



TRENDS-in-MEDICINE

BULLETIN: UPDATE ON CORONAVIRUS 4/6

April 6, 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 182 countries in the world. Most of the U.S. is on a near lockdown, with social distancing leaving our streets, schools, parks, and beaches almost a ghost town. Here are the latest news highlights. The U.S. estimate has been lowered for deaths to ~85,000 from a previous range of 100,000-240,000. The first peaks in cases are likely to be reached this week in a few places in the U.S., including New York, but the death rate will lag that, and the last case peaks in the country may hit in late May.

Our charts are on Pages 7-8. Watch the chart on *additional* cases per day to look for countries that are peaking. Remember that total deaths lag behind cases. There is a new figure in Chart #2 – a rate of cases per capita. That shows the U.S. rate is 0.11%, which is less than France, Germany, Italy, and Spain but more than the U.K.

We are only including the daily chart data in this report, but when we reach Week 4 (April 8) of our monitoring, we will again offer a look at weekly as well as daily numbers. If you want the weekly numbers in every report, let us know.

Some of the trends that pop out today include:

- Of the countries we are monitoring, only Spain showed a decrease in the latest numbers in the rate of **patient deaths** from Covid-19. However, both Spain and Italy appear to have peaked.
- The **per capita rate** of Covid-19 means that, roughly, nearly 1 in 5,000 people worldwide have been diagnosed with Covid-19. In the U.S., it is roughly 1 in 1,000.
- The **case fatality rate** has steadily increased worldwide and is now 5.5%. Spain, Italy, and the U.K. now have case fatality rates of 10% or more vs. 2.9% in the U.S.
- In the U.S. the top **hotspot** remains New York, with >130,000 cases – 36% of the country's total – and nearly 5,000 deaths, but other hotspots include, New Jersey, Michigan, Louisiana, and Illinois.

Tidbits

■ The world

- The **World Health Organization** (WHO) has come under heavy criticism for helping China to withhold or cover-up the threat the coronavirus posed. U.S. Sen. Rick Scott (R-FL) wants a congressional probe into WHO. The U.S. pays ~21% of the WHO budget, while China pays ~1%.

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- **France** had its worse coronavirus day so far on April 6.
- **Germany** has a surprising low death rate (1.8%), but cases are still mounting (>100,000). Yet, the government is making plans for how it will end the lockdown, which currently is set to end April 19. The plan is for a staged return to normalcy, accompanied by the ability to track more than 80% of people with whom an infected person comes in contact in the prior 24 hours. Then, infected people, along with those contacts, will be quarantined either at home or in hotels. The document **assumes the pandemic will last until 2021**.
- **Japan**. The prime minister is expected to declare a state of emergency that will last approximately 1 month.
- **U.K.**
 - ✓ **Prime Minister Boris Johnson** was admitted to the hospital for Covid-19 on April 5. The next day his condition worsened, and he was moved to the ICU. He is on oxygen but reportedly not on a ventilator. There is no formal plan of succession in the U.K. as there is in the U.S. Foreign Secretary Dominic Raab is temporarily taking over the prime minister's duties. President Trump said he talked with 4 drug companies, and they already have staff in London and will contact Johnson's doctors to see if they can be of help.
 - ✓ **Queen Elizabeth** addressed the nation, praising healthcare workers and urging citizens to stay home. This is only the fifth time in her 68-year rule that she has addressed the nation, outside of her annual Christmas Day message.

■ U.S.

