CDC/IDSA COVID-19 Clinician Call

October 23, 2021

Welcome & Introductions

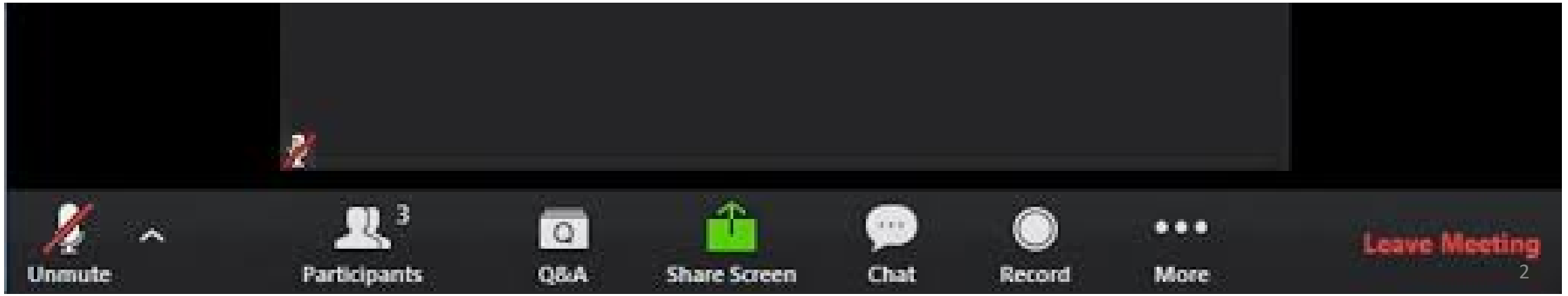
Dana Wollins, DrPH, MGC
Vice President, Clinical Affairs & Guidelines
IDSA

- 77th in a series of weekly calls, initiated by CDC as a forum for information sharing among frontline clinicians caring for patients with COVID-19
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

COVID-19 Real-Time Learning Network
Brought to you by CDC and IDSA

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button



COVID-19 Vaccine Boosters, the Immune Compromised & Protecting the Most Vulnerable

COVID-19 Boosters Update

Perspectives from VRBPAC

Archana Chatterjee, MD, PhD

Dean, Chicago Medical School

Vice President for Medical Affairs, Rosalind Franklin University

Member, Vaccines and Related Biological Products Advisory Committee

Considerations Regarding Authorization of COVID-19 Vaccine Boosters

Peter Marks, MD, PhD

Director, Center for Biologics Evaluation & Research

U.S. Food and Drug Administration

ACIP Recommendations for Additional and Booster Doses of COVID-19 Vaccines

Sarah Mbaeyi, MD, MPH

Chief Medical Officer, COVID-19 Vaccine Task Force

Centers for Disease Control and Prevention

Kimberley Fox, MD, MPH

Captain, U.S. Public Health Service

Vaccine Task Force Co-Lead

Centers for Disease Control and Prevention COVID-19 Response

COVID-19 Vaccine Boosters, the Immune Compromised & Protecting the Most Vulnerable

Protecting Our Most Vulnerable: Focus on the Immune Compromised

COVID-19 Prevention in Compromised Hosts

Lawrence Corey, MD
Co-PI, COVID-19 Prevention Network (CoVPN)
Professor of Medicine and Laboratory Medicine
Fred Hutchinson Cancer Center and University of Washington

Myron S. Cohen, MD
Yeargan-Bate Professor of Medicine, Microbiology and Epidemiology
Associate Vice Chancellor for Medical Affairs and Global Health
Director, Institute for Global Health and Infectious
University of North Carolina at Chapel Hill

COVID-19 in Patients with Cancer: A Uniquely Vulnerable Population

Jeremy L. Warner, MD, MS, FAMIA, FASCO
Associate Professor of Medicine (Hematology/Oncology) and Biomedical Informatics, Vanderbilt University
Co-Founder and Steering Committee Member
COVID-19 and Cancer Consortium (CCC19)
Director, CCC19 Research Coordinating Center

Perspectives from VRBPAC

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CDC/IDSA COVID-19 Clinician Call October 23, 2021: Perspectives from VRBPAC

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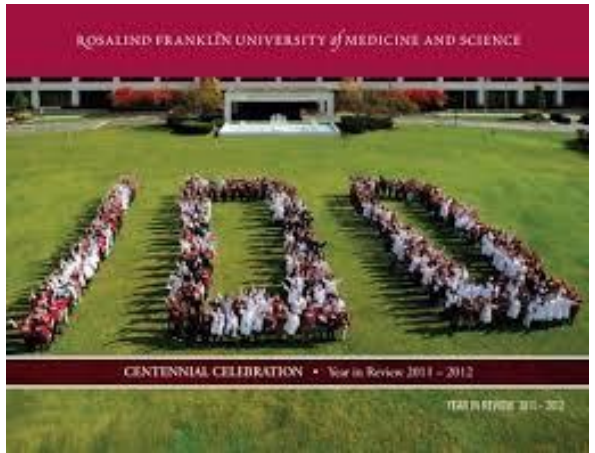

Overview of VRBPAC Meeting October 14-15, 2021

Day 1

- Issue 1: Update on the use of booster doses of vaccine in Israel
- Issue 2: Use of a booster dose of the Moderna COVID-19 vaccine following the Moderna COVID-19 primary series

Day 2

- Issue 3: Use of a booster dose of the Janssen COVID-19 vaccine following primary vaccination with the Janssen COVID-19 Vaccine
- Issue 4: Data on heterologous (mix-and-match) boosting using the currently available vaccines

Moderna Booster Dose

- Primary discussion by the VRBPAC was whether a booster should be administered at the same strength as the primary series or as a half dose, which demonstrated strong immune responses (not clinical outcomes) in the presented data.
- The Moderna data compared neutralizing antibody responses to D614G (a key mutation in the SARS-CoV-2 Spike protein) and Delta variant, and 94.6% of people age 65 and older who received a booster had what was judged to be an adequate immune response.
- VRBPAC unanimously recommended that a half dose (50 mcg instead of 100 mcg) be available to certain higher risk individuals who completed the primary two-dose series at least six months prior.
- The enumerated groups mirrored those in the FDA's expansion of the EUA for the Pfizer vaccine earlier this month:
  - Individuals 65 and older
  - Those 18-64 years old with risk of severe disease
  - Those 18-64 years old with high risk of infection as a result of occupational/institutional exposure

Janssen Booster Dose

- Janssen provided several studies that have evaluated safety and immunogenicity or efficacy of the vaccine as a second dose administered 2-3 months after the first dose or as a booster dose administered approximately 6 months after a single dose primary vaccination.
- While noting the small sample size for the clinical trial, the committee recommended that boosters be made available for those individuals who received the Janssen vaccine.
- Notably, the VRBPAC recommended that any person who received the vaccine at least two months ago should get a second dose regardless of age or risk factors, essentially voicing skepticism about whether the Janssen regimen should really have been a one-dose vaccine in the first place.
- There was also discussion about the lack of independent verification and analysis of the data by the FDA.

Mix-and-Match Boosters

- The VRBPAC engaged in a robust discussion about mix-and-match booster doses based on a study sponsored by the National Institute of Allergy and Infectious Diseases evaluating the immunogenicity of each of the vaccines following immunization with the same or a different primary series.
- Roughly 50 volunteers who had received their second dose of the vaccine at least 12 weeks prior and had no history of COVID-19 were selected for each mix-and-match group.
- The results were short term, 15 and 29 days after the booster dose, and the study was not powered to be used for comparison between arms.

Mix-and-Match Boosters cont.

- Reactogenicity of the vaccines was similar to the primary series, with skin pain, malaise, headache, and myalgias occurring in more than half the participants.
- At baseline, binding antibody concentrations for the Janssen vaccine were 3-15 times **lower** than the mRNA vaccines.
- Nearly all volunteers had a two-fold or greater boost in binding antibodies, regardless of which booster was used.
- The largest jump in antibodies was seen in volunteers who had Janssen as their primary vaccine followed by an mRNA vaccine booster. Volunteers who received Janssen as their primary vaccine and booster had 7-10 times **lower** binding antibody titers than those boosted with the mRNA vaccines.
- Overall, heterologous boosters were effective, and in every case provided neutralizing antibody titers that would be expected to be protective.

Mix-and-Match Boosters cont.

- No formal recommendations were made, but the committee stressed that expanding each EUA every time a new combination of vaccines was considered was unwieldy and that having broad flexibility for the use of any of the vaccines in boosters would make administration easier. It was also noted that not all individuals in the United States will have ready access to the same vaccine they received in the primary series.
- In summary, mixing-and-matching seems to be a reasonable strategy, at least in the short term.

Considerations Regarding Authorization of COVID-19 Vaccine Boosters

Peter Marks, MD, PhD
Director
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

Considerations Regarding Authorization of COVID-19 Vaccine Boosters

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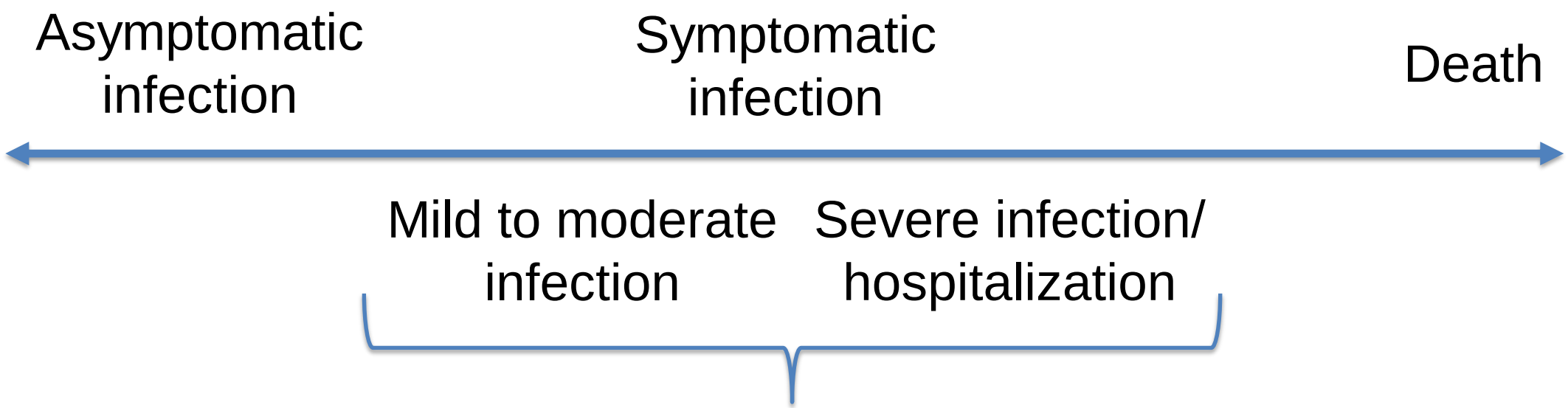
CDC-IDSA Meeting

October 23, 2021

The Spectrum of SARS-CoV-2 Infection



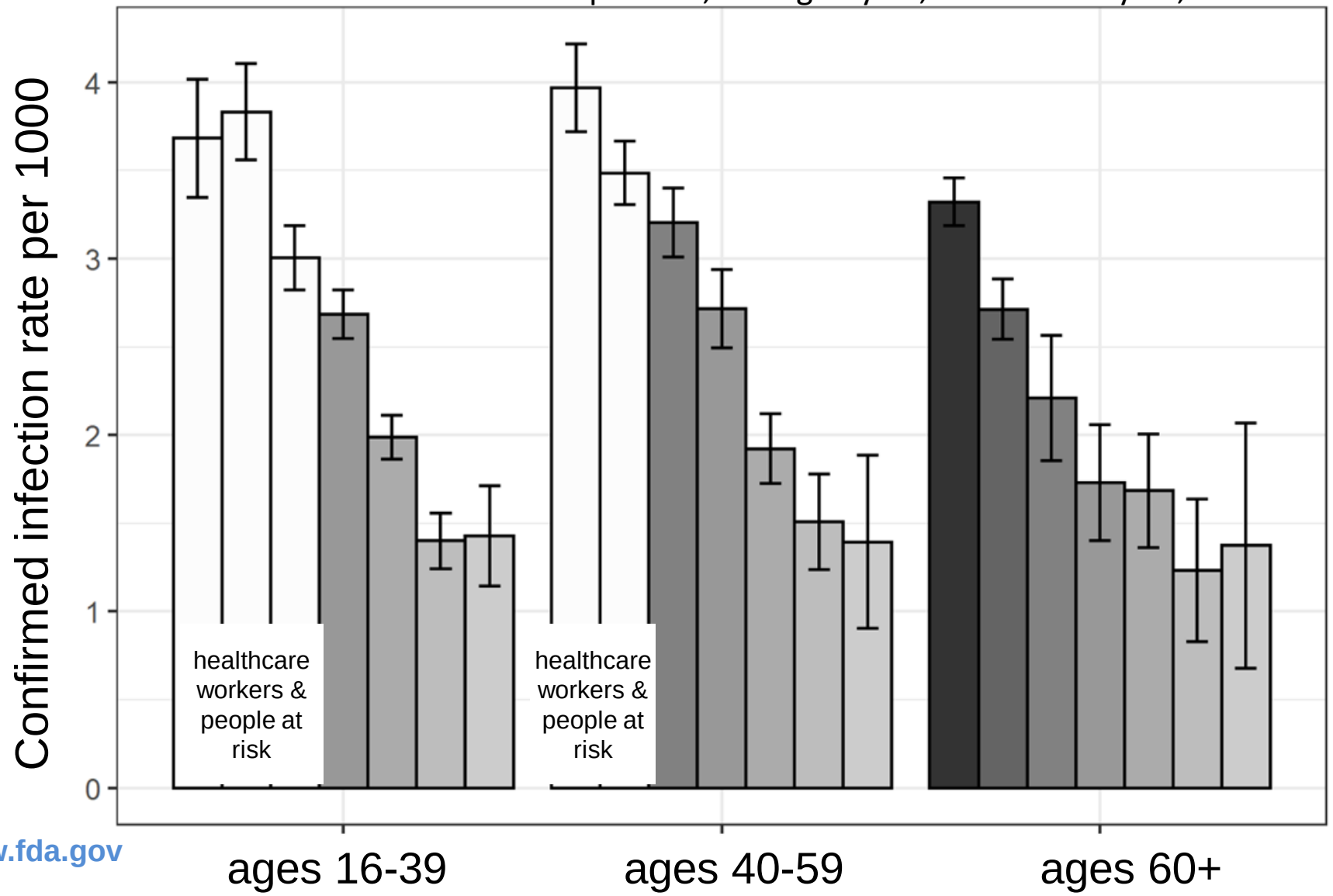
Potentially associated with Long COVID-19:
Cardiac, pulmonary, neurologic and other symptoms

Vaccine Effectiveness Over Time

- Pfizer-BioNTech, Moderna, and Janssen have all submitted data suggesting some waning of effectiveness over time
- Most evidence is based on neutralizing antibody titers or real-world evidence (RWE) on symptomatic infection
- Separating waning effectiveness from reduced effectiveness against variants, such as Delta, can be challenging
- Vaccines are still very effective against serious outcomes

Waning immunity in Israel across age groups

Rate of confirmed **SARS-CoV-2 infections** stratified by vaccination period and age group
Per 1000 persons, during July 11, 2021 and July 31, 2021



Goldberg et al.,
https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1

Booster reduces the rate of severe disease* in 60+ and 40-60 age groups

*Severe disease (NIH definition): resting respiratory rate >30 breaths per minute, or O2 saturation <94%, or PaO2/FiO2 <300

(**Poisson regression** controlling for age, gender, demographic group, 2nd dose period, and incidence in area of residence. Based on data from booster eligibility in age group until 9/29)

