

COVID-19: Public Health and Scientific Challenges

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National Institutes of Health



JAMA

The Journal of the American Medical Association

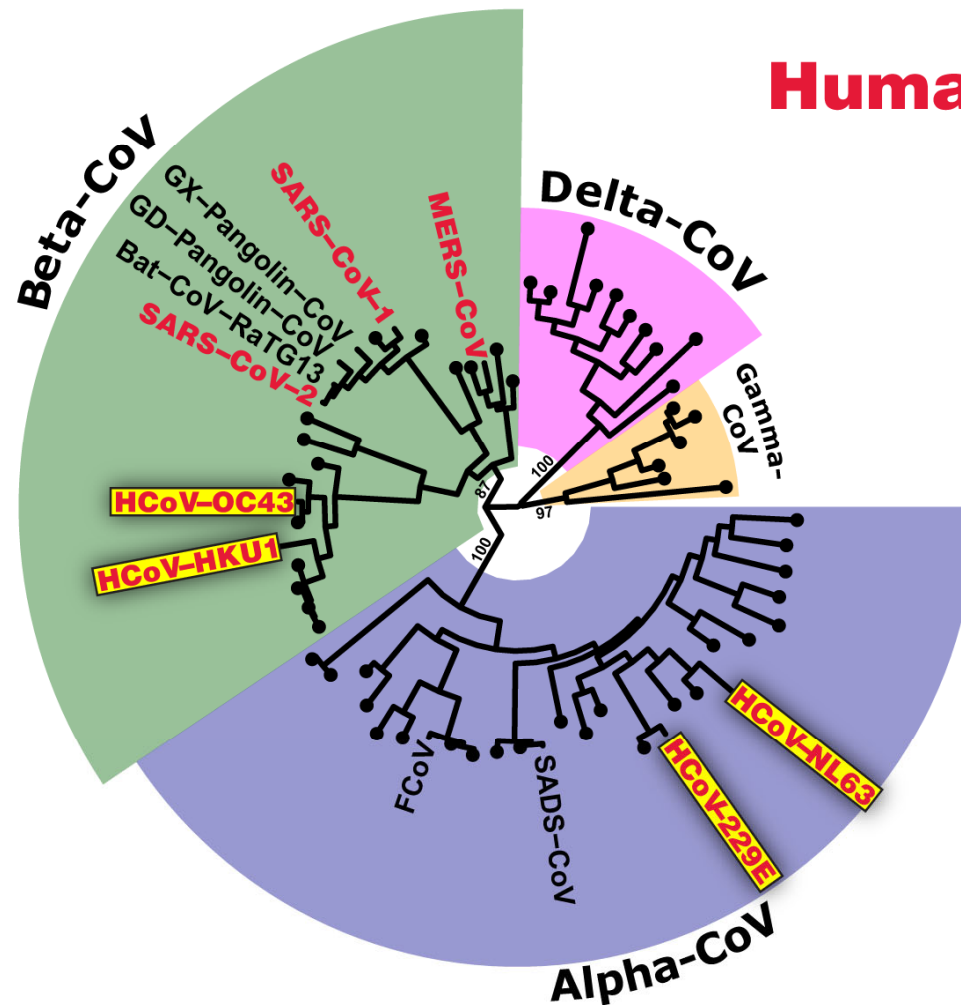
Published online
January 23, 2020

Viewpoint

Coronavirus Infections—More Than Just the Common Cold

CI Paules, HD Marston and AS Fauci

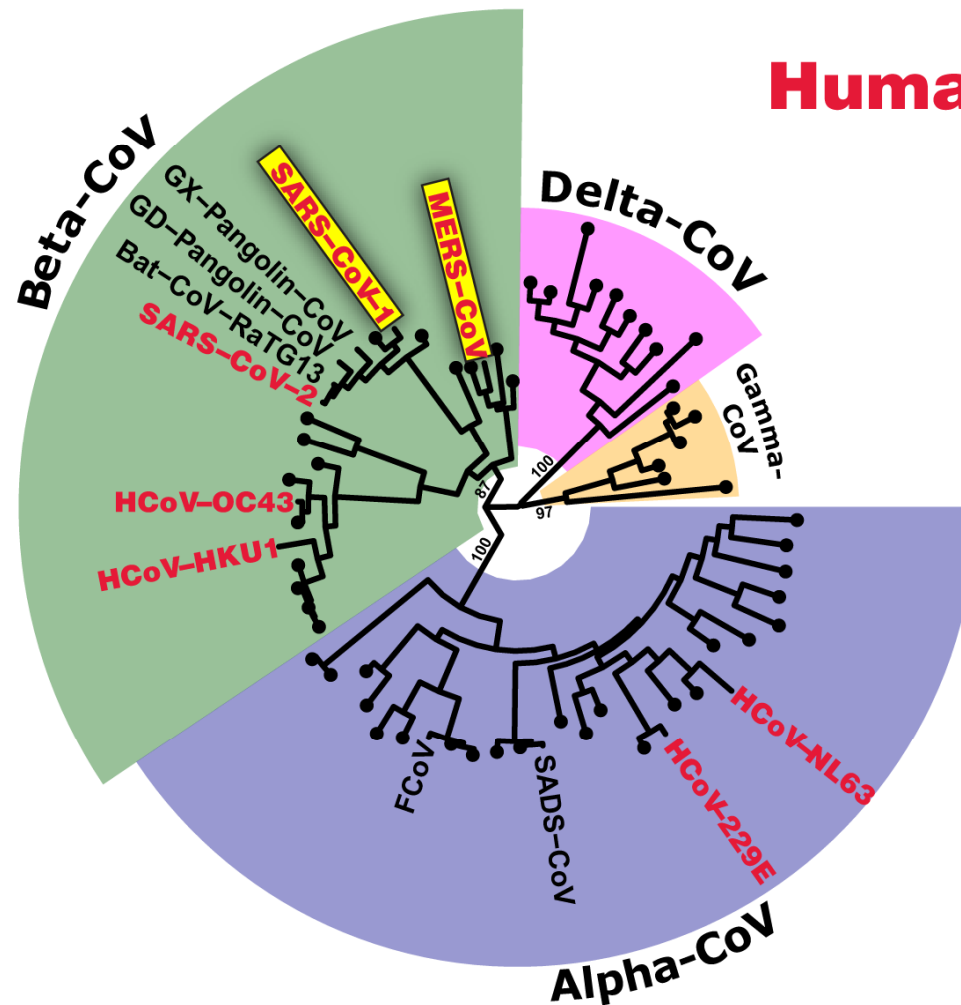
Coronavirus Phylogenetic Tree



Human coronaviruses

Source: SM Gygli, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.

Coronavirus Phylogenetic Tree

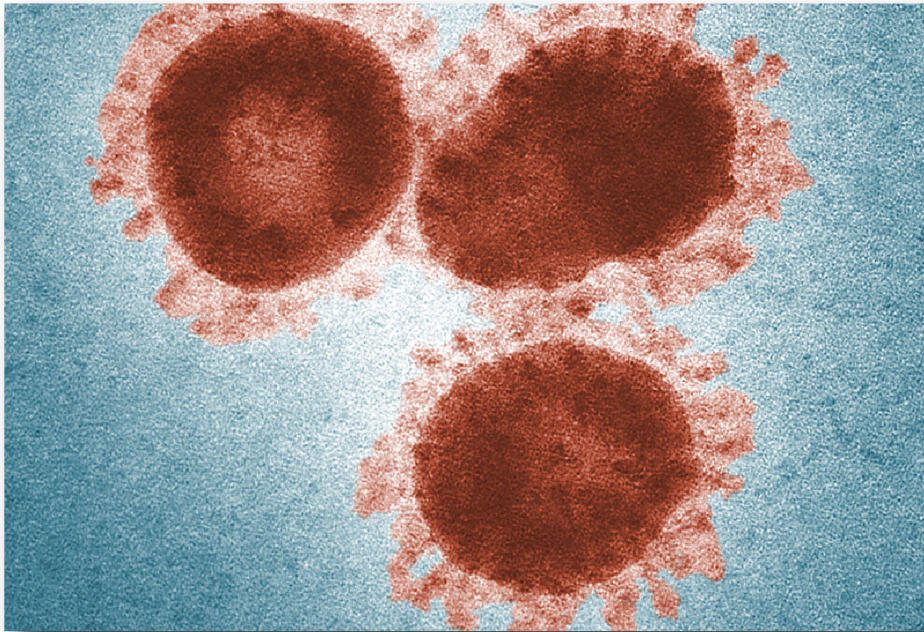


Human coronaviruses

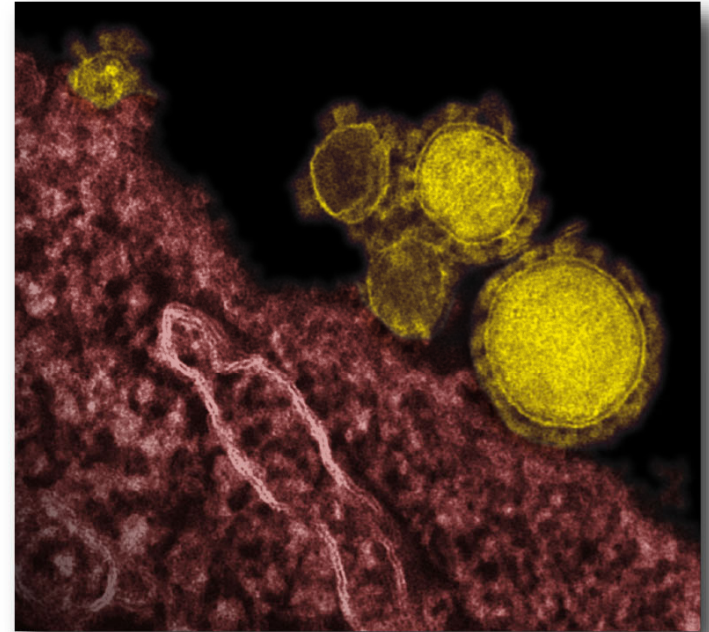
Source: SM Gygli, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.

