

# **TRENDS-in-MEDICINE**

### **BULLETIN:** UPDATE ON CORONAVIRUS 5/7

May 7, 2020 by Lynne Peterson

#### Be careful, be safe, and be well.

Mitigation efforts aimed at slowing the SARS-CoV-2 virus and Covid-19, the disease it causes, appear to be working in the U.S. and in many European countries. The peak likely has been reached in the U.S and in many European countries, and steps – mostly baby steps – are being taken to re-open economies. It seems increasingly unlikely that President Trump's prediction of a V-shaped U.S. recovery will occur in the U.S. or elsewhere. The outlook is for either a U-shaped recovery or a W-shaped recovery, if there is a second wave of Covid-19 this fall.

There are also predictions that there will be a second wave in the fall, likely coinciding with the annual flu season. A University of Buffalo epidemiologist predicted that social distancing will not be able to be discontinued in the U.S until mid-2020, and the pandemic won't really end until July 2022.

There will be another Coronavirus Update soon looking at the resumption of elective surgery and more.

**Worldwide**, more than 3.8 million people have been infected with the coronavirus. In the **United States**, total cases passed the 1.2 million mark. As of May 7, the virus has killed 268,887 people worldwide, with 28% of those in the U.S. (*See charts on Pages 14-16*)

Among the *countries* we are monitoring – looking over the past 10 days, not at just one point in time:

- The rate of *cases* per capita a good way to compare what is going on in different countries is highest in Spain at 0.54%, followed by the U.S. at 0.37% and Italy at 0.36%. This compares to a 0.05% rate worldwide. France, Italy, and Spain appear to have stabilized, but the U.K. continues to creep up. (See Chart 2A on Page 15)
- Looking at *fatality rates* (deaths per 100,000 people), Spain, again, is the worst at 55 (or roughly 1 in every 2,000 people). Germany is lowest at 9, followed by the U.S. at 22 (or roughly 1 in every 5,000 people), with most other European countries nearly double the U.S. rate (U.K. 45, France 39, Italy 49). Interestingly, Sweden has a higher rate (29) than the U.S., so its lack of a formal lockdown has not spared lives. In all the countries monitored, the fatality rate per 100,000 people rate has slowly but steadily increased over the last 10 days; none have stabilized, and worldwide, the rate has creeped up to 3.5. The comparison of France and the U.K. is particularly interesting, since they have comparable populations. (See Chart 2B on Page 15)
- On the key metric of *new cases per day*, there seems to be a steady increase worldwide. However, there is a flattening in Spain, Italy, and the U.S, though not the U.K. All of the states followed have flattened, and a couple New York and Washington are trending down. (See Chart 4 on Page 16)

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#### The virus

The **key questions** now about the virus include:

- *Did the virus accidentally escape from the Biosafety Level 4 laboratory in Wuhan, China?* Maybe, but that is still just a theory. What really has some governments around the world suspect was China's failure to give the world a timely alert (perhaps on purpose) about the dangers of this virus and to let experts into the country to study the virus. As President Trump pointed out, China banned flights out of Wuhan to other parts of China (e.g., Beijing) but continued to allow flights from Wuhan to other countries.
- *Is the virus man-made or genetically modified?* That idea appears to have been debunked. A statement by the U.S. Office of Director of National Intelligence said, "The Intelligence Community also concurs with the wide scientific consensus that the Covid-19 virus was not man-made or genetically modified."
- *Can patients get Covid-19 twice?* There were reports of 263 patients in South Korea who got the virus, cleared the virus, and then tested positive again, suggesting reinfections or reactivations, so no immunity. However, South Korean <u>researchers</u> now say the second positive tests were due to inactivated RNA from dead virus, not true positives because the RT-PCR tests used cannot differentiate between live and dead genetic viral material.
- **Do antibodies confer immunity to a new Covid-19 infection?** The FDA and other experts continue to caution that the presence of antibodies has not been proven to confer any immunity. And if there were immunity, there are no data on how long that immunity would last days, weeks, months, a year, forever?
- *Will the mutant strains all be susceptible to the same vaccine?* The original virus from China, which was the strain that first hit Washington state, is not the more contagious strain that has done so much harm in Europe and New York. Initially, the virus was not thought to mutate significantly, so the expectation was that a vaccine for SARS-CoV-2 would provide lifetime protection like a measles vaccine, rather than requiring a new vaccine yearly as with influenza.

The current thinking is that the spike mutations (and there are at least 14 of them) are not likely to make the virus immune to a general SARS-CoV-2 vaccine or to require a new vaccine each year because the mutations are not in a key area. However, that is still to be proven.

And a <u>study</u> – a computational analysis of 6,000 coronavirus sequences from around the world – by researchers at Los Alamos National Laboratory, posted on *BioRxiv.org*, found that the New York strain (D614G), while more highly transmissible, is not more lethal, but it may make people more vulnerable to a second infection. The researchers also warned that if the pandemic doesn't wane with summer, the virus could mutate further, potentially making the effectiveness of vaccines currently under study less effective and/or reducing any natural immunity from having Covid-19 the first time.

#### The world

- WHO. The World Health Organization extended its declaration that the Covid-19 pandemic continues to warrant a public health emergency of international concern. WHO's Covid-19 emergency committee recommended development of guidance for the resumption of passenger travel and expressed concern about disruptions of food and supply shipments in some countries.
- **BRIC.** China continues to report nearly flat cases and deaths (if those data are believable), but the other BRIC countries Brazil, Russia, and India are still in the upward trajectory. India is planning to repatriate hundreds of thousands of its citizens stranded abroad.
- International travel. Travel around the world has virtually ground to a halt, and there are no signs this is likely to improve in the near future (or even for many months). Many countries are banning travelers and/or quarantining new arrivals for 14 days, which pretty much ends movement. Australia and New Zealand are considering a "trans-Tasman bubble," that would allow travel between the two countries only.

Austria declared the outbreak now under control.

