## COVID-19 Update

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National Institutes of Health

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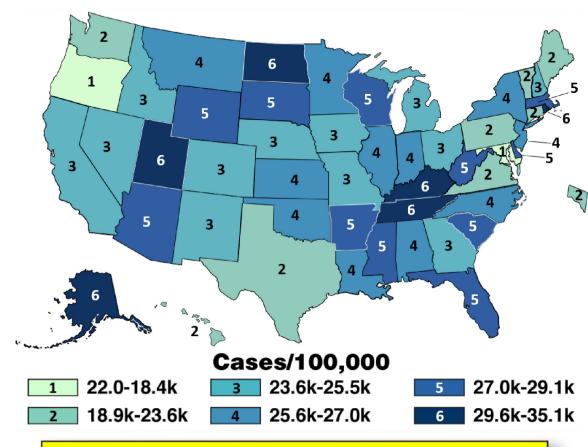
#### **The COVID-19 Pandemic**

#### **Globally**



Reported cases: 526.6 million Reported deaths: 6,287,117

#### **United States**

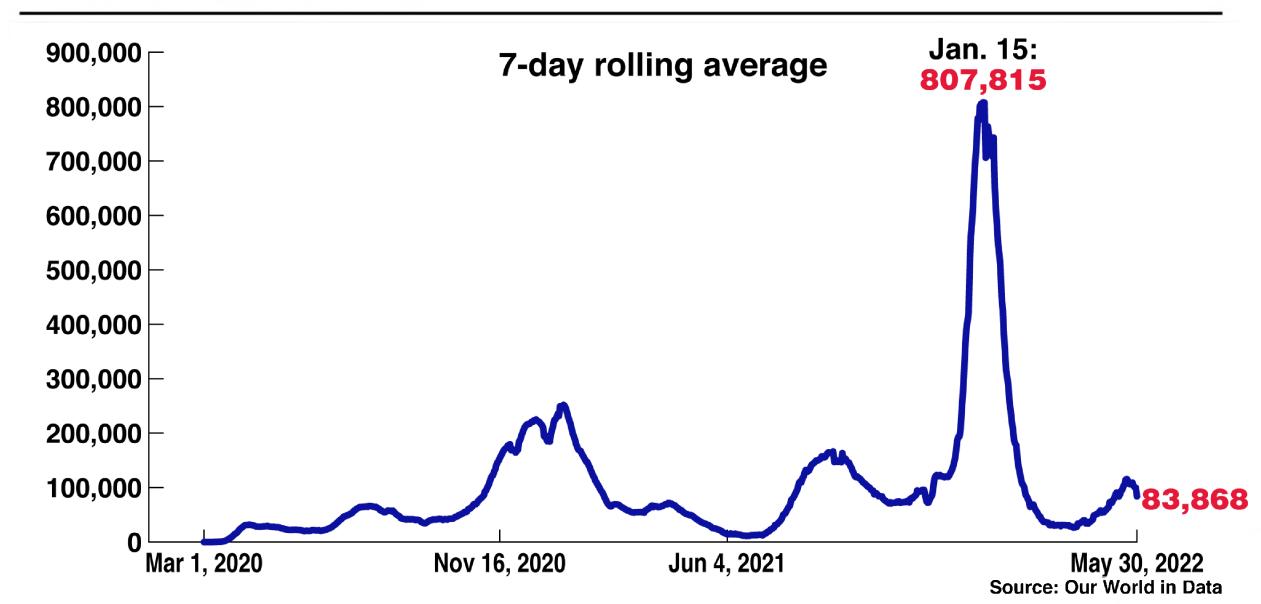


Reported cases: 84.0 million Reported deaths: 1,002,070

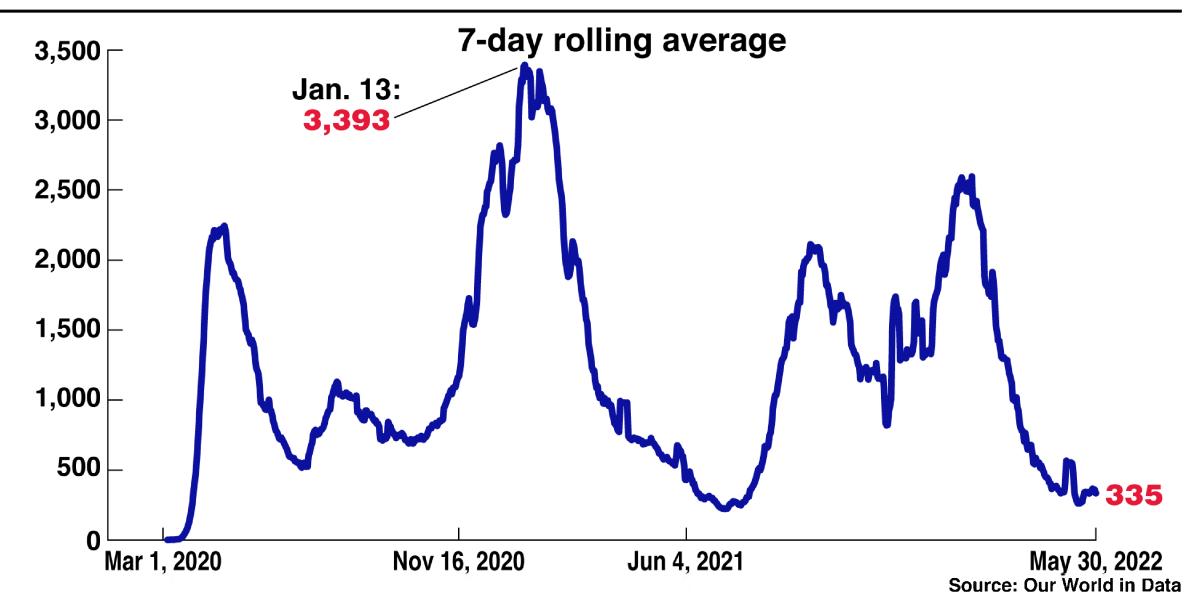
Sources: WHO: KFF. Data as of 5/31/2022.

Source: CDC. Data as of 5/31/2022.

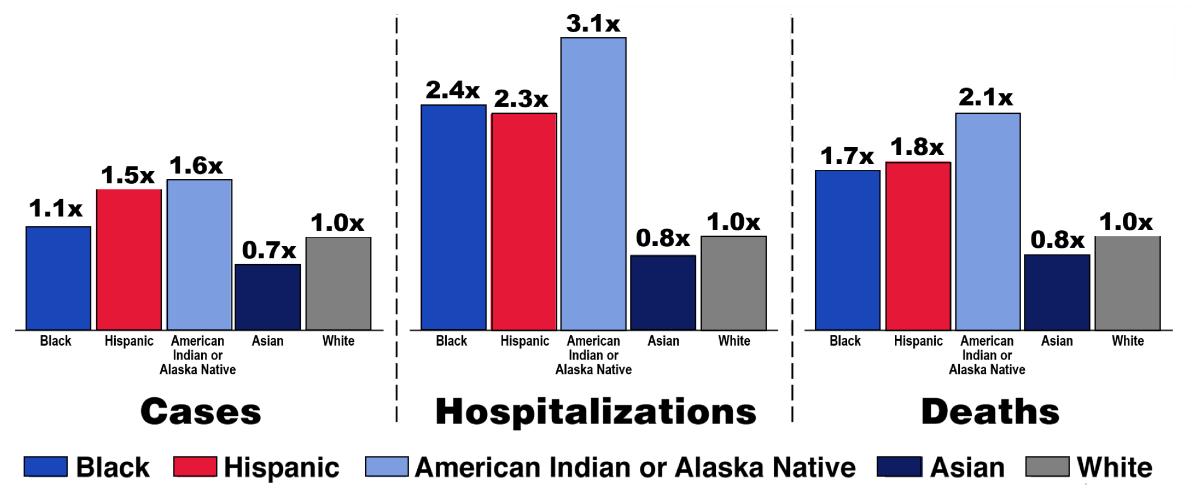
## Daily New Confirmed COVID-19 Cases, United States



## Daily New Confirmed COVID-19 Deaths, United States



## Age-Adjusted Risk of COVID-19 Infection, Hospitalization, and Death, Compared to White People in the United States



Source: CDC, 4/29/2022.

