Good morning.

Today very little new to report under COVID-19 News. FDA may act in the next week to authorize boosters to immunosuppressed persons and later to persons >65.

Under Journal Review I start with a small study concluding unvaccinated people who have had Covid-19 may be more than twice as likely to get infected again than those who also received vaccination. The second article confirms vaccine effectiveness against SARS-CoV-2 and infections among household and other close contacts. The third article reports on illness duration in children infected with SARS-CoV-2. As more children become infected the question of long haulers in children is becoming an important focus. Last is a report on myocarditis and pericarditis following mRNA vaccines.

I hope this week will be less stressful.

Ed

Journal Review

Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May-June 2021
MMWR August 6, 2021
The study, published by the CDC, examined the risk of reinfection during May and June among hundreds of Kentucky residents who tested positive for the virus in 2020. [natural immunity]

Those who did not get vaccinated had a risk of reinfection that was 2.34 higher than those who did get vaccinated. The study suggests that for those who had recovered from natural infection, the addition of a vaccine offered better protection than the natural immunity generated by their original infection.

| Vaccination status | No. (%) | | OR (95% CI)[†] |
	Case-patients	Control participants	
Not vaccinated	179 (72.8)	284 (57.7)	2.34 (1.58–3.47)
Partially vaccinated[¶]	17 (6.9)	39 (7.9)	1.56 (0.81–3.01)
Fully vaccinated[§]	50 (20.3)	169 (34.3)	Ref
Total	**246 (100)**	**492 (100)**	—

Comment: In this study unvaccinated people who have had Covid-19 may be more than twice as likely to get infected again than those who tested positive and bolstered their natural immunity with a vaccine, according to a small study that assessed the likelihood of reinfection. There are other studies which do not support this conclusion of this study (Cleveland Clinic). I would have liked to see a control group of unvaccinated uninfected patients as a comparison and any significant differences in severity of illness. Reinfection was not confirmed through WGS, which would be necessary to definitively prove that the reinfection was caused from a distinct virus relative to the first infection. In addition, persons who have been vaccinated are possibly less likely to get tested. Therefore, the association of reinfection and lack of vaccination might be overestimated. In addition, this is a retrospective study design using data from a single state during a 2-month period; therefore, these findings cannot be used to infer causation. Lastly, the lack of a significant association with partial versus full vaccination should be

interpreted with caution given the small numbers of partially vaccinated persons included in the analysis. Additional prospective studies with larger populations are clearly needed.

Vaccine Effectiveness Against SARS-CoV-2 and Infections Among Household and Other Close Contacts of Confirmed Cases, the Netherlands, February to May 2021
Eurosurveillance August 6, 2021
Based on routine contact monitoring data, the investigators estimated the vaccine effectiveness against transmission (VET) and the vaccine effectiveness against infection (VE) among household and other close contacts of confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the Netherlands, between 1 February and 27 May 2021. Alpha variant was the dominant variant. During the study period, household members and other close contacts of confirmed cases needed to quarantine for 10 days post exposure. All close contacts of a confirmed case were encouraged to get tested as soon as possible after exposure. In addition, a test was recommended on the 5th day after last exposure. If negative, contacts could end quarantine. Fully vaccinated was defined as having completed a two-dose schedule with a time since vaccination of at least 7 days, or the one-dose J&J with a time since vaccination of at least 14 days.

The attack was 31% among household contacts of unvaccinated index cases and 11% among household contacts of fully vaccinated index cases. Stratified by vaccine received by the index case, VET values were estimated at 58% for AZ, 70% for Pfizer, 88% for Moderna and 77% for the J&J vaccine. For all vaccines with a two-dose schedule, the adjusted VET (aVET) after one dose was considerably lower than after two doses: 15% for AZ, 26% for Pfizer, and 51% for Moderna.

