



TRENDS-in-MEDICINE

BULLETIN: UPDATE ON CORONAVIRUS 4/12

April 12, 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. The lockdowns in Europe, India, the U.S., and elsewhere are having an effect on the spread of the virus, but the economic toll is mounting, and how long people can and will continue it is uncertain. It is becoming increasingly clear that the U.S. will not re-open May 1, that there is no sudden switch that can be thrown that re-opens everything.

The questions are how much longer governments can maintain the closures, how to handle re-opening things, and whether any re-opening will cause a spike in Covid-19 cases/deaths.

Our charts are on Pages 12-13 (we did all the computations). Watch the charts on *additional* cases per day to look for countries/states that are peaking. Note that there are two new charts, one reflecting the rate of *cases* per capita and another on *deaths* per capita. These may be the best way to compare what is happening in different states and countries.

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

- The **U.S.** has more cases than any other country, 557,571. On the key metric of additional cases per day, the U.S. *may* have peaked, but that is not completely clear.
- **France, Italy, and Spain** have plateaued in terms of additional cases per day, a key metric. There is no decrease yet, but the flattening is encouraging.
- The worldwide **case fatality rate** continues to increase steadily and is now 6.2%. Spain, Italy, France, and the U.K. continue to have case fatality rates $\geq 10\%$ vs. 4.0% in the U.S. and 2.4% in Germany.
- On a **per capita basis**, the U.S. *case rate* is lower than France, Italy, and Spain but higher than the U.K., and close to Germany.
- On a **per capita basis**, the *fatality rate* in the U.S. is lower than even Sweden. Out of every 100,000 people in the U.S. 7 are dying from Covid-19, which compares to 37 in Spain, 33 in Italy, 22 in France, 16 in the U.K., and 9 in Sweden.
- **New York** remains the hottest hotspot in the U.S., with 188,694 cases, accounting for 34% of all the cases in the U.S. It appears to have peaked and plateaued, but the numbers aren't going down yet.

Trends-in-Medicine ■ 2731 N.E. Pinecrest Lakes Blvd ■ Jensen Beach FL 34957
772-285-0801 ■ Fax 772-334-0856 ■ www.trends-in-medicine.com

Trends-in-Medicine has no financial connections with any pharmaceutical or medical device company. The information and opinions expressed have been compiled or arrived at from sources believed to be reliable and in good faith, but no liability is assumed for information contained in this newsletter. Copyright ©2020.

This document may not be reproduced without written permission of the publisher.

The world

- **Europe** – The University of Washington’s Institute for Health Metrics and Evaluation ([IHME](#)) estimates that Belgium, France, Germany, Italy, and Spain may have peaked in daily Covid-19 deaths. The Netherlands and Switzerland are predicted to peak on May 4.
- **France** is extending its lockdown for a second time, past April 15, but how much past is unclear. President Emmanuel Macron will address the nation on Monday April 13.
- **India** – Prime Minister Modi extended the lockdown indefinitely.
- **Italy** – The country-wide lockdown, which was due to expire April 13, was extended until May 3, though a few shops – bookshops, stationers, and children’s clothing stores – will be allowed to re-open April 14.
- **Saudi Arabia** extended indefinitely a 24-hour nationwide curfew (in other words, a lockdown).
- **South Korea**
 - The health ministry will start putting tracking wristbands (bracelets) on people who disobey quarantine rules as soon as a sufficient quantity of the bands has been manufactured, which is expected to be soon.
 - There is a mandatory 14-day quarantine on incoming travelers from the U.S. and Europe.
 - The number of people who tested positive for the virus, recovered, and now are positive again has risen to 111. The question is whether they were re-infected or whether the virus was reactivated in them.
- **Spain** – Some industries – e.g., manufacturing and construction – will be allowed to restart on April 13 – after the government issued guidelines for people to return to work, loosening lockdown restrictions. Companies re-opening must provide workers with appropriate protective equipment and must ensure employees have the space to be 6 feet apart.
- **U.K.**
 - Prime Minister Boris Johnson was released from the hospital after being treated for Covid-19.
 - Queen Elizabeth delivered her first-ever Easter message, basically urging everyone to stay home.
- The **World Health Organization** (WHO) is investigating a report of some recovered coronavirus patients testing PCR-positive after initially testing negative. There have been sporadic reports of re-infections before the latest South Korea batch, but they were mostly dismissed as testing errors.

