3/11/2021

COVID-19 update 2021

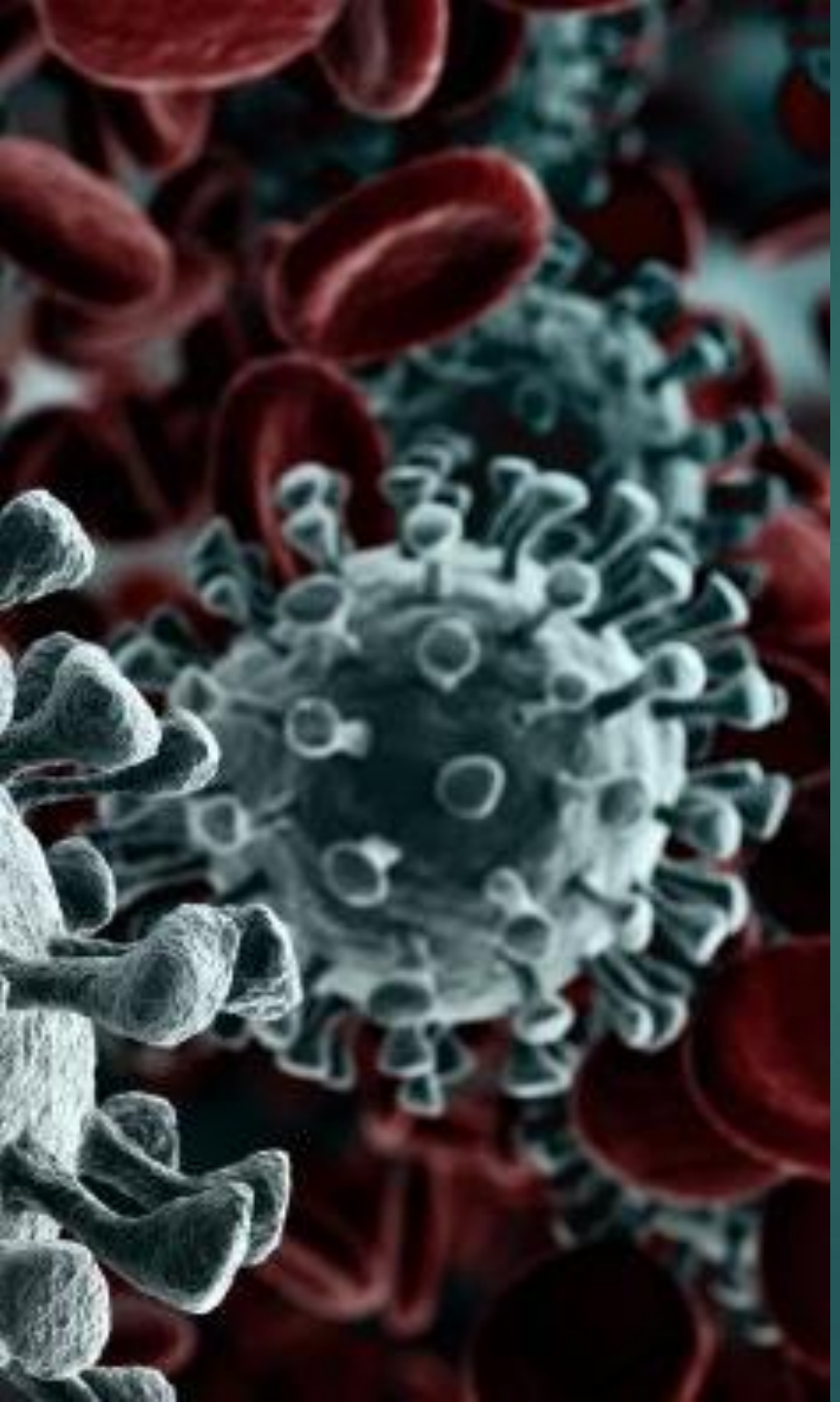
DANIEL RODRIGUE, M.D.

LEXINGTON INFECTIOUS DISEASE CONSULTANTS

Covid-19 update objectives

- Review latest epidemiology of Covid-19
- Review current treatment of Covid-19
- Prevention of Covid-19 and vaccines

- *No one involved in the planning or presentation of this activity discloses they have anything to disclose*
- Identify one knowledge deficit you had regarding clinical treatment or vaccinations prior to this educational offering



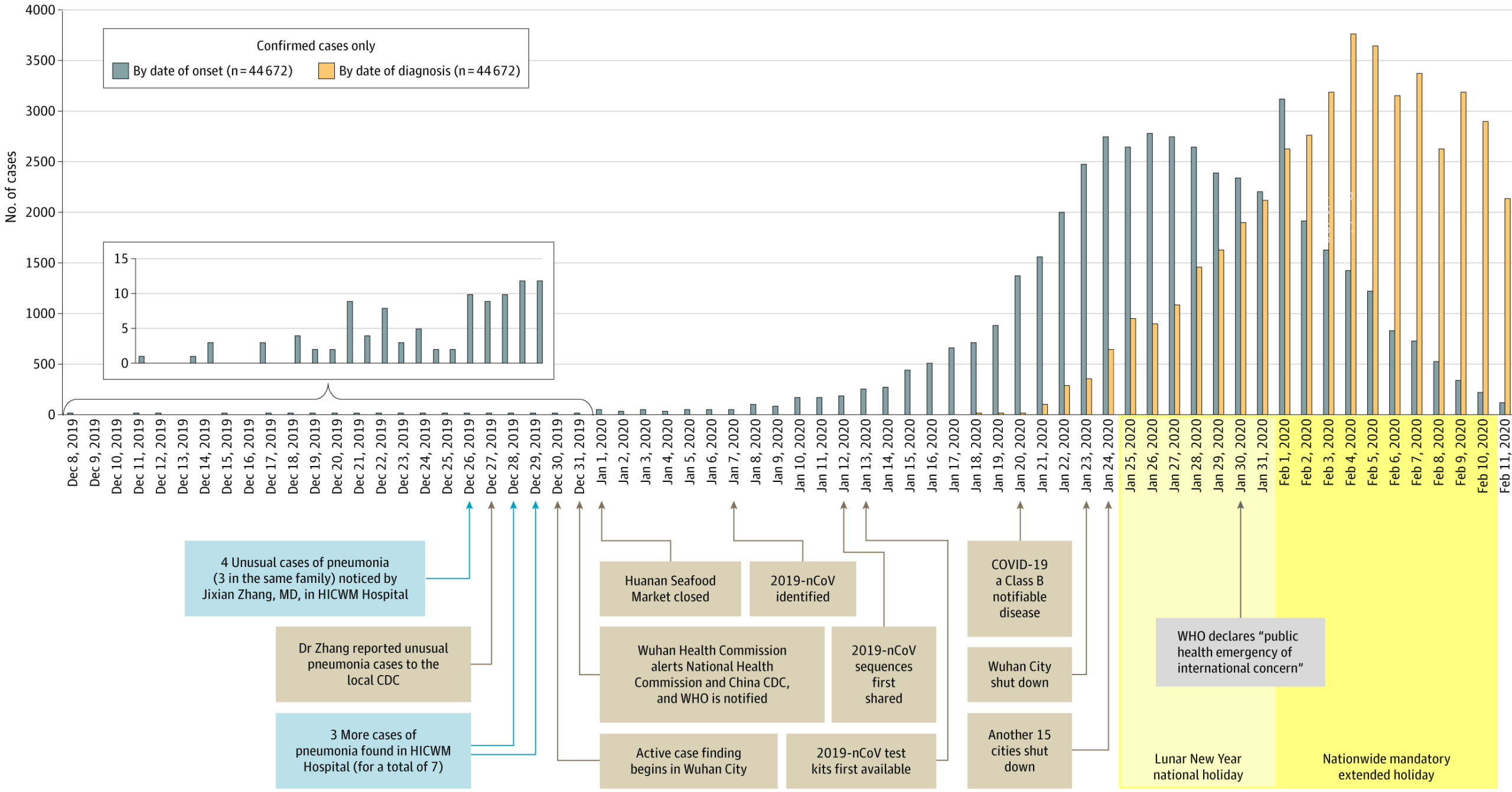
Covid-19 epidemiology

December 2019 a series of pneumonia cases emerged in Wuhan, Hubei, China

Sequenced as a novel coronavirus, now named SARS-Cov-2

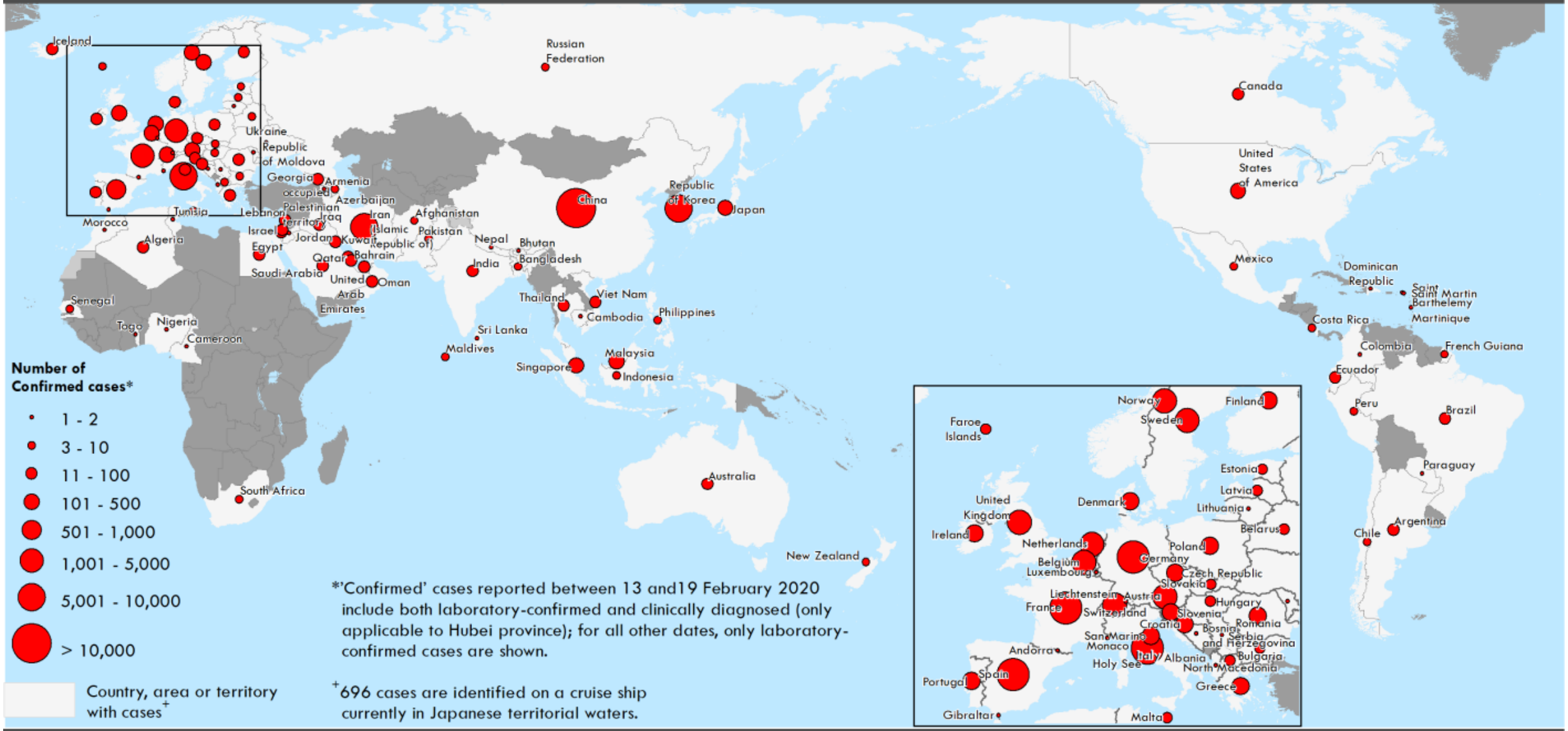
Rodrigue
4/1/20

Kroger grocery store during Covid-19 pandemic, KY, 3/2020


Confirmed cases only
By date of onset (n = 44 672)
By date of diagnosis (n = 44 672)
No. of cases
4000
3500
3000
2500
2000
1500
1000
500
0
15
10
5
0
Dec 8, 2019
Dec 9, 2019
Dec 10, 2019
Dec 11, 2019
Dec 12, 2019
Dec 13, 2019
Dec 14, 2019
Dec 15, 2019
Dec 16, 2019
Dec 17, 2019
Dec 18, 2019
Dec 19, 2019
Dec 20, 2019
Dec 21, 2019
Dec 22, 2019
Dec 23, 2019
Dec 24, 2019
Dec 25, 2019
Dec 26, 2019
Dec 27, 2019
Dec 28, 2019
Dec 29, 2019
Dec 30, 2019
Dec 31, 2019
Jan 1, 2020
Jan 2, 2020
Jan 3, 2020
Jan 4, 2020
Jan 5, 2020
Jan 6, 2020
Jan 7, 2020
Jan 8, 2020
Jan 9, 2020
Jan 10, 2020
Jan 11, 2020
Jan 12, 2020
Jan 13, 2020
Jan 14, 2020
Jan 15, 2020
Jan 16, 2020
Jan 17, 2020
Jan 18, 2020
Jan 19, 2020
Jan 20, 2020
Jan 21, 2020
Jan 22, 2020
Jan 23, 2020
Jan 24, 2020
Jan 25, 2020
Jan 26, 2020
Jan 27, 2020
Jan 28, 2020
Jan 29, 2020
Jan 30, 2020
Jan 31, 2020
Feb 1, 2020
Feb 2, 2020
Feb 3, 2020
Feb 4, 2020
Feb 5, 2020
Feb 6, 2020
Feb 7, 2020
Feb 8, 2020
Feb 9, 2020
Feb 10, 2020
Feb 11, 2020
4 Unusual cases of pneumonia (3 in the same family) noticed by Jixian Zhang, MD, in HICWM Hospital
Dr Zhang reported unusual pneumonia cases to the local CDC
3 More cases of pneumonia found in HICWM Hospital (for a total of 7)
Huanan Seafood Market closed
2019-nCoV identified
Wuhan Health Commission alerts National Health Commission and China CDC, and WHO is notified
2019-nCoV sequences first shared
Active case finding begins in Wuhan City
2019-nCoV test kits first available
COVID-19 a Class B notifiable disease
Wuhan City shut down
Another 15 cities shut down
WHO declares "public health emergency of international concern"
Lunar New Year national holiday
Nationwide mandatory extended holiday

Distribution of COVID-19 cases as of 09 March 2020

World Health Organization



*'Confirmed' cases reported between 13 and19 February 2020 include both laboratory-confirmed and clinically diagnosed (only applicable to Hubei province); for all other dates, only laboratory-confirmed cases are shown.

+696 cases are identified on a cruise ship currently in Japanese territorial waters.

Data Source: *World Health Organization*

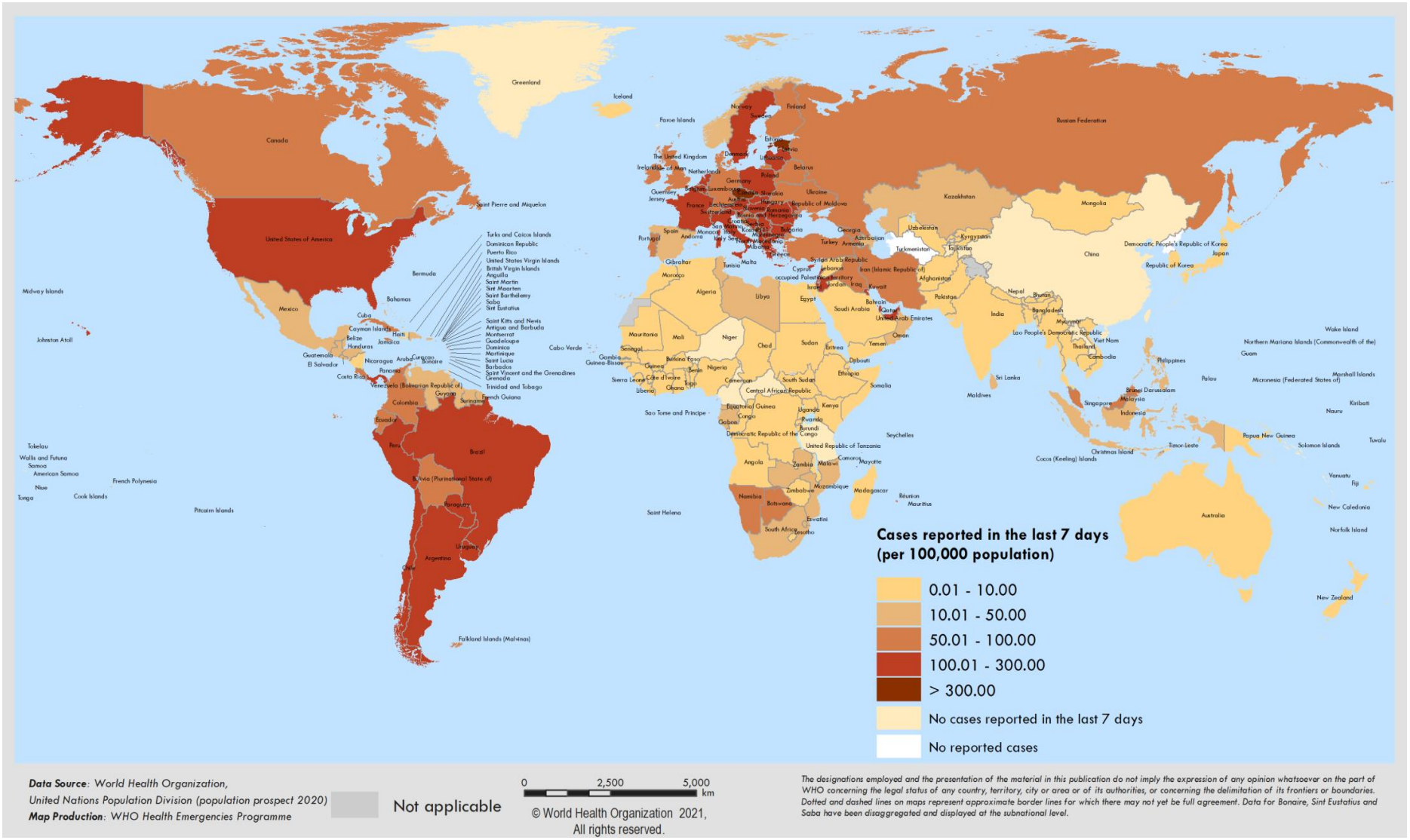
Map Production: *WHO Health Emergencies Programme*

Not applicable

0 2,500 5,000 km

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Figure 2. COVID-19 cases per 100 000 population reported in the last seven days by countries, territories and areas, 22 February through 28 February 2021**



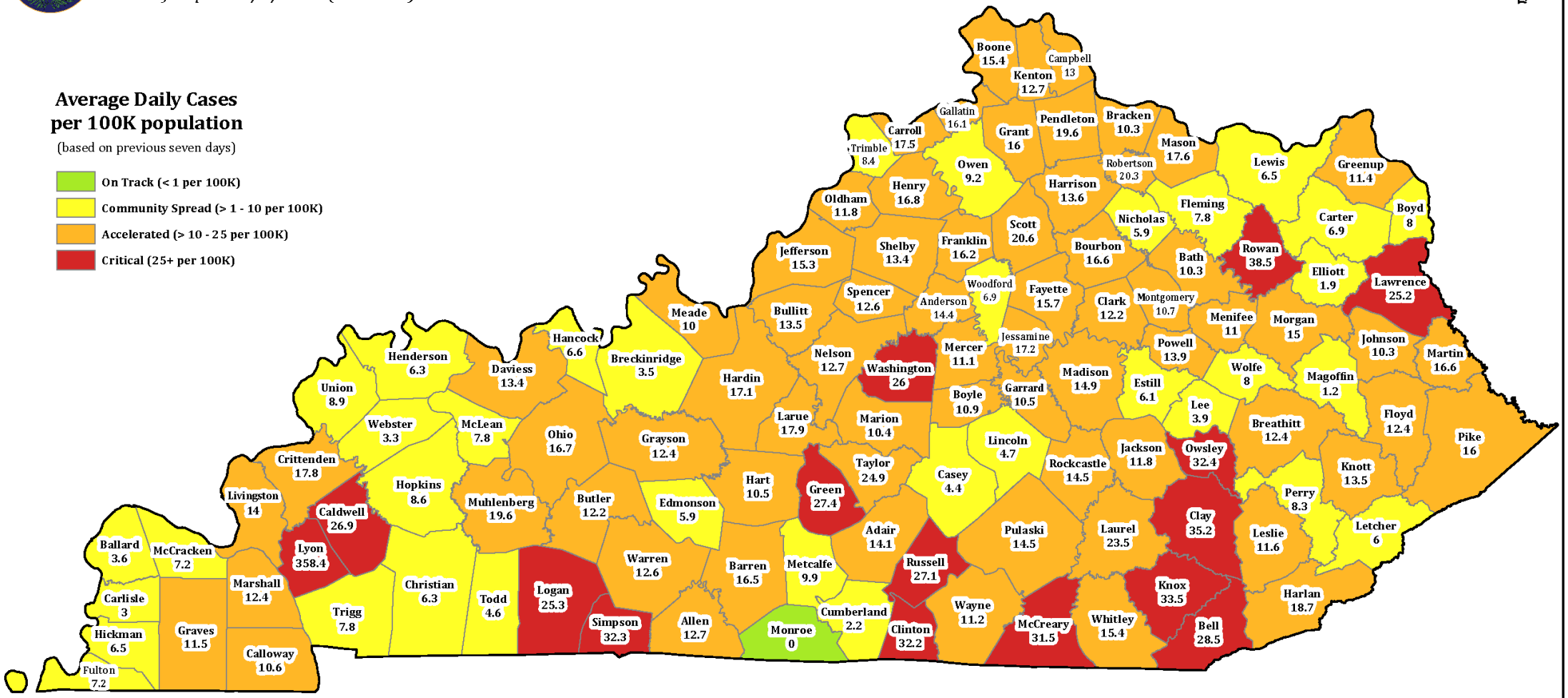
COVID-19 Current Incidence Rate in Kentucky

