I hope everyone is doing well and had a great weekend.

Today under Covid-19 News the FDA has revised the EUA for bamlanivimab and etesevimab (Lilly), administered together, to include emergency use as post-exposure prophylaxis for COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg). Next is a discussion on the FDA advisory board on boosters. This next goes to the CDC's ACIP for their recommendation. Next the announcement that the CDC plans to distribute $2.1 billion from the American Rescue Plan to boost the nation's infection control and prevention efforts. Last, the preliminary announcement by Pfizer on their trial on vaccinating children 5-11 years old.

Under Journal Review, I start with a CDC report on VE of three vaccines in preventing COVID-19 hospitalization March-August 2021. Next is an important study on "test-to-stay" policy as an alternative to home quarantine for exposed students in secondary schools and colleges. Last, is a report examining the percentage of completed COVID-19 vaccinations among nursing home residents and different staff types.

Have a great week.

Ed

COVID-19 News

FDA Authorizes Bamlanivimab and Etesevimab Monoclonal Antibody Therapy for Post-Exposure Prophylaxis for COVID-19
The FDA has revised the EUA for bamlanivimab and etesevimab (Lilly), administered together, to include emergency use as post-exposure prophylaxis for coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death.

Further, the agency said that post-exposure prophylaxis as authorized with bamlanivimab and etesevimab, administered together, is <u>not</u> a substitute for vaccination against COVID-19, and that the drugs may only be used as post-exposure prophylaxis for individuals who are:

- at high risk for progression to severe COVID-19, including hospitalization or death, **and**
- not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, people with immunocompromising conditions, including those taking immunosuppressive medications), **and**
    - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention, **or**
    - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example: nursing homes or prisons)

In addition, the FDA noted that bamlanivimab and etesevimab, administered together, also remain authorized for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

Comment: This EUA adds to EUA approval for postexposure for casirvimab+imdevimab (Regeneron).

FDA Panel Backs Pfizer Booster for Select Groups
An FDA advisory panel recommended EUA of a booster dose of the Pfizer/BioNTech COVID-19 vaccine for individuals 65 and older, and those judged to be at high risk of severe COVID-19. FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC) voted 18-0 that the known and potential benefits of a booster dose outweighed the known and potential risks for older adults, and for individuals 16 and up at high risk of severe disease. The committee also agreed but did not formally vote that HCWs and others at high risk for occupational exposure should be included, which included teachers. However, full approval of a booster dose was not recommended for all individuals ages 16 and older, by a vote of 16-2, with the committee mainly citing lack of safety data for the general population, including the risk for myocarditis in younger men.

Comment: Well, I guess I was right. 😊 This was a partial rebuff to the Biden administration, which had prematurely announced that boosters would be rolled out to the general public by September 20th. The panel also warned against drawing conclusions from short-term results from booster shots; data from Israel, for example, only included a follow-up period of several weeks for older adults. I think Paul Offit said it best. He questioned whether extra shots would do much at all to change the curve of the pandemic. He said: "We all agree that if we really want to impact this pandemic, we need to vaccinate the unvaccinated." Other public health advisers agree saying governments should give priority to vaccinating the unvaccinated, both in the U.S. and abroad. We live in a global community. Variants are more likely to arise in unvaccinated populations anywhere in the world and we have seen how fast variants can spread. What we need is an RCT in persons who have received two doses especially in the younger population. The risk benefit may be very different in younger people than the elderly.

Reminder – do not forget to get your flu vaccine!

CDC to Spend $2.1B to Bolster US Infection Control and Prevention Efforts
The CDC plans to distribute $2.1 billion from the American Rescue Plan to boost the nation's infection control and prevention efforts, marking a record federal investment in this sector. In October, the agency will distribute an initial $500 million to support strike teams that will assist nursing homes and long-term care facilities experiencing COVID-19 outbreaks and labor shortages.