United States

■ Re-opening the economy

- President Trump is not giving a date when the economy can re-open, and even if he did, it is state governors who ultimately control when businesses can re-open and how they re-open.
 - ✓ He said the decision of how and when to re-open the economy is “the biggest decision I’ve ever had to make.”
 - ✓ He is forming an Opening Our Country Task Force with doctors and business leaders, focused on the economic aspects. Details on the task force are expected April 14.
 - Thomas Frieden, MD, former director of the Centers for Disease Control and Prevention (CDC), said that re-opening has to have 4 features: wide testing, contact tracing (which he compared to a hurricane warning system), safe isolation, and quarantine. Dr. Frieden said contact tracing is what CDC knows how to do, but it needs to “build an army” of tracers, so the “faucet can gradually be loosened.” He said it will be a massive undertaking and is not going to happen overnight. He suggested there could be a new CCC – “Coronavirus Contact Corps.”
-

- Irwin Redlener, MD, director of Columbia University's National Center for Disaster Preparedness, said re-opening is going to be "slow and painful and could take until August before shelter-in-place is over."
 - **Cruise ships.** The CDC modified and extended the "no sail" order, banning *all* cruise ship sailings for at least *another 100 days*. CDC said that there currently are ~100 cruise ships roaming at sea off the coasts of the U.S., with nearly 80,000 crew onboard. There are also at least 20 cruise ships in port/anchorage in the U.S. with known/suspected Covid-19-infected crew members. CDC said some of these ships have crew onboard that are not critical to maintaining seaworthiness. The CDC is ordering ships in U.S. waters to develop a comprehensive, detailed operational plan, approved by CDC and the U.S. Coast Guard, to address the pandemic through maritime focused solutions that have *limited reliance* on state, local, and federal government support.
 - **Disaster declarations.** President Trump signed a disaster declaration for Wyoming, so now all 50 states, for the first time, are under a disaster declaration at the same time.
 - **Fatality peak.** The modelers at IHME believe Illinois, New Jersey, and New York daily deaths have peaked. Eduardo Sanchez, MD, MPH, Chief Medical Officer for Prevention at the American Heart Association, did some calculations of his own and concluded that, at this time, Covid-19 is likely the #9 cause of death in the U.S., falling between flu and kidney-related diseases.
 - **Food supply.** The report of an outbreak of Covid-19 among workers at a meat packing plant in Colorado raised, again, the question of whether the virus can be transferred through food. The FDA has said No, and the president of the American Farm Bureau said, "As I understand it, it cannot."
 - **Heart damage.** Studies suggest that the coronavirus can damage the heart, though it is not yet clear whether it directly invades the heart or if there is an immune reaction effect. Either way, effects on the heart are being seen in people without pre-existing cardiac conditions. A New York cardiologist expressed concern that uninfected people experiencing a heart attack at home may be delaying going to the hospital or not going at all out of fear of catching the virus, and she noted that a lot of them could be dying at home.
 - **Healthcare providers.** The Centers for Medicare and Medicaid Services (CMS) said that, in addition to allowing – paying for – telehealth, it will allow healthcare providers to practice across state lines and at the top of their license. That means nurse practitioners will be allowed to perform select medical exams for Medicare patients in skilled nursing facilities, even if those are not Covid-19-related exams; occupational therapists at home health agencies will be able to do initial assessments for homebound patients; and hospice nurses will no longer have to participate in hospice aide in-service activities. State licensing rules may still limit some of this.
 - **Military**
 - **USS Theodore Roosevelt.** At latest count, 92% of crew members on this nuclear-powered aircraft carrier which is docked in Guam had been tested for coronavirus, with 550 sailors testing positive and 3,696 sailors moved ashore.
 - **USS Nimitz** is scheduled to replace the Roosevelt in the South Pacific this summer. Asked if the sailors would all be tested for coronavirus before boarding the Nimitz, Thomas McCaffery, Assistant Secretary of Defense, said No because "the current test will show a considerable amount of false negatives... We don't believe that is the best way to allocate testing resources."
 - **Field hospitals and ships** are being under-used, but that is good news.
 - ✓ The USNS Comfort in New York harbor has the capacity to treat 500 Covid-19 patients but is only treating 64 patients. Instead, 366 medical personnel are going to New York City hospitals to help out.
 - ✓ 255 of the 2,500 Covid-19 beds at the Javits Center in New York City are in use.
 - ✓ 15 of the beds on the USNS Mercy in Los Angeles harbor are in use.
-

■ **Unemployment.** There are 17 million people unemployed in the U.S. right now, and the states with the highest rates of unemployment, in order, are: Louisiana, New Hampshire, Virginia, Georgia, and Mississippi. The ones with the lowest rates of unemployment are: Connecticut, Oregon, Wyoming, Wisconsin, and West Virginia. But even in the state with the smallest increase (Connecticut), unemployment is up 13-fold vs. the same period in 2019.