Household contact
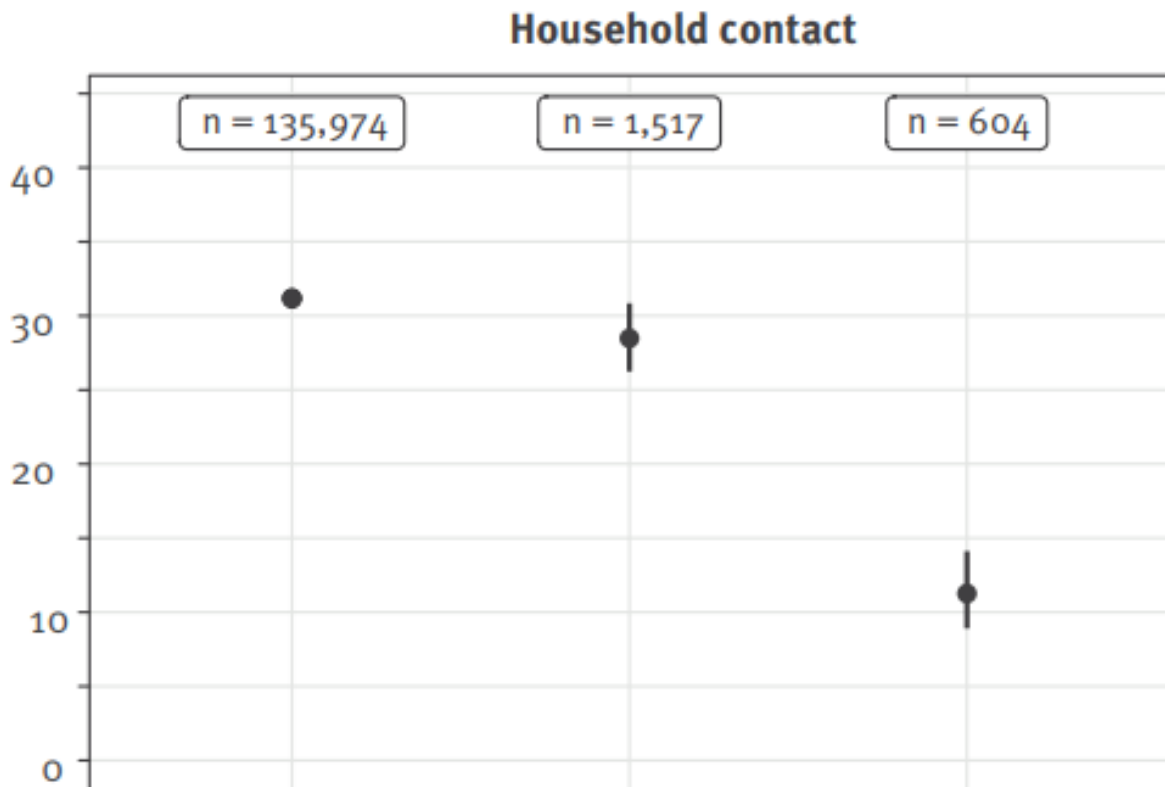
Comment: This study clearly shows the effectiveness of full vaccination for close contacts. As the Alpha variant of SARS-CoV-2 dominated during the study period, an important question is to what extent these VET and VE estimates hold in the context of the Delta variant which is now dominant and more transmissible.

Illness Duration and Symptom Profile in Symptomatic UK School-Aged Children Tested for SARS-CoV-2
Lancet Child Adolesc Health published online August 3, 2021
doi.org/10.1016/S2352-4642(21)00198-
This is a prospective cohort study, data from UK school-aged children (age 5-17 years) reported by an adult. Participants were voluntary and used a mobile application (app). Illness duration and symptom prevalence, duration, and burden were analyzed for children testing positive for SARS-CoV-2 for whom illness duration could be determined and were assessed overall and for younger (age 5-11 years) and older (age 12-17 years) groups. Data from symptomatic children testing negative for SARS-CoV-2, were matched 1:1 for age, gender, and week of testing.

