

TRENDS-in-MEDICINE

BULLETIN: UPDATE ON CORONAVIRUS 4/4

April 4, 2020 by Lynne Peterson

Be careful, be safe, and be well.

The SARS-CoV-2 virus and the disease it causes, Covid-19, not only dominate the news, they also dominate the everyday lives of many Americans. Here are the latest news highlights. The estimate now is that 100,000-240,000 Americans will die from Covid-19 if mitigation efforts are strong. If they aren't, the estimate is for 2.2 million Covid-19 deaths in the U.S.

Our charts are on Pages 11-13. The numbers are as of end of the day April 4. The charts have been broken into weekly (March 18, March 25, and April 1) as well as daily April views. The weekly charts can show you longer term progression, and the daily charts should help spot the apex. In particular watch the chart on *additional* cases per day (#6) to track the U.S. curve. Some of the trends that pop out from the charts:

- 151 nations are now affected by Covid-19. Iran and China have seen a decrease in the rate of **patient deaths** from Covid-19, but the numbers from both those countries are suspect. Italy may be at or near its peak, and Spain now has more cases than Italy, though a smaller population.
- The **fatality rate** continues to steadily increase worldwide and is now 5.4%. Italy is now 12.3%, but France is close behind at 10.0% followed by Spain at 9.4%.
- In the U.S. the top **hotspot** remains New York, but California, Louisiana, Massachusetts, and Michigan each has >10,000 cases and Florida and Illinois are almost at that level. President Trump and other U.S. experts predicted that the next couple of weeks are going to be "a very deadly period" in the U.S. All but five states have stay-at-home orders.
- The population of the U.S. is ~5.5-times that of Italy, though fewer people in the U.S. are age ≥65 (17% vs. 23%). One model shows that, if the U.S. follows the trajectory of Italy, there would be **93,000 deaths in the U.S.** That seems a low estimate since the current death toll in Italy is 14,681 and, even if Italy has peaked (which is not yet certain), that would suggest a death toll in Italy at the bottom of the hill would be at least double that (~30,000), and that would translate to 186,000 in the U.S.
- New York accounted for nearly half of U.S. cases of Covid-19 on March 25, but, while total cases have gone up substantially (New York's worst day yet on April 4), so have cases across the country. New York is 37% of all U.S. cases.
 - ✓ The number of cases in the state is continuing to increase, but there is a shift with a decrease in the percentage coming from New York City (from 75% to 65%) and an increasing percentage of the mix now coming from Long Island.

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- ✓ Long Island also went up as a share of state hospitalizations (from 17% to 22%).
- ✓ New York now is expected to crest in 5-14 days (likely around 7 days, April 11) instead of the end of April.

Tidbits

The world

- China The accuracy of the coronavirus numbers in China has always been viewed with some suspicion, but the suspicion is growing into outright disbelief and blame.
- Italy The outbreak of Covid-19 appears to be near the peak, but the question is whether it will <u>reignite</u>. So far, ~75% of Covid-19 cases have been in northern Italy, and the concern is that there could be a spike in the southern part of the country. All of Italy will remain on lockdown for at least another 2 weeks.
- Spain There are reports that hospitals overwhelmed with patients are refusing treatment to very elderly Covid-19 patients, giving the beds instead to younger patients.

U.S.

• The economy. Unemployment was 4.4% for March, with 701,000 jobs lost in March. 1 in 4 small businesses either closed or teetering on the edge of closure. White House Economic Adviser Larry Kudlow said it is going to get "much worse...There is no question it is going to be bad...[But] this is not going to last through the year, and we will see a strong recovery when this has played itself out."

President Trump and administration officials have insisted that the economy will bounce back – and do it quickly – once the virus is defeated. However, former FDA Commissioner Scott Gottlieb, MD, predicted that the virus will continue to disrupt daily life through the fall unless there is an effective drug to treat it. "If we don't have it [a treatment], this virus is going to come back in the fall, and it's going to continue to shut down parts of our lives. The consumer is not going to bounce back. People are going to be afraid to go out, and we're going to continue to see people succumb to this virus."