#### France

- The first case of Covid-19 in France was likely a patient in a hospital near Paris thought to have pneumonia on December 27, 2019, who actually had Covid-19. This indicates the virus reached Europe earlier than previously thought.
- The country will start to loosen restrictions on May 11. Prime Minister Édouard Philippe told Parliament, "We are going to have to learn to live with the virus. We must learn to live with Covid-19 and to protect ourselves from it."
- All incoming travelers will be quarantined for 14 days.
- Germany Federal tourism commissioner Thomas Bareiss said Germans may be able to travel for vacations this summer to certain European locations (e.g., Austria, Belgium, France, Greece, Majorca, Netherlands, Poland), but details are being worked out.
- India After a lockdown slowed/halted production in Baddi, India, this pharma production hub is back at work, though supply chain concerns remain.
- Iran allowed 132 mosques in lower risk areas and drive-in movie theaters (for the first time since 1979) to re-open.
- Japan The government extended the state of emergency until the end of May. The island of Hokkaido, which was the first place in the country hit with the virus, is back in lockdown after lifting the shutdown resulted in a new outbreak.
- U.K. The U.K. has become the hardest hit country in Europe, with the highest total number of deaths even higher than Spain or Italy but the U.K.'s per capita death rate is still lower than Spain or Italy. The best comparison for the U.K. may be France because the two countries have similar populations (~67 million), and the U.K. has a higher per capita case rate, a higher per capital death rate, more total cases, and more total deaths than France. Prime Minister Boris Johnson says the U.K. is "past the peak" of the coronavirus outbreak.

#### **United States**

- U.S. fatality rate. President Trump predicted that deaths from Covid-19 in the U.S. are likely to be about 100,000, far above the 74,073 estimate from the University of Washington's Institute for Health Metrics and Evaluation (IHME) on April 28. Then, the next day IHME once again raised its estimate of projected U.S. deaths through August 4, 2020, this time to 134,475, its highest estimate yet. The continuous changes in the IHME projections, first step-wise down from the initial 90,000, then steadily up, raise questions about the reliability of any of its estimates or "adjustments." This suggests that the estimate that the pandemic won't end until July 2022 might need to be given more credence.
- Contact tracing. As the economy opens up, testing and contact tracing gain even more importance. This is a well respected system for limiting disease outbreaks, but to use it in a pandemic situation requires a scale far above what Centers for Disease Control and Prevention (CDC) is capable of doing nationwide by itself. Contact tracing means anyone who a Covid-19-positive patient may have exposed will need to be contacted and tested. It's a big job. New York Gov. Andrew Cuomo estimated it will take an "army" of tracers, estimating that could mean 6,400-17,000 tracers in New York alone. In states with fewer cases of Covid-19, state and local health departments may be able to handle the tracing.
- **Cruises.** Carnival Cruise Line said it will resume cruises with just 8 of its 109 ships in August 2020 at ports where most passengers arrive by car instead of by plane, and it has a waiting list of people anxious to take a cruise. On the other hand, Norwegian Cruise Line said it may have to file for bankruptcy.

#### Economic situation

• Total unemployment in the last 6 weeks has risen to more than 33 million.

- Treasury Sec. Steven Mnuchin said that paycheck protection program (PPP) loans above \$2 million from the small business administration will get a full audit to make sure they are valid.
- Meat packing plants. Outbreaks have been extensive, leading to closures, creating backups in the supply chain and shortages at stores and restaurants. President Trump invoked the Defense Production Act (DPA) to order the plants to remain open. The problem is both finding a way to add social distancing to a workplace not conducive to that and finding workers not infected and willing to work. More than 6,500 workers (~3% of all workers) in 115 meat processing facilities across 19 states have been infected with 30 deaths. Note: The FDA insists the virus is not spread on or through food.
- Nursing homes and long-term care facilities. There are ~15,600 nursing homes in the U.S, with ~1.3 million residents. More than 7,000 nursing home patients in the U.S. have died from Covid-19 (including ~4,800 in New York, >1,500 in New Jersey, 395 in Texas, and 325 in Florida). Nursing home deaths account for ~64% of Covid-19 deaths in Colorado, 45% of Texas deaths, and ~10% nationally.

Pets. Two tigers, a lion, two cats, and a dog have caught Covid-19 in the U.S., and the CDC is now recommending social distancing for pets. But they don't need to wear masks.

- **Schools.** All but 4 states canceled school for the rest of this school year.
- Sequencing. The CDC announced a consortium aimed at expanding the use of whole genome sequencing (WGS) of the SARS-CoV-2 virus <u>SPHERES</u> (Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance). The national network will connect sequencing laboratories to speed release of SARS-CoV-2 sequence data into the public domain.
- **Stay-at-home orders.** At least 21 states loosened their stay-at-home orders on May 1, and 31 will have done that by May 11. However, Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), said he is "concerned that some states are leapfrogging over the first checkpoint [in the Task Force guidelines]."
- Toilet paper shortage. In the first few days/weeks of the stay-at-home orders, a shortage of toilet paper might have been understandable as people stocked up on that as well as food and other supplies. However, the shortage has continued. It is still hard to find toilet paper and other paper products. Why is the shortage continuing? One reason may be that, with people staying home, they are using their bathroom more often instead of public restrooms and public restroom toilet paper can't just be switched to consumer use.

#### Travel

- TSA said travel last week was up 20% over the previous week.
- Most airlines said they won't assign the middle seat, flight attendants will wear a mask, and passengers will be required to wear a mask. There is also discussion of some form of testing of passengers at airports, but those details are not yet worked out.
- White House Coronavirus Task Force. Vice President Pence said there are preliminary discussions ongoing at the White House about phasing out this task force on or before mid-June. President Trump initially said there needs to be a different group set up for the re-opening, but then he said that the Coronavirus Task Force will continue indefinitely.

#### **President Trump**

- Did not extend the federal government social distancing guideline when they expired on May 1, leaving re-opening decisions to the governors.
- Said Dr. Fauci will be allowed to testify before a Senate committee but that none of the White House Coronavirus Task Force members will be testifying at this time before any House committees.

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#### U.S. states and cities

Only a few states have not yet peaked in Covid-19 cases – Arkansas, Mississippi, Nebraska, North Dakota, South Dakota, and Utah. By May 15, all of these are expected to have peaked.

States are starting to re-open. By the end of this week at least 14 states are likely to have eased restrictions. Most of those opening have Republican governors, and most of the strictest closures are in states with Democratic governors. Most governors (even Republican governors) are *not* following the White House Coronavirus Task Force guidelines but are making their own decisions on timing and what to open. This prompted Dr. Fauci to say on CNN, "How many deaths and how much suffering are you willing to accept to get back to what you want to be some form of normality sooner rather than later?"

The things on which all governors appear to agree:

- Continuing the no visitation rule for nursing homes remains in place.
- When restaurants open, inside seating is or will be restricted to 25% capacity.
- No large gatherings or fans at sporting events. Dr. Fauci said, "We are not ready for sports to resume this year."
- At least some elective surgeries can resume.
- Masks should be used in public, but that is voluntary in some states and mandatory in others.

