UW Retirement Association – October 6, 2020

PANDEMIC COVID-19

What have we learned 9 months into the Pandemic of 2020? What are the unanswered questions?

Dennis G. Maki, MD

Divisions of Infectious Disease

and Pulmonary/Critical Care Medicine
Department of Medicine

University of Wisconsin
School of Medicine and Public Health

dgmaki@medicine.wisc.edu

CONFLICT OF INTEREST STATEMENT

I have no conflicts of interest to report.

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

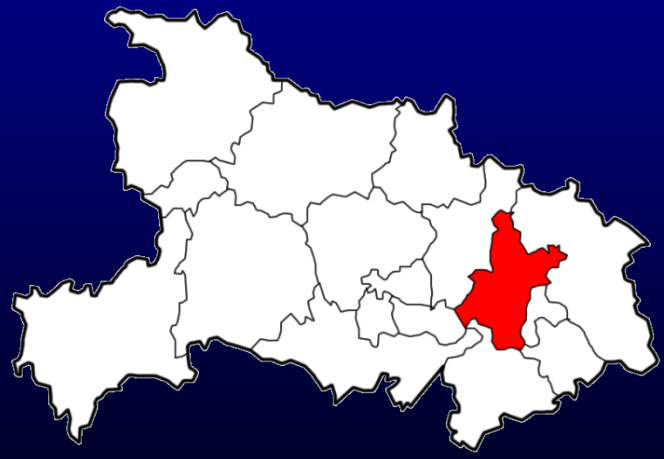
Goals*: To Understand*

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China
- The biology of coronaviruses
- Endemic human coronavirus infection
- What's new? *The 3rd Coronavirus pandemic of the 20th Century!*
- The extraordinary global spread of COVID-19 since January 2020
- Pathophysiology and epidemiology of COVID-19
- Clinical features of COVID-19 and its laboratory diagnosis
- The challenge of protecting healthcare providers
- Management of COVID-19.
- Prevention of COVID-19 and prospects for a vaccine
- What's going on in Wisconsin and the upper Midwest?
- Air travel and protecting oneself from COVID-19
- What have we learned? What are the big unanswered questions?

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China



TIME-LINE OF 2019-20 COVID-19 PANDEMIC

Dec 18 Dr Li Wenliang informs Chinese officials and reports a cluster of unusual pneumonias in Wuhan, subsequently punished by the Chinese Government

Dec 31 China informed WHO of 42 cases pneumonia in Wuhan Fish/Wild Animal Market

Jan 7 New Coronasvirus identified, named **SARS-CoV-2**

PANDEMIC NOMENCLATURE

- The novel pandemic coronavirus (nCoV) was formally named **SARS-CoV-2**

- **Infection** by **SARS-CoV-2** is now termed:

COVID-19

Corona
Virus
Infectious **D**isease
Virus identified in 20**19**

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Jan 7 New Coronasvirus identified, named SARS-CoV-2

Jan 20 200 Chinese cases, spread to S Korea Thailand, Hong Kong, Japan, Europe and North America. The U.S. had it's 1st recognized case

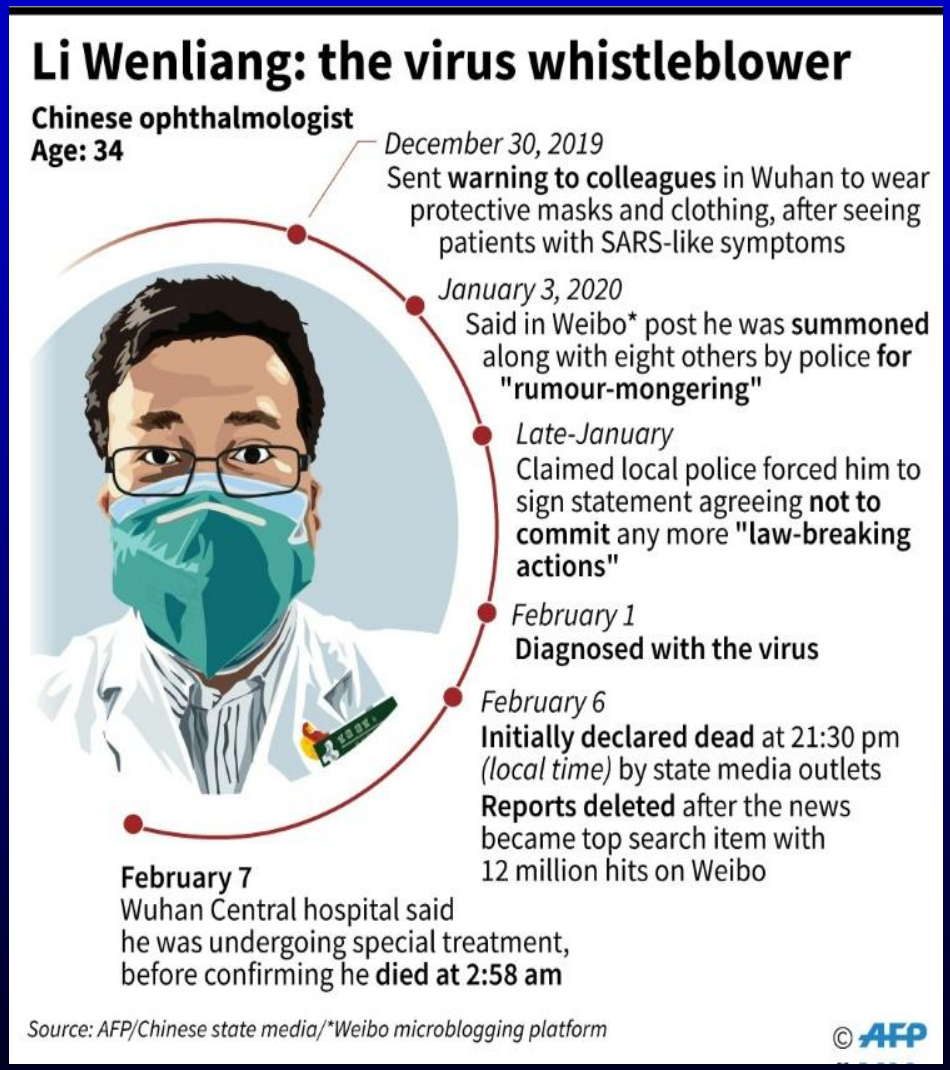
Jan 30 WHO declares "Emergency",

President Trump blocks travel from China,

Dr Fauci states "this is not a major threat to the United States and not something the citizens of the United States should be worried about"

Feb 7 **Dr Li Wenliang dies.**

AN INTERNTIONAL HERO



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Feb 7 Dr Li Wenliang dies.
10,000 Chinese cases, 811 deaths

Feb 12-21 Major Outbreaks in Iran, Italy, U.S. 89 cases on Mar 1

Mar 11 WHO declares *PANDEMIC, U.S has 1272 cases, Pres Trump decares BAN on travel from Europe, Chinese declare their outbreak over*, MLB, NBA, NCAAB CANCEL seasons, Cruise Lines SUSPEND activity