- Elective surgery is down, but that was expected as hospitals prepare for (or care for) Covid-19 patients. But thousands of healthcare workers are being laid off 42,500 healthcare jobs were lost in March because of a decrease in **outpatient care** as patients do telehealth or postpone doctor visits.
- The Democratic convention was postponed from mid-July to mid-August because of Covid-19. President Trump said there are no plans to postpone the Republican convention in August.
- Masks. The Centers for Disease Control and Prevention (CDC) issued new guidance, recommending that the public wear a <u>cloth face covering</u> in public settings where other social distancing measures are difficult to maintain (e.g., grocery stores and pharmacies) *especially* in areas of significant community-based transmission. The CDC specifically recommends *against* use of medical, surgical, or N95 masks, which should be reserved for healthcare providers and first responders. The change in guidance was explained as a result of studies that show asymptomatic people can transmit the virus. However, remember that cloth (or even medical masks) mostly prevent you from infecting anyone else; they are so leaky and are unlikely to be handled sufficiently carefully to provide the wearer with much protection. President Trump emphasized that this is a voluntary recommendation, and he doesn't plan to wear a mask.
- Mitigation. Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), said mitigation is working, "There is no doubt in my mind...that the mitigation activities the physical separation clearly

is having a positive impact...There is no doubt it is having an effect...The entire nation...absolutely needs to adhere to those recommendations...That is the only tool we have that we know is effective."

- **Prisons.** Attorney General William Barr ordered the Bureau of Prisons to expedite the release of eligible prisoners at high risk from Covid-19 at three federal prisons and an increase in the use of home confinement.
- Stimulus/relief money. The money is starting to get to work. Bank of America and other lenders made 17,500 small business loans the first day, totaling \$5.4 billion. President Trump said, "The numbers are far greater than we would have anticipated. Bank of America really stepped right up." Other officials suggest nearly 500 banks have made \$2 billion in small business loans.
- **USS Theodore Roosevelt.** At least 155 of the sailors on this nuclear aircraft carrier, which is docked in Guam, are Covid-19 positive. The captain of the ship, Brett Crozier, was relieved of his command by Acting Navy Sec. Thomas Modly but he will be reassigned rather than mustered out of the Navy after he emailed a letter pleading for help with the outbreak on the ship to ~30 people but not to his superior, who was on the ship with him. That letter was leaked to the media. Modly said Crozier used "poor judgement," "acted emotionally," and used an unsecure system to send the email. Deborah Brix, MD, the White House Coronavirus Response Coordinator, said, "The military will test all the sailors on the ship with an antibody test."

President Trump

- Energy. The President met with energy company leaders at the White House but said they did not ask for a bail out. He was optimistic about Russia and Saudi Arabia ending the oil battle that has depressed oil prices. He asked the Secretary of Interior to find more storage space, so the government could add to the strategic reserve at the current very low prices, "At these prices you would think you would want to fill up every cabinet we have...Check out other areas where you can store oil...At these prices, you should do it. Fill up the tank." He said he is not thinking about tariffs on Saudi oil at this point "but it is a tool in the toolbox."
- Infrastructure. President Trump said he plans to "do a big package" on infrastructure soon, "We have to fix our infrastructure...We are borrowing at zero interest...This is a great time...We can fix our infrastructure and have almost no interest. This is the time to do it."
- **Insurance.** He announced that BlueCross/Blue Shield will follow what Cigna, Humana, and Anthem already did and, for the next 60 days, cover testing and treatment of Covid-19 patients with no copays or deductibles and no balance billing. He also announced that the federal government will reimburse hospitals and healthcare providers (out of the stimulus package) *at Medicare rates* for treating uninsured Covid-19 patients.
- **Travel restrictions.** Asked if he is considering banning domestic flights from hotspot areas of the country, President Trump didn't commit to anything.
- Voting. President Trump expressed strong opposition to the idea of mail-in voting in the November election for president.

U.S. states and cities

- At least 15 state governors have issued executive orders that suspend scope of practice laws which restrict what nurse practitioners, physician assistants, and nurses can do, so they can help out as needed in treating Covid-19 patients.
- The federal government is building temporary hospitals for Covid-19 patients at the convention centers in Dallas and New Orleans like the one at the Javits Center in New York.

California – A Stanford <u>researcher</u> said his model shows that shelter-in-place might need to be continued for five months in order to completely suppress the epidemic. The concern is lifting the order too soon could lead to a second wave.

• Florida

- ✓ Gov. Ron DeSantis said 86% of the **deaths in Florida** have been people age ≥65. An epidemiologist predicted that Florida will have 6,897 deaths by August 4, 2020 (range 1,700-18,000).
- ✓ **Cruise ships.** Holland America's **MS Zaandam** cruise ship, with 4 dead and >200 Covid-19-positive passengers and crew among the 1,391 aboard, and its sister ship the **MS Rotterdam** (with 1,445 aboard), were both allowed to dock in Ft. Lauderdale. Thirteen critically ill passengers were taken to Florida hospitals, and healthy Florida residents were allowed to leave to drive home. The passengers who were fit for travel were taken by bus directly to the airport and to planes on the tarmac, not the terminal for chartered flights home to Atlanta, San Francisco, Toronto, Paris, and London. At least 36 passengers with "minor illnesses remained on the ship until they are fit for travel, and the crew will not disembark.

