



## BULLETIN: UPDATE ON CORONAVIRUS 4/9

April 9, 2020  
by Lynne Peterson

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

The SARS-CoV-2 virus and the disease it causes, Covid-19, now affect virtually every country in the world. Most of the U.S. is on a near lockdown, with social distancing leaving our streets, schools, parks, and beaches almost a ghost town. Here are the latest news highlights. The U.S. estimate has been lowered for deaths to ~63,000 from a previous range of 100,000-240,000. The first peaks in cases are likely to be reached this week in a few places in the U.S., including New York, but the death rate will lag that, and the last case peaks in the country may hit in late May.

Our charts are on Pages 11-12. Watch the charts on *additional* cases per day to look for countries/states that are peaking. Note that there is a new column in Chart #2 – reflecting the rate of cases per capita. And on Page 8 there is a look at other clinical trials that are being affected by Covid-19.

Some of the trends that pop out today *for the countries and states we are monitoring* include:

- Over the past three weeks, both the total number of cases and the case fatality rate have steadily increased for every **country** except Iran and China (if the numbers for either are believable).
- Looking at just April, no country has shown a decline in either the case rate or the fatality rate. Italy continues to appear to have peaked. Spain may have peaked, but that is less clear.
- While the **U.S.** had more cases than any other country, our fatality rate is still relatively low compared to other countries.
- **New York** remains the hottest hotspot in the U.S., accounting for 49% of the cases in the 9 states monitored. It may have peaked, but the numbers are ugly and sad.
- On a **per capita** basis, the U.S. rate is lower than all European countries except the U.K. Out of every 10,000 people: worldwide 2 have the coronavirus, 9 in the U.K., 13 in the U.S., 17 in France, 23 in Italy, and 32 in Spain.
- The **case fatality rate** has steadily increased worldwide and is now 5.8%. Spain, Italy, and the U.K. continue to have case fatality rates of  $\geq 10\%$  vs. 3.4% in the U.S.
- In the U.S. the top **hotspot** remains New York, with 149,316 cases – 35% of the country's total – and more than 6,000 deaths, but other hotspots include, New Jersey, Michigan, Louisiana, and Illinois.

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## Tidbits

### ■ The world

- **France** is extending its lockdown for a second time, until at least April 15.
- **Germany** – Here is a link to a plan for reopening the country after Covid-19:  
<https://www.ifo.de/en/publikationen/2020/monograph-authorship/making-fight-against-coronavirus-pandemic-sustainable>
- **India** withdrew its partial ban on exports of hydroxychloroquine. The U.S. imports 47% of its supply of this drug from India.
- **Italy** – Prime Minister Giuseppe Conte said the Covid-19 pandemic could lead to the breakup of the European Union.
- **Japan** declared a coronavirus emergency as infections rise to >5,000, asking people to self-isolate for a month.
- **Saudi Arabia**
  - ✓ At least 150 members of the royal family are infected with Covid-19, but not King Salman or Crown Prince Muhammed bin Salman, who are both secluded separately on an island near Jeddah.
  - ✓ Saudi Arabia declared a unilateral ceasefire in Yemen, effective April 9 out of concern about coronavirus spreading in Yemen.
- **Spain** – The government is taking steps to implant a basic income to help Spaniards get through the Covid-19 disaster. However, the Minister of Economic Affairs said the program will be temporary, not permanent.
- **U.K.**
  - ✓ **Prime Minister Boris Johnson** remains in the hospital but is no longer in intensive care.
  - ✓ The University of Washington's Institute for Health Metrics and Evaluation (IHME) – which overestimated the deaths expected in the U.S. – now is predicting that the U.K. will be the worst hit European country, but British experts are not convinced it is correct.

### ■ U.S.

- **African Americans.** African Americans don't appear to be catching Covid-19 more often than non-African Americans, but when they do get it, they are more likely to have a bad outcome. Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), said, "We have a particularly difficult problem of an exacerbation of a health disparity... We have known that diseases like obesity, diabetes, and asthma disproportionately affect minorities, particularly African Americans." And Covid-19 is more deadly in people with those comorbidities. The administration promised to start doing more demographic tracking and analyses.
  - **Death toll.** The IHME modelers initially predicted U.S. deaths from Covid-19 could reach as high as 100,000-240,000 even with mitigation – and 2.2 million without those steps – but then modelers brought the estimate down to 93,000. And now they say it is 60,415. That's good news, and officials of the White House Task Force on Coronavirus said this is due to Americans observing the stay-at-home orders. However, *it also suggests there could be problems with their modeling.*
  - **Economy.** In the last week, 6.6 million people filed for unemployment benefits, bringing unemployment claims to 16.6 million since the coronavirus pandemic struck.
  - **Heart damage.** Studies suggest that the SARS-CoV-2 virus can infect the heart muscle, causing cardiac damage in up to 20% of Covid-19 patients and leading to heart failure. The question is whether the heart damage is caused by the virus itself or the disease's stress on the heart.
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- **Medical conferences.** All medical conferences through the end of May have been canceled or turned into virtual meetings, and this now includes the annual American Medical Association (AMA), though that meeting will not be virtual.
- **Paycheck Payment Program.** In just a few days the program has committed \$100 billion in small business loans, but there are questions about what small businesses are getting this. That is because it is not easy to apply for the program. It is doubtful that many truly small business people will be able to navigate the paperwork and collect all the data that is required to qualify, especially small businesses that don't have an in-house accountant or the money to pay an outside accountant. Perhaps it is the larger small businesses that are getting applications completed.

