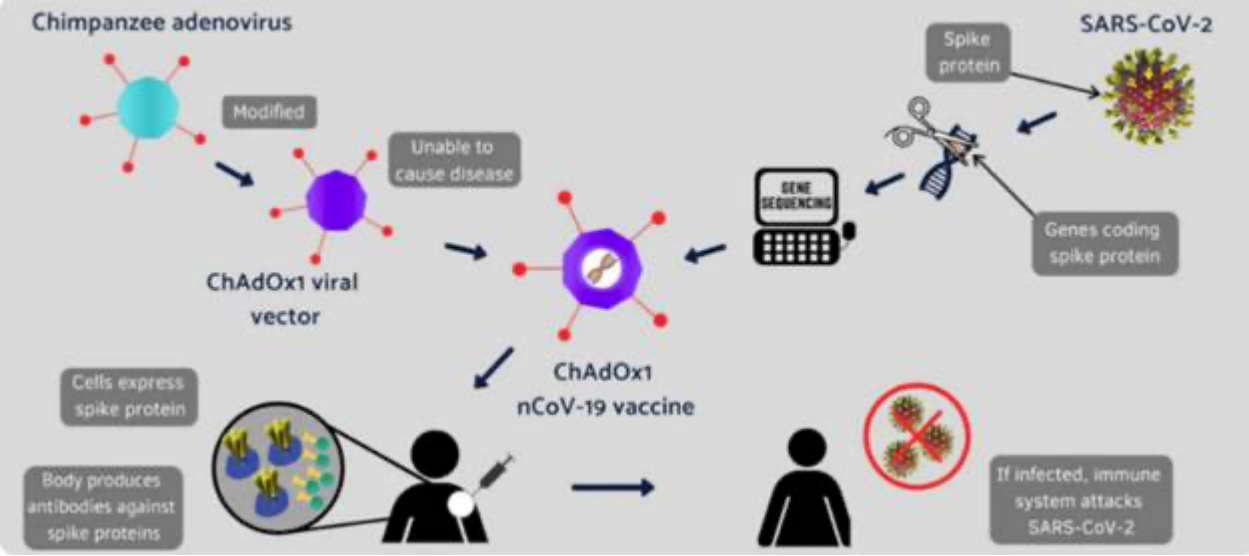
In the end I believe COVID-19 will become a manageable risk by mid-2021. Until then we must continue to practice safe behaviors-the 3 Ws and get vaccinated. I hope 2021 will be filled with optimism, hope and good health!



COVID-19 News

Novavax Vaccine Trial
The company announced the start of the phase 3 clinical trial of up to 30,000 people in the U.S. and Mexico. Novavax will become the fifth Covid-19 vaccine to enter final-stage testing in the U.S., and if results are positive it could receive authorization sometime during 2021. The results from the new study will likely be spring at the earliest. Novavax's vaccine contains proteins resembling the "spike" proteins found on the surface of the coronavirus, which are supposed to trigger an immune response to the virus once injected. Novavax manufactures the proteins in insect cells. It also contains an adjuvant, a substance designed to enhance immune responses. Novavax's adjuvant is derived from the bark of an evergreen tree native to Chile. This approach of combining a protein with an adjuvant is similar to the shingles vaccine, Shingrix.

Oxford-Astra Zeneca Vaccine approved in the UK
The UK government said the decision to approve the vaccine follows rigorous testing, with 100 million initially ordered for the first phase of the immunization program, and another 40 million due to be rolled out by March next year. This is an adenovirus-vectored vaccine using a chimpanzee adenovirus. The original adenovirus causes common cold in chimpanzees and it rarely, if ever, infects humans. The virus is further modified to ensure it cannot grow in people. This is also a two-dose vaccine. Awaiting results using half dose as initial dose followed by full dose at 4 weeks. When given in two, full-strength doses, AstraZeneca's vaccine showed 62 percent efficacy in clinical trials — considerably lower than the roughly 95 percent efficacy achieved by Pfizer and Moderna's shots. For reasons scientists do not yet understand, AstraZeneca's vaccine showed 90 percent efficacy in a smaller group of volunteers who were given a half-strength initial dose. However, other trial data for the full-dose regimen was more robust. It triggered an immune response that is 80 per cent effective at preventing COVID-19 disease over a three-month period. Vaccine response in older adults appears similar to younger adults. This vaccine is easier to make, less expensive, and easy to ship and store.



Comment: Overall this is good news. I would like to see more data on dosing and efficacy, but even if 60-80% is confirmed the additional number of persons that can be vaccinated will make a difference. The Oxford-AstraZeneca vaccine is poised to become the world's dominant form of inoculation. At $3 to $4 a dose, it is a fraction of the cost of some other vaccines. And it can be shipped and stored at normal refrigeration temperatures for six months, rather than in the ultracold freezers required by the Pfizer-BioNTech and Moderna vaccines, making it easier to administer to people in poorer and hard-to-reach areas. The FDA is likely to review in the next month. Stay tuned.

