

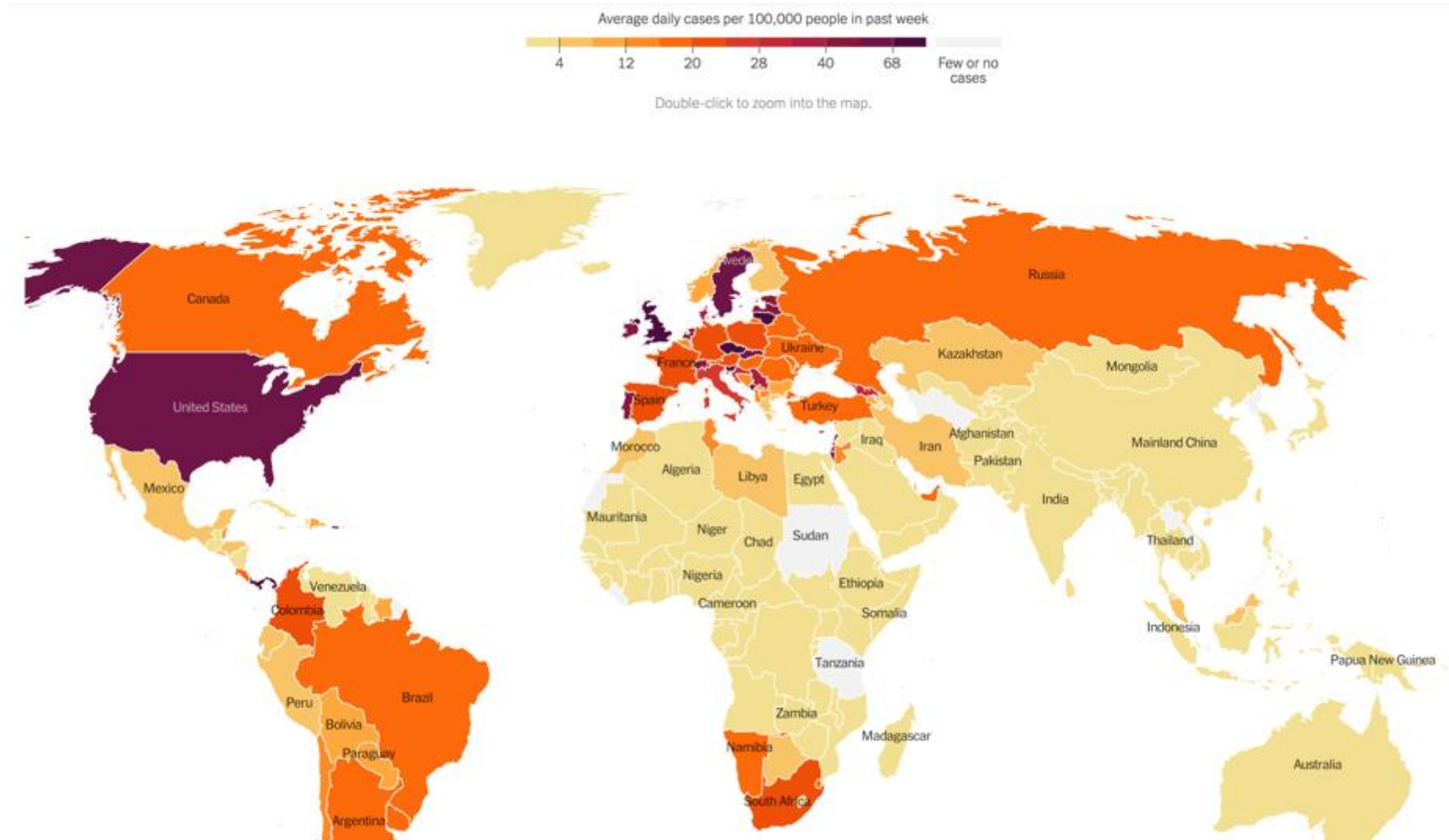
# IL-13 and COVID Pneumonia Research Response to a Pandemic

William A. Petri, Jr. MD, PhD

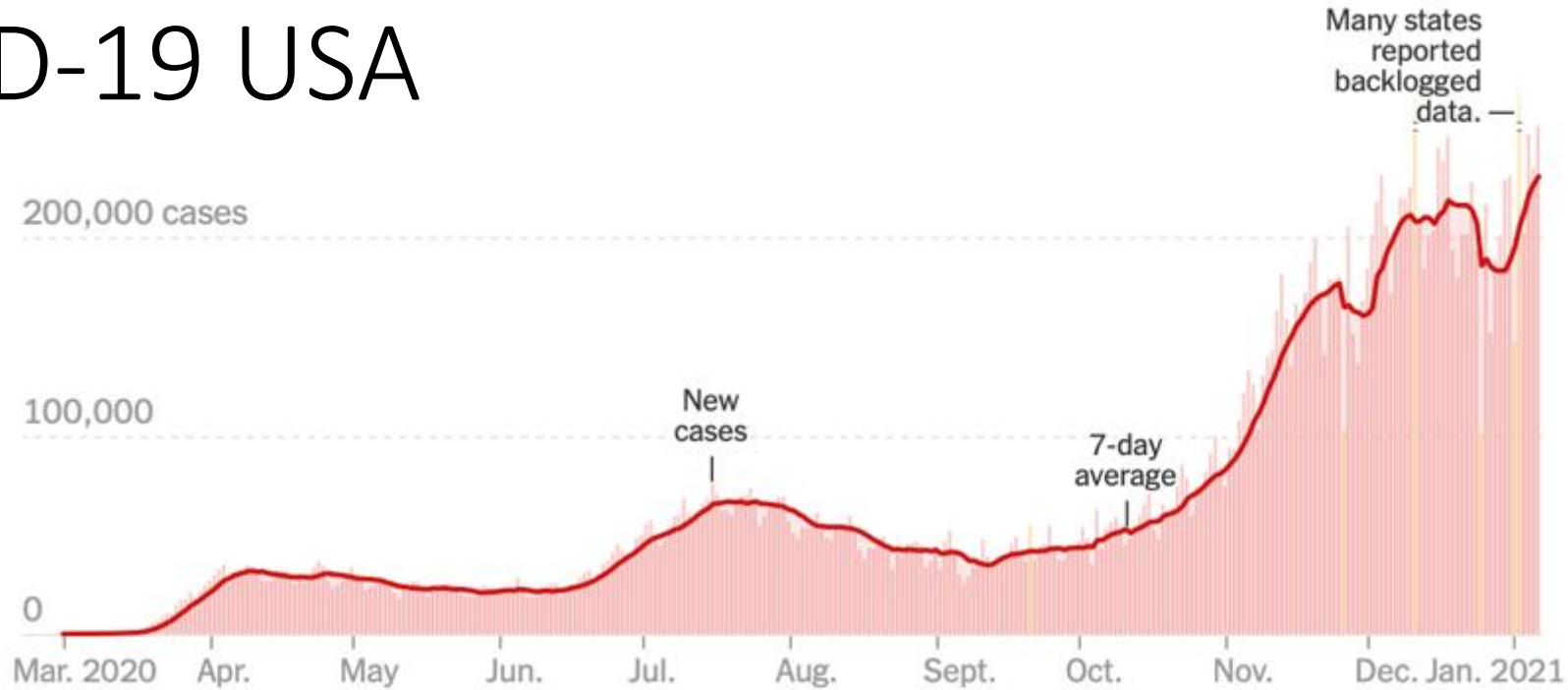
Infectious Diseases, Pathology and MIC

Setting the stage: impact, current treatment

# World daily cases per 100,000



# COVID-19 USA

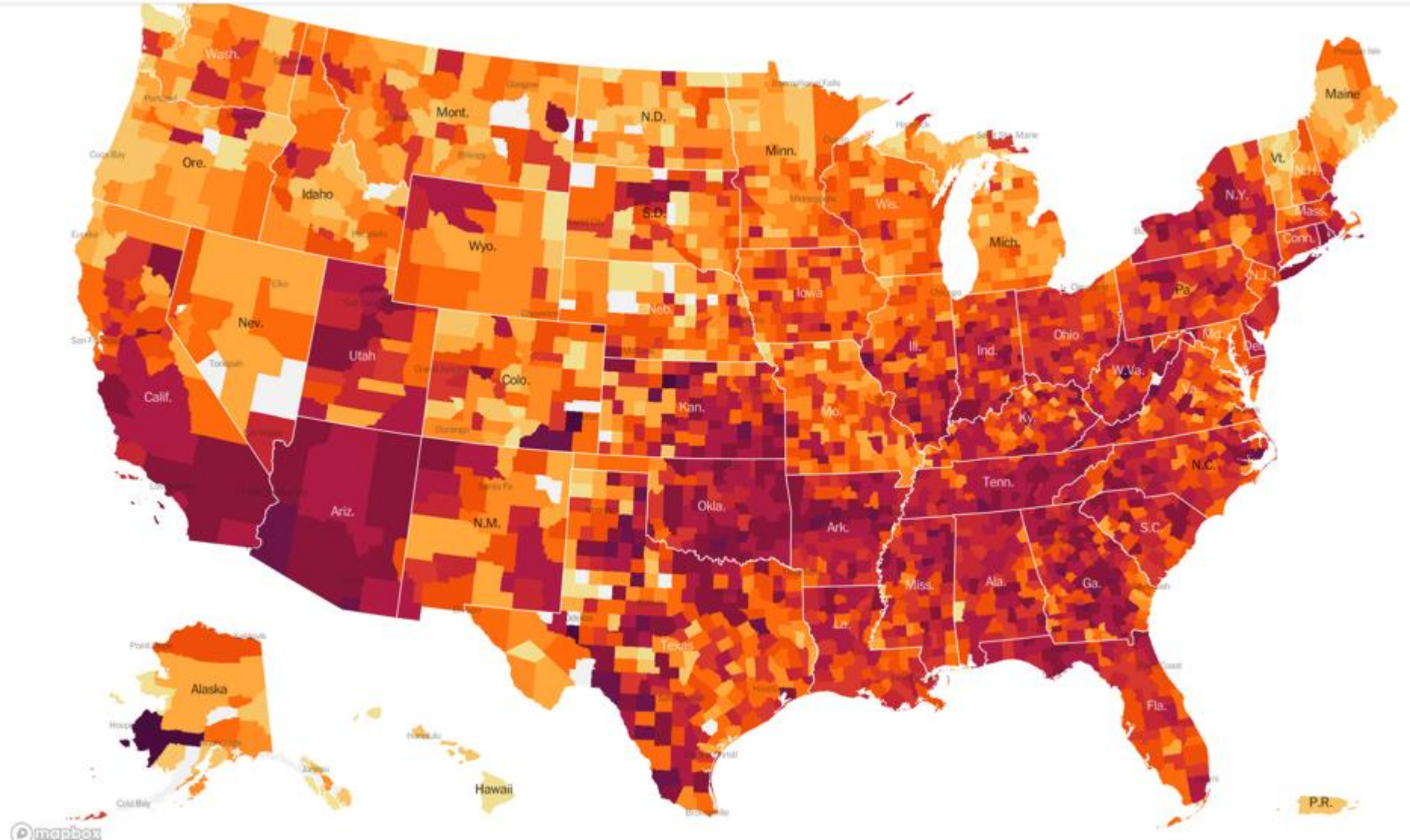


	TOTAL REPORTED	ON JAN. 6	14-DAY CHANGE
<b>Cases</b>	<b>21.4 million+</b>	<b>255,728</b>	<b>+8%</b> ↗
<b>Deaths</b>	<b>361,383</b>	<b>3,964</b>	<b>Flat</b> ↔
<b>Hospitalized</b>		<b>132,476</b>	<b>+10%</b> →