Mar 17 *Italy 31,506 cases, 2,503 deaths*

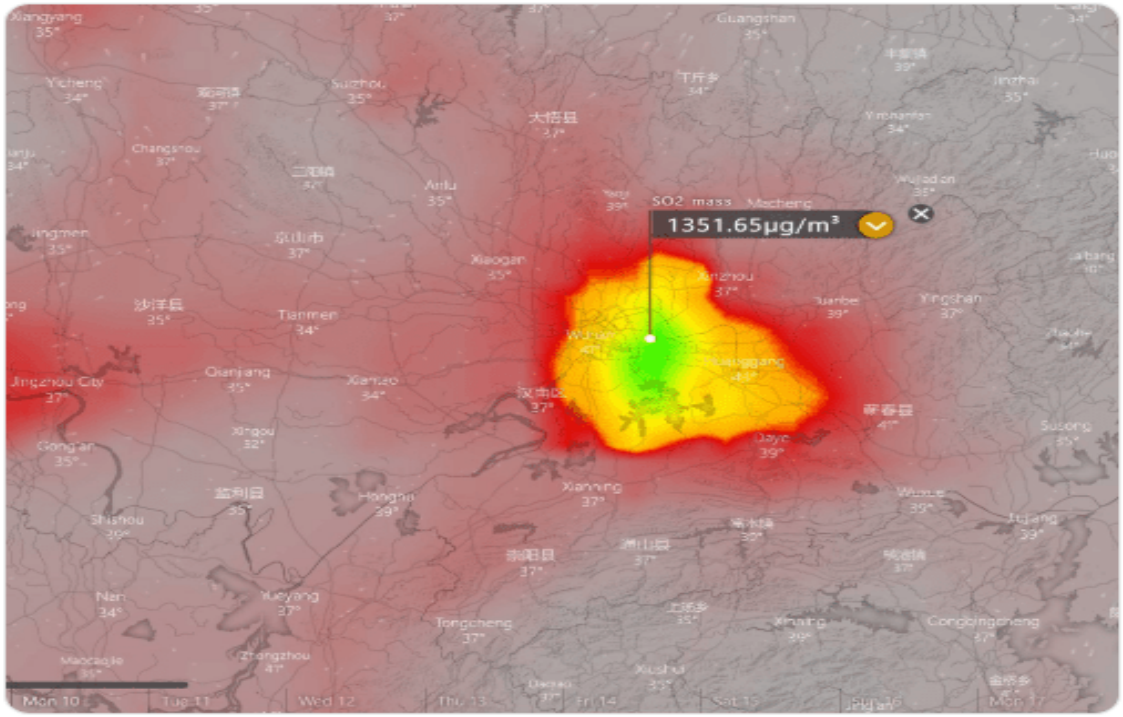
Mar 22 *34,000 U.S. cases, 413 deaths, NYC 11,000 cases, U.S. LOCKDOWN,*

Mar 29 *142,000 U.S. cases, 2500 deaths, 723,000 cases worldwide, 34,000 deaths. Large epidemics in Seattle, NYC, New Orleans, Milwaukee, Chicago, Florida*

Inteldotwav
@inteldotwav

Follow

Data from windy.com shows a massive release of sulfur dioxide gas from the outskirts of Wuhan, commonly associated with the burning of organic matters. Levels are elevated, even compared with the rest of China.