There is no agreement on the re-opening of:

- Barbershops and hair salons open in Georgia, closed in California.
- Movie theaters open in Texas, closed in most states.
- Beaches closed in Orange County, California; open in Texas and most of Florida.
- **California** Los Angeles is offering free coronavirus testing for all *residents*, and there is no limit on how many times a person can be tested (at least for now).
- Maryland will open Ocean City boardwalk beaches on May 9 but only to residents, though police reportedly will not be checking license plates or IDs. This sounds like a prescription for a crowd since relatively few people live there compared to the number of people who have vacation condos/homes there.
- Massachusetts started adding people who die at home from apparent, not necessarily confirmed, Covid-19 to the state's official numbers. The state also is going back and examining death certificates as far back as March 1, 2020, to catch victims who may have been missed in the official numbers.
- Michigan Gov. Gretchen Whitmer extended her blanket stay-at-home order until May 28, despite protests.
- New York
  - Gov. Andrew Cuomo said on April 29<sup>th</sup> that new hospitalizations had declined for 15 straight days, and on May 5<sup>th</sup> he said the state is coming down the other side of the mountain.
  - Preliminary results from a 3-day survey of 100 New York state hospitals found that 66% of the people hospitalized were people who claimed they had been staying at home (either retirees or unemployed) and 22% were from nursing homes and assisted living facilities. In New York City, 45% of patients in the survey were African-American or Latino. Gov. Cuomo called the findings "shocking." *How did people at home get the virus if they were really staying home?*
  - Gov. Cuomo ordered the closure of New York City subways every day from 1am to 5am for disinfecting. One thing being used to kill the coronavirus on subways is: ultraviolet light. (Yes, UV lights.)

- Thomas Frieden, MD, MPH, the former head of the CDC, said two months (March and April 2020) of deaths in New York were worse than any 2-month period during the 1917 Spanish flu.
- The emergency Covid-19 hospital that the Army Corps of Engineers created at the Javits Center Covid-19 hospital was dismantled, and the USNS Comfort returned to Norfolk.
- At least 25 children (mostly in New York but also elsewhere in the country) have been hospitalized with symptoms that *might* be related to the coronavirus. Instead of the respiratory symptoms generally seen in adults with Covid-19, the children are presenting with a rash, eye redness, and/or circulatory problems. The syndrome is being referred to as "pediatric multisystem inflammatory syndrome." It appears similar to Kawasaki disease, a rare childhood illness that can lead to inflammation of the blood vessels, particularly the coronary arteries. The children are generally responding to treatment.
- A federal judge ordered the state to hold its Democratic presidential primary on June 23, as originally planned.
- Texas Nearly half the people who have died in Texas were in a nursing home or assisted living facility (395 of 884 as of May 3).

#### **Regulatory news**

- The Centers for Medicare and Medicaid Services (CMS)
  - Increased payments for **telehealth** visits by  $\sim 140\%$  and agreed to cover telehealth physical therapy.
  - Suspended the **Advance Payment Program** for physicians that had been put in place in late March to help offset the financial damage to healthcare providers from the Covid-19 pandemic.
  - Eased the requirements for coverage of Covid-19 tests.
  - Detailed how hospitals can protect staff and patients as they re-open for non-emergent (and non-Covid-19) care.
- Litigation. Senate Majority Leader Mitch McConnell (R-KY) said the Senate will not pass more coronavirus relief unless there is also legislation to protect businesses from health and safety lawsuits related to Covid-19 in order to prevent a post outbreak "lawsuit pandemic."

#### The FDA

- Created a new "umbrella" pathway for serology (antibody) tests seeking an emergency use authorization (EUA). Under this pathway, the tests will be submitted to an interagency testing group and will be run against a panel of ~30 samples confirmed positive for anti-SARS-CoV-2 antibodies as well and 80 pre-Covid-19 samples that are antibody negative. This will help determine the test's specificity and sensitivity in a standardized fashion.
- The FDA released new <u>guidance</u> outlining exclusions and exemptions to certain Drug Supply Chain Security Act requirements as a result of Covid-19. The exemptions apply to distribution of drugs under an EUA and to other products approved for diagnosing, treating, preventing, mitigating, and curing Covid-19.
- Senate Democrats introduced a bill that would federalize the medical supply chain and increase production of personal protective equipment (PPE), testing supplies, and other items needed for Covid-19 treatment. The Senators said they would push to have this bill included in the next Covid-19 relief/stimulus package. The legislation would establish a new executive officer to oversee the production of supplies and to issue weekly reports on the supplies that are needed. The executive officer would then be required to issue purchase orders under the Defense Production Act for those needed supplies and oversee their distribution.

#### Medical supplies and drug shortages

**Antibiotics.** According to a 2019 <u>estimate</u>, 90% of the generic drugs Americans take come from either China or India. Of particular concern: no generic antibiotics are made in the U.S., and there haven't been any plants making penicillin in the U.S. since 2004. This dependence on China, and to a lesser extent, India, has some experts (and some legislators) very concerned.

**Disinfection.** Xenex Disinfection Services has a \$125,000 ultraviolet light <u>robot</u> for eradicating coronavirus from rooms and masks, and an analysis of the technology by the non-profit Texas Biomedical Research Institute said the device actually works. Texas Biomed estimated that the robot cleans surfaces in 2 minutes and N95 masks in 5 minutes.

#### Ventilators and related devices

- ALung Technologies' <u>Hemolung</u>, a respiratory assist system for reducing the need for invasive mechanical ventilation and intubation, was granted an EUA.
- Baxter's Oxiris filter set was granted an EUA to help reduce levels of inflammatory cytokines.
- NASA's Ventilator Intervention Technology Accessible Locally (VITAL), a high-pressure ventilator designed for Covid-19 patients, was granted an EUA.
- Nvidia's OP-Vent The design for this low-cost (~\$400), open-source ventilator a device that can be manufactured from off-the-shelf parts was made public.

#### **Diagnosis of Covid-19**

**CT.** In a study of 23 patients who were asymptomatic for Covid-19, published in the *American Journal of Roentgenology*, and who received an abdominopelvic CT for gastrointestinal symptoms found ground-glass opacities in the lower lungs of the patients, and 17 of those patients tested positive for Covid-19 on an RT-PCR test. The researchers suggested the findings should prompt radiologists identifying lung-base ground-glass opacities in abdominopelvic CTs to promptly alert the referring clinician that there is a possible Covid-19 infection.

