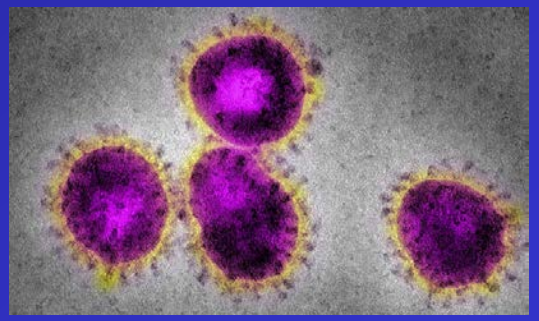
COVID-19 Vaccines

The only way out?



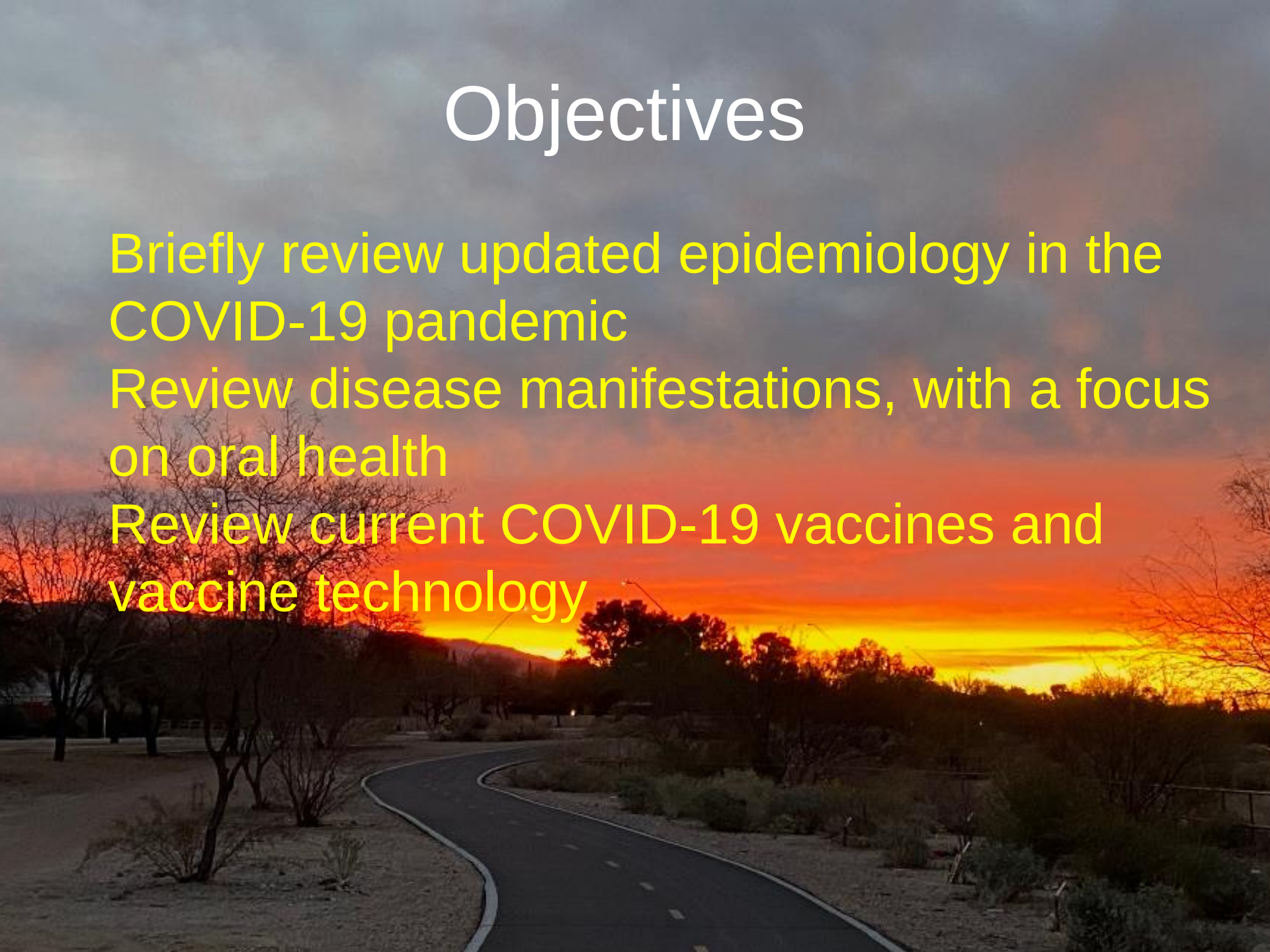
Stephen J Scholand, MD
1:00 – 1:30
Mar 4, 2021

Objectives

Briefly review updated epidemiology in the COVID-19 pandemic

Review disease manifestations, with a focus on oral health

Review current COVID-19 vaccines and vaccine technology

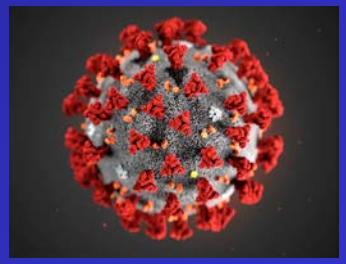


The Virus

- First identified in 12/2019 –Wuhan, China

  -SARS-CoV-2 - Severe acute respiratory syndrome coronavirus 2

- Transmitted from (?)



Enveloped, RNA virus

Pangolins

Bats: Horseshoe

www.wsj.com

Living planet

Opinion

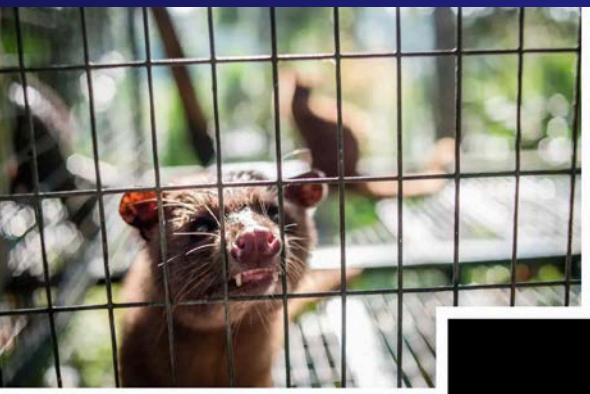
We Made the Coronavirus Epidemic

It may have started with a bat in a cave, but human activity set it loose.

By David Quammen

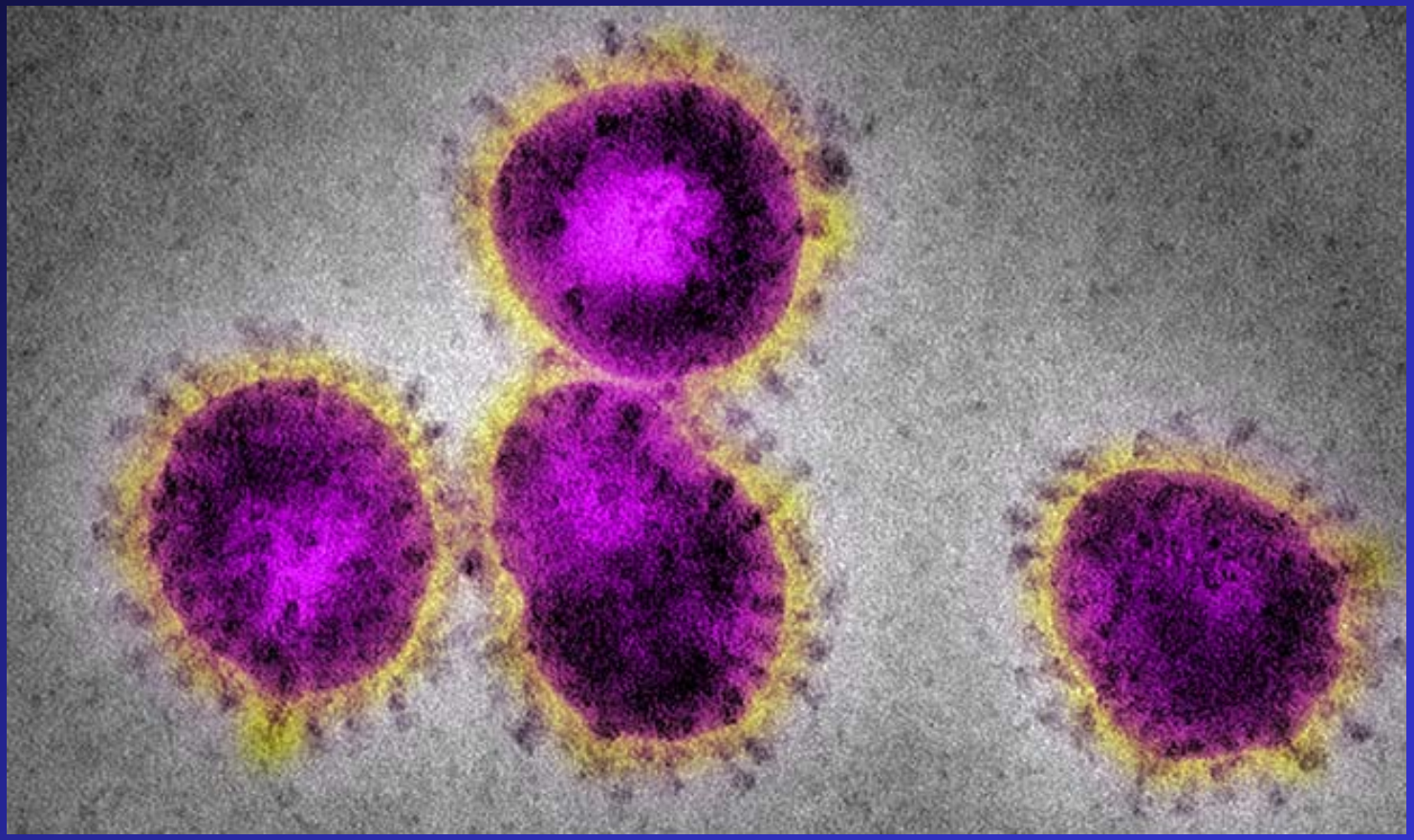
Mr. Quammen is the author of "Spillover: Animal Infections and the Next Human Pandemic."

New York Times



Wildlife Trade

Coronavirus



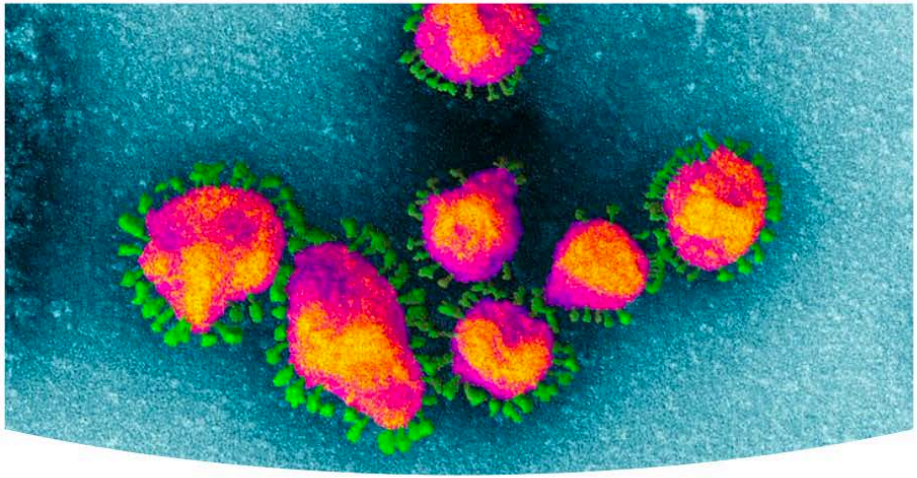
www.fredhutch.org

Human Coronaviruses

- Common cold Coronaviruses
  - Four HCoVs (229E, NL63, OC43, and HKU1)
  - 10% to 30% of upper respiratory tract infections in adults

Coronaviruses:

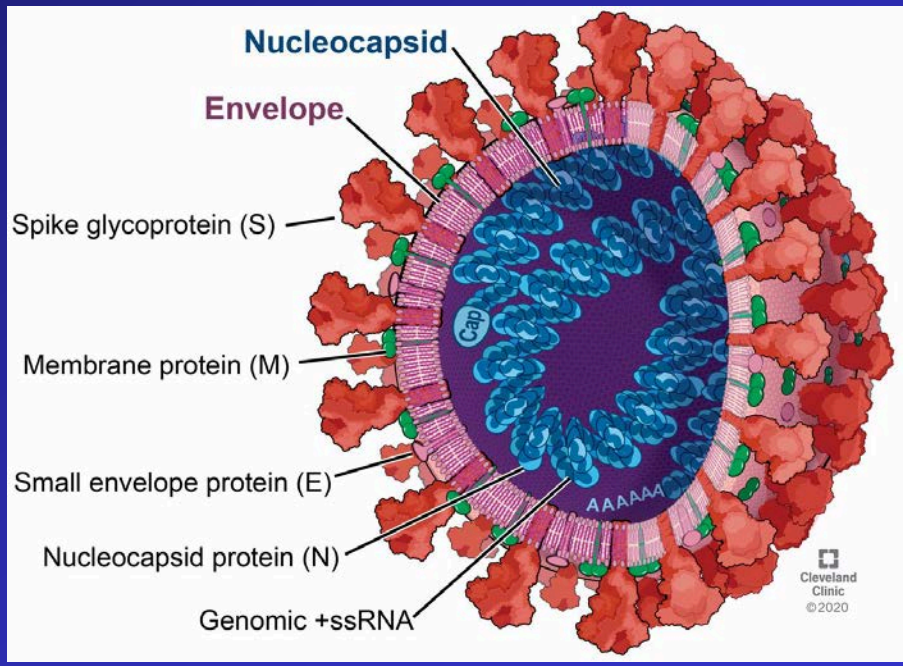
- 2002, SARS a novel, highly pathogenic CoV emerged in China
- 2012 MERS - Middle East respiratory syndrome. Continues to smolder
- 2019-nCoV; COVID-19, Wuhan, China