# COVID-19 USA

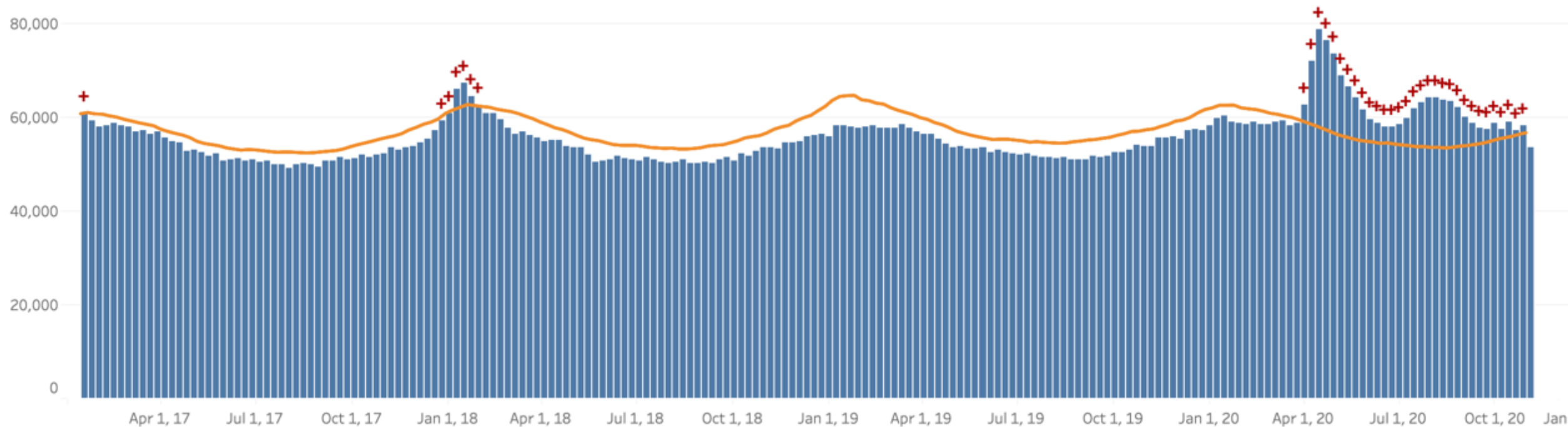
The New York Times

U.S. | Coronavirus in the U.S.: Latest Map and Case Count

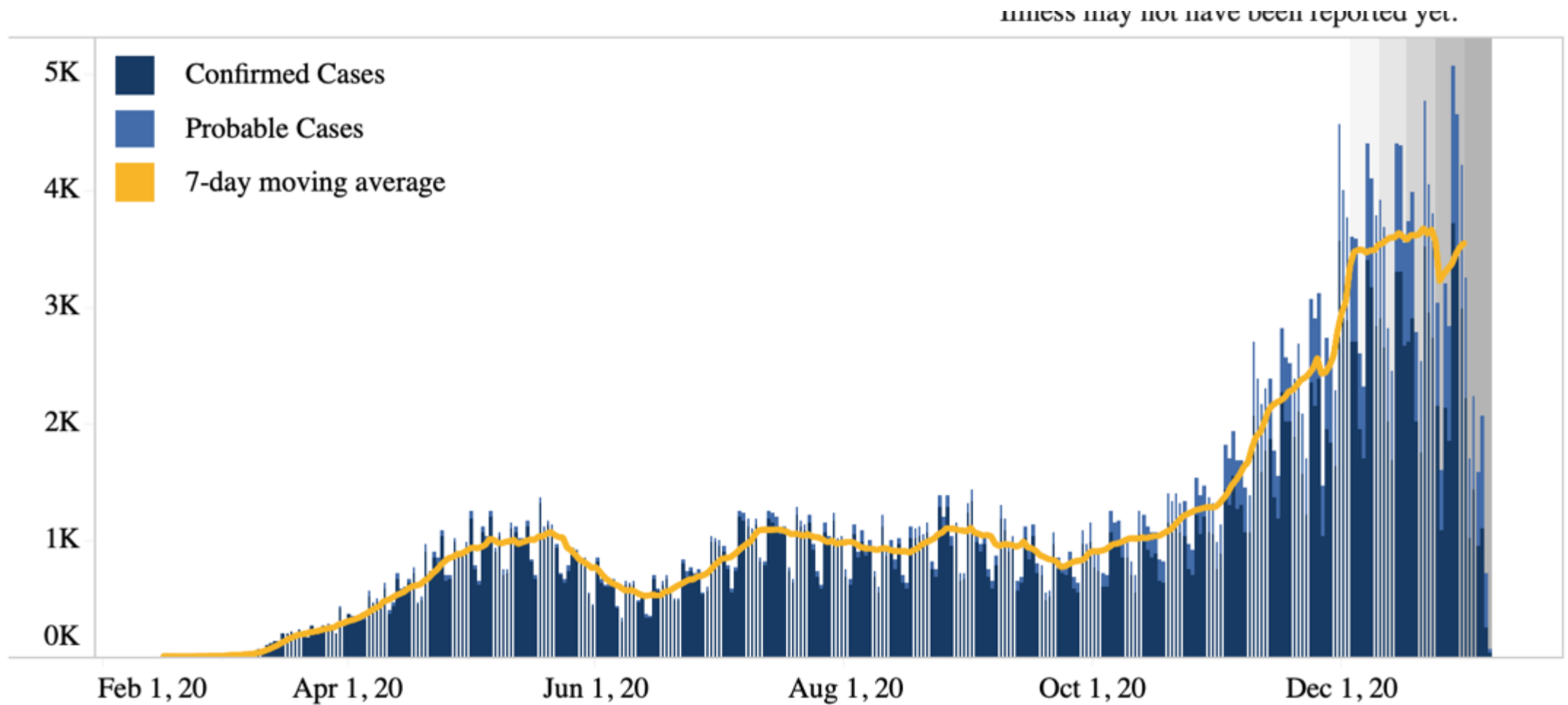


# 242,000-331,000 Excess Deaths United States Since February 1, 2020

Weekly number of deaths (from all causes)



# COVID-19 Virginia



# COVID-19 UVA

June 15<sup>th</sup>, 2020

## **UVA COVID-19 INPATIENT SNAPSHOT, 2:32 p.m.**

Under investigation for COVID-19: **4**  
Confirmed with COVID-19: **18**  
Confirmed with COVID-19 in ICU: **5**  
Confirmed with COVID-19 in ICU on ventilator: **4**

## **Discharged Since March 10**

Under investigation for COVID-19: **19**  
Confirmed with COVID-19: **135**

-

## **PPE INVENTORY UPDATE, 7:11 a.m.**

January 6<sup>th</sup>, 2021

## **Current Census**

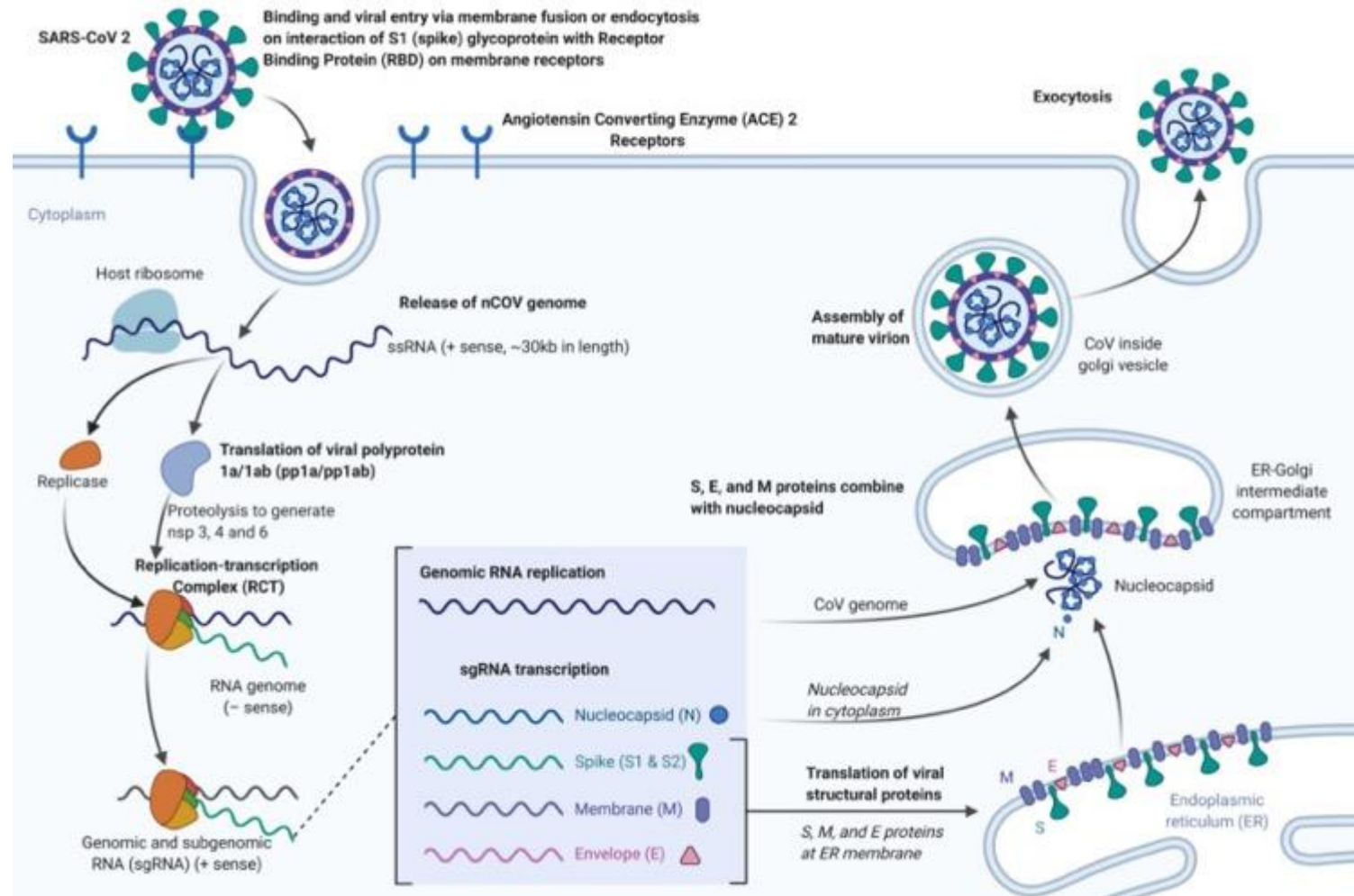
Under investigation for COVID-19: **0**  
Confirmed with COVID-19: **58**  
    Acute SPU (5S): 22  
    ICU SPU (4S): 20  
    3 South: 16  
Confirmed with COVID-19 on ventilator: **17**

## **Discharged Since March 10**

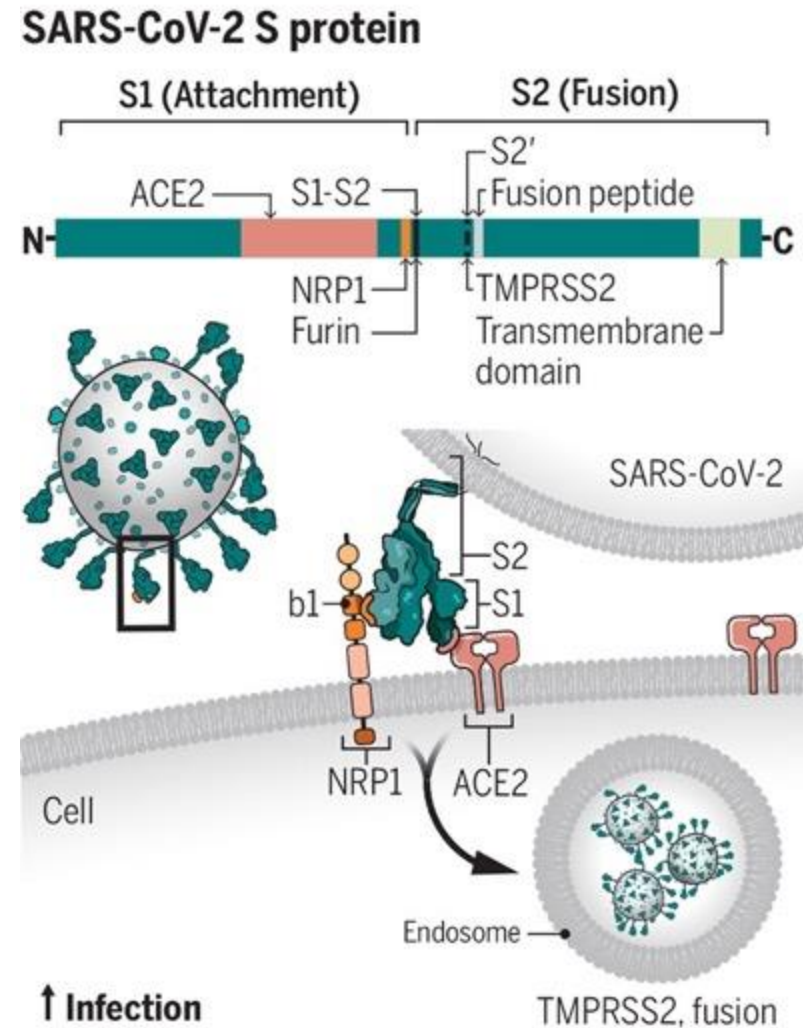
Under investigation for COVID-19: **190**  
Confirmed with COVID-19: **723**



