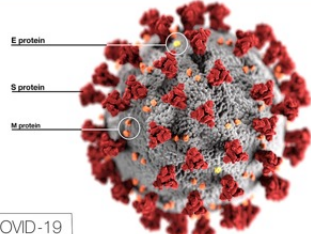


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**SARS-nCoV-2 → COVID-19: Global Pandemic 2020 → →**  
**Coronavirus Infections—More Than Just the Common Cold**




<p><b>FAMILY</b> of coronaviruses (<math>\alpha, \beta, \gamma, \delta</math>) (7 strains in humans) cause ~ 1/4 of common colds, but some cause more severe diseases (ie, SARS1, MERS, &amp; now COVID-19). SARS-nCoV-2 <math>\beta</math> is in the nidovirus viral order.</p>	 <p>COVID-19</p>	<p><b>JAMA</b> Published online January 23, 2020</p> <p><i>Thanks to many organizations &amp; colleagues for some slides: US CDC, NIH, WHO, JHU, SC DHEC, journals, &amp; others TNTC.</i></p> <p><b>Anthony S. Fauci, MD</b>          National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.</p>
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**COVID Update, Vaccine information 28 Jan. 2021**

<p align="center"><i>Robert T Ball Jr, MD MPH FACP</i>  <i>Assistant Professor: Medical University of SC/ USA</i>  <i>Department of Medicine,</i>  <i>Divisions of Infectious Diseases &amp; Public Health Sciences</i>  <i>(ballrt@musc.edu)</i></p>	 <p align="right"><small>R. Ball, MD MPH FACP</small></p>
<p>Hosted by Paul Webber      <a href="http://www.webbertraining.com">www.webbertraining.com</a></p>	

**Disclosures- Robert Ball, MD MPH FACP** 2

- No university research or pharmaceutical funding
- No conflicts of interest
- Dr. Ball to receive an honorarium from Webber Training.
- *Some (of many) upcoming free webinars to note:*

 <p><b>AMA WEBINAR</b>  <b>COVID-19: WHAT PHYSICIANS NEED TO KNOW</b></p> <p><small>New webinar! Register now: COVID-19 Vaccine Safety and Delivery</small>          Jan. 29 at 3 p.m. CT / 4 p.m. ET</p> <p><small>Host: Susan R. Bailey, MD, AMA President          Guest: Peter Marks, MD, PhD, Director of the Center for Biologics Evaluation and Research at the Food and Drug Administration (FDA).</small></p>	<p>ScienceWebinars   AAAS      FREE WEBINAR</p> <p>February 3, 2021          12:00 PM to 1:00 PM US Eastern Time</p>  <p><b>Monitoring the immune system to fight COVID-19: Investigating lymphocyte subsets as surrogate biomarkers to prioritize patient care</b></p> <p align="center"><b>Register now!</b></p>	<p><b>COCA Call</b>          CDC Clinician Outreach and Communication Activity</p> <p><b>Treating Long COVID: Clinician Experience with Post-Acute COVID-19 Care</b></p> <p><b>Overview</b></p> <p><small>For some people, the effects of COVID-19 can last well beyond the immediate illness. Patients and clinicians across the United States are reporting long-term effects of COVID-19, commonly referred to as long COVID. Symptoms may include cognitive difficulties, fatigue, and anorexia of breath. In some patients, critical illness from COVID-19 may be the cause of persistent symptoms, but many patients with long-term effects had mild or asymptomatic acute COVID-19 infection. During this COCA Call, presenters will share their firsthand experiences with treating long COVID.</small></p>  <p><small>Date: Thursday, January 28, 2021</small></p> <p align="right"><small>R. Ball, MD MPH FACP</small></p>
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**Families and Genera of Viruses Infecting Vertebrates**

**DNA**

**dsDNA**

**Smallpox**

Asfarviridae, Poxviridae, Iridoviridae

**ssDNA**

Circoviridae, Anelloviridae, Parvoviridae

**dsDNA (RT)**

Hepadnaviridae, Herpesviridae, Polyomaviridae, Adenoviridae

**Hepatitis A,B,C,D,E etc**

**Herpes**

**HPV**

**RNA**

**dsRNA**

Reoviridae, Birnaviridae

**ssRNA (-)**

Orthomyxoviridae, Rhabdoviridae, Paramyxoviridae, Bornaviridae, Arenaviridae, Bunyaviridae

**Rabies**

**HIV**

**ssRNA (+)**

Caliciviridae, Hepivirus, Nodaviridae, Betanodavirus, Togaviridae, Picornaviridae, Astroviridae, Flaviviridae, Coronaviridae, Arteriviridae

**Chickungunya & Mayaro**

**Zika**

**DNA viruses generally more stable**  
**RNA viruses mutate more often**

Slide courtesy of Eric Brenner, MD, Epidemiologist extraordinaire'  
 Modified by R. Ball, MD MPH FACP

**Genomic epidemiology of novel coronavirus**


3.2020 → 1.2021

Maintained by the **Nextstrain** team. Enabled by data from **GISAI**

Showing 84 of 838 genomes sampled between Jan 2020 and Mar 2020 and comprising 5 recencies, 5 locations, 5 divisions, 5 countries, 5 hosts, 5 re

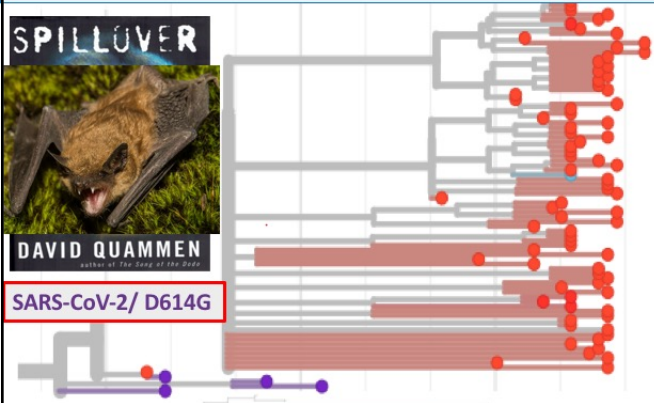
**Mutations: 1<sup>0</sup> = D614G in SARS-CoV-2 spike protein S1. + MUTANTS (Variants of Concern/VOC): 1<sup>st</sup>=20A.EU1/Y453F [in minks]; 19B= B.1.1.7 lineage (UK & now global), & L452R (EU), N501Y.V2 (So. Africa), Italy, USA. Brazil++ P.1 (20J/501.YV3). ↑infectivity, ?shedding, prob.↑ virulence**

**SPILLOVER**

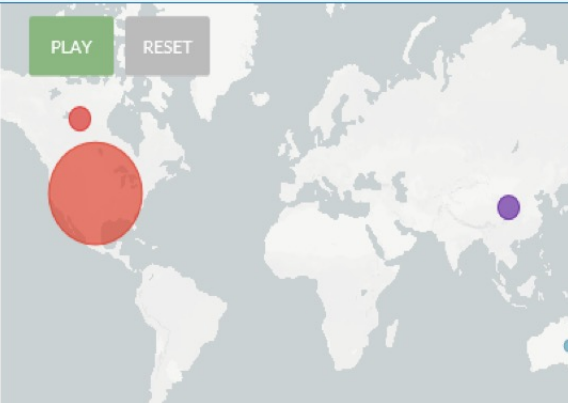


**DAVID QUAMMEN**  
author of *The Song of the Dodo*

**SARS-CoV-2/ D614G**



PLAY RESET



<https://nextstrain.org/narratives/ncov/sit-rep/2020-03-20?n=10>

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### Coronavirus Phylogenetic Tree

Source: SM Gygi, PhD, NIAID. Based on 440 bp nucleotide sequences of RNA-dependent RNA polymerase.

### Severe Human Coronavirus Disease: Past as Prologue

#### Severe Acute Respiratory Syndrome (SARS) (2002–2003)

#### Middle East Respiratory Syndrome (MERS) (2012–present)

Annual Meeting 2020 | Confronting Urgent Threats to Human Health & Society

**The Implications of Silent Transmission for the Control of COVID-19 Outbreaks**  
 SM Moghadas, AP Galvani et al.

Modeling study estimates that individuals without symptoms account for >50% of transmission

### Risk of Transmission

- Varies by type and duration of exposure, prevention measures used, and individual factors (e.g., viral load)
- Transmissions most common among household contacts, in congregate or health care settings when PPE not used, and in closed settings (e.g., cruise ships, nursing homes, prisons)
- Factors that may increase the risk of airborne transmission include:
  - Crowded, enclosed spaces with poor ventilation
  - Singing, speaking loudly, or breathing heavily

US Nat'l. Academy of Medicine 50th Annual mtng. 10.19.2020: COVID (Fauci et al.) R. Ball, MD MPH, FACP

## SARS-CoV-2 → COVID-19: déjà vu SARS pandemic?

JAMA March 5, 2019 Volume 321, Number 9

An **epidemic** occurs when a disease affects a greater number people than is usual for the locality or one that spreads to some areas not usually associated with the disease.

A **pandemic** is an **epidemic** of world-wide (border-crossing) proportions.

### The Spread of a Health Condition

- 1 **Endemic**  
A health condition that occurs at a steady rate among a population
- 2 **Outbreak**  
A condition that occurs above endemic levels
- 3 **Epidemic**  
An outbreak that has spread to a larger geographic area
- 4 **Pandemic**  
A health condition that has spread globally

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**CDC** THE BEST WEBSITE FOR USA INFO: [WWW.CDC.GOV](http://WWW.CDC.GOV) 2020  
Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives, Protecting People™  
Search  
Advanced Search

Diseases & Conditions ▾ Healthy Living ▾ Travelers' Health ▾ Emergency Preparedness ▾ More ▾

## Coronavirus Disease 2019

CDC is responding to the novel coronavirus outbreak.

[Learn More About COVID-19](#)

R. Ball, MD MPH FACP

Centers for Disease Control and Prevention  
Center for Preparedness and Response

## Clinical Management of Critically Ill Adults with COVID-19

CDC webinar April 2, 2020

### Median incubation period is 4-5 days (range: 2-14 days)

“Symptoms (infection) may appear 2-14 days (median ~5 days) after exposure to the virus”

Seafood Wholesale Market, as compared with 8.6% of the subsequent cases.

The mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0), with the 95th percentile of the distribution at 12.5 days.

In its early stages, the epidemic doubled in size every 7.4 days. With a mean serial interval of 7.5 days (95% CI, 5.3 to 19), the basic reproductive number was estimated to be 2.2 (95% CI, 1.4 to 3.9).

Proportion of Symptomatic Cases

Days Since Infection

R. Ball MD MPH FACP

Links: *Lauer Ann Intern Med 2020, Xu BMJ 2020, Guan NEJM 2020*

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**★ Primary Symptoms of COVID-19**

**Anthony Fauci, MD:**  
**9.11.2020 re COVID-19 transmission :** “It is now clear that about 40%-45% of infections are asymptomatic.” **BUT:**  
**“59% of all transmission came from asymptomatic transmission, comprising 35% from presymptomatic individuals, and 24% from individuals who never develop symptoms”**

**-SARS-CoV-2 Transmission From People Without COVID-19 Sx.**  
**- Johansson+ JAMA 01.07.2021**  
Li. J Med Virol. 2020;92:577. <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

**SARS-CoV-2 binds to many host cells via the ACE2 receptor (found in most organs). The S1 spike protein crosses the BBB. (Nature Neuroscience 12.2020)**

9

Slide credit: [clinicaloptions.com](https://clinicaloptions.com)

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**Single-cell RNA expression map of human coronavirus entry factors-Singh+ Ref: Cell Reports 9.3.2020**

Journal Pre-proof

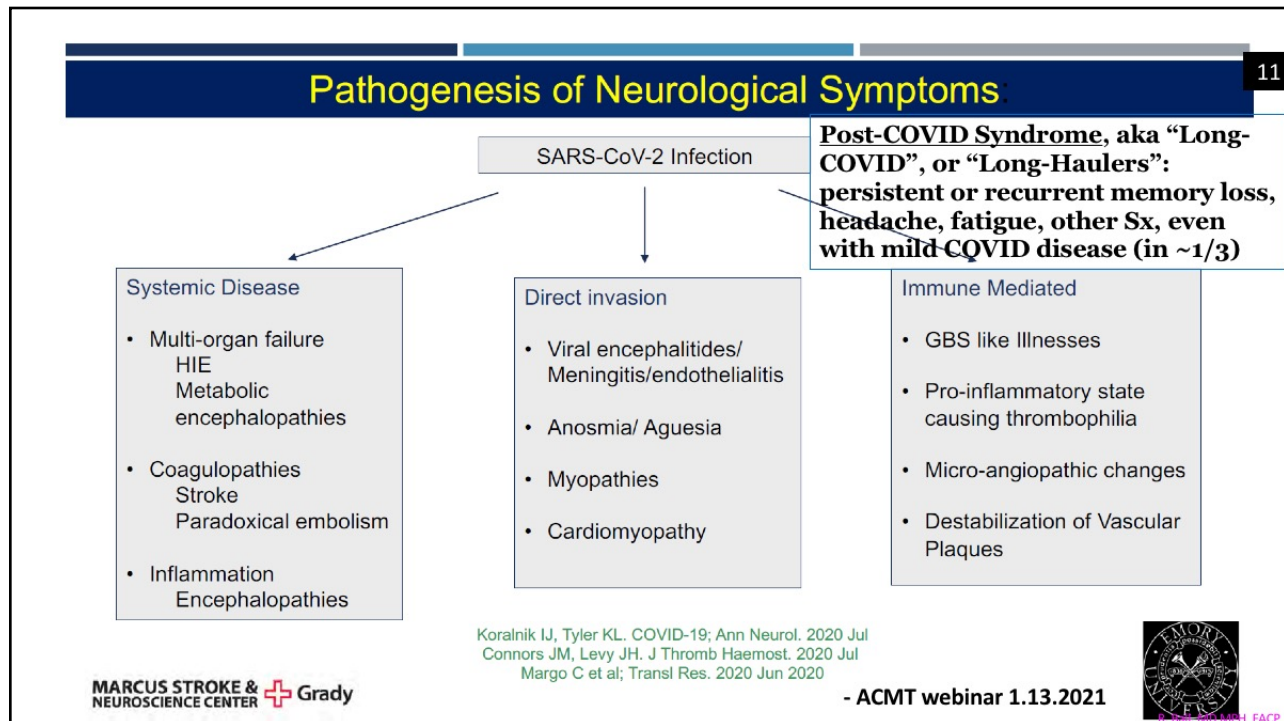
64 samples ~ 400K cells

10

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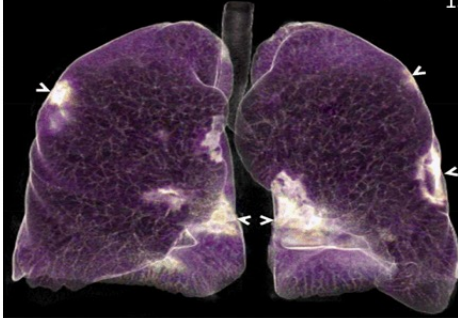
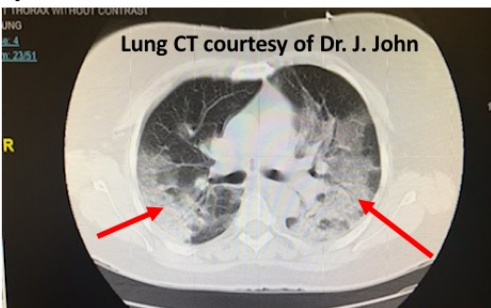
- 12
- ★ Some COVID Clinical Sx, Signs: [www.cdc.gov](http://www.cdc.gov) et al 2020
- **1<sup>o</sup>**: fever, cough, dyspnea, fatigue, anorexia, sore throat, headache, odd rashes...
  - Loss of **smell (anosmia)**, taste (ageusia) [direct infection: NP cells, cranial nerves]
  - CNS & peripheral neurologic events, including encephalopathies, meningitis, peripheral neuropathies, psychiatric anomalies (ie, psychosis), “brain fog”, others
  - **COMPLICATIONS**: severe pneumonia/ “ground-glass” ARDS (~ 1/3 need ventilators, ~ 1/3 never wean off, die); scattered thrombotic/ thromboembolic events in multiple body sites. Examples: cardiac [ie, MIs]; CNS [ie, strokes, incl. large vessel, even in young patients]; pulmonary [eg, pulm. embolism]; renal [ARN, etc]; limbs [eg, “COVID-toes”]; ~MG; diffuse “microthrombi” @ autopsy.
  - **Others** (rare): multiple Sx: Multisystem Inflammatory Syndrome in Children (MIS-C, MIS-Adults) ~Kawasaki disease (ongoing cytokine storm)→odd focal/ diffuse rashes; myo-pericarditis; peritonitis (abdominal pain+); shock; cardiac arrest.
- R. Ball, MD MPH, FACP

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[www.CDC.gov](http://www.CDC.gov) **Some COVID Respiratory Clinical Sx, Signs 2020** 13

<p><b>Clinical Presentation</b></p> <p>The signs and symptoms of COVID-19 present at illness onset vary, but over the course of the disease, most persons with COVID-19 will experience the following:</p> <ul style="list-style-type: none"> <li>• Fever (83–99%)</li> <li>• Cough (59–82%)</li> <li>• Fatigue (44–70%)</li> <li>• Anorexia (40–84%)</li> <li>• Shortness of breath (31–40%)</li> <li>• Sputum production (28–33%)</li> <li>• Myalgias (11–35%)</li> </ul> <p align="right"><b>Clinical Care Guidance</b></p>	<p><b>CXR &amp; CT scans: often as "PNEUMONIA"</b></p> <p><b>multiple diffuse (often "ground glass") opacities in various pulm. segments</b> →</p>	  <p>Lung CT courtesy of Dr. J. John</p> <p align="right"><small>R. Ball, MD MPH FACP</small></p>
<p><b>Therapeutic Options</b></p> <p><b>There are no drugs or other therapeutics approved by the U.S. Food and Drug Administration to prevent or treat COVID-19.</b> Use of investigational therapies for treatment of COVID-19 should ideally be done in the context of enrollment in randomized controlled trials.</p>		

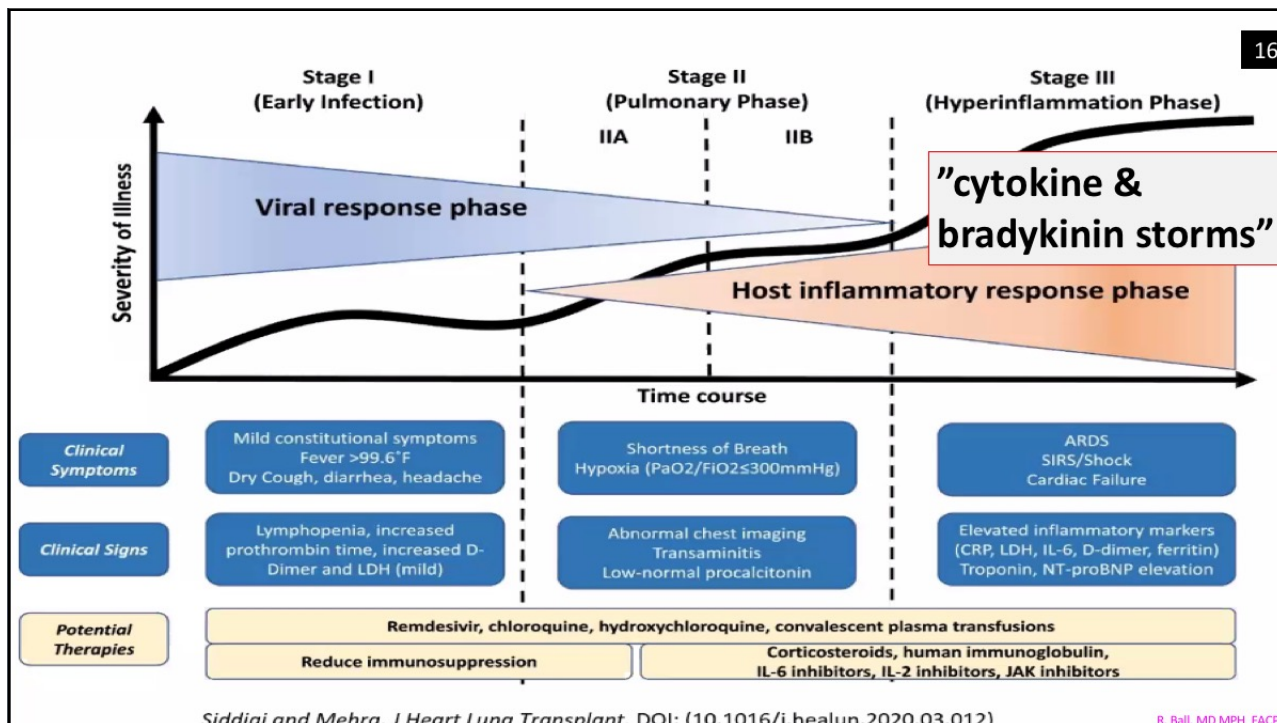
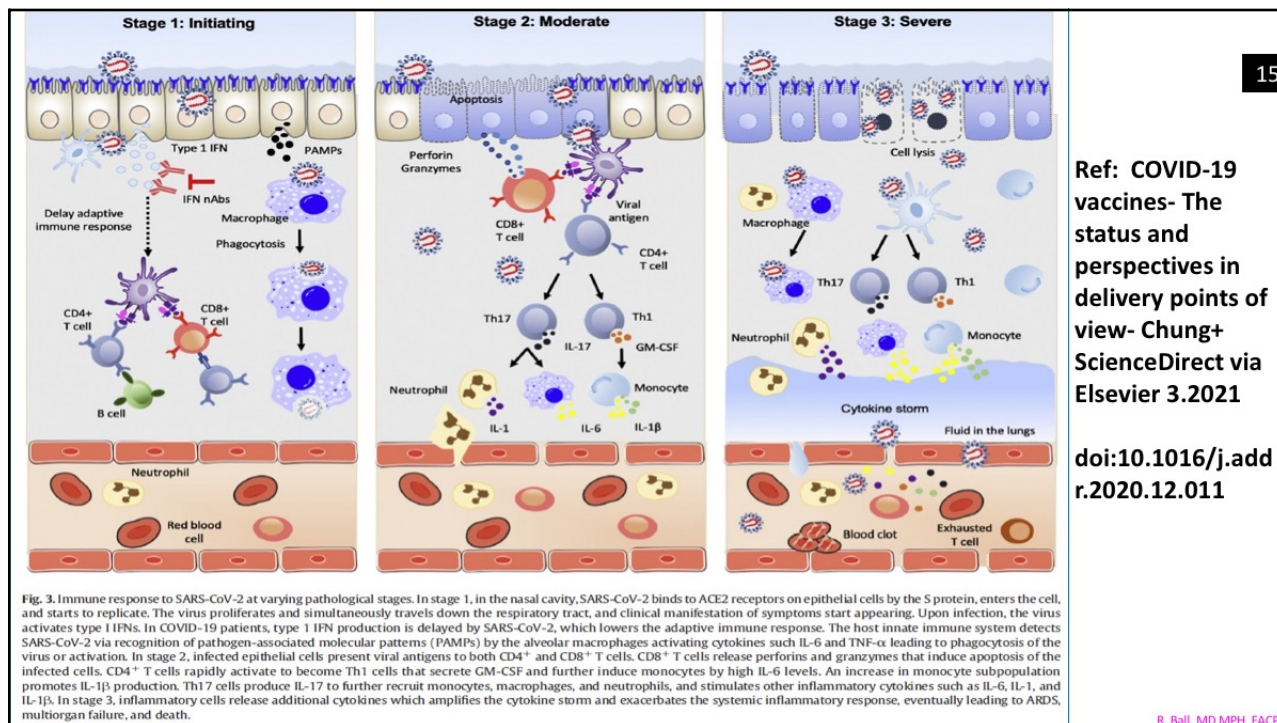
14