- Surgeon General Jerome Adams is calling this week America's "Pearl Harbor moment."
- Data from the Institute for Health Metrics and Evaluation (IHME) at the University of Washington suggest:
 - ✓ The shortage of **ventilators** and ICU beds may be less than previously thought.
 - ✓ **Total deaths** in the U.S. are expected to be less (81,766) than even the lowest number (100,000) the White House Task Force on Coronavirus has been using. And the range is lower: 49,421-136,401 instead of 100,000-240,000.
 - ✓ **New York** may peak in the next few days, with New Jersey a few days behind that.
 - ✓ Peaks will be **earlier than expected** in Florida (April 21), Virginia (April 22), Louisiana (April 10 if it hasn't already happened), and West Virginia (April 16).
- **When will elective surgeries resume?** One assumption is that states will gradually restart elective procedures ~30 days after peak hospital use. This suggests that all states may be able to restart elective procedures by late June.
- **Fatality rate error.** More people have died (and are dying) from Covid-19 than the official numbers reflect. The Centers for Disease Control and Prevention (CDC) said that this is because the official death numbers only include people who died after a positive Covid-19 test.
- **Animals.** It was known that dogs (occasionally) and cats (more commonly) can get infected with SARS-CoV-2, though it is not believed that they can transmit the disease, and it doesn't make them sick or kill them. Now, a tiger at the Bronx Zoo in New York has tested positive with Covid-19, and six other tigers and lions are exhibiting signs of Covid-19. The zoo believes they caught it from an asymptomatic zookeeper. A new Chinese study found that housecats can transmit the virus to other housecats. ***All of this raises the question of whether livestock can get the virus.***
- **Newborns.** The American Academy of Pediatrics recommends that infants born to mothers with Covid-19 should be temporarily separated from their mother to minimize the risk of the mother infecting the baby. In addition, the AAP recommends that mothers with Covid-19 pump their milk and have the baby fed by a designated caregiver, even though it does not appear that Covid-19 affects breast milk.

- **Nursing homes.** The recommendation is that all nursing home facilities assign the same staff to care for the same people and to make separate areas for healthy individuals. Both of these practices are likely to continue long after the pandemic is over, as a precaution.
- **Retirees.** More than 107,000 healthcare workers have come back from retirement to help with the coronavirus pandemic. At the same time, non-urgent care healthcare workers have been laid off. *Did anyone think about moving workers to areas in need the way they are moving supplies?*
- **USS Theodore Roosevelt.** Capt. Brett Crozier, who was removed from command of this nuclear-powered aircraft carrier for circulating a 5-page memo critical of the Navy's response to the coronavirus outbreak on his ship, tested positive for Covid-19 on his last day on the ship. So far, at least 155 sailors on the ship have tested positive, and one is in the hospital. Acting Navy Secretary Thomas Modly also came under fire for calling the captain "too naïve or too stupid" to command the ship. President Trump said Capt. Crozier was wrong, but he might intervene in the dispute and maybe he did because Sec. Modly later issued a statement apologizing to Capt. Crozier and his family (but not reinstating him).
- **Visas.** The State Department said it will resume processing visas needed by international doctors to enter the country and work here. Processing of visas was suspended on March 18, 2020, because of coronavirus. It still may be difficult for physicians who get a visa to travel to the U.S., and they may face quarantine for 14 days if and when they arrive.

U.S. states and cities

- **Georgia** – Gov. Brian Kemp is under fire for allowing public beaches to reopen, provided the beaches are used for exercise – with social distancing and without chairs, tents, or umbrellas.
 - **Louisiana** – The state had a spike of ~3,000 Covid-19 cases on April 2, a 42% one-day increase, which was attributed to an increase in testing, but now it looks like the state may peak earlier than expected. Gov. John Bel Edwards said 70% of Covid-19 deaths in the state have been African Americans.
 - **Maryland** – The governor predicted his state would be the next hotspot in the country, with a surge in mid-April.
 - **New York**
 - Gov. Andrew Cuomo said the number of Covid-19 positive patients, hospitalizations, and deaths have all grown by smaller numbers in recent days. The hope is that this is the start of a plateau – a flattening of the curve – but Gov. Cuomo is still concerned that, if it is a plateau, it will hold at this high level for too long before declining. (Like a mesa instead of a spire or a rolling hill).
 - At the governor's request, President Trump agreed to let the USNS Comfort hospital ship be used for Covid-19 patients – from both New York and New Jersey – instead of only non-Covid patients.
 - The closing of New York schools and non-essential businesses will continue until April 29.
 - The governor was unhappy with violations of the stay-at-home order and doubled the penalty from \$500 to \$1,000 per offense. He also was unhappy with reports of orthodox Jewish weddings and funerals violating the social distancing and gathering rules, saying the police should enforce those rules.
 - **Ohio** – Gov. Mike DeWine is considering releasing some non-violent prisoners to slow coronavirus spread in the state.
 - **Wisconsin** – The state Supreme Court blocked Gov. Tony Evers' executive order to postpone in-person voting in the April 7 state and local elections, and the U.S. Supreme Court ruled 5-4 that the state cannot accept absentee ballots postmarked after Tuesday (voting day).
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Drug shortages

Asked whether India has lifted its ban on exports of hydroxychloroquine and other drugs, President Trump said, “I would be surprised if he would [block exports]...He would have to tell me that...[if it doesn’t lift]...Of course, there would...But, of course, there may be retaliations. Why wouldn’t there be?”