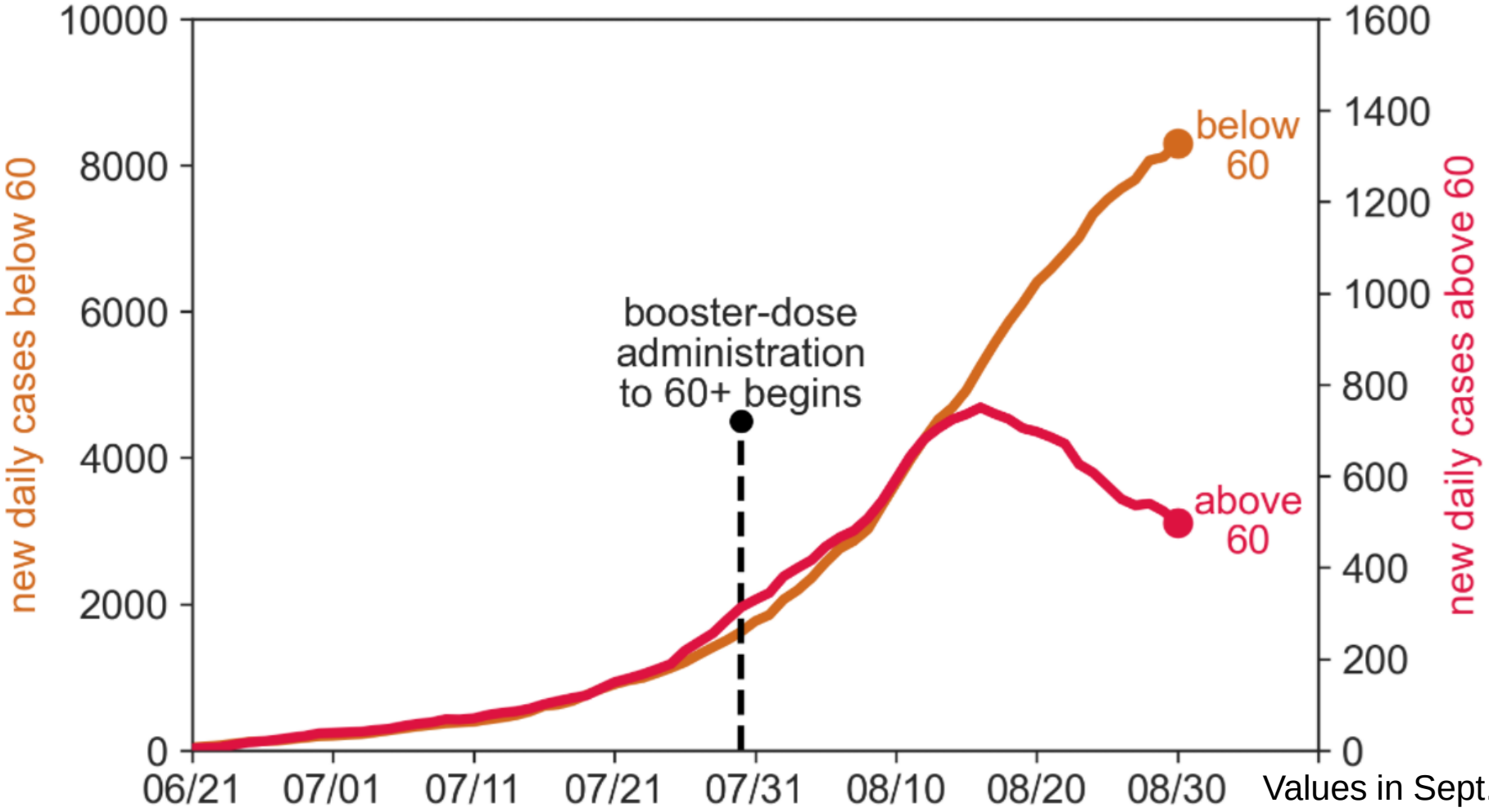
Age	Non-booster severe cases (person-days at risk)	Booster group severe cases - day 12+ (person-days at risk)	Rate ratio for **severe** cases day 12+ relative to non-booster [95% CI]
60+	957 (20,894,746)	150 (39,630,040)	**18.7** [15.7, 22.4]
40-59	160 (25,243,100)	7 (20,202,835)	**22** [10.3, 47]
16-39	23 (36,907,240)	1 (9,761,068)	too few cases to estimate reliably

Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Following the booster in Israel a decrease in confirmed infections was observed among people aged 60+

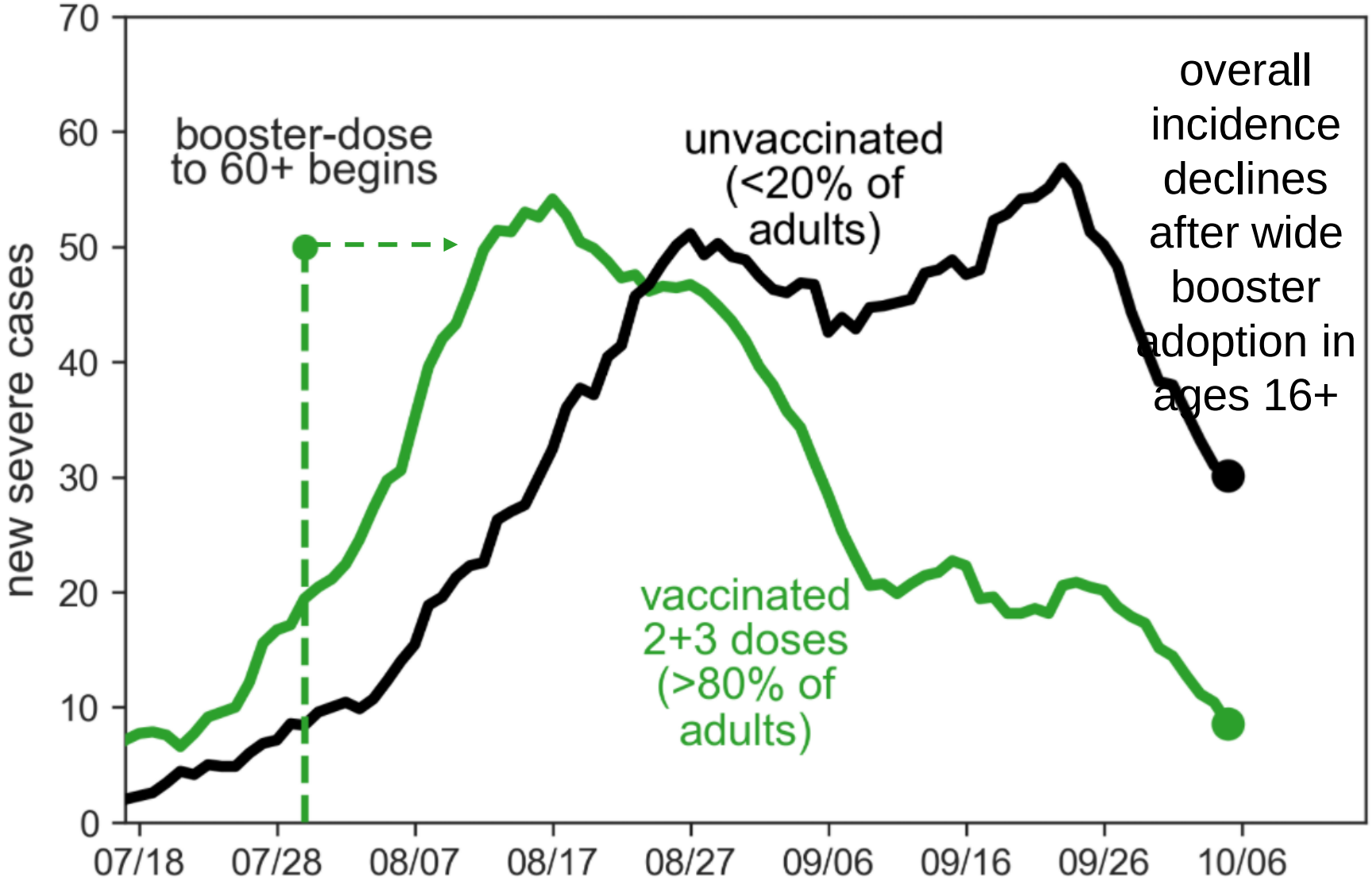
Based on PCR testing.

In Israel testing is performed either following symptoms or without symptoms for contact tracing and other reasons



Values in Sept. are affected by booster administered to age groups below 60

Following the third dose in Israel, severe cases among vaccinated decreased sharply



Myocarditis & perimyocarditis cases and number of vaccinees by age group and sex

Proactive surveillance. All cases reported in Israel Dec. 2020 - Oct. 10th, 2021

Sex	Age group	1st dose (0-21 days following vaccination)		2nd dose (0-30 days following vaccination)		3rd dose* (0-30 days following vaccination; For ages 30+, 80% with 30 days; For ages 16-29, 48% with 30 days)	
		Number of vaccinees	Number of cases reported	Number of vaccinees	Number of cases reported	Number of vaccinees	Number of cases reported
Female	12-15	204,729	**0**	162,297	**1**	279	**0**
	16-19	248,881	**0**	222,067	**2**	97,807	**0**
	20-24	263,845	**1**	242,697	**6**	141,910	**0**
	25-29	247,365	**0**	229,189	**1**	130,283	**0**
	+30	2,127,538	**3**	2,029,074	**7**	1,542,142	**0**
Male	12-15	192,014	**1**	151,081	**10**	292	**0**
	16-19	254,497	**3**	223,079	**36****	96,238	**5**
	20-24	275,235	**6**	251,672	**26**	139,015	**5**
	25-29	257,713	**3**	239,319	**20**	133,650	**1**
	+30	1,983,230	**10**	1,897,067	**32**	1,448,745	**6**

* Two more cases are currently under diagnosis review; For 2,548 individuals without gender information there were zero cases reported.

** One case – first dose Pfizer, second dose Moderna

Randomized Trial of Boosters - Pfizer

- All previously completed the primary series of the Pfizer-BioNTech vaccine
- Median age 53 years, 55.5% between 16 and 55 years, and 23.3% age ≥ 65 years
- Randomized 1:1 to receive either a 30-µg booster dose or placebo
- The median time between second dose and administration of the booster dose or placebo was approximately 11 months
- Symptomatic COVID-19 occurrence was measured from at least 7 days after booster or placebo, with a median follow-up of 2.5 months
- 5 cases of COVID-19 in the booster group, and 109 cases in the placebo group
- Observed relative vaccine efficacy of 95.6% (95% CI: 89.3, 98.6) in those without evidence of prior SARS-CoV-2 infection.

Heterologous Boosters (Mix and Match)

Janssen Primary	Moderna Primary	Pfizer-BioNTech Primary
Moderna Booster	**Moderna Booster**	**Moderna Booster**
75.9 (55.8-104.8)	10.2 (8.0-12.8)	31.7 (23.8-42.2)
Janssen Primary	**Moderna Primary**	**Pfizer-BioNTech Primary**
Janssen Booster	**Janssen Booster**	**Janssen Booster**
4.2 (3.0-5.8)	6.2 (4.5-8.5)	12.5 (8.7-17.9)
Janssen Primary	**Moderna Primary**	**Pfizer-BioNTech Primary**
Pfizer-BioNTech Booster	**Pfizer-BioNTech Booster**	**Pfizer-BioNTech Booster**
35.1 (23.9-51.6)	11.5 (9.0-14.8)	20.0 (14.6-27.4)

Source: NIH Heterologous Booster Study

Do I qualify for a COVID-19 vaccine booster and which one?

Which primary vaccine series did you complete?	Pfizer-BioNTech	Moderna	Janssen (J&J)
You can get a booster if:	It's been at least 6 months since completing the primary series AND you are:	It's been at least 6 months since completing the primary series AND you are:	It's been at least 2 months since completing the primary series AND you are:
	Age 65+	Age 65+	Age 18+
	OR	OR	
	Ages 18-64 and at high risk of severe COVID-19	Ages 18-64 and at high risk of severe COVID-19	
	OR	OR	
	Ages 18-64 with frequent institutional or occupational exposure to SARS-CoV-2	Ages 18-64 with frequent institutional or occupational exposure to SARS-CoV-2	
If eligible, you can get a booster of:	Pfizer-BioNTech Moderna Janssen (J&J)	Moderna Pfizer-BioNTech Janssen (J&J)	Janssen (J&J) Pfizer-BioNTech Moderna

For more information, visit www.fda.gov/covid19vaccines.

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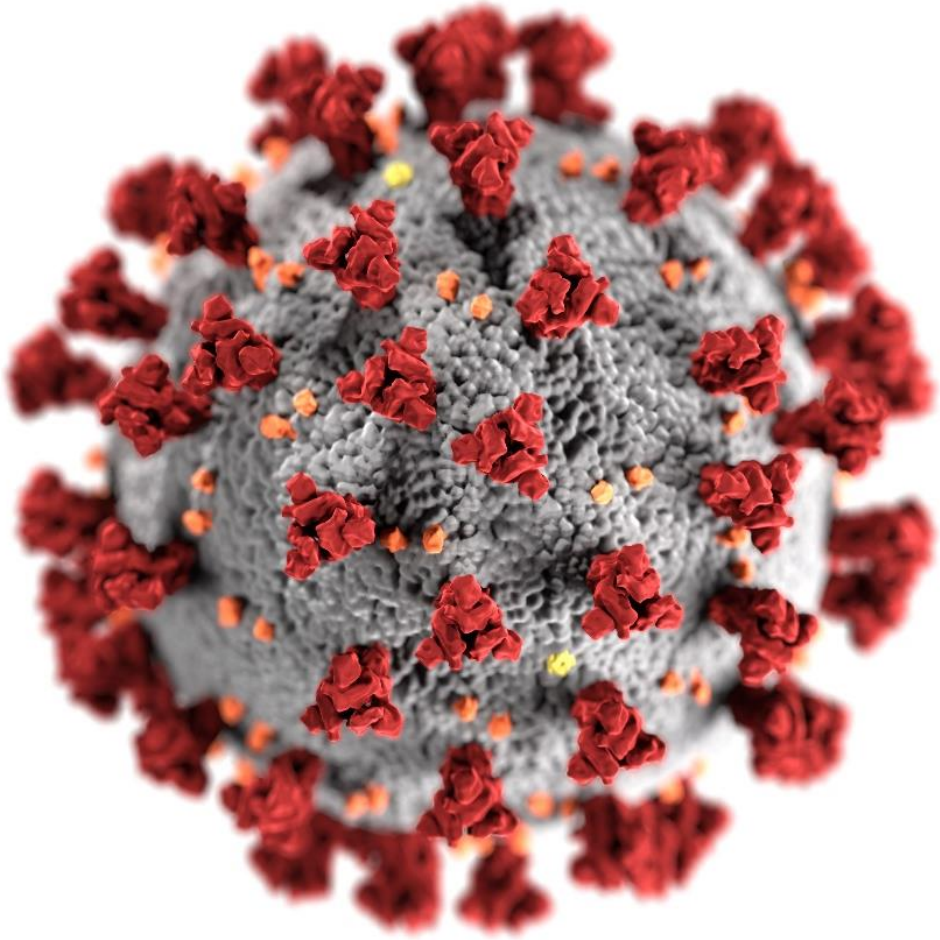
ACIP Recommendations for Additional and Booster Doses of COVID-19 Vaccines

Sarah Mbaeyi, MD, MPH
Chief Medical Officer, COVID-19 Vaccine Task Force
Centers for Disease Control and Prevention

