

Good morning to all

In today's COVID-19 News, I review the ACIP recommendations for Phase 1a for COVID-19 vaccination. The UK has given EUA for the Pfizer vaccine. Lastly, the CDC is about to release the revised quarantine recommendations.

Under literature reviews, the first article adapted a previously published model using contact information from Shanghai to model school reopening under various conditions. Bottom line: careful school reopening can proceed if mitigation strategies are in place and maintained. The second article looks at the role of transmission heterogeneity. The analysis revealed that 80% of secondary infections were connected to 15% of SARS-CoV-2 primary infections, indicating substantial transmission heterogeneities. While the lockdown period was shown to increase household transmission risk, healthcare contacts posed the lowest risk of transmission, reinforcing the importance of adequate protective measures taken in hospitals and healthcare centers. The next article looks at mental health in older people during the pandemic. The result of this study may surprise you. The last article is a terrific review on current treatment modalities for severe COVID-19. Bottom line: evolving science has confirmed that a purely antiviral approach is insufficient in treating critical SARS-CoV-2 infections.

Have a wonderful hump day!

Ed

COVID-19 News

ACIP Meeting

ACIP in an emergency meeting today, approved an interim recommendation for who should receive the first COVID-19 vaccine doses once authorized, which puts healthcare workers and nursing home residents at the front of the line. The two groups represent ~ 24 million people. [US population is ~330 million] ACIP also raised the possibility that, for the 1b phase, essential workers could be placed ahead of seniors and those with underlying medical conditions as a way to get people of color, known to be disproportionately affected by COVID-19 complications, higher on the priority list. ACIP will meet again shortly after FDA vaccine advisors meet on Dec 10 to discuss the EUA application for Pfizer's COVID-19 vaccine.

Pfizer Vaccine

UK became the first Western country to grant EUA and will be distributed within days. It is expected the US will follow next week.

Quarantine Period

The CDC is expected to release later today updated recommendations on length of quarantine after close contact with someone infected with SARS-CoV-2. The proposed change would allow persons to resume normal activities after 10 days [without testing] or seven days with a negative COVID-19 test. This is down from current recommendation of 14 days. Timing of when to obtain a COVID-19 test will be critical as well as which test the CDC will recommend. Part of the rationale is that most people become infectious and/or develop symptoms between 4-5 days after exposure. Since ~40% of persons are asymptomatic or presymptomatic, PCR is clearly better than rapid diagnostics for asymptomatic individuals. A person sheds virus 48 hours before symptoms. [if they develop symptoms] Therefore, a

PCR test obtained ~5-6 days after exposure maybe the optimal time but will wait for CDC's final recommendations later today.

Literature Reviews

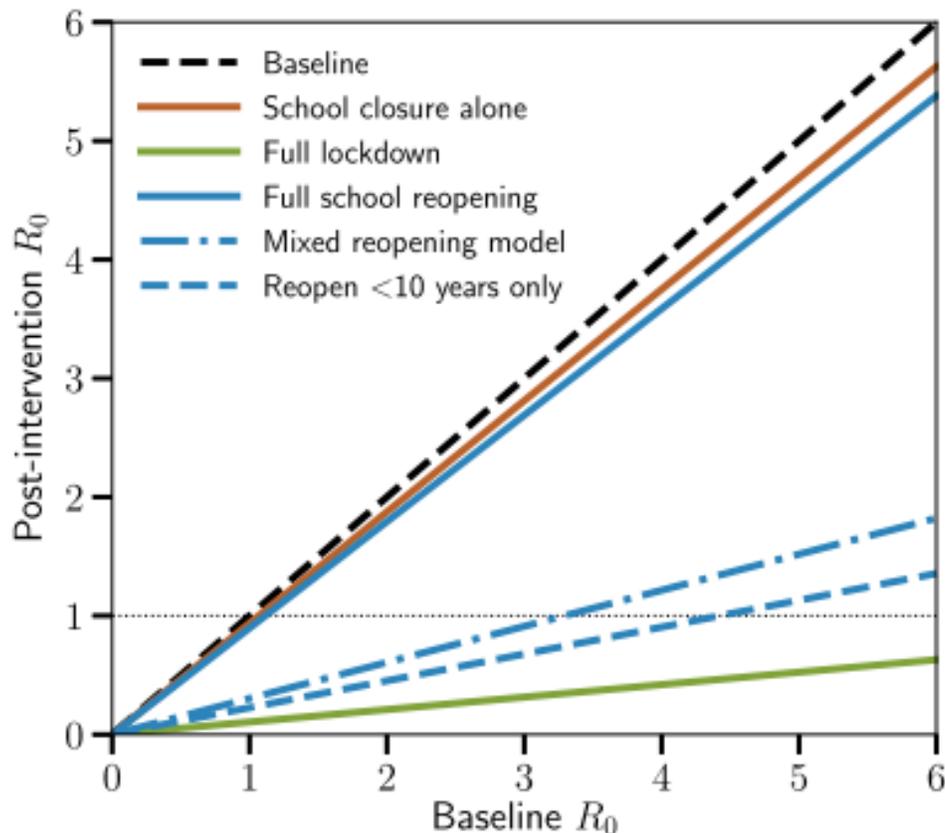
Modeling the Impact of School Reopening on SARS-CoV-2 Transmission Using Contact Structure Data from Shanghai

BMC Public Health published online November 16, 2020

doi.org/10.1186/s12889-020-09799-8

The authors adapted a previously published model using contact information from Shanghai to model school reopening under various conditions. We investigated different strategies by combining the contact patterns observed between different age groups during both baseline and "lockdown" periods. We also tested the robustness of our strategy to the assumption of lower susceptibility to infection in children under age 15 years.