The same applies to the new unemployment rules for self-employed people and independent contractors. In states that are in non-essential business lockdown, they have to be completed online, but many of those workers don't have or use computers.
- **Spine surgery.** The North American Spine Society created a task force on Covid-19, and they came up with some guidelines for patients and surgeons. The guidelines spell out what are *emergency* patients who have a procedure/treatment should not be postponed, urgent patients where a procedure/treatment can be done if the local situation and resources allow it, elective patients where the procedure/treatment should be postponed.
- **USNS Comfort.** A merchant mariner on the USNS Comfort, the hospital ship sent to New York, tested positive for Covid-19. The ship was transitioned from general medicine only to Covid-19 only, but that cut the number of usable beds from 500 to 1,000. And it meant housing the crew/staff off the ship in a hotel (a hotel just for them).
- **USS Theodore Roosevelt.** At latest count, 416 sailors on this nuclear-powered aircraft carrier have Covid-19. Acting Navy Secretary Thomas Modly, who removed Capt. Brett Crozier who circulated a lengthy critical memo – that went public – about the virus on the ship (when there were 90% fewer cases) resigned from the Navy after his rant at Capt. Crozier also went public.
- **World Health Organization (WHO).** President Trump said the U.S.'s >\$450 million contributions to WHO will be put on hold while WHO's behavior relating to Covid-19 is reviewed, "They've been wrong about a lot of things." Those things include: misleading him and the world by saying Covid-19 was not spread person-to-person when it clearly was, minimizing the threat from the virus, criticizing President Trump for cutting off travel from China to the U.S., and kowtowing to China. Asked if there should be a leadership change at WHO, U.S. Secretary of State Mike Pompeo said, "This is not the time to be doing that kind of change...There will be a lot of time to look back."

## President Trump

- Removed the inspector general overseeing the \$2.2 trillion coronavirus relief package. It is not yet clear who will replace him.
  - Proposed another stimulus bill, this one with \$250 billion for small business loans. Senate Majority Leader Mitch McConnell (R-KY) proposed simply changing the amount in the original bill from \$350 billion to \$600 billion instead of negotiating a new bill, with all the political wrangling that could entail. So far, the Democrats aren't buying that idea.
  - Has been putting blame on China for failing to disclose more information and for not doing that sooner about Covid-19. Secretary of State Pompeo said, "It started in China, so they had that special responsibility...This is not the time for retribution, but it is the time for clarity and transparency."
  - Asked when the company will be able to get back to work, President Trump said "We have to start planning restarting...We are not there...This is not a light switch we can just flip one day."
    - He said he hopes to put together a coordinated regional approach to opening back up.
    - Testing has to be a big part of that.
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- He is hoping an antibody test that the New York Department of Health has developed – but which still needs FDA clearance – will help.
- Other tests will be needed, “We are interested in those companies and in investing in those companies.”

### U.S. states and cities

- **Georgia** – Gov. Brian Kemp extended his shelter-in-place order, due to expire on April 13, to April 30.
- **Kansas** – The legislature struck down the governor’s directive limiting the size of religious gatherings to 10.
- **Maryland** – The state is preparing for the possibility that schools will not be able to open for the fall semester and that students will have to continue online learning.
- **New York**
  - Two separate studies by geneticists concluded that the Covid-19 outbreak in New York was due to travelers from Europe.
  - Gov. Andrew Cuomo ordered flags in the state flown at half mast in honor of all the people who have died from Covid-19.
  - *When will things get back to normal?* Gov. Cuomo said, “I don’t think we return to normal. I don’t think we return to yesterday. I think we return to a new normal.”
- **Wisconsin** – The courts refused to allow a last-minute extension of the time for mail-in voting, so the state held local elections on April 7. Lines were long as people tried to stay 6 feet apart as they waited to vote. No results yet.

### Drug shortages

FDA Commissioner Stephen Hahn, MD, said there’s **no** shortage of drugs – or active pharmaceutical ingredients (APIs) – that the U.S. gets from China. He said the FDA is monitoring the situation, but that isolated drug shortages in some areas of the U.S. were due to increased demand, not supply issues. In line with that, Johnson & Johnson said it had a “temporary” shortage of Tylenol (acetaminophen) because of increased demand.