Severe Human Coronavirus Disease: Past as Prologue

Severe Acute Respiratory Syndrome (SARS) (2002–2003)



Middle East Respiratory Syndrome (MERS) (2012–present)





Novel Human Virus? Pneumonia Cases Linked to Seafood Market in China Stir Concern

By Dennis Normile

PLANTS

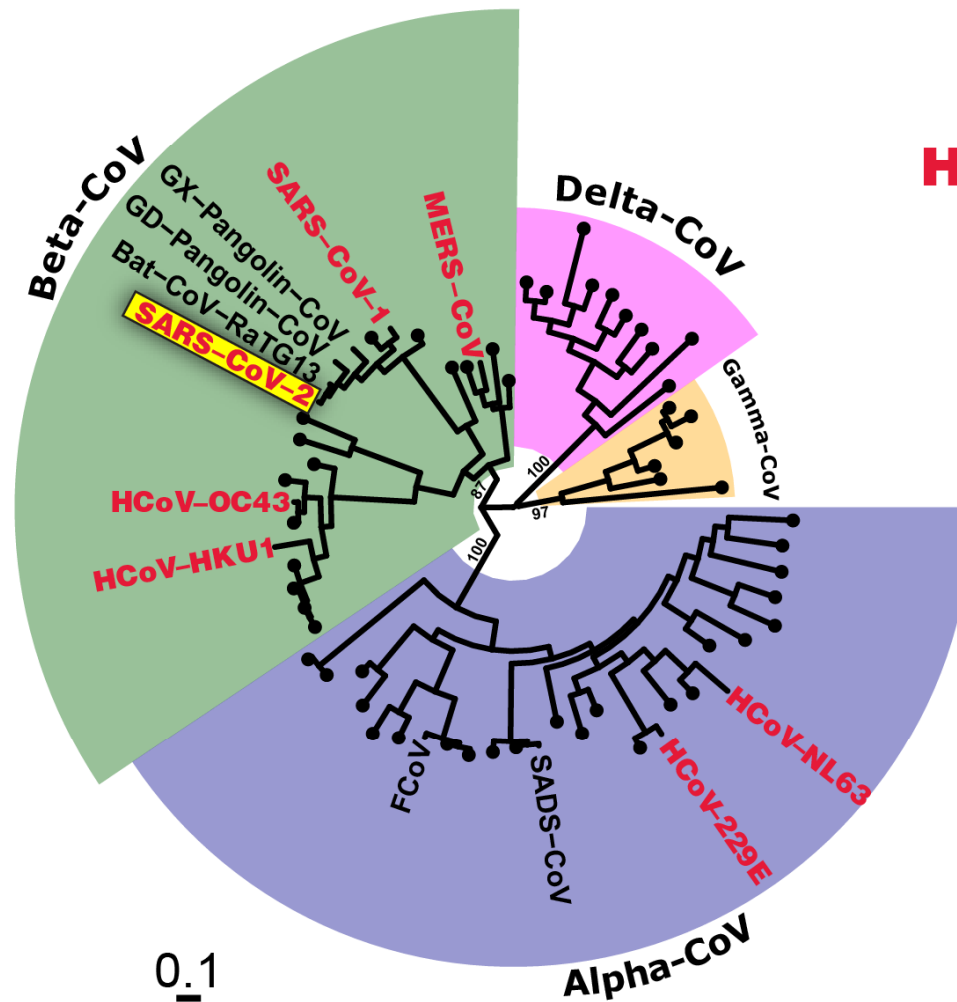
Convoluted shapes
from simple rules pp. 24 & 91

The Washington Post

January 9, 2020

China Identifies New Strain of Coronavirus as Source of Pneumonia Outbreak

Coronavirus Phylogenetic Tree

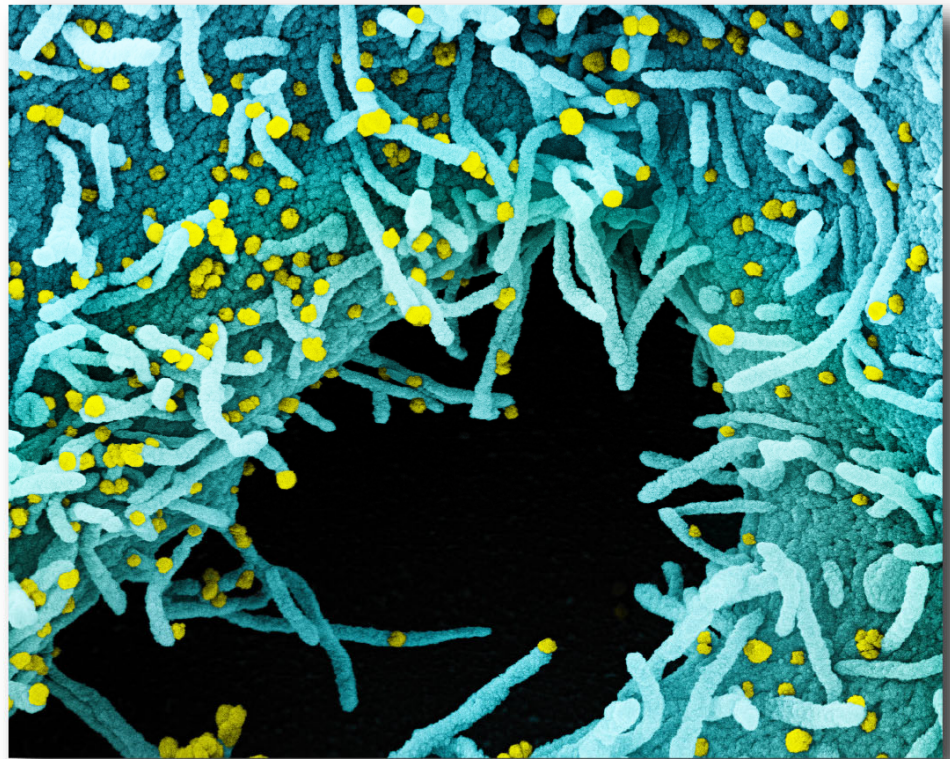
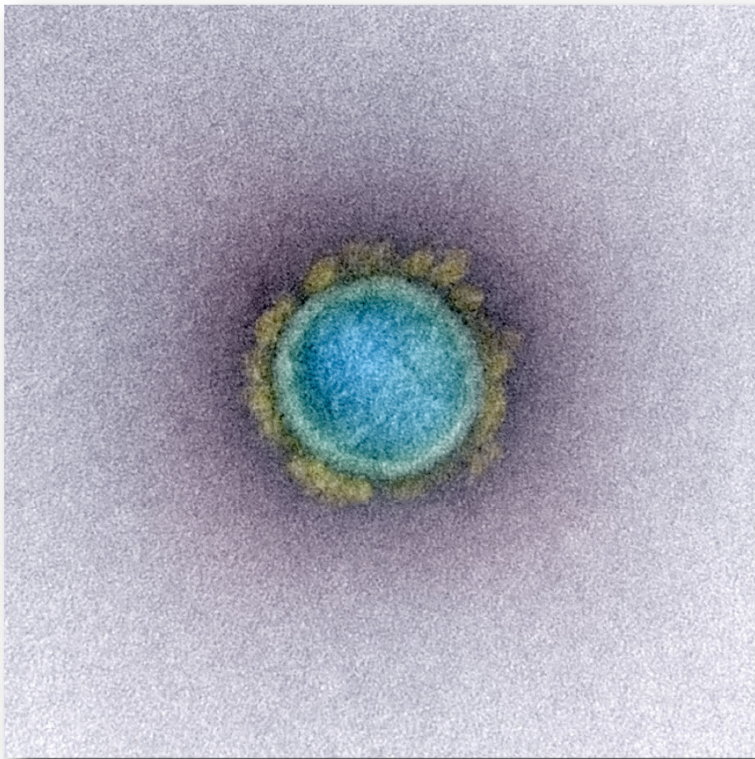


Human coronaviruses

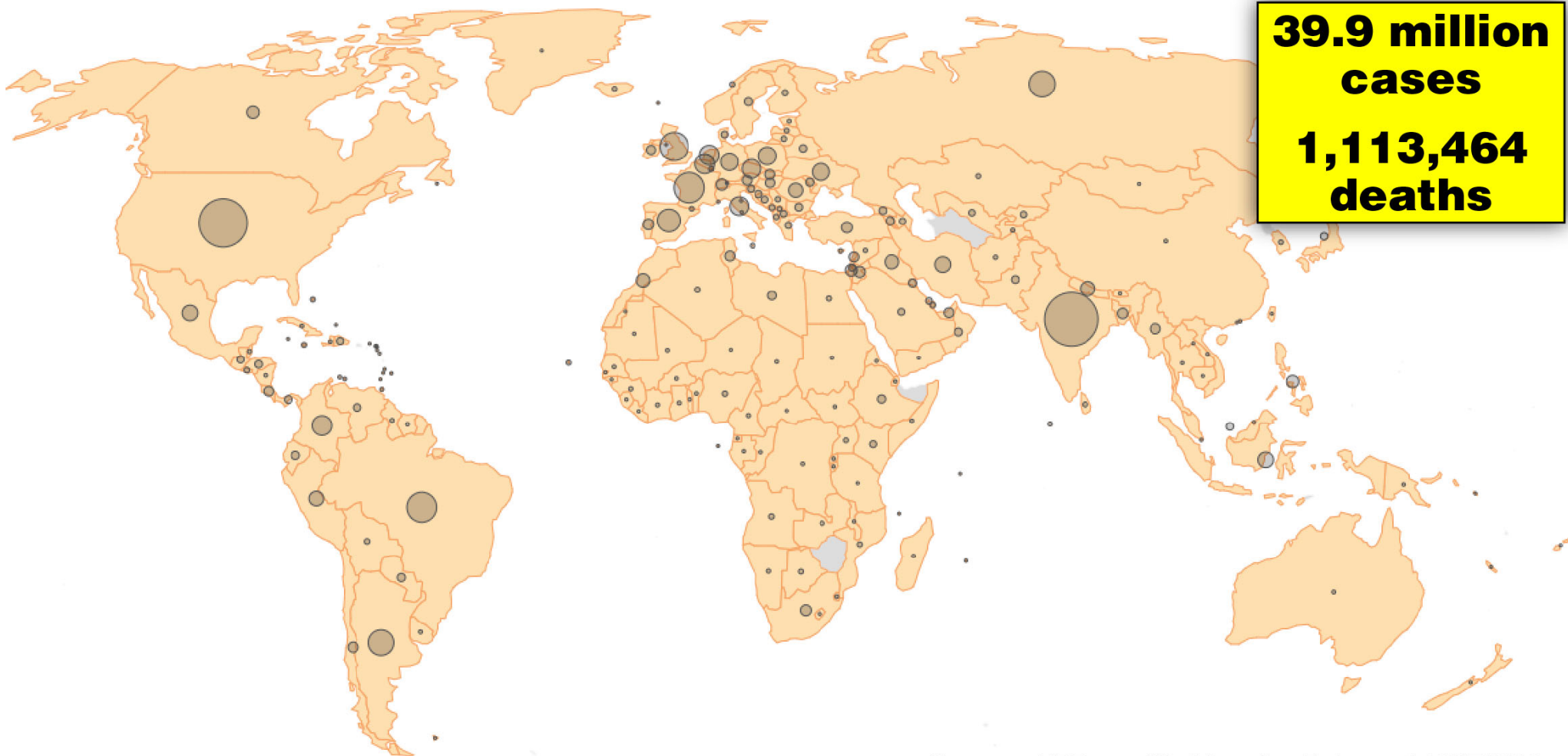
Figure courtesy of S.M. Gygli, Ph.D., NIAID.
Based on 440 bp nucleotide sequences of
RNA dependent RNA polymerase (RdRp).