Medical supplies

- **3M.** President Trump said the issues with 3M have been resolved, and 3M will deliver an additional 55.5 million high quality face masks each month (for three months). He said, “So, the 3M saga ends very happily.”
- **Hospital survey.** The Inspector General (IG) of the Department of Health and Human Services Ann Maxwell released the results of a survey of 323 American hospitals done March 23-27, 2020. The 34-page report found 75% of the hospitals had at least one Covid-19 patient. Among the complaints the hospitals had were:
 - A “severe” shortage of Covid-19 tests, with wait times of up to 7 days.
 - “Widespread” shortages of personal protective equipment (PPE).

President Trump challenged the findings, and Adm. Brett Giroir, MD, head of the administration’s testing effort, said that the study was done while testing was ramping up and has since improved. The American Hospital Association said the report “accurately captures the crisis that hospitals and health systems, physicians, and nurses face.”

- **VA survey.** The Inspector General of the Veterans Administration issued its own survey of 207 VA facilities, and that, too, found a shortage of supplies and drugs. Former VA Secretary David Shulkin said, “This was a wake-up inspection to say we have to do much more.” He said the VA is now moving things around the country. They have the ability to move resources.

Masks

- The truth is: Cloth masks – and medical masks (other than N95) – provide the user with very minimal protection from catching the coronavirus. However, they do prevent the wearer from spreading the virus if the wearer has Covid-19. And that was the finding of a study, published in *Nature Medicine*, that surgical face masks could prevent “transmission of human coronaviruses and influenza viruses from symptomatic individuals.”
- In the absence of a federal policy or recommendations on how to allocate resources, many state health departments and health systems are formulating their own policies.

Ventilators

- **Veterinarians** have been donating ventilators used for cats and dogs to hospitals for use on people with Covid-19.
- Several states have been **loaning** some of their ventilators to states with a greater need: Oregon sent New York 140 ventilators; Washington State sent 400 ventilators to New York; and California gave the federal government 500 ventilators for the national stockpile.

Testing

To date, 23 diagnostic tests have received an emergency use authorization (EUA) from the FDA to test for SARS-CoV-2. In addition, the FDA issued a broad EUA that allows eligible molecular-based laboratory-developed tests.

Among the newer tests are:

- **Becton Dickinson and BioMedomix** plan to launch a rapid diagnostic test – a simple, point-of-care blood test – for current or post exposure.

- **Biolidics'** fast Covid-19 test kit that detects the virus within 10 minutes, with ~95% accuracy was given provisional authorization by Singapore's Health Science Authority.
- **Rendu Biotechnology's SARS-CoV-2 nucleic acid detection kit** delivers results within 90 minutes was given emergency approval by China's National Medical Products Administration.

Transmission

- **Blood** – In a teleconference with reporters, Peter Marks, MD, PhD, director of the FDA's Center for Biologics Evaluation and Research (CBER), said the FDA believes the blood supply is safe from coronavirus, "It is true that patients who are extremely viremic can have coronavirus in their blood, and there is a thought that viremia could potentially transmit, but they would be too sick to donate blood. One qualification for donating is you have to be in good health. There are some reports in the literature finding coronavirus RNA – the genetic matter – in donated specimens. But there is no evidence...that that can actually be transmitted. We are in a very different place [from where we were in the early days of AIDS]...Back then, we couldn't do the kind of recombinant DNA testing...So, I'm pretty confident...that it is behaving like other respiratory viruses and will not be spread in that manner."
- **Food** – In another teleconference with reporters, Frank Yiannas, the FDA's Deputy Commissioner for Food Policy and Response, said, "There is no evidence it [coronavirus] can be transmitted through food." Unlike *e. coli*, Yiannas said the foodborne outbreaks have been primarily bacterial, not viral, "Virus on food is generally through some exposure to droplets. That is the route of contamination."

