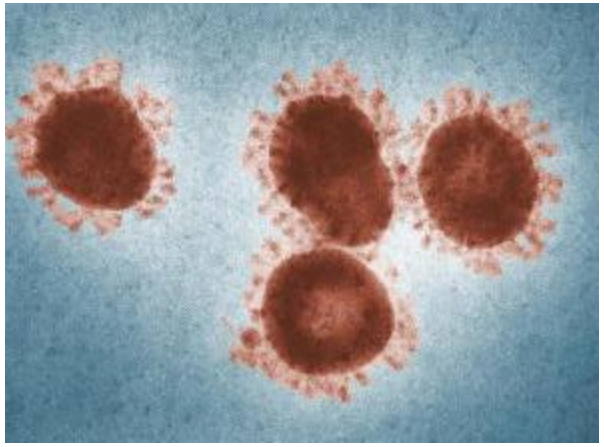
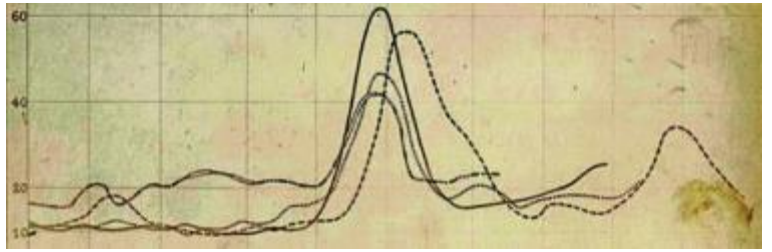
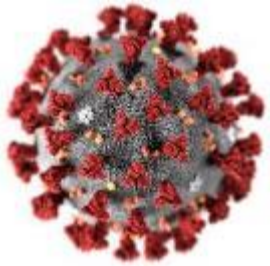
9-15-2020

Covid-19 Clinical Update 9/15/2020

George Washington University







COVID-19 UPDATES

CURRENT AS OF 09.15.2020

HANA AKSELROD, MD, MPH

GW DIVISION OF INFECTIOUS DISEASES

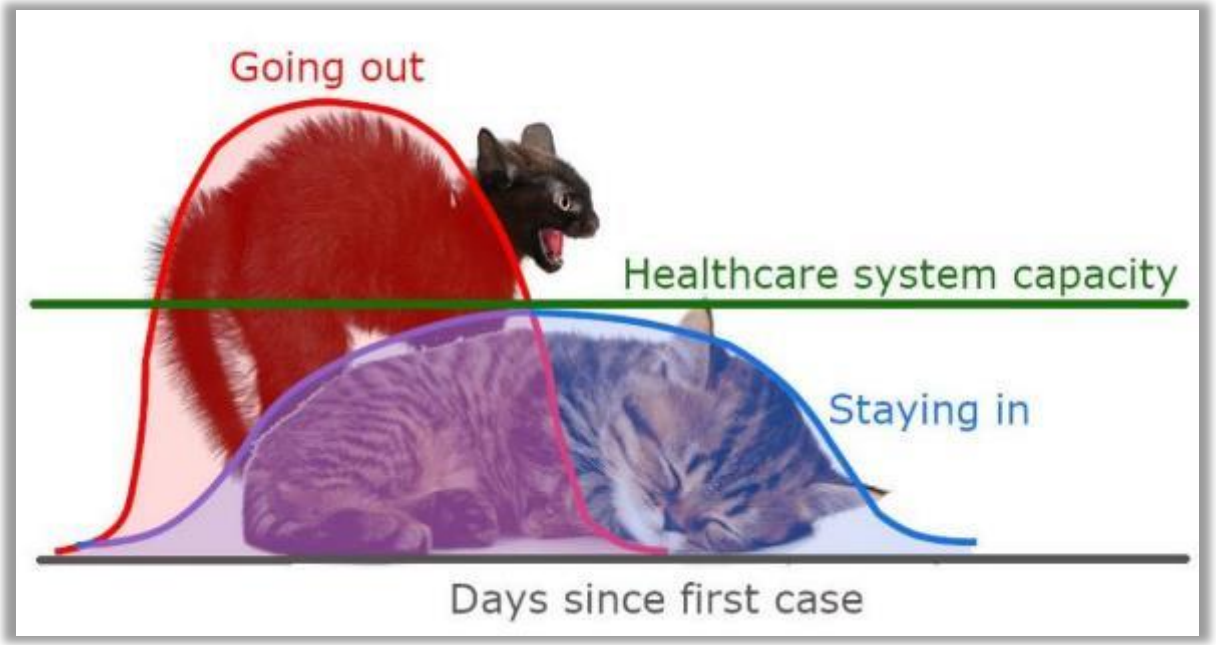
Disclosures

- No financial COI
- Investigator on Abbvie and Moderna COVID-19 trial protocols
- Pre-print information and investigational uses may be discussed

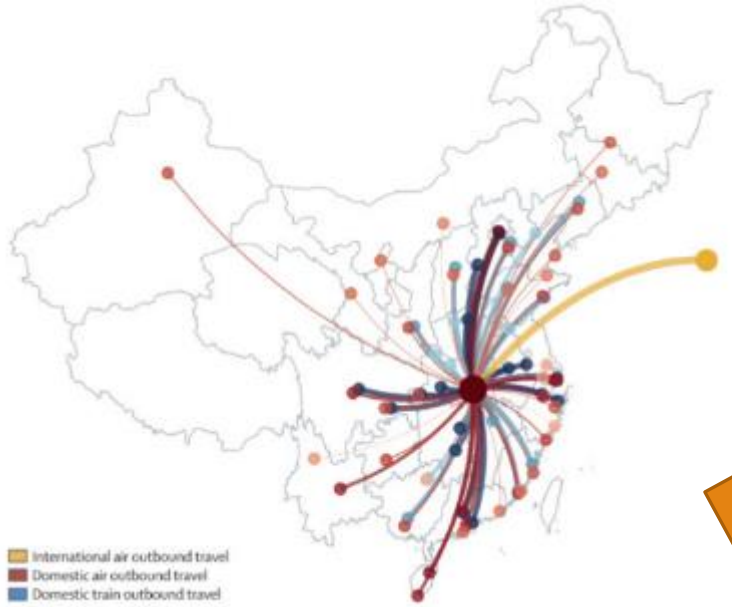
https://xkcd.com/2304/

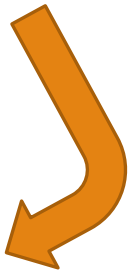
Overview

1. Epidemiology
2. Pathophysiology
3. Diagnostics
4. Treatment
5. Vaccines
6. What's Next?

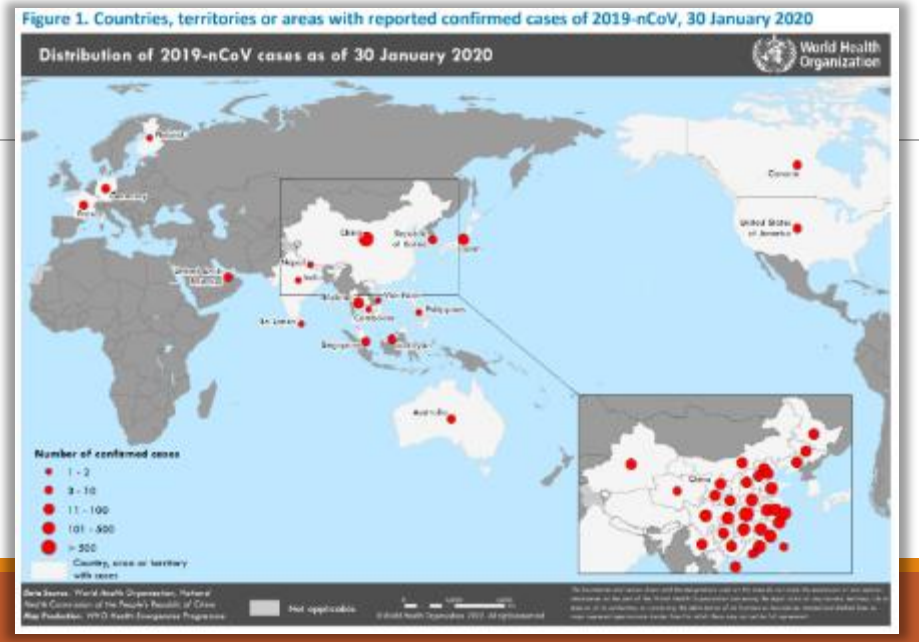


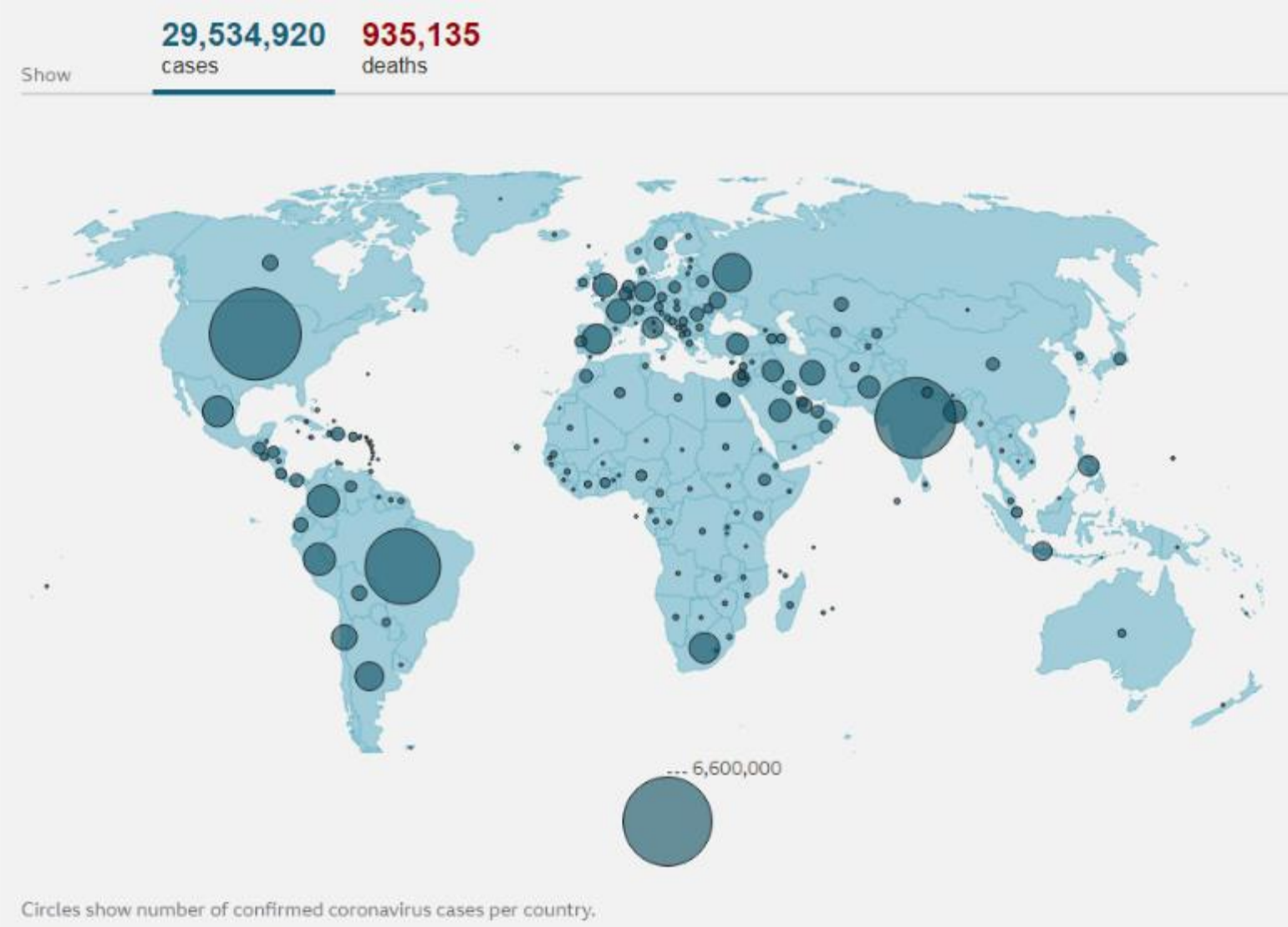
?

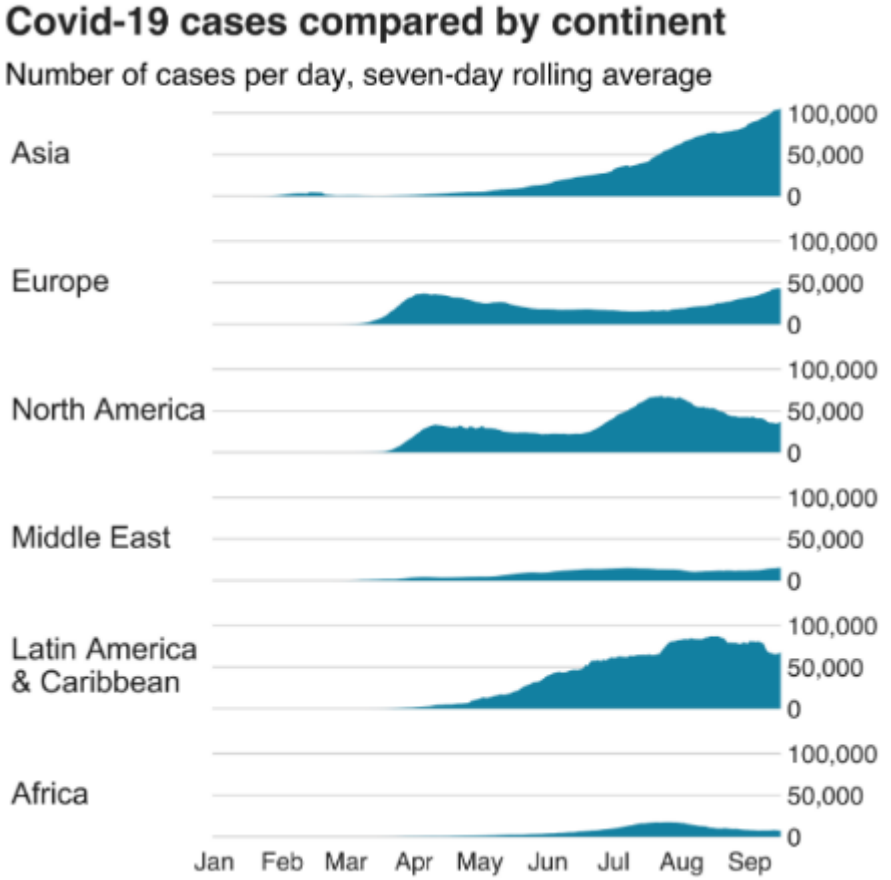




Epidemiology



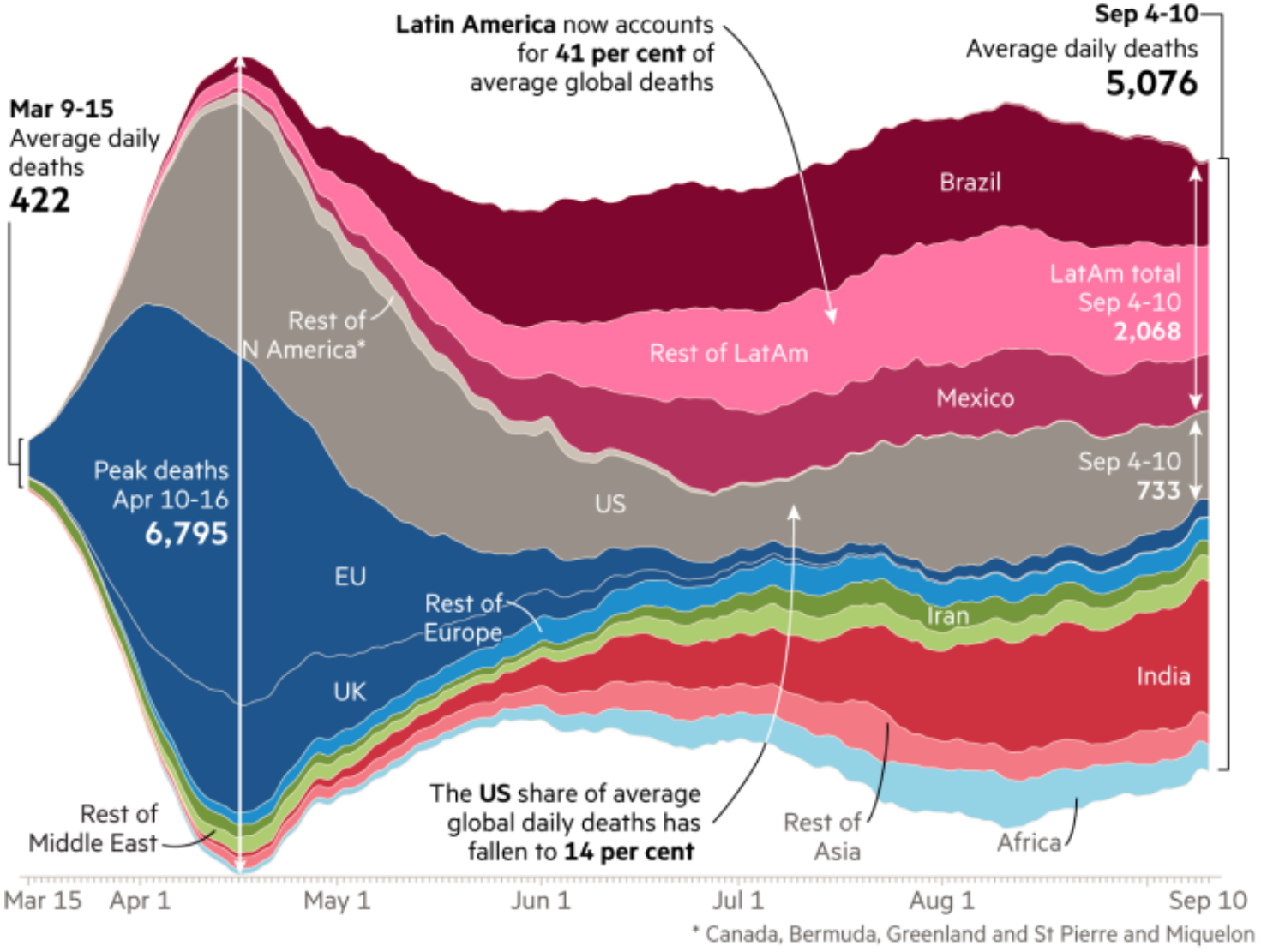




https://www.ft.com/content/a26fbf7e-48f8-11ea-aeb3-955839e06441
https://www.bbc.com/news/world-51235105

India's death toll surges as the Americas continue to struggle with Covid-19

Daily deaths of patients diagnosed with coronavirus (7-day rolling average)

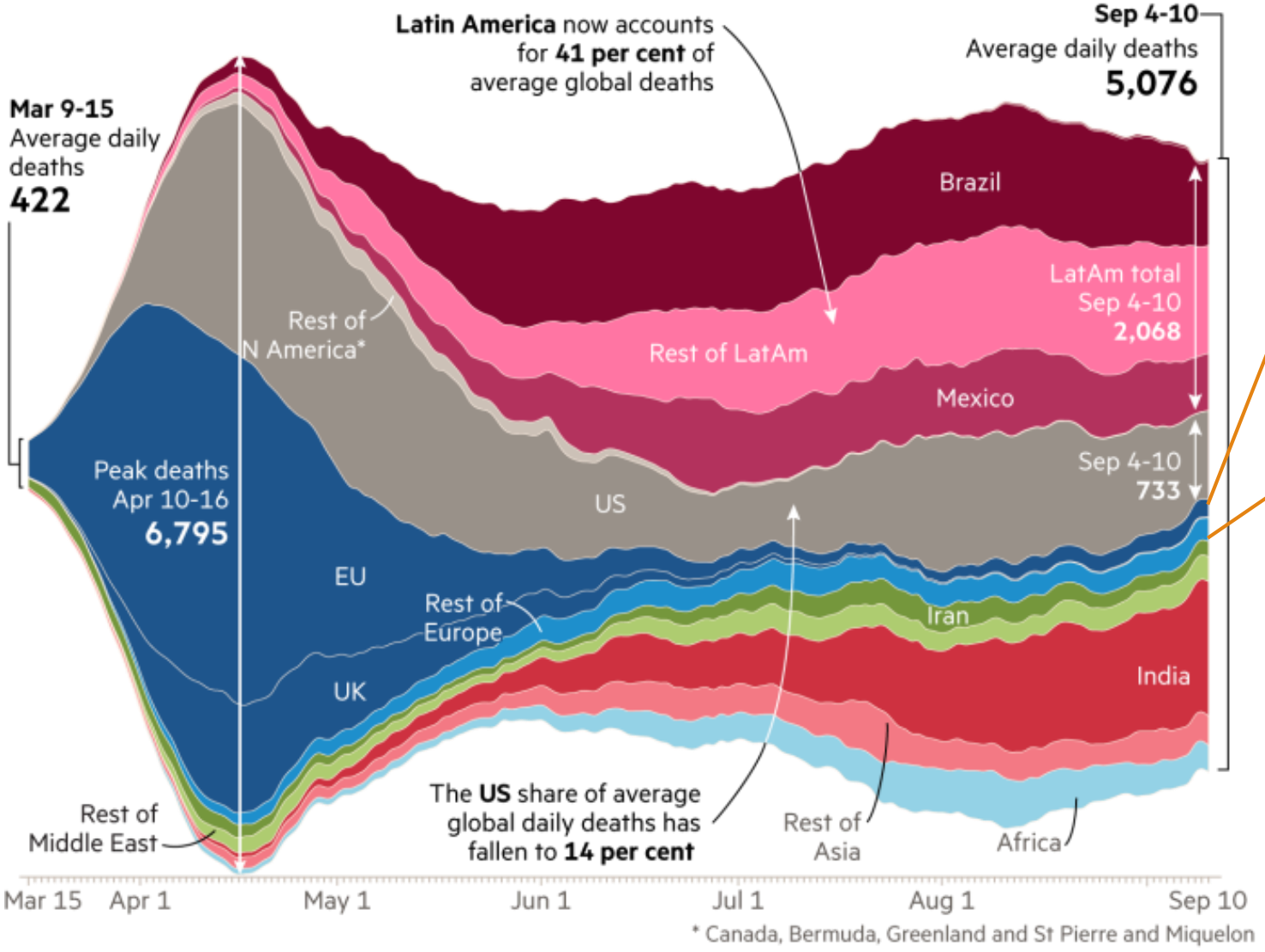


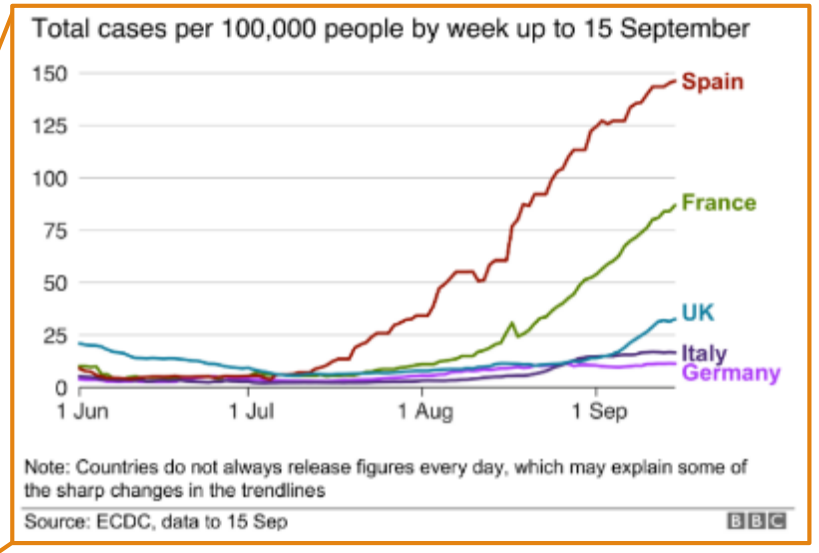
* Canada, Bermuda, Greenland and St Pierre and Miquelon

https://www.ft.com/content/a26fbf7e-48f8-11ea-aeb3-955839e06441
https://www.bbc.com/news/world-51235105

