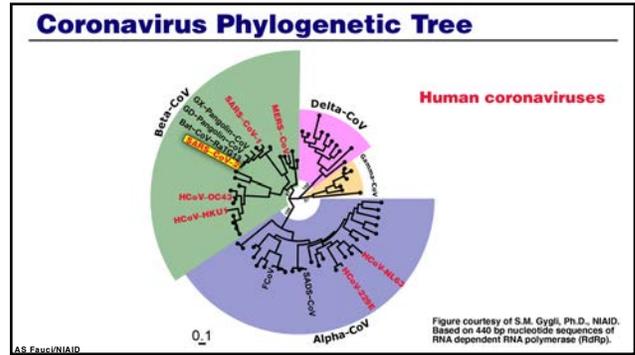


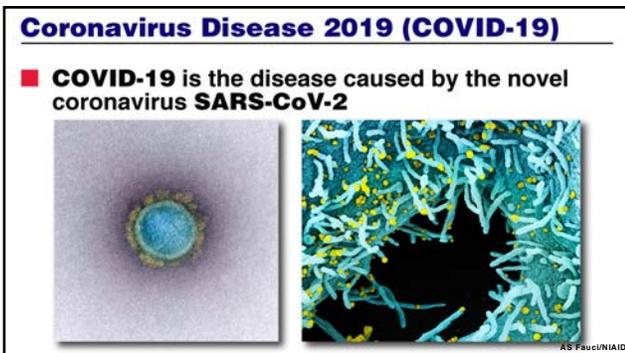




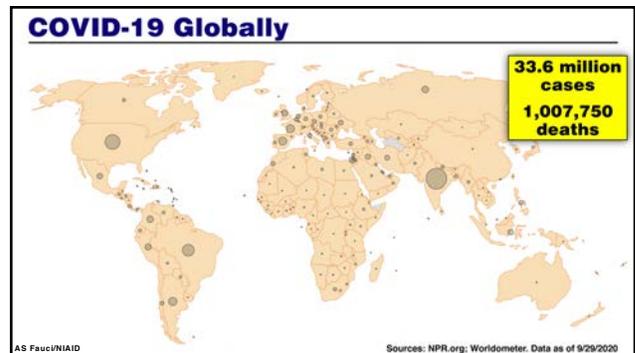
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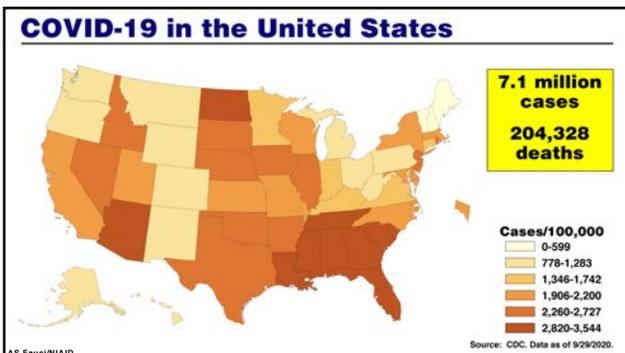
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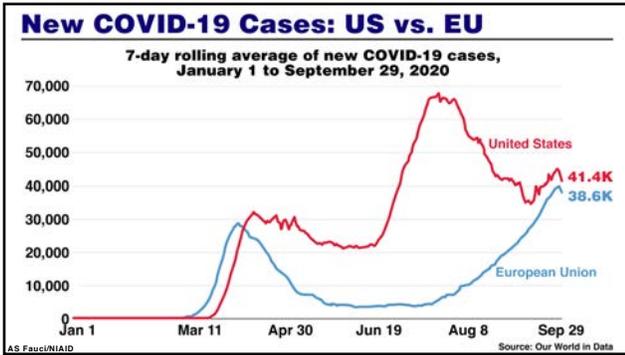
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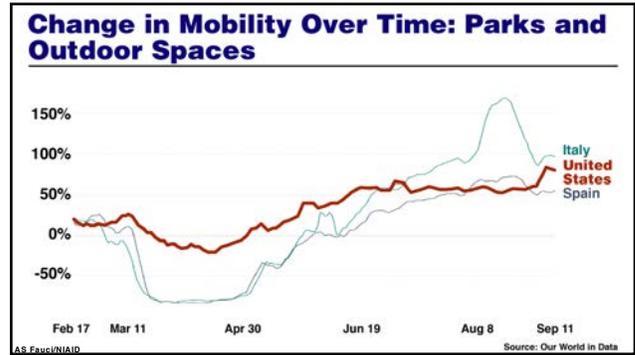
11

