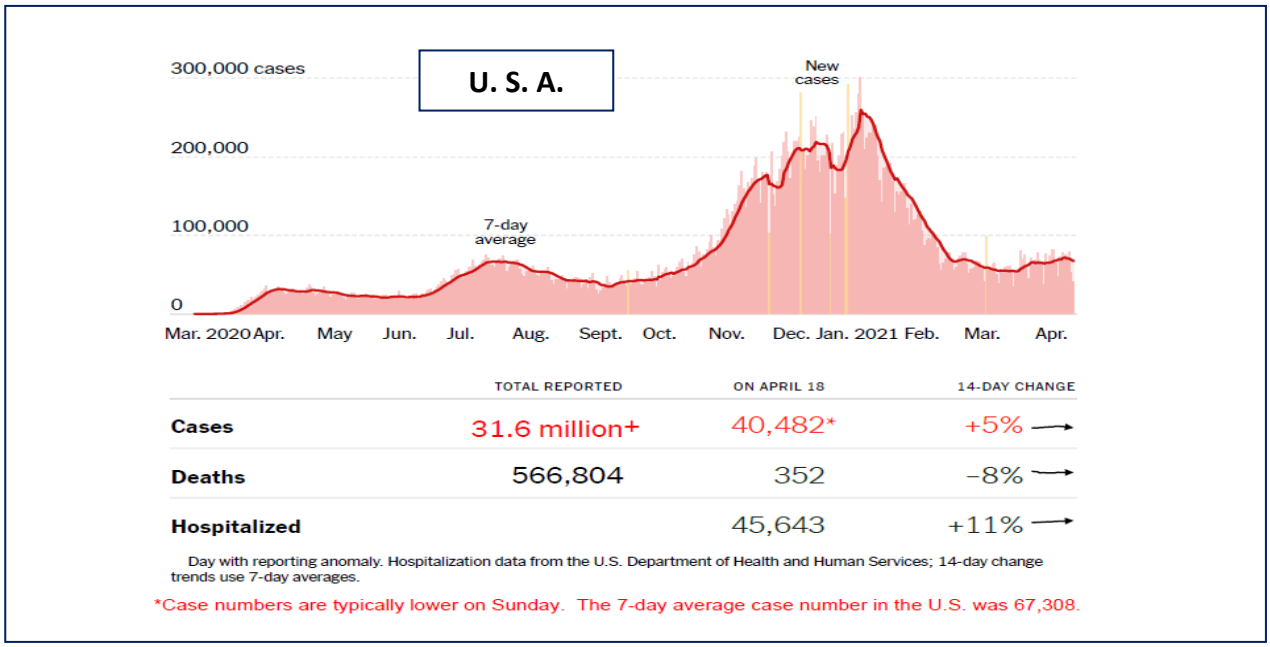
COVID-19 UPDATE – MONDAY, APRIL 19, 2021

Dear Members of the DoM Community,

Good morning to you. Here are what happened in the COVID-19 pandemic last week. I hope they keep you updated on the pandemic's status.

1. Nationwide COVID-19 Data

Fourteen-day average new case numbers are still on the rise in the U.S.



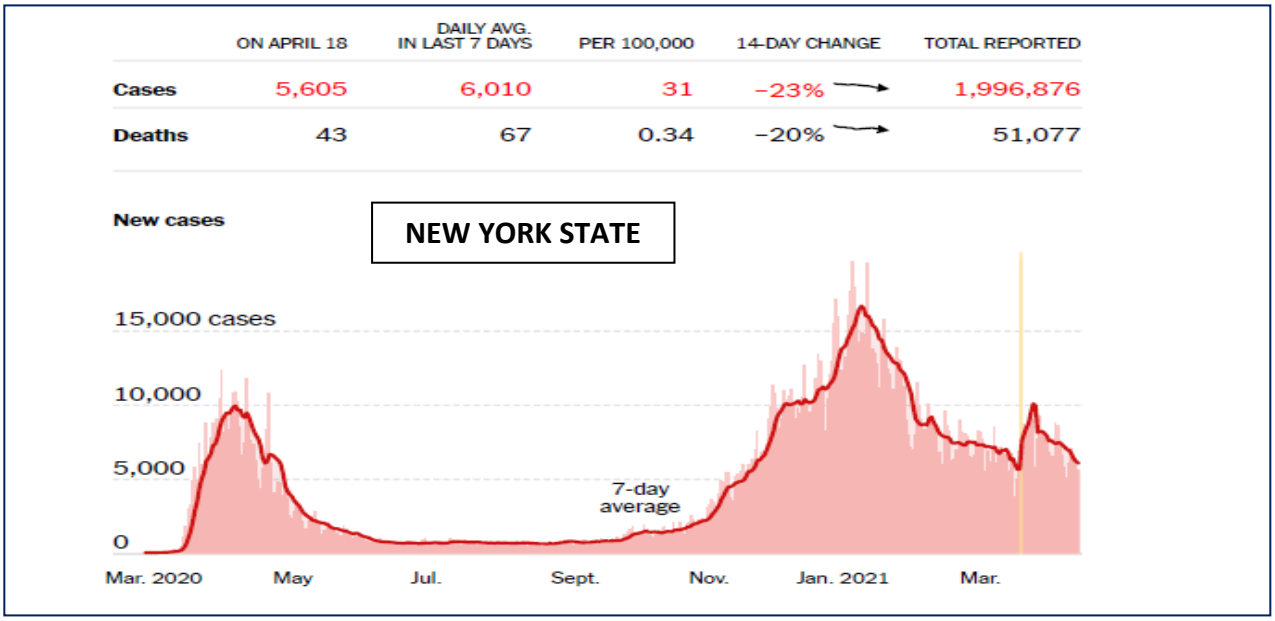
	TOTAL REPORTED	ON APRIL 18	14-DAY CHANGE
Cases	31.6 million+	40,482*	+5% →
Deaths	566,804	352	−8% →
Hospitalized		45,643	+11% →

