COVID-19 Updates and Insights with Dr. Zieg – October 8, 2020 Questions

I've heard some ideas on "Herd Immunity" wherein the enough of the population is immunized to protect the rest of the population. When you mentioned 9-12 months to vaccinate the entire population, does that take this into consideration? If not, is it likely that stay-at-home precautions may be lifted earlier?

The 9-12 months was the timeframe to when the general population (i.e. not the prioritized groups) will have access to a vaccine. It's unlikely we'll see uptake of a vaccine across the entire population – estimates are commonly 60-70% based on polls and annual flu vaccine uptake. If we saw exceptional efficacy of the vaccine candidates, 60-70% would likely be enough to reach herd immunity. If the vaccines only reach 50% efficacy (the floor for a vaccine to get EUA approval), we would see some impact around herd protection but would not likely reach "herd immunity" where we don't see outbreaks from time to time.

What are the statistics on false positive PCR tests? and Are there differences in "contagiousness" from one patient to another? (Meaning are some people more contagious than others over the course of the infection).

The reported rate of false ***negatives*** with in-lab RT-PCR is as low as 2% and as high as 37%. The false ***positive*** rate — that is, how often the test says you have the virus when you actually do not — should be close to zero but I have seen rates as high as potentially 4% reported (UK study). PCR testing is very specific so false positive rates are low, however, the lower the prevalence of COVID in a population, the higher the potential for false positives (a lower likelihood of a positive test lowers the positive predictive value). Most false-positive results are thought to be due to lab contamination or other problems with how the lab has performed the test, not limitations of the test itself.

Regarding contagiousness, it is likely there are differences between people infected and how easily they spread disease, but it's largely theory at this point. We do know some people are "super spreaders" which is likely driven by several factors – social behavior (talking a lot; jumping from person to person etc) and viral load (how much virus is accumulated in the body/nasal and oropharyngeal secretions).

How much of a "viral dose" is required to test positive and/or get sick?

The actual quantity isn't described in the literature. However, there is some evidence that suggests a low "viral dose" may lead to less severe illness or asymptomatic case. This theory is largely driven by case series that describe people wearing masks consistently were observed to be more likely to have asymptomatic infection, under the premise that a mask is at least somewhat protective and may reduce the viral load in an exposure. Some, however, also argue that an individual's immune system plays more of a factor in severity of illness than "viral dose".

Do masks protect against this smaller floating aeresolization?

Masks can help contain, to some degree, aerosolization of virus from the wearer. Masks may play a role in reducing viral load in exposure to droplets in the wearer, but most cotton masks/surgical masks do not *prevent* aerosolized particles from being inhaled…these particles are too small to be blocked by general use masks. A medical grade N-95 respirator that is properly fitted to the individual is needed to block aerosols from being inhaled, and these are typically reserved for healthcare workers.

Do asymptomatic individuals have natural antibodies to covid-19?

There have been reports that some people have antibodies from exposure to other coronaviruses (ex/common cold) that may cross react to and provide some protection from COVID-19. Other reports note the existence of B and T cells (other cells that are part of the immune response) that respond to COVID-19, likely the result of exposure to other coronaviruses in the past. These theories may explain the widespread differences in severity of illness, but data is very limited at this time.

You mentioned 50% efficacy of the Covid-19 vaccine. How does that compare with other vaccines?

It depends on the vaccine. Flu vaccine averages 30-50% efficacy but varies year to year. Best it has been is 60%. The measles vaccine, in contrast, is 97% efficacious after two doses, and most routine childhood vaccines are 85-95% effective. I haven't seen data on efficacy of the COVID-19 vaccines in phase 3 trials yet, but the FDA has set a benchmark of "*at least* 50% efficacious to be considered for EUA".

Are airplane's considered to be filtered enough in your opinion?

Yes, air filtration (they use HEPA) and turnover is excellent in commercial airlines. Thinking of the other factors though (TDNA), time, distance and number of people are risk factors to consider even though air circulation is lower risk.

What is the rationale behind using the PCR tests for employees at Mercury, when the results take 2+ days to receive; in the meantime, employees are working next to each other? Wouldn't a rapid test be more prudent?

In-lab PCR testing is the gold standard and most accurate. 2-day delay is a disadvantage to some degree, but in screening asymptomatic populations it's still reasonable. Rapid testing with molecular assays or antigen assays have their place in screening populations but they have advantages and disadvantages. As Mercury Systems continues its testing protocols, they may choose to move to another, rapid based strategy at some point but will depend on evolution of their strategy and availability of new testing assays.

I had rheumatic fever as a teen where my physician says there is not enough data to know how it will impact me... Recommended taking extra precautions... your thoughts?

I recommend that we all take extra precautions. This virus is tricky and can do some bad things to the body, including the heart. If someone had rheumatic fever that resulted in heart dysfunction (known as rheumatic heart disease) or other complications, this may represent the potential to be at higher risk for complications from COVID-19.

If I am on an elevator with a mask and another person gets on with a mask, can I stay on the elevator, or should I get off or take some other action?

Think of the acronym – TDNA – Time, Distance, Number of people, Airflow. Weigh the risks based on these factors. One other person also wearing a mask in an elevator for a 30 second ride, probably represents low risk overall even though distance and airflow represent higher risk.

How safe is it to stay in hotels? What are the key precautions you can take?