President Trump and the White House Task Force on Coronavirus

- The President renewed his call for a broad **payroll tax cut** to be included in a fourth economic stimulus package, if there is one.
- Ambassador Deborah Birx, MD, the White House Coronavirus Response Coordinator, said on April 10 that the U.S. was where Italy was a week ago.
- Agriculture Secretary Sonny Perdue was tasked with setting up a program to bring relief to farmers, ranchers, and producers and to make sure the food supply is safe and uninterrupted.
- President Trump said more than 2 million Covid-19 tests have been completed, with more than 100,000/day being done. He also said the FDA is currently validating antibody tests to be sure they are accurate – and doing that “at breakneck speed.”

U.S. states and cities

■ **Connecticut** is expected to peak on April 25, with **Florida** and **Massachusetts** peaking on April 27.

■ Florida

- The Florida Health Care Association, which represents the state’s nursing homes, sent a letter to Gov. Ron DeSantis asking him to protect nursing homes from Covid-19 lawsuits. And the governor is considering it.
- Broward County ordered all people age ≥ 2 (except people with breathing difficulties) to wear a facial covering when visiting essential businesses. The order also requires those providing essential services to wear a mask during in-person interactions with the public.

■ **Louisiana** extended the stay-at-home order until May 15.

■ New York

- New York City Mayor Bill de Blasio announced that New York City schools will remain closed for the rest of the school year, but Gov. Andrew Cuomo said that decision is his, and he has not decided yet.
- Intensive care unit (ICU) admissions were fewer than discharges/deaths – a net negative change – for the first time during the coronavirus outbreak.
- Gov. Cuomo signed an executive order that will allow more people to administer antibody tests than regulations currently allow.
- Overall, New York appears to be flattening the curve.

Drug supplies

■ **Pharmacies.** The FDA issued a guidance for pharmacy compounders that experience shortages of the personal protection equipment (PPE) they typically use to compound sterile human drugs, suggesting ways pharmacies may be able to preserve PPE when supplies are limited. The Agency also provided *limited regulatory flexibility* for compounders that cannot obtain sufficient supplies of PPE for sterile compounding, provided they adopt risk mitigation strategies that are described in the guidance.

Medical supplies

- **Reusable supplies.** FDA Commissioner Stephen Hahn, MD, said the FDA issued revised guidance on laundering medical cloth gowns. He noted that it is not something that normally happens around the country, but if hospitals want to do it, there is no information on how to do it properly. And he said reusing gowns was cleared with CMS.
- **Mask sterilization.** The FDA approved two more companies to provide machines that sterilize N95 masks, granting an emergency use authorization (EUA) for:
 - Advanced Sterilization Products' STERRAD Sterilization Cycles (STERRAD 100S Cycle, STERRAD NX Standard Cycle, or STERRAD 100NX Express Cycle), which uses vaporized hydrogen peroxide gas plasma sterilization, was granted an EUA. The FDA said there are ~9,930 of these sterilization systems in ~6,300 hospitals in the U.S. The reprocessing times vary from 24-55 minutes, and each can reprocess approximately 480 respirators per day.
 - STERIS' STERIS V-PRO 1 Plus, maX, and maX2 Low Temperature Sterilization Systems. Each of these machines, which use vaporized hydrogen peroxide, can decontaminate ~80,000 masks/day. And the FDA Commissioner said that 80,000 limit may be able to be increased for this and the Battelle devices.
- **Exports.** U.S. Customs and Border Protection (CBP) plans to seize exports of N95 respirator masks, surgical masks, gloves, and other PPE. The Federal Emergency Management Agency (FEMA) will then determine what can be released and what must stay in the U.S. during the pandemic.
- **Ventilators.** So far, there are no reports of a patient dying from Covid-19 because there wasn't an available ventilator. Mehmet Oz, MD, estimated that at his hospital, New York Presbyterian, ~50% of Covid-19 ventilator patients are dying.
 - Yet, ventilators are being rapidly manufactured, and new ideas are being proposed, such as:
 - ✓ Use of non-invasive ventilators to treat patients with less severe respiratory distress, which has been tried in Italy and China.
 - ✓ A low-cost ventilator, the Robertson Ventilator, created by researchers at the University of Mississippi Medical Center, that is made from adapters, valves, garden hose sections, a solenoid, and a lamp timer. The device was submitted to the FDA for an EUA.
 - ✓ Maingear, a gaming PC company, is producing a low-cost ventilator (~\$7,500) for New York City that it designed using off-the-shelf parts, the Maingear LIV.
 - ✓ Auburn University researchers are converting continuous positive airway pressure (CPAP) machines into low-cost ventilators called Re-InVent.
 - ✓ Irish researchers have created an adjustable ventilator that can be split to treat two patients at once.
 - A study, published in *Clinical Radiology*, found 3 of 4 respirators were unsafe to use in an MRI. The researchers called for MRI-approved masks to be designated by the WHO and for radiologists to test respirators with a handheld magnet (>1,000 gauss) before conducting an MRI on someone wearing the respirator.