Coronavirus Disease 2019 (COVID-19)

- **COVID-19** is the disease caused by the novel coronavirus **SARS-CoV-2**

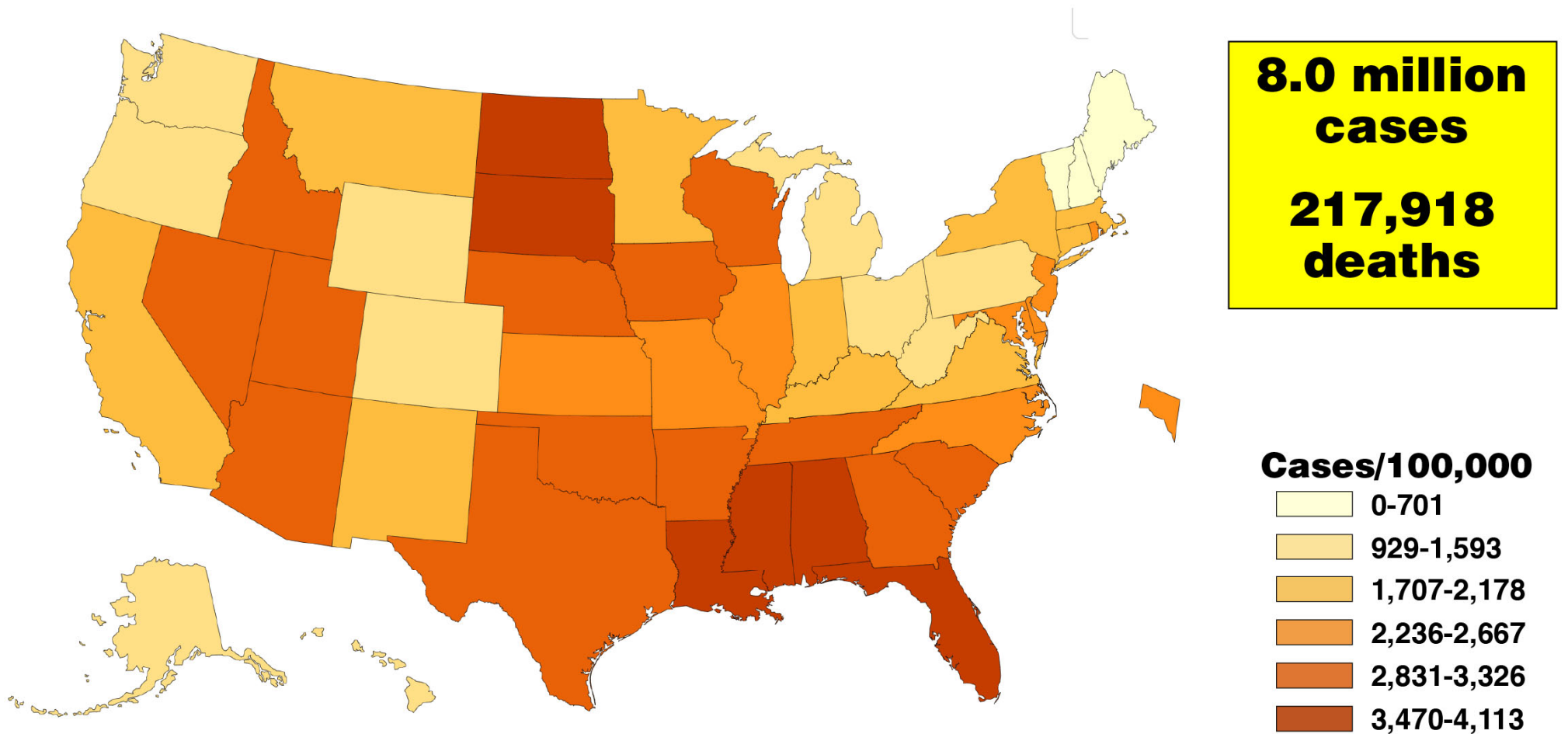


COVID-19 Globally



Sources: NPR.org; Worldometer. Data as of 10/17/2020

COVID-19 in the United States

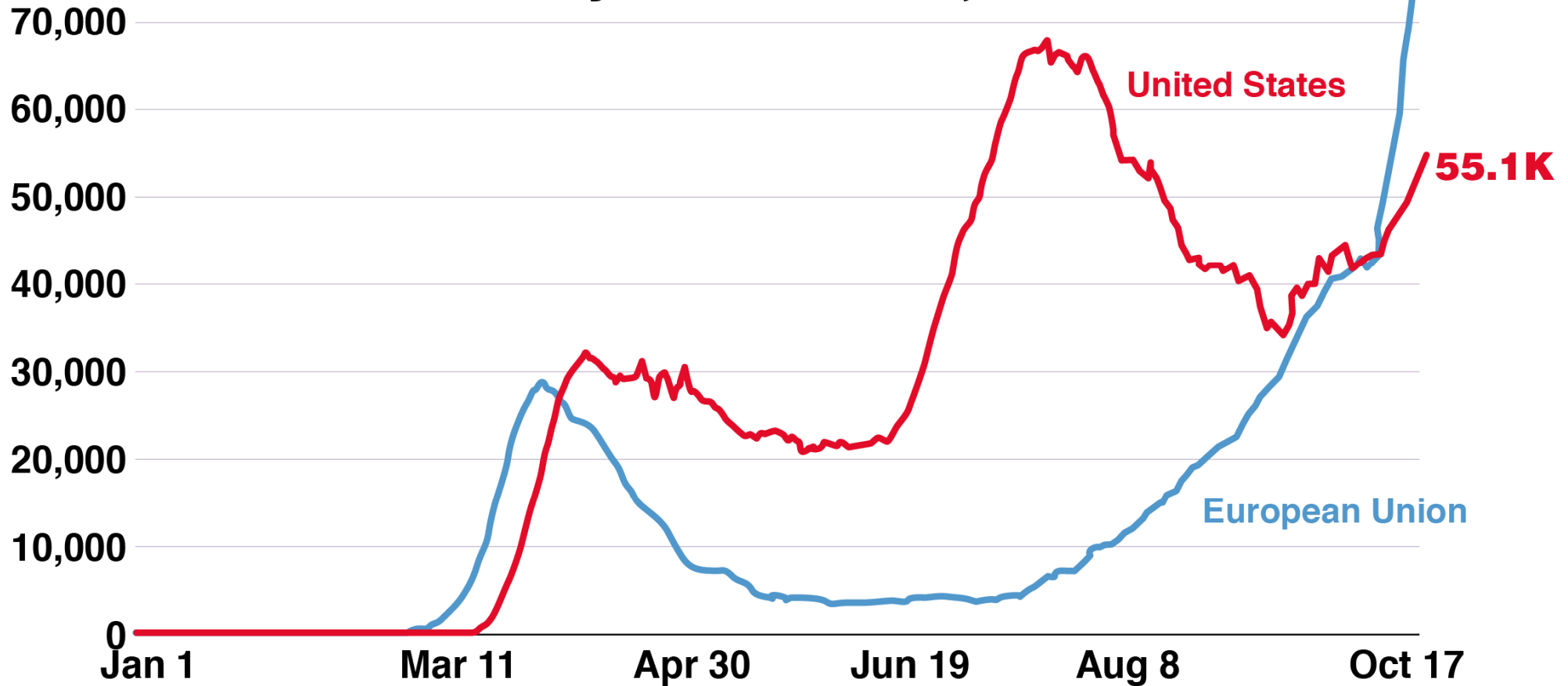


Source: CDC. Data as of 10/17/2020.