### COVID-19 Among Children (<18 Years) in the United States

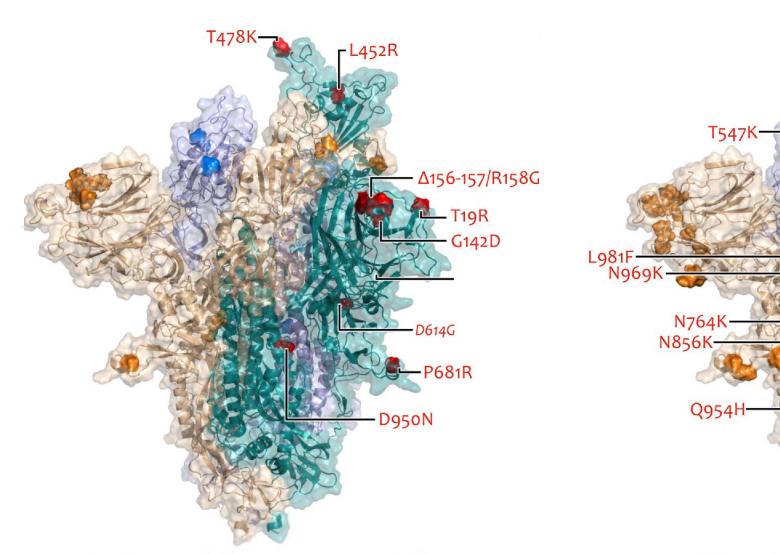
- Reported cases: 15,005,523
- **■** Hospital admissions: 126,809\*
- Multisystem Inflammatory Syndrome in Children (MISC-C) cases: 8,210
- **Deaths: 1,527**

#### WHO SARS-CoV-2 Variants of Concern (VOCs)

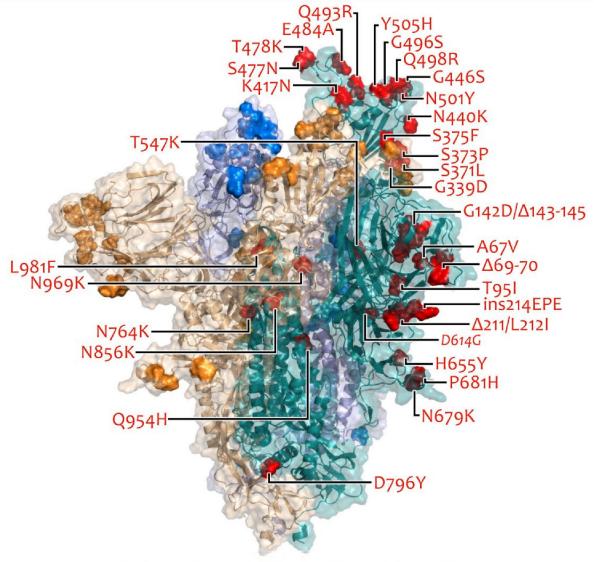
WHO name	Earliest documented samples			
Alpha	9/2020			
Beta	5/2020			
Gamma	11/2020			
Delta	10/2020			
Omicron	11/2021			

**Source: WHO** 

#### **SARS-CoV-2 Spike Protein Mutations**



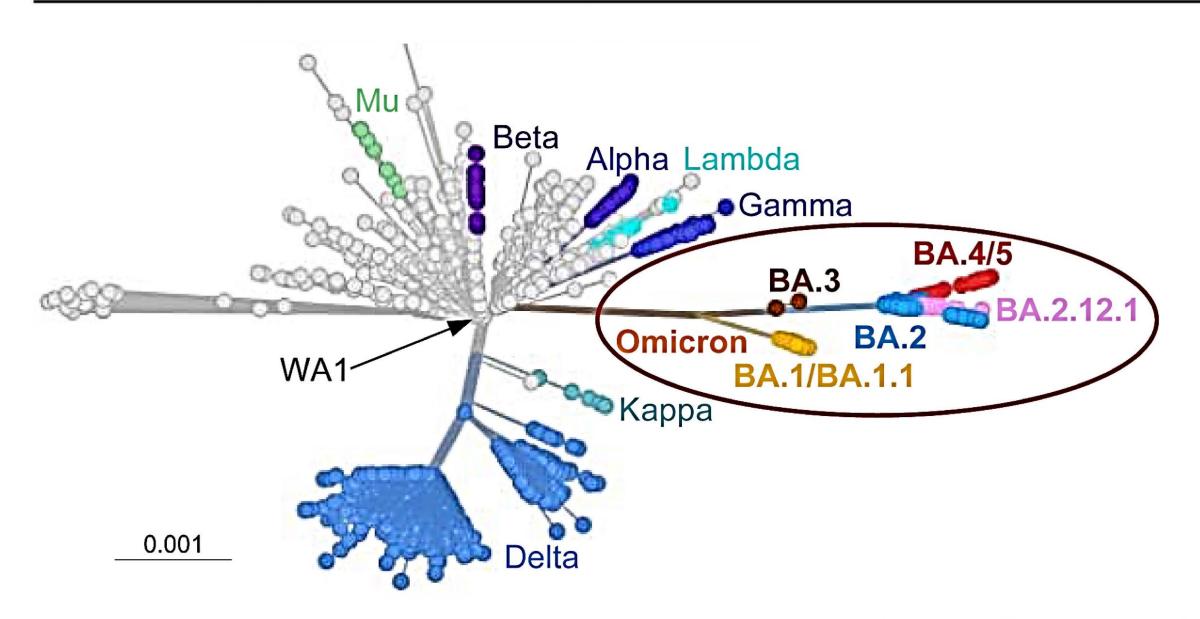
Delta (B.1.617.2)



