COVID-19 Now, Near and Far

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Disclosures-Research support

- Abioscope
- AstraZeneca Pharmaceuticals
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- Suven Life Sciences, Ltd.





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MERCYHEALTH

The New Hork Times						
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Covid in the U.S.: Latest Map and Case Count

By The New York Times Updated November 10, 2020, 8:06 A.M. E.T.

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100	000 casa	es.	-		Ne	es —
50,0	00		aver	age		
0 M	arch Ar	pril May	June July	Aug. S	ept. Oct.	Nov.
		TOTAL REPOR	TED	ON NOV 9	14-DAY CH	HANGE
Ca	ses 1	0.1 millio	on+ 1	30,553	+64%	
De	aths	238,77	76	745	+18%	-+
E Di Inclu trend	ay with de ides conf ts use 7-	ata reporting and irmed and proba day averages.	omaly, able cases wh	ere evailable. 1	4-day change	
Мар	1	Cases by stat	te	Hot sp	ots	Cluste

At least 745 new coronavirus deaths and 130,553 new cases were reported in the United States on Nov. 9. Over the past week, there has been an average of 116,448 cases per day, an increase of 64 percent from the average two weeks earlier.

As of Tuesday morning, more than 10,191,200 people in the United States have been infected with the coronavirus and at least 238,700 have died, according to a New York Times database.



The New York Times

SHOP NOW >	SHOP NOW >	SHOP NOW >
Shimmer Paisley Flounce Dress	Floral Tiered Midi Dress	Garden Split Neck Swing E
	的名称是非常能够得到的	

WORLD COUNTRIES U.S.A. STATES COLLEGES

Ohio Covid Map and Case Count

By The New York Times Updated November 10, 2020, 8:06 A.M. E.T.

1.000			New cases
4,000 cases		7-day average	
0 March Ap	ril May June	July Aug.	Sept. Oct. Nov.
	TOTAL REPORTED	ON NOV. 9	14-DAY CHANGE
Cases	254,974	4,706	+99%
Deaths	5,524	7	+30% 🖍
Hospitalized		2,533	+65%

Includes confirmed and probable cases where available. 14-day change trends use 7-day averages.

Map By county New cases Clusters

At least 7 new coronavirus deaths and 4,706 new cases were reported in Ohio on Nov. 9. Over the past week, there has been an average of 4,724 cases per day, an increase of 99 percent from the average two weeks earlier.

As of Tuesday morning, there have been at least 254,974 cases and 5,524 deaths in Ohio since the beginning of the pandemic, according to a New York Times database.



U.S. | Ohio Covid Map and Case Count



Sources: State and local health agencies. Population and demographic data from Census Bureau. About this data

The table below was recently changed to show the average number of cases per day in the last seven days instead of the total number of cases over the last seven days.

Reported cases and deaths by county

This table is sorted by places with the most cases per 100,000 residents in the last seven days. Charts are colored to reveal when outbreaks emerged.

Cases	Deaths	LUC	LUCAS				
				DAILY AVG.	G. ST ▼PER /S 100,000	WEEKLY CASES PER CAPITA	
	TOT/ DEATH	TOTAL DEATHS	OTAL PER ATHS 100,000	IN LAST 7 DAYS		FEWER	MORE
Ohio		5,524	47	26.3	0.2	March 1	Nov. S
Lucas		393	92	0.7	0.2		
			Show al	I			

▼ About this data:

Weekly cases per capita shows the share of population with a new reported case for each week. Weeks without a reported case are shaded gray. The daily average is calculated with cases and deaths that were reported in the last seven days.

The New York Times is engaged in a comprehensive effort to track details about every reported case in the United States, collecting information from federal, state and local officials around the clock.





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In some tests, polymerase chain reaction makes millions of copies of the transcribed DNA. Short, virus-specific oligonucleotide probes with a fluorophore on one end bind to the copies. An enzyme cleaves the probe, causing fluorescence and confirming infection.



Virus in a collected sample is chemically broken up in solution and added to a slide coated in antibodies. The antibodies bind to the viral proteins. Then, fluorescent antibodies are added, which attach to confirm a positive result.