ACIP Recommendations for Additional and Booster Doses of COVID-19 Vaccines

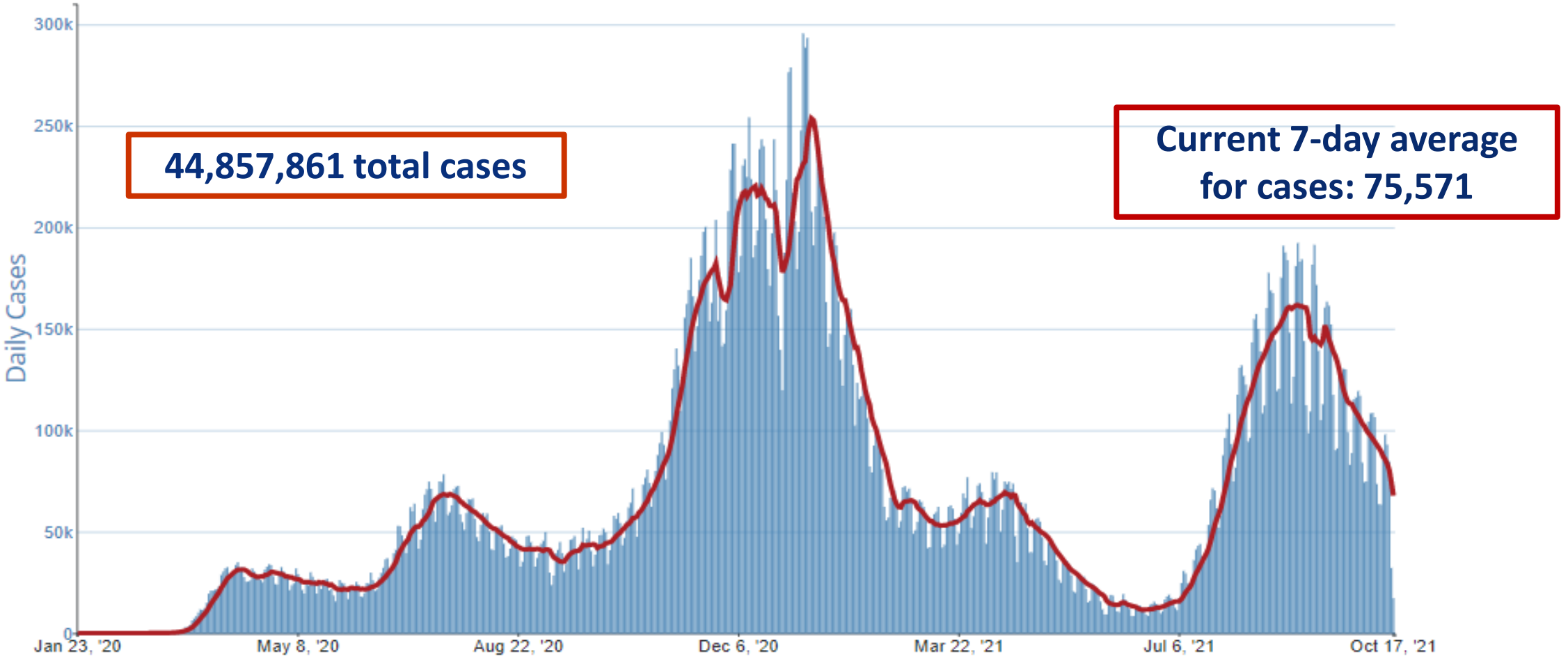


Dr. Sarah Mbaeyi, MD, MPH
October 22, 2021

cdc.gov/coronavirus

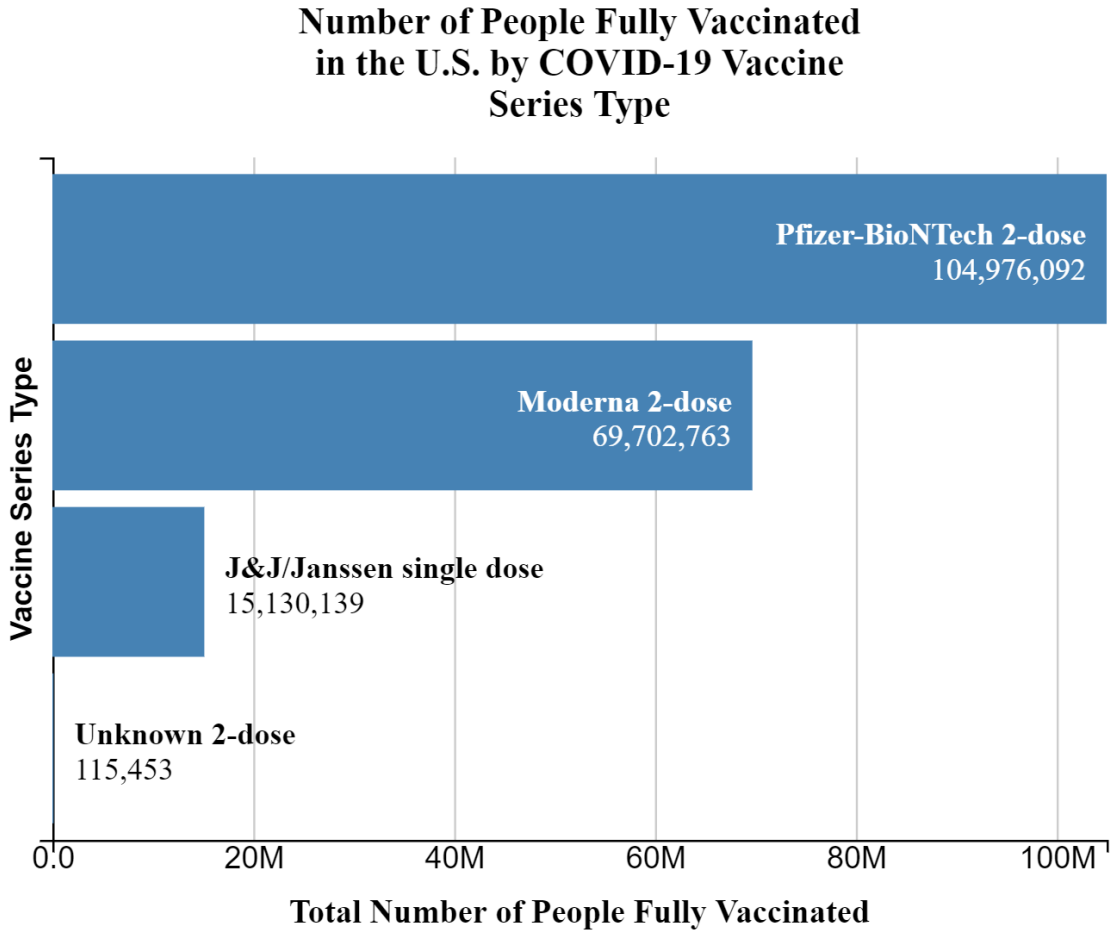
COVID-19 cases in the United States

January 23, 2020 – October 17, 2021



https://covid.cdc.gov/covid-data-tracker/#trends_dailycases. Accessed October 19, 2021

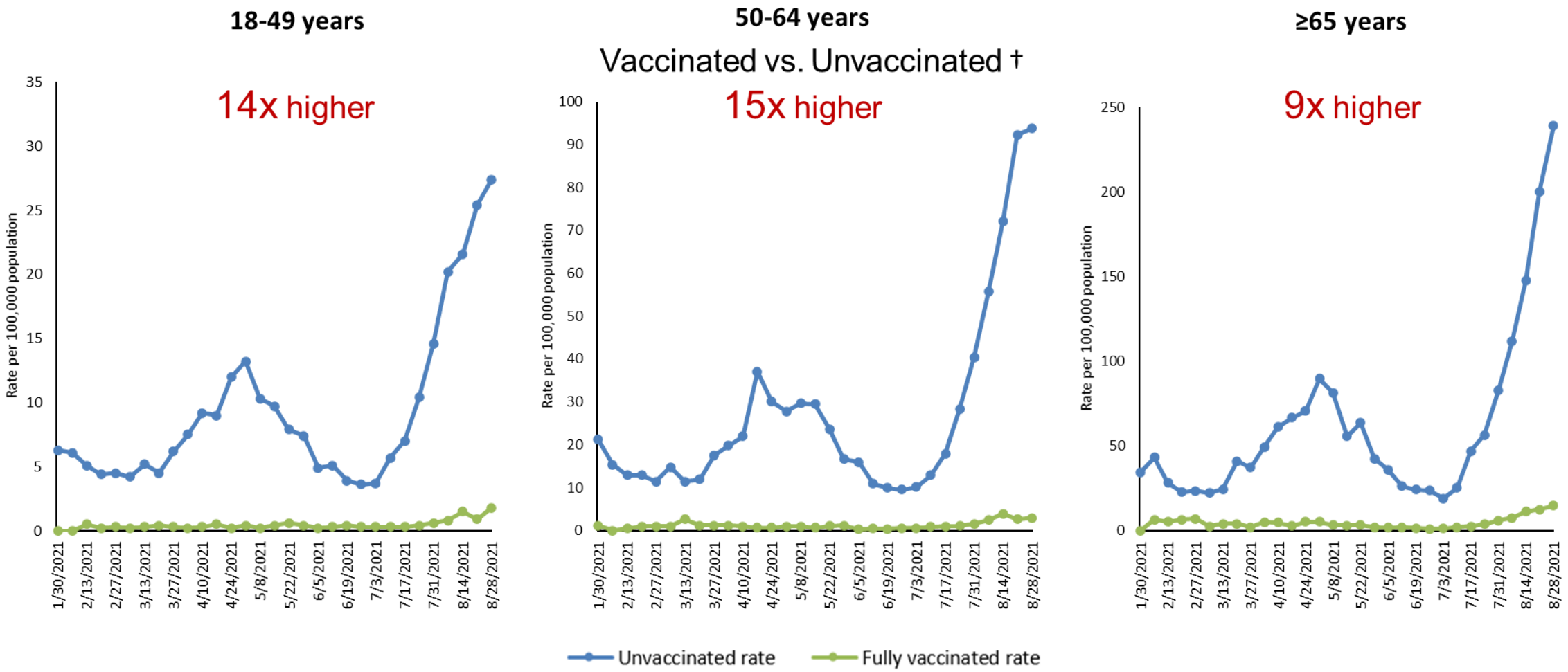
COVID-19 Vaccination in the United States



68.7% of population aged ≥18 years is fully vaccinated

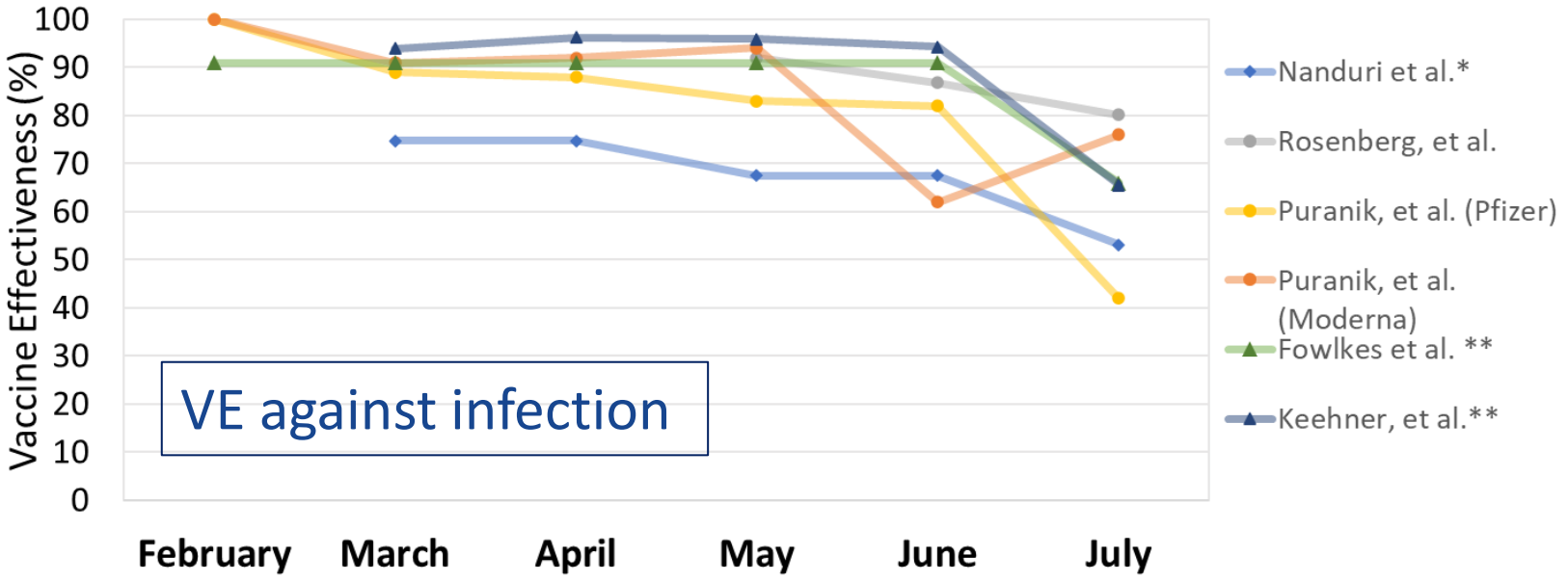
https://covid.cdc.gov/covid-data-tracker, as of October 22, 2021

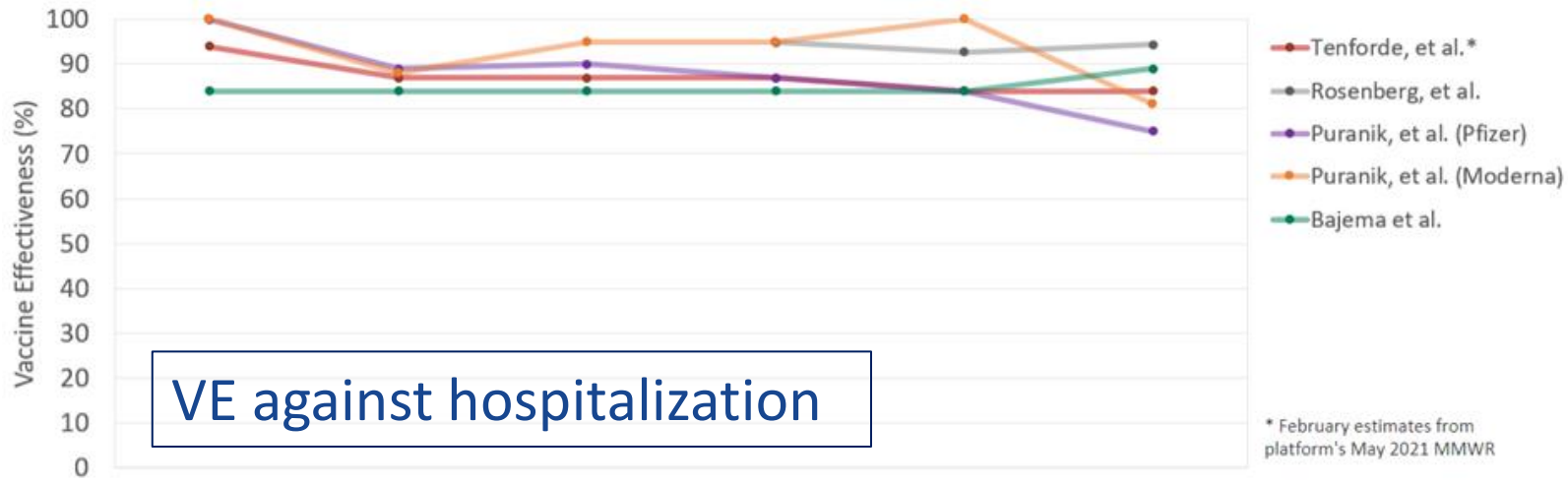
Unvaccinated persons at greatest risk for COVID-19-associated hospitalization



*Data are preliminary and case counts and rates for recent hospital admissions are subject to lag. As data are received each week, prior case counts and rates are updated accordingly.
†Cumulative rate ratio from January 24 – August 28, 2021.
COVID Data Tracker: https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

Vaccine effectiveness (VE) in persons aged ≥18 years

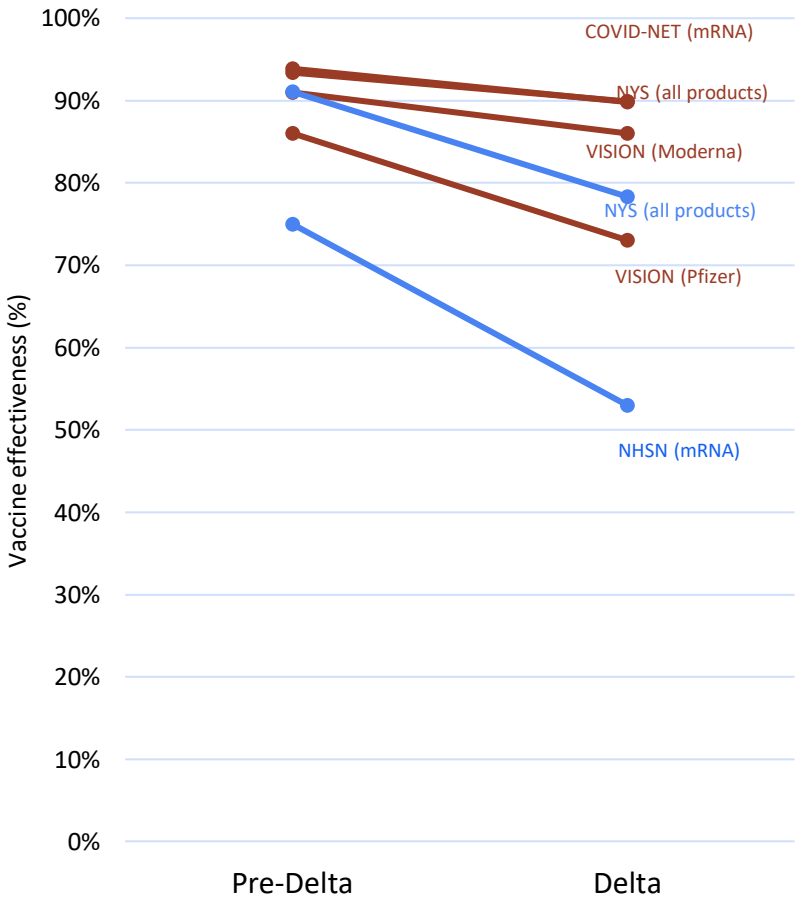




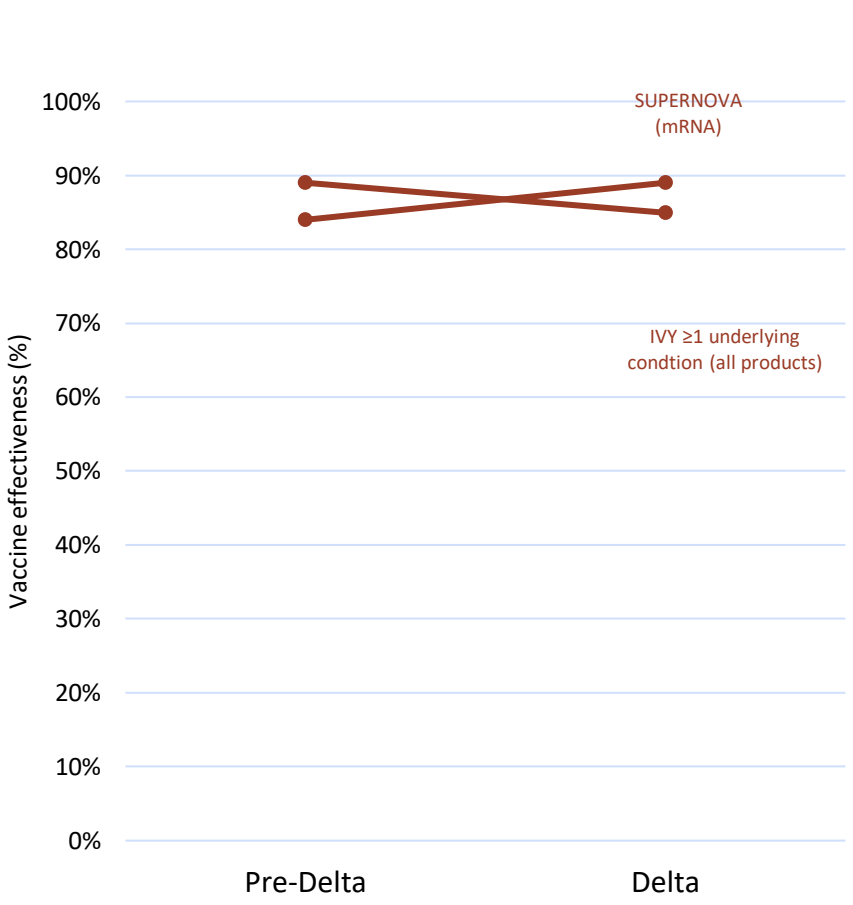
Rosenberg ES, et al. MMWR Morb Mortal Wkly Rep. ePub: 18 August 2021.; Nanduri S et al. MMWR Morbidity and Mortality Weekly Report. 2021 2021;70. ; Fowlkes A et al. MMWR Morb Mortal Wkly Rep. ePub: 24 August 2021; Puranik A et al. medRxiv 2021.08.06.21261707; Keehner J et al. NEJM, September 1, 2021. DOI: 10.1056/NEJMc2112981; Bajema KL et al. MMWR Morb Mortal Wkly Rep; Thompson MG et al. N Engl J Med 2021;385:320–9; Self WH et al. MMWR Morb Mortal Wkly Rep. ePub: 17 September 2021; Nunes et al. mRNA vaccines effectiveness against COVID-19 hospitalizations and deaths in older adults: a cohort study based on data-linkage of national health registries in Portugal. MedRXiv preprint.; Andrews et al. Vaccine effectiveness and duration of protection of Comirnaty, Vaxzevria and Spikevax against mild and severe COVID-19 in the UK. Preprint; Tartof S et al. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3909743