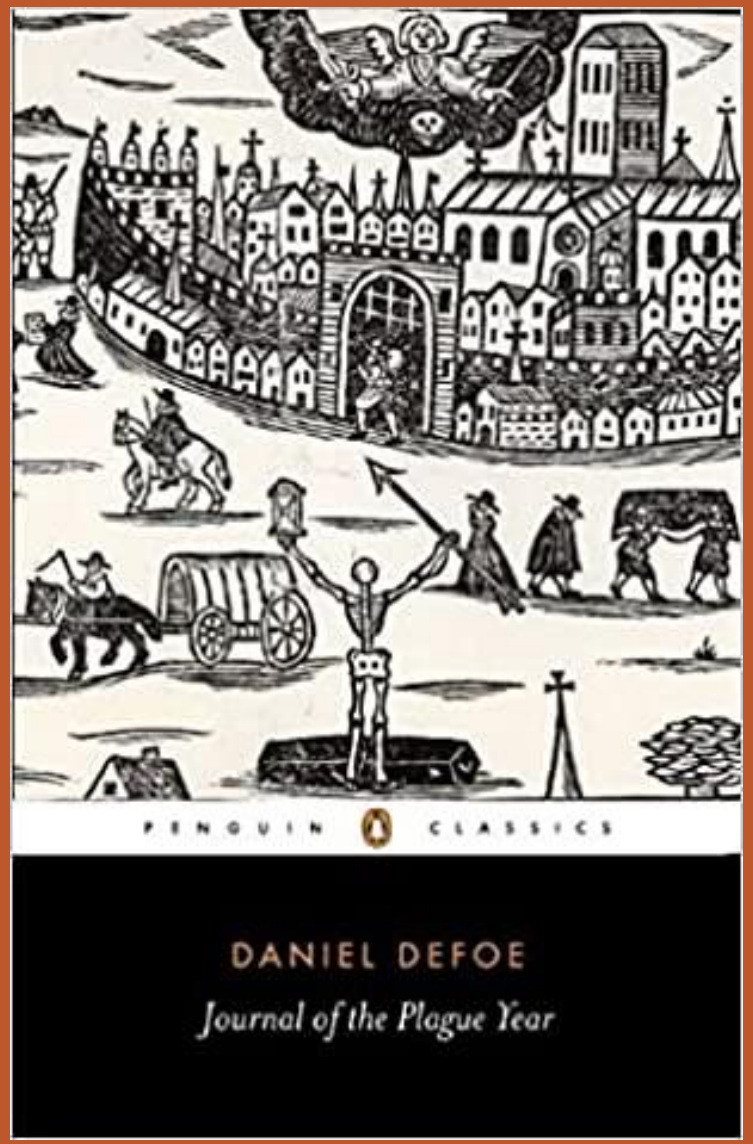
India's death toll surges as the Americas continue to struggle with Covid-19

Daily deaths of patients diagnosed with coronavirus (7-day rolling average)





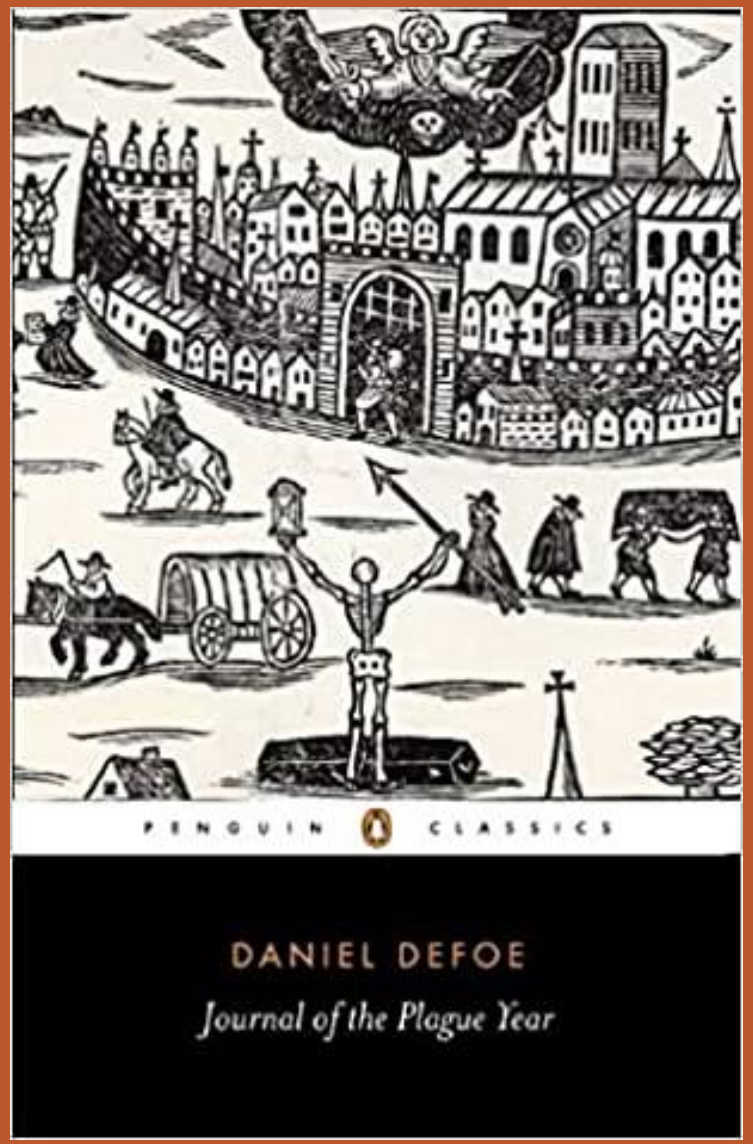
https://www.ft.com/content/a26fbf7e-48f8-11ea-aeb3-955839e06441
https://www.bbc.com/news/world-51235105



"When the Physicians assured us that the Danger was as well from the Sound (that is, the *seemingly sound*) as the Sick; and that those people who thought themselves entirely Free were oftentimes the most fatal; and that it came to be generally understood that people were sensible of it, and of the reason of it: Then, I say, they began to be jealous of every Body, and a vast Number of People lock'd themselves up, so as not to come abroad into any Company at all, nor suffer any that had been abroad in promiscuous Company to come into their Houses, or near them—at least not so near them as to be within the Reach of their Breath or of any Smell from them; and when they were oblig'd to converse at a Distance with Strangers, they would always have Preservatives in their Mouths and about their Cloths to repell and keep off the Infection.

It must be acknowledg'd that when People began to use these Cautions they were less exposed to Danger; and the Infection did not break into such Houses so furiously as it did into others before; and thousands of Families were preserved."

https://www.gutenberg.org/files/376/376-h/376-h.htm

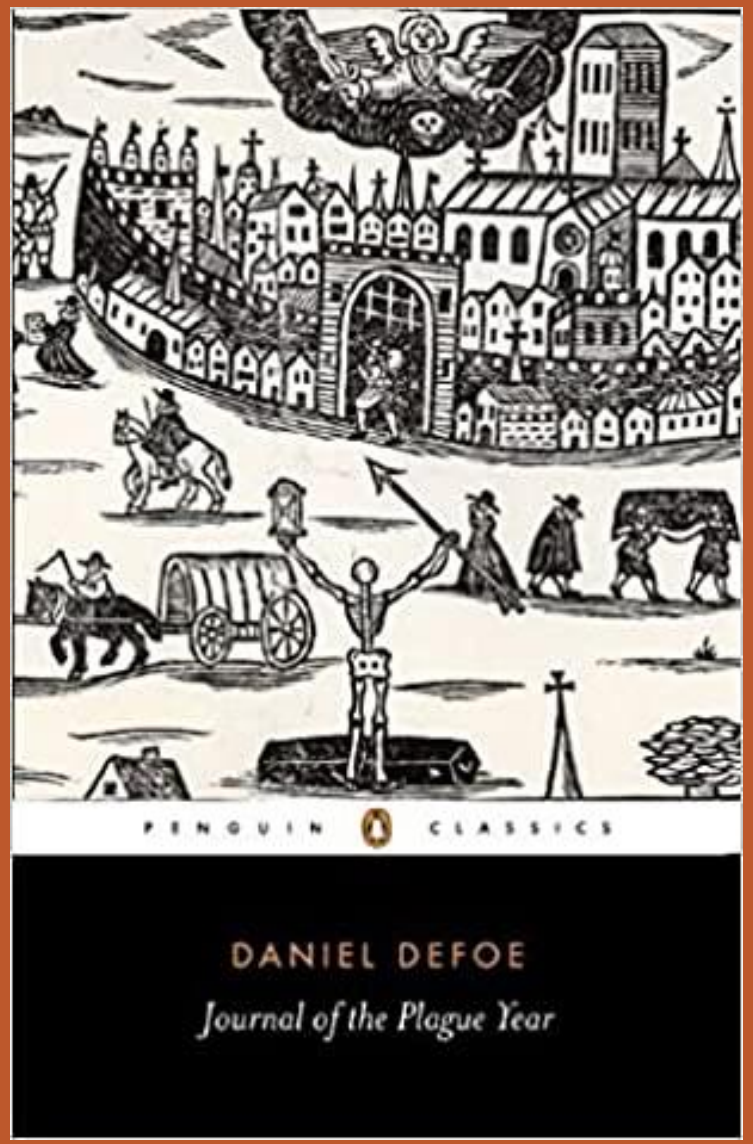


"The audacious . . . were so possessed with the first Joy, and so surpriz'd with the Satisfaction of seeing a vast Decrease in the weekly Bills, that they were impenetrable by any new Terrors, and would not be persuaded, but that the Bitterness of Death was pass'd; and it was to no more purpose to talk to them, than to an East-wind, but they open'd Shops, went about Streets, did Business, and conversed with any Body that came in their Way to converse with, whether with Business, or without, neither inquiring of their Health, or so much as being Apprehensive of any Danger from them, tho' they knew them not to be sound.

This impudent rash Conduct cost a great many their Lives, who had with great Care and Caution shut themselves up, and kept retir'd as it were from all Mankind, and had by that means, under God's Providence, been preserv'd thro' all the heat of that Infection. . .

The Consequence of this was, that the Bills encreas'd again.“

https://www.gutenberg.org/files/376/376-h/376-h.htm



"A dreadful plague in London was

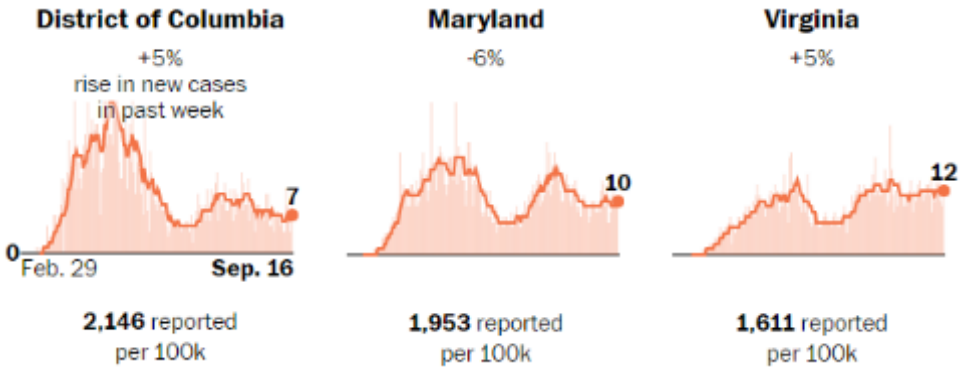
In the year sixty-five,

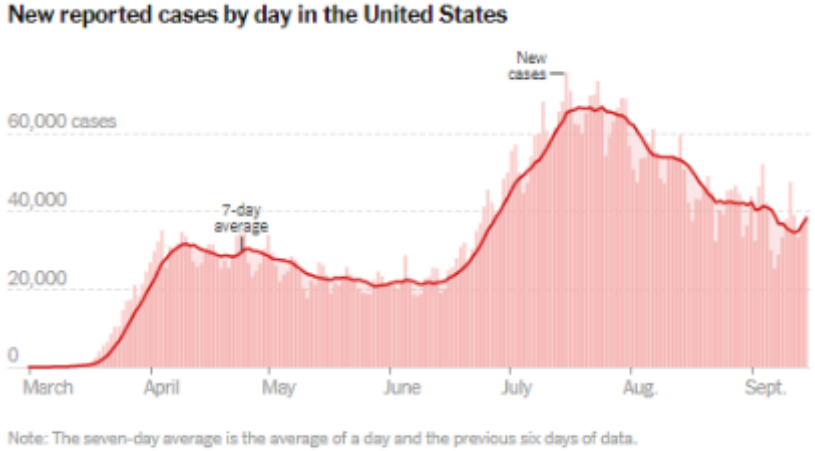
Which swept an hundred thousand souls

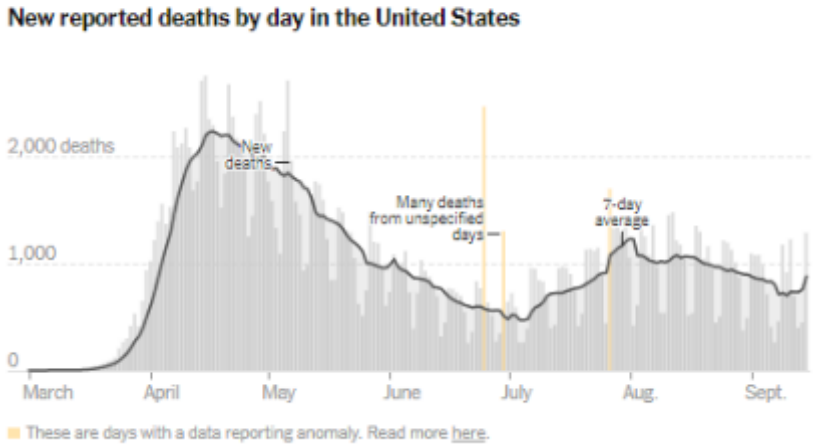
Away; yet I alive!"

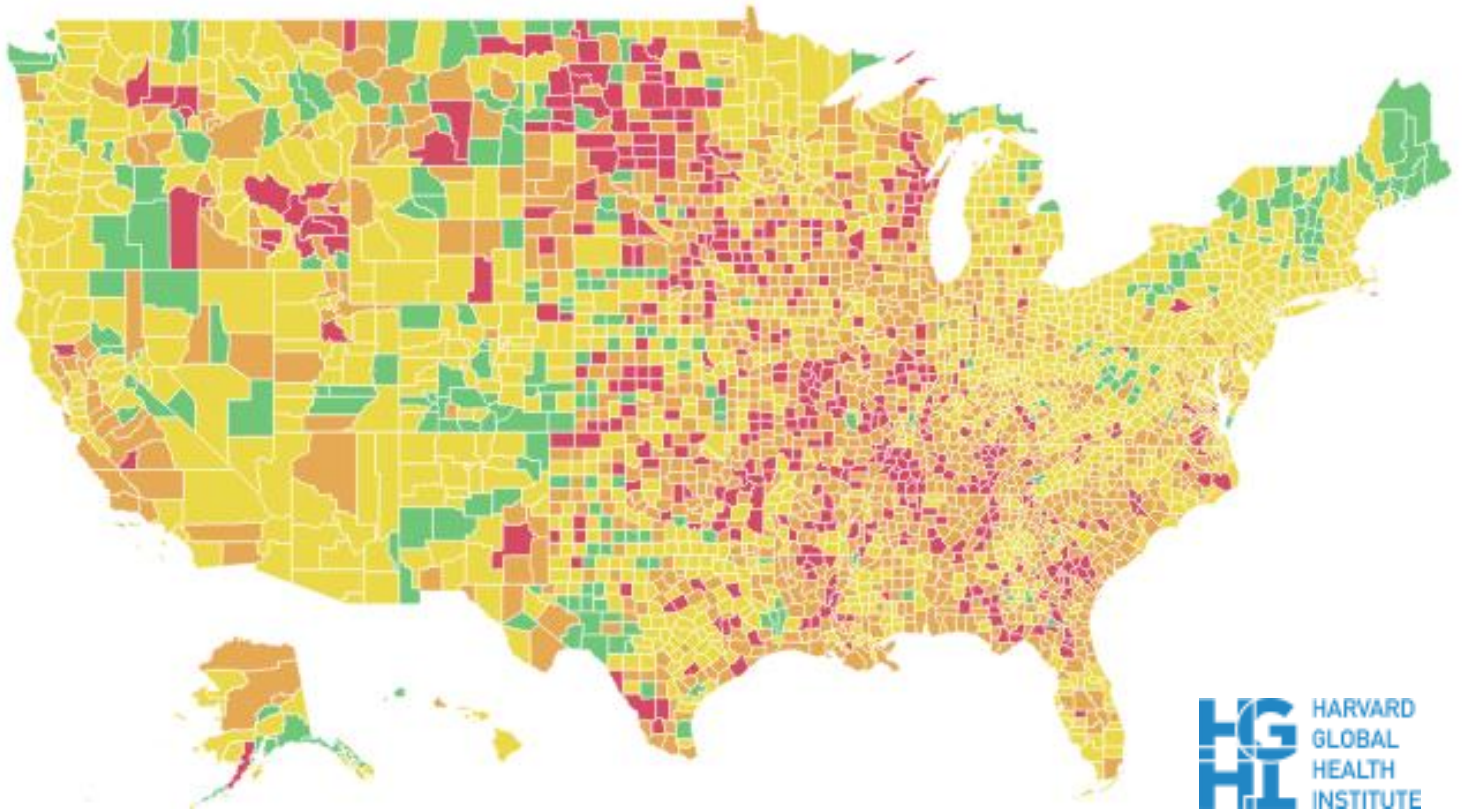
(1722 re: 1665-1666)

https://www.gutenberg.org/files/376/376-h/376-h.htm



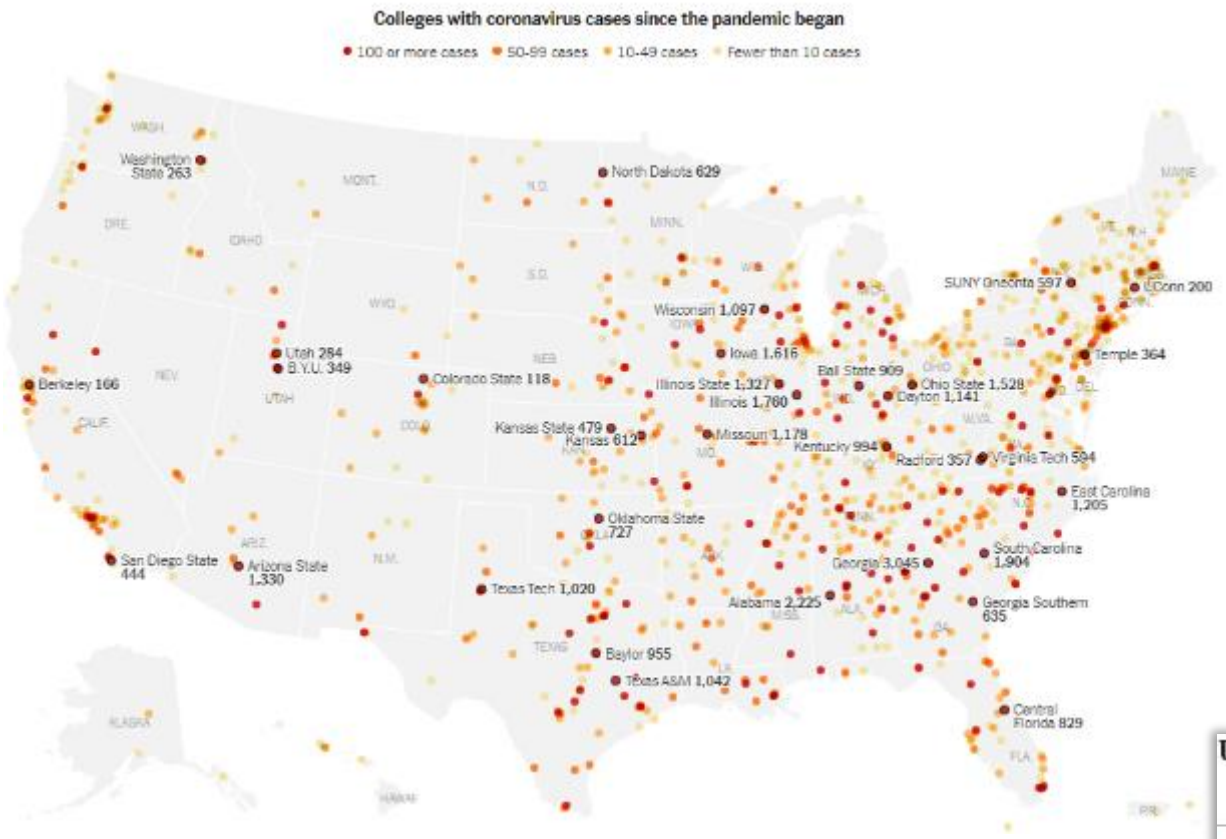


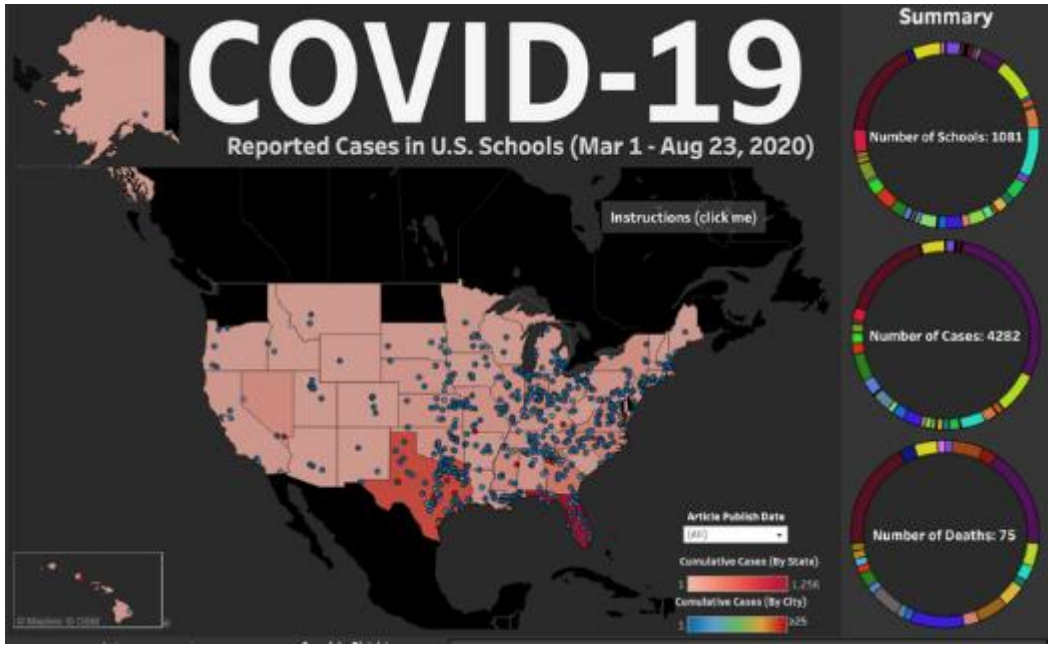




HARVARD GLOBAL HEALTH INSTITUTE

https://www.washingtonpost.com/graphics/local/dc-maryland-virginia-coronavirus-cases/
https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html
https://globalepidemics.org/key-metrics-for-covid-suppression/





WHSV

JMU seeks disciplinary action against over 100 students for not following COVID-19 guidelines

CBS News

Illinois university quarantines entire student body due to coronavirus outbreak

Dozens of cases crop up among thousands enrolled at Bradley University in Peoria, which is turning to remote learning for at least two weeks.

