I hope everyone is having a good week so far.

Today under Covid-19 News I share the latest cases in the US. Next is the Canadian decision to allow mixing of vaccines whose first dose was AstraZeneca. Last is the approval for SC injection for the Regeneron monoclonal.

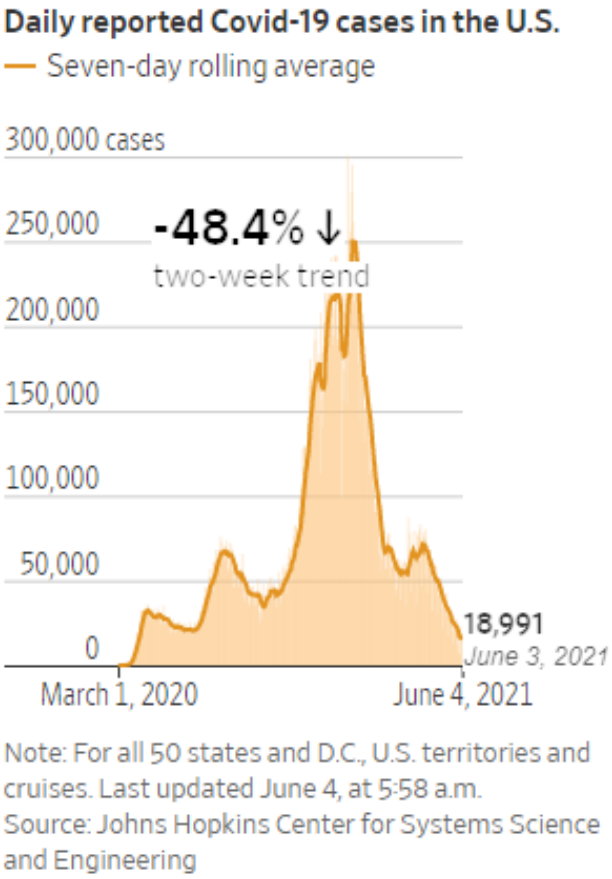
Under Journal Review is the CDC report on adolescent hospitalizations for Covid-19 compared to flu. Next is a report on myocarditis associated with the Pfizer vaccine in adolescents. Last is a nice report on incidence of co-bacterial infections in Covid-19 patients confirming incidence is very low and antibiotic use is very high.

Have a good rest of the week.

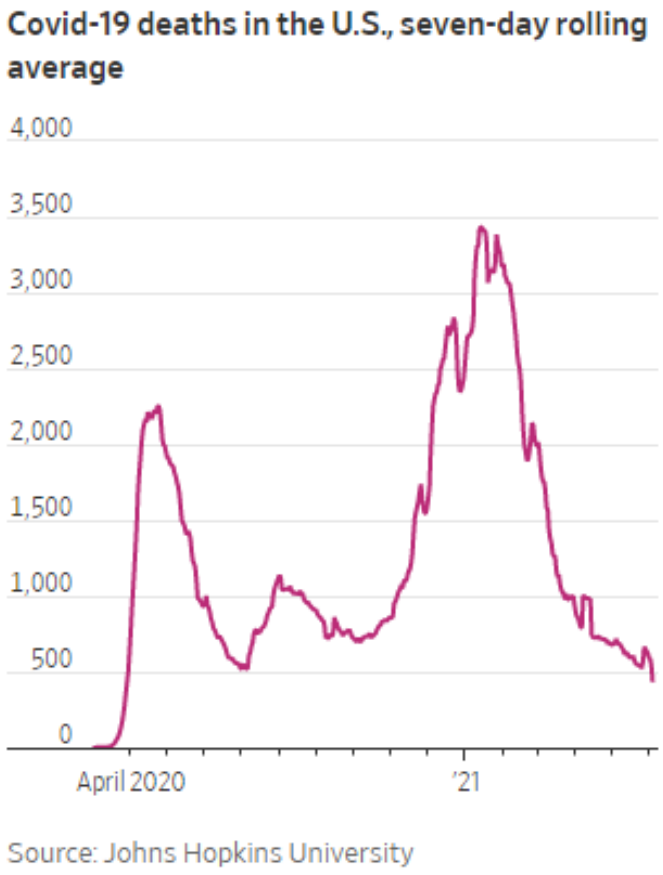
Next Briefing Friday.