A third cruise ship, the Carnival's **Coral Princess**, which also had Covid-91 infections on board, docked in Miami on April 4. Two critical passengers were taken to a local hospital, Most of the passengers – those who were not sick – were allowed to disembark. The sick passengers and crew remain on the ship.

- Louisiana The state had a spike of ~3,000 Covid-19 cases on April 2, a 42% one-day increase, which was attributed to an increase in testing.
- Maryland The governor predicted his state would be the next <u>hotspot</u> in the country, with a surge in mid-April.
- New York
 - Chris Cuomo. Gov. Andrew Cuomo's brother, Chris, who has Covid-19, appears to be doing well in isolation in his (finished) basement.
 - ✓ **Javits Center.** New York wanted to turn the Javits Center emergency hospital, which was set up to handle non-Covid overflow patients, into a Covid treatment center. President Trump agreed but said the federal government will take over care at the Javits Center and staff it with military doctors. *Maybe this means the federal government has to provide the ventilators for that facility. That could be one way to get more ventilators for New York.*
 - ✓ **Medical students.** Gov. Cuomo issued an executive order to allow medical students slated to graduate this spring to begin practicing now, so they can help with Covid-19 care.
 - ✓ Social distancing. Google <u>tracking data</u> suggest that New Yorkers are **not distancing** themselves in public as much as the French or Italians and are less likely to avoid public places and stay home than residents of hard-hit coronavirus hotspots in Europe. In New York state, foot traffic in public parks was down 47% vs. an ~90% drop in Italy and Spain and an ~80% drop in France.
 - ✓ **Transfers**. "Several dozen" patients have been transferred from New York City to upstate New York.
 - ✓ **USNS Comfort.** This medical ship was sent to New York, which said it needed more beds but so far <25 patients have been sent to the hospital ship. The Comfort was supposed to be restricted to non-Covid-19 patients, but there haven't been enough of them to need the Comfort. Gov. Cuomo said the social distancing has resulted in fewer car accidents, bicycle accidents, and criminal injuries, so there has been a serious decrease in non-Covid emergency patients, and elective surgeries have been largely eliminated.

President Trump said Comfort will remain Covid-patient free, but the chairman of the Joint Chiefs of Staff said that decision is being reassessed. The new complication: 4 Covid-19-positive patients were sent to the Comfort by mistake. They were later transferred, but what that means for decontamination or patients going forward is not yet clear.

✓ Ventilators. Gov. Cuomo signed an executive order giving the state authority to take ventilators and personal protective equipment (PPE) "from institutions that don't need them now and redeploy them to other parts of the state and hospitals that need them." He said the institutions will either get the equipment back or the state will pay them for it (later). The National Guard will be deployed to pick up the equipment and move it. The governor said he is not "seizing" private property, just "sharing resources," adding, "We are not going to have any part of the state that doesn't have the resources it needs because we didn't *share* resources."

Asked if this order will stand up in court, the governor said, "Yes. You think they want to sue me? Do they want to sue me for borrowing their excess ventilators?"

Gov. Cuomo said the "burn" rate for ventilators is ~300/day. That is much lower than just a week ago. He had repeatedly said that 20% of patients who test positive are being hospitalized and 25% of those need an ICU/ventilator bed. So either fewer patients who test positive are being hospitalized or fewer hospitalized patients are requiring a ventilator. He did not indicate which it is.

He also said that the Chinese government is *donating* 1,000 ventilators to the state, and they will arrive April 4. And the state of Oregon is *loaning* New York 140 ventilators.

- Ohio Gov. Mike DeWine ordered a halt to use of commercial labs for Covid-19 testing. He said the labs are too slow, so now tests will go to Ohio hospitals that can handle the tests more quickly e.g., Ohio State University, the Cleveland Clinic, Clinic University Hospitals, and MetroHealth.
- Texas Officials think the state could be an emerging hotspot. One Texas nursing home has 83 patients positive for Covid-19, and another has 75 Covid-19-positive patients. Oh, my!

Drug shortages

- Midazolam. The FDA listed this drug, which is used for sedating ventilator patients, on the list of drugs where supply is running short.
- Narcotics. Physician and pharmacy advocates sent a letter to the Drug Enforcement Administration (<u>DEA</u>) urging it to increase production limits of injectable fentanyl, hydromorphone, morphine, and other narcotics used for Covid-19 patients on ventilators to ensure hospitals have enough supplies during the pandemic. A DEA official said the issue is under review, though it believes the current limit is high enough to meet the surge in demand.