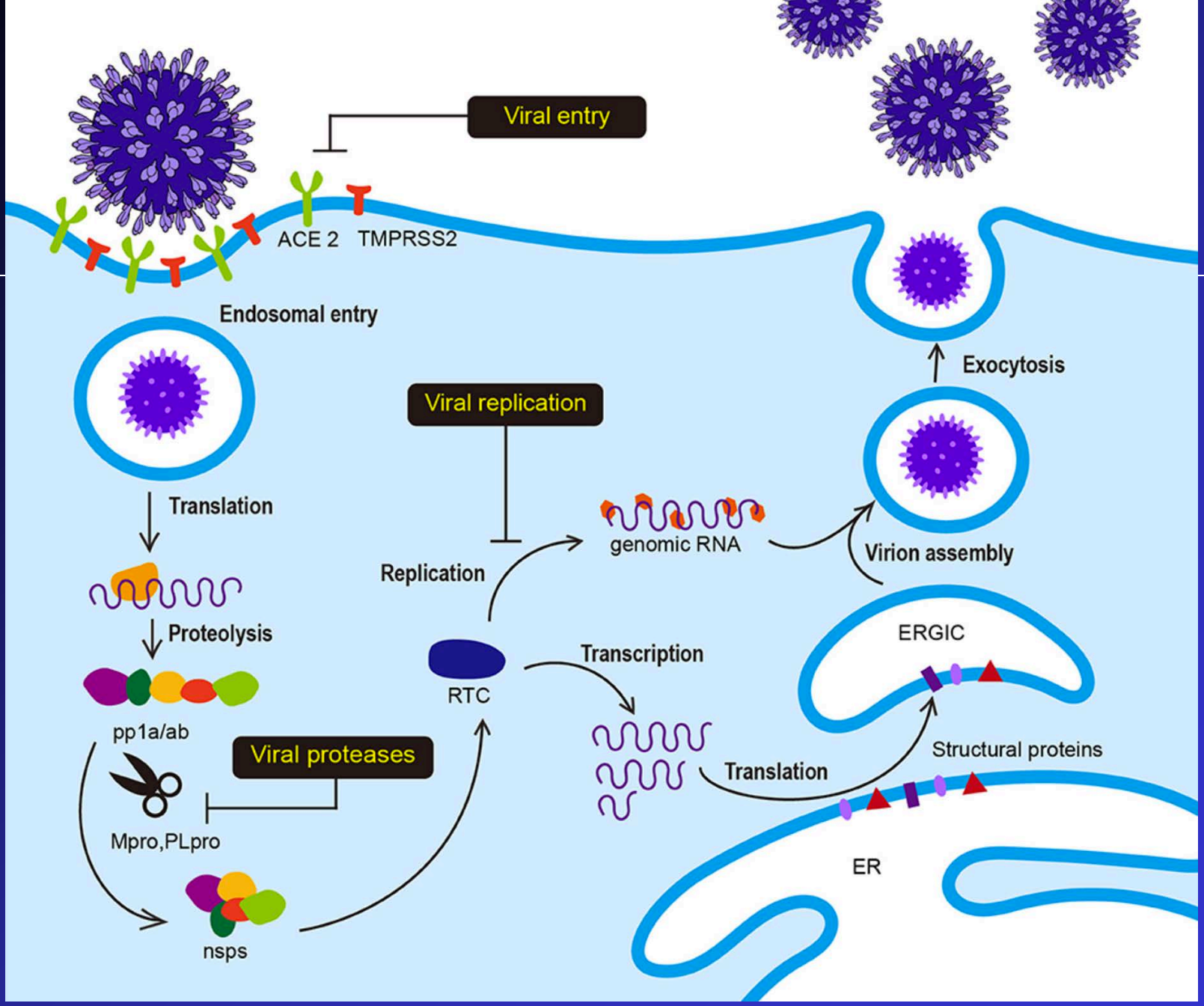
Virus anatomy

- Spherical enveloped virus;
  - single strand of positive-sense RNA (~26 to 32 kb)
- SPIKES: Club-shaped projections

  -resembling a crown or corona
- 3 other structural proteins:
  - envelope, membrane, and nucleocapsid proteins



Bergmann et al. COVID-19: Coronavirus replication, pathogenesis, and therapeutic strategies. Cleveland Clinic Journal of Medicine May 2020



Jeong GU, Therapeutic Strategies Against COVID-19 and Structural Characterization of SARS-CoV-2: A Review. Front. Microbiol., 14 July 2020

Transmission - Infection

- Respiratory
  Respiratory
  Respiratory

- Fomites (?)
  - Contamination of environmental surfaces
    - How long contaminated?
      - Surface
      - Temperatures/humidity

Clinical disease – COVID-19

- COVID – Coronavirus Disease 2019
- Symptoms:
  - Fever, dry cough, SOB
  - Additional: chills, fatigue, myalgias, headache, loss of taste or smell*, sore throat, congestion, runny nose, nausea, vomiting, diarrhea
  - Neurologic symptoms#(36%):
    - Central nervous system (dizziness, altered mental status, acute cerebrovascular disease, ataxia and seizure)
    - Peripheral nervous system (impairments in taste, smell, vision, and nerve pain)

* Upto 30% BMJ 2020;368:m1202

#Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol.* Published online April 10, 2020. doi:10.1001/jamaneurol.2020.1127

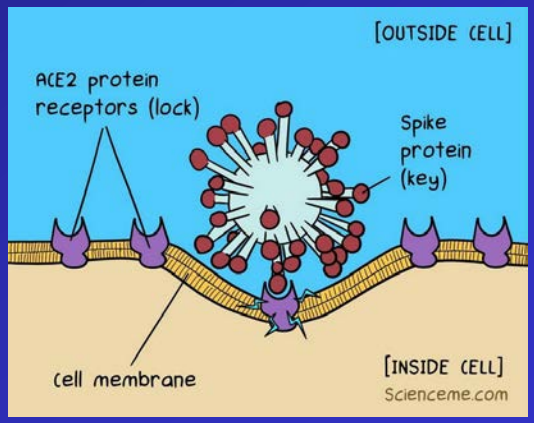
Top Mouth symptoms

- Gingival inflammation
- Xerostomia (dry mouth)
  - infection of salivary glands
- Oral ulcerations and gingival tissue breakdown
- Cracked teeth
  - Bruxism (stress)
- Loss of taste (ageusia) & smell (anosmia)

Figure 1: COVID-19–positive patient with ulceration on tongue. This patient had many ulcerations in the mouth that healed after disease resolution.

Clinical disease – COVID-19

- Alarming symptoms and syndromes (brought about by inflammation):
  - Strokes, venous-thromboembolism
    - endotheliitis
  - Pediatrics: Kawasaki like illness
    - Multisystem Inflammatory Syndrome in Children (MIS-C)
    - Multisystem Inflammatory Syndrome in Adults (MISC-A)

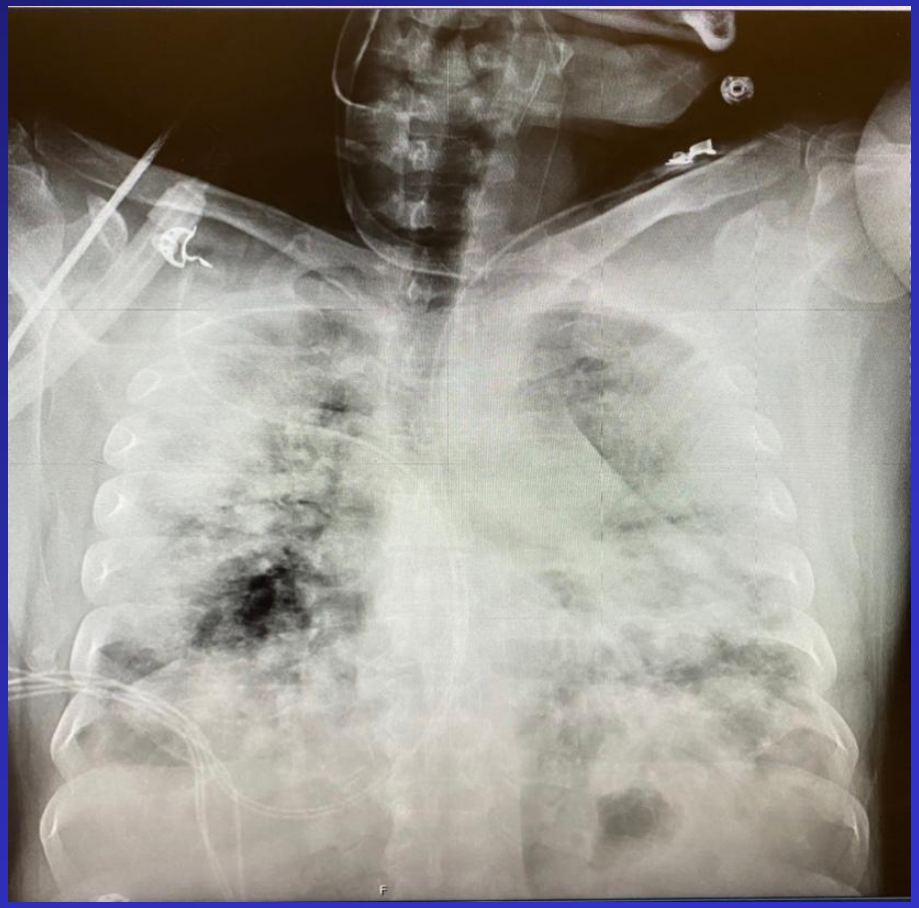


Spectrum of illness

- Asymptomatic
- Mild
- Moderate
- Severe

Patient factors:

  - Medical morbidities
  - Age



Spectrum of illness

- Asymptomatic
- Mild
- Moderate

} 81%

- Severe 14%
- CRITICAL 5%

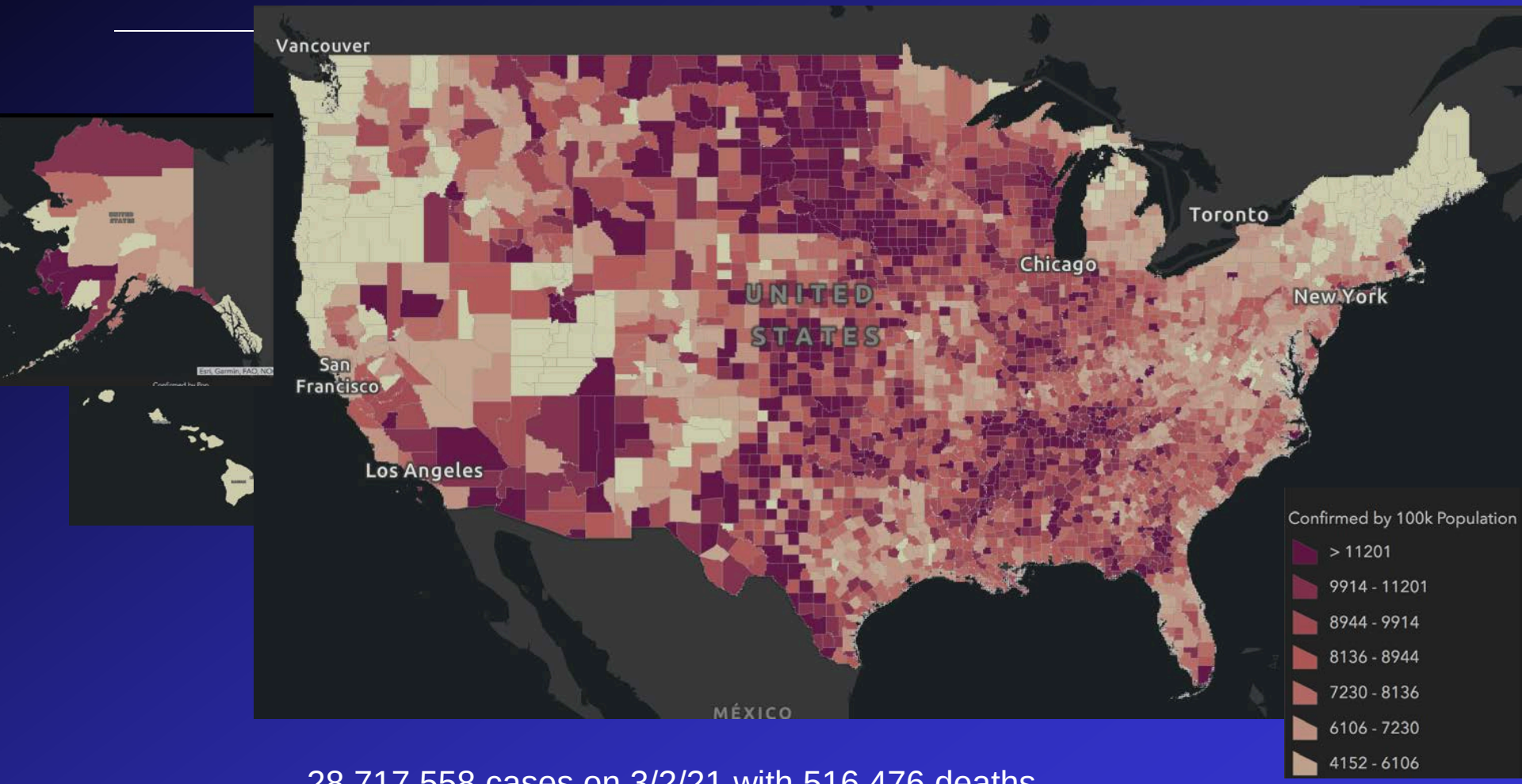
What might be some of the co-morbidities and conditions that could make COVID-19 worse?