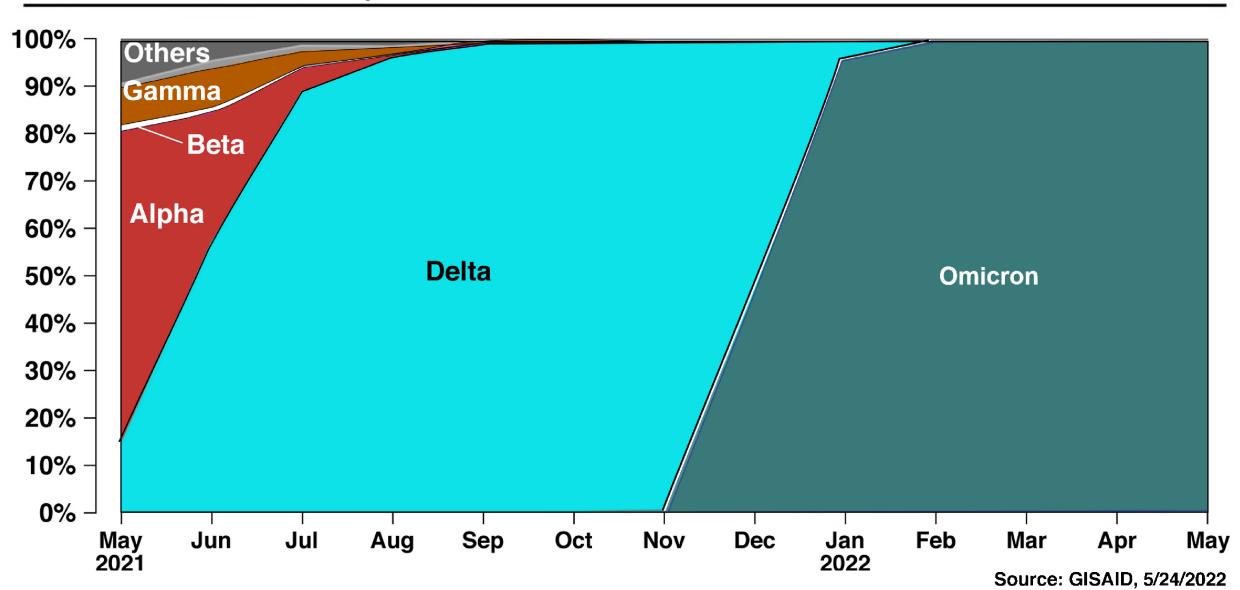
**Omicron (BA.1)** 

Source: COG-UK/Mutation Explorer, May 2022

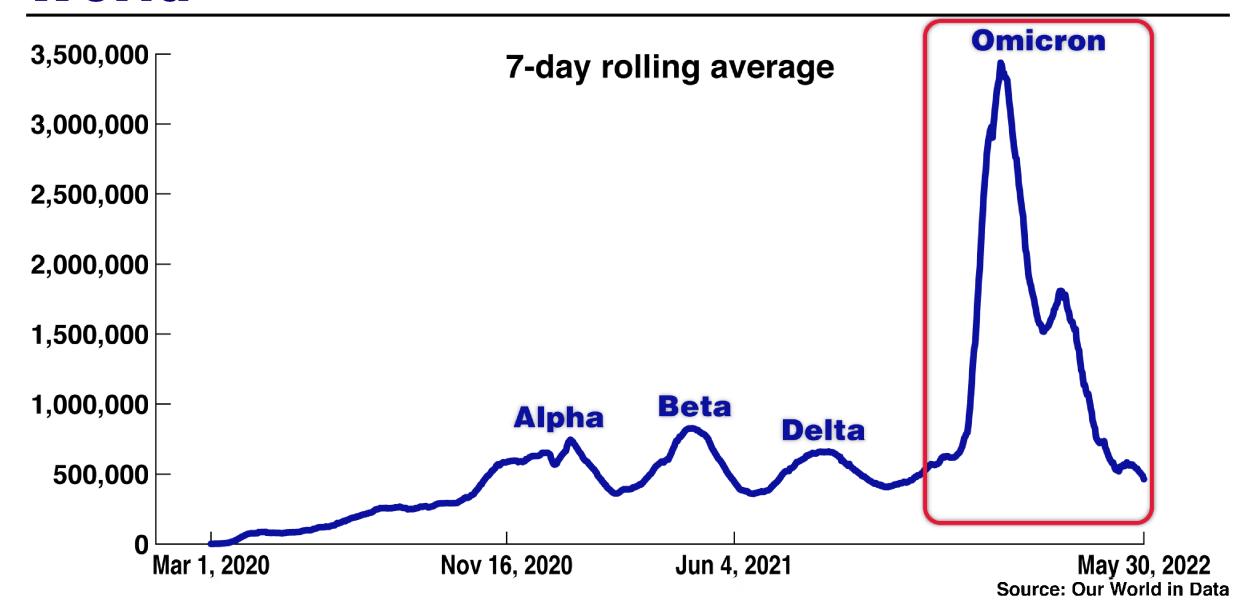
#### **SARS-CoV-2 "Family Tree"**



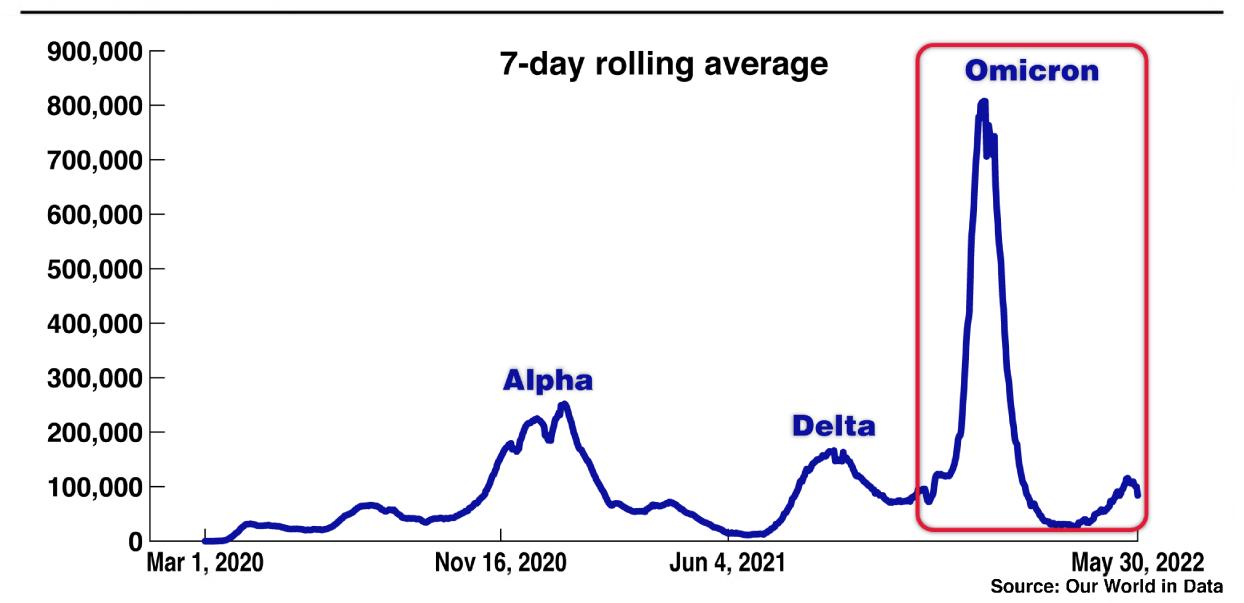
## Timecourse of SARS-CoV-2 Variant Distribution, Global



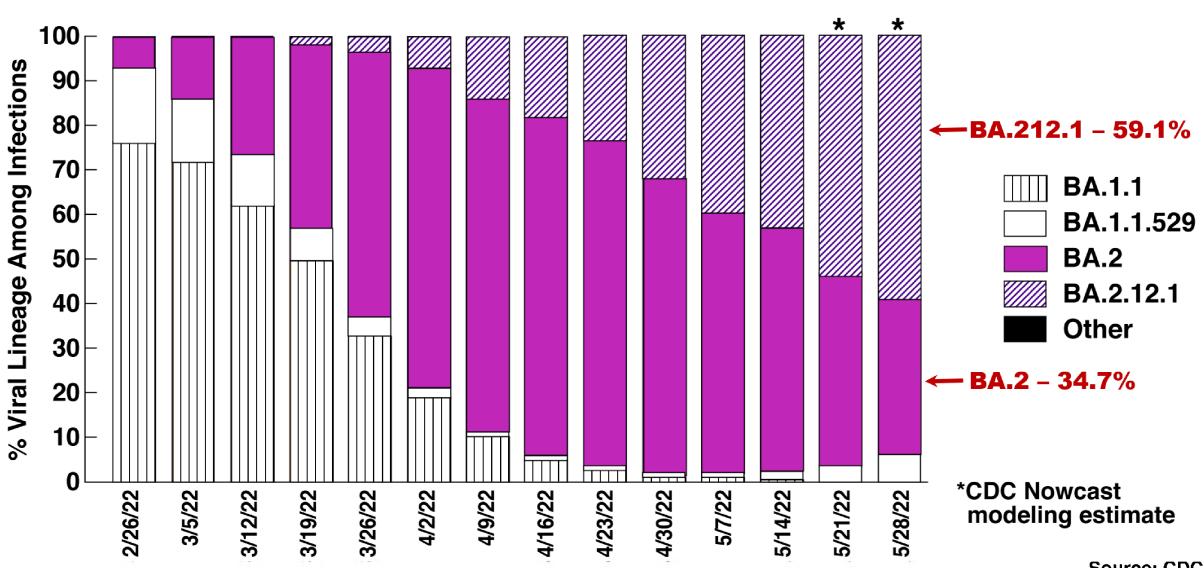
## Daily New Confirmed COVID-19 Cases, World



## Daily New Confirmed COVID-19 Cases, United States



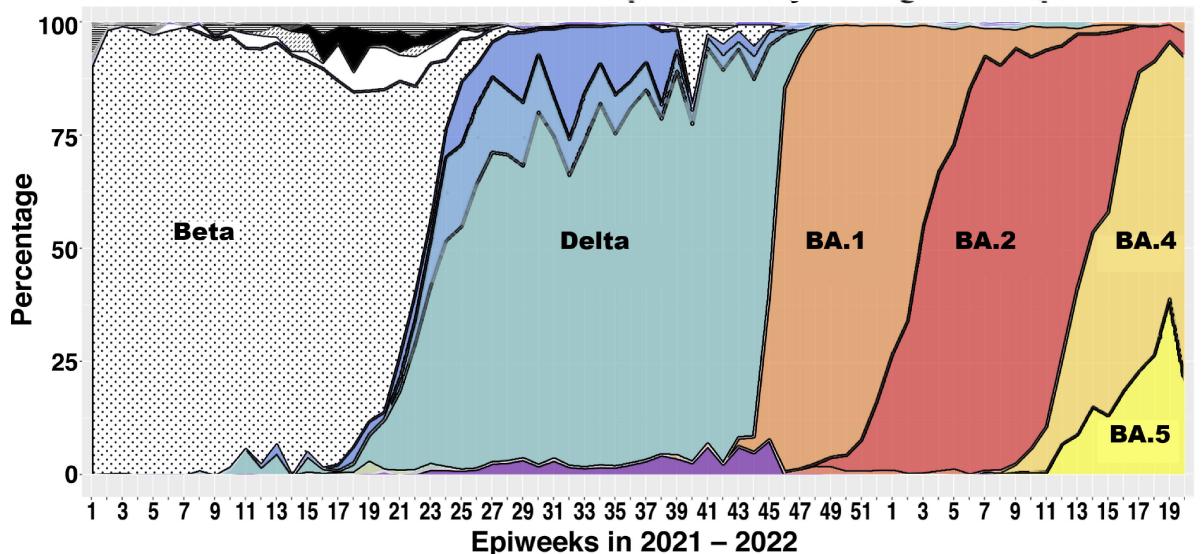
#### SARS-CoV-2 Variant Proportions, United States, Feb. 20 - May 28, 2022