<p>Ability to contain emerging virus in absence of countermeasures</p>		<p>Patients seek health care and can be diagnosed and isolated, and their contacts can be traced. A caveat is that coronaviruses have a propensity for nosocomial spread.</p> <p>Patients do not seek health care, do not receive a diagnosis, and may spread the virus to contacts.</p>
		<p>Emerging Infectious Diseases. CDC 5.2020</p>

**Pyramid much like many I.D.s, with an aSx base (often ~80%):**  
**Examples: AIDS v HIV/ WNV aSx v encephalitis / HPV v Cx CA**

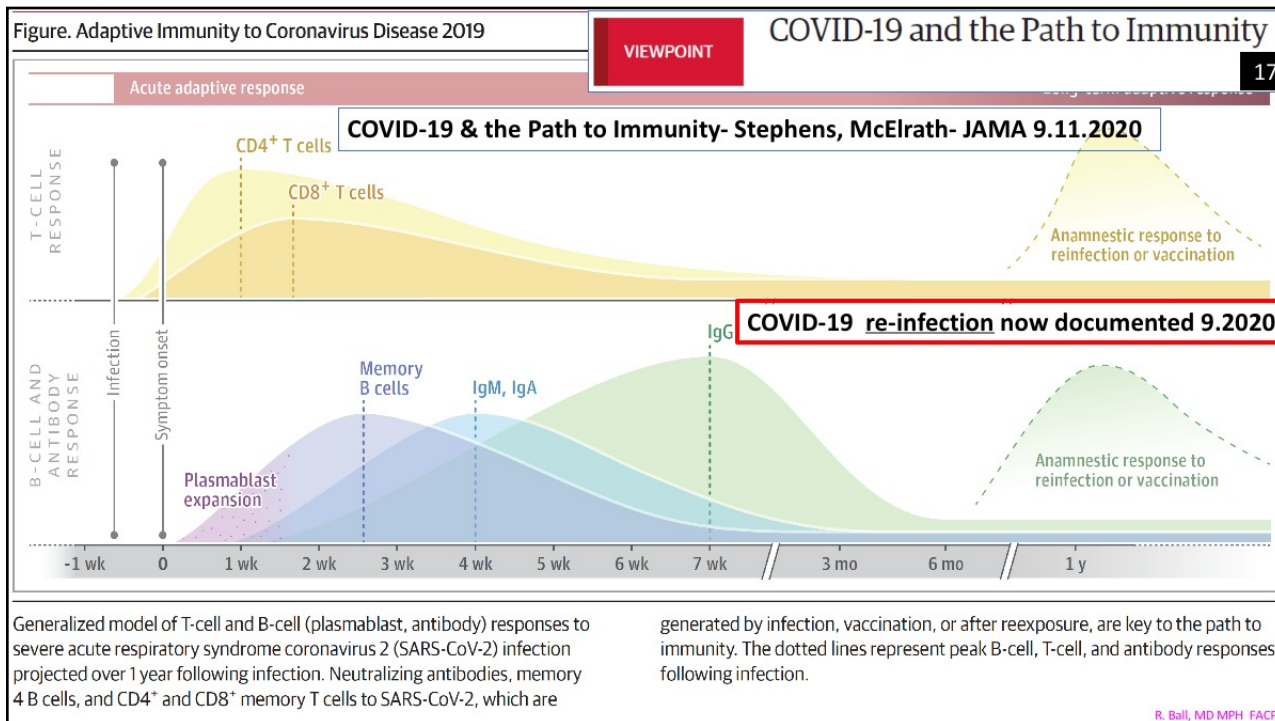
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**Table 1. Pathogenicity and Transmissibility Characteristics of Recently Emerged Viruses in Relation to Outbreak Containment.**

Virus	Case Fatality Rate (%)	Pandemic	Contained	Remarks
2019-nCoV	Unknown*	Unknown	No, efforts ongoing	
pH1N1	0.02–0.4	Yes	No, postpandemic circulation and establishment in human population	
H7N9	39	No	No, eradication efforts in poultry reservoir ongoing	
NL63	Unknown	Unknown	No, endemic in human population	
SARS-CoV	9.5	Yes	Yes, eradicated from intermediate animal reservoir	58% of cases result from nosocomial transmission
MERS-CoV	34.4	No	No, continuous circulation in animal reservoir and zoonotic spillover	70% of cases result from nosocomial transmission
Ebola virus (West Africa)	63	No	Yes	

\* Number will most likely continue to change until all infected persons recover.

**‘Novel Coronavirus Emerging in China- Key Questions for Impact Assessment’ e-NEJM 1.24.2020**

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## SARS-CoV-2 → COVID-19: Respiratory, Airborne, or both ?

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**R<sub>0</sub> = INFECTIVITY RATE:** 1 SARS-CoV-2 (+) patient → ≥3-5 exposed persons become infected.  
**PRIMARY ROUTE:** LARGE respiratory droplets > smaller > invisible microdroplets (aerosols).

**GLOBAL MORTALITY RATE** (from Johns Hopkins Univ. > data map): ↓ from ~3%-~5% to ~2% (since Feb. 2020, ongoing, w USA ~ 1.8% (of the known test+ cases)

**ULTIMATELY, Case Fatality Rate (CFR)** will ↓ WHEN we have mass Abs sero-surveys of MANY sub-populations to determine what % of general population really got infected with SARS-CoV-2. Most experts now think, that like many other pandemics, ~ 75-80% of the US (& global) population will have been infected by ~2023, most unknown & undiagnosed. Only then we will be able to determine the true CFR in retrospect.

**Surface survivability:** respiratory droplets ~ 2-3 hrs. (? longer in deep cough cloud) >> 3-6m.  
**Fomites:** ~4 hrs. on copper, 1 day on cardboard, 2-3 days on plastic/ stainless steel (low conc.)  
**BUT: Q is: How Infectious Are Fomites (& do we need extreme surface decontamination)?**  
**A: UNKNOWN, but probably MUCH less viral RNA likely than direct close respiratory contact with a (+) patient (CDC: ~6' apart for ≥15 minutes cumulatively = "close contact")**  
**Refs: NEJM 3.26.2020, CDC MMWR 10.2020**


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## Some nuances re transmission of SARS-2

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Virus	Incubation Period (typical cases)
Novel Coronavirus (COVID-19)	2-14 or 0-24 days *
SARS	2-7 days, as long as 10 days
MERS	5 days (range: 2-14)
Swine Flu	1-4 days, as long as 7 days
Seasonal Flu	2 days (1-4 range)

The odds of indoor transmission of SARS-CoV-2 is



**18.7X higher**  
 compared with outdoor transmission

Healio

**US CDC defines "Close Contact" = being within ≥6' of COVID+ person for ≥15 min (cumulative)/ 24 hrs indoors (standard room), w or w/o masks.**

**"Superspreaders" & "superspreader events" common. Ro often >10-15**

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**Respiratory Droplets &/or "Airborne" ? "cough cloud"**

Size of droplets (diameter)	Distance of droplets from mouth	Duration of infectivity
1-2 mm	~6 feet	1-2 hours (more on some fomites)
0.1-1mm	12-15 feet	6-12 hours (? 1+ days)
0.1-.001mm	?	???
~1-5 microns	??	weeks++

Droplet size	Role in transmission	Transmission	Duration in the air
Larger	Likely <b>more</b> important	Typically 1-6 feet	Less time (fall to the ground)
Smallest	Likely <b>less</b> important	Can float farther	More time (may stay suspended)

Eric Brenner MD

**Multiphase Turbulent Gas Cloud From a Human (Sneeze- Bourouiba) JAMA video 3.26.2020**  
**"A Sneeze"** <https://edhub.ama-assn.org/jn-learning/video-player/18357411>

Video Supplement to  
 Bourouiba L. Turbulent gas clouds and respiratory pathogen emissions: potential implications for reducing transmission of COVID-19. *JAMA*. Published online March 26, 2020. doi:10.1001/jama.2020.4756

**8 meters ~ 26.7 feet !**

≈ 7-8 m

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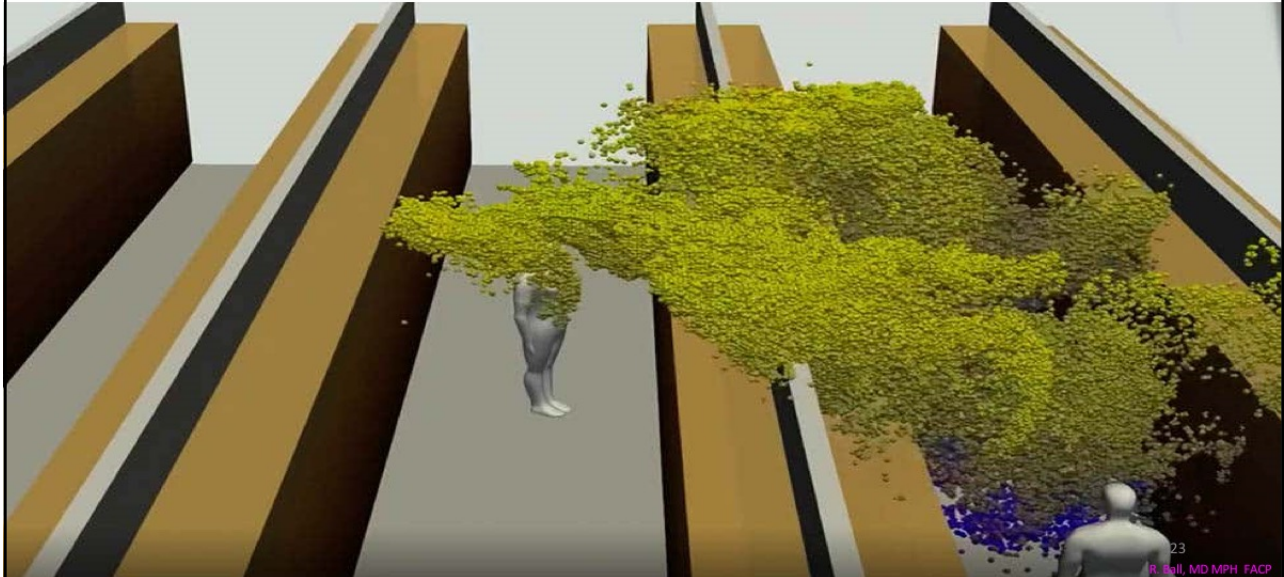
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Cough cloud in store: inhale, hasten down aisle, gather essentials, wait to exhale

<https://www.youtube.com/watch?v=vv9JQ0iPfgE>

23



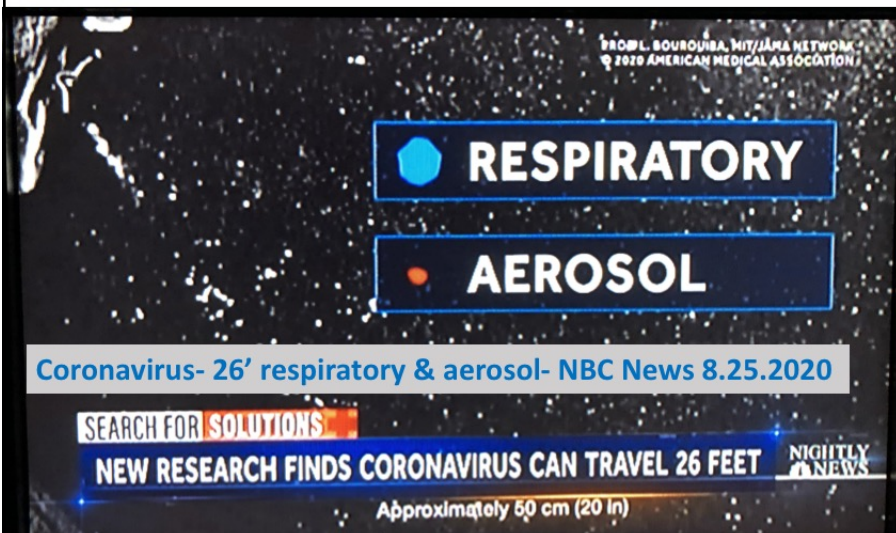
## Covid-19 superspreading event in Boston may have led to 20,000 cases, researcher says

24



By Jacqueline Howard and Carma Hassan, CNN

Updated 8:24 PM ET, Tue August 25, 2020



More from CNN

### CDC 2.2020 goofs:

- Keep  $\geq 6$  ft. "social" distance (**NO** distinction re indoors v outdoors)
- **NO** distinction re mask wearing or not.

### Jordan wedding 3.13.2020:

>350 wedding attendees  
→76 infected guests (1/5).

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### The Power of Masks

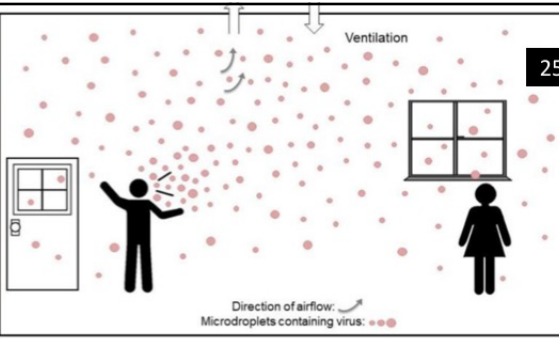
❖ **Masks decrease spread of virus-containing respiratory DROPLETS, the primary mode of SARS-CoV-2 transmission.**

- 6 feet = average distance large respiratory droplets from sneeze/cough travel before settling on to surfaces (based on pre-COVID studies)
- More recent **simulation** shows 12 feet (tracer droplets suspended midair for 3 min)
- Droplet spread decreased significantly w/ face coverings:
  - Bandana = 3 ft., 7 in.
  - Folded cotton handkerchief = 1 ft., 3 in.
  - Stitched quilted cotton mask = 2.5 in.
  - Cone-style mask = 8 in.

<https://phys.org/news/2020-06-mask-materials-droplets.html>

Dr. Allison Eckard  
 MUSC Peds.  
 9.2020





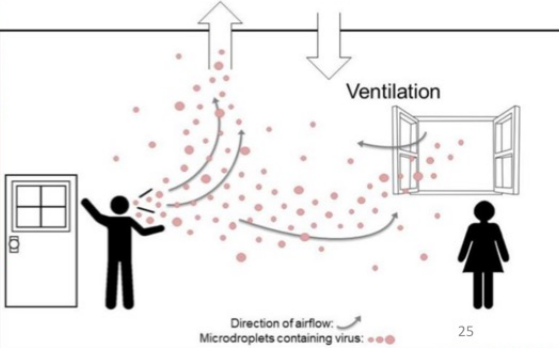
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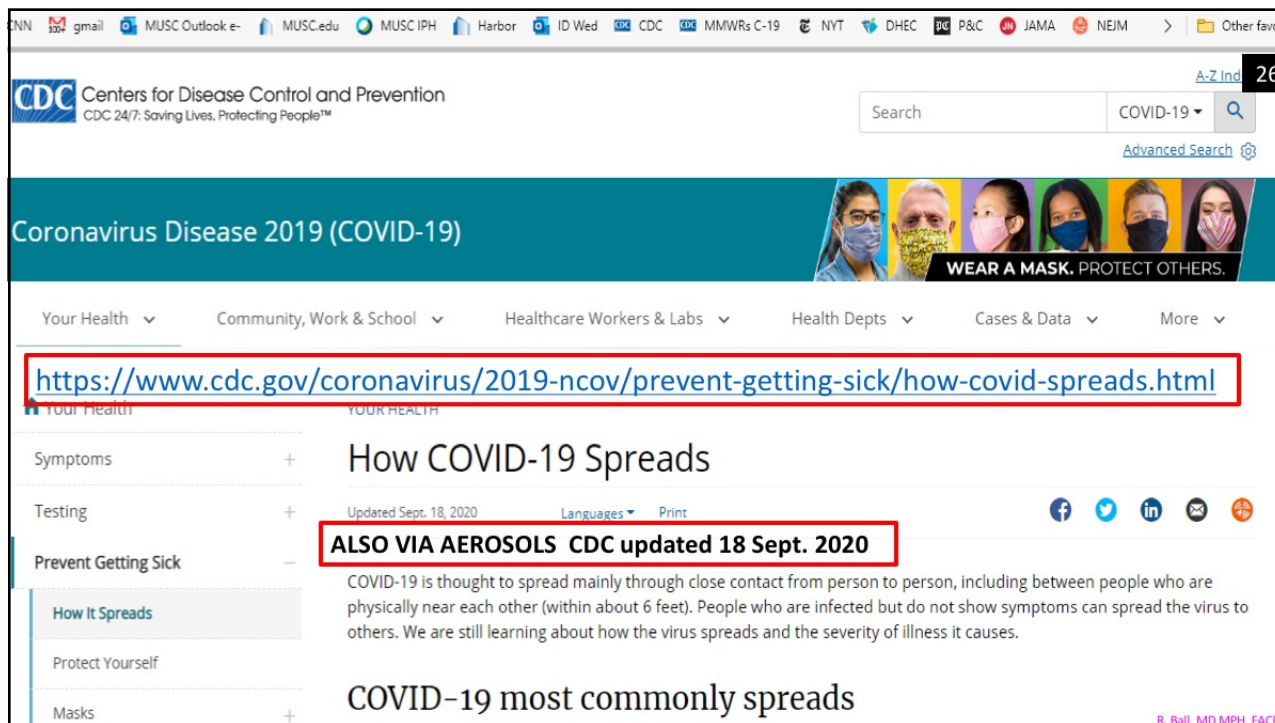
### It is Time to Address Airborne Transmission of COVID-19

Lidia Morawska<sup>1,2\*</sup>, Donald K. Milton<sup>2</sup>

**Clinical Infectious Diseases 7.6.2020**  
 doi:10.1093/cid/ciaa939 (Pres. Trump knew 1.2020)



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**ALSO VIA AEROSOLS CDC updated 18 Sept. 2020**

COVID-19 is thought to spread mainly through close contact from person to person, including between people who are physically near each other (within about 6 feet). People who are infected but do not show symptoms can spread the virus to others. We are still learning about how the virus spreads and the severity of illness it causes.

**COVID-19 most commonly spreads**

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# SARS-CoV-2: Pandemic Exponentiation

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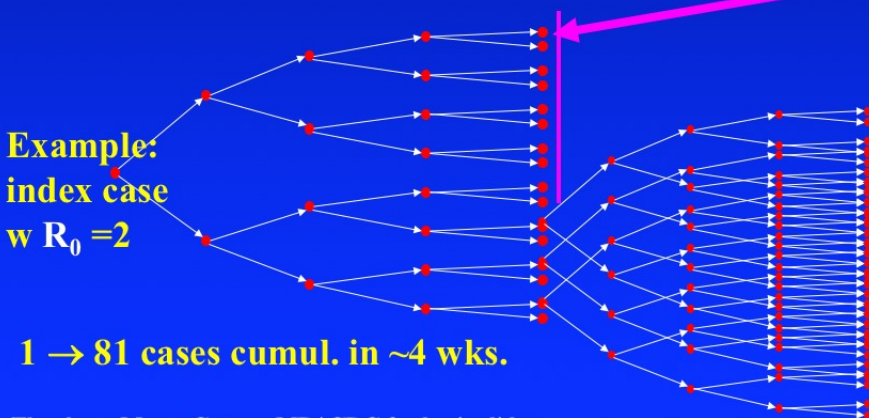
Early estimates:  $R_0$ : 1 primary case  $\rightarrow$   $\sim$ 3-5 or more secondary infections, now est.  $\sim$ 7-8+

If  $R_0 \geq 1$ ,  $\therefore$  progression (ie, if  $R_0$  1:3=1:9:27:81:243...

If incubation period  $\sim$ avg 5, up to 10 days, then:

Example:  
 index case  
 w  $R_0 = 2$

1  $\rightarrow$  81 cases cumul. in  $\sim$ 4 wks.



Maximal effective mitigation (ie, MASKS, distancing, etc) likely not to begin until weeks, months into pandemic i.e.,  $R_t$  then  $< 3$ . ideal:  $R_t \rightarrow < 1$

With little mitigation, we get  $> 243$  cases cumul. in  $\sim$ 6 wks.!