Magnitude of vaccine effectiveness (VE) against infection or hospitalization by Delta predominance and study, by risk group

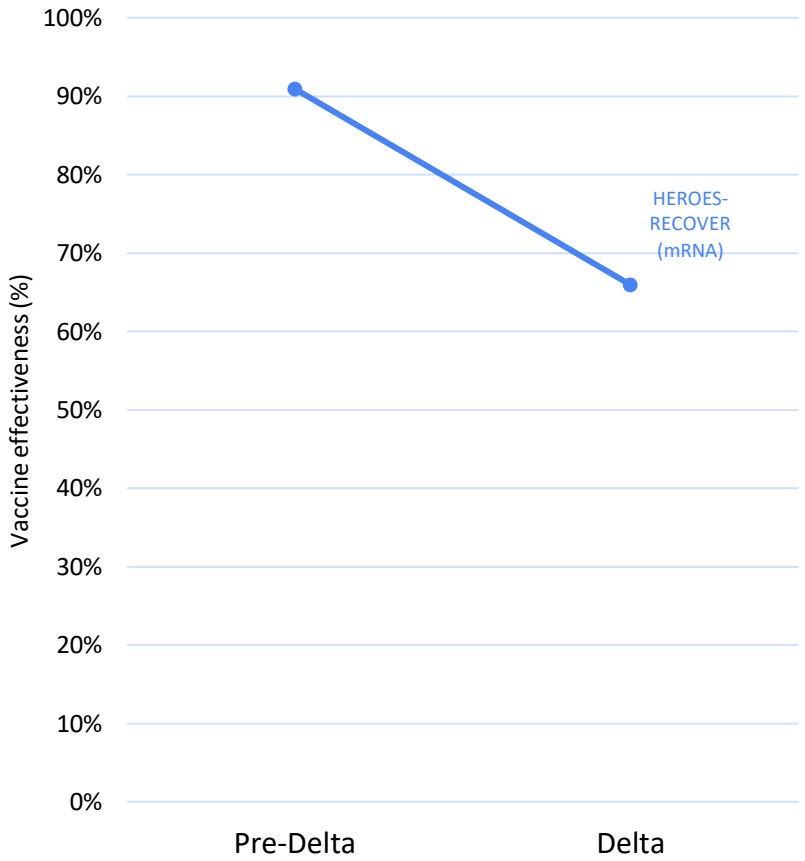
≥ 65 years of age



Underlying medical conditions



Frontline workers



NHSN: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm ; COVID-NET: CDC unpublished; VISION: https://www.nejm.org/doi/10.1056/NEJMoa2110362/https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm
IVY: CDC unpublished data; SUPERNOVA: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htmNYS: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm; HEROES-RECOVER: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm

Lower vaccine effectiveness of mRNA COVID-19 vaccines in immunocompromised persons

VE against SARS-CoV-2 infection

Immunocompromised: **71%** (CI 37-87%)

Overall: **90%** (CI 83-96%)

VE against COVID-19 associated hospitalization

Immunocompromised: **59%** (CI 12-81%)

Non-immunocompromised: **91%** (CI 86-95%)

Chodick et al. *Clinical Infectious Diseases*, ciab438, https://doi.org/10.1093/cid/ciab438; Khan et al. Gastroenterology (2021). https://www.gastrojournal.org/article/S0016-5085(21)03066-3/pdf; Tenforde et al. medRxiv preprint: https://doi.org/10.1101/2021.07.08.21259776

Summary

- Over 190 million people are fully vaccinated (~57% of total population)
- Hospitalization rates are 9-15 times higher in unvaccinated compared to vaccinated adults
- mRNA vaccine effectiveness:
  - Declines in VE against infection over time and during Delta period
  - Minimal-to-no declines in VE against hospitalization in younger adults; mild declines observed among older adults in some studies
- Janssen vaccine effectiveness: stable VE over time, but lower VE against infection and hospitalization than mRNA vaccines in most studies

Immunogenicity and safety of an additional mRNA vaccine dose in immunocompromised persons

- Among immunocompromised patients with no detectable antibody response to an initial mRNA vaccine series, **33-50%** developed an antibody response to an additional dose

- Local and systemic reactions reported after an additional dose were mostly mild to moderate and similar to those observed after previous doses

Kamar et al. (2021) NEJM Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients; Epsi et al. (2021) medRxiv doi: https://doi.org/10.1101/2021.07.02.21259913; Hall et al. (2021) NEJM. Randomized Trial of a Third Dose of mRNA-1273 Vaccine in Transplant Recipients. DOI: 10.1056/NEJMc2111462; Ducloux., et al. (2021). Humoral response after 3 doses of the BNT162b2 mRNA COVID-19 vaccine in patients on hemodialysis.“Kidney Int. 2021 Jun 30m doi: 10.1016/j.kint.2021.06.025

Immunogenicity and efficacy of a COVID-19 vaccine booster dose in persons who received a primary series

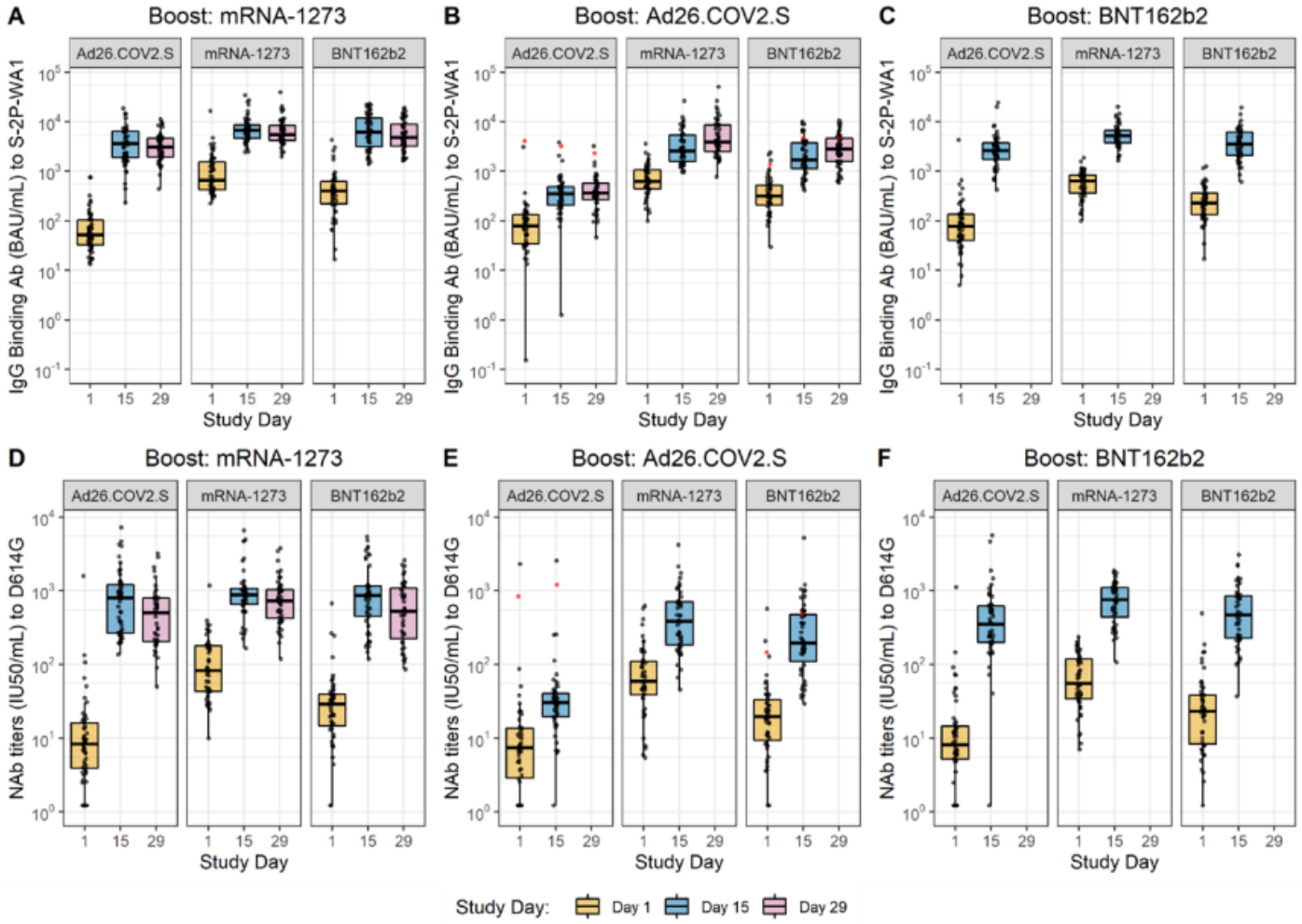
- **Immunogenicity**: Compared with geometric mean titers (GMTs) after the last dose in the primary series, GMTs after booster doses were increased by:
  - mRNA: **1.3 to 3.3-fold** (booster dose 6 months after primary series)
  - Janssen: **4.6 to 12-fold** (booster dose 2-6 months after primary dose)

- **Efficacy:** Janssen booster dose against moderate to severe COVID-19 for 2 doses administered 2 months apart vs. a single dose
  - Overall: **75%** (CI 55-87%) vs. **53%** (CI 47-58%)
  - U.S. study population: **94%** (CI 59-100%) vs. **70%** (61-77%)

- **Incremental effectiveness:** Pfizer-BioNTech booster compared to 2nd dose:
  - **70%** (CI 62-76%) in persons aged ≥ 40 years
  - **91%** (CI: 90-92%) in persons aged ≥ 60 years

https://www.fda.gov/media/152161/download; https://www.fda.gov/media/152953/download; https://www.fda.gov/media/152954/download; Bar-On YM et al. *N Engl J Med*. 2021;10.1056/NEJMoa2114255; Patalon et al. Short Term Reduction in the Odds of Testing Positive for SARS-CoV-2; a Comparison Between Two Doses and Three doses of the BNT162b2 Vaccine. MedRxiv https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html

Immunogenicity of heterologous (mix-and-match) booster dose administration



- Heterologous booster results in neutralizing antibody titers that are similar or higher to those following homologous booster vaccination

Atmar R, et al. Advisory Committee on Immunization Practices meeting, October 21. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/04-COVID-Atmar-508.pdf

Safety of a COVID-19 vaccine booster dose in persons who received a primary series

- Rates of local or systemic adverse events were similar or less frequent after a booster dose than after the last dose of primary vaccination

- Over 12 million persons in the United States have received an additional or booster dose (predominantly Pfizer-BioNTech) and no unexpected patterns of adverse events have been reported

https://www.fda.gov/media/152161/download; https://www.fda.gov/media/152953/download; https://www.fda.gov/media/152954/download; https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html

Current ACIP and CDC recommendations for additional and booster doses of COVID-19 vaccines

Definitions

- **Additional dose:** administration of an additional vaccine dose when the initial immune response following a primary vaccine series is likely to be insufficient

- **Booster dose:** a dose of vaccine administered when the initial sufficient immune response to a primary vaccine series is likely to have waned over time

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Additional dose of mRNA COVID-19 vaccine in immunocompromised persons

- Moderately-to-severely immunocompromised persons aged ≥12 years (Pfizer-BioNTech) or ≥18 years (Moderna) who completed an mRNA COVID-19 vaccine primary series **should** receive an additional mRNA vaccine dose at least 28 days after their second dose

- Recommendation does not apply to immunocompromised recipients of Janssen COVID-19 vaccine; these persons should follow the booster dose recommendations

Moderately and severely immunocompromised people

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of CAR-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge, Wiskott-Aldrich syndromes)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids (i.e., ≥20mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory

ACIP General Best Practice Guidelines for Immunization; CDC Yellow Book; 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

COVID-19 vaccine booster dose in persons who completed an mRNA primary series

Persons who <u>should</u> receive a COVID-19 booster dose

- Aged ≥65 years
- Aged ≥18 years and reside in long-term care settings
- Aged 50-64 years with certain underlying medical conditions

Persons who <u>may</u> receive a COVID-19 booster dose, based on individual benefits and risks

- Aged 18-49 years with certain underlying medical conditions*
- Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting

- Booster dose administered at least 6 months after completion of primary series
- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used for booster dose, regardless of vaccine received for primary series

* Includes pregnant people

COVID-19 vaccine booster dose in persons who received a dose of Janssen vaccine

- Persons aged ≥18 years who received primary vaccination with Janssen COVID-19 vaccine **should** receive a single COVID-19 vaccine booster dose at least 2 months later
- Any FDA-approved or authorized COVID-19 vaccine (Pfizer-BioNTech, Moderna, or Janssen) can be used as the booster dose, at an interval of at least 2 months since the primary Janssen vaccine dose

FDA-authorized or approved COVID-19 vaccines for primary or booster vaccination

Vaccine	Primary series/dose			Booster dose		
	Dose (volume)	No. doses (interval)	Age (yrs)	Dose (volume)	No. doses (interval since primary series)	Age (yrs)
Pfizer-BioNTech	30 µg (0.3 ml)	2 (21 days)	≥12	30 µg (0.3 ml)	1 (≥6 months)	≥18
Moderna	100 µg (0.5 ml)	2 (28 days)	≥18	**50 µg (0.25 ml)**	1 (≥6 months)	≥18
Janssen	5×10^{10} VP (0.5 ml)	1 (N/A)	≥18	5×10^{10} VP (0.5 ml)	1 (≥2 months)	≥18

- Any of the COVID-19 vaccines (Pfizer-BioNTech, Moderna, Janssen) can be used for booster vaccination, regardless of the vaccine product used for primary vaccination
- When a heterologous (mix-and-match) booster dose is administered, the eligible population and dosing intervals are those of the vaccine used for primary vaccination

Potential risks of COVID-19 vaccine booster doses, based on rare risks observed after primary vaccination

- Janssen:
  - Thrombosis with thrombocytopenia syndrome (TTS): highest risk in women aged 18-49 years
  - Guillain-Barre Syndromé (GBS): highest risk in men aged 50-64 years
- mRNA:
  - Myocarditis and pericarditis: highest risk in males aged 12-30 years

Definition of ‘fully vaccinated’

- People who have completed a primary vaccine series (i.e., 2-dose mRNA vaccine series or a single dose of the Janssen vaccine) are considered fully vaccinated ≥2 weeks after completion of the primary series

- Receipt of an additional or booster dose is not required to be considered fully vaccinated

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html

Coadministration with other vaccines

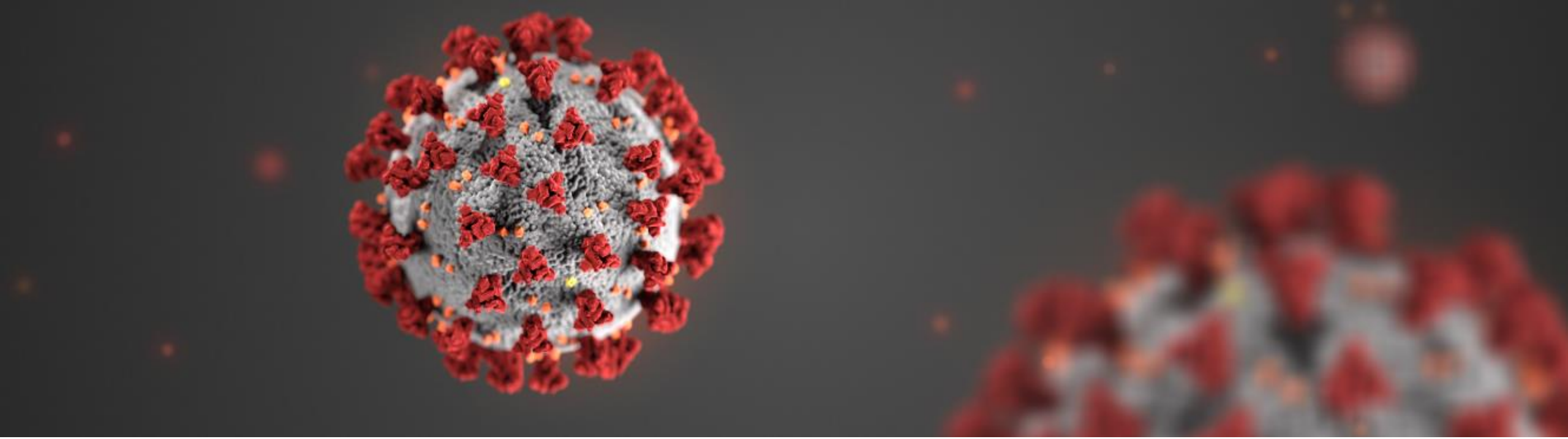
- COVID-19 vaccines (Pfizer-BioNTech, Moderna, or Janssen) may be given with other vaccines, without regard to timing.