The CDC will roll out the rest of the funds over the next three years to support state and local health departments in addressing a rise in HAIs. The money will help states expand lab testing capabilities, provide training for front-line healthcare staff, and support other initiatives aimed at preventing the spread of infectious diseases. Nearly $900 million of the funding will go to healthcare providers, academic institutions, and other nonprofit partners to establish new infection prevention and control measures.

Comment: This funding is welcomed. The pandemic has set us back in our journey to reduce HAIs. As was reported in the Briefing on Labor Day NHSN reported that since the pandemic started there have been significant increases in CLABSIs, CAUTIs, VAEs, and MRSA bacteremia in 2020.

Pfizer Preliminary Data on Vaccination of Children 5-11
September 20, 2021

Pfizer announced the results of their trial which included 2,268 children ages 5 to 11, two-thirds of whom received two doses of the vaccine three weeks apart; the rest were injected with two doses of saline. Given how rarely children become severely ill, the trial was not big enough to draw meaningful conclusions about the vaccine's ability to prevent Covid-19 or hospitalization. Instead, the investigators relied on measurements of the immune response, on the assumption that the protective levels of antibodies seen in older people would be as protective in younger children. The children who got the vaccine produced a strong immune response, comparable to the levels of antibodies seen in the earlier trials of participants aged 16 to 25 years. But children in the 5- to 11-year-old group achieved this response with 10 micrograms of the vaccine, a third of the dose given to older children and adults. At higher doses, the researchers observed more side effects in younger children, including fever, headache, and fatigue, although none were severe. With the 10-microgram dose, they reported that the second dose, had less fever, less chills than we see in the 16- to 25-year-olds.

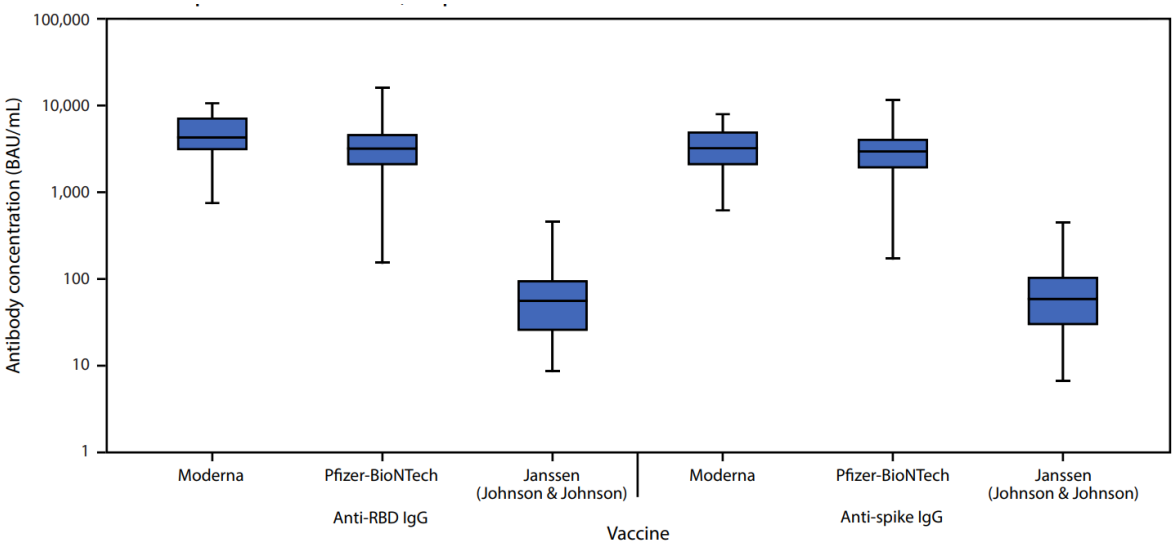
Pfizer plans to apply to the FDA in the next few weeks for authorization to use the vaccine in children 5-11. If the FDA review process goes well elementary school students could be eligible for vaccination by the end of October. Trial results for children younger than 5 are not expected till the fourth quarter of this year at the earliest.