### Medical supplies

A survey of 2,600 physicians by Doximity, Harvard Medical School, and RAND found that:

- 73.3% didn’t have the ability to test for Covid-19 quickly and easily.
- >50% have treated patients with symptoms that they weren’t able to test.
- >77% said their hospital or clinic would not have adequate medical supplies if the pandemic gets worse.

### ■ Ventilators

- So far, no patients have died because of lack of a needed ventilator, but what if there is a critical shortage?
  - ✓ A controversial guideline in **Alabama**’s disaster preparedness plan on who should receive a ventilator if there were a shortage prioritized able-bodied individuals over people with physical and intellectual disabilities. It’s been dropped.
  - ✓ The **Massachusetts** Department of Public Health issued voluntary guidelines that say the hospital staff should look at a patient’s chances of both short- and long-term survival. Things that should not be considered include: race, disability, gender, sexual orientation, gender identity, ethnicity, immigration status, incarceration, etc.

- The first **newly manufactured** ventilators from General Electric and Hamilton Medical have arrived at the Strategic National Stockpile.
- *Are ventilators being **over-used** for Covid-19 patients?* Some doctors think so, suggesting that blood oxygen levels may be misleading and causing ventilators to be used when less intensive respiratory support may be sufficient.
- **Johnson & Johnson/Ethicon** is partnering with **Prisma Health** to manufacture and distribute Prisma's VESper Ventilator Expansion Splitter, a Y-shaped connector that lets two patients share a ventilator. The device has emergency use authorization (EUA) from the FDA.
- **Medtronic's** ventilator was granted an EUA for use in treating Covid-19.
- **Mullen Technologies**, which normally makes electric cars, will manufacture its **Mullen 8** ventilator system, a portable, low-cost device for use when larger devices are not available.
- **Vortran Medical's Go2Vent – Xerox** partnered with Vortran to help mass produce these low-cost, disposable ventilators for use by first responders.

### Diagnostics

- **Babylon Health's COVID-19 Care Assistant**, an app to help patients check for symptoms of Covid-19, track disease progression, and have a virtual consultation with a doctor (if needed), was launched.
- **IQVIA** started a new Covid-19 trial "**matching service**" in the U.S.
- The FDA issued guidelines that relaxed regulatory requirements for:
  - Thermometers
  - Infusion pumps

### Testing

*Asked why more of the rapid Abbott tests haven't been done*, Vice President Mike Pence said there are 18,000 Abbott machines in the country that can run the test, but not all of them are being used. Ambassador Deborah Birx, MD, the White House Coronavirus Response Coordinator, said she is doing a call with lab directors around the country to get to the bottom of this and get them into use, "We only ran 88,000 tests with 1 million test kits...They could have screened 100% of healthcare workers in the last three weeks."

Starting on April 9, White House reporters had to pass an Abbott rapid Covid-19 test to get into the daily briefing. Experts agree that tests like these – and antibody tests – are key to getting the economy going again. Asked when the Abbott test is likely to be readily available, White House Economic Advisor Larry Kudlow estimated 4-8 weeks.

The list of tests is continuing to grow. There are almost too many to know how to choose. Among the newest entries to the list are:

- **Aid Genomics** is partnering with **BGI** on a coronavirus testing lab that can handle 3,000 tests/day in the Gaza Strip.
  - **Avacta** and **Cytiva** are collaborating on development of a Covid-19 rapid test.
  - **Becton Dickinson and BioGX's SARS-CoV-2 test**, which will run on the BD Max molecular diagnostic system, was granted an EUA by the FDA. The test will be used on-site at hospitals.
  - **Genetron Health's Detection Kit for Novel SARS-CoV-2 RNA** (PCR-Fluorescence Probing) was granted a CE Mark.
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- **Gnomegen's COVID-19 RT-Digital PCR Detection kit** received an EUA from the FDA. Its test runs on Thermo Fisher Scientific's Applied Biosystems QuantStudio 3D Digital PCR system.
- **Ipsium Diagnostics' COV-19 IDx**, which runs on Thermo Fisher Scientific's Applied Biosystems QuantStudio 12 K Flex instrument, was granted an EUA by the FDA.
- **MicroGen DX**, a CLIA-certified laboratory test that uses sputum and saliva, has been submitted to the FDA for EUA clearance.
- **OraSure Technologies** was awarded \$710,310 by the Biomedical Advanced Research and Development Authority (BARDA) for development of a 20-minute pan-SARS-coronavirus antigen self-test and to obtain an EUA for it from the FDA.
- **ScienCell Research Laboratories' ScienCell SARS-CoV-2 Coronavirus Real-time RT-PCR Detection Kit** was granted an EUA by the FDA.
- **Viracor Eurofins Clinical Diagnostics' Viracor SARS-CoV-2 assay**, a molecular laboratory-developed test that runs on Thermo Fisher Scientific's Applied Biosystems 7500 Real-Time PCR systems and uses BioMérieux's Nuclisens EasyMag for nucleic acid extractions, was granted emergency use authorization by the FDA.