Date of Report: 3/8/2021 (4:38 PM)

Average Daily Cases per 100K population

(based on previous seven days)

- On Track (< 1 per 100K)
- Community Spread (> 1 - 10 per 100K)
- Accelerated (> 10 - 25 per 100K)
- Critical (25+ per 100K)



Overall Current Incidence Rate

14.98

Population values from the 2019 US Census Bureau Estimates

Total number of cases used in the calculations: 411,032 Cases

Data Source: Kentucky Department for Public Health

Covid-19 epidemiology

3/11/2021

Cases > global 117 million to date, 2.6 million deaths (3/8/21), 216 countries, WHO pandemic called 3/11/20

United States, 29 million cases, total deaths 525,673 (3/8/21), US state of emergency called 3/13/20

Kentucky 411,040 cases, 4,829 deaths, 4.06% positivity tests (3/8/21), state incidence rate 15/100 K

Infection fatality risk of 1%, with highest risk factors for age > 65 y, comorbidities (obesity BMI > 30, COPD, DM2, CAD (or cardiomyopathies, CHF), CKD, cancer, sickle cell, solid organ transplant), smoking, pregnancy, Down syndrome; 8/10 deaths reported in US in adults > 65 y; 5 d incubation (2-14 d), ?race (AA), ?gender (male), blood type O—91 % of hospitalized adults w/ risk factor; 52% of children (most common obesity, neuro, asthma)

jhu.edu 3/7/21, kycovid19.ky.gov 3/7/21; cdc.gov 3/7/21

Covid-19 and undercounting cases

- Seroprevalence studies also demonstrate undercounting of cases of Covid-19.
  - Study of dialysis patients, July 2020, sample of 28,503 patients
  - 8.3% positive overall but varied by region.
  - Of those that were positive, only 10% were ever diagnosed, although some had symptoms. (Lancet 10/24/20)

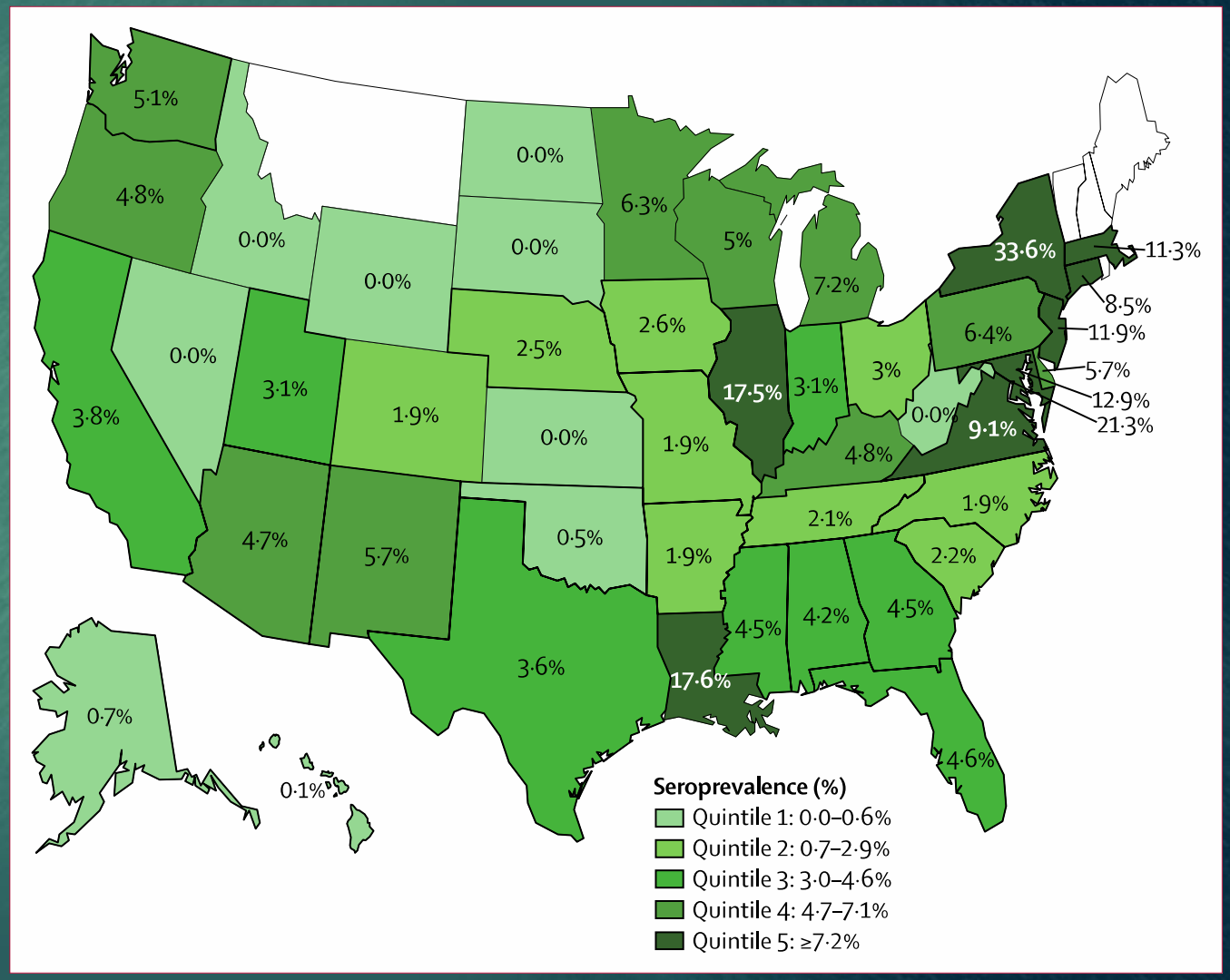
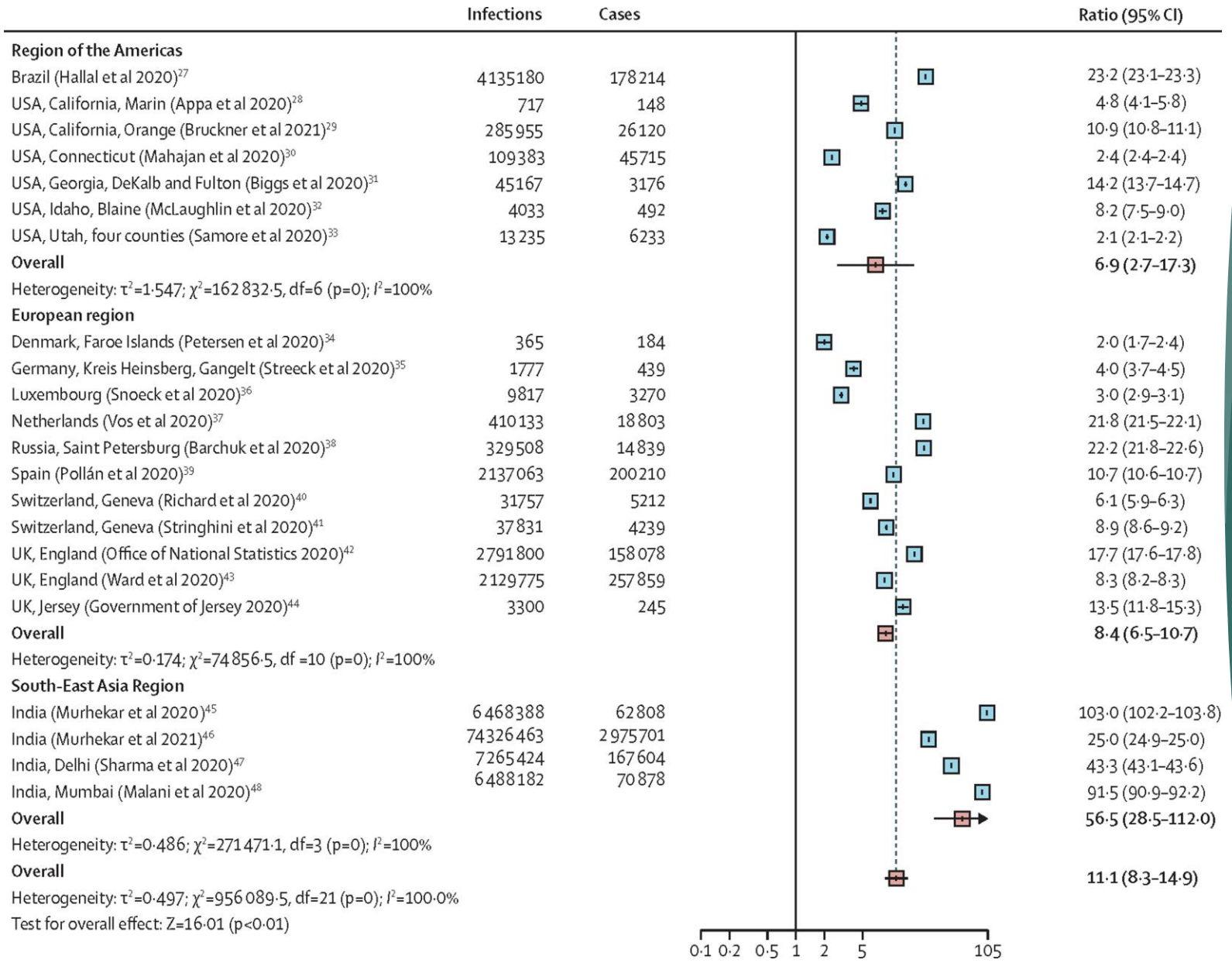


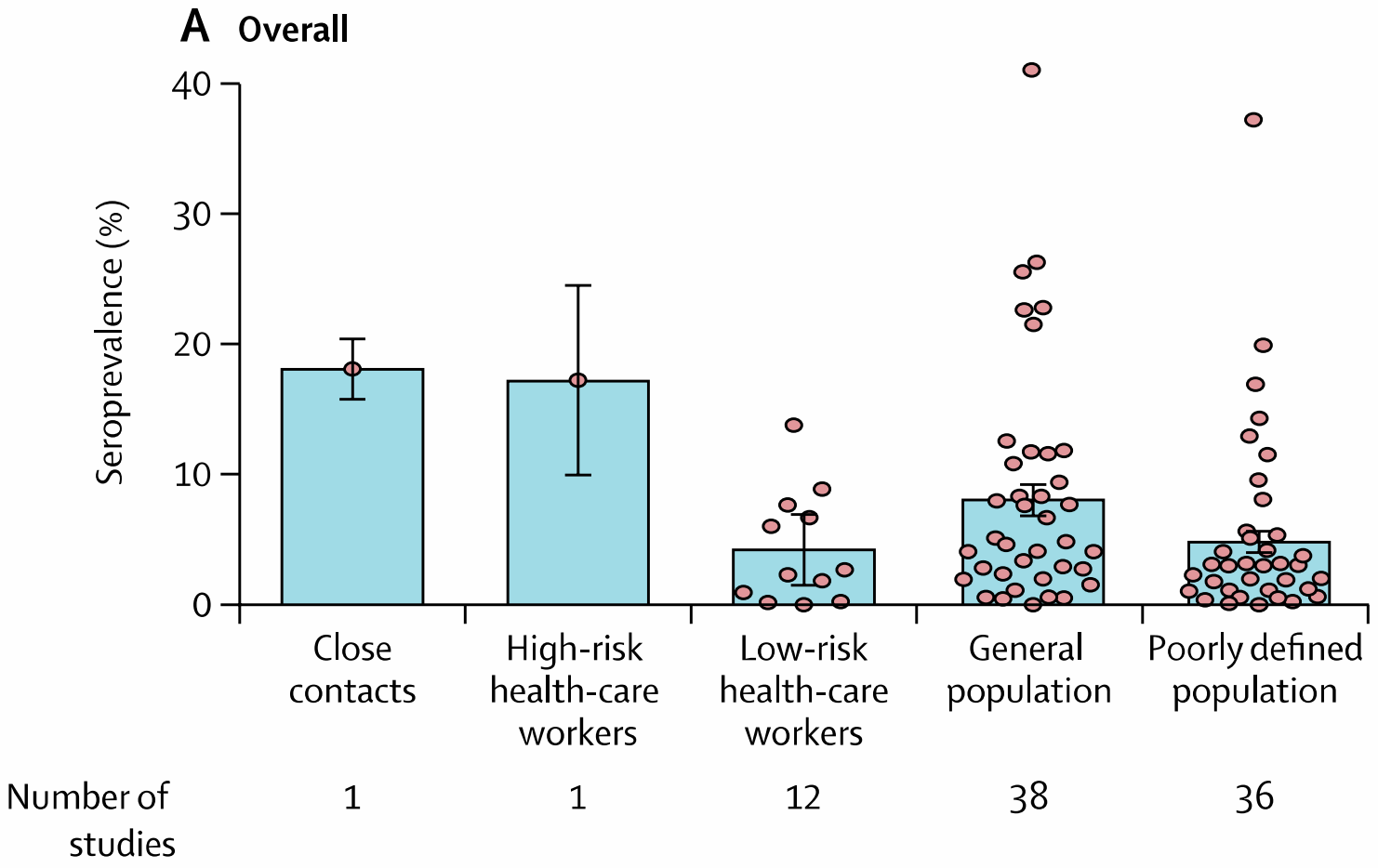
Figure 2: **Prevalence of SARS-CoV-2 antibodies in sampled population, by state**



Lancet 3/8/21

Covid-19 serosurveys globally

Overall seroprevalence of 8.0%, ranged from 1.7% in Western Pacific to 19.6% in SE Asia



Covid-19 serosurveys globally

Covid-19 epidemiology

- Primary transmission routes are respiratory **droplet from face to face contact**, and to a prob much lesser degree contact with contaminated surfaces. Aerosol spread may occur, (mostly related to procedures, crowded poorly ventilated spaces), but the role remains unclear. No good evidence for transmission by breastmilk, or vertical transmission. High viral load regardless of sx a risk factor for transmission (Lancet 2/2/21).
- Fomite transmission can occur but not common mode for transmission of COVID-19. Lab does not always translate to the field. Amount studies in lab often uses higher quant of virus, not representative of real life. (Goldman, Lancet Infect D, 7/30/20)
- Transmission may occur via pre-symptomatic carriers (2 d prior to symptom onset); asymptomatic pts do not transmit infxn as well as symptomatic (PLOS 10/8/20 meta-analysis)

Influenza Other Respi Viruses. 2020;00:1–2; Lancet 2020;395:809; J Hosp Infect 1/31/20; NEJM 3/15/20; JAMA 3/11/20; Gastroenterology 2/27/20 Xiao F, et al.; *JAMA*. doi:10.1001/jama.2020.12839; who.org 8/8/20; PLOS med 9/22/20

Ease of transmission of disease (R○)

Rodrigue
4/1/20

Ebola and Flu

1-2 people

SARS-CoV-2

2-3 people

Measles

12-18 people

R○ is a function of 3 primary parameters including the duration of contagiousness after a person becomes infected, the likelihood of infection per contact between a susceptible person and an infectious person, and the contact rate.

Emerg Infect Dis 2019;25:1

Covid-19 epidemiology
Risk of death increases w/ age

Table 3 Age-specific fatality rates for COVID-19 infections vs. accidental deaths (%)

Age group	COVID-19 IFR (95% CI)	Automobile fatalities		Other accidental fatalities	
		England	USA	England	USA
0–34	0.004 (0.003–0.005)	0.002	0.015	0.004	0.032
35–44	0.068 (0.058–0.078)	0.002	0.012	0.017	0.043
45–54	0.23 (0.20–0.26)	0.002	0..013	0.019	0.043
55–64	0.75 (0.66–0.87)	0.003	0.013	0.014	0.043
65–74	2.5 (2.1–3.0)	0.003	0.013	0.020	0.040
75–84	8.5 (6.9–10.4)	0.005	0.017	0.069	0.094
85 +	28.3 (21.8–36.6)	0.007	0.019	0.329	0.349

Kenya, only 3.9% of population > 65 yo, compared w/ 16.3% in US, and 23.3% in Italy

COVID-NET | A Weekly Summary of U.S. COVID-19 Hospitalization Data

Laboratory-Confirmed COVID-19-Associated Hospitalizations

Preliminary cumulative rates as of Feb 27, 2021

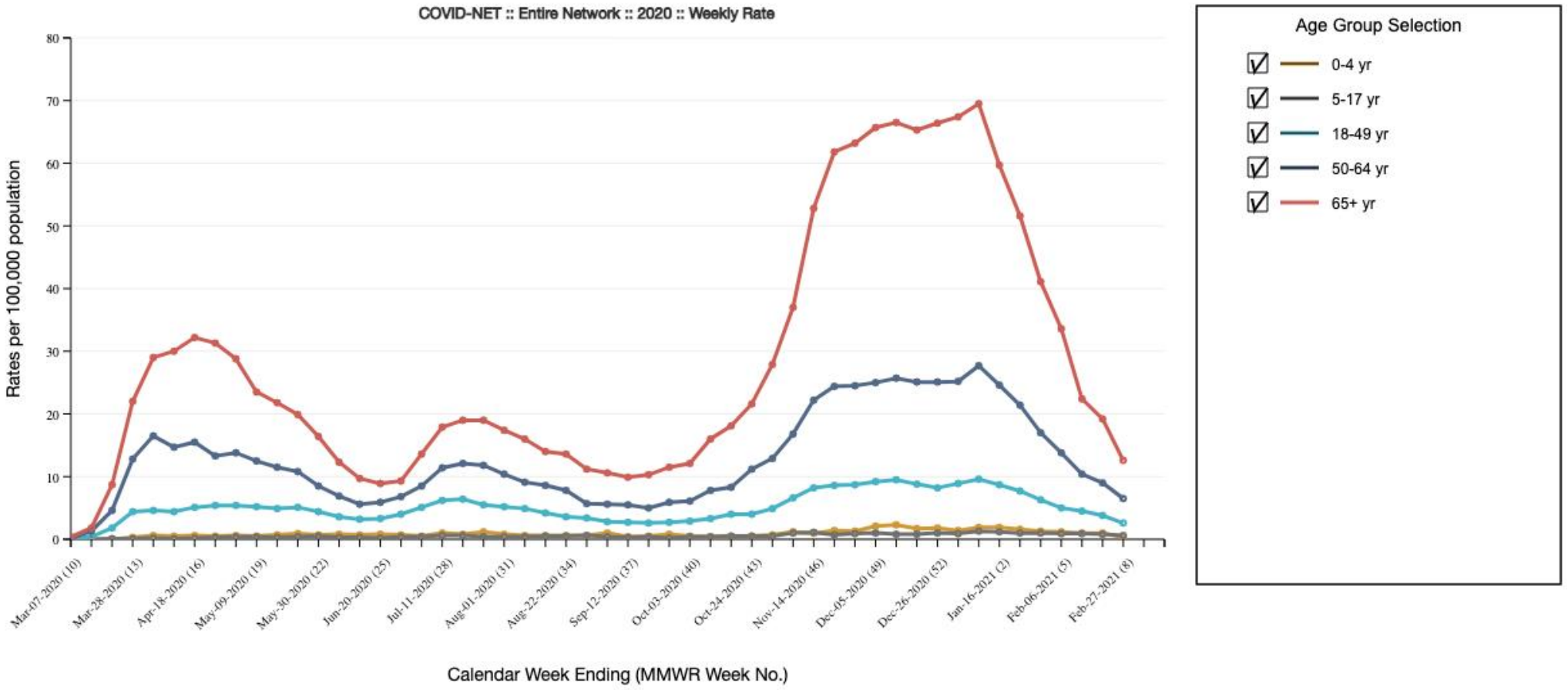
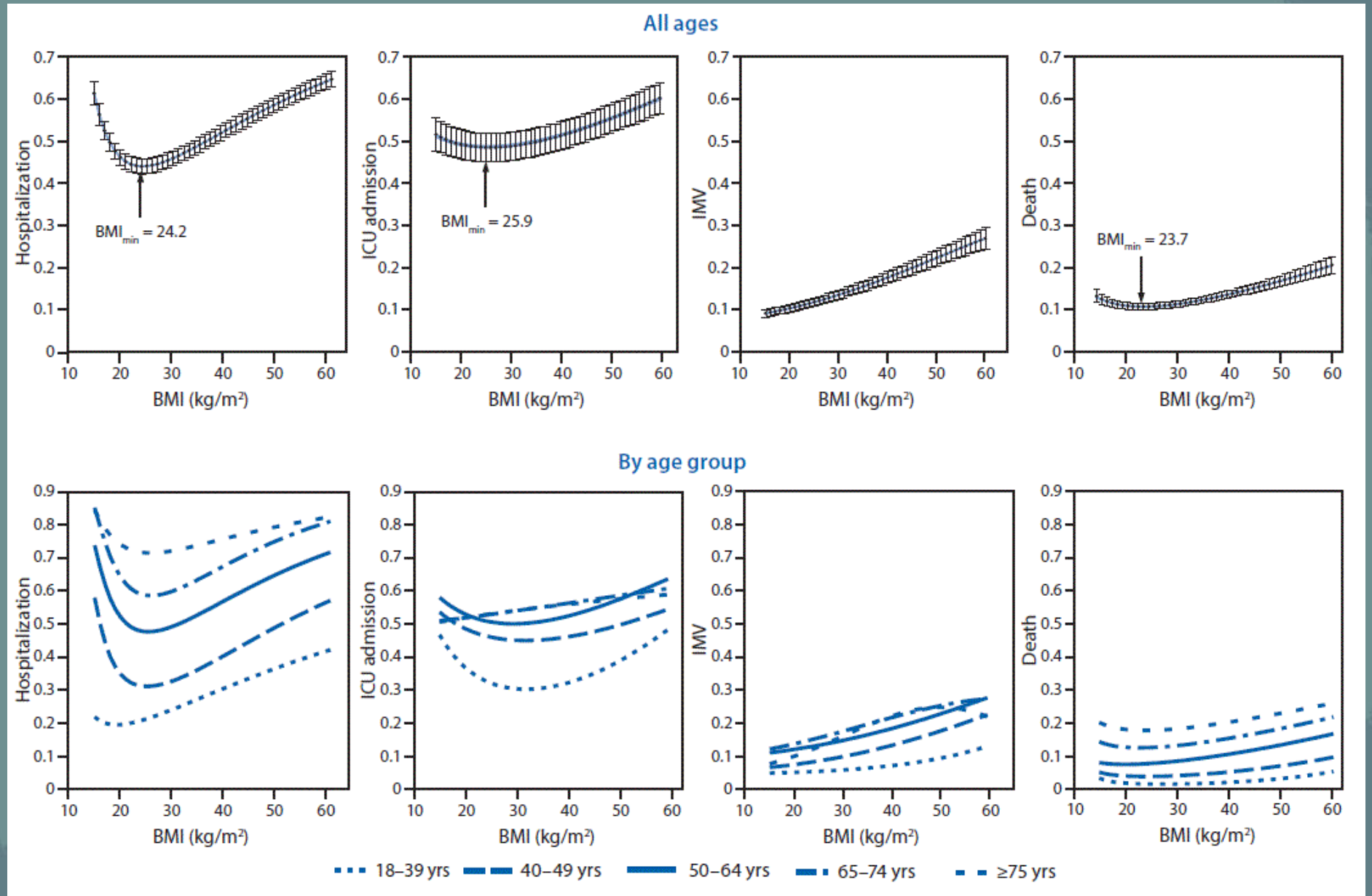