Ed

COVID-19 News



Note: For all 50 states and D.C., U.S. territories and cruises. Last updated June 4, at 5:58 a.m.
Source: Johns Hopkins Center for Systems Science and Engineering



Canada Panel Says COVID-19 Shots Can Be Mixed, Cases Fall Steadily
An official Canadian panel on Tuesday said people who received a first shot of AstraZeneca COVID-19 vaccine can choose to receive a different shot for their second dose**.** One reason for the recommendation by the National Advisory Committee on Immunization (NACI) was concern about rare and potentially fatal blood clots linked to the AstraZeneca vaccine. NACI said Denmark, Finland, France, Germany, Norway, Spain, and Sweden, citing the risk of clots, were already offering second doses from Moderna Inc or Pfizer Inc to people who had received their first shots from AstraZeneca.

Regeneron's COVID-19 Drug is Authorized for Injection
Under the new authorization, the FDA has approved Regeneron's monoclonal to be administered by SC injection where IV infusions are not feasible or would lead to a delay in treatment. In addition, the FDA allowed for the drug to be combined in a single vial, which could reduce the time it takes for nurses to prepare the treatment. The FDA also cleared a lower dose of the drug that is about half the strength of the originally authorized dose, which will increase the total number of doses available for patients under Regeneron's contract with the U.S. government.

Comment: This is great news. Monoclonals have been underutilized and one of the challenges has been arranging for the drug to be administered by IV infusion. This new formulation will certainly make it easier to provide monoclonals to high-risk patients.

Journal Review

Hospitalization of Adolescents Aged 12–17 Years with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, March 1, 2020-April 24, 2021

MMWR June 4, 2021

Data from FluSurv-NET, a surveillance system across 13 states, compared COVID-19 and flu-related hospitalizations among kids aged 12-17 from October to April, or most of the typical flu season. Rates were compared across three flu seasons starting in 2017.

Cumulative COVID-19-associated hospitalization rates during October 1, 2020-April 24, 2021, were 2.5-3.0 times higher than seasonal influenza-associated hospitalization rates during three recent influenza seasons. Results indicate upwards of 35 COVID-19 hospitalizations per 100,000 population, compared to approximately 15 flu hospitalizations per 100,000 population.