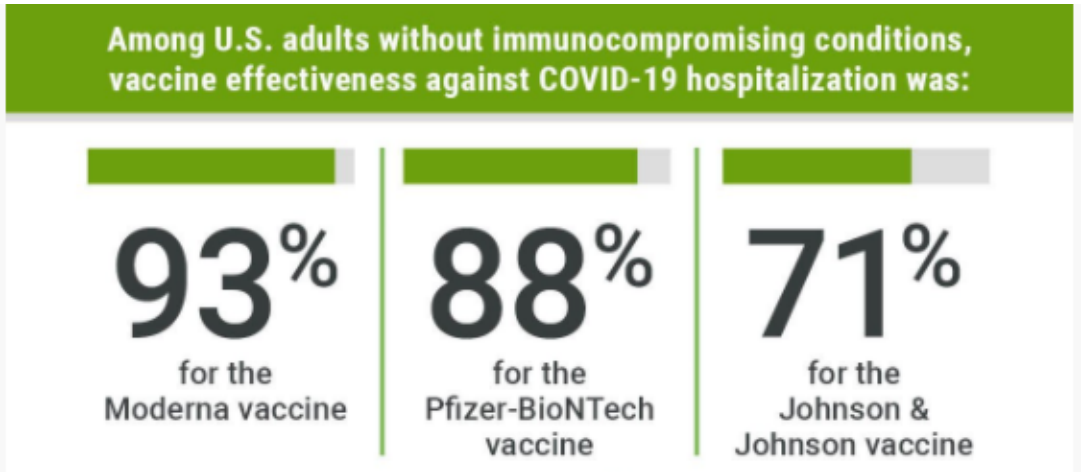
Comment: Children now account for one in five new cases in the US. Nearly 30,000 children were hospitalized for Covid-19 in August. Although children have a much lower risk of severe Covid-19 than adults, even when exposed to the Delta variant, still, some small number of infected children develop life-threatening MIS-C. Still others may have lingering symptoms for months. Infected children can also transmit to vulnerable unvaccinated adults. The study was not large enough to detect any extremely rare side effects, such as myocarditis.

Journal Review

Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions — United States, March-August 2021
MMWR September 17, 2021
To assess VE of three vaccines in preventing COVID-19 hospitalization, CDC and collaborators conducted a case-control analysis among 3,689 adults aged ≥18 years who were hospitalized at 21 U.S. hospitals across 18 states during March 11-August 15, 2021. An additional analysis compared serum antibody levels (anti-spike immunoglobulin G [IgG] and anti–receptor binding domain [RBD] IgG) to SARS-CoV-2, the virus that causes COVID-19, among 100 healthy volunteers enrolled at three hospitals 2-6 weeks after full vaccination with the Moderna, Pfizer, or J&J vaccines. Patients with immunocompromising conditions were excluded.

VE against COVID-19 hospitalizations was higher for the Moderna vaccine (93%; 95% confidence interval [CI] = 91%–95%) than for the Pfizer-BioNTech vaccine (88%; 95% CI = 85%–91%) ($p = 0.011$); VE for both mRNA vaccines was higher than that for the Janssen vaccine (71%; 95% CI = 56%–81%) (all $p < 0.001$). Protection for the Pfizer vaccine declined 4 months after vaccination. Postvaccination anti-spike IgG and anti-RBD IgG levels were significantly lower in persons vaccinated with the J&J vaccine than the Moderna or Pfizer vaccines.





