

Good morning and TGIF. I have much to share so let's get started.

I begin trying to make sense of the masking controversy. As I state, one size may not fit all, and I outline some questions to ask in evaluating your risk and whether you should consider masking. I do not have any easy answers, but I hope this provides some commonsense things to consider. Please let me know if I have failed to consider certain facts and if you have other suggestions.

Next since we have begun to hear about the Lambda variant, I have summarized what I believe to be the latest information. Next the AAP guidance on opening schools this fall. There are a few differences with the CDC especially regarding masks. Next an important report of HCW burnout which I can tell you is real. Lastly is the announcement that AHA now supports mandatory Covid-19 vaccinations for HCW.

Under Journal Review the first article demonstrates evidence that monoclonal antibodies work in COVID-19 outpatients and should be offered to eligible patients. Next an article reminding us of the importance of nurse staffing and outcomes. Next an important article that Pfizer and AZ vaccines hold up well against the Delta variant if you are fully vaccinated (2 doses). The last article looks at the J&J vaccine against VOC.

Have a wonderful weekend

Ed

VII: Is it Time to Return to Universal Masking?

My answer is it depends – one size does not fit all. Masks remain a sensible precaution in certain settings for both the vaccinated and unvaccinated. How often you use a mask will depend on your personal health tolerance and risk, the infection and vaccination rates in your community, and whom you are around.

Below are some considerations to evaluate your risk:

- Are the people I am with also vaccinated?
- What is the infection rate and vaccination rate in my community?
- Will I be in a poorly ventilated indoor space or outside?
- Will the potential increased risk of exposure last for a few minutes or for hours?
 - The more time you spend with unvaccinated people in enclosed spaces for long periods of time, the higher your risk of coming in contact with the Delta variant, or any other variants that may emerge.
- What is my personal risk and the risk for those around me for complications from Covid-19?
 - If you are older especially with underlying medical conditions or immune compromised your response to the vaccine may not be as robust as the response in a younger person.
 - If you are healthy and vaccinated but caring for an aging parent or spending time with others at high risk, you should consider their risk too when deciding whether to attend an event or wear a mask.
- Are going into enclosed public spaces where the chances of your encountering unvaccinated people are greater?

The bottom line for me: While being fully vaccinated protects against serious illness and hospitalization from Covid-19, no vaccine offers 100 percent protection. If large numbers of people remain unvaccinated and continue to spread SARS-CoV-2, vaccinated people will be exposed to the Delta

variant, and a small percentage of them will develop so-called breakthrough infections. Breakthrough cases are relatively rare. As of July 12, more than 159 million people in the United States had been fully vaccinated against Covid-19. Of those, just 5,492 had breakthrough cases that resulted in serious illness, including 1,063 who died. That is less than 0.0007 percent of the vaccinated population. Meanwhile, 99 percent of deaths from Covid-19 are among the unvaccinated. You may wish to adopt a “mask optional” policy to promote the message of prevention without stigmatizing mask wearers.

COVID-19 News

Lambda COVID-19 Variant

- Lambda has been detected in 29 countries, territories, or areas in five WHO regions, with the strongest presence in South America as of June 15.
- Eighty percent of all cases sequenced in Peru since April were linked to the variant, according to a June 15 WHO report. In Chile, 31 percent of cases sequenced to date are associated with lambda.
- The variant has been detected in less than 1 percent of samples sequenced in the U.S.
- The variant carries several mutations seen in other strains, including seven in the spike protein. While they have the potential to make the strain more infectious or make it more able to resist neutralizing antibodies, further study is needed. It has mutations at 14 positions including a long stretch of seven amino acids which has been deleted from a region of the spike protein called the N-terminal domain or NTD. Beyond these, Lambda also has mutations in the ORF1ab gene that are found in other variants of concern: Alpha, Beta, and Gamma. The ORF1ab gene encodes a large protein, parts of which help the coronavirus replicate and suppress the human immune response.
- Preliminary lab studies have found antibodies generated by the Pfizer and Moderna mRNA vaccines are less powerful against lambda compared to the original strain, though still able to neutralize it. There are very few studies on Lambda, but preliminary results suggest that current vaccines are still effective but perhaps less than against the original virus.
- It is still unclear whether lambda is more contagious or severe than other variants. It is also unclear if lambda will become a significant VOC in the US.

Comment: Of interest Gamma (B.1 Brazil) is the predominant variant in IL.

AAP Covid-19 Guidance for Safe Schools

July 18, 2021

AAP guidance is different from CDC in terms of masking recommendations – **wouldn’t it be nice if agencies would coordinate their guidance? AAP is a respected organization as is the CDC – this only adds to anxiety and confusion.** Here are some highlights. My comments are in brackets [].