US Case of COVID-19 Variant (B.1.1.7) Found in Colorado

The first reported U.S. case of the COVID-19 variant that has been seen in the UK has been discovered in Colorado. The variant was found in a man in his 20s who is in isolation southeast of Denver and has no travel history, state health officials said. The Colorado State Laboratory confirmed the virus variant, and the CDC has been notified. Public health officials are investigating other potential cases and performing contact tracing to determine the spread of the variant throughout the state.

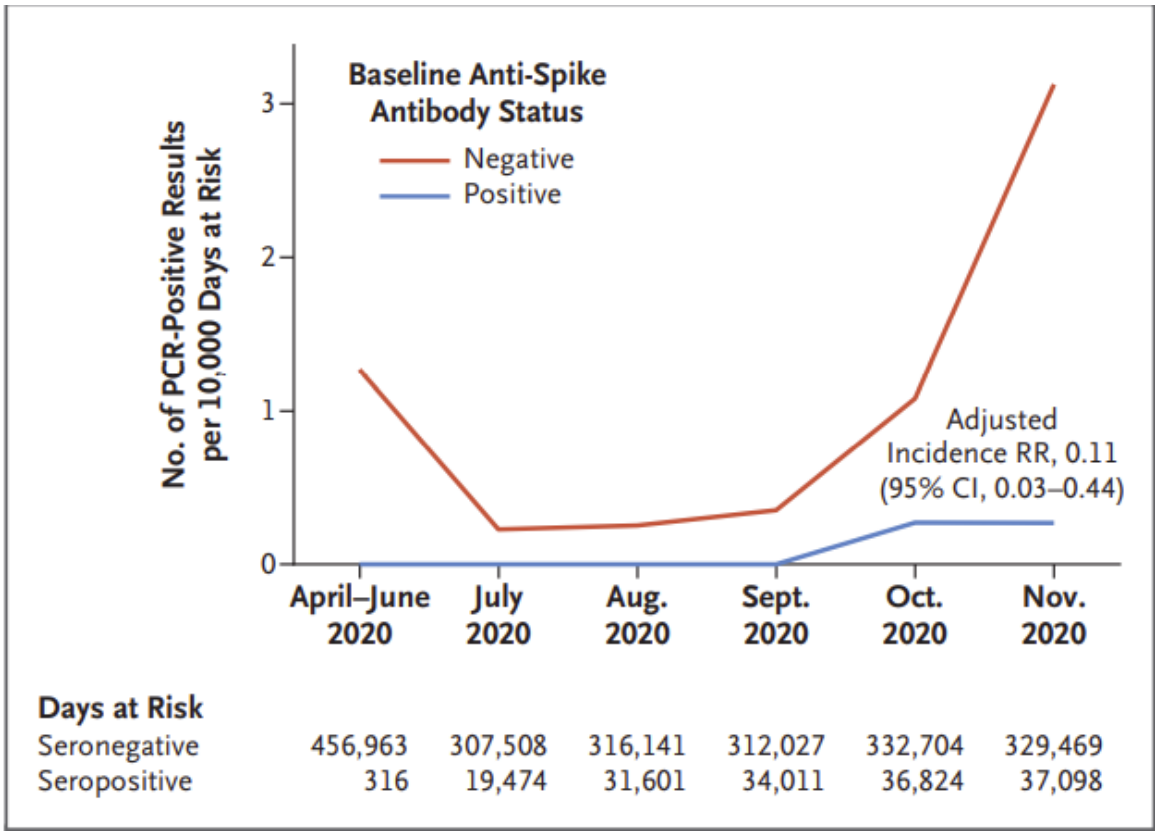
Scientists in the UK believe the new virus variant is more contagious (~56% more transmissible) than previously identified strains of the SARS-CoV-2. Currently there is no evidence this strain is more virulent. The current vaccines being administered now are thought to be effective against this variant.

Comment: This is not a surprise. RNA viruses regularly mutate. As we increase our genomic surveillance, I think we will see more widespread isolation of this strain. [any perhaps other mutations] There is no need to panic since it appears this mutant is not more virulent and current vaccines should be protective of this new strain. The proteins that coat the shell of SARS-CoV-2 would need to undergo significant genetic transformations to render the vaccines redundant – something that, at this stage, doesn't appear to have happened. Of the 23 mutations identified in the new variant, only a handful concern the virus' spike protein. Scientists have insisted there are many other components to its structure that will still be targeted by the antibodies and T-cells induced by the vaccines. We need to continue to modify our behavior to slow the transmission until we reach herd immunity.

