



TRENDS-in-MEDICINE

BULLETIN: UPDATE ON CORONAVIRUS

March 15, 2020
by Lynne Peterson

Be careful, be safe, and be well.

Based on the latest data available on March 15, 2020, this is what is known about the SARS-CoV-2 virus and the disease it causes, Covid-19. This update includes information on (in this order):

- Extent of the problem – worldwide, U.S., and hot spots
- What government is doing
- The impact on Americans
- Testing
- Treatments
- Vaccines
- Unanswered questions
- Major medical conference schedule/changes

Extent of the problem

- The World Health Organization (WHO) declared Covid-19 a **pandemic**.
- More than 169,000 people worldwide have been infected with SARS-CoV-2, and there have been 6,492 deaths from Covid-19, a fatality rate of 3.8%.
 - Italy has been especially hard hit, with 24,747 cases and 1,809 deaths, a fatality rate of 7.3%.
 - Spain, Italy, and France are all in lockdown, with almost everything canceled in Germany, which closed its borders. German Chancellor Angela Merkel estimated that 60%-70% of the German population will become infected.
- In the U.S., 3,499 people have been diagnosed with Covid-19, and 63 have died, a fatality rate of 1.8%. Coronavirus has been diagnosed in 49 states, the District of Columbia, and Puerto Rico. The hot spots, according to President Trump, are California, Washington state, New York, Massachusetts, and Florida (even though there are states with more cases than Florida).
- President Trump declared a **national emergency**, which waives a lot of federal regulations affecting doctors and hospitals. He said the “next eight weeks are critical.” He also imposed a ban on non-American travelers flying (directly or indirectly) from Europe, the U.K., and Ireland to the U.S., effective at midnight March 16.
- Several prominent people have tested positive, including Canadian Prime Minister Trudeau’s wife, the wife of the prime minister of Spain, the U.K. Health Minister, and actor Tom Hanks and his wife. President Trump tested negative.

What government is doing

- **Emergency declarations** – President Trump declared a national emergency, and several states have also declared a state of emergency. One city imposed a curfew to keep people home.

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- **Congressional action** – The House of Representatives passed an economic aid package, and the Senate is due to take it up on March 16.
- The **Federal Reserve** dropped interest rates a half point and just lowered them again by a full point to 0-0.25%. In addition, the Fed is going to purchase \$500 billion in treasuries and \$200 billion in mortgage-backed securities.
- **Public-private partnership** – On March 13, President Trump – surrounded by senior officials of Walmart, Target, CVS, Walgreens, LabCorp, Roche, Becton Dickinson, Quest, Signify Health, and LHC Group – announced a public private partnership to expand coronavirus testing. On March 15, President Trump said he had talked with the heads of most of the major grocery and food service companies, and they are committed to staying open and working “around the clock to keep their stores stocked...at a level beyond Christmas time...There is no need to hoard essential food supplies.”
- **Oil** – President Trump announced that the government will top off the strategic oil reserves with low-cost crude oil.

The impact on Americans

■ Closures

- **Events** are being canceled, including most major sporting events, concerts, Broadway shows, primary voting in two states, etc. Disney and Universal closed their theme parks!
- **FDA** canceled all meetings, including advisory committees, through the end of April.
- **Gatherings.** The Centers for Disease Control and Prevention (CDC) recommends no gatherings of ≥ 50 people for the next 8 weeks. That includes “conferences, festivals, parades, concerts, sporting events, weddings, and other types of assemblies.”
- **Schools and colleges** across the country are closing or moving to online classes – 29 states have closed all their schools, and the CDC suggests they should close for ≥ 8 weeks, not just 2-4, to slow coronavirus spread.
- **Stores and businesses** are closing (Apple) or cutting hours (e.g., Walmart, Publix, Kroger, H-E-B, Patagonia, Urban Outfitters, etc.) The cruise lines canceled cruises for 30 days, airlines cut flights drastically, and some Starbucks stores may become drive-through only. Several states – including Illinois, New York, and Ohio – have closed all bars and restaurants until further notice. California closed all bars, pubs, wineries, and clubs. However, major grocery stores have committed to remaining open and stocked.
- **Elective surgery** – Some hospitals are postponing elective procedures as they prepare for Covid-19. The question is whether they will have enough respirators for severe patients, but President Trump said, “We ordered a large number of respirators.” (I took my husband to our Cleveland Clinic-associated local Florida hospital on March 7 for something that turned out not to be serious. In the emergency room patients were on gurneys in the hall because all the ER rooms were full – and there were no coronavirus patients yet. So, while coronavirus patients are likely to be hustled out of the ER and into isolation, it shows that some hospitals may not have much spare capacity.)