FIGURE 2. Estimated risk for severe COVID-19–associated illness* among adults aged ≥18 years, by body mass index (BMI) and age group — Premier Healthcare Special COVID-19 Release (PHD-SR),† United States, March–December, 2020§



Covid-19 hospital outcomes, US, March 2020-Aug 2020

Table. Clinical Outcomes Among Adults Hospitalized With Coronavirus Disease 2019 at 555 US Medical Centers

Outcome	Patients, No./total No. (%)
In-hospital	
Mortality or discharged to hospice	32 060/192 550 (16.6)
Mortality	26 221/192 550 (13.6)
In-hospital mortality by mo of admission	
March	3657/16 517 (22.1)
April	11 880/65 475 (18.1)
May	4101/34 071 (12.0)
June	2204/24 088 (9.1)
July	3192/34 482 (9.2)
August	1154/17 776 (6.5)
In-hospital mortality by age, y	
18-29	179/12 644 (1.4)
30-39	471/17 172 (2.7)
40-49	1185/22 888 (5.2)
50-59	3047/34 532 (8.8)
60-69	5921/40 344 (14.7)
70-79	7141/33 835 (21.1)
≥80	8277/31 135 (26.6)
Length of stay, median (IQR), d	
Without ICU stay	6 (3-8)
With ICU stay	15 (6-20)
ICU admission	55 593/192 550 (28.9)
Median cost of stay, median (IQR), $	
Without ICU stay	10 520 (8031-14 550)
With ICU stay	39 825 (25 763-56 804)

JAMA Network Open. 2021;4(3):e210417. doi:10.1001/jamanetworkopen.2021.0417

Covid-19 and health care workers

- 6-11% of HCW infected in US, but depends on when and where serosurveys done. 6.9% of first responders, HCW, public safety workers in Detroit survey (MMWR 12/2020), with community exposure a primary risk factor. Use of PPE protective (Ann I M 2/9/21). 1/2020 to 3/4/21 14,699 Baptist KY employees quarantined, 3,959 positive, 482 BHL employees.
- Most are infected from community and personal contacts, and small amount from taking care of unsuspected Covid-19 patients. Virus sequencing can be helpful for determination if avail (EID 10/2020)
- Most common reasons given for HCW infection include insufficient knowledge and training in infection control, and shortage of PPE. Family exposure, and exposure in break rooms identified as contributing factors.
- Stress and burnout common among HCW taking care of Covid-19 patients.

Pregnant Women with COVID-19 who were hospitalized, United States, January 22, 2020 - March 1, 2021

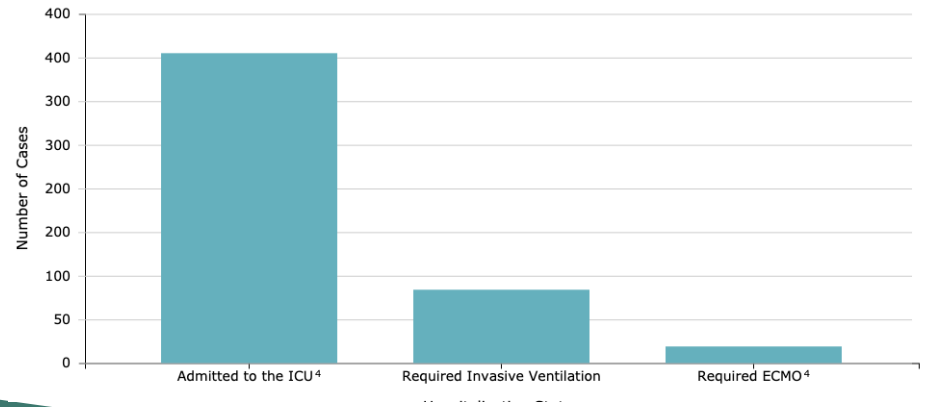
Data were collected from 73,617 women, but hospitalization data were only available for 59,976 (81.5%).

HOSPITALIZED CASES[3]

12,471

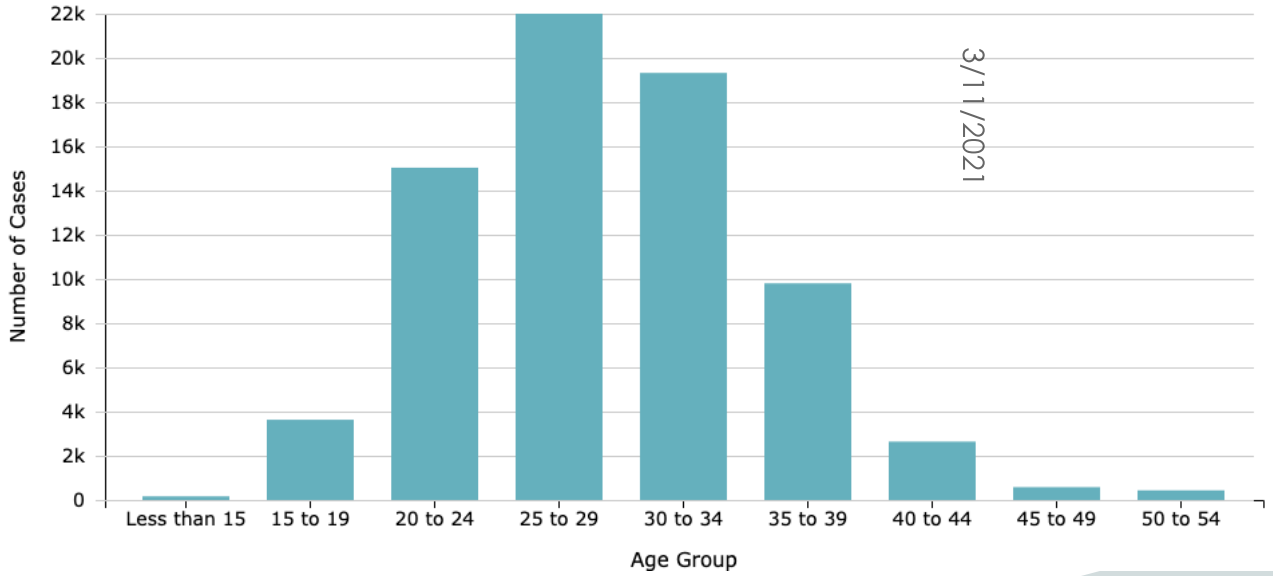
Pregnant women with COVID-19 admitted to the ICU, who required invasive ventilation, or who required ECMO, United States, January 22, 2020 - March 1, 2021

Data were collected from 73,617 women, but ICU admission data were only available for 11,028 (15%) women, invasive ventilation data were only available for 7,542 (10.2%) women, and ECMO data were only available for 8,168 (11.1%).



Pregnant women with COVID-19 by age, United States, January 22, 2020 - March 1, 2021

Data were collected from 73,617 women, and age was available for 73,617 (100%) women.



Covid-19 and pregnancy

How does Covid-19 compare to other pandemics

- 2009 Swine flu (Influenza A H1N1) estimated to have killed 151,000 to 575,000 worldwide (and worldwide infection rate of about 1/4), 61 million cases in US, 275,000 hospitalizations, 12,500 deaths in US, CFR 0.2-0.02%, elder with lower mortality.
- Spanish flu 1918 (H1N1) infected 500 million people worldwide (1/3 world's population), 50 million (to 100 million) deaths, and 675,000 deaths in US; CFR 2.5%, R 1.87. Killed an estimated 15,000 in Kentucky (1,000 in Lexington), and on Oct 7, 1918, all schools, churches, weddings, funerals, colleges and universities were closed. St. Joseph's hospital on 2nd street, and Good Samaritan Hospital were full. Outbreak lasted about 2 y (Feb 1918-April 1920). Three waves (spring 1918, autumn 1918, spring 1919). Secondary infxn caused death.

CDC.gov 4/1/20, Lex H Leader 4/1/20, CIDRAP 1/24/13

Pandemics collide with chronic disease

- US prevalence rates of chronic illness with obesity (40%), HTN (28%), cardiac disease exclude HTN (11%), diabetes (10%), COPD (5.9%) collided with SARS-CoV-2.
- Important impact of outpatient care needs to be reinforced. Population health management in health care systems opportunity for improvement. Vaccination rates for other illnesses decreased w/ pandemic.

https://doi.org/10.1016/S2352-3018(20)30113-2; MMWR 69(13);382–386

Covid-19 and structural vulnerability in the US, and waves

- First wave of infection with limited community transmission to a immunologically naïve population, reaching elderly and frail living in conglomerate settings. Feb to March 2020, 140 nursing homes, March to April 2020, > 2500 nursing home fueled by visitors and contacts w/ HCW, and group gatherings
- Second wave of transmission early March 2020 to Summer 2020 with sustained community transmission in cities with larger population density, high prev of chronic disease, all states involved by Mid-March 2020, service industry, day laborers, immigrants, delayed lockdown, insurance, then prison systems, food industry
- Third wave Fall 2020, with varying situation w/ reopening of restrictions in states, relaxing of control measures, surges w/ ongoing community spread, and holidays, increased in fall 2020, and holidays, 2021. Then decreasing into Feb/March 2021.

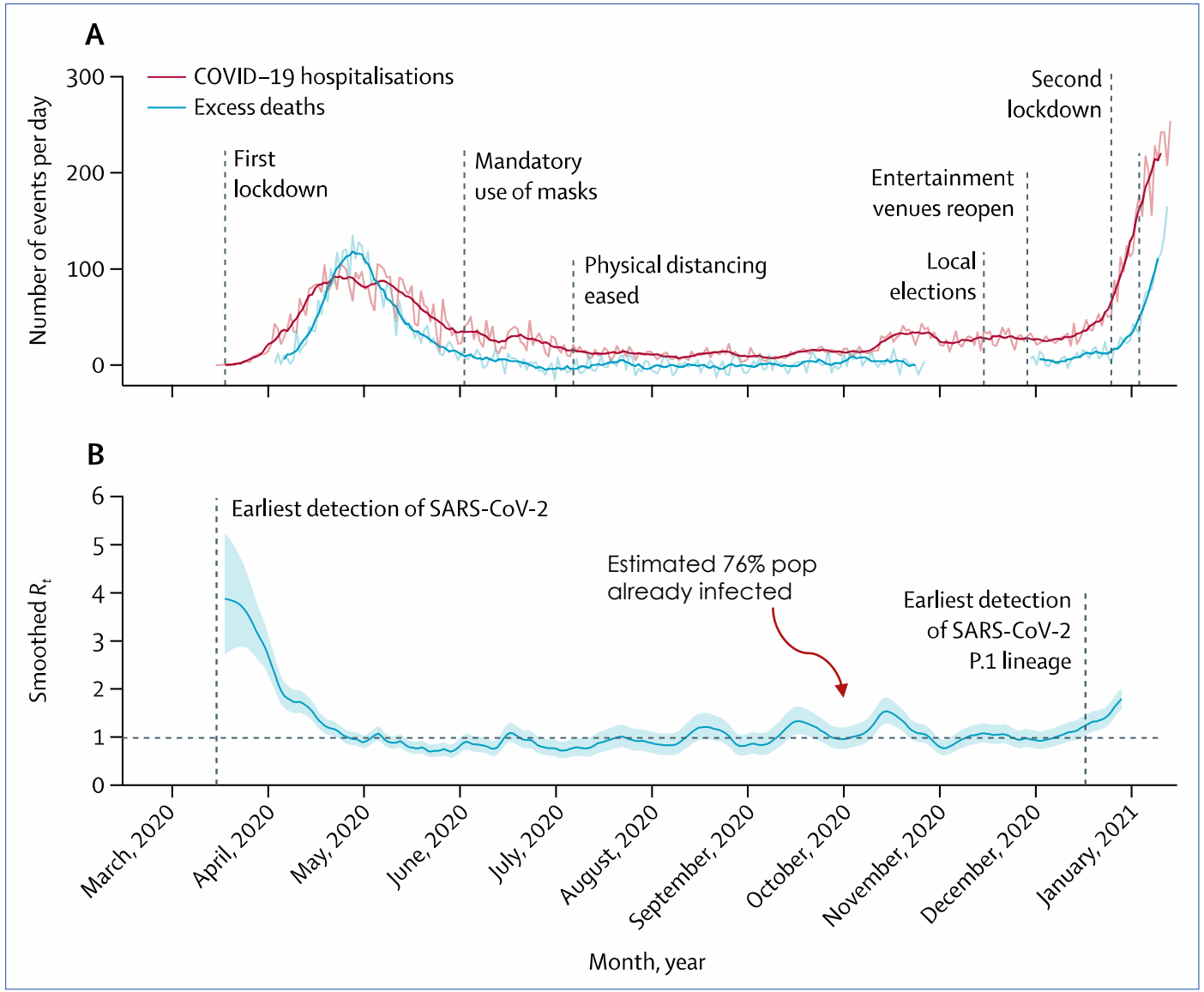
Am. J. Trop. Med. Hyg., 00(0), 2020, pp. 1–3, Solis, J, et al

Covid-19 variant epidemiology

- UK identified a variant called B.1.1.7 with large number of mutations (17) Sept 2020. 70% more transmissible, ? More virulent. Detected in US (Colorado) Dec 2020. One of the mutations N501Y binds ACE2 receptor more tightly. 1523 cases by 2/19/21 in US. 3037 by 3/7/21, 49 jurisdictions.
- South Africa variant B.1.351 detected 10/2020 share some mutations w/ B.1.1.7 (E484K, N501Y, K417N). Cases in US (S. Carolina, Maryland) in end of Jan 2021. E484K make ab more difficult to bind to spike. Less effective monoclonal. 21 cases in US 2/19/21, 81 cases 3/7/21. 20 jurisdictions.
- Brazil variant P.1, P.2 emerged in travelers from Brazil, tested at airport in Japan early Jan 2021. Additional mutations affecting its ability to be recogn by ab. In US (Minnesota, then OK, MD, FL, Alaska) at end of Jan 2021. 5 cases 2/19/21, 15 cases on 3/7/21. 9 jurisdictions.
- California L452R variant found in Santa Clara, Humboldt, Lake, Monterrey, San Bernardino, San Diego, SLO, originally identified in Denmark 2020; another Ca variant B.1.427/B.1.429 became dominant variant in Jan 2021.
- Strain surveillance in US. Nov 2020 state health dept sending samples to CDC, 750 samples per wk. Partnering w/ commercial labs to sequence 6000/wk. Partnering w/ university. SPHERES consortium outside of CDC.

cdc.Gov 3/8/21

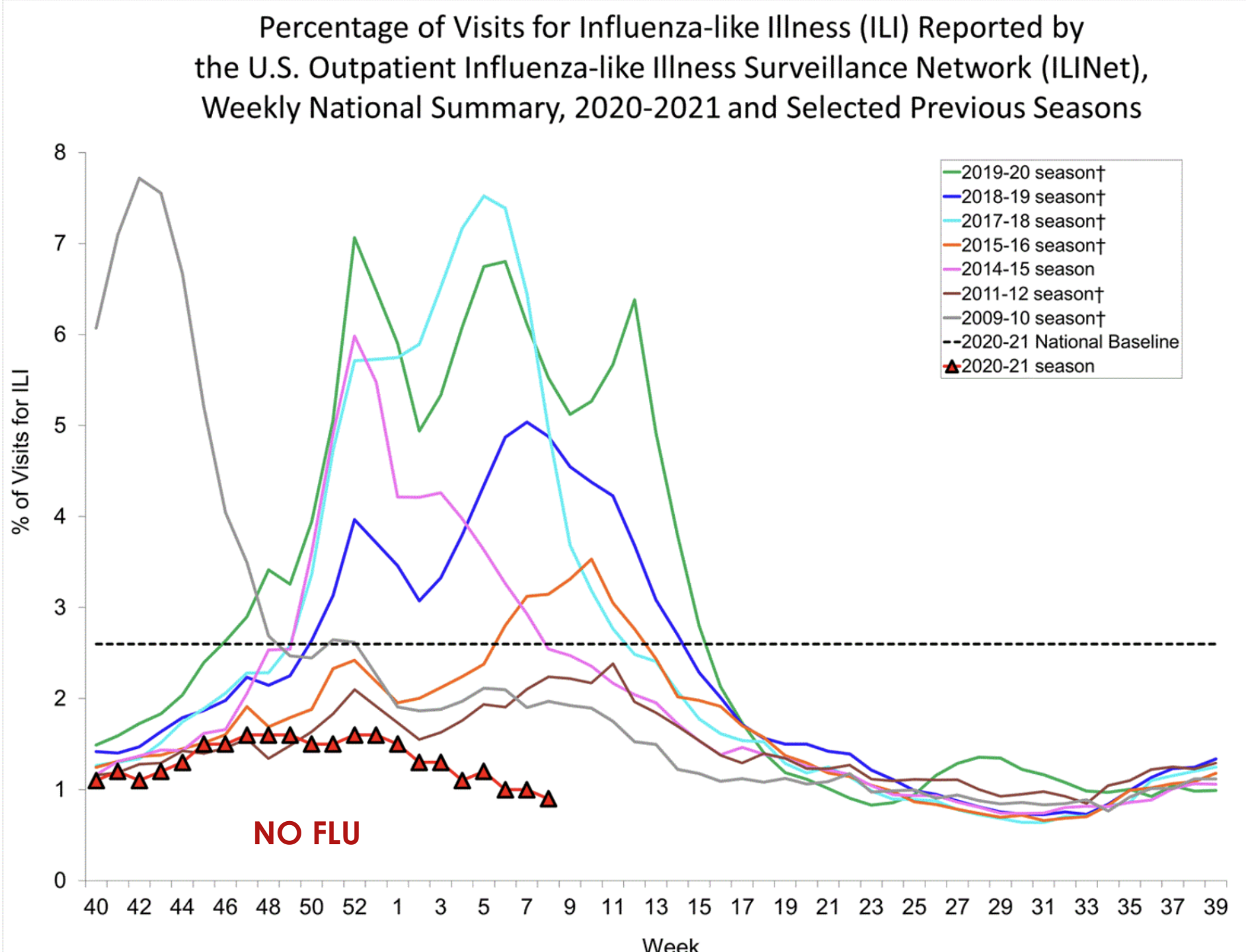
Effect of Covid-19 variant spread on hospitalizations in Brazil, Jan 2021



Lancet 1/27/21

3/11/2021

3/11/2021

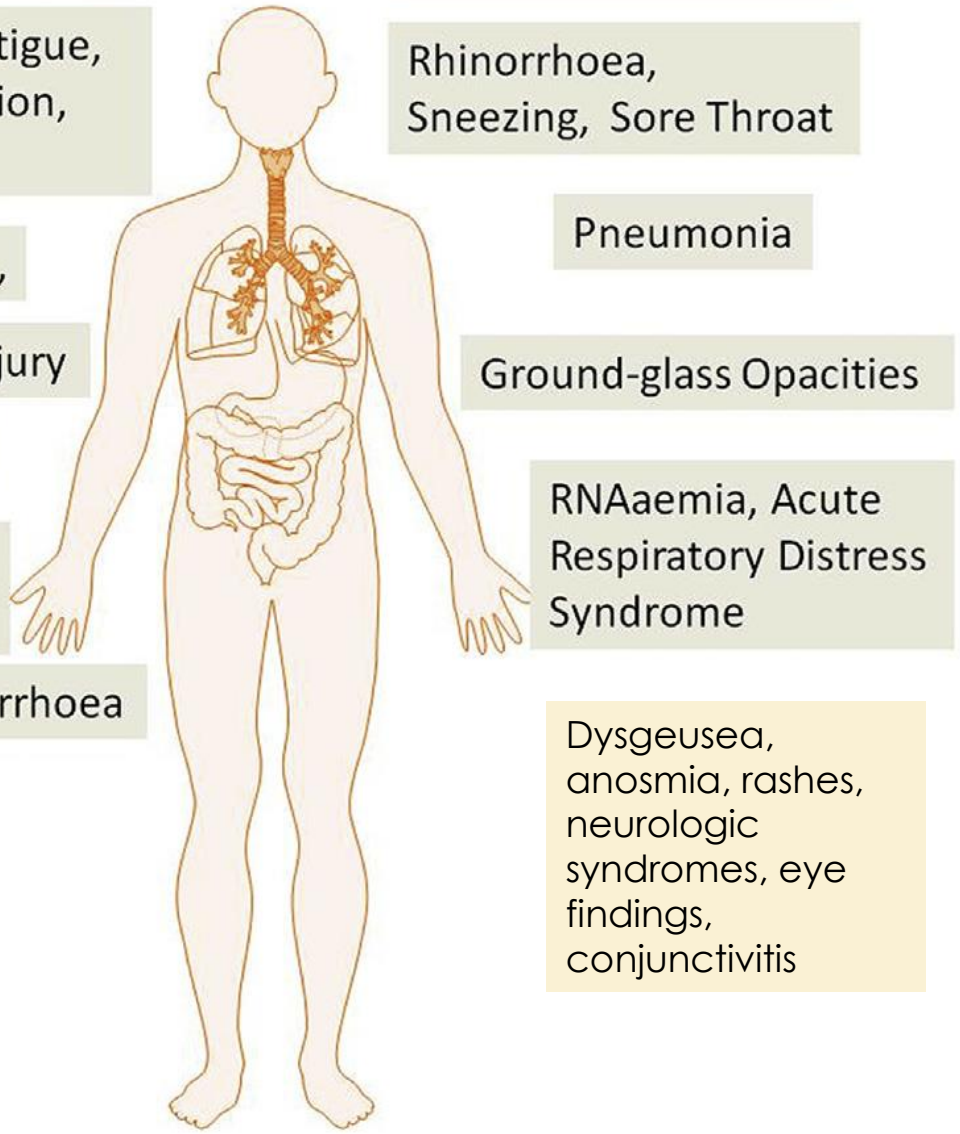

Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2020-2021 and Selected Previous Seasons
% of Visits for ILI
Week
2019-20 season†
2018-19 season†
2017-18 season†
2015-16 season†
2014-15 season
2011-12 season†
2009-10 season†
2020-21 National Baseline
2020-21 season
NO FLU