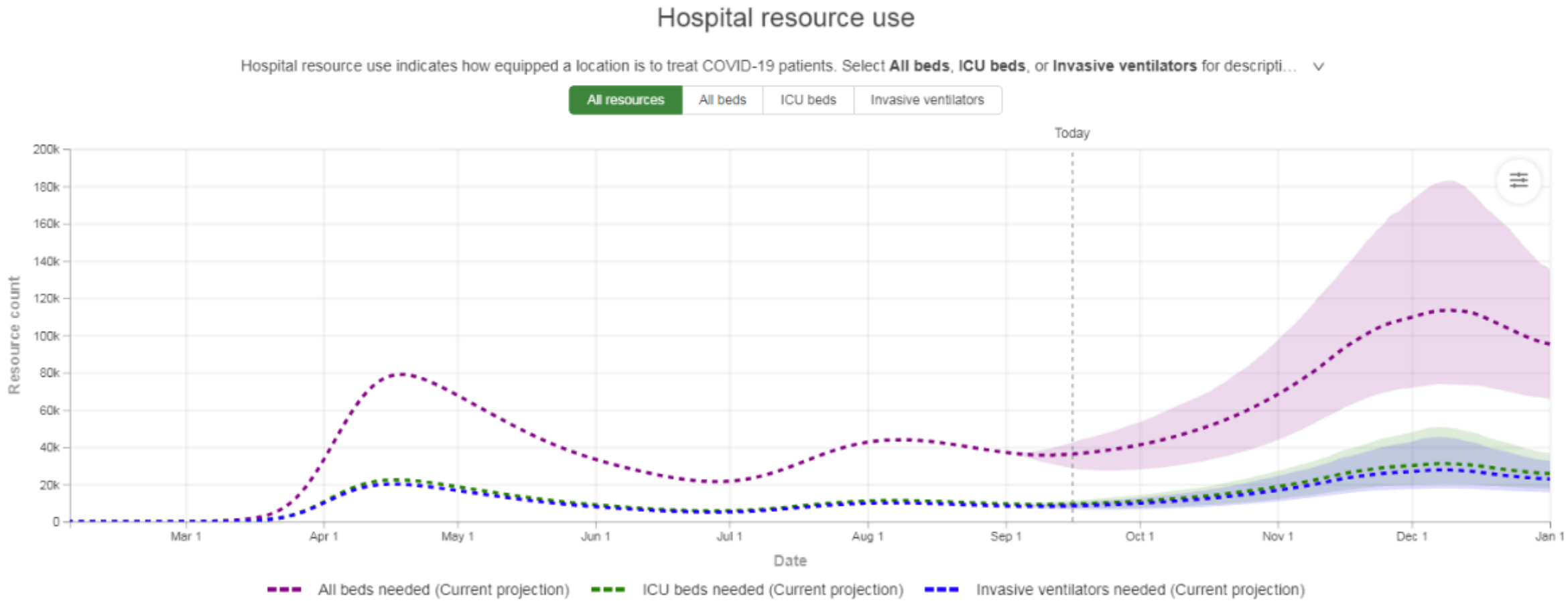
Northeastern is not the only school cracking down on students for partying

The virus moves off campus

https://www.nytimes.com/interactive/2020/us/covid-college-cases-tracker.html

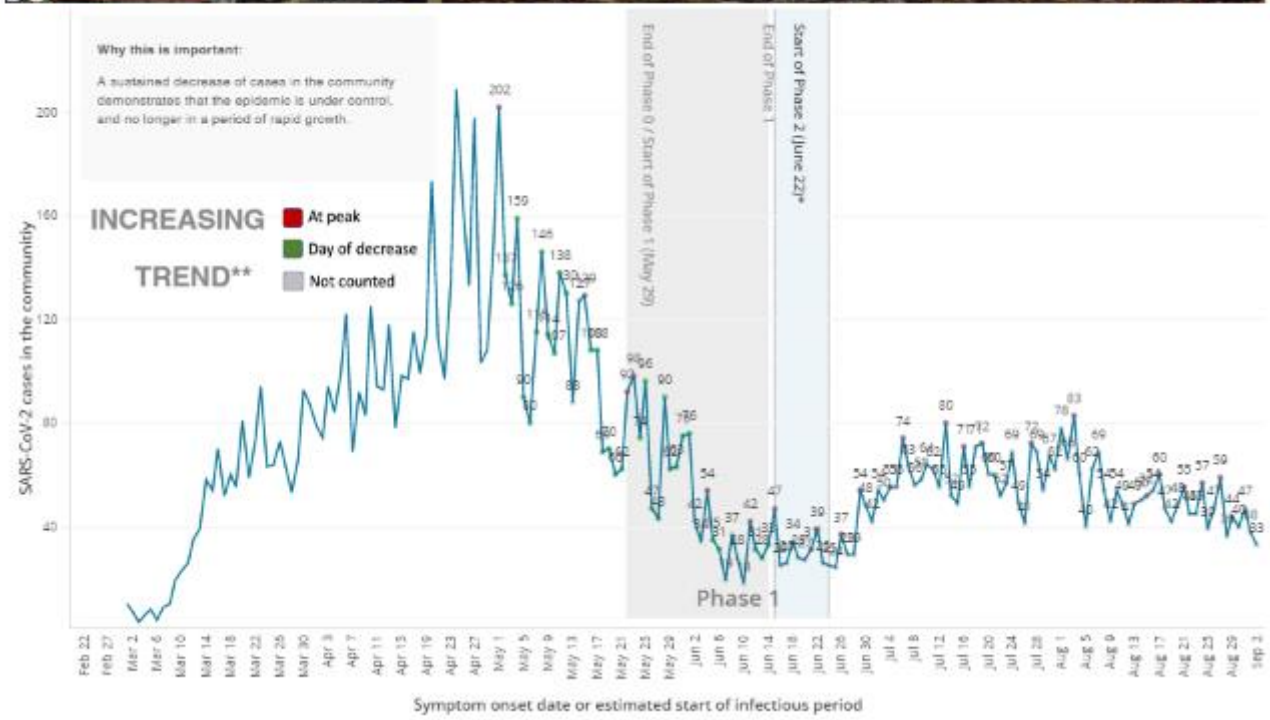
https://www.npr.org/sections/health-shots/2020/08/28/906263926/how-many-coronavirus-cases-are-happening-in-schools-this-tracker-keeps-count

Health Systems Capacity



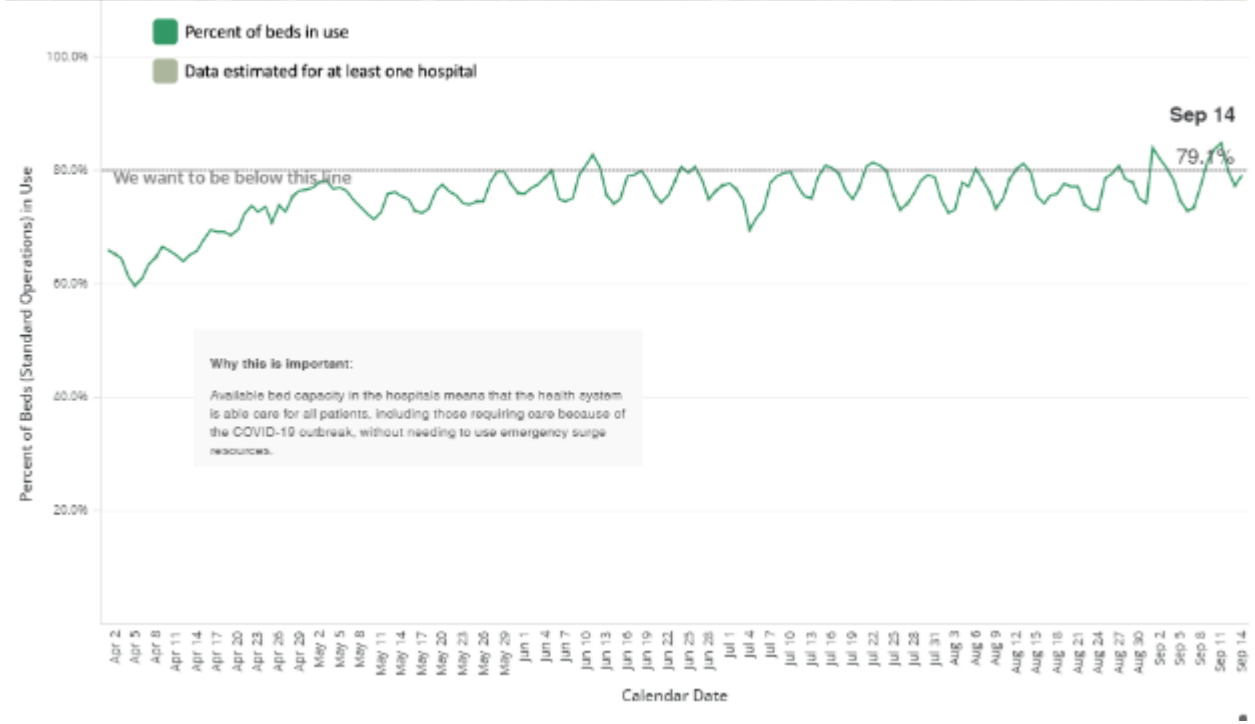
Not Achieved

Sustained Decrease in Cases within the Community



Achieved

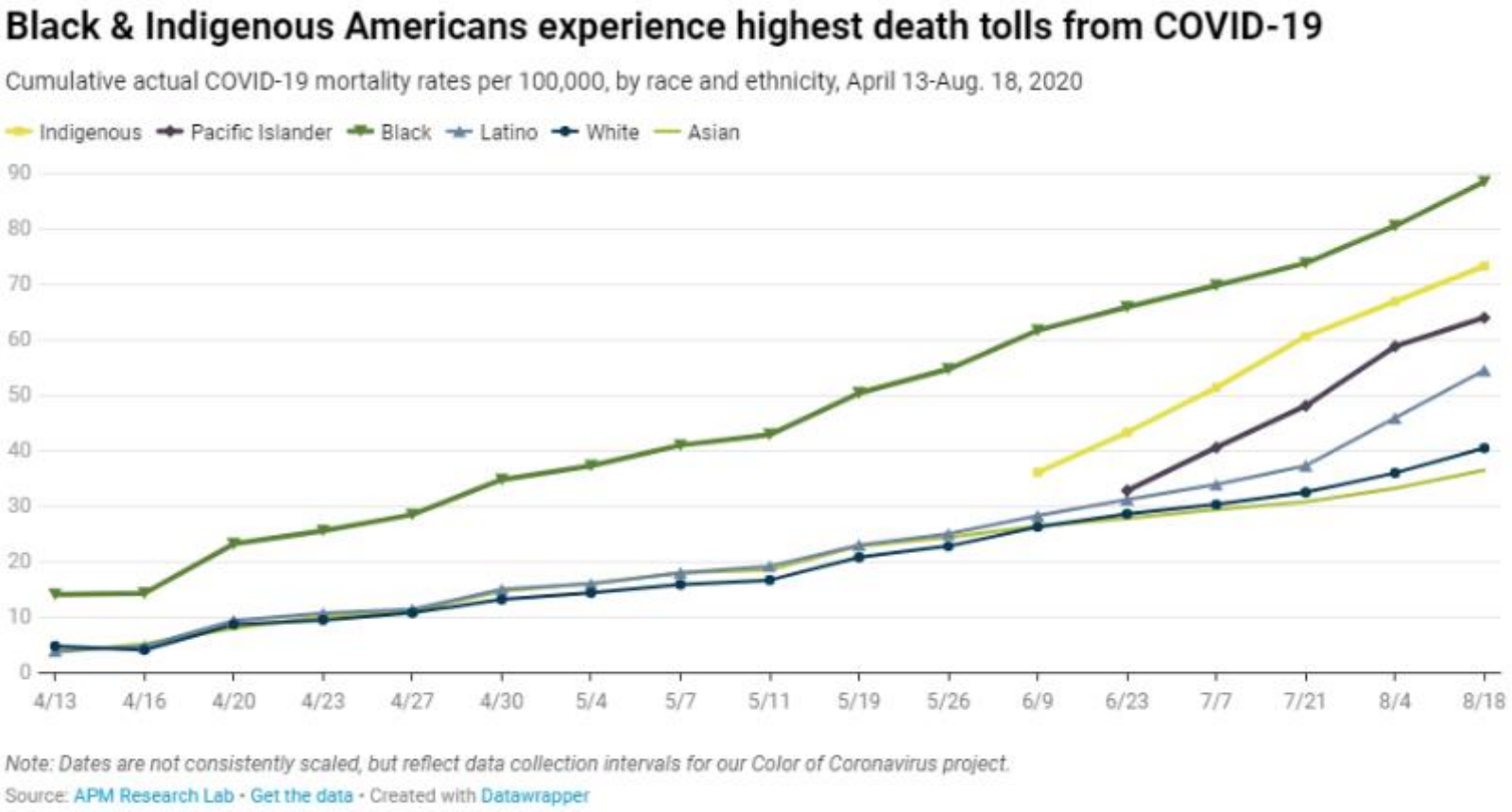
Utilization of beds at acute care hospitals

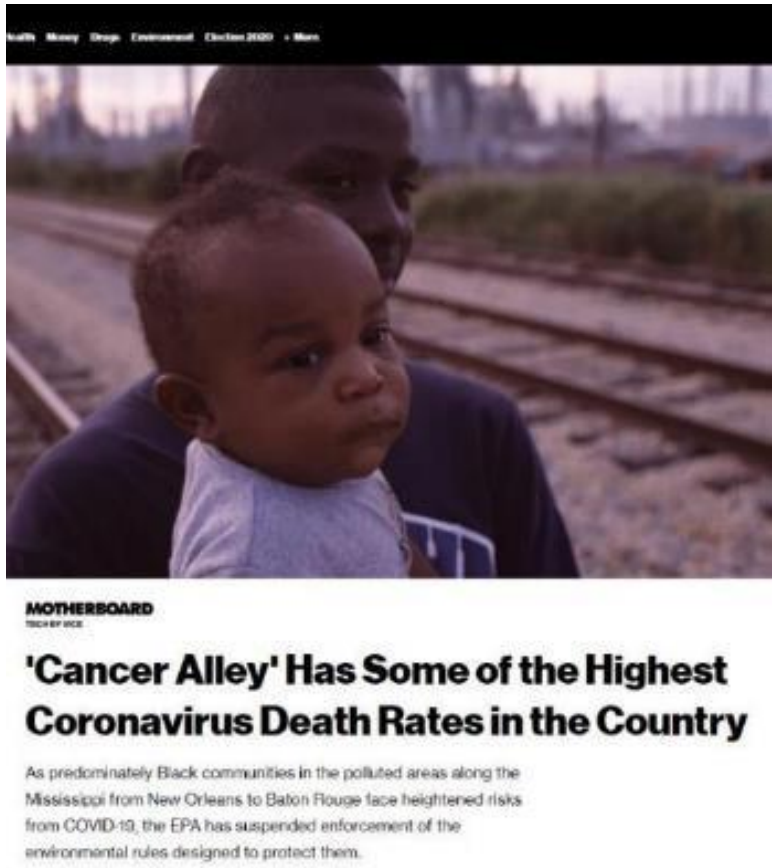


https://coronavirus.dc.gov/page/coronavirus-data

COVID-19:
The Disparities Amplifier

- **1 in 1,125 Black Americans has died** (or 88.4 deaths per 100,000)
- **1 in 1,375 Indigenous Americans has died** (or 73.2 deaths per 100,000)
- **1 in 1,575 Pacific Islander Americans has died** (or 63.9 deaths per 100,000)
- **1 in 1,850 Latino Americans has died** (or 54.4 deaths per 100,000)
- **1 in 2,450 White Americans has died** (or 40.4 deaths per 100,000)
- **1 in 2,750 Asian Americans has died** (or 36.4 deaths per 100,000)





https://www.apmresearchlab.org/covid/deaths-by-race
http://climatesofinequality.org/happening/louisianas-cancer-alley-and-covid-19/

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

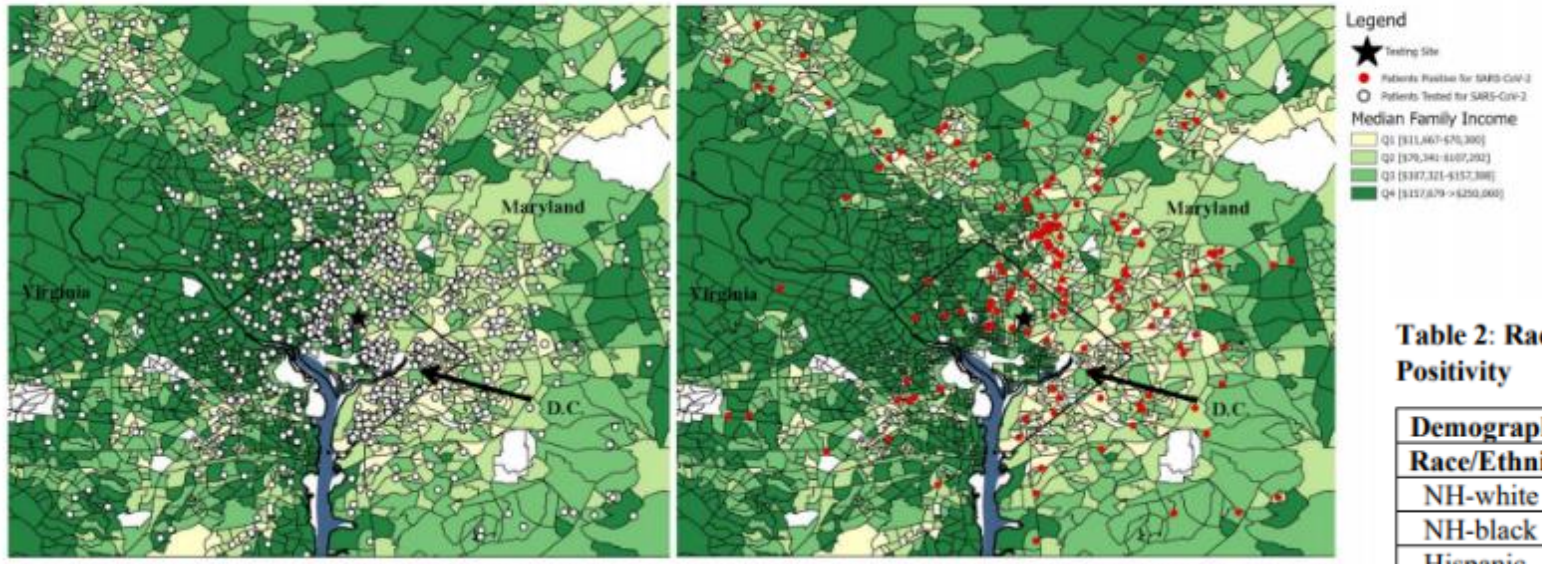
Pre-publication Release

Racial/Ethnic and Socioeconomic Disparities of SARS-CoV-2 Infection Among Children

Monika K. Goyal, Joelle N. Simpson, Meleah D. Boyle, Gia M. Badolato, Meghan Delaney, Robert McCarter and Denice Cora-Bramble

Pediatrics August 2020, e2020009951; DOI: https://doi.org/10.1542/peds.2020-009951

Figure 1. SARS-CoV-2 Testing and Positivity by Median Family Income



a) Geospatial distribution of patients tested for SARS-CoV-2 and median family income quartiles b) Geospatial distribution of patients positive for SARS-CoV-2 and median family income quartiles

Figure 2. Rates of SARS-CoV-2 Infection by Race/Ethnicity and Socioeconomic Status

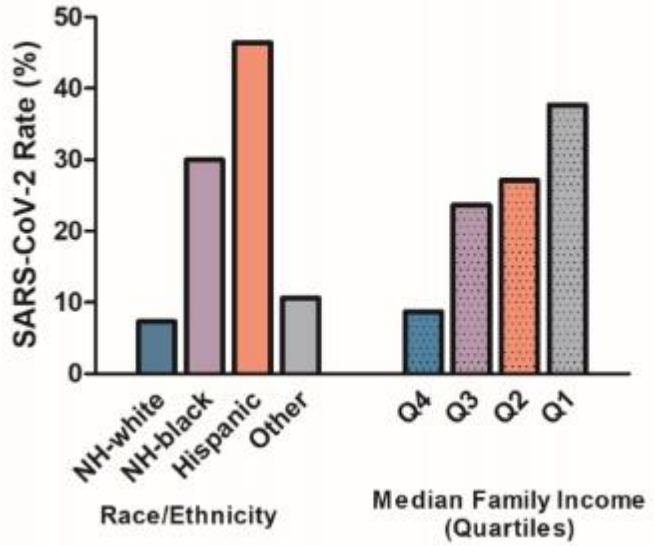


Table 2: Racial/Ethnic and Socioeconomic Factors Associated with SARS-CoV-2 Virus Positivity

Demographic Characteristic	OR (95% CI)	aOR (95% CI)[a]
Race/Ethnicity		
NH-white	Reference	Reference
NH-black	3.3 (1.8, 5.9)	2.3 (1.2, 4.4)
Hispanic	9.1 (5.1, 16.4)	6.3 (3.3, 11.9)
Other	1.9 (0.9, 3.8)	1.8 (0.9, 3.7)
Median Family Income (quartiles)		
Q4: $157,679->$250,000	Reference	Reference
Q3: $107,321-$157,308	3.2 (1.8, 5.6)	2.6 (1.4, 4.9)
Q2: $70,341-$107,292	3.8 (2.1, 6.6)	2.3 (1.2, 4.3)
Q1: $11,667-$70,300	5.9 (3.4, 10.3)	2.4 (1.3, 4.6)

[a] Adjusted for age, sex, race/ethnicity, and median family income.