A survey of ~60 orthopedic surgeons, interventional cardiologists, and anesthesiologists by an analyst at Jefferies found Covid-19 has already started to affect procedure volume, with 23% saying there has been an increase in delays/cancellations, down an average of 16%.

- **Hand sanitizer** – For anyone thinking of making their own hand sanitizer, the FDA issued guidance to pharmacists for compounding hand sanitizer, saying it should contain:
 1. Alcohol (ethanol) (80%, denatured) – or Isopropyl Alcohol (75%)
 2. Glycerol (1.45%)
 3. Hydrogen peroxide (0.125%)
 4. Sterile distilled water or boiled cold water.

The FDA also warned against adding other active or inactive ingredients because they may reduce the safety and effectiveness of the product.

- **Illness duration** – When someone does get Covid-19, Shoshana Ungerleider, MD, a California hospitalist told Fox News, the illness can last a few days to weeks or months. What kills patients is acute respiratory distress syndrome (ARDS), for which there is no treatment, making respirators a key last line of defense.
- **Immunity** – It still is not known if someone who gets the virus will be immune from it in the future. Children are generally not getting sick (though there is a case in Utah), but they may be infected and not showing the effect, so they could spread the virus.
- **Insurance** – Seema Verma, administrator of the Centers for Medicare and Medicaid Services (CMS), announced, after President Trump met with insurance industry executives at the White House, that insurers agreed to waive copays for Covid-19 testing, eliminate any surprise billing for Covid-19 testing/treatment and cover Covid-19 associated treatment. She also said CMS responded to a request from Medicare Advantage plans, agreeing to allow the plans to remove prior authorizations, waive prescription refill limits, offer mail delivery of prescriptions, and allow more telehealth services.
- **Nursing homes** and assisted living facilities – no outside visitors. Most hospitals also cut back visiting hours and who can visit patients.
- **Pregnancy** – In China, 9 pregnant women became infected with Covid-19, but all delivered normal babies. However, a newborn in the U.K. is positive, and the baby's mother tested Covid-19-positive days before the birth.
- **Risk assessment** – A Chinese retrospective cohort study, published in *The Lancet*, found that the key indicators of poor outcome in people who contract Covid-19 are: hypertension, d-dimer >1 µg/L, and SOFA score (a sepsis risk score).
- **Student loans** – President Trump announced that interest on federal student loans is waived until further notice.
- **Surfaces** – An unpublished study by the National Institutes of Health's Rocky Mountain Laboratories found the virus can live on hard surfaces (e.g., plastic and stainless steel) for up to 3 days (72 hours), on cardboard for up to 24 hours, but only for 4 hours on copper. It lasts a shorter time in direct sunlight. But it isn't known yet how long it lives on clothing or carpet. Food contamination is not thought to be an issue, but utensils can harbor the virus. The virus also can survive in the air for several hours.
- **Travel** – Non-essential U.S. travel is now being discouraged for everyone, but particularly for the elderly. Americans returning from Europe are being asked to self-isolate for 14 days. President Trump said there *could* be restrictions on *domestic* air travel in the U.S., particularly to hot spots.

