Good morning

The first ever virtual ID Week is over. Except for a few technical glitches I thought the meeting went well. I had no problems getting into a lecture hall or finding a seat, I had unobstructive view of the slides, I did not have to get on an airplane, or unpack in my hotel, and it cost a lot less! However, I missed seeing so many friends and colleagues and the networking that is such an important part of our meeting. Hopefully, next year we will have the option of attending in person or virtually. I wonder if we will transition to more virtual meetings in the future.

Today I wanted to concentrate of the new CDC definition of close contact and encourage each of you to weigh in on this change but sending me an email. I will gather your insights and at the end of the week will summarize for our readers. I have contact CDC to get additional information that may have led to this change.

In addition to reviewing the new definition of close contact and the MMWR publication, I also included an article on convalescent plasma, an IHME paper on modeling deaths based on several different scenarios, and lastly a paper on common nasal and oral products that may impact infection and transmission of SARS-CoV-2.

VII Comments on the New CDC Definition of Close Contact.
I have reviewed the revised CDC definition of "close contact" which I find problematic and difficult to execute. It appears the CDC has actually changed the definition based on this unusual jail exposure. The MMWR article (published October 23, 2020) concludes in correctional settings, frequent encounters of ≤6 feet between [incarcerated or detained persons] and facility staff members are necessary; now public health officials should consider transmission-risk implications of cumulative exposure time within such settings. Here are the facts: On July 28, a 20-year-old male correctional officer in Vermont had multiple brief encounters with six transferred incarcerated or detained people while their SARS-CoV-2 test results were pending. The six were asymptomatic at the time and were housed in a quarantine unit. The following day, all six inmates tested PCR-positive for COVID-19. On August 4, unfortunately, the correctional officer developed symptoms that included loss of smell and taste, myalgia, runny nose, cough, shortness of breath, headache, loss of appetite, and gastrointestinal symptoms. Video surveillance footage showed the correctional officer's limited contact with prisoners. The officer's 22 interactions with the inmates totaled 17 minutes throughout an eight-hour shift. The officer wore a mask, gown and eye protection during the encounters according to report though he sometimes didn't wear gloves. But inmates did not wear masks during several encounters in a cell doorway or the recreation room. Investigators could not determine the specific route of the officer's infection, whether it was through droplets, aerosols or touching the same object as an infected inmate. What about community exposure or exposures in the break room? Despite this the CDC still revised their definition. I have underlined or bolded several important sentences for your consideration.

The CDC altered its definition of a close contact, saying it is now someone who was within 6 feet of an infected person for a total of 15 minutes or more over a 24-hour period. Close contact, and public health officials should **consider** cumulative exposure time in settings such as correctional facilities, the report said. Someone who was within 6 feet of an infected person for a cumulative total of 15 minutes or more over a 24-hour period* starting from 2 days before illness onset (or, for asymptomatic patients, 2 days prior to test specimen collection) until the time the patient is isolated.

** Individual exposures added together over a 24-hour period (e.g., three 5-minute exposures for a total of 15 minutes). Data are limited, making it difficult to precisely define "close contact;" however, 15 cumulative minutes of exposure at a distance of 6 feet or less can be used as an operational definition for contact investigation. Factors to consider when defining close contact include proximity (closer distance likely increases exposure risk), the duration of exposure (longer exposure time likely increases exposure risk), whether the infected individual has symptoms (the period around onset of symptoms is associated with the highest levels of viral shedding), if the infected person was likely to generate respiratory aerosols (e.g., was coughing, singing, shouting), and other environmental factors (crowding, adequacy of ventilation, whether exposure was indoors or outdoors). Because the general public has not received training on proper selection and use of respiratory PPE, such as an N95, the determination of close contact should generally be made irrespective of whether the contact was wearing respiratory PPE. At this time, differential determination of close contact for those using fabric face coverings is not recommended.*

As you can read, they admit limited data making it difficult to define close contact but list factors to consider. (see below) Once again, they say close contact may be present regardless whether close contact was wearing a mask. Once again, they fail to discuss if BOTH are wearing a mask since the infected person is unlikely to generate respiratory aerosols as documented by the MMWR report in the 2 hairdressers who were infected but both hairdresser and client both wore masks and no infections occurred. We have not seen broad transmission even with the last definition so why change it now? I do believe, however that close contact in close quarters with poor ventilation with brief removal of masks or improper wearing of a mask may be problematic in a population where prevalence may be high.

The change could have significant consequences, since schools, businesses, and other establishments base decisions on who is allowed to enter their premises on whether they are a close contact of an infected person. It also could have implications for contact-tracing efforts, potentially expanding the number of close contacts for any one case that health agencies would have to track down.
In my opinion the new CDC's updated definition for all settings is a heavy lift especially outside of healthcare settings. It is going to make contact tracing much more difficult, subjective, and resource intensive, because there will be more contacts. Health departments have limited resources to do the boots on the ground contact tracing.