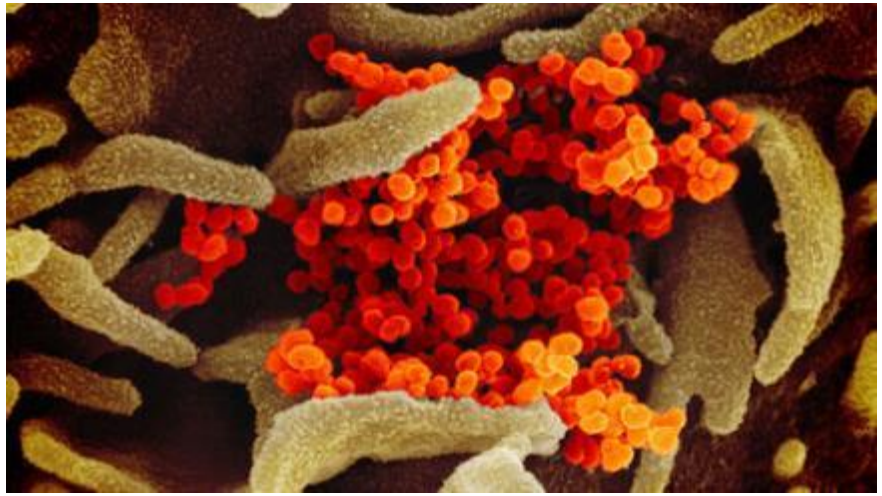
Risk Factors for Infection

MARYLAND

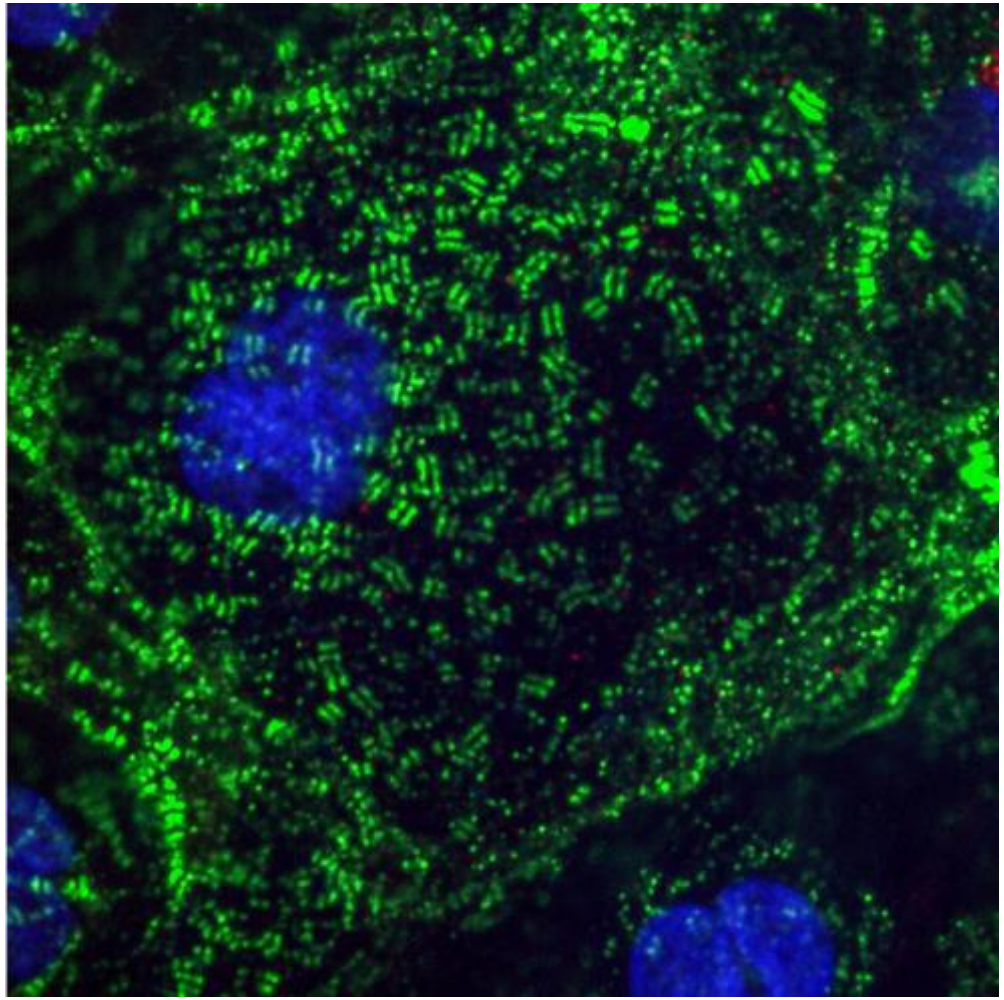
- Clipman et al., **"Rapid real-time tracking of non-pharmaceutical interventions and their association SARS-CoV-2 positivity: The COVID-19 Pandemic Pulse Study."** *Clin Infect Dis* 2020. PMID: 32766598.
- 1,030 individuals in Maryland in 06/2020 surveyed on non-pharmacologic intervention (NPI) adoption, access to SARS-CoV-2 testing, and self-reported SARS-CoV-2 positivity
- SARS-CoV-2 infection was negatively associated with **strict social distancing** (aOR: 0.10; 95% CI: 0.03-0.33)
- After adjusting for strict social distancing and demographics, only **public transport use** (aOR for ≥7 times vs. never: 4.29) and **visiting a place of worship** (aOR for ≥3 times vs. never: 16.0) remained significantly associated with SARS-CoV-2 infection

MASSACHUSETTS

- Figueroa et al., **"Community-Level Factors Associated With Racial And Ethnic Disparities In COVID-19 Rates In Massachusetts."** *Health Affairs* 2020. PMID: 32853056.
- Cross-sectional study of 351 municipalities in 01-05/2020
- Independent predictors of higher COVID-19 rates in the Latino/a population included the proportion of foreign-born non-citizens living in a community, mean household size, and share of food service workers.
- The association between the Black population and COVID-19 rates may be explained by other systemic inequities
- Efforts that **improve care for foreign born non-citizens**, **address crowded housing**, and **protect food-service workers** may help mitigate the spread of COVID-19 among minority communities



Pathophysiology



https://www.statnews.com/2020/09/04/carnage-in-lab-dish-shows-how-coronavirus-may-damage-heart/

Myocardial Damage

SARS-CoV-2 infection of human iPSC-derived cardiac cells predicts novel cytopathic features in hearts of COVID-19 patients

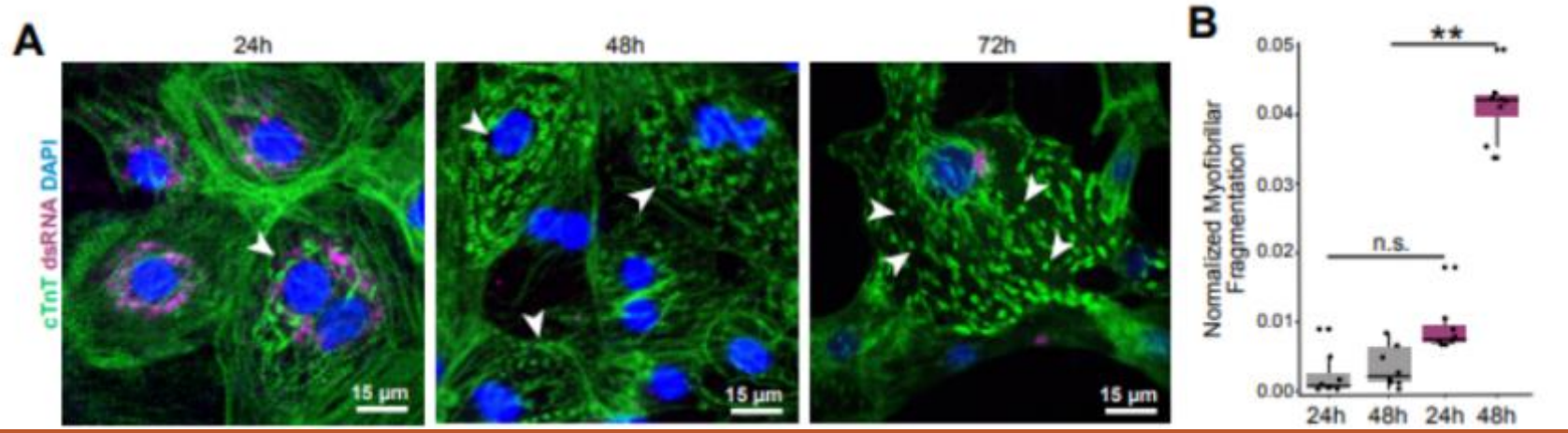
Juan A. Pérez-Bermejo, Serah Kang, Sarah J. Rockwood, Camille R. Simoneau, David A. Joy, Gokul N. Ramadoss, Ana C. Silva, Will R. Flanigan, Huihui Li, Ken Nakamura, Jeffrey D.Whitman, Melanie Ott, Bruce R. Conklin, Todd C. McDevitt

doi: https://doi.org/10.1101/2020.08.25.265561

- COVID-19 causes cardiac dysfunction in up to 25% of patients
- Exposure of human iPSC-derived heart cells to SARS-CoV-2 revealed productive infection and robust transcriptomic and morphological signatures of damage, particularly in cardiomyocytes
- Transcriptome signatures revealed disruption of structural proteins with myofibrillar fragmentation
- Human autopsy specimens from COVID19 patients displayed similar disruption

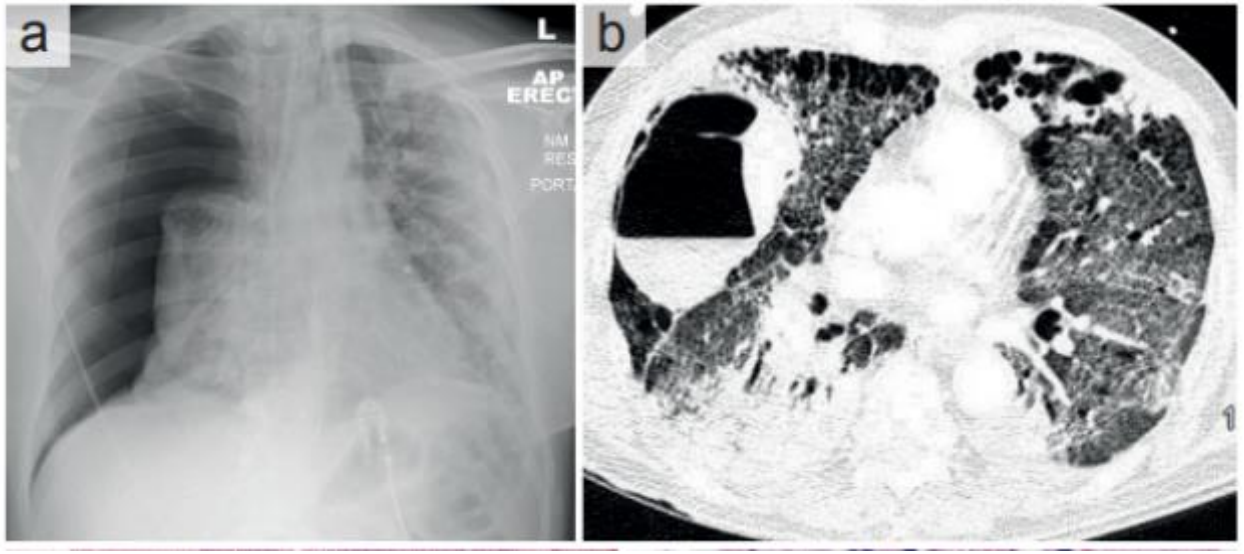
(A) Cardiomyocytes after exposure to SARS-CoV-2

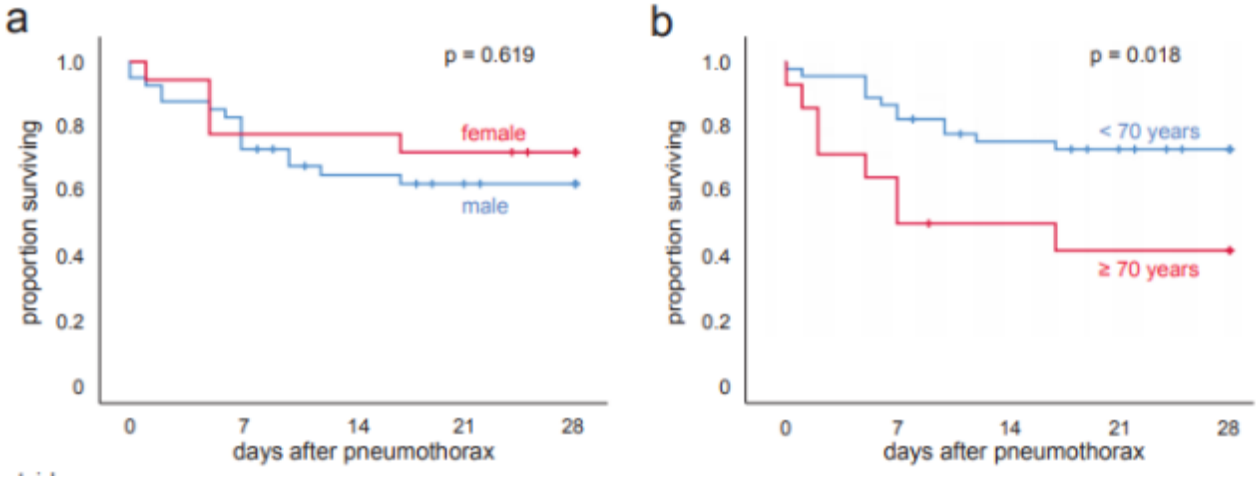
(B) Concentration of myofibril fragments



Pneumothoraces

- 71 cases of pneumothorax (60) or pneumomediastinum (11) or both (6) from 16 hospitals in UK
- 5% NIV, 44% ventilated, 20% ECMO
- 63% overall survival
- No difference in survival by sex
- Significant difference by age >70
- “We caution against therapeutic nihilism in the context of COVID-19 pneumothorax and active treatment should be continued where clinically possible.”

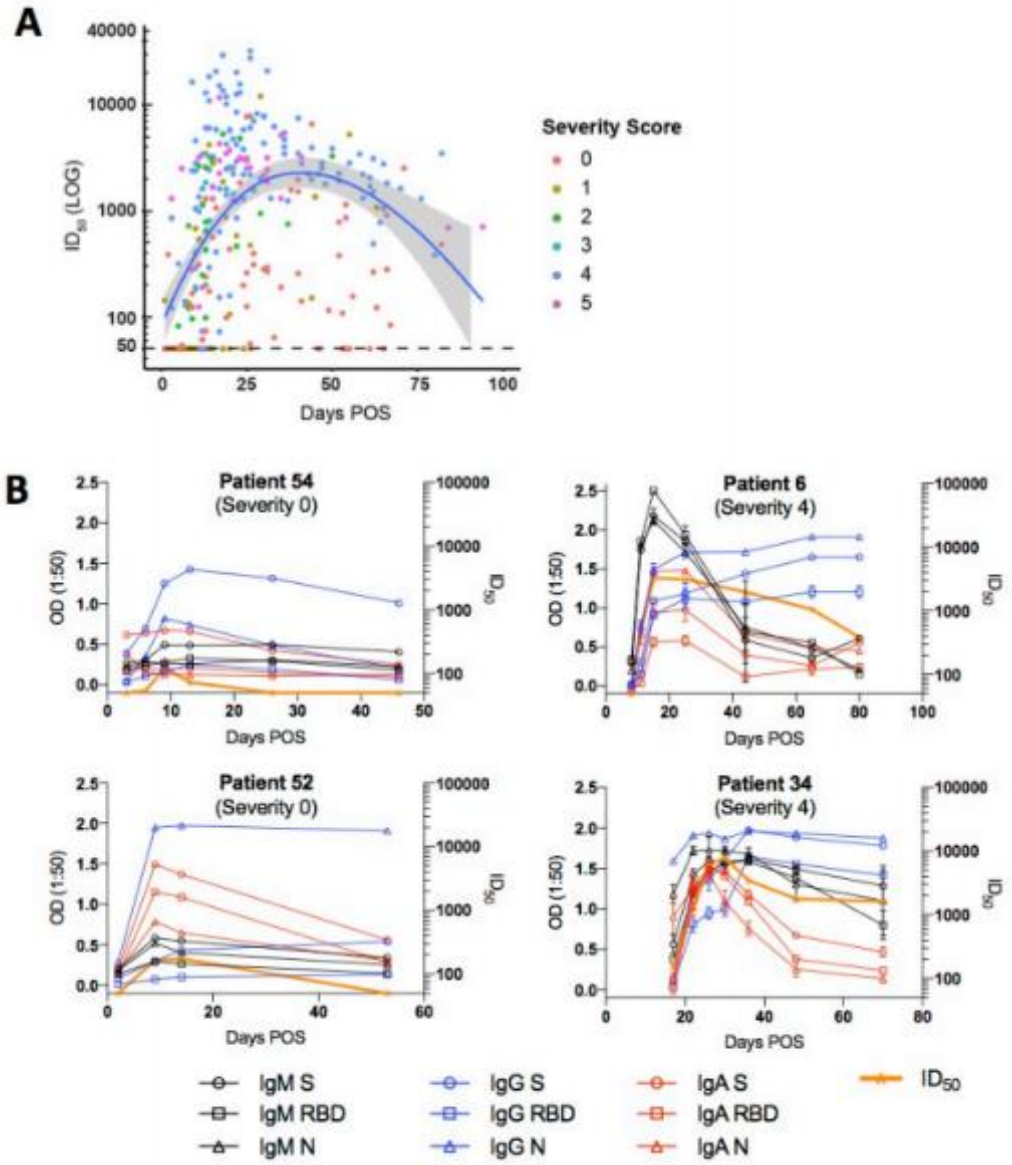




Martinelli et al. *European Respiratory Journal* 2020; **DOI:** 10.1183/13993003.02697-2020

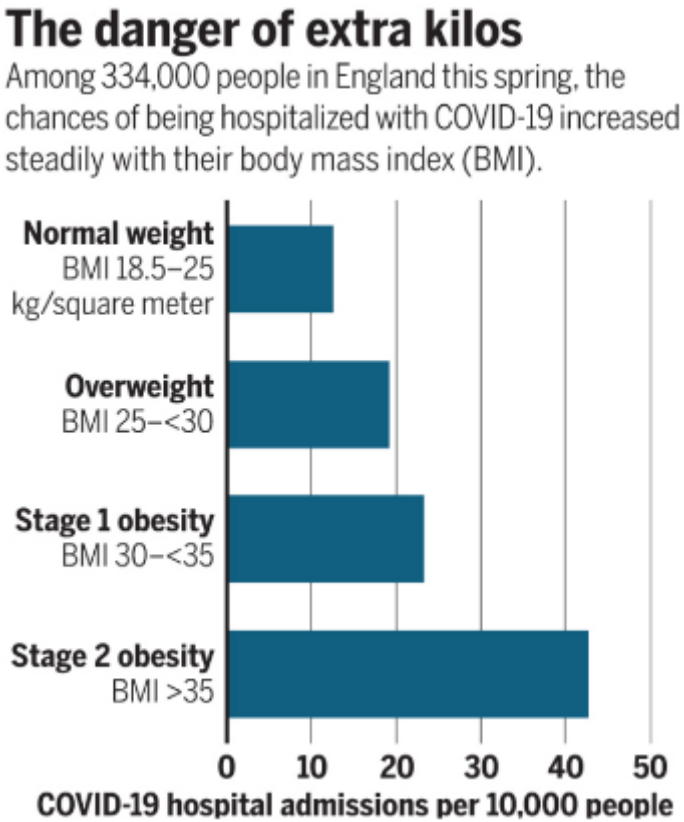
Longitudinal evaluation and decline of antibody responses in SARS-CoV-2 infection