Testing

Test *availability* has improved but still has a long way to go. Testing *eligibility* has lightened, but patients generally still have to be *symptomatic*. As much as test availability was an issue, testing *sites* were also an issue because doctors don't want sick patients coming to their offices/clinics for testing, labs don't want the patients going there either, and hospitals don't want test patients clogging their ERs and possibly exposing other people.

Drive-through testing sites are popping up around the country. These are a good partial solution because they protect the patients and staff from exposure to possibly infected people. Ten states reportedly have drive-through sites, and the number is increasing. In addition, testing "pods" will be deployed across the country, where needed, that can test 2,000-4,000 people/day, starting this coming week. However, even drive-through sites require patients to be symptomatic before testing in most cases.

- Vice President Mike Pence said the first people to be tested are going to be healthcare workers and first responders.
- Starting on March 16, 2,000 labs will be able to conduct coronavirus testing.
- Admiral Brett Giroir, MD, Assistant Secretary for Health and head of the Public Health Service, was named the Covid-19 testing czar.
- The FDA rapidly granted emergency use authorization for two new rapid tests:
 - **Roche's cobas SARS-CoV-2 Test**, an RT-PCR test for Covid-19 that is 10 times faster than the CDC's test. The test was also given a CE-IVD Mark, so it can be used in Europe as well.
 - **Thermo Fisher Scientific's TaqPath COVID-19 Combo Kit**.

- Other tests are in development.
 - CDC is working on two serological (blood) tests for use in asymptomatic patients or patients with mild symptoms.
 - **Chembio Diagnostics** and **LumiraDx** are collaborating on development of point-of-care diagnostic assays for SARS-CoV-2.
 - **GenMark Diagnostics' ePlex test** – An emergency use authorization was submitted to the FDA.
 - **Hologic** is getting \$699,000 from the Biomedical Advanced Research and Development Authority (BARDA) for development of a molecular diagnostic test for SARS-CoV-2 that can process ~ 1,000 tests in 24 hours using the Panther Fusion system.
- **CT scans** – A study, published in the journal *Radiology*, found that CT scans can help differentiate Covid-19 from usual pneumonia.

Treatments

There are no real treatments for Covid-19. A Chinese retrospective study, published in *The Lancet*, found that viral shedding can occur for 8-37 days in Covid-19 survivors and to death in infected patients, suggesting patients may need to be treated for at least 37 days if and when a treatment is identified.

Sen. Ted Cruz (R-TX) said he will introduce legislation that would allow the FDA to expedite approval of any drug, vaccine, or medical device endorsed by regulators in 36 other countries (including Canada, Australia, Japan, and New Zealand) to treat coronavirus.

The leading candidates for treatment are:

- **Gilead Sciences' remdesivir**, an antiviral developed for Ebola that failed, is getting the most attention – and use in the U.S. It is being tested in the U.S. in two Gilead trials and one NIH trial as well as in 2 trials in China. The Chinese trial initially had some enrollment issues because the protocol required that patients not have had any other therapy in the previous 30 days, but some results are now expected in April.

Remdesivir is available in the U.S. under compassionate use, and Gilead said it would provide the drug free to the U.S. military. There was a rumor that remdesivir is having some positive effects. CDC Commissioner Robert Redfield, MD, said the efficacy should be known by April 2020, when the first Chinese trial data are expected.

However, a pre-print of a paper to be published (but which has not yet been peer reviewed) on the first 12 U.S. patients, 3 of whom were treated with remdesivir under compassionate use at the time of clinical worsening, raise questions about its utility. There are side effects, and there was no “wow” response. The researchers reported:

- “All [patients on remdesivir] had transient gastrointestinal symptoms, including nausea, vomiting, gastroparesis, or rectal bleeding.” In one case these side effects were likely related to prior travel to Mexico. Three patients developed elevated aminotransferase elevation.
- Three patients “tolerated treatment with...remdesivir.”
- Remdesivir was discontinued after improvement in each patient’s respiratory symptoms, but the researchers made no statement that they improved because of remdesivir.
- The researchers concluded: “Because remdesivir use was not given as part of a randomized controlled trial, we are unable to assess its effectiveness or safety.”