Medical supplies

- **Hand sanitizer.** Johnson & Johnson is repurposing its Listerine plant in Pennsylvania to make hand sanitizer. Unlike distilleries, this plant can pump out huge quantities when the switch-over is complete.
- Masks
 - **3M.** President Trump said he is invoking the Defense Production Act (DPA) to "prohibit the export of scarce medical supplies by unscrupulous actors and profiteers...We need these items immediately for domestic use. We have to have them." The action was clearly aimed at **3M**, which reportedly has been selling its masks to other countries when the U.S. critically needs them. The President said, "I am not happy with 3M…We are not happy with 3M."

3M previously said it was upping production of N95 masks. The question appears to be to whom 3M is selling its masks, including that extra production. Are they selling to American hospitals and states or to foreign governments/entities? A Florida state emergency management official said 3M only sells through its distributors, and his N95 mask order was delayed (pushed down the queue) by the distributor because foreign buyers came with cash. There appears to be a question of where 3M's overseas production is going.

3M CEO Mike Roman said in an interview that it was "absurd" to suggest his company wasn't doing all it could to help the U.S. fight the pandemic. White House Trade Advisor Peter Navarro's response to that: "3M needs to stop whining and produce masks and get them to the American people...3M has been doing nothing but dissembling...We haven't been able to get information out of them. They have been behaving like a sovereign nation...The distributors, instead of filling orders domestically, are taking money and running offshore. That is going to stop...Attorney General [William] Barr is the sheriff in town, and we are cracking down on that...3M is going to basically help the American people fight this battle...There will still be exports to our friends in Mexico and Canada...but as to the rest of 3M production around the world, we will get our fair share...These guys have to stop whining and spinning and do the biasness for the American people." President Trump said he also would send masks to Italy or Spain if they need them.

- <u>KN95 masks</u>. The FDA is permitting imports of KN95 masks (the Chinese version of an N95 mask) during the current mask shortage, but the Agency warned importers to verify the authenticity of the masks.
- Sterilization. A combination of ozone + ultraviolet light is sometimes used to treat Lyme disease, and Massachusetts General Hospital reportedly is looking at giving it a try to sterilize PPE masks. There are even doctors suggesting use to treat Covid-19 patients.

Ventilators

- The Advanced Medical Technology Association said its 7 respiratory device companies have expanded their production capacity to the maximum in response to Covid-19, producing on average 2,000-3,000 ventilators per week, collectively, and they further expected to ramp production up to a total of 5,000-7,000/week.
- Smith & Nephew. The U.K. government contracted with Smith & Nephew to produce <u>OxVent ventilators</u>. The company is currently being reviewed by the Medicines and Healthcare products Regulatory Authority (MHRA), and production will begin as soon as the company receives design authorization.

Monitoring

- **PRA Health Sciences**, a contract research organization (CRO), has developed a <u>mobile app</u> aimed at tracking Covid-19 patients' physical and psychological symptoms.
- **Pulse oximeter.** This has become a hot consumer item online. Why? It can be used to measure oxygen levels in the blood in patients with symptoms of shortness of breath (a Covid-19 symptom).

Diagnosis/complications

Covid-19 symptom. A case study, published in *Radiology*, describes a female airline worker in her late 50s with Covid-19 who developed acute hemorrhagic necrotizing encephalopathy, an uncommon complication linked to cytokine storms caused by excessive immune cell production. She had non-contrast head CT images that showed symmetric hypoattenuation in the bilateral medial thalami, as well as MRI scans that showed hemorrhagic rim enhancing lesions in the medial temporal lobes, bilateral thalami, and subinsular brain regions. Those images suggest that a subgroup of patients with severe Covid-19 might have a cytokine storm syndrome.

Imaging. The Medical Imaging and Technology Alliance (<u>MITA</u>) urged the FDA to prioritize review and clearance of mobile x-ray, ultrasound, and CT systems that can help radiologists in the Covid-19 pandemic.

Neurologic symptoms. A small subset of Covid-19 patients appears to have serious neurologic impairment – altered mental status or encephalopathy – due to viral inflammation of the brain. The symptoms can be any of these: inability to speak, false seizure, confusion, headache, acute necrotizing encephalopathy, lethargy, strange behavior staring off into space, etc. These symptoms can occur before or after the more usual symptoms of Covid-19 appear.

A neurologist suggested this could indicate the coronavirus can invade the brain in some (rare?) circumstances. European doctors have also reported strokes, seizures, encephalitis-like symptoms, and blood clots, acroparathesia, and delirium. These neurological symptoms can occur even before the patient develops fever or respiratory illness.