- All eligible individuals should receive the COVID-19 vaccine.
 - It may become necessary for schools to collect COVID-19 vaccine information of staff and students and for schools to require COVID-19 vaccination for in-person learning. Adequate and timely COVID-19 vaccination resources for the whole school community must be available and accessible.
- Preponderance of evidence indicates that children and adolescents are less likely to have severe disease resulting from SARS-CoV-2 infection. At present, it appears that children younger than

10 years are less likely to become infected and less likely to spread the infection to others, although further studies are needed. Some data suggest children older than 10 years may spread SARS-CoV-2 as efficiently as adults. [agree]

- All students older than 2 years and all school staff should wear face masks at school [this is different from CDC's guidance – it is important to remember that masks are good at stopping people from spreading the disease, not as good at preventing from getting it]. Here are the reasons AAP recommends universal masking:
 - A significant portion of the student population is not eligible for vaccination [yes children < age 12 but they are less likely to become infected and spread disease]
 - Protection of unvaccinated students from COVID-19 and to reduce transmission
 - Lack of a system to monitor vaccine status among students, teachers, and staff [this depends on the school and state – to me not having universal vaccine registries is a shame and missed opportunity]
 - Potential difficulty in monitoring or enforcing mask policies for those who are not vaccinated; in the absence of schools being able to conduct this monitoring, universal masking is the best and most effective strategy to create consistent messages, expectations, enforcement, and compliance without the added burden of needing to monitor vaccination status
 - Possibility of low vaccination uptake within the surrounding school community [varies by community]
 - Continued concerns for variants that are more easily spread among children, adolescents, and adults [i.e. delta]
- Adult Staff and Educators: Universal use of face masks is recommended, given that certain teachers must cross-over to multiple classes, such as special teachers, special educators, and secondary school teachers, and in consideration of new SARS-CoV-2 variants.
 - At this time, this recommendation for use of face masks includes staff and educators who have been fully vaccinated, especially for teachers with students who are unvaccinated (including pre-K, kindergarten, and elementary schools). School staff working with students who are unable to wear a face mask or who are unable to manage secretions, who require high-touch (hand over hand) instruction, and who must be in close proximity to these students should consider wearing a surgical mask in combination with a face shield [again the key – especially for teachers – what if this is a highly vaccinated high school?]
- An added benefit of universal masking is protection of students and staff against other respiratory illnesses that would take time away from school – this is probably true. [So, if you agree with this statement masks should probably become a “standard” during the respiratory virus season, but better to enforce a culture to stay home when ill.]
- It is critically important to develop strategies that can be revised and adapted depending on the level of viral transmission and test positivity rate throughout the community and schools, recognizing the differences between school districts, including urban, suburban, and rural districts [agree and this should also apply to individual schools including vaccination rates – if a high school has very high vaccination rates in students as well as staff do they still need to use universal masking?]
- Schools must continue to take a multi-pronged, layered approach to protect students, teachers, and staff (i.e., vaccination, universal mask use, ventilation, testing, quarantining, and cleaning and disinfecting). Combining these layers of protection will make in-person learning safe and possible. Schools should monitor the implementation and effectiveness of these policies.

- Behavioral Health/Emotional Support for Children and Adolescents [this is a very important section]
- There is a link on testing, but not discussed in this document [I think the CDC document and guidance on testing is worth considering.]

Comment: This document is written for the average school as a template for opening schools. It may be more applicable to public school settings where vaccination rates may not be known and may vary from school to school. Personally, I would advise vaccinations and reinstate masks indoors where social distancing is not possible (e.g., grocery stores, pharmacies, sporting events etc.) in communities or settings with low vaccination rates and rising cases and positivity until we see numbers going back down again. Changing information about Covid-19 as well as shifting and sometimes contradictory guidance from public health agencies and medical organizations have increased confusion and fear.

Half of Health Workers Report Burnout Amid COVID-19

AMA

48% of U.S. doctors reported burnout in 2020, with more than 25% having high stress, anxiety. Other health professionals suffered even more. This is a serious challenge which will be with us for some time. See article below on nurse staffing and outcomes.

AHA Supports Mandatory COVID-19 Vaccination Policies for Healthcare Personnel

July 21, 2021

The American Hospital Association (AHA) expressed its support for mandatory COVID-19 vaccinations. The AHA said in a policy statement, “To protect all patients, communities and personnel from the known and substantial risks of COVID-19, the AHA strongly urges the vaccination of all health care personnel. [...] The AHA also supports hospitals and health systems that adopt mandatory COVID-19 vaccination policies for health care personnel, with local factors and circumstances shaping whether and how these policies are implemented.”

