

COVID-19: Public Health and Scientific Challenges

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1

Disclosures

- No relevant financial relationships with commercial interests

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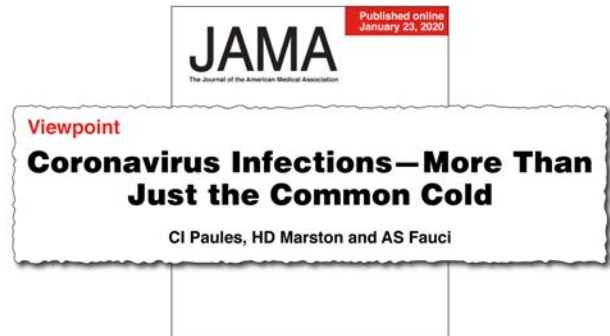
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Objectives

- Discuss the mechanisms and risk factors for SARS-CoV-2 transmission, as well as fundamental principles to prevent transmission.
- Describe the clinical presentation of COVID-19 and risk factors for severe illness.
- Discuss the current COVID-19 therapeutics landscape, including agents under investigation and those under EUA/approved by the FDA.
- Describe the current state of COVID-19 vaccine development and deployment in the United States.

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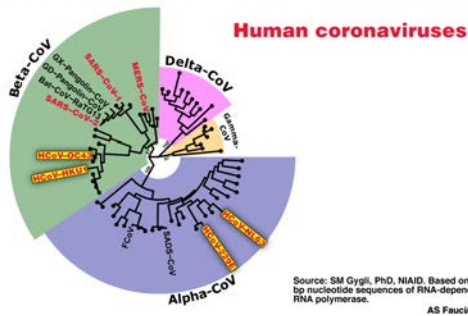
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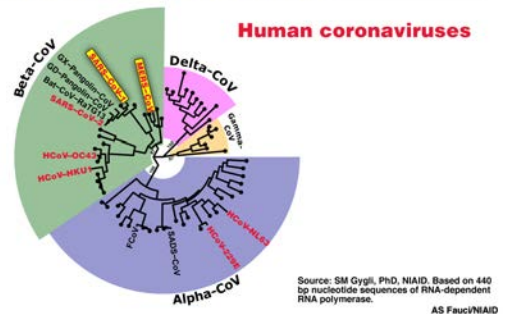
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Coronavirus Phylogenetic Tree



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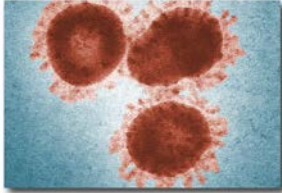
Coronavirus Phylogenetic Tree



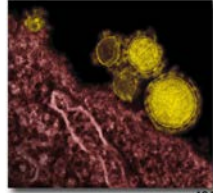
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Severe Human Coronavirus Disease: Past as Prologue

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

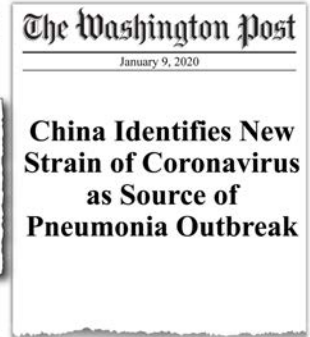


Middle East Respiratory Syndrome (MERS) (2012–present)



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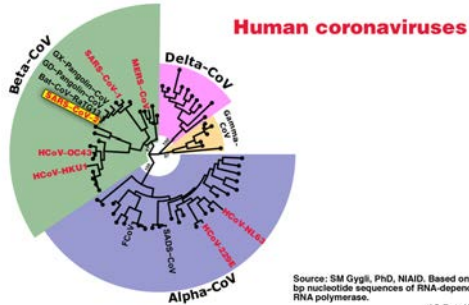
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8