Increased risk of severe illness

- Cancer
- Chronic kidney disease
- COPD
- Down Syndrome
- Heart conditions
  - heart failure, coronary artery disease, cardiomyopathies
- Immunocompromised
  - (i.e. organ transplant)
- Obesity
  (body mass index [BMI] of 30 kg/m^2 or higher
  Severe Obesity
  (BMI ≥ 40 kg/m^2)
- Pregnancy
- Sickle cell disease
- Smoking
- Type 2 diabetes mellitus

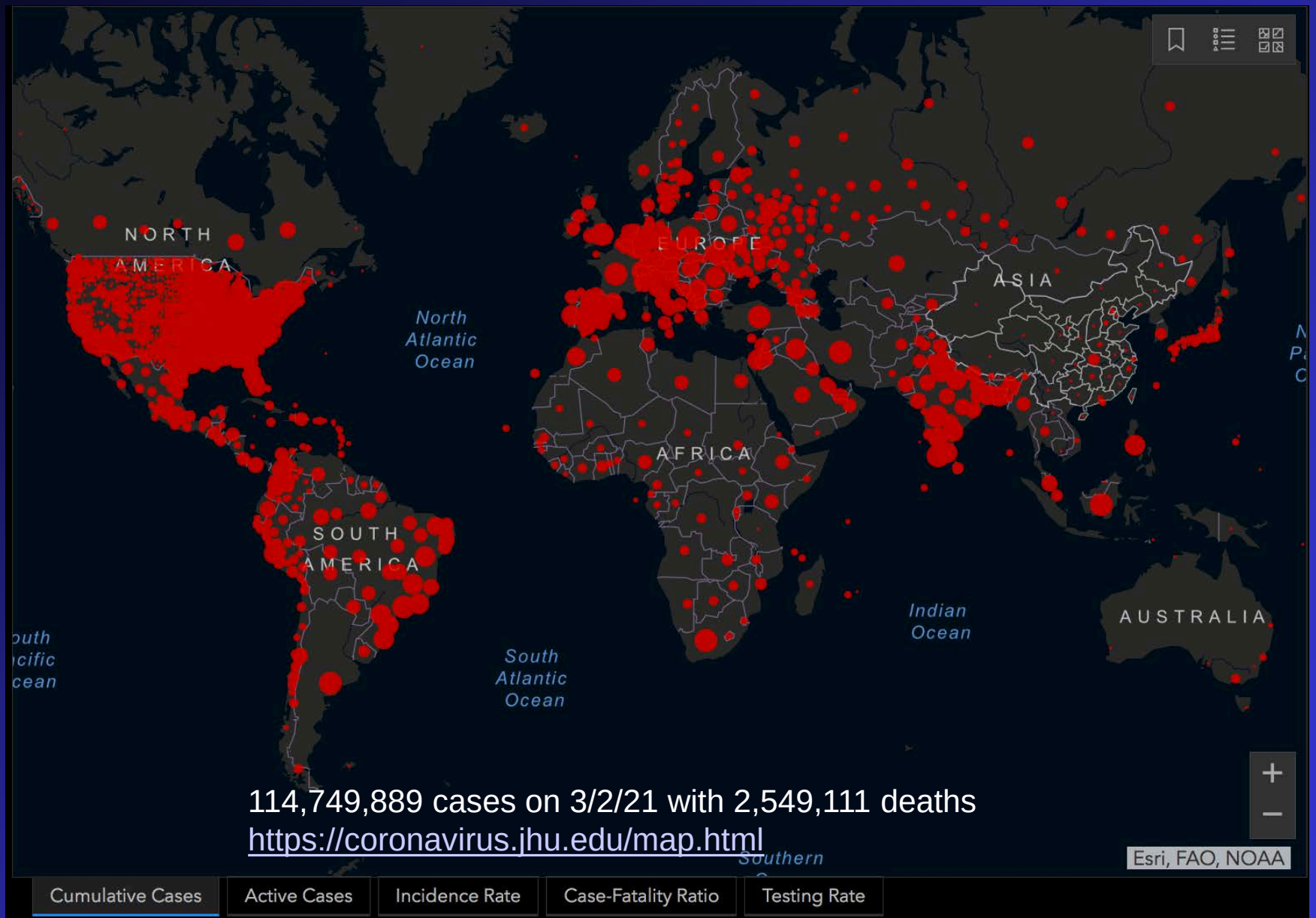
www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

COVID-19 in the United States



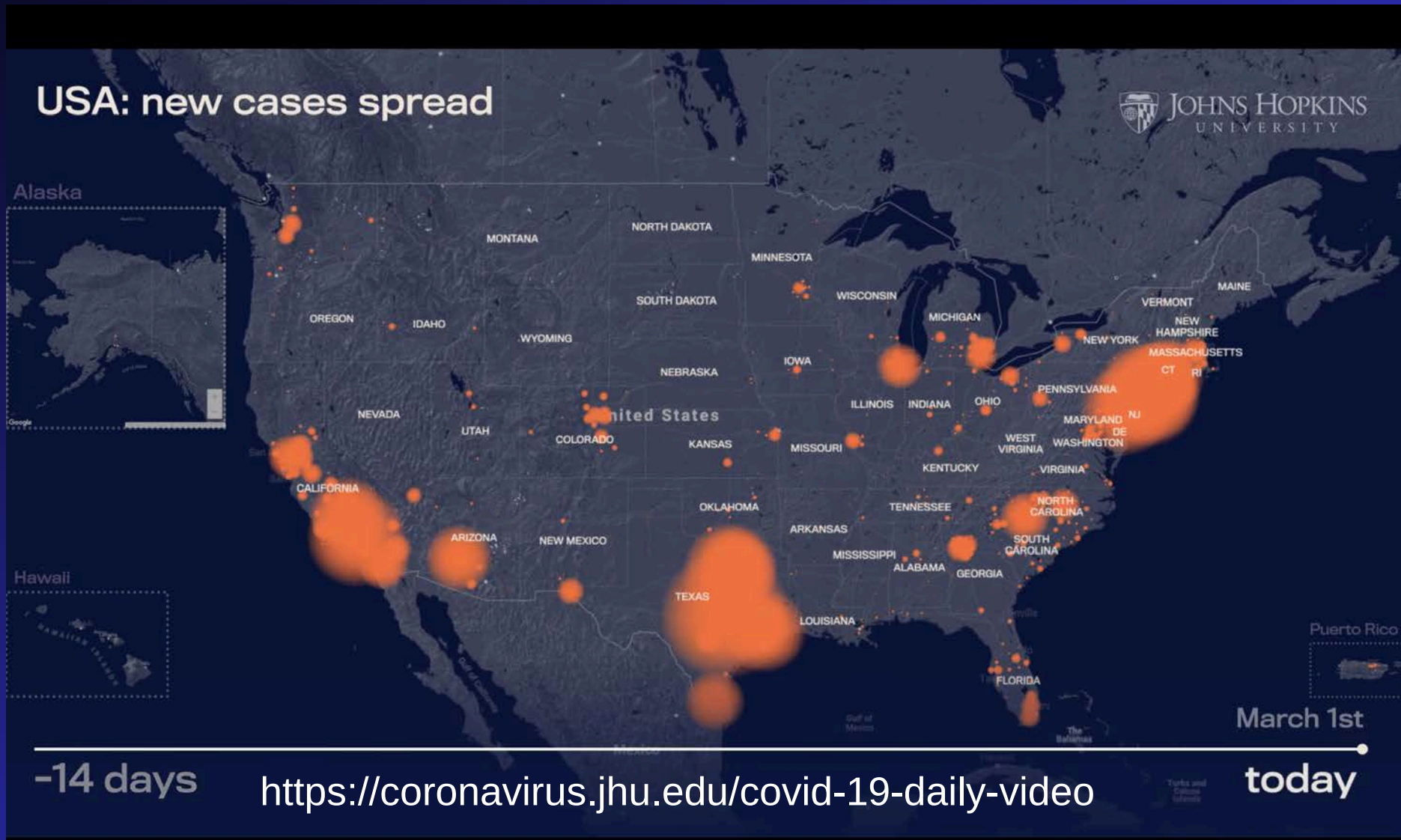
28,717,558 cases on 3/2/21 with 516,476 deaths
https://coronavirus.jhu.edu/us-map

COVID-19 Across the World



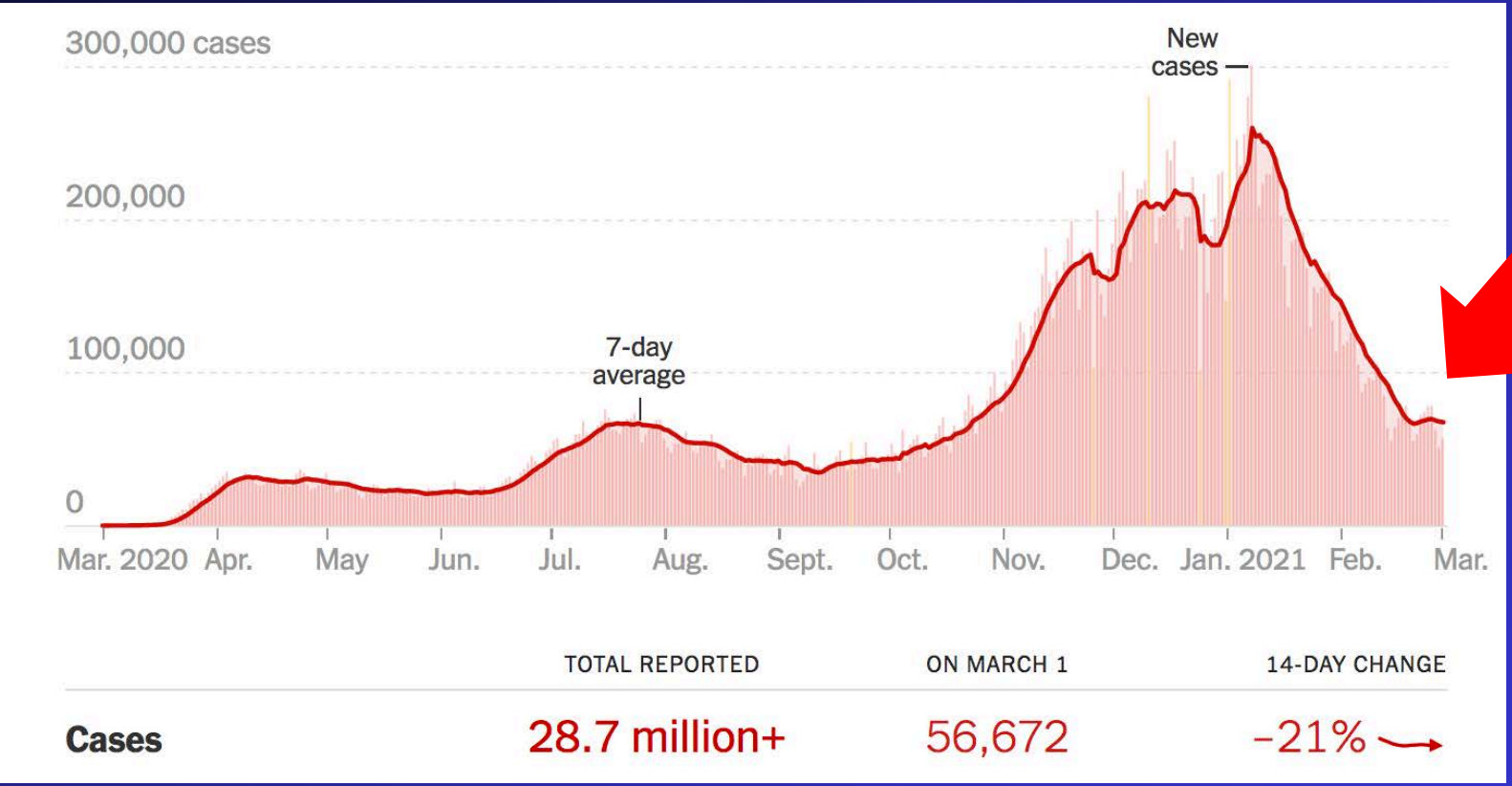
114,749,889 cases on 3/2/21 with 2,549,111 deaths
https://coronavirus.jhu.edu/map.html