Thanks to Marty Cetron, MD/ CDC for basic slide

R. Ball, MD MPH, FACP

## COVID-19 most commonly spreads

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- Between people who are in close contact with one another (within about 6 feet).
- Through respiratory droplets or small particles, such as those in aerosols, produced when an infected person coughs, sneezes, sings, talks, or breathes.
  - These particles can be inhaled into the nose, mouth, airways, and lungs and cause infection. This is thought to be the main way the virus spreads.
  - Droplets can also land on surfaces and objects and be transferred by touch. A person may get COVID-19 by touching the surface or object that has the virus on it and then touching their own mouth, nose, or eyes. Spread from touching surfaces is not thought to be the main way the virus spreads.
- It is possible that COVID-19 may spread through the droplets and airborne particles that are formed when a person who has COVID-19 coughs, sneezes, sings, talks, or breathes. There is growing evidence that droplets and airborne particles can remain suspended in the air and be breathed in by others, and travel distances beyond 6 feet (for example, during choir practice, in restaurants, or in fitness classes). In general, indoor environments without good ventilation increase this risk.

Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients- Lednický et al- medRxiv preprint 8.3.2020

## COVID-19 spreads very easily from person to person

How easily a virus spreads from person to person can vary. Airborne viruses, including COVID-19, are among the most contagious and easily spread. Some viruses are highly contagious, like measles, while other viruses do not spread as easily. The virus that causes COVID-19 appears to spread more efficiently than influenza, but not as efficiently as measles, which is highly contagious. In general, the more closely a person with COVID-19 interacts with others and the longer that interaction, the higher the risk of COVID-19 spread.

R. Ball, MD MPH, FACP



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Although there is not yet solid evidence of airborne transmission of SARS-CoV-2, the coronavirus that causes COVID-19, a “reasonable assumption” can be made that it may occur, said Anthony S. Fauci, MD

Clin. Infect. Dis. 7.6.2020.

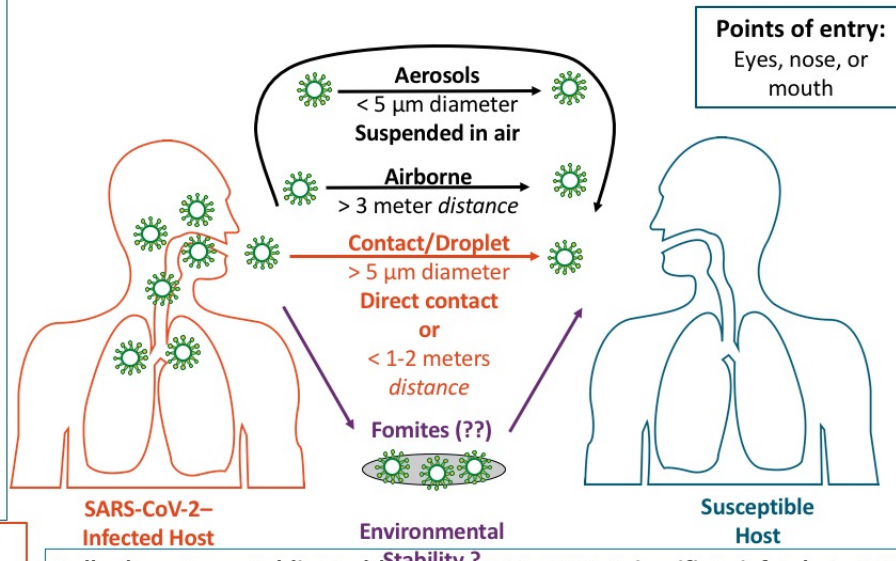
The commentary, which was supported by **239 scientists**, explained that several retrospective studies performed after the SARS epidemic in the early 2000s showed airborne transmission was the “most likely mechanism” to explain the spatial pattern of infections. According to the authors, a retrospective analysis demonstrated the same to be true for SARS-CoV-2

**What about urine & feces?**

RNA found in both; live virus cultivated from some specimens

**Proposed Routes of SARS-CoV-2 Transmission**

29



Galbadage. Front Public Health. 2020;8:163. WHO. Scientific Brief. July 9, 2020

slide credit: [clinicaloptions.com](http://clinicaloptions.com)

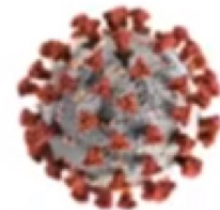
R. Ball, MD MPH FACP

**SARS-CoV-2 Transmission**

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US Nat'l. Academy of Medicine 50th Annual mtng. 10.19.2020: COVID (Fauci et al.)

- Mainly through exposure to respiratory droplets when close (≤6 ft) to an infected person
- Sometimes through particles that remain in the air over time (“aerosol”) and distances (>6 feet)
- Less commonly through contact with contaminated surfaces
- Virus found in stool, blood, semen and ocular secretions; role in transmission unknown
- Animals (including domesticated) not major source of human infection



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**Figure 1. Concepts of the Effective Reproduction Number**

The effective reproduction number ( $R_t$ ) of a viral infection is the mean number of additional infections caused by an initial infection in a population at a specific time.

Thomas V. Inglesby, MD JAMA 5.1.2020

**$R_t = 1$**   
Initial infection  
1 secondary infection is caused by the initial infection  
The single secondary infection causes 1 more infection  
Each additional infection causes 1 more subsequent infection

**$R_t = 4$**   
Initial infection  
4 secondary infections are caused by the initial infection  
**If  $R_0 = 1 \rightarrow 4$**   
Each secondary infection causes 4 more infections  
Each additional infection causes 4 more subsequent infections

**After choir practice with one symptomatic person, 87% of group developed COVID-19**

**COVID-19 spreads easily**

- Avoid groups
- Stay at least 6 feet apart
- Wear face coverings

**Summary** MMWR / May 15, 2020 / Vol. 69 / No. 19  
**What is already known about this topic?**  
 Superspreading events involving SARS-CoV-2, the virus that causes COVID-19, have been reported.  
**What is added by this report?**  
 Following a 2.5-hour choir practice attended by 61 persons, including a symptomatic index patient, 32 confirmed and 20 probable secondary COVID-19 cases occurred (attack rate = 53.3% to 86.7%); three patients were hospitalized, and two died. Transmission was likely facilitated by close proximity (within 6 feet) during practice and augmented by the act of singing.  
**What are the implications for public health practice?**  
 The potential for superspreader events underscores the importance of physical distancing, including avoiding gathering in large groups, to control spread of COVID-19. Enhancing community awareness can encourage symptomatic persons and contacts of ill persons to isolate or self-quarantine to prevent ongoing transmission.

**SARS-CoV-2 → COVID-19: Mitigation CY 2020**

**SLOW THE SPREAD OF THE VIRUS**

**“flattening the curve”**

**Proactive measures slow the spread of disease and reduce the burden on hospitals.**  
 This includes social distancing such as telecommuting, limiting large gatherings, reducing travel, or more assertive approaches.

**Most hospitals now @/near capacity! Now w HCU burnout Epidemic!**

**POPULATION INFECTED**

**TIME SINCE FIRST CASE**

**Health care system capacity (ICU beds, ER visits, etc.)**

**WITHOUT social distancing measures**

**WITH social distancing measures**

**USA “peaks” in spring & summer 2020, w plateaus & worse peaks depend on people reopening, resurgence ... prior to Rx’s in 2020, then vaccine(s) in ? late 2020 → mass vax. early 2021 - per national & local experts**

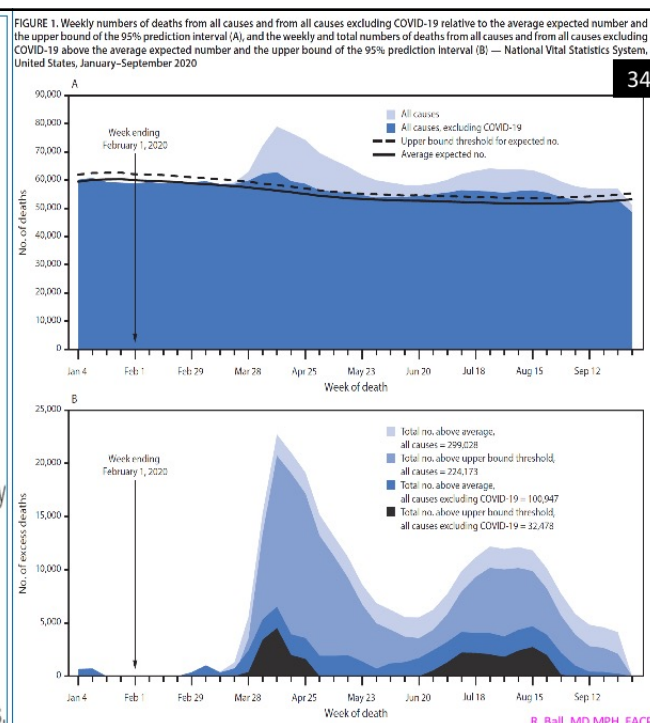
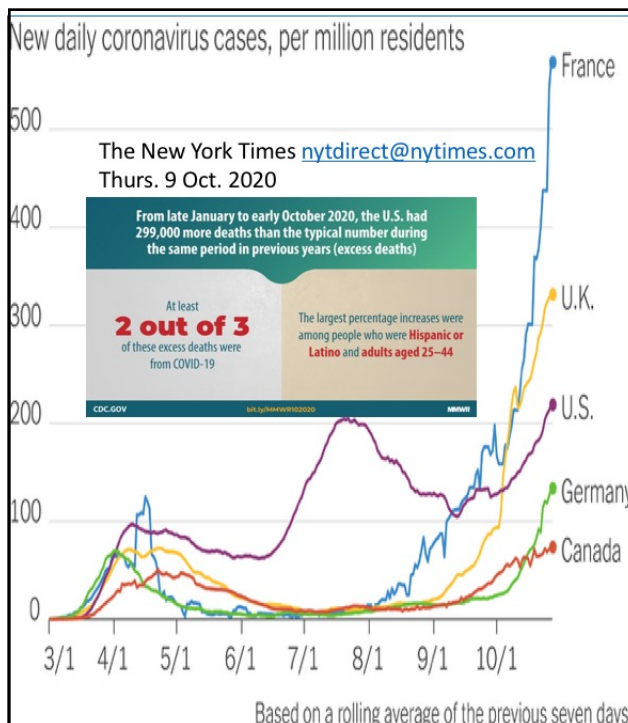
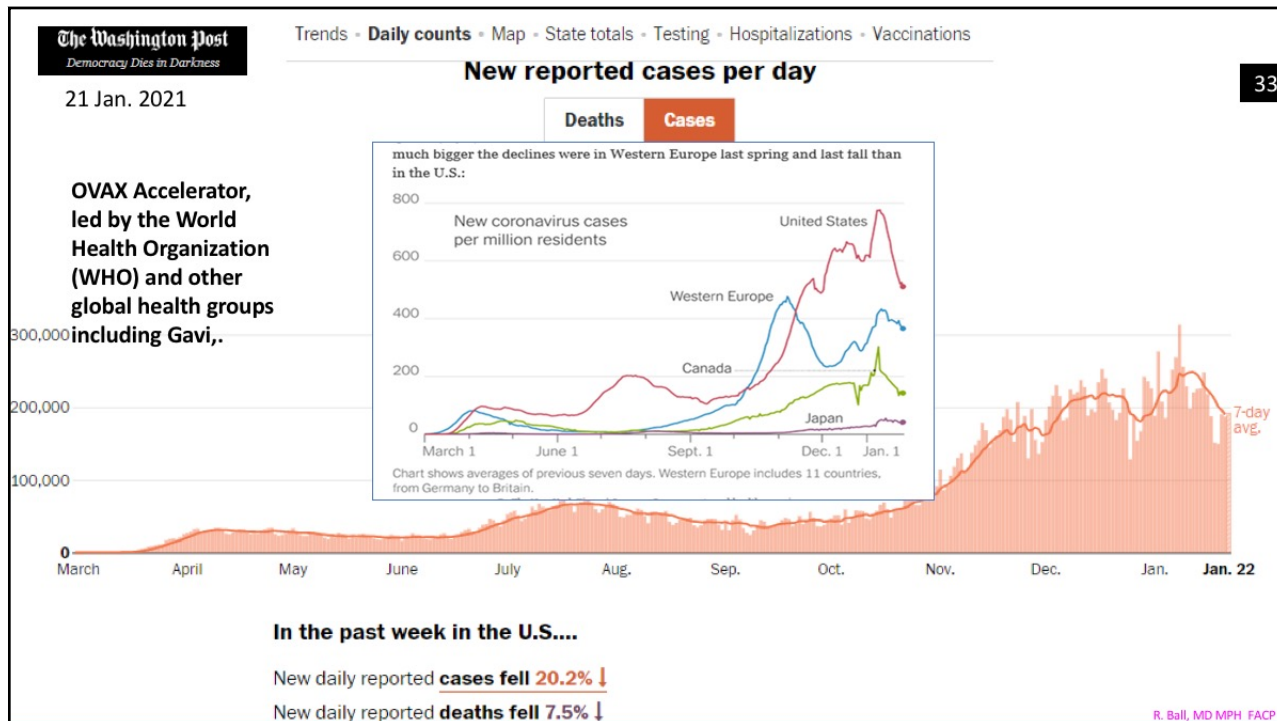
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# COVID Update: Focus on Vaccines

## Dr. Robert T. Ball, University of South Carolina

### A Webber Training Teleclass



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# COVID Update: Focus on Vaccines

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**JAMA Insights**  
**“Herd Immunity”** JAMA 10.19.2020  
**Herd Immunity and Implications for SARS-CoV-2 Control**

Saad B. Omer, MBS, MPH, PhD; Inci Yildirim, MD, PhD, MSc; Howard P. Forman, MD, MBA

Herd immunity, also known as indirect protection, community immunity, or community protection, refers to the protection of susceptible individuals against an infection when a sufficiently large proportion of the population has been infected or vaccinated. Herd immunity breaks will extinguish and endemic transmission of the pathogen will be interrupted. In the simplest model, the herd immunity threshold depends on the basic reproduction number ( $R_0$ ), the average number of secondary infections produced by one infected individual in a population of susceptible individuals.

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The population of the US is about 330 million. Based on WHO estimates of an infection fatality rate of ~0.5%, about 198 m. individuals in the US are needed to be immune to reach a herd immunity threshold of **≥ 60%**, which would lead to **several hundred thousand additional deaths**. Assuming that less than 10% of the population has been infected so far, with an infection-induced immunity lasting 2 to 3 years (duration unknown), infection-induced herd immunity is not realistic at this point to control the pandemic. SARS-CoV-2 vaccines will help to reach the herd immunity threshold, but the effectiveness of the vaccine(s) and the vaccine coverage are TBD.

**Figure. Herd Immunity Thresholds by Disease**

Disease	Location	Year	Basic reproduction number ( $R_0$ )	Herd immunity threshold (%)
Measles	Ghana	1960-1968	~14.5	~93
Poliomyelitis	Europe	1955-1960	~4.5	~78
Smallpox	Indian subcontinent	1968-1973	~4.0	~75
1918 H1N1 influenza	Geneva	Fall wave	~3.5	~72
SARS epidemic	-	2002-2003	~2.5	~60
SARS-CoV-2	-	2020	~1.5	60
Zika	South America	2015-2016	~2.0	~50
H2N2 influenza pandemic	United States	1957	~1.8	~40
1918 H1N1 influenza	Geneva	Spring wave	~1.5	~35
Ebola	Guinea	2014	~1.5	~25
H1N1 influenza	South Africa	2009	~1.5	~25

The locations included are the locations in which the threshold was measured.

**“Why not just let all Americans get it & get it over with?” - Dr. S. Atlas, (has NO Inf. Dis. or Public Health experience)- but was new Trump White House COVID Taskforce Director 10.2020**

MD MPH FACP

<https://www.worldometers.info/coronavirus/coronavirus-cases/#total-cases>

28 Jan. 2021

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**COVID-19 CORONAVIRUS PANDEMIC**

Last updated: January 28, 2021, 16:19 GMT

[Graphs](#) - [Countries](#) - [News](#)

**Coronavirus Cases:**

**101,647,819**

[view by country](#)

**Deaths:**

**2,190,145**

~ 2% current mortality rate. USA ~1/4 of all global deaths.

**Recovered:**

**73,494,420**

**ACTIVE CASES**

**25,959,776**

Currently Infected Patients

**25,853,028 (99.6%)** **110,226 (0.4%)**

In Mild Condition    Serious or Critical

[Show Graph](#)

**CLOSED CASES**

**75,688,043**

Cases which had an outcome:

**73,494,420 (97%)** **2,190,145 (3%)**

Recovered / Discharged    Deaths

[Show Graph](#)

daily linear logarithmic

**Daily New Cases**

Cases per Day  
Data as of 0:00 GMT+0

daily linear logarithmic

**Daily Deaths**

Deaths per Day  
Data as of 0:00 GMT+0

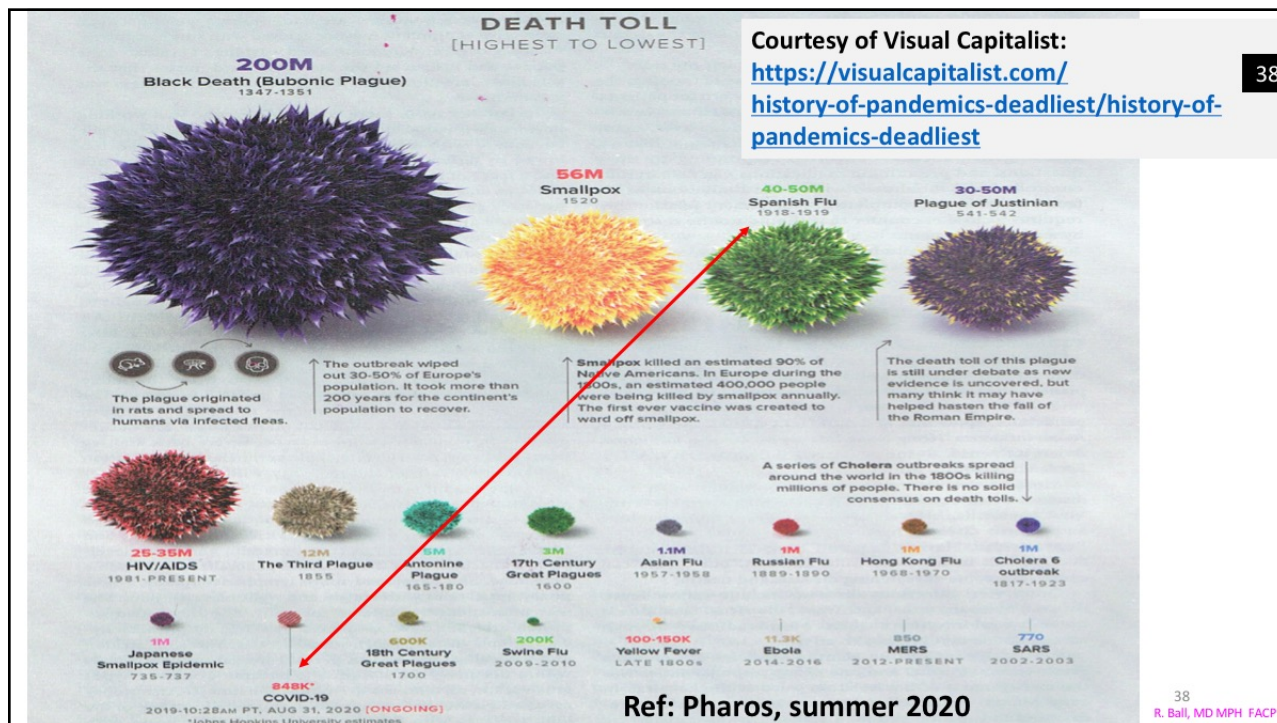
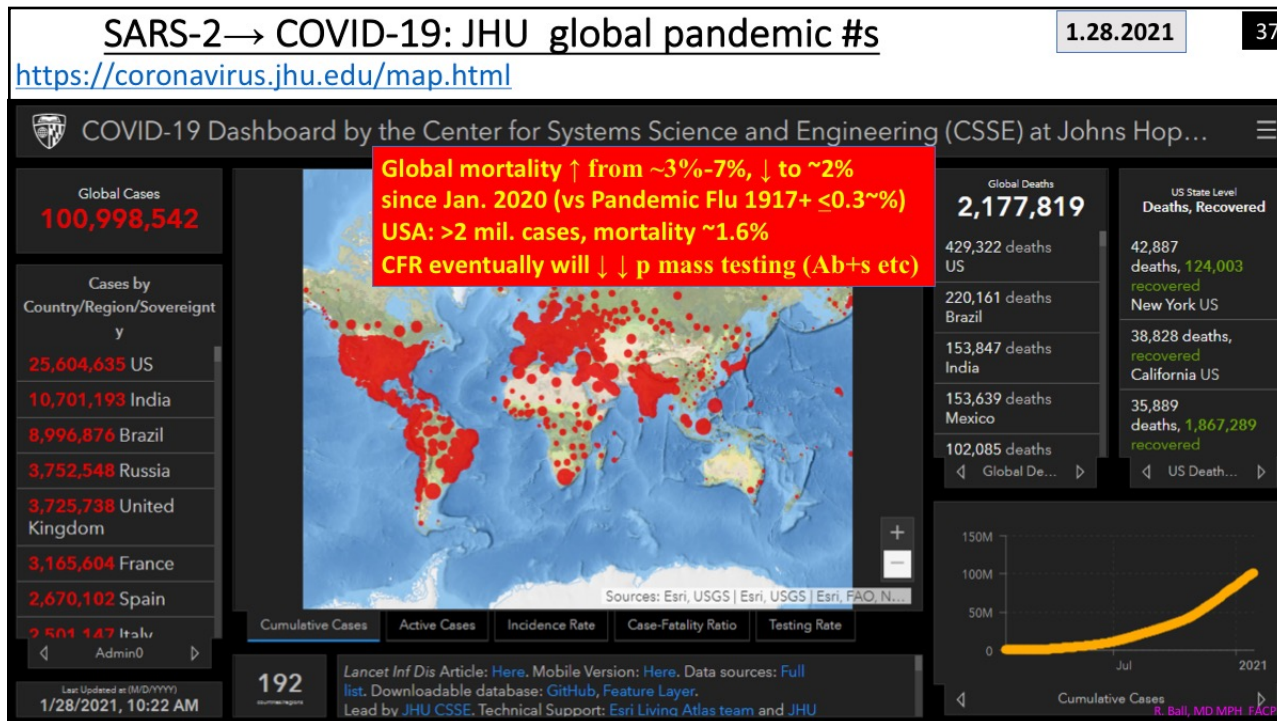
#	Country/Other	Total Cases	New Cases	Total Deaths	New Deaths	Total Recovered	Active Cases	Serious, Critical	Tot Cases/1M pop	Deaths/1M pop	Total Tests	Tests/1M pop	Population
1	USA	26,192,314	+26,891	440,257	+736	15,946,080	9,805,977	25,851	78.864	1.326	304,556,824	917.011	332,119,170
2	India	10,702,730	+699	153,896	+10	10,373,649	175,186	8,944	7.712	111	194,338,773	140.035	1,387,790,010
3	Brazil	9,000,485		220,237		7,798,665	981,593	8,318	42.171	1,032	28,600,000	134.003	210,427,920
4	Russia	3,793,810	+15,138	71,651	+875	3,229,258	492,901	2,300	25.990	491	100,700,000	689.865	145,970,672
5	UK	3,743,734	+28,680	103,126	+1,209	1,673,936	1,966,672	3,937	64.981	1,615	70,872,402	1,040.845	68,091,217