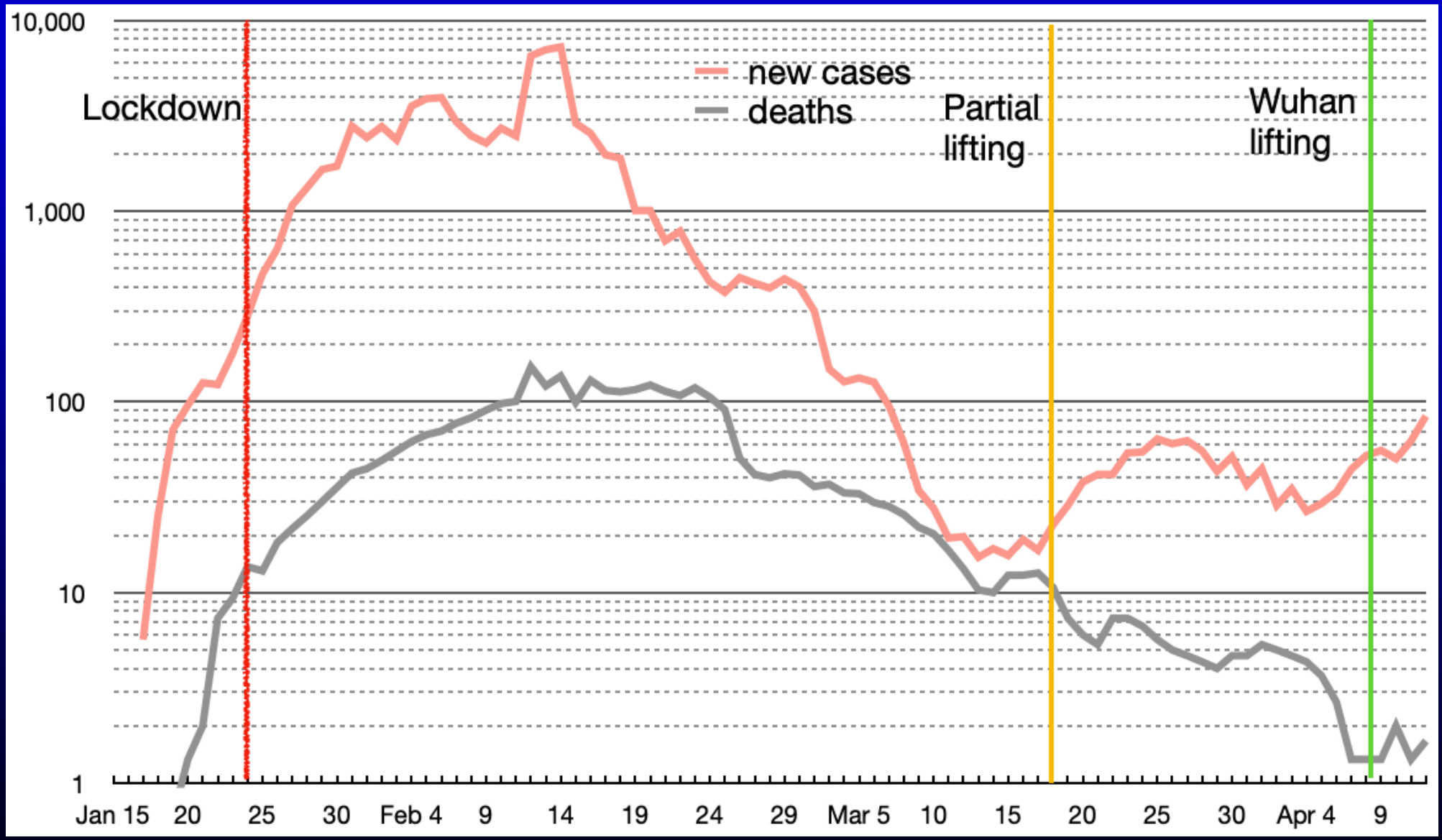


2:12 PM - 8 Feb 2020

12,231 Retweets **15,971** Likes

959 12K 16K

CHINA'S EPIDEMIC OF COVID-19



SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

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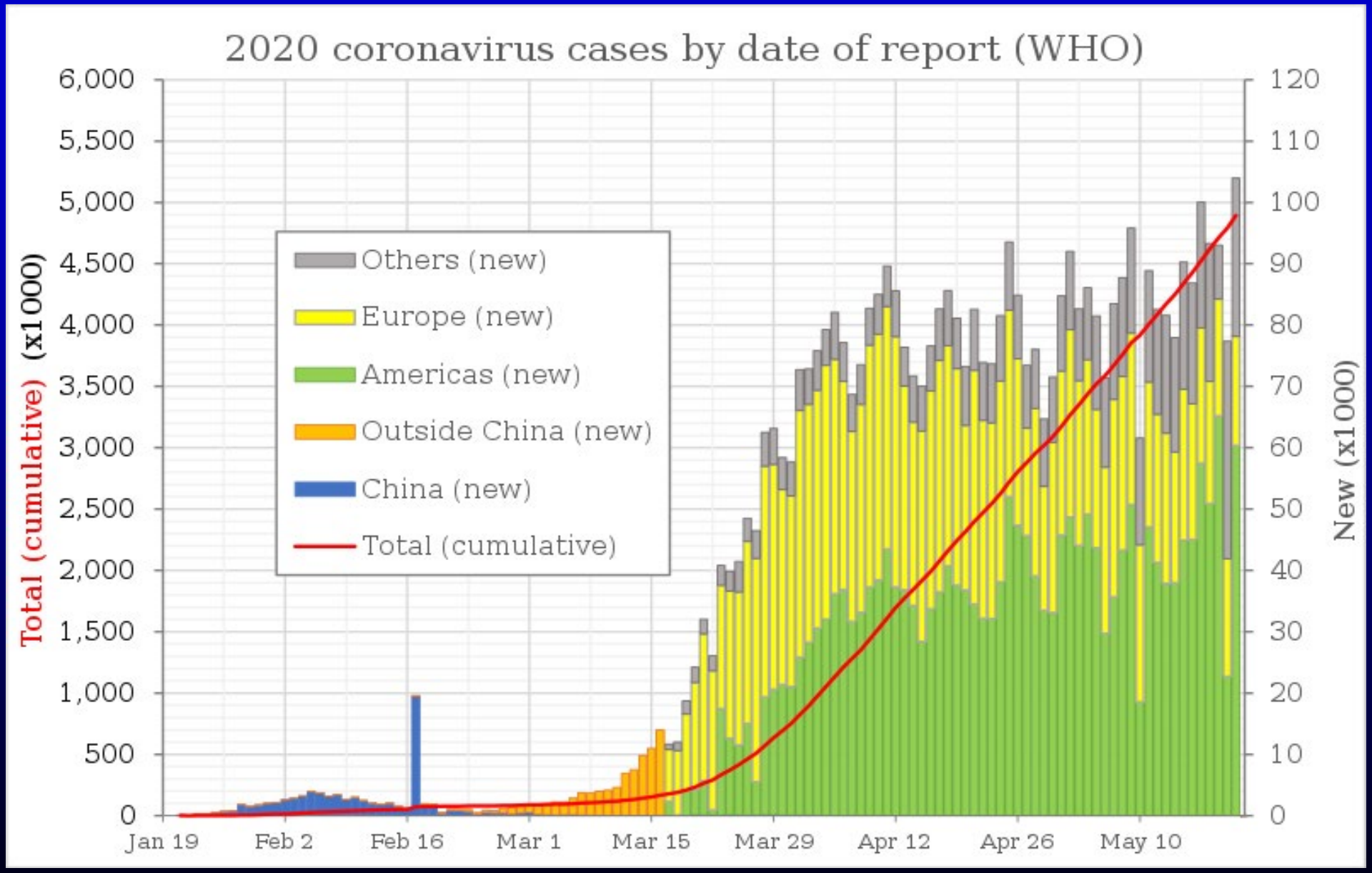
COVID-19 GLOBAL PANDEMIC CURVE



COVID-19 IN THE U.S. AS OF Oct 5, 2020

Global Figures

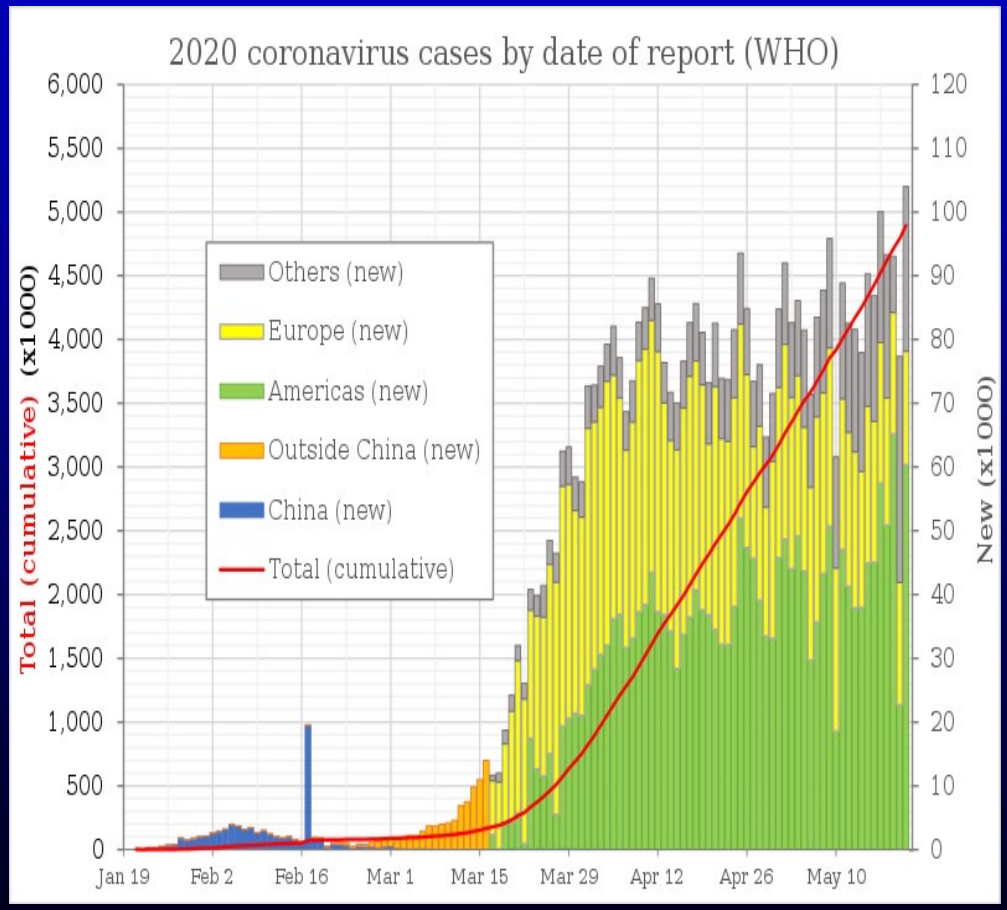
35,631,438 cases

1,044,556 dead (2.9 %)

U.S. Figures:

7,667,817 cases

214,884 deaths (2.8 %)