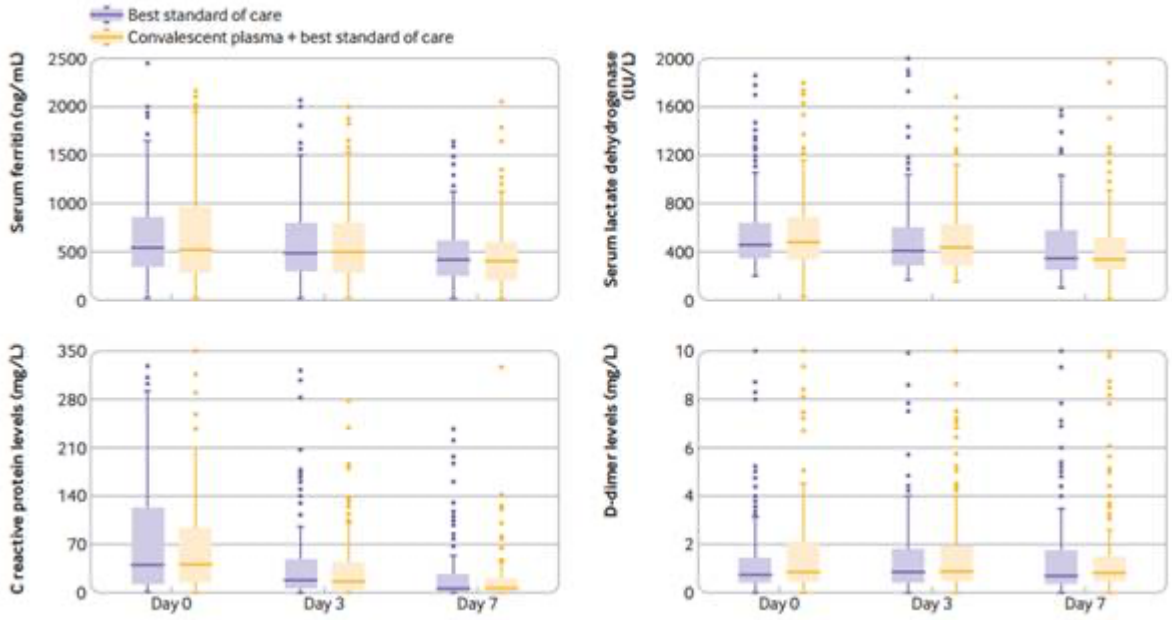
The four factors that have been associated with higher risk for transmission are the proximity of each encounter, its duration [CDC has now added over a 24-hour period], whether an interaction takes place indoors or outdoors, and the number of people encountered. Some studies would add if the person was symptomatic. I do agree with the CDC that not all exposures are the same and they have listed factors to consider. This means each of us in our roles may have to make clinical judgments on whether the incident in question a close contact is or not. This may be subjective and become emotional for the individual(s) potentially exposed. Clearly, an exposure in a crowded bar indoors with people speaking loudly may be quite different than an exposure outside at a picnic.

I would also like a clear statement about both parties are correctly wearing masks. Curious of how you read this and how this will impact our work especially if we get the big second or third wave which is predicted and is already impacting many areas of the country.

Convalescent Plasma in the Management of Moderate Covid-19 in Adults in India: Open Label Phase II Multicentre Randomized Controlled Trial (PLACID Trial)
BMJ published online October 22, 2020

464 adults admitted to the hospital were screened with confirmed moderate Covid-19 (partial pressure of oxygen in arterial blood/fraction of inspired oxygen (PaO2/FiO2) ratio between 200 mm Hg and 300 mm Hg or a respiratory rate of more than 24/min with oxygen saturation 93% or less on room air): 235 were assigned to convalescent plasma with best standard of care (intervention arm) and 229 to best standard of care only (control arm). Participants in the intervention arm received two doses of 200 mL convalescent plasma, transfused 24 hours apart. The presence and levels of neutralizing antibodies were not measured prior to transfusion; however, stored samples were assayed at the end of the study. The primary outcomes were composite of progression to severe disease (PaO2/ FiO 2 <100 mm Hg) or all-cause mortality at 28 days post-enrolment.