- This includes simultaneous administration of COVID-19 vaccines and other vaccines on the same day.

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Coadministration

Updates to additional clinical resources

Updates will be posted at:
https://www.cdc.gov/vaccines/covid-19/info-by-product/index.html



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Q&A/Discussion

COVID-19 Prevention in Compromised Hosts

Lawrence Corey, MD
Co-PI, COVID-19 Prevention Network (CoVPN)
Professor of Medicine and Laboratory Medicine
Fred Hutchinson Cancer Center and University of Washington

Myron S. Cohen, MD
Yeargan-Bate Professor of Medicine, Microbiology and Epidemiology
Associate Vice Chancellor for Medical Affairs and Global Health
Director, Institute for Global Health and Infectious
University of North Carolina at Chapel Hill

COVID-19
Prevention Network

Protecting Our Most Vulnerable—Focus on the Immune Compromised

- Lawrence Corey, MD
- Myron S. Cohen, MD

Immunocompromised people and SARS-CoV-2 infection

- Immunocompromised people comprise ~2.7% of U.S. adults (~7 million adults)[1]
- More likely to get severely ill from COVID-19[1,2]
- Higher risk for:
  - Prolonged SARS-CoV-2 infection and shedding[3-7, 14-16]
  - Viral evolution during infection and treatment (hospitalized patients)[3,6,8-10,14,17]
- Lower antibody/neutralization titers to SARS-CoV-2 variants compared to non-immunocompromised people[12]
- More likely to transmit SARS-CoV-2 to household contacts[11]

COVID-19 Prevention Network

See reference slide at end

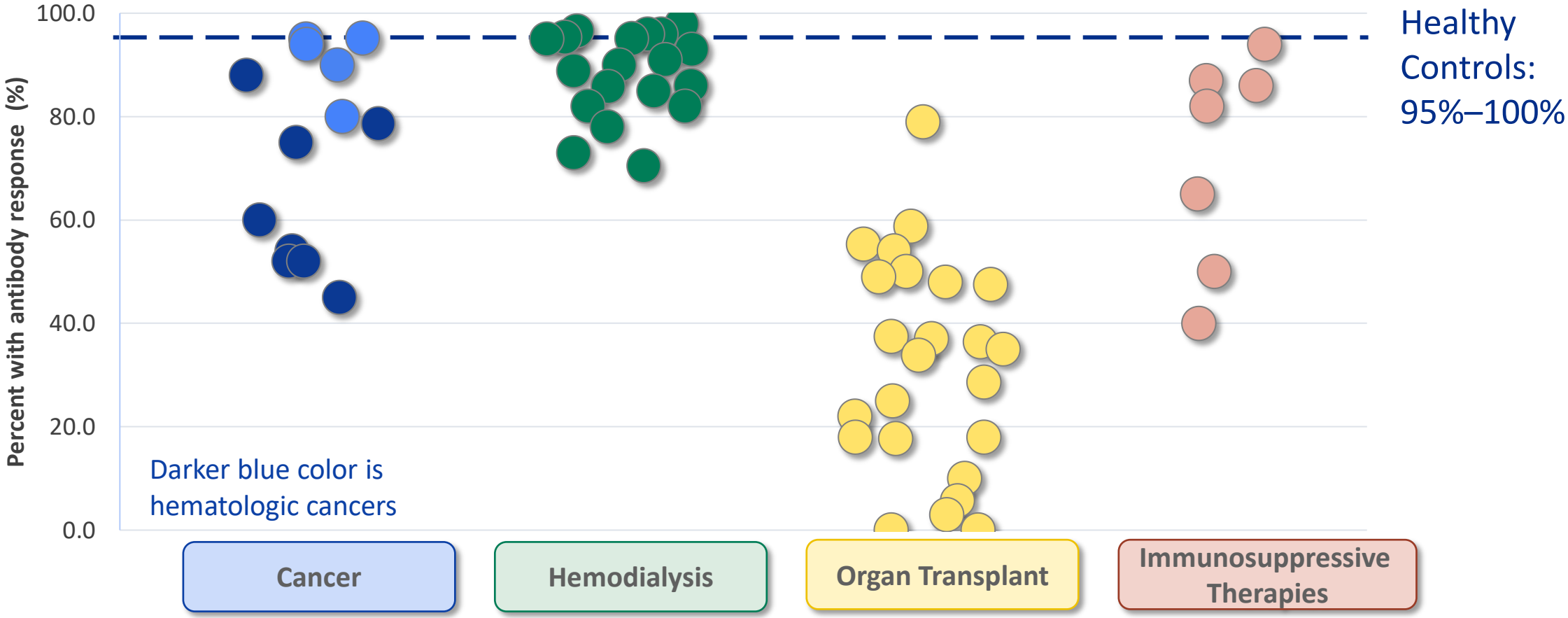
Immunocompromised people and infections in vaccinated persons

- More likely to have breakthrough infection
  - 40-44% of hospitalized breakthrough cases are immunocompromised people in US study[1-2]
- Lower vaccine effectiveness
  - 59-72% VE among immunocompromised people compared to 90-94% among non-immunocompromised people after second dose[1, 3-5]

COVID-19 Prevention Network

See reference slide at end

Percent of subjects with antibody response after two mRNA COVID-19 vaccine doses by immunocompromising condition and study (n=63)



- Studies that compared response after first and second dose demonstrated less robust response after dose 1
- Antibody measurement and threshold levels vary by study protocol

COVID-19 Prevention Network

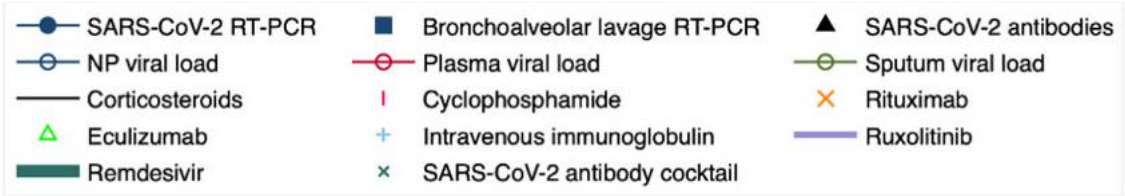
See reference slide at end

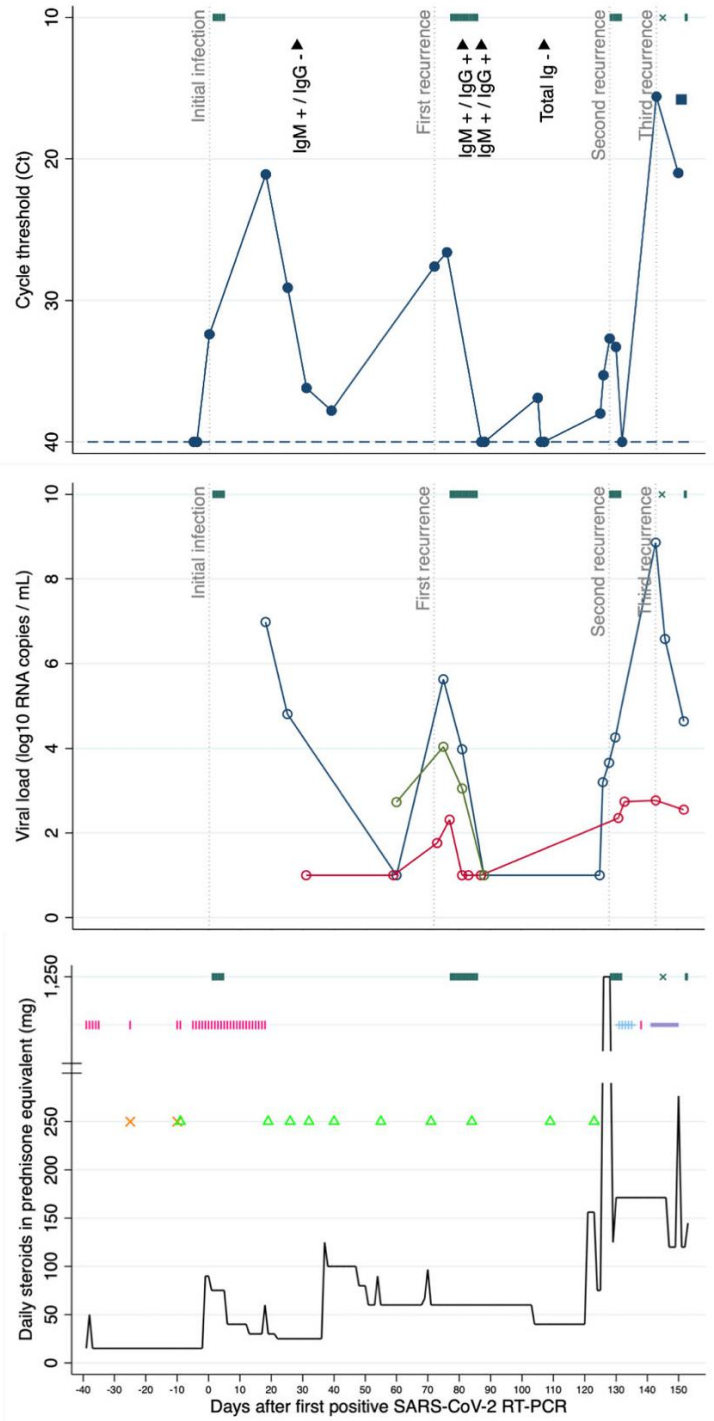
Levels of SARS-CoV-2 viral RNA and time course of immunosuppressive and antiviral treatments

Top panel: Nasopharyngeal and bronchoalveolar lavage SARS-CoV-2 RT-PCR cycle threshold (Ct) values (dashed line represents cutoff for positivity at 40) and SARS-CoV-2 antibody testing. Day 0 represents day of first positive SARSCoV-2 nasopharyngeal swab RT-PCR. Prior nasopharyngeal swab RT-PCR from Days -5 and -4 were negative.

Middle panel: SARS-CoV-2 RNA viral loads in nasopharyngeal, plasma, and sputum by quantitative RT-PCR assay. Viral load not obtained on Day 132, the day of negative RT-PCR before third recurrence.

Bottom panel: Immunosuppressive and antiviral treatments.

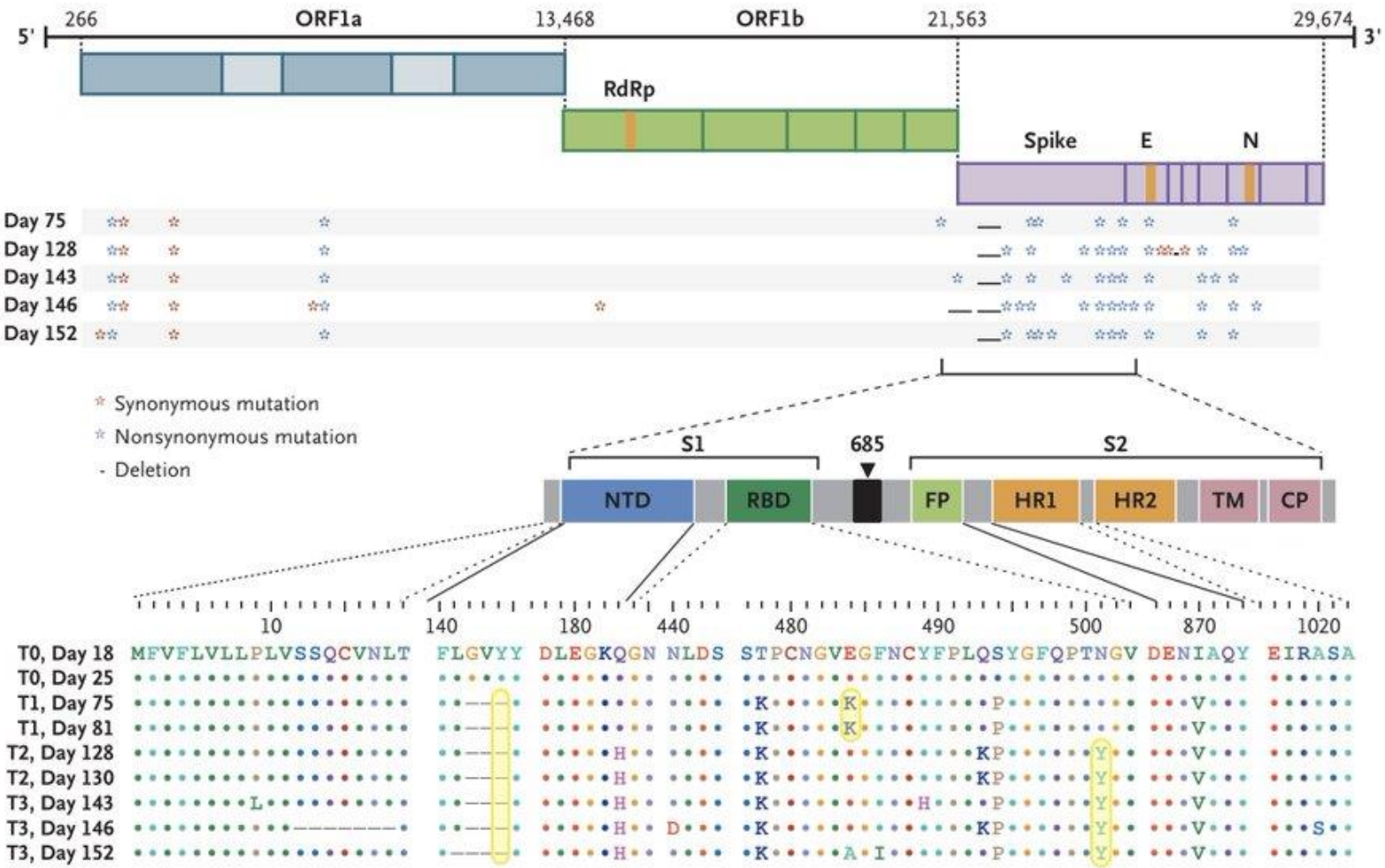




COVID-19 Prevention Network

Choi B, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host. NEJM 2020;383:2291-3.

