

Once again, we have come to the end of another stressful week in the fight against SARS-CoV-2 and **we will win this fight**. I am reminded of the JFK speech about choosing to go to the moon. He said “not because they are easy, but because they are hard, because the goal will serve to organize and measure the best energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one we intend to win.”

So, for today lots to share: Under Covid-19 News I start with a preliminary report from J&J on booster doses. Next an alarming report of the use of ivermectin and over the counter formulations not intended for human use resulting in ADE. [People are scared and getting desperate] Last is the updated weekly report from AAP on pediatric cases and hospitalizations.

Under Journal Review first a report on SARS-CoV-2 infections by vaccination status. Next a CDC report on VE among HCWs during the delta surge. The third article highlights how many deaths have been averted in the US due to vaccinations. The last article uses data from the largest health care organization in Israel to evaluate the safety of the Pfizer vaccine. I have included 2 figures which I think are powerful taking points when speaking to vaccine hesitant persons.

I sincerely hope we all find some time this weekend to relax and recharge our batteries for the coming week ahead.

Ed

COVID-19 News

Booster Doses from J&J and Pfizer Give Immune Boost August 25, 2021

New studies from J&J and Pfizer demonstrated that extra shots can dramatically raise antibodies against the coronavirus.

In its new study, J&J tracked 17 volunteers from last year’s clinical trial. When given a booster shot at six months, their antibodies against SARS-CoV-2 jumped nine times as high as after the first dose. The data has not yet been published in a scientific journal and involved only 17 volunteers. Pfizer released new data from 306 people showing that a third dose given five to eight months after the second caused a strong immune response with antibodies against SAR-CoV-2 more than tripled.

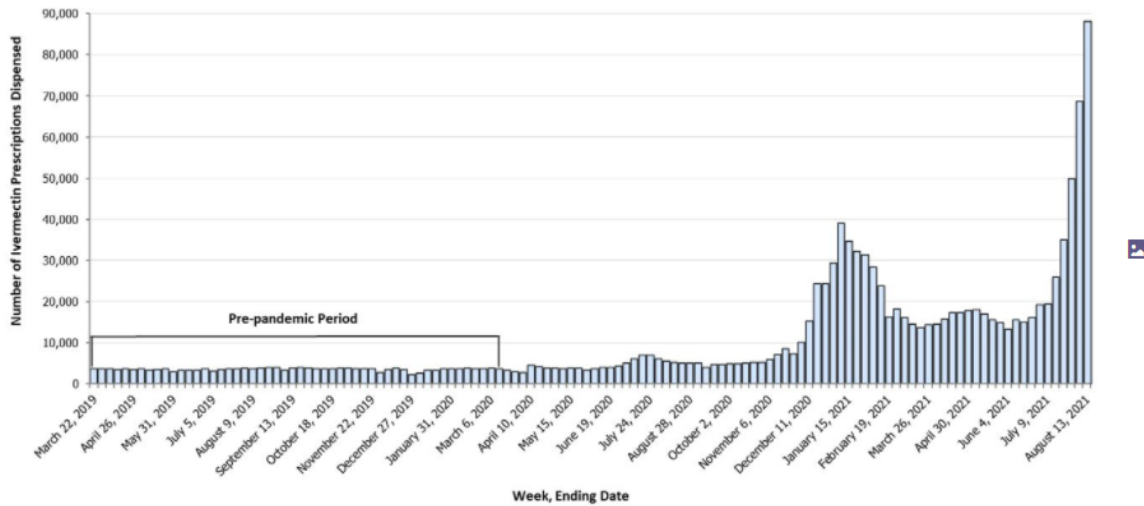
Comment: ACIP will meet this Monday to discuss the data if booster doses are indicated. I hope they take up the J&J vaccine as well. Stay tuned.

Rapid Increase in Ivermectin Prescriptions and Reports of Severe Illness Associated with Use of Products Containing Ivermectin to Prevent or Treat COVID-19

August 26, 2021

During this pandemic ivermectin dispensing by retail pharmacies has increased, as has use of veterinary formulations available over the counter but not intended for human use. FDA has cautioned about the potential risks of use for prevention or treatment of COVID-19. Adverse effects associated with ivermectin misuse and overdose are increasing, as shown by a rise in calls to poison control centers reporting overdoses and more people experiencing adverse effects. In 2021, poison control centers across the U.S. received a three-fold increase in the number of calls for human exposures to ivermectin in January 2021 compared to the pre-pandemic baseline. In July 2021, ivermectin calls have continued

to sharply increase, to a five-fold increase from baseline. These reports are also associated with increased frequency of adverse effects and emergency department/hospital visits.