Day with reporting anomaly. Hospitalization data from the U.S. Department of Health and Human Services; 14-day change trends use 7-day averages.

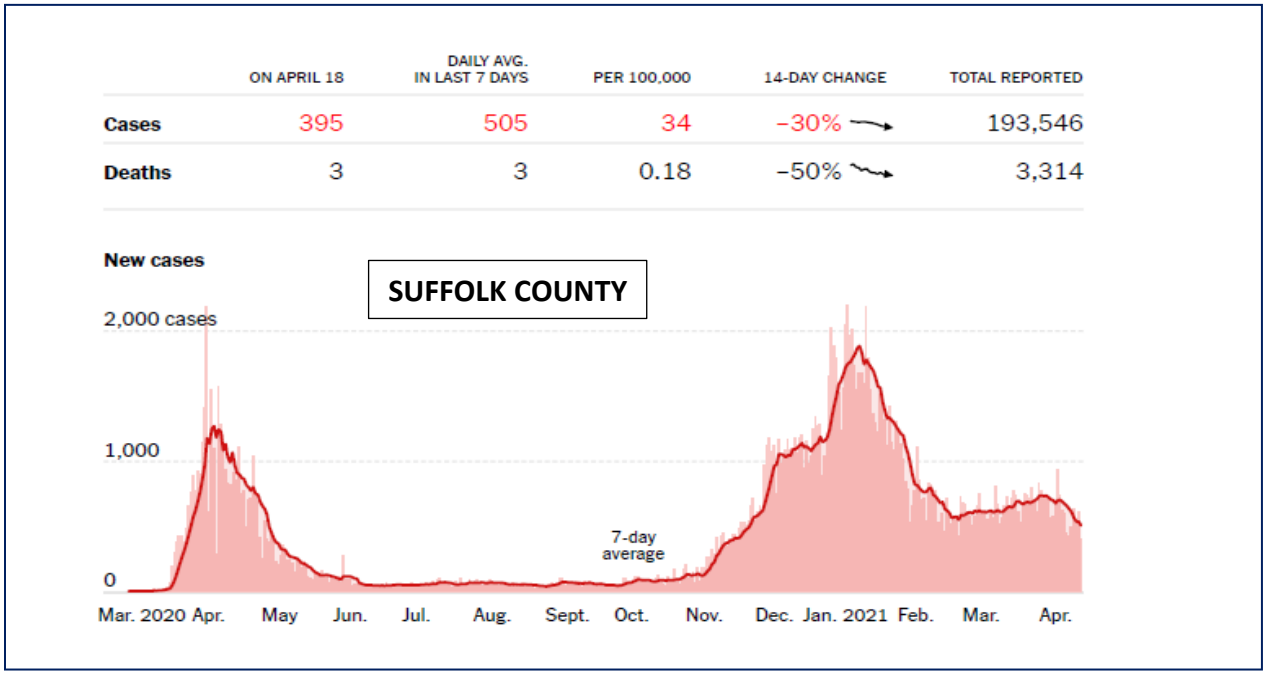
*Case numbers are typically lower on Sunday. The 7-day average case number in the U.S. was 67,308.

2. New case numbers in New York State continue to decrease (the recent spike was in part due to a data reporting anomaly on March 24 when several days' worth of data were combined.)

	ON APRIL 18	DAILY AVG. IN LAST 7 DAYS	PER 100,000	14-DAY CHANGE	TOTAL REPORTED
Cases	5,605	6,010	31	−23% →	1,996,876
Deaths	43	67	0.34	−20% →	51,077