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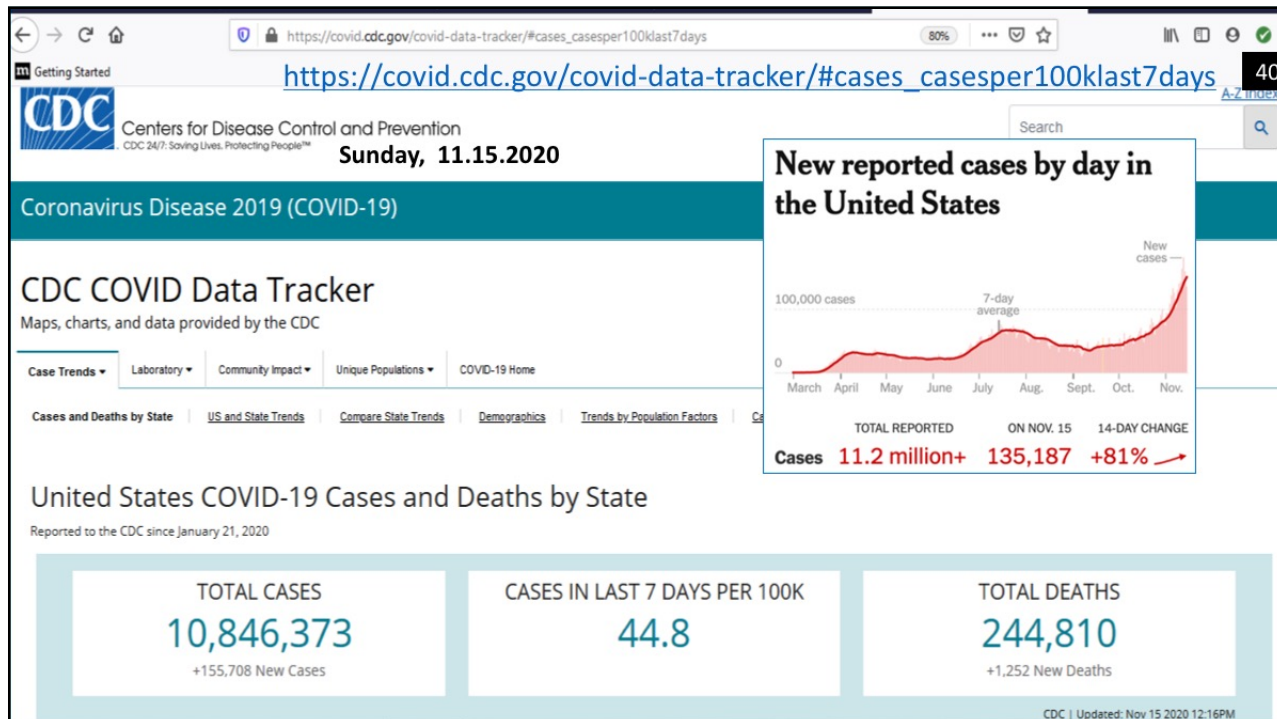
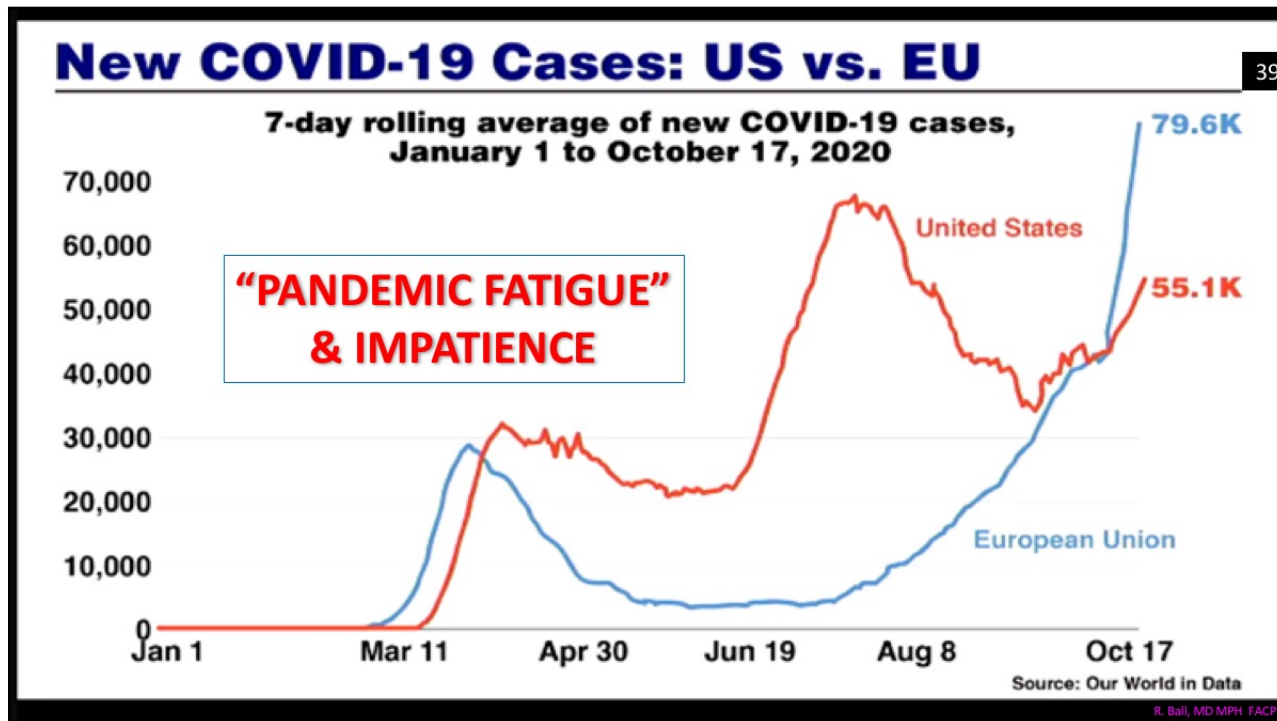


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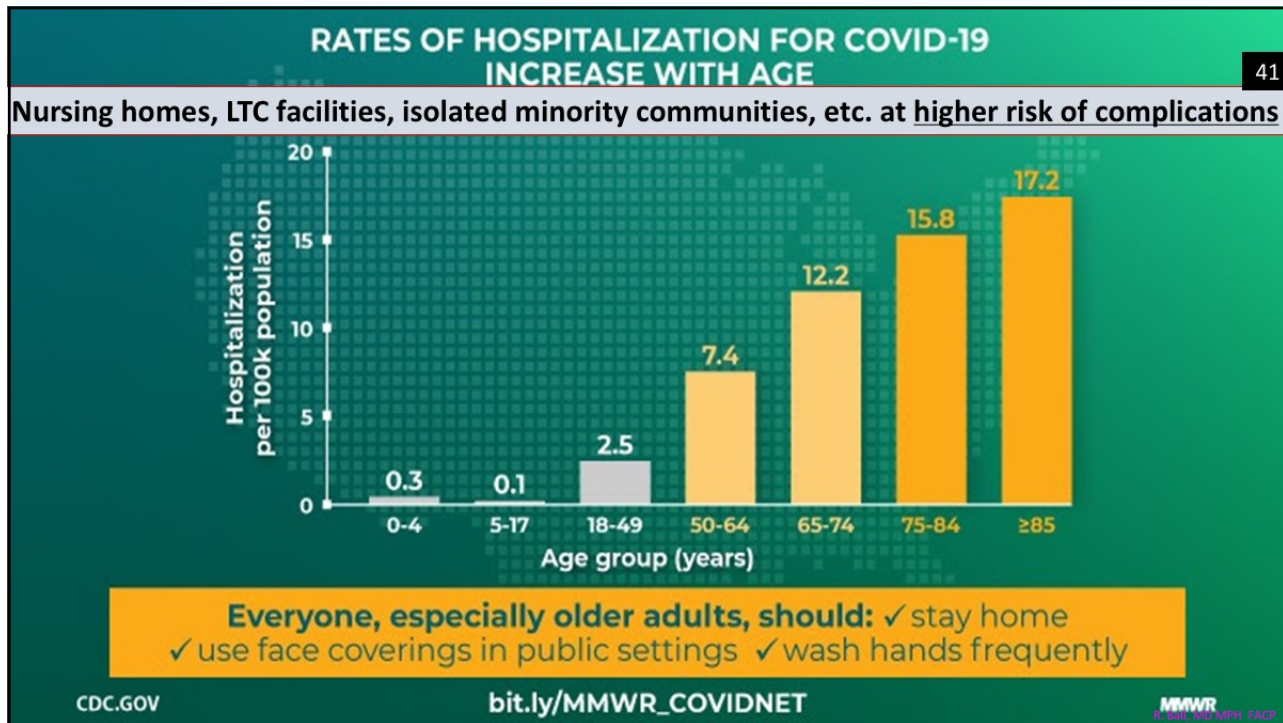
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TABLE 1. Total population and racial/ethnic disparities<sup>a</sup> in cumulative COVID-19 cases among 79 counties identified as hotspots during June 5–18, 2020, with any disparity identified — 22 states, February–June 2020

NMA Health Institute and the National Urban League.

NHLBI and NIMHD are collaborating on this event through the NIH Community Engagement Alliance (CEAL) Against COVID-19 Disparities. <https://covid19community.nih.gov/>

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**Summary**

**What is already known about this topic?**  
 Long-standing health and social inequities have resulted in increased risk for infection, severe illness, and death from COVID-19 among communities of color.

**What is added by this report?**  
 Among 79 counties identified as hotspots during June 5–18, 2020 that also had sufficient data on race, a disproportionate number of COVID-19 cases among underrepresented racial/ethnic groups occurred in almost all areas during February–June 2020.

**What are the implications for public health practice?**  
 Identifying health disparities in COVID-19 hotspot counties can inform testing and prevention efforts. Addressing the pandemic's disproportionate incidence among communities of color can improve community-wide health outcomes related to COVID-19.

State	No. of persons living in analyzed hotspot counties <sup>a</sup>	No. of (col %) hotspot counties analyzed <sup>a</sup>	No. of counties with disparities in COVID-19 cases among each racial/ethnic group <sup>b</sup>				
			Hispanic	Black	NHPI	Asian	AI/AN
South Carolina	1,000,000–3,000,000	9 (11.4)	6	4	2	—	—

**Disparities in Incidence of COVID-19 Among Underrepresented Racial/Ethnic Groups in Counties Identified as Hotspots During June 5–18, 2020 — 22 States, February–June 2020**

Jazmyn T. Moore, MSc, MPH<sup>1</sup>; Jessica N. Ricaldi, MD, PhD<sup>1</sup>; Charles E. Rose, PhD<sup>1</sup>; Jennifer Fuld, PhD<sup>1</sup>; Monica Parise, MD<sup>1</sup>; Gloria J. Kang, PhD<sup>1</sup>; Anne K. Driscoll, PhD<sup>1</sup>; Tina Norris, PhD<sup>1</sup>; Nana Wilson, PhD<sup>1</sup>; Gabriel Rainisch, MPH<sup>1</sup>; Eduardo Valverde, DrPH<sup>1</sup>; Vladislav Beresovsky, PhD<sup>1</sup>; Christine Agnew Brune, PhD<sup>1</sup>; Nadia L. Oussayef, JD<sup>1</sup>; Dale A. Rose, PhD<sup>1</sup>; Laura E. Adams, DVM<sup>1</sup>; Sindoo Awel<sup>1</sup>; Julie Villanueva, PhD<sup>1</sup>; Dana Meaney-Delman, MD<sup>1</sup>; Margaret A. Honein, PhD<sup>1</sup>; COVID-19 State, Tribal, Local, and Territorial Response Team.

**Mid-2020: SC had 2<sup>nd</sup> highest # of “hotspots” in US. NC was #1**

R. Ball, MD MPH, FACP


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# COVID-19:

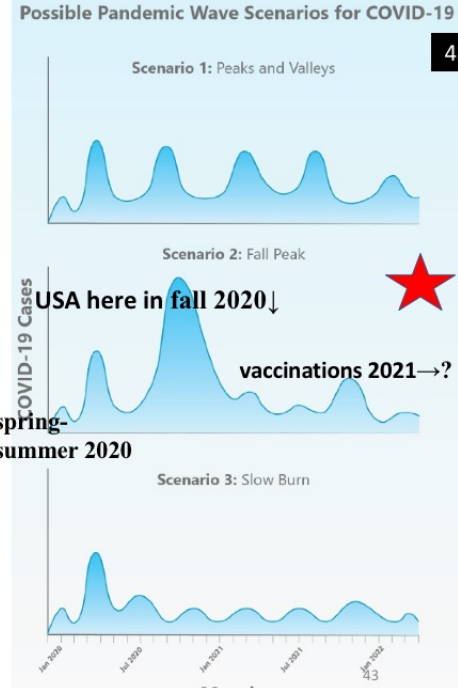
## The CIDRAP Viewpoint

4.30.2020

**COVID-19: The CIDRAP Viewpoint working group:**  
 Michael T. Osterholm, PhD, MPH, CIDRAP director



**Possible Pandemic Wave Scenarios for COVID-19**



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*R. Ball, MD MPH FACP*

Full Menu Environment Health Vital Records Maps & Apps

### Coronavirus Disease 2019 (COVID-19)

<https://www.scdhec.gov/coronavirus>

DHEC continues to work with federal, state and local partners as it investigates COVID-19 cases in South Carolina. DHEC's top priority remains protecting the public during this national and state emergency.

COVID-19 Stop the Spread of Germs PSA

## Stop the Spread of Germs

Help prevent the spread of respiratory viruses like COVID-19 and flu.

Detenga la Propagación de Microbios (COVID-19 & Gripe)

How to Protect Yourself & Your Family

What to do if You Feel Sick

Cloth Face Coverings (Homemade Masks)

**What you need to know**

6'

Watch for symptoms

Call ahead

Have a general question about COVID-19?  
 Call the DHEC Care Line at 1-855-472-3432 between 8 a.m. and 6 p.m. daily.

Full Menu Environment Health Vital Records Maps & Apps

Home \ Health Professionals \ Current Page

### South Carolina Health Alert Network (HAN)

This page lists the current health alerts of public health importance from DHEC.

- **Health Alert:** conveys the highest level of importance; warrants immediate action or attention.
- **Health Advisory:** provides important information for a specific incident or situation; may not require immediate action.
- **Health Update:** provides updated information regarding an incident or situation; unlikely to require immediate action.
- **Info Service:** Provides general information that is not necessarily considered to be of an emergent nature.

If you are a public health professional interested in receiving health notifications from the South Carolina Health Alert Network via email, you may sign up by clicking on the link below and completing the registration form. If you are approved to join the Health Alert Network, then your contact information will be added to the CodeRED system which is used to distribute health alerts. *R. Ball, MD MPH FACP*

6.2020

**Practice social distancing**

We tend to spend the most amount of time interacting with those who live closest to us. When around others, keep **6 feet between you when possible**. If you're sick, stay at home and don't attend public gatherings.

[Learn more](#)

**Watch for symptoms**

Before you act, know your symptoms so you can make the best decision for care.

Adults age 65 and older, and people with underlying conditions, should take extra precautions.

[Learn more](#)

**Call ahead**

If you have fever, cough or shortness of breath, please call your healthcare provider.

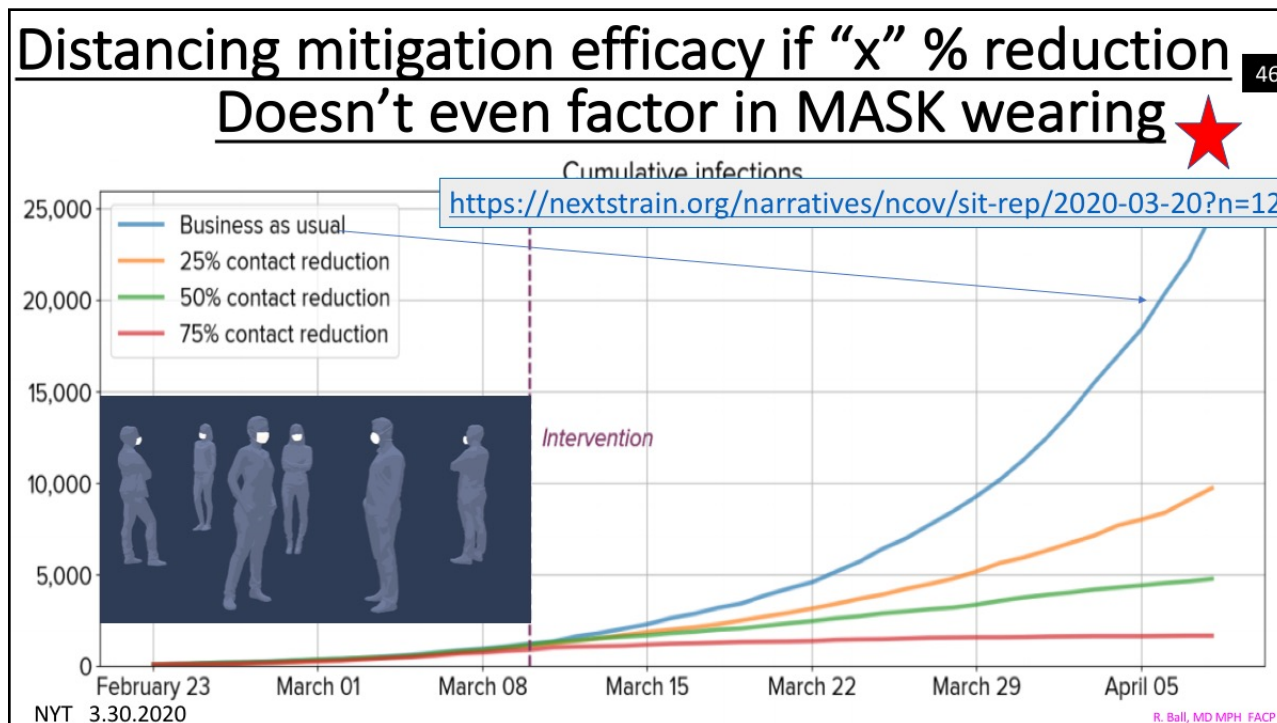
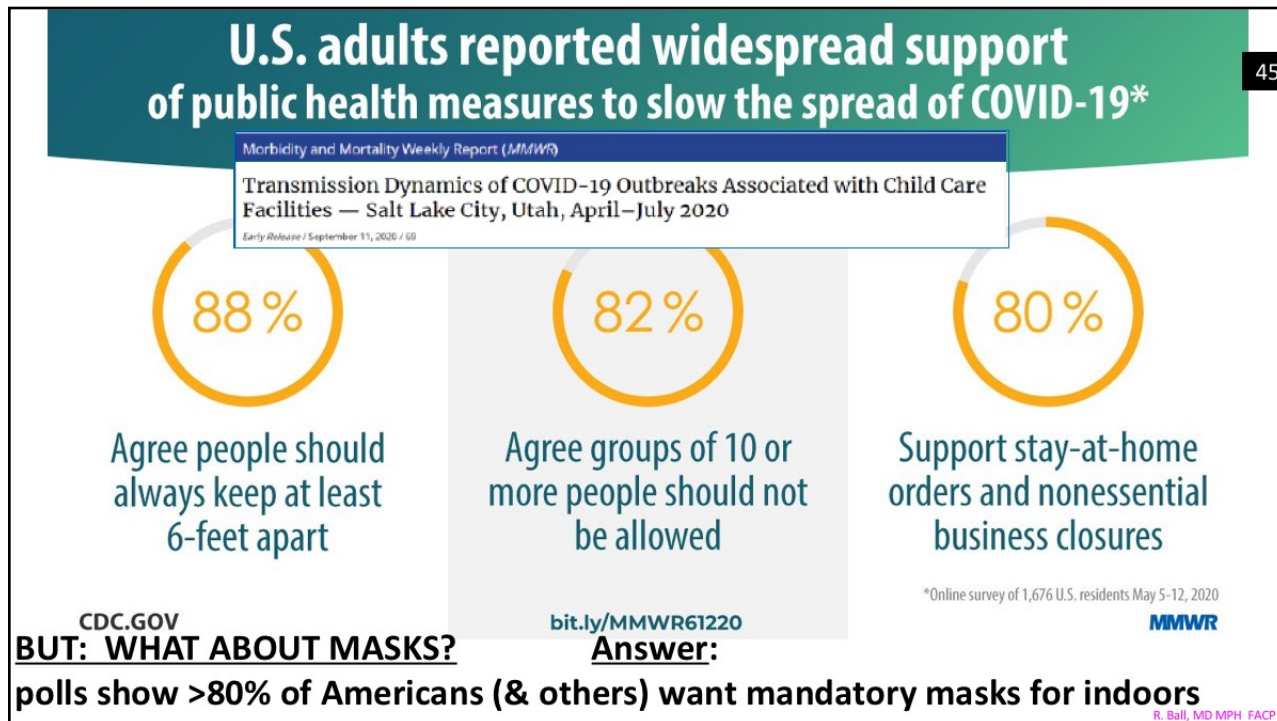
Please also see our listing of telehealth virtual care providers in South Carolina.