**United States vs. Europe**

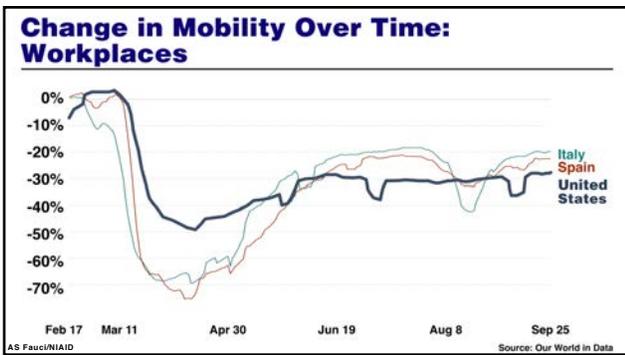
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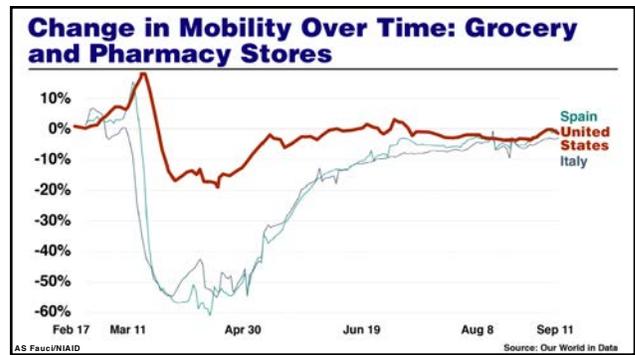
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# Virology

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### SARS-CoV-2 Virology

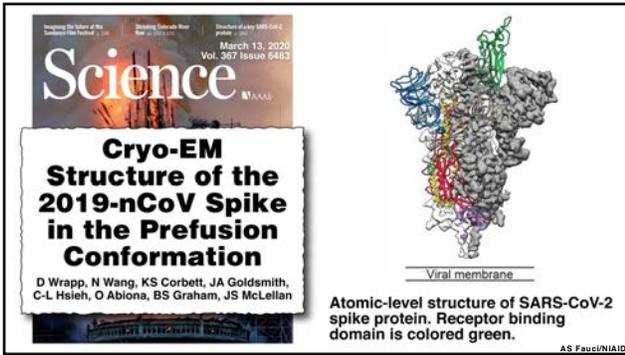
- **Beta-CoV:** same subgenus as SARS CoV-1 and some bat CoVs
- **RNA virus:** enveloped, positive-sense, single-stranded
- **Large genome:** ~30,000 Kb
- **4 structural proteins:** S, E, M, N
  - S allows virus to attach to and fuse with cell membrane
- **ACE2 receptor:** cell receptor

not to scale

Images: Florian Kramer; NIAID VRC

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**Science**  
 March 13, 2020  
 Vol. 367 Issue 6483

**Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation**  
 D Wrapp, N Wang, KS Corbett, JA Goldsmith, C-L Hsieh, O Abiona, BS Graham, JS McLellan

Atomic-level structure of SARS-CoV-2 spike protein. Receptor binding domain is colored green.

