I hope everyone had a good weekend. Covid-19 rates are beginning to come down in many areas, but not all.

Today I start with some reflections on the conversation over vaccinations and boosters. I also show the recent CDC death toll from Covid-19 which now surpasses the 1918 pandemic.

Under Journal Review I reviewed two articles on impact of masking in K-12. The last article looks at the impact of routine Covid testing of students and staff.

Have a great week.

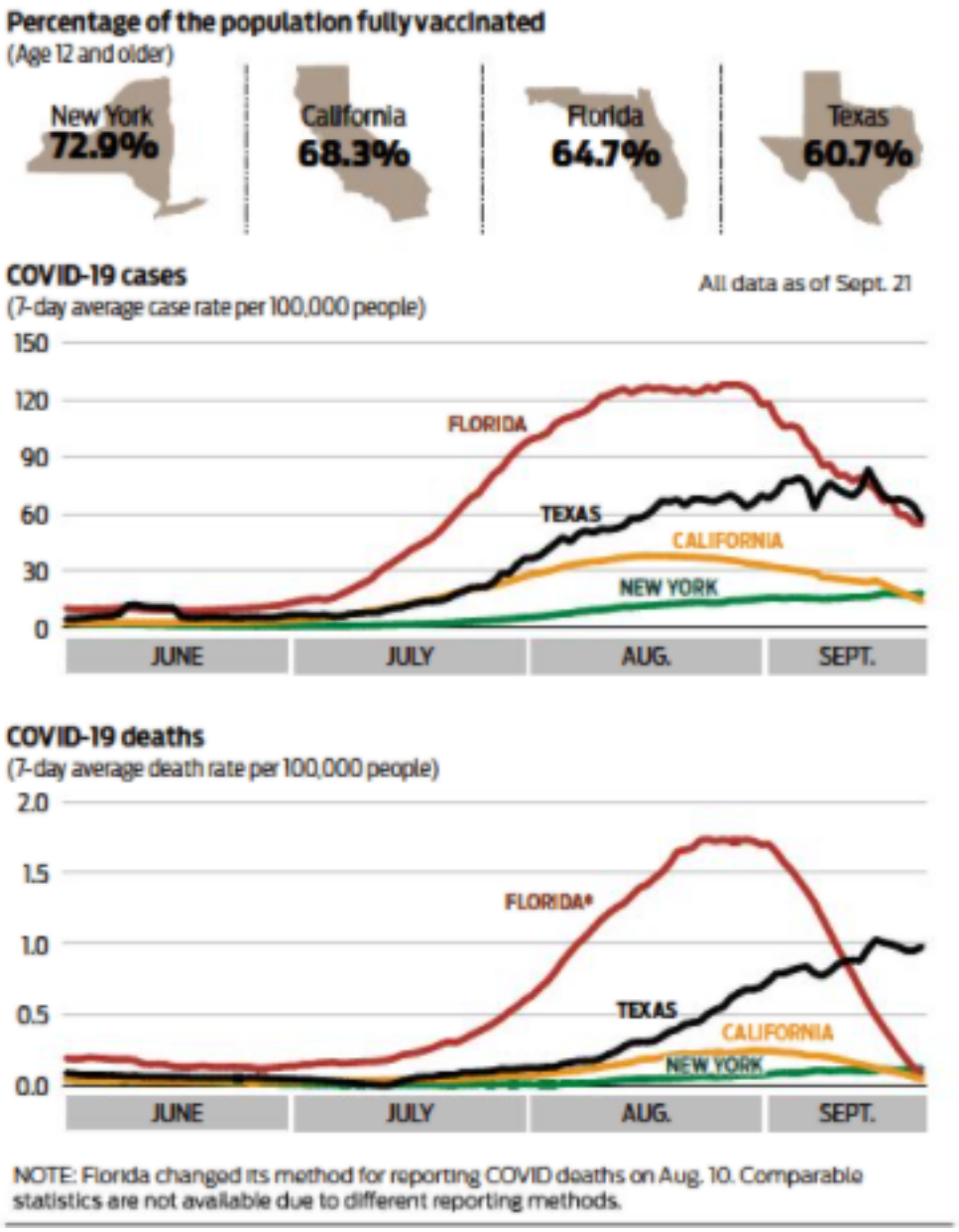
Ed

VII Reflections

Americans have reached the booster worry/confusion/frustration stage of the pandemic—and the CDC's announcement on Friday backing a third shot for some people, but not all, has left many with more questions than answers. For HCPs, the queries are coming fast and furious: Am I eligible for a booster? After six months or eight months? What if I got Moderna or Johnson & Johnson? The booster conversation has everyone's heads spinning. I know I have whiplash. [occupational hazard during the pandemic]