- Sequential serum samples from 65 RT-qPCR confirmed pts
- Neutralizing antibody (nAb) response detected in >95% of cases
- Magnitude but not kinetics of nAb response dependent upon disease severity
- Declining nAb titers observed at 3-4 months
- While some individuals with high peak ID50 (>10,000) maintained titers >1,000 at >60 days POS, some with lower peak ID50 had titers approaching baseline within the follow up period
- Similar decline in nAb titres was also observed in a cohort of seropositive healthcare workers
- Transient nAb response is a feature shared by both a SARS-CoV-2 infection that causes low disease severity and the circulating seasonal coronaviruses that are associated with common colds



Obesity

- 40% of US adults are obese and 32% are overweight
- Metabolic syndrome substantially increases the risks of ICU admission, ventilation, and death. BMI is a strong independent risk factor for severe COVID-19 after adjusting for age, sex, social class, diabetes, and heart conditions
- Of nearly 17,000 patients hospitalized with COVID-19 in the US, 77% were overweight (29%) or obese (48%)
- More than one mechanism proposed:
  - Coagulopathy
  - T-cell response less robust
  - Cytokine response more robust
  - Hypoventilation of obesity and other cardiopulmonary problems
  - Health care access, poverty, and stigma

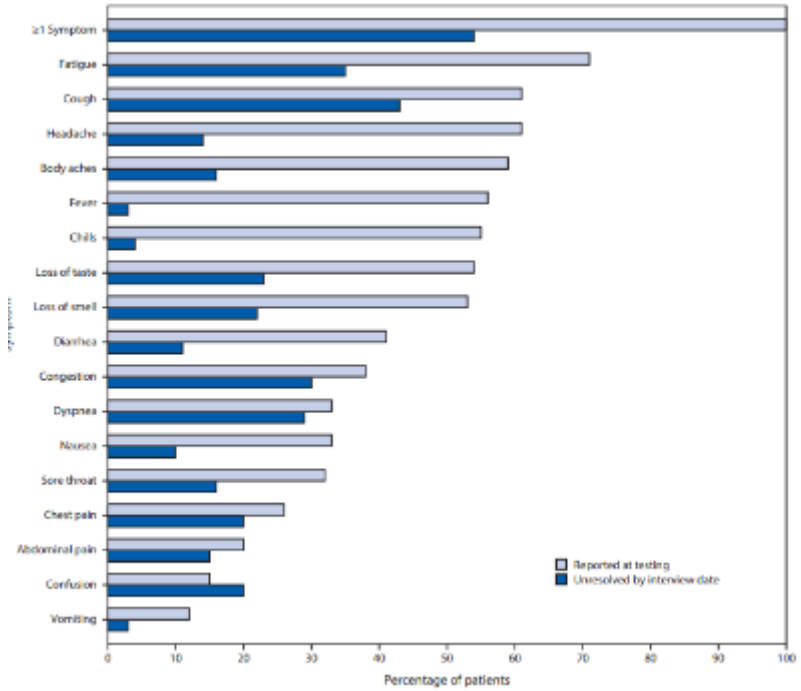


https://science.sciencemag.org/content/369/6509/1280

Duration of Symptoms / “Long-Haulers”

Morbidity and Mortality Weekly Report

Symptom Duration and Risk Factors for Delayed Return to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network — United States, March–June 2020



https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6930e1-H.pdf

ERS Studies Highlight Long-Term Effects of COVID-19

SEP 16, 2020 | BRIAN DUNLEAVY

In May, Brazilian president Jair Bolsonaro famously (or infamously) referred to COVID-19 as the “little flu.”

Clearly, the grim figures on deaths attributed to the virus—in his country, and elsewhere—have proved him wrong, but research presented during the European Respiratory Society International Congress on September 7 should also cause him to take note.

Together, the 2 studies suggest that COVID-19 patients may suffer long-term lung and heart damage—although, for many, it resolves over time.

For the first paper, researchers working in a COVID-19 “hotspot” in Austria recruited their first 86 consecutive patients in May and early June (they now have more than 150 enrolled). The patients returned for evaluation 6, 12 and 24 weeks following their discharge from St. Vinzenz Hospital in Zams and underwent clinical examination, laboratory test, analysis of the amounts of oxygen and carbon dioxide in arterial blood, lung function tests (FEV1 and DLCO), computed tomography (CT) scans, and echocardiograms at each visit.

https://www.contagionlive.com/news/ers-studies-highlight-longterm-effects-of-covid19

Reinfection Case Reports

ACCEPTED MANUSCRIPT

COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing FREE

Kelvin Kai-Wang To, Ivan Fan-Ngai Hung, Jonathan Daniel Ip, Allen Wing-Ho Chu, Wan-Mui Chan, Anthony Raymond Tam, Carol Ho-Yan Fong, Shuofeng Yuan, Hoi-Wah Tsoi, Anthony Chin-Ki Ng ... Show more

Author Notes

Clinical Infectious Diseases, ciaa1275, https://doi.org/10.1093/cid/ciaa1275

Published: 25 August 2020 **Article history** ▾

- 33 yo M with no chronic medical problems
- Diagnosis by SARS-CoV-2 RT-PCR both times
- First symptomatic episode in March 2020
  - Sore throat, cough, fever, headache; hospitalized for 2 weeks
- Second asymptomatic episode 142 days later (August 2020)
  - Diagnosed at airport screening while traveling from Spain → UK → HK
  - Elevated CRP, positive SARS-CoV-2 IgG
- Whole-genome sequencing showed two different clades/lineages of virus between episodes
- Compared to viral genomes in GISAID, the first virus genome has a stop codon at position 64 of orf8 leading to a truncation of 58 amino acids, and was phylogenetically closely related to strains collected in March/April 2020, while the second virus genome was closely related to strains collected in July/August 2020.
- Another 23 nucleotide and 13 amino acid differences located in 9 different proteins, including positions of B and T cell epitopes, were found between viruses from the first and second episodes.

Diagnostics

Testing News

The Good

- Growing selection of antigen tests
- Most require NP or nasal turbinates
- Most require laboratory processing
- Abbott Binax Now lateral flow assay approved by FDA (Sn 97.1%, Sp 98.5% c/w gold-standard PCR)
- “Lower barrier” but may miss infection with lower virus; prone to false-positives in a low-prevalence population
- May be useful for mass testing to identify and isolate those at highest risk of transmitting virus

The Bad

The Ugly

(CNN) — In a shift that perplexed some doctors, the US Centers for Disease Control and Prevention has changed its Covid-19 testing guidelines to say some people without symptoms may not need to be tested, eve
the virus.

Previously, the CDC said viral te
exposure, even if they were asy

Related Article: CDC was pressure
'from the top down' to change
coronavirus testing guidance, offici

CIDRAP Center for Infectious Disease Research and Policy

News & Perspective | Infectious Disease Topics | Antimicrobial Stewardship | Ongoing Programs

FEATURED NEWS TOPICS Novel Coronavirus | Ebola | MERS-CoV | Chronic Wasting Disease

Feds OK COVID-19 tests without FDA approval

Filed Under: COVID-19

Stephanie Soucheray | News Reporter | CIDRAP News | Aug 20, 2020

Share | Tweet | LinkedIn | Email | Print & PDF

Yesterday, the US Department Health and Human Services rescinded guidance that mandated that COVID-19 tests gain approval from the Food and Drug Administration (FDA) before use, under an executive order from President Donald Trump.

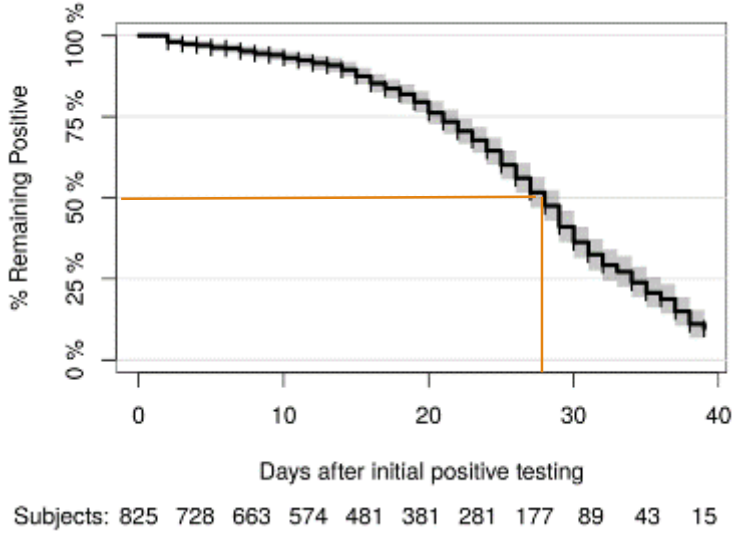
"As part of HHS's ongoing department-wide review of regulatory flexibilities enacted since the start of COVID-19, the department has determined that the Food and Drug Administration ("FDA") will not require premarket review of laboratory developed tests ("LDT") absent notice-and-comment rule making," HHS said in a document posted to its website yesterday.

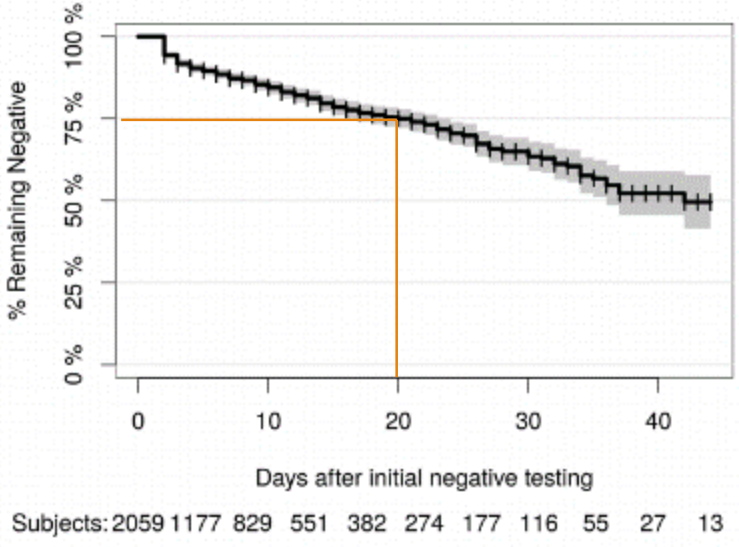
Governor Tom Wolf / Flickr cc

The decision will allow private and commercial laboratories to manufacture and administer tests, including labs controlled by Quest Diagnostics and LabCorp. According to Politico, most COVID-19 tests currently used in the United States are made by device manufacturers and thus subject to FDA review.

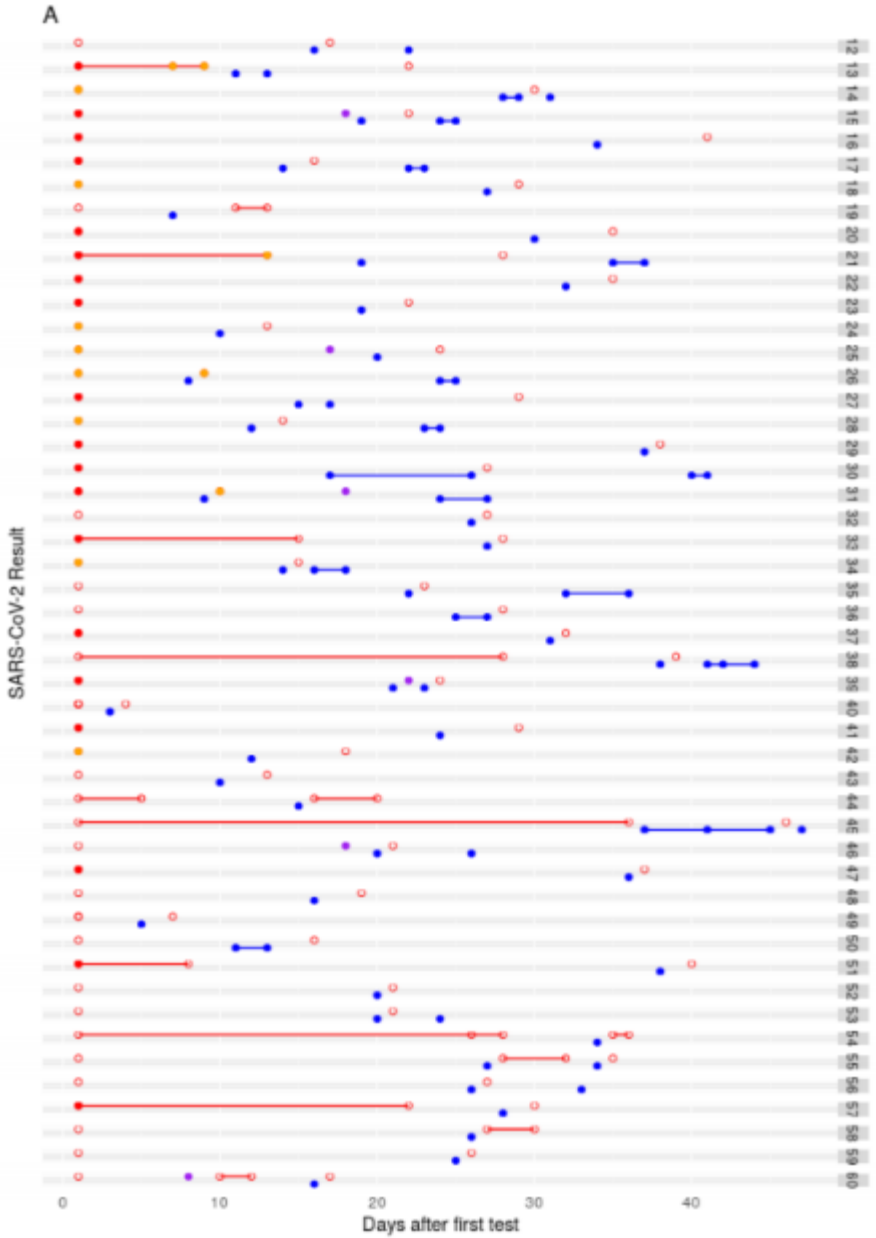
Clinical Performance of PCR Tests for SARS-CoV-2

- Clinical performance of PCR for SARS-CoV-2 is still incompletely understood
- 3/10/2020-5/1/2020, NY-Pres, 27,377 SARS-CoV-2 molecular assays from 22,338 patients
  - Roche Cobas system and Cornell-NYP in-house molecular assay under FDA EUA
  - Repeat testing for 3,432 (15%) patients (2,413 had initial negative, 802 initial positive)
- Repeat-tested patients were more likely to have severe disease and low viral loads
  - Positive patients more likely to be male, >44 years, African-American or Hispanic/Latino (p<0.0001)
  - Patients with positive PCR had higher mortality (6.2% vs. 3.8%, 159 p=0.048), presence of symptoms (91.8% vs. 72.4%, p=0.004), need for intubation (10.7% 160 vs. 7%, p=0.026) and frequency of decompensation (13.4% vs. 8.4%, p=0.005)
  - **NPV** of the first day result among repeat-tested patients was **81.3%**
- Clinical sensitivity of SARS-CoV-2 molecular assays was estimated between 58% and 96%
- Conversion from (+) to (-) was unlikely to occur before 15-20 days after initial testing or 20-30 days after onset of symptoms, with **50% conversion occurring at 28 days after initial testing**
- Conversion from (-) to (+) increased linearly with each day of testing, reaching **25% in 20 days**
- 60 patients fluctuated between positive and negative results over several weeks
- Suggests time frame for appropriate repeat testing is **15-20 days after a positive test** and the **same or next 2 days after a negative test in patients with high suspicion** for COVID-19

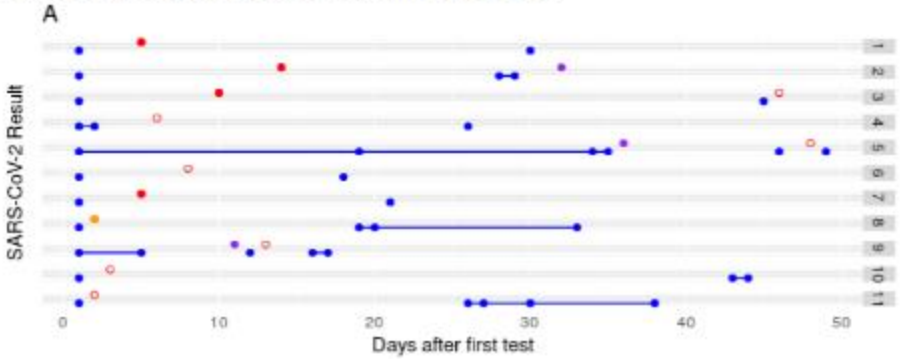




https://jcm.asm.org/content/early/2020/06/08/JCM.00995-20



Supplementary Figure 2: SARS-CoV-2 results from repeat-tested patients that converted from negative to positive and back to negative (**A**) or from positive to negative and back to positive (**B**). SARS-CoV-2 negative results are represented by blue dots, indeterminate results by purple dots, and positive results are in orange (Target1 Ct value > 30), filled red (Target1 Ct value <= 30), or open red dots (Ct not available), plotted on a time scale from the date of the first test



https://jcm.asm.org/content/early/2020/06/08/JCM.00995-20

Lowering the Barrier: Saliva Testing

› Clin Infect Dis. 2020 Aug 6;ciaa1156. doi: 10.1093/cid/ciaa1156. Online ahead of print.

Comparing nasopharyngeal swab and early morning saliva for the identification of SARS-CoV-2

Mohan Rao [1], Fairuz A Rashid [1], Fashihah S A H Sabri [1], Nur Nadia Jamil [1], Rozainanee Zain [1], Rohaidah Hashim [1], Fairuz Amran [1], Huey Tean Kok [2], Md Anuar Abd Samad [2], Norazah Ahmad [1]

› Clin Infect Dis. 2020 Sep 2;ciaa1314. doi: 10.1093/cid/ciaa1314. Online ahead of print.

No One Likes a Stick up Their Nose: Making the Case for Saliva-Based Testing for COVID-19

Farhana Ali [1], Daniel A Sweeney [2]