The mechanism of action for neurological symptoms is not yet known, but Chinese researchers have suggested that there is some evidence that other coronaviruses are not confined to the respiratory tract and invaded the central nervous system – and that could contribute to respiratory failures. What is particularly interesting is that there generally isn't significant respiratory illness in these patients. And a study, published in the *British Medical Journal* in March 2020, found that 22% of 113 patients who died had neurological symptoms, ranging from somnolence to deep coma vs. 1% of patients who recovered.

The CDC includes "new confusion or inability to rouse" as warning signs that should be reported to the doctor.

Testing

Cellex's qSARS-CoV-2 IgG/IgM Rapid Test — The FDA granted emergency use authorization (EUA) for the first antibody (serology) test. It can detect past coronavirus infections but may be less effective at identifying more recent infections because antibodies can take time to develop and be detectable. Blood is collected through a vein and must be sent to a certified lab to run the test.

This will be useful, but it is not the test that is needed to get people back to work. Dr. Birx said that what is needed for that is a simple antibody test, "The antibody piece is critical because...we have to know how many people have become infected...We want the test like for HIV and malaria – fingerpicks into a cassette, then a line shows if it is positive, and if it is negative, there is no line. In the meantime we are asking for an ELISA-based assay which requires a tube of blood."

Bodysphere – The FDA did *not* issue an EUA for this Covid-19 test, so don't believe it if you see a story that said it was granted an EUA.

- Genetic Signatures' SARS-CoV-2 test kit was cleared for use in the European Union.
- **Fakes.** Not all antibody tests are equally accurate. The FDA warned people to be cautious of false coronavirus tests, drugs, and devices.

Transmission

Food is not a transmission source for coronavirus, according to the FDA. Frank Yiannas, Deputy Commissioner for Food Policy and Response at the FDA, said, "The food supply in the U.S. remains safe for both people and animals. There is no evidence of food or food pathogens associated with the transmission of coronavirus. This is not a GI virus...It is not known to be transmitted by exposure to food."

Asked if coronavirus could be carried on produce such as lettuce (like *e. coli*), Yiannas said, "I'm not aware of any specific tests for this coronavirus. There is no evidence it is transmitted through food...Food-borne outbreaks in [lettuce and leafy

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greens] is generally due to some exposure to droplets. That is the route of contamination...There is no evidence [SARS-CoV-2] is transmitted by food."

Asked about transmission on food packaging, he said, "That is a question we are hearing more and more. The virus is not transmitted by food...but a surface could be contaminated....While there have been some studies that talk about survivability of the virus on certain types of material, we don't think it survives for a long period, so we think the risk is low...We don't think food packaging is a common source of transmission. I personally don't sanitize food items brought into my house."

Treatment

Treatment tracking

- Health and Human Services Sec. Alex Azar announced that Oracle has donated a web portal for use in collecting crowdsourced real-time information on how Covid-19 patients respond to therapies, "It won't replace a trial, but it will give us data rapidly. If you are a doctor or provider, you can sign up today at **covid19.oracle.com**." Oracle has described this as a Covid-19 Therapeutics Learning System.
- The American Heart Association is developing a free registry through its Get With The Guidelines hospital quality improvement program to aggregate data on research, treatment protocols, and risk factors related to adverse cardiovascular outcomes in Covid-19 patients. The registry is up and starting now, and initial sites should be operable in early May. Some initial information could be available as early as August 2020.

Hydroxychloroquine

- In a survey of >6,000 doctors by Semo, this anti-malarial drug was the most highly rated treatment for Covid-19 out of a list of 15 possibilities, with 37% of respondents saying it is the "most effective therapy." The drugs these doctors prescribe most often for Covid-19 were: analgesics (56%), azithromycin (41%), and hydroxychloroquine (33%). Asked about this survey, Dr. Fauci said, "We don't care what doctors 'think."
- President Trump continues to be optimistic about this drug, saying on April 3, "It is looking like it is having some good results...We have it now in 1,500 people in New York...It has been there about 3.5 days...and many other places are being tested. We have a tremendous supply in case it works. We'll see what happens."
- India halted exports of hydroxychloroquine (among a few other drugs), and President Trumps said he talked with India's Prime Minister Modi about this, "I said I would appreciate it if you would release the materials we ordered, and they are giving that serious consideration."
- Some New York doctors and patients also are complaining that access to hydroxychloroquine is extremely limited there. If they can't get in a trial, New York pharmacists are not allowed, by executive order of the governor, to dispense it for a non-FDA approved indication (i.e., they can't fill it for Covid-19).
- The European Medicines Agency (<u>EMA</u>) restricted use of both chloroquine and hydroxychloroquine to clinical trials or emergency use programs.
- Anecdotally, David Lat, founder of Above the Law, tweeted that he was being discharged from a New York hospital where he had been treated for Covid-19 for 17 days including 6 days on a ventilator. He was given hydroxy-chloroquine + azithromycin in the New York trial, but (and this is a big but) he was also treated with all the leading investigational drugs three IL-6 inhibitors [Roche's Actemra (tocilizumab), Regeneron Pharmaceuticals and Sanofi's Kevzara (sarilumab), and Vitaeris' clazakizumab] and Gilead Sciences' remdesivir so it isn't possible to know how much of his recovery was due to the hydroxychloroquine or any of the other drugs.