Source: CDC

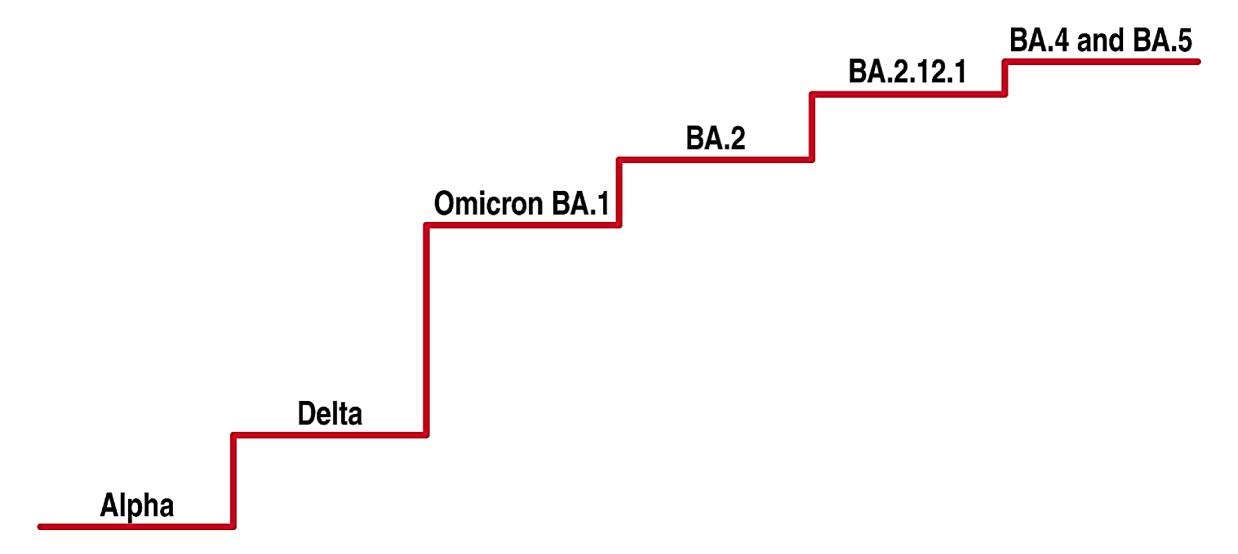
#### South Africa: BA.4, BA.5 Now Dominant

Prevalence of SARS-CoV-2 sequences by lineage and epiweek



Source: Network for Genomic Surveillance in South Africa (NGS-SA), May 27, 2022

## **SARS-CoV-2 Variants: Ladder of Transmissibility**



Waning immunity to prior infection and/or vaccination

Increased transmissibility of new variants

Relaxation of mitigations (masking, indoor congregating)

Increase in COVID-19 Cases

## Medical Management of the SARS-CoV-2-Infected Patient

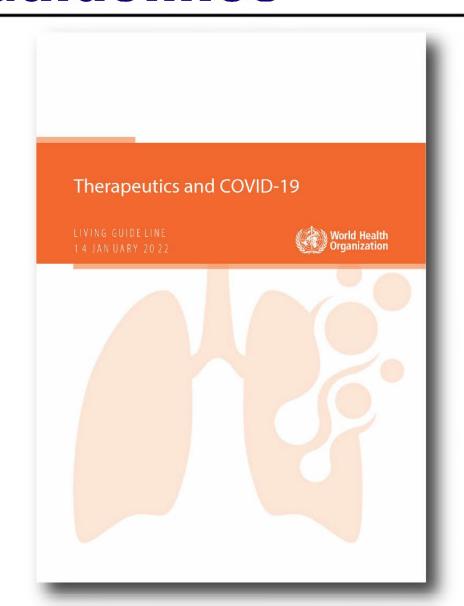
### Medical Management of the SARS-CoV-2-Infected Patient

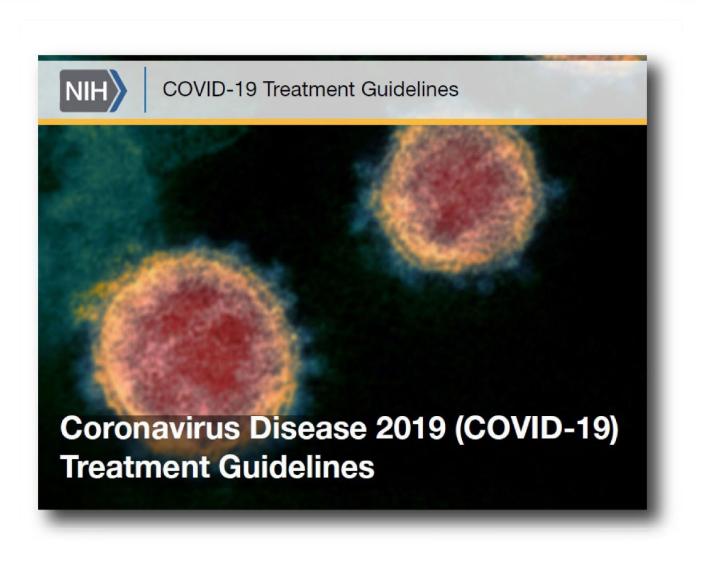
Control of symptoms

End-organ support

Antivirals and immunomodulators

## **COVID-19 Treatment: WHO and NIH Guidelines**





#### **Key COVID-19 Therapeutics, June 2022**

#### **Targeting the virus**

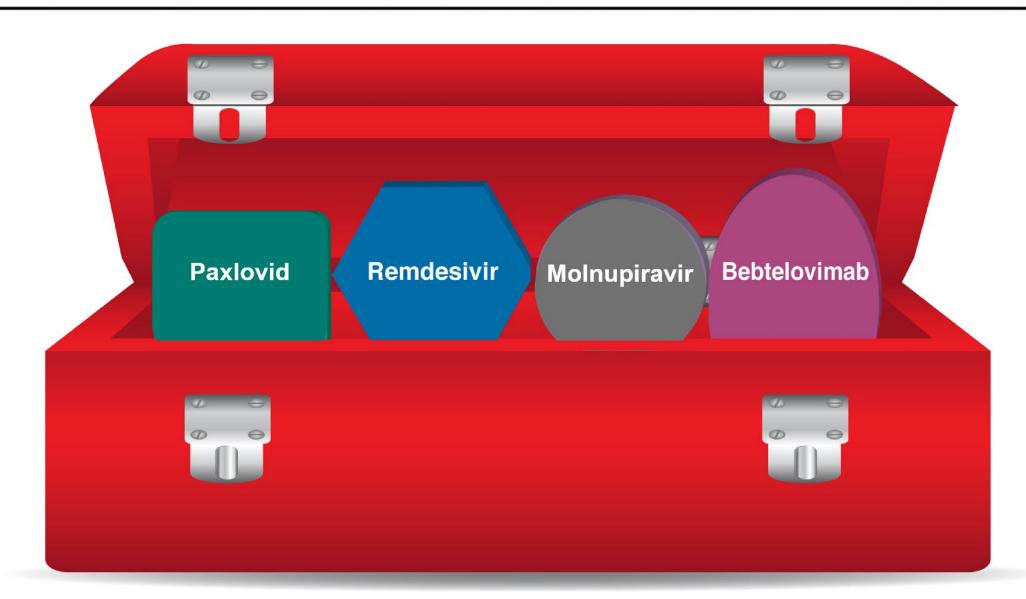
- Remdesivir FDA approved
- Paxlovid EUA
- Molnupiravir EUA
- Anti-SARS-CoV-2 monoclonal antibodies
  - Bebtelovimab (EUA)



#### **Moderating host responses**

- Dexamethasone recommended for hospitalized patients on oxygen
- Tocilizumab (EUA) or baricitinib (FDA approved) recommended for certain patients on dexamethasone
- Other immunomodulators clinical trials
- Anticoagulants recommended for certain hospitalized patients

### Therapeutic "Toolkit" for Non-Hospitalized Patients with COVID-19 in the Omicron Era





# Fact Sheet: Biden Administration Launches Nationwide Test-to-Treat Initiative Ensuring Rapid 'On the Spot' Access to Lifesaving COVID Treatments

