Good morning.

Under COVID-19 News the CDC announced a one week postponement on if they will recommend a third dose for the general population. Next a report on pediatric hospitalizations during this surge and finally the FDA report on the approval of the Pfizer vaccine for persons ≥16 years of age.

Under Journal Review I start with a pre-publication report on the virological characteristics of breakthrough cases in HCWs. Next is an interesting report on SARS-CoV-2 dynamics in close contacts. Last is a publication comparing saliva PCR compared to NP PCR.

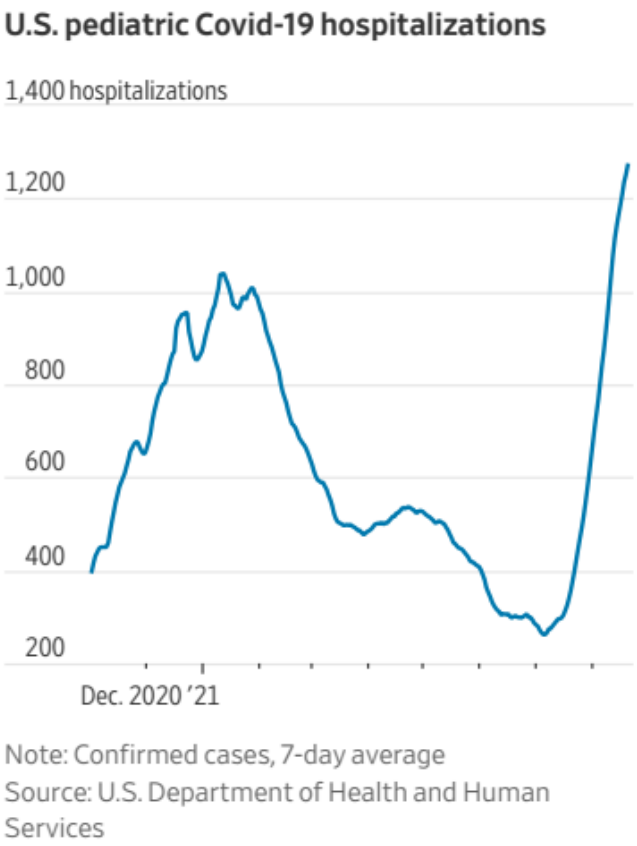
Have a great day and week

Ed

CDC/ACIP and Third Dose
The CDC has pushed back the ACIP meeting to discuss COVID-19 booster shots for the general population by one week to make sure the information is available to review and to ensure a robust deliberation. Medical experts are divided over whether third doses are necessary for the general population and if so, when, and the WHO has called for wealthy countries to hold off on giving third doses until less vaccinated countries catch up.

Comment: I have two concerns about this conversation. First, I worry it could undercut confidence in vaccines. The announcement suggests that people who consider themselves fully vaccinated were not fully protected but that is the wrong message, because you are protected against serious illness. Second, we need to make sure the 40% who are not fully vaccinated get vaccinated. As I wrote last week based on current evidence there does appear to be a role of a third shot for persons over age 60 and persons with certain immunocompromised conditions at least 6 months after they received their second dose.

More Children Are Hospitalized with Covid-19
Although children are much less likely than adults to develop severe Covid-19 or die from the virus, recent data from HHS show pediatric hospitalizations for Covid-19 are at the highest point since the agency began tracking them last year, driven by states that have been hit hard by the Delta variant. Children's hospitals are bracing for even more cases as schools reopen.



Comment: It has become clear; we are seeing a surge in pediatric hospitalization due to Covid-19. Delta has changed the landscape in pediatrics as well as adults. Children < age 12 cannot be vaccinated and adolescents ≥12 can be vaccinated but only 30-35% are fully vaccinated. All this supports the CDC and AAP in recommending universal masking in areas with substantial or high spread of Covid-19.