TEST BENEFITS AND LIMITATIONS



These tests give accurate results early in the infection. Patients can collect their own swab samples at home and mail them to a lab for testing.



Accuracy of the test drops later in infection. It can only tell you if you have an infection now-it can't tell if you had an infection in the past.

ANTIBODY TESTS

TEST BENEFITS AND LIMITATIONS



These tests are faster and cheaper than most nucleic acid tests. Like some rapid nucleic acid tests, they can be carried out at the point of care.



They can only report whether you have an infection now. The tests are also less accurate than nucleic acid tests, particularly if the level of virus in the sample is low.

COMPARING TESTS

TIME TAKEN



As reported in The Washington Post:"Restaurants, gyms, and coffee shops rank high among locations where the corona virus is likely to spread outside the home..."

Chang, S., Pierson, E., Koh, P.W.*et al.* Mobility network models of COVID-19 explain inequities and inform reopening. *Nature*(2020). https://doi.org/10.1038/s41586-020-2923-



SLOW THE SPREAD OF COVID-19 cdc.gov/coronavirus





Scientific Brief: Community Use of Cloth Masks to Control the Spread of SARS-CoV-2 Updated Nov. 10, 2020 https://www.cdc.gov/

 Source Control to Block Exhaled Virus & Filtration for Personal Protection Seven studies have confirmed the benefit of universal masking in community level analyses: in a unified hospital system, a German city, a U.S. state, a panel of 15 U.S. states and Washington, D.C., as well as both Canada and the U.S. nationally. Each analysis demonstrated that, following directives from organizational and political leadership for universal masking, new infections fell significantly. Two of these studies and an additional analysis of data from 200 countries that included the U.S. also demonstrated reductions in mortality. An economic analysis using U.S. data found that, given these effects, increasing universal masking by 15% could prevent the need for lockdowns and reduce associated losses of up to \$1 trillion or about 5% of gross domestic product.



Symptoms of COVID-19: Onset 2-14 days after exposure

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea



Figure 1. Recommendations for Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS (Recommendations are listed in order of preference in each category below; however, all options are considered acceptable.)
Not Hospitalized or Hospitalized but Does Not Require Supplemental Oxygen	No specific antiviral or immunomodulatory therapy recommended The Panel recommends against the use of dexamethasone (AI) See the Remdesivir section for a discussion of the data on using this drug in hospitalized patients with moderate COVID-19.ª
Hospitalized and Requires Supplemental Oxygen (but Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO)	Remdesivir 200 mg IV for one day, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge, whichever comes first (AI) ^{b,c,d} or Remdesivir (dose and duration as above) plus dexamethasone° 6 mg IV or PO for up to 10 days or until hospital discharge, whichever comes first (BIII) ^r If remdesivir cannot be used, dexamethasone° may be used instead (BIII)
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Dexamethasone ⁴ plus remdesivir at the doses and durations discussed above (AIII) ⁷ or Dexamethasone ^{d,e} at the dose and duration discussed above (AI)
Hospitalized and Requires Invasive Mechanical Ventilation or ECMO	Dexamethasone ^{d,e} at the dose and duration discussed above (AI) or Dexamethasone ^e plus remdesivir for patients who have recently been intubated at the doses and durations discussed above (CIII) ^r
Rating of Recommendations: A = Strong; B = Modera Rating of Evidence: I = One or more randomized trials well-designed, nonrandomized trials or observational c	te; C = Optional with clinical outcomes and/or validated laboratory endpoints; II = One or more cohort studies; III = Expert opinion
The Panel recognizes that there may be situations in which a moderate COVID-19 (e.g., a patient who is at a particularly h	a clinician judges that remdesivir is an appropriate treatment for a hospitalized patient with nigh risk for clinical deterioration). However, the Panel finds the data insufficient to recommen

- either for or against using remdesivir as routine treatment for all hospitalized patients with moderate COVID-19.
- ^b Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.
- The Panel recognizes there is a theoretical rationale for initiating remdesivir plus dexamethasone in patients with rapidly progressing COVID-19.
- ^d For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.
- If dexamethasone is not available, equivalent doses of other corticosteroids, such as prednisone, methylprednisolone, or hydrocortisone, may be used.
 See <u>Corticosteroids</u> for more information.
- ¹ The combination of dexamethasone and remdesivir has not been studied in clinical trials; see text for the rationale for using this combination.