### Transmission

- A wastewater study in one community in Massachusetts found a virus particle level in sewage that suggests at least 2,300 people were infected, but at the time there were only 446 official cases.
- A CDC study found that **infected people** may be much more infectious than previously thought. Epidemiologists use the reproduction number ( $R_0$ ) to represent the number of cases, on average, an infected person will cause during the infectious period. Measles is very infective with an  $R_0$  of 12-18; flu is less infective with an  $R_0$  of 2-3. SARS-CoV-2 was thought to have an  $R_0$  of 2-3.5, but now the CDC estimates it has an  $R_0$  of 5.7, making it much worse than flu but not as bad as measles.
- The CDC issued new guidelines for which **essential workers** – e.g., healthcare workers, food suppliers – can **return to work** after exposure to Covid-19 but no signs or symptoms of the disease.
  - **Yes if employees** – If they take their temperature before work, wear a face mask at all times, practice social distancing at work, go home if they become sick, don't share headsets or objects used near the face, and don't congregate in the break room or elsewhere.
  - **Yes if employers** – If they take the employees' temperature and assess for symptoms prior to the employee starting work, increase the frequency of cleaning, increase air exchange in the building, send sick workers home immediately, and test the use of face masks to be sure they don't interfere with workflow.

### Treatment

#### ■ Hydroxychloroquine

- The FDA approved an abbreviated new drug application (ANDA) from Accord Healthcare as another generic treatment for lupus, rheumatoid arthritis, and malaria. This approval did not cover Covid-19.
  - The CDC removed **guidance** from its website on antimalarial dosing information on use of hydroxychloroquine and chloroquine after criticism from physicians and other experts.
  - Henry Ford Hospital in Detroit, Michigan, is running the 3,000-patient, 8-week WHIP COVID-19 **trial** of hydroxychloroquine vs. placebo as a prophylaxis for healthcare workers and first responders. The principal investigator
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is William O'Neill, MD, a well-known interventional cardiologist and experienced trialist. Mylan is providing the hydroxychloroquine to the FDA which will give it to Henry Ford.

- The National Heart, Lung, and Blood Institute started the randomized ORCHID trial in >500 hospitalized Covid-19 patients, with the first patients enrolled at Vanderbilt University Medical Center.
- *Asked when the results of any of the U.S. tests with hydroxychloroquine will be available*, FDA Commissioner Dr. Hahn said, **"The trials will take several months."**
- Joint guidance from the American Heart Association (AHA), the American College of Cardiology (ACC), and the Heart Rhythm Society (HRS) – published in *Circulation*, the *Journal of the American College of Cardiology*, and the *Heart Rhythm Journal* – on considerations for drug interaction (QT prolongation) when Covid-19 is treated with hydroxychloroquine and azithromycin recommended:
  - ✓ Electrocardiographic/QT interval monitoring
  - ✓ Withholding the drugs in patients with baseline QT prolongation or congenital long QT syndrome
  - ✓ Monitoring cardiac rhythm and QT interval
  - ✓ Optimal electrocardiographic interval and rhythm monitoring may not be possible
  - ✓ Correction of hypokalemia and hypomagnesemia
  - ✓ Avoiding other QTc prolonging agents

#### ■ The European Medicines Agency (EMA)

- Established a task force (COVID-ETF) to take quick and coordinated action on development, authorization, and safety monitoring of therapeutics and vaccines for Covid-19. The task force pulls together the chair and vice-chair of the key regulatory agencies in the EU.
- Issued a report that concludes that a randomized clinical trial is the best and fastest way to help patients.
- Approved compassionate use of **Gilead Sciences' remdesivir** for Covid-19 even though it didn't do that for hydroxychloroquine.

#### ■ Fujifilm's Avigan (favipiravir) – Together, three Massachusetts hospitals are launching the first U.S. trial of this RNA polymerase inhibitor in Covid-19.

#### ■ Gilead Sciences' remdesivir – The company said it is ramping up production and plans to donate (for free) 1.5 million doses of this antiviral.

#### ■ Pfizer announced that it has identified a lead drug to treat Covid-19 that, if successful, would be given early in the disease process, when patients are admitted to the hospital. Pfizer expects to be ready to start a trial in "a few months."