COVID-19 IN THE U.S. ON Oct 5, 2020

Global Figures

35,631,438 cases

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214,884 deaths (2.8 %)

New York City

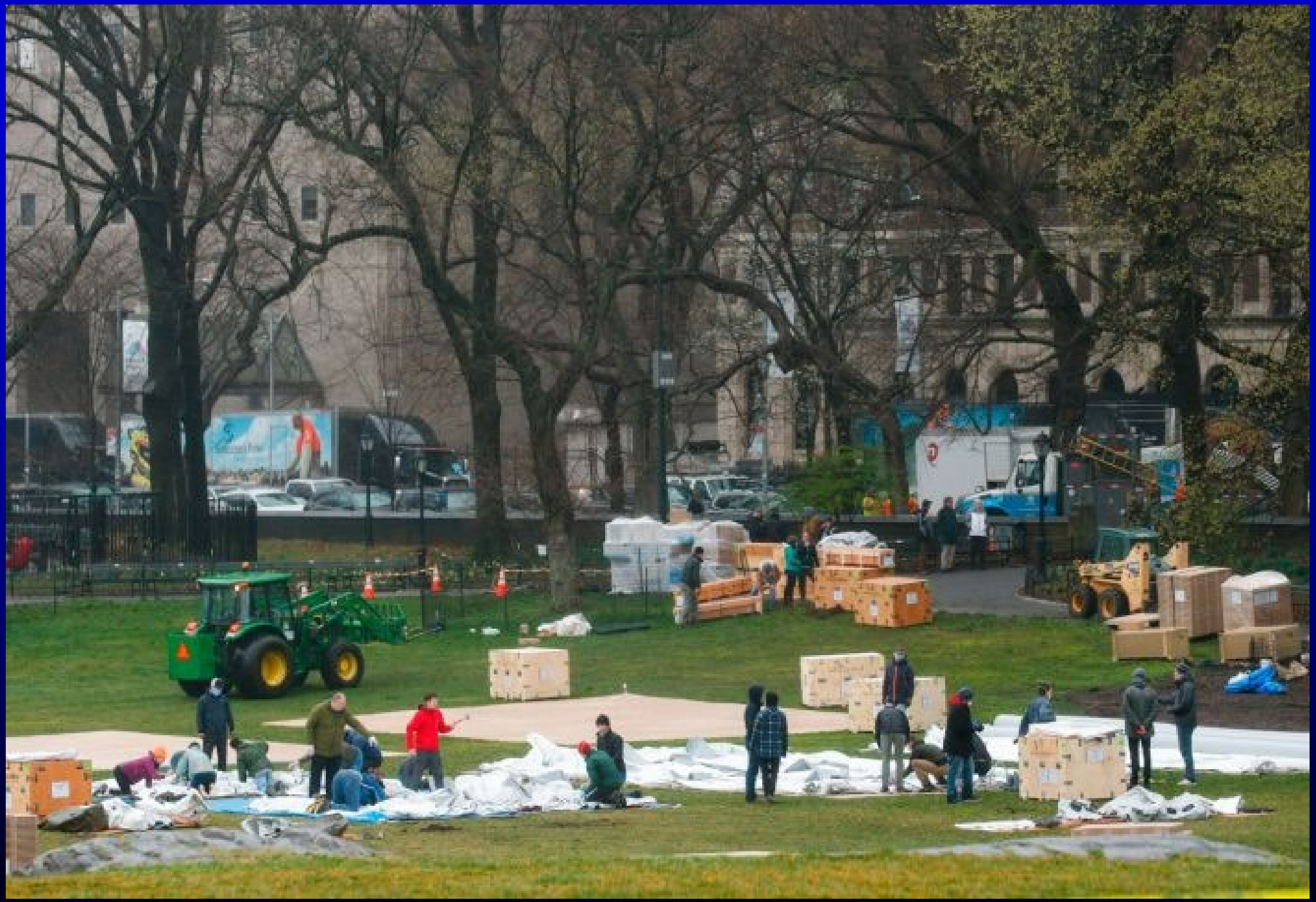
246,885 cases

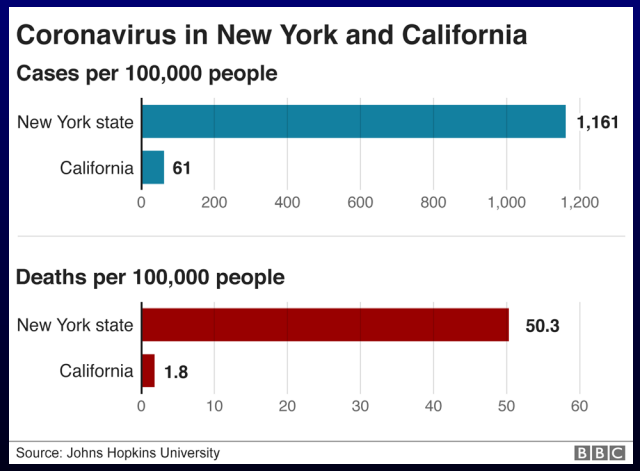
52% < 50 years-old

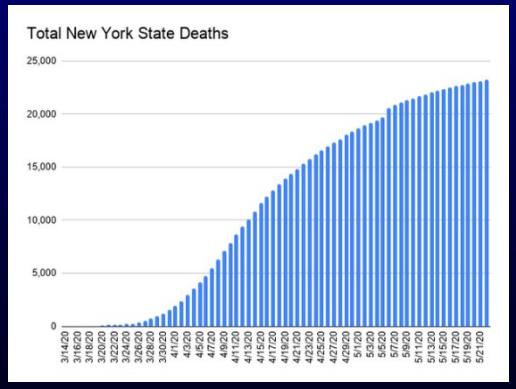
23,861 deaths (9.8%)

75% >65 yo, 2/3 male


GENCY




Coronavirus in New York and California
Cases per 100,000 people
New York state
1,161
California
61
0
200
400
600
800
1,000
1,200
Deaths per 100,000 people
New York state
50.3
California
1.8
0
10
20
30
40
50
60
Source: Johns Hopkins University
BBC


Total New York State Deaths
25,000
20,000
15,000
10,000
5,000
0

COVID-19 IN THE U.S. ON Oct 5, 2020

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214,884 deaths (2.8 %)

