



TRENDS-in-MEDICINE

BULLETIN: UPDATE ON CORONAVIRUS 4/16

April 16, 2020
by Lynne Peterson

Be careful, be safe, and be well.

The SARS-CoV-2 virus and the disease it causes continue to have much of the world on pause. In the U.S. and most of Europe, the rate of infection appears to have peaked/plateaued, and countries are trying to figure out how to safely get things restarted again.

Worldwide, more than 2 million people have been infected with the coronavirus. In the **U.S.**, total cases are 639,664, with 30,985 deaths.

The case-related fatality rate is higher everywhere than the U.S. Centers for Disease Control and Prevention (CDC) had predicted (2.0%-2.5%) and is even higher than our prediction of at least 3.4%. Worldwide it is 6.6%, with the U.S. at 4.8%, and Italy and the U.K. at 13%.

On a per capita basis, for the countries followed:

- The **case rate** is 0.03% worldwide and (among the countries in our coverage) highest in Spain at 0.36%. The U.S. falls in the middle of that at 0.18%, similar to Germany at 0.16% and lowest in Sweden at 0.11%.
- The **fatality rate** per 100,000 people has been slowly but steadily climbing everywhere (except China, whose numbers are suspect). Spain is the highest at 40, Germany is lowest at 4.6, and the U.S. comes in at 9 which is lower than Sweden (12).

In the U.S.:

- **New York**, the No. 1 hotspot, accounts for 33% of all cases (down from 35% a few days ago) and 37% of all deaths. New Jersey has the second most cases and deaths, accounting for 11% of all the cases in the country and 10% of the deaths.
- The good news is that the **rates have flattened** for the country and for New York, though there are other hotspots: Louisiana (especially New Orleans), Massachusetts, Michigan, and New Jersey (which has not yet crested).
- **Total Covid-19 deaths** when this is all over is now predicted to be a little higher (68,841 vs. 61,545), so the country is not quite at the halfway point in deaths.
- The only clear trends on the key trend chart – **additional cases each day** – are:
 - ✓ Decrease in Italy, Louisiana, Michigan, and New York – and *maybe* the U.K.
 - ✓ A flattening in Spain, Florida, and Illinois.

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European countries have started announcing dates and plans to start easing their lockdowns.

- **Denmark** already re-opened its schools and nurseries.
- **Spain** has allowed construction and manufacturing work to restart, particularly around Madrid.
- **Austria** re-opened smaller shops already and will allow tennis, golf, and athletics starting May 1.
- **Germany** will allow small shops (8,600 sf), car dealers, bicycle shops, and book stores to restart on April 19, schools on May 4, and hairdressers on May 4.
- In **France** restrictions will start to lift May 11.

President Trump and state governors are talking about plans for **re-opening the U.S. economy**, gradually, though no dates or specific plans have been announced yet – just some hints that it will be “soon.” President Trump said 29 states don’t have much of a problem, and some of these may re-open before May 1, gradually. The issue in the U.S., particularly in more heavily affected states, is testing, and testing is still fragmented, sporadic, not widely available, and inconsistent. President Trump says testing is a state responsibility, and some governors are saying the federal government has to provide help because the job is too big for them.