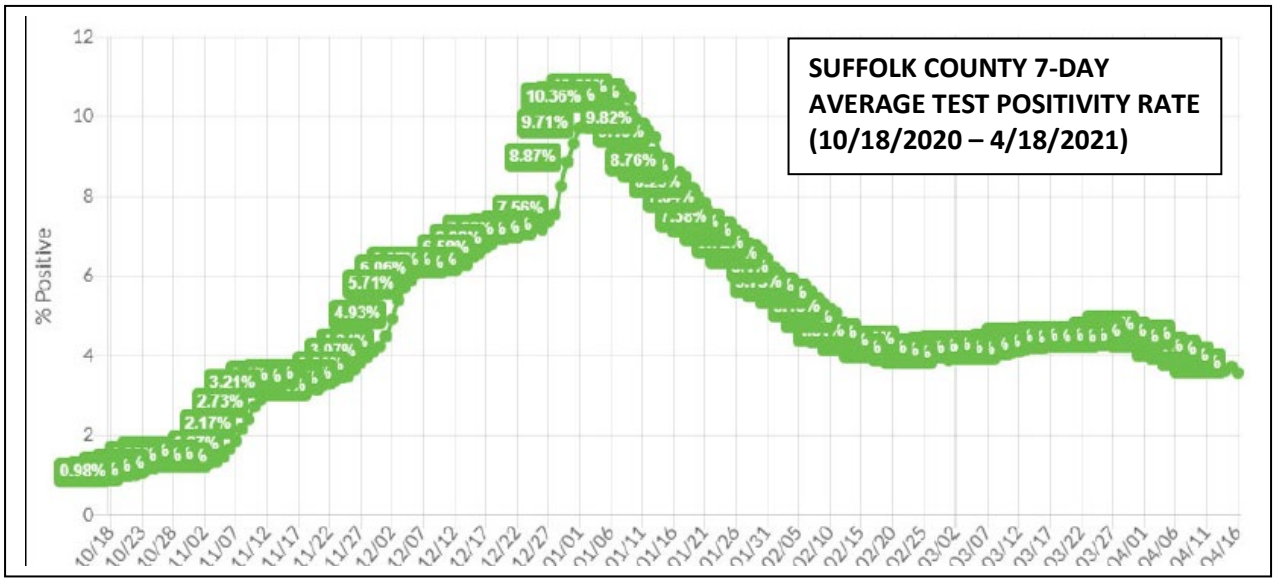


3. ***Cases in Suffolk County also continue to decline, now at a very high risk level (defined as between 11 and 41 per 100,000) at a 7-day average of 34 per 100,000 population.***



COVID-19 Testing in Suffolk County on April 18:

- 16,099 COVID-19 tests were administered.
- 395 new cases were reported.; 7-day average = 505, a **decrease of 162** from one week ago.
- 193,546 total cases have been reported since March of 2020.
- Seven-day average test positivity rate = 3.4%, a **decrease of 0.6%** from a week before (6-month trend below).



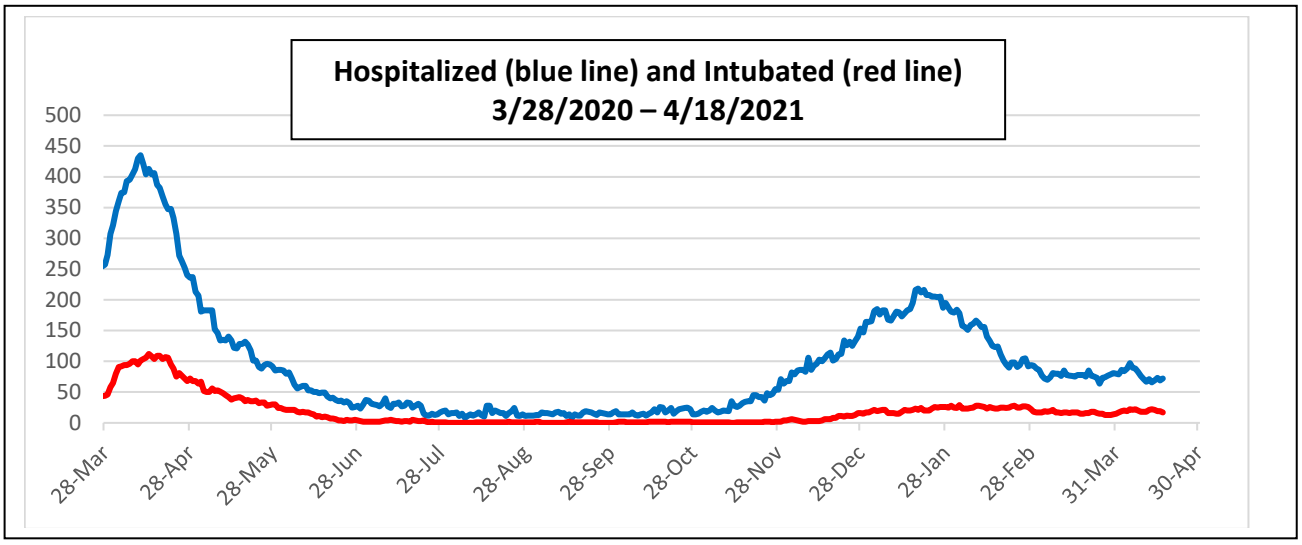
Fatalities:

- 3,314 total fatalities, an **increase of 19** from one week before.

COVID-19 Hospitalizations:

- 282 individuals were hospitalized, a **decrease of 34** from one week before.
- 71 patients were in the Intensive Care Unit (ICU), a **decrease of 4** from a week ago.