[Learn more](#)

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**PPE (“3 Ws”): WEAR a MASK, Watch your 6’+ distance, frequent handWashing,. Also: proper cough/ sneeze etiquette (into elbow), NO shaking hands (use “prayer hands” & a bow), avoid touching common surfaces, AVOID crowds (espec indoors), & use common sense! Schools=??**

A SEVERE SHORTAGE OF SURGICAL MASKS PROMPTS SOME PEOPLE TO THINK

**Cover your Cough**

R. Ball, MD MPH FACP

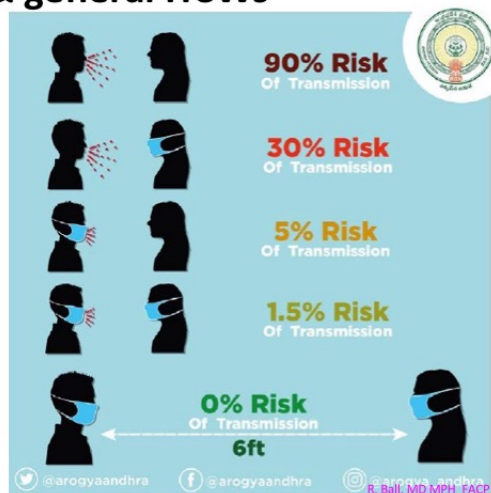
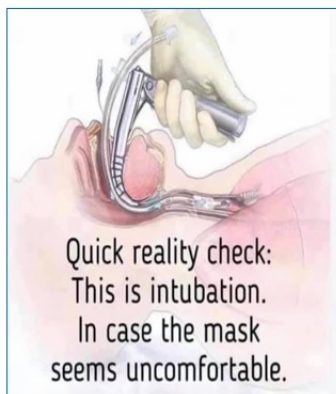
**PREVENTIVE MEASURES: MOSTLY MASKS!**



“surgical masks”: cheap, commonly worn by public & general HCWs



HCW medical N95 “respirators” filter ~95% large droplets





Anthony S. Fauci, the nation's top infectious-disease expert, endorsed a national mask mandate Wednesday (Wash. Post 10.28.2020) after months of reluctance. "What we can't have is this very inconsistent wearing that you see, where some states absolutely refuse to wear a mask," [Fauci said in an interview on CNBC](#). When the host asked if the government should force compliance, Fauci replied: "You know, yes."

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The Washington Post

BUT:  
American has many anti-maskers



R. Ball, MD MPH FACP

## Some reasons why SARS-CoV-2 is such a wildfire in USA

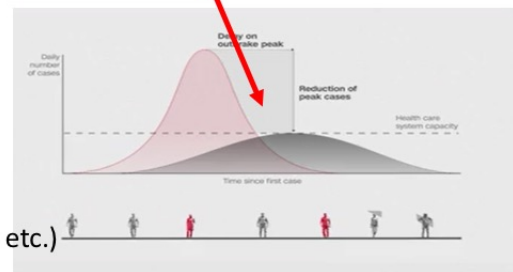
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### • PUBLIC IGNORANCE, APATHY, DENIAL/ REFUSAL

- General refusal to use COMMON SENSE PREVENTATIVES (ie, MASKS, > 6'+ social distancing, handwashing, avoid crowds espec. indoors, etc.)
- Political beliefs ("yahoos" vs common sense), often anti-government, anti-science, anti-public health, anti-mask "libertarians"

### • VIRAL FACTORS:

- Asymptomatic cases shed & infect others (incl. peds)
- Very high transmissibility
- Moderately short hort incubation period
- "Hot spots/ super-spreader events & people"  
(certain areas in many states) generate & propagate more cases (ie, WH Rose Garden; Charleston, SC mid-2020, etc.)



**Isolation** separates sick people with a contagious disease from people who are not sick.

**Quarantine** separates & restricts the movement of people who were exposed to a contagious disease to see if they become sick (from Latin *quadraginta* meaning "forty").

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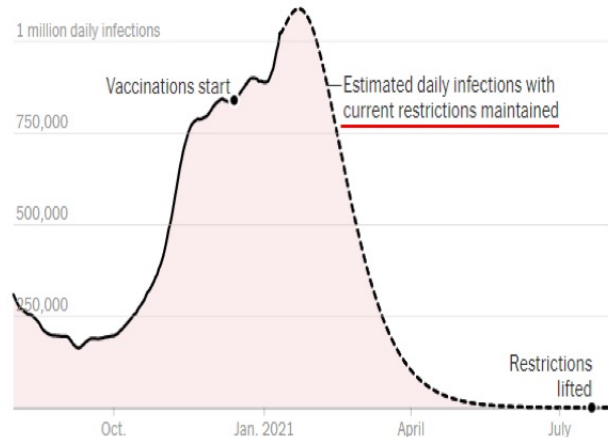
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**Q: continue restrictions (lockdowns), or lift (public pressure) ?**

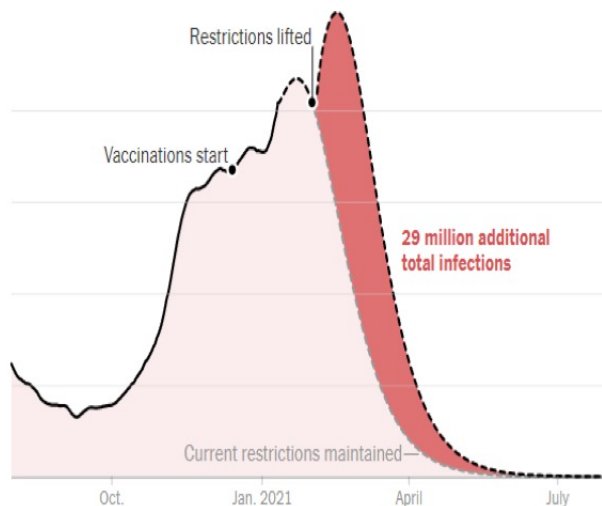
*The New York Times* 22 Jan. 2021

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**If current restrictions remain in place until late July**



**If restrictions are lifted in February**



R. Ball, MD MPH FACP

**SARS-nCoV-2/ COVID testing 2020**

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**3 basic types →**



1) current **NP PCR (nasal swab, or even saliva)** detects **RNA fragments** of SARS-CoV-2, whether in high or low concentrations (# of PCR cycles= Cn). Is **THE** diagnostic test (“gold standard”) to detect (+) virus in folk for several months; it’s still necessary (for now). ~ 99% sensitive, specific.

2) 3) New nasal swab tests for **Antigen (Ag)** got **EUA approval by US FDA 5.2020**, detect some CoV-2 proteins & can be done **rapidly** (like the flu nasal swab for influenza A&B Ag), with a result within an hour or less. Currently Quidel’s Sofia2 & Abbott’s BINAX-NOW, IDNOW have suboptimal sensitivity but decent specificity. These rapid tests, when validated, are likely to become commonplace.

3) **>50 new Antibody (Ab)** tests: (ie, Abbott Labs & others). Some have FDA EUA (requires blood-fingerstick or venipuncture) & detects (+) Ab of the IgG type (“G” for Geriatric, or older Ab, which last months/years, usually indicative of older/past infection), BUT some recent articles show that some COVID patients have trace IgG Ab and still harbor the virus (in very small amounts). And there are no data to prove binding Ab are fully or even partially “protective” or if so, for how long (months/ years/ ?). IgM Ab occurs sooner but w shorter duration. Neutralizing Ab better...

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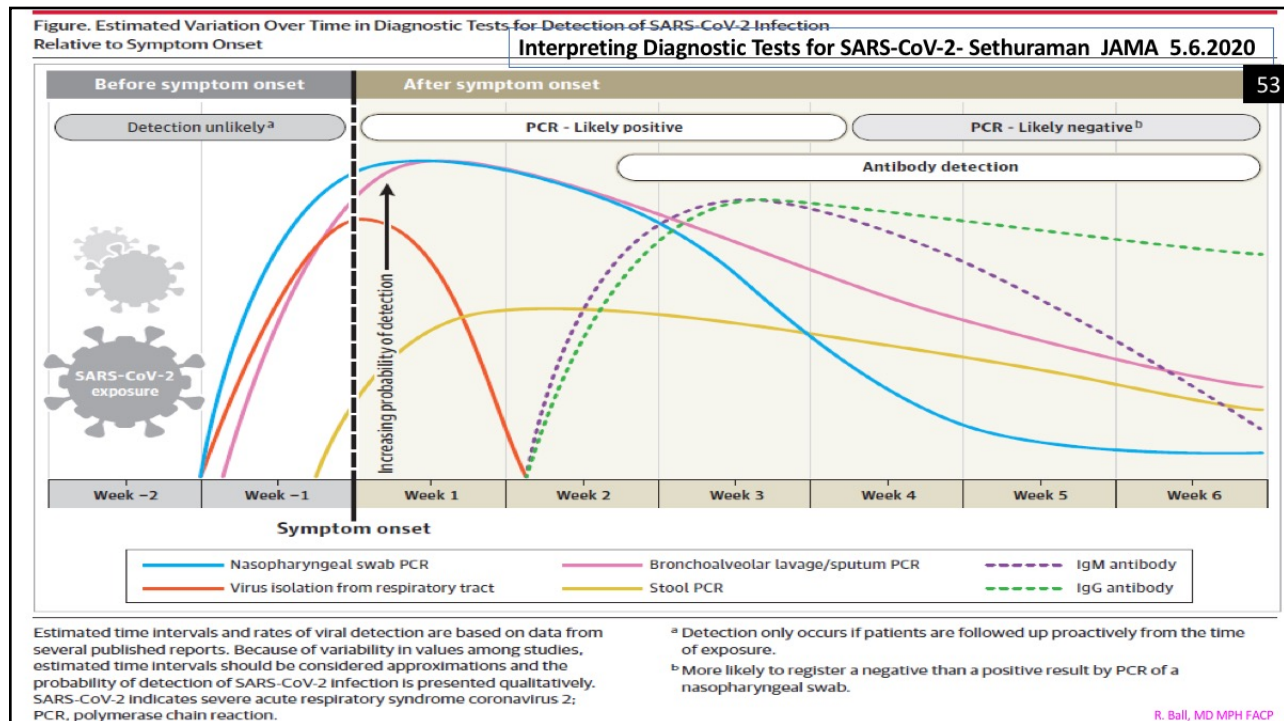
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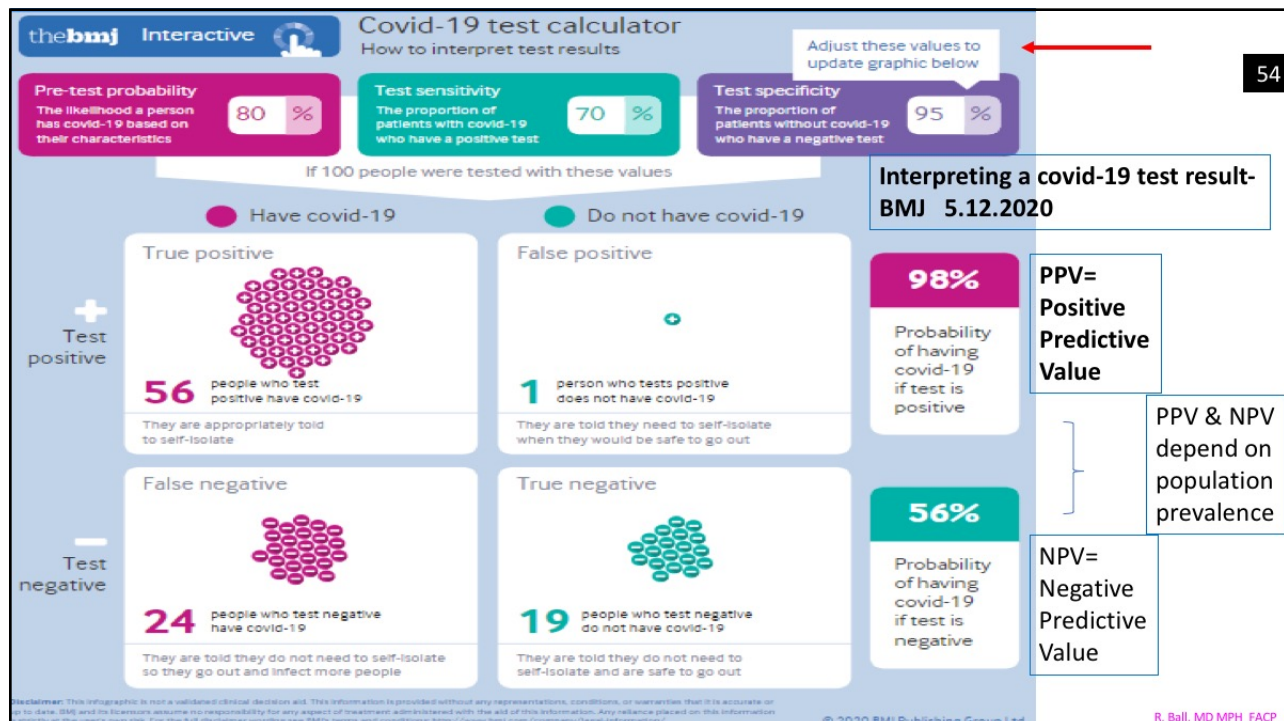
# COVID Update: Focus on Vaccines

## Dr. Robert T. Ball, University of South Carolina

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## Estimated Sensitivity and Specificity Based on Clinical Sample Collection

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**IDSA PCR Testing Guidelines**  
SE AETC webinar 6.9.2020

Test, % (95% CI)	Sensitivity	Specificity
Sample location (3 studies)		
▪ Upper respiratory tract	76 (51-100)	100 (99-100)
▪ Lower respiratory tract	89 (84-94)	100 (99-100)
Upper respiratory tract samples (11 studies)*		
▪ Oral	56 (35-77)	99 (99-100)
▪ Nasal	76 (59-94)	100 (99-100)
▪ Nasopharyngeal	97 (92-100)	100 (99-100)
▪ Nasal (vs nasopharyngeal)	95 (87-100)	100 (99-100)
▪ Saliva	85 (69-94)	100 (99-100)
▪ Mid-turbinate <span style="color: red; font-size: 1.2em;">→</span>	100 (93-100)	100 (99-100)
Repeat testing (via nasopharyngeal swabs; 3 studies)		
▪ Single test	71 (65-77)	100 (99-100)
▪ Repeat test	88 (80-96)	100 (99-100)

\*Not head-to-head comparisons. Not all specimens were collected from the same patients at the same time point, the time of collection from symptom onset was not provided in all studies, and the studies used various approaches for establishing SARS-CoV-2 positivity to define positive results.

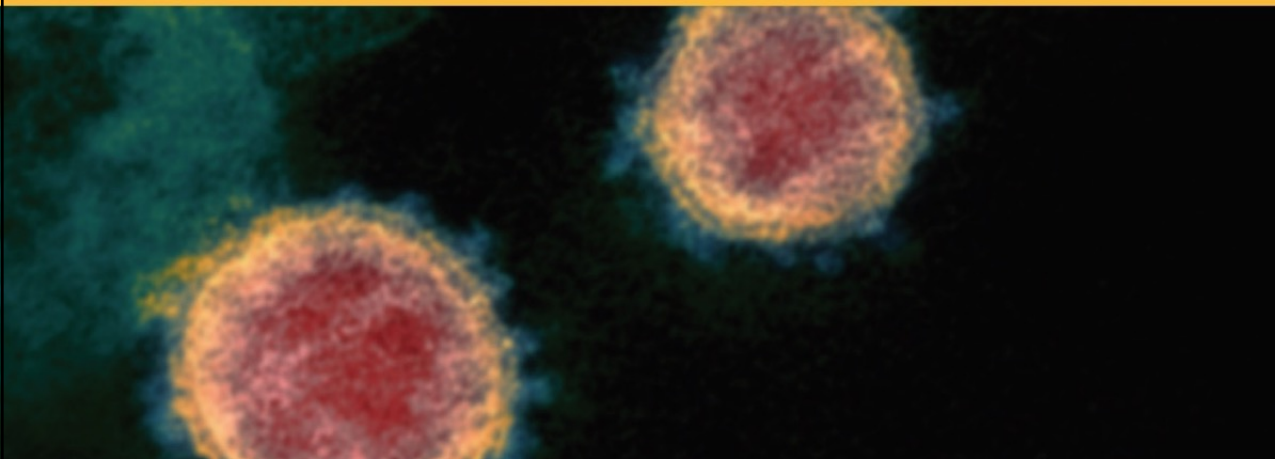
IDSA. COVID-19 Guideline, Part 3: Diagnostics. Version 1.0.1. Slide credit: [clinicaloptions.com](http://clinicaloptions.com)  
R. Ball, MD MPH, FACP

NIH

COVID-19 Treatment Guidelines

2020

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# Coronavirus Disease 2019 (COVID-19)


## Treatment Guidelines


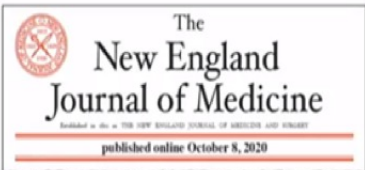

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**COVID Update: Focus on Vaccines**  
**Dr. Robert T. Ball, University of South Carolina**  
**A Webber Training Teleclass**

Annals of Internal Medicine	5.27.2020	REVIEW	Journal Pre-proof	1.9.2021	
<b>Hydroxychloroquine or Chloroquine for Treatment or Prophylaxis of COVID-19 NOT to be used except in clinical trials</b>			<b>? use of Vit. D in treatment</b>		
<b>A Living Systematic Review</b>			Vitamin D Status is Associated With In-hospital Mortality and Mechanical Ventilation: A Cohort of COVID-19 Hospitalized Patients		
Adrian V. Hernandez, MD, PhD; Yuani M. Roman, MD, MPH; Vinay Pasupuleti, MD, MS, PhD; Joshua J. Barboza, MSc; and C. Michael White, PharmD			Angeliki M. Angelidi, MD PhD, Matthew J. Belanger, MD, Michael K. Lorinsky, MD, Dimitrios Karamanis, PhD, Natalia Chamorro-Pareja, MD, Jennifer Ognibene, BA, Leonidas Palaolimos, MD MSc, Christos S. Mantzoros, MD DSc		
<b>Background:</b> Hydroxychloroquine and chloroquine have antiviral effects in vitro against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).			logic clearance with antigen testing. Several studies found that patients receiving hydroxychloroquine developed a QTc interval of 500 ms or greater, but the proportion of patients with this finding varied among the studies. Two studies assessed the efficacy of chloroquine; 1 trial, which compared higher-dose (600 mg twice daily for 10 days) with lower-dose (450 mg twice daily on day 1 and once daily for 4 days) therapy, was stopped owing to concern that the higher dose therapy increased lethality and QTc interval prolongation. An observational study that compared adults with COVID-19 receiving chloroquine phosphate, 500 mg once or twice daily, with patients not receiving chloroquine found minor fever resolution and virologic clearance benefits with chloroquine.		
<b>Purpose:</b> To summarize evidence about the benefits and harms of hydroxychloroquine or chloroquine for the treatment or prophylaxis of coronavirus disease 2019 (COVID-19).			<b>“Conclusion: Among patients admitted with laboratory-confirmed COVID-19, 25(OH)D levels <math>\geq 30</math> ng/mL were inversely associated with in-hospital mortality and the need for invasive mechanical ventilation. Further observational studies are needed to confirm these findings and randomized clinical trials to assess the role of vitamin D administration in improving the morbidity and mortality of COVID-19.”</b>		
<b>Data Sources:</b> PubMed (via MEDLINE), EMBASE (via Ovid), Scopus, Web of Science, Cochrane Library, bioRxiv, Preprints, ClinicalTrials.gov, World Health Organization International Clinical Trials Registry Platform, and the Chinese Clinical Trials Registry from 1 December 2019 until 8 May 2020.			<b>Limitation:</b> There were few controlled studies, and control for confounding was inadequate in observational studies.		
<b>Study Selection:</b> Studies in any language reporting efficacy or safety outcomes from hydroxychloroquine or chloroquine use in any setting in adults or children with suspected COVID-19 or at risk for SARS-CoV-2 infection.			<b>Conclusion:</b> Evidence on the benefits and harms of using hydroxychloroquine or chloroquine to treat COVID-19 is very weak and conflicting.		
<b>Data Extraction:</b> Independent, dually performed data extraction and quality assessments.			<b>Primary Funding Source:</b> Agency for Healthcare Research and Quality.		
<b>Data Synthesis:</b> Four randomized controlled trials, 10 cohort studies, and 9 case series assessed treatment effects of the medications, but no studies evaluated prophylaxis. Evidence was conflicting and insufficient regarding the effect of hydroxychloroquine on such outcomes as all-cause mortality, progression to severe disease, clinical symptoms, and upper respiratory viro-			<small>Annu Intern Med. 2020;173:287-296. doi:10.7326/M20-2496</small> <small>Annals.org</small> <small>For author, article, and disclosure information, see end of text.</small> <small>This article was published at Annals.org on 27 May 2020.</small>		
					<small>R. Ball, MD MPH FACP</small>

<b>Annual Meeting 2020   Confronting Urgent Threats to Human Health &amp; Society</b>	
<b>Superior clinical status and recovery rates with 5 days of remdesivir</b>	<div data-bbox="781 1283 1143 1451">  </div> <div data-bbox="581 1455 1344 1612"> <p align="center"><b>Remdesivir for the Treatment of Covid-19 — Final Report</b></p> <p align="center">JH Beigel, HC Lane et al. for the ACTT-1 Study Group Members</p> </div> <div data-bbox="561 1625 1365 1822"> <ul style="list-style-type: none"> <li><span style="background-color: yellow;">■ Hospitalized patients on remdesivir recovered more quickly than those on placebo (median 10 days vs 15 days, P&lt;0.001)</span></li> <li><span style="background-color: yellow;">■ A trend toward decreased mortality: hazard ratio = 0.73 (95% CI: 0.52–1.03)</span></li> <li><span style="background-color: yellow;">■ 1,062 patients from 10 countries: U.S., Europe and Asia</span></li> </ul> </div>
	58
National Academy of Medicine Ann. Mtng. 10.19.2020	<small>R. Ball, MD MPH FACP</small>

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## Therapeutics for COVID-19

National Academy of Medicine  
 Ann. Mtng. 10.19.2020 (Fauci)

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### Recommended by the NIH COVID-19 Treatment Guidelines Panel for Certain Patients

- Remdesivir (investigational antiviral)
- Dexamethasone (corticosteroid)

### Examples of Other Investigational Therapies

- Antivirals
- Blood-derived products, e.g., convalescent plasma, hyperimmune globulin
- Monoclonal antibodies against SARS-CoV-2
- Immunomodulators, e.g., cytokine inhibitors, interferons
- Adjunct therapies, e.g., anticoagulants



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## MONOCLONAL ANTIBODY THERAPY FOR MILD-MODERATELY ILL COVID PATIENTS AT HIGH RISK OF HOSPITALISATION AND COMPLICATIONS

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### NIH Guidelines – update Nov 18 2020

- On November 9, 2020, the FDA issued an Emergency Use Authorization for bamlanivimab (LY-CoV555)
  - Treatment of non-hospitalized patients who are at high risk of progressing to severe COVID-19
- There are insufficient data to recommend either for or against the use of bamlanivimab for the treatment of outpatients with mild to moderate COVID-19.
- Patients who are hospitalized for COVID-19 should not receive bamlanivimab outside of a clinical trial.
- Given the possibility of a limited supply of bamlanivimab, as well as challenges distributing and administering the drug, patients at highest risk for COVID-19 progression should be prioritized for use of the drug through the EUA.