Treatment

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

The latest agents – none of which were specially mentioned by the President – include:

- **Amgen and Adaptive Biotechnologies** are collaborating on fully human neutralizing antibodies against Covid-19, either as a treatment or a preventive.
- **Brii Biosciences** is working with Tsinghua University and Shenzhen No. 3 People's Hospital on development of antibodies against Covid-19.
- **Celularity's CYNK-001** – The FDA approved an investigational new drug (IND) application clearing the way for a Phase I/II trial of this natural killer cell-based therapy for Covid-19.
- **Merck MSD's Stromectol (ivermectin) and generics** – Why would a lice treatment (an antiparasitic) work for Covid-19? An *in vitro* study showed this FDA-approved drug inhibits replication of SARS-CoV-2.
- **Novartis and Incyte's Jakafi (ruxolitinib)** – A double-blind Phase III trial will begin soon testing standard of care ± this JAK inhibitor as a treatment for cytokine storm in severe Covid-19 patients.
- **Synairgen's SNG-001** – A Phase II trial of this inhaled formulation of interferon beta-1a has shown efficacy in treating asthma patients with a respiratory viral infection.
- **Hydroxychloroquine**. The debate continues on whether this anti-malaria drug is effective in treating or preventing Covid-19, but the anecdotal data look promising.
 - President Trump continues to believe in this as a treatment, saying, "Why not try it? What do you have to lose?" And the President suggested it may be a good prophylactic, "If you are a doctor, nurse, first responder, they say taking it before the fact is good."

- Gov. Cuomo said “The anecdotal evidence is promising...That is why we are going ahead...Anecdotally, it has been positive, and if we get additional supply – which the federal government said we will lift the 14-day limit...The tests in the hospital are too short to get a scientific report. Hospital administrators and doctors want to have a significant dataset before they give a formal option.”
- **Convalescent plasma** – In an interview, FDA Commissioner Stephen Hahn, MD, said, “We absolutely need to get back to work...and balance that with public health issues...Once we determine that [convalescent plasma] is safe and effective, then we move to hyperimmune globulin. That is in parallel...It can work as a treatment potentially but also as a prophylactic and act as a **bridge to a vaccine**...There are manufacturers that have a lot of experience with monoclonal antibodies, and we have been working with them for several weeks to try to scale that up as a bridge to a vaccine.”
- **Roche’s Actemra (tocilizumab)** – A case study from China, published in *Blood Advances*, suggests this anti-IL-6 may be an effective treatment for very ill Covid-19 patients.

Vaccines

What is really needed to get the world back to normal is a vaccine for Covid-19. And there are several in development, including:

- **Inovio Pharmaceuticals’ INO-4800** – After the FDA approved an investigational new drug (IND) application, the company began dosing healthy volunteers in a 40-patient Phase I trial of this DNA vaccine.
- **GlaxoSmithKline and Inovax Biotech**

FDA Commissioner Dr. Hahn said, “We really need redundancy in the medical supply chain – drugs, ventilators, masks. We can’t be dependent on any single country. We need redundancy in our manufacturing.”

China is a potential vaccine competitor. China could be ready to release a vaccine this fall, inject it in people, and if it works, the question is whether the U.S. will use it. Asked if the FDA is ready to review this to make it available in the U.S. Dr. Hahn said, “We have been working with vaccine manufacturers for weeks now...We will look at the data from any source, but we will measure safety of any medical products, including a vaccine.”

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

- ? Are the **neurological symptoms/effects** reversible in some, all, most patients?
- ? Do people with lupus or rheumatoid arthritis who are taking **hydroxychloroquine** (Sanofi’s Plaquenil) have a lower rate of getting Covid-19? Experts agree this is a good question, and the Medicare or Kaiser databases should be able to answer it, but no one has offered those data yet.
- ? Is **hydroxychloroquine** being prescribed for the right patients – and who are those patients (mild/moderate, severe, ventilator)?
- ? People who get mild Covid-19 and recover continue to shed virus for up to 8 days or more **after symptoms resolve**. Is that virus capable of infecting other people? Should those people be quarantined longer?
- ? What do we know about Covid-19 patients who are put on a ventilator and **recover**? What percent recover and is it a *functional* recovery?
- ? Are there **long-term effects** from getting Covid-19, even mild Covid-19? Will there be long-lasting lung abnormalities or pulmonary fibrosis?
- ? Is there a **reservoir** in the body where SARS-CoV-2 might hide and later come back to cause a disease flare or even spread the disease as with HIV or Ebola? Experts still say they don’t know.