Key: ECMO = extracorporeal membrane oxygenation; IV = intravenously; PO = orally

Convalescent Plasma

Last Updated: October 9, 2020

Plasma from donors who have recovered from COVID-19 may contain antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that may help suppress the virus and modify the inflammatory response.1

Recommendation

•There are insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of COVID-19 convalescent plasma for the treatment of COVID-19



CDC Revises Guidance on Isolation After Positive COVID-19 Test, Reports Prolonged COVID-19 Illness Among Nonhospitalized Patients

Assymptomatic, mild, moderate illness, isolate for 10 days provided afebrile x 24 hrs and symptoms improved
Severe or critical illness, isolate for 20 days provided afebrile x 24 hrs and symptoms improved



COVID-19 is a complex illness that might require ongoing clinical care even after being discharged from the hospital

1 in 11

patients hospitalized for COVID-19 were readmitted to the same hospital within 2 months

Premier Healthcare Database includes data from 865 nongovernmental, community, and teaching hospitals that contributed data during the study period

CDC.GOV

Patients who were readmitted were more likely to:



Be 65 years of age or older



Have been hospitalized within the 3 months preceding the first COVID-19 hospitalization

bit.ly/MMWR11920



Have a chronic medical condition



Have been discharged to a skilled nursing facility or with home health care

MMWR



TABLE 3. Generalized estimating equation model showing the adjusted odds of readmission among persons hospitalized with COVID-19 — United States, March–August 2020 MMWR 69:2020

Characteristic	Odds ratio (95%Cl)	Standard error*	P-value					
Age group (yrs), (referent = 18–39 yrs)								
<18	1.03 (0.80-1.33)	0.13	0.806					
40-49	0.94 (0.84-1.04)	0.05	0.204					
50-64	1.08 (0.99-1.17)	0.04	0.078					
65-74	1.22 (1.12–1.34)	0.05	⊲0.001					
75-84	1.32 (1.20–1.46)	0.05	⊲0.001					
285	1.37 (1.23-1.53)	0.06	<0.001					
Race/Ethnicity (referent = White, non-Hispanic)								
Asian, non-Hispanic	0.82 (0.71-0.95)	0.07	0.007					
Black, non-Hispanic	0.90 (0.85–0.95)	0.03	⊲0.001					
Hispanic	0.75 (0.71-0.81)	0.03	⊲0.001					
Other	0.80 (0.74-0.87)	0.04	<0.001					
Sex (referent = male)	Sex (referent = male)							
Female	0.94 (0.90-0.99)	0.02	0.015					
Chronic conditions								
COPD	1.35 (1.28-1.42)	0.03	⊲0.001					
Heart failure	1.58 (1.48-1.67)	0.03	<0.001					
Diabetes	1.21 (1.14-1.28)	0.03	<0.001					
Chronic kidney disease	1.64 (1.55-1.74)	0.03	<0.001					
Obesity	0.95 (0.90-1.00)	0.03	0.049					
Previous hospitalization+ (yes versus no)	2.61 (2.45-2.78)	0.03	⊲0.001					
Severity measures at index hospitalization								
Length of stay, days	0.99 (0.99–1.00)	00.0	0.001					
ICU admission	0.94 (0.89-0.99)	0.03	0.014					
Mechanical ventilation	1.15 (1.04–1.27)	0.05	0.006					
Noninvasive ventilation	0.86 (0.81-0.90)	0.03	⊲0.001					
Discharge category from index hospitalization (referent = home/self-care)								
SNF	1.37 (1.29-1.47)	0.03	<0.001					
Home health organization	1.30 (1.21-1.39)	0.04	<0.001					
Hospice	0.24 (0.20-0.29)	0.09	⊲0.001					
Ongoing care								