FDA Approves Pfizer's COVID-19 Vaccine
Pfizer vaccine has received full approval for persons ≥16 years of age. Pfizer's vaccine will still be under an EUA for recipients ages 12 to 15, and for immunocompromised individuals who qualify for a third dose of the vaccine 28 days after their second dose.

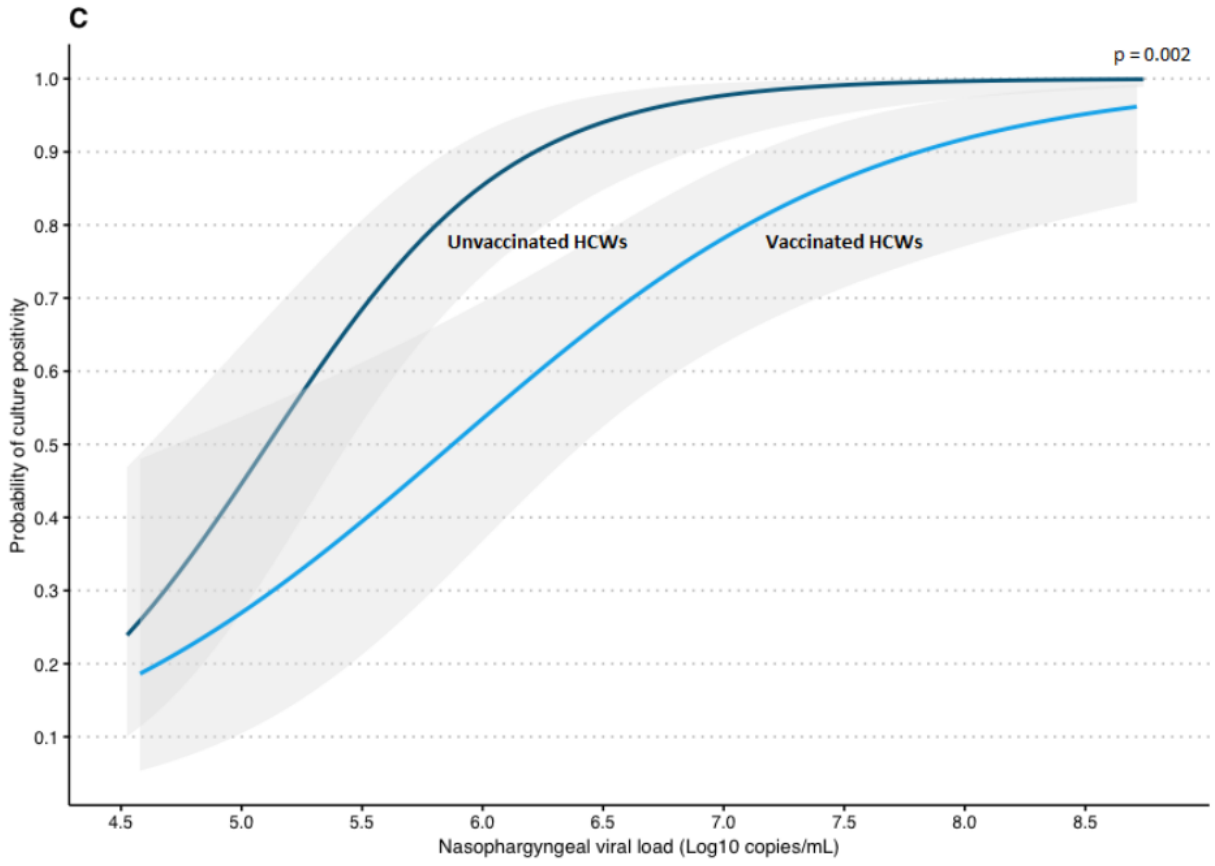
Comment: Hallelujah. A full approval allows more businesses, schools, and organizations to mandate vaccine use among employees and students and offers legitimacy to a vaccine some people believe has been rushed through safety evaluations and protocols. The mRNA vaccines are incredibly efficacious and safe.