Testing

- The Trump administration said it will require insurance companies to provide free *antibody* tests as well as free diagnostic tests. Who will pay for antibody tests for the uninsured is not clear.
 - The FDA said:
 - It has worked with >300 test developers who plan to submit an EUA request for tests to detect the coronavirus.
 - So far, 33 EUAs have been issued for diagnostic tests.
 - 170 laboratories have begun testing under the policies set forth in our COVID-19 Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency Guidance.
-

- >70 test developers are marketing serologic (antibody) tests without prior FDA review under special guidance the FDA issued for the pandemic. However, some of the companies are falsely claiming that their test is FDA approved/authorized. Only one test has an EUA, and that test is intended for use by clinical laboratories, **Ortho Clinical Diagnostics'** VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack. These test kits are expected to be available in a few weeks.
 - The Agency warned that antibody tests are not for diagnosing Covid-19 but to identify people who have been exposed to the virus, making them potential convalescent plasma donors and likely immune to re-infection (though for how long is uncertain).
- **Antibody test accuracy.** An Oxford University researcher, Sir John Bell, MD, writing in a university [blog](#), noted, “There are many challenges to creating accurate tests; hence these tests need to be validated carefully. Other countries such as Spain have already sent tests back because they don’t work. There are 100 or more such tests kits from different suppliers available for identifying Covid-19 antibodies, and it is important that each of these is checked for accuracy before making them available to the public.”
- However, finding an accurate test is not easy. Dr. Bell wrote, “Sadly, the tests we have looked at to date have not performed well. We see many false negatives...and we also see false positives. None of the tests we have validated would meet the criteria for a good test.”
- **Iceland**, which has not imposed a lockdown (though large gatherings are banned), has randomly [tested](#) ~10% of its population and found that 0.3%-0.8% have coronavirus, and 50% don’t know it because they are asymptomatic.
- **Apple**, in partnership with Stanford Medicine, has developed an [app](#) – the First Responder COVID-19 Guide – to connect first responders to Covid-19 drive-through testing sites if they show symptoms.
- **BillionToOne** is developing a qSanger-COVID-19 test, a quantitative Covid-19 assay based on Sanger sequencing, that can increase the capacity of diagnostic tests for Covid-19 by hundreds of thousands per day and avoid the reagent supplies issue.
- **Darwin Biosciences' SickStick.** Working with researchers at the University of Colorado, Darwin is developing what it claims will be an affordable, rapid, and simple test that will be able to diagnose Covid-19 before a person has any symptoms. The user spits in a cup, sticks in a strip that soaks up the saliva, and within minutes – much like with an at-home pregnancy test – a series of lines appear on the strip. The company hopes to have the test on the market in 6 months.
- **Stanford Medicine** researchers have developed an antibody [test](#), but it takes 2-3 days to get the results.

Monitoring

- **Serosurvey.** The National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the National Center for Advancing Translational Sciences (NCATS), and the National Cancer Institute (NCI) are collaborating on an antibody study – a “serosurvey” – using an NIH-developed ELISA assay to quantify how many people have or have had Covid-19 but are undetected. The study wants to recruit 10,000 healthy volunteers from across the country who will donate a collected-at-home blood sample.

In blood samples found to have antibodies against SARS-CoV-2, the researchers may perform additional tests to evaluate the volunteers’ immune responses to the virus to try to understand why those people had less severe cases than patients who were hospitalized.

Transmission

- **Spread.** The coronavirus has a reproduction rate (R_0 , pronounced R-naught) of 5.7, which means that each infected person is expected to infect 5.7 other people. Dr. Birx said, “No one has buried R-naughts like that without a vaccine.”
- **Fecal transplants.** Citing the risk of transmission of SARS-CoV-2 through fecal transplants, the FDA banned clinical use of fecal microbiota transplantation (FMT) manufactured on stool donated on or after December 1, 2019, until new screening and testing procedures are implemented that ensure the samples are free of SARS-CoV-2 – and the FDA spelled out how that must be done.
- **Reactivation.** South Korea continues to be cited as an example of good testing, but South Korea also is reporting a small but significant number (111) of cases of people whose Covid-19 was reactivated. Those patients tested negative and were classified as cured and then tested positive again after being released from quarantine. Korea’s Centers for Disease Control and Prevention is conducting an investigation. There also have been at least 2 similar cases in Japan.

Treatment

Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), noted that there are a lot of candidate interventions and predicted it would “probably be months before we see which is working.”