**Rapid Acceleration of Diagnostics (RADx) initiative.** The National Institutes of Health (NIH) announced a \$1.5 billion push (with stimulus funds) to develop Covid-19 diagnostics – not antibody tests. NIH issued a "national Covid-19 testing challenge," urging scientists, inventors, and innovators to compete for a share of a \$500 million pool earmarked for diagnostic development. Successful entrants will be matched with manufacturers and business experts who can help to scale up production quickly of any tests developed during the project.

In RADx, NIH will work closely with the FDA, CDC, and the Biomedical Advanced Research and Development Authority (BARDA). NIH Director Francis Collins, MD, PhD, said he hopes to harness "American ingenuity" to solve the problem of a simple, inexpensive, readily available Covid-19 test, one that can be scaled up quickly (by late summer or fall) so that millions of tests can be deployed weekly.

There are four phases to this challenge, which will be overseen by Bruce Tromberg, PhD, director of NIH's National Institute of Biomedical Imaging and Bioengineering (NIBIB):

- 1. Submissions, rather like a "Shark Tank" and NIH expects about 100 applications to be submitted.
- 2. Validation
- 3. Risk assessment
- 4. Clinical testing and regulatory approvals

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Among the Covid-19 *diagnostic* tests that recently got an EUA from the FDA are:

- AIT Laboratories' SARS-CoV-2 Test
- Altona Diagnostics' RealStar SARS-CoV-2, real-time PCR kit for research use only
- Autobio Diagnostics' Anti-SARS-CoV-2 Rapid Test
- Biocerna's RT-PCR test, a modified version of Thermo Fisher Scientific's TaqPath Covid-19 test
- GenoSensor's GS Covid-19 RT-PCR kit
- Hologic's Aptima SARS-CoV-2 test, a molecular test that runs on its Panther system, was submitted for an EUA
- KorvaLabs' Curative-Korva SARS-CoV-2 Assay
- LabGenomics' LabGun Covid-19 RT-PCR Kit
- MicroGenDX' Covid-19 Key assay
- Nationwide Children's Hospital's SARS-CoV-2 assay
- Ortho Clinical Diagnostics' VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack and Calibrators
- Rheonix's Rheonix Covid-19 MDx Assay
- SD Biosensor's Standard M nCoV Real-Time Detection kit
- Seasun Biomaterials' U-TOP Covid-19 Detection Kit
- Ultimate Dx's UDX SARS-CoV-2 Molecular Assay

And the European Medicines Agency (EMA) granted a CE-IVD Mark to some additional tests, including:

- BAG Diagnostics' ViroQ SARS-CoV-2 rapid PCR test
- JN Medsys' ProTect Covid-19 RT-qPCR kit
- Vela Diagnostics' ViroKey SARS-CoV-2 RT-PCR Test

Tests on the horizon:

• **E25Bio** is developing a Covid-19 antigen <u>test</u> that uses nasal swab from a patient, puts it into a solution, then exposes the solution to one end of a series of paper strips (rather like a home pregnancy test). The strips contain artificial antibodies specially designed to bind to coronavirus antigens. As the solution moves up the strip, any antigens that are present will bind to it and give a visual readout. The whole thing takes less than 30 minutes, and it doesn't require special equipment or training. A company official said it could be priced as low as \$10.

But before you get too excited about this, Alan Wells, MD, DMSc, the medical director of clinical laboratories at the University of Pittsburgh Medical Center, cautions, "It won't work." Why? He explained that antigen tests are good for bacterial diseases but not viruses, and the efficacy may depend on the ability to collect a good nasal swab. For example, the sensitivity of an antigen test for influenza has a sensitivity of 70%-80%, even with a good nasal swab.

• Sanofi is partnering with Luminostics to develop a smartphone-based Covid-19 test.

#### Antibody (serology) testing

Demand for these tests has skyrocketed but so has the misunderstanding about what they can and cannot do. Basically, these tests can identify people who have antibodies to Covid-19, which means they were exposed to the virus, whether they got sick and recovered or were asymptomatic. Antibody positivity makes people potential donors for convalescent plasma, and it provides epidemiologists with a picture of the spread of the virus within the general population.

The problem is there still is no evidence that a person with antibodies has any immunity to SARS-CoV-2 or, if there is immunity, how long it lasts.

The FDA and NIH continue to remind people of this, but there remains a popular misconception about immunity related to a positive test. And the specificity and sensitivity of the tests are still unclear. The White House proposed that, in some circumstances, <u>two antibody tests</u> be administered to the same person. And the WHO <u>warned against plans</u> for proposed "immunity passports," which would allow people who have recovered from the coronavirus to resume unrestricted travel and work.

Yet, there are a growing number of antibody tests getting either an EUA from the FDA or a CE Mark from the EMA, and there are more than 180 in development. The latest antibody tests include:

- Abbott's SARS-CoV-2 IgG antibody test, which claims 99% sensitivity and specificity EUA and CE Mark
- Erba Mannheim's ErbaLisa Covid-19 antibody Elisa detection kit CE Mark
- **Quest Diagnostics**' Covid-19 antibody test, which consumers can buy online for \$119.
- Quotient's MosaiQ Covid-19 antibody microarray test, which claims 99.8% accuracy CE Mark
- Roche's Elecsys Anti-SARS-CoV-2 antibody test, which claims specificity >99.8% and sensitivity of 100% EUA and CE Mark
- Siemens Healthineers' fast total antibody test for SARS-CoV-2, which claims specificity and sensitivity of >99% not yet approved

## The question is why any consumer would pay for any of these tests since there is no useable information beyond the ability to donate plasma.

#### Treatments

■ Gilead Sciences' <u>remdesivir</u>, a direct-acting antiviral (an RNA polymerase inhibitor), was granted an EUA – not approval – for treating *hospitalized* Covid-19 patients. This is the first drug with an EAU for treating Covid-19 that has randomized trial data to back it up. Dr. Fauci called the results of that trial "quite good news," adding, "This is really quite important. What it has proven is that a drug can block this virus." He said remdesivir is now the "new standard of care" for all other trials.

In preliminary results from the 1,063-patient <u>ACTT</u> trial (at 47 sites in the U.S and 21 in Europe and Asia) sponsored by NIAID, remdesivir was shown to shorten the time to recovery from 15 days to 11 days, on average, a significant improvement vs. placebo (p<0.001). However, it did *not* have a significant effect on mortality (8.0% vs. 11.6%, p=0.059), the secondary endpoint, which means it failed on that endpoint, and describing it as a "trend toward a benefit" is inappropriate. And those were the only trial results or details released.