United States vs. Europe

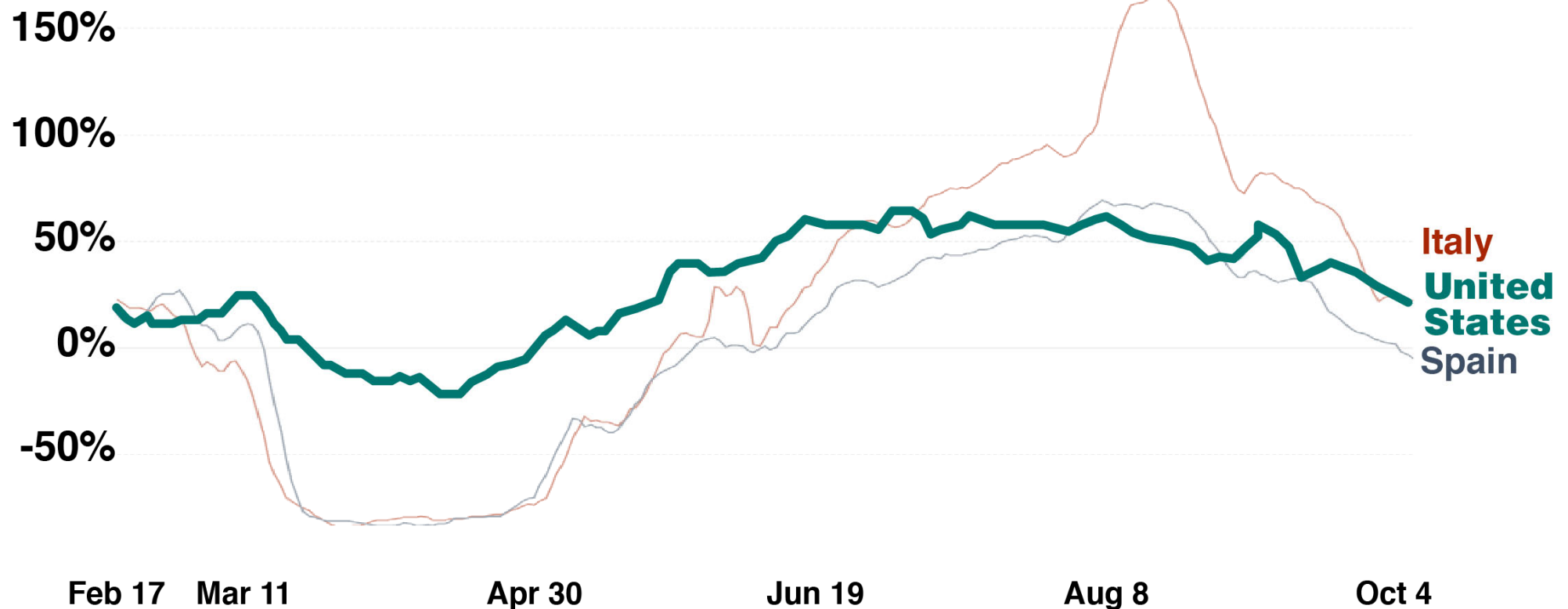
New COVID-19 Cases: US vs. EU

7-day rolling average of new COVID-19 cases,
January 1 to October 17, 2020



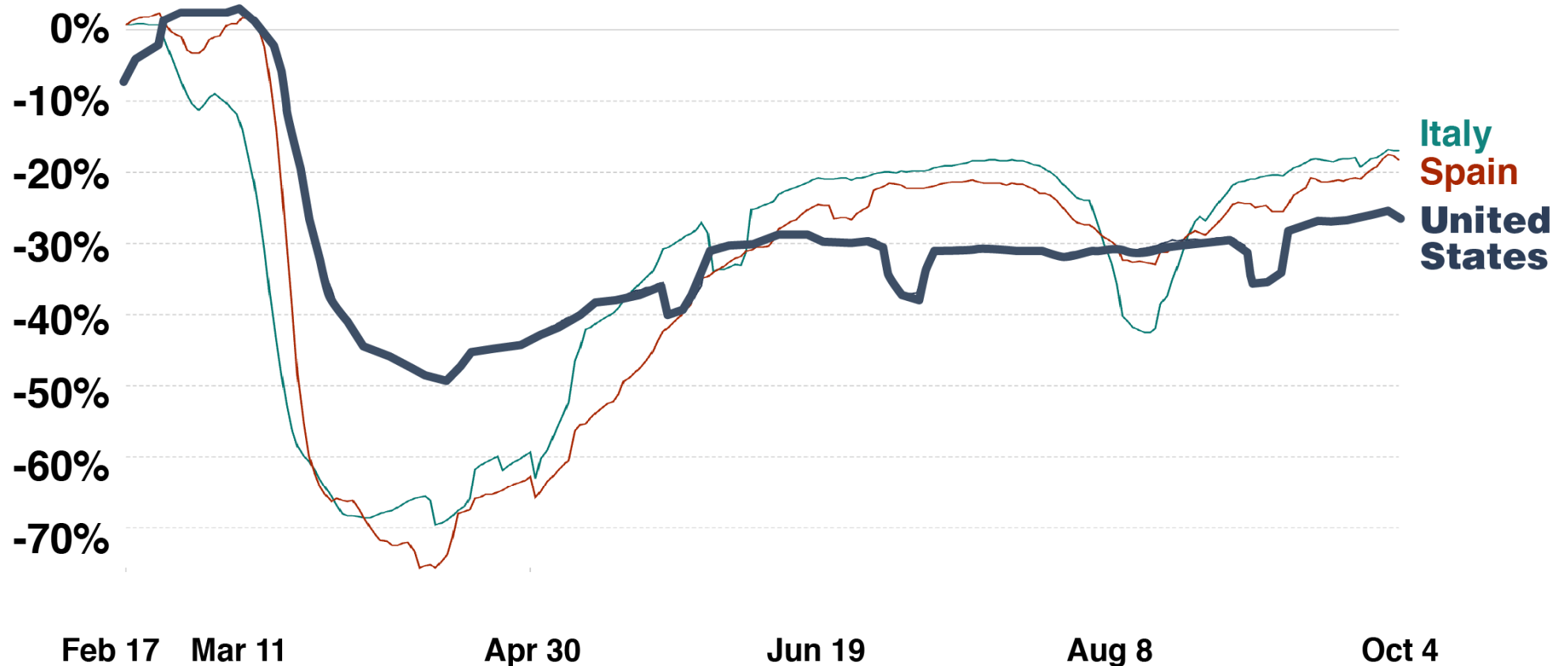
Source: Our World in Data

Change in Mobility Over Time: Parks and Outdoor Spaces



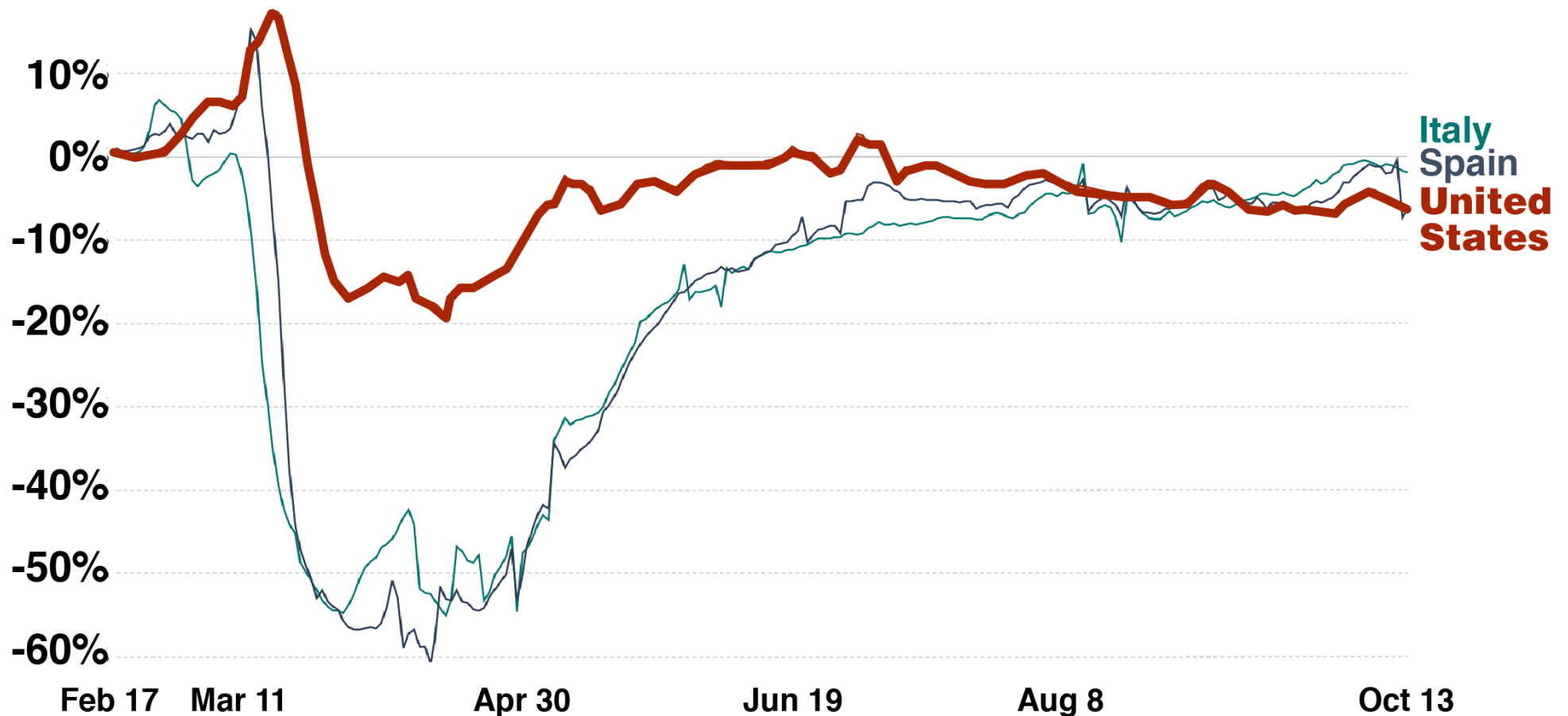
Source: Our World in Data

Change in Mobility Over Time: Workplaces



Source: Our World in Data

Change in Mobility Over Time: Grocery and Pharmacy Stores

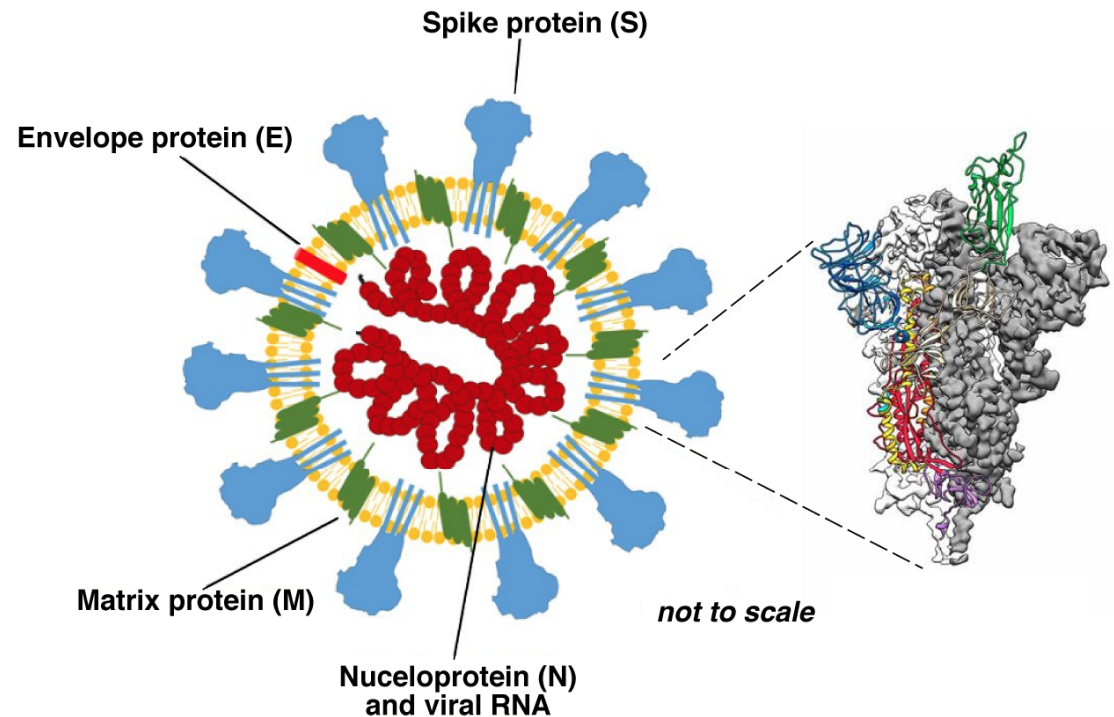


Source: Our World in Data

Virology

SARS-CoV-2 Virology

- **Beta-CoV:** same subgenus as SARS CoV-1 and some bat CoVs
- **RNA virus:** enveloped, positive-sense, single-stranded
- **Large genome:**
~30,000 Kb
- **4 structural proteins: S, E, M, N**
 - **S** allows virus to attach to and fuse with cell membrane
- **ACE2 receptor:** cell receptor

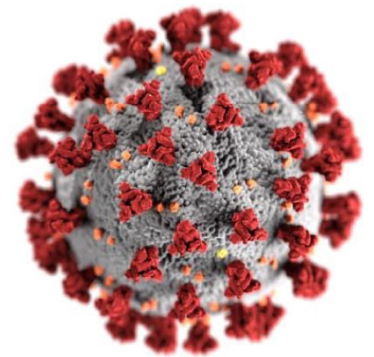


Images: Florian Krammer; NIAID VRC

Transmission

SARS-CoV-2 Transmission

- **Mainly through exposure to respiratory droplets when close (≤ 6 ft) to an infected person**
- **Sometimes through droplets or particles that remain in the air (aerosols) over time and various distances ($>$ or < 6 ft)**
- **Less commonly through contact with contaminated surfaces**
- **Virus found in stool, blood, semen and ocular secretions; role in transmission unknown**





Source: *NEJM*

Risk of Transmission

- **Varies by type and duration of exposure, prevention measures used, and individual factors (e.g., viral load)**
- **Transmissions most common among household contacts, in congregate or health care settings when PPE not used, and in closed settings (e.g., cruise ships, nursing homes, prisons)**
- **Factors that may increase the risk of airborne transmission include:**