Hot spots around the USA



https://coronavirus.jhu.edu/covid-19-daily-video

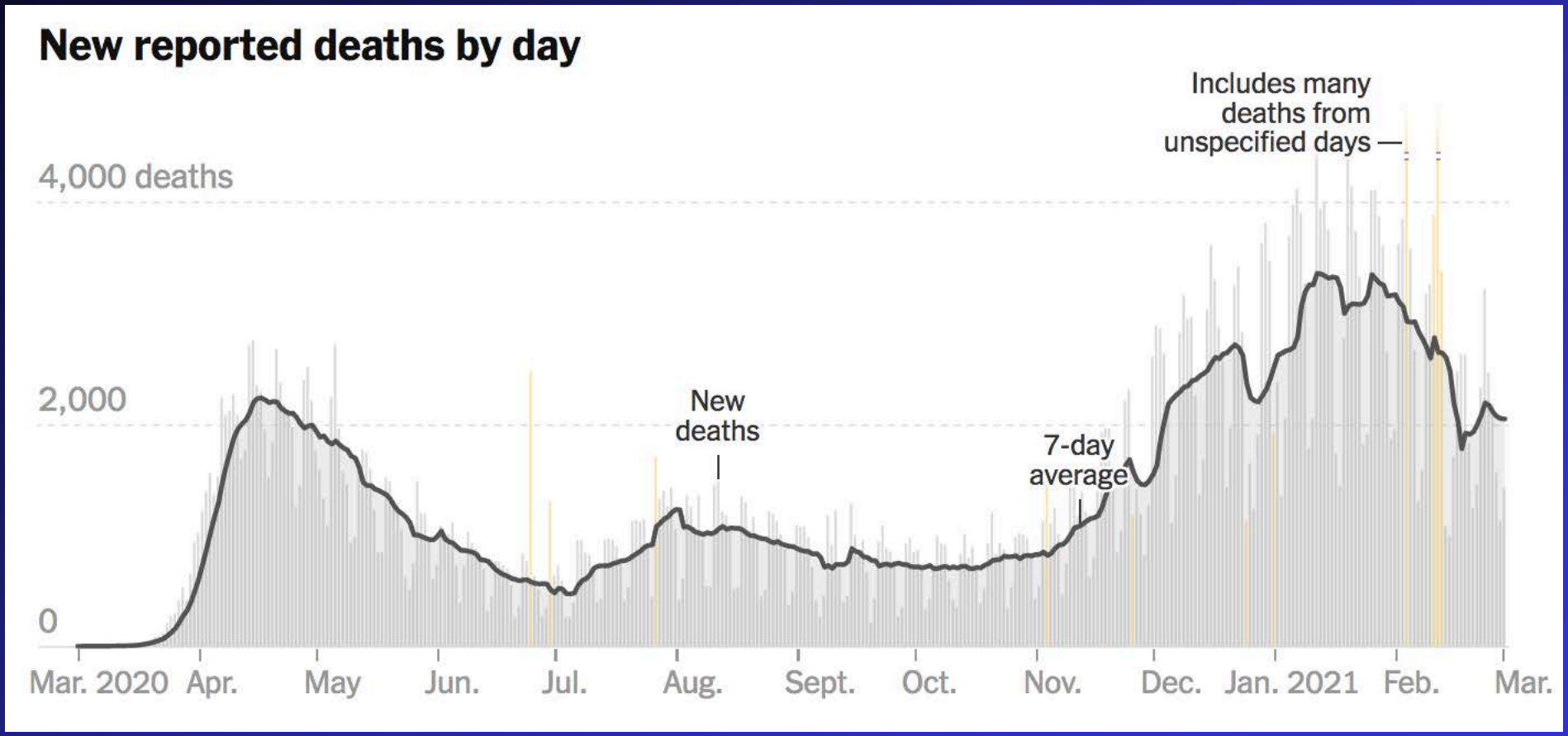
Cases in the USA



Cases declined; now stopped. What does it mean?

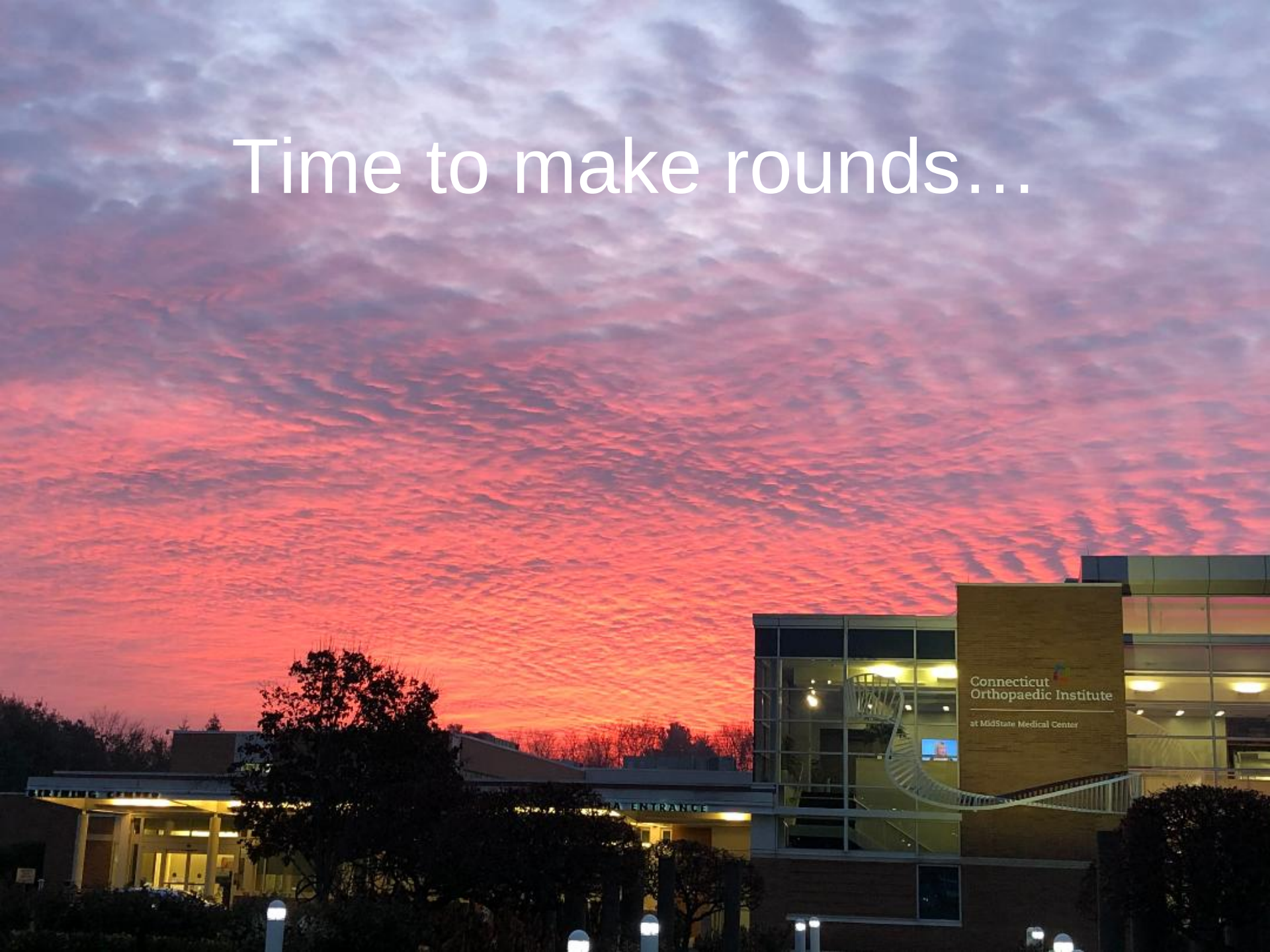
https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html

How many ‘jet liners’? A320 seats 182 passengers



Deaths	516,283	1,425	−17% ↘

Time to make rounds…



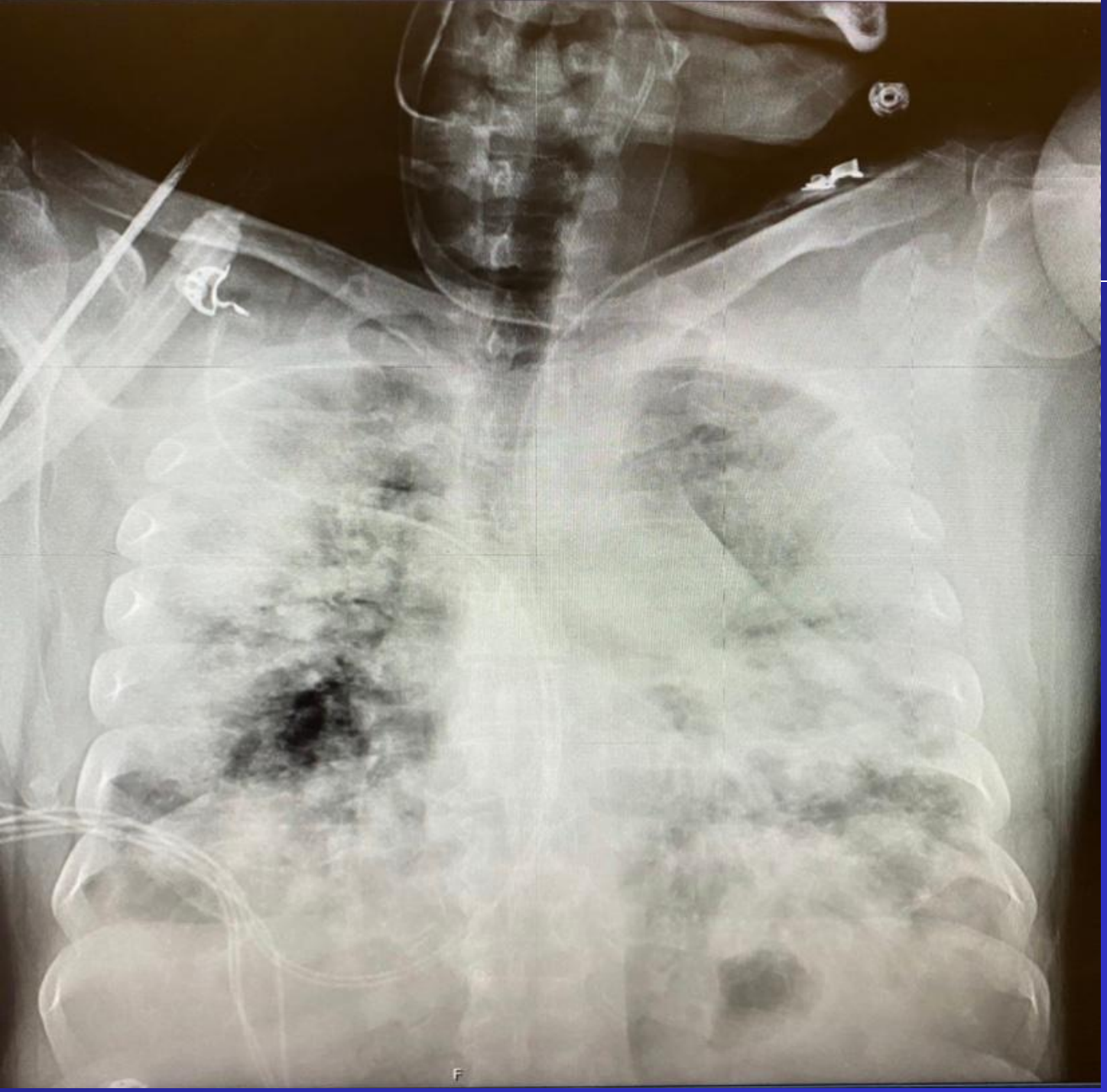
Case

- 61 yo HM
- Uncontrolled DM, obesity (BMI 31.3), HTN, HLD, hypothyroidism
- Worked as a chef in a group home
  - Cough, SOB, myalgias, N, D, anorexia
  - Tested positive on 5/4/20
  - Wife also COVID-19 positive; recovered
- P.E. T 99.3 P 93 RR 30s sat 71% R.A.

