



TRENDS-in-MEDICINE

BULLETIN:

UPDATE ON CORONAVIRUS 01/19/2021

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Be careful, be safe, and be well...while you wait for your turn for a Covid-19 vaccine.

The numbers

- **The world.** There have been 95,860,637 cases of Covid-19, with 2,048,811 deaths. In comparison, about 500 million people contracted the Spanish flu in 1917/1918, with 10% (50 million) dying. The countries with the highest number of cases continue to be, in order: The U.S., India, Brazil, Russia, the U.K., France, and Italy.
- **Europe.** There have been 30,808,389 cases (a per capita rate of 4.2%), with 674,202 deaths (a per capita rate of 91 per 100,000). Europe now accounts for 33% of worldwide deaths (up from 29% nine days ago).
- **U.S.** There have been 24,163,707 cases (a per capita rate of 7%) and 400,022 deaths (a per capita rate of 121 per 100,000 – or 1.2 per thousand). This is 19.5% of worldwide deaths.
 - The Department of Health and Human Services (HHS) extended the Covid-19 public health emergency until April 2021, which continues telehealth options.
 - Data from Humana offers a look at the impact of the pandemic on elective procedures in the U.S. Humana reported:
 - ✓ A significant increase in Covid-19 hospital admissions in nearly all the markets in which it operates – for Medicare Advantage, Medicaid, and group commercial plans.
 - ✓ A corresponding decline in non-Covid utilization in all service categories. Medicare non-Covid utilization is ~15% below usual levels for the same time of year.
 - ✓ These trends are expected to continue through at least the first few months of 2021.
- **China.**
 - China has reported only 98,226 cases, with 4,799 deaths. If true, this means the number of cases has only increased by 6,332 in two months – and only 57 additional deaths in those two months.
 - An increasing number of regions in China are under “shelter in place” or lockdown orders, including two regions near Beijing and two in the northern part of the country. There are – if you can believe the Chinese numbers – roughly 89,000 cases in all of China. This begs the question: *Why is virtually all of the rest of the world inundated with cases while China is barely affected?*

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How do people get vaccinated?

It may not be easy, is mostly hit or miss, and in some states is really difficult.

The Centers for Disease Control and Prevention (CDC) reported that, as of January 13, 10.3 million doses of the Moderna and Pfizer/BioNTech vaccines had been administered out of 29 million doses distributed. At long-term care facilities, 1.1 million people have gotten a first dose – out of 4.6 million doses distributed for use in long-term-care facilities.

Bloomberg's Vaccine Tracker estimates that 14.7 million shots have been given in the U.S., with an average of 776,901 doses given daily in the last week. That translates to 4.7% of the U.S. population getting at least one vaccine dose. Some states are doing a better job than others. For example:

- On the high end: 8.6% of West Virginians, 7.5% of Alaskans, 5.9% of Mainers, and 5.2% of Floridians have had at least one dose.
- On the low end: 3.0% of Alabamans, 3.2% of Nevadans, and 3.3% of Californians have had at least one dose.
- The national vaccine usage rate is 38.8%, with the worse usage rates Alabama (21.2%) and California (27.5%).

Here is a look at one state (Florida) and one county there (Martin). The CDC prioritized healthcare workers and nursing home residents in Phase Ia. The governor of Florida (and a few other states) decided to do it differently, prioritizing seniors (residents and non-residents) and healthcare workers along with nursing home residents/staff in Phase Ia. CVS and Walgreens are handling the nursing homes, and, at least in Florida, that appears to be moving along well.

According to the Florida Department of Health's latest [report](#), 769,765 people across the state have been given the first dose of a Covid-19 vaccine. Another 79,552 people have had both doses, with 40,661 people *overdue* for their second dose. Florida was the first state in the country to vaccinate more than 500,000 seniors (age ≥ 65), and seniors have gotten $\sim 60\%$ of total vaccinations in the state. A quick look at the numbers county-by-county suggests that doses are being distributed on a population basis, as promised.

For the individual senior, the state's vaccination program is moving but slowly and rather like a lottery, with the odds of winning a vaccine slot nearly as elusive as a lottery prize. If you could get a number like a draft number and wait your turn, at least you would know your turn is coming.

There are health departments in all of Florida's 67 counties, but they are run by the state health department, not the county government. Some counties appear to be doing a better vaccine job than others. The health departments were closed for the New Year and Martin Luther King holidays, but in many (if not all) counties, many staff members were working behind the scenes.