Journal Review

Real-World Clinical Outcomes of Bamlanivimab and Casirivimab-Imdevimab among High-Risk Patients with Mild to Moderate Coronavirus Disease

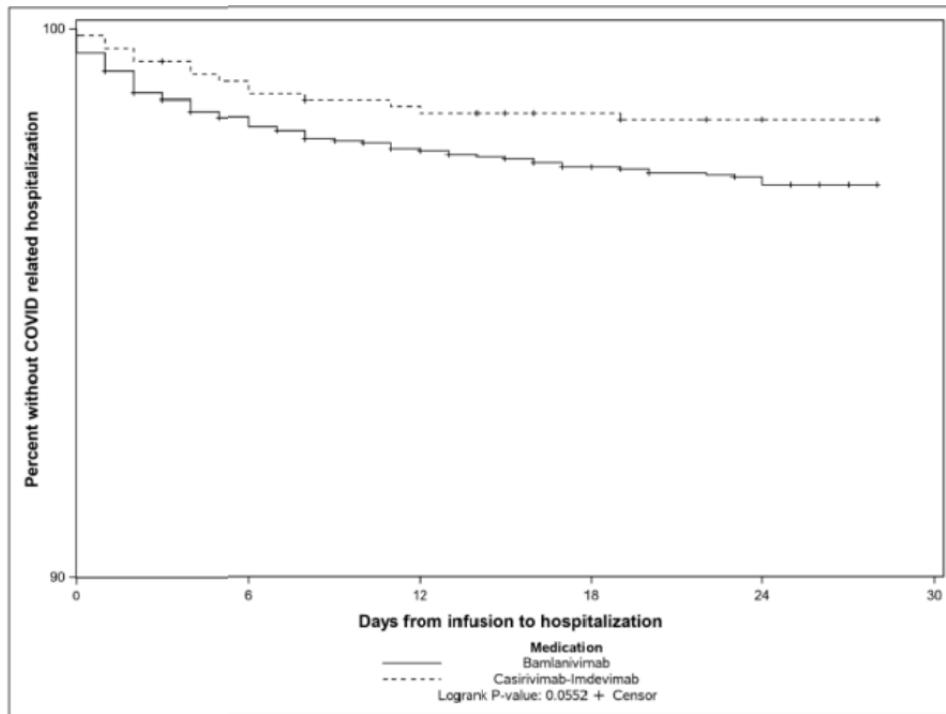
J Infect Dis published online July 19, 2021

doi.org/10.1093/infdis/jiab377

This is an observational study using electronic health records to compare 28-day all-cause death rates and COVID-19-related hospital admissions in 2,747 patients who received an infusion of bamlanivimab and 849 given casirivimab-imdevimab from Nov 19, 2020, to Feb 11, 2021. The drugs were started within 10 days of symptom onset.

The overall all-cause 28-day death rate was 3.98% (five bamlanivimab recipients and three casirivimab-imdevimab recipients), and 2.56% were hospitalized for COVID-19. After adjustment for underlying diseases, all-cause death rates and coronavirus-related hospitalizations did not differ between the bamlanivimab and casirivimab-imdevimab groups (adjusted hazard ratios, 1.4 and 1.6, respectively). Patients who had chronic kidney, respiratory, and cardiovascular diseases, high blood pressure, or were immunocompromised were at higher risk of hospitalization (odds ratios [ORs], 6.10, 1.67, 2.20, 1.67, and 2.78, respectively). Men and divorced participants were more likely to be hospitalized (ORs, 1.49 and 1.84, respectively).

The rates of 28-day all-cause and COVID-19-related hospitalization appeared higher among patients who received bamlanivimab monotherapy compared to casirivimab-imdevimab combination, although this did not reach statistical significance.



Comment: The study adds to mounting evidence that monoclonal antibodies work in COVID-19 outpatients and should be offered to eligible patients. More recent data show some variants are not as responsive to bamlanivimab and hence guidance has now changed to not use bamlanivimab as variants have changed.