Coronavirus Phylogenetic Tree

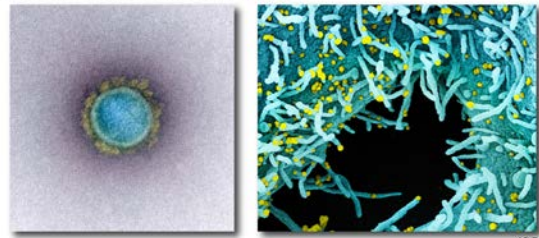


Source: SM Gygi, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase. AS Fauci/NIAD

9

Coronavirus Disease 2019 (COVID-19)

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



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10

COVID-19 Globally

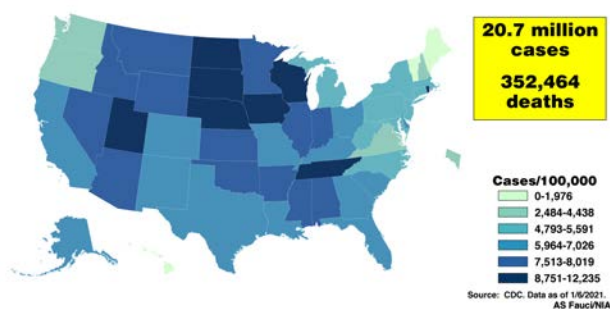


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Sources: NPR.org; Worldometer. Data as of 1/6/2021

11

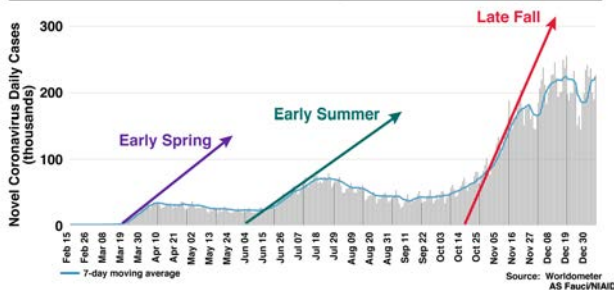
COVID-19 in the United States



Source: CDC. Data as of 1/6/2021. AS Fauci/NIAD

12

Daily New COVID-19 Cases Reported in the United States – Slopes of 3 Surges



13

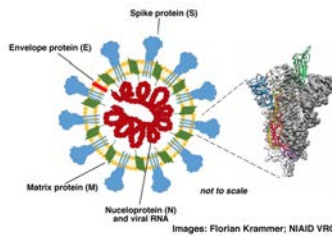
Virology

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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



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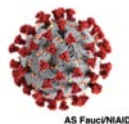
Transmission

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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



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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

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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

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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

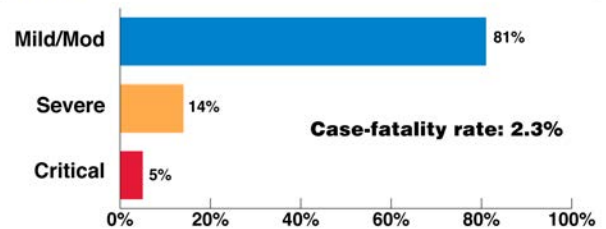
Other non-specific symptoms reported

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

Source: WHO, 5/2020
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21

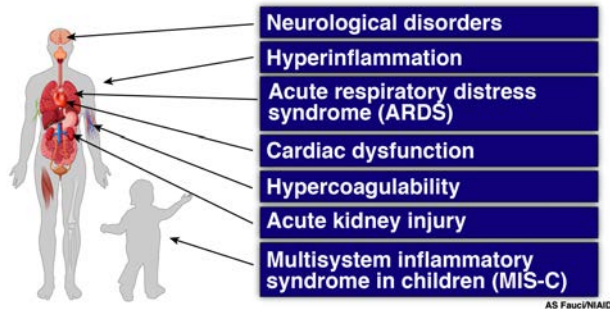
Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China



Source: Z Wu & JM McGoogan, JAMA 323:1239, 2020
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Manifestations of Severe COVID-19