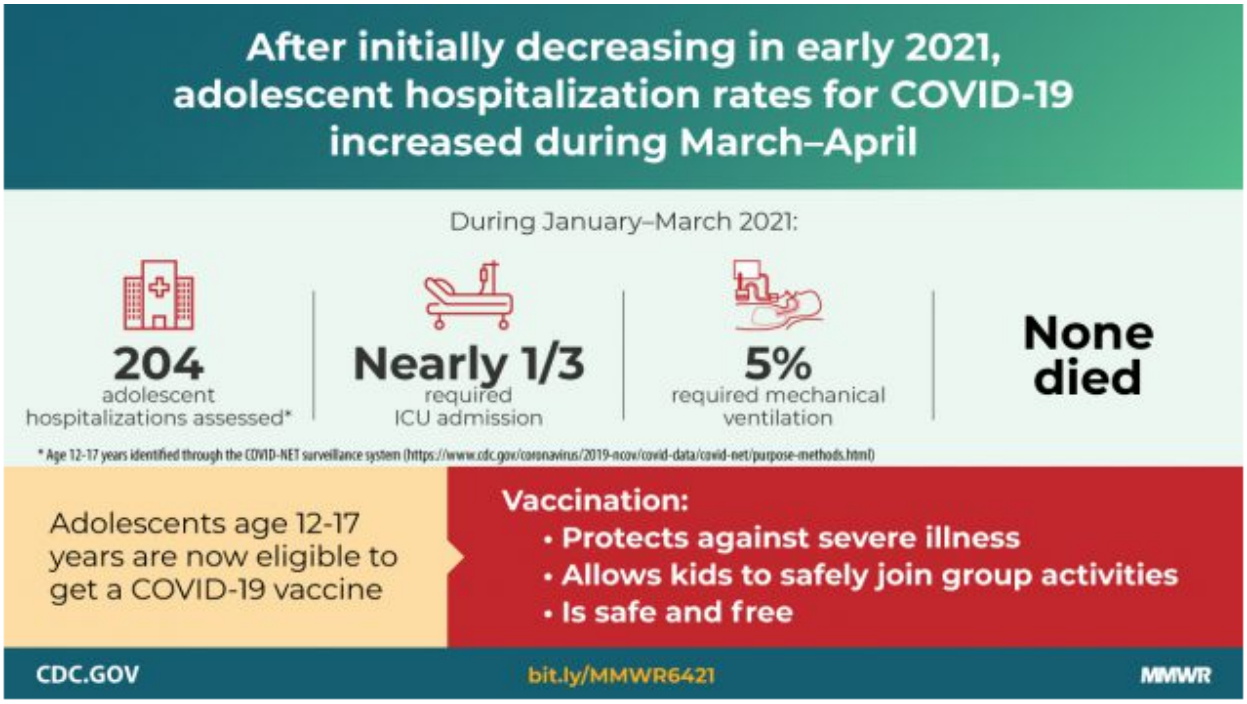


FIGURE 1. Three-week moving average COVID-19–associated hospitalization rates* among children and adolescents aged <18 years, by age group — COVID-NET, 14 states,† March 1, 2020–April 24, 2021

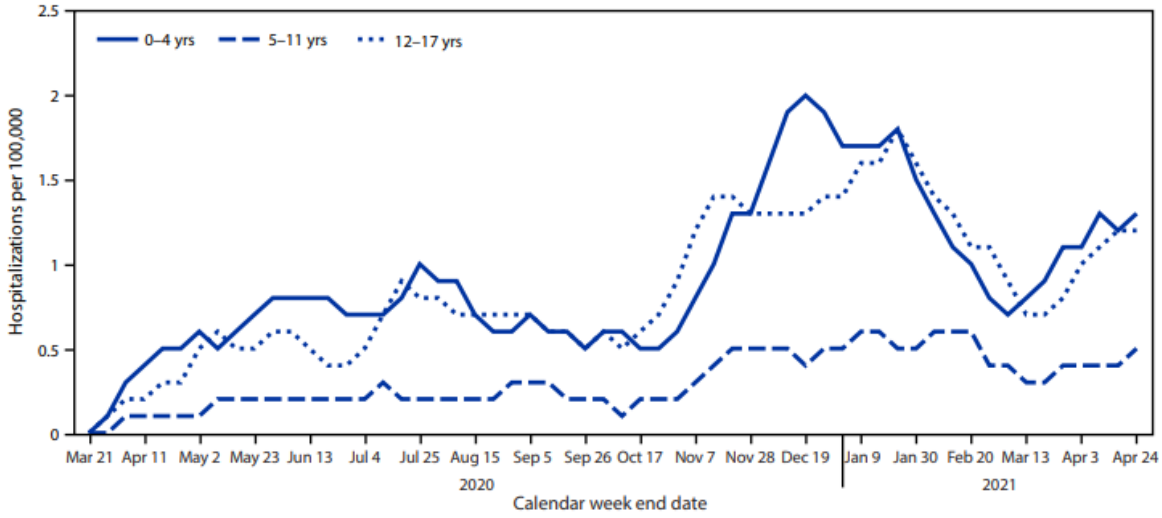
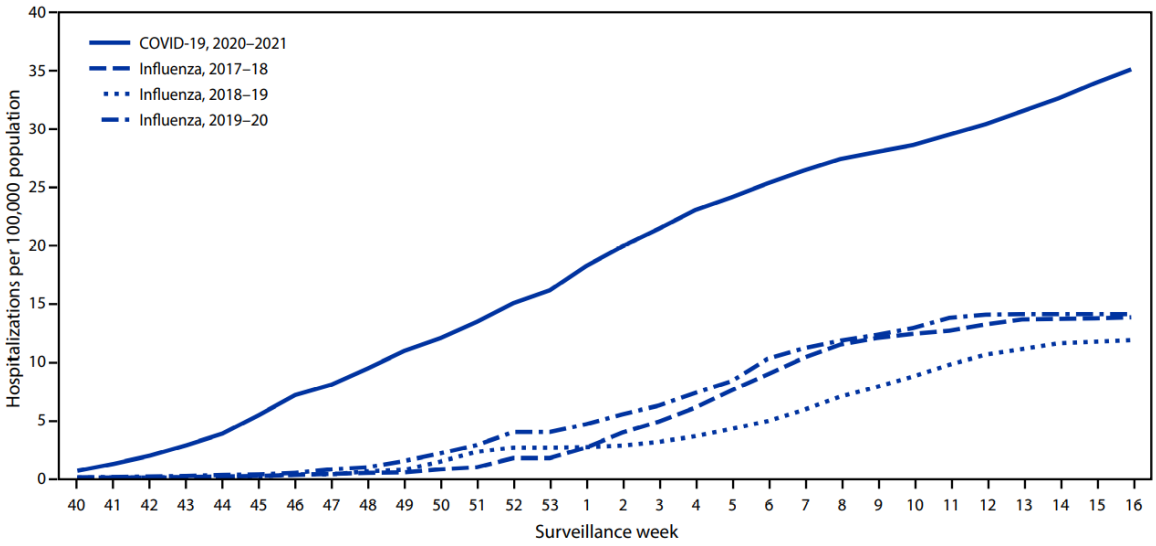