Progression to severe disease or all-cause mortality at 28 days after enrolment occurred in 44 (19%) participants in the intervention arm and 41 (18%) in the control arm (risk difference 0.008 (95% confidence interval -0.062 to 0.078); risk ratio 1.04, 95% confidence interval 0.71 to 1.54). Additionally, outcomes did not differ between participants receiving convalescent plasma with detectable neutralizing antibody titers compared with participants receiving best standard of care alone; or between those receiving convalescent plasma with neutralizing antibody titer of 1:80 or higher and those receiving best standard of care alone. Treatment with convalescent plasma, however, was associated with a higher resolution of shortness of breath and fatigue on day 7. [study was not blinded] A higher proportion of participants in the intervention arm showed negative conversion of SARS-CoV-2 RNA on day 7 post-enrolment. The intervention did not, however, show anti-inflammatory properties as they could not detect any difference in the levels of inflammatory markers such as ferritin, CRP, D-dimer, or LDH between the trial arms. This study was underpowered but did not find any benefit from convalescent plasma being administered within three days of symptom onset in Covid-19. Neutralizing antibody titer were measured in 418 trial participants; 348 (83%) had detectable neutralizing antibodies at enrolment!



Comment: The mechanism of benefit from convalescent plasma is through direct antiviral action of neutralizing antibodies on SARS-CoV-2 RNA.1 In the PLACID Trial, a statistically significant 20% higher rate of conversion to a negative result for SARS-CoV-2 RNA occurred on day 7 among patients in the

intervention arm. This has been reported by others, but as this paper points out, convalescent plasma has no impact on the inflammatory response. This observation helps explain the Mayo Clinic pre-publication results which reported for convalescent plasma to improve outcomes treatment needed to be given early and with high titer plasma before the evolution into the inflammatory stage. Like other studies, many patients who received convalescent plasma already had antibodies. Future research should include effectiveness of convalescent plasma among neutralizing antibody negative patients and the use of convalescent plasma with high neutralizing antibody titer given early in disease. The challenge will be to find both suitable patients and suitable plasma donors. It is unclear how generalizable the findings are because many of the units of plasma had either very low or no antibody titers [but they did analyze the subgroup who received plasma with 1:80 and higher] and because the plasma was given late in the course of the disease in many patients. The question remains where do monoclonal antibodies fit, and should these interventions be offered for patients with mild symptoms that do not require hospitalization at time of diagnosis?

Modeling COVID-19 Scenarios for the United States: IHME COVID-19 Forecasting Team
Nat Med published online October 23, 2020
The investigators from the Institute for Health Metrics and Evaluation delimited three possible future scenarios of the course of the COVID-19 epidemic in the United States, at the state level—mandate easing, plausible reference and universal mask-use scenarios— to help frame and inform a national discussion on what actions could be taken during the fall of 2020 and the public health, economic and political influences that these decisions will have for the rest of the winter (here defined as the end of February 2021). As of September 21^{st,} only 49% of Americans say they always wear a mask in public.

Scenario 1 States continue to ease their social distancing mandates at their current pace: According to the model a total of 1,053,206 American may lose their lives to COVID-19 with over 150 million infections by end of February 2021.

Scenario 2 is a better than scenario 1 States begin tightening restrictions or maintaining certain restrictions back in place. This would result reducing deaths to a little over 500,000 by February 2021.

Scenario 3 would improve by increasing 95% of people wearing masks outside their home up from current 49%. This would result in reducing death toll to 381,798, meaning almost 700,000 fewer deaths compared to the status quo.

Scenario 4 same as scenario 3, but instead of 95% of population wearing masks outside the home to 85%. [this may be more realistic] The researchers estimate deaths would be 415,000 by February 2021.

In addition, the implementation of social distancing mandates as soon as individual states reach a threshold of 8 daily deaths per million could dramatically reduce the effects of the disease; achieving near-universal mask(85-95% use could delay, or in many states, possibly prevent, this threshold from ever being reached and has the potential to save the most lives.

Comment: The potential life-saving benefit of increasing mask use in the coming fall and winter cannot be overstated. Longer term, the future of COVID-19 in the United States will be determined by the deployment of an efficacious vaccine and the evolution of herd immunity. Until then we need to continue to execute on the "3Ws": wash hands, wear a mask, and watch your distance. This include reducing crowds [this includes weddings, bars, and large family gatherings etc.] especially indoors. There are limitations in any modeling study. Specifically, (1) these models are approximations of real-world

scenarios, and the investigators have simplified many aspects of the epidemiological process of disease transmission to make these models computationally feasible; (2) these models are driven strongly by mortality data with all of its fidelity and recording imperfections; (3) these models are also informed by a wealth of other data types that each have differential availability, as well as detection and measurement bias issues for which we can never fully calibrate; (4) these models make particular assumptions about covariates, including seasonality, that while evidence-based and explicitly stated, are subject to sensitivity analyses because their effects could be substantial; and (5) our knowledge of this dynamic pandemic improves daily and may change trajectory. They conclude "Finally, it is especially important for decision-makers that we emphasize that we are not forecasting a future, but rather a range of outcomes that we believe are more probable given the scenarios tested, based on the data observed so far and our model assumptions. These forecasts are best considered as helpful guides, rather than definitive maps."