Persistent Symptoms in Patients After Acute COVID-19

- Carfi, AJuly 9, 2020. doi:10.1001/jama.2020.12603
- 87.4% of 143 hospitalized pts had at least 1 symptom 2 moslater
- Only 12.6% symptom free
- 32% had 2 symptoms
- 55% had 3 or more symptoms
- None had symptoms of acute illness and all PCR neg
- Fatigue, dyspnea, joint pain and chest pain;44% worsened QOL
- NIVV 14.7% and invasive vent 4.9%



"Long-haulers"

- Typically mild disease
- Fatigue
- Headache
- Vertigo
- Impairment of cognition, hair loss, diminished cardiorespiratory function
- Myocarditis



COVID-19 **Neurocritical Care**



Associated Clinical Findings

- CNS*: Encephalitis, postviral encephalopathy, acute demyelinating encephalomyelitis, stroke (ischemic and hemorrhagic), seizures, status epilepticus
- PNS^: Myositis, critical illness myopathy/neuropathy

Phases

- Viremic phase: Neuroinvasive potential
- Inflammatory phase: Immune dysregulation
- Coagulopathy and endotheliopathy
- Treatment-related adverse effects

Wide spectrum of neurological complications

Similar treatment strategies as those for non-COVID-19 patients



Diagnostic Considerations

- High clinical suspicion
- Diagnostic challenges due to sedation, paralysis, limitations in imaging, continuous EEG capabilities
- Electrodiagnostic studies
- Cerebrospinal fluid sampling

Outcomes

- Short-term outcomes determined by severity of COVID-19 + neurological manifestation
- Long-term outcomes: TBD
- Post-intensive care syndrome (PICS), fatigue, "brain fog"

*CNS: central nervous system, ^PNS: peripheral nervous system







currently postulated to combine to produce weakness in critically ill patients



Long term effects of Critical Illness

- 80% develop neurocognitive deficits
- High incidence of delirium. May lead to dementia
- Critical Illness Polyneuropathy
- Cognitive deficits
- PTSD
- Increased risk for mortality for at least 2 yrsout.
- Many never regain pre-illness functional status



CMR Findings in athletes recovering from COVID-19

- 26 collegiate athletes eith mild or asymptomatic COVID-19
- 4showed CMR evidence for acute myocarditis; 2 had mild SOB
- 8 showed scaring suggesting previous myocarditis
- Pericardial effusion present in 2
- All had nI ECG, Echo, and troponins

 Current recommendations call for 2week convalescence. Further workup may be indicated.

A Steady-state free precession cine, patient 1

D Steady-state free precession cine, patient 2

B T2 map, patient 1



E T2 map, patient 2





F Phase-sensitive inversion recovery with late gadolinium enhancement, patient 2





 Rajpal, s, JAMA Cardiol.doi:10.1001/jamacardio.2020.4 916



"Cytokine Storm" & COVID-19

TNF, IFN-a/B, **IL-6**, IL-1B



Cytokine Storm

- Overwhelming inflammatory immune response to an illness or trigger with release of:
 - Interferon (IFN), interleukins (IL), tumor-necrosis factor (TNF), chemokines
- Results in cell and tissue damage

COVID-19

- Pathogenesis of lung injury & multiple organ dysfunction syndrome remain uncertain
 - Cytokine storm is on proposed theory of pathogenesis in severe COVID-19 illness

Acute Respiratory Distress Syndrome (ARDS)

- IL-6 plays a key role in pathogenesis in several known viral etiologies²
- eg, Influenza & SARS-CoV
- Mechanisms other than cytokine storm may contribute to COVID-19 ARDS
 - Median levels of IL-6 in COVID-19 ARDS are ↑ but reported ≤ than median levels seen in typical ARDS³

Therapies

- Clinical trials are evaluating IL-6 pathway targeted treatments such as:
 - Tocilizumab (IL-6 receptor inhibitor)
 - Sarilumab (IL-6 receptor antagonist)
 - Siltuximab (monoclonal antibody with high affinity for IL-6 receptor)

Further study is needed to evaluate the role of cytokine storm in the pathogenesis and severity of COVID-19 disease. **SCHEST**

¹Qin C et al. Clin Infect Dis. 2020. ²Wang W et al. Clin Infect Dis. 2004. ³Sinha P et al. JAMA Intern Med. 2020.