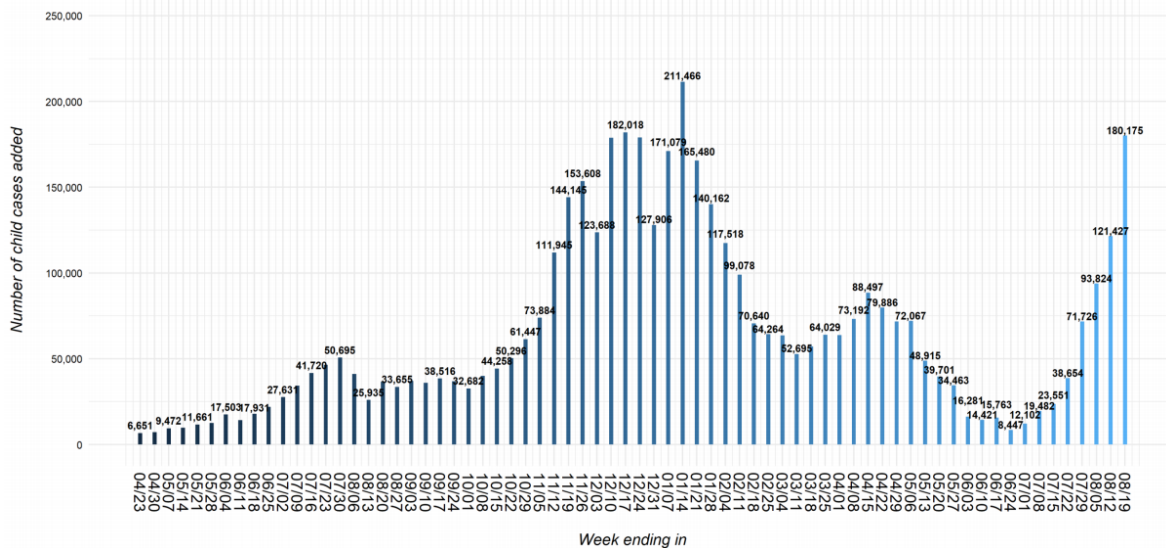
Comment: Ivermectin is not authorized or approved by FDA for prevention or treatment of COVID-19. The NIH COVID-19 Treatment Guidelines Panel has also determined that there are currently insufficient data to recommend ivermectin for treatment of COVID-19. [Reviewed in Briefing August 13, 2021]

US Pediatric COVID-19 Cases

AAP August 19, 2021

More than 180,000 COVID-19 cases in US children were recorded in the week ending on August 19, 2021, reaching levels of the winter surge, according to the latest data from the AAP. More than one in five (22.4%) reported cases that week were in children. A four-fold increase has been reported in the past month, rising from about 38,000 cases the week ending July 22nd to 180,000 the past week. Recent update this week: pediatric COVID-19-related hospitalizations have hit all-time highs in the US.