The world

- Experts are predicting that the SARS-CoV-2 virus will be affecting the world for a long time – until there is a vaccine.
 - There is growing suspicion that the SARS-CoV-2 outbreak did not begin in a Wuhan, China, wet market but through an *accident* at a Chinese lab, the Wuhan Institute of Virology, China’s only Level 4 biosafety research lab. U.S. Embassy officials in Beijing visited the lab two years ago and sent official warnings back to the State Department about inadequate safety at the lab – which was conducting studies on coronaviruses.
 - **Mutation.** In a study, available on the pre-print site [biorxiv.org](https://www.biorxiv.org), scientists in Taiwan and Australia reported that a strain of SARS-CoV-2 found in India showed a mutation that could make vaccines currently under investigation ineffective. Those vaccines are generally targeting the spike protein that lets the virus attach to the ACE2 receptor, and the mutation makes that site less important. However, it is also possible that the mutation is a laboratory error.
 - **World Health Organization (WHO)**
 - President Trump suspended U.S. contributions to WHO and ordered a “review to assess its role in severely mismanaging and covering up the spread of the coronavirus.” The announcement met with strong reactions.
 - WHO claimed the global coronavirus peak has not been reached yet.
 - WHO cautioned global leaders against lifting quarantine restrictions prematurely, predicting a “deadly resurgence” of the virus if the openings were too soon.
 - **China** is getting roundly criticized for not providing more information about the origin of the coronavirus outbreak.
 - **France**
 - A judge ordered Amazon to deliver only essential goods – food, medical supplies, and hygiene products – in France, and Amazon responded by temporarily suspending all operations there.
 - French President Emmanuel Macron set May 11 as the day the lockdown would end, with a gradual lifting of restrictions – starting with nurseries, K-12 schools, and some shops – in 2-3 week increments. No festivals will be allowed until at least mid-July.
 - About a third of the crews on the aircraft carrier Charles de Gaulle and its escort vessels have Covid-19.
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- **India** – Prime Minister Modi extended the nationwide lockdown to May 3.
- **Italy** – The government would like to increase use of convalescent plasma but that requires an antibody test, and Italy doesn't have one – yet. A test is in development and is expected to be ready for use by the end of April.
- **Japan** – The health minister warned that 400,000 people could die in Japan if social distancing is not imposed.
- **U.K.** – Total deaths for this outbreak are predicted to top at 23,791 (down from >37,000 previously).

United States

- **Antibodies and immunity.** There is a huge emphasis, at least in the U.S. on the importance of antibody testing, to find people who have had Covid-19, have antibodies, and are now immune, so they can't pass the virus on to anyone else and can return to work. But how long do they remain in the body, do they have immunity, and if so, how long is that immunity? And do people exposed to another more common coronavirus have some degree of immunity against SARS-CoV-2?
 - Among the companies working on development of antibodies to treat Covid-19 are: AbCellera, Berkeley Lights, GenScript, Regeneron Pharmaceuticals, and VIR Biotechnology.
 - George Rutherford, MD, head of infectious disease and global epidemiology at the University of California San Francisco, said these are questions that are “going to take a while to figure out.”
 - David Walt, PhD, a pathologist from Harvard Medical School and Brigham and Women's Hospital, said, “There is no proof at this point that the development of an antibody response will be protective...There is no evidence yet that people can't be reinfected with the virus.”
 - Marc Lipsitch, D.Phil, an epidemiologist from Harvard's School of Public Health and director of Harvard's Center for Communicable Disease Dynamics, said that experiments with SARS-1 and MERS suggest antibodies to SARS-1 persist for 2 years and antibodies to MERS for nearly 3 years. However, their neutralizing ability was declining during this period, so how long the antibodies are protective isn't clear.

A peer-reviewed study of 12 Covid-19 patients by Dutch researchers found that the patients developed antibodies after infection with SARS-CoV-2. Dr. Lipsitch said he and colleagues (and students) statistically analyzed thousands of seasonal coronavirus cases in the U.S. and estimate that immunity to SARS-CoV-2 for >1 year is likely.

However, Dr. Lipsitch also pointed out that a 175-patient study from China suggests that not every case of infection contributes to herd immunity. In that study, 70 of patients with mild symptoms developed a strong antibody response, ~25% developed a low response, and ~5 had no detectable response at all. That means mild illness might not always be protective. That raises the question of what, if any, immunity asymptomatic Covid-19 patients have.
- At a press conference in Geneva, WHO officials said not everyone who recovers from Covid-19 has antibodies to fight a second infection. This raises a question about whether patients develop immunity after surviving Covid-19. Michael Ryan, MD, executive director of WHO's health emergencies program, said, “With regards to recovery and then re-infection, I believe we do not have the answers to that. That is an unknown.” Maria Van Kerkhove, MD, WHO's lead scientist on Covid-19, said that early results from a Chinese study found that some patients had “no detectable antibody response” while others had a very high response. She added that whether patients with a strong antibody response had immunity to a second infection is “a separate question.”
- **The downside to immunity:** In some cases, immunity to a coronavirus can exacerbate an infection rather than prevent or mitigate it. Research on SARS and MERS is starting to clarify how this works, suggesting there may be a way around it.
- The National Cancer Institute is going to evaluate Covid-19 antibody tests for the FDA, testing them for accuracy.