 - **Crowded, enclosed spaces with poor ventilation**
 - **Singing, speaking loudly, or breathing heavily**

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Early Release

May 12, 2020

High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice – Skagit County, Washington, March 2020

L Hamner, H Leibrand et al.

After choir practice with one symptomatic person,
87% of group developed COVID-19



● index case ● 32 confirmed and 20 probable cases ● unaffected person

COVID-19 spreads easily

- Avoid groups
- Stay at least 6 feet apart
- Wear face coverings

CDC.GOV

bit.ly/MMWR51220

MMWR



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

April 17, 2020

Morbidity and Mortality Weekly Report (MMWR)

Community Transmission of SARS-CoV-2 at Two Family Gatherings — Chicago, Illinois, February–March 2020

I Ghiai, JE Layden et al.



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

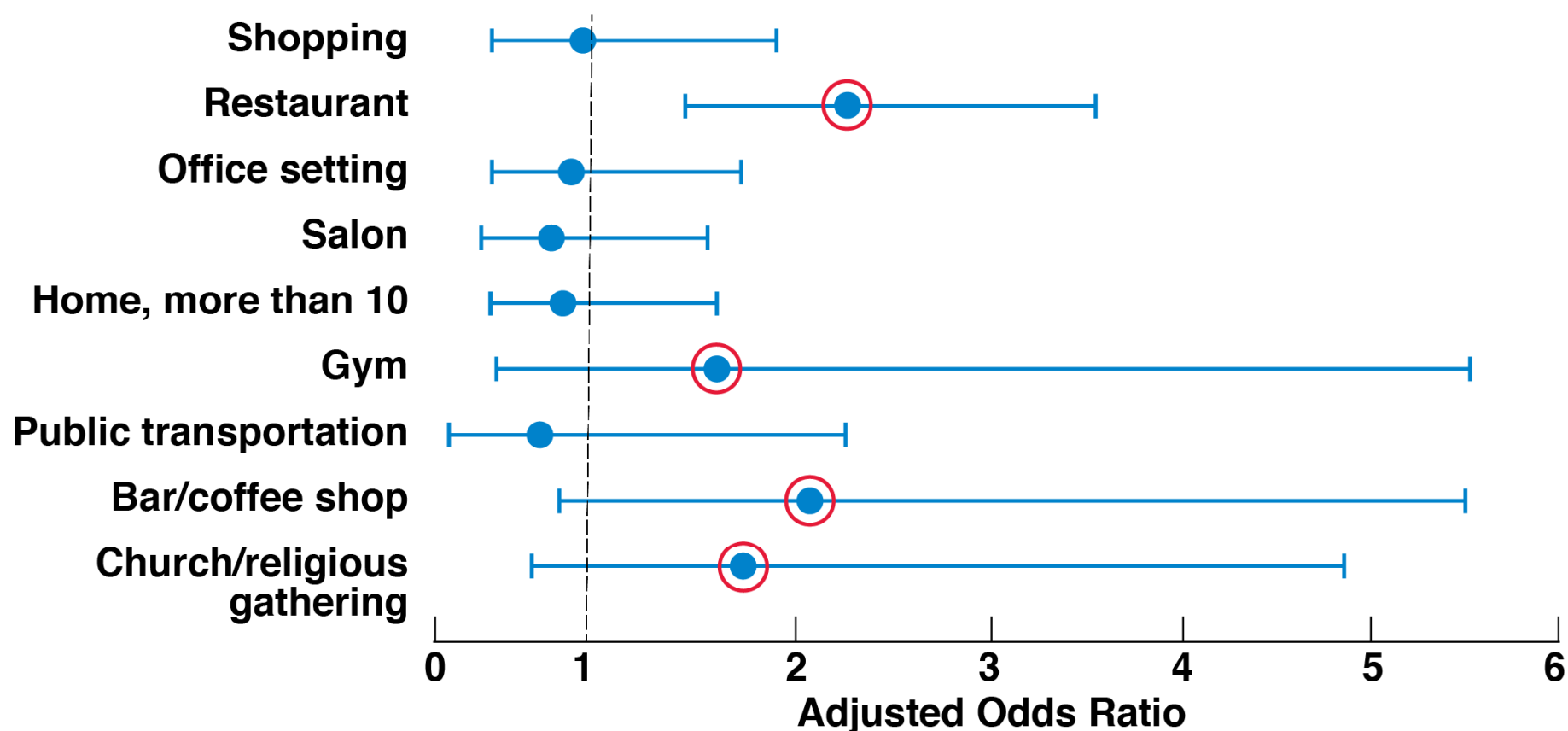
May 22, 2020

Morbidity and Mortality Weekly Report (MMWR)

High COVID-19 Attack Rate Among Attendees at Events at a Church — Arkansas, March 2020

A James, H Kirking et al.

Community Exposures among Symptomatic Adults – 11 U.S. Healthcare Facilities



Source: KA Fisher et al.
MMWR 69:1258, 2020.

Annals of Internal Medicine

Established in 1927 by the American College of Physicians

June 3, 2020

Prevalence of Asymptomatic SARS-CoV-2 Infection

A Narrative Review

DP Oran and EJ Topol

- Data from 16 cohorts, total n= 45,000+
- Asymptomatic persons account for ~40-45% of SARS-CoV-2 infections

July 28, 2020 | vol. 117 | no. 30

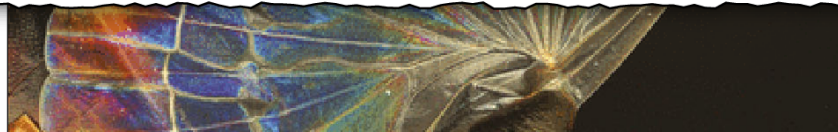
PNAS

Proceedings of the National Academy of Sciences of the United States of America

BRIEF REPORT

The Implications of Silent Transmission for the Control of COVID-19 Outbreaks

SM Moghadas, AP Galvani et al.