What else was learned from those 12 patients, who were not really severe patients?

- Nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, and sputum samples were the most accurate in determining Covid-19 continued infection. Urine and serum were not accurate.
 - Median symptom duration was 14 days (range 6-20 days).
 - Hospitalized patients worsened in Week 2.
 - All patients recovered or are recovering.
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- Viral RNA was detected for as long as 29 days in some patients. Viral RNA levels and duration of RNA detection did not appear to correlate with illness severity.
 - Viral RNA was detected in the stool of multiple patients, but it is not known yet if this is viable virus.
- **AbbVie's Kaletra (lopinavir + ritonavir)**, an HIV drug, is being tried but rumors are that it has not been very effective.
- **Chloroquine**, an old anti-malarial, reportedly is flying out of distributors' warehouses, but there is no information on where or how it is being used. South Korea reportedly is using this drug. China's Ministry of Science and Technology also suggested that chloroquine should be included in the standard regimen for treating Covid-19.
- **Roche's Actemra (tocilizumab)**, an anti-IL-6 for rheumatoid arthritis that is also used to treat cytokine release syndrome in immunotherapy patients, is in the Chinese [guidelines](#) for Covid-19, but there are no reports about its use in the U.S. for that.
- Other investigational therapies being explored:
- **AIM ImmunoTech's Ampligen (rintatolimod)**— The National Institute of Infectious Diseases in Japan plans to start testing this.
 - **BioCryst Pharmaceuticals' galidesivir** — The company is working with BARDA on repurposing this antiviral to treat Covid-19.
 - **Enanta Pharmaceuticals** is searching its library.
 - **Johnson & Johnson/Janssen** expanded its partnership with BARDA to include Covid-19 and will see if an existing drug can be repurposed for Covid-19.
 - **Lilly and AbCellera Biologics** hope to have a treatment in the clinic by summer. They are working on identifying neutralizing antibodies in people who recovered from Covid-19 in the hopes of finding a treatment.
 - **NanoViricides** is the latest company to announce it is working on a treatment, in this case a broad-spectrum virus-binding ligand.
 - **Parallax Diagnostics** is looking for a partner to help develop an inexpensive, fast coronavirus test to use with its VT-1000 Immunoassay diagnostic platform.
 - **Regeneron and Sanofi's Kevzara (sarilumab)** — The companies are looking to repurpose this anti-IL-6 rheumatoid arthritis drug.
 - **Ruxin Medical Systems' CoughSync** — This Israeli-developed non-invasive *device* is under review by Chinese regulators as a way to clear secretions from Covid-19 patient airways. It is already approved in Europe.
 - **Sirnaomics** is exploring gene-silencing techniques to see if it can find a way to turn off key genes in the virus.
 - **Takeda's TAK-888**, a plasma-derived therapy made from the blood of Covid-19 patients who have recovered, is under development.
 - **Vir Biotechnology** is collaborating with National Institute of Allergy and Infectious Diseases (NIAID) to advance the characterization and development of human monoclonal antibodies against coronaviruses, including SARS-CoV-2, SARS, and MERS. Vir also is working with **WuXi Biologics**, a Chinese pharma, on finding a treatment for Covid-19.
 - **Zhejiang Hisun Pharma's Favilavir (favipiravir)** — This flu drug, which is approved in Japan, is under review by China's Ministry of Science and Technology as a potential treatment for Covid-19.