- **Guidelines.** The Infectious Diseases Society of America issued guidelines for treating Covid-19 patients. They concluded that they could “not make a determination whether the benefits outweigh the harms for most treatments,” but they offered 7 recommendations for hospitalized patients:
 - Hydroxychloroquine/chloroquine in a clinical trial.
 - Hydroxychloroquine/chloroquine + azithromycin *only* in a clinical trial.
 - Lopinavir/ritonavir (AbbVie’s Kaletra, an HIV drug) *only* in a clinical trial.
 - *Against* the use of corticosteroids in Covid-19 patients with pneumonia.
 - Corticosteroids in Covid-19 patients with Covid-19-caused ARDS [acute respiratory distress syndrome) but in a clinical trial.
 - Tocilizumab (Roche’s Actemra), an anti-IL-6, but *only* in a clinical trial.
 - Convalescent plasma in a clinical trial.
- **BioCryst Pharmaceuticals’ galidesivir (BCX-4430).** The company started enrolling patients in a trial of this antiviral, an adenosine nucleoside analog that has shown *in vitro* activity against MERS and SARS viruses. The drug was originally being explored to treat yellow fever, so the trial will be in Brazil where that study was due to take place. Part 1 will enroll 24 hospitalized moderate-to-severe Covid-19 patients to find a dose, then 42 patients in Part 2, with mortality determined at Day 56.
- **CalciMedica’s CM-4620-IE,** a CRAC channel inhibitor – that down regulates IL-6, IL-17, and TNF-alpha, and more – is being tested vs. standard of care in a Phase II trial in Covid-19 patients with severe pneumonia. The hope is that it will prevent/reduce cytokine storms.
- **Cipla’s albuterol sulfate inhalation** – a generic of Merck’s Proventil HFA (albuterol sulfate) metered dose inhaler – was approved by the FDA to treat or prevent bronchospasm in patients age ≥ 4 with reversible obstructive airway disease and to prevent exercise-induced bronchospasm in that age group. It should also come in handy for Covid-19 patients, too, because the use of albuterol inhalers for Covid-19 patients has been so common that there has been a shortage for other patients.

- **Convalescent plasma.** The FDA and the European Commission both issues new guidelines on convalescent plasma from people who have recovered from Covid-19 for use as a treatment for other Covid-19 patients. The FDA guidance discusses clinical trials, expanded access, single patient (N of 1) studies and how to obtain them, as well as information on patient eligibility and the collection of Covid-19 convalescent plasma. The European Commission guidance discusses convalescent plasma collection, testing, processing, storage, and distribution as well as how to test donated plasma and how to submit data.
 - **Generics.** An Axcella Health executive suggested establishing a public benefit entity to gather data, submit applications for regulatory approval, and allow makers of generic drugs to add a Covid-19 indication to drugs approved for other diseases.
 - **Gilead Sciences' remdesivir**
 - Data on 53 French patients with severe Covid-19 given this nucleotide analog prodrug under compassionate use, published in the *New England Journal of Medicine*, found that
 - ✓ At Day 18 after the first dose:
 - 36 patients (68%) showed improvement in oxygen support, and 8 (15%) worsened.
 - All 12 non-ventilator patients improved, and 71% of high-flow supplemental oxygen.
 - 57% of ventilator patients were extubated, and 75% of patients on extracorporeal membrane oxygenation (ECMO) stopped receiving it – and all of the patients were still alive at follow-up.
 - ✓ At Day 28, 84% showed clinical improvement or live discharge, with improvement less frequent in ventilator patients and in patients age ≥ 70 .
 - ✓ 7 patients (13%) died after completion of the remdesivir treatment, including 18% of ventilator patients and 5% of non-invasive oxygen patients. The mean time between remdesivir initiation and death was 15 days. This compares to 28-day mortality of 22% with AbbVie's Kaletra in a Chinese trial with fewer ventilator patients.
 - ✓ No viral load data were collected.
 - The company also made several changes to the two ongoing open-label U.S. trials, one in severe Covid-19 and another in moderate Covid-19.
 - ✓ From 400 to 2,400 patients and the other in moderate Covid-19 from 600 to 1,600 patients. It isn't clear whether the primary endpoint will be the original patient number or the new number. *Does this mean that the effect is so modest that to get statistical significance, that many patients are needed?*
 - ✓ The primary endpoint was also changed to an improvement on a 7-point clinical assessment scale instead of normalization of fever/oxygen for severe patients and hospital discharge for moderate patients. *Will this make it easier to show a benefit?*
 - **Hydroxychloroquine / chloroquine**
 - The trials are proliferating. The latest is one by the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH).
 - The **French study** that started the enthusiasm for hydroxychloroquine is now up to 1,061 patients, and the principal investigator, Didier Raoult, MD, PhD, said that he has had a 91% success rate. But this is not a controlled trial.
 - France's drug safety agency reported 43 cases of **cardiac side effects** linked to hydroxychloroquine used in Covid-19 patients, advising that it "should only be used in hospitals, under close medical supervision."
 - The 3,000-patient study being run at **Henry Ford** in first responders and healthcare workers is testing only hydroxychloroquine – not in combination with azithromycin and/or zinc.
-

- **Chloroquine safety issue.** The high dose arm of a Phase IIb trial in Brazil of *chloroquine* was halted for safety – excess QTc prolongation and death. At the time, only 81 of the planned 440 patients had been enrolled in this double-blind study ([NCT04323527](#)) in hospitalized patients with Covid-19-related ARDS. The trial was testing both a high dose (600 mg BID for 10 days) and a low dose (450 mg BID on Day 1, then 450 mg QD for 5 days). All patients in the study were also receiving ceftriaxone and azithromycin. Since there was no placebo comparator in this two-arm, the trial was effectively ended. The [results](#) are available in pre-print form at [medRxiv](#).