  (day 5 of illness)
  - Gen: obese HM
  - Resp: tachypnea; no crackles; no wheezing
  - Derm: no rashes

Case (cont'd)

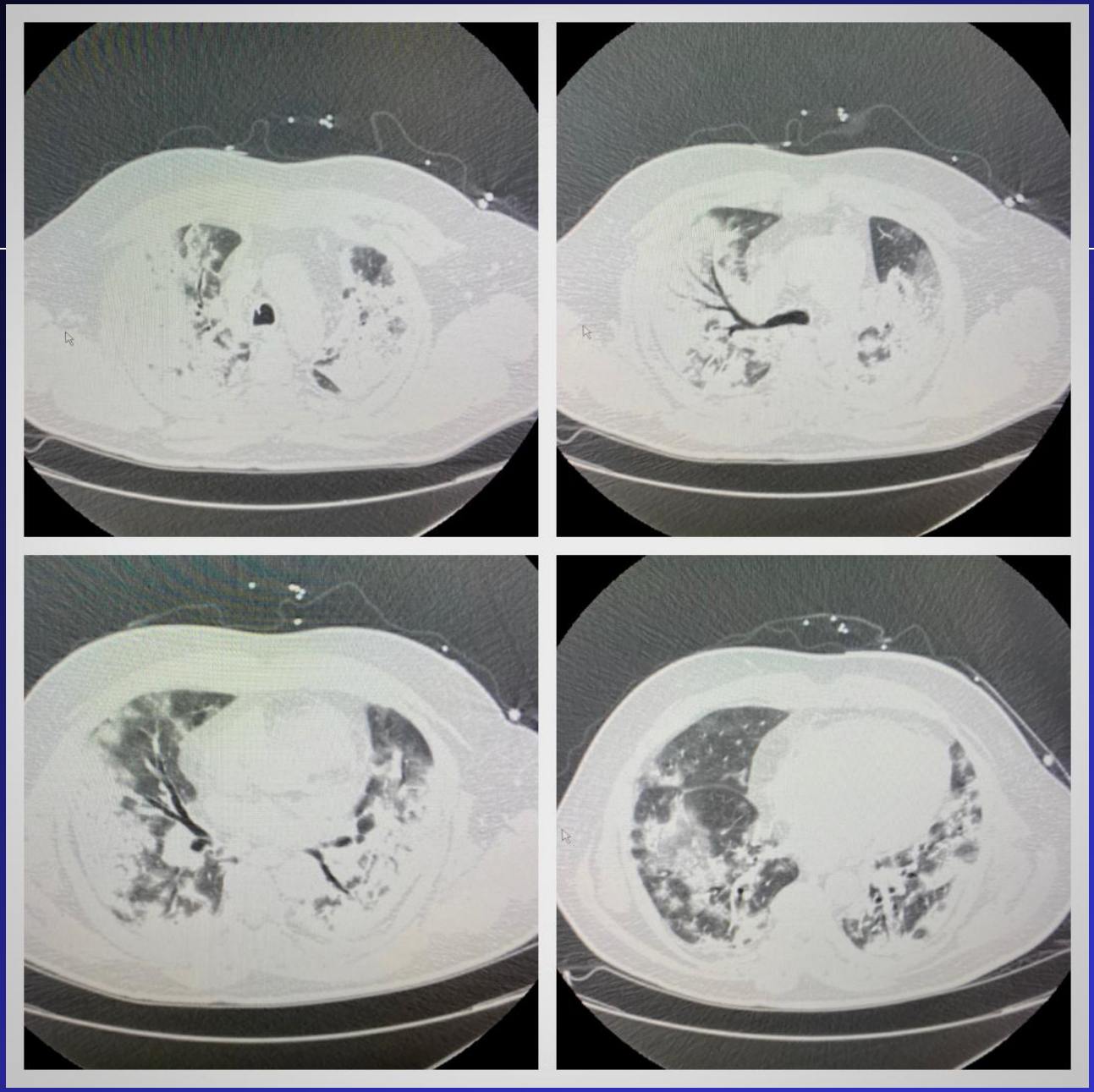
- Labs:
  - WBC 9.9 L% 5.8 (ABS 580)
  - ESR > 90; LDH 622; Ferritin 1870; CRP 22.28
  - BNP neg; Na 132, K 3.9, Cr 0.7, Glc 268
  - ABG: 7.41 PCO 36 PO 77 HCO 22
  - D-dimer 508; fibrinogen 1314 (high)



5 days later:
Desaturating despite Hi-Flo, self-proning

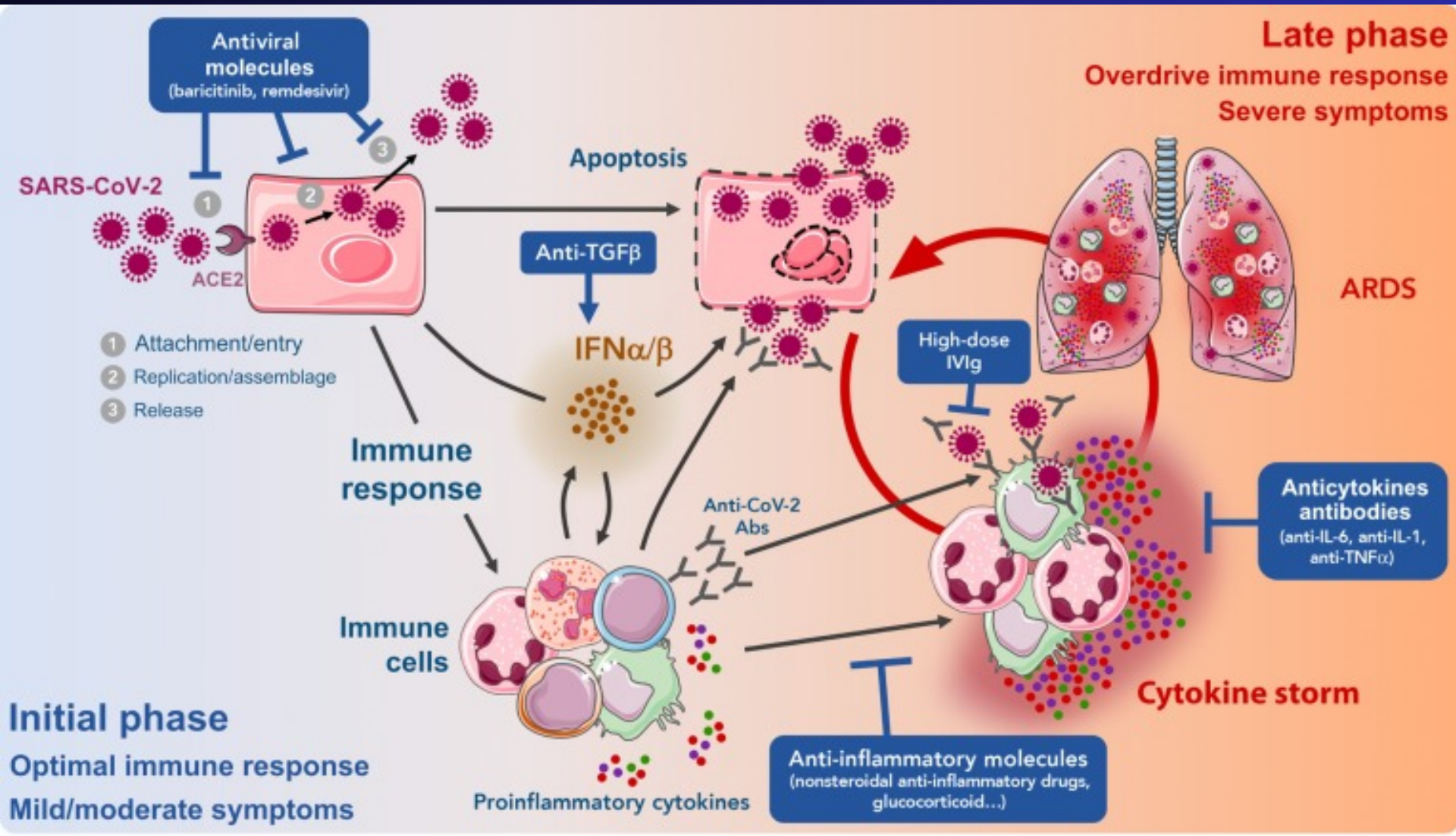
Transfer to ICU
Intubation…
(day 10 illness)

High PEEPs 15
(ARDS)