- **Prisons and jails.** At least 17 states are freeing non-violent criminals because of the risk of Covid-19 in the prisons. Immigration and Customs Enforcement (ICE) is releasing ~700 illegal immigrants.
- **Re-opening the economy**
 - Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), said it will be a “rolling” re-opening but said a May 1 target is “a bit overly optimistic.”
 - Governors are forming regional alliances to work together on joint recommendations for re-opening their economies.
 - ✓ Northeast: 7 states – Connecticut, Delaware, Massachusetts, New Jersey, New York, Pennsylvania, and Rhode Island.
 - ✓ West: 3 states – California, Oregon, and Washington.
 - ✓ Central: 3 states – Indiana, Kentucky, and Ohio.
- **Seasonality.** For Covid-19, maybe there is, and maybe there isn't. A Michigan study, published in the *Journal of Infectious Diseases*, analyzed four different coronaviruses – not SARS-CoV-2 – over 8 years and found the viruses were detected in a limited timeframe, from December to April and May, with a peak during January and February. However, one thing that may suggest that SARS-CoV-2 may be different: the highest rate of infection with the non SARS-CoV-2 coronaviruses was in children age <5, and SARS-CoV-2 rarely infects children in a noticeable way.
- **USNS Comfort and Javits Center.** More than 400 Covid-19 patients have been treated at these two military sites in New York City, with 4 deaths. Medical personnel from both sites have also been helping out at city hospitals.
- **USNS Mercy.** Seven crew members on this hospital ship docked at the port of Los Angeles have tested positive for Covid-19 and are being treated off the ship.
- **USS Theodore Roosevelt.** A Navy sailor died from Covid-19, and 585 others have contracted Covid-19. It now looks like the outbreak was not due to a stopover in Vietnam but to the flight crews.
- **World Health Organization (WHO).** President Trump said he was putting a hold on WHO funding – and the U.S. gives WHO ~\$50 million/year – while a review of its role in “mismanaging and covering up the spread of the coronavirus...and opposing the travel restriction [on China].”

President Trump

- Threatened to apply a never-used provision of the U.S. Constitution to adjourn Congress and fill the **vacancies** with recess appointments, saying Congress has taken way too long to consider/approve nominees for government positions. There are 129 nominees awaiting Senate action, and some of them have been waiting longer than 2 years.
 - Got into a dispute with governors about who has the **authority to order the re-opening** of the economy. The President initially said he had the ultimate authority. The governors pushed back, with New York Gov. Andrew Cuomo noting that Trump is not king. But it all seemed to blow over, with Gov. Cuomo saying, “I look forward to working with the President...I put my hand out to say, ‘Let’s do this together.’” The President then agreed the decisions are up to the governors, and the federal role is to help and advise. He said he will announce on April 16 some federal guidelines for re-opening.
 - Met at the White House with **Covid-19 patients** who have recovered – a Democratic legislator that recovered with hydroxychloroquine, a Diamond Princess cruise ship survivor, a traveler who initially had trouble getting tested, a man who got it and had few symptoms but whose wife was very ill, and former NFL football player Mark Campbell who thought he got Covid-19 from pumping gas at the gas station in Michigan and was very ill until he asked for hydroxychloroquine + azithromycin. He said he is about 95% recovered but his lung capacity “is still not as good as it was.”
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- Announced a hospital-led **ventilator sharing program** – the Dynamic Ventilator Reserve – a public-private partnership that will allow hospitals to lend ventilators to each other. The program was developed in partnership with the American Hospital Association which will help coordinate where they are needed and where they can be borrowed.
- Announced a long list of **business people** from across the spectrum of business in the U.S. who agreed to participate in an outside advisory council. However, some of those business leaders said testing is needed before they can go back to work.