# SARS-CoV-2 Infection of Epithelial Cells

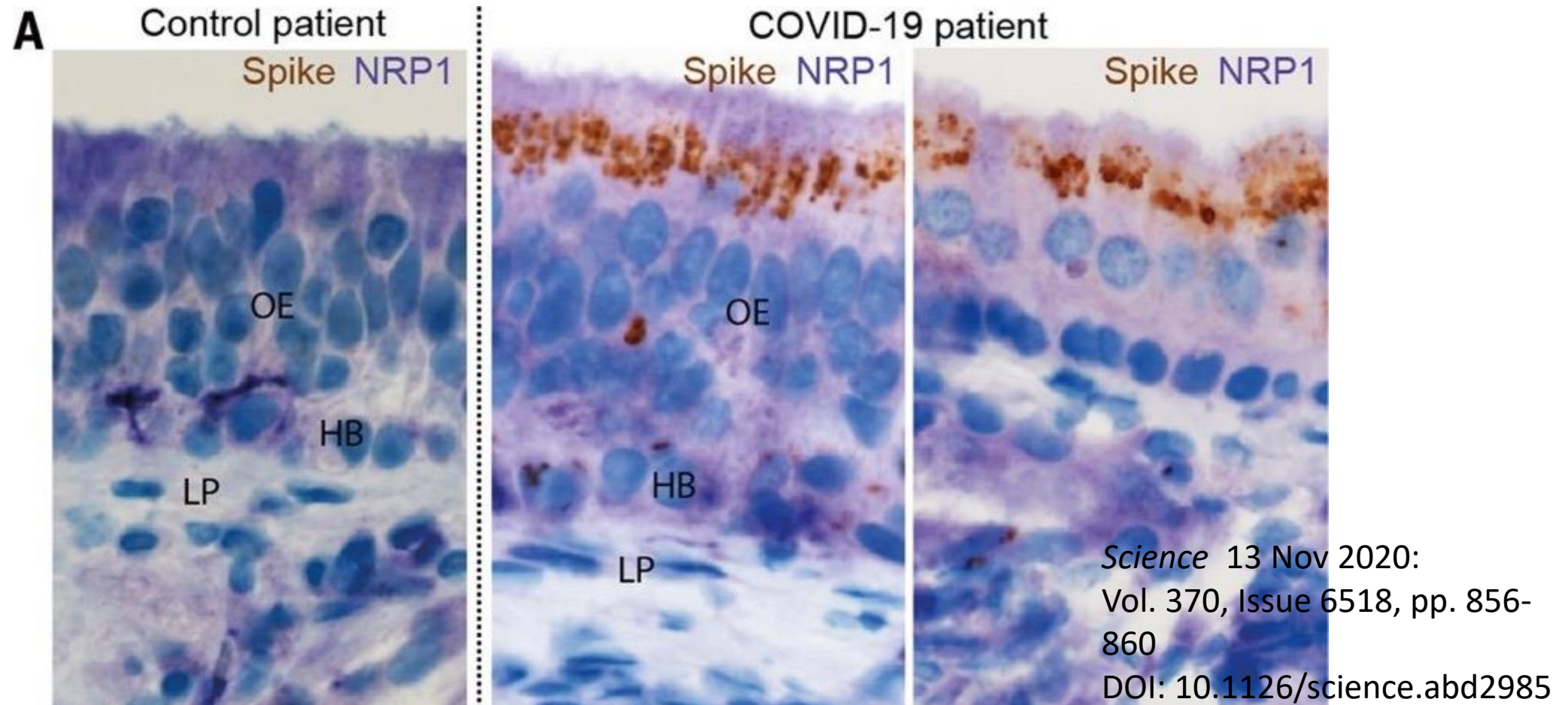


# SARS-CoV-2 Cell Entry via Spike Glycoprotein

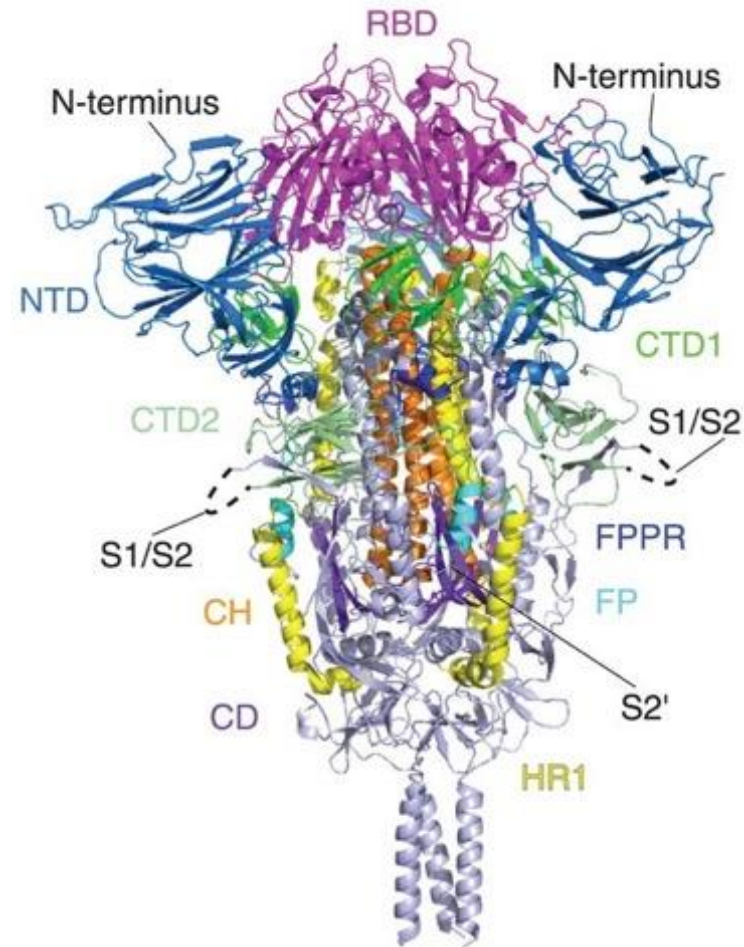


ACE2, angiotensin-converting enzyme 2; NRP1, neuropilin 1; S, spike; SARS-CoV, severe acute respiratory syndrome coronavirus; TMPRSS2, transmembrane protease with serine 2

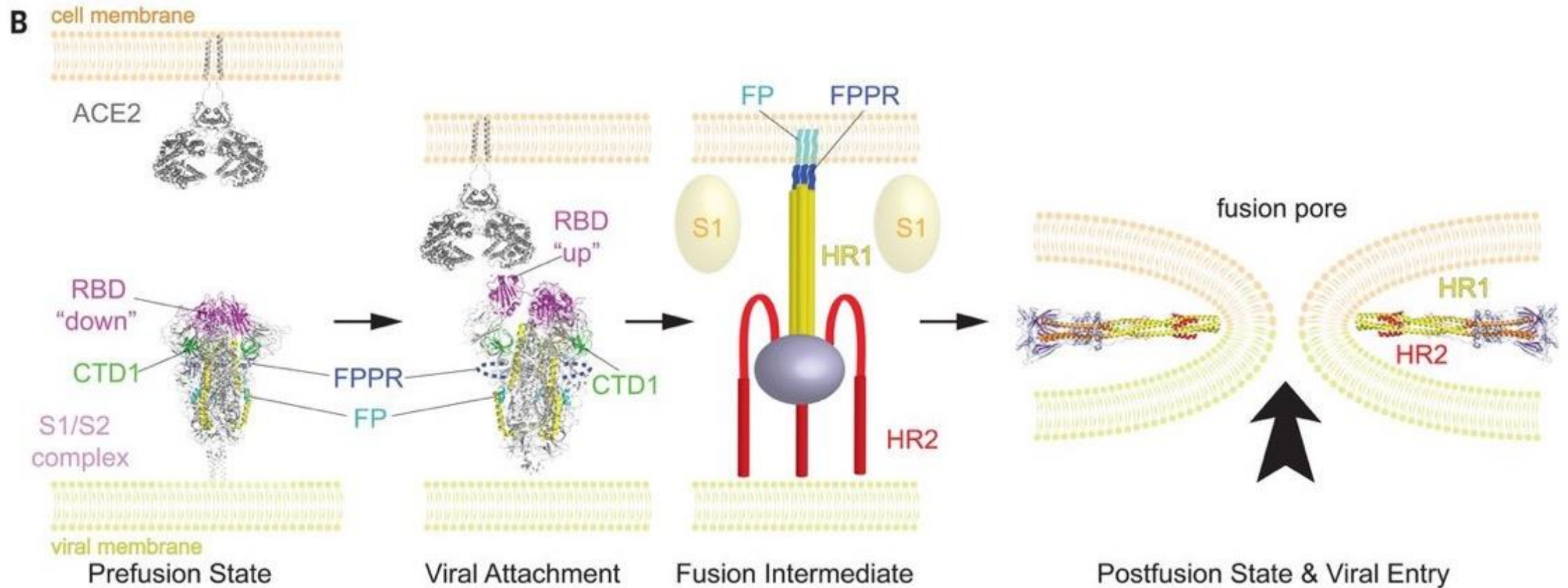
# Olfactory epithelium of patient with COVID-19 demonstrating co-localization of SARS-CoV-2 and neuropilin 1