In Martin County, FL, for example, there are $\sim 161,000$ people (not counting snowbirds), and $\sim 32\%$ ($\sim 50,000$) are seniors. In the first two weeks of vaccinations, the county was allocated $\sim 3,300$ doses, enough to inoculate $\sim 2\%$ of the county population (without counting snowbirds). So, demand has – and continues to – outstrip supply. The health department is gearing up, but it is taking time.

You probably saw pictures in December 2020 of senior citizens standing in line (or sitting in chairs they lugged along) overnight or for hours to get a Covid-19 vaccination in Florida. That is still happening. Here is a picture taken January 16, 2021, of a line in St. Lucie County, Florida, where seniors (including this writer) spent up to 11 hours *outside* in line to get their first dose of the Moderna vaccine.

The mismatch between demand and supply is why people are willing to spend hours in line. When there is a site with some doses, it fills up quickly. Local hospitals offer vaccinations on their website, but there are virtually no appointments. Checking 10-20 times a day for a week may turn up one appointment time, but the time disappears when you try to capture it.



Most appointments have to be done through either a smartphone app or a computer. Many seniors are not able to navigate that technology and don't have a family member or friend to do it for them. Those with internet access are spending hours searching for an appointment or for a site with a first-come, first-serve vaccination announcement. Appointments are advertised but almost impossible

to obtain. Some Publix grocery stores in Florida will start making online appointments this week to give vaccinations, and that could be an improvement, but the website is likely to be overloaded quickly. Walgreens and CVS are expected to start vaccinations, though no start date for that has been announced.

So, when a family practice group – Florida Community Health Centers (FCHC) – offered first-come, first-serve vaccinations for seniors and qualified healthcare personnel at five of its 12 locations on January 16, people flocked to them. At their Port St. Lucie office (just north of Martin County), which is in a strip mall, the seniors in the picture (see page 2) started lining up *outside* at 4am for an office that would open at 9am. That meant the shortest wait for anyone was more than 5 hours. And it was cold for Florida (about 55 degrees).

By 8am, there were 327 seniors in the line, most of them from St. Lucie County, but others from Martin County and at least one from Illinois (snowbird?). The local police put up yellow tape and turned other “late” arrivals away. The practice only had 200 doses, but the business manager, Gino Tabet, MBA, the practice’s director of business intelligence, promised that everyone already in the line would get a vaccine. And he made good on that promise, “liberating” an additional 100 doses from another location and 27 more doses from a third site. With just 3-4 people doing injections, only about 32 people an hour could get the vaccine, so it took a long time.

Two truly amazing things happened over those 11 hours: (1) Everyone in line was polite, friendly, and orderly the entire day. There was zero line-cutting, no arguments, no trouble. (2) The FCHC staff was *always* calm, polite, friendly, and helpful. Despite working a very long day and dealing with all these people, no one on the staff got even a little cranky or brusque with anyone. It was remarkable.

By 11am everyone in line had their paperwork, with a number showing their place in line. People could go get some lunch, do a little shopping, listen to the radio in the car, go to the ice cream shop for a milkshake, etc. Most checked back hourly to be sure they didn’t get missed in case inoculations had speeded up.

What do seniors do who can’t get an appointment or physically get in a line? There doesn’t appear to be any plan for that. Home health nurses are not administering the vaccine for logistical reasons. This writer’s husband has a home health nurse, five local specialists, and four more specialists at the Cleveland Clinic in Weston, Florida, and none of them stepped up to help arrange his vaccination, which is complicated because he had foot surgery and can’t walk or stand in line for even a couple of minutes. The staff at FCHC made arrangements for him to have a no-wait *appointment* on another day. That is service!

Other Covid-19 News

Recovery. A study, published in *Annals of the American Thoracic Society*, found that only 4% of patients who recovered from Covid-19 had lung scarring on chest CT scans, even when abnormalities were observed in early chest x-rays, suggesting there is no correlation between Covid-19 and significant fibrosis. The study did find an elevated prevalence of post-Covid-19 breathlessness, fatigue, and poor health, but those symptoms were not linked to the severity of the initial infection.

Testing

- Cambridge University researchers have developed a DNA test to identify secondary, hospital-acquired infections in Covid-19 patients.
- The first in a series of monthly surveys by **Oxford Immunotec Global** of 100 medical professionals found that:
 - ✓ 82% trust PCR tests for Covid-19.
 - ✓ 57% trust serology tests.
 - ✓ 75% had unanswered diagnostic questions.
 - ✓ >60% said alternatives to serology tests would be valuable.