4. Daily COVID-19 Hospitalization Data in SBUH

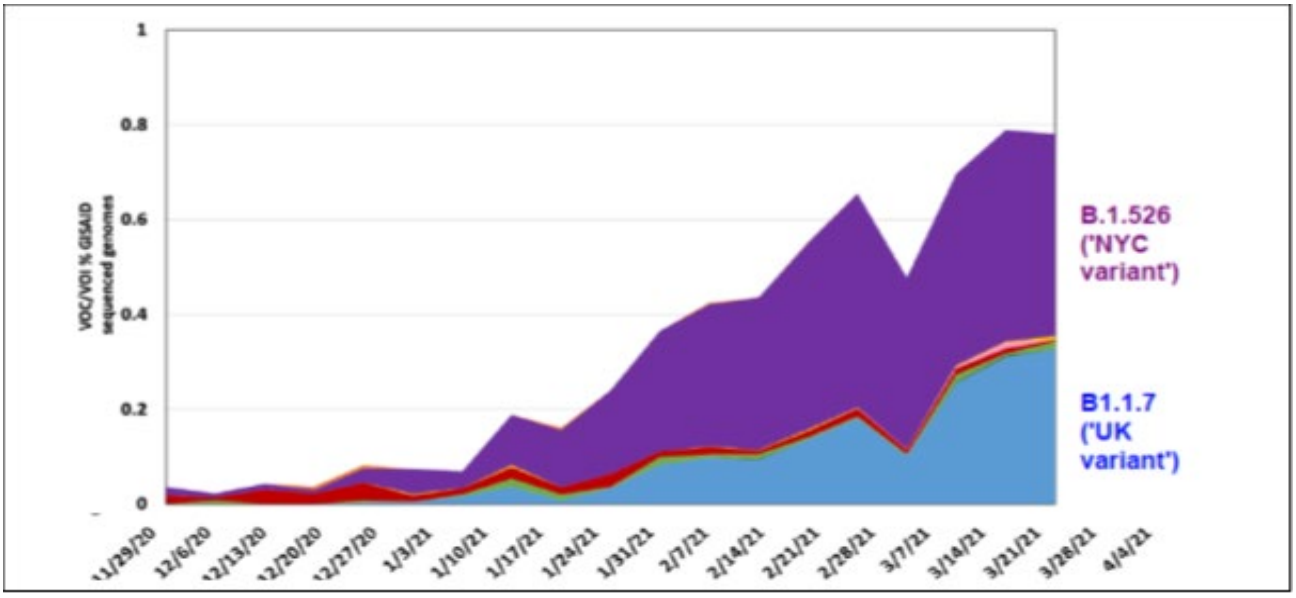


At midnight Sunday, April 18, SBUH census is as follows (see figure above for all-time trend of hospitalization).

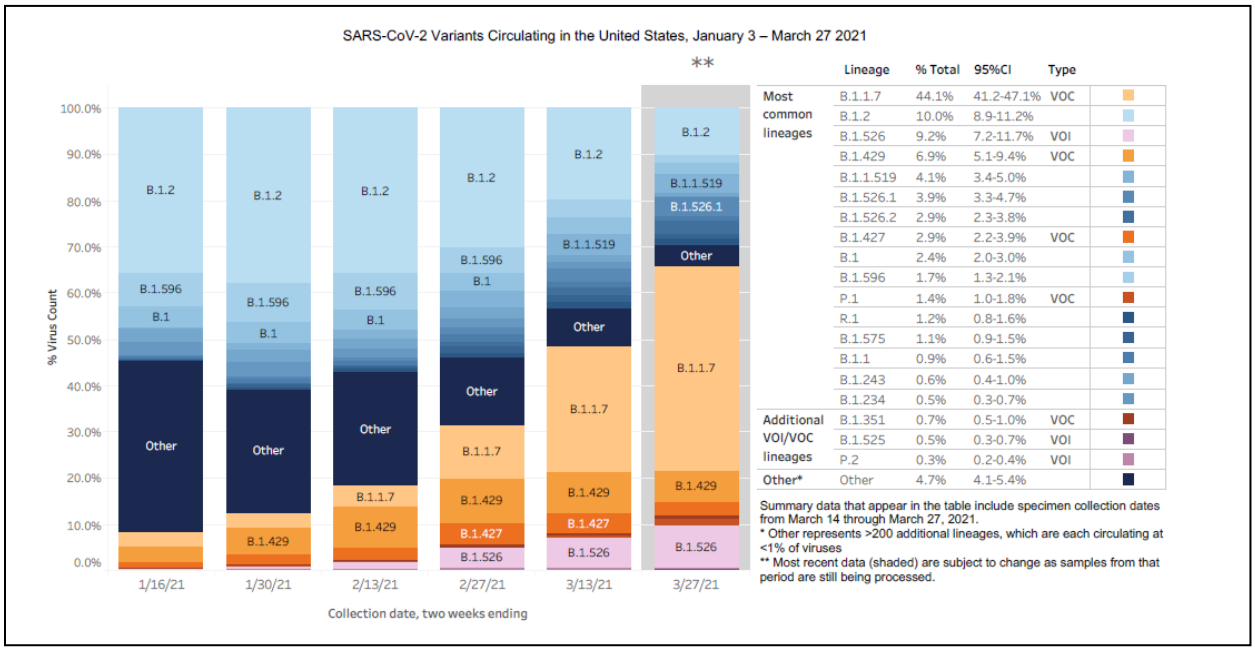
- 74 COVID + inpatients; 7-day average = 71, a **decrease of 10** from one week before.
    - 19 patients were in ICU level of care; 16 on ventilators; 11 in ICR.
    - COVID admissions on Sunday = 9.
    - COVID live discharges =4.
    - COVID-related deaths = 1.
- Total hospital census = 589; Med/Surg = 451 (102%).