FIGURE 2. Cumulative rates for COVID-19–associated hospitalizations* compared with influenza-associated hospitalizations† among adolescents aged 12–17 years, by surveillance week§ — COVID-NET¶ and FluSurv-NET, 14 states,†† 2017–2021§§**



Comment: Recent increased hospitalization rates in spring 2021 and potential for severe disease reinforce the importance of continued COVID-19 prevention measures, including vaccination and correct and consistent mask wearing among persons not fully vaccinated.

The study had its limitations, including how uneven testing rates between COVID-19 and influenza were not adjusted for, potentially disproportionately affecting flu rates. In addition, the Pfizer COVID-19 vaccine had been approved for and administered to adolescents aged 16-17 years during this study period; therefore, rates of COVID-19-associated hospitalization in adolescents aged 16-17 years might differ from those in adolescents aged 12-15 years who were not previously eligible for vaccination and could affect the overall hospitalization rate for all adolescents.

Symptomatic Acute Myocarditis in Seven Adolescents Following Pfizer-BioNTech COVID-19 Vaccination

Pediatrics published online May 4, 2021
DOI: 10.1542/peds.2021-052478

The authors report seven cases of acute myocarditis or myopericarditis in healthy male adolescents who presented with chest pain all within four days after the second dose of Pfizer COVID-19 vaccination. Five patients had fever around the time of presentation. Acute COVID-19 was ruled out in all 7 cases based on negative SARS-CoV-2 real-time PCR tests of specimens obtained using nasopharyngeal swabs. None of the patients met criteria for multisystem inflammatory syndrome in children (MIS-C). Six of the 7 patients had negative SARS-CoV-2 nucleocapsid antibody assays. All patients had an elevated troponin level. Cardiac MRI revealed late gadolinium enhancement characteristic of myocarditis. All 7 patients resolved their symptoms rapidly. Three patients were treated with NSAIDs only and 4 received intravenous IVIG and corticosteroids. No causal relationship between vaccine administration and myocarditis could be established.