Hospital Nurse Staffing and Patient Outcomes in Chile: A Multilevel Cross-Sectional Study

Lancet Global Health published online July 2, 2021

[doi.org/10.1016/S2214-109X\(21\)00209-6](https://doi.org/10.1016/S2214-109X(21)00209-6)

This is a multilevel cross-sectional study, using data from surveys of hospital nurses to measure staffing and work environments in public and private Chilean adult high-complexity hospitals, which were linked with patient satisfaction survey and discharge data from the national diagnosis-related groups database for inpatients. All adult patients on medical and surgical units whose conditions permitted and who had been hospitalized for more than 48 hours were invited to participate in the patient experience survey until 50 responses were obtained in each hospital. The authors estimated associations between nurse staffing and work environment quality with inpatient 30-day mortality, 30-day readmission, length of stay (LOS), patient experience, and care quality using multilevel random-effects logistic regression models and zero-truncated negative binomial regression models, with clustering of patients within hospitals.

Nurse staffing was significantly related to all outcomes, including mortality, after adjusting for patient characteristics, and the work environment was related to patient experience and nurses' quality assessments. Each patient added to nurses' workloads increased mortality (odds ratio 1.04, 95% CI 1.01-

1·07, $p<0·01$), readmissions (1·02, 1·01–1·03, $p<0·01$), and LOS (incident rate ratio 1·04, 95% CI 1·01–1·06, $p<0·05$). Nurse workloads across hospitals varied from six to 24 patients per nurse. Patients in hospitals with 18 patients per nurse, compared with those in hospitals with eight patients per nurse, had 41% higher odds of dying, 20% higher odds of being readmitted, 41% higher odds of staying longer, and 68% lower odds of rating their hospital highly. They estimated that savings from reduced readmissions and shorter stays would exceed the costs of adding nurses by US\$1·2 million and \$5·4 million if the additional nurses resulted in average workloads of 12 or ten patients per nurse, respectively.

Comment: The substantial amount of evidence supporting an association between better hospital nurse staffing and work environments and better patient outcomes is in my mind enough to warrant action. As mentioned above, healthcare worker burnout is real and will last years after the pandemic. A limitation of this study is its cross-sectional design, which is insufficient to establish causal relationships between nursing resources and patient outcomes.

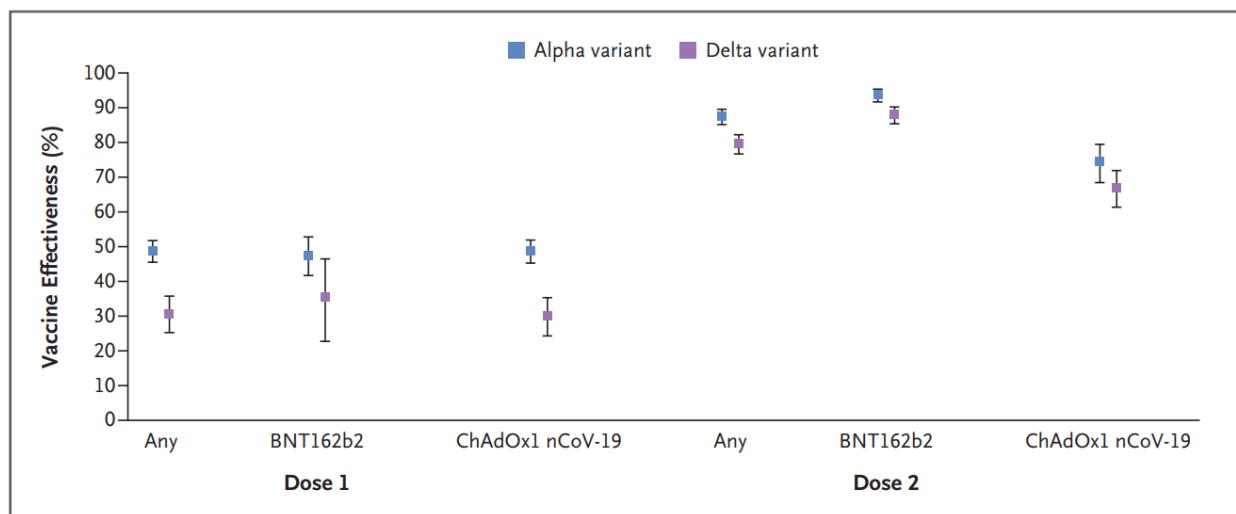
Effectiveness of Covid-19 Vaccines Against the B.1.617.2 (Delta) Variant

N Engl J Med published online July 21, 2021

DOI: 10.1056/NEJMoa2108891

The investigators (Public Health England) used a test-negative case-control design to estimate the effectiveness of vaccination against symptomatic disease caused by the delta variant or the predominant strain (B.1.1.7, or alpha variant) over the period that the delta variant began circulating. Variants were identified with the use of sequencing and on the basis of the spike (*S*) gene status. Data on all symptomatic sequenced cases of Covid-19 in UK were used to estimate the proportion of cases with either variant according to the patients' vaccination status.