Wisconsin

32,663 cases

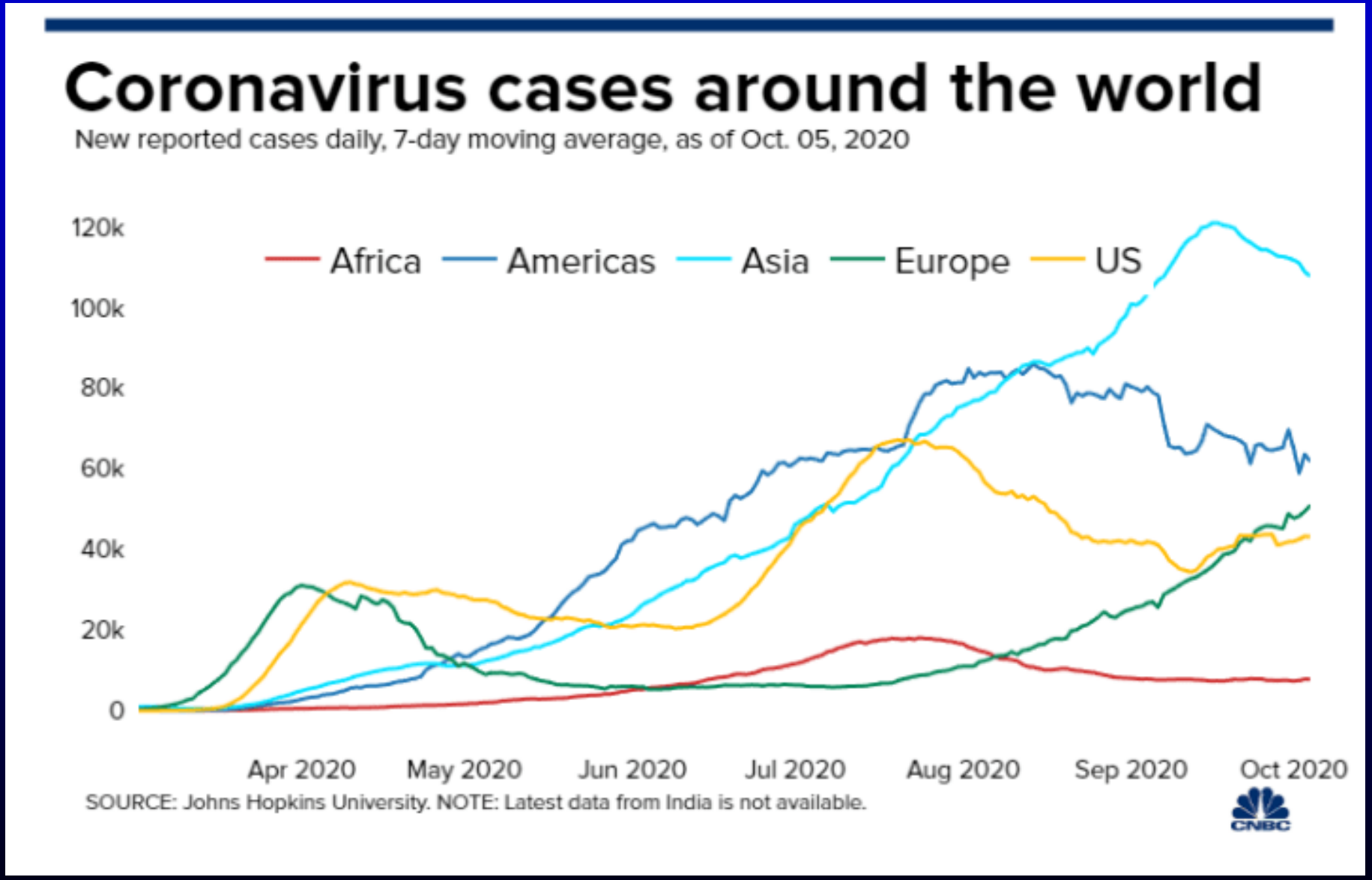
1377 deaths (1.3%)

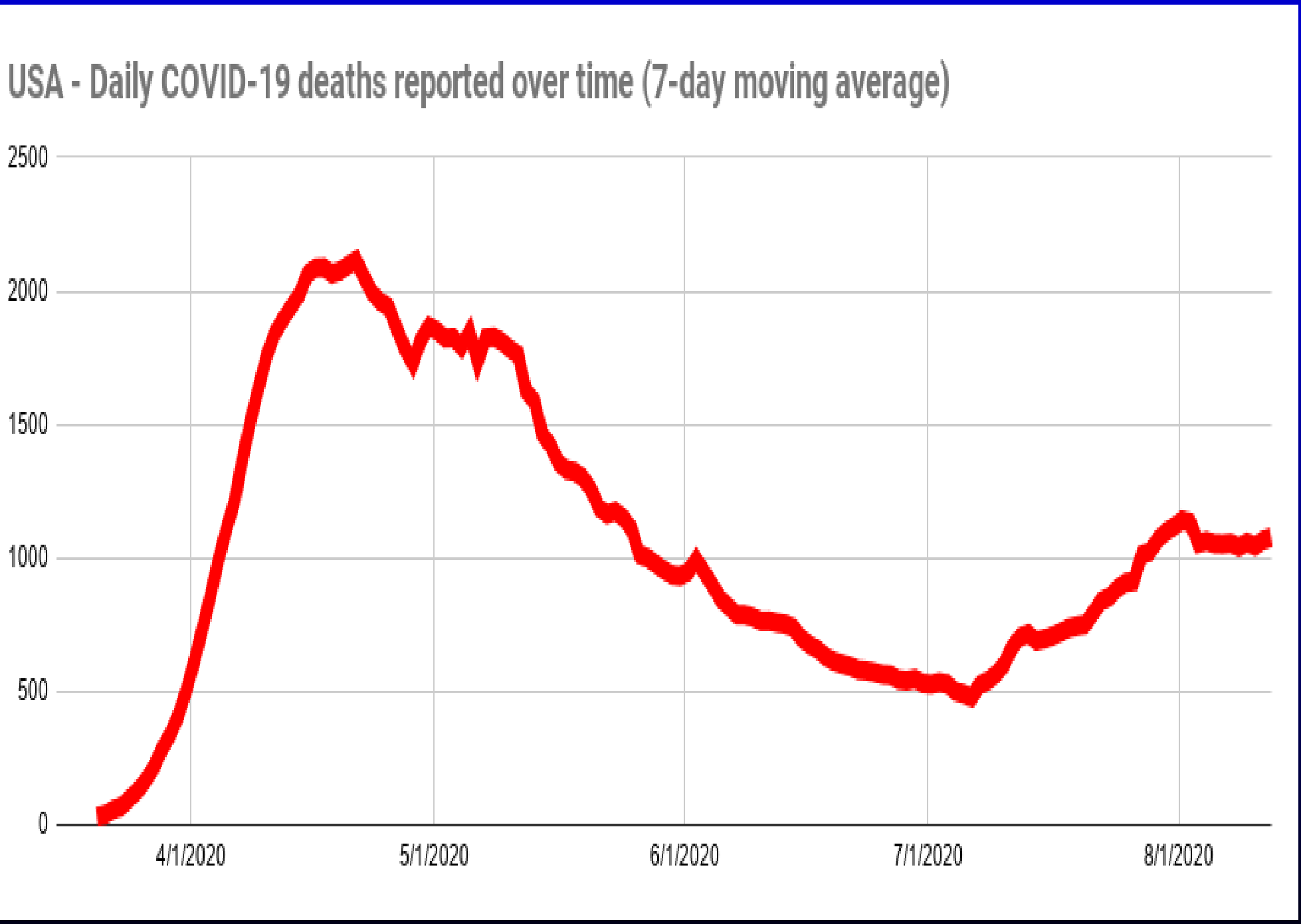
Dane County

10,426 cases

83 deaths (0.8%)

NEW CASES OF COVID-19 FROM 7 REGIONS OF THE WORLD




USA - Daily COVID-19 deaths reported over time (7-day moving average)
2500
2000
1500
1000
500
0
4/1/2020
5/1/2020
6/1/2020
7/1/2020
8/1/2020

