Summary of Recent COVID-19-related Research June 23, 2020

PREVENTION

 Covid Transmission (WSJ): A growing body of research indicates surface contamination and brief, transitory contact with infected individuals won't readily spread Covid. Extended interactions with infected individuals over a long period provide optimal conditions for infection. Aerosolization of the virus through normal breathing by infected individuals releases sufficient viral load over time to infect healthy individuals. The chart below (Yahoo!) ranks 36 activities based on risk (mLIVE):

9	BARS	LARGE MUSIC CONCERTS	
8	BUFFETS SPORTS STADIUMS	• GYMS • AMUSEMENT PARKS	CHURCHES
7	BASKETBALL	PUBLIC POOLS	SCHOOLS
6	CASINOS RESTAURANTS, INDOOR SEATING	PLAYGROUNDS AHAIR SALONS, BARBERSHOPS	PONTOON BOAT RIDES MOVIE THEATERS
5	DINNER PARTIES AT A House Airplanes	BACKYARD BARBECUES MALLS	BEACHES BOWLING
4	DENTIST'S OFFICE WALKING IN A BUSY DOWNTOWN	OFFICES DOCTOR'S WAITING ROOMS	EATING OUTSIDE AT A RESTAURANT
3	GETTING GROCERIES CAMPING	HOTELS GOLFING	LIBRARIES AND MUSEUMS
2	• GOING FOR A WALK, RUN OR BIKE RIDE WITH OTHERS	• GETTING FUEL	
1	GETTING TAKEOUT FROM A RESTAURANT	• PLAYING TENNIS	

Indoor Activity (The Atlantic): Take precautions with prolonged exposure (>15 mins) to others in enclosed spaces (use masks, social distancing). Avoid indoor activities that involve active breathing that could easily spread the virus (intense workouts, choir practice, etc.)

Outdoor Activity: Research suggests outdoor activities pose a much lower risk for virus transmission, even intensive activities such as running, biking, etc. In an abundance of caution, it's worth considering wearing a mask if social distancing isn't feasible, even outdoors.

- Masks (<u>Science Daily</u>): The best advice currently available is that we should all wear a mask when there's a higher risk of Covid spread. There are indications that wearing a mask reduces transmission by >50% which matches the protection a vaccination will likely provide. A leading scientist we've spoken to affirms that this, along with social distancing, is by far the simplest, most effective way to prevent Covid transmission and stay healthy.
- Health Monitoring (<u>Bloomberg</u>): New technology may allow active monitoring via wearables such as an Apple Watch that detect physiological changes (e.g., heart rate) associated with viral infections. This is still in the early, unproven state, but very interesting.
- **Blood Type** (<u>NEJM</u>): New research suggests that people with Type O blood have some protection against severe Covid infections (fewer acute cases, fewer intubations). Those with Type A blood type tend to have worse outcomes on average. This is early research and may not hold up over time.

• **Diagnostic Testing**: Testing for *presence* of the Covid virus (RT-PCR tests) continues to rapidly expand with easier access, less invasive methods, and faster results. However, the prevalence of testing remains far behind where it needs to be. One expert estimated the

country could fully reopen if we could perform 30 million tests per week (~\$1.5 billion / week). In many regions, testing is now available for non-symptomatic people without a doctor referral.

 Antibody Testing (Johns Hopkins): Serology tests to identify whether an individual has been exposed to Covid and has antibodies present in his or her blood are rapidly growing in availability and accuracy. These tests can identify asymptomatic carriers which helps researchers understand the prevalence of the virus. The best estimates suggest ~5% of Americans have been infected with the virus to date. Antibody testing is readily available in most regions through Quest Diagnostics and other labs without a doctor referral. At home tests aren't yet recommended due to poor accuracy.