AETC

Lilly: LY-CoV555 bamlanivimab (single monoclonal Ab Tx):  
 dose IV. USA: FDA EUA on 11.9.2020  
 Requirements: age  $\geq 12$ yo, high-risk for hospitalization, etc.

### Regeneron (double monoclonal Ab Tx):

USA: FDA EUA on 11.21.2020

Casirivimab + Imdevimab = REGN10933 and REGN10987

One IV dose x 5 days.

Requirements: age  $\geq 12$ yo, high-risk for hospitalization, etc.

### Other investigational antivirals for treatment of mild COVID-19

- MK-4482 - molnupiravir
  - orally bioavailable ribonucleoside inhibitor that was originally developed for influenza
  - administered orally every 12 hours for 5 days (10 doses total), ([NCT04575597](#))
- SNG001
  - Nebulized formulation of interferon- $\beta$ 1a developed for viral infections in patients with chronic obstructive pulmonary disease ([NCT04385095](#))
- Camostat mesylate, 200mg taken 7 days.
  - serine protease inhibitor approved for treatment of chronic pancreatitis and postoperative reflux esophagitis ([NCT04353284](#)).

AETC

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**Ref: COVID-19 vaccines- The status and perspectives in delivery points of view- Chung+ ScienceDirect via Elsevier March 2021** doi:10.1016/j.addr.2020.12.011

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Repurposed drugs for COVID-19.

Category	Drugs	Mechanism of action	Status of clinical use
Anti-viral	Remdesivir	Inhibition of viral replication	Approved by the FDA
	Favipiravir	Inhibition of viral-RNA dependent RNA polymerase	Under clinical trials
	Lopinavir-Ritonavir	Inhibition of protease enzymes (HIV reverse transcriptase inhibitors)	Under clinical trials
	Umifenovir	Inhibition of viral and cellular membrane fusion	Under clinical trials
	Camostat (TMPRSS2 inhibitor)	Blockade of viral maturation and entry to host cells	Under clinical trials
	Hydroxychloroquine	Inhibition of virus entry, elevate endosomal pH and interfere with ACE2 glycosylation	Emergency use terminated by the FDA (Serious cardiac events)
	Azithromycin	Indirect immunomodulatory effects	Under clinical trials
Anti-inflammatory	Tocilizumab	Blockade of IL-6 receptors and its downstream signaling pathways	Under clinical trials
	Anakinra	Blockade of IL-1 receptors and its downstream signaling pathways	Under clinical trials
	Ruxolitinib	JAK signaling inhibition, Immune suppression	Under clinical trials
	Baricitinib	Inhibition of viral invasion and JAK signaling, Immune suppression	Under clinical trials
	Thalidomide	Reduction of inflammatory cell infiltration, reduce cytokine storm	Under clinical trials
	Glucocorticoids	Suppression of immune and inflammatory response	Dexamethasone authorized use in critically ill patients
Monoclonal antibody	Bamlanivimab	Inhibit viral entry into host cells	Emergency Use Authorization
	Casirivimab and imdevimab	Inhibit viral entry into host cells	Emergency Use Authorization
Plasma therapy	Convalescent plasma	Virus elimination via virus-specific antibodies	Under clinical trials
Cell-based therapy	Mesenchymal stem cell	Facilitate tissue regeneration and immune suppression	Under clinical trials
	NK cell	Strengthen immune response	Under clinical trials

**COVID-19 Therapeutics, vaccines: ~summary**

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**1.2021**

- **ANTI-VIRALS:** IV **Remdesivir** (Veklury): a nucleoside analog (polymerase-inhibitor) with good antiviral activity. +in USA. 4.2020: Adaptive Clinical Trials (NIH/ NIAID ACTIV)-> FDA EUA 5.1.2020, **approved 10.23.2020 for >12yo.** Others: ?Favipiravir (oral RT inhibitor); other antivirals (~HIV) Rx (ie, lopinavir, Kaletra +/-?)
- **CONVALESCENT PLASMA (CP) Antibodies [IgG]** from recovered COVID-19 patients: in several case series reports, CP allowed faster recovery times and prevented deaths & hospitalizations, but more RCTs are needed to validate.
- **ANTI-CYTOKINE STORM (↑ IL-6+) AGENTS:** **steroids**=dexamethasone FDA EUA+; tocilizumab (TCZ)- (Roche 3.23.2020: US FDA approved;), others... (? ribavirin+ interferon +/-)
- **MONOCLONAL neutralizing B-Cell Antibodies v surface "S" spike glycoprotein.** Lilly Co. mAb Bamlanivimab. Trials of IL-6 inhibitors: ramlavimabab, sarilumab, others...
- **>40+ VACCINES- 4 platforms:** (mRNA, repl.-defective viral vectors, adjuvanted subunit protein, live attenuated) **Early: Pfizer+ BioNTech & Moderna** (m-RNA); **AstraZeneca-Oxford AZD1222** (A.E.9.9.20, used now in UK); **J&J/Janssen (1 shot); Novavax;** Univ. of Miami School of Medicine+ Heat Biologics-Sinovac; & many more. **Results?** late fall-winter 2020→2021++ Medico-ethical issues include: which groups get first doses (Phases 1a,1b,1c, 2...) 1a:HCWS, hi-risk folk, minorities, etc.). **BIG Qs:** the anti-vaxxers (polls 10.2020 ~30-40% of US popul.). Booster vax needed @21/28 d. Pfizer requires ultracold storage (-74<sup>o</sup> F!). **Ideal:** refrig/ room temp.



**Studies +/- on other Rx's** (ie, [anticoagulants ~ASA+] colchicine, famotidine [H2 blocker], ^dose Vit. D, fluvoxamine, melatonin, ^ivermectin, etc.). Hydroxychloroquine NOT effective (can ↑mortality).

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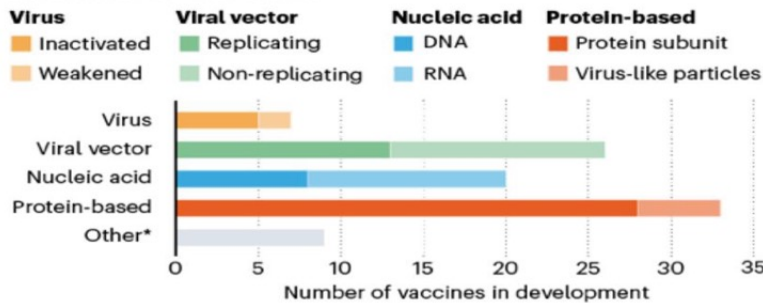
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**Dr. Robert T. Ball, University of South Carolina**  
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**How modern vaccines work**

**COVAX Accelerator, led by the World Health Organization (WHO) and other global health groups including Gavi**

**AN ARRAY OF VACCINES**



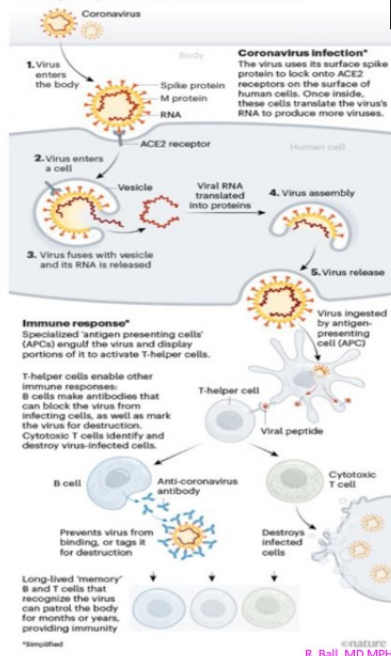
\* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

enature

slide courtesy of Carlos del Rio MD, Emory Univ., Atlanta

**VACCINE BASICS: HOW WE DEVELOP IMMUNITY**

The body's adaptive immune system can learn to recognize new, invading pathogens, such as the coronavirus SARS-CoV-2.

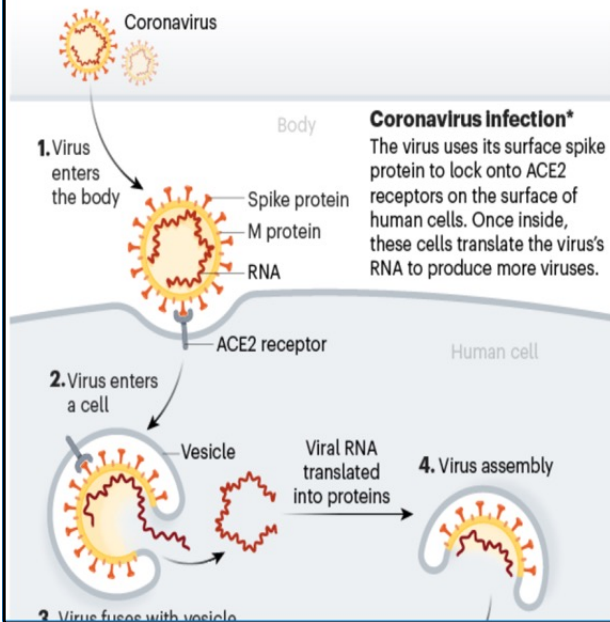


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**VACCINE BASICS: HOW WE DEVELOP IMMUNITY**

The body's adaptive immune system can learn to recognize new, invading pathogens, such as the coronavirus SARS-CoV-2.



**Advanced Candidates—January 2021**

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- mRNA
  - BNT162b2 (Pfizer-BioNTech) – EUA granted 12/11/2020
  - mRNA-1273 (Moderna) – EUA granted 12/18/2020
- Non-Replicating Viral Vector
  - ChAdOx1 (Astra Zeneca-Oxford)
  - Ad26.COV2.S (Janssen)
- Protein Subunit
  - NVX-CoV2373 (Novavax)
  - MRT5500 (Sanofi-Translate Bio)

NFID webinar 1.06.2021  
 Trade names used for clarification purposes only



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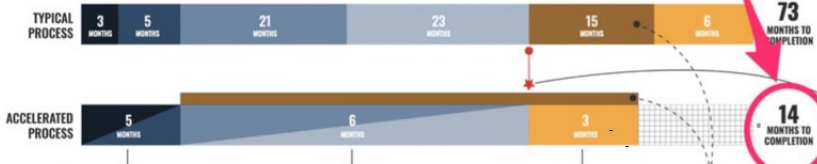


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Op. Warp Speed only designed for prevention of hospitalization, death- NOT to prevent aSx infection or transmission (TBD).

## OPERATION WARP SPEED ACCELERATED VACCINE PROCESS

**MISSION: Deliver 300 million doses of safe and effective vaccine by 1 January 2021.**



- A typical 8-month process is accelerated by:
  - Creating vaccine candidates immediately after viral genome sequence is available.
  - Using vaccine platforms developed for other diseases.
- A typical 42-month process is accelerated by:
  - Large scale Phase III clinical trials of 30,000 volunteers allowing for rapid collection and earlier analysis of safety and efficacy data of demographically diverse populations by the FDA, reducing the typical 12-month approval process to three months.
  - Two promising candidates began Phase III clinical trials in July, with others to follow quickly in coming months. Before beginning Phase III, candidates must show safety data from animal and human studies.
  - The U.S. Government funding at-risk, large-scale manufacturing of the most promising vaccine candidates during Phase III clinical trials to ensure any vaccine proven to be safe and effective is available immediately upon FDA Emergency Use Authorization (EUA) approval or licensure.
- A typical 6-month process is accelerated by:
  - A tiered approach based on CDC recommended allocation methodology used as part of pandemic flu planning and the COVID-19 response will be used to determine vaccine distribution.
- A typical 15-month process is accelerated by:
  - Planning for infrastructure and distribution before the vaccines are approved or authorized.
  - CDC leading distribution planning with DoD augmentation.
- A typical 12-month FDA review for EUA approval or licensure is accelerated by:

Op. Warp Speed only had 20 million doses on hand 12.31.2020, & just 12.4 million of those had been distributed to states @ end 2020.

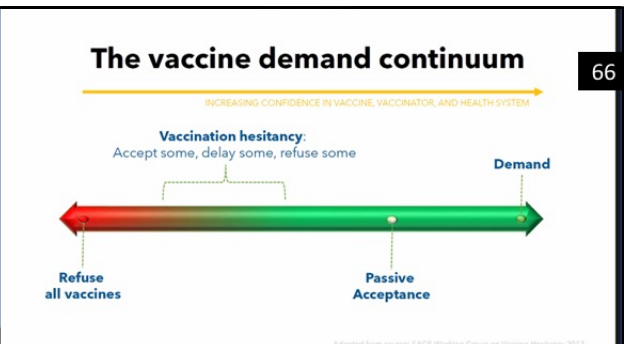
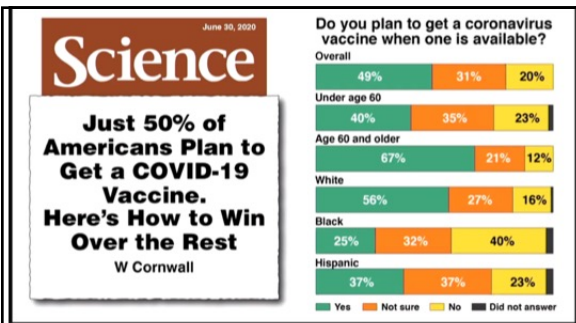
■ R&D - Preclinical Trials Vaccine Candidate/s Identified ■ Phase II Clinical Trials  
 ■ Phase I Clinical Trials ■ Phase III Clinical Trials ■ Manufacturing ■ Distribution

<https://media.defense.gov/2020/Aug/13/2002476369/-1/-1/0/200813-D-ZZ999-100.JPG>

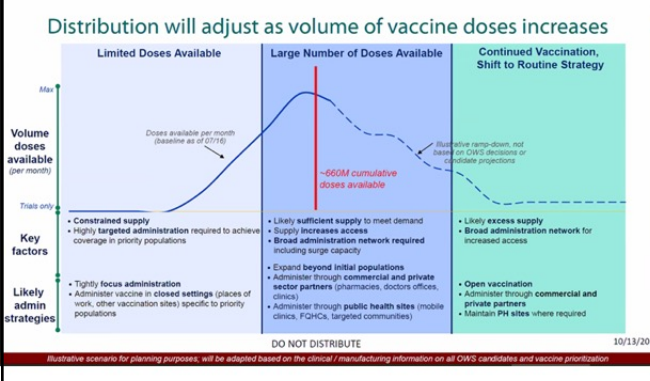
44 in clinical trials  
154 in preclinical eval

- 2 mRNA**
- Pfizer mRNA BNT162b2; Phase 3: Jul 27; >42K → 44K (>35K dose 2)
  - Moderna mRNA-1273; Phase 3: Jul 27; 30K (>25K dose 2)
- 2 viral-vectored**
- AstraZeneca ChAd-Spike; Phase 3: Aug 31; On hold until 23OCT
  - Janssen Ad26-Spike; Phase 3: Sep 23; On hold until 23OCT
- 2 S protein-based**
- Novavax NVX-CoV2373
  - Sanofi/GSK

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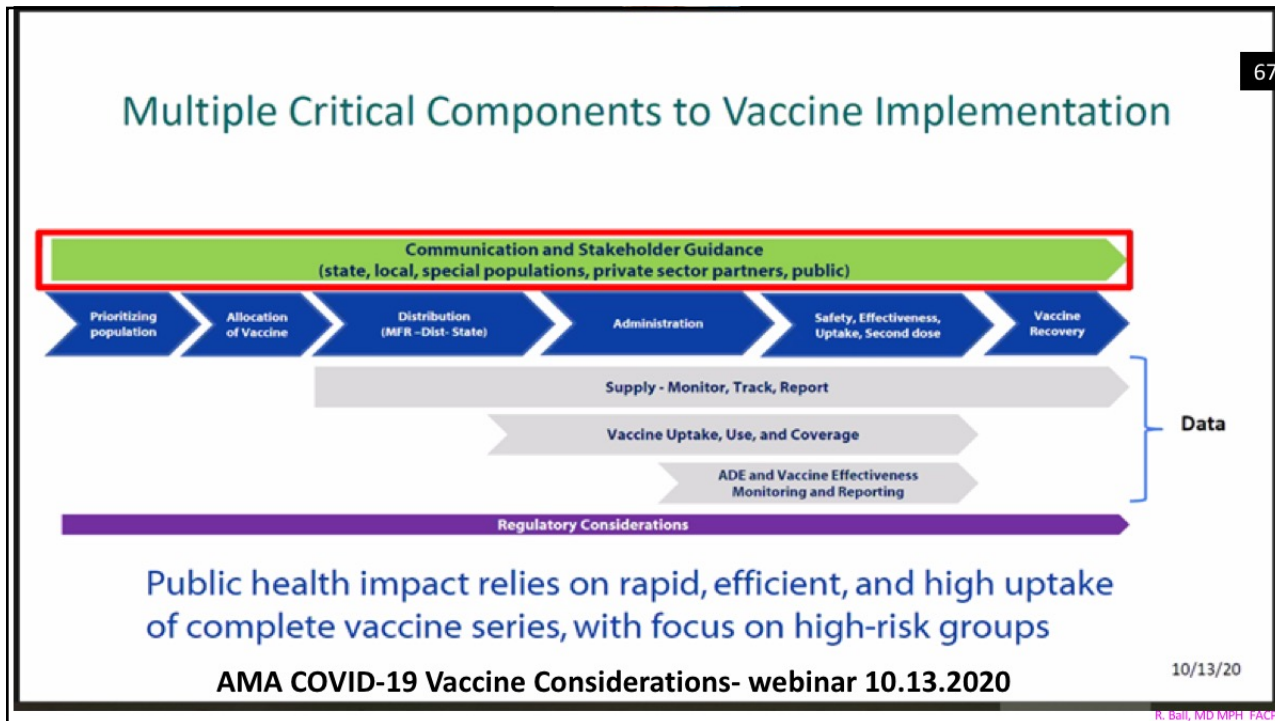


Platform	Developer	Phase 1/2	Phase 2/3
Nucleic acid	moderna	Enrolled	Ongoing
	BIONTECH	Enrolled	Ongoing
Viral vector	OXFORD or AstraZeneca	Enrolled	Ongoing
	janssen	Enrolled	Ongoing
	MERCK	Ongoing	--
Protein subunit	NOVAVAX	Ongoing	Ongoing
	gsk SANOFI	Ongoing	--

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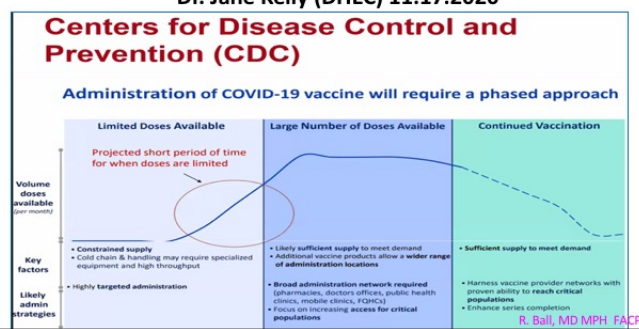
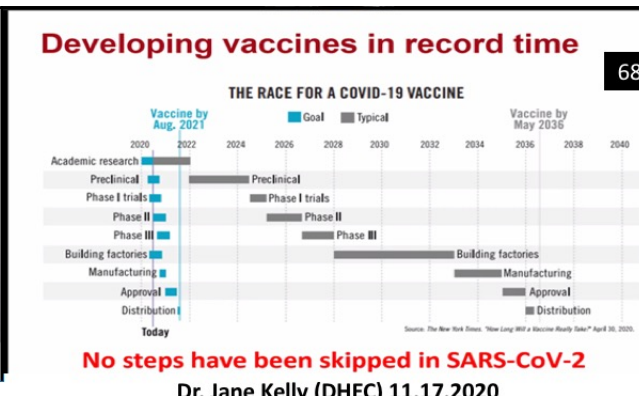
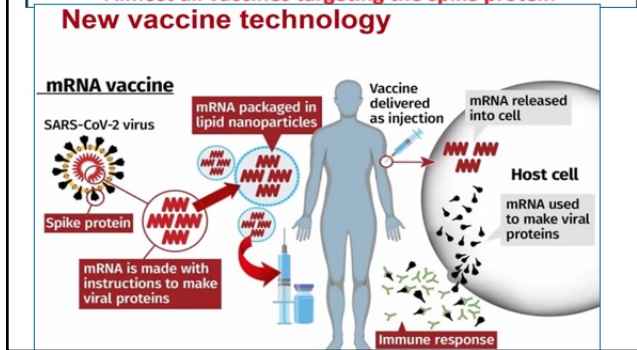