5. SARS-CoV-2 Viral Variants Update (source = CDC; NYC Health Department)

- The Health Department in New York City has identified multiple variants of interest and variants of concern, notably the **B.1.1.7** and the **B.1.526** variants:
    - **B.1.1.7** (first identified in the UK) is classified by CDC as a **variant of concern**, which means that there is evidence that it increases transmissibility and the severity of disease. Specifically, B.1.1.7 has been found to be 50% more transmissible and cause more severe infections.
    - **B.1.526** (first identified in NYC) is classified by CDC as a **variant of interest**, because there are signs that it increases transmissibility. Studies are ongoing regarding the impact of B.1.526 on disease severity, reinfection, and vaccine effectiveness.



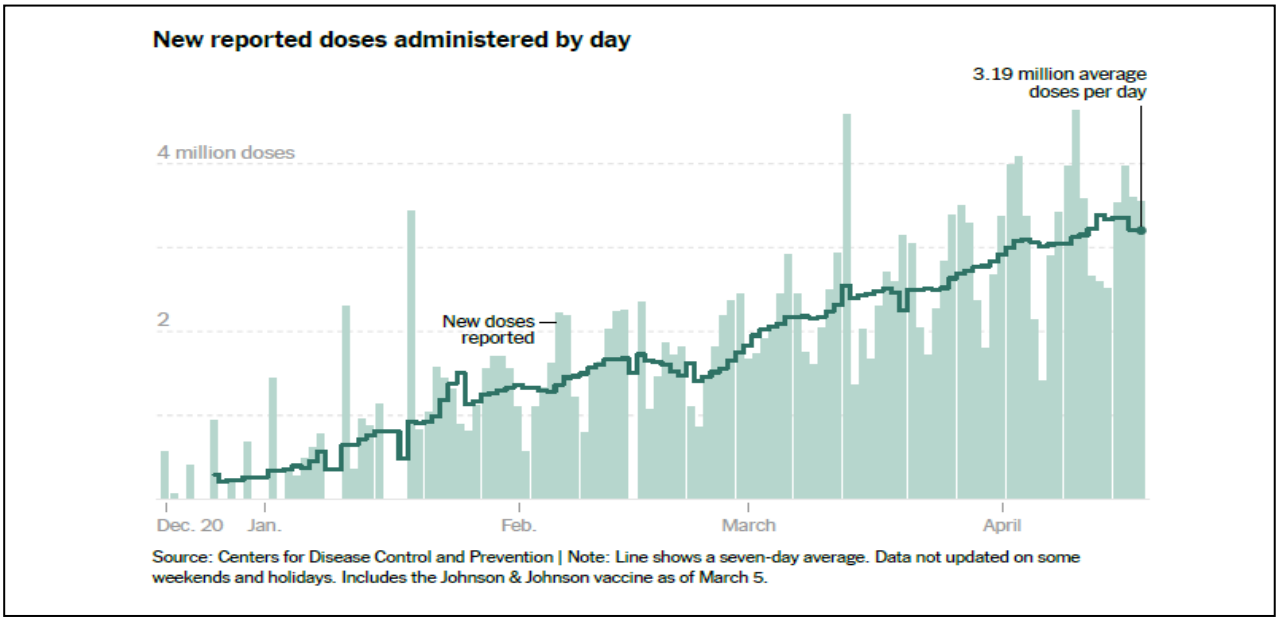
- **In the U.S., B.1.1.7 is the predominant variant strain.**



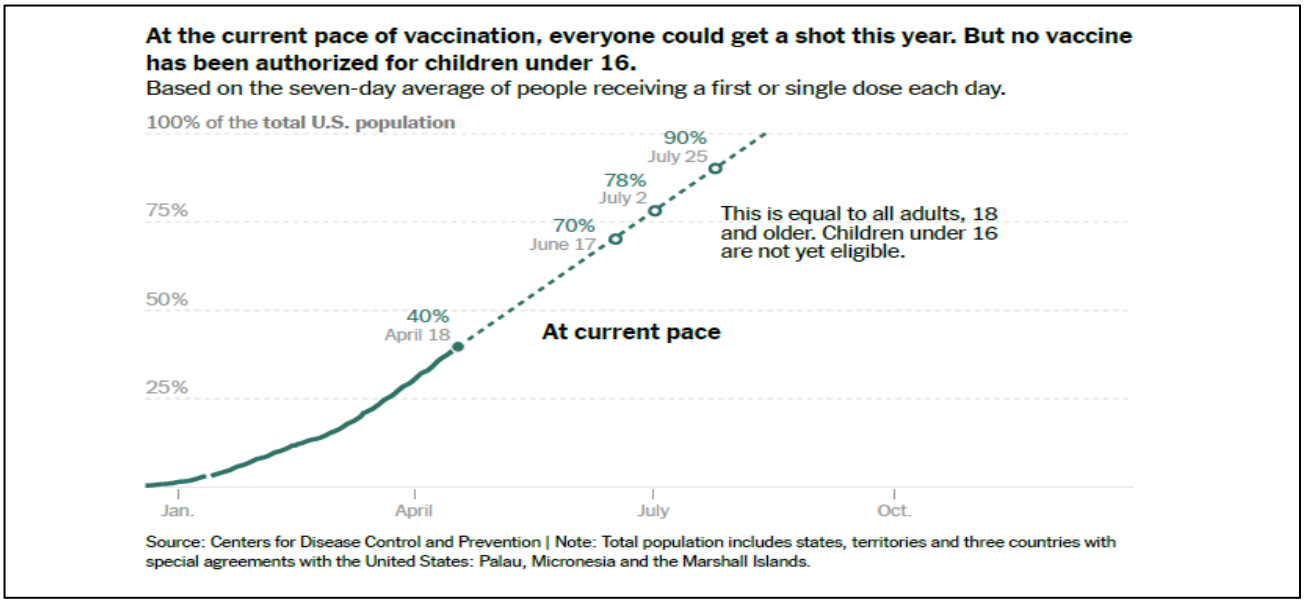
- For more information on variants of concern and variants of interest, visit cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html.