Affiliations + expand

PMID: 32875330 DOI: 10.1093/cid/ciaa1314

Figure 1

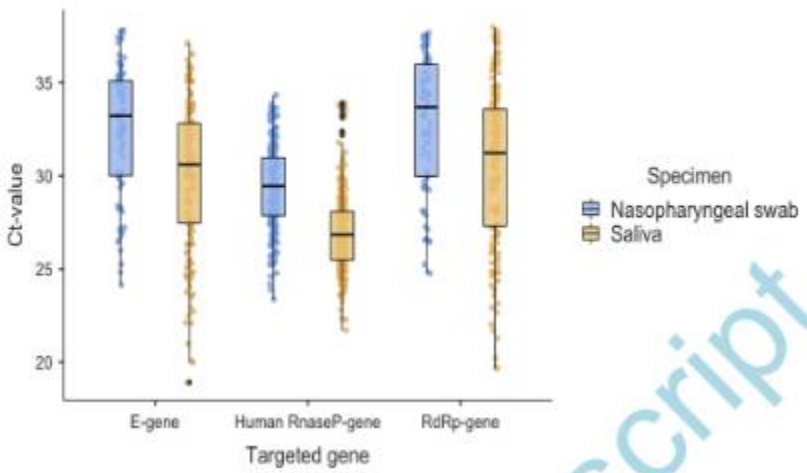
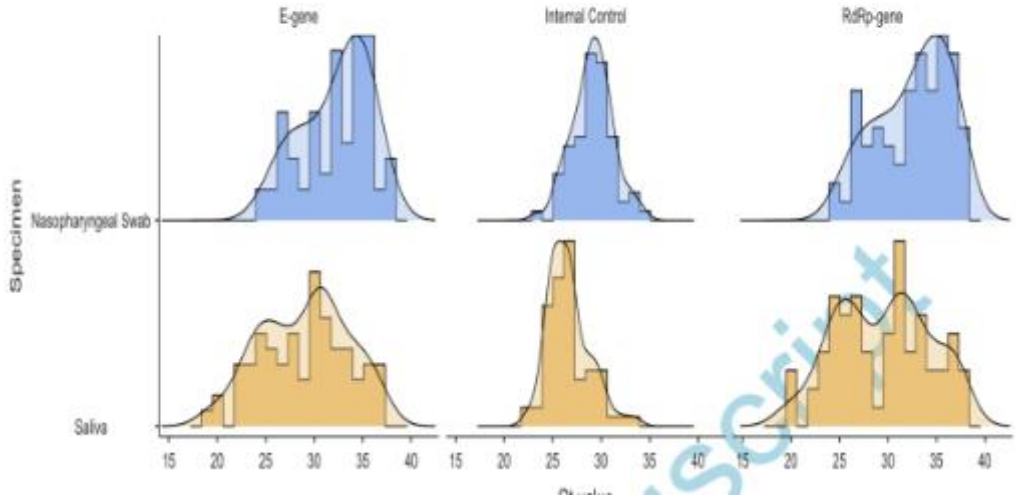
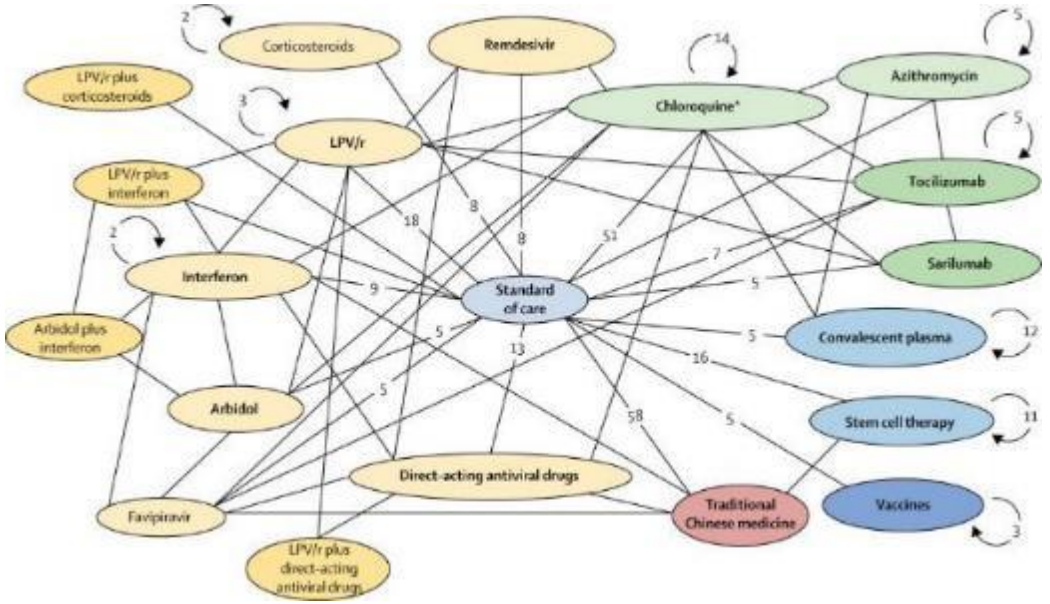
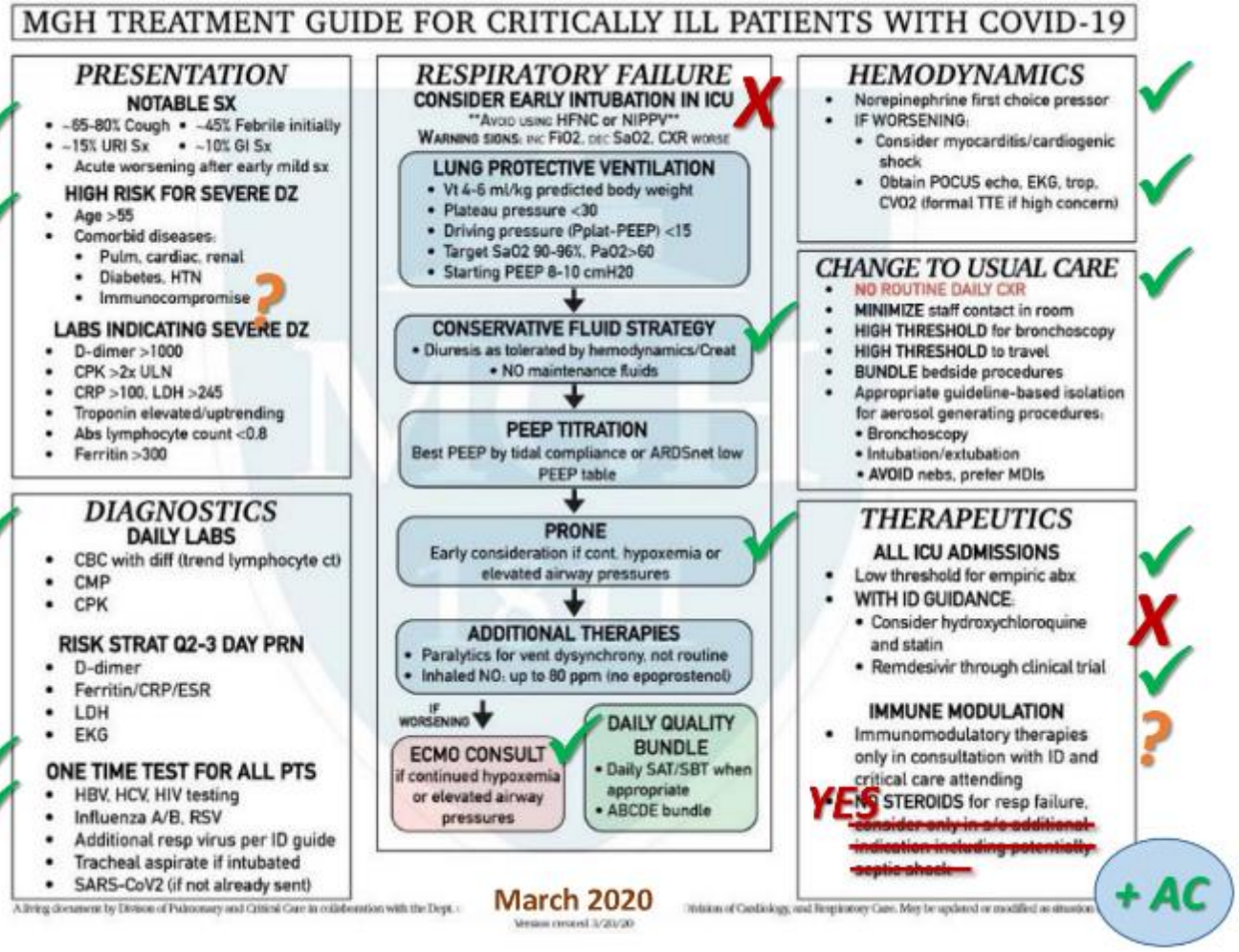


Figure 2




Corticosteroids
Remdesivir
Azithromycin
Chloroquine*
LPV/r plus corticosteroids
LPV/r
LPV/r plus interferon
Tocilizumab
Sarilumab
Interferon
Standard of care
Arbidol plus interferon
Convalescent plasma
Arbidol
Stem cell therapy
Direct-acting antiviral drugs
Favipiravir
Traditional Chinese medicine
Vaccines
LPV/r plus direct-acting antiviral drugs

Treatment

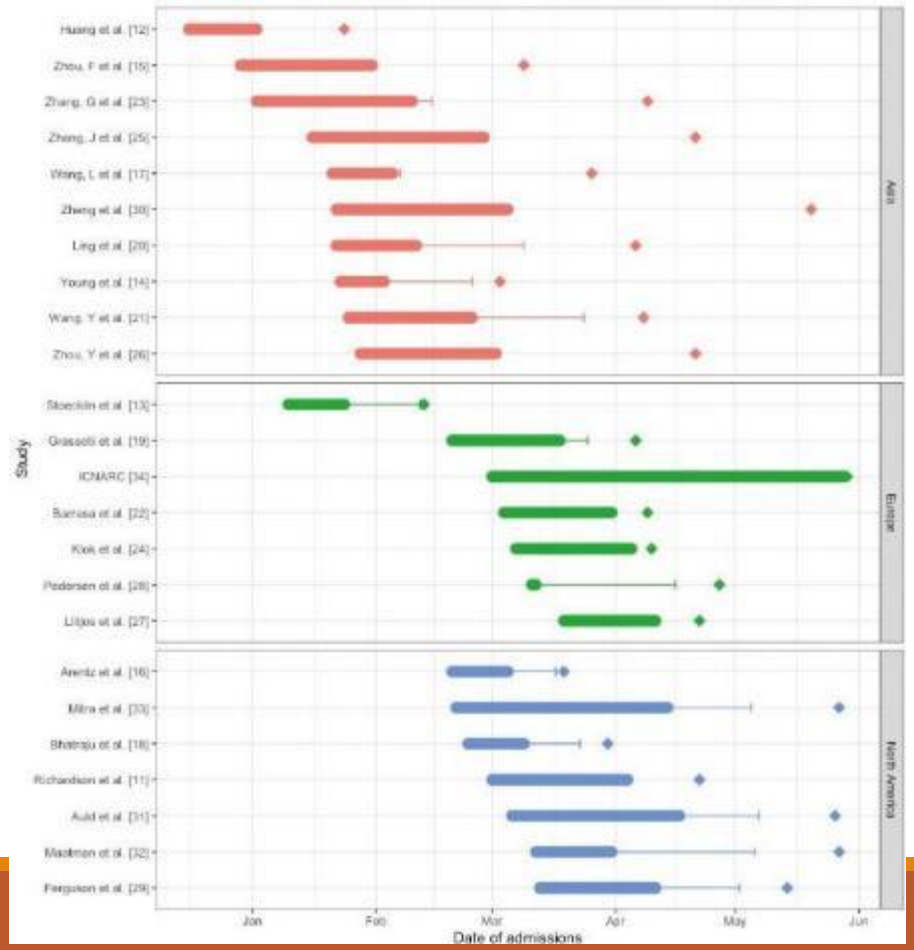

MGH TREATMENT GUIDE FOR CRITICALLY ILL PATIENTS WITH COVID-19
PRESENTATION
NOTABLE SX
~65-80% Cough • ~45% Febrile initially
~15% URI Sx • ~10% GI Sx
Acute worsening after early mild sx
HIGH RISK FOR SEVERE DZ
Age >55
Comorbid diseases:
Pulm, cardiac, renal
Diabetes, HTN
Immunocompromise
LABS INDICATING SEVERE DZ
D-dimer >1000
CPK >2x ULN
CRP >100, LDH >245
Troponin elevated/uptrending
Abs lymphocyte count <0.8
Ferritin >300
DIAGNOSTICS
DAILY LABS
CBC with diff (trend lymphocyte ct)
CMP
CPK
RISK STRAT Q2-3 DAY PRN
D-dimer
Ferritin/CRP/ESR
LDH
EKG
ONE TIME TEST FOR ALL PTS
HBV, HCV, HIV testing
Influenza A/B, RSV
Additional resp virus per ID guide
Tracheal aspirate if intubated
SARS-CoV2 (if not already sent)
RESPIRATORY FAILURE
CONSIDER EARLY INTUBATION IN ICU
Avoid using HFNC or NIPPV
Warning signs: inc FiO2, dec SaO2, CXR worse
LUNG PROTECTIVE VENTILATION
Vt 4-6 ml/kg predicted body weight
Plateau pressure <30
Driving pressure (Pplat-PEEP) <15
Target SaO2 90-96%, PaO2>60
Starting PEEP 8-10 cmH20
CONSERVATIVE FLUID STRATEGY
Diuresis as tolerated by hemodynamics/Creat
NO maintenance fluids
PEEP TITRATION
Best PEEP by tidal compliance or ARDSnet low PEEP table
PRONE
Early consideration if cont. hypoxemia or elevated airway pressures
ADDITIONAL THERAPIES
Paralytics for vent dysynchrony, not routine
Inhaled NO: up to 80 ppm (no epoprostenol)
IF WORSENING
ECMO CONSULT
if continued hypoxemia or elevated airway pressures
DAILY QUALITY BUNDLE
Daily SAT/SBT when appropriate
ABCDE bundle
HEMODYNAMICS
Norepinephrine first choice pressor
IF WORSENING:
Consider myocarditis/cardiogenic shock
Obtain POCUS echo, EKG, trop, CVO2 (formal TTE if high concern)
CHANGE TO USUAL CARE
NO ROUTINE DAILY CXR
MINIMIZE staff contact in room
HIGH THRESHOLD for bronchoscopy
HIGH THRESHOLD to travel
BUNDLE bedside procedures
Appropriate guideline-based isolation for aerosol generating procedures:
Bronchoscopy
Intubation/extubation
AVOID nebs, prefer MDIs
THERAPEUTICS
ALL ICU ADMISSIONS
Low threshold for empiric abx
WITH ID GUIDANCE:
Consider hydroxychloroquine and statin
Remdesivir through clinical trial
IMMUNE MODULATION
Immunomodulatory therapies only in consultation with ID and critical care attending
NO STEROIDS for resp failure,
YES
March 2020
+ AC

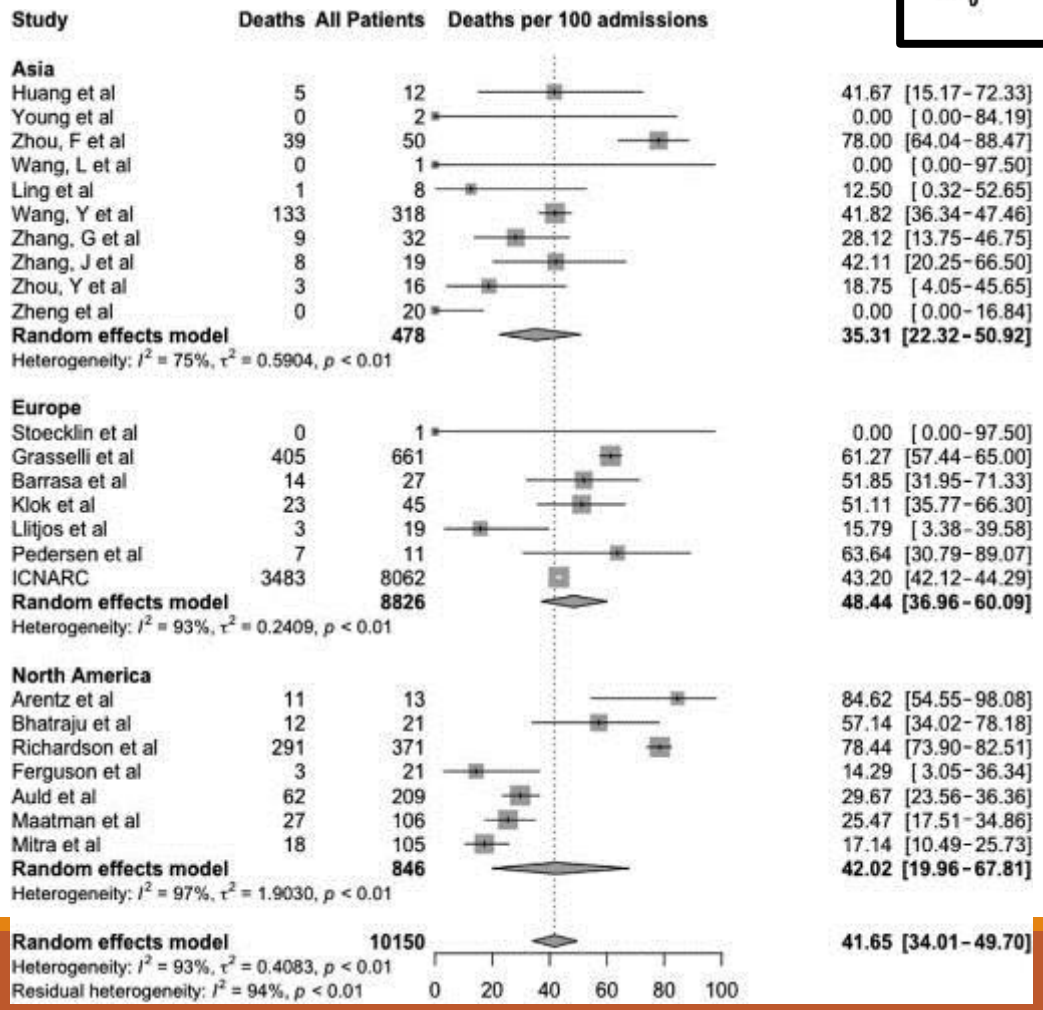
Anaesthesia
Peri-operative medicine, critical care and pain
Association of Anaesthetists

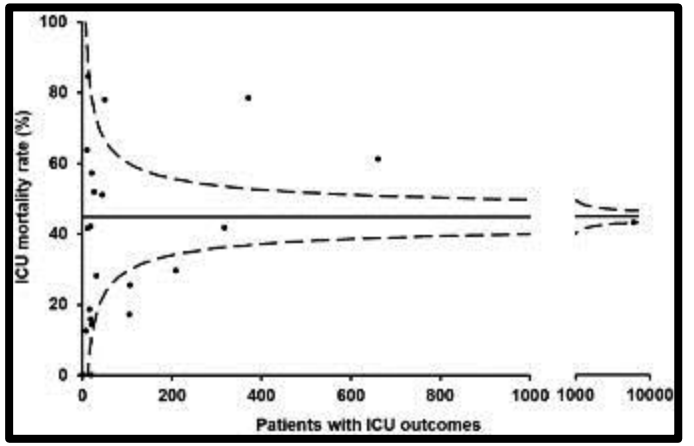
Review Article | Free Access

Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies

R. A. Armstrong, A. D. Kane, T. M. Cook



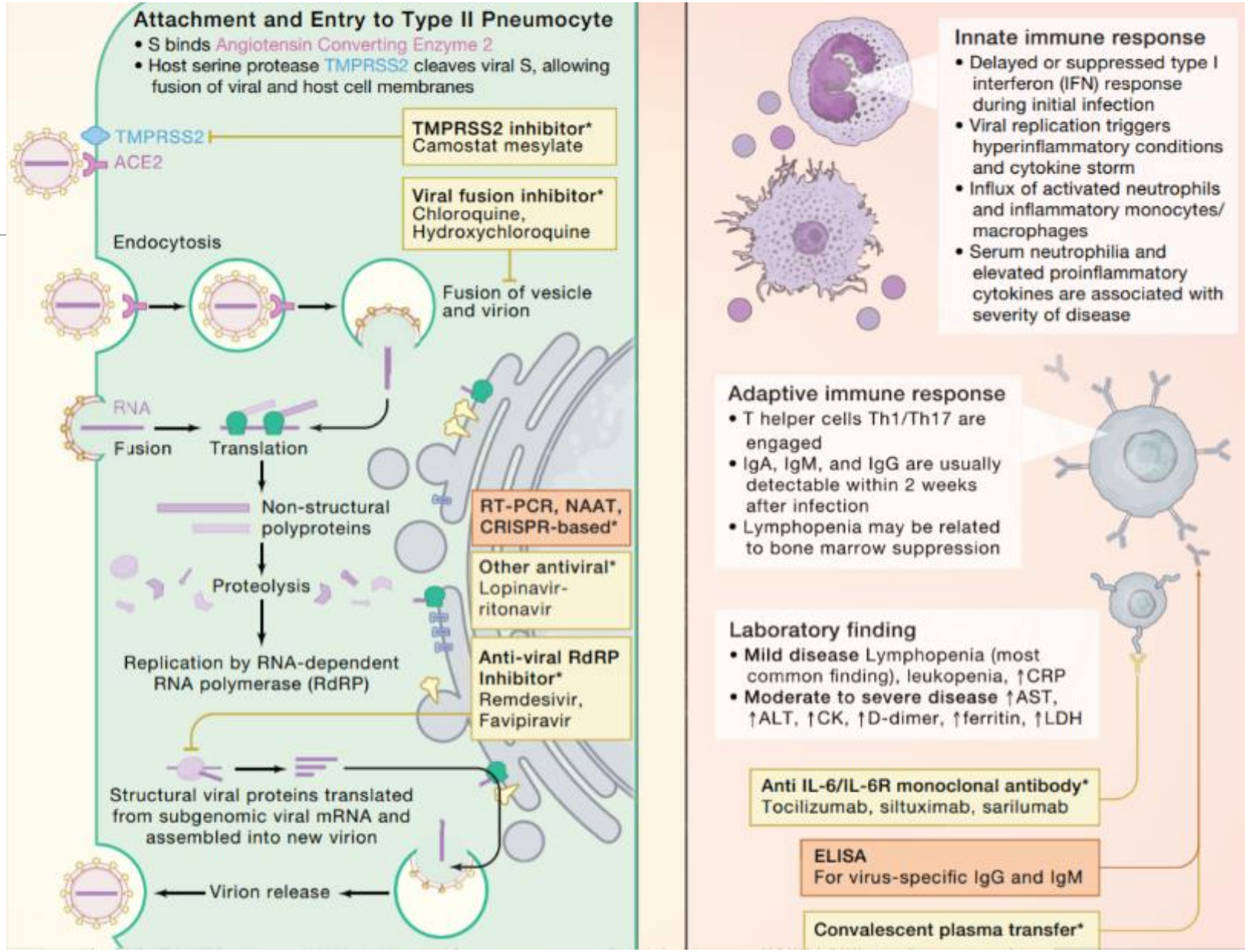




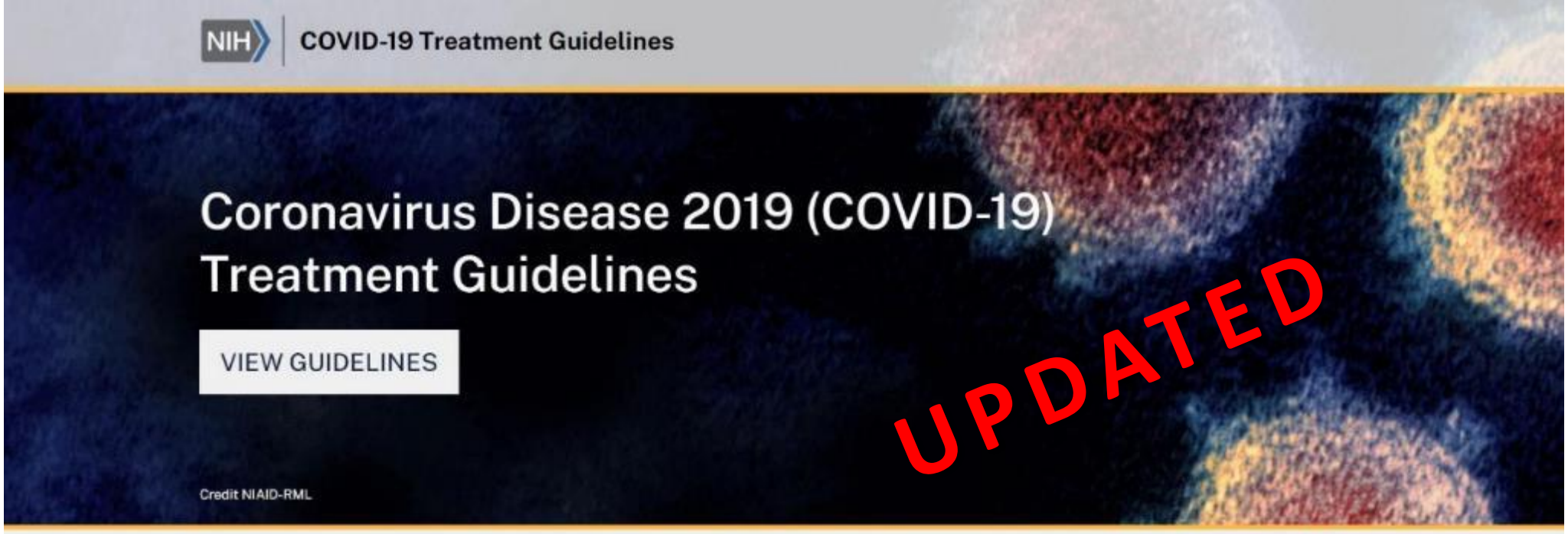
Targets

1. Cell entry
2. Viral replication
3. Inflammatory cascade
4. Passive immunity (IgG)
5. Active immunity (vax)

6. Supportive care
7. Doing No Harm

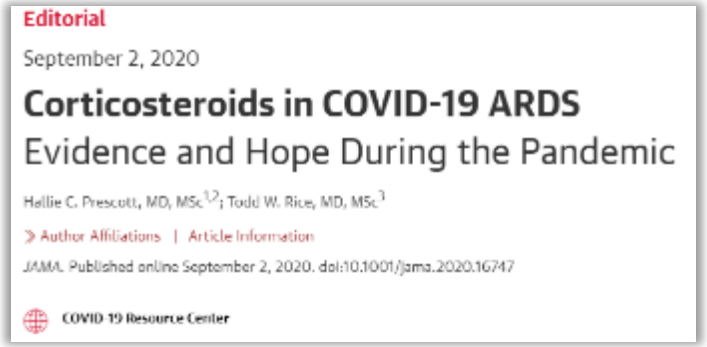


Oberfeld et al., Cell, May 2020



- There are **insufficient data** to recommend either for or against the use of convalescent plasma for the treatment of COVID-19. Convalescent plasma should not be considered the standard of care for the treatment of patients with COVID-19.
- The Panel **recommends against** the use of anti-IL-6 receptor monoclonal antibodies (**e.g., sarilumab, tocilizumab**) or an anti-IL-6 monoclonal antibody (**siltuximab**) for the treatment of COVID-19, except in a clinical trial **(BI)**.
- The Panel **recommends against** the use of **chloroquine** or **hydroxychloroquine** for the treatment of COVID-19 in hospitalized patients **(AI)**.
- In nonhospitalized patients, the Panel **recommends against** the use of **chloroquine** or **hydroxychloroquine** for the treatment of COVID-19, except in a clinical trial **(AI)**.
- The Panel **recommends against** the use of **ivermectin** for the treatment of COVID-19, except in a clinical trial **(AIII)**.