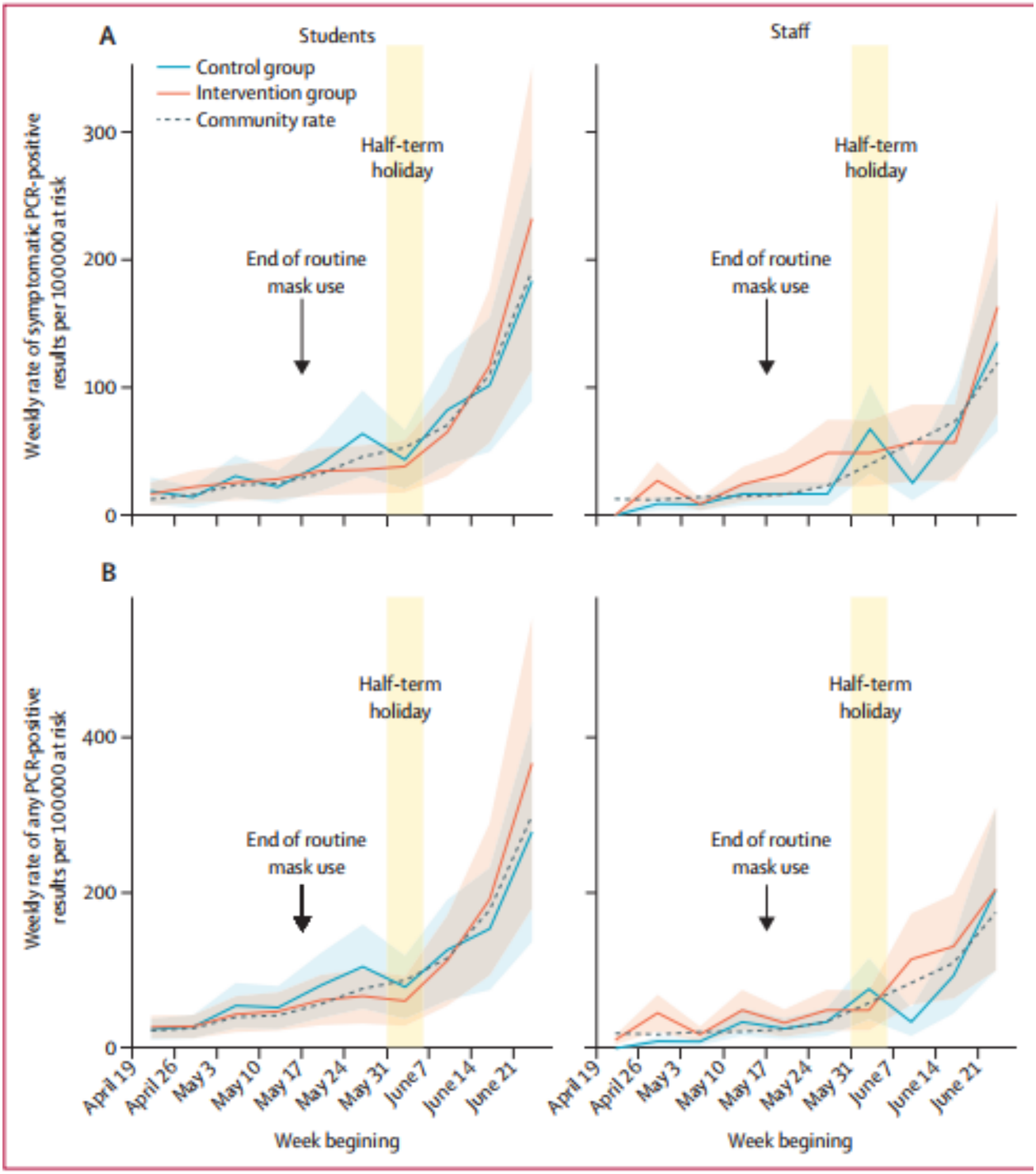
Comment: Two-dose regimens of the Moderna and Pfizer mRNA vaccines provided a remarkable level of protection against COVID-19 hospitalizations in a real-world evaluation at 21 U.S. hospitals during March-August 2021. Although these real-world data suggest some variation in levels of protection by vaccine, all FDA-approved or authorized COVID-19 vaccines still provide substantial protection against severe COVID-19 hospitalization and deaths. mRNA vaccines outperformed J&J. This study did not consider children, immunocompromised adults, or VE against COVID-19 that did not result in hospitalization. The CIs for the J&J VE estimates were wide because of the relatively small number of patients who received this vaccine. Follow-up time was limited to approximately 29 weeks since receipt of full vaccination. Although VE estimates were adjusted for relevant potential confounders, residual confounding is possible. Lastly vaccine specific VE by variant, including against Delta variants and AY sublineages, was not evaluated. I continue to wait for the FDA to authorize a second dose for persons who received the J&J vaccine.