258,790 children aged 5-17 years were reported by an adult between March 24, 2020, and Feb 22, 2021, of whom 75,529 had valid test results for SARS-CoV-2. 1734 children (588 younger and 1146 older children) had a positive SARS-CoV-2 test result and calculable illness duration within the study timeframe (illness onset between Sept 1, 2021, and Jan 24, 2021). The most common symptoms were headache (62·2%), and fatigue (55%). Median illness duration was 6 days (IQR 3-11) versus 3 days (2-7) in children testing negative and was positively associated with age p<0·0001. Median illness duration was longer for older children (7 days, IQR 3-12) than younger children (5 days, 2-9). 4·4% of children had illness duration of at least 28 days, more commonly in older than younger children (5·1% of 1146 older children vs 3·1% of 588 younger children; p=0·046). The most common symptoms experienced by these children during the first 4 weeks of illness were fatigue (84·4%), headache (77·9%), and anosmia (77·9%); however, after day 28 the symptom burden was low (median 2 symptoms, IQR 1-4) compared with the first week of illness (median 6 symptoms, 4-8). Only 25 (1·8%) of 1379 children experienced symptoms for at least 56 days.
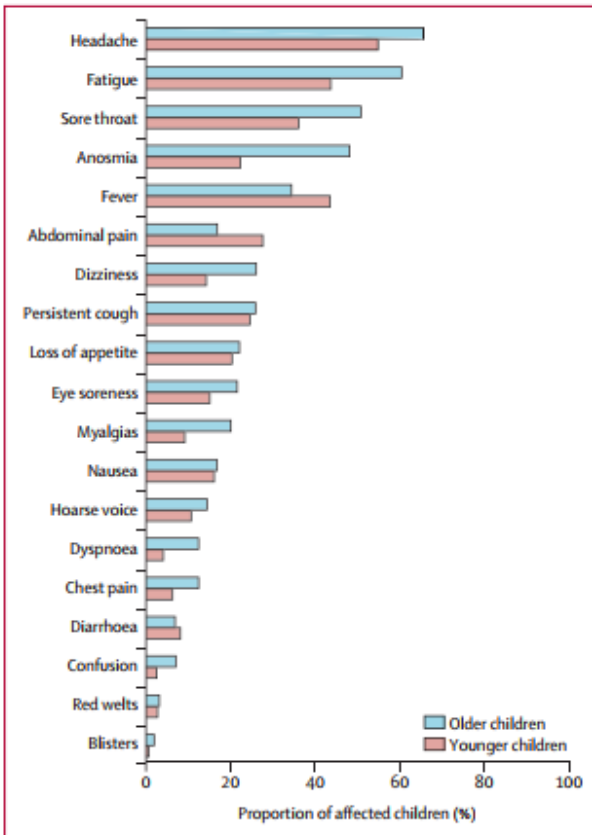
Figure 2: Prevalence of symptoms reported over the course of illness in younger (age 5–11 years, n=588) and older (age 12–17 years, n=1146) children testing positive for SARS-CoV-2
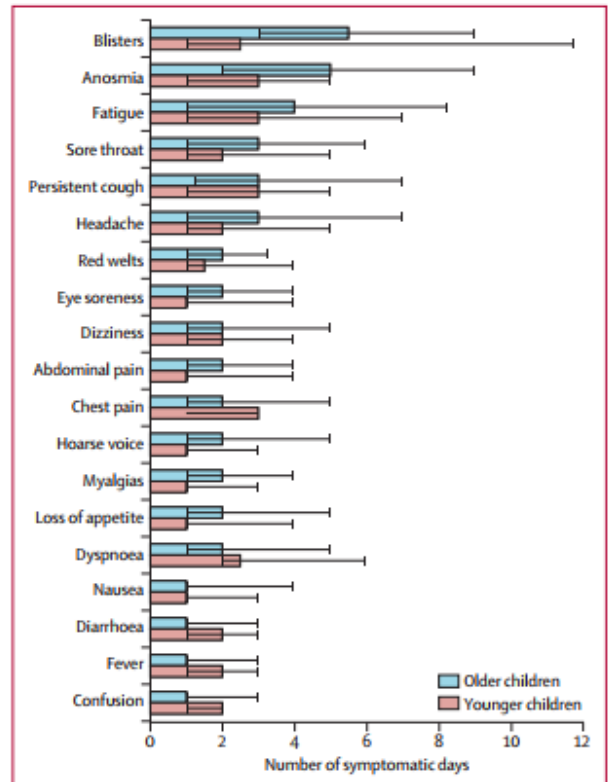

Figure 3: Median duration of each symptom and IQR in younger (age 5–11 years) and older (age 12–17 years) children
Data refers to children with symptom onset between Sept 1, 2020, and Jan 24, 2021. Black bars represent IQRs.