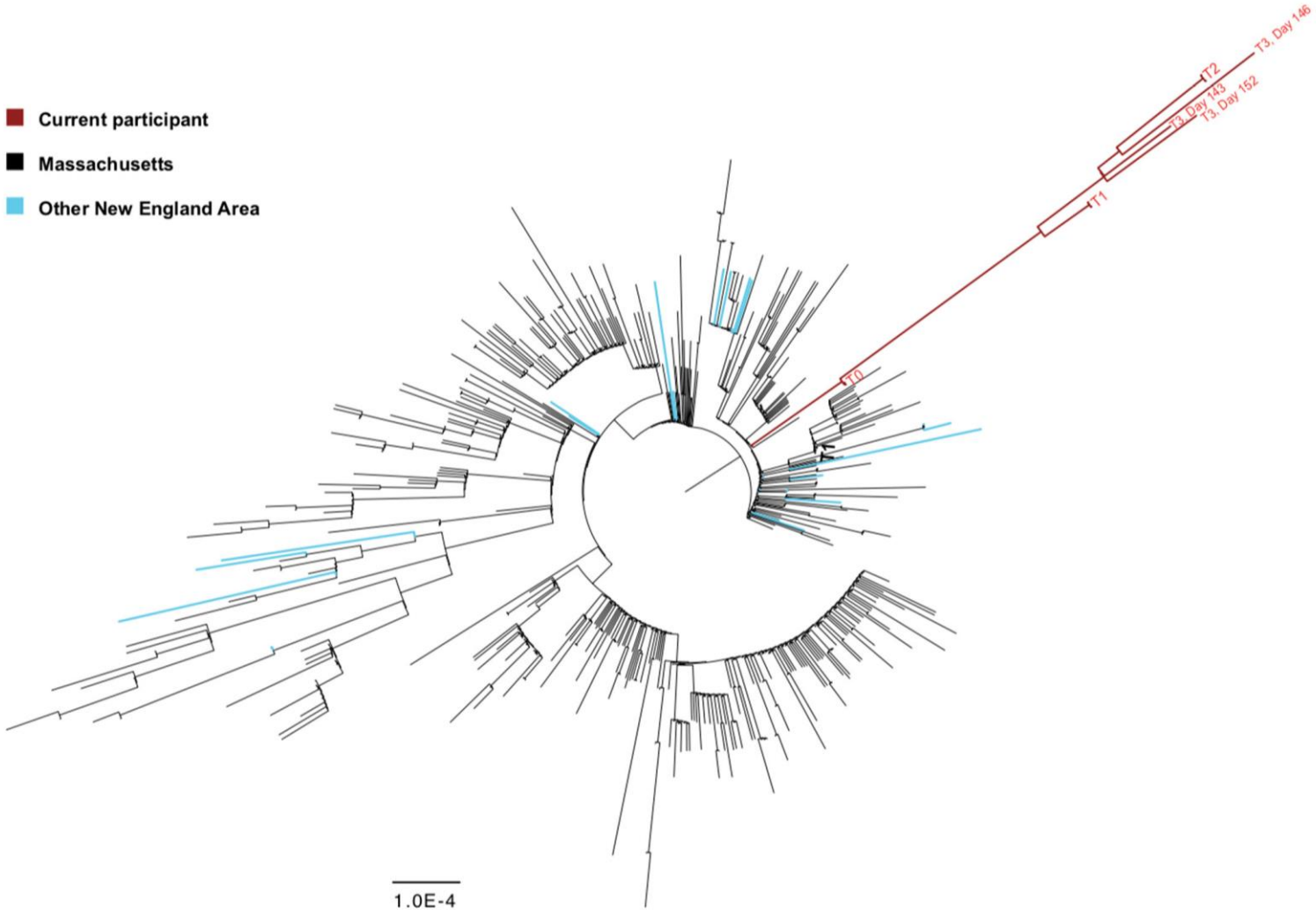
This patient with chronic COVID-19 infection evolved some of the exact same mutations seen in these variant viruses including 484K, 501Y and a 144 deletion



Choi, et al. Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host. N Engl J Med. 2020 Dec 3;383(23):2291-2293.

COVID-19 Prevention Network

Maximum likelihood phylogenetic tree with patient sequences (red) at three time points, T0 (Day 18, 25), T1 (Day 75, 81), T2 (Day 128, 130), and T3 (Days 143, 146, 152) compared to representative sequences from the state (Massachusetts) and region (Other New England Area)



COVID-19 Prevention Network

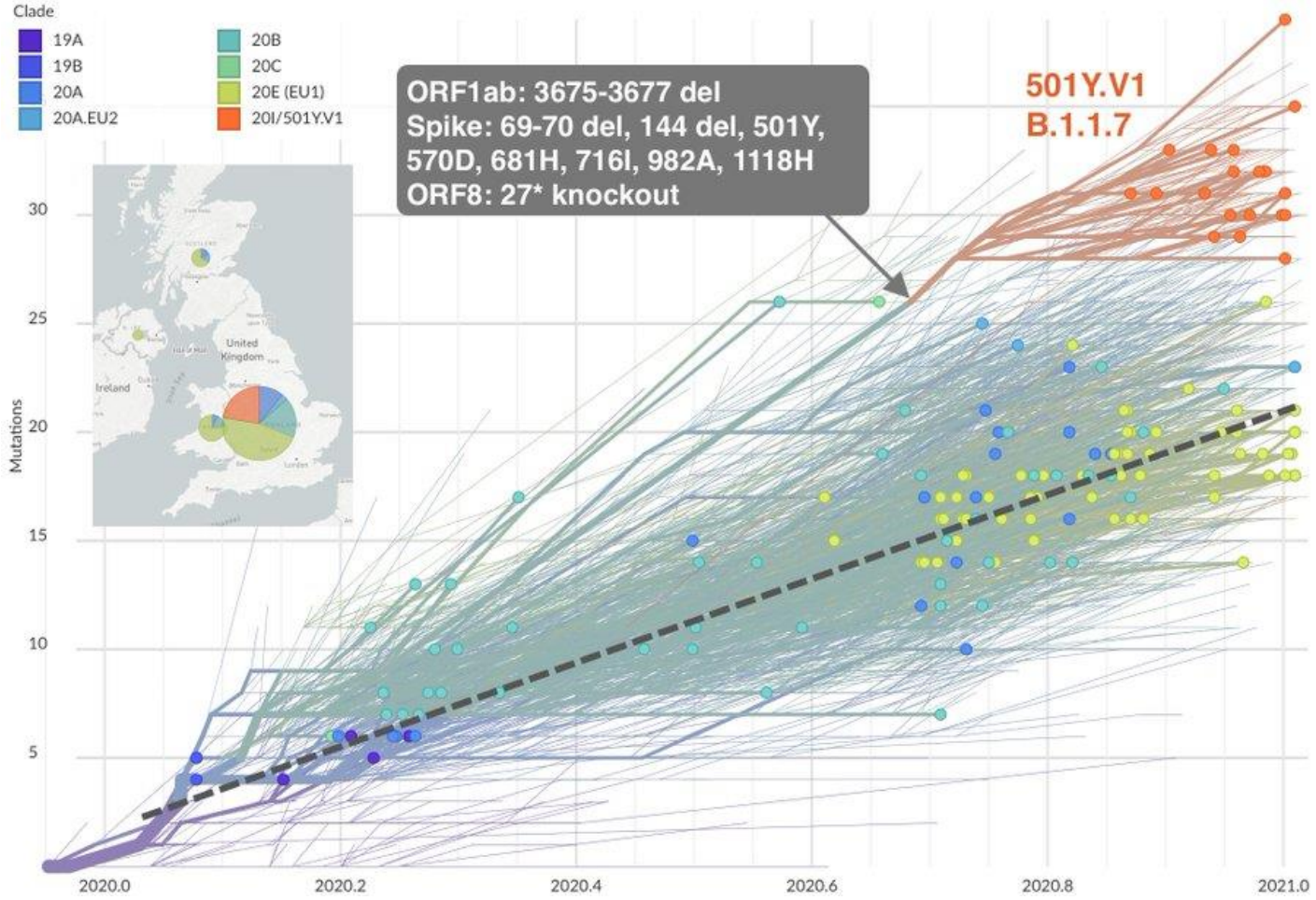
Choi B, et al. Persistence and evolution of SARS-CoV-2 in an immunocompromised host. NEJM 2020;383:2291-3.

Year-long COVID-19 infection reveals within-host evolution of SARS-CoV-2 in a patient with B cell depletion

Veronique Nussenblatt, M.D.[1*], Allison E Roder, Ph.D.[2*], Sanchita Das, M.D.[3], Emmie de Wit, Ph.D.[4], Jung-Ho Youn, Ph.D.[3], Stephanie Banakis, M.S.[2], Alexandra Mushegian, Ph.D.[2], Christopher Mederos, B.S.[2], Wei Wang, M.S.[2], Matthew Chung, Ph.D[2]., Lizzette Pérez-Pérez, M.S.[4], Tara Palmore, M.D.[5], Jennifer N. Brudno, M.D.[6], James N. Kochenderfer, M.D.[6], Elodie Ghedin, Ph.D.[2]

medRxiv preprint doi: https://doi.org/10.1101/2021.10.02.21264267

The variant emerging in the UK possesses 8 mutations in spike, a 3 amino acid deletion in ORF1ab and an ORF8 knockout mutation



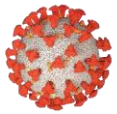
This figure is a "root-to-tip" plot showing number of mutations in sampled viruses against date of collection.
The dashed line represents average accumulation of mutations of about 1 mutation every 2 weeks.
The 501Y.V1 variant stands out here with additional mutations.

https://nextstrain.org/ncov/europe?branchLabel=none&f_country=United%20Kingdom&l=clock&m=div&r=division

COVID-19 Prevention Network

Issues to Discuss

- Prevention of infection in the severely immunocompromised host has been, with essentially every viral disease, better than treatment; especially if they are lymphopenic (personal benefit).
- Asymptomatic acquisition is common in the immune compromised host and hence prolonged shedding and transmission (infectivity to particle ratio).
- Both of the above are amenable to reduction by effective prophylaxis.
- Vaccination, monoclonals, antivirals, vaccination plus monoclonals?



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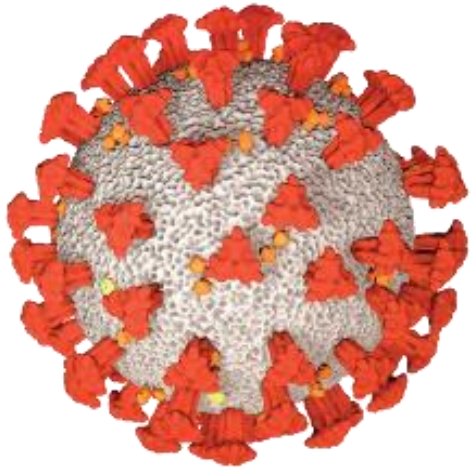
COVID-19 Prevention in Compromised Hosts



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Myron S. Cohen, MD

Yeargan-Bate Professor of Medicine, Microbiology and Epidemiology
Associate Vice Chancellor for Medical Affairs and Global Health
Director, Institute for Global Health and Infectious Diseases

UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

130 Mason Farm Road, Suite 2115, CB 7030 | Chapel Hill, NC
http://globalhealth.unc.edu | https://www.med.unc.edu/infdis

Research

JAMA | Original Investigation

Effect of Bamlanivimab vs Placebo on Incidence of COVID-19 Among Residents and Staff of Skilled Nursing and Assisted Living Facilities A Randomized Clinical Trial

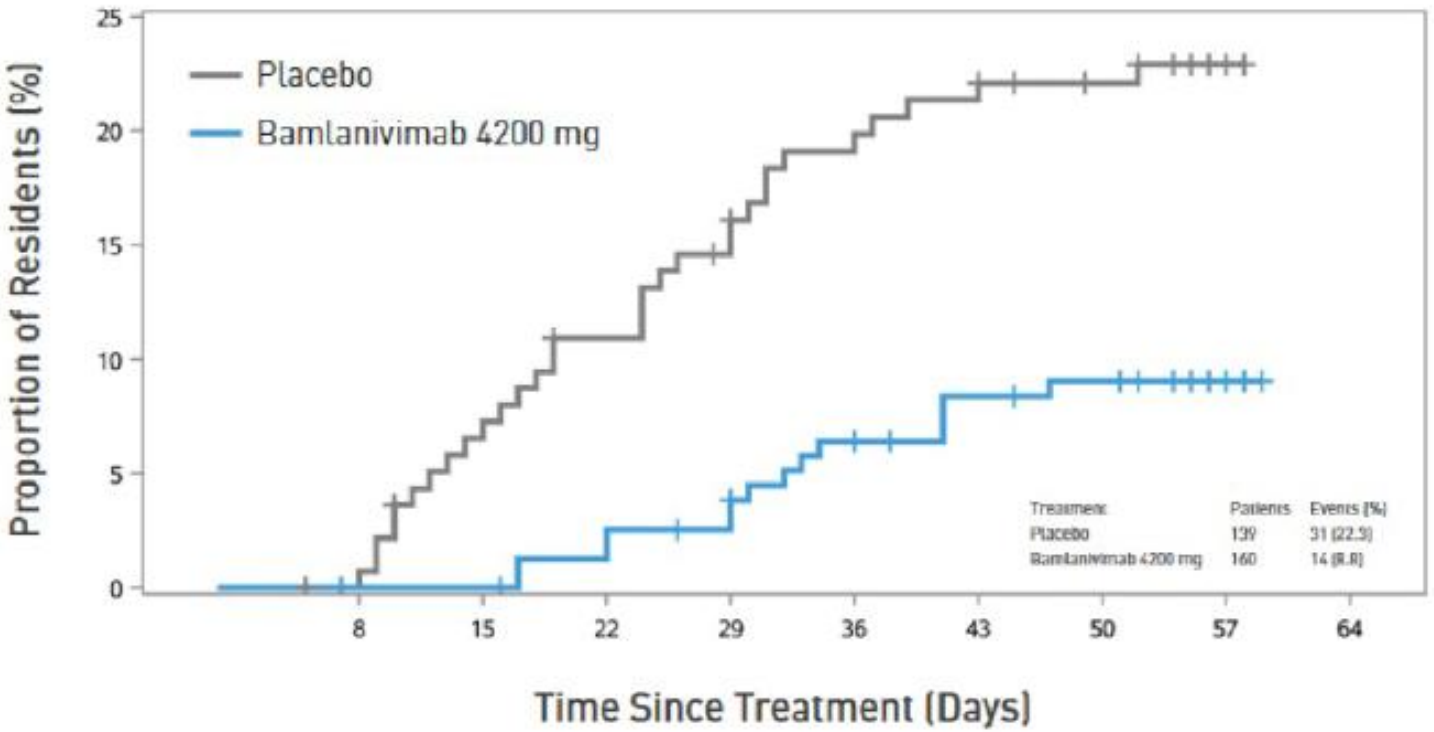
Myron S. Cohen, MD; Ajay Nirula, MD, PhD; Mark J. Mulligan, MD; Richard M. Novak, MD; Mary Marovich, MD; Catherine Yen, MD; Alexander Stemer, MD; Stockton M. Mayer, DO; David Wohl, MD; Blair Brengle, MD; Brian T. Montague, DO; Ian Frank, MD; Russell J. McCulloh, MD; Carl J. Fichtenbaum, MD; Brad Lipson, DO; Nashwa Gabra, MD; Julio A. Ramirez, MD; Christine Thai, MD; Wairimu Chege, MD, MPH; Margarita M. Gomez Lorenzo, MD; Nirupama Sista, PhD; Jennifer Farrior, MS; Meredith E. Clement, MD; Elizabeth R. Brown, ScD; Kenneth L. Custer, PhD; Jacob Van Naarden, BS; Andrew C. Adams, PhD; Andrew E. Schade, MD, PhD; Matan C. Dabora, MD; Jack Knorr, PhD; Karen L. Price, PhD; Janelle Sabo, PharmD; Jay L. Tuttle, PhD; Paul Klekotka, MD, PhD; Lei Shen, PhD; Daniel M. Skovronsky, MD, PhD; for the BLAZE-2 Investigators

IMPORTANCE Preventive interventions are needed to protect residents and staff of skilled nursing and assisted living facilities from COVID-19 during outbreaks in their facilities. Bamlanivimab, a neutralizing monoclonal antibody against SARS-CoV-2, may confer rapid protection from SARS-CoV-2 infection and COVID-19.

OBJECTIVE To determine the effect of bamlanivimab on the incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities.

JAMA. 2021 Feb 16;325(7):632-644.

RESIDENTS WITH SYMPTOMATIC COVID-19 (Prevention Population)



COVID-19 PREVENTION

Odds ratio: 0.20
p-value: 0.00026

Up to 80% reduction in risk

DEATH DUE TO COVID-19

Placebo: 4 of 139 residents
Bamlanivimab: 0 of 160 residents

No deaths due to COVID-19 on bamlanivimab

Notes:
No significant effect in rate of COVID-19 diagnosis, which was relatively low, in staff.
Lower viral loads at time of detection among those getting the mAb

DEATH DUE TO ANY CAUSE (RESIDENTS)

	N	Deaths	Rate
Placebo	24	4	17%
Bamlanivimab 4200 mg	17	0	0%

https://investor.lilly.com/news-releases/news-release-details/lillys-neutralizing-antibody-bamlanivimab-ly-cov555-prevented

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19

M.P. O'Brien, E. Forleo-Neto, B.J. Musser, F. Isa, K.-C. Chan, N. Sarkar, K.J. Bar, R.V. Barnabas, D.H. Barouch, M.S. Cohen, C.B. Hurt, D.R. Burwen, M.A. Marovich, P. Hou, I. Heirman, J.D. Davis, K.C. Turner, D. Ramesh, A. Mahmood, A.T. Hooper, J.D. Hamilton, Y. Kim, L.A. Purcell, A. Baum, C.A. Kyratsous, J. Krainson, R. Perez-Perez, R. Mohseni, B. Kowal, A.T. DiCioccio, N. Stahl, L. Lipsich, N. Braunstein, G. Herman, G.D. Yancopoulos, and D.M. Weinreich, for the Covid-19 Phase 3 Prevention Trial Team*

ABSTRACT

BACKGROUND

REGEN-COV (previously known as REGN-COV2), a combination of the monoclonal antibodies casirivimab and imdevimab, has been shown to markedly reduce the risk of hospitalization or death among high-risk persons with coronavirus disease 2019 (Covid-19). Whether subcutaneous REGEN-COV prevents severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and subsequent Covid-19 in persons at high risk for infection because of household exposure to a person with SARS-CoV-2 infection is unknown.

mAbs for COVID-19 Prevention

Casirivimab and Imdevimab (REGEN-COV); Bamlanivimab and Etesevimab

- Post-exposure prophylaxis (PEP) for adults and pediatric individuals (12 years of age and older weighing at least 40 kg) who are:
- At high risk for progression to severe COVID-19, including hospitalization or death, **and**
- Not fully vaccinated **or** *who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, people with immunocompromising conditions, including those taking immunosuppressive medications),* **and**
    - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC), **or**
    - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes or prisons)

mAbs for Prevention of COVID-19: Forward?