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### Vaccine Platform Technologies

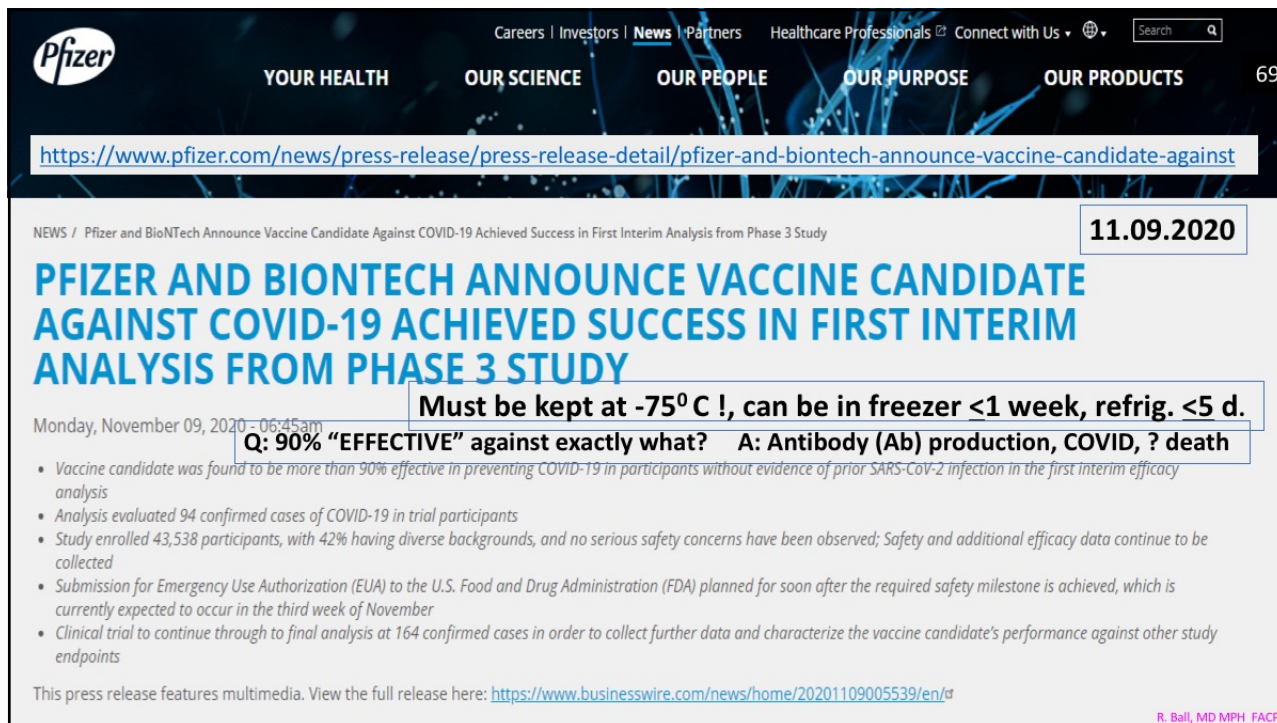
Genetic immunization (DNA and RNA vaccines) SARS, MERS, West Nile, Zika, RSV	Nanoparticles (viral protein on particle) Influenza, Malaria, RSV
Viral vector (e.g., VSV, adenovirus) Ebola, Marburg, Zika	Virus-like particle (VLP) (no RNA or DNA; non-infectious) Chikungunya, Zika, WEVEE
Recombinant protein Influenza, RSV	Adjuvants (e.g., AS01, MF59)

**Almost all vaccines targeting the spike protein**





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<https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-vaccine-candidate-against>

NEWS / Pfizer and BioNTech Announce Vaccine Candidate Against COVID-19 Achieved Success in First Interim Analysis from Phase 3 Study **11.09.2020**

## PFIZER AND BIONTECH ANNOUNCE VACCINE CANDIDATE AGAINST COVID-19 ACHIEVED SUCCESS IN FIRST INTERIM ANALYSIS FROM PHASE 3 STUDY

Monday, November 09, 2020 - 06:45am

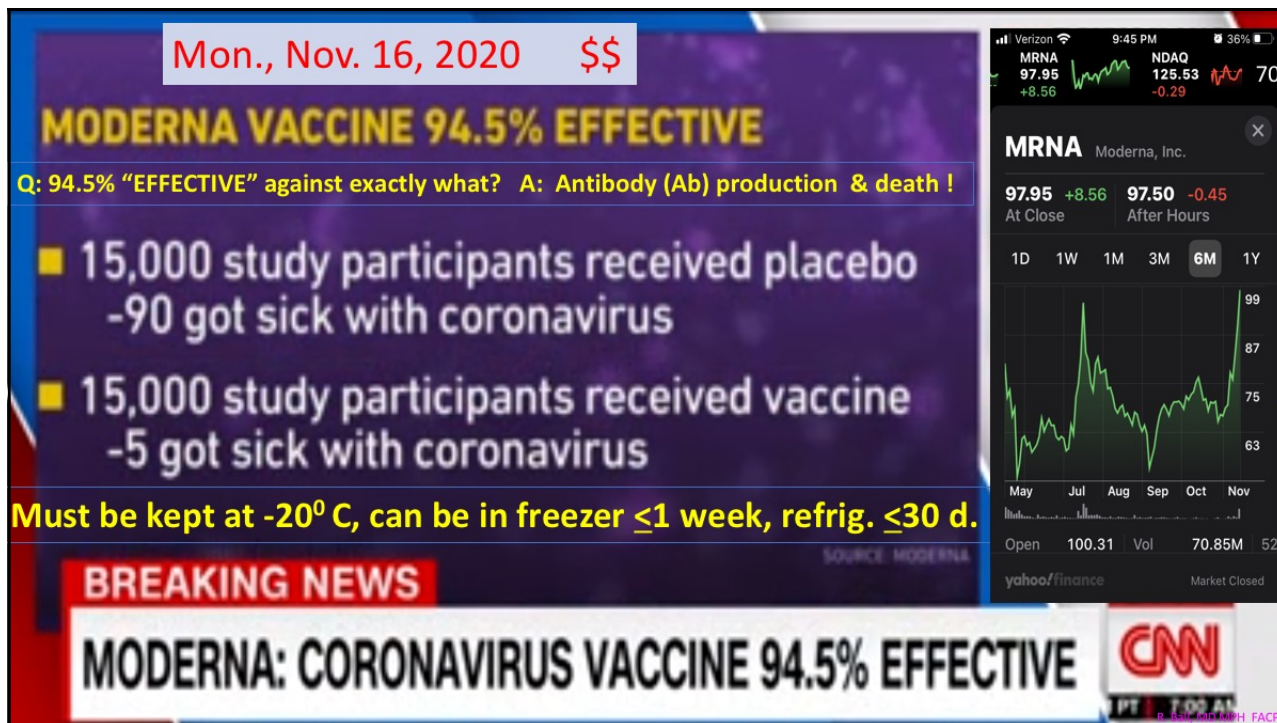
**Must be kept at -75° C !, can be in freezer <1 week, refrig. <5 d.**

**Q: 90% "EFFECTIVE" against exactly what?   A: Antibody (Ab) production, COVID, ? death**

- Vaccine candidate was found to be more than 90% effective in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection in the first interim efficacy analysis
- Analysis evaluated 94 confirmed cases of COVID-19 in trial participants
- Study enrolled 43,538 participants, with 42% having diverse backgrounds, and no serious safety concerns have been observed; Safety and additional efficacy data continue to be collected
- Submission for Emergency Use Authorization (EUA) to the U.S. Food and Drug Administration (FDA) planned for soon after the required safety milestone is achieved, which is currently expected to occur in the third week of November
- Clinical trial to continue through to final analysis at 164 confirmed cases in order to collect further data and characterize the vaccine candidate's performance against other study endpoints

This press release features multimedia. View the full release here: <https://www.businesswire.com/news/home/20201109005539/en/>

R. Ball, MD MPH FACP



**Mon., Nov. 16, 2020   \$\$**

## MODERNA VACCINE 94.5% EFFECTIVE

**Q: 94.5% "EFFECTIVE" against exactly what?   A: Antibody (Ab) production & death !**

- 15,000 study participants received placebo -90 got sick with coronavirus
- 15,000 study participants received vaccine -5 got sick with coronavirus

**Must be kept at -20° C, can be in freezer <1 week, refrig. <30 d.**

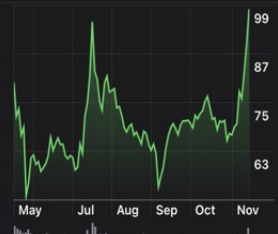
SOURCE: MODERNA

**MRNA** Moderna, Inc.

**97.95** +8.56   **97.50** -0.45

At Close   After Hours

1D 1W 1M 3M **6M** 1Y



May Jul Aug Sep Oct Nov

Open 100.31   Vol 70.85M 52

yahoo/finance   Market Closed

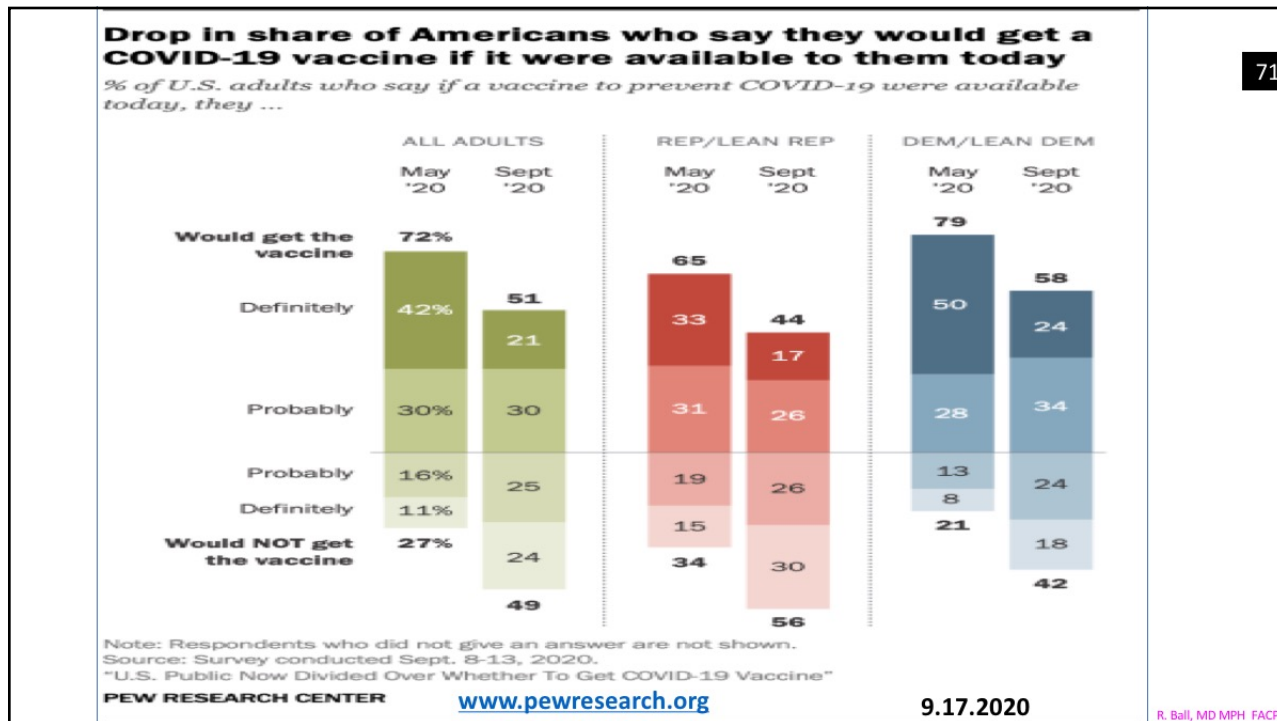
**BREAKING NEWS**

## MODERNA: CORONAVIRUS VACCINE 94.5% EFFECTIVE

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[F.D.A. Grants Emergency Authorization of Antibody Treatment-The New York Times \(nytimes.com\)](https://www.nytimes.com)

The treatment, made by the biotech company Regeneron, is a cocktail of two powerful antibodies that have shown promise for people who get it early in the course of the disease.

The treatment, made by the [biotech company Regeneron](#), is a cocktail of two powerful antibodies that have shown promise in early studies at keeping the infection in check, reducing medical visits in patients who get the drug early in the course of their disease. A similar treatment, made by Eli Lilly, was given emergency approval [earlier this month](#).



**Estimating Herd Immunity Thresholds for SARS-CoV-2**

- Estimates of herd immunity threshold for SARS-CoV-2 use various assumptions of  $R_0$  varying rates of heterogenous contact<sup>[1,2]</sup>
- Various epidemiological models of the herd immunity threshold for SARS-CoV-2 currently range from 50% to 75% of the population<sup>[1,2]</sup>
  - Assume that infection provides lasting protection against reinfection
  - This equates to 200 million people in the US and 5.6 billion people worldwide<sup>[1]</sup>

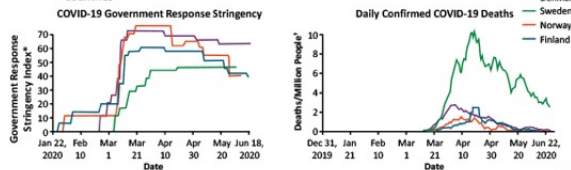
1. Bloom, NEJM, 2020 (Epub). 2. Britton, Science, 2020;369:846.

Slide credit: clinicaloptions.com

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**Less Stringent Mitigation Measures: Sweden Compared to Other Scandinavian Countries**

- Sweden permitted limited infection to continue by controlled viral spread to potentially reach herd immunity
  - To July 2020, higher mortality rate and prolonged outbreak compared to other Scandinavian countries



Slide credit: clinicaloptions.com

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<p><b>mRNA vaccines</b></p> <p>US FDA approved for 16+ y.o.</p> <p><b>Pfizer</b></p> <ul style="list-style-type: none"> <li>• New technology</li> <li>• Store at -70°C</li> <li>• 2 injections 21 days apart</li> <li>• Shipped in lots of ~1000 doses</li> <li>• Phase 3 interim analysis: 90% efficacy</li> <li>• May apply for EUA this week</li> <li>• First doses may be available mid-December</li> </ul> <p><b>US FDA EUA: 12.11.2020</b>  <b>UK EUA: 12.30.2020</b></p>	<p><b>mRNA vaccines</b></p> <p>US FDA approved for 18+ y.o.</p> <p><b>Moderna</b></p> <ul style="list-style-type: none"> <li>• Store at -20°C</li> <li>• Refrigerated 30 days</li> <li>• 2 injections 28 days apart</li> <li>• Phase 3 interim analysis: 94.5% efficacy</li> </ul> <p><b>Both vaccines:</b></p> <ul style="list-style-type: none"> <li>• New technology</li> <li>• mRNA is labile so need coat with lipid</li> <li>• Systemic symptoms, e.g., fever in 40-60%</li> <li>• RNA vaccines appear to be safe but need more time to discover rare side effects</li> </ul> <p><b>US FDA EUA on 12.18.2020</b>  <b>UK EUA on 12.30.2020</b></p> <p>Lot# 41L20A:          ↑ allergic rxns</p>
<p><b>Side Effects:</b> myalgias, h/a, fatigue, fever, etc...          4 vaccine recipients developed Bell's Palsy to date.          Allergic reactions: RARE (observe on site 15-30 min.)</p>	<p><b>Side Effects:</b> myalgias, h/a, fatigue, fever, etc...          3 vaccine recipients developed Bell's Palsy to date.          Allergic reactions: RARE (observe on site 15-30 min.)</p>

## Moderna mRNA vaccine

- NP swab PCR testing at baseline and at 4 weeks (when returned for 2<sup>nd</sup> dose)
- Among those negative at baseline and without symptoms who tested positive at 4 weeks:
  - 39 (0.3%) placebo group
  - 15 (0.1%) vaccine group
- Suggests some protective effect after 1 dose
- Need more data on transmission prevention

<https://www.nejm.org/covid-vaccine/faq>

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## Replication-defective vaccines

### Johnson & Johnson

- Attenuated adenovirus vector
- 60K enrolled Phase 3 internationally
- Same proven technology as used for Ebola, Zika, RSV vaccines: >100K people have received these w/o serious side effects
- Refrigerated, not frozen
- Testing 1 and 2 doses



## Johnson & Johnson vaccine

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- Phase 1-2 trial showed Ad26.COVS vaccine safe and immunogenic after single dose
- Neutralizing antibodies and T cell response in 90% overall on day 29 after the first vaccine dose
- Antibody levels increased/stabilized 71 days after 1 dose
- Added benefit of 2<sup>nd</sup> dose being studied (age 65+)
- Phase 3 trial began Sept 2020, recruited 45,000, results expected late January
- Possibly apply EUA in February 2021
- Non-human primate studies: near complete prevention of viral replication in the nose

<https://www.nejm.org/doi/pdf/10.1056/NEJMoa2034201?articleTools=true>

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## COVID-19 UPDATE

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Oxford/AstraZeneca mRNA AZD1222 vaccine trial began 8.26.2020, paused 9.9.2020 (UK woman developed transverse myelitis, little other info). Trials resumed 9.12.2020 in Europe+. Death in Brazil in placebo recipient. In USA (ie, MUSC), vaccine trials resumed 10.30.2020.

Aug. 26, 2020



AZD1222 uses a replication-deficient chimpanzee viral vector based on a weakened version of a common cold virus (adenovirus) that causes infections in chimpanzees and contains the **genetic material of the SARS-CoV-2 virus spike protein**. After vaccination, the surface spike protein is produced, priming the immune system to attack the SARS-CoV-2 virus if it later infects the body.

### Vaccine trial

Last week, MUSC Health in Charleston announced that it will be one of the first locations in the nation to test a promising vaccine for COVID-19. MUSC researchers are enrolling volunteers now.

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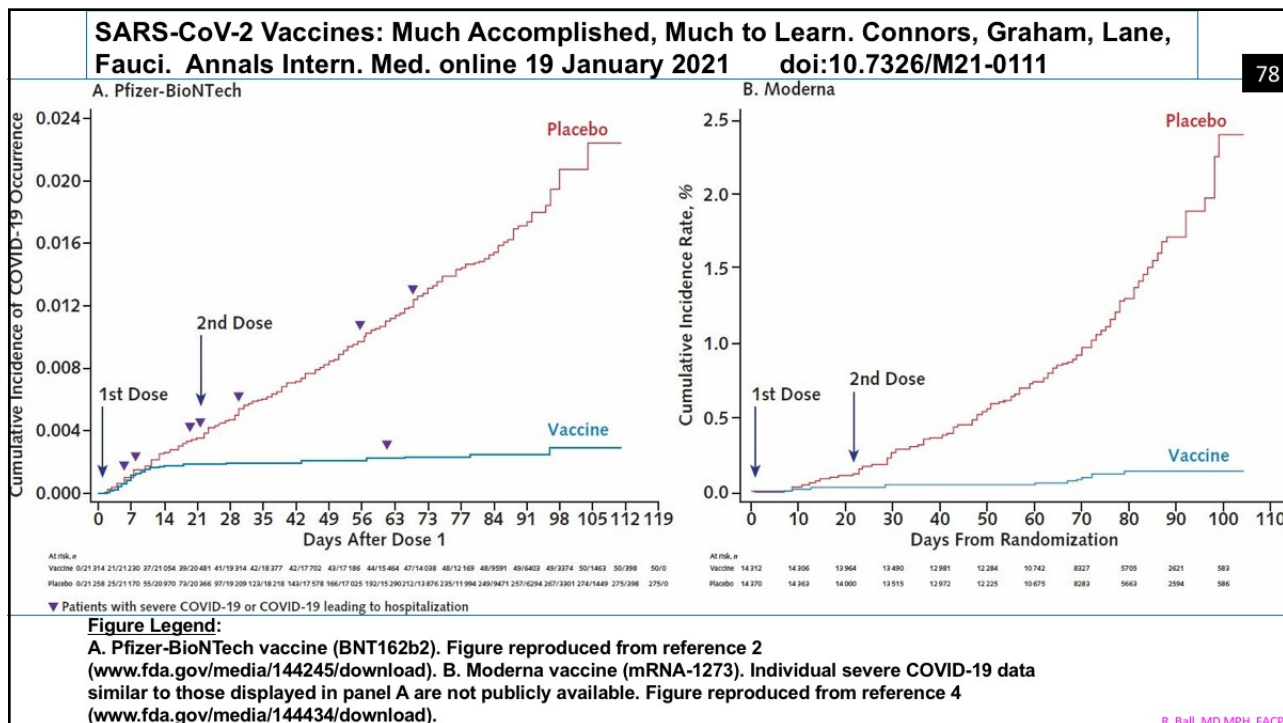
Manufacturer	Platform	Status In the U.S.	Doses and Interval	Phase 3 Sample Size	Efficacy Against Symptomatic Disease (95% CI)	Efficacy Against Severe Disease†	Reactogenicity	Storage and Temperature
Pfizer/BioNTech	mRNA	EUA	2 at 3 wk apart	43 661	95.0% (90.3%–97.6%)	9 vs. 1	Fatigue, muscle aches, chills, fever, local reactions	–70 °C for 6 mo 2–8 °C for 5 d
Moderna	mRNA	EUA	2 at 4 wk apart	30 351	94.1% (89.3%–96.8%)	30 vs. 0	Local pain, fatigue, headache, myalgia, arthralgia, chills, fever	–20 °C for 6 mo 2–8 °C for 30 d RT for 12 h
AstraZeneca	Recombinant chimpanzee adenovirus (nonreplicating)	Enrolling phase 3	2 at 4 wk apart	~30 000	NA	NA	Local pain, fatigue, headache, fever, myalgia	2–8 °C for 6 mo
Johnson & Johnson/Janssen	Recombinant human adenovirus 26 (nonreplicating)	Completed phase 3 enrollment	1	~45 000	NA	NA	Local pain, fatigue, headache, myalgia	2–8 °C
Novavax	Recombinant protein	Enrolling phase 3	2 at 3 wk apart	~30 000	NA	NA	Local pain, fatigue, headache, myalgia	2–8 °C
Sanofi/GlaxoSmithKline	Recombinant protein	Phase 2	1 or 2 at 3 wk apart	NA	NA	NA	NA	2–8 °C
Merck	Recombinant vesicular stomatitis virus (replicating)	Phase 1	1	NA	NA	NA	NA	–70 °C

**SARS-CoV-2 Vaccines: Much Accomplished, Much to Learn**  
**Connors, Graham, Lane, Fauci. Annals Intern. Med. online 1.19.2021**

EUA = emergency use authorization; NA = not available; RT = room temperature  
 \*All vaccines are directed toward the spike protein of SARS-CoV-2.  
 † Number of severe cases of COVID-19 (placebo vs. vaccine group)

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# COVID Update: Focus on Vaccines

## Dr. Robert T. Ball, University of South Carolina

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**Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial**

**Folegatti et al- Lancet 7.20.2020**

**Summary**  
Background The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, reactogenicity, and immunogenicity of a viral vectored coronavirus vaccine that expresses the spike protein of SARS-CoV-2.