Dr. Fauci compared remdesivir to AZT for HIV, saying, "When I was looking at these data with our team, it was reminiscent of 34 years ago in 1986 when we were struggling for drugs for HIV...and there were a lot of anecdotal

reports...We did the first randomized trial with AZT...which had a modest effect...That was not the end game...but building on that...we had better drugs."

Dr. Fauci said remdesivir is "opening the door" to other improved therapies. The next step for NIAID is going to be a trial of remdesivir with a monoclonal antibody – reportedly Lilly's Olumiant (baricitinib), a JAK inhibitor. Dr. Fauci predicted, "As more investigators get involved, it will get better and better."

Asked if remdesivir will change the vaccine timeline, Dr. Fauci said No.

Asked about a negative study out of China, and published in **The Lancet**, which found no significant benefit to remdesivir, Dr. Fauci said that study was "underpowered...That was not an adequate study, and everyone in the field feels that way."

Conditions on use. The FDA put some specific conditions on the use of remdesivir:

- Distribution has to be controlled by the government, with Gilead supplying remdesivir to authorized distributors or directly to a U.S. government agency, who will distribute it to hospitals and other healthcare facilities, in collaboration with state/local authorities.
- Patients must have suspected or laboratory confirmed Covid-19.
- Patients must have severe disease, defined as blood oxygen saturation ≤94% on room air, the need for supplemental oxygen or mechanical ventilation or extracorporeal membrane oxygenation (ECMO).
- Remdesivir must be administered in an inpatient hospital setting. *Remember, it is an IV drug.*
- Use must be accompanied by a Fact Sheet for healthcare providers and another one for patients and parents/caregivers.

**Price.** Gilead is donating 1.5 million doses to the government (enough to treat 140,000 patients). Beyond that, there is no word yet on how Gilead will price the drug. The Institute for Clinical and Economic Review (<u>ICER</u>) said remdesivir would be cost-effective at \$4,460 per course of treatment.

**Supply.** The next question is whether Gilead can meet demand for remdesivir. The company hopes to have enough remdesivir to treat another 360,000 patients by October 2020 and 1 million patients by the end of 2020. While the company is considering possible licensing applications, it is concerned about not creating a shortage of the active pharmaceutical ingredients. **And** President Trump said the drug is not easy to make.

**Distribution.** The authorized distributor is AmerisourceBergen, but it is only the physical distributor. The Federal Emergency Management Administration (FEMA) said the Department of Health and Human Services (HHS) is making the decisions about where the drug goes. How HHS is choosing which hospitals get the drug is still unclear. There is an unconfirmed report that ~2 hospitals have gotten remdesivir. Massachusetts General Hospital is one of them. Mass Gen got enough remdesivir for ~170 patients, though it had 381 Covid-19 patients at the time, while other Boston hospitals with Covid-19 patients (e.g., Beth Israel Deaconess Medical Center with 248 cases and Boston Medical Center with 238 cases) didn't get any. Likewise, Northwestern Medical Center, the University of California San Francisco, and the University of Michigan didn't get any.

Outside the U.S., the demand is also going to be high, and Gilead will have to balance that with U.S. demand.

- Japanese Prime Minister Shinzo Abe said remdesivir is expected to get a fast track review after approval elsewhere (i.e., the U.S.) to treat Covid-19.
- The EMA started a rolling review of remdesivir.

**Treatment duration.** The open-label, Phase III SIMPLE trial compared a 10-day course of remdesivir treatment with a 5-day course, and in top-line results the shorter course was the winner.

- Improvement in clinical status was comparable.
- Time to improvement for 50% of patients was 10 days with the short course and 11 days with the longer course.
- 60.0% of short-course patients were discharged from the hospital by Day 14 vs. 52.3% of longer course patients.
- At Day 14, 64.5% of the short-course patients vs. 53.8% of longer course patients achieved clinical recovery.
- Outside of Italy, overall mortality at Day 14 was 7% with both regimens, with 64% vs. 61% of patients discharged from the hospital.
- In an exploratory analysis, patients who received remdesivir within 10 days of symptom onset had improved outcomes vs. patients treated >10 days after onset of symptoms. When data were pooled across treatment arms, by Day 14 62% of patients treated early were able to be discharged from the hospital vs. 49% of patients who were treated late.
- No new safety signals were identified.
- The most common adverse events with both regimens were nausea (10.0% vs. 8.6%), acute respiratory failure (6.0% vs. 10.7%). Grade ≥3 ALT elevations occurred in 7.3% of patients, with 3.0% discontinuing treatment as a result.

#### Convalescent plasma

- There have been anecdotal reports of the efficacy of this therapy, but it has been used in 7,200 people in the past couple of months. Data on those patients are being analyzed, will be released in a couple of weeks, and should offer some useful insights, but it is not a randomized study.
- The FDA issued <u>guidance</u> for healthcare providers and investigators on the administration and study of *investigational* convalescent plasma collected from people who have recovered from Covid-19, with recommendations on patient eligibility, donor eligibility/qualifications, labeling, recordkeeping, and more.
- Johns Hopkins plans to start enrolling patients next week into two randomized clinical trials of convalescent plasma in the *outpatient* setting, with results expected in a couple of months:
  - ✓ A preventive study in nursing home patients to see if convalescent plasma will prevent them from catching Covid-19.
  - ✓ A treatment study in people with confirmed Covid-19 who are remaining at home to see if giving them convalescent plasma at home will prevent them from worsening to the point they need to be hospitalized.

Asked how many recovered Covid-19 patients would qualify to donate plasma, Arturo Casadevall, MD, PhD, chair of the Department of Molecular Microbiology and Immunology at the Johns Hopkins Bloomberg School of Public Health, said, "The majority have high titers of antibodies...However, a small percentage have antibodies but not very high levels...And it depends on the antibody test used. They are not standardized very well. We are using an Elisa test developed at Mount Sinai."

Hydroxychloroquine (HCQ). President Trump is one of the few people still speaking out positively about HCQ, though he isn't pushing it as hard as he used to do. Some states are still stockpiling it. So, is it safe? Does it work? Two non-definitive but positive trials were reported recently.

- A 568-patient retrospective Chinese study, available as a <u>preprint</u> on **medRxiv.org**, looked at critically ill Covid-19 patients who had severe acute respiratory distress syndrome (ARDS) despite antiviral + antibiotic therapy. Of the 568 patients, 48 also received HCQ (200 mg BID for 7-10 days).
  - ✓ Mortality (the primary endpoint) was 18.8% with HCQ vs. 45.8% without it.
  - ✓ Length of stay before death was 15 days with HCQ and 8 days without it.