More info: <a href="mailto:aspr.hhs.gov/COVID-19/Therapeutics">aspr.hhs.gov/COVID-19/Therapeutics</a>

#### COVID-19 Vaccines

## **COVID-19 Vaccines in U.S. Government Development Portfolio**

Platform	Immunoge	en	Developer	Status
Nucleic Acid (mRNA)	S2P	linn.	moderna	■ BLA (Age 18+)
	S2P	mul	BIONTECH Pfizer	■ BLA (Age 16+); EUA (Age 5-15)
Adenovirus Vector	S2P		Johnson-Johnson	■ EUA (Age 18+)
	Wild-type spike	Stood Proces	AstraZeneca	EUA/BLATBD
Recombinant Protein and Adjuvant	S2P		gsk SANOFI 🕠	EUA request 2/2022
	S2P	+	NOVAVAX Creating Tomorrow's Vaccines Today	EUA request 1/2022

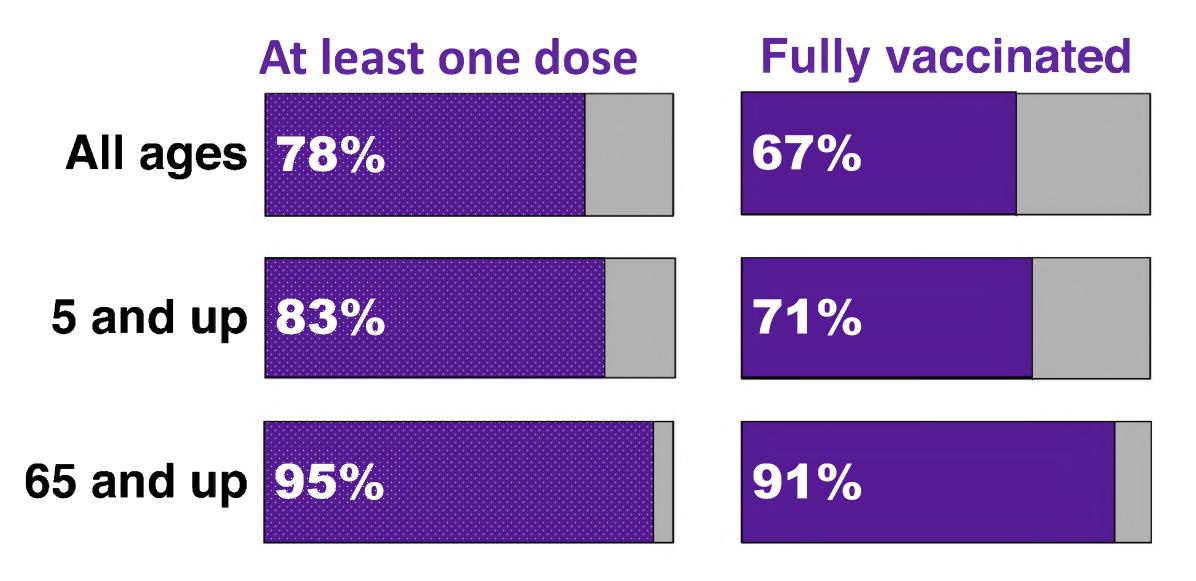


## Estimates of COVID-19-Attributable Deaths, Hospitalizations, Infections, and Health Care Costs Averted by the U.S. Vaccination Program, 12/12/2020 – 3/31/2022

- **Deaths: 2,265,222**
- Hospitalizations: 17,003,960
- Infections: 66,159,093
- **■** Health care costs: \$899.4 billion

Source: EC Schneider, A Galvani et al. Commonwealth Fund analysis, Apr. 8, 2022.

#### **Vaccination Profile in the United States**

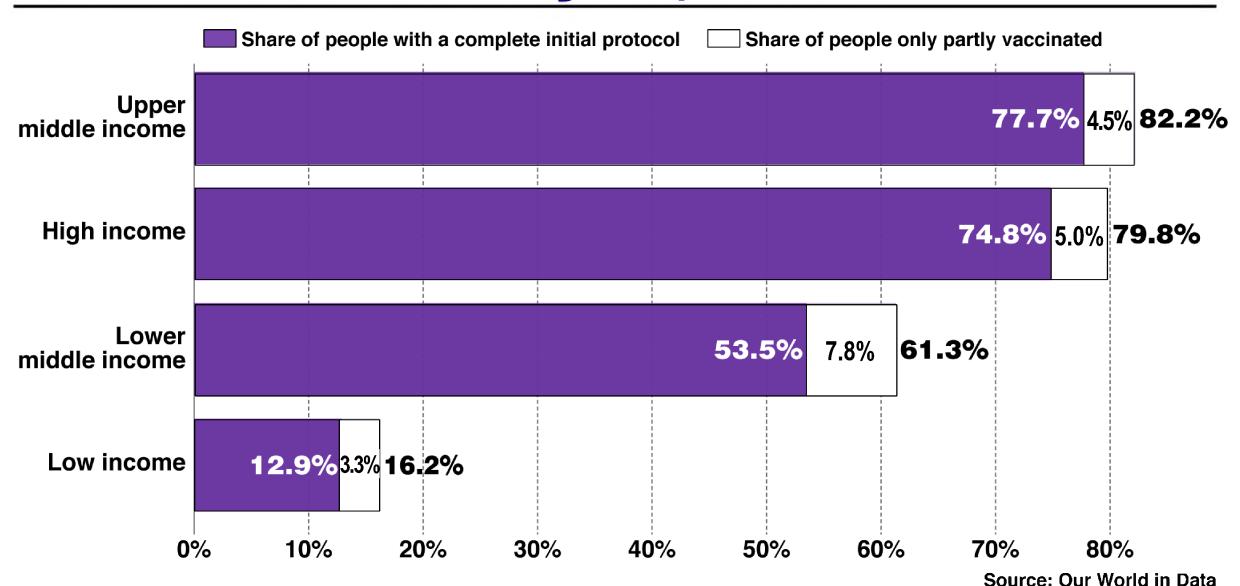


Source: CDC COVID Data tracker, 5/31/2022.

## FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC): Upcoming Meetings on COVID-19 Vaccines for Children

- June 14, 2022 Discussion of Moderna's Emergency Use Authorization (EUA) request for children 6 years through 17 years of age
- June 15, 2022 Discussion of Moderna's EUA request for children 6 months through 5 years of age and Pfizer-BioNTech's EUA request for children 6 months through 4 years of age

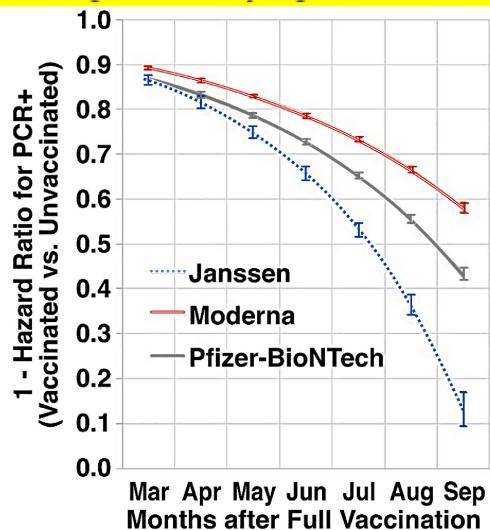
## Share of People Vaccinated Against COVID-19 as of May 30, 2022



## Booster Shots for SARS-CoV-2 Vaccines

## Waning Immunity after COVID-19 Vaccination Among U.S. Veterans, 2021

#### Waning immunity against infection

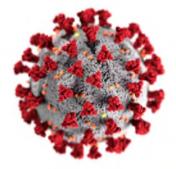


- Vaccine effectiveness (VE) against SARS-CoV-2 infection declined from 87.9% to 48.1% from Feb. to Oct., 2021
- From July to October 2021 (Delta predominant period), VE against COVID-19 death:
  - age <65 years: 73.0% for Janssen, 81.5% for Moderna, 84.3% for Pfizer-BioNTech
  - age ≥65 years: 52.2% for Janssen, 75.5% for Moderna, 70.1% for Pfizer-BioNTech