Covid-19 clinical

- Symptoms are not easily distinguished from other viral illness, incubation period about 5 days (2-14 d), 97.5% develop symptoms within 11.5 d
- **Most common sx in hospitalized patients include, fever 70-90%, cough 60-86%, SOB 53-80%, fatigue 38%, myalgias 15-44%, n/v/d 15-39%, HA, weak 25%, rhinor 7%; loss of taste (dysgeusea), and smell (anosmia) can be presenting signs. 1st week (5-10 d) usually milder (viral load high, dev ab) into 2nd week where you can develop severe illness (watching RR, sob, hypoxia).**

Lancet. 2020;395(10223):497-50, Lancet. 2020;395(10224):565-574; N Engl J Med. 2020;382(8):727-7336, Lancet 2020; 295:200; BMJ 2020;368:m606; JAMA 323:1061 March; ENT UK, Laryngoscope 2007;117:272

Covid-19 clinical symptoms signs

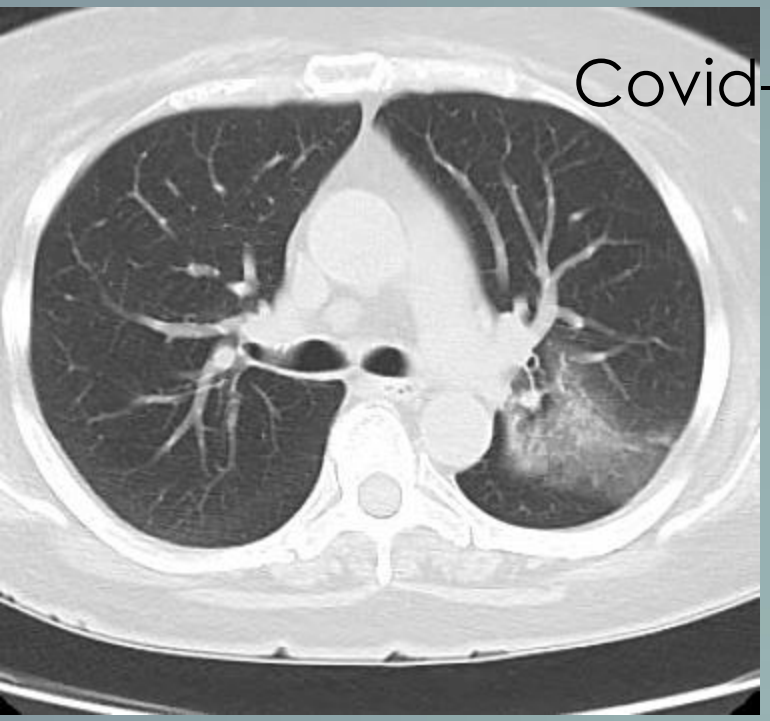


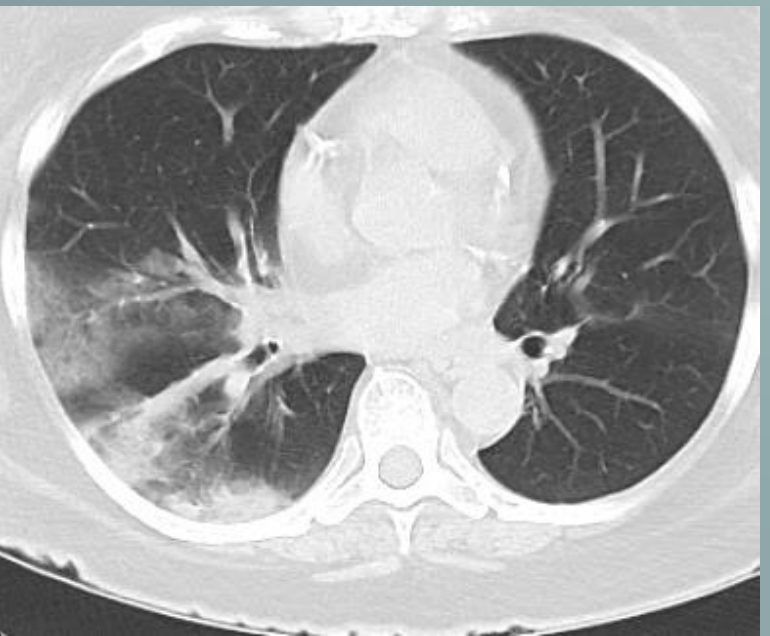
Less common presentations:

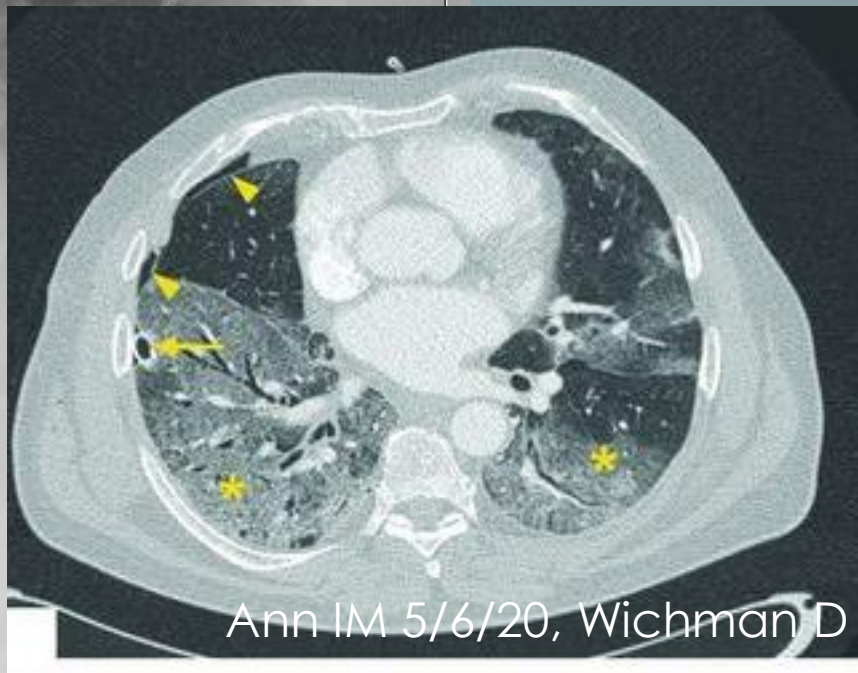
Stroke
Myocardial infarct
Rash, toes
Red eye
Guillain-Barre
DVT/PE
Seizures
Renal failure
Bell's palsy
Pre-op testing

Adapted doi.org/10.1016/j.jaut.2020.102433

Covid-19 patient hospital day 1, illness day 3, KY







Ann IM 5/6/20, Wichman D

3/11/2021

CDC 2019-nCoV ID: ☐

Form Approved: OMB: 0920-1011 Exp. 4/23/2020

……PATIENT IDENTIFIER INFORMATION IS NOT TRANSMITTED TO CDC……

Patient first name _____ Patient last name _____ Date of birth (MM/DD/YYYY): ____/_____/_____

……PATIENT IDENTIFIER INFORMATION IS NOT TRANSMITTED TO CDC……

Human Infection with 2019 Novel Coronavirus
Person Under Investigation (PUI) and Case Report Form

Reporting jurisdiction: _____ Case state/local ID: _____
Reporting health department: _____ CDC 2019-nCoV ID: _____
Contact ID [a]: _____ NNDSS loc. rec. ID/Case ID [b]: _____

a. Only complete if case-patient is a known contact of prior source case-patient. Assign Contact ID using CDC 2019-nCoV ID and sequential contact ID, e.g., Confirmed case CA102034567 has contacts CA102034567 -01 and CA102034567 -02. [b]For NNDSS reporters, use GenV2 or NETSS patient identifier.

Interviewer information

Name of interviewer: Last _____ First_____

Affiliation/Organization: _____ Telephone _____ Email _____

Basic information

What is the current status of this person?
☐ Patient under investigation (PUI)
☐ Laboratory-confirmed case

Report date of PUI to CDC (MM/DD/YYYY):
_____

Report date of case to CDC (MM/DD/YYYY):
_____

County of residence: _____
State of residence: _____

Ethnicity:
☐ Hispanic/Latino
☐ Non-Hispanic/ Latino
☐ Not specified

Sex:
☐ Male
☐ Female
☐ Unknown
☐ Other

Race (check all that apply):
☐ Asian
☐ American Indian/Alaska Native
☐ Black
☐ Native Hawaiian/Other Pacific Islander
☐ White
☐ Unknown
☐ Other, specify: _____

Date of birth (MM/DD/YYYY): ____/_____/_____
Age: _____
Age units(yr/mo/day): _____

Date of first positive specimen collection (MM/DD/YYYY):
____/_____/_____
☐ Unknown ☐ N/A

Did the patient develop pneumonia?
☐ Yes ☐ Unknown
☐ No

Did the patient have acute respiratory distress syndrome?
☐ Yes ☐ Unknown
☐ No

Did the patient have another diagnosis/etiology for their illness?
☐ Yes ☐ Unknown
☐ No

Did the patient have an abnormal chest X-ray?
☐ Yes ☐ Unknown
☐ No

Was the patient hospitalized?
☐ Yes ☐ No ☐ Unknown

If yes, admission date 1
___/___/___ (MM/DD/YYYY)
If yes, discharge date 1
__/___/____ (MM/DD/YYYY)

Was the patient admitted to an intensive care unit (ICU)?
☐ Yes ☐ No ☐ Unknown

Did the patient receive mechanical ventilation (MV)/intubation?
☐ Yes ☐ No ☐ Unknown
If yes, total days with MV (days)
_____

Did the patient receive ECMO?
☐ Yes ☐ No ☐ Unknown

Did the patient die as a result of this illness?
☐ Yes ☐ No ☐ Unknown

Date of death (MM/DD/YYYY):
____/_____/_____
☐ Unknown date of death

Symptoms present during course of illness:
☐ Symptomatic
☐ Asymptomatic
☐ Unknown

If symptomatic, onset date (MM/DD/YYYY):
____/_____/_____
☐ Unknown

If symptomatic, date of symptom resolution (MM/DD/YYYY):
____/_____/_____
☐ Still symptomatic ☐ Unknown symptom status
☐ Symptoms resolved, unknown date

Is the patient a health care worker in the United States? ☐ Yes ☐ No ☐ Unknown
Does the patient have a history of being in a healthcare facility (as a patient, worker or visitor) in China? ☐ Yes ☐ No ☐ Unknown
In the 14 days prior to illness onset, did the patient have any of the following exposures (check all that apply):
☐ Travel to Wuhan
☐ Travel to Hubei
☐ Travel to mainland China
☐ Travel to other non-US country specify:_____
☐ Household contact with another lab-confirmed COVID-19 case-patient
☐ Community contact with another lab-confirmed COVID-19 case-patient
☐ Any healthcare contact with another lab-confirmed COVID-19 case-patient
☐ Patient ☐ Visitor ☐ HCW
☐ Animal exposure
☐ Exposure to a cluster of patients with severe acute lower respiratory distress of unknown etiology
☐ Other, specify:_____
☐ Unknown
If the patient had contact with another COVID-19 case, was this person a U.S. case? ☐ Yes, nCoV ID of source case: _____ ☐ No ☐ Unknown ☐ N/A

Under what process was the PUI or case first identified? (check all that apply): ☐ Clinical evaluation leading to PUI determination
☐ Contact tracing of case patient ☐ Routine surveillance ☐ EpiX notification of travelers; if checked, DGMQID_____
☐ Unknown ☐ Other, specify:_____

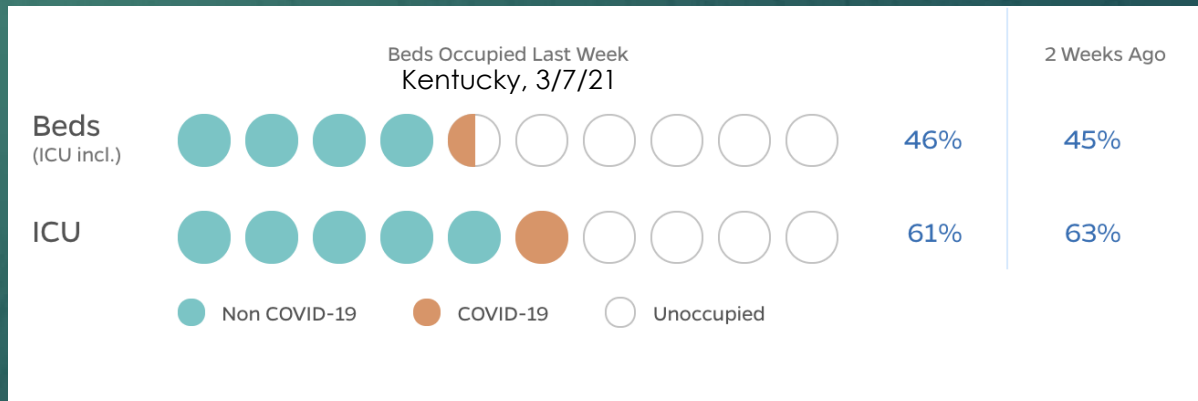
Covid-19 severe disease and death

- Cause of death ARDS, thromboembolic dz, multiorgan thrombosis, sepsis. Prospective autopsy study of 12 consecutive deaths found DVT in 58% in whom venous thromboembolism not suspected. All patients had high conc of SARS-CoV-2 in lung, and 5/12 w/ evidence of virus in lung, kidney, heart. Another study of 11 autopsy found virus in mult organs, but inflammation primarily in lung.
- NYU autopsy study of 7 patients with evidence of multiorgan thrombosis including lungs, heart, hepatic, renal, and did not find significant myocarditis.
- 20-43% of ICU patients may have DVT/PE in some series.

Lancet 2/21/20, Ann IM 5/6/20, doi.org/10.7326/M20-2003; *JAMA*. doi:10.1001/jama.2020.12839, 7/10/20; https://doi.org/10.1016/j.eclinm.2020.100434; https://doi.org/10.1101/2020.07.02.20145003

Covid-19 treatment general

- Supportive care in hospital patient
  - Oxygen often required, especially in high risk populations with ventilator use in as many as 6.1% reported from Wuhan, but less in Singapore study. 41% of hospitalized patient require O2, and 70% of severe cases. Global shortage of oxygen in some developing countries (Lancet 3/6/21)
  - In Italy, 9-11% patients between 3/1/20 and 3/11/20 required ICU care. Ventilators became a scarce resource in some places.
  - Proning



Ann IM, 5/7/20, Halpern S et al, JHU 3/7/21

Covid-19 treatment general

- Antibiotic use common because of difficulty in distinguishing bacterial infection and were used in 53% of non-severe, and > 90% of severe disease. Secondary bacterial infections in one study of critically ill patients 11%, and Zhou (15%), but meta-analysis 6% or less. Initially, risk is low, but 3 wks later, increase.
- **Anticoagulation treatment consider** in patients w/ elevated d dimers, with enhanced prophylactic anticoagulation depending on coagulopathy, with attention to bleeding risk factors (higher risk if age > 60 y, hep fail, GFR < 30 ml/m, ICU, CCU, central venous cath, RA, CA, male, PUD, bleeding 3 mo prior, plt < 50, INR > 1.5, recent major surgery). Duration of anticoagulation not clear.
- Modified IMPROVE VTE risk score >= 4

3/11/2021

Lancet 4 9 20 doi.org/10.1016/S2352-3026(20)30109-5

Multiplatform RCT (mpRCT)

A collaboration between three trial platforms

- ATTACC: Antithrombotic therapy to ameliorate complications of COVID-19 – 58 sites in Canada, USA, Brazil, Mexico
- REMAP-CAP: Randomized embedded multi-factorial, adaptive platform trial – 290 sites in Canada, USA, UK, Ireland, EU, Saudi Arabia, Australia, New Zealand, Nepal, India, Pakistan
- ACTIV-4a: Accelerating COVID-19 therapeutic interventions and vaccines – 60 activated sites in USA and Spain

Release date: 1/28/21

ATTACC, REMAP-CAP, and ACTIV IV-4a mpRCT Primary outcome

State & D-dimer Strata	Proportional Odds Ratio Median (95% CrI)	Trial Statistical Conclusion
Moderate state, low D-dimer	1.57 (1.14 - 2.19)	**Superiority** [Probability of OR>1 = 0.997]
Moderate state, high D-dimer	1.53 (1.09 - 2.17)	**Superiority** [Probability of OR>1 = 0.991]
Moderate state, missing D-dimer	1.51 (1.06 – 2.15)	n/a[⏃]
Severe state	0.76 (0.60 – 0.97)	**Futility*** [Probability of OR>1.2 < 0.001]

Covid-19 treatment
Convalescent plasma

- Benefit seen in Argentine study 160 patients randomized, **received high titer (> 1:1000 IgG), and mild symptoms < 72 h**.
- Showed a 48% risk reduction of progression to severe disease. NEJM 1/6/21.
- Similar to Houston study (25 pts), and analysis of Mayo clinic CP expanded access data.
- How to apply to hospitalized patients
  - Most of hospitalized patients **are probably outside the 72 h window**, including those severely ill, where viral replication is not the issue, but inflammatory process is the issue.
  - Convalescent plasma can have side effects such as a procoagulant effect, among others. Should not be routine therapy for hospital patients. 2/23/21.
  - PlamaAr study of 228 patients (sx median time **8 d**) no benefit NEJM 11/24/20

Covid-19 treatment
Monoclonal antibody

- REGN-COV2 trial (n=275) casirivimab and imdevimab monoclonal ab against different regions of spike protein (RBD) given within 7 d and test positive within 72 h showed a decrease in viral load, and about a 50% decrease in medical visit (NEJM 1/21/21). Granted FDA EUA Nov 2020.
- Bamlanivimab (Eli Lilly, BLAZE trials) monoclonal ab also against spike protein given FDA EUA Nov 2020 for outpatients w/ mild to mod Covid—9 based on interim results of phase 2 studies showing a reduction in hospital visits (1.6% v 6.3%). Feb 2021 FDA EUA for bamlanivimab and etesevimab based on study of 592 outpt showed a 70% risk reduction in hospitalization and death, and a dec in viral load.
- Both products halted studies in Oct 2020 in hospitalized patients w/ O2 requirements as not having a benefit (ACTIV-3, and REGN-COV2)

Covid-19 treatment
Remdesivir

- Remdesivir (Adaptive Covid-19 Treatment Trial) ACTT-1 trial (n=1062) reported those on O2 had a shorter recovery time (median 10 d vs 15 for placebo). Enrolled from 2/21/20-4/19/20. No difference if on ventilator, or not requiring O2. NEJM 11/5/20. FDA approved 10/22/20.
- SOLIDARITY (n=5472) trial open label did not find a significant difference in mortality between the remdesivir (Velkury) arm and standard of care.
- Recent review Ann Int Med 2/9/21 of RCT and data reported that remdesivir probably results in little to no diff in mortality, but prob improves the percentage recovered and reduces serious adverse events. 5 d prob same outcome as 10 d treatment.

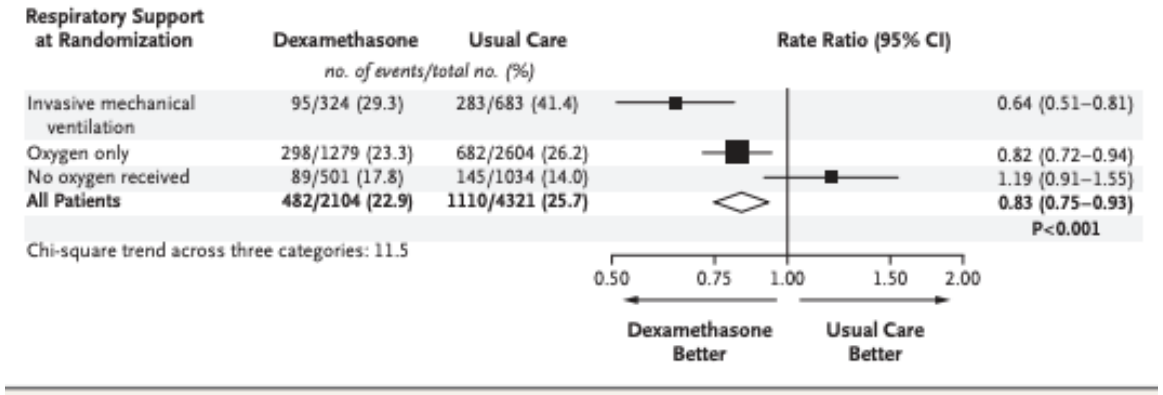
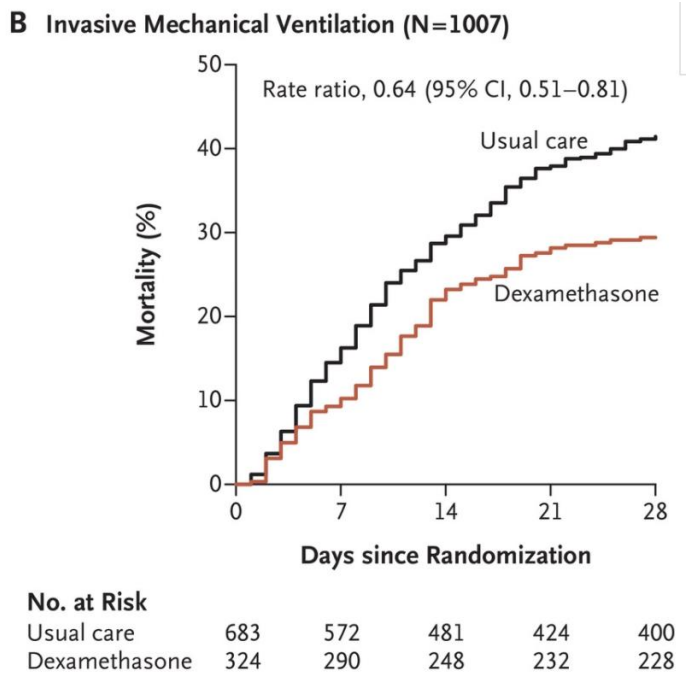


Figure 3. Effect of Dexamethasone on 28-Day Mortality, According to Respiratory Support at Randomization.