- Astra Zenica (IM AZD7442 Combination PROVENT Trial

- 5,197 participants in a 2:1 randomization AZD7442 to placebo

-77% reduction in SARS-CoV-2 in symptomatic infection

- REGEN-COV SubQ PrEP for IC hosts with vaccine “failure”
  - Multinational trial with >8000 subjects planned
  -Three arms with a placebo “rescue” design

nature
International weekly journal of science

Article

SARS-CoV-2 evolution during treatment of chronic infection

https://doi.org/10.1038/s41586-021-03291-y

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Published online: 5 February 2021

Check for updates

Steven A. Kemp[1,148], Dami A. Collier[1,2,3,148], Rawlings P. Datir[2,3,148], Isabella A. T. M. Ferreira[2,3], Salma Gayed[4], Aminu Jahun[5], Myra Hosmillo[5], Chloe Rees-Spear[1], Petra Mlcochova[2,3], Ines Ushiro Lumb[6], David J. Roberts[6], Anita Chandra[2,3], Nigel Temperton[7], The CITIID-NIHR BioResource COVID-19 Collaboration*, The COVID-19 Genomics UK (COG-UK) Consortium*, Katherine Sharrocks[4], Elizabeth Blane[3], Yorgo Modis[2,3,8], Kendra E. Leigh[2,3,8], John A. G. Briggs[8], Marit J. van Gils[9], Kenneth G. C. Smith[2,3], John R. Bradley[3,10], Chris Smith[11], Rainer Doffinger[12], Lourdes Ceron-Gutierrez[12], Gabriela Barcenas-Morales[12,13], David D. Pollock[14], Richard A. Goldstein[1], Anna Smielewska[5,11], Jordan P. Skittrall[4,15,16], Theodore Gouliouris[4], Ian G. Goodfellow[5], Effrossyni Gkrania-Klotsas[4], Christopher J. R. Illingworth[15,17], Laura E. McCoy[1] & Ravindra K. Gupta[2,3,18]

Nature. 2021 Apr;592(7853):277-282. doi: 10.1038/s41586-021-03291-y.

NIH Studies of COVID-19 Vaccines in IC HOSTS

- **NCT04969263**

-Kidney transplant pilot study (booster doses only; no immunosuppression reduction) with 82 participants with detailed evaluation of antibodies and T-Cells

- **NCT05077254**

-A multi-site study is expected to launch in early November; will enroll kidney and liver recipients who are Roche Elecsys negative/non-detectable (<0.8/0.4) after a full course of a COVID-19 vaccine and randomize to immunosuppression reduction vs. maintenance surrounding administration of a booster vaccine.

- **NCT05000216**

-A multi-site study enrolling patients with one of 5 autoimmune diseases and Roche Elecsys titers <50U/ml after a full course of a COVID-19 vaccine and on MMF, MTX, or B cell depleting regimens. Participants on MMF or MTX will be randomized to transient immunosuppression withdrawal vs. maintenance surrounding administration of a booster vaccine. Those on B cell depleting regimens will receive a booster vaccine close to the next dose of the B cell depleting agent.

COVID-19 in Patients with Cancer: A Uniquely Vulnerable Population

Jeremy L. Warner, MD, MS, FAMIA, FASCO
Associate Professor of Medicine (Hematology/Oncology)
and Biomedical Informatics
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Co-Founder and Steering Committee Member
COVID-19 and Cancer Consortium (CCC19)
Director, CCC19 Research Coordinating Center

The COVID-19 & Cancer Consortium

COVID-19 in Patients with Cancer: A Uniquely Vulnerable Population

Jeremy L. Warner, MD, MS, FAMIA, FASCO

October 23, 2021

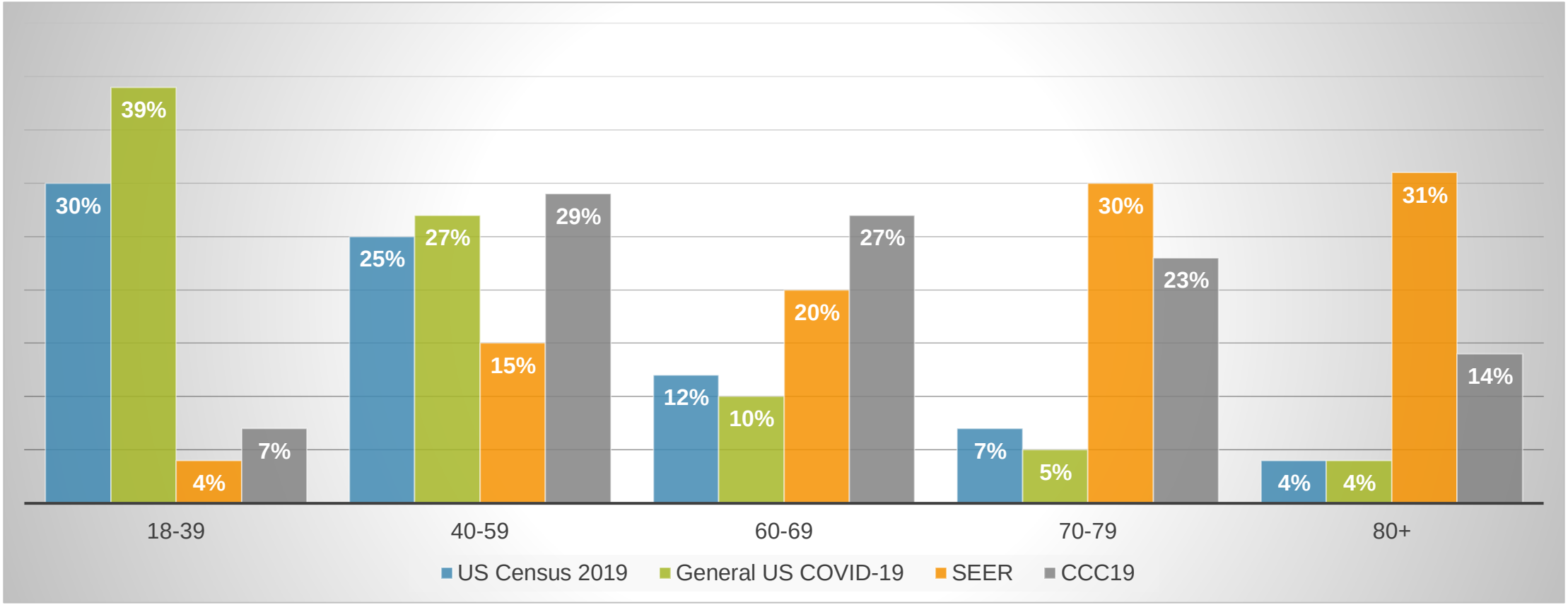
Disclosures

- Grant funding: NIH, AACR
- Consulting: Westat, Roche, Melax Tech, Flatiron Health
- Ownership: HemOnc.org LLC

Patients with Cancer are often Immunocompromised on a Spectrum

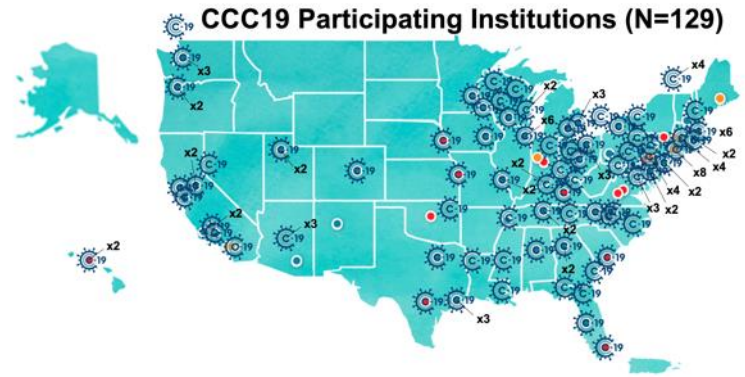
- A patient with **multiple myeloma** who is taking **dexamethasone** 20 mg PO weekly as part of an anticancer regimen
- A patient with ovarian cancer taking **dexamethasone** 8 mg PO twice per day the day before, the day of, and day after chemotherapy
- A patient with diffuse large B-cell lymphoma taking **prednisone** 100 mg PO per day x 5 days every 3 weeks, and **rituximab**, as part of R-CHOP
- A patient with **chronic lymphocytic leukemia**, who may or may not be taking a **BTK inhibitor**
- A patient taking **tacrolimus** after a liver transplant for hepatocellular carcinoma
- A patient continuing **anti-PD-1 immunotherapy** while also receiving **infliximab** to stabilize ICI-induced colitis

Patients with Cancer are Older



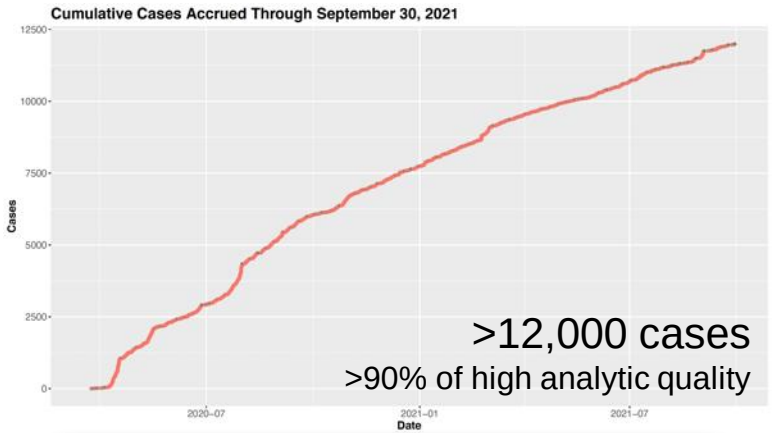
General US COVID-19: https://www.statista.com/statistics/1254271/us-total-number-of-covid-cases-by-age-group/
SEER: Delay-adjusted incidence rates by age at diagnosis, all cancer types. Source: SEER 21 2013–2017, all races, both sexes.
CCC19: Data through September 30, 2021

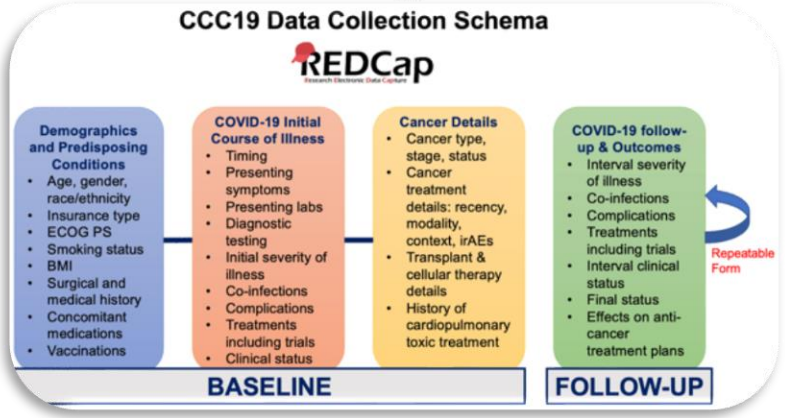
The COVID-19 and Cancer Consortium (CCC19)



>550 investigators

CANCER CENTER · COMPREHENSIVE CANCER CENTER · BASIC LABORATORY





Publications with aggregate >1300 citations

Major findings to date

- Patients with cancer have a **high rate of mortality** and other complications
- Older age, male sex, Black race, Hispanic ethnicity, comorbidities, and performance status are major adverse non-cancer factors
- Progressing cancer, hematologic, and thoracic malignancy are major adverse cancer factors
- No apparent increased risk with cancer treatment overall, but certain treatments/timing may carry risk
- In early data, HCQ and steroids have not shown benefit; remdesivir is of questionable benefit
- Access to certain COVID-19 treatments appears to be driven by non-clinical factors, e.g., race
- Convalescent plasma may improve survival in patients with hematologic malignancy

NCT04354701 www.ccc19.org

More than 550 investigators

Maheen Abidi; David M. Aboulafia; Melissa K. Accordino; Jared D. Acoba; Daniel Addison; Shailesh Advani; Muhammad Zubair Afzal; Neeraj Agarwal; Manmeet S. Ahluwalia; Syed A. Ahmad; Archana Ajmera; Mojtaba Akhtari; Mariam Alexander; Saif I. Alimohamed; Mohammed E. Alomar; Jessica Altman; Celina Ang; Anne H. Angevine; Susan K. Ayre; Nilo Azad; Nadia Bahadur; Julian Bailey; Ziad Bakouny; Michael H. Bar; Aditya Bardia; Jill S. Barnholtz-Sloan; Briana Barrow McCollough; Babar Bashir; Arnab Basu; Gerald Batist; Mónica Patricia Bejarano Rosales; Tanios Bekaii-Saab; Rimma Belenkaya; Jeffrey Berenberg; Stephanie Berg; Eric H. Bernicker; Christine Bestvina; Divaya Bhutani; Neal Bhutiani; Ragneel Bijjula; Mehmet A. Bilen; Poorva Bindal; Rohit Bishnoi; Danielle S. Bitterman; Sibel H. Blau; Pamela Bohachek; Genevieve Boland; Mark Bonnen; Gabrielle Bouchard; Nathaniel Bouganim; Mateo Bover Larroya; Daniel W. Bowles; Sharon S. Brouha; CarrieAnn Brown; Leanna Bryd; Robin A. Buerki; Fiona J. 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CCC19 30-day mortality, by age and cancer type

Age, yrs	Mortality
18-39	4%
40-59	6%
60-69	9%
70-79	16%
80+	25%

Overall
N=12,022

Age, yrs	Mortality
18-39	3.5%
40-59	5%
60-69	9%
70-79	15%
80+	25%

Solid tumors
N=9825[a]

Age, yrs	Mortality
18-39	5%
40-59	9%
60-69	11%
70-79	19%
80+	28%

Hematologic malignancy
N=2585[a]

[a]Numbers add to more than 100% because some patients have multiple malignancies

Unpublished data
ccc19.org

CCC19 30-day mortality by age, stratified by immunosuppression

Age, yrs	Mortality
18-39	2%
40-59	3%
60-69	7%
70-79	14%
80+	24%

NOT immunosuppressed at baseline
N=7429

Age, yrs	Mortality
18-39	7.5%
40-59	11%
60-69	15%
70-79	20%
80+	30%

Immunosuppressed[1] at baseline
N=3515

[1]Defined as any of the following: general immunosuppressed state; chronic steroids at a dose of >20 mg prednisone dose equivalent/day; cytotoxic chemotherapy or BTK inhibitor within 3 mo of COVID-19; anti-CD20 antibody or stem cell transplant/cellular therapy within 12 mo of COVID-19

Unpublished data

ccc19.org

CCC19 30-day mortality by age, stratified by immunosuppression and cancer status

Age, yrs	Mortality
18-39	0%
40-59	2%
60-69	4%
70-79	11%
80+	22%

NOT immunosuppressed, cancer inactive
N=3036

Age, yrs	Mortality
18-39	8%
40-59	12%
60-69	15.5%
70-79	21%
80+	30%

Immunosuppressed, cancer active[1]
N=3220

[1]Defined as any of the following: receipt of anticancer treatment within 12 mo of COVID-19; detectable (measurable) cancer, regardless of progression; presence of metastatic cancer; diagnosis of cancer within 12 mo of COVID-19