U.S. states and cities

■ California

- Gov. Gavin Newsom said he wants to see **hospitalization numbers** flatten and decline before he begins rolling back stay-at-home orders. When restaurants re-open, he said waiters likely will be wearing masks and gloves, and public schools may stagger start times to maintain social distancing.
- **Illegal immigrants** will get \$500 per person or \$1,000 per household from a new Disaster Relief Fund, using \$7 million in state funds and \$50 million from philanthropic groups.
- The mayor of Los Angeles, Eric Garcetti, said that **large gatherings** – concerts, sporting events – will likely be banned until 2021.

■ **District of Columbia** – The mayor extended the shutdown and school closures until May 15.

■ **Florida** – Gov. Ron DeSantis ordered the state National Guard to send “strike teams” to help patrol and do testing to identify asymptomatic carriers at nursing homes, assisted living facilities, and long-term care facilities in the state. However, Gov. DeSantis said he won’t reveal which nursing homes have the virus – and at least 93 nursing homes in the state have at least one case.

■ **Georgia** – Gov. Brian Kemp signed an executive order temporarily suspending a 1951 law that made it a misdemeanor to conceal your identity on public property – an anti-Klu Klux Klan law – so people can wear masks to protect against the spread of Covid-19.

■ **Illinois** – A judge ordered the McHenry County Department of Health to provide the police department with the name of people who have tested positive to the coronavirus so that officers assigned to 911 calls to those addressed can take necessary health precautions.

■ Louisiana

- Gov. John Bel Edwards extended the school closure until the end of the school year.
- The mayor of New Orleans extended the lockdown there until May 16, and she “recommended” that no large events be held in the city before 2021.

■ **Massachusetts** – Boston University said it may cancel all live, on-campus classes until January 2021. Other colleges also are thinking about that.

■ Michigan

- Last week Gov. Gretchen Whitmer issued a very strict stay-at-home order (one of the strictest in the state), and it prompted thousands of demonstrators to descend on the state capital, some in cars and honking horns but others on foot. It wasn’t so much that people objected to staying at home, but they found the rules arbitrary – lottery tickets were legal to buy in person but lawn care services were not, motor boats were banned but not canoes, etc.