# Cryo-EM structure of the SARS-CoV-2 S protein in the prefusion conformation

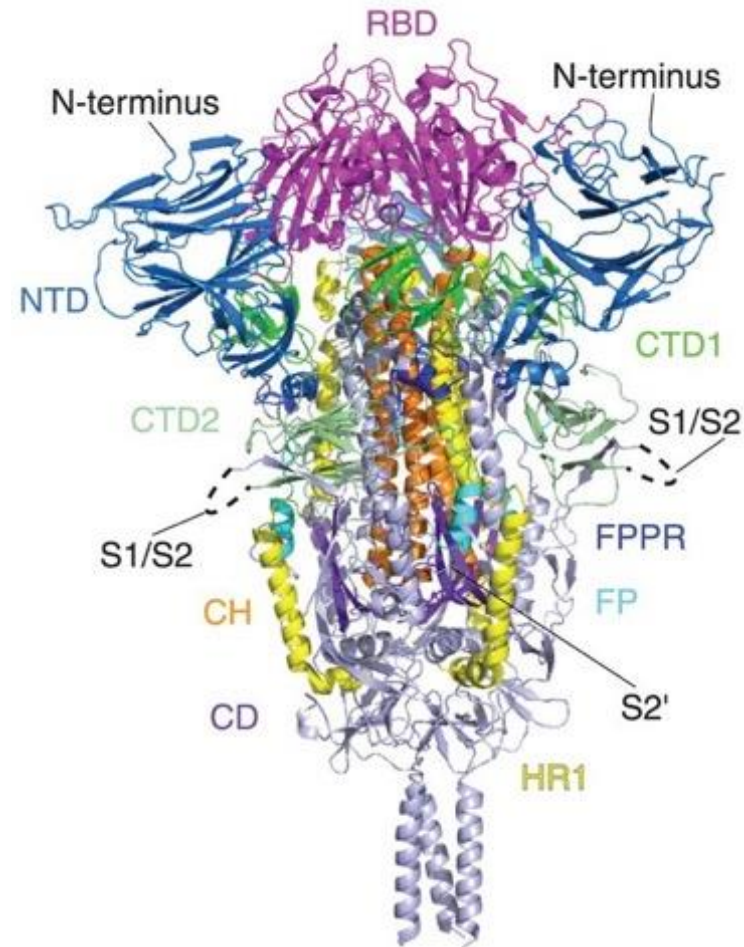


# Prefusion to fusion change in Spike

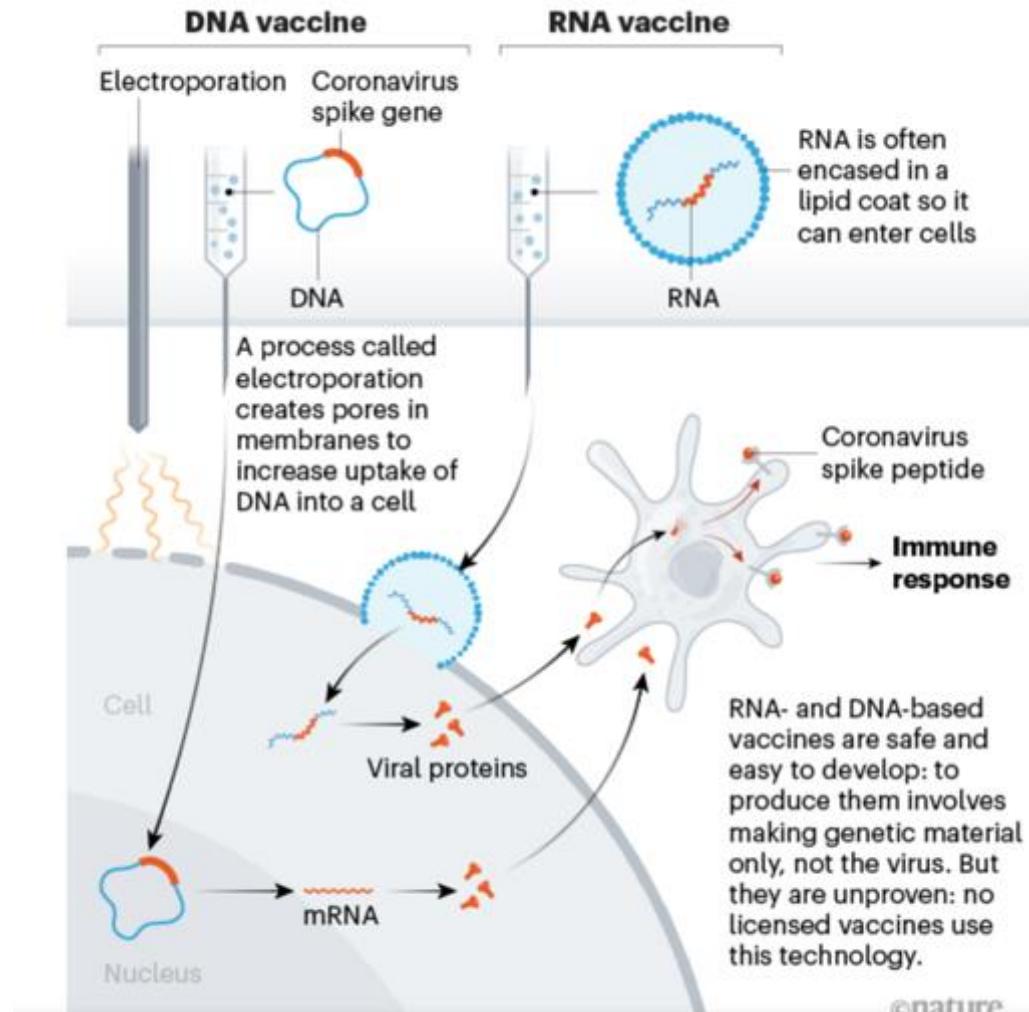


Yongfei Cai et al. *Science* 2020;369:1586-1592

# Goal: lock the SARS-CoV-2 S protein in the prefusion conformation



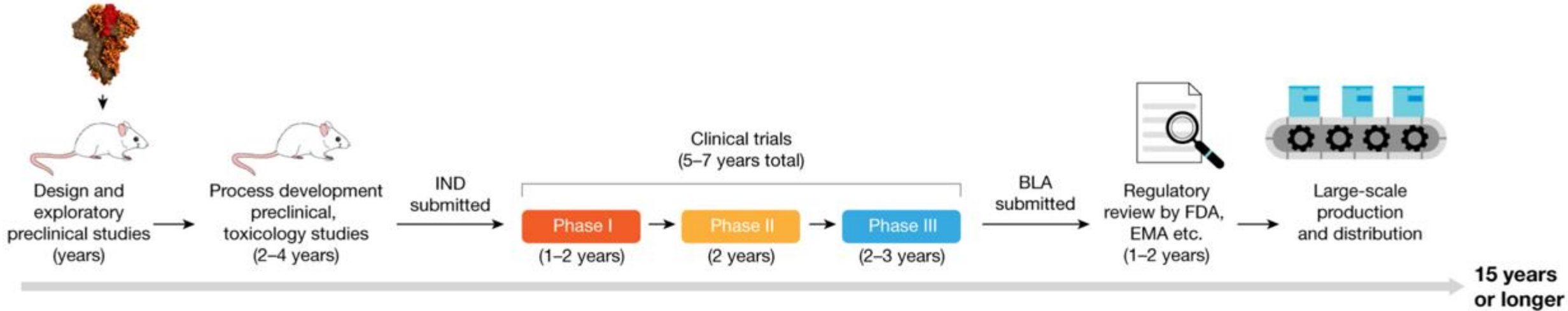
# RNA vs DNA Vaccines



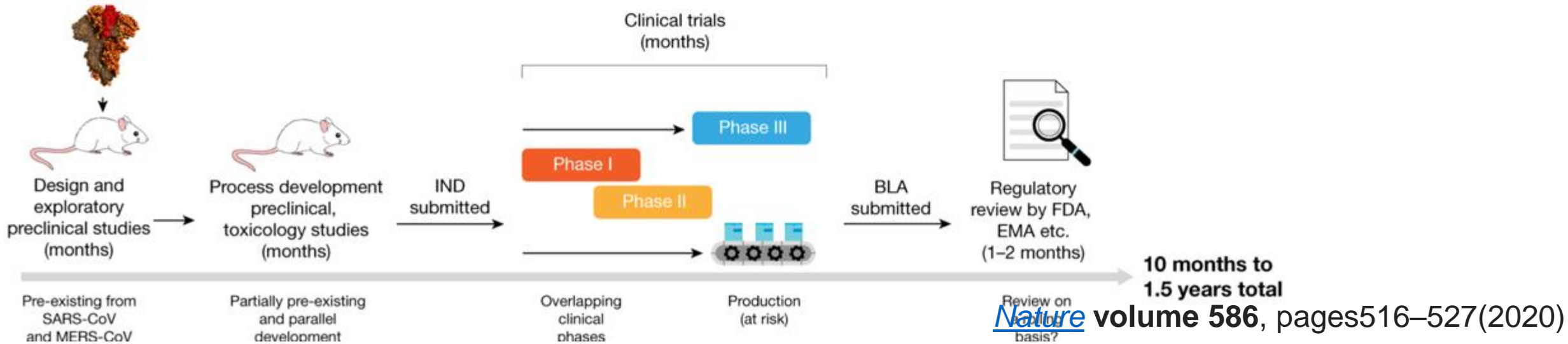
[\*Nature\* volume 586](#), pages 516–527(2020)

# Accelerated development of vaccine

## Traditional development



## SARS-CoV-2 vaccine development

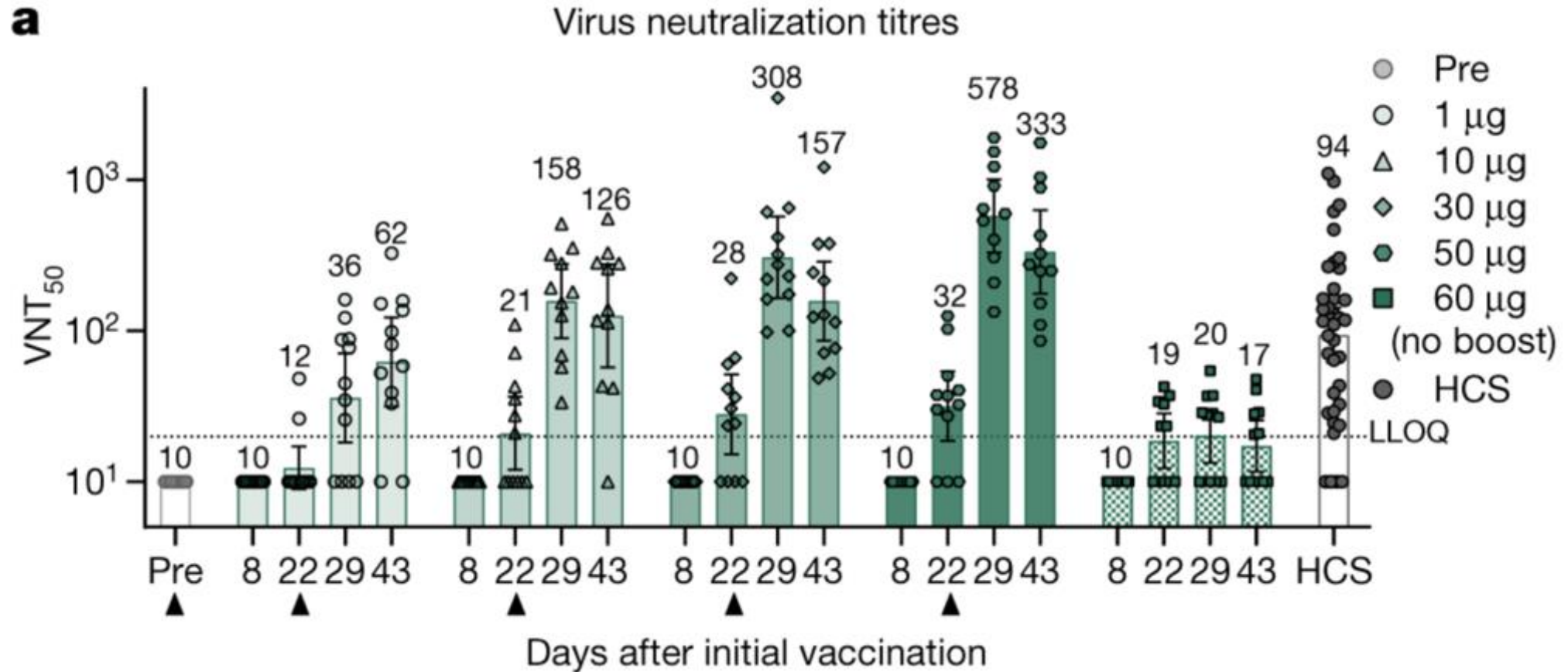




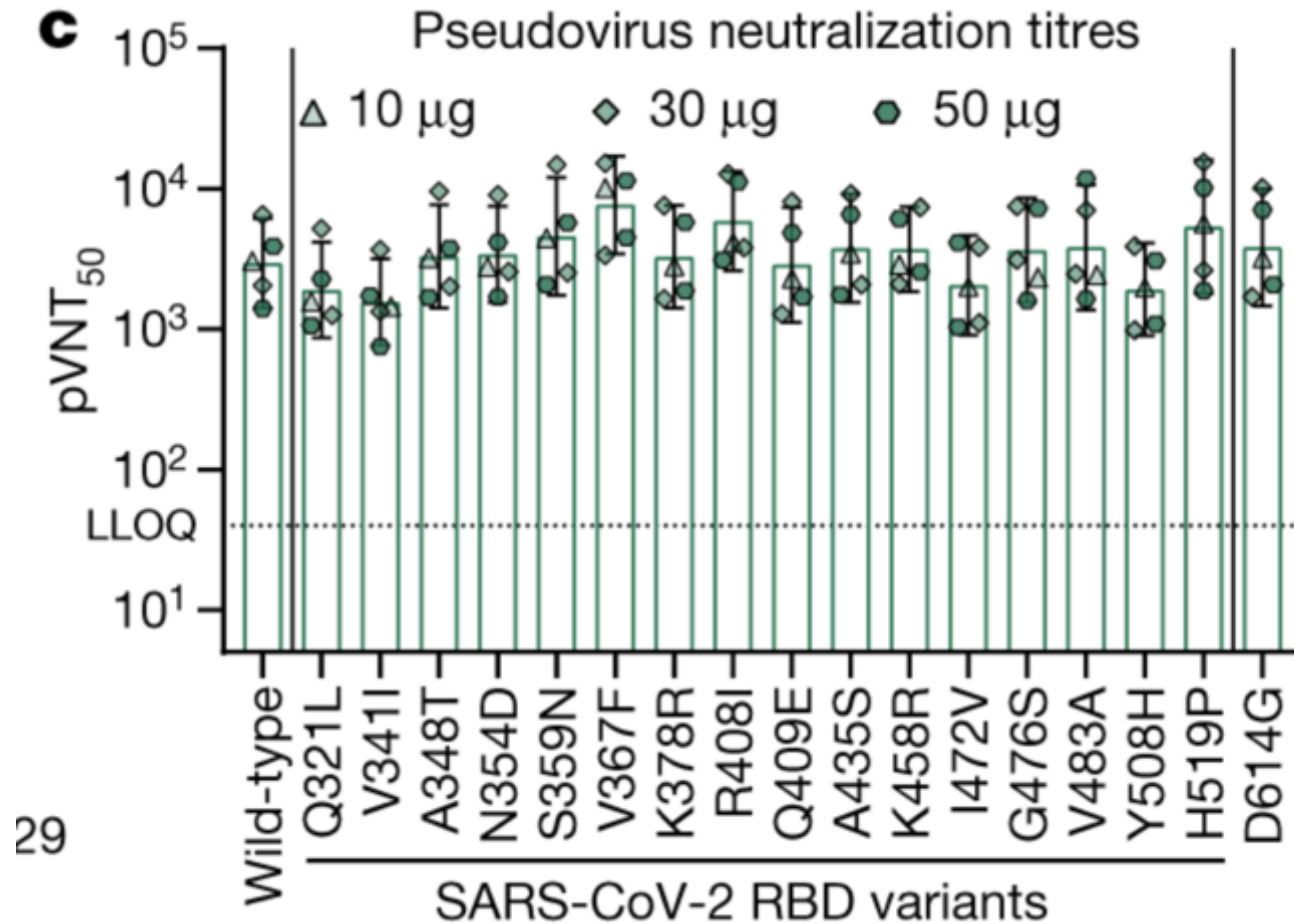
# Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)

- SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA and formulated in lipid nanoparticles
- The Pfizer-BioNTech COVID-19 Vaccine, BNT162b2 (30  $\mu\text{g}$ ), is administered intramuscularly (IM) as a series of two 30  $\mu\text{g}$  doses (0.3 mL each) 21 days apart.