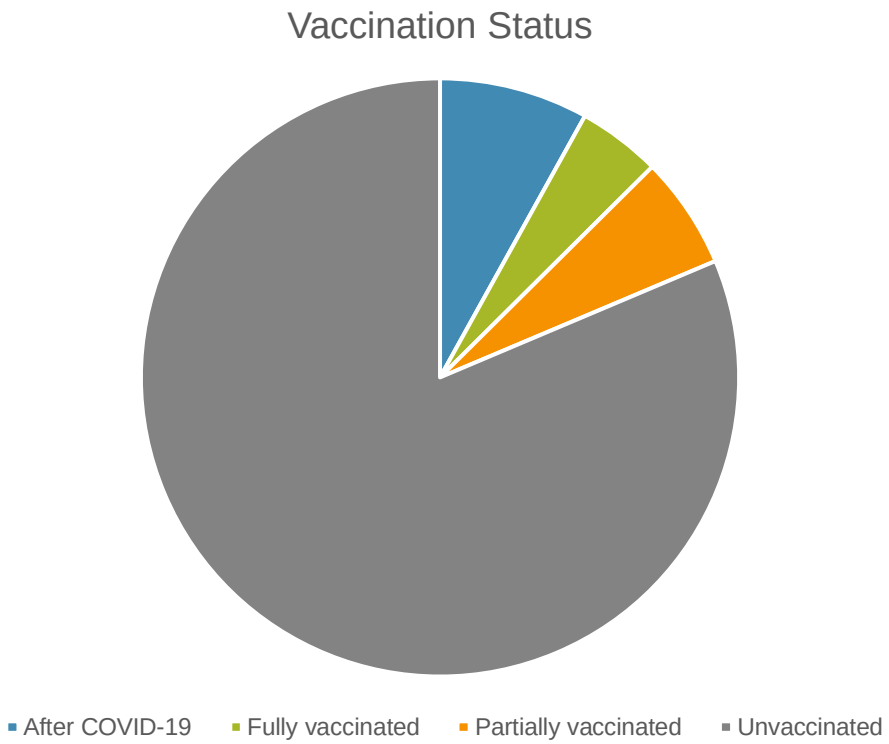
Unpublished data
ccc19.org

Changing the Natural History of SARS-CoV-2 Infection in Patients with Cancer

1. Vaccination
2. Convalescent plasma
3. Monoclonal antibodies

Vaccination in the CCC19 registry

- N=2420 patients with *potential access* to COVID-19 vaccine and known vaccination status



Status	30d Mortality
Unvaccinated	12%
Partially vaccinated	10%
Fully vaccinated	15%
After COVID-19[a]	<2.5%

[a]Lead-time bias precludes interpretation of this endpoint

Manuscript under review

Convalescent Plasma

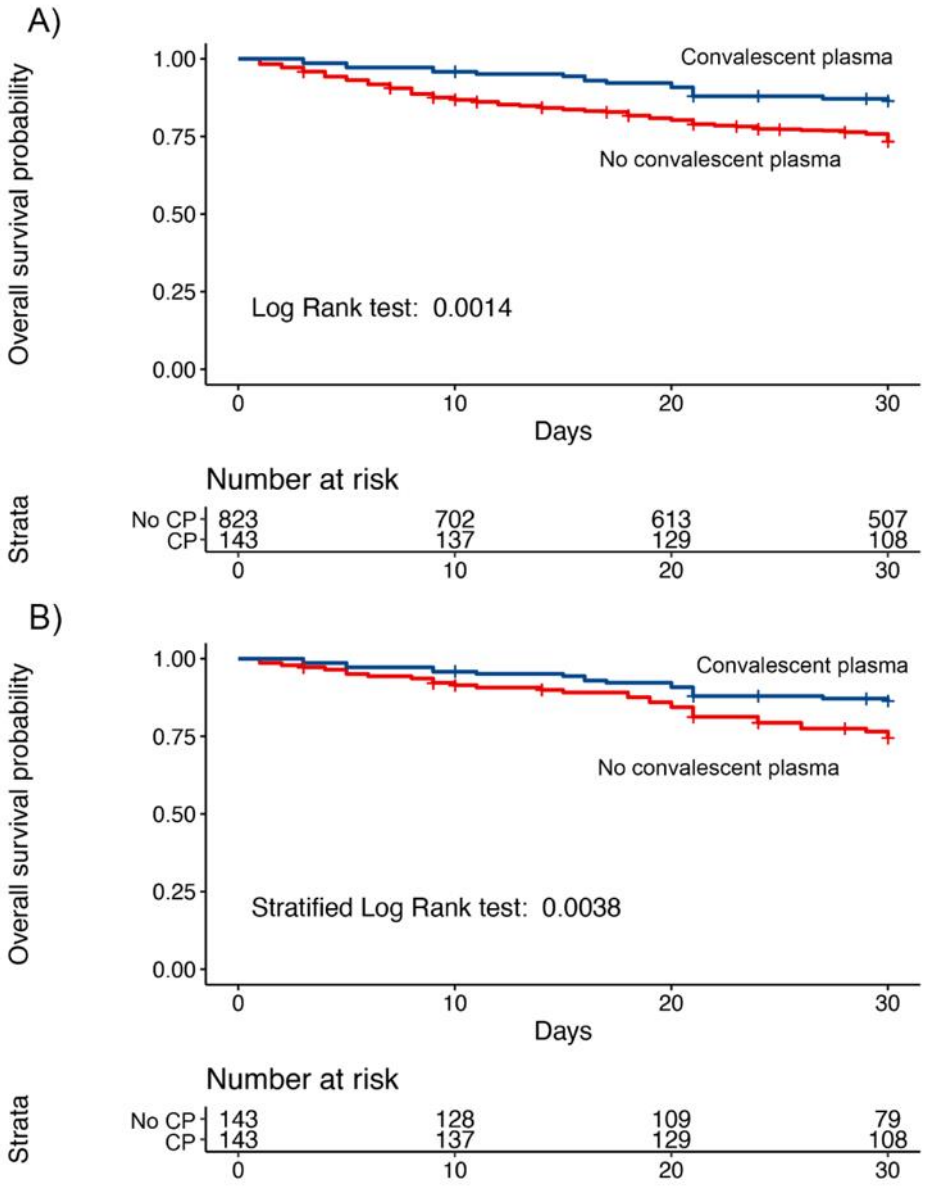


Figure 1: Primary Outcome in the A) Overall Population and B) Propensity-Score Matched Population

Table 3: Association between Convalescent Plasma use and Death in the Crude Analysis, Multivariable Analysis, and Propensity-Score Analyses.

Analysis	Death in 30 days
Overall Population	
No. of events/no. of patients at risk (%)	223/966 (23.1%)
Convalescent plasma	19/143 (13.3%)
No convalescent plasma	204/823 (24.8%)
Crude analysis — hazard ratio (95% CI)[a]	0.47 (0.30 – 0.76)
Multivariable analysis — hazard ratio (95% CI)[b]	0.60 (0.37 – 0.97)
Propensity-score matching — hazard ratio (95% CI)[c]	0.52 (0.29 – 0.92)
Subgroup requiring intensive care unit admission	
No. of events/no. of patients at risk (%)	135/338 (39.9%)
Convalescent Plasma	12/76 (15.8%)
No Convalescent Plasma	123/262 (46.9%)
Crude analysis — hazard ratio (95% CI)[a]	0.26 (0.14 – 0.47)
Multivariable analysis — hazard ratio (95% CI)[b]	0.30 (0.16 – 0.56)
Propensity-score matching — hazard ratio (95% CI)[c]	0.40 (0.20 – 0.80)
Subgroup requiring mechanical ventilation	
No. of events/no. of patients at risk (%)	105/227 (46.3%)
Convalescent Plasma	8/45 (17.8%)
No Convalescent Plasma	97/182 (53.3%)
Crude analysis — hazard ratio (95% CI)[a]	0.24 (0.16 – 0.49)
Multivariable analysis — hazard ratio (95% CI)[b]	0.23 (0.10 – 0.50)
Propensity-score matching — hazard ratio (95% CI)[c]	0.32 (0.14 – 0.72)

[a]Hazard ratio from bivariable model in all patients from the unmatched study cohort
[b]Hazard ratio form multivariable stratified Cox proportional-hazard model, with stratification by trimester of diagnosis with additional covariate adjustment
[c]Marginal hazard ratio from propensity-score matched sample, constructed using 1:1 nearest neighbor matching with calipers of width equal to 0.2 of the standard deviation of the distance measure.

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Monoclonal antibodies

- N=225 patients have received 1 or more doses of monoclonal antibodies (bamlanivimab, bamlanivimab/etesevimab, or casirivimab/imdevimab)

Initial Severity[1]	N (%)
Mild	167 (74%)
Moderate	49 (22%)
Severe	9 (4%)

Outcome	N (%)
No complications	142 (63%)
Hospitalized	81 (36%)
Required ICU	19 (8%)
Req'd intubation	7 (3%)
Died within 30 days	7 (3%)

[1]Mild: no hospitalization indicated; Moderate: hospitalization indicated; Severe: ICU indicated

Unpublished data

Limitations and Conclusions

- Although a large international effort, the CCC19 registry is an observational cohort with all the usual biases:
  - Ascertainment bias (e.g., incomplete reporting; predominance of AMCs)
  - Unmeasured confounding (e.g., SDOH not available in EHRs)
  - Incomplete follow-up (although, 86% of patients not known to be deceased have at least 30 days of follow-up)
- Despite these limitations, the CCC19 registry offers an opportunity to learn about real-world outcomes for vulnerable patients who have not typically been included in prospective studies of COVID-19 interventions

Acknowledgments

- **The patients and their families**
- 129 institutions & >550 active participants
- The Findhorn Foundation for transferring ccc19.org
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Q&A/Discussion

Today's Links

- Slide 1 - This webinar is being recorded and can be found with the slides online at https://www.idsociety.org/cliniciancalls
- Slide 17 - https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1
- Slide 18 - https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf
- Slide 28 - https://covid.cdc.gov/covid-data-tracker/#trends_dailycases
- Slide 29 - https://covid.cdc.gov/covid-data-tracker
- Slide 30 - https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination
- Slide 32- https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm
  - COVID-NET: CDC unpublished; VISION: https://www.nejm.org/doi/10.1056/NEJMoa2110362/https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm
  - IVY: CDC unpublished data; SUPERNOVA: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htmNYS : https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm;
  - HEROES-RECOVER: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm
- Slide 33 – https://doi.org/10.1093/cid/ciab438;
  - https://www.gastrojournal.org/article/S0016-5085(21)03066-3/pdf;
  - https://doi.org/10.1101/2021.07.08.21259776
- Slide 35 - https://doi.org/10.1101/2021.07.02.21259913
- Slide 36 - https://www.fda.gov/media/152161/download; https://www.fda.gov/media/152953/download; https://www.fda.gov/media/152954/download; https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html

Today's Links Continued…

- Slide 37 - https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/04-COVID-Atmar-508.pdf
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  - https://www.fda.gov/media/152953/download
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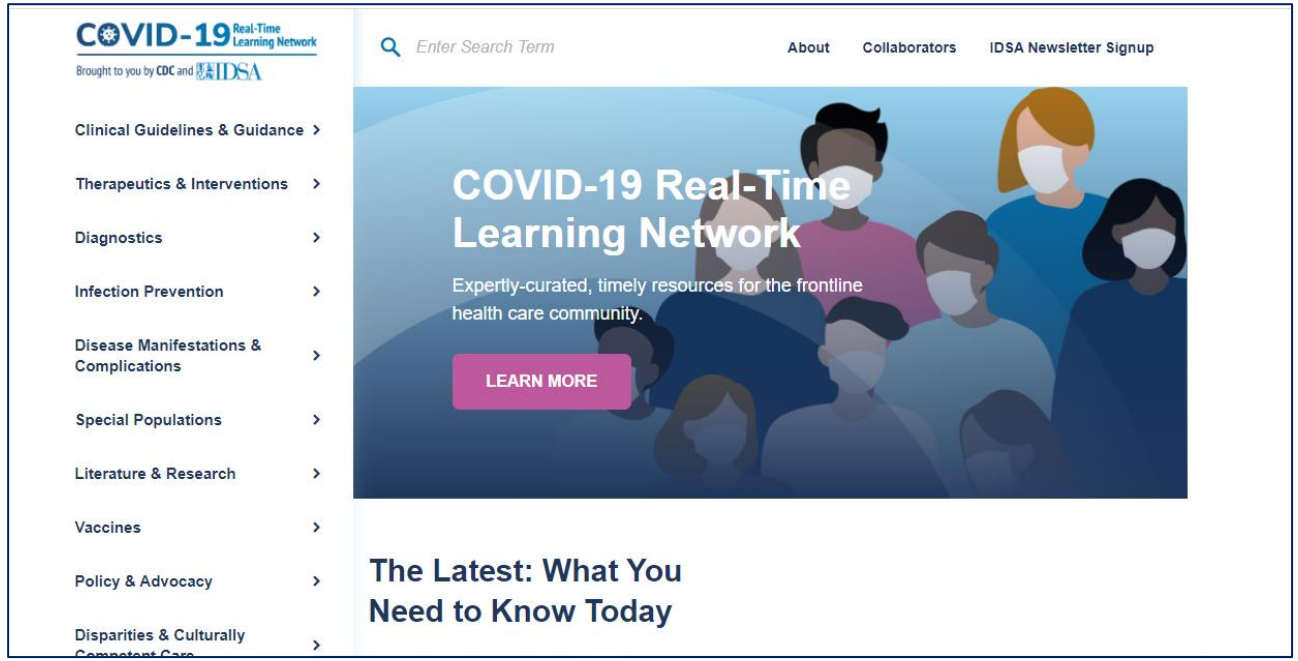
  - https://www.cdc.gov/vaccines/acip/meetings/slides-2021-10-20-21.html
- Slide 40 - https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html
- Slide 47 - https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html
- Slide 48 - https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Coadministration
- Slide 49 - https://www.cdc.gov/vaccines/covid-19/info-by-product/index.html
- Slide 60 - https://doi.org/10.1101/2021.10.02.21264267
- Slide 61 - https://nextstrain.org/ncov/europe?branchLabel=none&f_country=United%20Kingdom&l=clock&m=div&r=division
- Slide 66 - https://investor.lilly.com/news-releases/news-release-details/lillys-neutralizing-antibody-bamlanivimab-ly-cov555-prevented
- Slide 76 https://www.statista.com/statistics/1254271/us-total-number-of-covid-cases-by-age-group/
- Slide 77 - https://ccc19.org/
- Slide 85 - https://doi.org/10.1001/jamaoncol.2021.1799

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



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CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

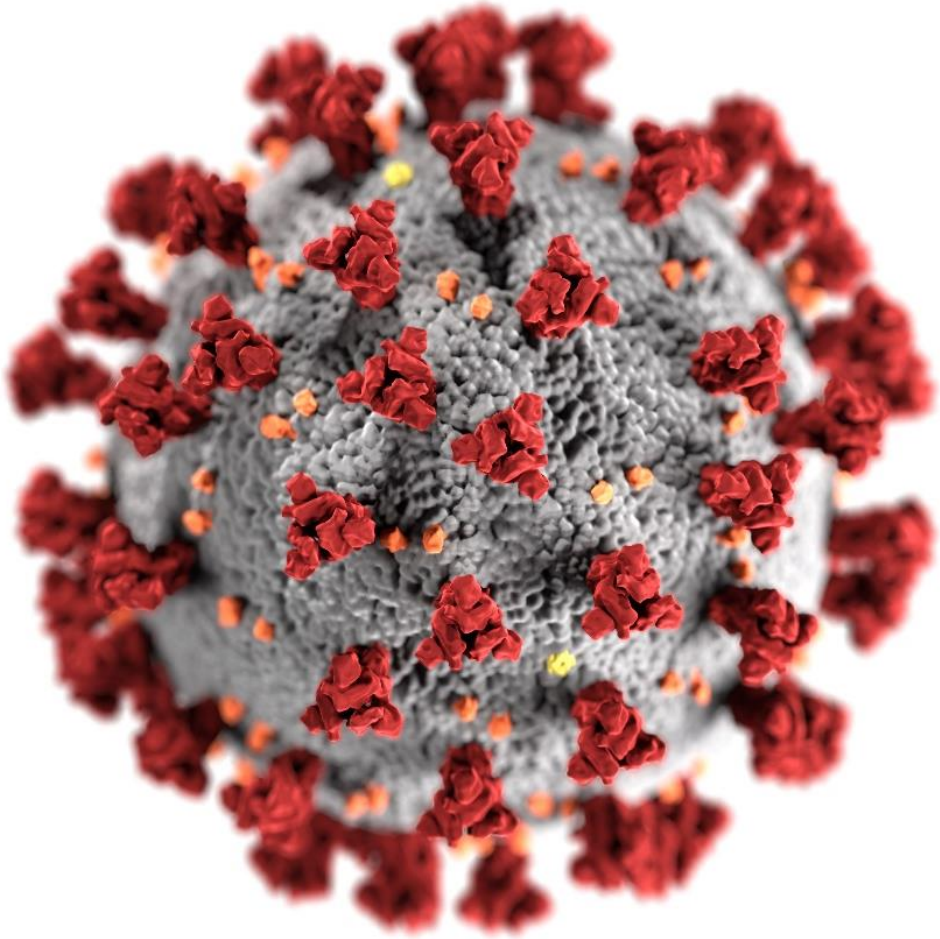
- Clinicians who have questions about the clinical management of COVID-19

WHAT?

- Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form



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Infectious Diseases Society of America

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We want to hear from you!

Please complete the post-call survey.

Next Call:

Saturday, Nov. 6th

A recording of this call will be posted at
www.idsociety.org/cliniciancalls

-- library of all past calls now available --

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Deirdre Lewis (dlewis@idsociety.org)