Fig 6. United States: Number of Child COVID-19 Cases Added in Past Week*



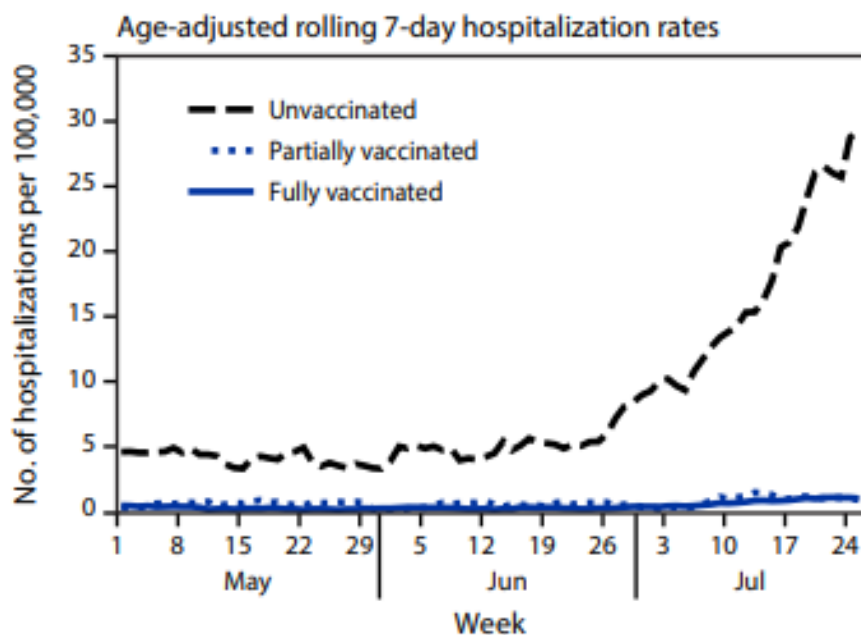
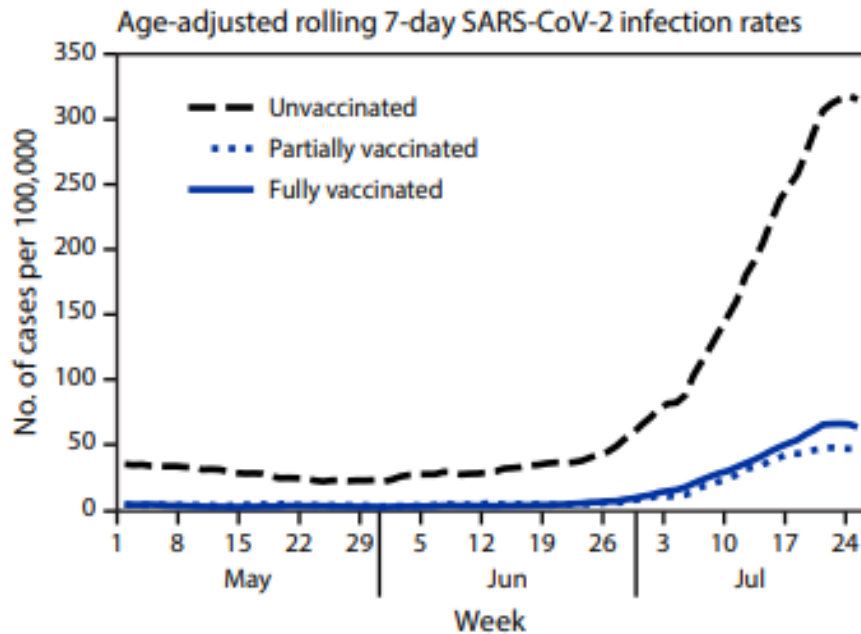
Comment: Since the start of the pandemic, over 4.5 million children have tested positive for COVID-19. Hospitalization and deaths remain low for pediatric patients, but cases are expected to continue surging as the school year begins and vaccines remain unauthorized for children under 12. Among states reporting, children were 0.00%-0.22% of all COVID-19 deaths, and 7 states reported zero child deaths. Most who have died have had an underlying medical condition.

Journal Review

SARS-CoV-2 Infections and Hospitalizations Among Persons Aged ≥ 16 Years, by Vaccination Status — Los Angeles County, California, May 1-July 25, 2021

MMWR published online August 24, 2021

During May 1-July 25, 2021, among 43,127 SARS-CoV-2 infections in residents of Los Angeles County, California, 10,895 (25.3%) were in fully vaccinated persons, 1,431 (3.3%) were in partially vaccinated persons, and 30,801 (71.4%) were in unvaccinated persons. On July 25, infection and hospitalization rates among unvaccinated persons were 4.9 and 29.2 times, respectively, those in fully vaccinated persons. In July, when the Delta variant was predominant, cycle threshold values were similar for unvaccinated, partially vaccinated, and vaccinated persons.



Comment: CDC's new data from Los Angeles County collected from May to July shows unvaccinated people were 5 times more likely to get COVID-19 than vaccinated peers and 29 times more likely to be hospitalized for their infections. This report may have case ascertainment since it is based on passive surveillance, with known underreporting that might differ by vaccination status. Similarly, screening and testing behaviors might differ among groups. Lineage and Ct values were available only for a sample of SARS-CoV-2 cases. In addition, all the assays used to generate Ct values for comparison were qualitative, and none is approved for use in quantitating the amount of viral nucleic acid present. Bottom line this is more evidence that the pandemic in the United States is a pandemic of the unvaccinated.

Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance — Eight U.S. Locations, December 2020-August 2021

MMWR published online August 24, 2021

During December 14, 2020-April 10, 2021, data from the HEROES-RECOVER Cohorts, a network of prospective cohorts among frontline workers, showed that the Pfizer and Moderna vaccines were approximately 90% effective in preventing symptomatic and asymptomatic infection with SARS-CoV-2. This report updates vaccine effectiveness (VE) estimates including all COVID-19 vaccines available through August 14, 2021 and examines whether VE differs for adults with increasing time since completion of all recommended vaccine doses. VE before and during SARS-CoV-2 Delta variant dominance, which coincided with an increase in reported COVID-19 vaccine breakthrough infections, were compared. HCP, first responders, and other essential and frontline workers in eight U.S. locations across six states were tested weekly for SARS-CoV-2 infection by PCR and upon the onset of any COVID-19-like illness.

Among 4,217 participants, 3,483 (83%) were vaccinated; 2,278 (65%) received Pfizer-BioNTech, 1,138 (33%) Moderna, and 67 (2%) Janssen (Johnson & Johnson) COVID-19 vaccines. Cox proportional hazards models were used to calculate ratios of unvaccinated to fully vaccinated (≥ 14 days after receipt of all recommended COVID-19 vaccine doses) infection rates, adjusted for occupation, site, and local viral circulation, and weighted for inverse probability of vaccination using sociodemographic characteristics, health information, frequency of close social contact, and mask use.

During December 14, 2020-August 14, 2021, full vaccination with COVID-19 vaccines was 80% effective in preventing PCR-confirmed SARS-CoV-2 infection among frontline workers, further affirming the highly protective benefit of full vaccination up to and through the most recent summer U.S. COVID-19 pandemic waves. The VE point estimates declined from 91% before predominance of the SARS-CoV-2 Delta variant to 66% since the SARS-CoV-2 Delta variant became predominant.

Comment: These findings must be interpreted with caution, as vaccine effectiveness might wane over time and the estimates of efficacy were imprecise. As with all observational VE studies, unmeasured and residual confounding might be present. Although these findings suggest a moderate reduction in VE of COVID-19 vaccines in preventing infection, a two thirds reduction in infection risk underscores the ongoing benefits of COVID-19 vaccination. In addition, the mRNA vaccines still have a 90% benefit in preventing severe disease, hospitalizations, and deaths. The CDC will review if a third dose will provide additional benefit for the general population. The preliminary data from Israel suggests significant additional benefit in persons over age 60.

Vaccinations Against COVID-19 May Have Averted Up To 140,000 Deaths in the United States

Health Affairs September 2021

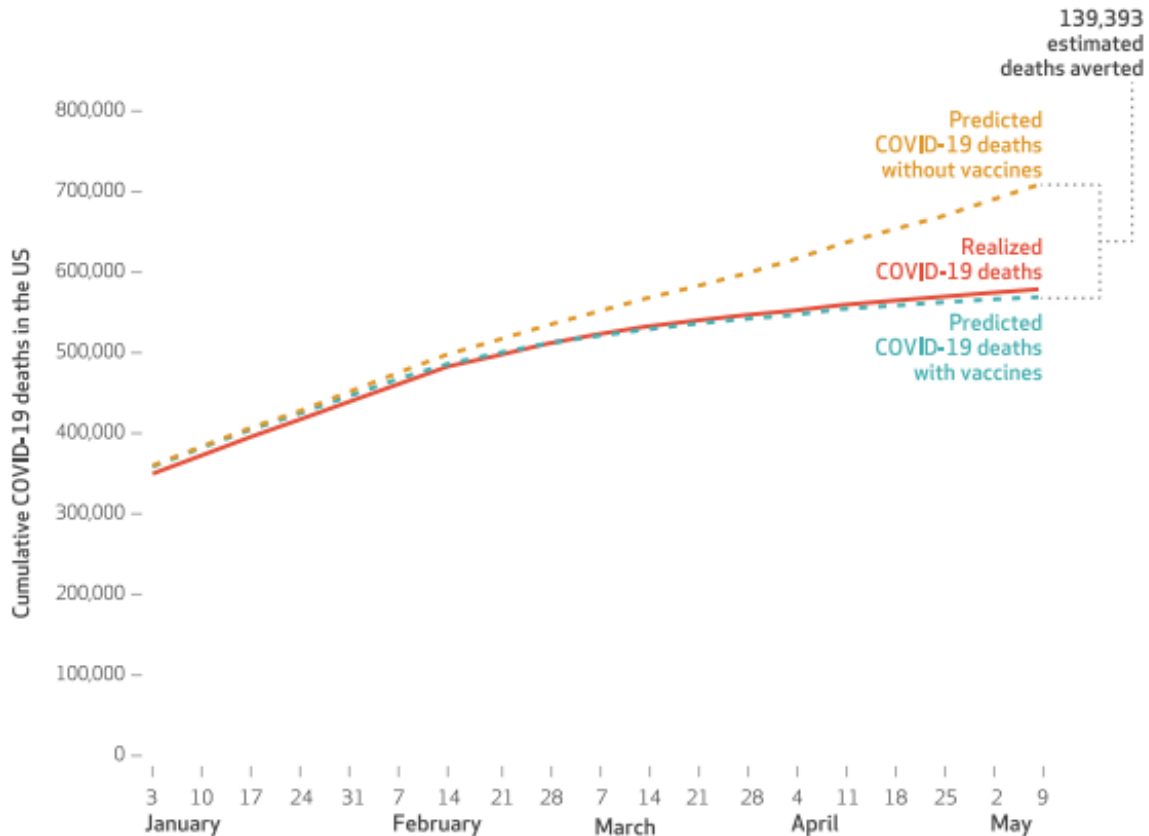
doi: [10.1377/hlthaff.2021.00619](https://doi.org/10.1377/hlthaff.2021.00619)