One quarter of patients in the high-dose arm had QTc prolongation. There was also a trend toward higher mortality with the high dose by Day 6 (17%). And only 1 patient on the high dose cleared virus from respiratory secretions during the study.

The researchers concluded, “The higher chloroquine dosage (10-day regimen) should not be recommended for Covid-19 treatment because of its potential safety hazards.” They also said the study had too few patients in the low-dose arm to estimate a clear benefit of chloroquine in patients with severe ARDS.

- **Lilly’s Olumiant (baricitinib)** is being tested in an NIH adaptive Covid-19 trial, with results expected in ~2 months. This is the second JAK inhibitor to be tested in Covid-19.

- **Merck MSD’s Stromectol (ivermectin) and generics**

- Australian investigators reported in the journal *Antiviral Research* that they discovered that this anti-parasitic halted replication of SARS-CoV-2 in lab-grown cells within two days. They wrote, “We found that even a single dose could essentially remove all viral RNA by 48 hours and that even at 24 hours there was a really significant reduction in it.”
- However, the FDA issued a warning that people should not self-medicate with versions of ivermectin that are *intended for animals* either to treat or prevent Covid-19. In humans, ivermectin is used to treat onchocerciasis (river blindness) and other parasitic infections. There is a pre-publication paper that suggests that the drug is effective against SARS-CoV-2 *in a petri dish*. The FDA is concerned that people will self-medicate with animal treatments containing ivermectin.

- **Mesoblast’s Ryoncil (remestemcel-L).** Remestemcel-L, this allogeneic stem cell therapy, has previously been tested in bone marrow transplant patients with graft-versus-host disease (GVHD), who can experience an overactive immune response similar to that seen in severe Covid-19. Mount Sinai Health System was the first hospital to use it in Covid-19, treating 10 patients under compassionate use. Keren Osman, MD, medical director of the Cellular Therapy Service in the Bone Marrow and Stem Cell Transplantation Program at The Tisch Cancer Institute at Mount Sinai, reported encouraging results.

Mount Sinai now is participating in a 240-patient randomized, U.S./Canadian trial in Covid-19 patients with severe ARDS and will be the clinical and data coordinating center for that trial, which is a public-private partnership between NIH’s Cardiothoracic Surgical Trials Network and the company.

- **Takeda and CSL Behring** set up an [alliance](#) to ramp up development of one, unbranded anti-SARS-CoV-2 polyclonal hyperimmune immunoglobulin for Covid-19, and other companies are joining the alliance and bringing their work on plasma treatments, including Octapharma, Biotest, Bio Products Laboratory, and LFB. Takeda is giving the alliance the work it has done on TAK-888.
 - **Terumo BCT’s Spectra Optima Apheresis System**, combined with **Marker Therapeutics’ Depuro D2000 Adsorption Cartridge devices**, blood purification systems for treating adults with confirmed Covid-19 in the intensive care unit with confirmed/imminent respiratory failures, were granted EUA.
-

Patients who recover from Covid-19

Information is starting to trickle in on how patients fare after a serious bout of Covid-19 requiring hospitalization and ventilator therapy.

- The state of Maryland is opening a “registry” for Maryland residents who have recovered from Covid-19, COVIDConnect. It is intended as a “community platform to share experiences and to lend support to others who are coping with the recovery process.”
- **Ventilator patients.** In an interview with *Kaiser Health News*, Kenneth Lyn-Kew, a pulmonologist at National Jewish Health in Denver, talked about what patients are like who recover from Covid-19 after two weeks on a ventilator, “If we’re able to do everything right, these people are up and walking around with the ventilator. Those patients come out on the other end looking pretty good. Maybe they’ll have some weakness, some weight loss, a little PTSD [post-traumatic stress disorder]. The patients who are sicker and more intolerant of the technology, they tend to come out weak, forgetful, confused, deconditioned, maybe not even able to get out of bed. Sometimes, in spite of our best efforts, they’ll have skin wounds. Some of these patients have significant lung fibrosis – scarring of the lungs and reduced lung function. This might be a short-term part of their recovery or it could be long-term.”