Viral membrane

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**nature microbiology**  
 April 2020

**Functional Assessment of Cell Entry and Receptor Usage for SARS-CoV-2 and Other Lineage B Betacoronaviruses**  
 M Letko, A Marzi and V Munster

Uncovering coronavirus entry

■ Human ACE2 is the receptor for SARS-CoV-2

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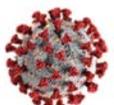
**Transmission**

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**SARS-CoV-2 Transmission**

- Transmission between people in close contact
- Transmission via particles that remain in the air over time and distance
- Infected surfaces
- Virus found in stool, blood, semen and ocular secretions; role in transmission unknown
- Animals (including domesticated) not major source of human infection



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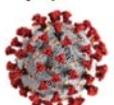
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Source: NEJM

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**Risk of Transmission**

- Varies by the type and duration of exposure, use of preventive measures, and individual factors (e.g., the amount of virus in respiratory secretions)
- Secondary infections most common among household contacts, in congregate or health care settings when personal protective equipment not used, and in closed settings (e.g., cruise ships)
- Numerous clusters of cases after social or work gatherings highlight the risk of transmission through close, non-household contact



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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

COVID-19 spreads easily

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

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CDC 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.

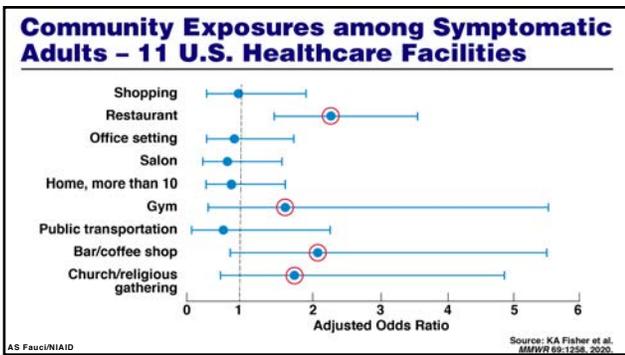
CDC Centers for Disease Control and Prevention  
 CDC 24/7: Saving Lives, Protecting People™ May 22, 2020

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.

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Annals of Internal Medicine  
 Established in 1937 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

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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

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**Fundamentals for Prevention of Acquisition and Transmission of SARS-CoV-2**

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

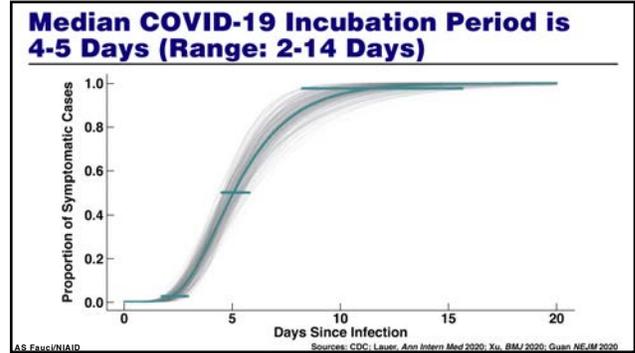
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# Clinical Manifestations

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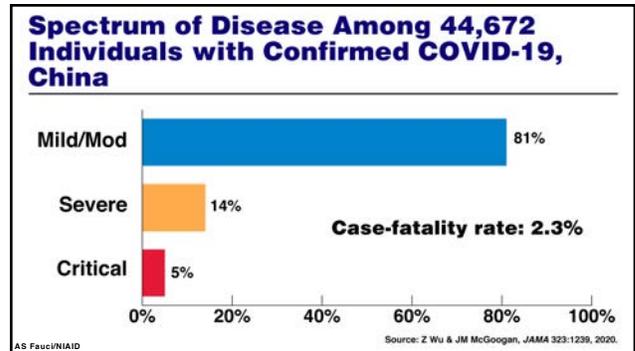
### COVID-19 Clinical Presentation

■ 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.