# Goal of Vaccination: Neutralizing Antibodies to Spike

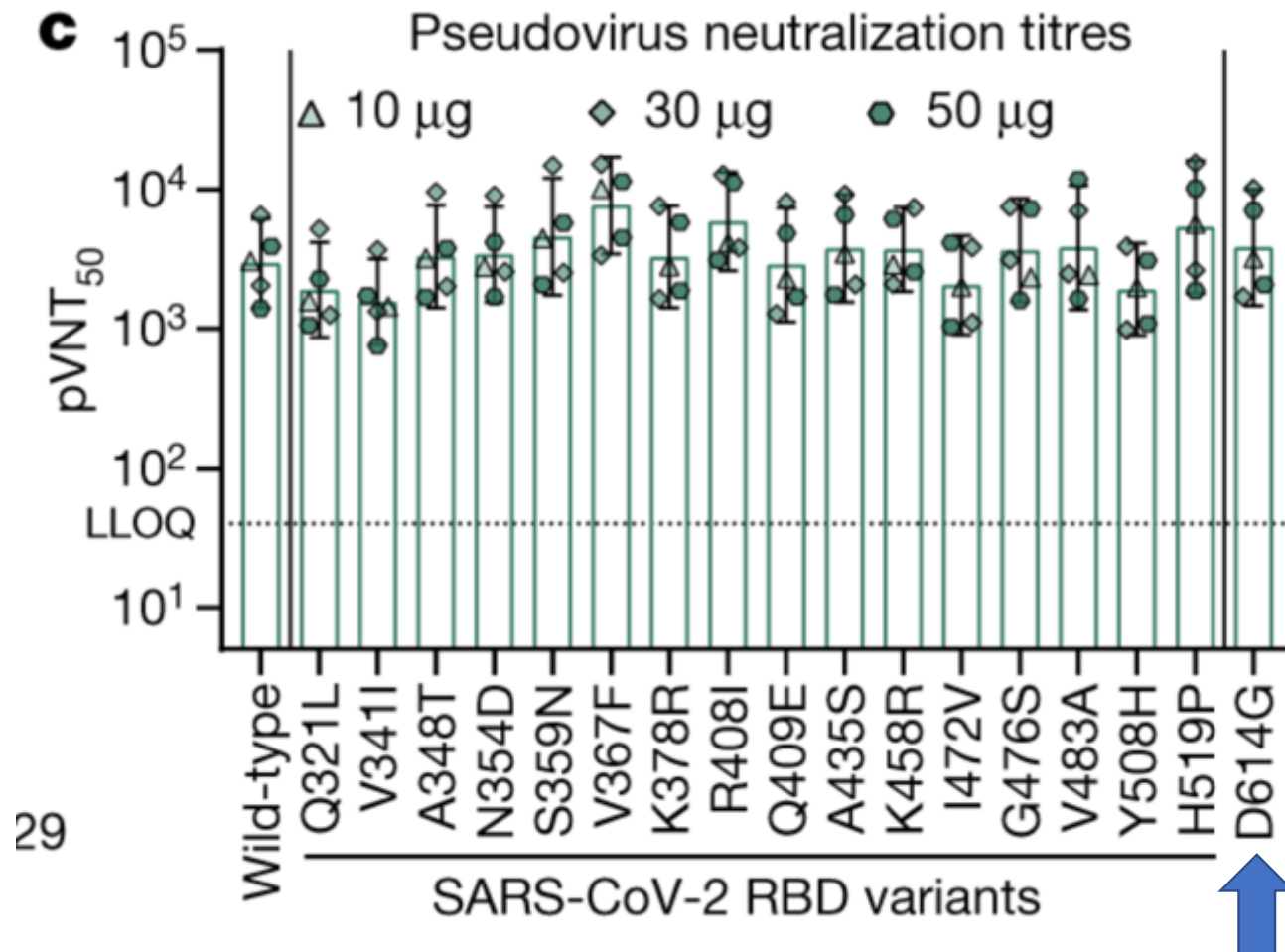


# Receptor binding domain variants are also neutralized



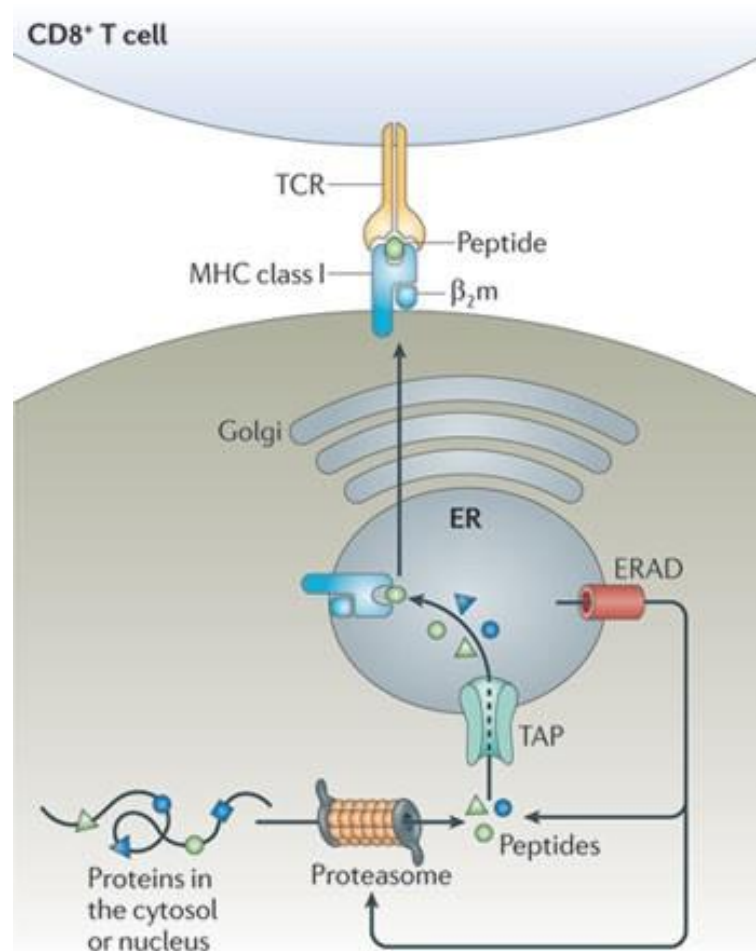
29

# Receptor binding domain variants are also neutralized

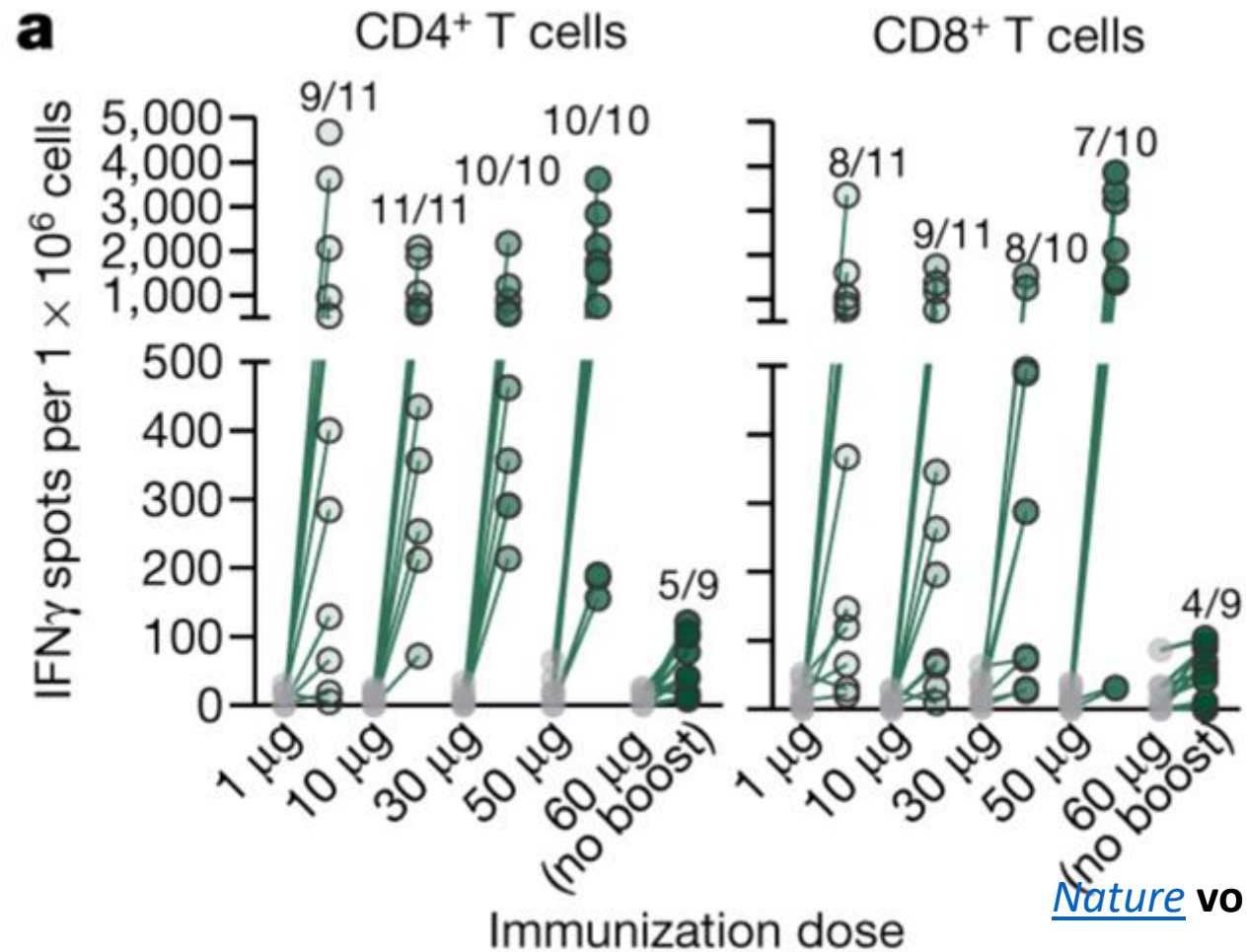


29

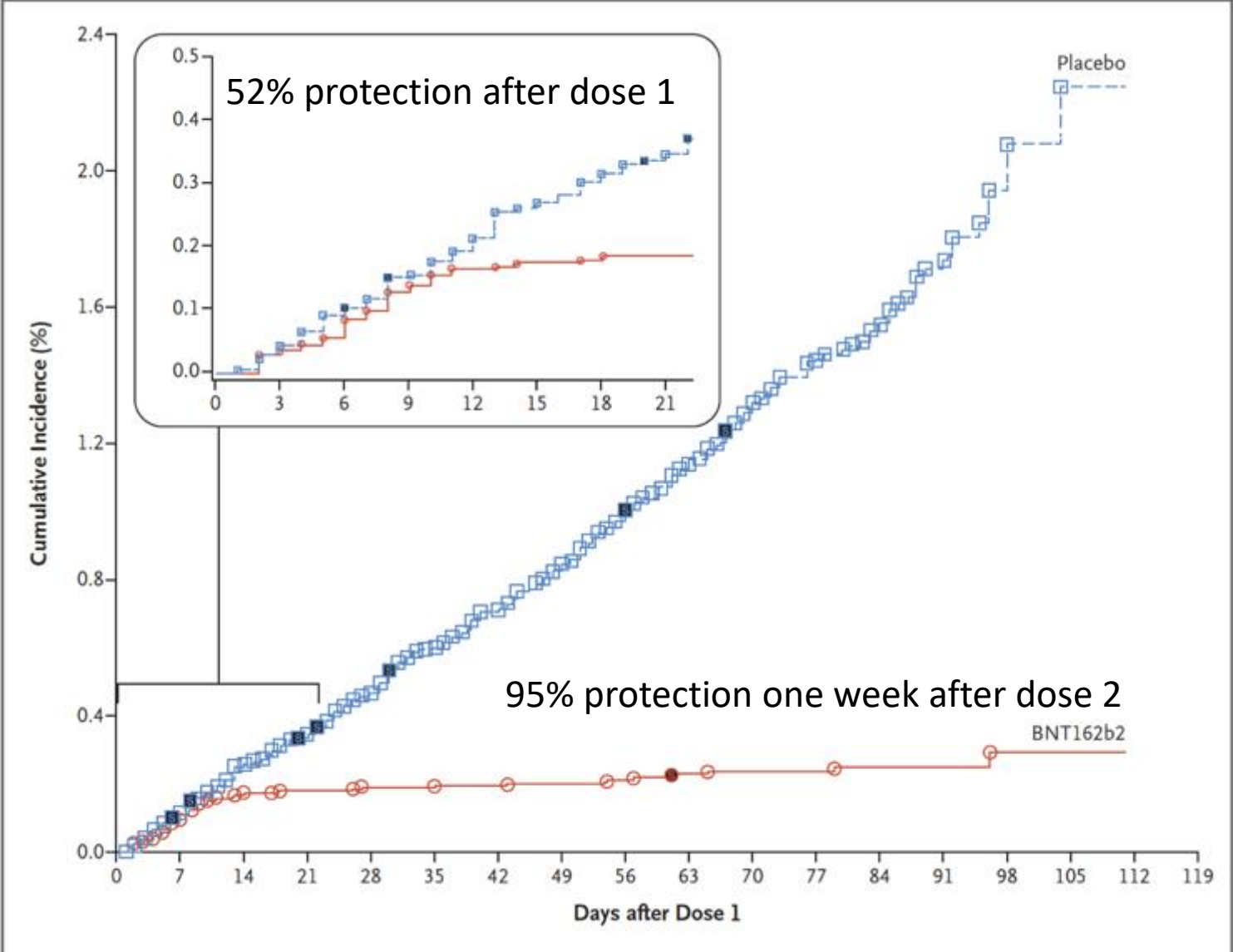
# Not just antibodies: T cells mediate immunity to COVID-19



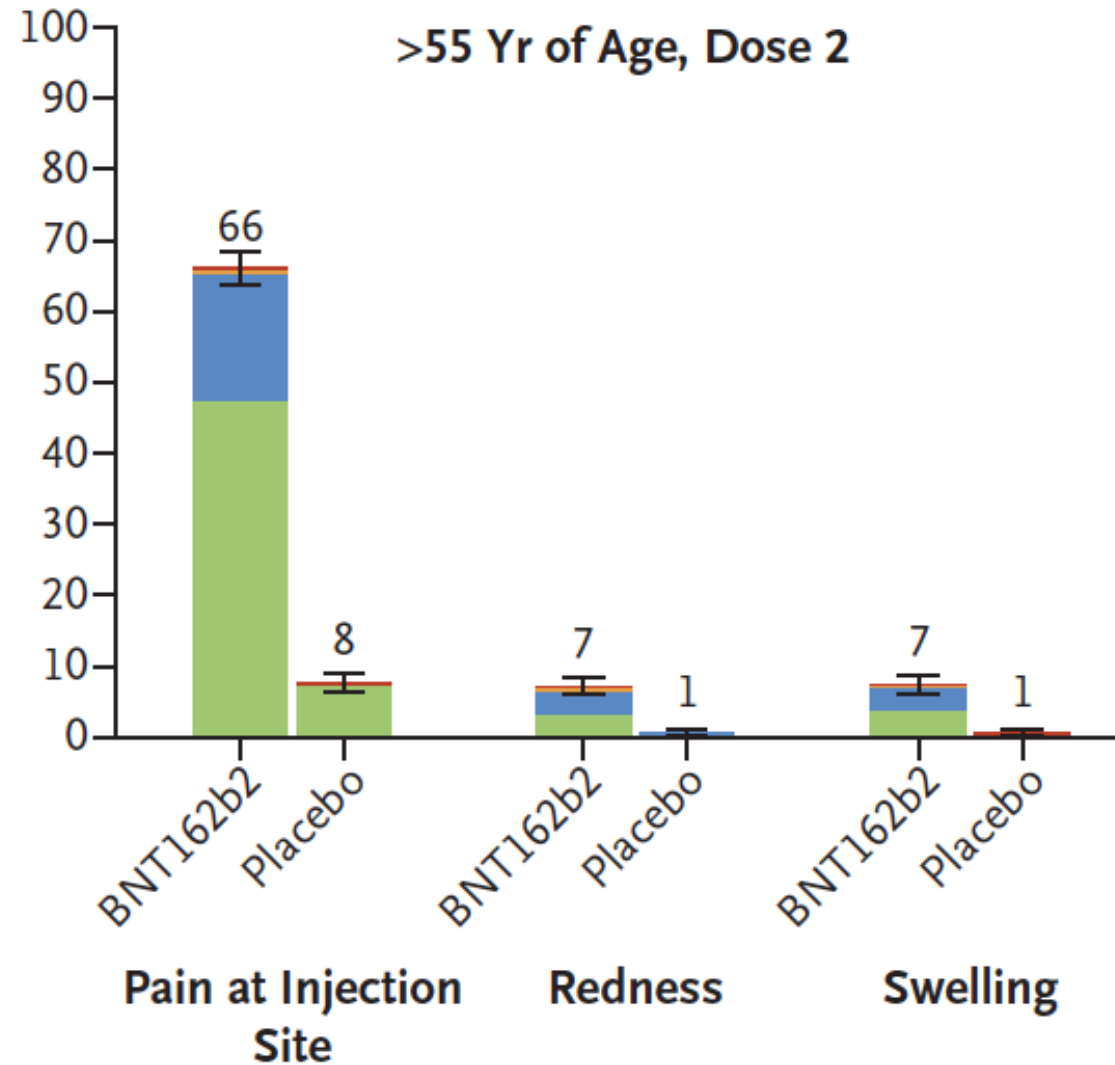
# T cell immune responses to vaccination



# Efficacy to prevent symptomatic COVID-19

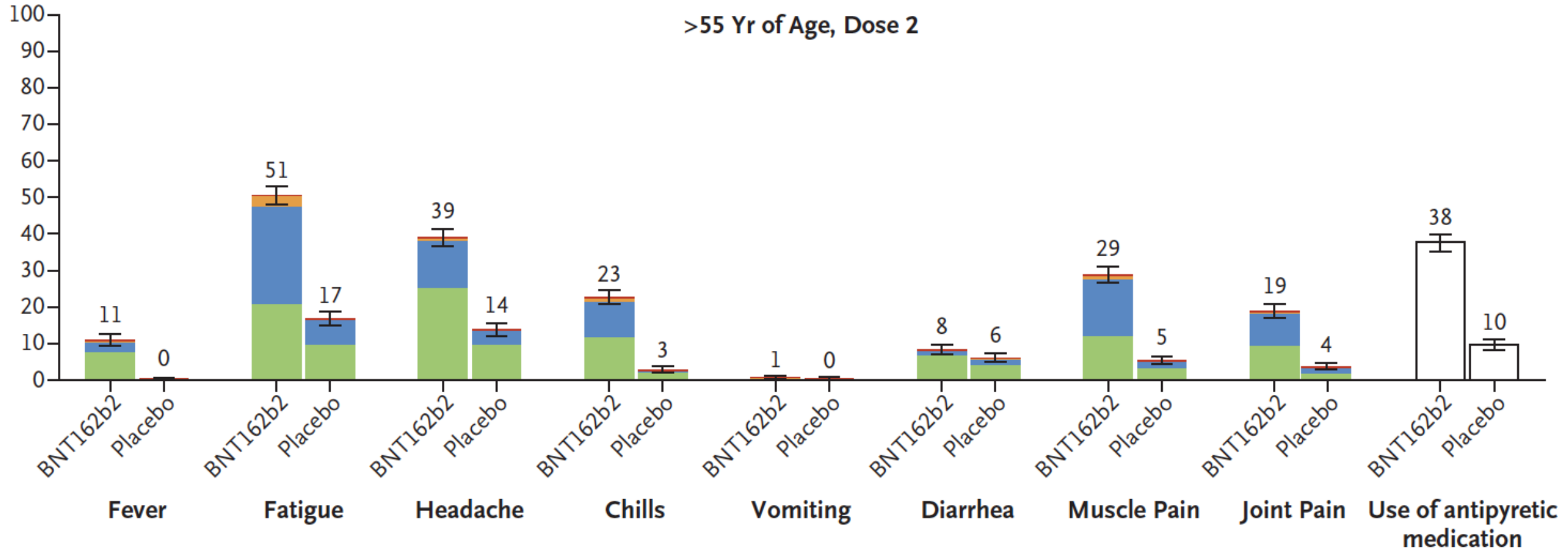


# Local side effects





# Systemic side effects



VAERS Home

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Report Using a PDF Form

VAERS Data **+**

Resources **+**

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## Report an Adverse Event to VAERS

VAERS is a passive reporting system, meaning it relies on individuals to send in reports of their experiences. Anyone can submit a report to VAERS, including parents and patients.

Healthcare providers are **required by law** to report to VAERS:

- Any adverse event listed in the [VAERS Table of Reportable Events Following Vaccination](#) that occurs within the specified time period after vaccinations
- An adverse event listed by the vaccine manufacturer as a contraindication to further doses of the vaccine

Healthcare providers are strongly **encouraged** to report to VAERS:

- Any adverse event that occurs after the administration of a vaccine licensed in the United States, whether it is or is not clear that a vaccine caused the adverse event
- Vaccine administration errors

Vaccine manufacturers are required to report to VAERS all adverse events that come to their attention.

Online reporting is strongly encouraged. Please report clinically important adverse events that occur after vaccination of adults and children, even if you are not sure whether the vaccine caused the adverse event.