- ✓ IL-6 levels were significantly lowered by the end of treatment with HCQ but not without it.
- The researchers concluded that HCQ significantly decreased mortality in critically ill patients through attenuation of inflammatory cytokine storm and should be prescribed for treatment of critically ill Covid-19 patients.
- A 1,061-patient retrospective analysis of HCQ in Marseille, <u>France</u>, in preprint, in which HCQ was combined with azithromycin, found that:
  - ✓ 91.7% had a good clinical outcome and virological cure within 10 days.
  - ✓ 4.3% of patients had a poor clinical outcome, and 8 died (0.75%). All the deaths were from respiratory failure, not cardiac toxicity.
  - ✓ Poor clinical outcome was associated with older age, severity at admission, and low HCQ serum concentration.
  - The researchers concluded that the combination of HCQ + azithromycin is safe and associated with a very low fatality rate.
- The **negative news.** A <u>report</u> on 90 Covid-19 patients treated at a Boston hospital, published in *JAMA Cardiology*, found a potential for serious cardiac arrhythmias significant QTc prolongation (>500 ms). One patient developed torsade de pointe when given HCQ + azithromycin.
- Roche's Actemra (tocilizumab). This anti-IL-6R met the primary endpoint in the 129-patient French CORIMUNO-19 trial in hospitalized patients with moderate-to-severe Covid-19, with significantly fewer patients needing ventilation (mechanical or non-invasive) or dying by Day 14. The results have not yet been published. This drug makes sense because it is already used to treat cytokine storms in immunotherapy patients, and a key issue with Covid-19 is cytokine storm.
- **WHO** announced the launch of Access to COVID-19 Tools Accelerator, a global project focused on developing and producing new treatments, vaccines, and tests for Covid-19, while ensuring global access to the products.
- Among *other therapies* to add to the long list of drugs in development to treat Covid-19 are:
  - AbCellera and Lilly are collaborating on research for development of an antibody to treat Covid-19, and AbCellera got some help (up to \$175.6 million) from the Canadian government's Innovation, Science, and Economic Development Canada Strategic Innovation Fund.
  - BerGenBio's bemcentinib, an oral selective AXL inhibitor A 120-patient Phase II trial has started in the U.K. in hospitalized Covid-19 patients.
  - CAR T Researchers at Duke-NUS Medical School in Singapore are studying whether there might be utility for CAR-T and/or TCR-T therapies in Covid-19.
  - Karyopharm Therapeutics' Xpovio (selinexor) The company announced the first patient was dosed with this cancer drug in a Phase II trial in severely ill Covid-19 patients.
  - Johnson & Johnson and Merck's Pepcid (<u>famotidine</u>) given IV at a dose 9-times the over-the-counter dose of this heartburn drug is being tested in a clinical trial in New York City by Northwell Health.
  - **Sarepta Therapeutics** is initiating a discovery program to see if some of its antisense oligonucleotides can inhibit viral infection.

Repurpo	sed Drugs Bein	g Investigated	for Covid-19
Company	Brand name	Generic name	Target
Alexion Pharmaceuticals	Ultomiris	ravulizumab	C5 complement inhibitor
Amgen	Otezla	apremilast	PDE4 inhibitor
AstraZeneca	Farxiga	dapagliflozin	SGLT2 inhibitor
Johnson & Johnson and Merck	Pepcid	famotidine	H2 blocker
Novartis and Incyte	Jakafi	ruxolitinib	oral JAK inhibitor (for ventilator patients)
	Cosentyx	secukinumab	anti-IL-17A
Novartis	Diovan	valsartan	ARB
	Ilaris	canakinumab	interleukin-1 $\beta$ inhibitor
	Xolair	omalizumab	IgE inhibitor
Pulmotect		inhaled superoxide	
Synairgen		SNG-001	inhaled interferon beta-1a

#### Vaccines

- AstraZeneca is collaborating with Oxford University on the vaccine Oxford developed. Oxford took an existing chimp vaccine and engineered it to work for SARS-CoV-2, did efficacy studies in monkeys, and has now started a Phase I safety trial in healthy volunteers. The researchers predicted the vaccine could be ready by fall 2020.
- **Leukocare, ReiThera,** and **Univercells** are collaborating on development of a novel adenoviral vector-based vaccine for Covid-19. They hope to launch a clinical trial this summer and begin manufacturing alongside clinical development.
- Moderna, which has the lead in vaccine development and the support of NIAID, is advertising to fill a number of positions across Clinical, Quality, Technical Development, Drug Manufacturing, and Digital.
- The Trump administration is working on a Manhattan Project-style initiative, Operation Warp Speed, to spur rapid development of a SARS-CoV-2 vaccine, with the aim of having a vaccine ready for use by the end of this year. The hope is that 3-4 of the 14 promising vaccines already in development will survive and be successful.

May 7, 2020/Coronavirus

#1A Worldwide Covid-19 Statistics – Daily Cases													
		April 26		ļ	April 27		A	pril 28			April 29		
Country	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	
Worldwide	2,972,315	206,565	6.9%	3,057,957	211,894	6.9%	3,116,398	217,153	7.0%	3,193,886	227,638	7.1%	
U.S.	965,910	54,876	5.7%	988,197	56,253	5.7%	1,012,517	58,355	5.8%	1,039,909	60,966	5.9%	
Spain	226,629	23,190	10.2%	229,422	23,521	10.3%	232,128	23,822	10.3%	236,899	24,275	10.2%	
Italy	197,675	26,644	13.5%	199,414	26,977	13.5%	201,505	27,359	13.0%	203,591	27,682	13.6%	
France	162,220	22,890	14.1%	165,842	23,293	14.0%	169,053	23,694	14.0%	166,543	24,121	14.5%	
U.K.	154,037	20,795	13.5%	157,149	21,092	13.4%	162,350	21,745	13.4%	166,441	26,166	15.7%	
Germany	157,770	5,976	3.8%	158,758	6,126	3.9%	159,912	6,314	3.9%	161,539	6,467	4.0%	
Sweden	18,640	2,194	11.8%	18,926	2,274	12.0%	19,621	2,355	12.0%	20,302	2,462	12.1%	
China	83,912	4,637	5.5%	83,938	4,637	5.5%	83,938	4,637	5.5%	83,944	4,637	5.5%	

https://coronavirus.jhu.edu/map.html www.statista.com/statistics/1102203/cumulative-coronavirus-cases-in-sweden/ www.worldometers.info/coronavirus/country/uk/