While access to and use of vaccines has varied substantially across states and sub-populations during early stages of the U.S. vaccine campaign, COVID-19 deaths have fallen sharply since vaccination programs began.

Researchers from RAND and Indiana University created models to estimate the number of COVID-19 deaths that would have occurred in the absence of vaccinations. By the week May 9, 2021, about 550,000 people had died of COVID-19 in the US. Researchers determined that, without the vaccinations, that number would have reached 709,000, the study says. The economic value of the lives saved during

the study period is estimated to be between \$625 billion and \$1.4 trillion. Through the end of 2020, the U.S. federal government had allocated \$13 billion dollars for vaccine development and manufacturing.

Estimated COVID-19 deaths averted through vaccination among US adults, by week, 2021



Comment: This study implies that without the vaccinations of early 2021, the cumulative number of COVID-19 deaths in the U.S. would be much higher than their current level. This study was done before delta. From recent data >90% of recent hospitalizations and >95% of deaths are in unvaccinated persons during this current surge in the US. The results support further efforts to vaccinate populations globally and in a coordinated fashion which is critical to achieving greater control of the COVID-19 pandemic. [See first article above] The U.S. is projected to see nearly 100,000 more COVID-19 deaths between now and Dec. 1, according to forecasting models. Behavior is going to determine if, when, and how sustainably the current wave will last.