They report that reopening schools for all children would maintain a post-intervention $R_0 < 1$ up to a baseline R_0 of approximately 3.3 provided that daily contacts among children 10–19 years are reduced to 33% of baseline. This finding was robust to various estimates of susceptibility to infection in children relative to adults (up to 50%) and to estimates of various levels of concomitant reopening in the rest of the community (up to 40%). However, full school reopening without any degree of contact reduction in the school setting returned R_0 virtually back to baseline, highlighting the importance of mitigation measures. Results remained robust after varying children's susceptibility to the virus and gradual increases in contacts in the wider community.



Comment: School closures and re-openings have been a subject of heated debate throughout the pandemic. Evidence suggests children under 10-years-old are less susceptible to SARS-CoV-2 and less likely to transmit the virus to adults. In addition, school closures may have severe consequences for children's support networks and development. However, while school closure alone does not have a major impact on transmission, full school reopening during a "lockdown" without mitigation measures in the school setting can return transmission to its baseline value. That being said, the findings here support that careful school reopening can proceed while maintaining post-intervention $R_0 < 1$ under a wide range of both baseline R_0 levels and estimates of susceptibility to infection in children, provided that appropriate measures are taken in the school and community settings to reduce the number of daily contacts among both children and school and community members. The challenge is how to reduce exposure in the community setting outside of school.

Transmission Heterogeneities, Kinetics, and Controllability of SARS-CoV-2

Science published online November 24, 2020

[10.1126/science.abe2424](https://doi.org/10.1126/science.abe2424) (2020)

A team of investigators from China and the US analyzed epidemiological data on 1,178 COVID-19 patients and their 15,648 contacts in Hunan, China, to investigate the role of transmission heterogeneity. The analysis revealed that 80% of secondary infections were connected to 15% of SARS-CoV-2 primary infections, indicating substantial transmission heterogeneities. While the lockdown period was shown to increase household transmission risk, healthcare contacts posed the lowest risk of transmission, reinforcing the importance of adequate protective measures taken in hospitals and healthcare centers.

Transmission risk scales positively with the duration of exposure and the closeness of social interactions and is modulated by demographic and clinical factors. The lockdown period increases transmission risk in the family and households, while isolation and quarantine reduce risks across all types of contacts. The reconstructed infectiousness profile of a typical SARS-CoV-2 patient peaks just before symptom presentation.

Comment: Modeling indicates SARS-CoV-2 control requires the synergistic efforts of case isolation, contact quarantine, and population-level interventions, owing to the specific transmission kinetics of this virus. Symptomatic cases represent 86.5% of all SARS-CoV-2 infections in their dataset. This is higher than most studies. Infectiousness profile of a typical SARS-CoV-2 patient peaked just before symptom onset, complicating epidemic control efforts and stressing the importance of targeted mitigation strategies and continuous testing. The investigators could not evaluate the risk of transmission in schools, workplaces, conferences, prisons, or factories, as no contacts in these settings were reported in the Hunan dataset. In addition, this study is likely underpowered to assess the transmission potential of asymptomatic individuals given the relatively small fraction of these infections in their dataset.

Older Adults and the Mental Health Effects of COVID-19

JAMA published online November 23, 2020

[doi:10.1001/jama.2020.21753](https://doi.org/10.1001/jama.2020.21753)

The investigators summarized evidence on the impact that the COVID-19 pandemic has had on the mental health of older adults. Evidence suggested that even though older adults have been disproportionately affected by the COVID-19 pandemic, they may be less negatively affected by mental health outcomes than other age groups. A survey from CDC conducted in June 2020 demonstrated that among the 933 participants aged 65 years or older, few reported anxiety disorder (6.2%), depressive

disorder (5.8%), or trauma- or stress-related disorder (TSRD) (9.2%), whereas the percentages among 895 participants aged 45 - 64 years, were 16.1%, 14.4%, 17.2%, respectively.

Comment: The finding here may surprise some, but in other recent studies, a significant inverse correlation was demonstrated between loneliness and wisdom, and loneliness and empathy, leading the authors to suggest that wisdom and empathy may partially contribute to the resilience enabling the older adults to deal with the adverse effects of the pandemic. However, the authors emphasized that studies on mental health during the COVID-19 pandemic may only deal with short-term outcomes and that findings from population-level studies may not capture heterogeneity at the individual, community, or environmental level.