- ? Is the **blood supply** safe? This question is back on the list, even though the FDA insists the blood supply is safe, because that pronouncement was based on the *assumption* that a respiratory virus wouldn't be transmitted in blood. There have been no studies to confirm this. If the virus can't survive in blood but could, possibly, survive in other bodily fluids, doesn't that mean it has some durability and could possibly be transmitted?
- ? Can people get Covid-19 **more than once**? There are still conflicting reports on this.
- ? What more can be done to protect **nursing home** residents? Visitors can't be banned forever.

#2 Worldwide Covid-19 Statistics – Daily

Country	April 1			April 4			April 5			April 6			Per capita case rate
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	
Worldwide	932,605	46,809	5.0%	1,197,405	64,606	5.4%	1,275,856	69,514	5.4%	1,345,048	74,565	5.5%	0.02%
U.S.	213,372	4,757	2.2%	308,850	8,407	2.7%	337,638	9,647	2.9%	366,614	10,783	2.9%	0.11%
Italy	110,574	13,155	11.9%	124,632	15,362	12.3%	128,948	15,887	12.3%	132,547	16,523	12.5%	0.22%
Spain	104,118	9,387	9.0%	126,168	11,947	9.5%	131,646	12,641	10.0%	136,675	13,341	9.8%	0.29%
China	82,261	3,316	4.0%	82,543	3,330	4.0%	82,644	3,335	4.0%	82,665	3,335	4.0%	0.006%
Germany	77,872	920	1.2%	96,092	1,444	1.5%	100,123	1,584	1.6%	103,374	1,810	1.8%	0.12%
France	57,749	4,043	9.5%	90,848	7,574	8.3%	93,780	8,093	8.6%	98,963	8,926	9.0%	0.15%
Iran	47,593	3,036	6.4%	55,743	3,452	6.2%	58,226	3,603	6.2%	60,500	3,739	6.2%	0.07%
U.K.	29,865	2,357	7.9%	42,477	4,320	10.0%	48,440	4,943	10.2%	52,279	5,385	10.3%	0.08%

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

#4 U.S. Covid-19 Statistics – Daily

State	April 1			April 4			April 5			April 6		
	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate	Cases	Deaths	Fatality rate
New York	83,712	1,941	2.3%	113,704	3,565	3.1%	122,031	4,159	3.4%	130,689	4,758	3.6%
New Jersey	11,255	355	3.2%	34,124	846	2.5%	37,505	917	2.4%	41,090	1,003	2.4%
Michigan	9,334	337	3.6%	14,225	540	3.8%	15,718	617	3.9%	17,221	727	4.2%
Louisiana	6,424	273	4.2%	12,496	409	3.3%	13,010	477	3.7%	14,867	512	3.4%
California	8,155	171	2.1%	12,026	276	2.3%	13,438	319	2.4%	14,336	343	2.4%
Massachusetts	7,738	133	1.7%	11,736	216	1.8%	12,500	231	1.8%	13,837	260	1.9%
Florida	6,955	87	1.3%	11,111	191	1.8%	12,350	221	1.8%	13,324	236	1.8%
Illinois	6,980	141	2.0%	10,357	243	2.3%	11,256	274	2.4%	12,262	307	2.5%
Washington	5,634	224	4.0%	6,966	284	4.1%	7,591	310	4.1%	7,984	338	4.2%

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

#6 Watching for When the Coronavirus Curve Flattens

*APRIL 2020

(Additional cases each day, not total cases)

Location	April 1	April 2	April 3	April 4	April 5	April 6
Worldwide	75,687	81,068	84,175	98,557	78,451	69,192
U.S.	25,200	31,306	33,150	31,022	28,788	28,976
China	7	172	78	32	101	21
Spain	8,195	7,947	7,134	6,969	5,478	5,029
Italy	4,782	4,668	4,585	4,805	4,316	3,599
Iran	2,898	2,875	2,715	2,560	2,483	2,274
New York	7,917	8,669	10,482	10,841	8,327	8,658

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

#8 Death Toll Increases

(Additional deaths, not total deaths)

Location	April 1	April 2	April 3	April 4	April 5	April 6
Worldwide	4,811	6,164	5,898	5,735	4,908	5,051
China	7	6	4	4	5	0
Italy	727	760	766	681	525	636
Spain	923	961	850	749	694	700
U.S.	884	1,154	1,230	1,266	1,240	1,136
New York	441	432	562	630	594	599