Shown are subgroup-specific rate ratios for all the patients and for those who were receiving no oxygen, receiving oxygen only, or undergoing invasive mechanical ventilation at the time of randomization. Rate ratios are plotted as squares, with the size of each square proportional to the amount of statistical information that was available; the horizontal lines represent 95% confidence intervals.



3/11/2021

Covid-19 treatment Steroids

STEROIDS AND RECOVERY TRIAL

Covid-19 treatment
Tocilizumab

- NIH changed rec to cannot rec or not recommend on 2/3/21 based on REMAP-CAP trial 803 patients of which 353 tocilizumab, 48 sarilumab, vs standard of care 402 patients. One or two doses of toci decreased in-hosp mortality (28% vs 36%) in critically ill patients hospit < 15 d, and admitted to ICU < 24 h, and increased number of organ support-free days. > 80T received steroids.
- Recovery trial 4116 pts randomized, mortality benefit, and less invasive ventilation, additional to benefit from steroids. Medrxiv 2/11/21. Reduce mortality by ½ in those on vent.
- EMPACTA trial w/ 389 patients showed a trend favoring toci, but no diff in all cause mortality at d 28.
- COVACTA trial w/ 452 pts, no diff in mortality, but shorter time to hosp discharge. COVINTOC study India no effect, JAMA 3/4/21.

Covid-19 treatment
Tocilizumab

- Baptist Lexington Data, n = 26 between 3/23/20 to 12/1/20, Unpub, Marafat, L.
  - Median age 66 y, BMI 30.9, 7 d from test to admin, 69% ICU stay, 38% required intubation, Hospital LOS 17, CRP 101.9 mg/L, 92% also with steroids, duration 13.5 d, 2/26 died.
  - Deceased patients died 17 and 29 d after toci given, w/ infection and multiorg failure as reasons, and had longer courses of steroids.

Covid-19 treatment
Baricitinib

- FDA EUA 11/19/21 largely based on ACTT-2 multinational trial 1033 hospitalized patients randomized 1:1 for up to 14 d. 10.9% of pts in baricit plus remdesivir group vs 12.9% in placebo group received steroids. Median time to recovery shorter in the baricit group by 1 d. **High flow O2 group w/ highest difference (10 d) vs (18 d) in placebo**. Serious adverse events less freq in the baricit group. No diff in mort at d 28. NEJM 12/11/20.
- BHL eval of 35 pts, median age 69, BMI 33.73, LOS 11, 17 pts admitted to ICU, median days of tx 8, days since Covid to start 7 d, days since admit 2, 6 pts on IMV, 3 pts started IMV after baricit, all pts received steroids, 2 pts w/ infxn doc after starting; 6/35 died. Unpub data. Marafat, L.

Covid-19 treatment
Other

- Other treatments not supported at this time include hydroxychloroquine, azithromycin, and under continued investigation ivermectin (possible applicable to strongyloidiasis in KY, no change in symptoms in mild Covid-19 disease JAMA 3/4/21), vit C, zinc, vit D, famotidine, colchicine, fluvoxetine (SSRI, JAMA 11/12/20); outpatient treatments under investigation include above plus budesonide, and **Molnupiravir** (oral antiviral, Merck/Ridgeback Pharm)

Covid-19 treatment

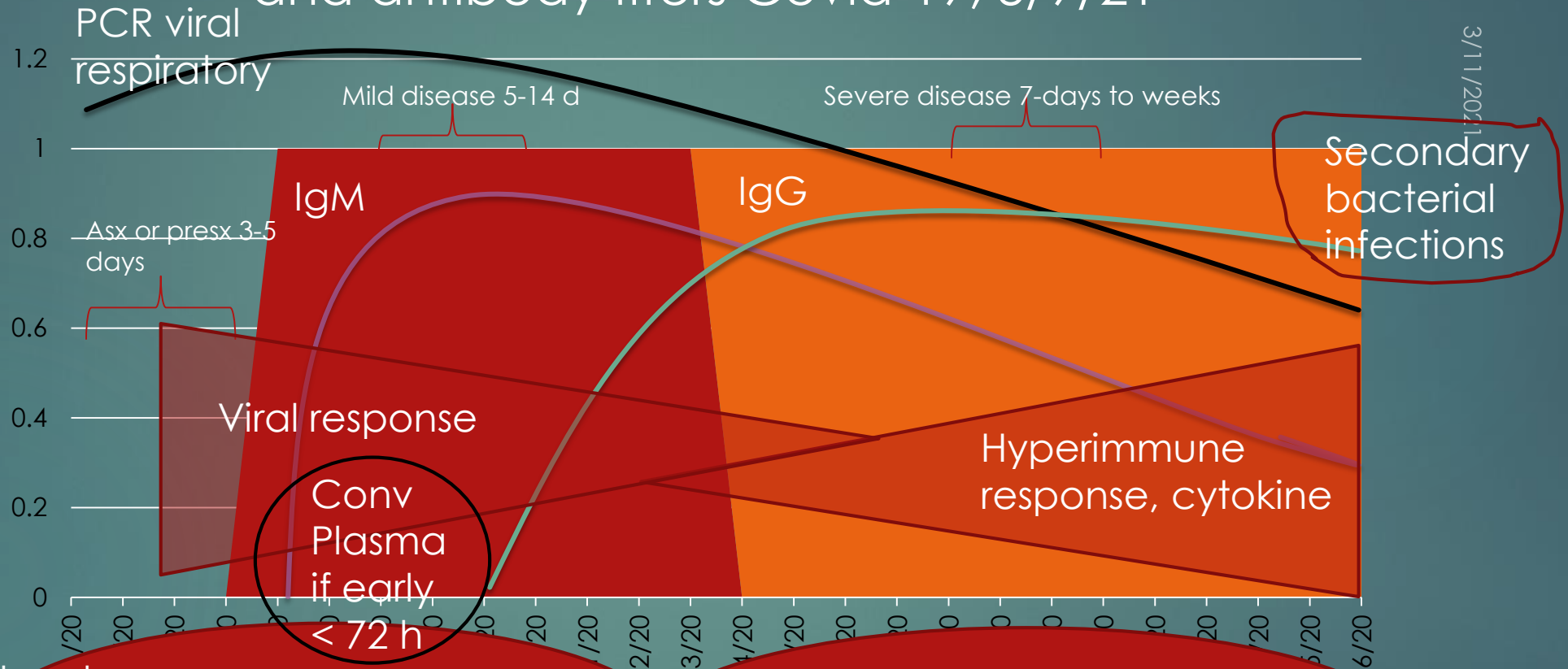
- Steroids beneficial in treatment of Covid-19 in early clinical trials (Recovery trial)
- **Treatments 3/9/21**
  - **Steroids (decadron (or equivalent) 6 mg/d x 10 d), Remdesivir for 5 d (10 d if on bariticinib), convalescent plasma (if < 72 h, and high titer EUA 8/32/20 and 2/4/21), Tocilizumab IL-6 inhibitor w/ elevated CRP and 24 h or within 48 h of ICU care/intubation.** Baricitnib for patients on high flow oxygen (EUA 11/19/20).
  - **Monoclonal antibody treatment for nonhospitalized high risk (bamlanivimab EUA 11/9/20, bam plus etesevimab 2/9/21 , casirivimab imdevimab EUA 11/21/20, Regeneron), especially if < 72 h.**

Nature Rev 2020;19:149, JID 2017;216:203; Roche

3/11/2021

Draft subject to change

Representative clinical timeline with PCR and antibody titers Covid-19, 3/9/21



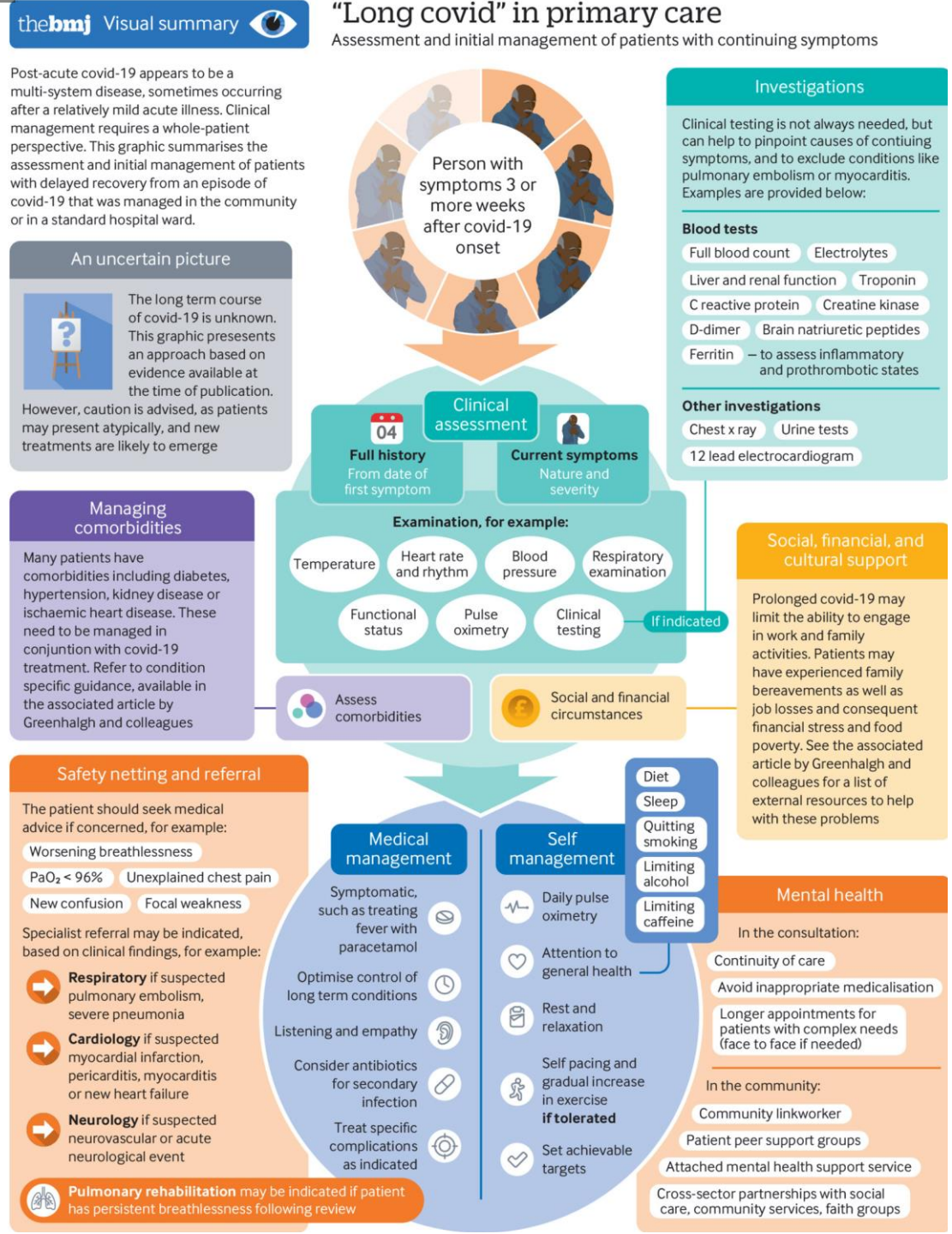
Monoclonal prior to admit if early symptoms, < 72 h?

Decadron, Remdesivir

Immune control steroids, tocilizumab, baricitnib, for pts w/ progressive resp fail and high flow oxygen, prior to ICU if possible

Long Covid-19

- Italian study reported that 87% of discharged patients reported at least one sx 60 d after onset.
- Included fatigue (53%), sob (43%), joint pain (27%), and chest pain (22%), and 2/5 reported worse quality of life.
- UK study of 1733 patients at 6 m reported fatigue or muscle weakness (63%), sleep difficult (26%), anxiety/depr (23%). If severely ill, exercise intol, and diffusion impairment common (29-56%) Lancet 1/26/21



BMJ 2020;370:m3026 | doi: 10.1136/bmj.m3026
JAMA 2020;9. doi: 10.1001/jama.2020.12603

Community prevention of Covid-19 KY

- Masking, recommended general public in US 4/2020
- Social distancing
- Hand hygiene and avoid touching face
- Vaccination
  - Pfizer and Moderna mRNA vaccines
  - Johnson and Johnson Ad26.Cov2, vector vaccine

Pedestrians in Hong Kong wear face masks as a precautionary measure against the coronavirus on May 14, 2020. | Antony Wallace/AFP via Getty Images

Kycovid19.gov 2/23/21

Preventative effect of wearing mask in transmission of Covid-19

TABLE 1. Characteristics* of clients (N = 139) who visited hair salon A and were exposed to stylists A and B with COVID-19 —Springfield, Missouri, May 2020

Characteristic	Value
Demographic characteristic	
Male, no. (%)	79 (56.8)
Age, yrs. mean (range)	52 (21–93)
Encounter information	
Appointment date range	May 12–20 (days 0–8†)
Exposure to stylist A, no. (%)	84 (60.4)
Exposure to stylist B, no. (%)	55 (39.6)
Appointment duration, mins, median (range)	15 (15–45)
Client testing	
Clients tested, no. (%)	67 (48.2)
Negative tests, no. (%)§	67 (100)

Maximizing fit for masks

A. Unknotted medical procedure mask blocked 56.1% particles
B. Cloth mask over med proc mask blocked 85.4% (cloth mask alone blocked 51.4%)
C. Knotted and tucked med procedure mask blocked 77.0% MMWR 2/19/21

Masks reduce exhaled respiratory droplets and aerosols from infected wearere and reduce exposure to others; also reduce inoculum to mask wearer (J Gen Intern Med 35(10):3063–6)

3/11/2021

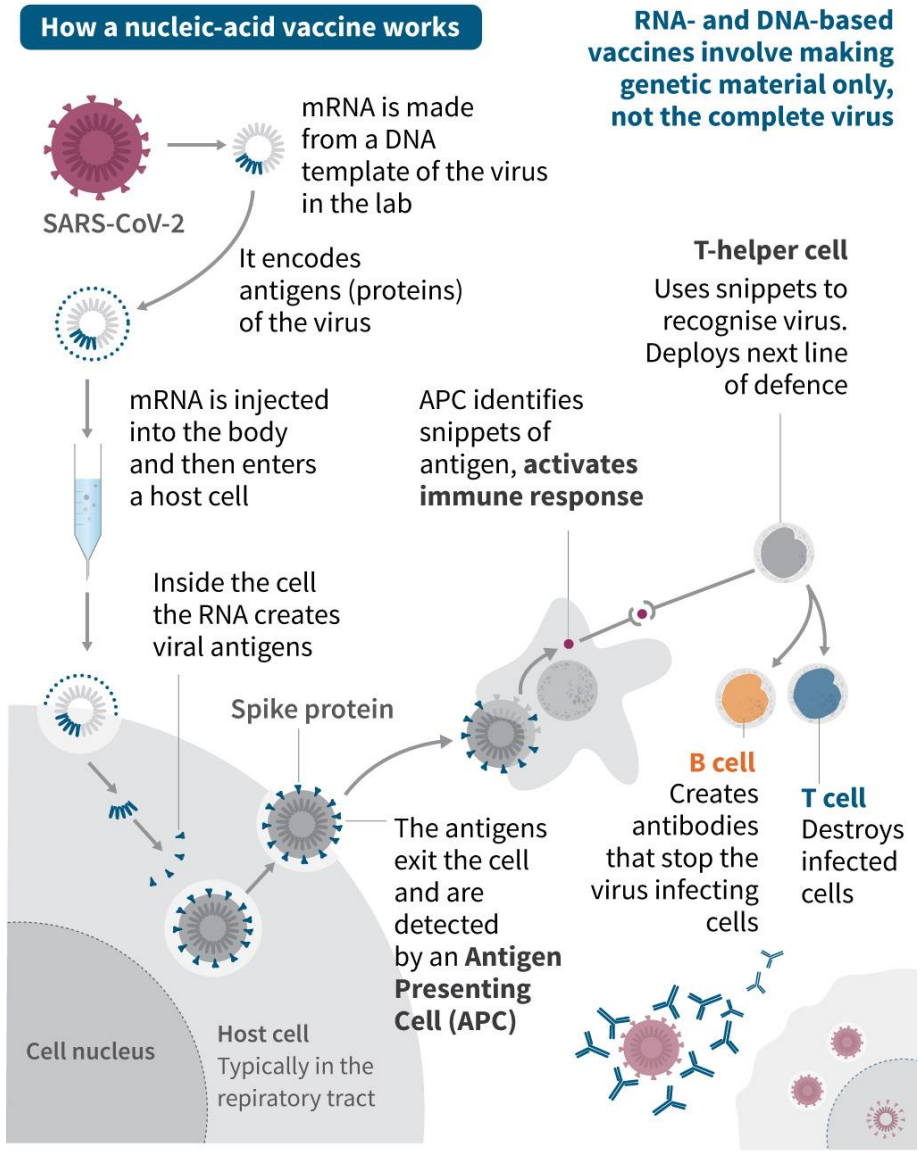
Covid-19 vaccines

- Technology differs—Goal of Operation Warp Speed was 300 million doses of vaccine by Jan 2021
  - BioNTech/Fosun Pharma/Pfizer uses mRNA similar tech lipid nanoparticle encapsulated for spike protein, FDA EUA December 11, 2020, 2 dose, 3 wk apart
  - Moderna uses mRNA vaccine (lipid nanoparticle encapsulated) for the SARS-CoV2 spike protein (m-RNA-1273) FDA EUA December 18, 2020, 2 dose, 4 wk apart
  - Johnson and Johnson/Janssen Pharmaceuticals adenovirus vaccine that delivers DNA encoding mRNA from SARS-CoV2, single dose. FDA EUA 2/27/21.
  - AstraZeneca/Univ of Oxford simian adenovirus 26 vector, replication defective

JAMA August 4, 2020 Volume 324, Number 5; NEJM DOI: 10.1056/NEJMoa2022483

Triggering immunity from genetic code

The Pfizer Covid-19 vaccine is a **nucleic-acid* vaccine**. It uses a lab-made SARS-CoV-2 messenger RNA (mRNA) to trigger the body's natural defences



*The cell's main information-carrying molecules, which direct protein production

Source: Vaccine pipeline/Nature journal/pfizer.co.uk

AFP

Pfizer mRNA vaccine BNT162b2

- Lipid nanoparticle formulated nucleoside-modified RNA encoding spike protein
- Early phase w/ success eliciting neutralizing ab and antigen specific CD8 and Th1-type CD4 T cell response.
- Phase 3 trial age 16 y and older randomized 43,548 persons between 7/27/20 and 11/14/20.
- 2 doses of vaccine, 21 d apart, storage in ultra-cold freezer (-112F to -76F), needs to be thawed, mixed w/ diluent
- Prelim data from Israel reported a VE of 85% after 15-28 d from 1st dose (Lancet 2/18/21), and stability data of vaccine in regular freezers submitted to FDA 2/2021

Moderna mRNA 1273 vaccine

- Lipid-nanoparticle encapsulated mRNA vaccine expressing the prefusion-stabilized spike protein
- Animal models, and early phase w/ success
- Phase 3 trial of 18 yo and older between 7/27/20 and 10/23/20 30,420 underwent randomization
- 2 doses, 28 days apart, stored at 35.6-46.4 F, doses could be held up to 8 h at room temp before admin, no dilution

Johnson and Johnson Ad26Cov.2.5 vaccine

- Recombinant vector vaccine using a human adenovirus to express the spike protein. Same viral vector used against Ebola virus (Ad26 ZEBOV, and MVN-BN-Filo)
- Phase 3 ENSEMBLE trial randomized 44,325 persons in Argentina, Brazil, Chile, Columbia, Mexico, Peru, South Africa, and the United States
- 66% effective at preventing moderate and severe COVID-19 at 28 d post vaccination. 72% in the US, 57% in S. Africa. 85% effective in preventing severe/critical COVID-19. No deaths related to COVID-19 in vaccine group. Had efficacy against variants in S. Africa and Brazil.
- Single vaccination. FDA EUA approval 2/27/21 Easier storage requirements, 3 months in regular refrigerator, or 2 y in reg freezer

Covid-19 vaccine additional information

- Preliminary data suggest that in the Moderna trial, vaccine recipients were 2/3 less likely than placebo to also test positive after the first dose.
- Efficacy of Janssen Covid-19 asymptomatic seroconversion was 74% in a subset of trial participants.
- All three vaccine trials differed in their calendar time and geography.
- Vaccines were tested in settings with different Covid-19 background incidence and circulating variants.
- The 3 vaccines have some benefit against the current variants including B.1.117, to date in lab, and in the trials. No deaths from Covid-19 in vaccine recipients in trials despite variants.