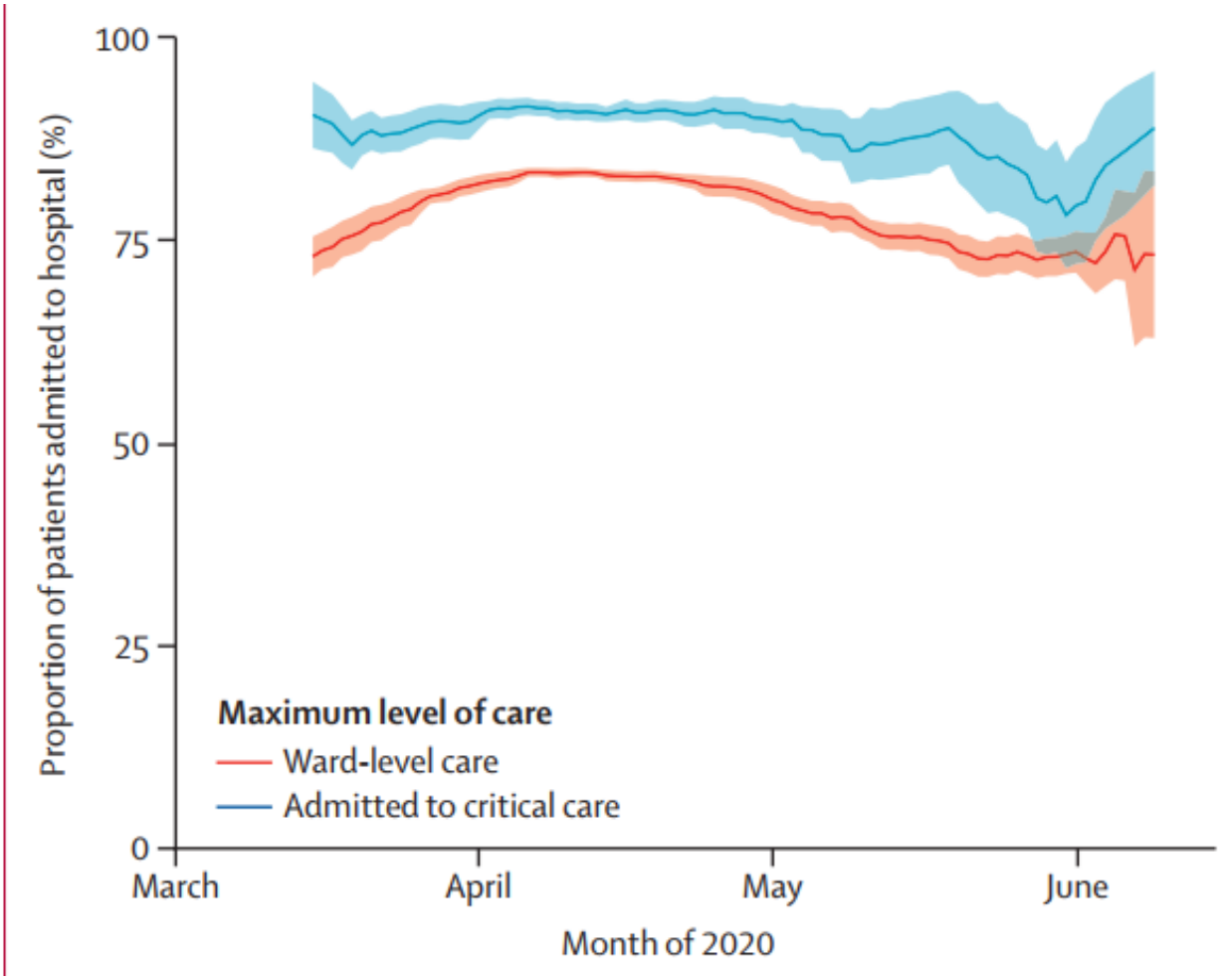
Comment: While the authors correctly point out that a causal relationship between vaccination and myocarditis could not be established at this time, the temporal association of these cases with vaccination as well as the striking similarity in the clinical and laboratory presentations raise the possibility that such a relationship may exist. In addition, there were very few other circulating

respiratory viruses. However, the pathogenesis of viral myocarditis involves direct viral infection of the myocardium which would not apply in these cases. The authors also acknowledge that a significant limitation in their report is that they compiled cases through personal communication rather than through a systematic surveillance system. Clearly, this approach could introduce reporting bias. Bottom line continued monitoring and reporting to the FDA Vaccine Adverse Event Reporting System (VAERS) is strongly recommended. To date the benefits of vaccination clearly outweigh the potential risks.

Co-Infections, Secondary Infections, and Antimicrobial Use in Patients Hospitalised with COVID-19 During the First Pandemic Wave from the ISARIC WHO CCP-UK Study: A Multicentre, Prospective Cohort Study

Lancet Microbe published online June 2,2021
doi.org/10.1016/ S2666-5247(21)00090-2

The investigators analyzed data from 48,902 patients admitted to the hospital between Feb 6 and June 8, 2020, in the UK. The median patient age was 74 years (IQR 59–84) and 20,786 (42·6%) of 48,765 patients were female. Microbiological investigations were recorded for 8,649 (17·7%) of 48,902 patients, with clinically significant COVID-19-related respiratory or bloodstream culture results recorded for 1,107 patients. 762 (70·6%) of 1,080 infections were healthcare-associated (HAI), occurring more than 2 days after hospital admission. *S. aureus* and *H. influenzae* were the most common pathogens causing respiratory co-infections (diagnosed ≤2 days after admission), with Enterobacteriaceae and *S aureus* most common in secondary respiratory infections. Bloodstream infections were most frequently caused by *E. coli* and *S aureus.* Among patients with available data, 13,390 (37·0%) of 36,145 had received antimicrobials in the community for this illness episode before hospital admission and 39,258 (85·2%) of 46,061 patients with inpatient antimicrobial data received one or more antimicrobials at some point during their admission (highest for patients in critical care). We identified frequent use of broad-spectrum agents and use of carbapenems rather than carbapenem-sparing alternatives. Below is the percent of patients admitted to the hospital who were prescribed antibiotics.



Comment: As other studies have reported, bacterial co-infections and secondary infections are rare in patients admitted to the hospital with COVID-19. The frequency and nature of antimicrobial use is disturbing, heightening the need for stronger antimicrobial stewardship.