#### ■ Roche/Chugai's Actemra (tocilizumab)

- Chugai started a Phase III trial of this anti-IL-6 in Covid-19 in Japan.
- A case report, published in the journal *Blood Advances*, describes a 60-year-old man with multiple myeloma and confirmed Covid-19 who was given this anti-IL-6 on Day 9 of his hospitalization. The patient's chest tightness resolved on Day 12, the ground-glass opacity in his chest was significantly improved on Day 19, and he was discharged.

#### ■ Other new drugs keep being added to the list of things being explored as treatments for Covid-19. President Trump said there are 10 therapeutics currently in active studies, adding, "Some are looking incredibly successful, but we have to go through a process."

- **Alexion Pharmaceuticals' Soliris (eculizumab)** – The company plans to start a 10-patient Phase II proof-of-concept trial of this Complement 5 inhibitor in Covid-19.



- **Johnson & Johnson's darunavir** – A preprint study (see at [medRxiv](#)) this HIV antiviral showed “no activity” against SARS-CoV-2. Gilead's remdesivir was the control, and it did show “potent antiviral activity.”
  - **Neurimmune** and **Ethris** are partnering on creation of messenger RNA antibodies that can be inhaled and delivered directly into a patient's lungs to neutralize SARS-CoV-2.
- An American Thoracic Society-led international task force released guidance on managing Covid-19 patients, with **suggestions** (not recommendations) for treatment, based on scarce direct evidence, indirect evidence, and clinical observations, including:
- Perform **prone** ventilation in patients who have refractory hypoxemia and Covid-19 pneumonia (i.e., acute respiratory distress syndrome, ARDS).
  - Consider extracorporeal membrane oxygenation (ECMO) in patients who have refractory hypoxemia, ARDS, and failed prone ventilation.
  - Prescribe hydroxychloroquine (or chloroquine) to hospitalized patients with Covid-19 pneumonia if all of the following apply: a) shared decision-making is possible, b) data can be collected, c) the illness is sufficiently severe to warrant investigational therapy, and d) the drug is not in short supply.

### Vaccines

**What's new:** **Voltron Therapeutics** and **Hoth Therapeutics' HaloVax** was developed with vaccine technology from Massachusetts General Hospital, and it will start animal trials this month.

### Clinical trial update

Both the FDA and the European Medicines Agency (EMA) issued comments on clinical trial operations during Covid-19.

- **EMA.** The EMA issued a draft guideline, saying sponsors should consider the implications of Covid-19 on methodological aspects of ongoing trials. Though the EMA said it was “not possible to give general applicable advice on how the different aspects related to the pandemic should be handled, as implications on clinical trials are expected to be manifold,” sponsors were urged to “pre-plan how systematic deviations resulting from the measures and individual decisions related to the Covid-19 pandemic are captured.” And the EMA said sponsors should record deviations and the related reasons for them.
- **FDA.** The FDA acknowledged that protocol modifications may be required and that there may be protocol deviations due to Covid-19. One FDA suggestion: virtual visits.

Covid-19 **is** affecting clinical trials. A March 19, 2020, survey by Clinical Research IO found that 24% of trial investigators have stopped enrolling new patients due to patient safety concerns, and half of the others were considering halting new patient enrollment. In addition, some sites reported a 9% decrease in patient retention. Among the issues:

- Weighing the potential risks and benefits of missed treatments vs. possible exposure to Covid-19. Some sponsors are considering arranging home visits for injectable drugs.
- Uneven site closing – for example, sites in New York may close but sites in Japan continue – changing the patient mix.

Here is what is happening to some specific research projects that have been affected. This is not intended to be a complete list, just studies that have caught our attention:

- **Addex Therapeutics' dipraglurant** – A pivotal trial of this Parkinson's disease drug is postponed indefinitely.
  - **Alzheimer's disease** – Enrollment of new participants has been halted everywhere. Observational studies in Alzheimer's disease have been stopped almost everywhere, though there are a few exceptions (e.g., the DIAN trial in Argentina).
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- **Atara Biotherapeutics' ATA-188** – Patient enrollment was paused in the second (randomized) part of an ongoing Phase I trial in progressive forms (secondary and primary progressive) of multiple sclerosis (MS). Patients in the first, open-label part of this trial are continuing to be monitored.
  - **bluebird bio's Zynteglo (LentiGlobin, BB-305)** – Some of the assays required for the rolling biologics license application (BLA) submission for this gene therapy for beta thalassemia are expected to be impacted by Covid-19, and the company now does not expect the submission to be completed until mid-2021. In addition, the commercial launch of Zynteglo in Germany is likely to be delayed until 2H20.
  - **Bristol-Myers Squibb** temporarily suspended all screening, enrollment, and apheresis in gene therapy trials, and no new sites will be activated until at least April 13, though existing sites can continue to recruit new patients.
  - **CRISPR Therapeutics' CTX-001** – Patient enrollment was halted in a study in transfusion-dependent beta thalassemia and another in severe sickle cell disease because of hospital beds being reserved for Covid-19 patients.
  - **Enanta Pharmaceuticals** paused recruitment and dosing in the Phase IIb ARGON-2 trial of EDP-105 in NASH and paused enrollment in Part 2 of a Phase Ia/Ib trial of EDP-514 in hepatitis B.
  - **Equillium's itolizumab (EQ-001)** – Two Phase Ib trials (one in asthma and another in lupus nephritis) were halted due to the coronavirus outbreak, but a Phase Ib/II trial in acute graft-versus-host disease is continuing. The rights to this anti-CD6 antibody were licensed from **Biocon** for the U.S., Canada, Australia, and New Zealand.
  - **Genfit's elafibranor (GFT-505)** – The company said that the Phase III RESOLVE-IT trial of this PPAR $\alpha/\gamma$  agonist for non-alcoholic steatohepatitis (NASH) is fully enrolled, and the read-out should not be delayed, and the extension study is continuing. However, the Phase I trials necessary to support a regulatory submission of elafibranor have been halted, and new trials in NASH and primary biliary cholangitis (PBC) have been put on hold.
  - **Intercept Pharmaceuticals' Ocaliva (obeticholic acid)** – The FDA advisory committee review of this drug to treat NASH was delayed until June 9 because of Covid-19. The PDUFA date was March 26, so it is delayed at least 3 months.
  - **Ironwood Pharmaceuticals' IW-3718** – Enrollment in Phase III trials of this treatment for refractory gastroesophageal reflux disease (GERD) has been impacted, delaying the expectation for top-line data until 2H20.
  - **IVERIC bio's Zimura (avacincaptad pegol)** – The start of enrollment was delayed in a second pivotal Phase II trial in geographic atrophy secondary to dry age-related macular degeneration (AMD).
  - **Lilly** halted new enrollment in ongoing trials, continuing dosing in existing trials, and not starting new trials. This means mirikizumab (an anti-IL-23 for Crohn's disease and ulcerative colitis) and tirzepatide (a dual GIP/GLP-1 receptor agonist for diabetes) are delayed.
  - **Merck MSD** is temporarily suspending enrollment in ongoing trials and is not starting new studies, except in China where work is "on track" and actually "scaling up."
  - **Moderna's mRNA-1273** – This coronavirus vaccine trial is continuing, but the company has paused a number of other trials in infectious and rare diseases, including a Phase I trial of mRNA-3704 in methylmalonic acidemia and another of mRNA-3927 in propionic acidemia. Neither of those trials had enrolled any patients. And an age de-escalation pediatric trial of a respiratory vaccine, mRNA-1653, was paused.
  - **Novocure's Optune (tumor treating fields, TTF)** – Completion of studies for expanding indications is expected to be delayed by about 6 months.
  - **Pfizer** halted recruitment in new and ongoing "interventional" trials for 3 weeks but with some exceptions. The pause does not affect sites in China, Japan, and South Korea or to trials recruiting patients with life-threatening conditions with
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few/no other options – e.g., some oncology studies and Duchenne muscular dystrophy (DMD) studies. Fully enrolled trials are not affected.

- **Provention Bio's teplizumab (PRV-031)** – Recruitment was suspended in the Phase III PROTECT trial of this anti-CD3 antibody in newly diagnosed Type 1 diabetics. Patients already enrolled will be allowed to complete treatment.
- **Reata Pharmaceuticals' bardoxolone methyl** – The Phase III CATALYST trial and the RANGER extension study in connective tissue disease-associated pulmonary arterial hypertension (PAH) were halted because those patients are considered high-risk for Covid-19. The company also paused enrollment of new patients in two Phase III kidney trials, CARDINAL in Alport syndrome and FALCON in autosomal dominant polycystic kidney disease.
- **Servier and Allogene's UCART19** – Recruitment was stopped in the PALL and CALM trials of this allogeneic CAR T therapy in patients with relapsed/refractory acute lymphoblastic leukemia (ALL).
- **Vertex Pharmaceuticals** halted enrollment in some studies and may delay the start of new studies.
- The **U.K.'s NIHR Clinical Research Network** shut down due to Covid-19 and is pausing all trials, redeploying medical staff to fight Covid-19.