5 days later: Extensive confluent airspace opacities + air bronchograms

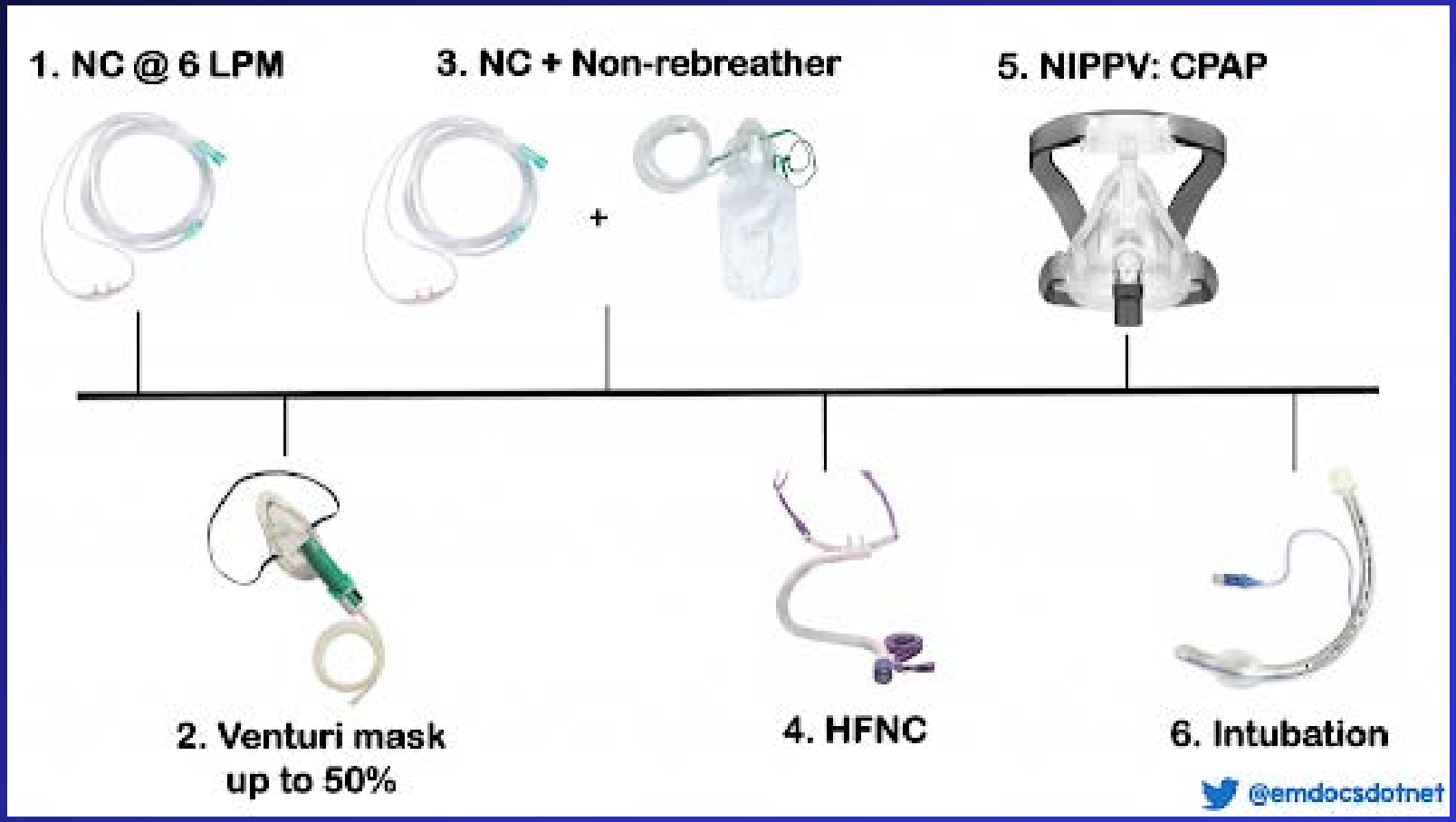
Pathophysiology



www.cell.com/trends/immunology/fulltext/S1471-4906(20)30261-1

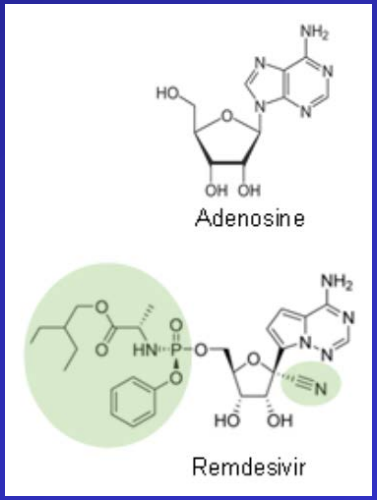
Treatment

Oxygen delivery



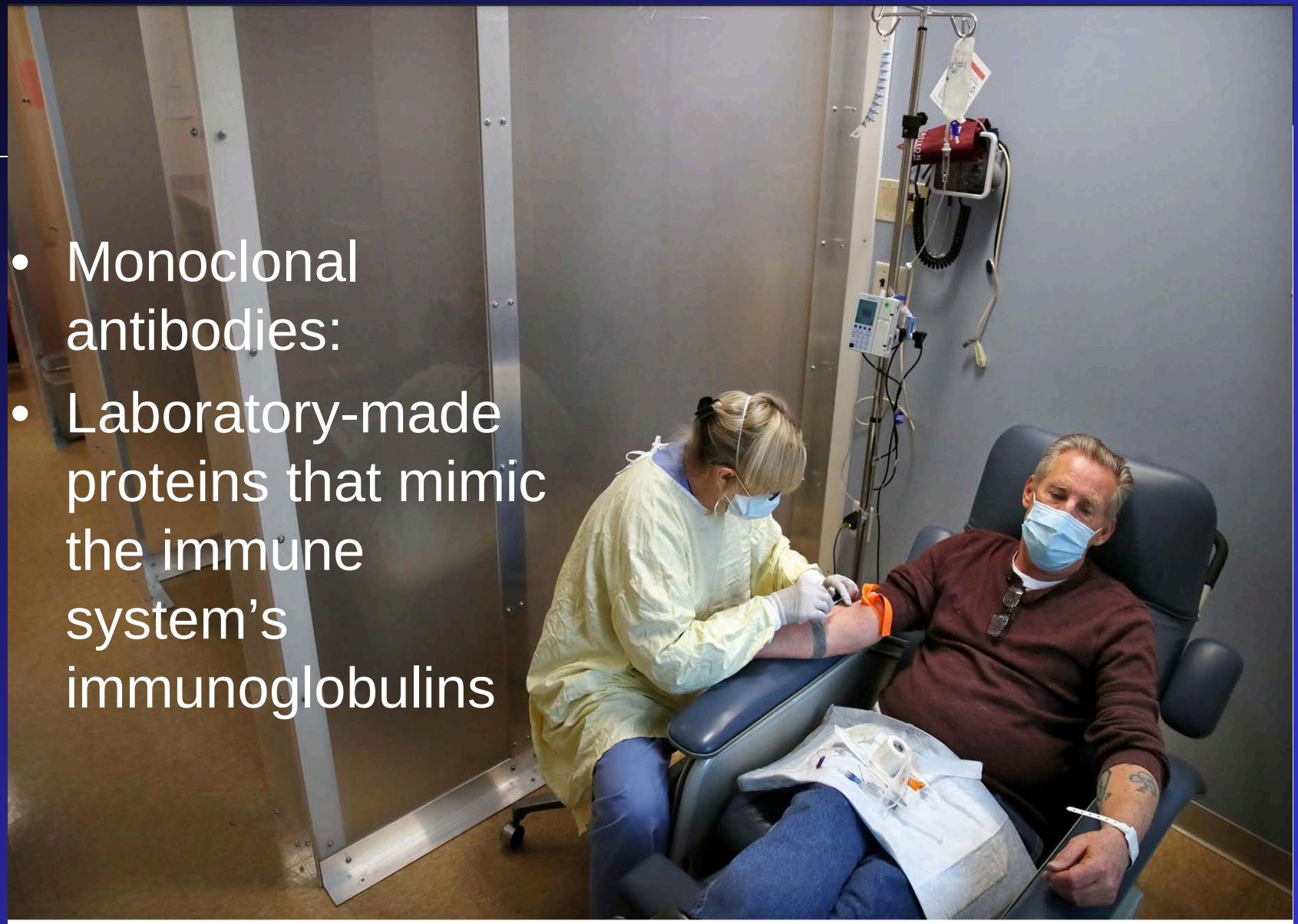
Antivirals

- Remdesivir (VEKLURY®)
  - nucleotide prodrug of an adenosine analog
  - binds to the viral RNA-dependent RNA polymerase, inhibiting viral replication
    - premature termination of RNA transcription
  - S.E.'s: GI (nausea), elevated transaminase levels, increase in prothrombin time, and hypersensitivity
    - Check LFTs, PT (10x ALT elevation)
    - Check Cr (GFR > 30)
      - Contains SBECD -sulfobutylether-beta-cyclodextrin sodium



Monoclonals

- Monoclonal antibodies:
- Laboratory-made proteins that mimic the immune system's immunoglobulins



Nurse Janet Gilleran treats a coronavirus patient, Mike Mokler, with bamlanivimab, a monoclonal antibody, in at Tufts Medical Center in Boston

Bamlanivimab:

- EUA 12 years of age and older
- weighing at least 40 kg and
- at high risk for progressing to severe COVID-19 and/or hospitalization
- for the treatment of mild to moderate COVID-19
- **includes 65 y.o., and those with chronic medical conditions**
- *NOT: for hospitalized due to COVID-19 or require oxygen*

-Eli Lilly

Casirivimab and Imdevimab:

- EUA 12 years of age and older
- weighing at least 40 kg
- at high risk for progressing to severe COVID-19 and/or hospitalization
- for the treatment of mild to moderate COVID-19
- **includes 65 y.o., and those with chronic medical conditions**

-Regeneron

Bamlanivimab:

- shown in clinical trials to reduce COVID-19-related hospitalization or ER visits:
- *Only 3% of bamlanivimab-treated pts vs 10% in placebo*
- benefit of bamlanivimab treatment has not been shown in hospitalized due to COVID-19
- may be associated with worse clinical outcomes when given to hospitalized patients on high flow O2 or mechanical ventilation
- *SEs:* anaphylaxis and infusion-related reactions, N/V, diarrhea dizziness, HA, itching

Casirivimab and Imdevimab:

Similar benefit:

- 3% of casirivimab & imdevimab-treated patients needed ER visit or hospitalization vs. 9% in placebo group
- -Viral load reduction at 7 days
- -SEs: anaphylaxis and infusion-related reactions, fever, chills, hives, itching and flushing

Monoclonal usage

- *<u>The only available therapy that can potentially keep patients out of the hospital</u>*
- Save lives;

  Ease strain on hospital systems
- <u>WHY NOT?</u>
- Timing: Must be given within 1 week of illness (issues with testing)
- Resources: Available? Time to infuse (1 hr)

  ”If we had this pandemic under control, we could set up infusion centers” Dr. Cohen, Harvard
- AWARENESS!

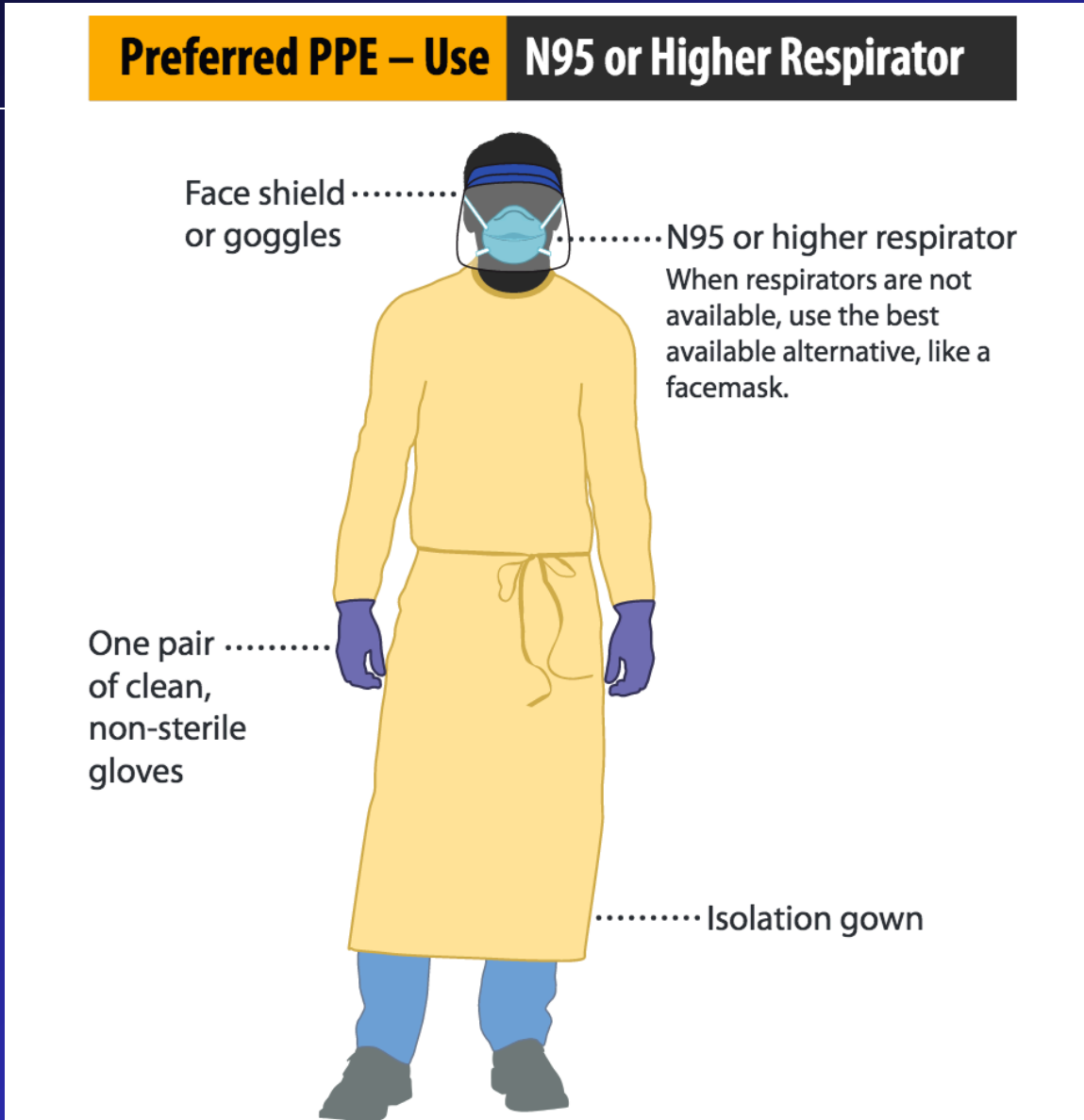
Nicholas Capote of the pharmacy department displays a treatment of bamlanivimab, a monoclonal antibody, in the Respiratory Infection Clinic at Tufts Medical Center in Boston on Dec. 31.

COVID-19 prevention

- Masks
  - Surgical masks 70 – 83%
  - N95 masks > 99%
- Physical Distancing
- Hygiene
  - Hand washing
  - Cough etiquette
- VACCINE