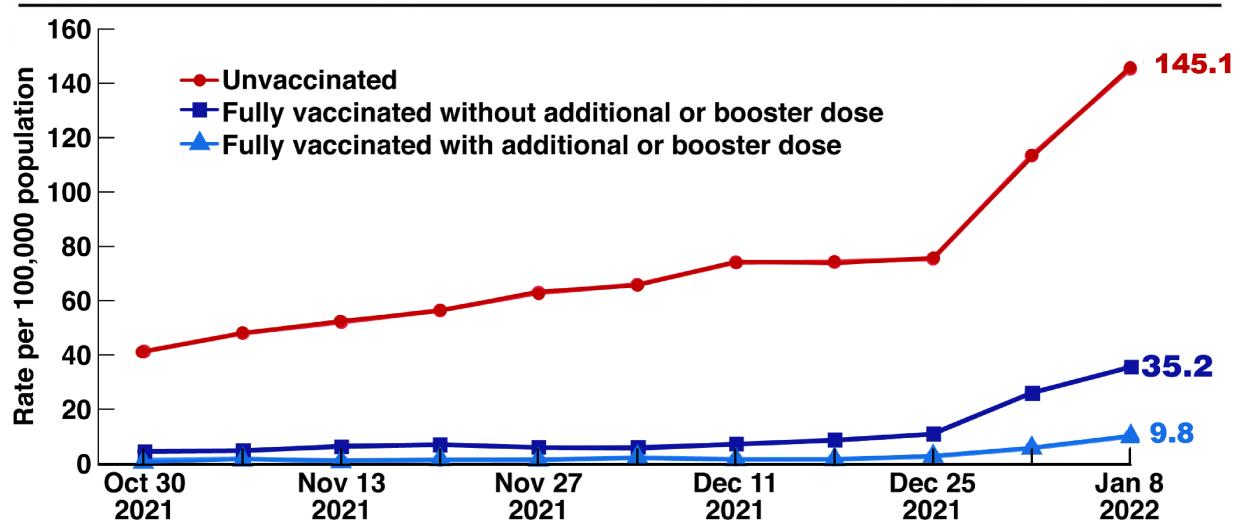
Source: BA Cohn et al. Science, 11/4/2021.

Numerous studies of the real-world effectiveness COVID-19 vaccines show that booster doses reconstitute waning immune protection for at least several months

The effect of booster doses is most pronounced against severe disease, hospitalization and death



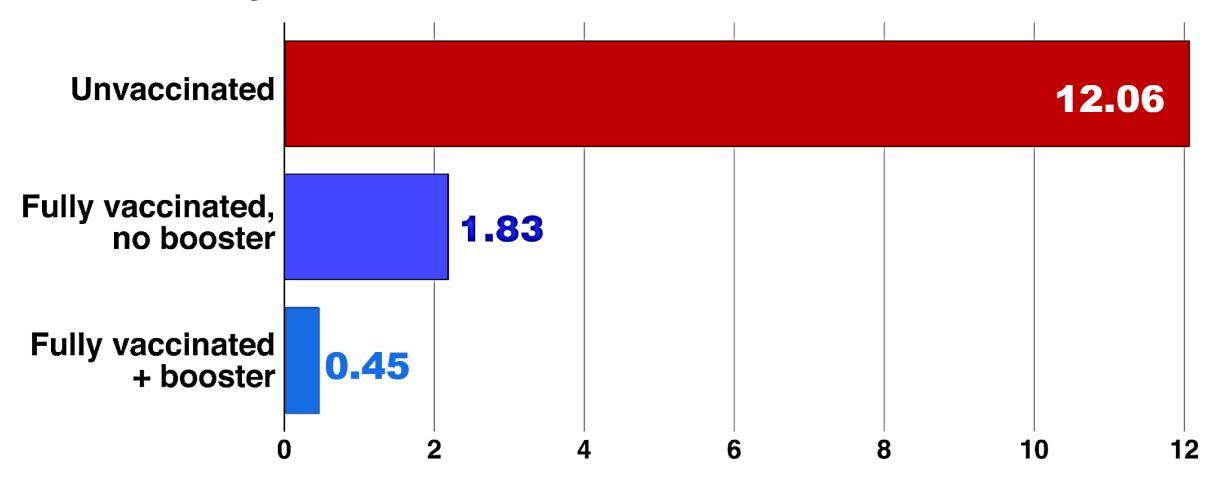
## Age-Adjusted Rates of COVID-19-Associated Hospitalizations by Vaccination Status in Adults Ages ≥18 Years, October 2021–January 2022



Source: CDC

#### **COVID-19 Vaccination and Boosters Work!**

### COVID-19 weekly death rate/100,000 population by vaccination status, USA, 1/2022



Sources: CDC; Our World in Data

## Impact of COVID-19 Booster Doses in the United States

#### In March 2022 (Omicron variant predominant):

- Unvaccinated people aged 18+ years had a 5x increased risk of COVID-19-associated hospitalization compared to people vaccinated with a primary series and a booster dose
- Unvaccinated people aged 12+ years had a 17x increased risk of dying from COVID-19 compared to people vaccinated with a primary series and a booster dose

Source: covid.cdc.gov/covid-data-tracker, May 2022

# FDA Expands Eligibility for Pfizer-BioNTech COVID-19 Vaccine Booster Dose to Children 5 through 11 Years

## Considerations for a Second COVID-19 Booster Shot

## Waning Effectiveness of 1st COVID-19 Vaccine Booster Restored by 2nd Booster Dose

- First booster doses restore the waning vaccine effectiveness of a primary vaccination series, including against severe disease and hospitalization associated with the Omicron variant
- However, the effectiveness of a first booster dose wanes over time
- Growing evidence indicates that a second COVID-19 vaccine booster dose can restore vaccine effectiveness for certain populations, at least in short term



## Protection by a Fourth Dose of BNT162b2 against Omicron in Israel

YM Bar-On, R Milo et al.

- >1.2 million people aged 60+ years and eligible for fourth dose, Israeli Ministry of Health database
- An additional booster dose of Pfizer/BioNTech vaccine at 4 months after a 1st booster resulted in a 3.5-fold lower rate of severe illness
- Protection against severe illness did not wane during 6 weeks of follow up

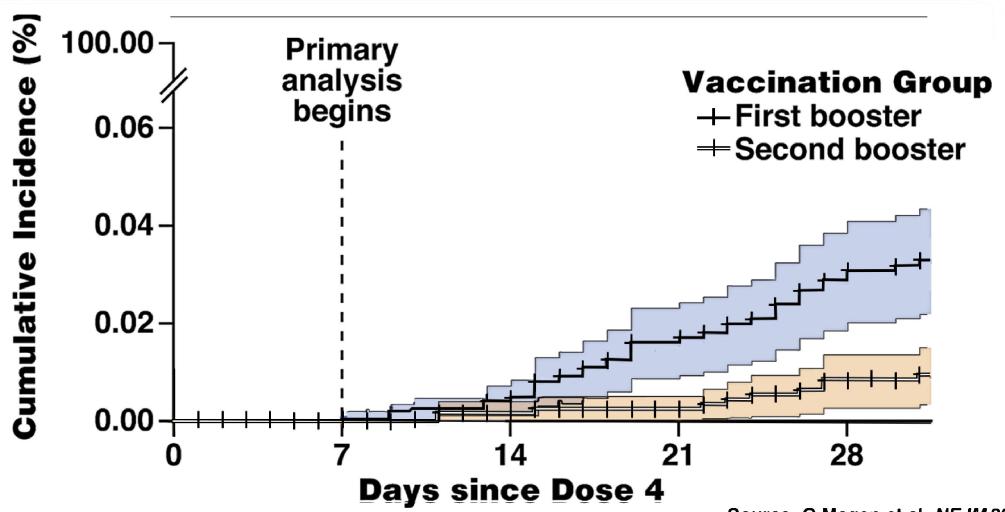


## Fourth Dose of BNT162b2 mRNA COVID-19 Vaccine in a Nationwide Setting

O Magen, N Dagan et al.