Dexamethasone


Editorial

September 2, 2020

Corticosteroids in COVID-19 ARDS

Evidence and Hope During the Pandemic

Hallie C. Prescott, MD, MSc[1,2]; Todd W. Rice, MD, MSc[3]

Author Affiliations | Article Information

JAMA. Published online September 2, 2020. doi:10.1001/jama.2020.16747

COVID-19 Resource Center

- **CODEX Trial:** IV dexamethasone plus standard care, compared with standard of care alone, resulted in a statistically significant increase in the number of days alive and free of mechanical ventilation (6.6 days vs 4.0 days) over 28 days in this RCT involving 299 patients in Brazil.
- **WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group:** In this prospective meta-analysis of 7 randomized trials that included 1703 patients of whom 647 died, 28-day all-cause mortality was lower among patients who received corticosteroids compared with those who received usual care or placebo (summary odds ratio, 0.66).
- **REMAP-CAP Trial:** In this Bayesian RCT of 403 patients, a 7-day fixed-dose course of hydrocortisone or shock-dependent dosing of hydrocortisone, compared with no hydrocortisone, resulted in 93% and 80% probabilities of superiority, respectively, in odds of improvement in organ support–free days within 21 days. Although suggestive of benefit for hydrocortisone in patients with severe COVID-19, the trial was stopped early and no treatment strategy met prespecified criteria for statistical superiority, precluding definitive conclusions.
- **NCT02517489:** In this RCT of 149 patients in France which was terminated early following the recommendation of the data and safety monitoring board, there was no significant difference in the rate of treatment failure (defined as death or persistent respiratory support with mechanical ventilation or high-flow oxygen therapy) on day 21 between the hydrocortisone and placebo groups (42.1% vs 50.7%, respectively).

Remdesivir


Original Investigation ONLINE FIRST FREE

August 21, 2020

Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19

A Randomized Clinical Trial

Christoph D. Spinner, MD[1]; Robert L. Gottlieb, MD, PhD[2]; Gerard J. Criner, MD[3]; et al

> Author Affiliations | Article Information

JAMA. Published online August 21, 2020. doi:10.1001/jama.2020.16349

JAMA Network

QUESTION Does remdesivir provide a benefit on clinical status for patients hospitalized with moderate COVID-19 pneumonia?

CONCLUSION This clinical trial found that hospitalized patients with moderate COVID-19 randomized to a 5-day course, but not a 10-day course, of remdesivir had a statistically significant better clinical status vs standard care at 11 days, but the difference was of uncertain clinical importance.

POPULATION

357 Men
227 Women

Patients hospitalized with moderate COVID-19 pneumonia (pulmonary infiltrates plus room air oxygen >94%)

Median age: **57** years

LOCATIONS

105 Hospitals in the United States, Europe, and Asia

INTERVENTION

596 Patients randomized
584 Patients analyzed

193 10-Day remdesivir
IV remdesivir, 200 mg on day 1, followed by 100 mg/d

191 5-Day remdesivir
IV remdesivir, 200 mg on day 1, followed by 100 mg/d

200 Standard care

PRIMARY OUTCOME

Clinical status on day 11 rated on a categorical scale (1 = death , 7 = discharged) reported as odds ratio (OR >1 indicates difference in clinical status toward category 7 for remdesivir)

FINDINGS

Clinical status on day 11

The difference in the primary outcome indicating better clinical status at day 11 was **statistically significant** for the 5-day remdesivir group compared with the standard care group:

OR = **1.65** (95% CI, 1.09 to 2.48);
5-day remdesivir vs standard care, *P* = .02

The difference in the primary outcome indicating better clinical status at day 11 was **not statistically significant** for the 10-day remdesivir group compared with the standard care group:

10-day remdesivir vs standard care, *P* = .18

Spinner CD, Gottlieb RL, Criner GJ, et al; for the GS-US-540-5774 Investigators. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. *JAMA*. Published online August 21, 2020. doi:10.1001/jama.2020.16349

Remdesivir

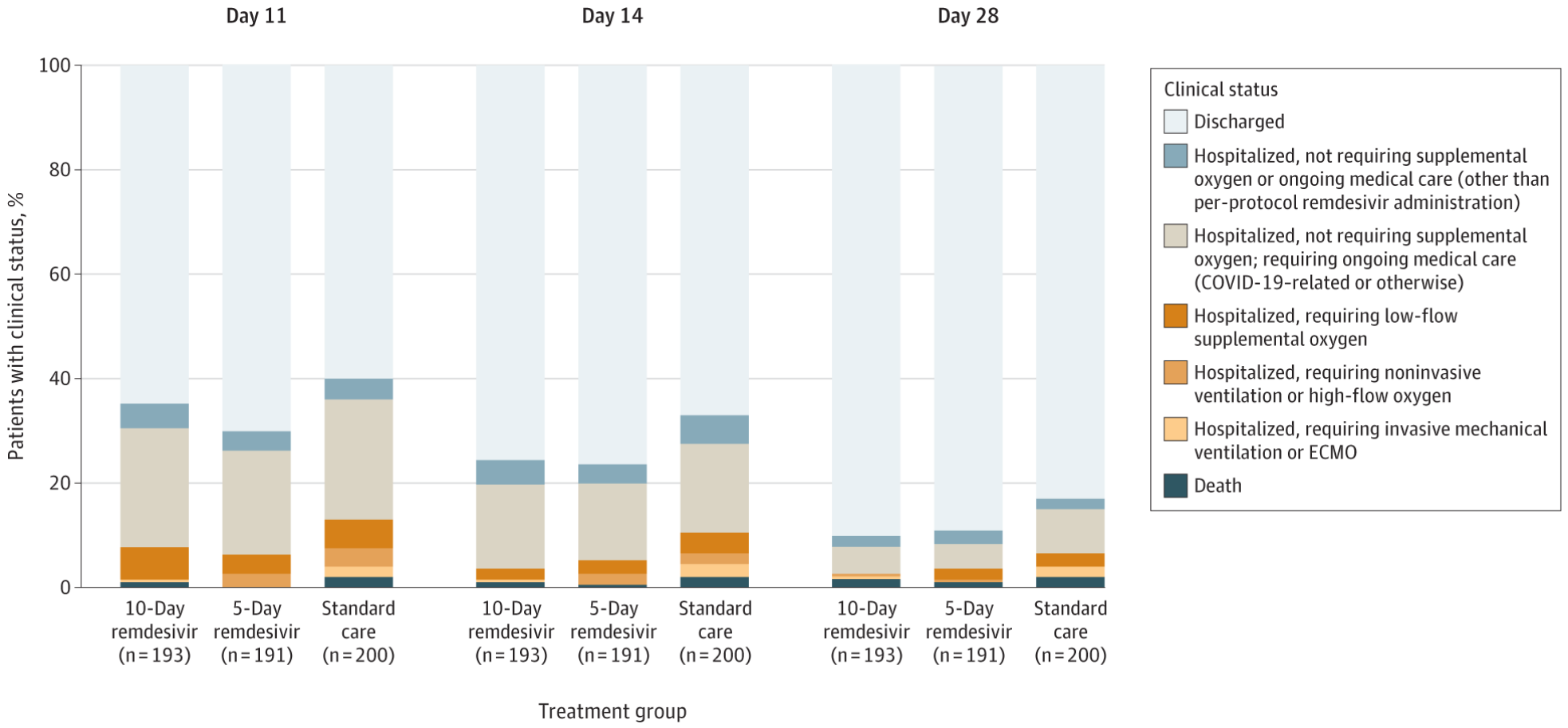
Original Investigation
ONLINE FIRST FREE
August 21, 2020

Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19

A Randomized Clinical Trial

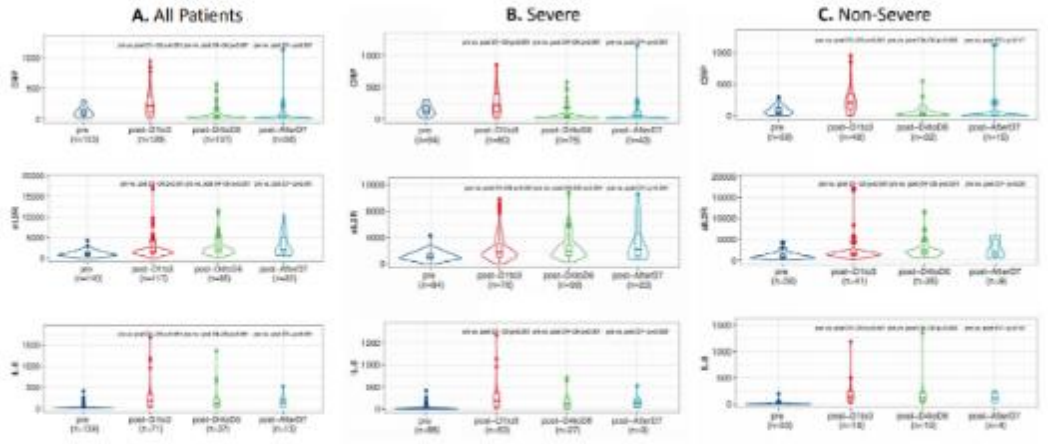
Christoph D. Spinner, MD[1]; Robert L. Gottlieb, MD, PhD[2]; Gerard J. Criner, MD[3]; et al
> Author Affiliations | Article Information

JAMA. Published online August 21, 2020. doi:10.1001/jama.2020.16349



Tocilizumab

Figure 3B: Inflammatory biomarker status relative to pre-tocilizumab administration over 14 days*



* hsCRP and IL-6 levels significantly decreased over 14 days, initially with an increase in IL-6 levels during the first 72 hours after administration. sIL2R levels, however, significantly increased over time for both severe and non-severe patients. D-dimer levels (not depicted here), significantly increased for non-severe (+0·67, 95%CI 0·31, 1·3; p<0.001) and severe patients (+1·09, 0·62, 1·9; p<0.001). Temperature also significantly decreased a similar amount in both non-severe and non-severe (-1·35, 95%CI -1·65, -1; p<0.001).

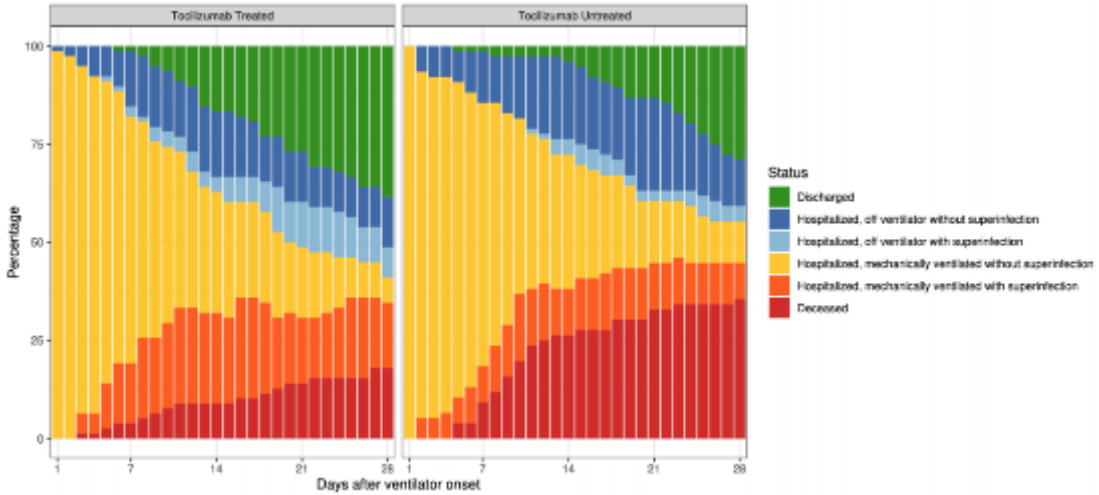
Price et al., *Chest*, DOI: https://doi.org/10.1016/j.chest.2020.06.006

ACCEPTED MANUSCRIPT

Tocilizumab for treatment of mechanically ventilated patients with COVID-19

Emily C Somers, PhD ScM, Gregory A Eschenauer, PharmD, Jonathan P Troost, PhD, Jonathan L Golob, MD PhD, Tejal N Gandhi, MD, Lu Wang, PhD, Nina Zhou, MS, Lindsay A Petty, MD, Ji Hoon Baang, MD, Nicholas O Dillman, PharmD ... Show more
Author Notes

Clinical Infectious Diseases, ciaa954, https://doi.org/10.1093/cid/ciaa954
Published: 11 July 2020 **Article history**



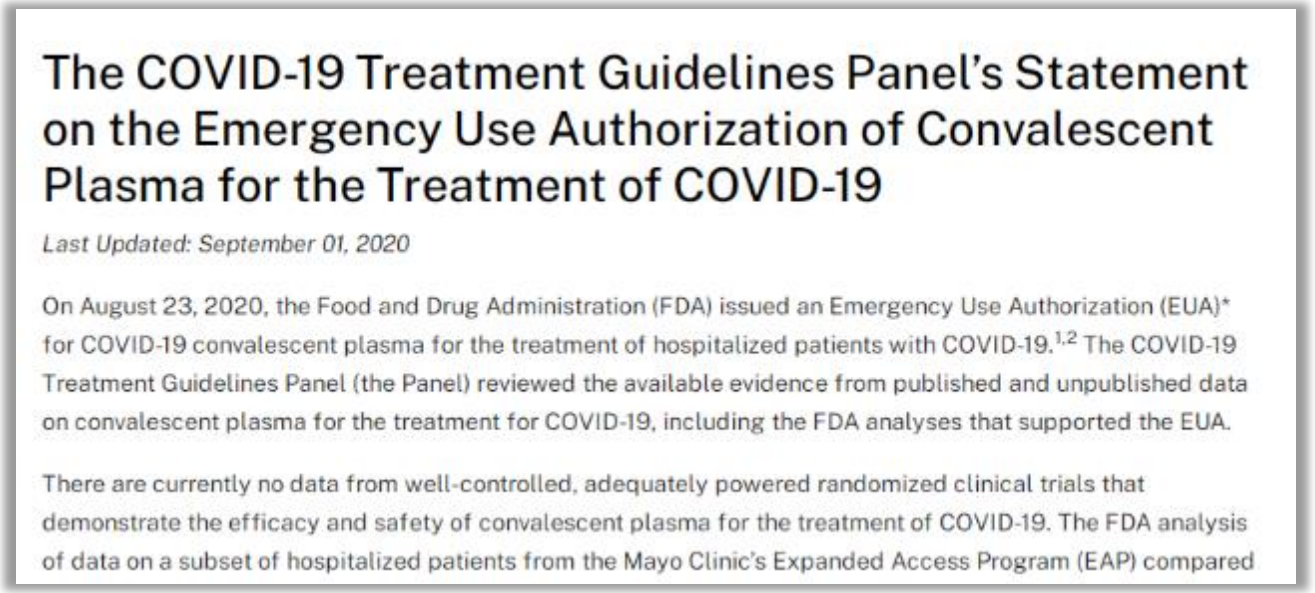
Convalescent Plasma

FDA NEWS RELEASE

FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID-19 Treatment, Another Achievement in Administration's Fight Against Pandemic

Share Tweet LinkedIn Email Print

For Immediate Release: August 23, 2020



The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Convalescent Plasma for the Treatment of COVID-19

Last Updated: September 01, 2020

On August 23, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA)* for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19.[1,2] The COVID-19 Treatment Guidelines Panel (the Panel) reviewed the available evidence from published and unpublished data on convalescent plasma for the treatment for COVID-19, including the FDA analyses that supported the EUA.

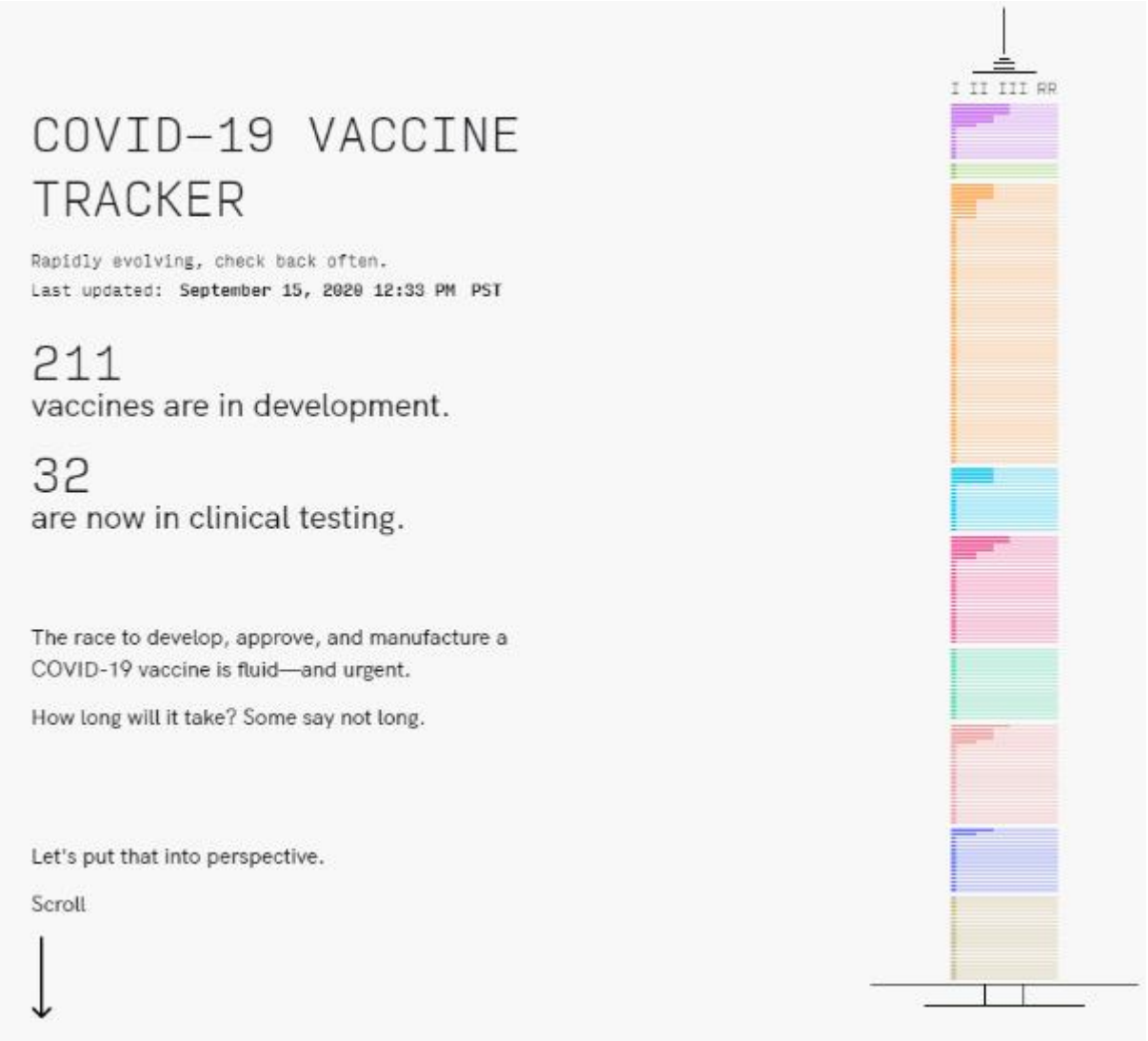
There are currently no data from well-controlled, adequately powered randomized clinical trials that demonstrate the efficacy and safety of convalescent plasma for the treatment of COVID-19. The FDA analysis of data on a subset of hospitalized patients from the Mayo Clinic's Expanded Access Program (EAP) compared

Key limitations:

- Neutralizing antibody titers
- Stage of disease at which given
- Difficulty in attributing effects when multiple modalities of treatment given

https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment

Vaccine Development



https://www.covid-19vaccinetracker.org/

SPUTNIK-V

- 76 participants in Phase I/II studies
- Gamaleya Institute in Moscow, funded by Russian Direct Investment Fund
- Phase III trials with 40,000 participants ongoing, vaccine released for use in Russia
- Recombinant adenovirus type 26 (rAd26) and type 5 (rAd5) vectors carrying gene for SARS-CoV-2 spike protein
- Reported strong positive antibody response through day 42 and good safety profile
- Data availability and validity in question

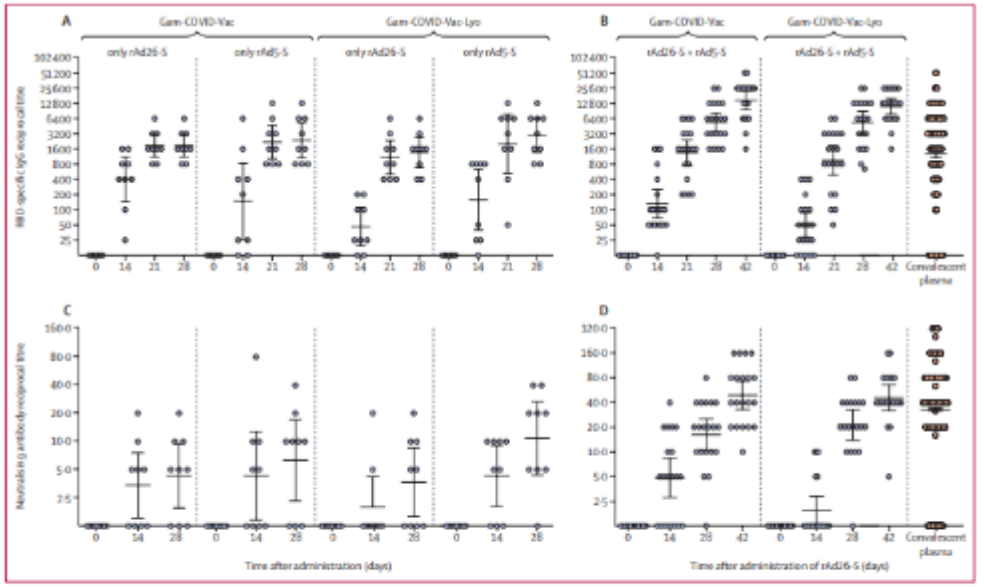


Figure 2: Humoral immune response
Data are geometric mean titres and 95% CIs. (A) RBD-specific antibodies on days 0, 14, 21, and 28, as measured by ELISA, in participants vaccinated with rAd26-S or rAd5-S only. (B) RBD-specific antibodies on days 0, 14, 21, 28, and 42, as measured by ELISA, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. (C) Neutralising antibodies on days 0, 14, and 28, as measured by neutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S or rAd5-S only. (D) Neutralising antibodies on days 0, 14, 28, and 42, as measured by microneutralisation assay with 100 TCID50, in participants vaccinated with rAd26-S on day 0 and rAd5-S on day 21. RBD-specific IgGs and neutralising antibodies of in convalescent plasma are also shown in (B) and (D).
Gam-COVID-Vac=frozen vaccine formulation. Gam-COVID-Vac-Lyo=lyophilised vaccine formulation. rAd26-S=recombinant adenovirus type 26 carrying the gene for SARS-CoV-2 full-length glycoprotein S. rAd5-S=recombinant adenovirus type 5 carrying the gene for SARS-CoV-2 full-length glycoprotein S. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. RBD=receptor-binding domain. TCID50=50% tissue culture infective dose.

https://cattiviscienziati.com/2020/09/07/note-of-concern/

AstraZeneca

EXCLUSIVE

AstraZeneca Covid-19 vaccine study put on hold due to suspected adverse reaction in participant in the U.K.