- **Modeling study estimates that individuals without symptoms account for >50% of transmission**

Fundamentals to Prevent Acquiring and Transmitting SARS-CoV-2

- **Universal wearing of masks/cloth face coverings**
- **Maintain physical distance – at least 6 feet**
- **Avoid crowds and congregate settings**
- **Outdoors better than indoors**
- **Frequent washing of hands**

Clinical Manifestations

COVID-19 Clinical Presentation

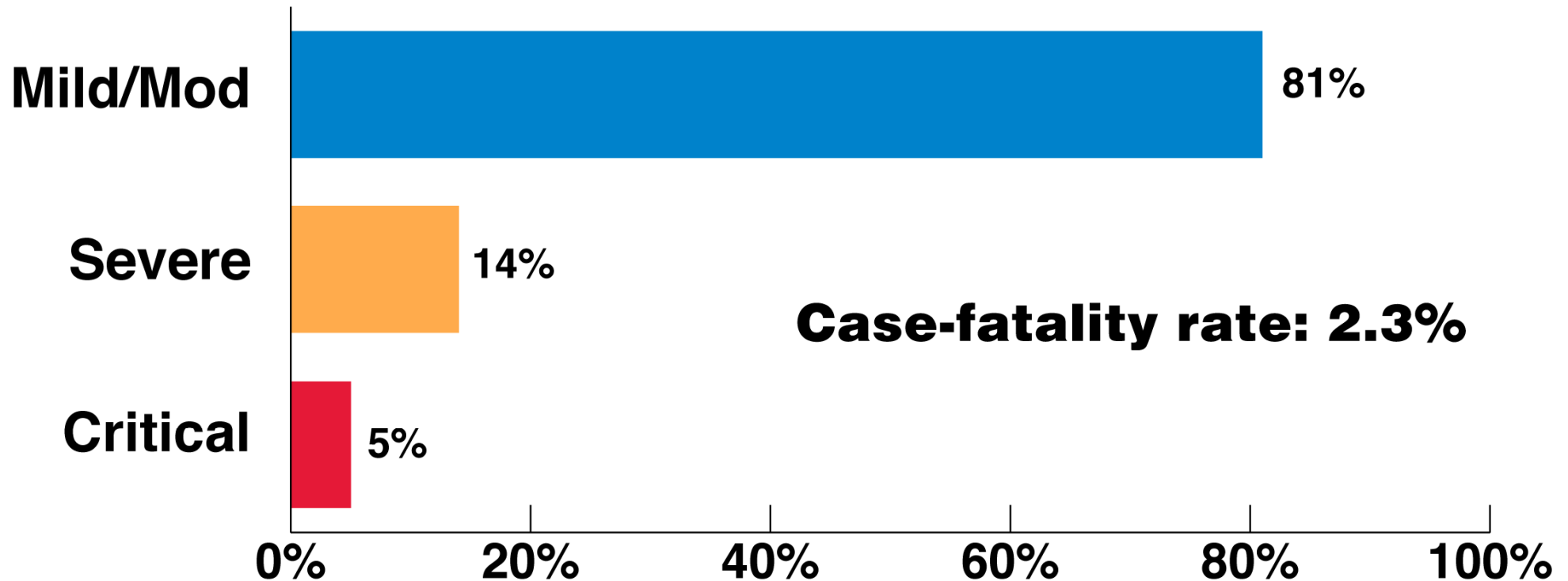
■ Fever	83–99%
■ Cough	59–82
■ Fatigue	44–70
■ Anorexia	40–84
■ Shortness of breath	31–40
■ Myalgias	11–35

Other non-specific symptoms reported

- Sore throat, nasal congestion, headache, diarrhea, nausea, vomiting. Loss of smell/taste preceding the onset of respiratory symptoms.

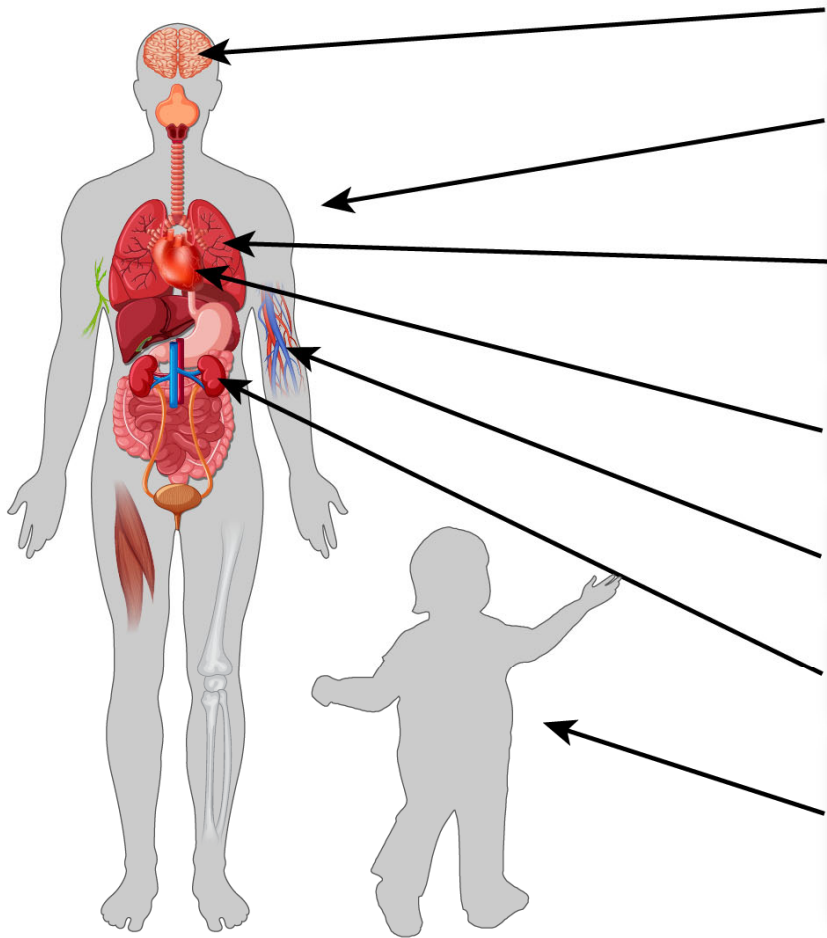
Source: WHO, 5/2020

Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China



Source: Z Wu & JM McGoogan, *JAMA* 323:1239, 2020.

Manifestations of Severe COVID-19



Neurological disorders

Hyperinflammation

Acute respiratory distress syndrome (ARDS)

Cardiac dysfunction

Hypercoagulability

Acute kidney injury

Multisystem inflammatory syndrome in children (MIS-C)