The patients who die

A study of 85 Covid-19 patients in Wuhan, China, by Chinese and American researchers, published in the *American Journal* of *Respiratory and Critical Care Medicine*, reported on the most common characteristics of the patients who died in the early stages of the pandemic found despite treatment:

- More males over 50 with non-communicable chronic diseases (e.g., hypertension, coronary heart disease, and diabetes). 72.9% of the patients were men.
- Mean age 65.8.
- >80% had very low counts of eosinophils on admission (eosinophilopenia)
- Complications included respiratory failure, shock, acute respiratory distress syndrome (ARDS), and cardiac arrhythmia.
- Most patients received antibiotics, antivirals, and glucocorticoids. Some patients were given intravenous immunoglobulin or interferon alpha-2b.

Important findings:

- While respiratory symptoms may not develop until a week after presentation, once they do there can be a rapid decline, as indicated by the short duration between time of admission and death (6.35 days on average) in our study."
- ✓ Abnormally low levels of eosinophils may indicate a poor prognosis.
- ✓ A combination of antimicrobial drugs (antivirals, antibiotics) did not significantly help these patients.
- ✓ The majority of patients died from multiple organ failure.

Vaccines

- University of Pittsburgh's PittCoVacc Researchers reported that this protein subunit vaccine (which is much like a traditional flu vaccine) targets a protein on the surface of the SARS-CoV-2 virus. The vaccine is administered in a Band-Aid like patch with hundreds of small microneedles. Louis Falo, MD, PhD, the chairman of the Department of Dermatology, said they were ahead of the game because they had already been working on SARS and MERS vaccines. An investigational new drug (IND) application for PittCoVacc has been submitted to the FDA, and, if it is granted, a Phase I healthy volunteer trial could start immediately.
- Johnson & Johnson, which is partnered with the Biomedical Advanced Research and Development Authority (BARDA), said it expects to be able to start trials of its <u>Covid-19 vaccine</u>. Together J&J and BARDA committed >\$1 billion to Covid-19 vaccine research and development. In addition, J&J will establish a new U.S. vaccine manufacturing capability with the ability to supply >1 billion doses, with additional production capacity outside the U.S.

Paul Stoffels, MD, chief scientific officer for J&J, said the vaccine is primarily for urgent cases – care providers in intensive care (e.g., nurses, doctors, and ambulance drivers), "They are the first candidates. It is up to health authorities to determine who follows, perhaps older people. For example, the vaccine will be administered gradually." He said the aim is for the vaccine to be available to a wide audience by the end of 2021 and through 2022. He said the vaccine would be distributed at cost, about \$10 or $\notin 10$.

President Trump mentioned it at a briefing, saying, "It seems to be leading in terms of studies." Maybe he had it confused with the Moderna vaccine – or maybe he likes this one better.

Some things to keep in mind:

- It's been known for weeks that *asymptomatic* people can spread Covid-19.
- The main reason for the average individual to wear a **mask** would be to protect someone else from the wearer, not to protect the wearer from other people.
- A 14-day quarantine period may not be long enough.
- Recently, a group of people at **higher risk** of dying from Covid-19 men, blood type A, comorbid conditions was identified.
- Covid-19 **deaths** occurred more often in the elderly especially elderly with comorbid conditions, and people with preexisting conditions, but they are not the only people at risk.
- The virus does not appear to be temperature sensitive, so unlike the flu, it is unlikely to go away when **summer** arrives. And it may cause a second wave in the fall.
- The idea of using an **anti-IL-6** both Roche's Actemra (tocilizumab) and Regeneron and Sanofi's Kevzara (sarilumab) to treat Covid-19 was mostly ignored for many weeks, but it is starting to get more attention.
- Pregnant women who are Covid-19 do not appear to pass the virus to the fetus. However, the newborn can quickly catch it from its mother after birth.
- The percent of people who test positive for Covid-19 that need to be **hospitalized** has remained relatively steady at 20%, and ~25% of hospitalized patients need an ICU bed/ventilator (or 5% of positive patients). Mortality is high among ventilator patients. It is generally at least 30%, but no one has offered statistics on Covid-19 ventilator patient survival.
- New York Gov. Cuomo could be a dark horse for the **Democratic nomination** for president.