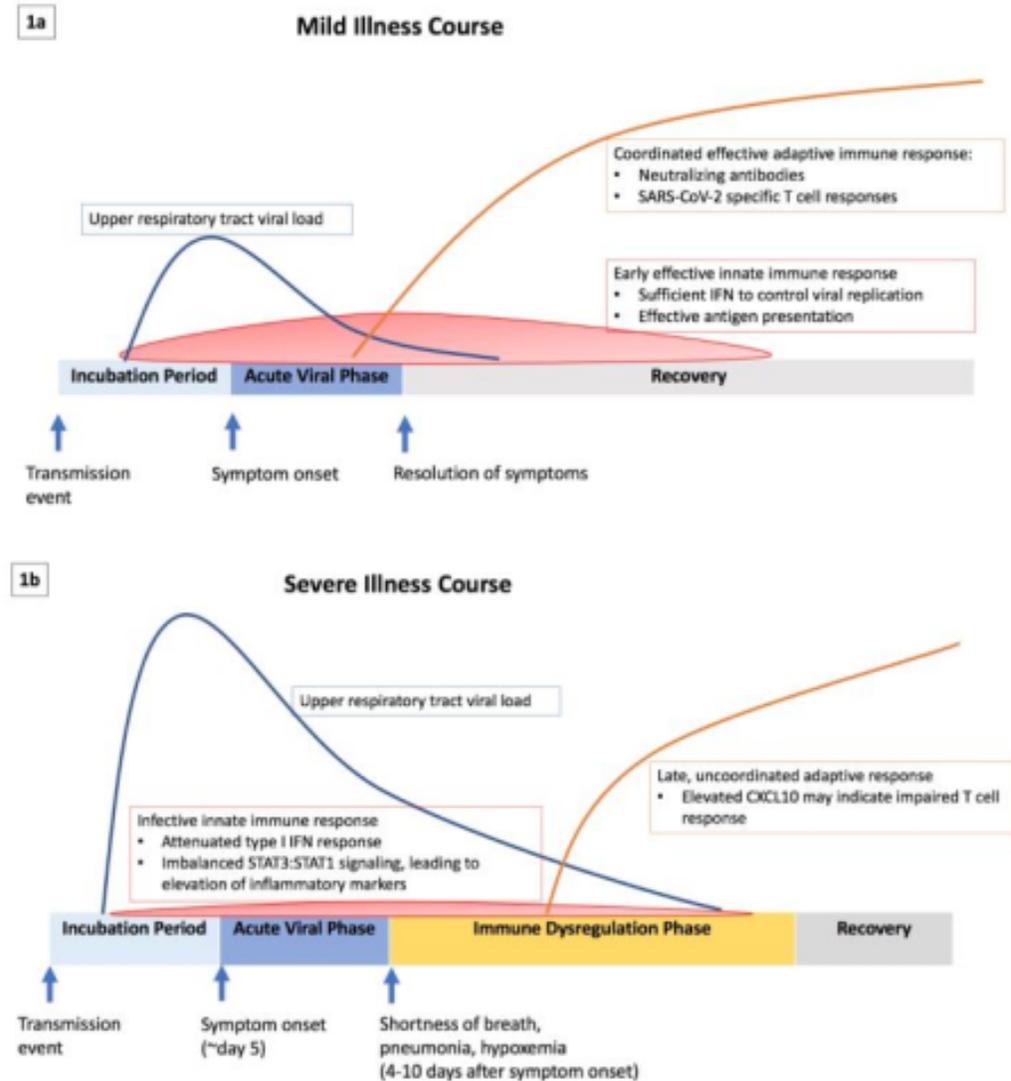
Immunomodulation as Treatment for Severe COVID-19: A Systematic Review of Current Modalities and Future Directions

Clin Infect Dis published online November 20, 2020

[Doi.org/10.1093/cid/ciaa1759](https://doi.org/10.1093/cid/ciaa1759)

This is a wonderful systematic review on current treatment modalities for severe COVID-19. They review that in SARS-CoV-2 infection that viral load peaks early and then set off a cascade of immune dysregulation that can persist well after viral clearance. Severe/critical disease is characterized by aberrant innate and adaptive immune responses with abnormal cytokine response and multiorgan dysfunction. Antiviral treatments have not shown benefit later in critical illness. [ACTT-1, Solidarity] A number of immunomodulatory strategies are being tested, including corticosteroids, cytokine and anticytokine therapies, small molecule inhibitors, and cellular therapeutics. The only drug to date to show a mortality benefit for COVID-19 in a randomized control trial is dexamethasone, but long-term complications including secondary infections remain a concern. This paper reviews the existing data around various immunomodulatory strategies and future studies. There are tables on steroids, IL-6 inhibitors, anakinra, baricitinib, and other antivirals reviewing studies and level of evidence.

Figure 1: Comparing Mild and Severe COVID-19 Illness Course



Comment: I think it is clear evolving science has confirmed that a purely antiviral approach is insufficient in treating critical SARS-CoV-2 infections. Trials on combination therapies are now underway such as the ACTT-2 trial combining remdesivir and baricitinib. Given the heterogeneity of COVID-19 clinical presentations, a one size fits all approach may not provide optimal outcomes. Hopefully, RCTs will help optimize the right drug, dose, and timing in relationship to stage of disease.