Post-COVID-19 Syndrome

July 31, 2020

Science

**From 'Brain Fog' to
Heart Damage,
COVID-19's Lingering
Problems Alarm
Scientists**

J Couzin-Frankel

August 12, 2020

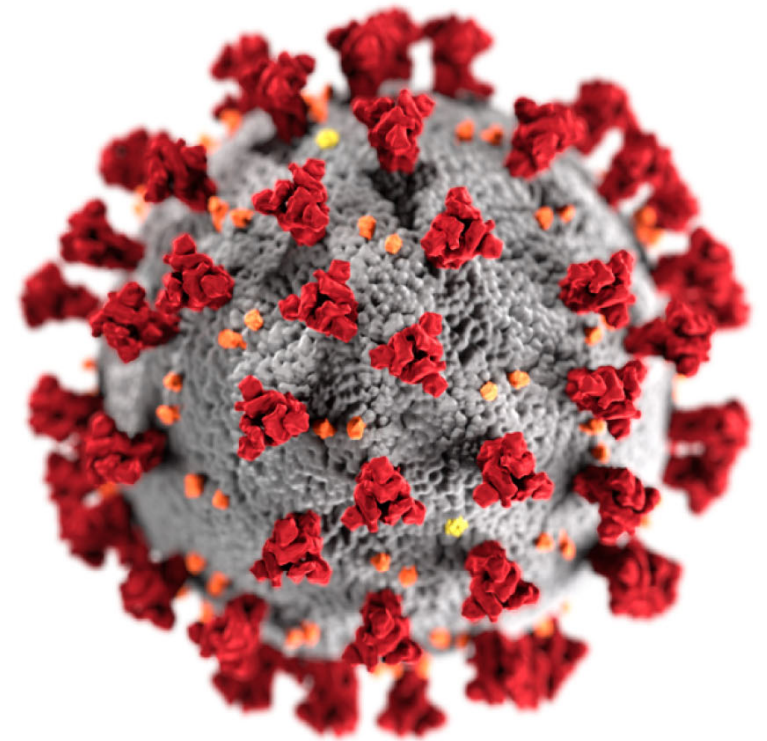
STAT

**Long After the Fire
of a COVID-19
Infection, Mental
and Neurological
Effects Can Still
Smolder**

E Cooney

People at Increased Risk for Severe COVID-19 Illness

- Older adults
- People of any age with certain underlying medical conditions

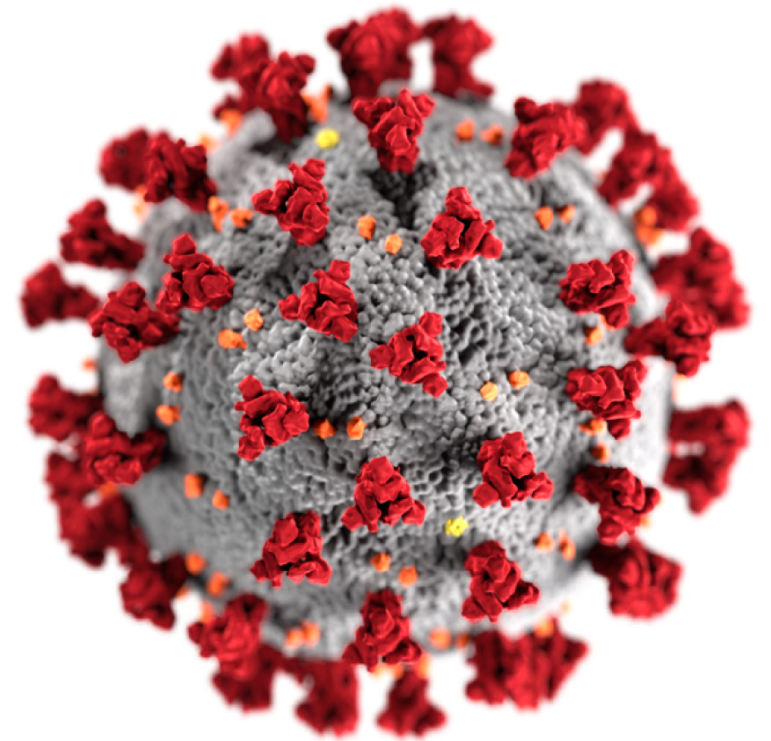


Source: CDC, 6/25/2020

People at Increased Risk for Severe COVID-19 Illness

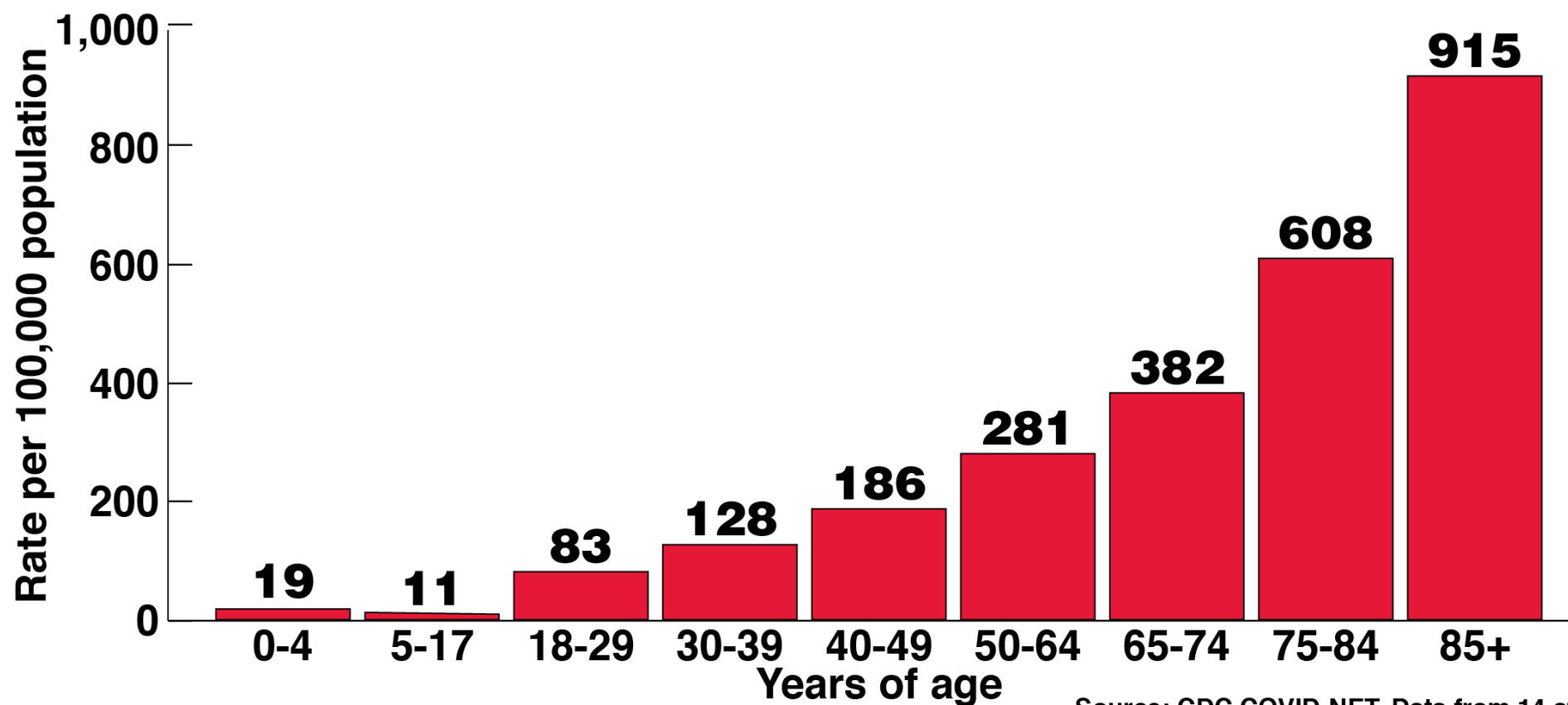
■ Older adults

■ People of any age with certain underlying medical conditions



Source: CDC, 6/25/2020

Cumulative Rates of Laboratory-Confirmed COVID-19-Associated Hospitalizations by Age, United States, March 1 – October 10, 2020

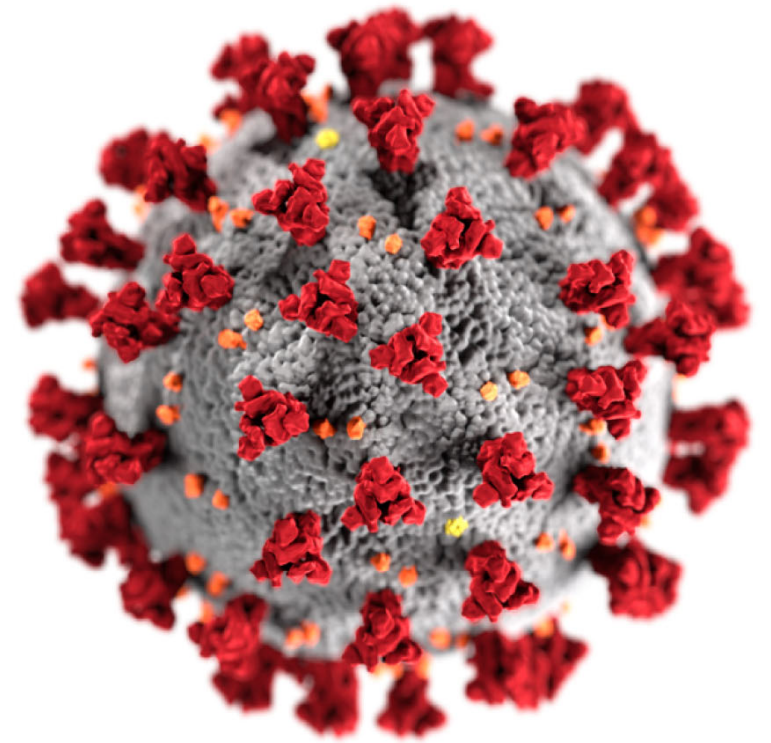


Source: CDC COVID-NET. Data from 14 states.

People at Increased Risk for Severe COVID-19 Illness

■ Older adults

■ People of any age with certain underlying medical conditions



Source: CDC, 6/25/2020

Underlying Medical Conditions Associated with Increased Risk for Severe COVID-19 Illness

- **Cancer**
- **Chronic kidney disease**
- **Chronic obstructive pulmonary disease (COPD)**
- **Diabetes, type 2**
- **Heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)**
- **Immunocompromised state from solid organ transplant**
- **Obesity (BMI \geq 30)**
- **Sickle cell disease**
- **Smoking**

Source: CDC, 10/6/2020

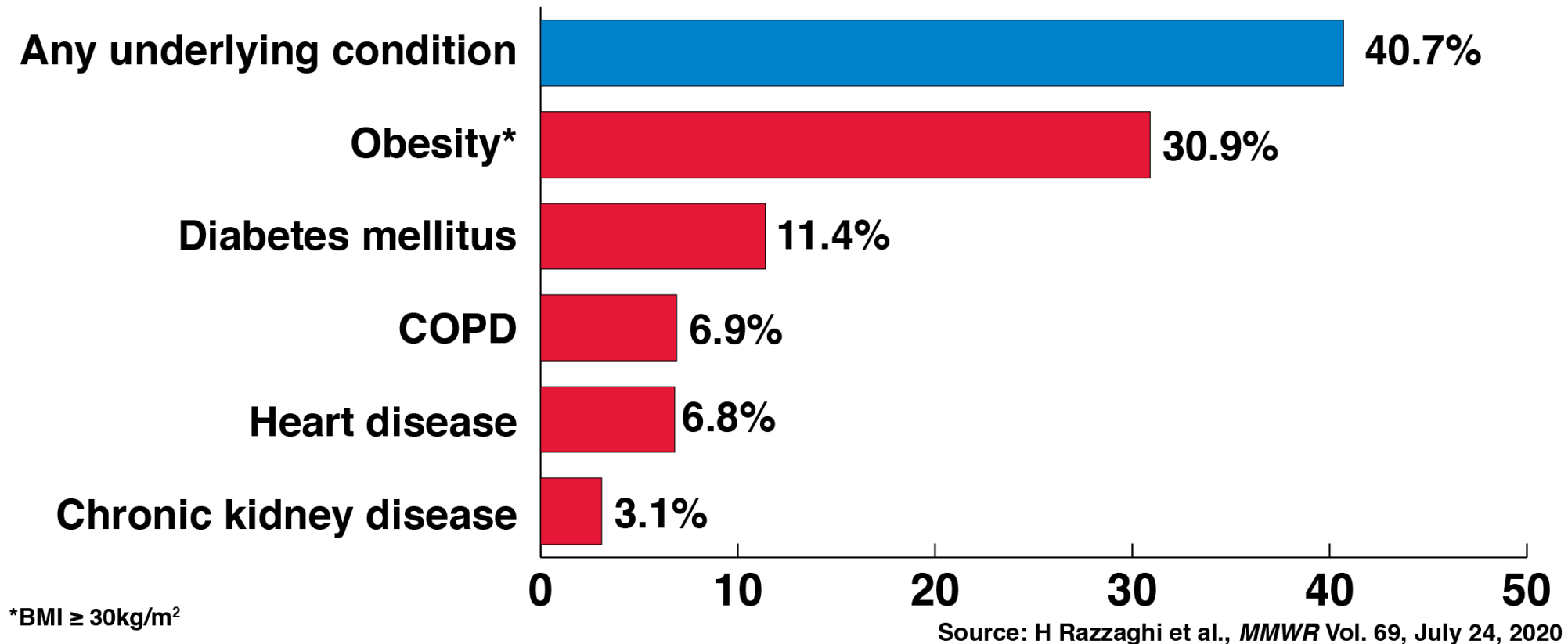
Underlying Medical Conditions That May Confer Increased Risk for Severe COVID-19 Illness