Oxford Immunotec is developing a T-SPOT Discovery SARS-CoV-2 assay using the same technology as for its T-SPOT TB test.

Travel. Starting January 26, 2021, anyone flying into the U.S. must present a negative Covid-19 test conducted within the prior 72 hours – even if they have been vaccinated.

Treatments

- **Alexion Pharmaceuticals' Ultomiris (ravulizumab-cwvz)** – Enrollment in a global Phase III trial of this C5 inhibitor was halted at the recommendation of the independent data monitoring committee after it reviewed interim data and concluded the trial would miss the primary endpoint, failing to improve efficacy when added to best supportive care in adult Covid-19 patients on a ventilator.
- **Celltrion's CT-P59** – Top line data from 327 patients in a Phase II/III [trial](#) of this infused antibody showed it reduced the risk of progression to severe disease by 54%, shortened the time to clinical recovery, and reduced viral load.
- **DiosCURE Therapeutics' DIOS-202 and DIOS-203** – Preclinical data, published in *Science*, suggest that fusing a nanobody derived from a llama with another nanobody from an alpaca creates a therapeutic that could be effective in treating Covid-19, and DiosCURE plans to take two of these nanobody pairs into clinical trials this year.
- **Gilead Sciences' Veklury (remdesivir)**
 - Is being tested against the U.K. and South African variants to prove what company scientists believe: that the antibody is effective against variants.
 - Reportedly is being used in about half of hospitalized U.S. Covid-19 patients.
- **Regeneron Pharmaceuticals' casirivimab + imdevimab (REGN-10933 + REGN-10987)** – Company officials said “it’s a problem” how few Covid-19 patients are getting antibody cocktail treatments – both this and **Lilly's antibody cocktail bamlanivimab (LY-CoV555)**. The FDA's Janet Woodcock, MD, agrees the drugs are underutilized and is encouraging hospitals to boost use.
- **Synairgen's SNG-001 (inhaled interferon beta-1a)** – A big concern with this potential therapy for Covid-19 was resolved with a study, published in *Nature Genetics*, by U.K. researchers who found that the drug does increase ACE2 receptors – an entry point for the virus – but the ACE2 is a “short form” that SARS-CoV-2 can't use to enter cells. In fact, the product may actually help protect against Covid-19 as well as treating it.