Journal Review

Virological Characteristics of SARS-CoV-2 Vaccine Breakthrough Infections in Health Care Workers
Media published online August 21, 2021
doi.org/10.1101/2021.08.20.21262158

The investigators analyzed the virological characteristics of 161 vaccine breakthrough infections in a population of 24,706 vaccinated healthcare workers (HCWs), using RT-PCR and virus culture. Virus culture was performed on all samples collected by inoculating Vero cells. All cultures were performed in twofold, with one replicate for immunofluorescence analysis after acetone fixation at 48h of incubation. The second replicate was microscopically examined for the presence of cytopathic effect daily for 2 weeks. Viral culture was considered negative if no cytopathic effect was observed after 14 days of incubation. To investigate how the probability of the binary outcome (culture positivity) depends on viral load and vaccination, the culture results were analyzed using probit regression.

The study showed that 68.6% of 161 COVID-19 breakthrough infections had positive nasopharyngeal swabs compared with 84.9% of infections in unvaccinated patients. Despite similar Ct-values, the investigators demonstrated lower probability of infectious virus detection in respiratory samples of vaccinated HCWs with breakthrough infections compared to unvaccinated HCWs with primary SARS-CoV-2 infections. The delta variant was identified in the majority of cases.



Comment: The data support that the SARS-CoV-2 infectious virus shedding is lower in vaccinated individuals with breakthrough infections (caused by primarily the delta variant) than in unvaccinated individuals with primary infections (caused by SARS-CoV-2 D614G – ancestral strain). Nevertheless, virus culture was positive in 68.6% of breakthrough infections. Despite the reduced viral viability, the infectivity of individuals with breakthrough infections should not be overlooked. In an article reviewed in

the Briefing on August 3rd, persons who had breakthrough infections were associated with a faster decline in viral RNA load compared with unvaccinated persons.

COVID-19 Transmission Dynamics Among Close Contacts of Index Patients With COVID-19
JAMA Intern Med published online August 23, 2021
doi:10.1001/jamainternmed.2021.4686
This study used a large, population-based cohort of 730 individuals (index patients) who received a diagnosis of COVID-19 from January 8 to July 30, 2020, along with a contact tracing surveillance program. Field workers visited 8852 close contacts of the index patients and evaluated them for COVID-19 through August 2020. A timeline was constructed to characterize different exposure periods between index patients and their contacts.

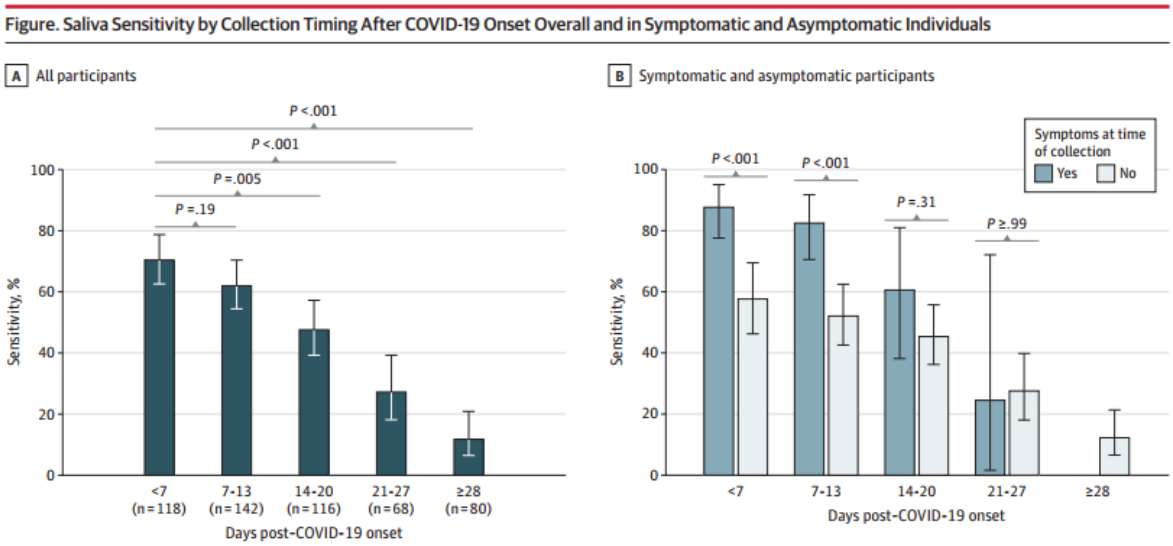
In this cohort study of 730 index patients with a COVID-19 diagnosis and 8852 close contacts, transmission potential was greatest in the first 2 days before and 3 days after onset of symptoms in the index patient. When contacts received a diagnosis of COVID-19 infection, they were more likely to present asymptomatically if they had been exposed to an asymptomatic patient.