By REBECCA ROBBINS @rebeccadrobbins, ADAM FEUERSTEIN @adamfeuerstein, and HELEN BRANSWELL @HelenBranswell
/ SEPTEMBER 8, 2020

Reprints

EXCLUSIVE

Covid-19 vaccine trial participant had serious neurological symptoms, but could be discharged today, AstraZeneca CEO says

By ADAM FEUERSTEIN @adamfeuerstein / SEPTEMBER 9, 2020

Reprints

https://www.statnews.com/2020/09/09/astrazeneca-covid19-vaccine-trial-hold-patient-report/

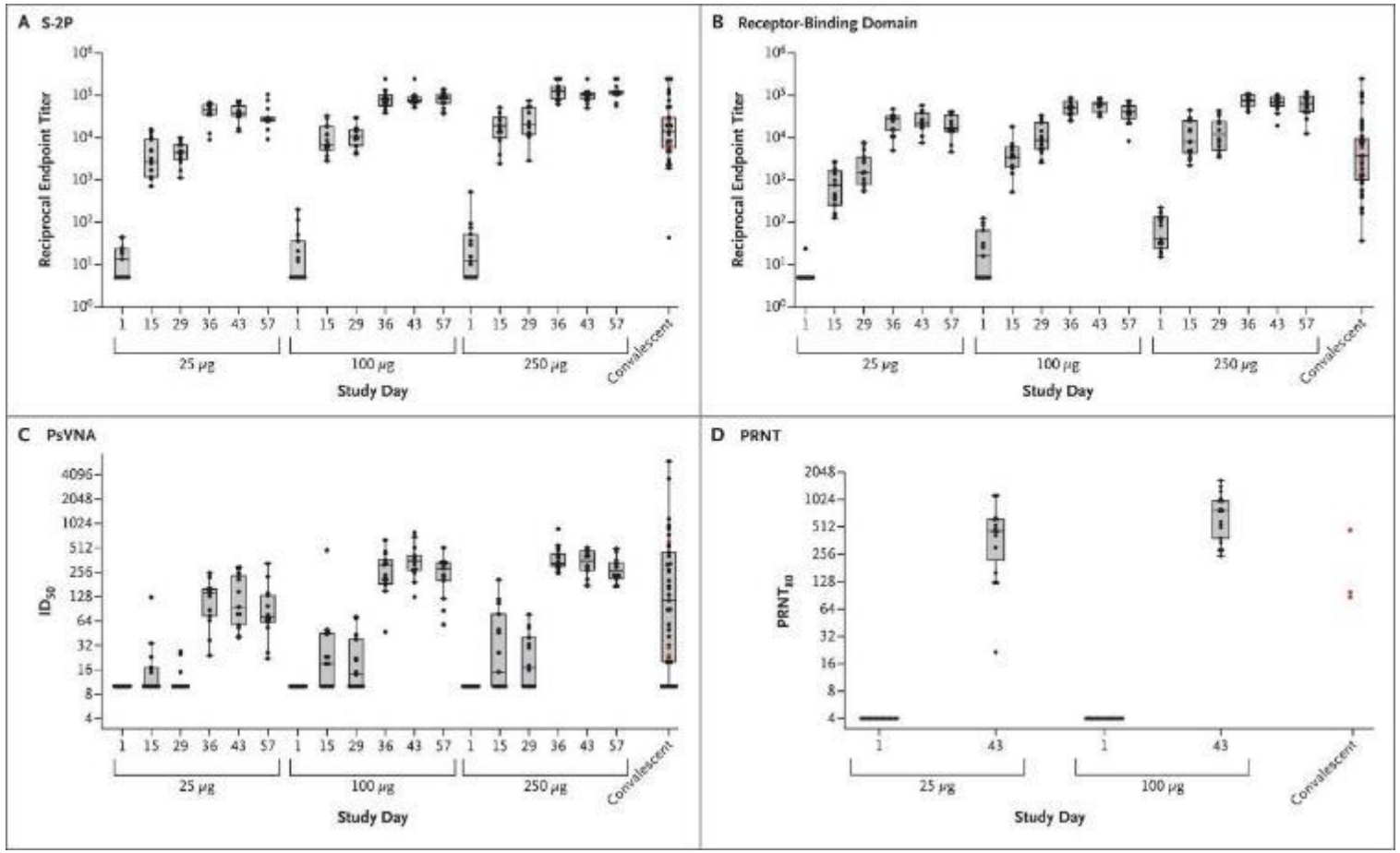
Moderna mRNA Vaccine Candidate

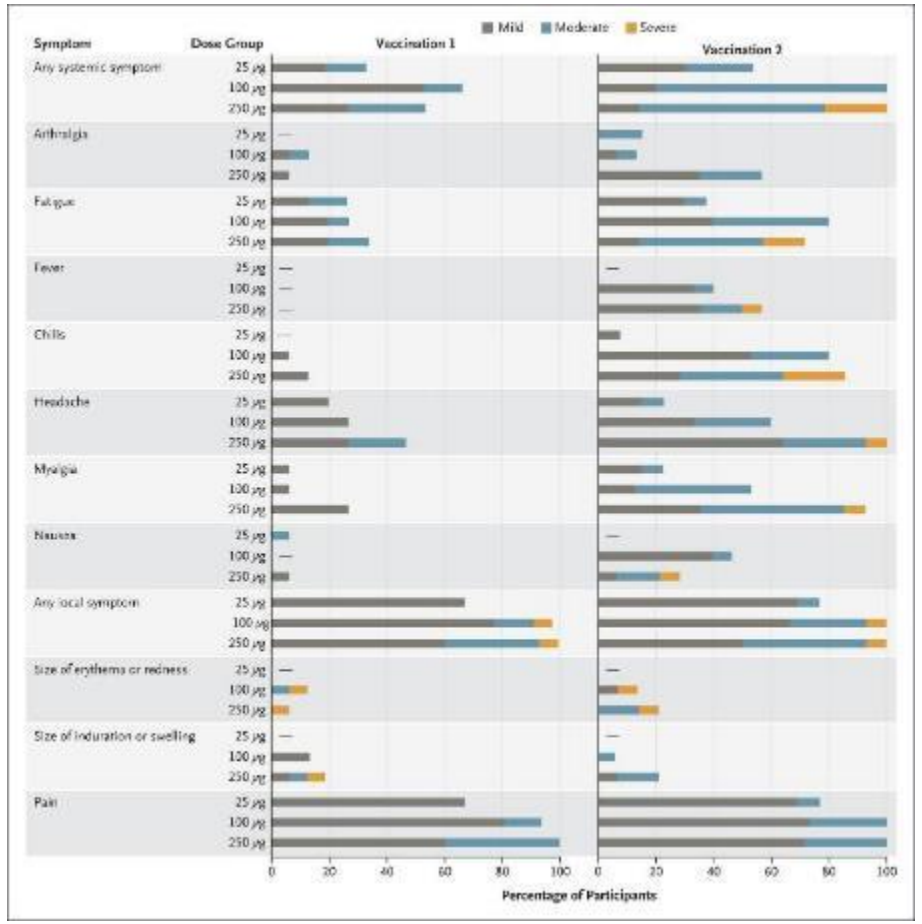
- Phase 1, dose-escalation, open-label trial including 45 healthy adults, 18 to 55 years of age, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25 µg, 100 µg, or 250 µg.
- After the first vaccination, antibody responses were higher with higher dose (day 29 enzyme-linked immunosorbent assay anti–S-2P antibody geometric mean titer [GMT], 40,227 in the 25-µg group, 109,209 in the 100-µg group, and 213,526 in the 250-µg group).
- After the second vaccination, the titers increased (day 57 GMT, 299,751, 782,719, and 1,192,154).
- After the second vaccination, serum-neutralizing activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens.
- Solicited adverse events that occurred in more than half the participants included fatigue, chills, headache, myalgia, and pain at the injection site.
- Systemic adverse events were more common after the second vaccination, particularly with the highest dose, and three participants (21%) in the 250-µg dose group reported one or more severe adverse events.

ORIGINAL ARTICLE

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

Lisa A. Jackson, M.D., M.P.H., Evan J. Anderson, M.D., Nadine G. Rouphael, M.D., Paul C. Roberts, Ph.D., Mamodikoe Makhene, M.D., M.P.H., Rhea N. Coler, Ph.D., Michele P. McCullough, M.P.H., James D. Chappell, M.D., Ph.D., Mark R. Denison, M.D., Laura J. Stevens, M.S., Andrea J. Pruijssers, Ph.D., Adrian McDermott, Ph.D., et al., for the mRNA-1273 Study Group*





Local

GWU's covid-19 clinical trial has met one early goal — getting Black and Latino people to join

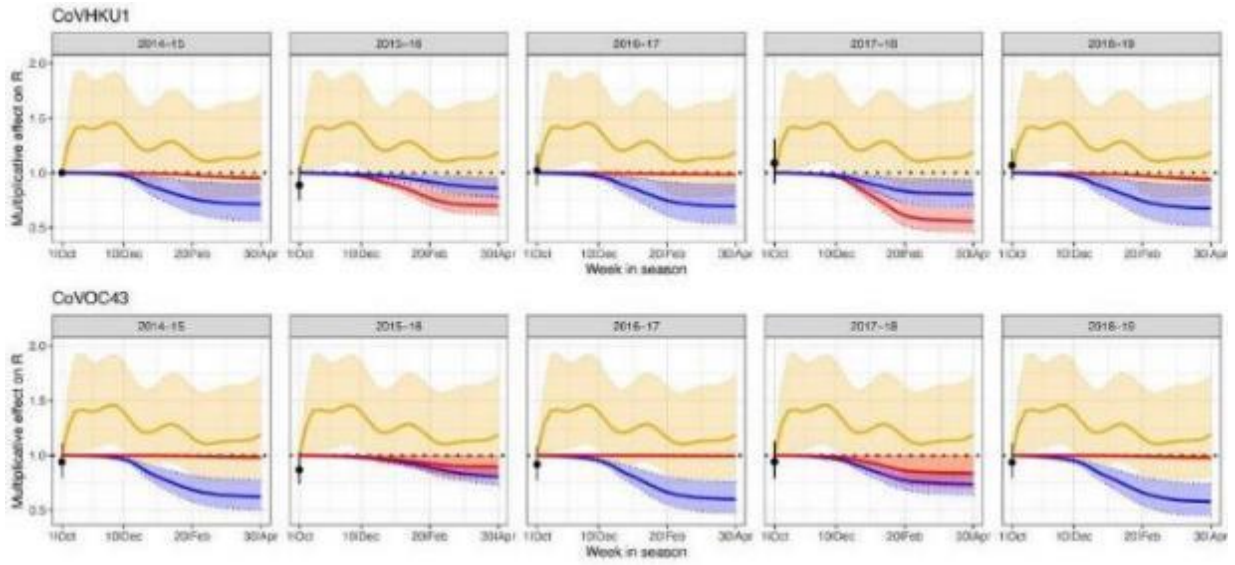
Mark M. Spradley, 66, volunteered to be a test subject in George Washington University's clinical trial for a vaccine for the coronavirus. (Sarah L. Voisin/The Washington Post)

Covering Ebola Didn't Prepare Me for This: I Volunteered for the Covid-19 Vaccine Trial

George Washington University invited me to participate in Moderna's vaccine trial because I am triple-risk: a Black woman, a Type 1 diabetic and asthmatic.

Helene Cooper during an exam at George Washington University Hospital in Washington, D.C. Ms. Cooper, a New York Times correspondent, is participating in the Moderna vaccine trial. Erin Schaff/The New York Times

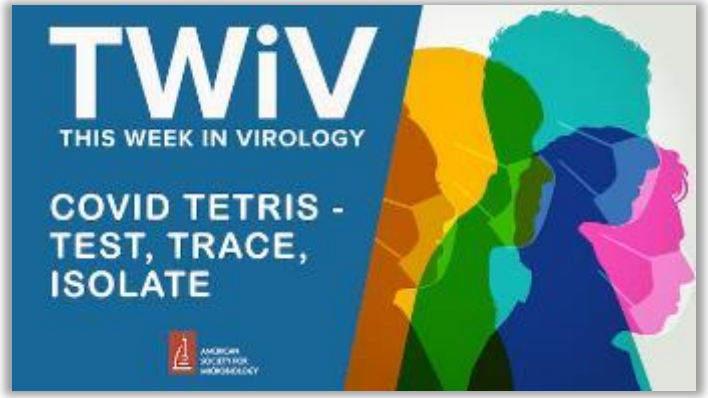
By Helene Cooper



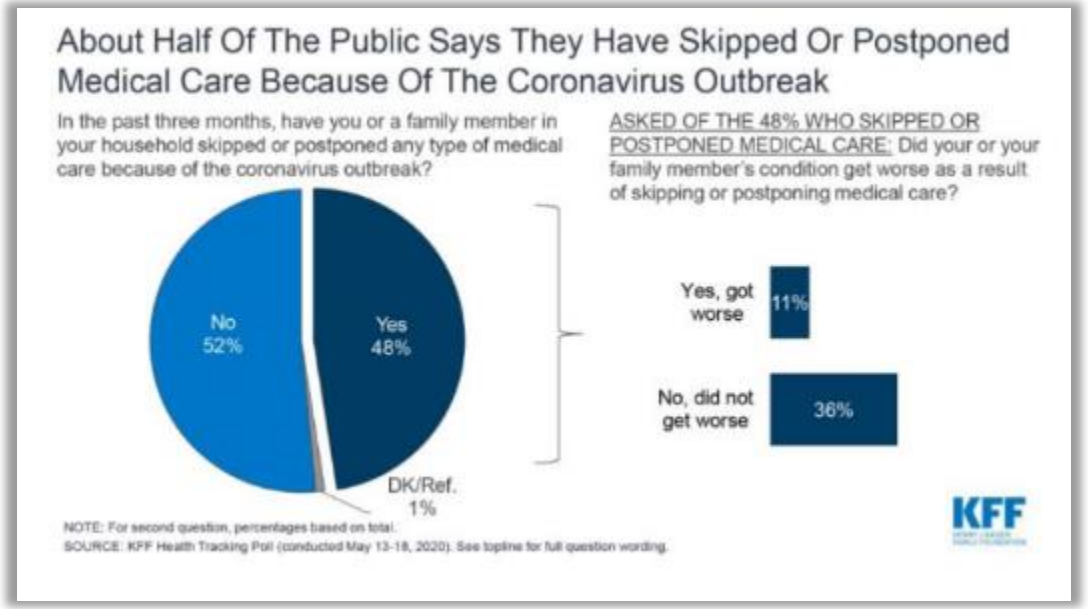
What Comes Next?


May 5, 2020
Hey Washington D.C.!
YOU SAVED
2,719 lives
by staying home for 45 days.
On March 30, Washington D.C.'s stay-at-home order went into effect.
While we are all aware of the rising death toll and the economic costs of COVID-19, it is important to recognize the positive difference we are all making to reduce the severity of this pandemic.
45
days home
25,427
people not in hospital
2,719
lives saved
60
days home
29,711
people not in hospital
3,078
lives saved
We are making an important difference everyday by staying home. Let's keep staying home and continue to save lives, Washington D.C.!
Using epidemiologists' models available through The New York Times, we can estimate the number of hospitalizations and deaths we can prevent by continuing to socially distance. The models are based on a variety of assumptions related to weather patterns, infectiousness of disease, and the aggressiveness of regulatory measures. As such, these numbers are only estimating the collective impact you and your neighbors are making to help save lives and are not actual hospitalizations or lives saved.
See the The New York Times model: bit.ly/NYTimesModel
BIG CITIES HEALTH COALITION
DREXEL UNIVERSITY
Urban Health Collaborative
Based on the infographic created by Community Information Now: bit.ly/CommInfoNow


TETRIS


TWiV
THIS WEEK IN VIROLOGY
COVID TETRIS - TEST, TRACE, ISOLATE


ACP Internist Weekly
COVID-19
AUGUST 11, 2020
Latest research shows impact of COVID-19 on other health care
Hospitalizations for stroke and myocardial infarction, ED visits, cancer diagnoses, and trials for conditions other than COVID-19 all dropped during the pandemic, recent studies show.


About Half Of The Public Says They Have Skipped Or Postponed Medical Care Because Of The Coronavirus Outbreak
In the past three months, have you or a family member in your household skipped or postponed any type of medical care because of the coronavirus outbreak?
No 52%
Yes 48%
DK/Ref. 1%
ASKED OF THE 48% WHO SKIPPED OR POSTPONED MEDICAL CARE: Did your or your family member's condition get worse as a result of skipping or postponing medical care?
Yes, got worse 11%
No, did not get worse 36%
NOTE: For second question, percentages based on total.
SOURCE: KFF Health Tracking Poll (conducted May 13-18, 2020). See topline for full question wording.
KFF

frontiers in Public Health

REVIEW

published: 15 September 2020

Seasonality of Respiratory Viral Infections: Will COVID-19 Follow Suit?

Amani Audi[1,2], Malak AlIbrahim[1,3], Malak Kaddoura[1,2], Ghina Hijazi[1,2], Hadi M. Yassine[3] and Hassan Zaraket[1,2*]*

Natural Disasters, Severe Weather, and COVID-19

Know how the COVID-19 pandemic can affect disaster preparedness and recovery, and what you can do to keep yourself and others safe.

Going to a Public Disaster Shelter During the COVID-19 Pandemic

NIH.gov | Blog Home | Director's Album

Citizen Scientists Take on the Challenge of Long-Haul COVID-19

Posted on September 3rd, 2020 by Dr. Francis Collins

THE CONVERSATION

COVID-19 Arts + Culture Economy + Business Education Environment + Energy Ethics + Religion Health Politics/Election '20 Science + Technology

Smoke from wildfires can worsen COVID-19 risk, putting firefighters in even more danger

September 11, 2020 8.19am EDT

September 15, 2020 | 2 min read

SAVE

Ex-CDC director Frieden: Vaccine 'not going to take COVID-19 off the table'

ADD TOPIC TO EMAIL ALERTS

Former CDC director **Tom Frieden, MD, MPH,** said the world will need more than a COVID-19 vaccine to end the pandemic.

"The bottom line is, for a vaccine to work, it has to be not only safe, effective and available — but also trusted," Frieden, now president and CEO of the global health initiative Resolve to Save Lives, said during a press conference hosted by the Infectious Diseases Society of America.

"One thing that's very important to understand is that even if we have a safe available, accessible, effective and trusted vaccine, it's not going to take COVID-19 off the table," Frieden said. "There is no one thing that's going to make this pandemic magically disappear."

https://www.healio.com/news/infectious-disease/20200915/excdc-director-frieden-vaccine-not-going-to-take-covid19-off-the-table
https://www.cdc.gov/disasters/hurricanes/covid-19/public-disaster-shelter-during-covid.html

At GW

- COVID-19 registry (EM, Crit Care)
- Specimen Bank study (Hospital Med, DGIM, ID)
- Therapeutic trials (coordinated through ID)
- Moderna-NIH vaccine trial (ID, Milken School)
- COVID-19 Recovery Clinic (DGIM, ID)
- Community & Public Health (SMHS, Milken School, Rodham Institute)
- Educational Mission (GWU, SMHS)
- Developmental Strategy (All-GW)

GW COVID-19 Intelligence Reports now monthly: https://guides.himmelfarb.gwu.edu/SituationReport

Emerging Disease Threats

Health Equity

Research

Thank You