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Source: WHO, 5/2020

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- ### Manifestations of Severe COVID-19 Disease
- Acute respiratory distress syndrome (ARDS)
  - Hyperinflammation
  - Acute cardiac injury, arrhythmias, cardiomyopathy
  - Acute kidney injury
  - Neurological disorders
  - Hypercoagulability leading to thromboembolic complications, including pulmonary embolism and acute stroke
  - Multisystem inflammatory syndrome in children (MIS-C)
- AS Fauci/NIID

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### COVID "Long-Haulers"

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

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# Collateral Negative Effects of COVID-19 on Other Health Issues

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**CDC** Centers for Disease Control and Prevention  
 CDC 24/7: Saving Lives, Protecting People™ June 26, 2020

**Morbidity and Mortality Weekly Report (MMWR)**

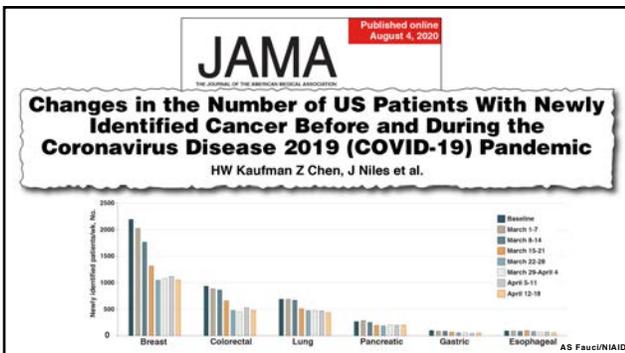
**Potential Indirect Effects of the COVID-19 Pandemic on Use of Emergency Departments for Acute Life-Threatening Conditions — United States, January–May 2020**  
 SJ Lange, Q Yang et al.

In the 10 weeks following the declaration of the COVID-19 national emergency, visits to emergency departments declined for:

Heart attack	Stroke	Uncontrolled high blood sugar
23%	20%	10%

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Public Policy Resources

**COVID-19 Pandemic Ongoing Impact on the Cancer Community: May 2020**

- 17% of patients in active treatment who reported delays to their cancer therapy
- 67% of cancer patients and survivors expressed concern about health as shelter in place orders lifted

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**Science** June 19, 2020  
 VOL 368 Issue 6457 pp. 3980

**COVID-19 and Cancer**  
 NE Sharpless

- COVID-19-related reductions in cancer screening and treatment over the next decade could result in 10,000 excess deaths from breast and colorectal cancer
- Beyond clinical care, the COVID-19 pandemic has caused an unprecedented disruption throughout the cancer research community, shuttering many labs and slowing down cancer clinical trial operations

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**People at Increased Risk for Severe COVID-19 Illness**

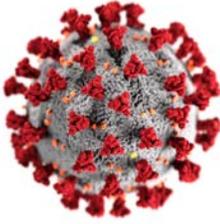
- Older adults
- People of any age with certain underlying medical conditions

Source: CDC, 6/25/2020

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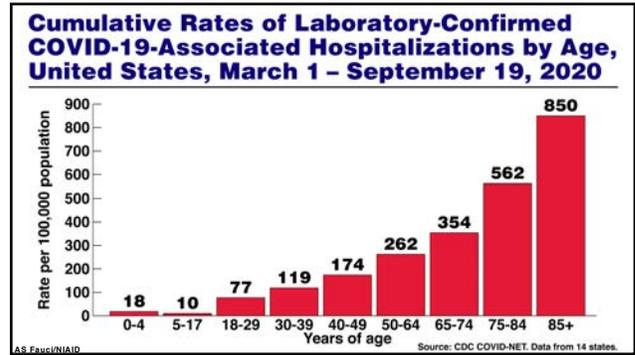
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AS Fauci/NIID Source: CDC, 6/25/2020

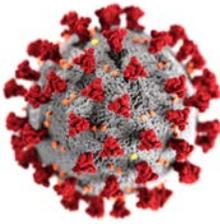
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### People at Increased Risk for Severe COVID-19 Illness

- Older adults
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AS Fauci/NIID Source: CDC, 6/25/2020

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

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

AS Fauci/NIID Source: CDC, 7/28/2020

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

■ Asthma	■ Inherited metabolic disorders
■ Other chronic lung diseases	■ Neurologic conditions
■ Cerebrovascular disease	■ Liver disease
■ Diabetes, type 1	■ Pregnancy
■ Hypertension	■ Smoking
■ Immunocompromised state from bone marrow transplant, immune deficiencies, HIV, use of corticosteroids or other immunosuppressive medications	■ Thalassemia