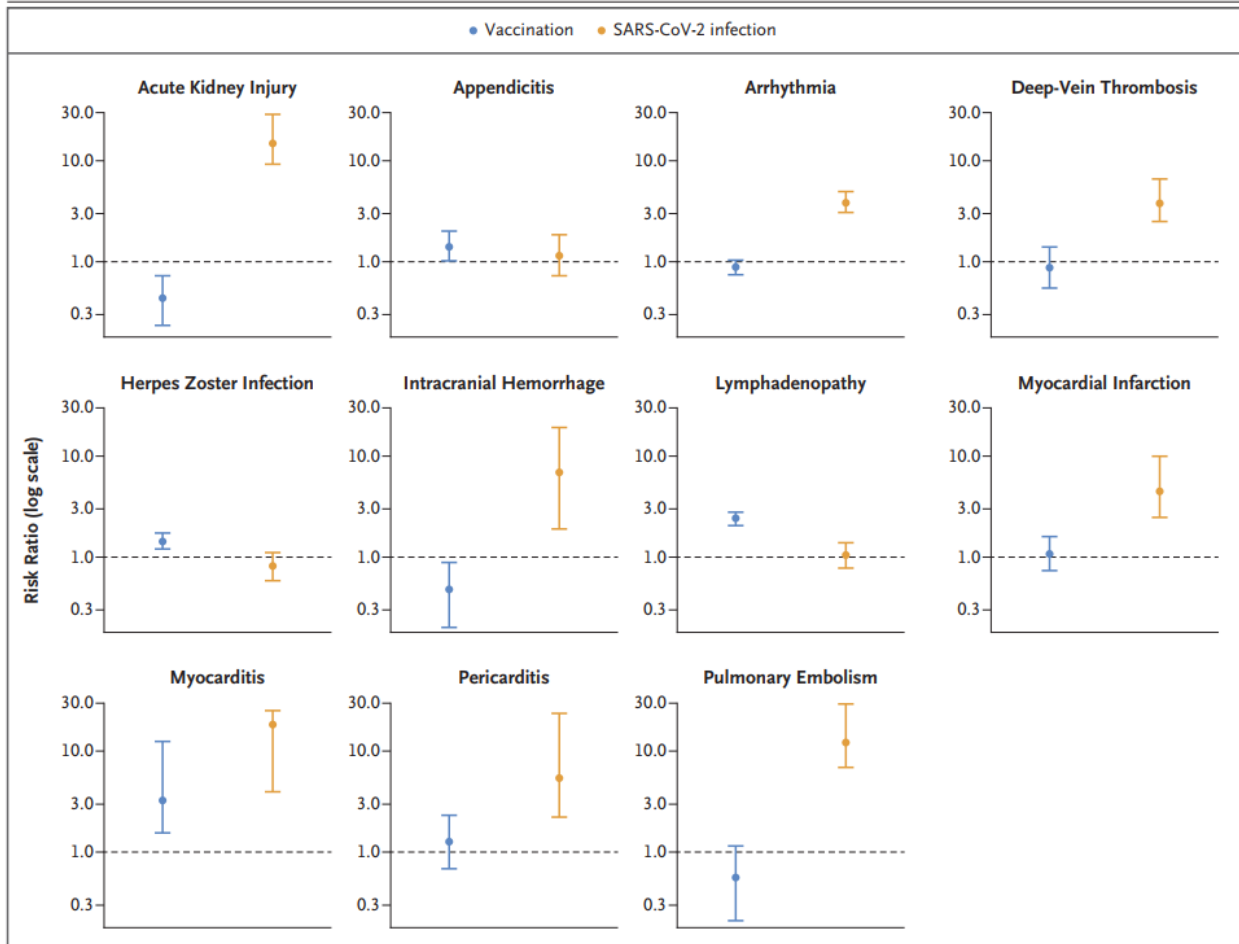
Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

N Engl J Med published online August 25, 2021

DOI: [10.1056/NEJMoa2110475](https://doi.org/10.1056/NEJMoa2110475)

The investigators used data from the largest health care organization in Israel to evaluate the safety of the Pfizer vaccine. For each potential adverse event, in a population of persons with no previous diagnosis of that event, they individually matched vaccinated persons to unvaccinated persons according to sociodemographic and clinical variables. Risk ratios and risk differences at 42 days after vaccination were derived with the use of the Kaplan-Meier estimator. They also performed a similar analysis involving SARS-CoV-2-infected persons matched to uninfected persons.

The risk ratios for myocarditis were 3.24 (95% confidence interval [CI], 1.55 to 12.44) after vaccination and 18.28 (95% CI, 3.95 to 25.12) after SARS-CoV-2 infection, with risk differences of 2.7 events per 100,000 persons (95% CI, 1.0 to 4.6) and 11.0 events per 100,000 persons (95% CI, 5.6 to 15.8), respectively. There was a substantial protective effect of vaccines with respect to adverse events such as acute kidney injury, intracranial hemorrhage, and anemia, probably because infection was prevented. Furthermore, the persons with SARS-CoV-2 infection appeared to be at substantially higher risk for arrhythmia, myocardial infarction, deep-vein thrombosis, pulmonary embolism, pericarditis, intracerebral hemorrhage, and thrombocytopenia than those who received the Pfizer vaccine.