#1B Worldwide Covid-19 Statistics – Daily Cases													
		April 30			May 1		1	May 2			May 3		
Country	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	
Worldwide	3,276,373	233,997	7.1%	3,344,402	238,787	7.1%	3,427,343	243,808	7.1%	3,506,924	247,473	7.1%	
U.S.	1,095,023	63,856	5.8%	1,103,781	65,068	5.9%	1,132,539	66,369	5.9%	1,158,041	67,682	5.8%	
Spain	239,639	24,543	10.2%	242,979	24,543	10.1%	245,589	25,100	10.2%	246,133	25,264	10.3%	
Italy	205,463	27,976	13.6%	207,428	28,236	13.6%	209,328	28,710	13.7%	210,717	28,884	13.7%	
France	167,178	24,376	14.6%	167,305	24,628	14.7%	168,518	24,763	14.7%	168,925	24,900	14.7%	
U.K.	171,253	26,771	15.6%	178,685	27,583	15.4%	183,500	28,205	15.4%	187,842	28,520	15.2%	
Germany	163,009	6,623	4.1%	164,777	6,736	4.1%	164,967	6,812	4.1%	165,664	6,866	4.1%	
Sweden	21,092	2,586	12.3%	21,520	2,653	12.3%	22,082	2,669	12.1%	22,317	2,679	12.0%	
China	83,944	4,637	5.5%	83,959	4,637	5.5%	83,959	4,637	5.5%	83,964	4,637	5.5%	

	#1C Worldwide Covid-19 Statistics – Daily Cases													
		May 4			May 5			May 6						
Country	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate					
Worldwide	3,582,469	251,510	7.0%	3,662,691	257,207	7.0%	3,769,150	264,111	7.0%					
U.S.	1,180,634	68,934	5.8%	1,204,351	71,064	<b>5.9</b> %	1,228,609	73,431	6.0%					
Spain	248,301	25,428	10.2%	250,561	25,613	10.2%	253,682	25,857	10.2%					
Italy	211,938	29,079	13.7%	213,013	29,315	13.8%	214,457	29,684	13.8%					
France	169,583	25,204	14.9%	170,687	25,537	15.0%	174,224	25,812	14.8%					
U.K.	191,832	28,809	15.0%	196,243	29,501	15.0%	202,359	30,150	14.9%					
Germany	166,152	6,993	4.2%	167,007	6,993	4.2%	168,162	7,275	4.3%					
Sweden	22,721	2,760	12.1%	23,216	2,854	12.3%	23,918	2,941	12.3%					
China	83,966	4,637	5.5%	83,968	4,637	5.5%	83,970	4,637	5.5%					

#### May 7, 2020/Coronavirus

#2A Worldwide Per Capita <i>Case</i> Rate													
Country	Population	April 25	April 26	April 27	April 28	April 29	April 30	May 1	May 2	May 3	May 4	May 5	May 6
Worldwide	7,577 million	0.04%	0.04%	0.04%	0.04%	0.04%	0.04%	0.04%	0.05%	0.05%	0.05%	0.05%	0.05%
U.S.	330 million	0.28%	0.29%	0.30%	0.31%	0.32%	0.33%	0.33%	0.34%	0.35%	0.36%	0.36%	0.37%
Spain	47 million	0.48%	0.48%	0.49%	0.49%	0.50%	0.51%	0.45%	0.46%	0.46%	0.46%	0.47%	0.54%
Italy	60 million	0.33%	0.33%	0.33%	0.35%	0.34%	0.34%	0.35%	0.35%	0.35%	0.35%	0.36%	0.36%
France	67 million	0.24%	0.24%	0.25%	0.25%	028%	0.25%	0.25%	0.25%	0.25%	0.25%	0.25%	0.26%
U.K.	67 million	0.22%	0.23%	0.23%	0.24%	0.25%	0.26%	0.27%	0.27%	0.28%	0.29%	0.29%	0.30%
Germany	83 million	0.19%	0.19%	0.19%	0.19%	0.19%	0.20%	0.20%	0.20%	0.20%	0.20%	0.20%	0.20%
Sweden	10 million	0.18%	0.19%	0.19%	0.20%	0.20%	0.21%	0.22%	0.22%	0.22%	0.23%	0.23%	0.24%
China	1,386 million	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%	0.006%

Source: https://covidtracking.com/data/

#2B Worldwide Per Capita <i>Fatality</i> Rate: Deaths per 100,000 People													
Country	Population	April 25	April 26	April 27	April 28	April 29	April 30	May 1	May 2	May 3	May 4	May 5	May 6
Worldwide	7,577 million	2.7	2.7	2.8	2.9	3.0	3.0	3.2	3.2	3.3	3.3	3.4	3.5
U.S.	330 million	16	17	17	18	18	19	20	20	21	21	22	22
Spain	47 million	49	49	50	51	52	52	52	53	54	54	54	55
Italy	60 million	44	44	45	46	46	47	47	48	48	48	49	49
France	67 million	34	34	35	35	36	36	37	37	37	38	38	39
U.K.	67 million	30	31	31	32	32	40	41	42	43	43	44	45
Germany	83 million	7.1	7.2	7.4	7.6	7.8	8.0	8.1	8.2	8.3	8.4	8.4	8.8
Sweden	10 million	22	22	23	24	25	26	27	27	27	28	29	29
China	1,386 million	0.46	033	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33

#3A U.S. Covid-19 Statistics – Daily Cases														
		April 26		ŀ	April 27		A	pril 28			April 29			
State	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate		
California	42,164	1,710	4.0%	43,464	1,755	4.0%	45,031	1,809	4.0%	46,500	1,887	4.1%		
Florida	31,528	1,094	3.5%	32,138	1,101	3.4%	32,846	1,154	3.5%	33, 193	1,240	3.7%		
Illinois	43,903	1,933	4.4%	45,883	1,983	4.3%	48,102	2,125	4.4%	50,355	2,215	4.4%		
Louisiana	26,773	1,670	6.2%	27,068	1,670	6.2%	27,286	1,801	6.6%	27,660	1,845	6.7%		
Massachusetts	54,938	2,899	5.3%	56,462	3,003	5.3%	58,302	3,153	5.4%	60,265	3,405	5.7%		
Michigan	37,778	3,315	8.8%	38,210	3,407	8.9%	39,262	3,567	9.1%	40,399	3,670	9.1%		
New Jersey	109,038	5,938	5.4%	111,188	6,044	5.4%	113,856	6,442	5.7%	116,264	6,770	5.8%		
New York	288,045	16,966	5.9%	291,996	17,303	<b>5.9</b> %	295,106	17,638	<b>6.0%</b>	299,691	18,015	<b>6.0</b> %		
Washington	13,521	738	5.5%	13,521	749	5.5%	13,686	765	5.6%	13,842	786	5.7%		