AS Fauci/NIID Source: CDC, 7/28/2020

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May 11, 2020

# JAMA

The Journal of the American Medical Association

**Viewpoint**

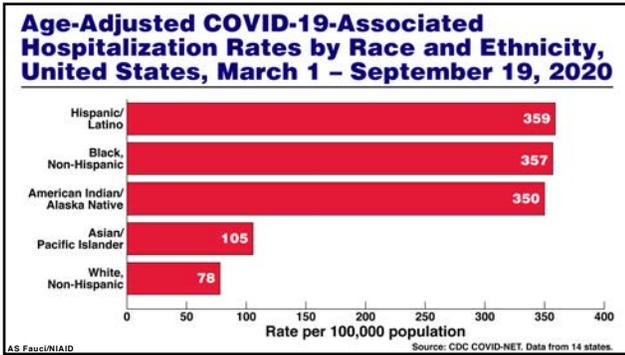
## COVID-19 and Racial/Ethnic Disparities

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.”*

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# Therapeutics

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NIH 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

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### 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

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The New England Journal of Medicine  
published online May 22, 2020

### Remdesivir for the Treatment of Covid-19 – Preliminary Report

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

- Patients who received remdesivir had a 32% faster time to recovery than those who received placebo (p<0.001)
- Results also suggested a survival benefit
- N=1,063 patients from 10 countries in U.S., Europe, Asia

54

The New England Journal of Medicine  
 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

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**Monoclonal Antibody Studies in COVID-19**

- Outpatient
- Inpatient
- Family prophylaxis
- Nursing home prophylaxis

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**Vaccines**

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Science  
 May 29, 2020

**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.

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**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
Protein subunit		Ongoing	--
		Ongoing	Ongoing
		Ongoing	--

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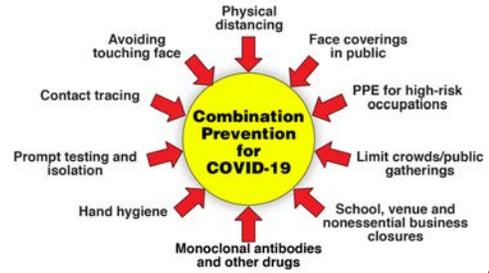
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# When will we return to normal?

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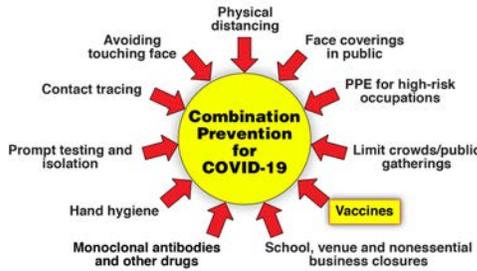
## Prevention of COVID-19 in the Absence of a Vaccine



AS Fauci/NIH/ID

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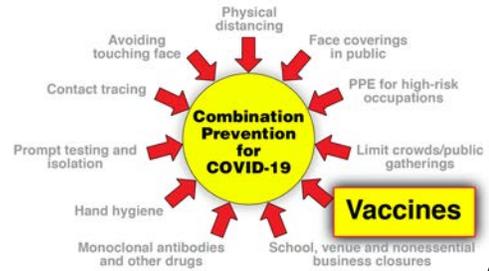
## Prevention of COVID-19 with a Moderately Effective Vaccine and Moderate Uptake



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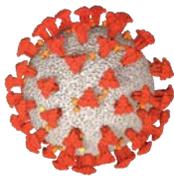
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## Prevention of COVID-19 with a Highly Effective Vaccine and Widespread Uptake



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# COVID-19 Prevention Network

[coronaviruspreventionnetwork.org](https://coronaviruspreventionnetwork.org)

AS Fauci/NIH/ID

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