Think of the acronym TDNA – Time, Distance, Number of people, Airflow. If you can avoid groups of people, your risk of being exposed by staying in a hotel would be pretty low. Hotels are cleaning regularly which likely reduces risk, but bring your own wipes and hand sanitizer and use them frequently.

Does a false negative mean you are not contagious? Are you only contagious once the test is positive?

A false negative means the test came back negative even though the disease is present, so you would be contagious.

Assuming no more than 33 % full, would you trust going to a indoor, large movie theater auditorium?

Personally, I would not… think of the acronym TDNA – Time, Distance, Number of people, Airflow when assessing your risks. Time, number of people and likely airflow are against you here…even if 33% full allows for distancing. Probably not worth the risk.

Is playing ice hockey safe enough to play because the rink is large and the number of players are limited? or would players breathing hard during game/practice increase risks?

I personally would not feel comfortable with the exposure risk of playing hockey given the reasons you note. In addition to the acronym TDNA – Time, Distance, Number of people, Airflow, *activity* plays a part too. Breathing heavy during exercise increases risk, as does singing, yelling etc.

What constitutes being in the risk population?

The CDC has a lot of information. I'll paste some of the key information from the CDC here:

Risk for Severe Illness Increases with Age

As you get older, your risk for severe illness from COVID-19 increases. For example, people in their 50s are at higher risk for severe illness than people in their 40s. Similarly, people in their 60s or 70s are, in general, at higher risk for severe illness than people in their 50s. The greatest risk for severe illness from COVID-19 is among those aged 85 or older.

Adults of any age with certain underlying medical conditions are at increased risk for severe illness from the virus that causes COVID-19:

Adults of any age with the following conditions **are at increased risk** of severe illness from the virus that causes COVID-19:

- Cancer
- Chronic kidney disease
- COPD (chronic obstructive pulmonary disease)
- Heart conditions, such as heart failure, coronary artery disease, or cardiomyopathies
- Immunocompromised state (weakened immune system) from solid organ transplant
- Obesity (body mass index [BMI] of 30 kg/m^2 or higher but < 40 kg/m^2)
- Severe Obesity (BMI ≥ 40 kg/m^2)
- Sickle cell disease
- Smoking
- Type 2 diabetes mellitus

COVID-19 is a new disease. Currently there are limited data and information about the impact of underlying medical conditions and whether they increase the risk for severe illness from COVID-19. Based on what we know at this time, adults of any age with the following conditions **might be at an increased risk** for severe illness from the virus that causes COVID-19:

- Asthma (moderate-to-severe)
- Cerebrovascular disease (affects blood vessels and blood supply to the brain)
- Cystic fibrosis
- Hypertension or high blood pressure
- Immunocompromised state (weakened immune system) from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune weakening medicines
- Neurologic conditions, such as dementia
- Liver disease
- Overweight (BMI > 25 kg/m^2, but < 30 kg/m^2)
- Pregnancy
- Pulmonary fibrosis (having damaged or scarred lung tissues)
- Thalassemia (a type of blood disorder)
- Type 1 diabetes mellitus

Why do we talk of raw numbers (800000 in CA, 400000 in TX, etc.) when percentages are a much more valuable comparison?

Various metrics are reported, and total cases in each state being one of them just as each country's total is reported. I think the incidence x/100,000 (i.e. current caseload) is most impactful and obviously accounts for population differences.

Is there speculation on how long masks will continue to be enforced as a mandatory apparel item?

Likely until we see containment which isn't likely until widespread vaccination occurs.

With the possibility of false positives, should we follow up positive test results with another test before we remove them from the testing pool for 3 months?

In situations where incidence is very low, the positive predictive value is lower and this strategy might be reasonable to consider especially under certain circumstances. Another way to say it is if it is highly unlikely to find a positive test result, a positive test result found is more likely to be false. False positive rates on in-lab PCR though are very low when looking at the quality assays - close to 0 under most circumstances. Most false-positive results are thought to be due to lab contamination or other problems with how the lab has performed the test, not limitations of the test itself.

If you are working from home, social distancing, wearing masks, and only go to the grocery store, what would be a reason to get tested? If we don't feel any symptoms, aren't around people, do we need to get tested?

If you are only working from home and following all of these precautions, I would suggest that you would not need to be tested.

Can we share your graphic about Contagious Period with family and friends?

I will share it but it should be taken in context – it is based on small studies, estimations and assumptions and should not be read "literally", but rather as a general guide around a potential timeline.

I have been told after getting vaccinated for the flu you can test positive for COVID-19, is this true?

No, absolutely not.

When you say "immune" in herd immunity, do you mean they have tested positive within 90 days? or how are you defining immune?

Regarding herd immunity, I was referring to having some level of *lasting immune protection* from COVID-19, which is required to reach herd immunity. This is still being studied and the information we have on what immunity to this virus actually looks like is limited.

Are there any numbers around how many of the positive reported cases were symptomatic vs asymptomatic?

Best estimate I've seen is between 40-50% of all COVID-19 cases are asymptomatic – not all of these were reported given asymptomatic people don't commonly seek testing, so it's an extrapolation from limited data that does exist.

Will you be able to choose which manufacturer you get your vaccine from when it's available to the general public?

Eventually this may be possible but given the limited supply and how this is shaping up, it's likely we'll need to take what we can get initially.