TREATMENT

- **Dexamethasone** (<u>Nature</u>): This cheap and readily available steroid apparently reduces mortality >30% in patients with severe Covid infections. The study was done in the UK on patients who had already been placed on a ventilator. It's the first drug proven to reduce deaths from Covid. There remains some skepticism due to the number of studies retracted recently as steroids also suppress the immune system.
- Anticoagulants (<u>Stat News</u>): Covid causes a high rate of blood clotting. As a result, the standard of care for patients admitted to the hospital with Covid now generally includes a low dose of blood thinner (e.g. Warfarin). A leading scientist puts this at the top of the list of drugs he'd immediately consider taking if he tests positive.
- **Remdesivir** (<u>New England Journal of Medicine</u>): This intravenous drug was superior to a placebo in shortening time to recovery for Covid-infected adults with evidence of lower respiratory tract infection. The difference was 11 days vs 14 days with some indications of lower mortality. There are reports that the US government's current supply runs out at the end of the month and new inventory may be sporadic through July as Gilead ramps up manufacturing (<u>CNN</u>). Separately, Gilead has started testing a version of the drug taken via an inhaler rather than intravenously.
- **Hydroxychloroquine** (<u>Stat News</u>): The largest studies now show the malaria drug offers no benefit for Covid-infected patients. The WHO removed it from its massive Covid drug trial. Rigorous studies also found the drug does not prevent people exposed to the virus from getting sick. The FDA revoked emergency use authorization for Hydroxychloroquine earlier this week.
- Other Treatments (NPR): Research is under way on several other Covid treatments, none of which has yet proven to provide clinical benefits: Convalescent Plasma (Mayo Clinic); Antivirals EIDD-2801 (Science); Monoclonal Antibodies (NPR); and Immune Modulators. The US government is funding the Covid-19 High Performance Computing Consortium (HPC Consortium) to bring together the Federal government, industry, and academic leaders and provide high performance computing resources in support of Covid research.

VACCINES

According to WebMD, there are over 160 potential vaccines in different phases of research trials (<u>WebMD</u>). A leading scientist working with an organization that is raising funds to support vaccine trials and help build vaccine manufacturing capacity, feels there are two candidates most likely to succeed – Moderna's mRNA-1273 and AstraZeneca's AZD1222.

Any vaccine will require vaccination levels of at least 50% (if not more) to ensure herd immunity. In addition, it's possible that vaccine candidates won't stop Covid infection but may protect people from the most devastating effects of the disease.

A critical outstanding issue for any approved vaccine will be how to allocate it geographically and across categories of recipients. It's expected that the highest risk patients (individuals age 60+, frontline healthcare workers, first responders, etc.) will receive the vaccine first. In the US, the government will likely provide a framework for distributing the vaccine.

Here's more background on the two leading Covid vaccine candidates:

- Moderna mRNA-1273 (Moderna): mRNA-1273 is an RNA vaccine, a brand new type of vaccine that tricks the body into producing some of the viral proteins itself using messenger RNA. There are no mRNA vaccines currently licensed for production and use. Starting in July, mRNA-1273 will be the first experimental Covid vaccine to enter phase 3 trials (Fierce Biotech). The primary objective of this phase is to assess the vaccine's ability to prevent symptomatic Covid disease. In addition, the trial will assess the ability of the vaccine to prevent hospitalization and asymptomatic infection. A leading scientist has expressed concern about scaling up manufacturing of mRNA-1273 as there's no precedent for a fully commercialized messenger RNA vaccine.
- AstraZeneca AZD1222 (<u>AstraZeneca</u>): ADZ1222 is a recombinant adenovirus-based Covid vaccine candidate discovered by University of Oxford researchers that AstraZeneca will commercialize and manufacture. The vaccine contains the genetic material of Covid to trigger the body into producing its spike protein and attack the coronavirus upon infection. Given these types of vaccines are common, it's hoped that AZD1222 will pass through trials quickly. Phase 2 started in mid-May and will conclude shortly. A leading scientist believes this will be the most likely vaccine to be available at scale first with over 400 million doses already under contract (300 million of which will be delivered to the US) (<u>Fierce Pharma</u>).

Finally, there's some early findings from a big data research project suggesting that **individuals** who have received a Measles/Mumps/Rubella (MMR) or Shingles vaccine within the past 24 months may have up to 80% lower risk of Covid infection. The hypothesis is that the formulation of the MMR and Shingles vaccine using a live virus creates a strong antibody response in the body that helps protect against Covid. *This study has not yet been published nor peer reviewed.*