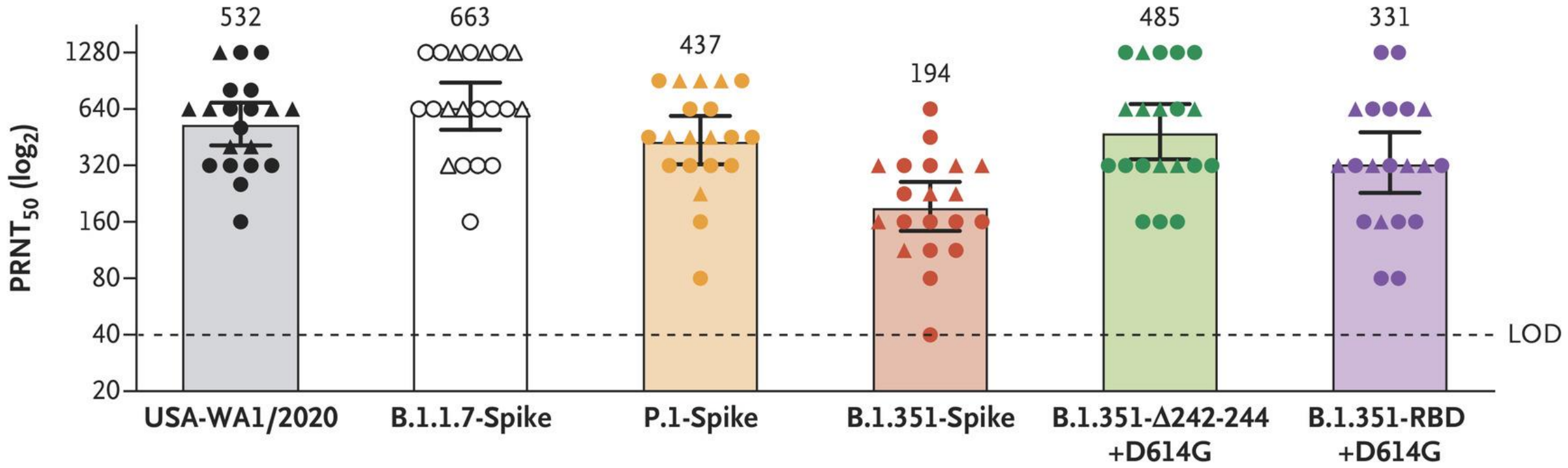
cdc.Gov 3/8/21

3/11/2021

Covid-19 vaccine additional information

3/11/2021

Serum neutralization of variant strains of Covid-19 after second dose of BNT162b2, NEJM 3/8/21



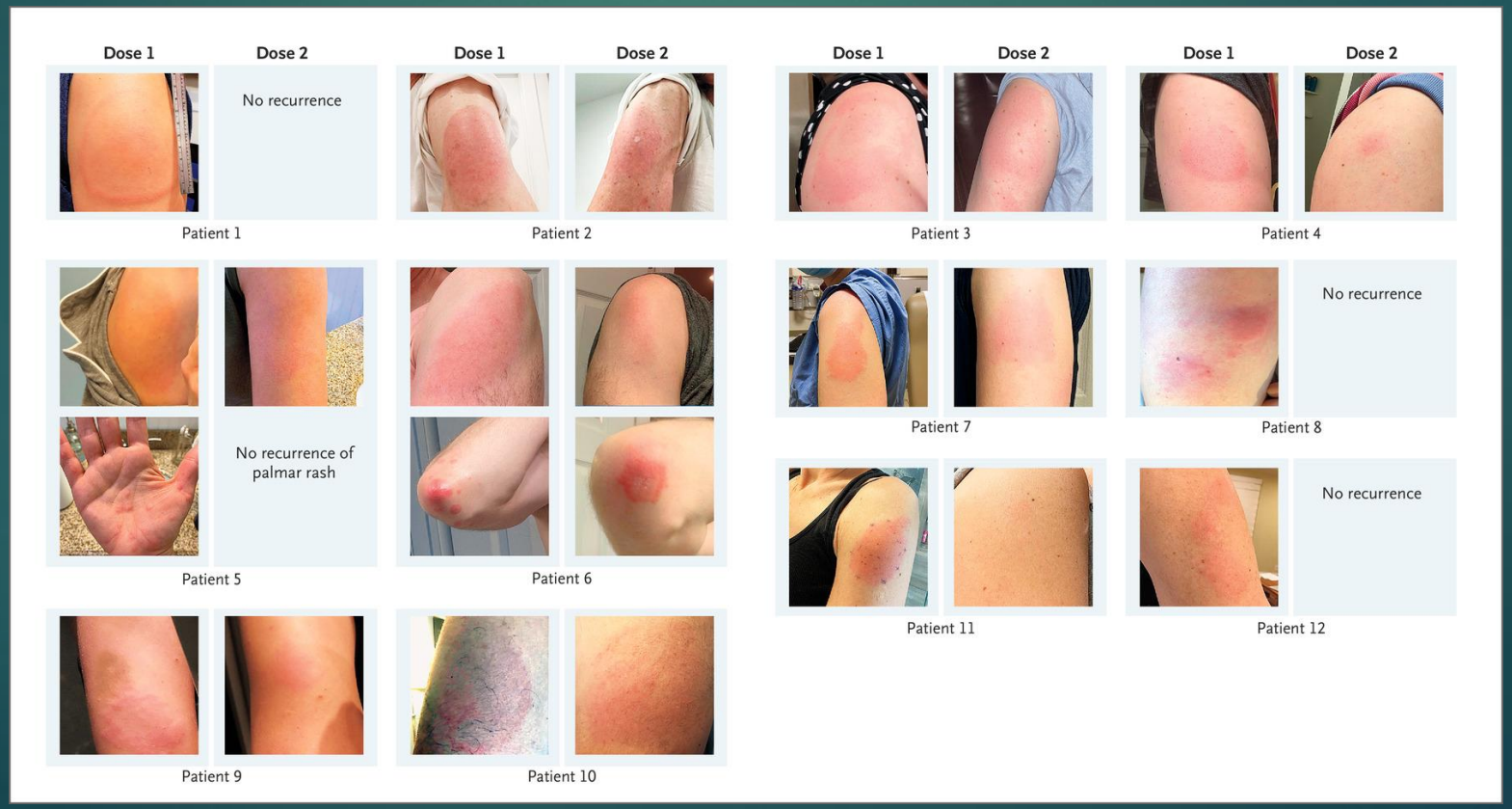
Covid-19 vaccine adverse events
12/4/20-1/13/21 data

3/11/2021

- 13,794,904 doses administered
- 6,994 reports of adverse events (91% nonserious)
- Anaphylaxis uncommon 4.5 cases per million doses (similar to flu vaccine 1.4/million, pneumococcal polysac 2.5/million, and zoster (9.6/million)
- Most common side effect HA, fatigue, dizziness, injection site soreness. MMWR 2/19/21.

Covid-19 and delayed cutaneous reactions to m-RNA-1273

- Report on 12 pts w/ median onset d 8 after 1st dose, and some have had after 2nd dose, resolve usually w/in 6 d (NEJM 3/4/21). Not contraindication to receive future vaccine.



Covid-19 vaccination strategy US 2021

Work Group considerations: Balancing Goals

3/11/2021

	Prevention of Morbidity & Mortality	Preservation of Societal Functioning
1a	LTCF residents 3 million	Health care personnel 21 million
1b	Persons 75 years and older 21 million	Frontline Essential Workers 30 million
1c	Persons 65 - 74 years 32 million Persons 16 - 64 with high-risk medical conditions >110 million	Other Essential Workers 57 million

- Ensure safety and effectiveness of COVID-19 vaccines
- Ensure equity in vaccine allocation and distribution

COVID-19 Vaccinations in the United States

Overall US COVID-19 Vaccine | Deliveries and Administration; Maps, charts, and data provided by the CDC, updated daily by 8 pm ET†
Represents all vaccine partners including jurisdictional partner clinics, retail pharmacies, long-term care facilities, Federal Emergency Management Agency and Health Resources and Services Administration partner sites, and federal entity facilities.

Total Vaccine Doses

Delivered	116,378,615
Administered	92,089,852

Learn more about the distribution of vaccines.

People Vaccinated	At Least One Dose	Fully Vaccinated
Total	60,005,231	31,493,040
% of Total Population	18.1%	9.5%
Population ≥ 18 Years of Age	59,945,907	31,470,910
% of Population ≥ 18 Years of Age	23.5%	12.3%
Population ≥ 65 Years of Age	32,074,651	16,035,530
% of Population ≥ 65 Years of Age	59.3%	29.7%

Read more about how these data are reported.

CDC | Data as of: Mar 08 2021 6:00am ET | Posted: Mar 8 2021 12:26PM ET

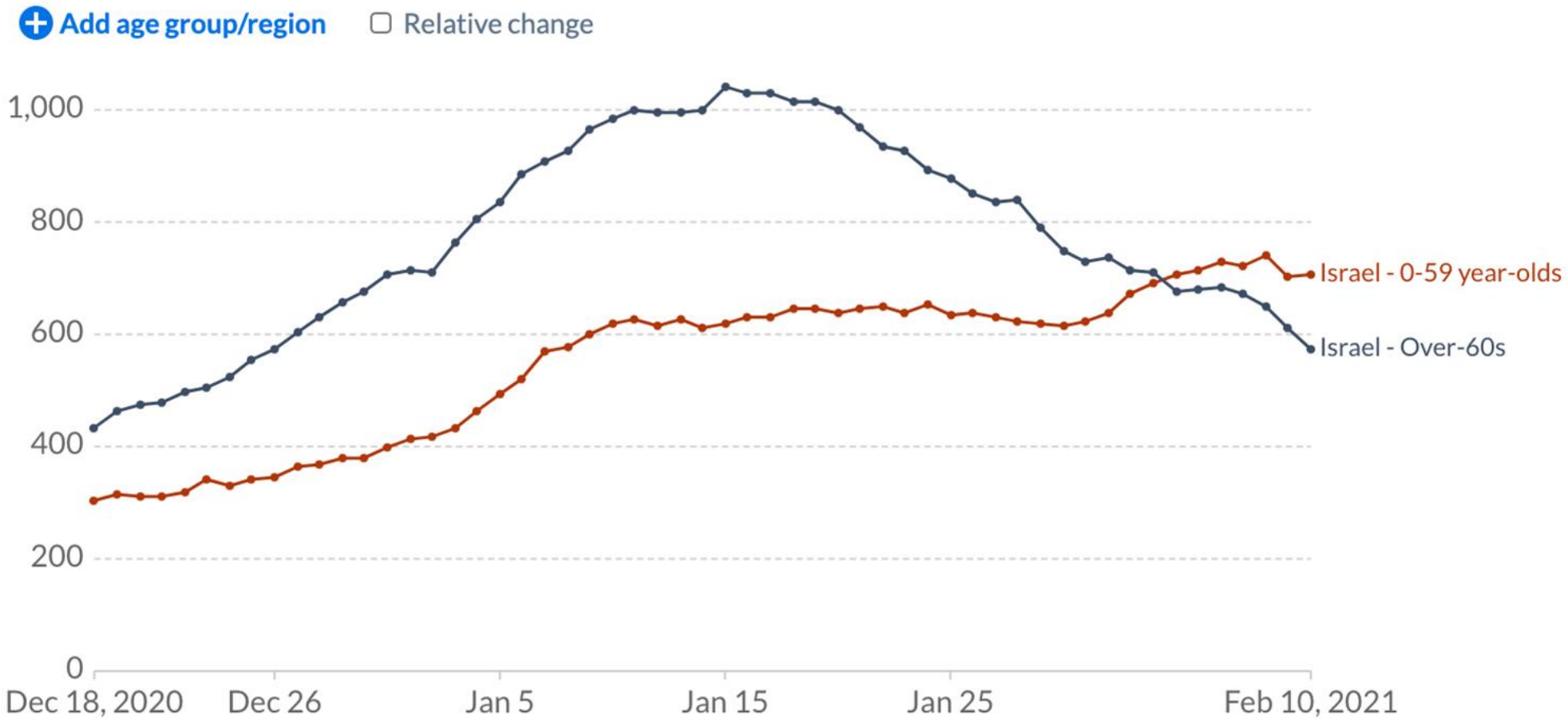
World doses 300,189,934 total, 65,405,366 fully vaccinated, 0.86% (JHU 3/7/21)
KY 834,130 persons received at least one dose by 3/8/21.

Israel: New hospitalizations for COVID-19 by age

Our World in Data

Shown is the rolling weekly sum of COVID-19 hospitalizations. Data is available at the national level, plus breakdown by regions where vaccination began early or late.

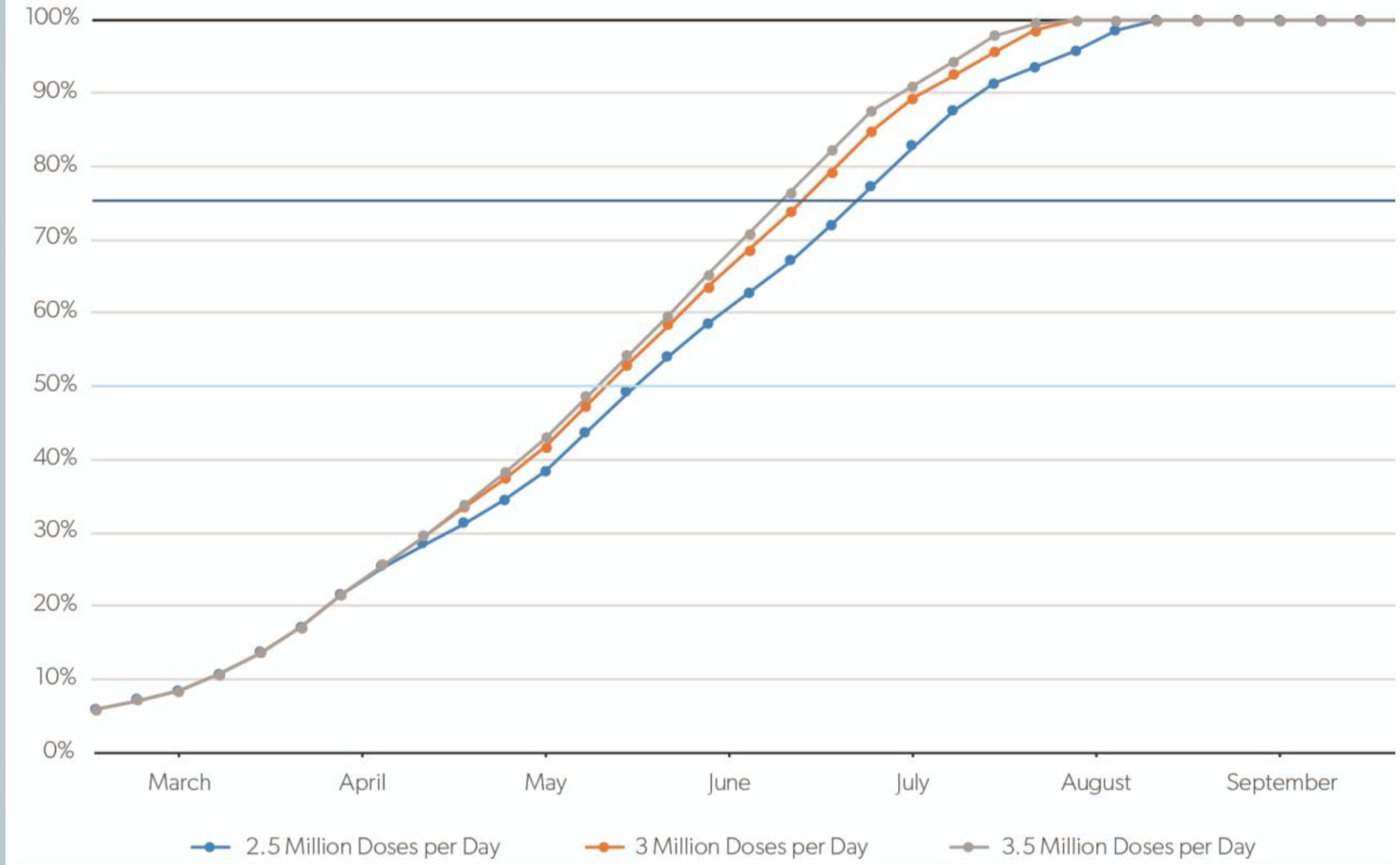
Vaccination in Israel began on December 19 2020. Israel imposed a third national lockdown on January 8 2021.



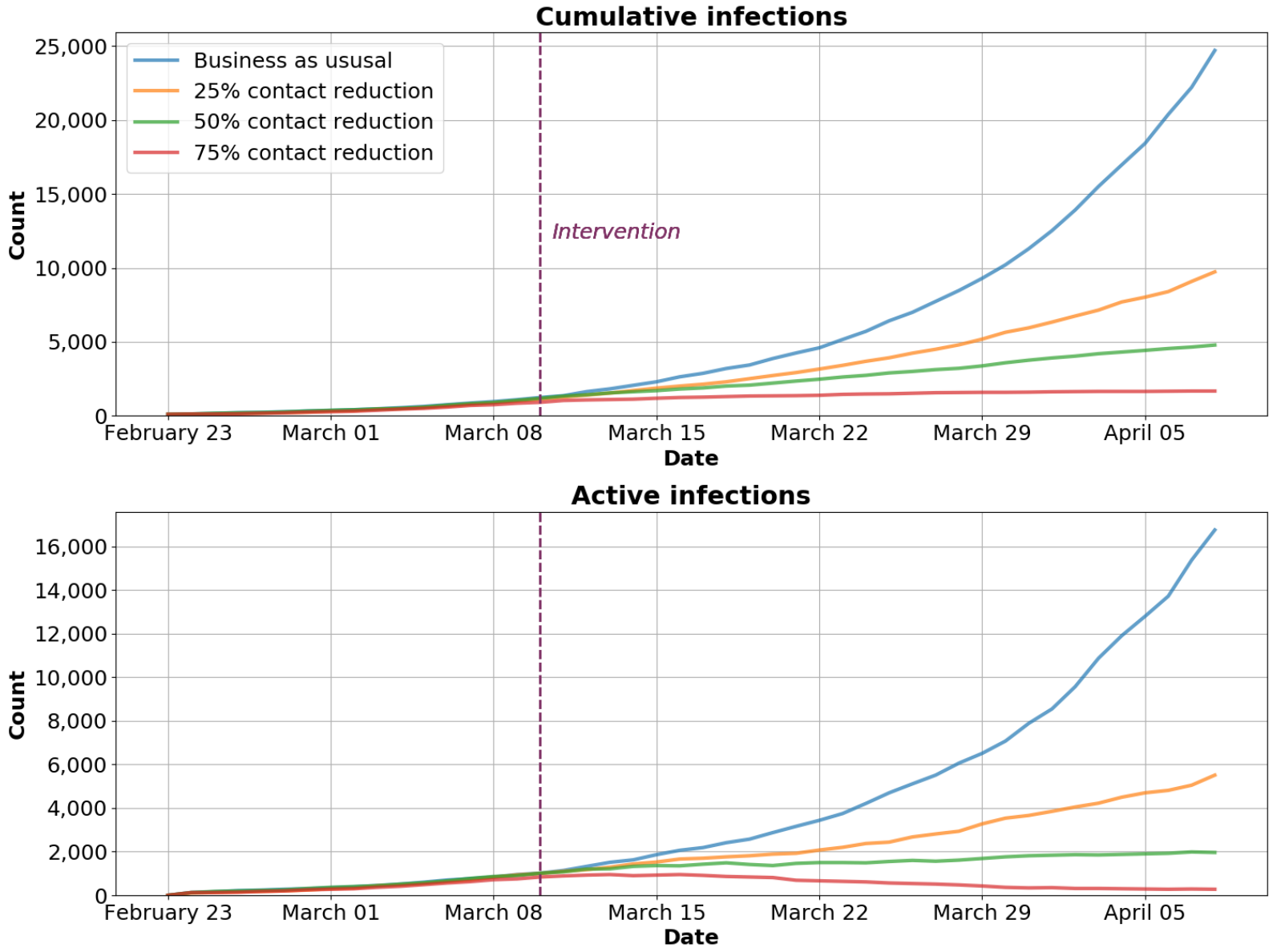
Source: Rossman, Shilo, Meir, Gorfine, Shalit & Segal (2021). Patterns of COVID-19 pandemic dynamics following deployment of a broad national immunization program.