- 365,000 members of Clalit Health Services aged 60+ years
- Relative effectiveness of a 4th vaccine dose after 14-30 days compared to a 3rd third dose given at least 4 months earlier
  - + 61% vs. symptomatic COVID-19
  - + 72% vs. COVID-19-related hospitalization
  - +64% vs. severe COVID-19
  - + 76% vs. COVID-19-related death

## Cumulative COVID-19 Mortality Rates in Israeli Adults 60+ Years Receiving 1 or 2 Booster Doses of BNT162b2 Vaccine



Source: O Magen et al. NEJM 386:1603, 2022



For Immediate Release

March 29, 2022





For Immediate Release

May 19, 2022

# CDC Strengthens Recommendations and Expands Eligibility for COVID-19 Booster Shots

### **COVID-19 mRNA Vaccine Dose Eligibility, Age**

		0-4	5-11	12-17	18-49	50+
Number of doses	First dose	X				
	Second dose	X				
	Third dose/ booster	X			<b>√</b>	
	Fourth dose/ booster	X	X	*	*	

**Source: CDC** 



#### **News Release**

#### NIH Begins Clinical Trial Evaluating Second COVID-19 Booster Shots in Adults

Study Includes Multiple Variant Vaccines

- COVID-19 Variant Immunologic Landscape (COVAIL) trial
- Assessing different 4th dose vaccine regimens prototype and variant vaccines alone and in combinations—to see if they broaden immunity in adults who have already had one booster dose



#### The Future



Published online December 15, 2021

## Perspective Universal Coronavirus Vaccines — An Urgent Need

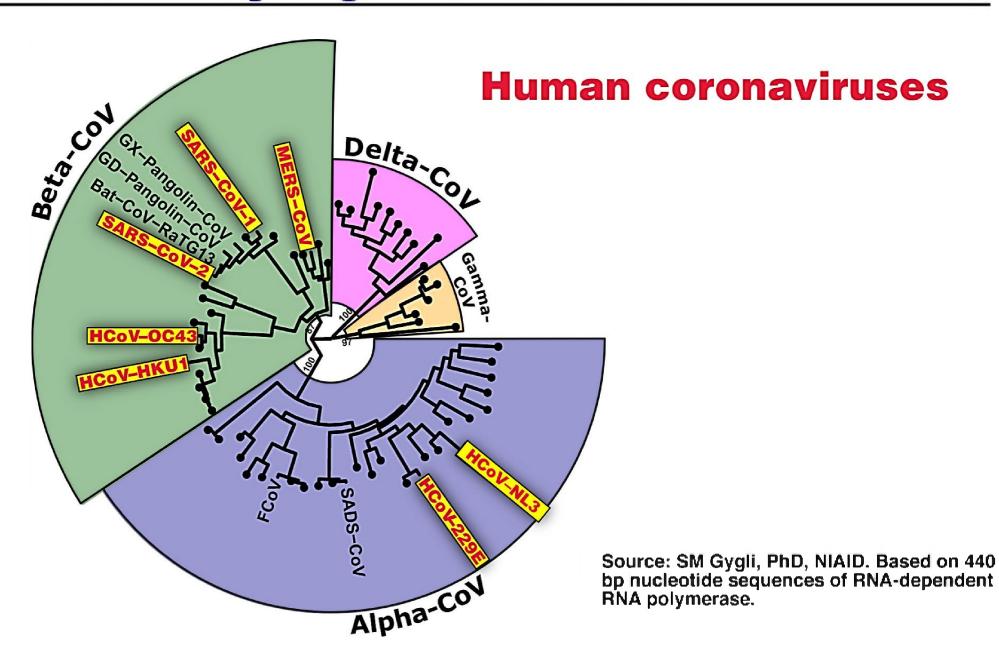
David M. Morens, M.D., Jeffery K. Taubenberger, M.D., Ph.D., and Anthony S. Fauci, M.D.

- In the past 20 years, three coronaviruses have caused major disease outbreaks – SARS, MERS, COVID-19
- Since September 2020, five SARS-CoV-2 Variants of Concern have emerged – alpha, beta, gamma, delta, omicron
- Innovative approaches are needed to induce broad and durable protection against coronaviruses, known and unknown



**Pan-Coronavirus Vaccines** 

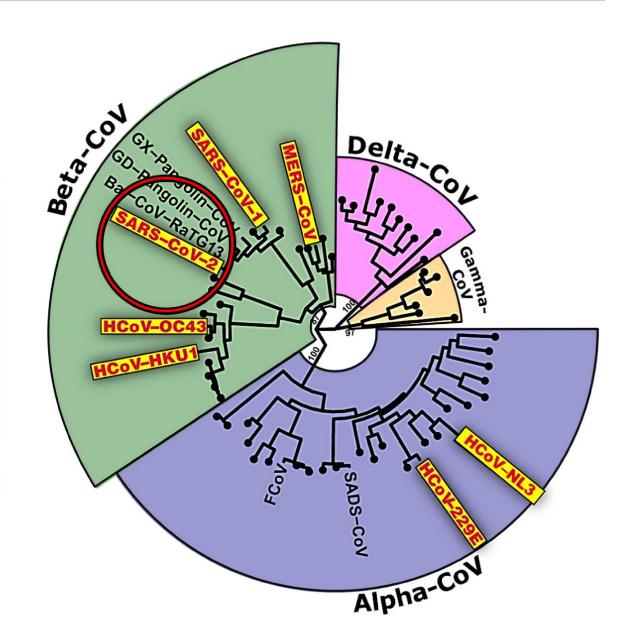
#### **Coronavirus Phylogenetic Tree**



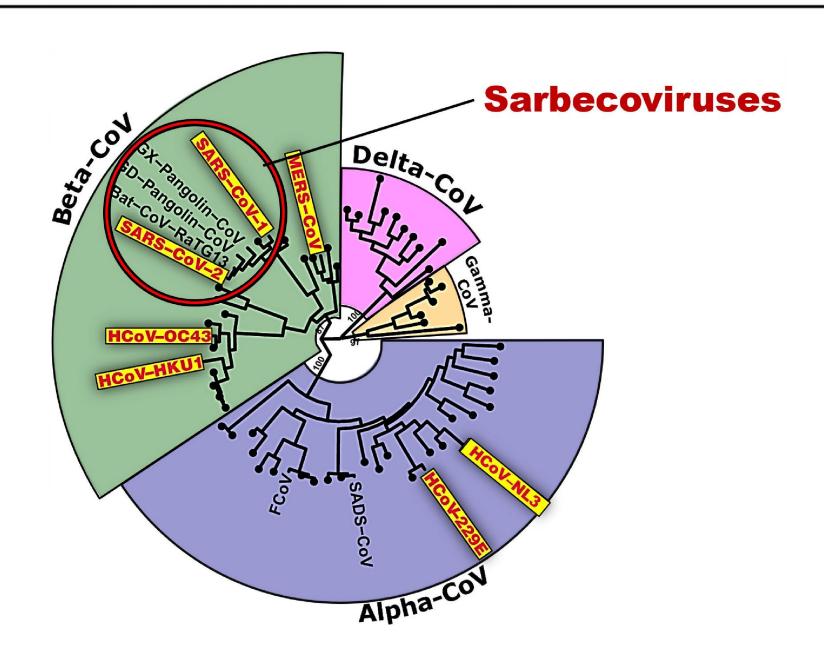
#### Pan-SARS-CoV-2 Vaccine

#### **WHO Variants of Concern:**

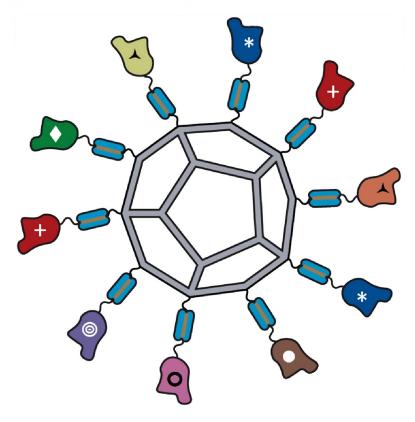
- Alpha
- Beta
- Gamma
- Delta
- Omicron



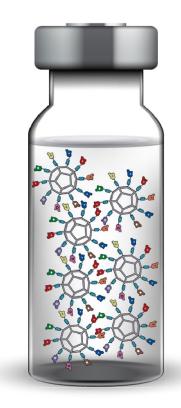
#### **Pan-Sarbecovirus Vaccine**



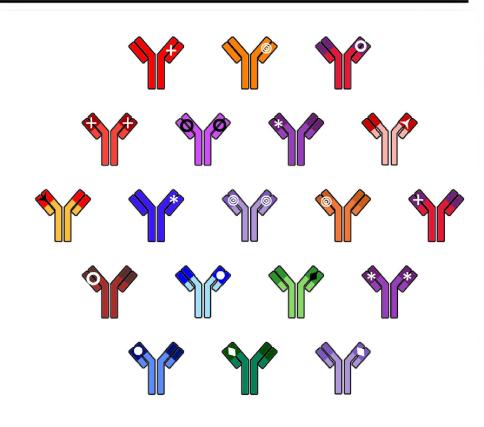
### Example of a Pan-Coronavirus Vaccine Concept