Vaccines

- **Data.** Microsoft, Epic, and the Mayo Clinic are collaborating to accelerate digital Covid-19 vaccine [records](#).
 - **Distribution.** Premier wrote to President-elect Biden and Vice President-elect Harris to say “vaccinations must be administered much more quickly,” and to do that “swift intervention from the Federal government is needed.” To that end, Premier said that, after polling its members, it has identified “five systemic issues in need of immediate remediation.” Those are:
 - **Vaccine hesitancy**, with some hospitals seeing as much as 80% of the staff hesitant to be vaccinated.
 - **Clinical staffing limitations**, with clinical staff qualified to administer vaccines “extremely scarce and on the verge of burnout.” As of November 2020, 53% of Premier members surveyed said lack of clinical staff was the top challenge to their Covid-19 response efforts, and that situation has gotten worse with the surge in cases. Premier members reported an almost 30% attrition rate in clinical staff.
 - **Distribution challenges** from the decentralized Operation Warp Speed distribution scheme. In addition, vaccination sites “are beginning to report **gray market offers** for vaccines.”
 - **Supply shortages**, with vaccine vials containing overfill but not enough needles and syringes for the extra doses. Premier members reported an inability to order more of these needles through their traditional distributors, which has caused spot shortages. And gloves – which do not come in the ancillary kit accompanying the vaccine – have been on backorder for months. Gloves are not required to give a vaccine, but the Premier data show a 40% increase in glove demand since vaccination began, and 78% of Premier members said their vaccinators prefer to wear gloves.
 - **Communication gaps**, with vaccination sites reporting widespread confusion over who is making decisions, where to turn to solve problems, how to provide feedback, how essential workers are defined, etc.
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- **President-elect Biden announced his plan to improve the vaccination rate. It includes:**
 - ✓ Ordering increased production of syringes, vials, and other supplies – and using the Defense Production Act (DPA), if necessary, to accomplish this. The DPA might be used to support vaccine refrigeration and storage.
 - ✓ Have federal disaster-relief workers set up thousands of vaccination centers, where retired doctors would administer shots to teachers, grocery store workers, people age ≥65, and other groups who do not currently qualify.
 - **AstraZeneca’s AZD-1222** is now approved in Argentina, Dominican Republic, El Salvador, Mexico, Morocco, Pakistan, and the U.K. – but not yet in the U.S. or European Union.
 - **Bharat Biotech’s Covaxin** – After two people inoculated with this died, the company warned that people with “any allergy” or who are immunocompromised should not get this intranasal vaccine.
 - **Codagenix’s COVI-VAC**, an intranasal Covid-19 vaccine, started a Phase I clinical trial in the U.K.
 - **Johnson & Johnson’s Ad26.COV2.S (JNJ-78436735)** – The interim results of a Phase I/II trial in healthy adults age 18-55 of this adenovirus vaccine, published in the *New England Journal of Medicine*, showed good safety and tolerability, with typical Covid-19 vaccine side effects – fatigue, headache, myalgia, and injection site pain. Reactogenicity was lower after the second dose.
 - **Moderna’s mRNA-1273**
 - The company needs ≥3,000 adolescents aged 12-17 for a trial it started in mid-December 2020, but it is having trouble getting them to enroll.
 - The CDC and the FDA are investigating one lot of Moderna vaccine administered in San Diego after an unusually high number of people (~10) had a severe allergic reaction.
 - Moderna plans to test whether a third dose – a “booster” given one year after the initial vaccination – will affect the duration of protection. The trial is expected to start in July 2021 and enroll patients from the earlier trials.
 - Switzerland approved emergency use of this vaccine. Regulators there had already authorized emergency use of the Pfizer/BioNTech vaccine.
 - Moderna CEO Stéphane Bancel said – without offering any data to support it – that his company’s vaccine should provide protection “potentially for at least a couple of years.”
 - **Pfizer and BioNTech’s BNT162b2** (Comirnaty in Europe)
 - The CDC and Pfizer are investigating the death of a 56-year-old male doctor in Florida who got this vaccine, developed severe acute immune thrombocytopenia, and died from a brain hemorrhage 16 days after the vaccination.
 - Israel, which has already vaccinated a large percentage of its population, is trading health information for more doses of the Pfizer vaccine.
 - New York Gov. Andrew Cuomo tried, unsuccessfully, to buy more doses of the Pfizer vaccine directly from Pfizer.
 - Despite the death of 23 elderly people (all age >80) in Norway who got this vaccine, Norway is not halting use. Health officials there noted that there is still no excess mortality among the elderly or any causal connection. Sigurd Hortemo, MD, chief physician at the Norwegian Medicines Agency, said that common vaccine side effects – fever and nausea – “may have contributed to a fatal outcome in some frail patients.” And he said the deaths have not changed the country’s vaccination program.
 - **Sinopharm/China National Biotec Group (CNBG)’s BBIBP-CorV** – The company claimed this Chinese vaccine is safe in children age ≥3. It was recently approved for use in Pakistan.
 - **Sinovac Biotech’s CoronaVac** – This Chinese vaccine was approved in Indonesia, but in Brazil researchers are backtracking on reports that the vaccine showed a 78% efficacy rate in a Brazilian study, saying it was actually only 50.4% effective. That’s high enough for conditional/emergency approval, but far below the Pfizer and Moderna efficacy rates. Why the new data? The Brazilian researchers said that the 78% efficacy was against mild-to-severe cases, but when “very mild” cases were included, efficacy dropped to 50.4%.
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- **Valneva's VLA-2001** – In a collaboration, **Oxford Immunotec Global's T-Spot Discovery SARS-CoV-2 test** is being used to measure T cell levels in participants in a Phase I/II trial of this inactivated Covid-19 vaccine in healthy participants. The hypothesis is that high T cell levels will provide information on the level of protection the vaccine provides.

Variants

First, there was the super-transmissible U.K. variant (B.1.1.7 or 20I/501Y.V1) and the South African variant (20H/501Y.V2 or B.1.351). The U.K. variant has now been reported in at least 12 U.S. states, and the CDC predicted that this variant will be the predominant source of Covid-19 infections in the U.S. by March 2021. Somewhat more concerning is a growing number of *other variants* that are springing up around the world – and in the U.S. (e.g., the COH.20G/501Y in Ohio). So far, the current vaccines appear to protect against all of the variants identified, but the variants may be resistant (to varying degrees) to some or all of the antibodies.

Issues to watch

The key unanswered questions right now are:

- How long do the vaccines provide protection?
- Are new variants developing that can evade current vaccines?