Interim Covid recommendations related to vaccine status, US, 3/8/21

Figure 6. Proportion of the US Population Vaccinated Assuming Approval of the Johnson & Johnson Vaccine



Managing the beginning of the Covid-19 outbreak, March 2020



Covid-19 and some pandemic lessons

- Communication is critical
  - Leadership (trust important, motivation), collaboration (working together for mitigation and containment, sharing best practice to inform process), science and risk communication crucial.
  - Relationships are important (and the need to strengthen them between families, communities, health systems, public health, government)
  - Misinformation and disinformation also spread like a virus
- Manage operations critical to maintain safety, deliver health care
- Flexibility and our ability to adapt increased from the increase in telehealth to masking, social gatherings changes, education
- Public health infrastructure and preparedness need continued attention and investment
- Health and social issues require commitment to improve

Covid-19 and the new normal

3/11/2021

- Vaccine and therapeutics work continue
- Public health measures continue
  - Masking and hand hygiene in school settings, office and work settings depending on disease incidence and prevalence
  - Testing (cheaper, faster), and transmission disruption, especially as cases are less common
  - Surveillance, including variant sequencing
- Community cooperation, public, private partnership

Cent for Am Progress, Emmanuel Z, 4/3/20; Am Ent Instit, Gottlieb S, 4/10/20; Rockefeller Foundation White Paper, 4/21/20, Allen, D, et al; Duke Margolis Center, McClellan M, 4/7/20

Thank you to all who served

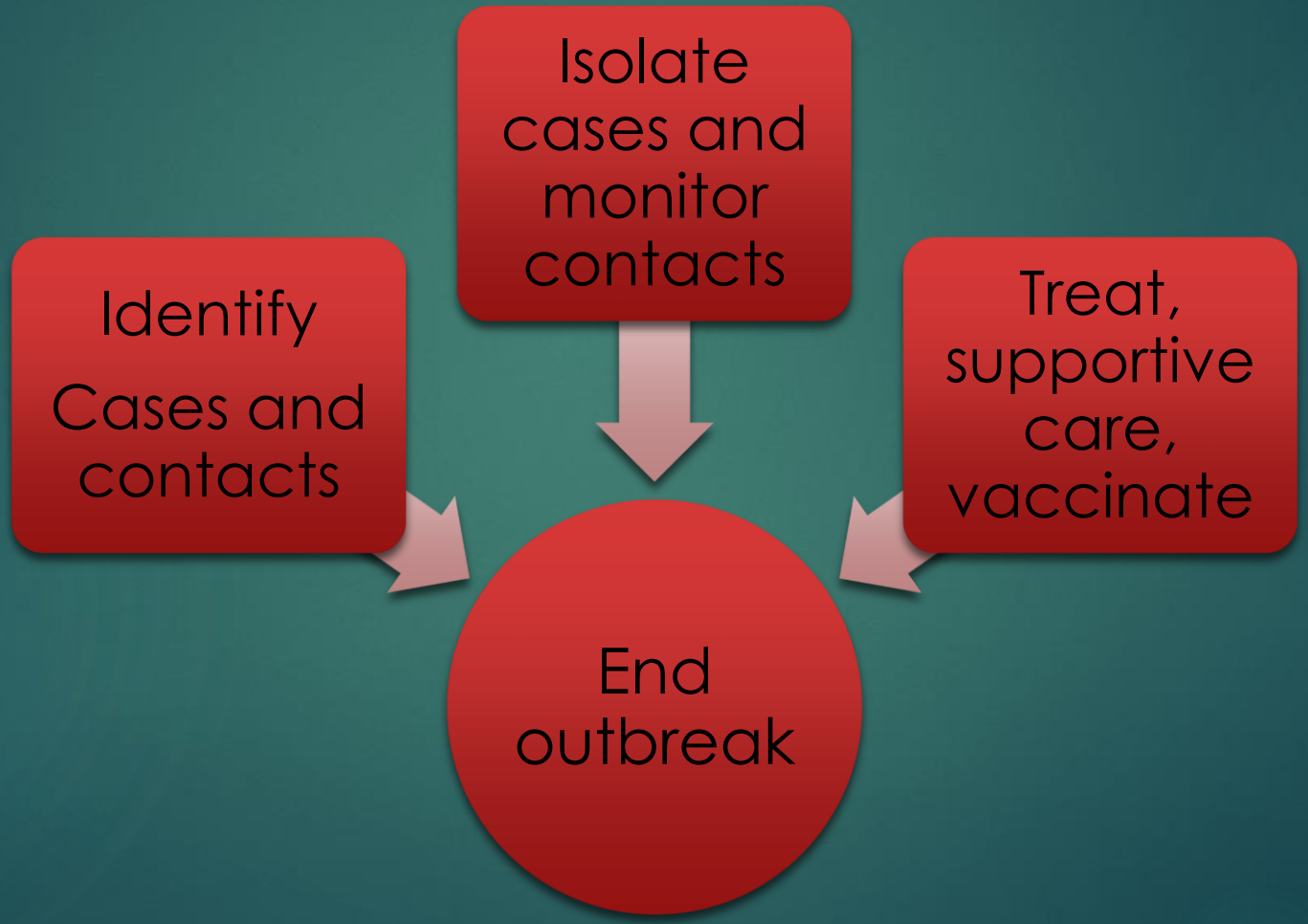
3/11/2021

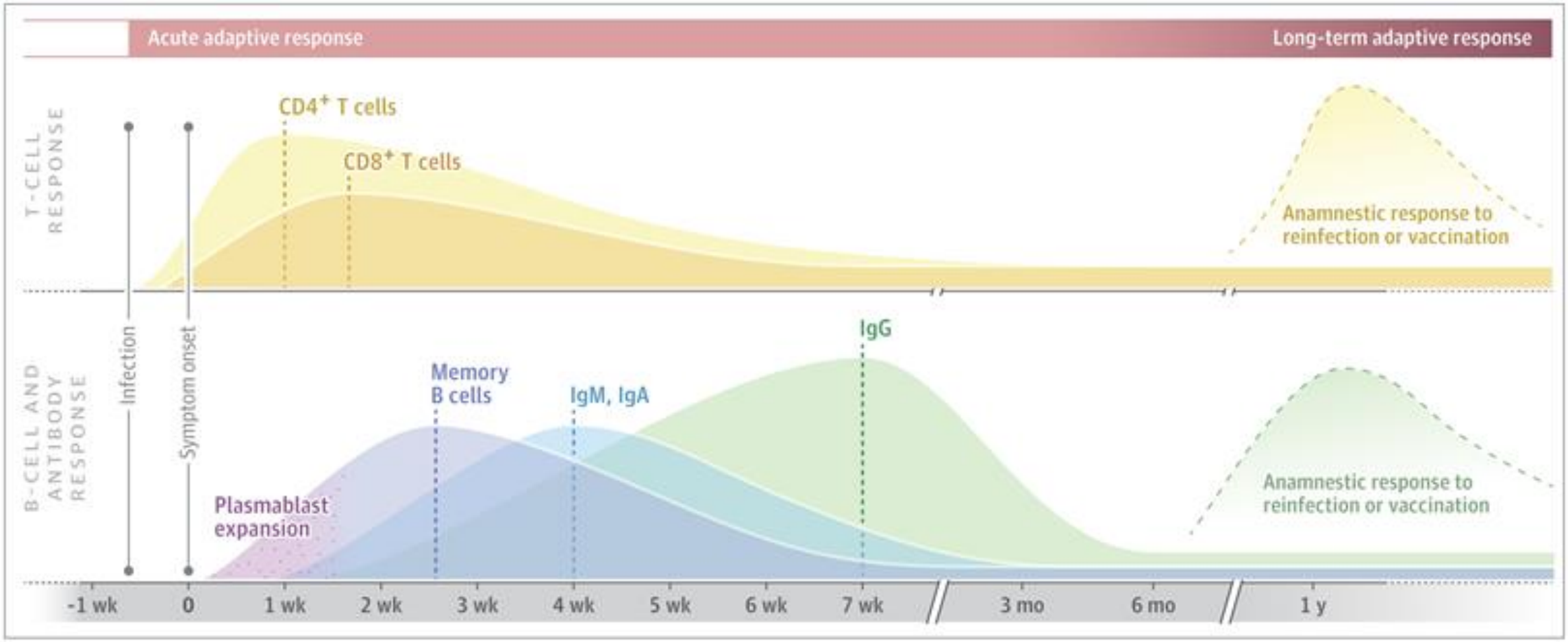
Reopening schools (13,500 school districts In the US)

- Full in person learning where < 50 cases/100,000 people in a week, and a 7-d positivity rate of < 8%.
  - Wear masks, social distance, hand hygiene, enhanced cleaning and ventilation, cohorting, podding of students.
- Hybrid learning where 50-100 new cases/100,000 people in a week, or a 7-d positivity rate of 8-10%.
- Remote learning if rate 100 or greater cases/100,000 people in a week or 7-d positive rate of 10% or greater. Can shift to hybrid learning if offer weekly covid tests for students and staff to detect asymptomatic cases.
- Vaccination of teachers and staff

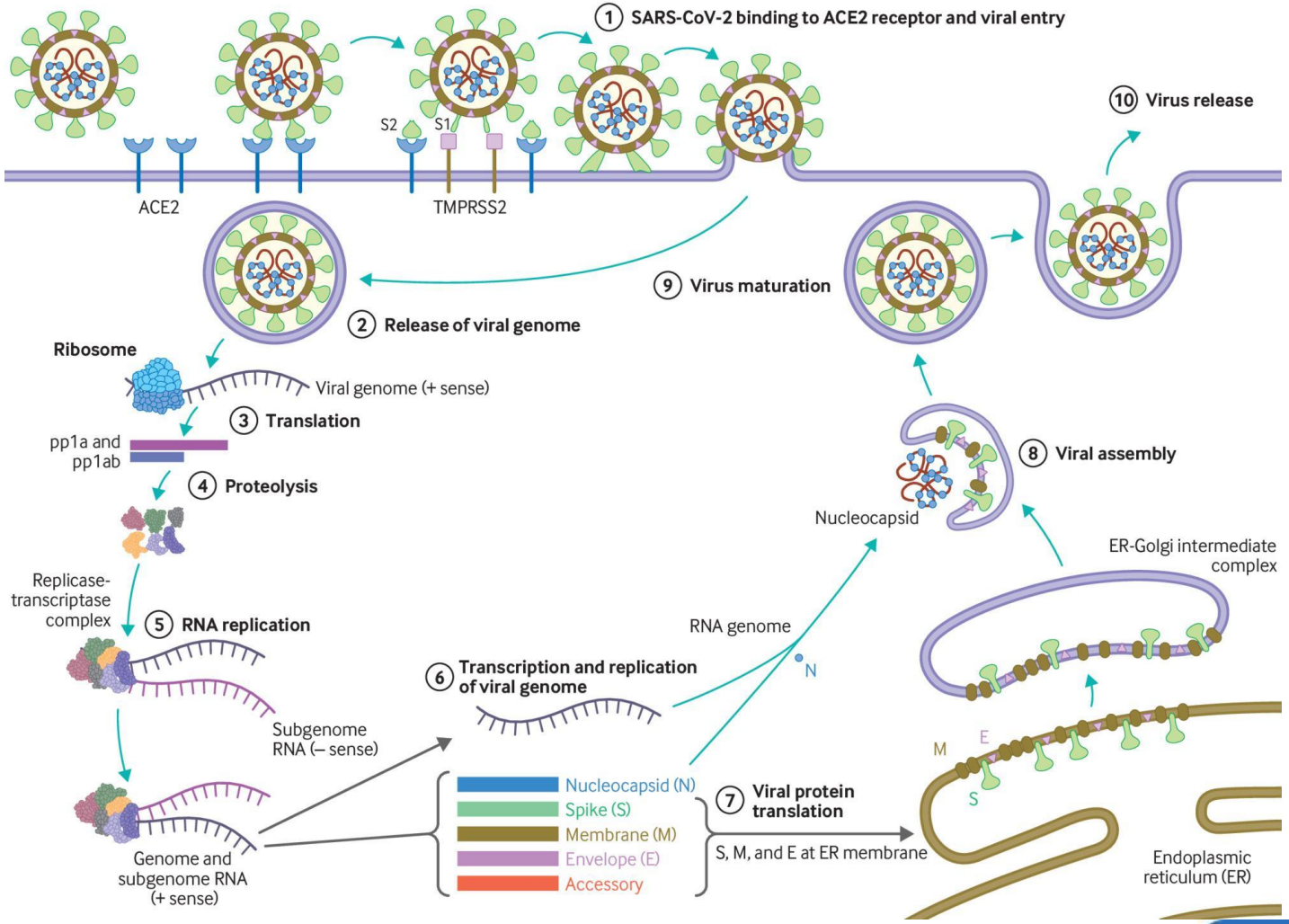
CDC.Gov Operational strategy for K-12 schools through phased mitigation. 2/26/21.

How do we control the Covid-19 outbreak?




Acute adaptive response
Long-term adaptive response
T-CELL RESPONSE
CD4+ T cells
CD8+ T cells
Anamnestic response to reinfection or vaccination
B-CELL AND ANTIBODY RESPONSE
Infection
Symptom onset
IgG
Memory B cells
IgM, IgA
Plasmablast expansion
Anamnestic response to reinfection or vaccination
-1 wk
0
1 wk
2 wk
3 wk
4 wk
5 wk
6 wk
7 wk
3 mo
6 mo
1 y

(1) The virus binds to ACE 2 as the host target cell receptor in synergy with the host's transmembrane serine protease 2 (cell surface protein), which is principally expressed in the airway epithelial cells and vascular endothelial cells



Muge Cevik et al. BMJ 2020;371:bmj.m3862

Predictive value of screening antibody Covid-19 test w/ 95%, sensitivity and 95% specificity

3/11/2021

	Disease				
Test	**Present**	**n**	**Absent**	**n**	**Total**
Positive	True Positive	a= 95	False Positive	c= 5	a + c = **100**
Negative	False Negative	b= 5	True Negative	d= 95	b + d = **100**
Total		a + b = **100**		c + d = **100**	

Disease prevalence

If the ratio of cases in the Disease Present and Disease Absent groups does not reflect the disease prevalence, enter:

disease prevalence (%): 4

Statistic	Value	95% CI
Sensitivity	95.00%	88.72% to 98.36%
Specificity	95.00%	88.72% to 98.36%
Positive Likelihood Ratio	19.00	8.08 to 44.70
Negative Likelihood Ratio	0.05	0.02 to 0.12
Disease prevalence (*)	4.00%	
Positive Predictive Value (*)	44.19%	25.18% to 65.07%
Negative Predictive Value (*)	99.78%	99.49% to 99.91%
Accuracy (*)	95.00%	91.00% to 97.58%

Positive test in this setting not useful and more likely false positive

Covid-19 and feasibility of quarantine at home

- 2017 American Housing Survey
  - Isolation or quarantine impossible in 21% of all US residential units
  - Native American, Hispanic persons, 2-3 times more likely, Black and Asian 1.7 time higher odds of occupying units unsuitable for isolation.

https://doi.org/10.7326/M20-4331, Annals IM 7/21/20

Quarantine and isolation for Covid-19

- Quarantine keeps someone who was in close contact with someone with Covid-19 away from others to prevent transmission and lasts 7 days w/ neg test, or 10 d if asymptomatic
- Isolation keeps someone who is sick or tested positive for Covid-19 (even if they have no symptoms) away from others to prevent transmission
  - If you were only mildly ill or asymptomatic, then you are isolated for 10 days since symptoms first appeared, and at least 24 h with no fever without meds, and symptoms improved. If no symptoms but positive test then 10 days from your positive test
  - If you were severely ill, then you are isolated for 20 days since symptoms first appeared, and at least 24 h with no fever without meds, and symptoms improved.
  - Test based strategy based on 2 negative PCR respiratory specimens collected 24 h apart, and at least 24 h with no fever without meds, and symptoms improved

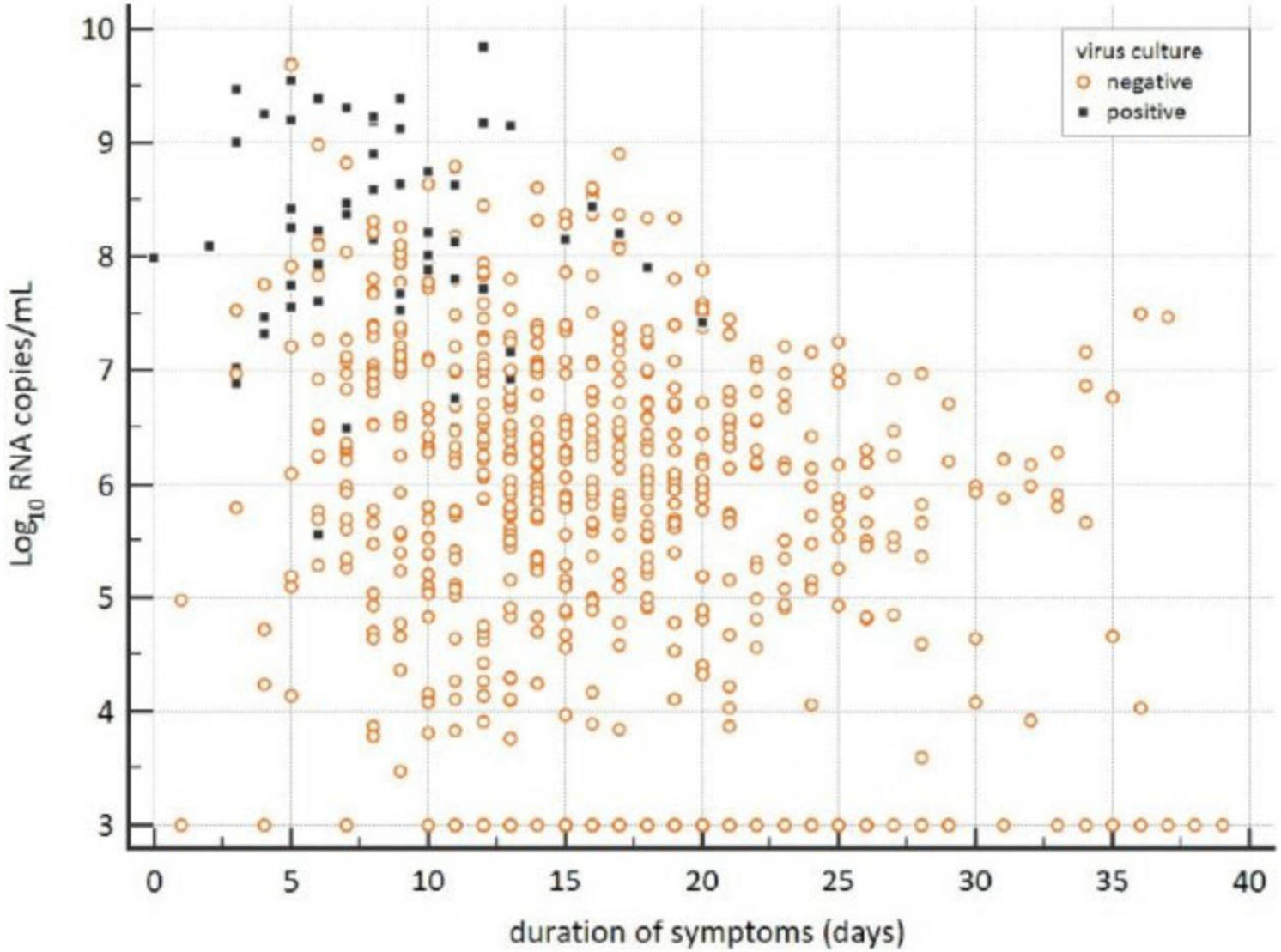
cdc.Gov updated 1/17/21

Covid-19 and time course of virus excretion

- SARS-CoV-2 declines during the course of illness
- Mild to mod Covid-19 no viable virus recovered after 10 d
- Severe illness in some cases complicated by immunocompromised status documented live virus between 10-20 d after sx onset. However, 88%, and 95% of their specimens no longer yielded replication competent virus after 10 and 15 days, respectively, following sx onset.

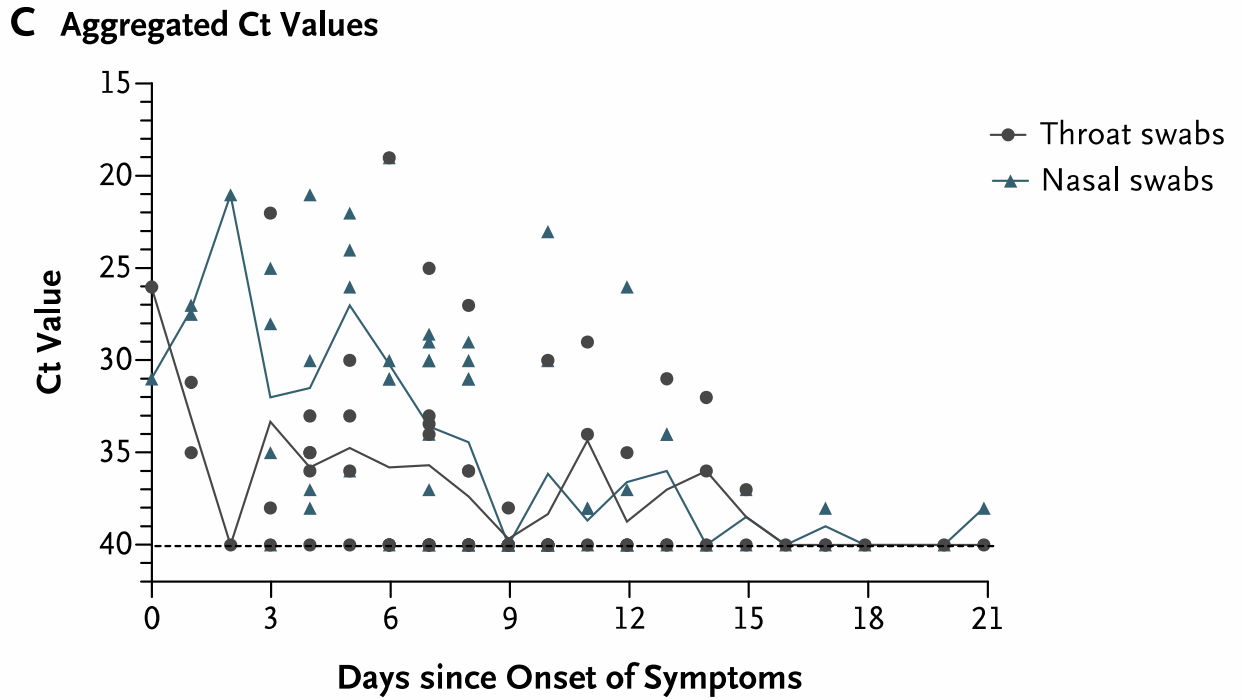
cdc.gov 8/11/20

Figure 3. From van Kampen *et al.*, demonstrating declining viral RNA loads (Log_{10} RNA copies/mL) and likelihood of positive viral culture for SARS-CoV-2 in the upper respiratory samples from a sample of severely ill patients, including some post -solid organ or -bone marrow transplant. Black boxes represent samples that yielded replication-competent virus.



Covid-19 viral dynamics

- 18 patients were evaluated in Wuhan, including 1 who never had symptoms) within 2 family clusters
- Measured sequential PCR in nasal and oral specimens related to onset of symptoms and found there was a high viral load from the onset of symptoms, and in the 1 asymptomatic patient that was as high as the symptomatic patients
- PCR decreased over time with a sharp decline by day 7-9 of illness, then a gradual decline at 2 weeks from onset of illness.