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

- ? When someone develops **antibodies** to the coronavirus, how long are those antibodies protective – months, years, a lifetime?
- ? Are the **neurological symptoms/effects** reversible in some, all, most patients?
- ? 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 or Kaiser databases 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)?
- ? 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**? What percent recover and 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

Country	March 18			March 25 (1 week)			April 1 (2 weeks)			April 8 (3 weeks)		
	Cases	Deaths	Fatality rate	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%	1,511,104	88,338	5.8%
Italy	35,713	2,978	8.3%	74,386	7,503	10.1%	110,574	13,155	11.9%	139,422	17,669	12.7%
Spain	13,176	638	4.8%	49,515	3,647	7.4%	104,118	9,387	9.0%	148,220	14,792	10.0%
<b>U.S.</b>	<b>9,249</b>	<b>145</b>	<b>1.6%</b>	<b>68,960</b>	<b>1,041</b>	<b>1.5%</b>	<b>213,372</b>	<b>4,757</b>	<b>2.2%</b>	<b>429,052</b>	<b>14,695</b>	<b>3.4%</b>
France	n/a	n/a	n/a	n/a	n/a	n/a	57,749	4,043	9.5%	113,959	10,887	9.6%
U.K.	>2,600	104	4.0%	9,640	466	4.8%	29,865	2,357	7.9%	61,474	7,111	11.6%
Iran	17,061	1,135	6.7%	27,017	2,077	7.7%	47,593	3,036	6.4%	64,586	3,993	6.2%
China	81,137	3,130	3.9%	81,667	3,285	4.0%	82,261	3,316	4.0%	82,809	3,337	4.0%
Germany	12,327	28	0.2%	37,323	206	0.6%	77,872	920	1.2%	113,296	2,349	2.1%

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

## #2 Worldwide Covid-19 Statistics – Daily

Country	April 5			April 6			April 7			April 8			Per capita case rate	
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	April 6	April 8
Worldwide	1,275,856	69,514	5.4%	1,345,048	74,565	5.5%	1,426,096	81,865	5.7%	1,511,104	88,338	5.8%	0.02%	0.02%
Italy	128,948	15,887	12.3%	132,547	16,523	12.5%	135,586	17,127	12.6%	139,422	17,669	12.7%	0.22%	0.23%
Spain	131,646	12,641	10.0%	136,675	13,341	9.8%	141,942	14,045	9.9%	148,220	14,792	10.0%	0.29%	0.32%
<b>U.S.</b>	<b>337,638</b>	<b>9,647</b>	<b>2.9%</b>	<b>366,614</b>	<b>10,783</b>	<b>2.9%</b>	<b>396,223</b>	<b>12,722</b>	<b>3.2%</b>	<b>429,052</b>	<b>14,695</b>	<b>3.4%</b>	<b>0.11%</b>	<b>0.13%</b>
France	93,780	8,093	8.6%	98,963	8,926	9.0%	110,065	10,343	9.4%	113,959	10,887	9.6%	0.15%	0.17%
U.K.	48,440	4,943	10.2%	52,279	5,385	10.3%	55,949	6,171	11.0%	61,474	7,111	11.6%	0.08%	0.09%
Iran	58,226	3,603	6.2%	60,500	3,739	6.2%	62,589	3,872	6.2%	64,586	3,993	6.2%	0.07%	0.08%
China	82,644	3,335	4.0%	82,665	3,335	4.0%	82,718	3,335	4.0%	82,809	3,337	4.0%	0.006%	0.006%
Germany	100,123	1,584	1.6%	103,374	1,810	1.8%	107,663	2,016	1.9%	113,296	2,349	2.1%	0.12%	0.15%

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

## #3 U.S. Covid-19 Statistics – Weekly

State	March 18			March 25 (1 week)			April 1 (2 weeks)			April 8 (3 weeks)		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
<b>New York</b>	<b>2,382</b>	<b>12</b>	<b>0.05%</b>	<b>30,811</b>	<b>285</b>	<b>0.9%</b>	<b>83,712</b>	<b>1,941</b>	<b>2.3%</b>	<b>149,316</b>	<b>6,268</b>	<b>4.2%</b>
New Jersey	427	5	1.2%	4,402	62	1.2%	11,255	355	3.2%	47,437	1,504	3.2%
Washington	1,012	52	5.1%	2,469	123	5.0%	5,634	224	4.0%	8,682	394	4.5%
California	611	13	2.1%	2,102	40	1.9%	8,155	171	2.1%	16,957	442	2.6%
Michigan	80	0	0	2,294	43	1.3%	9,334	337	3.6%	20,346	959	4.7%
Illinois	289	1	0.3%	1,884	19	1.0%	6,980	141	2.0%	15,078	462	3.1%
Florida	314	7	2.2%	1,682	22	1.3%	6,955	87	1.3%	15,455	309	2.0%
Louisiana	240	6	2.5%	1,795	65	3.3%	6,424	273	4.2%	17,030	652	3.8%
Massachusetts	256	0	0	1,838	15	0.7%	7,738	133	1.7%	16,790	433	2.6%
<b>U.S.</b>	<b>9,249</b>	<b>145</b>	<b>1.6%</b>	<b>68,960</b>	<b>1,041</b>	<b>1.5%</b>	<b>213,372</b>	<b>4,757</b>	<b>2.2%</b>	<b>429,052</b>	<b>14,695</b>	<b>3.4%</b>