Nanoparticle with different spike protein fragments



**Vaccine** 



Diverse antibody response

Source: Bjorkman et al. 2021 Science

## **Example of a Universal Beta-Coronavirus Vaccine Concept**



vaccine consisting of SARS-CoV-2 and

several different

coronaviruses delivered

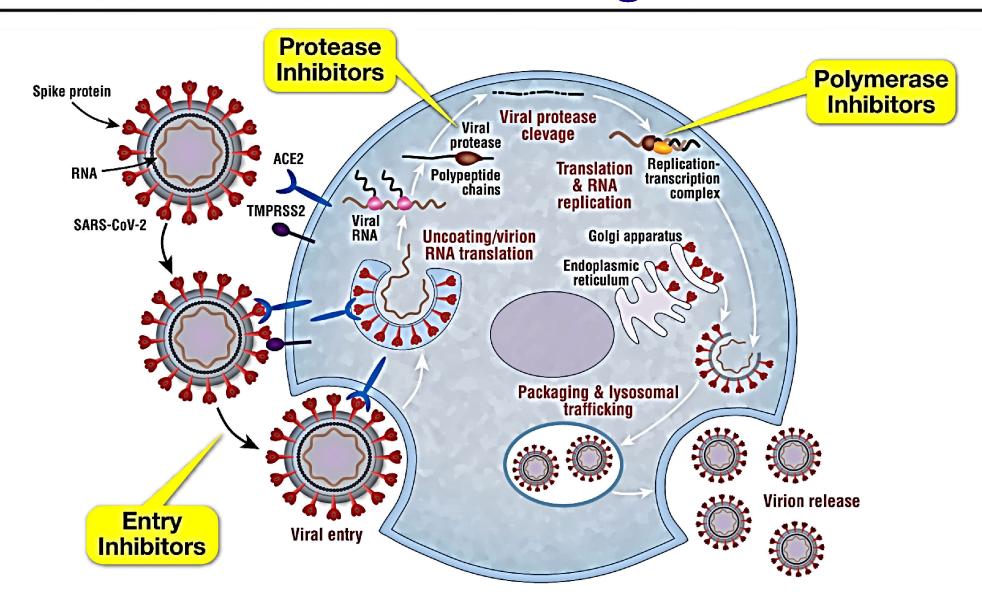
by intranasal mist

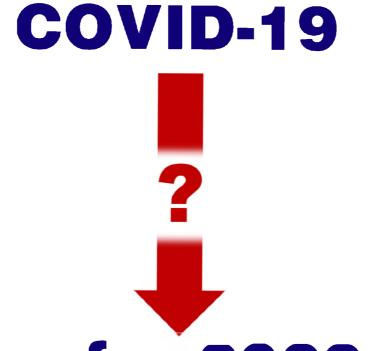
Source: Taubenberger, et al. 2022 Unpublished



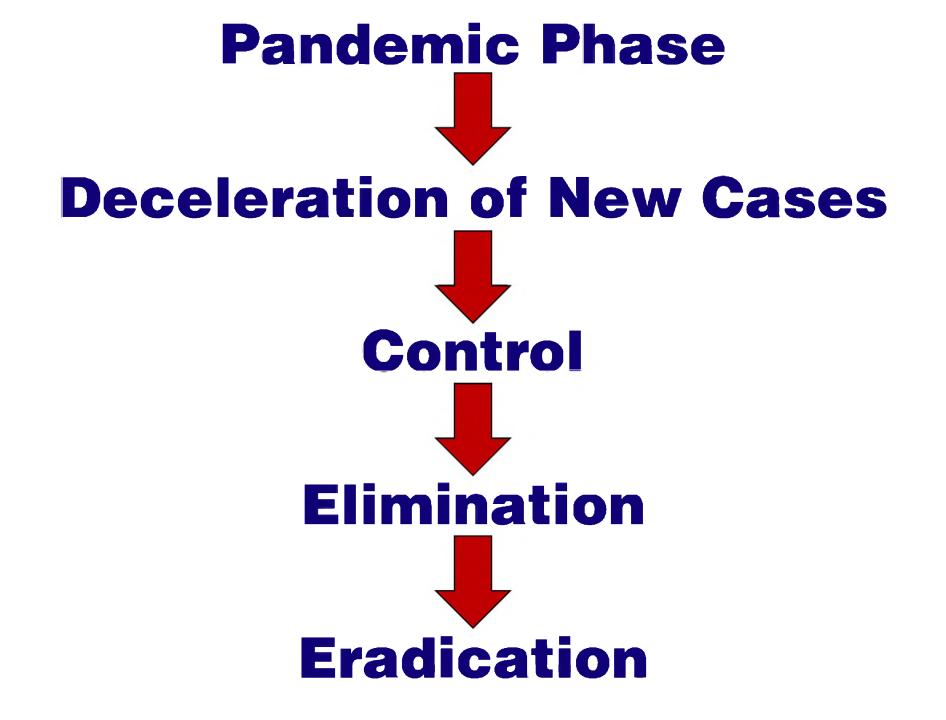
#### **The Antiviral Program for** Pandemics (APP) aims to catalyze the development of new medicines to combat COVID-19 and prepare for other pandemic threats

### **Bolstering COVID-19 Therapeutic Armamentarium: New Targets for Antivirals**

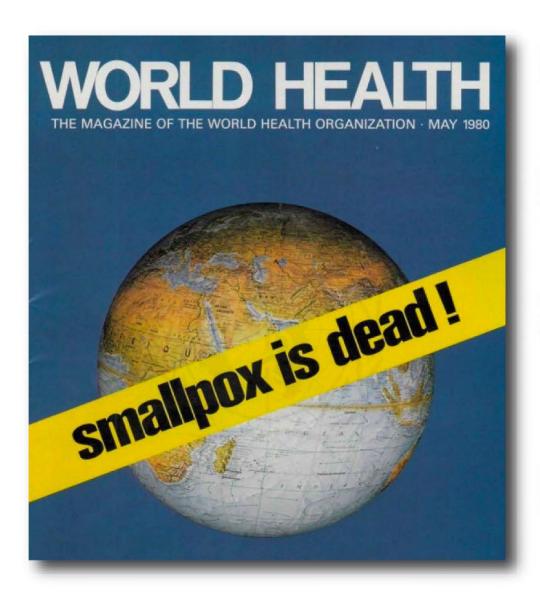




#### The End Game for 2022 and Beyond



#### **Smallpox Eradication**



Lack of animal reservoir

Phenotypically stable virus

Widely accepted global vaccination campaign

Durability of vaccine- and infection-induced immunity

### Elimination of Polio and Measles in the United States

Polio elimination: 1979



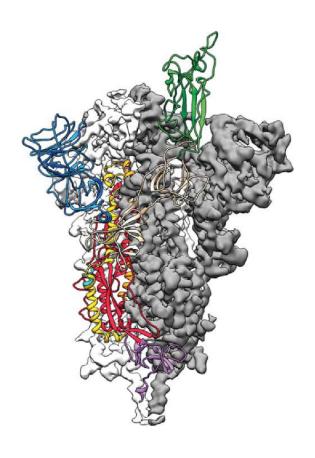


Measles elimination: 2000

Lack of animal reservoir

- Phenotypically stable virus
- Widely accepted national vaccination campaign

Durability of vaccine- and infection-induced immunity



SARS-CoV-2 (Spike Protein)

- Established animal reservoirs
- Evolution of genotypically and phenotypically diverse variants
- Lack of a wide acceptance of safe and effective vaccines
- Waning of vaccine- and infection-induced immunity

Common sense respiratory hygiene, voluntary masking, attention to ventilation

Return to "Normalcy"

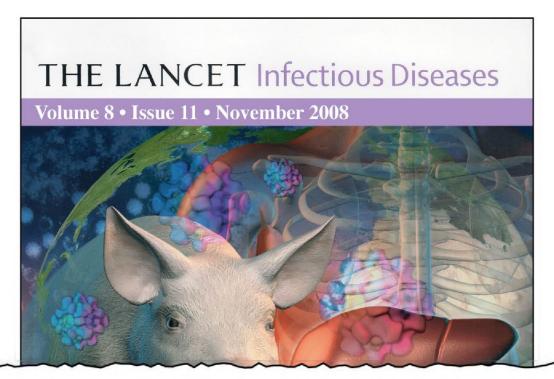
Requirement for intermittent vaccination

Control

**Endemicity** 

Availability of effective antivirals and monoclonal Abs

Similar to other respiratory viruses: RSV, common cold coronaviruses, influenza, etc.



## Emerging Infections: A Perpetual Challenge

DM Morens, GK Folkers, and AS Fauci

Review

Intervening in HIV immunopathogenesis

See page 675

People, pigs, and hepatitis E
See page 698

Emerging infections: from ancient
Greece to AIDS
See page 710