The CDC said Pfizer vaccine recipients who are 65 and over, as well as people ages 50 to 64 with certain underlying medical conditions, can get boosters. They also recommended other groups of people who may get boosters, based on their risk levels and potential benefits, prompting a host of new questions and how do you define risk level? [see below] If you live in a community with high transmission does that mean everyone? For recipients of the Moderna and J&J vaccines, the FDA and CDC have said that they need more time to review data. The biggest gray area now is for people ages 18 to 49. The guidelines give physicians a lot of flexibility for 18- to 49-year-olds. All that said, although the CDC has made mistakes during the pandemic, I think Dr. Walensky made the right call on boosters, but I am not sure if it was based on politics versus the science. A booster shot costs the government $20 compared to $2,100 for a monoclonal antibody treatment. A non-ICU Covid hospitalization costs $33,525.

As I have written in the Briefing multiple times, all this is a distraction from the real problem; the unvaccinated. We still have <60% of our eligible population fully vaccinated. We have produced and administered several very effective vaccines <340 days after the genetic sequenced was published! This accomplishment is nothing short of extraordinary, yet the pandemic continues to surge, now dominated by the SARS-CoV-2 variant Delta. It is sobering to note that despite the great progress on vaccinations and some on therapeutics, the numbers of COVID-19 cases and deaths have continued to rise since the day the first vaccine was administered in the US. We have now recorded more death for this pandemic than the 1918 pandemic (see below). There are several potential causes, including decline in protective behaviors such as handwashing, social distancing, and mask wearing, the increased transmissibility of emerging variants, or a combination of factors, but it is clear that the challenge before us in the US will be to double down on getting vaccines into eligible arms. Below shows the different trajectories in the four most populous states. One picture (graph from CDC) speaks a thousand words: The most vaccinated states have the lowest number of Covid-19 cases and deaths!



Vaccine hesitancy remains strong. When I speak of vaccine hesitancy, I mean a delay in acceptance or refusal of the vaccination despite availability. Studies have shown that confidence in vaccine safety and efficacy has been diminished because of the politicization of vaccine development and because marginalized communities were not engaged early as vaccines were being developed. [Am J Public Health 2021; 111:366–8] In addition the messaging has been inconsistent at best. The public hears of vaccine breakthrough, need for boosters, and side effects. To many the message is these vaccines are not that effective and they have significant side effects. To be clear these are amazing vaccines. You are more likely to die in a car accident or of influenza than die from Covid-19 if you are fully vaccinated. We also continue to ignore discussing the role of natural immunity.

In an article reviewed several months ago in the Briefing [J Infect Dis 2021; 224:938-948] The investigators demonstrated even incremental gains in vaccine coverage rates really matter, averting

millions of cases, tens of thousands of hospitalizations, and thousands of deaths as well as saving billions of dollars in direct medical and indirect costs. Second, coverage rates matter as much as the efficacy of the vaccine. Increasing coverage rates can avert more COVID-19 cases than a similar increase in vaccine efficacy, and even at lower vaccine efficacy (e.g., 50%), and incremental gains in coverage can provide measurable benefit in terms of cases averted. There are limitations to this model to predict the future. SARS-CoV-2 continues to surprise us with its lack of seasonality and the continued emergence of variants that are more transmissible and may be associated with more severe COVID-19. Further, behavioral changes (NPI), such as masking, vary widely across the US. Although these factors may affect the threshold needed for herd immunity, they do not change the need for vaccination as the graph above highlights.