Effectiveness after one dose of vaccine (Pfizer or AZ) was notably lower among persons with the delta variant (30.7%; 95% confidence interval [CI], 25.2 to 35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5 to 51.7); the results were similar for both vaccines. With the Pfizer vaccine, the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant. With the AZ vaccine, the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant.



Comment: This study strongly supports efforts to provide two doses among vulnerable populations. Overall, vaccine effectiveness after one dose was lower by approximately 12 to 19 percentage points against the delta variant than against the alpha variant. After two doses, the difference in vaccine effectiveness was notably less, approximately 6 percentage points (94% vs 88%). Since the investigators cannot randomize variants, comparing their effects must be observational. This article described an alternative nonrandomized study comparing the effectiveness of the Pfizer and AZ vaccines against two variants (B.1.1.7 [alpha] and B.1.617.2 [delta]) after one or two doses. This study used a test-negative design to assess vaccine effectiveness. This design is a form of case-control study in which persons testing positive for a disease after seeking health care (or because of a surveillance test) constitute the cases, whereas controls are selected from persons who test negative in the same situation, with each participant having their vaccination status recorded. The odds of vaccination are then compared between cases and controls, with vaccine effectiveness derived from the odds ratio subtracted from 1, expressed as a percentage. A recent test-negative design study in Canada showed positive findings regarding vaccine effectiveness with the Pfizer, Moderna, and AZ vaccines against symptomatic disease with the alpha, beta (B.1.351), gamma, and delta variants.

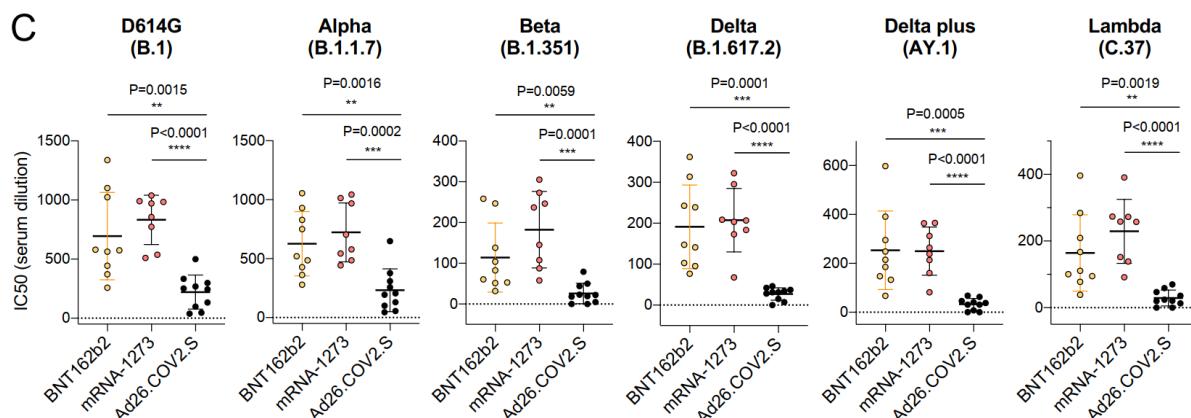
[<https://www.medrxiv.org/content/10.1101/2021.06.28.21259420v1>] In the United States, an estimated 279,000 deaths and up to 1.25 million hospitalizations have been averted as of the end of June 2021. [Commonwealth report reviewed in the Briefing July 9, 2021] As the delta variant spreads (now 83% in the US) the current imperative is to vaccinate as many people as possible, as quickly as possible.

Comparison of Neutralizing Antibody Titers Elicited by mRNA and Adenoviral Vector Vaccine against SARS-CoV-2 Variants

bioRxiv published online July 19, 2021

doi.org/10.1101/2021.07.19.452771

The investigators looked at neutralizing antibody titers elicited by an mRNA-based and an adenoviral vector-based vaccine against variant pseudotyped viruses were compared. Pfizer- and Moderna-elicited antibodies showed modest neutralization resistance against Beta, Delta, Delta plus, and Lambda variants whereas J&J elicited antibodies from a significant fraction of vaccinated individuals were of low neutralizing titer ($IC_{50} < 50$).



Comment: Several recent studies have shown that boosting a single immunization of the AZ (another adeno vector vaccine) with Pfizer resulted in high neutralizing titer against the VOCs. It is likely that neutralizing antibody titers against the VOCs elicited by the single shot of J&J could similarly be

improved by boosting with a second immunization or by a heterologous boost with one of the mRNA vaccines. This suggests the benefit of a second immunization following J&J vaccine could increase protection against the variants.