- Henry Ford Health System in Michigan has been reporting its Covid-19 statistics each day, and there were some interesting numbers:
 - ✓ 61 of the people they tested were positive for Covid-19.
 - ✓ Average hospital stays are 8 days
 - ✓ Average ICU stays are 9 days.
 - **New Jersey** – Seventeen bodies were found at a 500-bed nursing home after an anonymous tip. And that was the tip of the iceberg. It turns out that 68 people at that home died from Covid-19, and another 76 tested positive, plus 40 staff members are positive. Congressman Josh Gottheimer called the situation “horrific.” An understatement.
 - **New York**
 - Gov. Cuomo extended the stay-at-home order for New York state until **May 15**.
 - The situation has improved so much that New York is sending **ventilators** to other states to help them out – 50 to Maryland, 100 to Michigan, and 100 to New Jersey.
 - Gov. Cuomo said, “The good news is we showed we can change the **curve**...and we can control the spread...but you still have ~2,000 people a day who are...going into the hospital system, so it is still a serious public health issue.”
 - He said a “bridge” is needed from shutdown to **re-opening**, adding, “It is not a re-opening in that we will open what was. We are going to a different place, to a better place.” He said the re-opening will be a phased operation, an almost business-by-business decision, based on how essential the business is and what the risk of infection is at that business.
 - He also said the single best tool to re-open is **large scale testing**, but he said the states need federal help with the test-trace-isolate approach, “Tell FEMA [the Federal Emergency Management Agency] to buy all the tests...and then allocate them to the states.”
 - When will this be over? “When we have a **vaccine**. When people know they are 100% safe.” He added that New York state is volunteering to be a laboratory, to test a vaccine, “If you need a place to test it in large numbers, think of New York.”
 - Currently, **hydroxychloroquine** can only be prescribed in a hospital as part of a trial by the governor’s executive order, but he said he would lift that if the federal government would give the state more supply of the drug.
 - He signed an executive order requiring everyone to wear a **mask** in public when they can’t distance themselves. Initially, there will be no penalties for violations, but civil penalties could follow if people don’t wear a mask. He clarified that Uber drivers, taxi drivers, and people taking any form of public transport must wear a mask.
 - An MIT study blames **mass transit** – subways and buses – for the spread of the virus in New York City.
 - Asked what **nursing homes** in the state have had cases of Covid-19, Gov. Cuomo said he didn’t know off the top of his head but would provide that information – in stark contrast to Florida Gov. DeSantis’ refusal to disclose the nursing homes with cases in his state.
 - **Pennsylvania** – Gov. Tom Wolf said he will veto legislation passed by the legislature that would have allowed a significant number of businesses in the state to re-open by re-defining what is an essential business and by providing a roadmap for employers to re-open, provided they take safety precautions.
 - **South Dakota** – The Smithfield Foods pork plant in Sioux Falls – which processes ~5% of the U.S. pork supply – has at least 545 confirmed cases of Covid-19 – 55% of all the cases in the state – and the mayor, in conjunction with the governor, ordered the plant closed for at least two weeks. The Smithfield plant is not the only meat packing plant to have a Covid-19 outbreak – dozens of employees at a Tyson Fresh Meats beef plant in Washington state and 150 workers at a Cargill plant in Colorado have also tested positive.
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■ **Virginia** – Gov. Ralph Northam extended the shutdown order for non-essential businesses until May 8.

Drug shortages

Two additional sedatives used for Covid-19 patients on a ventilator – propofol and dexmedetomidine – are now on the FDA shortage list.

Insurance

The Trump administration issued guidance clarifying coverage requirements for private payors, specifying that commercial health plans are required to provide access to Covid-19 testing, doctor visits (in person and by telehealth), and treatment – whether at a doctor’s office, an urgent care center, or a hospital emergency room – at no cost to the patient. The Centers for Medicare and Medicaid Services (CMS) also specified that this will include antibody testing.

CMS also said it will pay almost double for high-throughput Covid-19 tests.

Medical supplies

■ Infusion pumps

- **B. Braun Medical’s Perfusor**, a space syringe infusion pump, the **Outlook ES** pump systems, and the **Infusomat** space volumetric infusion pumps were all granted emergency use authorization (EUA) by the FDA to be used with nebulizers to treat Covid-19 patients.

■ Ventilators

- **Philips’ Respironics E30** – The company is ramping up production of this smaller, emergency-use ventilator that can deliver high-flow oxygen both invasively and non-invasively and can include air filters to help minimize healthcare worker exposure to the virus. The goal is to produce 15,000 units/week by the end of this month. These devices are particularly suited for use at converted medical sites – convention centers, university dorms, hotels, etc.
- **Safe Flight Instrument’s Quad/Vent Splitter**, a ventilator splitter that lets *four* patients (not just one or two) share the same ventilator at the same time, was submitted to the FDA.
- **Somnetics International’s Transcend** – The company plans to convert its existing supply of these CPAP machines to non-invasive ventilators for use in treating Covid-19 patients.

Diagnostics/screening

- A New York hospital screened all expectant mothers and found 13.8% were asymptomatic or positive for Covid-19.
- Researchers at Cork University Hospital in Ireland have developed a temperature-based remote early warning system that can detect a rise in the temperature of healthcare providers.