One last thought. An increasing number of local and federal governments, businesses, school districts, and more than 1,000 colleges and universities adopted at least some vaccination requirements for employees and students. But without a unified approach to verify compliance, ideally through federal leadership, verification will be inaccurate and potentially insecure especially since counterfeit vaccine cards are already in circulation. The White House has rejected federal verification guidelines. Vaccination verification in the US, however, is not new. Almost every state has a vaccine register system on immunization which consolidates vaccine records. Every state already requires the MMR vaccination and other specified inoculations for school admission. Many hospitals and nursing homes require staff members to show proof they have received an annual influenza vaccine. But the problem is that we have multiple Covid-19 vaccination verification systems, each with its own user interface, validation, and security codes and protocols, which will make it difficult to verify vaccination status quickly and securely across state lines. Without federal guidance verifiers are adopting different methods to confirm individuals' identity, define adequate protection, and confirm vaccination status. We need a system that works. The system needs to be accurate. Covid-19-specific vaccination data should be stored in and verified by a computerized immunization information system — essentially an online record of vaccinations people have received — that allows for sharing between systems. It needs to be secure and maintain privacy. People who don't wish to or cannot participate in an electronic verification system should be able to use paper vaccination records with additional verification, such as a photo ID. Verifiers could then check this information against existing databases. Lastly it needs to be real-time so, like going through passport control, it can be verified quickly which can help going through airport security. Vaccination mandates are already here and will continue to expand. We need to make verification systems accurate, secure, and user friendly. Why the CDC and others did not put this in place before rolling out Covid-19 vaccinations is another missed opportunity.

The final victory against COVID-19 will be accomplished in local communities, one individual at a time. Solutions to vaccine hesitancy will be multifaceted from respectfully answering questions to making it easier to get vaccinated and packaged to fit local culture and medical literacy. Successful vaccination programs seek out where individuals and communities are along the vaccine hesitancy continuum from refusal to acceptance and develop strategies tailored to their need. Indeed, study after study has shown that the single most powerful tool to increase vaccination is through an individual's health care provider [Pediatrics 2006;118: e1287-92]. And it's no different for COVID-19 vaccines. As Nat Turner said: "Good communication is the bridge between confusion and clarity." This is a journey as John Kennedy said: "We choose to go to the moon in this decade and do other things, 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." Our success in creating and sustaining a safe environment for our communities depends on our commitment to one another.

CDC: Pfizer-BioNTech COVID-19 Vaccine Booster Shot

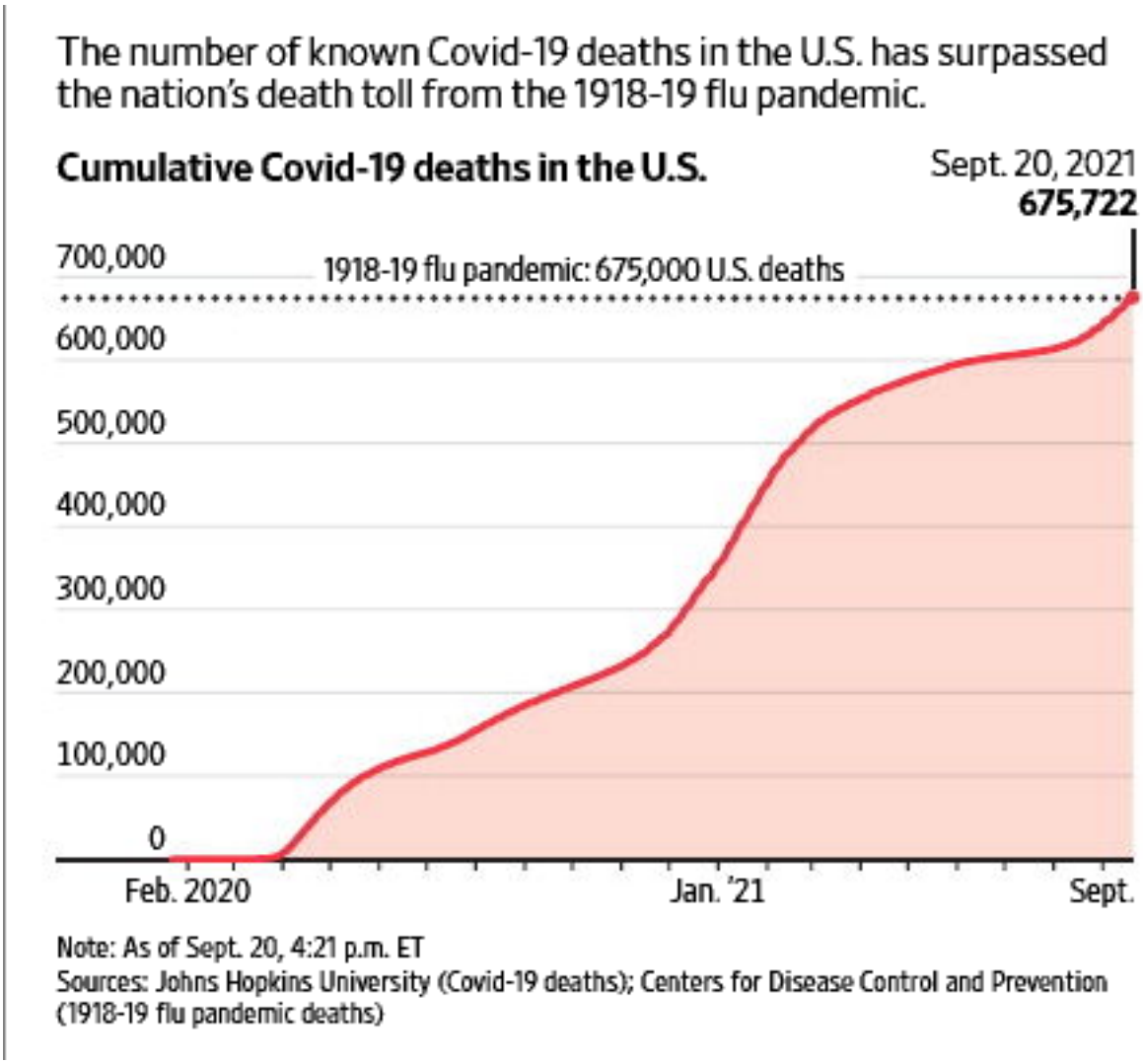
CDC recommends that people in the following groups should receive a booster shot of Pfizer-BioNTech's COVID-19 Vaccine at least 6 months after completion of their 2-dose Pfizer series:

- People ages 65 years and older
- Adults 18+ living in long-term care settings
- People ages 50-64 years with certain underlying medical conditions

People who **may** receive a Pfizer-BioNTech COVID-19 Vaccine booster include:

- People ages 18-49 with an underlying medical condition
- People ages 18-64 who are at increased risk for COVID-19 exposure and transmission due to working or residing in certain settings

U.S. Covid-19 Death Toll Surpasses 1918 Flu Fatalities



Comment: On September 20th we crossed the threshold of 675,000 reported Covid-19 deaths, according to Johns Hopkins University. There are several differences between the current pandemic and the one that claimed nearly as many lives more than 100 years ago. The U.S. at that time was roughly

one-third its current size, so the flu pandemic took a proportionally bigger toll on the population. That pandemic had a devastating effect on young people, including small children and young-to-middle-aged adults, while Covid-19 has hit older people hardest. Additionally, there was no vaccine for the flu a century ago, nor antibiotics to treat secondary bacterial infections. Despite having these tools available today we're still seeing this virus claim too many lives. This is very troublesome. We can prevent many of those deaths by changing our behavior and getting serious about public policy and vaccinations.

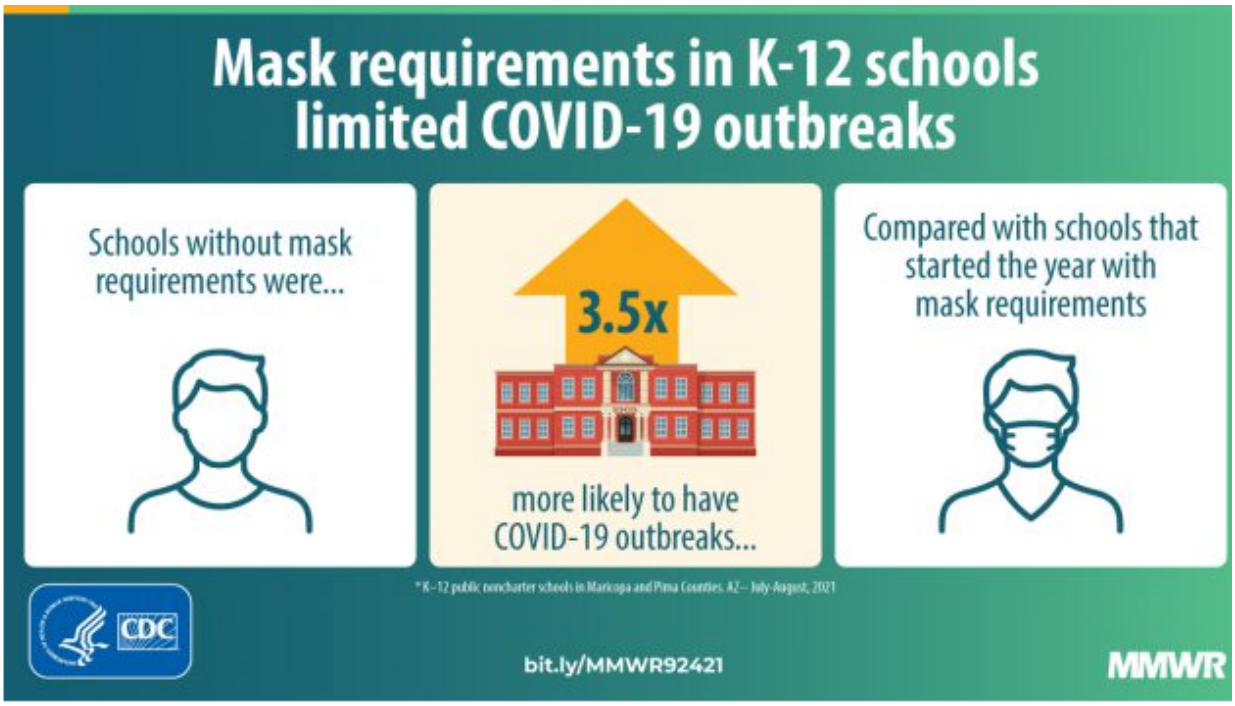
Journal Review

Association Between K-12 School Mask Policies and School-Associated COVID-19 Outbreaks — Maricopa and Pima Counties, Arizona, July-August 2021

MMWR September 24, 2021

CDC recommends universal indoor masking by students, staff members, faculty, and visitors in kindergarten through grade 12 (K-12) schools, regardless of vaccination status, to reduce transmission of SARS-CoV-2. Schools in Maricopa and Pima Counties, which account for >75% of Arizona's population, resumed in-person learning for the 2021-22 academic year during late July through early August 2021. In mid-July, county-wide 7-day case rates were 161 and 105 per 100,000 persons in Maricopa and Pima Counties, respectively, and 47.6% of Maricopa County residents and 59.2% of Pima County residents had received at least 1 dose of a COVID-19 vaccine. School districts in both counties implemented variable mask policies at the start of the 2021-22 academic year. The association between school mask policies and school-associated COVID-19 outbreaks in K-12 public noncharter schools open for in-person learning in Maricopa and Pima Counties during July 15-August 31, 2021, was evaluated.

Among the 999 (96.0%) schools included in the analysis, 210 (21.0%) had an early mask requirement, 309 (30.9%) had a late mask requirement enacted a median of 15 days after school started (interquartile range = 9-17 days), and 480 (48.0%) had no mask requirement. During July 15-August 31, 2021, 191 school-associated outbreaks occurred, 16 (8.4%) in schools with early mask requirements, 62 (32.5%) in schools with late mask requirements, and 113 (59.2%) in schools without a mask requirement. In the crude analysis, the odds of a school-associated COVID-19 outbreak in schools with no mask requirement were 3.7 times higher than those in schools with an early mask requirement (odds ratio [OR] = 3.7; 95% CI = 2.2–6.5). After adjusting for potential confounders, the odds of a school-associated COVID-19 outbreak in schools without a mask requirement were 3.5 times higher than those in schools with an early mask requirement (OR = 3.5; 95% CI = 1.8–6.9).