SARS-CoV-2 and COVID-19

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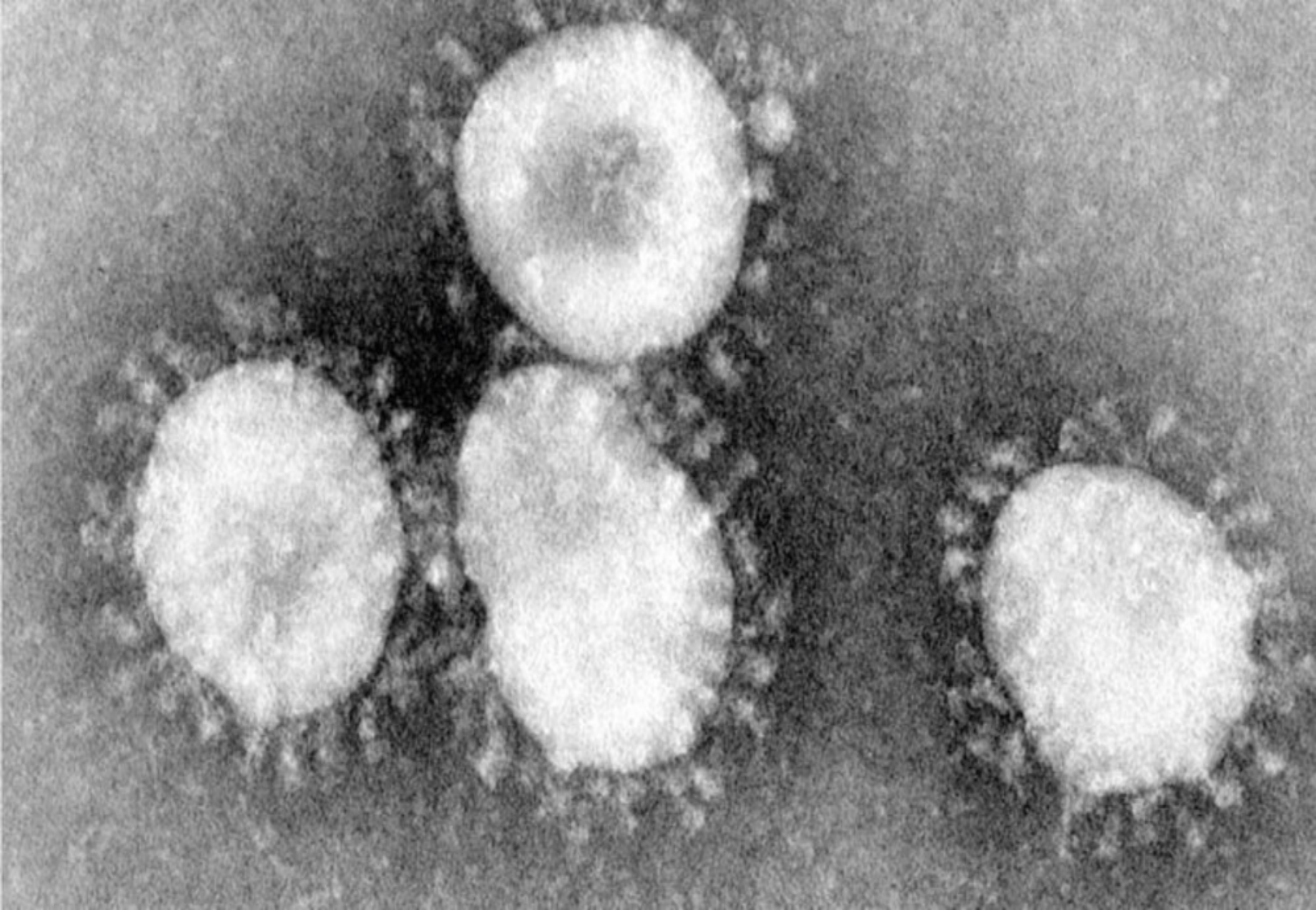
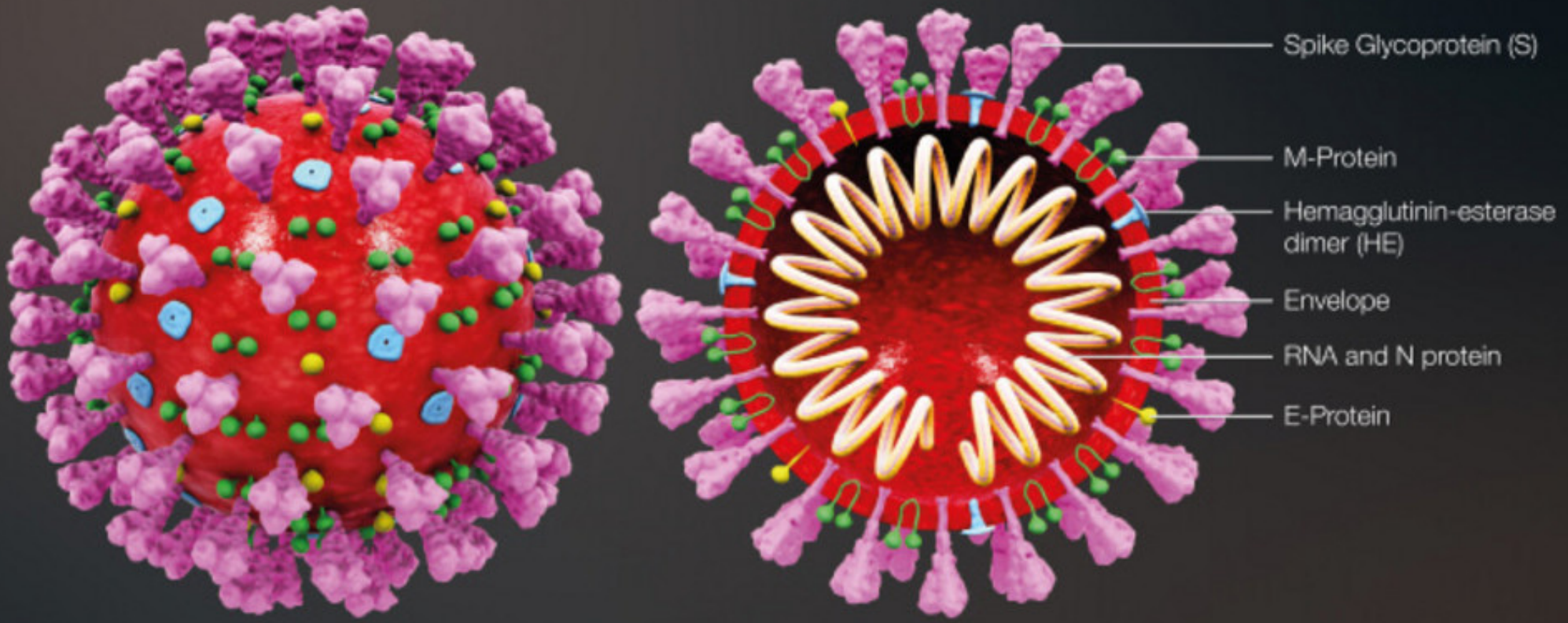
- **The biology of coronaviruses**




Spike Glycoprotein (S)
M-Protein
Hemagglutinin-esterase dimer (HE)
Envelope
RNA and N protein
E-Protein

BIOLOGY OF CORONAVIRUSES

- Coronaviruses are nonsegmented, positive-sense, enveloped single-stranded RNA viruses 27-34 kbases with projections resembling a crown (corona), and emerged only 10,000 years ago.