Comment: Although COVID-19 in children is usually of short duration with low symptom burden, some children with COVID-19 experience prolonged illness duration. Reassuringly, symptom burden in these children did not increase with time, and most recovered by day 56. Most children do recover over time. Short-term and long-term effects of COVID-19 on school performance and learning have been a matter of concern. In this cohort, attentional problems, memory complaints, and anxiety were not reported, and cases of low mood and irritability were consistent with previous school-aged population data. However, estimates from the handful of other studies of children so far vary widely. A recent study suggested that between 11 percent and 15 percent of infected youths might end up with this long-term consequence. There are reports of long Covid patients from across the country. They are seeing things like fatigue, headaches, brain fog, memory and concentration difficulties, sleep disturbances, and ongoing change in smell and taste. An April study by the United Kingdom's Office for National Statistics found that 9.8 percent of 2-to-11-year-olds and 13 percent of 12-to-16-year-olds infected with the coronavirus reported continuing symptoms five weeks later. After 12 weeks, rates remained significant: 7.4 percent in the younger group and 8.2 percent in the older group.

The challenge moving forward is that pediatric Covid-19 cases are rising sharply, driven in part by the Delta variant and the fact that only ~30% of 12-to-17-year-olds are fully vaccinated and children under 12 are still ineligible for vaccines. There is not yet enough evidence to conclude that Delta causes more severe disease in children compared to other variants.

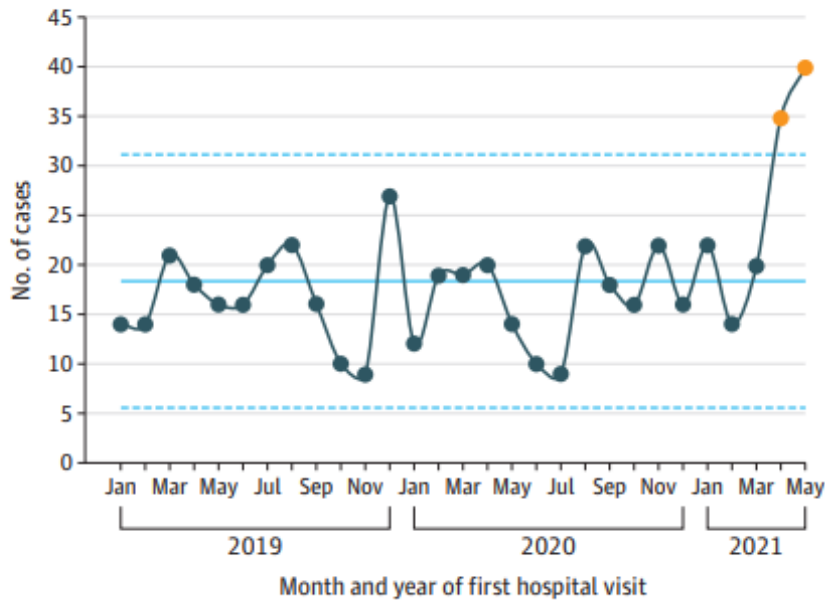**Myocarditis and Pericarditis After Vaccination for COVID-19**

Forty hospitals in Washington, Oregon, Montana, and Los Angeles County, California, that were part of the Providence health care system and used the same EMR were included. All patients with documented COVID-19 vaccinations administered inside the system or recorded in state registries at any time through May 25, 2021, were identified. Vaccinated patients who subsequently had emergency department or inpatient encounters with diagnoses of myocarditis, myopericarditis, or pericarditis were ascertained from EMRs.