Testing

- The FDA issued EUAs for lab-developed RT-PCR tests for SARS-CoV-2 from:
 - Integrity Laboratories
 - Baptist Hospital Miami’s pathology laboratory
- **Abbott’s IgG antibody test**, a lab-based serology test for detecting IgG, was cleared for use. It will run on Abbott’s ARCHITECT instruments, and there are >2,000 in U.S. labs. The machines can run 100-200 tests/hour. Abbott is

scaling up manufacturing of this test and expects to ship ~1 million tests this week and 4 million tests by the end of April, with 20 million expected to be shipped in June and after that as it expands the tests to run on the new Alinity system. The test is expected to be priced at \$5-6/each.

- **Nanomix** got \$569,647 from the Biomedical Advanced Research and Development Authority (BARDA) to develop a fast (15 minute) point-of-care Covid-19 assay.
- **Rutgers' RUCDR Infinite Biologics** saliva test for SARS-CoV-2, which was developed in partnership with Spectrum Solutions and Accurate Diagnostic Labs, was granted an EUA. It's easy to administer, but the time to get results is 24-48 hours. It can be a drive-through test, but it also could be used in any healthcare setting, and most large hospital networks in New Jersey reportedly are planning to use it.
- **Major league baseball** is testing 10,000 employees from 27 teams – executives, players, families, ushers, hot dog vendors – with a fingerprick antibody test *this week*. The results will be published, hopefully soon.

The patients with Covid-19

- The COVID Human Genetic Effort is studying the **genomes** of previously healthy people age <50 – those with no underlying medical conditions – who got severe Covid-19 to see if there are genetic defects that explain why they got severe disease.
- A 161-patient, retrospective Chinese study found that Covid-19 patients admitted to the hospital had the virus in their system for an average of 26 days (longest 50 days). The time was longer in older patients than patients age <60. The researchers concluded that Covid-19 may have longer and stronger **infectivity** than SARS-1.
- New York Gov. Cuomo said that **80% of Covid-19 ventilator patients die**.

Treatment

- **The European Medicines Agency (EMA)** created a task force (COVID-ETF) to oversee development of Covid-19 drugs and vaccines. The focus will be requesting data to identify promising candidates, evaluating scientific data on treatments, and offering scientific support for clinical studies.
 - **Anti-polymerase drugs** – In a study available at *ScienceDirect*, on the RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2 found that anti-polymerase **drugs** – e.g., ribavirin; Gilead Sciences' remdesivir, Sovaldi (sofosbuvir), and tenofovir; and BioCrys Pharmaceuticals' galidesivir – are potent against SARS-CoV-2 because they tightly bind to its RNA-dependent RNA polymerase (RdRp). The study also suggested that a guanosine derivative (Merck MSD's IDX-184, a nucleoside inhibitor) and Roche's setrobuvir (which was discontinued) hold promise because they tightly bind to the RdRp of SARS-CoV-2.
 - **AstraZeneca's Calquence (acalabrutinib)**, a BTK inhibitor for leukemia/lymphoma is being tested in the CALAVI trial in Covid-19 patients experiencing a cytokine storm. The goal is to reduce the need for a ventilator.
 - **BioCryst Pharmaceuticals' galidesivir**, a broad-spectrum IV antiviral, is being tested vs. placebo in a 2-part Phase I trial, funded by NIAID, in 66 hospitalized moderate-to-severe Covid-19 patients in Brazil.
 - **Convalescent Plasma** – Johns Hopkins researchers published a how-to guide for doctors who want to treat Covid-19 patients with this approach.
 - **CytoDyn's leronlimab (PRO-140)** – The company said that five patients with mild-to-moderate Covid-19 were able to get off oxygen after taking this viral entry inhibitor (originally for HIV). The company is running two trials: a Phase II trial in mild-to-moderate disease and a 390-patient Phase IIb/III trial in severe disease.
 - **CytoSorbents' CytoSorb**, a blood purification technology for treating inflammation in critically ill patients undergoing cardiac surgery, was granted an EUA to treat Covid-19 patients.
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- **Tiziana Life Sciences' TZLS-501** – The company is developing a technology that allows anti-IL-6 receptor monoclonal antibodies like this to be delivered directly into the lungs of Covid-19 patients with either a nebulizer or a handheld inhaler.
- **Hydroxychloroquine**
 - The **FDA**:
 - ✓ Issued new product-specific guidance designed to make it easier for development of generic versions of hydroxychloroquine and chloroquine.
 - ✓ Said it will prioritize review of any newly submitted abbreviated new drug application (ANDA) for chloroquine phosphate and hydroxychloroquine sulfate.
 - The **FAA** banned **pilots** from flying for 48 hours after taking hydroxychloroquine.
 - A **French retrospective study**, published on *medRxiv.org*, of the medical records of 181 Covid-19 patients with Covid-19 who had pneumonia and required supplemental oxygen, 84 who had taken hydroxychloroquine within 48 hours of being admitted to the hospital and 97 who had not. The study did not find a significant benefit to hydroxychloroquine.
 - ✓ Admission to the ICU or death within 7 days occurred in 20.2% of hydroxychloroquine patients vs. 22.1% of control (p<0.05).
 - ✓ Safety concerns were reported: 8 patients on the drug developed abnormal heart rhythms and had to stop taking it.
 - ✓ 2.8% of the hydroxychloroquine patients died vs. 4.6% of control (p<0.05).