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- **Most species infect animals**, causing RTI (pneumonia) in birds, GI infection (diarrhea) in pigs and cattle.

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- **In humans, 4 endemic strains cause colds and rare mild pneumonia:**

  229E, NL63, OC43, HKU1

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- The biology of coronaviruses
- Endemic human coronavirus infection
- **Why should we be surprised? We were warned!** ***This is only the 3rd Coronavirus pandemic of the 20th Century!***

BIOLOGY OF CORONAVIRUSES

- Coronaviruses are nonsegmented, positive-sense, enveloped single-stranded RNA viruses 27-34 kbases with projections resembling a crown (corona), emerged only 10,000 years ago.

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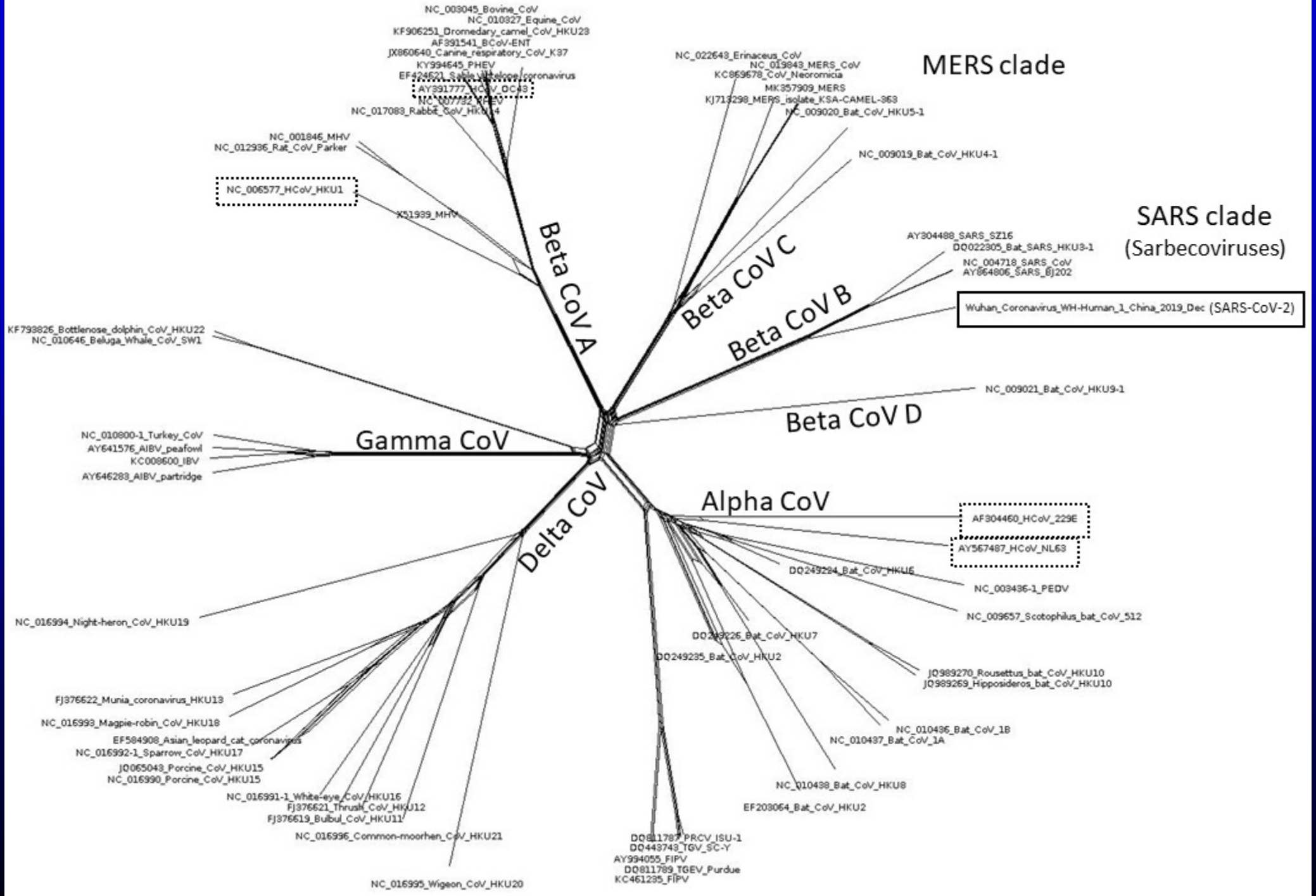
- In humans, 4 strains cause colds and rare mild pneumonia, 229E, NL63, OC43, and HKU1.

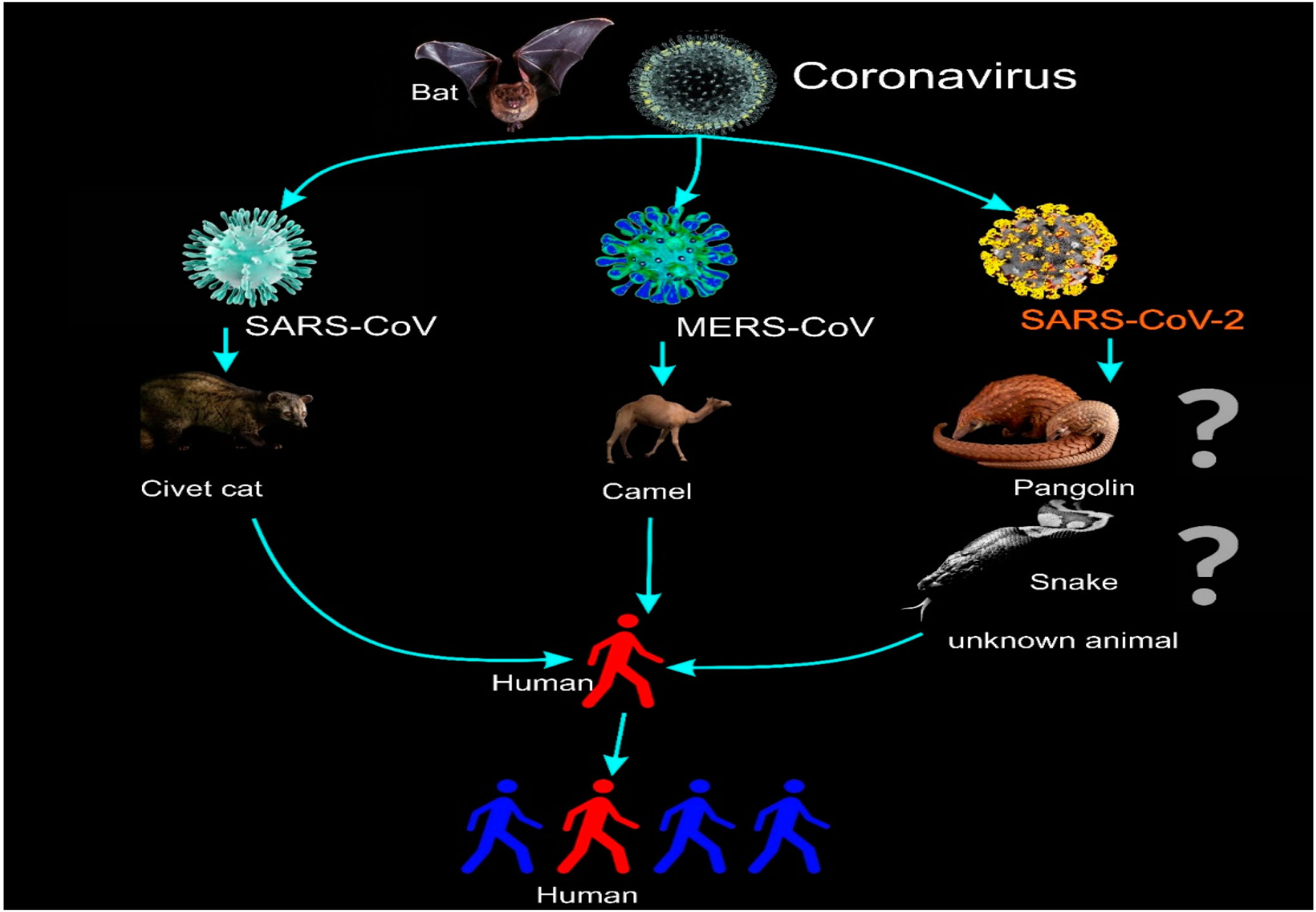
- **Three virulent coronaviruses have emerged from bat coronaviruses to cause pandemic life-threatening disease since 2003,**