Among 2,000,287 individuals receiving at least 1 COVID-19 vaccination, 58.9% were women, the median age was 57 years, 76.5% received more than 1 dose, 52.6% received the Pfizer, 44.1% received Moderna, and 3.1% received the J&J vaccine. Twenty individuals had vaccine related myocarditis (1.0 [95% CI, 0.61-1.54] per 100 000) and 37 had pericarditis (1.8 [95% CI, 1.30-2.55] per 100,000). Myocarditis occurred a median of 3.5 days after vaccination (Moderna vaccine, 11 cases [55%]; Pfizer vaccine, 9 cases). 75% were male, and the median age was 36 years (IQR, 26-48 years). 20% developed symptoms after the first vaccination and 80% developed symptoms after the second. Nineteen patients were admitted to the hospital. All were discharged after a median of 2 days. There were no readmissions or deaths. Two patients received a second vaccination after onset of myocarditis; neither had worsening of symptoms. At last available follow-up 13 patients had symptom resolution and 7 were improving.
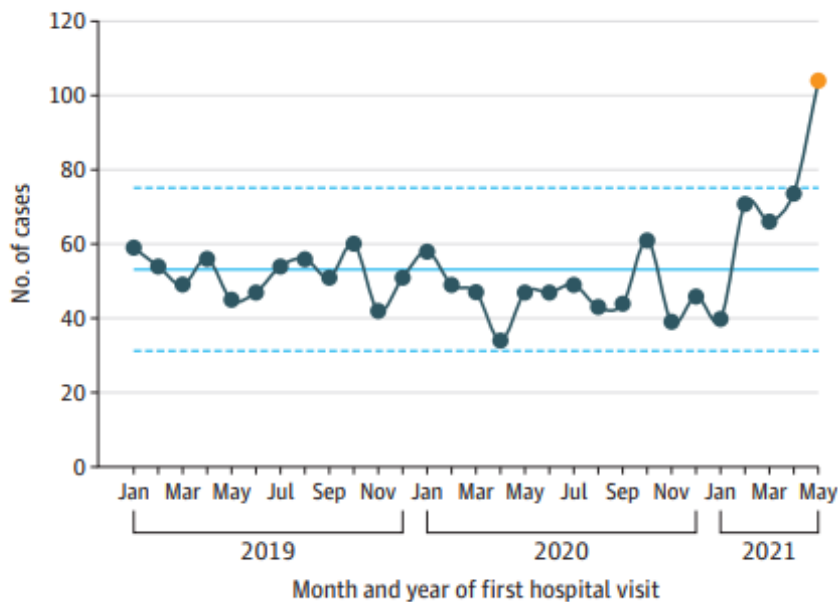
Pericarditis developed after the first immunization in 15 cases and after the second immunization in 22 cases (Moderna vaccine, 12 cases [32%]; Pfizer vaccine, 23 cases [62%]; J&J vaccine, 2 cases [5%]). Median onset was 20 days after the most recent vaccination. Thirteen (35%) were admitted to the hospital, none to intensive care. Median stay was 1 day (IQR, 1-2 days). Seven patients with pericarditis received a second vaccination. The median age was 59. No patient died. At last available follow-up (median, 28 days), 7 patients (19%) had resolved symptoms and 23 (62%) were improving.

The mean monthly number of cases of myocarditis or myopericarditis during the prevaccine period was 16.9 (95% CI, 15.3-18.6) vs 27.3 (95% CI, 22.4-32.9) during the vaccine period (P < .001). The mean numbers of pericarditis cases during the same periods were 49.1 (95% CI, 46.4-51.9) and 78.8 (95% CI, 70.3-87.9), respectively (P < .001).

A Incident cases of myocarditis

B Incident cases of pericarditis

Comment: Two distinct self-limited syndromes, myocarditis and pericarditis, were observed after COVID-19 vaccination (mRNA). Myocarditis developed rapidly in younger patients, mostly after the second vaccination. Pericarditis affected older patients later, after either the first or second dose. The CDC reported a possible association between COVID-19 mRNA vaccines and myocarditis, primarily in younger male individuals within a few days after the second vaccination, at an incidence of about 4.8 cases per 1 million. This current study shows a similar pattern, although at a higher incidence, suggesting vaccine adverse events may be underreporting. Additionally, pericarditis may be more common than myocarditis among older patients. The good news is patients did well.