JAMA. 2020;323(18):1837-1838. doi:10.1001/jama.2020.4756

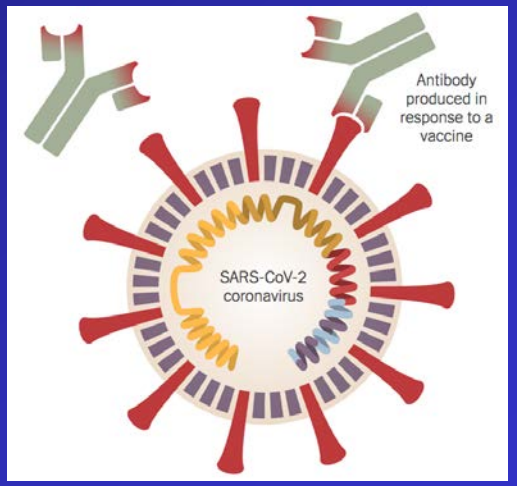
Know how to protect yourself



COVID-19 Vaccines

COVID-19 Vaccine overview

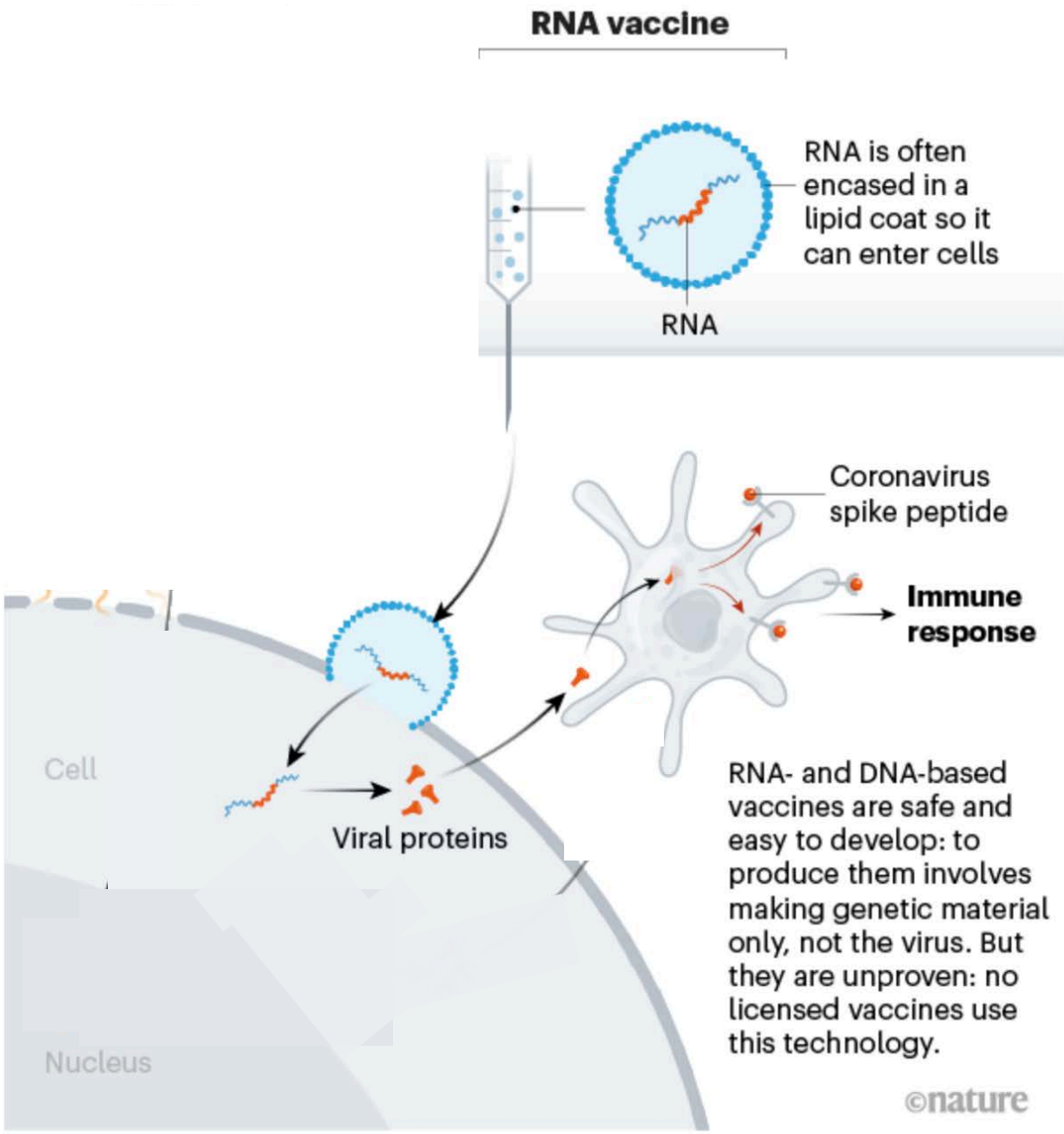
- 170 COVID-19 vaccine candidates under development*, #
  - 60 are in clinical development



- Different platforms:
  - Inactivated, non-replicating viral vector, protein subunit, RNA, DNA, VLP, replicating viral vector…

* https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines
# https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

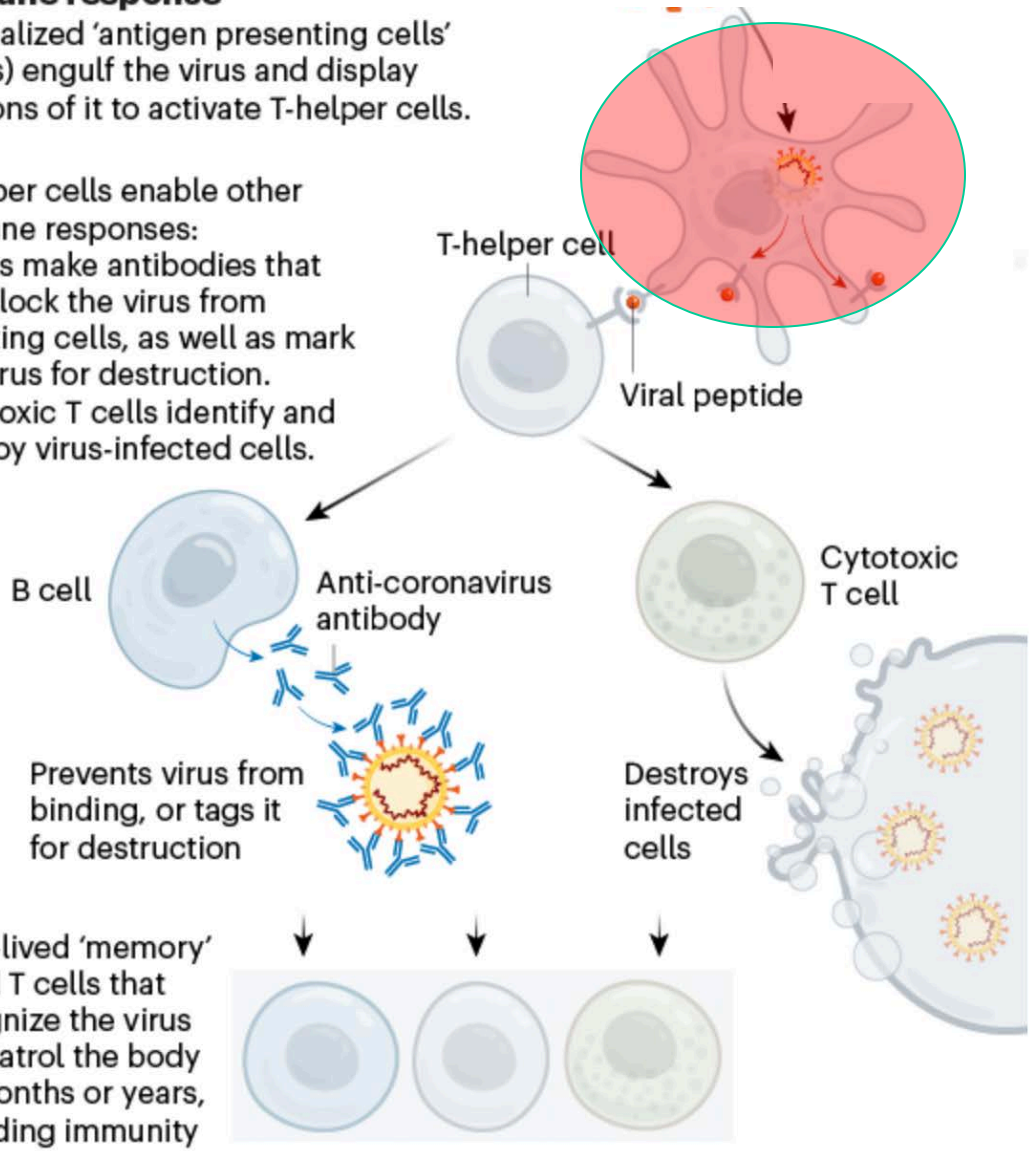
NUCLEIC-ACID VACCINES



Immune response*

Specialized 'antigen presenting cells' (APCs) engulf the virus and display portions of it to activate T-helper cells.

T-helper cells enable other immune responses:
B cells make antibodies that can block the virus from infecting cells, as well as mark the virus for destruction.
Cytotoxic T cells identify and destroy virus-infected cells.



Long-lived 'memory' B and T cells that recognize the virus can patrol the body for months or years, providing immunity

*Simplified

What are the available vaccines?

- Pfizer mRNA
- Moderna mRNA
- J&J
  - recombinant, replication-incompetent adenovirus type 26 (Ad26) vector, constructed to encode (SARS-CoV-2) spike (S) protein
- *Astra Zeneca/University of Oxford*
  - *Modified chimp adenovirus vector (ChAdOx1)*

Pfizer vaccine

- mRNA vaccine, BNT162b2
  - Lipid nanoparticles mRNA encoding spike glycoprotein (S)
    - thee target of virus neutralizing antibodies
- 43,000 participants; & children aged 12
- 2 doses: mild to moderate side effects
  - Minus 80 Celsius (112 Fahrenheit)

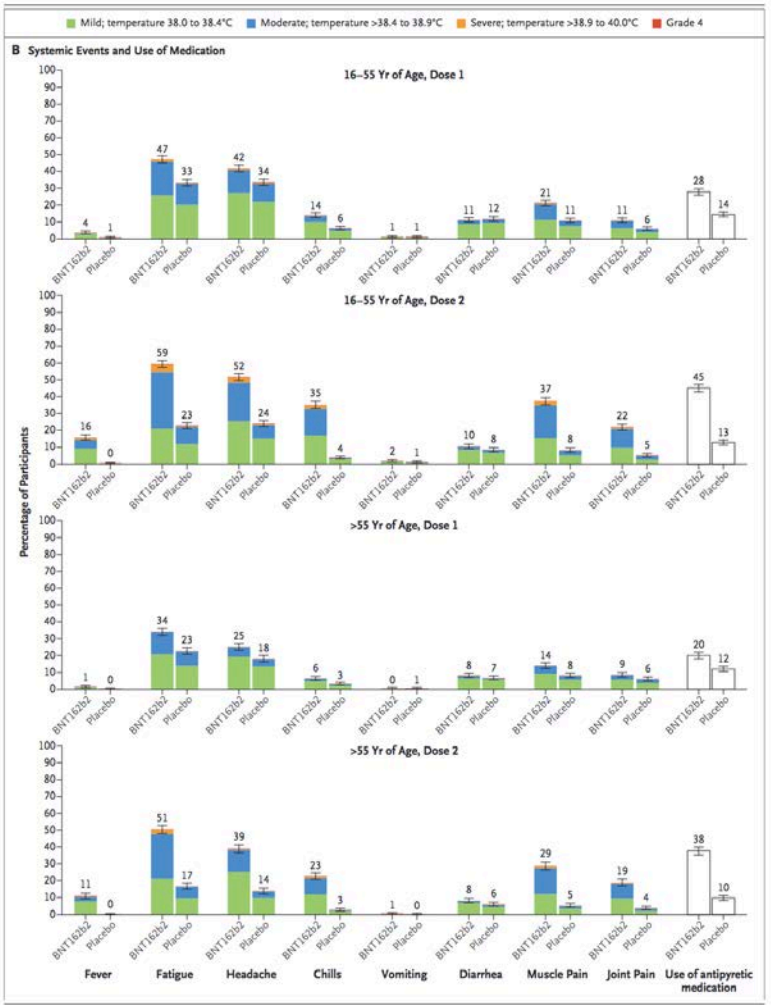
Vaccines

Pfizer-BioNTech

Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16–89	16–91	16–91
Body-mass index‡			
≥30.0: obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.



Polack et al., Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine NEJM Dec 10, 2020

Real World data

- Pfizer-BioNTech Shot Stops Covid Spread, Israeli Study Shows
  - *Israel has given more Covid vaccines per capita than anywhere else. ~half of the population has had at least one dose*
  - Vaccine reported to be 89% effective at preventing infections
  - Stopping virus transmission is key to ending Covid-19 pandemic
- Israelis –Pfizer vaccine was 99% effective at preventing death

J & J Vaccine

-Human adenovirus viral vector developed by Janssen Pharmaceuticals,
  a subsidiary of Johnson & Johnson
-Replication-incompetent recombinant adenovirus type 26 (Ad26) vector expressing the SARS-CoV-2 spike (S) protein
-66% effective in a one-dose regimen in preventing symptomatic COVID-19, with an 85% efficacy in preventing severe COVID-19
-Granted EUA – unanimous decision
-Safety: Very large study - 43,783 participants
-8 countries, ~ 34 percent over age 60
-From USA: 74% White; 15% Hispanic; 13% Black; 6% Asian and 1% Native American
-41% had comorbidities - increased risk for severe COVID-19
-no anaphylaxis was observed in participants

Vaccine ingredients: citric acid monohydrate, trisodium citrate dihydrate, ethanol (alcohol), 2-hydroxypropyl-β-cyclodextrin (HBCD) (hydroxypropyl betadex), polysorbate 80, sodium chloride, sodium hydroxide, and hydrochloric acid

J & J Vaccine

~72% efficacy rate against mild to severe/critical disease in US trials
-Yes, slightly lower numbers vs other [mRNA] vaccines but it was tested later -new variants were spreading
(i.e. the troubling B.1.351 strain)
Still gave strong protection vs severe illness

~3.9 million doses started distribution!
~16 million more doses by end of March
-Does not need to be frozen, a refrigerator is OK
-Easy to transport
-Allows for expanded availability in most community settings and mobile sites as supply scales up