**Immunogenicity**

- Vaccine doses Days 1+28
- 2 doses were needed
- Binding and pseudoneutralizing antibodies
- Rapid increase by 7 days after boost
- No current correlate of protection
  - Comparable to convalescent sera

**Safety**

<https://www.statnews.com/2020/09/08/astrazeneca-covid-19-vaccine-study-put-on-hold-due-to-suspected-adverse-reaction-in-participants/>

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

- Off safety hold 23OCT

**SARS-CoV-2 Vaccines: Much Accomplished, Much to Learn**  
Annals Intern. Med. Published online: 19 January 2021 doi:10.7326/M21-0111

**80**

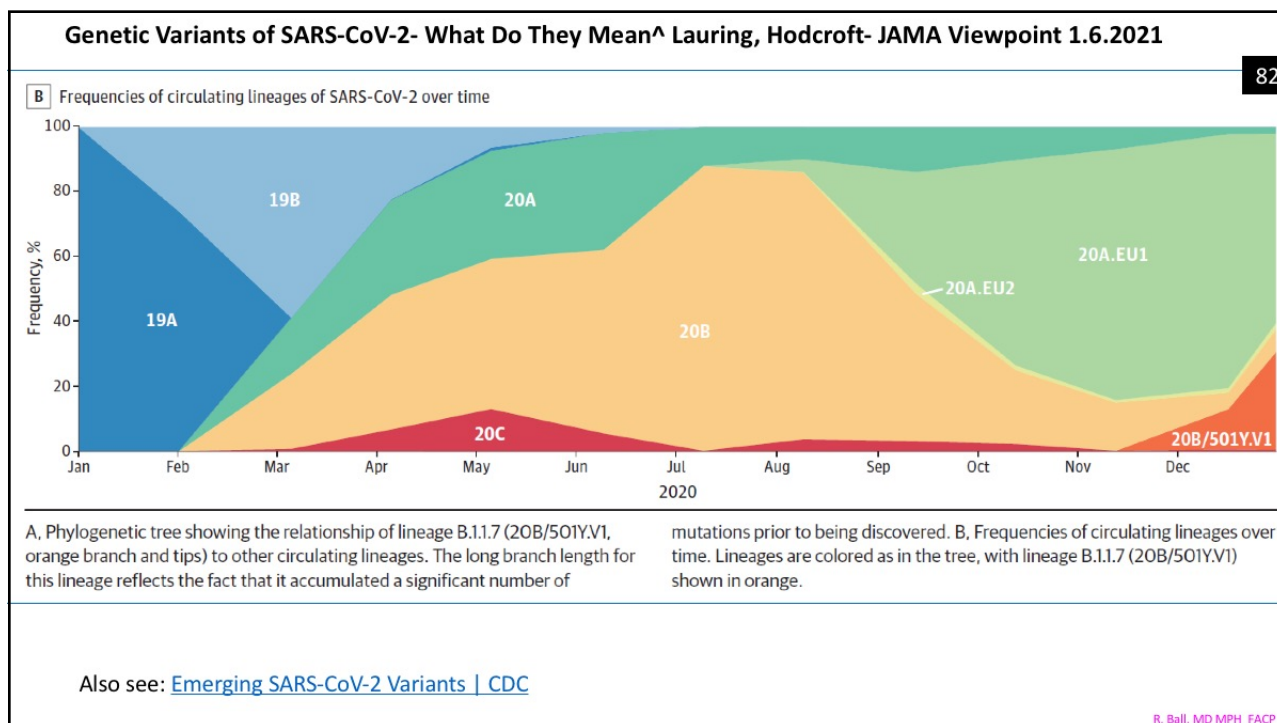
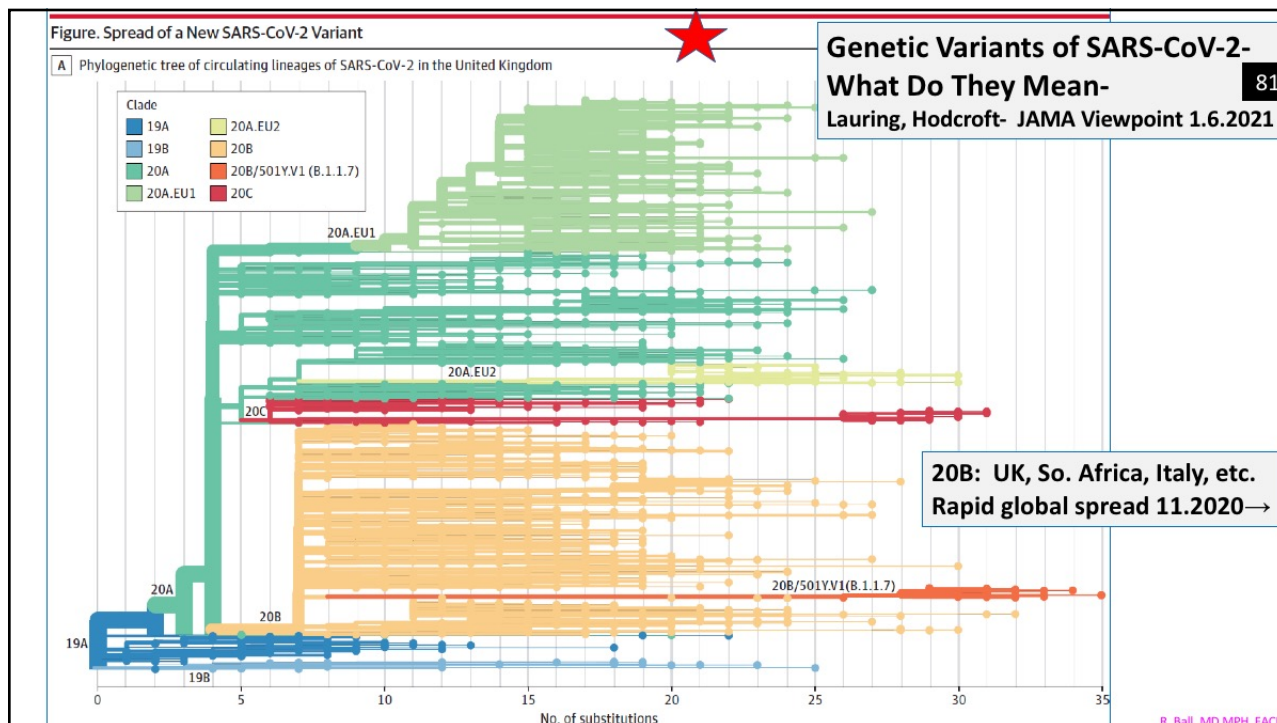
**Table 1. CDC Priorities for Distribution of COVID-19 Vaccines\***

Priority Group	Persons Eligible (Number of Unique Individuals)
1a	Health care providers (21 million) Residents of long-term care facilities (3 million)
1b	Persons aged 75 years or older (19 million) Frontline essential workers (30 million)
1c	Persons aged 65–74 years (28 million) Persons aged 16–64 years with high-risk medical conditions (81 million) Other essential workers (20 million)

CDC = Centers for Disease Control and Prevention; COVID-19 = coronavirus disease 2019.  
\* Data from Dooling K. Phased allocation of COVID-19 vaccines [presentation]. CDC; 20 December 2020. Accessed at [www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-12/slides-12-20/02-COVID-Dooling.pdf](http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-12/slides-12-20/02-COVID-Dooling.pdf) on 8 January 2021.



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The U.K. variant is also known as **B.1.1.7**, 20I/501Y.V1, and VOC (Variant of Concern) 202012/01. *NERVTAG note 1.21.2021 on B.1.1.7: ↑ transmission (50-70%) & possibly disease severity, even death.*

The South Africa variant is sometimes called **B.1.351** or 20C/501Y.V2.

The Brazil variant is known as **P.1** or 20J/501Y.V3. “Immune escape” from current vaccines is possible.

**SPIKE PROTEIN**

**MUTATION OF AMINO ACID**

may spread more easily from person to person.

**New virus variants that spread more easily could lead to a rapid rise in COVID-19 cases**

**NOW, more than ever, it is important to slow the spread**

**In the U.S.**

- ⚠ New cases are the highest ever and rising
- ⚠ Some health care systems are at or near capacity
- ⚠ New variants are emerging that spread more easily

**MORE SPREAD → MORE CASES → MORE DEATHS**

- 🧑‍🤝🧑 Wear a mask
- 📏 Stay at least 6 feet apart
- 🚫 Avoid crowds
- 💉 Get vaccinated when available to you

**SOUTH AFRICA**

infecting younger people more this time around.

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Britain's MHRA gave EUA to Pfizer, Moderna, & Oxford/AZ vaccines 12.30.2020

Israel's COVID vaccine rollout fastest & more complete in the world; next UK, UAE, ...

**As of 1.28.2021, ≥ 60 countries have (multiple) mutants**

**1.2021: SARS-CoV-2 variants deemed 50-70% more transmissible & ~30% more virulent**

**The Canberra Times**  
TO SERVE THE NATIONAL CITY

Therapeutic Goods Administration (TGA) considering Pfizer vaccine 01.2021

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# BioNTech-Pfizer vaccine likely to protect against highly infectious UK variant

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Most current vaccines are “expected” to protect against most current global variants

bioRxiv preprint doi: <https://doi.org/10.1101/2021.01.18.426984>; this version posted January 19, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

01.19.2021

## Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera

**Authors:** Alexander Muik<sup>1</sup>, Ann-Kathrin Wallisch<sup>1</sup>, Bianca Sanger<sup>1</sup>, Kena A. Swanson<sup>2</sup>, Julia Muhl<sup>1</sup>, Wei Chen<sup>2</sup>, Hui Cai<sup>2</sup>, Ritu Sarkar<sup>2</sup>, ozlem Tureci<sup>1</sup>, Philip R. Dormitzer<sup>2</sup>, Ugur Sahin<sup>1,3\*</sup>

### Affiliations:

<sup>1</sup>BioNTech, An der Goldgrube 12, 55131 Mainz, Germany.

<sup>2</sup>Pfizer, 401 N Middletown Rd., Pearl River, NY 10960, U.S.A.

<sup>3</sup>TRON gGmbH – Translational Oncology at the University Medical Center of the Johannes Gutenberg, University Freiligrathstrae 12, 55131 Mainz, Germany.

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Moderna is developing a booster candidate, mRNA-1273.351, to test v spike proteins specific to the B.1.351 variant, first detected in South Africa.

THE CORONAVIRUS PANDEMIC

1.19.2021

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Coronavirus / Europe

## Coronavirus: Norway raises concern over Pfizer vaccine jabs for elderly as Australia seeks information

- Pfizer-BioNTech vaccine comes into focus as Norway raises death toll and lowers age range of people thought to be affected
- Australia’s Therapeutic Goods Administration said it would seek additional information on the vaccine from Pfizer and Norway’s medical regulator



Bloomberg

Published: 7:17pm, 17 Jan, 2021

Why you can trust SCMP

[Coronavirus: Norway raises concern over Pfizer vaccine jabs for elderly as Australia seeks information | South China Morning Post \(scmp.com\)](https://www.scmp.com/news/health/coronavirus/article/2021-01-17/norway-concern-over-pfizer-vaccine-elderly-australia-seeks-information)

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## Summary: Triage of persons presenting for mRNA COVID-19 vaccination

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**COVID-19 Vaccines- Update on Allergic Reactions (ie, anaphylaxis),  
 Contraindications, & Precautions- US CDC COCA webinar 12.30.2020**

MAY PROCEED WITH VACCINATION	PRECAUTION TO VACCINATION	CONTRAINDICATION TO VACCINATION
<p><b>ALLERGIES</b>            History of allergies that are unrelated to components of an mRNA COVID-19 vaccine<sup>†</sup>, other vaccines, or injectable therapies, such as:</p> <ul style="list-style-type: none"> <li>• Allergy to oral medications (including the oral equivalent of an injectable medication)</li> <li>• History of food, pet, insect, venom, environmental, latex, etc., allergies</li> <li>• Family history of allergies</li> </ul> <p><b>ACTIONS</b></p> <ul style="list-style-type: none"> <li>• 30 minute observation period: Persons with a history of anaphylaxis (due to any cause)</li> <li>• 15 minute observation period: All other persons</li> </ul>	<p><b>ALLERGIES</b></p> <ul style="list-style-type: none"> <li>• History of any immediate allergic reaction<sup>‡</sup> to vaccines or injectable therapies (except those related to component of mRNA COVID-19 vaccines<sup>†</sup> or polysorbate, as these are contraindicated)</li> </ul> <p><b>ACTIONS:</b></p> <ul style="list-style-type: none"> <li>• Risk assessment</li> <li>• Consider deferral of vaccination and/or referral to allergist-immunologist</li> <li>• 30 minute observation period if vaccinated</li> </ul>	<p><b>ALLERGIES</b>            History of the following are contraindications to receiving either of the mRNA COVID-19 vaccines<sup>†</sup>:</p> <ul style="list-style-type: none"> <li>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components</li> <li>• Immediate allergic reaction<sup>‡</sup> of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components<sup>§</sup> (including polyethylene glycol)<sup>#</sup></li> <li>• Immediate allergic reaction of any severity to polysorbate <sup>#</sup></li> </ul> <p><b>ACTIONS</b></p> <ul style="list-style-type: none"> <li>• Do not vaccinate<sup>#</sup></li> <li>• Consider referral to allergist-immunologist</li> </ul>

<sup>†</sup> Refers only to mRNA COVID-19 vaccines currently authorized in the United States (i.e., Pfizer-BioNTech, Moderna COVID-19 vaccines)

<sup>‡</sup> Immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms consistent with urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.

<sup>§</sup> See Appendix A for a list of ingredients. Note: Polyethylene glycol (PEG), an ingredient in both mRNA COVID-19 vaccines, is structurally related to polysorbate and cross-reactive hypersensitivity between these compounds may occur. Information on ingredients of a vaccine or medication (including PEG, a PEG derivative, or polysorbates) can be found in the package insert.

<sup>#</sup> These persons should not receive mRNA COVID-19 vaccination at this time unless they have been evaluated by an allergist-immunologist and it is determined that the person can safely receive the vaccine (e.g., under observation, in a setting with advanced medical care available)

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## Key messages

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### Preparing for the potential management of anaphylaxis at COVID-19 vaccination sites

Pfizer vaccine-induced anaphylaxis: ~5 per million doses administered (had been ~11 per million).  
 Moderna vaccine-induced anaphylaxis remained stable ~2.8 per million. -CDC

Early recognition of anaphylaxis symptoms



Prompt treatment with epinephrine



Activation of emergency medical services



<https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html>

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## Distinguishing allergic reactions from other types of reactions

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Characteristic	Immediate allergic reactions (including anaphylaxis)	Vasovagal reaction	Vaccine side effects (local and systemic)
Timing after vaccination	Most occur within 15-30 minutes of vaccination	Most occur within 15 minutes	Median of 1 to 3 days after vaccination (with most occurring day after vaccination)
<b>Signs and symptoms</b>			
<b>Constitutional</b>	Feeling of impending doom	Feeling warm or cold	Fever, chills, fatigue
<b>Cutaneous</b>	Skin symptoms present in ~90% of people with anaphylaxis, including pruritus, urticaria, flushing, angioedema	Pallor, diaphoresis, clammy skin, sensation of facial warmth	Pain, erythema or swelling at injection site; lymphadenopathy in same arm as vaccination
<b>Neurologic</b>	Confusion, disorientation, dizziness, lightheadedness, weakness, loss of consciousness	Dizziness, lightheadedness, syncope (often after prodromal symptoms for a few seconds or minutes), weakness, changes in vision (such as spots of flickering lights, tunnel vision), changes in hearing	Headache
<b>Respiratory</b>	Shortness of breath, wheezing, bronchospasm, stridor, hypoxia	Variable; if accompanied by anxiety, may have an elevated respiratory rate	N/A
<b>Cardiovascular</b>	Hypotension, tachycardia	Variable; may have hypotension or bradycardia during syncopal event	N/A
<b>Gastrointestinal</b>	Nausea, vomiting, abdominal cramps, diarrhea	Nausea, vomiting	Vomiting or diarrhea may occur
<b>Musculoskeletal</b>	N/A	N/A	Myalgia, arthralgia
<b>Vaccine recommendations</b>			
Receive 2 <sup>nd</sup> dose of mRNA COVID-19 vaccine?	No	Yes	Yes

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1/4/21

## “Vaccine Hesitancy” & “Anti-vaccine” people

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Original research

BMJ Global Health

Social media and vaccine hesitancy

Steven Lloyd Wilson,<sup>1</sup> Charles Wiysonge<sup>2</sup>

**To cite:** Wilson SL, Wiysonge C. Social media and vaccine hesitancy. *BMJ Global Health* 2020;5:e004206. doi:10.1136/bmjgh-2020-004206

**Handling editor** Seye Abimbola

Received 14 October 2020  
Accepted 17 October 2020

**ABSTRACT**

**Background** Understanding the threat posed by anti-vaccination efforts on social media is critically important with the forth coming need for world wide COVID-19 vaccination programs. We globally evaluate the effect of social media and online foreign disinformation campaigns on vaccination rates and attitudes towards vaccine safety.

**Methods** We use a large-n cross-country regression framework to evaluate the effect of social media on vaccine hesitancy globally. To do so, we operationalize social media usage in two dimensions: the use of it by the public to organize action (using Digital Society Project indicators), and the level of negatively oriented discourse about vaccines on social media (using a data set of all geocoded tweets in the world from 2018-2019). In addition, we measure the level of foreign-sourced coordinated disinformation operations on social media in each country (using Digital Society Project indicators). The outcome of vaccine hesitancy is measured in two ways. First, we use polls of what proportion of the public

**Key questions**

**What is already known?**

- ▶ Vaccine hesitant groups on social media have an alarming foot print, with studies demonstrating that large proportions of the content about vaccines on popular social media sites are anti-vaccination messages.
- ▶ Organized campaigns have been traced to Russian pseudo-state actors promoting anti-vaccination content on social media abroad.

**What are the new findings?**

- ▶ At a national level, the use of social media to organize offline action is highly predictive of the belief that vaccinations are unsafe, with such beliefs mounting as more organization occur on social media.
- ▶ Foreign disinformation campaigns online are associated with a drop in both mean vaccination coverage over time and negative discussion of vaccines on social media.

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## Negotiating with “Vaccine Hesitancy” & “Anti-vaccine” folk

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### **FIRST, ask if they are just “hesitant” and why, or are they strictly “anti-vaccine” (and why).**

- If just hesitant (most reasonable folk), ask why. Ask if they would listen to some medical facts to help allay their concerns.
- And be prepared with scientific knowledge, but offer your opinion if asked.
- Note the “common good” beneficence (“Do unto others...”)

If strictly “anti-vaxxers”, ask why, but be prepared to face criticism and step back. You may note the direct benefit just to them (personalize).

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**Thank you for your attention.**

**(ballrt@musc.edu)**

*“Those who carry on great public schemes  
must be proof against the most fatiguing delays,  
the most mortifying disappointments,  
the most shocking insults,  
and what is worst of all,  
the presumptuous judgments of the ignorant.”*

**- Edmund Burke (1729 - 1797)**

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<a href="http://www.webbertraining.com/schedulep1.php">www.webbertraining.com/schedulep1.php</a>	
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February 9, 2021	<a href="#"><u>ANTIMICROBIAL STEWARDSHIP IN ASIA PACIFIC - GLOBAL BELLWEATHER?</u></a> Speaker: <b>Prof. Anucha Apisarntharak</b> , Thammasat University Hospital, Thailand <i>(South Pacific Teleclass)</i>
February 17, 2021	<a href="#"><u>THE NEW ZEALAND COVID-19 RESPONSE - LESSONS LEARNED</u></a> Speaker: <b>Prof. Ian Town</b> , Ministry of Health, New Zealand
February 25, 2021	<a href="#"><u>CONTINUOUS ACTIVE ANTI-VIRAL COATINGS</u></a> Speaker: <b>Prof. Charles Gerba</b> , University of Arizona <i>(FREE European Teleclass)</i>
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