# The Advisory Committee on Immunization Practices' Interim Recommendation for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020

*Weekly* / December 11, 2020 / 69(49);1857-1859

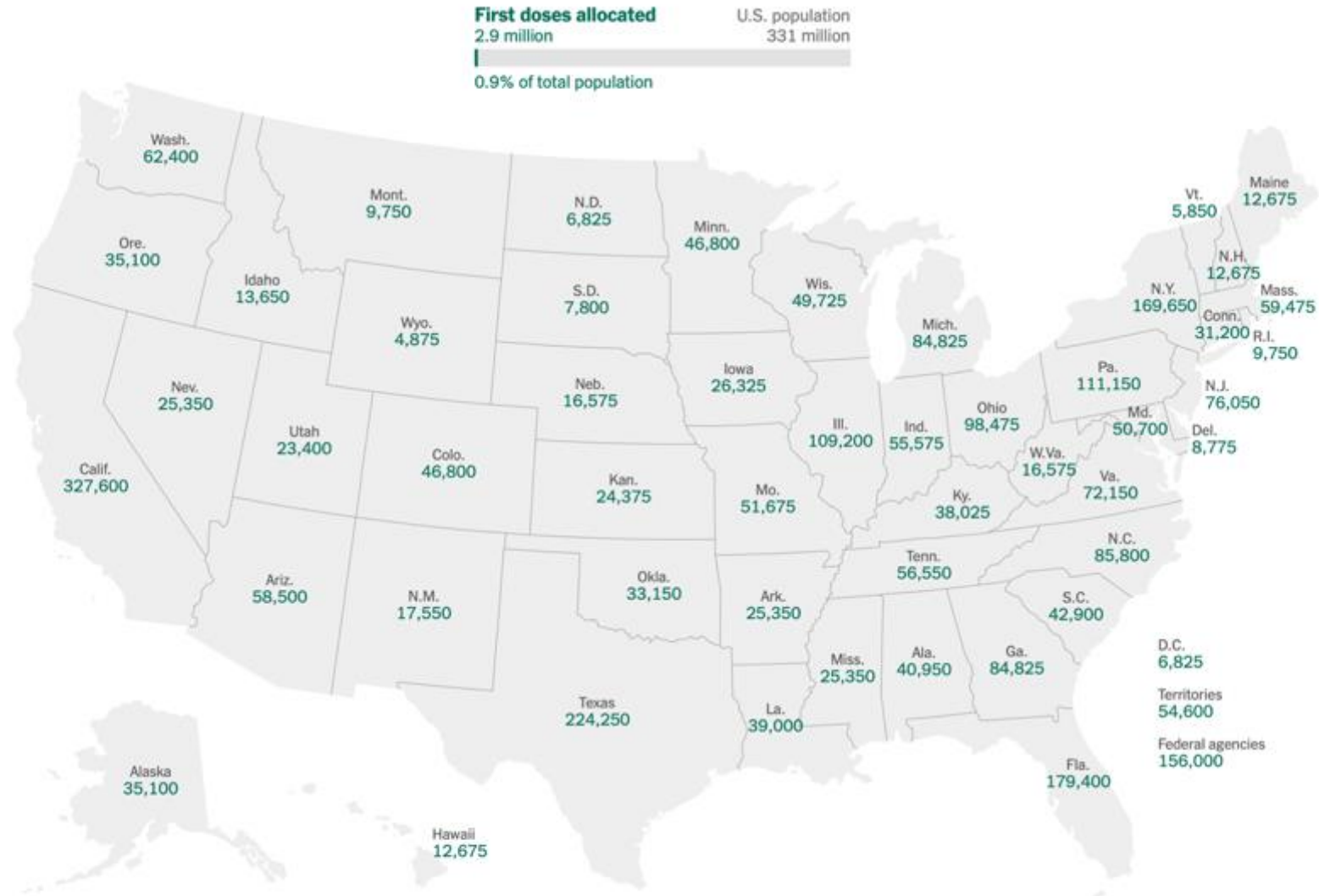
*On December 3, 2020, this report was posted online as an MMWR Early Release.*

Kathleen Dooling, MD<sup>1</sup>; Nancy McClung, PhD<sup>1</sup>; Mary Chamberland, MD<sup>1,2</sup>; Mona Marin, MD<sup>1</sup>; Megan Wallace, DrPH<sup>1,3</sup>; Beth P. Bell, MD<sup>4</sup>; Grace M. Lee, MD<sup>5</sup>; H. Keipp Talbot, MD<sup>6</sup>; José R. Romero, MD<sup>7</sup>; Sara E. Oliver, MD<sup>1</sup> ([View author affiliations](#))

Initial phase of vaccination program:

- 1) health care personnel (21 million; 858 deaths) and
- 2) residents of long-term care facilities (3 million; 70,000 deaths)

# Vaccine allocation in the US



Source: U.S. Department of Health and Human Services [data](#) - Note: The federal agencies include the Defense Department, Department of Veterans Affairs, Indian Health Service, State Department and Federal Bureau of Prisons

# Virginia COVID-19 Vaccination Prioritization Guidance

- **Phase 1a – Healthcare Workers and Long-Term Care Residents**
- **Phase 1b – Essential Workers**
- **Phase 1c – High Risk Adults**
- Virginia will get 480,000 vaccines in December and they will be distributed to the 500,000 healthcare workers and long-term care residents in Virginia.

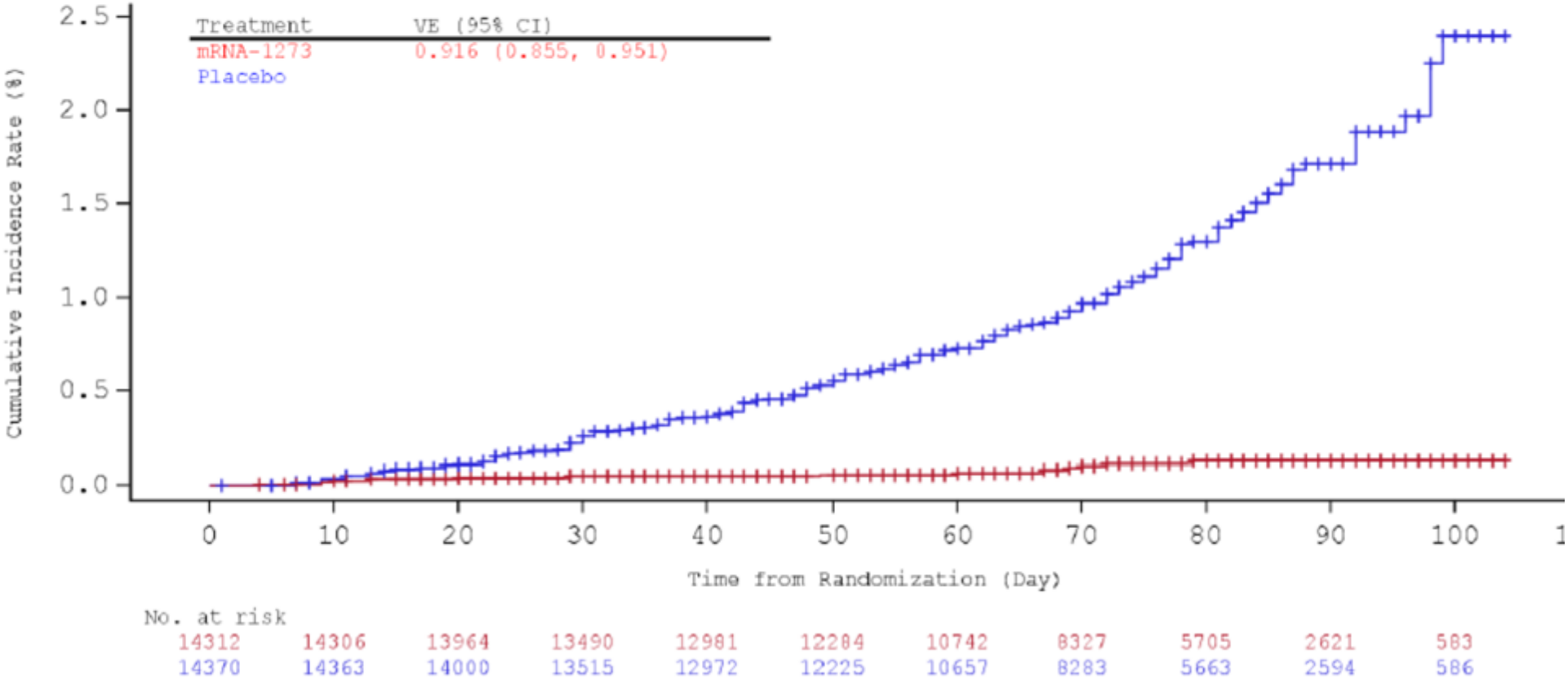
# UVA Prioritization – next set (Group 2) of vaccinations

- When scheduling, individuals will be asked to evaluate their risk for workplace exposure risks as well as personal risk for complications or other factors (e.g.. age, comorbidities, other factors).
- If they have many risk factors, they'll be advised to schedule early. If they have few, they'll be asked to please wait a few weeks.
- In essence, it will be based on the honor system. Our goal is to ramp up vaccination rapidly enough that those who are advised to wait a few weeks don't feel it's a significant burden.

# Next: Moderna mRNA vaccine

**Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Randomization, mITT Set**

<https://www.fda.gov/meda/144434/download>



# Does the vaccine prevent asymptomatic infection and transmission?

- Unpublished data submitted by Moderna to the FDA reported that at the time of the second dose 38 in placebo vs 14 vaccine recipients (67% reduction in asymptomatic infection after one dose).



# Vaccine administration

- Arrives in dry ice; store at -60 to -80° C
- Thaw and store undiluted vials for up to 5 days in a refrigerator
- Dilute with 1.8 ml normal saline; discard any unused vaccine within 6 hours after dilution
- Administer 0.3 ml of the diluted vaccine intramuscularly
- Individuals age 16 years and older
- Second dose 3 weeks later (17-21 days)

# Second dose

- If you miss the second dose, get it when you can. No recommendation to repeat the first if you are late with the second dose.
- No systematic data on efficacy of just one dose
- 14 day interval from other vaccines
- Do not interchange one COVID-19 vaccine for another
- Regardless of prior COVID-19 infection (which likely provides 90 days protection) still vaccinate
- If you received antibodies against COVID-19 (monoclonal antibodies or convalescent sera) wait for 90 days to be vaccinated.

# Pregnancy

- ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on ACIP-recommended priority groups.
- COVID-19 vaccines should be offered to lactating individuals similar to non-lactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP.

# Immunocompromise

- Unknown for HIV, organ transplants etc.
- Potential for a decrease in the immune response to vaccination.
- Protective efficacy not known.

# Prior COVID-19

- Prior COVID-19 provides a minimum of 90 days of protection from reinfection.
- Recommendation is to immunize, but can delay for 90 days post-infection

# Allergic reactions

- History of anaphylaxis to any of the vaccine components: do not vaccinate.
- History of anaphylaxis: observe for 30 minutes post-vaccine
- No allergies: observe for 15 minutes

# Maintain vigilance even after vaccination

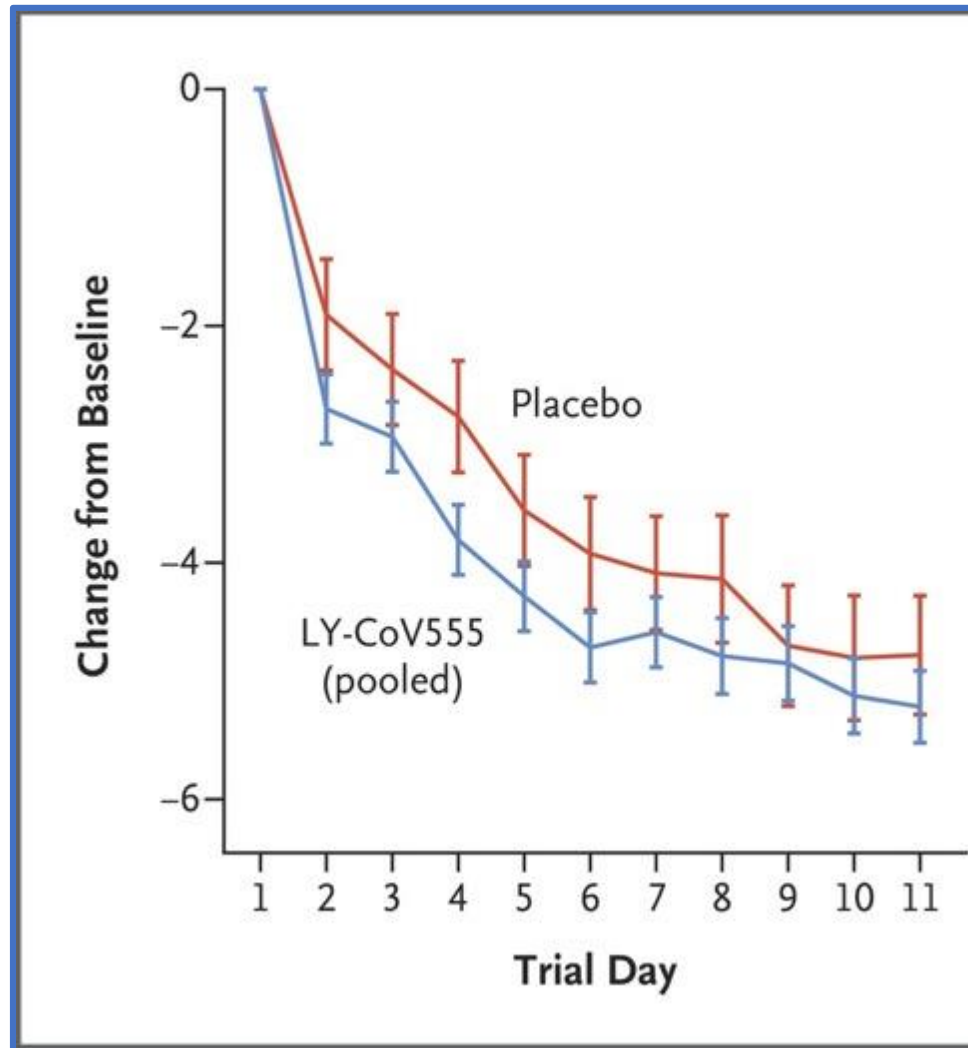
- Even after completing vaccination:
  - Wear a mask
  - Stay 6 feet away from others
  - Avoid crowds
  - Wash your hands
  - Follow CDC travel guidelines