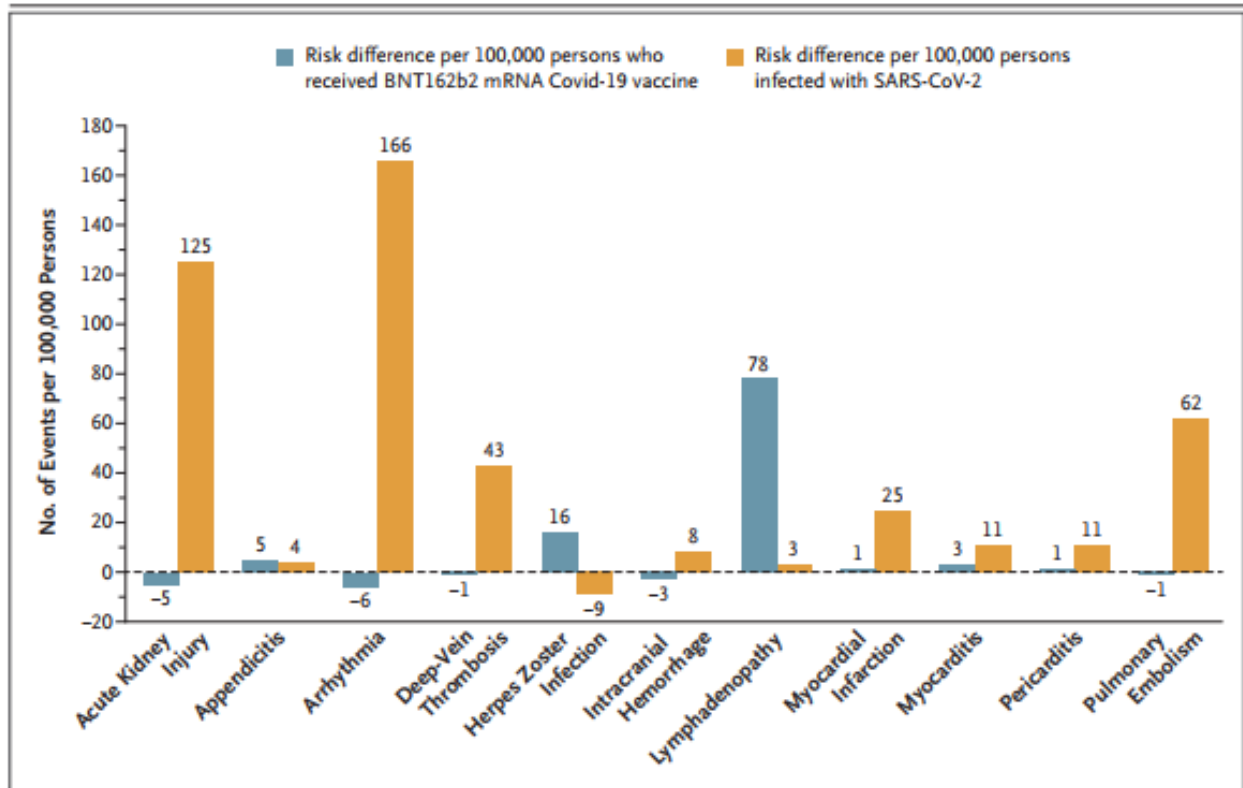


Figure 4. Absolute Excess Risk of Various Adverse Events after Vaccination or SARS-CoV-2 Infection.

Comment: In this study, the investigators sought to place the increased risk of adverse events caused by the Pfizer vaccine in context by contrasting this risk with that of the same adverse events after documented infection with SARS-CoV-2. To place these risks in context, they appropriately also examined data on more than 240,000 infected persons to estimate the effects of a documented SARS-CoV-2 infection on the incidence of the same adverse events. When the authors did adjust for events/100,000, SARS-CoV-2 infection was not estimated to have a meaningful effect on the incidence of lymphadenopathy, herpes zoster infection, or appendicitis [Figure 4]. In this study the Pfizer vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). In contrast the risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection. In this study there were no risk estimates according to age group and sex and there was a paucity of data regarding younger teens and children. The study was not randomly assigned according to exposures (vaccinations and SARS-CoV-2 infections); this may have introduced confounding at baseline and selection bias at censoring, especially since a single set of confounders was used for adjustment in the assessment of many disparate adverse events. In an editorial by Dr. Grace Lee, she explains “National discussions about benefit-risk balance often focus on the benefits of preventing symptomatic disease, hospitalization, or death due to Covid-19 and the risks of serious adverse events after vaccination. As specific adverse events such as myocarditis are highlighted, however, the lack of corresponding specificity about benefits can hamper efforts to communicate effectively with patients.” As this article demonstrates, the risk of natural disease far outweighs the risk of vaccination.