Journal Reviews

Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers
N Engl J Med published online December 23, 2020
DOI: 10.1056/NEJMoa203454
The authors investigated the incidence of SARS-CoV-2 infection confirmed by PCR in seropositive and seronegative health care workers attending testing of asymptomatic and symptomatic staff at Oxford University Hospitals in the United Kingdom. Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays, and staff members were followed for up to 31 weeks. We estimated the relative incidence of PCR-positive test results and new symptomatic infection according to antibody status, adjusting for age, participant-reported gender, and changes in incidence over time. Asymptomatic health care workers were invited to participate in voluntary nasal and oropharyngeal swab PCR testing every 2 weeks and serologic testing every 2 months.

A total of 12,541 health care workers participated and had anti-spike IgG measured; 11,364 were followed up after negative antibody results and 1265 after positive results, including 88 in whom seroconversion occurred during follow-up. A total of 223 anti-spike–seronegative health care workers had a positive PCR test (1.09 per 10,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic, whereas only 2 anti-spike–seropositive health care workers had a positive PCR test (0.13 per 10,000 days at risk), and both workers were asymptomatic when tested (adjusted incidence rate ratio, 0.11; 95% confidence interval, 0.03 to 0.44; P=0.002). There were no symptomatic infections in workers with anti-spike antibodies.



Comment: This is incredibly good news: the presence of anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection for at least 6 months. This study was predominantly healthy adult health care workers 65 years of age or younger; further studies are needed to assess postinfection immunity in other populations, including children, older adults, and persons with coexisting conditions, including immunosuppression.

The Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Molecular Diagnostic Testing

published December 23, 2020

review suggested by Dr. Andrew Chou

Recommendation 1: The IDSA panel recommends a SARS-CoV-2 NAAT in symptomatic individuals in the community suspected of having COVID-19, even when the clinical suspicion for COVID-19 is low (strong recommendation, very low certainty of evidence).

Recommendation 2: The IDSA panel suggests collecting a nasopharyngeal swab, mid-turbinate swab, anterior nasal swab, saliva or a combined anterior nasal/oropharyngeal swab rather than an oropharyngeal swab alone for SARS-CoV-2 RNA testing in symptomatic individuals suspected of having COVID-19 *(conditional recommendation, very low certainty of evidence)*.

Sample site	Saliva without coughing	Saliva with coughing	OP swab	AN swab	MT swab	Combined AN/OP swab
Sensitivity	0.90 (95% CI: 0.85 to 0.93)	0.99 (95% CI: 0.94 to 1.00)	0.76 (95% CI: 0.58 to 0.88)	0.89 (95% CI: 0.83 to 0.94)	0.95 (95% CI: 0.83 to 0.99)	0.95 (95% CI: 0.69 to 0.99)
Specificity	0.98 (95% CI: 0.93 to 1.00)	0.96 (95% CI: 0.83 to 0.99)	0.98 (95% CI: 0.96 to 0.99)	1.00 (95% CI: 0.99 to 1.00)	1.00 (95% CI: 0.89 to 1.00)	0.99 (95% CI: 0.92 to 1.00)
Outcome	**Effect per 1,000 patients tested** **Pre-test probability of 10%** [a,f]					
True positives (patients with COVID-19)	90 (85 to 93)	99 (94 to 100)	76 (58 to 88)	89 (83 to 94)	95 (83 to 99)	95 (69 to 99)
False negatives (patients incorrectly classified as not having COVID-19)	10 (7 to 15)	1 (0 to 6)	24 (12 to 42)	11 (6 to 17)	5 (1 to 17)	5 (1 to 31)
Quality of the evidence[b,c,d]	9 studies 387 patients ⊕⊕◯◯ LOW[b]	3 studies 137 patients ⊕⊕◯◯ LOW[b]	4 studies 64 patients ⊕◯◯◯ Very LOW[b,d,e]	2 studies 130 patients ⊕⊕◯◯ LOW[b]	5 studies 855 patients ⊕⊕◯◯ LOW[b]	2 studies 61 patients ⊕◯◯◯ Very LOW[b,d,e]
True negatives (patients without COVID-19)	882 (837 to 900)	864 (747 to 891)	882 (864 to 891)	900 (891 to 900)	900 (801 to 900)	891 (828 to 900)
False positives (patients incorrectly classified as having COVID-19)	18 (0 to 63)	36 (9 to 153)	18 (9 to 36)	0 (0 to 9)	0 (0 to 99)	9 (0 to 72)

Recommendation 3: The IDSA panel suggests that anterior nasal and mid-turbinate swab specimens may be collected for SARS-CoV-2 RNA testing by either patients or healthcare providers, in symptomatic individuals with upper respiratory tract infection (URTI) or influenza-like illness suspected of having COVID-19 *(conditional recommendation, low certainty of evidence)*.