The researchers concluded: “These results do not support the use of [hydroxychloroquine] in patients hospitalized for documented SARS-CoV-2-positive hypoxic pneumonia.”

Trial data

Inato, a marketplace that helps biopharmaceutical companies increase the pool of available patients for clinical trials, introduced an **anti-covid platform**. It's a comprehensive, central repository for all existing clinical trials for SARS-CoV-2. The platform is public, free to access, and offers search and filtering capabilities.

Already there have been some interesting findings from the platform:

- Nearly 1,000 Covid-19 trials were launched or anticipated in the past 4 months.
- China has the most trials, but Italy, France, and the U.S. have significantly increased their trials recently.
- Early signals suggest some antiviral agents could be *ineffective* for treating Covid-19 (at least in seriously ill patients), even though there is still a significant focus on the drugs in those trials.
- Chloroquine/hydroxychloroquine is a focus, with >50,000 people currently participating in trials in the U.S.
- The most frequently tested therapeutic classes are antiviral agents, chloroquine/hydroxychloroquine and traditional/Chinese medicine.

Vaccines

- **Moderna's mRNA-1273** – In an interview on *CNBC*, a Moderna official said dosing may be an issue with the vaccine. A vaccine is particularly tricky with this virus because vaccines tend to be less effective in older people, “The trick will be getting the dose high enough for older people who are most affected by the coronavirus and being sure it is not lethal for young people, infants, and pregnant women.” He said the dose being used in Phase I in healthy adults is in one-quarter

the dose used in cancer, adding, “We believe we have a lot of room to maneuver...**It is possible there will be a different dose for the elderly**... You might need to boost it every 3 or so years or more often in the elderly.”

- **Novavax’s NVX-CoV2373** – The company plans to start a Phase I trial of this vaccine in 130 healthy volunteers by mid-May 2020.
- **Sanofi** is partnering with **GlaxoSmithKline** on a coronavirus vaccine. The companies expect to start human testing by the end of 2020, with availability around the end of 2020.