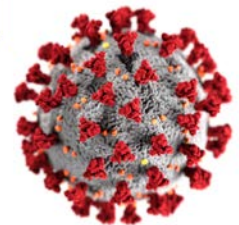


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People at Increased Risk for Severe COVID-19 Illness

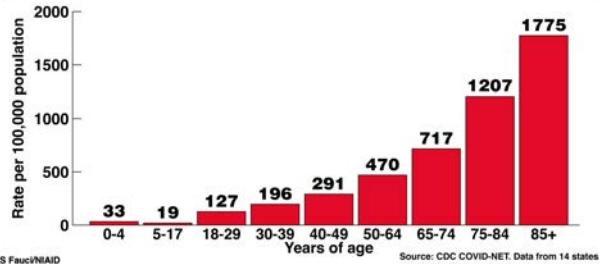
- Older adults
- People of any age with certain underlying medical conditions



Source: CDC, 6/25/2020
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24

Cumulative Rates of Laboratory-Confirmed COVID-19-Associated Hospitalizations by Age, United States, March 1 – December 26, 2020



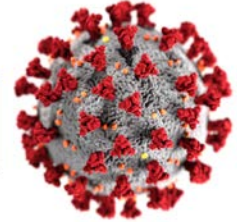
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People at Increased Risk for Severe COVID-19 Illness

Older adults

People of any age with certain underlying medical conditions



Source: CDC, 6/25/2020 AS Fauc/NIAID

26

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

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

Source: CDC, 12/29/2020 AS Fauc/NIAID

27

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)
- Pulmonary fibrosis
- Thalassemia

Source: CDC, 11/2/2020 AS Fauc/NIAID

28

May 11, 2020

JAMA
The Journal of the American Medical Association

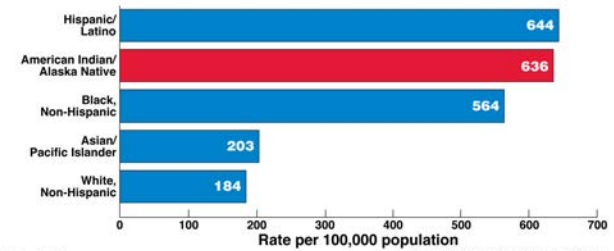
Viewpoint
COVID-19 and Racial/Ethnic Disparities
MW Hooper, AM Nápoles and EJ Pérez-Stable

“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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29

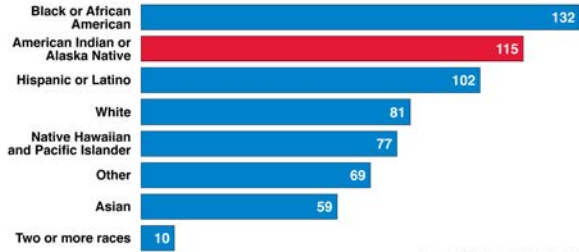
Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – December 26, 2020



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30

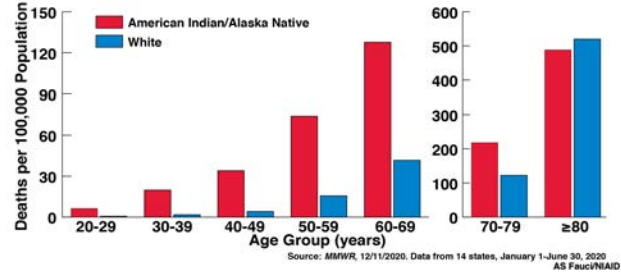
COVID-19 Deaths per 100,000 People by Race or Ethnicity, United States



Source: COVID Tracking Project, 1/8/2021
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31

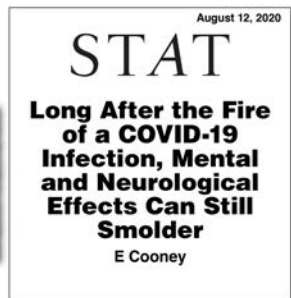
Rates of COVID-19-Associated Deaths Among American Indian/Alaska Native and Non-Hispanic White Persons Aged ≥20 Years, United States