Unanswered questions (Items will remain on this list until answered.)

- ? Do people with lupus or rheumatoid arthritis who are taking **hydroxychloroquine** (Sanofi's Plaquenil) have a lower rate of getting Covid-19? Experts agree this is a good question, and the Medicare database should be able to answer it, but no one has offered those data yet.
- ? Is **hydroxychloroquine** being prescribed for the right patients and who are those patients (mild/moderate, severe, ventilator)?
- ? Are the **neurological symptoms/effects** reversible in some, all, most patients?
- ? People who get mild Covid-19 and recover continue to shed virus for up to 8 days or more *after* symptoms resolve. Is that virus capable of infecting other people? Should those people be quarantined longer?
- ? What do we know about Covid-19 patients who are put on a ventilator and *recover*? Is it a *functional* recovery?
- ? Are there **long-term effects** from getting Covid-19, even mild Covid-19? Will there be long-lasting lung abnormalities or pulmonary fibrosis?
- ? Is there a **reservoir** in the body where SARS-CoV-2 might hide and later come back to cause a disease flare or even spread the disease as with HIV or Ebola? Experts still say they don't know.
- ? Is the **blood supply** safe? This question is back on the list, even though the FDA insists the blood supply is safe, because that pronouncement was based on the *assumption* that a respiratory virus wouldn't be transmitted in blood. There have been no studies to confirm this. If the virus can't survive in blood but could, possibly, survive in other bodily fluids, doesn't that mean it has some durability and could possibly be transmitted?

- ? Can people get Covid-19 more than once? There are still conflicting reports on this.
- ? What more can be done to protect **nursing home** residents? Visitors can't be banned forever.

	#1 Worldwide Covid-19 Statistics – Weekly										
	A	s of March 1	L8	As of M	arch 25 (1 v	veek)	As of	April 1 (2 w	April 1 (2 weeks)		
Country	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate		
Worldwide	217,242	8,704	4.0%	470,973	21,287	4.5%	932,605	46,809	5.0%		
U.S.	9,249	145	1.6%	68,960	1,041	1.5%	213,372	4,757	2.2%		
Italy	35,713	2,978	8.3%	74,386	7,503	10.1%	110,574	13,155	11.9%		
Spain	13,176	638	4.8%	49,515	3,647	7.4%	104,118	9,387	9.0%		
China	81,137	3,130	3.9%	81,667	3,285	4.0%	82,261	3,316	4.0%		
Germany	12,327	28	0.2%	37,323	206	0.6%	77,872	920	1.2%		
France	n/a	n/a	n/a	n/a	n/a	n/a	57,749	4,043	9.5%		
Iran	17,061	1,135	6.7%	27,017	2,077	7.7%	47,593	3,036	6.4%		
U.K.	>2,600	104	4.0%	9,640	466	4.8%	29,865	2,357	7.9%		

Source: https://coronavirus.jhu.edu/map.html

	#2 Worldwide Covid-19 Statistics – Daily											
		April 1			April 2		April 3 April			April 4		
Country	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
Worldwide	932,605	46,809	5.0%	1,014,673	52,973	5.2%	1,098,848	58,871	5.4%	1,197,405	64,606	5.4%
U.S.	213,372	4,757	2.2%	244,678	5,911	2.4%	277,828	7,141	2.6%	308,850	8,407	2.7%
Italy	110,574	13,155	11.9%	115,242	13,915	12.1%	119,827	14,681	12.3%	124,632	15,362	12.3%
Spain	104,118	9,387	9.0%	112,065	10,348	9.2%	119,199	11,198	9.4%	126,168	11,947	9.5%
China	82,261	3,316	4.0%	82,433	3,322	4.0%	82,511	3,326	4.0%	82,543	3,330	4.0%
Germany	77,872	920	1.2%	84,794	1,107	1.3%	91,159	1,275	1.4%	96,092	1,444	1.5%
France	57,749	4,043	9.5%	59,929	5,398	9.0%	65,202	6,520	10.0%	90,848	7,574	8.3%
Iran	47,593	3,036	6.4%	50,468	3,160	6.3%	53,183	3,294	6.2%	55,743	3,452	6.2%
U.K.	29,865	2,357	7.9%	34,173	2,926	8.6%	38,690	3,611	9.3%	42,477	4,320	10.0%