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. Watch the results from the Beaumont Health antibody study in Michigan when they are available.
 - ? 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? Does it work?
 - ? 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 are 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 of re-infected people 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.
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#3 U.S. Covid-19 Statistics – Daily Cases															
State	April 10			April 12			April 13			April 14			April 15		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
California	19,472	541	2.8%	21,794	651	3.0%	22,348	687	3.1%	23,338	758	3.4%	24,424	821	3.4%
Florida	17,531	390	2.2%	19,355	465	2.4%	21,019	513	2.4%	21,367	537	2.5%	22,511	609	2.7%
Illinois	17,887	596	3.3%	20,852	720	3.5%	22,025	794	3.6%	23,247	868	3.7%	24,593	948	3.9%
Louisiana	19,253	755	3.9%	20,595	840	4.1%	21,016	884	4.2%	21,518	1,013	4.7%	21,951	1,103	5.0%
Massachusetts	20,974	599	2.9%	25,475	756	3.0%	26,867	844	3.1%	28,163	957	3.4%	29,918	1,108	3.7%
Michigan	22,783	1,281	5.6%	24,638	1,487	6.0%	25,635	1,602	6.2%	27,001	1,768	6.5%	28,059	1,921	6.8%
New Jersey	54,588	1,932	3.5%	61,850	2,350	3.8%	64,584	2,443	3.8%	68,824	2,805	4.1%	71,030	3,156	4.4%
New York	170,512	7,844	4.6%	188,694	9,385	5.0%	195,031	10,056	5.2%	202,208	10,834	5.4%	213,779	11,586	5.4%
Washington	10,224	446	4.4%	10,224	491	4.8%	10,411	508	4.9%	10,538	516	4.9%	10,694	541	5.1%

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

The most important chart

#4 Watching for When the Coronavirus Curve Flattens - *APRIL 2020 - World and U.S. (Additional CASES each day, not total cases)										
Location	April 6	April 7	April 8	April 9	April 10	April 11	April 12	April 13	April 14	April 15
Worldwide	69,192	81,048	85,008	106,100	81,607	79,246	73,290	68,048	61,148	92225
China	21	53	91	131	36	38	121	2	0	1
Spain	5,029	5,267	6,278	5,002	5,051	4,754	3,804	3,268	3,901	6,599
Italy	3,599	3,039	3,836	4,204	3,951	4,694	4,092	3,153	2,972	2,667
U.K.	3,839	3,670	5,525	3,603	9,528	5,280	5,323	4,363	5,274	2,543
U.S.	28,976	29,609	32,829	37,247	35,002	28,586	27,684	24,108	26,779	31,206
California	898	1,529	1,092	1,352	1,163	0	2,322	554	990	1,086
Florida	1,173	1,423	708	909	1,167	963	861	1,664	348	1,144
Illinois	1,370	1,287	1,529	1,344	1,465	1,293	1,672	1,173	1,222	1,346
Louisiana	1,857	1,417	746	1,253	970	761	581	421	502	433
Massachusetts	1,337	1,365	1,588	2,151	2,033	1,886	2,615	1,392	1,296	1,755
Michigan	1,503	1,749	1,376	1,158	1,279	1,210	645	997	1,366	1,058
New Jersey	3,585	3,326	3,057	3,590	3,561	3,563	3,699	2,734	4,240	2,206
New York	8,658	8,174	10,453	10,621	11,676	9,946	8,236	5,337	7,177	11,571 **
Washington	326	337	N/A	1,087	455	0	0	87	127	156

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

**High due to a changing with inclusion of people who died at home.

#5 Death Toll Increases - APRIL 2020 - World and U.S.										
(Additional DEATHS, not total deaths)										
Location	April 6	April 7	April 8	April 9	April 10	April 11	April 12	April 13	April 14	April 15
Worldwide	5,051	7,300	6,473	8,701	5,714	6,109	5,389	5,337	6,969	4,993
China	0	0	2	3	3	0	0	2	0	1
Italy	636	604	542	610	570	619	431	566	602	578
Spain	700	704	747	655	634	525	603	547	499	557
U.K.	442	786	940	867	996	918	737	718	782	765
U.S.	1,136	1,939	1,973	1,996	2,067	1,846	1,504	1,496	2,388	4,993
California	24	31	68	50	49	0	110	36	71	63
Florida	18	60	13	45	36	48	27	48	24	72
Illinois	33	73	82	66	68	81	43	74	74	80
Louisiana	35	70	70	50	53	51	36	44	129	0 *
Massachusetts	29	96	77	70	96	87	70	88	113	151
Michigan	110	118	114	117	205	111	95	115	166	153
New Jersey	86	229	272	196	232	251	167	93	362	351
New York	599	731	779	799	777	783	758	671	778	752
Washington	10	12	19	66	0	45	0	17	8	25

* likely reporting was delayed