6. Vaccination Program Update (sources = CDC, NYS DOH, and NYT)

On April 18, the 7-day average of COVID vaccine administered in the U.S. was 3.19 million, for a total of 209+ million doses administered since the beginning of the rollout.



40% of the U.S. population have received at least one dose (NY state is at 43% and Suffolk County is 40%). At the current rate of administration, all adults 18 and older will receive at least one shot by early July.



7. CDC Health Alert on Johnson & Johnson (Janssen) Vaccine.

Distributed via the CDC Health Alert Network
April 13, 2021
CDCHAN-00442

Cases of Cerebral Venous Sinus Thrombosis with Thrombocytopenia afterReceipt of the Johnson & Johnson COVID-19 Vaccine

Summary

As of April 12, 2021, approximately 6.85 million doses of the Johnson & Johnson (J&J) COVID-19 vaccine (Janssen) havebeen administered in the United States. The Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA) are reviewing data involving six U.S. cases of a rare type of blood clot in individuals after receiving the J&J COVID-19 vaccine that were reported to the Vaccine Adverse Events Reporting System (VAERS). In these cases, a type of blood clot called cerebral venous sinus thrombosis (CVST) was seen in combination with low levelsof blood platelets (thrombocytopenia). All six cases occurred among women aged 18–48 years. The interval from vaccine receipt to symptom onset ranged from 6–13 days. One patient died. Providers should maintain a high index of suspensionfor symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J COVID-19 vaccine. When these specific type of blood clots are observed following J&J COVID-19 vaccination, treatment is different from the treatment that might typically be administered for blood clots. Based on studies conducted among the patients diagnosed with immune thrombotic thrombocytopenia after the AstraZeneca COVID-19 vaccine in Europe, the pathogenesis of these rare and unusual adverse events after vaccination may be associated with platelet- activating antibodies against platelet factor-4 (PF4), a type of protein. Usually, the anticoagulant drug called heparin is used to treat blood clots. In this setting, the use of heparin may be harmful, and alternative treatments need to be given.

CDC has convened an emergency meeting of the Advisory Committee on Immunization Practices (ACIP) on Wednesday, April 14, 2021, to further review these cases and assess potential implications on vaccine policy. FDA will review that analysis as it also investigates these cases. Until that process is complete, CDC and FDA are recommending a pause for 10 days in the use of the J&J COVID-19 vaccine out of an abundance of caution. The purpose of this Health Alert is, in part, to ensure that the healthcare provider community is aware of the potential for these adverse events and can provide propermanagement due to the unique treatment required with this type of blood clot.

Background

VAERS is a national passive surveillance system jointly managed by CDC and FDA that monitors adverse events after vaccinations. The six patients (after 6.85 million vaccine doses administered) described in these VAERS reports came to attention in the latter half of March and early April of 2021 and developed symptoms a median of 9 days (range = 6–13 days) after receiving the J&J COVID-19 vaccine. Initial presenting symptoms were notable for headache in five of six patients, and back pain in the sixth who subsequently developed a headache. One patient also had abdominal pain, nausea, and vomiting. Four developed focal neurological symptoms (focal weakness, aphasia, visual disturbance) prompting presentation for emergency care. The median days from vaccination to hospital admission was 15 days (range = 10–17 days). All were eventually diagnosed with CVST by intracranial imaging; two patients were also diagnosed with splanchnic* and portal vein thrombosis. Unusual for patients presenting with thrombotic events, all six patients showed evidence of thrombocytopenia (<150,000 platelets per microliter of blood), consistent with a condition known as thrombotic thrombocytopenia, with platelet nadir counts ranging from 10,000 to 127,000 during their hospitalizations. Fourpatients developed intraparenchymal brain hemorrhage and one subsequently died. All data presented in this HAN are preliminary and investigations of these VAERS reports are ongoing. The Clinical Immunization Safety Assessment (CISA) project which includes experts in infectious disease and hematology are also reviewing these cases. To date, VAERS has received no reports of CVST with thrombocytopenia among persons who received either of the two mRNA-based COVID-19 vaccines.

These reports following the J&J COVID-19 vaccine are similar to reports of thrombotic events with thrombocytopenia afterreceipt of the AstraZeneca COVID-19 vaccine in Europe. Both vaccines contain replication-incompetent adenoviral vectors (human [Ad26.COV2.S] for J&J and chimpanzee [ChAdOx1] for AstraZeneca) that encode the spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Based on studies conducted among the patients diagnosed with immune thrombotic thrombocytopenia after the AstraZeneca COVID-19 vaccine in Europe, the pathogenesis of these rareand unusual adverse events may be associated with platelet-activating antibodies against platelet factor 4 (PF4). Anti- PF4, also known as heparin-PF4 antibody, can induce thrombotic thrombocytopenia in a small percentage of persons exposed to heparin. However, none of the cases reported from Europe had recent heparin exposure. As with heparin- induced thrombocytopenia, the administration of the anticoagulant heparin should be avoided in patients with potential vaccine-associated immune thrombotic thrombocytopenia (VITT), unless heparin-induced thrombocytopenia (HIT) testing is negative. Non-heparin anticoagulants and high-dose intravenous immune globulin should be considered in treatment ofpatients who present with immune-mediated thrombotic events with thrombocytopenia after J&J COVID-19 vaccination. Consultation with hematology specialists is strongly recommended.