Daily Testing for Contacts of Individuals with SARS-CoV-2 Infection and Attendance and SARS-CoV-2 Transmission in English Secondary Schools and Colleges: An Open-Label, Cluster-Randomised Trial
Lancet published online September 14, 2021
doi.org/10.1016/S0140-6736(21)01908-5

The investigators studied whether daily testing of close contacts could be an alternative to home quarantine. To answer this question, they did an open-label, cluster-randomized, controlled trial in secondary schools and further education colleges in England. Schools were randomly assigned (1:1) to self-isolation of school-based COVID-19 contacts for 10 days (control) or to voluntary daily lateral flow device (LFD) testing for 7 days with LFD-negative contacts remaining at school (intervention). Randomization was stratified according to school type and size, presence of residential students, and proportion of students eligible for free school meals. Coprimary outcomes in all students and staff were COVID-19-related school absence and symptomatic PCR-confirmed COVID-19, adjusted for community case rates, to estimate within-school transmission.

201 schools were randomly assigned (control group n=99, intervention group n=102) in the 10-week study (April 19-May 10, 2021), which continued until the pre-appointed stop date (June 27, 2021). 76 control group schools and 86 intervention group schools actively participated. Routine mask use was discontinued during the trial on May 17, 2021, but other precautions were maintained.

2432 (42·4%) of 5763 intervention group contacts participated in daily contact testing. There were 657 symptomatic PCR-confirmed infections during 7,782,537 days-at-risk (59·1 per 100,000 per week) in the control group and 740 during 8,379,749 days-at-risk (61·8 per 100000 per week) in the intervention group (intention-to-treat adjusted incidence rate ratio [aIRR] 0·96 [95% CI 0·75–1·22]; p=0·72; CACE aIRR 0·86 [0·55–1·34]). Among students and staff, there were 59,422 (1·62%) COVID-19-related absences during 3,659,017 person-schooldays in the control group and 51,541 (1·34%) during 3,845,208 person-school-days in the intervention group (intention-to-treat aIRR 0·80 [95% CI 0·54–1·19]; p=0·27; CACE aIRR 0·61 [0·30–1·23]).