# Treatments for COVID-19

- Outpatient
  - Anti-viral
    - Casirivimab plus Imdevimab
    - bamlanivimab
- Inpatient
  - Anti-viral for early stage
    - Remdesivir
  - Anti-inflammatory Rx for later stages
    - Dexamethasone
    - Baracitinib

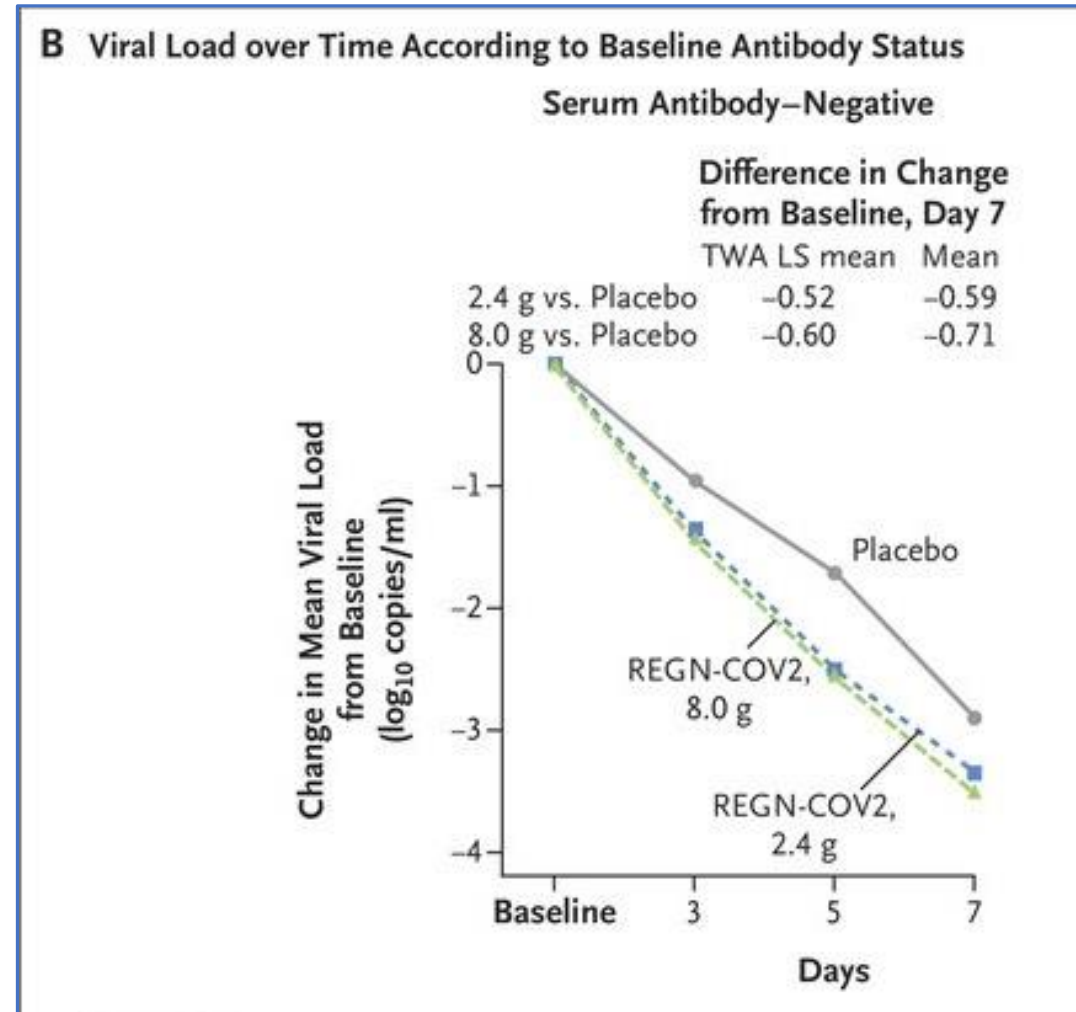


# Anti-Spike mAb bamlanivimab hastens symptom resolution for outpatients



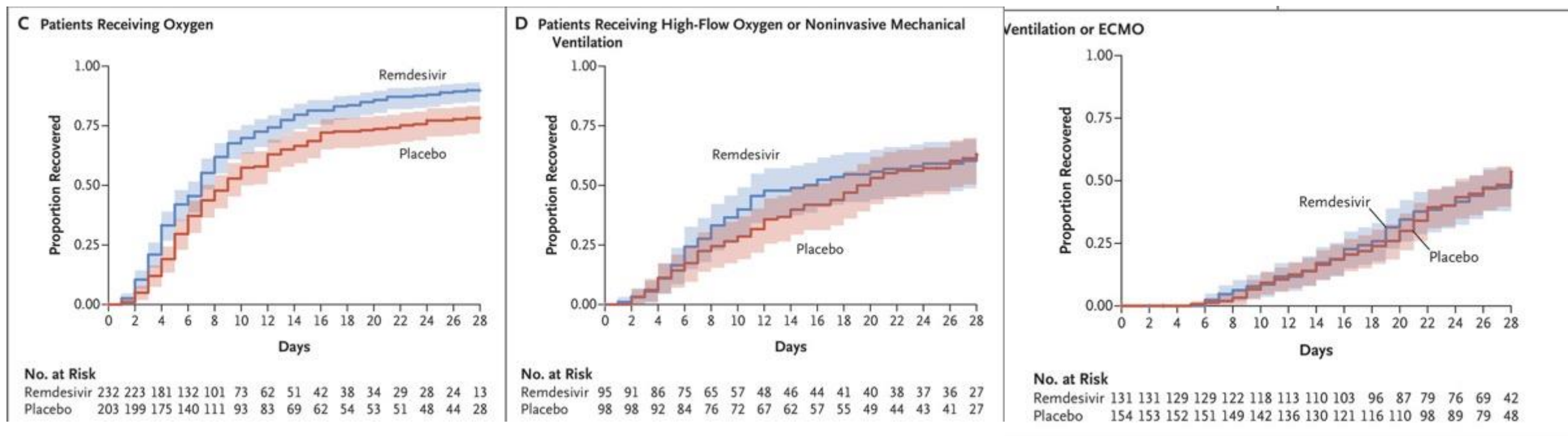
Chen et al. N  
Engl J Med  
2020. DOI:  
10.1056/NEJ  
Moa2029849

# Anti-Spike mAb casirivimab plus imdevimab combination decreases viral load early



DM Weinreich et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2035002

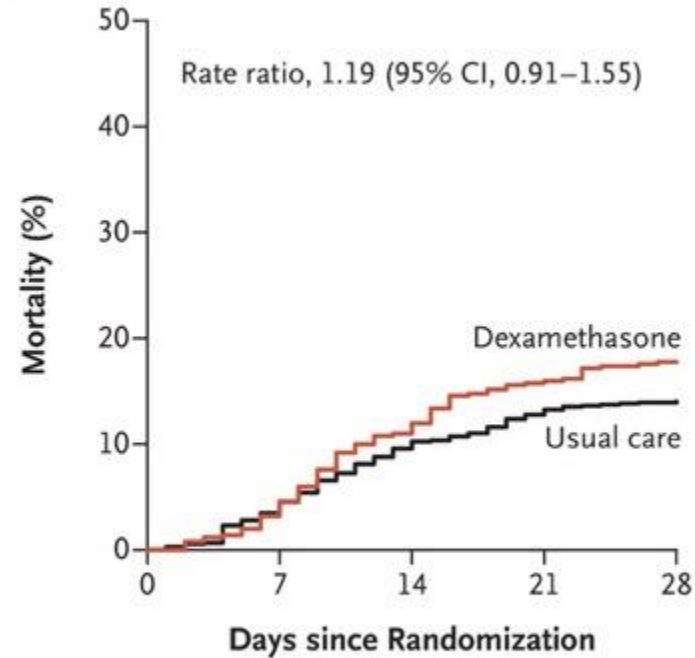
# Remdesivir (anti-viral) works best early



JH Beigel et al. N Engl J Med 2020;383:1813-1826.

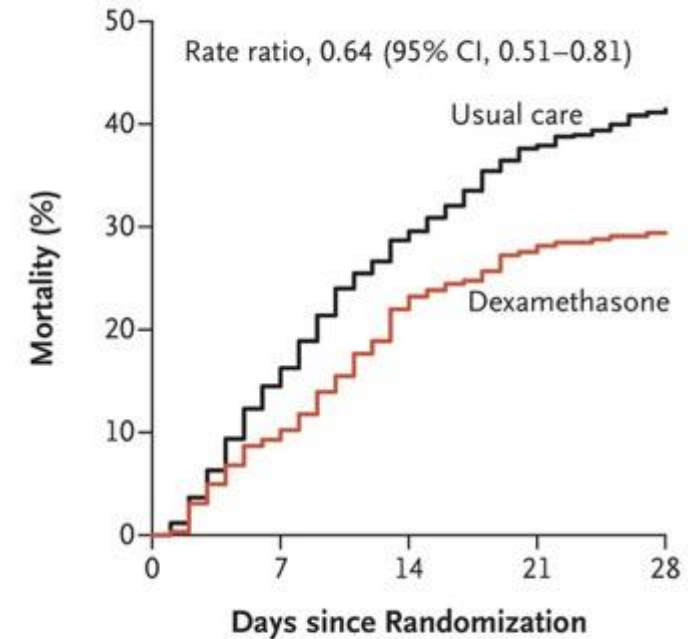
# Dexamethasone (anti-inflammatory) acts best late

**D** No Oxygen Received (N=1535)



No. at Risk	0	7	14	21	28
Usual care	1034	987	928	897	889
Dexamethasone	501	478	441	421	412

**B** Invasive Mechanical Ventilation (N=1007)



No. at Risk	0	7	14	21	28
Usual care	683	572	481	424	400
Dexamethasone	324	290	248	232	228

**The RECOVERY  
Collaborative Group. N  
Engl J Med 2020. DOI:  
10.1056/NEJMoa20214  
36**

<https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/>

## DISEASE SEVERITY

## PANEL'S RECOMMENDATIONS

Not Hospitalized,  
Mild to Moderate COVID-19

There are insufficient data to recommend either for or against any specific antiviral or antibody therapy. SARS-CoV-2 neutralizing antibodies (**bamlanivimab** or **casirivimab plus imdevimab**) are available through EUAs for outpatients who are at high risk of disease progression.<sup>a</sup> These EUAs do not authorize use in hospitalized patients.

**Dexamethasone** should not be used (**AIII**).

Hospitalized<sup>a</sup> But Does Not Require  
Supplemental Oxygen

**Dexamethasone** should not be used (**AIIa**).

There are insufficient data to recommend either for or against the routine use of **remdesivir**. For patients at high risk of disease progression, the use of remdesivir may be appropriate.

Hospitalized<sup>a</sup> and Requires  
Supplemental Oxygen

(But Does Not Require Oxygen Delivery  
Through a High-Flow Device,  
Noninvasive Ventilation, Invasive  
Mechanical Ventilation, or ECMO)

Use one of the following options:

- **Remdesivir<sup>b,c</sup>** (e.g., for patients who require minimal supplemental oxygen) (**BIIa**)
- **Dexamethasone<sup>d</sup> plus remdesivir<sup>b,c</sup>** (e.g., for patients who require increasing amounts of supplemental oxygen) (**BIII**)<sup>e,f</sup>
- **Dexamethasone<sup>d</sup>** (e.g., when combination therapy with remdesivir cannot be used or is not available) (**BI**)

Hospitalized<sup>a</sup> and Requires Oxygen  
Delivery Through a High-Flow Device  
or Noninvasive Ventilation

Use one of the following options:

- **Dexamethasone<sup>d,f</sup>** (**AI**)
- **Dexamethasone<sup>d</sup> plus remdesivir<sup>b,c</sup>** (**BIII**)<sup>e,f</sup>

Hospitalized<sup>a</sup> and Requires Invasive  
Mechanical Ventilation or ECMO

**Dexamethasone<sup>d</sup>** (**AI**)<sup>g</sup>

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

# Special Pathogens Unit

On 5 South with  
Ian Crane MD,  
Kajal Shah MD and  
Jane Forbes MD