Recommendations

For Clinicians:

1. Pause the use of the J&J COVID-19 vaccine until the ACIP is able to further review these CVST cases in thecontext of thrombocytopenia and assess their potential significance.
2. Maintain a high index of suspension for symptoms that might represent serious thrombotic events or thrombocytopenia in patients who have recently received the J&J COVID-19 vaccine, including severe headache,backache, new neurologic symptoms, severe abdominal pain, shortness of breath, leg swelling, petechiae (tiny red spots on the skin), or new or easy bruising. Obtain platelet counts and screen for evidence of immune thrombotic thrombocytopenia.
3. In patients with a thrombotic event and thrombocytopenia after the J&J COVID-19 vaccine, evaluate initially with a screening PF4 enzyme-linked immunosorbent (ELISA) assay as would be performed for autoimmune HIT. Consultation with a hematologist is strongly recommended.
4. Do not treat patients with thrombotic events and thrombocytopenia following receipt of J&J COVID-19 vaccinewith heparin, unless HIT testing is negative.
5. If HIT testing is positive or unable to be performed in patient with thrombotic events and thrombocytopenia following receipt of J&J COVID-19 vaccine, non-heparin anticoagulants and high-dose intravenous immuneglobulin should be strongly considered.
6. Report adverse events to VAERS, including serious and life-threatening adverse events and deaths in patients following receipt of COVID-19 vaccines as required under the Emergency Use Authorizations

for COVID-19 vaccines.

For Public Health:

1. Pause the use of the J&J COVID-19 vaccine in public health clinics until the ACIP is able to further review theseCVST cases in the context of thrombocytopenia and assess their potential significance.
2. Encourage healthcare providers and the public to report all serious and life-threatening adverse events and deaths following receipt of COVID-19 vaccines to VAERS as required under the EUAs for COVID-19 vaccines.
3. Disseminate this alert to healthcare providers in your jurisdictions.

For the Public:

1. If you have received the J&J COVID-19 vaccine and develop severe headache, abdominal pain, leg pain, or shortness of breath within three weeks after vaccination, contact your healthcare provider, or seek medical care.
2. Report adverse events following receipt of any COVID-19 vaccine to VAERS.
3. If you are scheduled to receive the J&J vaccine, please contact your healthcare provider, vaccination location, or clinic to learn about additional vaccine availability.

For More Information

- Resources on thrombotic thrombocytopenia after AstraZeneca COVID-19 vaccine https://www.nejm.org/doi/full/10.1056/NEJMoa2104840, https://www.nejm.org/doi/full/10.1056/NEJMoa2104882
- Frequently asked questions about VAERS reporting for COVID-19 vaccines VAERS - FAQs (hhs.gov)
- How to report to VAERS
- CDC materials on stroke and NIH materials on thrombocytopenia

8. Monoclonal Antibodies from Regeneron (REGEN-COV) Protects Household Contacts from Exposure to SARS-CoV-2 at Home.

Phase 3 Prevention Trial Showed 81% Reduced Risk of Symptomatic SARS-CoV-2 Infections withSubcutaneous Administration of REGEN-COV™ (casirivimab with imdevimab)

For detailed information, see https://investor.regeneron.com/news-releases/news-release-details/phase-3-prevention-trial-showed-81-reduced-risk-symptomatic-sars
April 12, 2021

REGEN-COV rapidly protected household contacts from exposure to SARS-CoV-2 at home, with 72% protection against symptomaticinfections in the first week, and 93% in subsequent weeks.

Among individuals who developed symptomatic infections, REGEN-COV recipients cleared the virus faster and had much shorter symptom duration.

Regeneron will share data with U.S. FDA and request EUA expansion to include COVID prevention for appropriate populations, using a1,200 mg subcutaneous dose.

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced positive results from a Phase 3 trial (2069A) assessing the ability of REGEN-COV™ (casirivimab with imdevimab) to reduce the risk and burden of COVID-19 infection among household contacts of SARS-CoV-2 infected individuals. The trial, which was jointly run with the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), met its primary and key secondary endpoints, showing that REGEN-COV 1,200 mg administered subcutaneously (SC) reduced the risk of symptomatic infections by 81% in those who were not infected when they entered the trial.

"These data suggest that REGEN-COV can complement widespread vaccination strategies, particularly for those at high risk of infection. Importantly, to date REGEN-COV has been shown *in vitro* to retain its potency against emerging COVID-19 variants of concern," said Myron Cohen, M.D., who leads the monoclonal antibody efforts for

the NIH-sponsored COVID Prevention Network (CoVPN) and is Director of the Institute for Global Health & Infectious Diseases at the University of North Carolina at Chapel Hill. "Despite standard precautions to reduce transmission, nearly 10% of unvaccinated individuals living with an infected person developed symptomatic infections if they did not receive REGEN-COV. If authorized, convenient subcutaneous administration of REGEN-COV could help control outbreaks in high-risk settings where individuals have not yet been vaccinated, including individual households and group living settings."