Comment: This cohort study found that individuals with COVID-19 were most infectious a few days before and after symptom onset. These results are consistent with recent results suggesting that viral load may peak at 2 days before symptom onset and decline quickly after 1 week of symptoms. Infected contacts of asymptomatic index patients were less likely to present with COVID-19 symptoms, suggesting that quantity of exposure (VL) may be associated with clinical presentation in close contacts. Compared with moderate and mild index cases, asymptomatic index patients were the least likely to transmit to contacts. Not all contacts were traced and screened with PCR testing. Because of this, contacts with asymptomatic disease may have been missed. NPI were widely employed early in 2020 to reduce transmission risk. Therefore, caution is needed when applying these results to other settings with limited NPI compliance. This study was pre-Delta.

Change in Saliva RT-PCR Sensitivity Over the Course of SARS-CoV-2 Infection
JAMA published online August 13, 2021
doi:10.1001/jama.2021.1396
Between June 17, 2020, and February 15, 2021, a sample of individuals exposed to a household member with PCR-confirmed SARS-CoV-2 within 2 weeks were recruited from Children's Hospital Los Angeles and nearby community testing sites into the Household Exposure and Respiratory Virus Transmission and Immunity Study (HEARTS). Paired nasopharyngeal and saliva samples were collected every 3 to 7 days for up to 4 weeks or until 2 negative nasopharyngeal test results. RT-PCR for SARS-CoV-2 N1 and N2 genes was performed. Saliva sensitivity was calculated using nasopharyngeal positive PCR as the reference standard.

The investigators tested 889 paired nasopharyngeal swab-saliva samples from 404 participants, of which SARS-CoV-2 was detected in 524 nasopharyngeal (58.9%) and 318 saliva (35.7%) specimens. SARS-CoV-2 was detected in both specimens in 258 pairs (29.0%). Of the 256 nasopharyngeal SARS-CoV-2-positive participants (63.4%), the mean age was 28.2 years (range, 3.0-84.5); 108 (42.2%) were male. Ninety-three participants (3 the 6.3%) were asymptomatic throughout their infection; 126 (77.3%) of 163 symptomatic individuals reported mild severity. Saliva sensitivity was highest in samples collected during the first week of infection at 71.2% (95% CI, 62.6%-78.8%) but decreased each subsequent week. Participants who presented with COVID-19-associated symptoms on the specimen collection day during

week 1 of infection had significantly higher saliva sensitivity compared with asymptomatic participants (88.2% [95% CI, 77.6%-95.1%] vs 58.2% [95% CI, 46.3%- 69.5%];*P* < .001).



Comment: Saliva was sensitive for detecting SARS-CoV-2 in symptomatic individuals during the initial week of infection, but sensitivity in asymptomatic SARS-CoV-2 carriers was less than 60% at all time points. Low saliva sensitivity in asymptomatic infections must be considered. This study suggests saliva-based PCR should not be used for asymptomatic COVID-19 screening. These results are similar to the performance of rapid antigen tests.