Vaccines

NIAID director Anthony Fauci, MD, PhD, said there as many as 10 vaccines in development, but it appears there are even more than that, including:

- **China's** Center for Disease Control and Prevention is working on development of a vaccine.
- **Alnylam Pharmaceuticals and Vir Biotechnology** are collaborating and claim to be “relatively close” to identification of an RNAi candidate for treating Covid-19.
- **CureVac**, a German biopharmaceutical company, is collaborating with the Coalition for Epidemic Preparedness Innovations (CEPI) on a vaccine and hopes to have a candidate by June or July.
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- **GlaxoSmithKline** is collaborating with **Clover Biopharmaceuticals** on COVID-19 S-Trimer, a protein-based vaccine.
- **Inovio Pharmaceuticals' INO-4800** – The company got a \$5 million grant from the Bill & Melinda Gates Foundation as well as funding from CEPI for development of a vaccine using its DNA medicine platform. Inovio hopes to have animal data on this vaccine candidate soon but will need a manufacturer for scale-up.
- **Johnson & Johnson** is working on a vaccine, though a J&J official said the company is starting from scratch and that could mean it will be up to a year before the vaccine is available for testing in patients.
- **Migal Research Institute** in Israel, which had been developing a coronavirus vaccine for chickens, is now modifying it for humans. Human trials are expected to start in a few months.
- **Moderna and NIAID's mRNA-1273.** The only data on this mRNA vaccine so far is from non-human cell cultures; there are *no preclinical animal data*. Asked about that, Tal Zaks, MD, PhD, chief medical officer of Moderna, told *Stat*, “I don't think proving this in an animal model is on the critical path to getting this to a clinical trial.” Dr. Zaks said NIAID is working on animal data now. A 45-patient Phase I safety trial started enrolling patients at Kaiser Permanente in Seattle in early March and should be completed by June 1, 2020. Dr. Fauci said it will be three months before it is known if the vaccine is safe enough to start a Phase II trial. However, it will be a minimum of a year before efficacy is known. CEPI also is providing some funding. Moderna and NIH reportedly had been (still are?) looking for a manufacturer to make the vaccine if and when it is ready for commercialization.
- **Novavax** reportedly expects to develop a vaccine candidate from the genetic sequence of the SARS-CoV-2 coronavirus.
- **Pasteur Institute Foundation** in France hopes to have a vaccine available by 2021.
- **Pfizer** reportedly is considering working with **BioNTech** on an mRNA vaccine.
- **Sanofi** is collaborating with the Department of Health and Human Services and BARDA on development of a recombinant DNA vaccine, based on research conducted by a flu vaccine company Sanofi bought, Protein Sciences.
- **Vaxart** initiated a coronavirus program based on its proprietary oral vaccine platform, VAAST.

Unanswered questions

- ? How does the *outbreak end*? Will it end or will it become a regularly circulating virus, infecting people like the common cold – until there is a reliable vaccine?
- ? What percent of severe patients who survive get or will get *pulmonary fibrosis*? Would **Boehringer Ingelheim's Ofev** (nintedanib) help these patients?
- ? If a *vaccine* is developed, will it work like a measles vaccine – once and done – or will it be more like a flu vaccine that has to be modified each year? And could the virus mutate between now and when the vaccine is ready so the vaccine doesn't work?
- ? Officials continue to say that they don't know if there is a SARS-CoV-2 *reservoir* in the body that persists as with HIV or Ebola, so this remains an open question.
- ? Is the U.S. *blood supply* safe? How is it being tested?

Major medical conferences

Those not mentioned here are canceled through May 15. The award for the *worst response* to the impact of Covid-19 on medical conferences goes to the president of the World Institute of Pain, Giustino Varrassi, MD, PhD. The meeting is scheduled for May 20-23 in Rome, Italy, and this message from him was on the meeting website as of March 15:

“I feel confident in reassuring everyone who is willing to participate in the WIP World Congress in Rome that, by May 20-23, COVID19 like any other flu will be only a distant memory.”

Still scheduled – expect many/most/all of these to cancel or go virtual, given the CDC call for no gatherings of ≥50 people

American Association of Clinical Endocrinologists (AACE), May 6-10, Washington, DC

American Society of Cataract and Refractive Surgery (ASCRS) – ASOA annual meeting, May 15-19, Boston

American Society of Clinical Oncology, May 29-June 2, Chicago. The current message is:

“At this time, we are planning to hold the meeting in Chicago as scheduled. However, because the situation and public health guidance are changing rapidly, we are **actively planning alternative scenarios**, should they be needed.”