Patients generally do not go home directly from an ICU. Some are able to go home after 2-3 more days on a medical/surgical ward, but Dr. Lyn-Kew said, “Other people take another week or two to regain some strength. Some will go to an acute rehabilitation facility to get rehab three times a day. Others can go to a skilled nursing facility, where they’ll get rehab over a couple of months and then go home.”

Dr. Lyn-Kew also pointed out that there can be issues with patients getting post-hospitalization care, “With such a high number of sick people, it’s harder to do things to maximize recovery, such as bringing in physical therapy and occupational therapy. People aren’t able to get as much therapy because there are only so many therapists and some hospitals are limiting who can come in.”

Vaccines

- Researchers at the University of Iowa and the University of Georgia suggest a virus that causes kennel cough in dogs could be used to create a vaccine against SARS-CoV-2. A mouse study, published in the journal *mBio*, showed that a vaccine based on the parainfluenza virus 5 (PIV5) protected all the mice from MERS. Now, they want to try it for 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? Antibody testing may help get this answer.
 - ? 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? 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)? And is azithromycin and/or zinc important to the efficacy?
 - ? 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? Data is starting to come in on this, but much more information is needed.
 - ? Are there **long-term effects** from getting Covid-19, even mild Covid-19? Will there be long-lasting lung abnormalities or pulmonary fibrosis?
-

- ? Can people get Covid-19 **more than once**? There are still conflicting reports on this, but the numbers are growing.
 - ? 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, but there are a small but growing number of cases of people who have been re-infected, and it is not clear if it is the same infection rearing its head again, a loss of immunity that allows new infection, or just testing errors.
 - ? 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? Since it can be transmitted through a fecal transplant, it obviously doesn't survive only in the airway.
-

#1 Worldwide Covid-19 Statistics – Daily Cases

Country	April 8			April 9			April 10			April 11			April 12		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
Worldwide	1,511,104	88,338	5.8%	1,617,204	97,039	6.0%	1,698,271	102,753	6.1%	1,777,517	108,862	6.1%	1,850,807	114,251	6.2%
U.S.	429,052	14,695	3.4%	466,299	16,691	3.6%	501,301	18,758	3.7%	529,887	20,604	3.9%	557,571	22,108	4.0%
Spain	148,220	14,792	10.0%	153,222	15,447	10.1%	158,273	16,081	10.2%	163,027	16,606	10.2%	166,831	17,209	10.3%
Italy	139,422	17,669	12.7%	143,626	18,279	12.7%	147,577	18,849	12.8%	152,271	19,468	12.8%	156,363	19,899	12.7%
France	113,959	10,887	9.6%	117,749	12,210	10.4%	125,931	13,215	10.5%	130,730	13,851	10.6%	133,670	14,412	10.8%
U.K.	61,474	7,111	11.6%	65,077	7,978	12.3%	74,605	8,974	12.0%	79,885	9,892	12.4%	85,208	10,629	12.5%
Germany	113,296	2,349	2.1%	118,236	2,607	2.2%	122,172	2,736	2.2%	125,452	2,871	2.3%	127,854	3,022	2.4%
Sweden	8,519	687	8.1%	9,241	793	8.6%	9,685	870	9.0%	10,151	887	8.7%	10,483	899	8.6%
Iran	64,586	3,993	6.2%	66,220	4,110	6.2%	68,192	4,323	6.3%	70,029	4,357	6.2%	71,686	4,474	6.2%
China	82,809	3,337	4.0%	82,940	3,340	4.0%	82,976	3,343	4.0%	83,014	3,343	4.0%	83,135	3,343	4.0%

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

#2A Worldwide Per Capita Case Rate

Country	Population	April 6	April 8	April 10	April 11	April 12
Worldwide	7.577 billion	0.02%	0.02%	0.013%	0.02%	0.02%
U.S.	330 million	0.11%	0.13%	0.15%	0.16%	0.17%
Spain	47 million	0.29%	0.32%	0.34%	0.35%	0.35%
Italy	60 million	0.22%	0.23%	0.25%	0.25%	0.26%
France	67 million	0.15%	0.17%	0.19%	0.20%	0.20%
U.K.	67 million	0.08%	0.09%	0.11%	0.12%	0.13%
Germany	83 million	0.12%	0.15%	0.15%	0.15%	0.15%
Sweden	10 million	N/A	0.09%	0.10%	0.10%	0.10%
Iran	81 million	0.07%	0.08%	0.08%	0.09%	0.09%
China	1.386 billion	0.006%	0.006%	0.006%	0.006%	0.006%

#2B Worldwide Per Capita Fatality Rate
Deaths per 100,000 People

Country	Population	April 10	April 11	April 12
Worldwide	7,577 million	1.4	1.4	1.5
U.S.	330 million	6	6	7
Spain	47 million	34	35	37
Italy	60 million	31	29	33
France	67 million	20	21	22
U.K.	67 million	13	15	16
Germany	83 million	3.3	3.5	3.6
Sweden	10 million	9	9	9
Iran	81 million	5	5	6
China	1,386 million	0.24	0.24	0.24