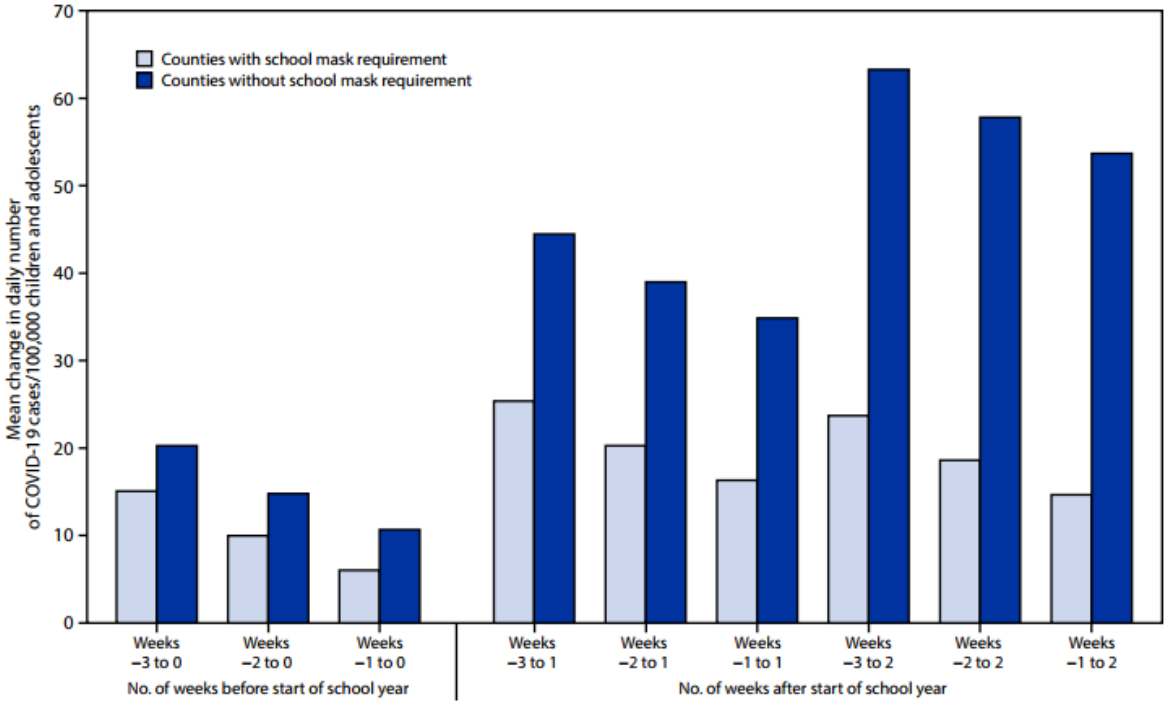


Comment: In this study the odds of a school-associated COVID-19 outbreak were 3.5 times higher in schools with no mask requirement than in those with a mask requirement implemented at the time school started. It has also been shown that lapses in universal masking contribute to COVID-19 outbreaks in school settings [MMWR 2021; 70:1214–9]. CDC K-12 school guidance continues to recommend multiple prevention strategies (NPI). In addition to universal masking, vaccination should be strongly recommended for all eligible students, staff members, and faculty.

Pediatric COVID-19 Cases in Counties With and Without School Mask Requirements — United States, July 1-September 4, 2021
MMWR September 24, 2021
Using data from July 1-September 4, 2021, counties that met the following criteria were included in the analysis: 1) a valid school start date included a known school mask requirement for at least one district; 2) in districts with known school mask requirements, a uniform mask requirement for all students or no students; and 3) at least 3 weeks with 7 full days of case data since the start of the 2021-22 school year. For counties with multiple school districts, the median school start date was used. Counties with conflicting school mask requirements were excluded from this analysis; only those counties with the same known mask requirements for all schools were included. County-specific pediatric COVID-19 rates (number of cases per 100,000 population aged <18 years) from CDC's COVID Data Tracker were tabulated and aggregated by school start week. The analysis was adjusted for age, race and ethnicity, pediatric COVID-19 vaccination rate, COVID-19 community transmission, population density, social vulnerability index score, percentage uninsured, and percentage living in poverty.

Counties without school mask requirements experienced larger increases in pediatric COVID-19 case rates after the start of school compared with counties that had school mask requirements ($p<0.001$). The average change from week -1 (1-7 days before the start of school) to week 1 (7-13 days after the start of school) for counties with school mask requirements (16.32 cases per 100,000 children and adolescents aged <18 years per day) was 18.53 cases per 100,000 per day lower than the average

change for counties without school mask requirements (34.85 per 100,000 per day) (p<0.001). Comparisons between pediatric COVID-19 case rates during the weeks before (weeks -3, -2, and -1) and after (weeks 0, 1, and 2) the start of school indicate that counties without school mask requirements experienced larger increases than those with school mask requirements (p<0.05). After controlling for covariates, school mask requirements remained associated with lower daily case rates of pediatric COVID-19 (β = -1.31; 95% confidence interval = -1.51 to -1.11) (p<0.001).