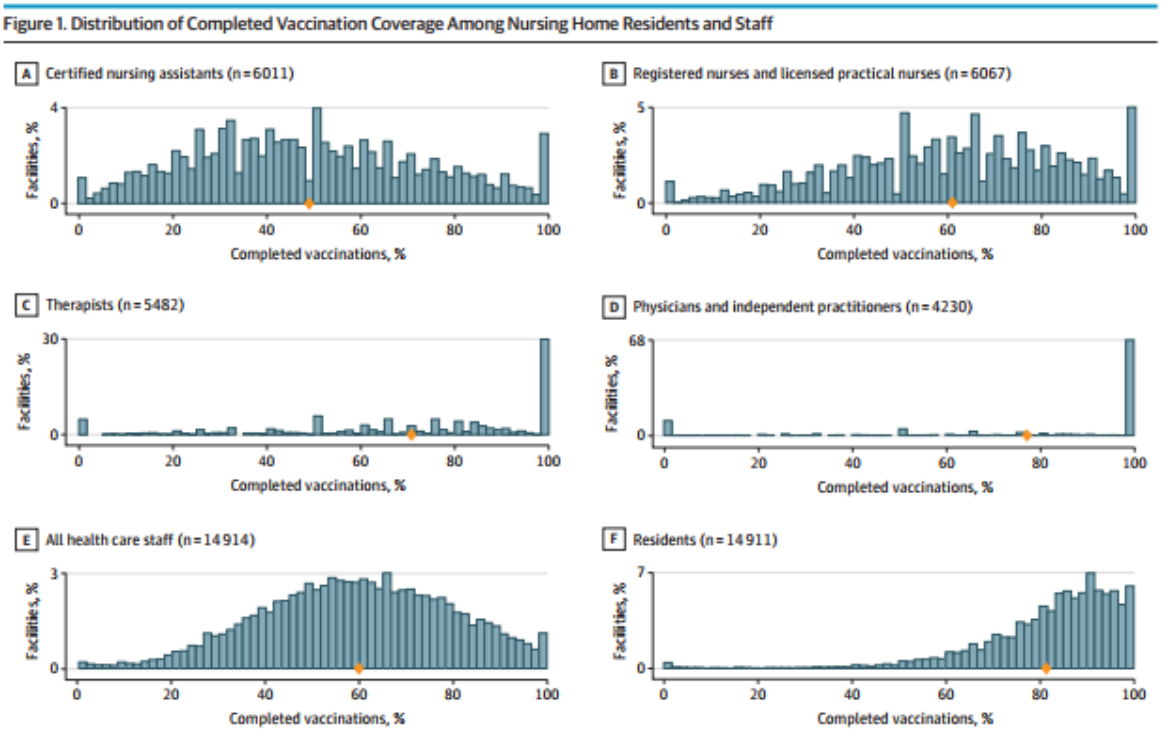


Comment: Daily contact testing of school-based contacts was non-inferior to self-isolation for control of COVID-19 transmission, with similar rates of symptomatic infections among students and staff with both approaches. Infection rates in school-based contacts were low, with very few school contacts testing positive. Roughly 2 percent of school-based close contacts ultimately tested positive for the virus, researchers found, which means that schools were keeping 49 uninfected students out of class every time one student tested positive. Many other schools in Utah have had similar experiences using daily testing to keep classrooms open and safe. This trial was done during periods of low to moderate SARS-

CoV-2 incidence. Therefore, they could not estimate the impact of daily contact testing in high incidence settings. Whether the extent of transmission and performance of LFDs is sufficient to make contact testing necessary and cost-effective will require careful discussion and might vary with changes in incidence, virus transmissibility, or the prevalence of potential new variants. Future work should include WGS of positive samples from school members and from the community, which would help better understand transmission. Currently the CDC does not endorse "test-to-stay" policy. Can we use rapid antigen tests rather than LFDs?

Association of Nursing Home Characteristics with Staff and Resident COVID-19 Vaccination Coverage
JAMA Intern Med published online September 16, 2021
doi:10.1001/jamainternmed.2021.5890
The authors examined the percentage of completed COVID-19 vaccinations among nursing home residents and different staff types at each facility, including all health care personnel eligible to work in the nursing home in the prior week, registered nurses and licensed practical nurses, certified nursing assistants (CNAs), therapists, and physicians and independent practitioners. Estimated means were weighted by the relevant population size (resident census and staff counts).

Among the more than 14,900 nursing homes (NH) reporting vaccination data by July 18, 2021, 60.0% of staff and 81.4% of residents were fully vaccinated on average. Average vaccination coverage was lowest among CNAs (49.2%) and registered nurses and licensed practical nurses (61.0%), with higher coverages noted among therapists (70.9%) and physicians and independent practitioners (77.3%). Greater percentages of staff and residents who were non-White (i.e., American Indian or Alaska Native, Asian, Black, Pacific Islander or Native Hawaiian, and 2 or more races) were associated with lower vaccination coverages for both groups.



Comment: They also found that nonprofit and nonchain nursing homes, facilities with higher Medicare star ratings, and facilities with longer-tenured staff achieved greater vaccine coverage, suggesting that organizational characteristics and culture, including ownership structure, quality, and ability to retain staff, may be key in facilities' ability to vaccinate residents and staff. This analysis is limited by the potential for unobserved confounders, which limits generalizability of the findings. In the end I am still amazed that staff working in NH are not fully vaccinated as a condition for employment. Like influenza, staff can be the index case for outbreaks putting our most vulnerable at risk.