#3 U.S. Covid-19 Statistics – Daily Cases

State	April 8			April 9			April 10			April 11			April 12		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
New York	149,316	6,268	4.2%	159,937	7,067	4.4%	170,512	7,844	4.6%	180,458	8,627	4.8%	188,694	9,385	5.0%
New Jersey	47,437	1,504	3.2%	51,027	1,700	3.3%	54,588	1,932	3.5%	58,151	2,183	3.8%	61,850	2,350	3.8%
Michigan	20,346	959	4.7%	21,504	1,076	5.0%	22,783	1,281	5.6%	23,993	1,392	5.8%	24,638	1,487	6.0%
Louisiana	17,030	652	3.8%	18,283	702	3.8%	19,253	755	3.9%	20,014	806	4.0%	20,595	840	4.1%
California	16,957	442	2.6%	18,309	492	2.7%	19,472	541	2.8%	19,472	541	2.8%	21,794	651	3.0%
Massachusetts	16,790	433	2.6%	18,941	503	2.7%	20,974	599	2.9%	22,860	686	3.0%	25,475	756	3.0%
Florida	15,455	309	2.0%	16,364	354	2.2%	17,531	390	2.2%	18,494	438	2.4%	19,355	465	2.4%
Illinois	15,078	462	3.1%	16,422	528	3.2%	17,887	596	3.3%	19,180	677	3.5%	20,852	720	3.5%
Washington	8,682	394	4.5%	9,769	446	4.6%	10,224	446	4.4%	10,224	491	4.8%	10,224	491	4.8%

Source: <https://covidtracking.com/data/>#4 Watching for When the Coronavirus Curve Flattens - *APRIL 2020 - World and U.S.
(Additional CASES each day, not total cases)

Location	April 2	April 3	April 4	April 5	April 6	April 7	April 8	April 9	April 10	April 11	April 12
Worldwide	81,068	84,175	98,557	78,451	69,192	81,048	85,008	106,100	81,607	79,246	73,290
China	172	78	32	101	21	53	91	131	36	38	121
Spain	7,947	7,134	6,969	5,478	5,029	5,267	6,278	5,002	5,051	4,754	3,804
Italy	4,668	4,585	4,805	4,316	3,599	3,039	3,836	4,204	3,951	4,694	4,092
Iran	2,875	2,715	2,560	2,483	2,274	2,089	1,997	1,634	1,972	1,837	1,657
U.S.	31,306	33,150	31,022	28,788	28,976	29,609	32,829	37,247	35,002	28,586	27,684
New Jersey	3,335	4,305	4,229	3,381	3,585	3,326	3,057	3,590	3,561	3,563	3,699
Michigan	1,457	1,953	1,481	1,493	1,503	1,749	1,376	1,158	1,279	1,210	645
Louisiana	2,726	1,147	2,199	514	1,857	1,417	746	1,253	970	761	581
California	1,036	1,510	1,325	1,412	898	1,529	1,092	1,352	1,163	0	2,322
Massachusetts	1,228	1,436	1,334	764	1,337	1,365	1,588	2,151	2,033	1,886	2,615
Florida	1,055	1,575	1,526	1,040	1,173	1,423	708	909	1,167	963	861
Illinois	715	1,209	1,453	899	1,370	1,287	1,529	1,344	1,465	1,293	1,672
Washington	376	612	405	396	326	337	N/A	1,087	455	0	0
New York	8,669	10,482	10,841	8,327	8,658	8,174	10,453	10,621	11,676	9,946	8,236

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

#5 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	April 9	April 10	April 11	April 12
Worldwide	4,811	6,164	5,898	5,735	4,908	5,051	7,300	6,473	8,701	5,714	6,109	5,389
China	7	6	4	4	5	0	0	2	3	3	0	0
Italy	727	760	766	681	525	636	604	542	610	570	619	431
Spain	923	961	850	749	694	700	704	747	655	634	525	603
U.S.	884	1,154	1,230	1,266	1,240	1,136	1,939	1,973	1,996	2,067	1,846	1,504
New Jersey	88	82	109	200	71	86	229	272	196	232	251	167
Michigan	78	80	62	61	77	110	118	114	117	205	111	95
Louisiana	34	37	60	39	66	35	70	70	50	53	51	36
California	18	32	34	39	43	24	31	68	50	49	0	110
Massachusetts	33	32	38	24	15	29	96	77	70	96	87	70
Florida	10	41	35	28	27	18	60	13	45	36	48	27
Illinois	42	16	53	33	31	33	73	82	66	68	81	43
Washington	18	26	24	20	13	10	12	19	66	0	45	0
New York	441	432	562	630	594	599	731	779	799	777	783	758