Source: https://coronavirus.jhu.edu/map.html

	#3 U.S. Covid-19 Statistics – Weekly									
		As of Marc	h 18	As of M	arch 25 (1	week)	As of	April 1 (2 w	eeks)	
Country	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	
New York *	2,382	12	0.05%	30,811	285	0.9%	83,712	1,941	2.3%	
New Jersey	427	5	1.2%	4,402	62	1.2%	11,255	355	3.2%	
Washington	1,012	52	5.1%	2,469	123	5.0%	5,634	224	4.0%	
California	611	13	2.1%	2,102	40	1.9%	8,155	171	2.1%	
Michigan	80	0	0	2,294	43	1.3%	9,334	337	3.6%	
Illinois	289	1	0.3%	1,884	19	1.0%	6,980	141	2.0%	
Florida	314	7	2.2%	1,682	22	1.3%	6,955	87	1.3%	
Louisiana	240	6	2.5%	1,795	65	3.3%	6,424	273	4.2%	
Massachusetts	256	0	0	1,838	15	0.7%	7,738	133	1.7%	

	#4 U.S. Covid-19 Statistics – Daily											
		April 1			April 2			April 3			April 4	
Country	Cases	Deat hs	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
New York	83,712	1,941	2.3%	92,381	2,373	2.6%	102,863	2,935	2.9%	113,704	3,565	3.1%
New Jersey	11,255	355	3.2%	25,590	537	2.1%	29,895	646	2.2%	34,124	846	2.5%
Washington	5,634	224	4.0%	5,984	247	4.1%	6,585	262	4.0%	6,966	284	4.1%
California	8,155	171	2.1%	9,191	203	2.2%	10,701	237	2.2%	12,026	276	2.3%
Michigan	9,334	337	3.6%	10,791	417	3.9%	12,744	479	3.8%	14,225	540	3.8%
Illinois	6,980	141	2.0%	7,695	157	2.0%	8,904	210	2.4%	10,357	243	2.3%
Florida	6,955	87	1.3%	8,010	128	1.6%	9,585	163	1.7%	11,111	191	1.8%
Louisiana	6,424	273	4.2%	9,150	310	3.4%	10,297	370	3.4%	12,496	409	3.3%
Massachusetts	7,738	133	1.7%	8,966	154	1.7%	10,402	192	1.8%	11,736	216	1.8%

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

	#5 Watching for When the Coronavirus Curve Flattens *MARCH 2020 (<i>Additional</i> cases each day, not total cases)								
Location	March 23	March 24	March 25	March 26	March 27	March 28	March 30	March 31	
Worldwide	45,321	36,289	53,391	60,711	58,910	75,022	120,612	70,690	
U.S.	13,056	7,328	14,912	16,545	15,212	23,969	39,917	23,569	
China	107	77	76	115	1115	164	179	39	
Spain	6,368	4,749	9,630	8,271	6,499	8,950	14,721	7,967	
3Italy	4,789	5,249	5,210	6,203	5,909	5,974	7,267	4,053	
Iran	1,411	1,762	2,206	2,389	2,926	3,076	6,087	3,110	
New York	6,521	6,976	5,146	6,447	7,377	7,683	14,179	9,298	

* This is the metric that Dr. Birx said to watch.

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#6 Watching for When the Coronavirus Curve Flattens *APRIL 2020 (<i>Additional</i> cases each day, not total cases)									
Location April 1 April 2 April 3 April 4									
Worldwide	75,687	81,068	84,175	98.557					
U.S.	25,200	31,306	33,150	31,022					
China	7	172	78	32					
Spain	8,195	7,947	7,134	6,969					
Italy	4,782	4,668	4,585	4,805					
Iran 2,898 2,875 2,715 2,560									
New York	7,917	8,669	10,482	10,841					

* This is the metric that Dr. Birx said to watch.

	#7 Death Toll Increases (Additional deaths, not total deaths) – MARCH									
Location	March 23	March 24	March 25	March 26	March 27	March 28	March 30	March 31		
Worldwide	1,940	2,040	2,664	3,217	2,889	3,914	6,963	4,178		
China	107	7	4	6	5	8	5	0		
Italy	601	743	683	712	919	889	1,568	837		
Spain	539	497	839	718	575	1,042	1,734	748		
U.S.	193	93	328	248	255	648	978	703		
New York	43	53	75	100	134	209	490	332		

#8 Death Toll Increases (<i>Additional</i> deaths, not total deaths)									
Location	April 1	April 2	April 3	April 4					
Worldwide	4,811	6,164	5,898	5,735					
China	7	6	4	4					
Italy	727	760	766	681					
Spain	923	961	850	749					
U.S.	U.S. 884 1,154 1,230 1,266								
New York									