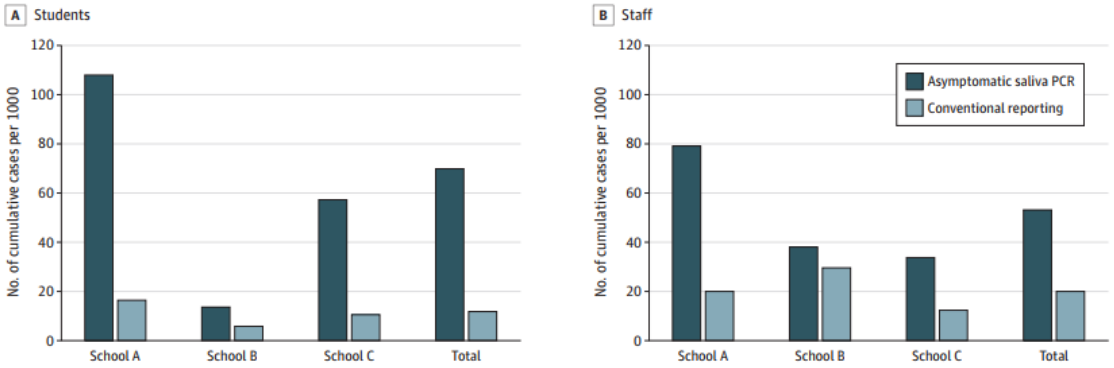
Comment: The results of this analysis indicate that increases in pediatric COVID-19 case rates during the start of the 2021-22 school year were smaller in U.S. counties with school mask requirements than in those without school mask requirements. School mask requirements, in combination with other NPI strategies, plus COVID-19 vaccination, are key to reduce the spread of COVID-19 in schools. Pediatric COVID-19 case counts and rates included all cases in children and adolescents aged <18 years. Further analyses will hopefully focus on cases in different school-age children and adolescents. County-level teacher vaccination rate and school testing data were not controlled in these analyses. These two studies support universal masking especially in areas with substantial or high rates of transmission.

Assessment of a Program for SARS-CoV-2 Screening and Environmental Monitoring in an Urban Public School District

JAMA Netw Open 2021;4(9):e2126447
doi:10.1001/jamanetworkopen.2021.26447

This pilot quality improvement program engaged 3 schools in Omaha, Nebraska, for weekly saliva polymerase chain reaction testing of staff and students participating in in-person learning over a 5-week period from November 9 to December 11, 2020. Wastewater, air, and surface samples were collected weekly and tested for SARS-CoV-2 RNA to evaluate surrogacy for case detection and interrogate transmission risk of in-building activities. The main outcomes were SARS-CoV-2 detection in saliva and environmental samples and risk factors for SARS-CoV-2 infection. SARS-CoV-2 genomes from positive saliva samples were sequenced to investigate transmission chains within cases identified by our testing program.

Weekly school-based saliva PCR testing at 3 urban public schools was associated with increased case detection among staff and students compared with symptom-based strategies, exceeding county-level case rates. SARS-CoV-2 was detected in school wastewater samples each week as well as air and surface.



Comment: This study suggests that routine SARS-CoV-2 testing may identify infected staff and students who are not identified through conventional case detection and may provide insight into disease burdens of undertested communities. Experiences differed among schools, and virus sequencing and geographical analyses suggested a dynamic interplay of school-based and community-derived transmission risk. This data does not permit firm conclusions about comparative incidence or transmission events within schools. Genomic sequencing identified potential transmission links among students and staff members in 2 clusters at school A, but the detection of the virus from saliva samples in our pilot demonstrated mostly a mix of multiple disparate transmission chains compatible with a broader community transmission. This study was conducted before alpha and delta variant penetration. This is a nice study to go along with the article I reviewed in the Briefing on September 21st using daily antigen testing to reduce disruption in school.