Source: MMWR, 12/11/2020. Data from 14 states, January 1-June 30, 2020
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Post-COVID-19 Syndrome



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33

Therapeutics

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34

Selected Therapeutics for COVID-19

Therapeutics for early/moderate disease

- Remdesivir – FDA approved
- Monoclonal antibodies – EUA
 - Bamlanivimab; casirivimab+imdevimab
- Other antivirals – clinical trials
- Convalescent plasma – EUA
- Hyperimmune globulin – clinical trials

Therapies for moderate/advanced disease

- Baricitinib+remdesivir – EUA
- Immunomodulators – clinical trials
- Dexamethasone – standard of care

Adjunct therapies

- Anticoagulants – clinical trials



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Vaccines

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■ 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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37

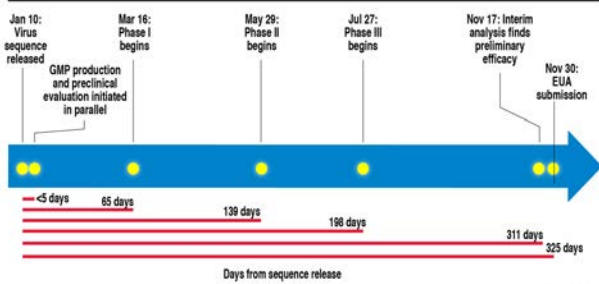
Selected COVID-19 Vaccine Candidates

Platform	Developer	Phase 1/2	Phase 2/3
Nucleic acid	moderna	Enrolled	Enrolled
	BIONTECH Pfizer	Enrolled	Enrolled
Viral vector	UNIVERSITY OF OXFORD AstraZeneca	Enrolled	Ongoing
	Janssen Johnson & Johnson	Enrolled	Enrolled
Protein subunit	NOVAVAX <small>Creating Tomorrow's Vaccines Today</small>	Enrolled	Ongoing

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38

SARS-CoV-2 Vaccine Development: mRNA-1273



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39

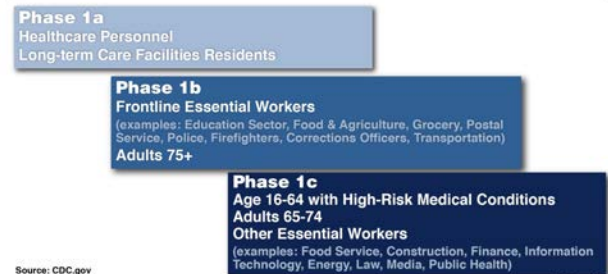


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40

Vaccine Distribution

CDC Recommendations for Vaccine Prioritization- Phase 1



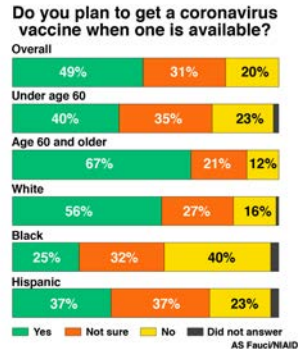
Source: CDC.gov

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41

42



43



44

Collins, Fauci, Azar Receive Moderna COVID-19 Vaccine at NIH, 12/22/2020



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45



Preventing the Spread of SARS-CoV-2 With Masks and Other "Low-tech" Interventions

AM Lerner, GK Folkers and AS Fauci

"While results of phase 3 trials for multiple candidate vaccines are on the near horizon, "low-tech" tools to prevent the spread of SARS-CoV-2 are essential, and it must be emphasized that these interventions will still be needed after a vaccine is initially available."

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46



Universal Coronavirus Vaccines: The Time to Start Is Now

LT Giurgea, A Han and MJ Memoli

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47