The danger of variant strains

UK quarantined

B 1.1.1.7 strain - up to 57% more transmissible

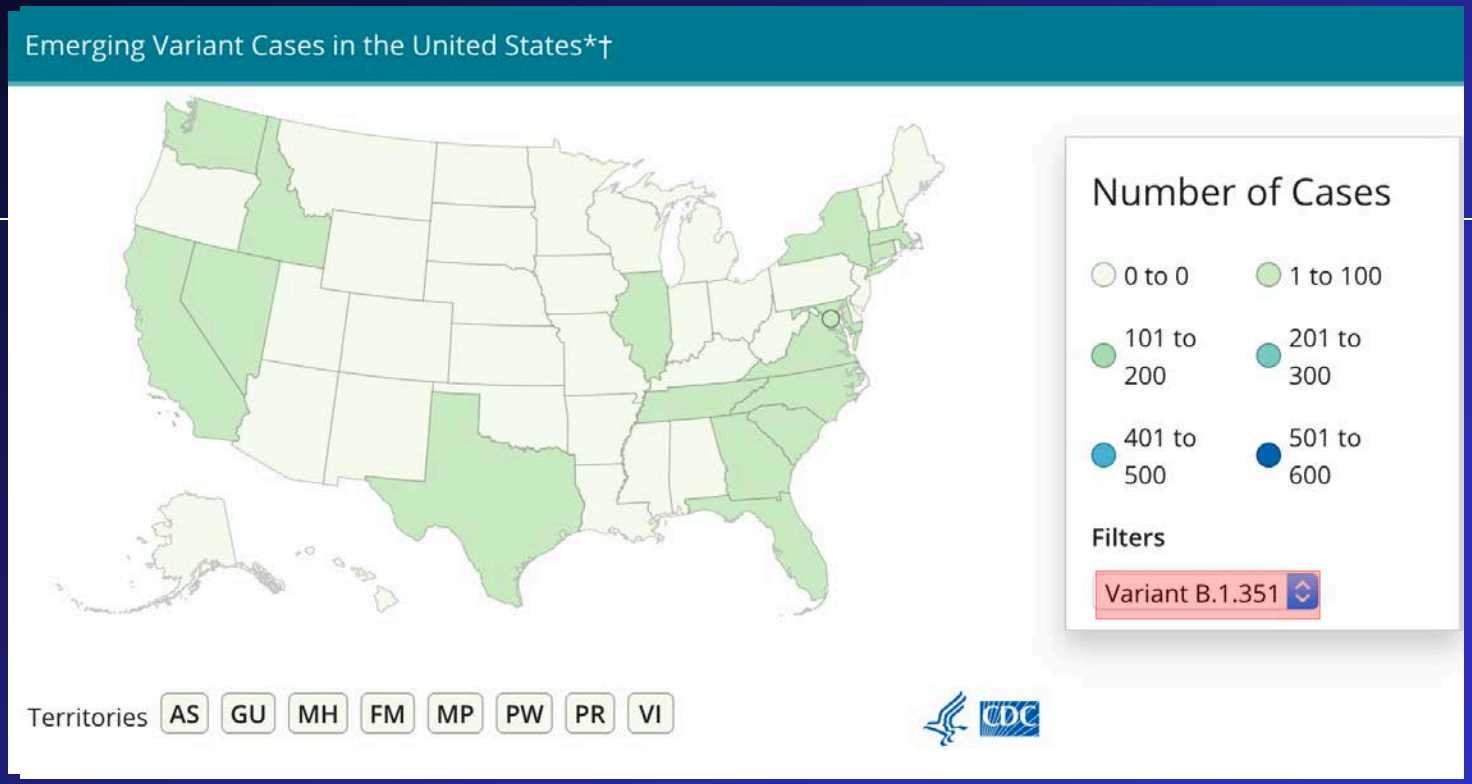
The danger of variants

"Please hear me clearly: At this level of cases with variants spreading, we stand to completely lose the hard-earned ground we have gained,"
-Dr. Rochelle Walensky, Director of the CDC

-The CDC said the highly contagious B.1.1.7 variant will become the dominant strain in the US this month

-New variant B.1.526 found in New York
  Shares a mutation in common with B1.351 and P1
-Unknown transmissibility, lethality, or vaccine effectiveness

Strains threatening the United States

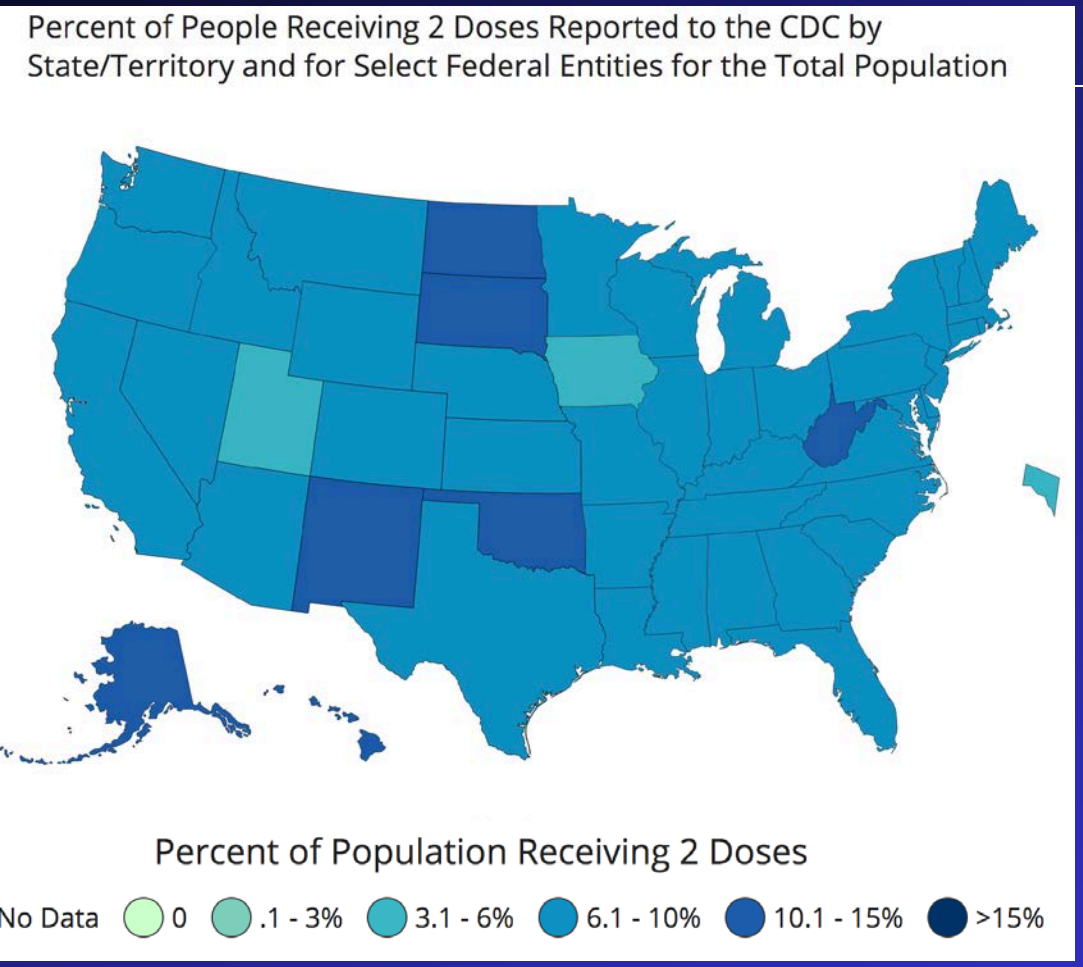


-At least 46 States B117 strain
  -2506 total: FL (599), MI (421) CA (212), NY (136), CT (42) MO (1)
-Other strains:
  -B.1.351 (17 States) – 65 cases
  -P.1 (5 States) – 10 cases

Variant	Reported Cases in US	Number of Jurisdictions Reporting
B.1.1.7	2506	46
B.1.351	65	17
P.1	10	5

www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html

COVID-19 Vaccinations across the US

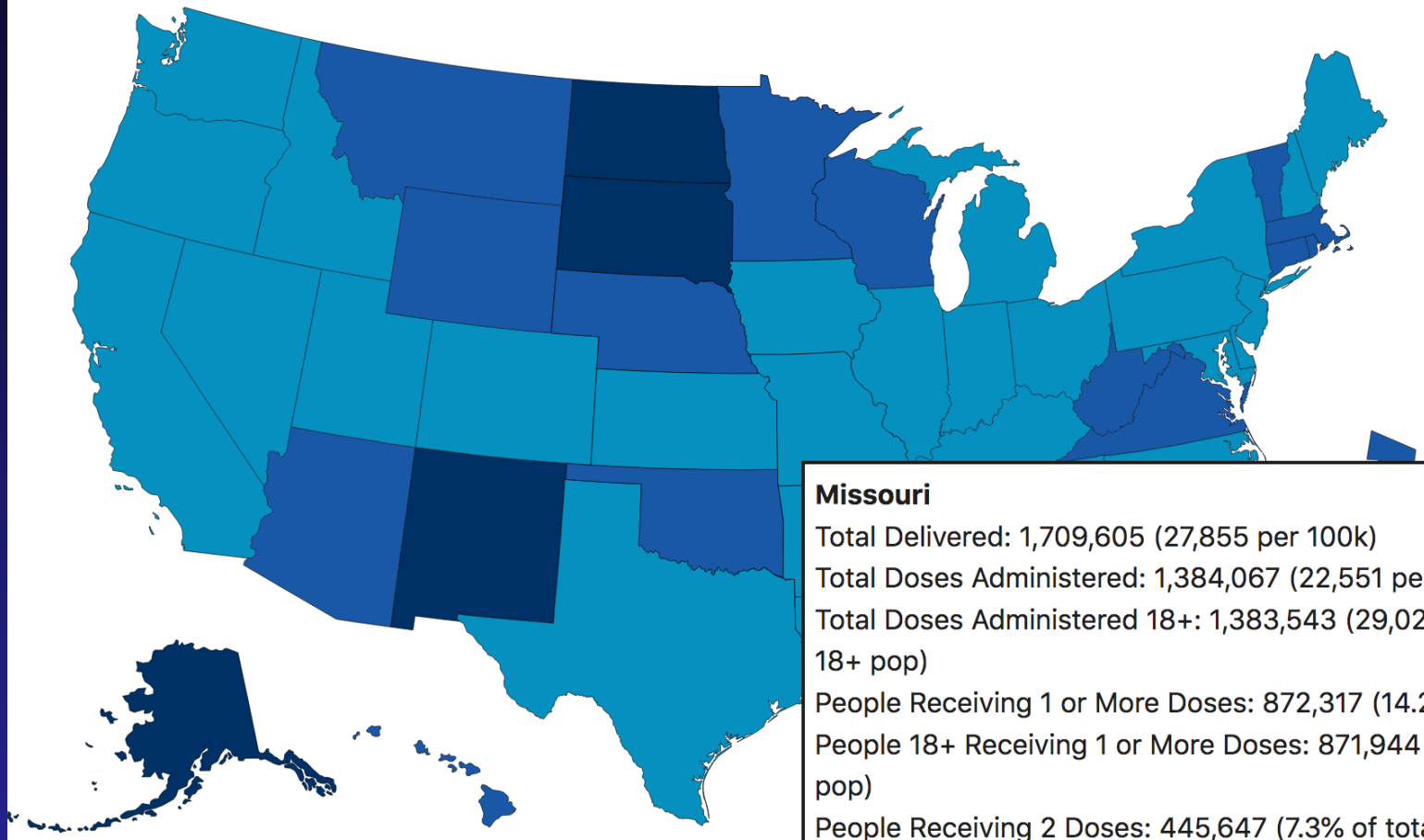


-As of 3/2, ~52 million had received at least one dose of Covid-19 vaccine
-about 26 million received 2 doses
-Averaging ~1.7 million doses/d
-J&J vaccine approved!

https://covid.cdc.gov/covid-data-tracker/#vaccinations

Vaccinations in Missouri

Total Doses Administered Reported to the CDC by State/Territory and for Select Federal Entities per 100,000 of the Total Population



Missouri

Total Delivered: 1,709,605 (27,855 per 100k)

Total Doses Administered: 1,384,067 (22,551 per 100k)

Total Doses Administered 18+: 1,383,543 (29,024 per 100k of 18+ pop)

People Receiving 1 or More Doses: 872,317 (14.2% of total pop)

People 18+ Receiving 1 or More Doses: 871,944 (18.3% of 18+ pop)

People Receiving 2 Doses: 445,647 (7.3% of total pop)

People 18+ Receiving 2 Doses: 445,529 (9.3% of 18+ pop)

Click on map to learn more about vaccine data in Missouri

https://covid.cdc.gov/covid-data-tracker/#vaccinations

Continue to fight

Elimination of Covid-19?
will depend on

- Genetic changes in the virus that might enable it to escape vaccine-induced immunity
- Potential “reservoirs” of SARS-CoV-2 in animals, and
- The ability to stop transmission across the world

-Dr Petousis-Harris

Questions?

Resources

- Nuvance health 2300+ articles reviewed:

https://spark.adobe.com/page/cisEJsZBgFEiG/

CDC:

https://www.cdc.gov/coronavirus/2019-ncov/index.html

https://emergency.cdc.gov/coca/calls/2021/

https://emergency.cdc.gov/coca/calls/2021/callinfo_030221.asp

- WHO:

https://www.who.int/emergencies/diseases/novel-coronavirus-2019

- Johns Hopkins:

https://coronavirus.jhu.edu/map.html

- Others

https://www.thelancet.com/coronavirus

https://covidactnow.org/

To be continued…

- Teamwork, preparations
  -supporting each other