Source: https://covidtracking.com/data/

#3B U.S. Covid-19 Statistics – Daily Cases													
		April 30			May 1			May 2			May 3		
State	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	
California	48,917	1,982	4.1%	50,442	2,073	4.1%	52,197	2,171	4.2%	53,616	2,215	4.1%	
Florida	33,690	1,290	3.8%	34,728	1,314	3.8%	35,463	1,388	3.9%	36,078	1,403	3.9%	
Illinois	52,908	2,355	4.5%	56,055	2,457	4.4%	58,505	2,559	4.4%	61,499	2,618	4.3%	
Louisiana	28,001	1,862	6.6%	28,711	1,927	6.7%	29,140	1,950	6.7%	29,340	1,969	6,7%	
Massachusetts	62,205	3,562	5.7%	64,311	3,716	5.8%	66,263	3,846	5.8%	68,087	4,004	5.9%	
Michigan	41,379	3,789	9.2%	42,356	3,866	9.1%	43,207	4,020	9.3%	43,754	4,049	9.3%	
New Jersey	118,652	7,228	6.1%	121,190	7,538	6.2%	123,717	7,742	6.3%	126,744	7,871	6.2%	
New York	304,342	18,321	<b>6.0</b> %	308,314	18,610	<b>6.0</b> %	312,977	18,909	<b>6.0</b> %	316,415	19,189	<b>6.1%</b>	
Washington	14,070	801	5.7%	14,327	814	5.7%	14,637	824	5.6%	15,003	830	5.5%	

#3C US. Covid-19 Statistics – Daily Cases													
		May 4			May 5			May 6					
State	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate				
California	54,937	2,254	4.1%	56,282	2,317	4.1%	58,815	2,412	4.1%				
Florida	36,897	1,423	3.9%	37,439	1,536	4.1%	38,002	1,605	4.2%				
Illinois	63,840	2,662	4.2%	65,962	2,838	4.3%	68,232	2,974	4.4%				
Louisiana	29,673	2,064	7.0%	29,996	2,115	7.1%	30,399	2,115	7.0%				
Massachusetts	69,087	4,090	5.9%	70,271	4,212	6.0%	72,025	4,420	6.1%				
Michigan	43,754	4,049	9.3%	44,397	4,179	9.4%	45,054	4,250	9.4%				
New Jersey	128,269	7,910	6.2%	130,593	8,244	6.3%	131,890	8,549	6.5%				
New York	318,953	19,415	<b>6.1%</b>	321,192	19,645	<b>6.1%</b>	323,978	19,877	<b>6.1%</b>				
Washington	15,185	834	5.5%	15,462	841	5.4%	15,594	862	5.5%				

#### The most important chart

#4 Watching for When the Coronavirus Curve Flattens - *APRIL/MAY 2020 - World and U.S.												
(Additional CASES each day, not total cases)												
Location	April 26	April 27	April 28	April 29	April 30	May 1	May 2	May 3	May 4	May 5	May 6	
Worldwide	75,569	85,642	58,441	77,488	82,487	68,029	82,941	79,581	75,545	90,222	106,459	
China	4	26	0	6	0	15	0	5	2	2	2	
Spain	2,870	2,793	2,706	4,771	2,740	3,340	2,610	533	2,179	2,260	3,121	
Italy	2,324	1,739	2,091	2,086	1,872	1,964	1,900	1,389	1,221	1,075	1,444	
U.K.	4,468	3,112	5,201	4,091	4,812	7,412	4,815	4,342	3,990	4,411	6,116	
U.S.	27,838	22,287	24,320	27,392	55,114	8,758	28,758	25,502	22,593	23,717	24,258	
California	1,027	1,300	1,567	1,469	2,417	1,515	1,755	1,419	1,321	1,345	2,533	
Florida	689	610	708	348	497	1,038	615	615	819	542	563	
Illinois	2,126	1,980	2,219	2,253	2,553	3,147	2,450	2,994	2,341	2,122	2.270	
Louisiana	261	295	218	374	341	710	429	200	333	323	403	
Massachusetts	1,590	1,524	1,840	1,963	1,940	2,106	1,952	1,824	1,000	1,184	1,754	
Michigan	575	432	1,052	1,137	980	977	851	547	0	1,643	657	
New Jersey	3,278	2,150	2,668	2,408	2,388	2,538	2,527	3,027	1,525	2,324	1,297	
New York	5,902	3,951	3,110	4,585	4,651	3,972	4,663	3,438	2,538	2,239	2,786	
Washington	544	0	165	156	228	257	310	376	182	277	132	

\* This is the metric to watch to find when the curve flattens.

#5 Death Toll Increases - APRIL/MAY 2020 - World and U.S.												
			(Additio	onal DEATH	HS, not tot	al deaths)						
Location	April 26	April 27	April 28	April 29	April 30	May 1	May 2	May 3	May 4	May 5	May 6	
Worldwide	3,719	5,329	5,259	10,485	6,359	4,790	5,021	3,665	4,037	5,697	6,904	
China	1	0	0	0	0	0	0	0	0	0	0	
Spain	288	331	301	77	268	0	557	164	164	185	244	
Italy	260	333	382	323	294	260	474	174	195	236	369	
U.K.	414	297	653	4,421	605	812	622	315	289	692	649	
U.S.	1,121	1,377	3,479	2,611	2,890	1,212	1,301	1,313	1,252	2,130	2,367	
California	59	45	54	86	95	91	198	44	39	63	95	
Florida	19	7	53	96	50	24	74	15	20	113	69	
Illinois	59	50	42	90	140	102	102	59	44	176	136	
Louisiana	26	0	131	44	17	65	23	19	95	51	0	
Massachusetts	169	104	150	152	157	154	130	158	86	122	208	
Michigan	41	92	160	103	119	77	54	29	0	130	71	
New Jersey	75	106	398	328	458	310	204	129	39	334	305	
New York	367	337	335	377	306	289	299	280	226	230	232	
Washington	15	9	16	21	15	13	10	6	4	7	21	