American Society of Gene & Cell Therapy (ASGCT), May 12-15, Boston

American Thoracic Society International Conference (ATS), May 15-20, Philadelphia

Digestive Disease Week (DDW), May 2-5, Chicago

ESMO Breast Cancer, May 7-9, Berlin, Germany

Food and Drug Law Institute (FDLI) Conference, May 7-8, Washington, DC – *not canceled but some remote viewing planned*

Global Embolization Symposium and Technologies (GEST), May 14-17, New York City

Heart Rhythm Society Scientific Sessions, May 6-9, San Diego

Society for Cardiovascular Angiography and Interventions (SCAI), May 13-16, Atlanta

Society of Biological Psychiatry, April 30-May 2, New York City

Virtual meeting or partial virtual meeting option

Advances in Alzheimer's and Parkinson's Therapies, an AAT-AD/PD Focus Meeting, scheduled for April 2-5 in Vienna, Austria.

Virtual meeting

American College of Cardiology (ACC), scheduled for March 28-30 in Chicago. **Some virtual options**

American Society of Addiction Medicine (ASAM) in Denver April 2-5. **Virtual meeting**

American Urological Association (AUA), May 15-18 in Washington, DC. **Canceled but possibly some virtual sessions/data**

Health Care Compliance Association's (HCCA) Compliance Institute, March 29-April 1 in Nashville TN. **Canceled but a virtual option available**

Postponed – with new date announced

American Society of Interventional Pain Physicians (ASIPP), scheduled for April 2-4 in Dallas. *Postponed* to September 4-6.

European Association for the Study of the Liver (EASL): International Liver Congress (ILC), April 15-19 in London.

Postponed to August 25-28.

European Breast Cancer Conference (EBCC) in Barcelona, Spain, March 18-20. *Postponed* to September 30-October 2.

European Society for Radiotherapy and Oncology (ESTRO) scheduled for April 3-7 in Vienna, Austria.

Postponed to July 31-August 4.

European Stroke Organization Conference, scheduled for May 12-15 in Vienna, Austria. *Postponed* to November 6-9.

Immunotherapy of Cancer (IIOC) conference April 2-4 in Munich. *Postponed* to October 3-5.

International Papillomavirus Conference (IPVC), scheduled for March 23-27 in Barcelona, Spain. *Postponed* to July 20-24.

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), scheduled for April 1-4 in Cleveland.

Postponed to August 12-15.

Society of Surgical Oncology (SSO) International Conference on Surgical Cancer Care 2020, scheduled for March 25-28 in Boston.

Postponed to August 17-20.

Venous Symposium in New York City scheduled for March 19-21. *Postponed* until July 30-August 1. The Aesthetic Vein Session and the Latin Session will still take place July 29, 2020.

World Congress on Neurology and Mental Disorders, May 11-12, Tokyo. *Postponed and location changed* to September 10-11 in Vancouver, Canada.

World Congress on Osteoporosis, Osteoarthritis, & Musculoskeletal Diseases (WCO-IOF) scheduled for April 2-5 in Barcelona, Spain.

Postponed to August 20-23.

World Vaccine Congress, scheduled for April 7-9 in Washington, DC. *Postponed* to September 27-29.

Postponed – no new date available

European Heart Rhythm Association (EHRA) Congress (formerly EUROPACE), scheduled for March 29-31 in Vienna.

Canceled but may be held later this year.

Gene Therapy for Rare Disorders conference, scheduled for March 30-April 2 in Boston. *Postponed to 2021.*

International Conference on Re-Emerging Infectious Diseases (ICREID) in Addis Ababa, Ethiopia, March 18-20. There was supposed to be a special symposium on Covid-19. *Postponed* – perhaps October 2020

National Comprehensive Cancer Network (NCCN) annual conference, scheduled for March 19-22 in Orlando.