The Phase 3, double-blind, placebo-controlled trial assessed the effect of REGEN-COV on uninfected individuals without anti-SARS-CoV-2 antibodies or any COVID-19 symptoms, who lived in the same household as an individual who tested positive for SARS-CoV-2 within the prior 4 days. The trial enrolled 1,505 people who were not infected with SARS-CoV-2 at baseline and randomized to receive either 1 dose of REGEN-COV (1,200 mg) or placebo, administered as SC injections.

"These findings are very encouraging and suggest that REGEN-COV is highly effective at preventing symptomatic COVID-19 in household contacts of SARS-CoV-2 infected individuals," said Dan H. Barouch, M.D., Ph.D., co-principal investigator of the trial and Director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center and Professor of Medicine at Harvard Medical School. "The rapid and robust protection,together with the subcutaneous route of administration, support the practical utility of these antibodies in protecting against COVID-19 in multiple settings, including after high-risk exposures. These antibodies may be particularly useful in individuals who are not yet vaccinated, and may also have potential in those who are immunosuppressed and may not respond well to vaccines."

On average, individuals treated with REGEN-COV who experienced a symptomatic infection resolved their symptoms in 1 week, compared to 3 weeks with placebo. Infected individuals also cleared the virus faster with REGEN-COV. "With more than 60,000 Americans continuing to be diagnosed with COVID-19 every day, the REGEN-COV antibody cocktail may help provide immediate protection to unvaccinated people who are exposed to the virus, and we are also working to understand its potential to provide ongoingprotection for immunocompromised patients who may not respond well to vaccines," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "We thank the individuals, investigators and our collaborators involved in the trial, and look forward to rapidly discussing these results with regulatory authorities."

TABLE: Key Results from Phase 3 Trial for the Prevention ofCOVID-19 in Uninfected Individuals[1]

	REGEN-COV (single 1,200 mg dose)	**Placebo**
	n=753	n=752
Risk of symptomatic SARS-CoV-2 infection		
Through day 29 (primary endpoint)		
Risk reduction	**81%** (p<0.0001)	
# of patients with events	11 (1.5%)	59 (7.8%)
Within 1 week[2]		
Risk reduction	**72%** (nominal p=0.0002)	
# of individuals with events	9 (1.2%)	32 (4.3%)

Post-1 week[2]		
Risk reduction	**93%** (nominal p<0.0001)	
# of individuals with events	2 (0.3%)	27 (3.6%)
Symptoms and viral load		
Total weeks with symptoms		
Reduction	93% (p<0.0001)	
Total # of weeks (cumulative for all individuals in each arm)	13	188
# of weeks with symptoms (average) in symptomatic individuals	1.2	3.2
Total weeks with high viral load (>10^4 copies/mL)		
Reduction	90% (p<0.0001)	
Total # of weeks (cumulative for all individuals in each arm)	14	136
# of weeks with high viral load (average) in qPCR positive subjects	0.4	1.3

[1.] Based on the seronegative modified Full Analysis Set population, which includes all randomized subjects without evidence of current or prior SARS-CoV-2 infection (i.e., a negative RT-qPCR test and a negative antibody test) at randomization.

[2.] These analyses were not part of the pre-planned statistical analysis plan, so p-values are nominal.

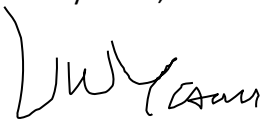
Adverse events (AEs) occurred in 20% (n=265 out of 1,311) of REGEN-COV participants and 29% (n=379 out of 1,306) of placebo participants, and serious AEs occurred in 1% (n=10) of REGEN-COV and 1% (n=15) of placebo participants. There were 0 REGEN-COV and 4 placebo participants who were either hospitalized or visited the emergency room because of COVID-19 during the 29-day efficacy assessment period. Injection site reactions, all of which were grades 1-2, occurred in 4% (n=55) of REGEN-COV and 2% (n=19) of placebo participants. No individuals from either group withdrew from the trial due to AEs, and none of the deaths in the trial (2 REGEN-COV, 2 placebo) were attributed to COVID-19 or study drug.

REGEN-COV continues to be evaluated in clinical trials in multiple settings for COVID-19: for the prevention of COVID-19 in household contacts of infected individuals, and in non-hospitalized and certain hospitalized patients, including the open-label RECOVERY trial of hospitalized patients in the UK. As of April 2021, more than 25,000 people have participated in clinical trials involving REGEN-COV.

The development and manufacturing of REGEN-COV have been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services, Office of the Assistant Secretary for Preparedness and Response, under OT number: HHSO100201700020C.

Once again, I hope the information provided here is useful to you in keeping track of the progression of the pandemic. While the increasing rollout of COVID vaccines is an encouraging trend, we are not out of the woods. It is important for everyone to remain vigilant until the storm passes. Please keep safe and healthy.

Sincerely Yours,



Vincent W. Yang, MD, PhD
Simons Chair of Medicine
Professor of Medicine, Biomedical Informatics, and Physiology and Biophysics