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

## #4 U.S. Covid-19 Statistics – Daily

State	April 4			April 5			April 6			April 7			April 8		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
New York	113,704	3,565	3.1%	122,031	4,159	3.4%	130,689	4,758	3.6%	138,863	5,489	4.0%	149,316	6,268	4.2%
New Jersey	34,124	846	2.5%	37,505	917	2.4%	41,090	1,003	2.4%	44,416	1,232	2.8%	47,437	1,504	3.2%
Michigan	14,225	540	3.8%	15,718	617	3.9%	17,221	727	4.2%	18,970	845	4.5%	20,346	959	4.7%
Louisiana	12,496	409	3.3%	13,010	477	3.7%	14,867	512	3.4%	16,284	582	3.6%	17,030	652	3.8%
California	12,026	276	2.3%	13,438	319	2.4%	14,336	343	2.4%	15,865	374	2.4%	16,957	442	2.6%
Massachusetts	11,736	216	1.8%	12,500	231	1.8%	13,837	260	1.9%	15,202	356	2.3%	16,790	433	2.6%
Florida	11,111	191	1.8%	12,350	221	1.8%	13,324	236	1.8%	14,747	296	2.0%	15,455	309	2.0%
Illinois	10,357	243	2.3%	11,256	274	2.4%	12,262	307	2.5%	13,549	380	2.8%	15,078	462	3.1%
Washington	6,966	284	4.1%	7,591	310	4.1%	7,984	338	4.2%	8,384	372	4.4%	8,682	394	4.5%

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

## #5 Watching for When the Coronavirus Curve Flattens - \*APRIL 2020 - World and U.S.

(Additional CASES each day, not total cases)

Location	April 1	April 2	April 3	April 4	April 5	April 6	April 7	April 8
Worldwide	75,687	81,068	84,175	98,557	78,451	69,192	81,048	85,008
China	7	172	78	32	101	21	53	91
Spain	8,195	7,947	7,134	6,969	5,478	5,029	5,267	6,278
Italy	4,782	4,668	4,585	4,805	4,316	3,599	3,039	3,836
Iran	2,898	2,875	2,715	2,560	2,483	2,274	2,089	1,997
<b>U.S.</b>	<b>25,200</b>	<b>31,306</b>	<b>33,150</b>	<b>31,022</b>	<b>28,788</b>	<b>28,976</b>	<b>29,609</b>	<b>32,829</b>
New Jersey	3,559	3,335	4,305	4,229	3,381	3,585	3,326	3,057
Michigan	1,719	1,457	1,953	1,481	1,493	1,503	1,749	1,376
Louisiana	1,187	2,726	1,147	2,199	514	1,857	1,417	746
California	673	1,036	1,510	1,325	1,412	898	1,529	1,092
Massachusetts	1,118	1,228	1,436	1,334	764	1,337	1,365	1,588
Florida	617	1,055	1,575	1,526	1,040	1,173	1,423	708
Illinois	986	715	1,209	1,453	899	1,370	1,287	1,529
Washington	597	376	612	405	396	326	337	N/A
<b>New York</b>	<b>7,917</b>	<b>8,669</b>	<b>10,482</b>	<b>10,841</b>	<b>8,327</b>	<b>8,658</b>	<b>8,174</b>	<b>10,453</b>

\* This is the metric that Dr. Birx said to watch to find when the curve flattens.

## #6 Death Toll Increases - APRIL 2020 - World and U.S.

(Additional DEATHS, not total deaths)

Location	April 1	April 2	April 3	April 4	April 5	April 6	April 7	April 8
Worldwide	4,811	6,164	5,898	5,735	4,908	5,051	7,300	6,473
China	7	6	4	4	5	0	0	2
Italy	727	760	766	681	525	636	604	542
Spain	923	961	850	749	694	700	704	747
<b>U.S.</b>	<b>884</b>	<b>1,154</b>	<b>1,230</b>	<b>1,266</b>	<b>1,240</b>	<b>1,136</b>	<b>1,939</b>	<b>1,973</b>
New Jersey	88	82	109	200	71	86	229	272
Michigan	78	80	62	61	77	110	118	114
Louisiana	34	37	60	39	66	35	70	70
California	18	32	34	39	43	24	31	68
Massachusetts	33	32	38	24	15	29	96	77
Florida	10	41	35	28	27	18	60	13
Illinois	42	16	53	33	31	33	73	82
Washington	18	26	24	20	13	10	12	19
<b>New York</b>	<b>441</b>	<b>432</b>	<b>562</b>	<b>630</b>	<b>594</b>	<b>599</b>	<b>731</b>	<b>779</b>