Lowering the Transmission and Spread of Human Coronavirus
J Med Virol published online October 2020
Nasal rinses and mouthwashes, which directly impact the major sites of reception and transmission of human coronaviruses (HCoV), may provide an additional level of protection against the virus. Common over-the-counter nasal rinses and mouthwashes were tested for their ability to inactivate high concentrations of HCoV using contact times of 30 s, 1 min, and 2 min. Reductions in titers were measured by using the tissue culture infectious dose 50 (TCID50) assay.

A 1% baby shampoo nasal rinse solution inactivated HCoV greater than 99.9% with a 2-min contact time. Several over-the-counter mouthwash/gargle products including Listerine and Listerine-like products were highly effective at inactivating infectious virus with greater than 99.9% even with a 30-s contact time. In this publication the investigators demonstrated that several commonly available healthcare products have significant virucidal properties with respect to HCoV.

TABLE 2 The effect of nasal rinses on HCoV

Nasal rinses	log10 Decrease contact time: 2 min (% inactivation)	log10 Decrease contact time: 1 min (% inactivation)	log10 Decrease contact time: 30 sec (% inactivation)
Neti Pot	No change (0%)	No change (0%)	No change (0%)
1% Baby Shampoo J&J	between >3 and >4 $\log_{10}$ (>99.9% to >99.99%)	between >2 and <3 $\log_{10}$ (>99% to <99.9%)	between <1 and <3 $\log_{10}$ (<90% to <99.9%)

TABLE 3 The effect of mouth wash/gargles on HCoV

Mouth Wash/gargle	log10 Decrease contact time: 2 min (% inactivation)	log10 Decrease contact time: 1 min (% inactivation)	log10 Decrease contact time: 30 sec (% inactivation)
Peroxide Sore Mouth	between >1 and <2 $\log_{10}$ (>90% to <99%)	between >1 and <3 $\log_{10}$ (>90% to <99.9%)	between <1 and <2 $\log_{10}$ (<90% to 99%)
Orajel Antiseptic Rinse	between <1 and <2 $\log_{10}$ (<90% to <99%)	between ≥1 and <2 $\log_{10}$ (≥90% to <99%)	between >1 and <2 $\log_{10}$ (>90% to <99%)
1.5% H_2O_2	<1 log10 (<90%)	between <1 and <3 $\log_{10}$ (<90% to <99.9%)	between <1 and <2 $\log_{10}$ (<90% to <99%)
Crest Pro Health	between ≥3 and >4 $\log_{10}$ (≥99.9% to >99.99%)	>4 $\log_{10}$ (>99.99%)	between ≥3 and <4 $\log_{10}$ (≥99.9% to <99.99%)
Listerine Antiseptic	>4 $\log_{10}$[a] (>99.99%)	>4 $\log_{10}$[a] (>99.99%)	>4 $\log_{10}$ (>99.99%)
Listerine Ultra	≥4 $\log_{10}$ (≥99.99%)	≥4 $\log_{10}$ (≥99.99%)	between ≥3 and <4 $\log_{10}$ (≥99.9% to <99.99%)
Equate Antiseptic	between >3 and ≥4 $\log_{10}$ (>99.9% to ≥99.99%)	between >2 and <4 $\log_{10}$ (>99% to <99.99%)	between >2 and <4 $\log_{10}$ (>99% to <99.99%)
CVS Antiseptic Mouth Wash	between ≥3 and ≥4 $\log_{10}$ (≥99.9% to ≥99.99%)	between ≥3 and ≥4 $\log_{10}$ (≥99.9% to ≥99.99%)	between >3 and <4 $\log_{10}$ (>99.9% to <99.99%)
Betadine 5%	>4 $\log_{10}$ (>99.99%)	between >3 and >4 $\log_{10}$ (>99.9% to >99.99%)	between >3 and <4 $\log_{10}$ (>99.9% to <99.99%)

Comment: The most significant mode of transmission is still considered through aerosolized droplets. We know wearing masks and social distancing can significantly decrease transmission and spread. (see model above) However, these practices have not been universally accepted. [only 49% are wearing masks outside the home!] Therefore, additional strategies may be necessary to reduce transmission. Nasal rinses and mouthwashes, which directly treat the major sites of reception and transmission of HCoV, may provide an additional level of protection against the virus. This article is one of several published in the last few months that confirm the activity of several commonly used nasal and oral rinses. [several reviewed in the Daily Briefing in the last several months] Clinical trials are necessary to study these interventions both for prevention of transmission, prophylaxis after exposure and reduction of viral load early in the early stages of infection which may prevent progression.