NEJM 2020;382;12

Covid-19 and case mortality over time

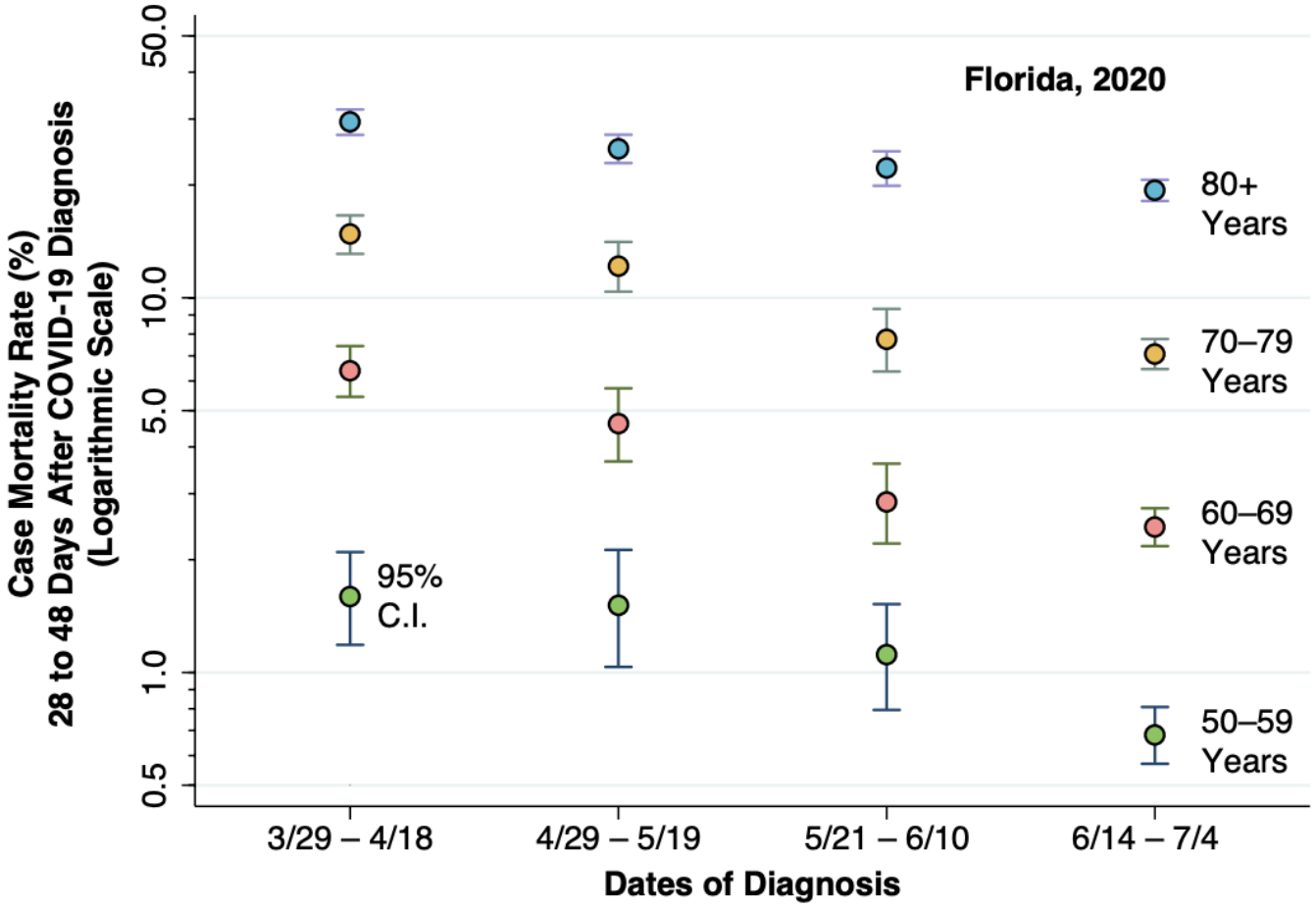
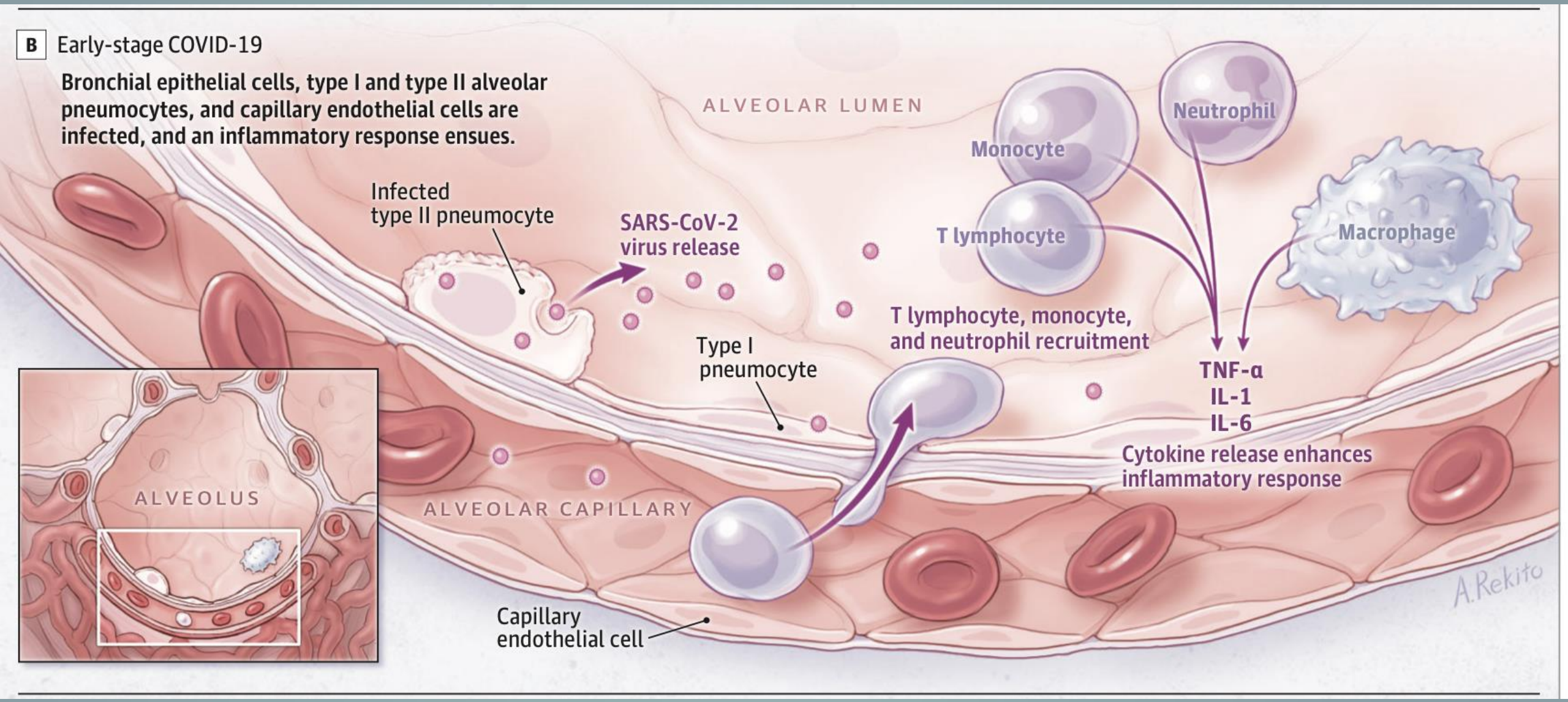
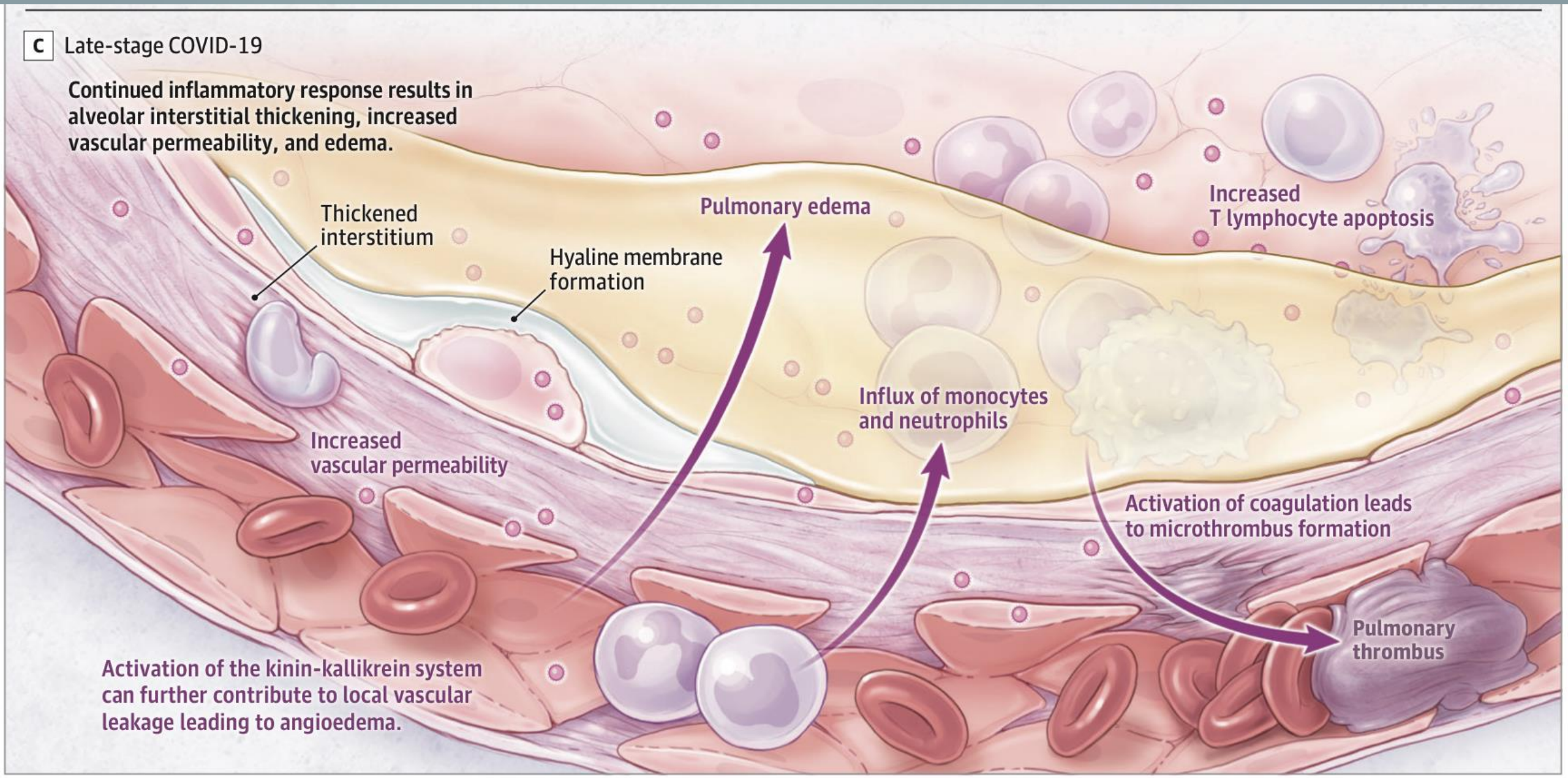


Figure 1. Case Mortality Rate 28 to 48 Days After COVID-19 Diagnosis by Age Group During Four Nonoverlapping Diagnostic Intervals, Florida, 2020

https://doi.org/10.1101/2020.08.03.20167338


B Early-stage COVID-19
Bronchial epithelial cells, type I and type II alveolar pneumocytes, and capillary endothelial cells are infected, and an inflammatory response ensues.
ALVEOLAR LUMEN
Monocyte
Neutrophil
T lymphocyte
Macrophage
Infected type II pneumocyte
SARS-CoV-2 virus release
T lymphocyte, monocyte, and neutrophil recruitment
Type I pneumocyte
TNF-α
IL-1
IL-6
Cytokine release enhances inflammatory response
ALVEOLUS
ALVEOLAR CAPILLARY
Capillary endothelial cell
A.Rekito



JAMA. doi:10.1001/jama.2020.12839

SCHOOLS DURING THE COVID-19 PANDEMIC

The purpose of this tool is to assist administrators in making (re)opening decisions regarding K-12 schools during the COVID-19 pandemic. It is important to check with state and local health officials and other partners to determine the most appropriate actions while adjusting to meet the unique needs and circumstances of the local community.

Should you consider opening?

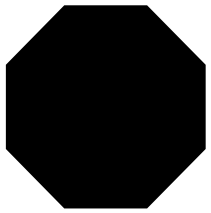
- ✓ Will reopening be consistent with applicable state and local orders?
- ✓ Is the school ready to protect children and employees at higher risk for severe illness?
- ✓ Are you able to screen students and employees upon arrival for symptoms and history of exposure?

ANY NO → **DO NOT OPEN**

ALL YES →

Are recommended health and safety actions in place?

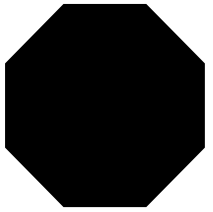
- ✓ Promote healthy hygiene practices such as hand washing and employees wearing a cloth face covering, as feasible
- ✓ Intensify cleaning, disinfection, and ventilation
- ✓ Encourage social distancing through increased spacing, small groups and limited mixing between groups, if feasible
- ✓ Train all employees on health and safety protocols

ANY NO → 

ALL YES →

Is ongoing monitoring in place?

- ✓ Develop and implement procedures to check for signs and symptoms of students and employees daily upon arrival, as feasible
- ✓ Encourage anyone who is sick to stay home
- ✓ Plan for if students or employees get sick
- ✓ Regularly communicate and monitor developments with local authorities, employees, and families regarding cases, exposures, and updates to policies and procedures
- ✓ Monitor student and employee absences and have flexible leave policies and practices
- ✓ Be ready to consult with the local health authorities if there are cases in the facility or an increase in cases in the local area

ANY NO → 

ALL YES → **OPEN AND MONITOR**

CDC

cdc.gov/coronavirus

FIGURE. Reported symptoms among 164 patients with laboratory-confirmed COVID-19, by age and hospitalization status*[,†,§] — United States, January–April 2020

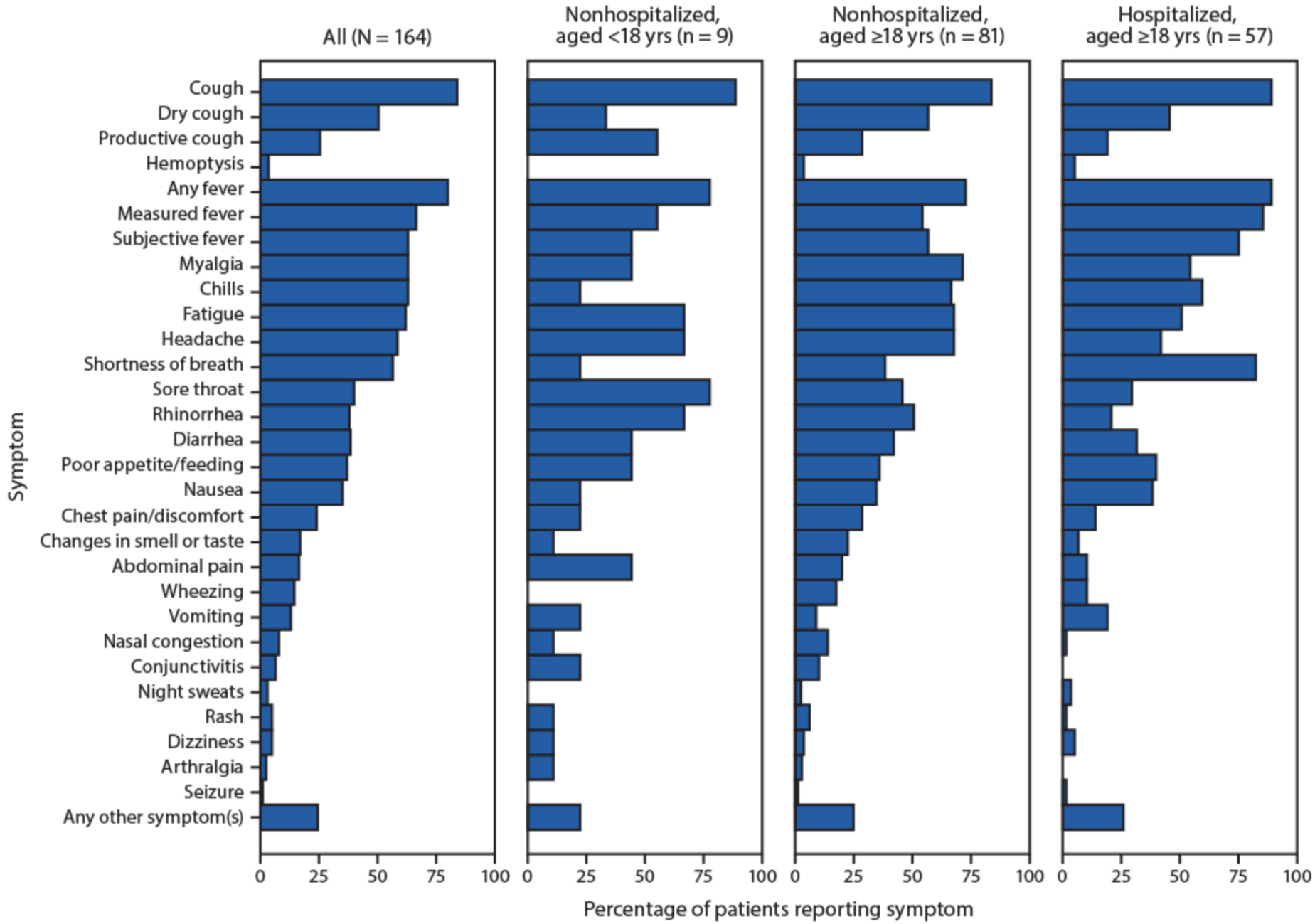
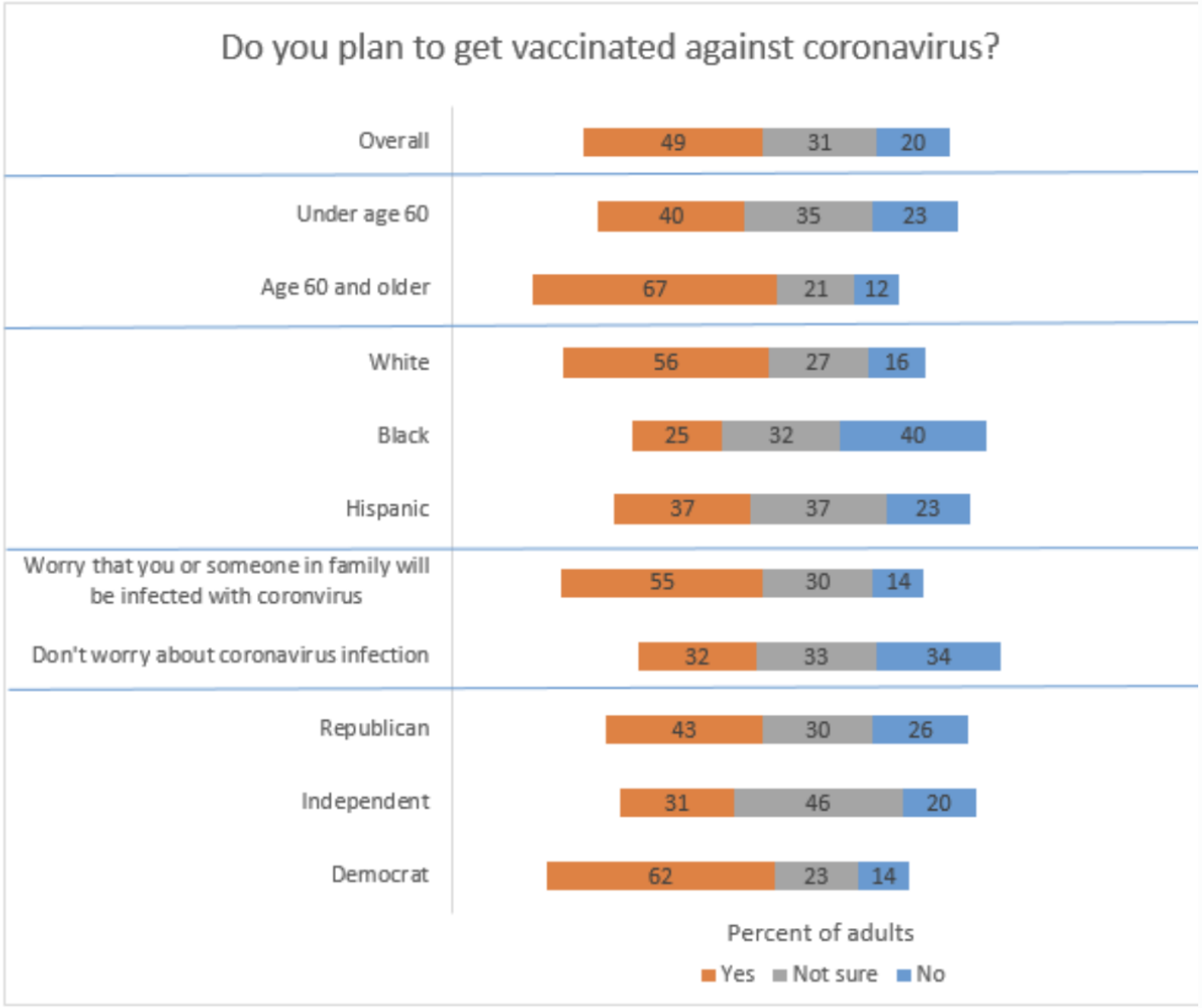


TABLE. Hospitalization, intensive care unit (ICU) admission, and case–fatality percentages for reported COVID–19 cases, by age group — United States, February 12–March 16, 2020

Age group (yrs) (no. of cases)	%*		
	Hospitalization	ICU admission	Case-fatality
0–19 (123)	1.6–2.5	0	0
20–44 (705)	14.3–20.8	2.0–4.2	0.1–0.2
45–54 (429)	21.2–28.3	5.4–10.4	0.5–0.8
55–64 (429)	20.5–30.1	4.7–11.2	1.4–2.6
65–74 (409)	28.6–43.5	8.1–18.8	2.7–4.9
75–84 (210)	30.5–58.7	10.5–31.0	4.3–10.5
≥85 (144)	31.3–70.3	6.3–29.0	10.4–27.3
Total (2,449)	**20.7–31.4**	**4.9–11.5**	**1.8–3.4**



Question: If a vaccine against the coronavirus becomes available, do you plan to get vaccinated, or not?

Source: AP-NORC Poll conducted May 14-18, 2020 with 1,056 adults