Recommendation 4**:** The IDSA panel suggests a strategy of initially obtaining an upper respiratory tract sample (e.g., nasopharyngeal swab) rather than a lower respiratory sample for SARS-CoV-2 RNA testing

in hospitalized patients with suspected COVID-19 lower respiratory tract infection. If the initial upper respiratory sample result is negative, and the suspicion for disease remains high, the IDSA panel suggests collecting a lower respiratory tract sample (e.g., sputum, bronchoalveolar lavage fluid, tracheal aspirate) rather than collecting another upper respiratory sample *(conditional recommendations, very low certainty of evidence)*.

Recommendation 5**:** The IDSA panel suggests performing a single viral RNA test and not repeating testing in symptomatic individuals with a low clinical suspicion of COVID-19 *(conditional recommendation, low certainty of evidence)*.

Recommendation 6: The IDSA panel suggests repeating viral RNA testing when the initial test is negative (*versus* performing a single test) in symptomatic individuals with an intermediate or high clinical suspicion of COVID-19 *(conditional recommendation, low certainty of evidence)*.

Recommendation 7**:** The IDSA panel suggests using either rapid RT-PCR or standard laboratory-based NAATs over rapid isothermal NAAT in symptomatic individuals suspected of having COVID-19 *(conditional recommendation, low certainty of evidence).*

- The sensitivity of rapid RT-PCR and standard laboratory-based NAAT appear to be essentially equivalent. In contrast, the rapid isothermal NAATs evaluated were less sensitive than either rapid RT-PCR or standard laboratory based NAATs.

Recommendation 8**:** The IDSA panel suggests SARS-CoV-2 RNA testing in asymptomatic individuals who are either known or suspected to have been exposed to COVID-19 *(conditional recommendation, very low certainty of evidence)*.

- Studies on the ideal time and collection method to test asymptomatic individuals who have been exposed to COVID-19 should be performed [current recommendation is to test ~5-7 days after exposure]

Recommendation 9: The IDSA panel suggests against SARS-CoV-2 RNA testing in asymptomatic individuals with no known contact with COVID-19 who are being hospitalized in areas with a low prevalence of COVID-19 in the community *(conditional recommendation, very low certainty of evidence)*.

Recommendation 10: The IDSA panel suggests direct SARS-CoV-2 RNA testing in asymptomatic individuals with no known contact with COVID-19 who are being hospitalized in areas with a high prevalence of COVID-19 in the community (i.e., hotspots) *(conditional recommendation, very low certainty of evidence)*.

- A high prevalence of COVID-19 in the community was considered communities with a prevalence of 10%.
- The decision to test asymptomatic patients (including when the prevalence is between 2 and 9%) will be dependent on the availability of testing resources.

Recommendation 11: The IDSA panel recommends SARS-CoV-2 RNA testing in immunocompromised asymptomatic individuals who are being admitted to the hospital regardless of exposure to COVID-19 *(strong recommendation, very low certainty of evidence)*.

Recommendation 12: The IDSA panel makes no recommendations for or against SARS-CoV-2 RNA testing before initiating immunosuppressive therapy in asymptomatic individuals with cancer *(evidence gap)*.

Recommendation 13: The IDSA panel makes no recommendations for or against SARS-CoV-2 RNA testing before the initiation of immunosuppressive therapy in asymptomatic individuals with autoimmune disease *(evidence gap)*.

Recommendation 14: The IDSA panel suggests SARS-CoV-2 RNA testing in asymptomatic individuals (without known exposure to COVID-19) who are undergoing major time-sensitive surgeries *(conditional recommendation, very low certainty of evidence)*.

Recommendation 15: The IDSA panel suggests against SARS-CoV-2 RNA testing in asymptomatic individuals without a known exposure to COVID-19 who are undergoing a time-sensitive aerosol

generating procedure (e.g., bronchoscopy) when PPE is available *(conditional recommendation, very low certainty of evidence)*.
Recommendation 16: The IDSA panel suggests SARS-CoV-2 RNA testing in asymptomatic individuals without a known exposure to COVID-19 who are undergoing a time-sensitive aerosol generating procedure (e.g., bronchoscopy) when PPE is limited, and testing is available *(conditional recommendation, very low certainty of evidence)*.

Comment: SARS-CoV-2 antigen detection tests have recently become available. IDSA anticipate systematically reviewing the clinical utility of these tests as data accumulates on their performance in comparison to NAAT. This is a major disappointment of this update. It is particularly important that IDSA quickly updates this guidance to include rapid antigen tests. Studies suggests rapid antigen tests are not as sensitive in asymptomatic people but may be acceptable to test people who are symptomatic. The issue of false positives is not addressed. mRNA vaccines designed that encode the SARS-CoV-2 spike protein have received emergency use authorization. There is currently no evidence that receipt of the vaccine would interfere with SARS-CoV-2 molecular diagnostic testing.