Prevention, Diagnosis, & Treatment of VTE in Patients with COVID- 19

- All acutely and critically ill patients should receive anticoagulation prophylaxis. LMWH and fondaparinux preferred.
- Recommend against antiplatelet treatment
- Regardless of markers, rec standard dose over weight-based, full dose
- Rec against extended prophylaxis
- Use mechanical prophylaxis unless chemical contraindicated
- Rec against routine venous US
- For patients with confirmed VTE rec wt adjusted LMWH. Oral apixaban or rivaroxaban if no interactions
- Duration of treatment is at least 3 mos (provoked VTE)
- Recurrent VTE despite anticoagulation increase dose of LMWH 25-30%; if on NOAC or VKA then wt based LMWH



• CHEST 2020; 158(3):1143-1163

Use of NIVV and HFNO in COVID-19





Duan, J. Am J Emerg Med. 2020 Jul 2930

NIVV and HFNO

- In early days of pandemic, early intubation was advocated to protect staff
- Although no good model to estimate risk of aerosolization with NIVV and HFNO, currently used widely and no observed increase in workplace infections.
- Decreases need for mechanical ventilation and bridge therapy post intubation
- Settings same as non-COVID patients





Vaccines

Many in various stages of testing

- Unprecedented effort
- Safety and efficacy will need to be determined on relatively small number of subjects
- Remember: vaccine is not vaccination
- Logistics of manufacture and distribution daunting. Some require deep freezing
- 50% of public state they will hesitate



Coronavirus Vaccine Tracker

By Jonathan Corum, Sui-Lee Wee and Carl Zimmer

Updated October 3, 2020



NIVV and **HFNO**

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Current Research Trials at St. Vincent

Genetech

 MSTT1041A (Astegolimab) IgG2 monoclonal Ab which blocks signaling of IL-33 to prevent progression to ARDS/hasten recovery or placebo v. UTTR1147A (an IL-2 which augments barrier function of the lung and GI epithelial cells

GlaxoSmithKlein

Otilimab single dose for proinflammatory phase of COVID-19



Current Research Trials at St. Vincent

Bellerophon PULSE COV19-001

(COViNOX)

- iNO a vasodilator
- High concentrations of nitric oxide suppress viral replication
- Randomized placebo v. iNO125 mcg/kg IBW/hr 12-24hr daily

Boehringer-Ingelheim BI764198

Efficacy and safety in prevention/progression of ARDS









Commercial platform sold to Mallinckrodt for \$2.3B

- Continuous flow iNO delivery system
- Approved for use in persistent pulmonary hypertension in neonates
- Bulky device with large cylinders designed for use in acute hospital settings



R&D Platform spun-out to form Bellerophon Therapeutics

- Pulsatile iNO delivery system
- Pulsed iNO can deliver equivalent dose as continuous delivery with 5% of the volume
- Dynamic pulse delivers the prescribed dose accurately throughout the day
- Small portable ~2.5 lbs. device allows ambulatory use in chronic in-home setting





INOpulse Delivery System: Lightweight, Portable and **User Friendly**





SIREN (CP30) Trial

- Convalescent plasma v. placebo in pts with mild disease
- Single infusion of convalescent plasma
- End-point to determine if prevents progression of illness
- Outpatient study



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ILLUSTRATED CURRENT NEWS



To Prevent Influenza!

Us not take any person's breath. Keep the mouth and treth sliens. Aroid these that cough and success. Due't visit possily ventilated places. Keep warm, get fresh air and susshine.

- Don't nor common draking supt, towels, etc.
- Cover your month when you cough and unexes.
- Avoid Worry, Four and Fatigue. Stay at house if you have a sold. Walk to your work or office. In sick rooms wears a game mask like in disstration.