- Asthma (moderate-to-severe)
- Cerebrovascular disease
- Cystic fibrosis
- Diabetes, type 1
- Hypertension
- Immunocompromised state from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids or other immune-weakening medicines
- Neurologic conditions (e.g. dementia)
- Liver disease
- Overweight (BMI > 25 but < 30)
- Pregnancy
- Pulmonary fibrosis
- Thalassemia

Source: CDC, 10/6/2020

More Than 40% Of U.S. Adults Are Susceptible To Severe COVID-19

Prevalence of underlying conditions in U.S. adults in 2018



JAMA

The Journal of the American Medical Association

May 11, 2020

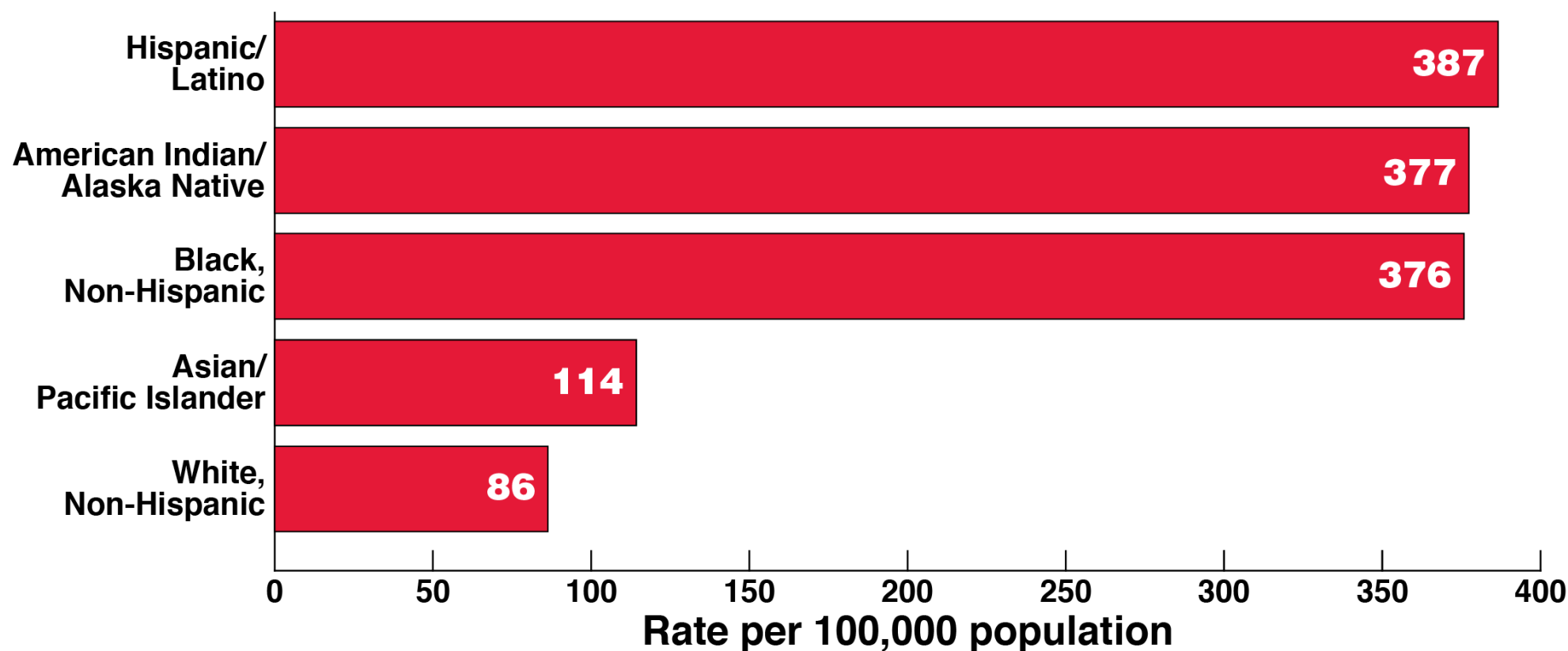
Viewpoint

COVID-19 and Racial/Ethnic Disparities

MW Hooper, AM Nápoles and EJ Pérez-Stable

“The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations.”

Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – October 10, 2020



Source: CDC COVID-NET. Data from 14 states.

Therapeutics



National Institutes of Health
Turning Discovery Into Health

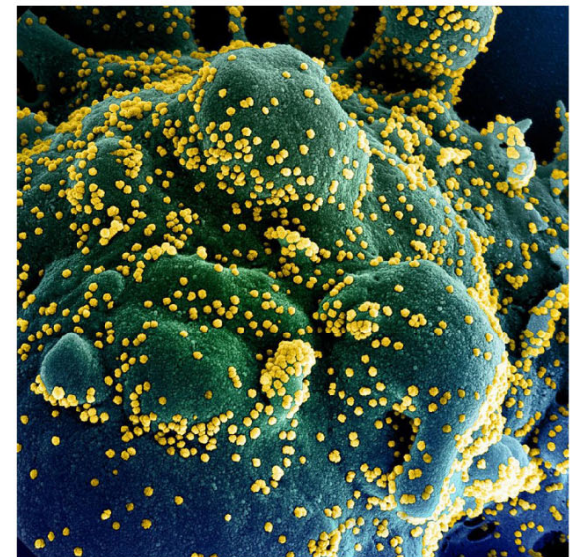
Tuesday, April 21, 2020

News Release

Expert U.S. Panel Develops NIH Treatment Guidelines for COVID-19

“Living document” expected to be updated often as new clinical data accrue

■ [Covid19treatmentguidelines.nih.gov](https://www.covid19treatmentguidelines.nih.gov)



Therapeutics for COVID-19

Recommended by the NIH COVID-19 Treatment Guidelines Panel for Certain Patients

- Remdesivir (investigational antiviral)
- Dexamethasone (corticosteroid)

Examples of Other Investigational Therapies

- Antivirals
- Blood-derived products, e.g., convalescent plasma, hyperimmune globulin
- Monoclonal antibodies against SARS-CoV-2
- Immunomodulators, e.g., cytokine inhibitors, interferons
- Adjunct therapies, e.g., anticoagulants





The
New England
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

published online October 8, 2020

Remdesivir for the Treatment of Covid-19 — Final Report

JH Beigel, HC Lane et al. for the ACTT-1 Study Group Members

- Hospitalized patients on remdesivir recovered more quickly than those on placebo (median 10 days vs 15 days, $P < 0.001$)
- A trend toward decreased mortality: hazard ratio = 0.73 (95% CI: 0.52–1.03)
- 1,062 patients from 10 countries: U.S., Europe and Asia



The
**New England
Journal of Medicine**

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Published online July 17, 2020

Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report

The RECOVERY Collaborative Group

- RECOVERY trial in UK -- 6,425 patients randomized to receive dexamethasone 6 mg once per day (oral or IV) for up to ten days or usual care alone
- Dexamethasone reduced 28-day mortality by 36% in ventilated patients and by 18% in other patients receiving oxygen
- No benefit for patients not receiving respiratory support

Vaccines










A Strategic Approach to COVID-19 Vaccine R&D

L Corey, JR Mascola, AS Fauci & FS Collins

- **Unprecedented collaboration and resources will be required to research and develop safe and effective vaccines for COVID-19 that can be manufactured and delivered in the scale of billions of doses to people globally.**

Selected COVID-19 Vaccine Candidates

Platform	Developer	Phase 1/2	Phase 2/3
Nucleic acid		Enrolled	Ongoing
		Enrolled	Ongoing
Viral vector		Enrolled	Ongoing
		Enrolled	Ongoing
		Ongoing	--
Protein subunit		Ongoing	Ongoing
		Ongoing	--

June 30, 2020

Science

**Just 50% of
Americans Plan to
Get a COVID-19
Vaccine.
Here's How to Win
Over the Rest**

W Cornwall

Do you plan to get a coronavirus vaccine when one is available?

Overall



Under age 60



Age 60 and older



White



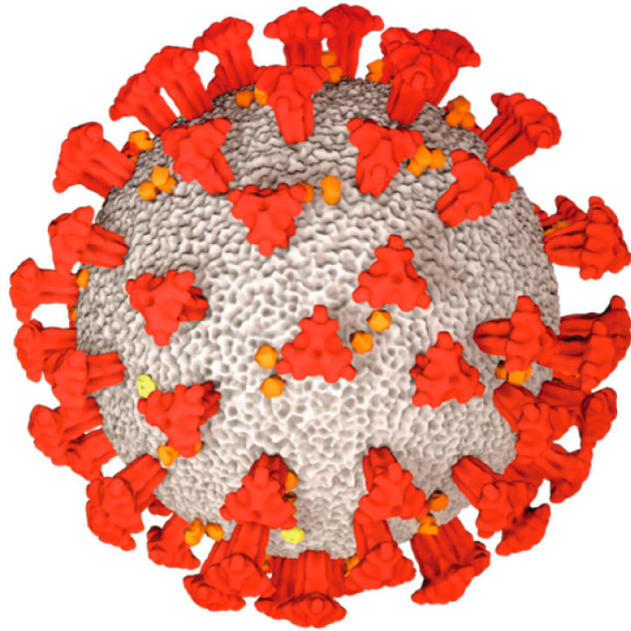
Black



Hispanic



Yes Not sure No Did not answer



COVID-19

Prevention Network

www.preventcovid.org