  SARS-CoV, MERS-CoV and SARS-CoV-2


MERS clade
SARS clade
(Sarbecoviruses)
Beta CoV A
Beta CoV C
Beta CoV B
Beta CoV D
Gamma CoV
Delta CoV
Alpha CoV
NC_003045_Bovine_CoV
NC_010327_Equine_CoV
KF906251_Dromedary_camel_CoV_HKU23
AF391541_BCoV-ENT
JX860640_Canine_respiratory_CoV_K37
KY994645_PHEV
EF424621_Sable_Whitetoe_coronavirus
AY391777_HCoV_OC43
NC_017083_Rabbit_CoV_HKU14
NC_001846_MHV
NC_012936_Rat_CoV_Parker
NC_006577_HCoV_HKU1
X51939_MHV
NC_022643_Erinaceus_CoV
NC_019843_MERS_CoV
KC869678_CoV_Neoromicia
MK357909_MERS
KJ713298_MERS_isolate_KSA-CAMEL-363
NC_009020_Bat_CoV_HKU5-1
NC_009019_Bat_CoV_HKU4-1
AY304488_SARS_SZ16
DQ022305_Bat_SARS_HKU3-1
NC_004718_SARS_CoV
AY864806_SARS_BJ202
Wuhan_Coronavirus_WH-Human_1_China_2019_Dec (SARS-CoV-2)
NC_009021_Bat_CoV_HKU9-1
KF793826_Bottlenose_dolphin_CoV_HKU22
NC_010646_Beluga_Whale_CoV_SW1
NC_010800-1_Turkey_CoV
AY641576_AIBV_peafowl
KC008600_IBV
AY646283_AIBV_partridge
AF304460_HCoV_229E
AY567487_HCoV_NL63
DQ249224_Bat_CoV_HKU6
NC_003436-1_PEDV
NC_009657_Scotophilus_bat_CoV_512
NC_016994_Night-heron_CoV_HKU19
DQ249226_Bat_CoV_HKU7
DQ249235_Bat_CoV_HKU2
JQ989270_Rousettus_bat_CoV_HKU10
JQ989269_Hipposideros_bat_CoV_HKU10
FJ376622_Munia_coronavirus_HKU13
NC_016993_Magpie-robin_CoV_HKU18
EF584908_Asian_leopard_cat_coronavirus
NC_016992-1_Sparrow_CoV_HKU17
JQ065043_Porcine_CoV_HKU15
NC_016990_Porcine_CoV_HKU15
NC_010436_Bat_CoV_1B
NC_010437_Bat_CoV_1A
NC_016991-1_White-eye_CoV_HKU16
Fj376621_Thrush_CoV_HKU12
FJ376619_Bulbul_CoV_HKU11
NC_010438_Bat_CoV_HKU8
EF203064_Bat_CoV_HKU2
NC_016996_Common-moorhen_CoV_HKU21
DQ811787_PRCV_ISU-1
DQ443743_TGV_SC-Y
AY994055_FIPV
DQ811789_TGEV_Purdue
KC461235_FIPV
NC_016995_Wigeon_CoV_HKU20

PANDEMIC CORONAVIRUSES OF THE 20TH CENTURY

	SARS	MERS	COVID-19
Virus	SARS-CoV	MERS-CoV	SARS-CoV-2
Host	Bat-Civet	Bat-Camel	Bat-Snake or Pangollin
Year, Origin (no. countries)	2002-3 China	2012…China	2019…China
Incub Period	5.2d (2-14)	7d (2-10)	5.5d (2-10)
Ro	2-5	0.3-0.8	2-4
Clinical	Pneumonia	Pneumonia	Pneumonia
Case Fatality	11%	34%	2-10%
No. cases (No. countries)	8,442 (29)	2518 (24) through April 2020	775,000 (200+) as of Mar 2020


Bat
Coronavirus
SARS-CoV
MERS-CoV
SARS-CoV-2
Civet cat
Camel
Pangolin
?
Snake
?
unknown animal
Human
Human

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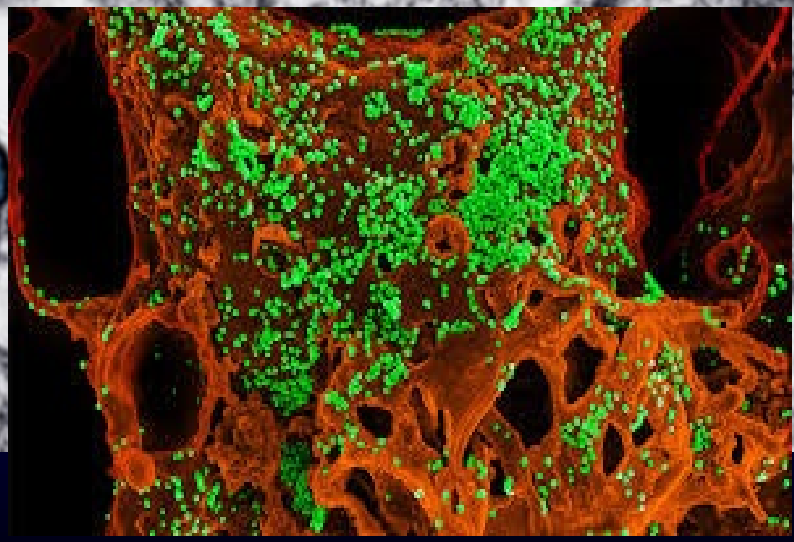
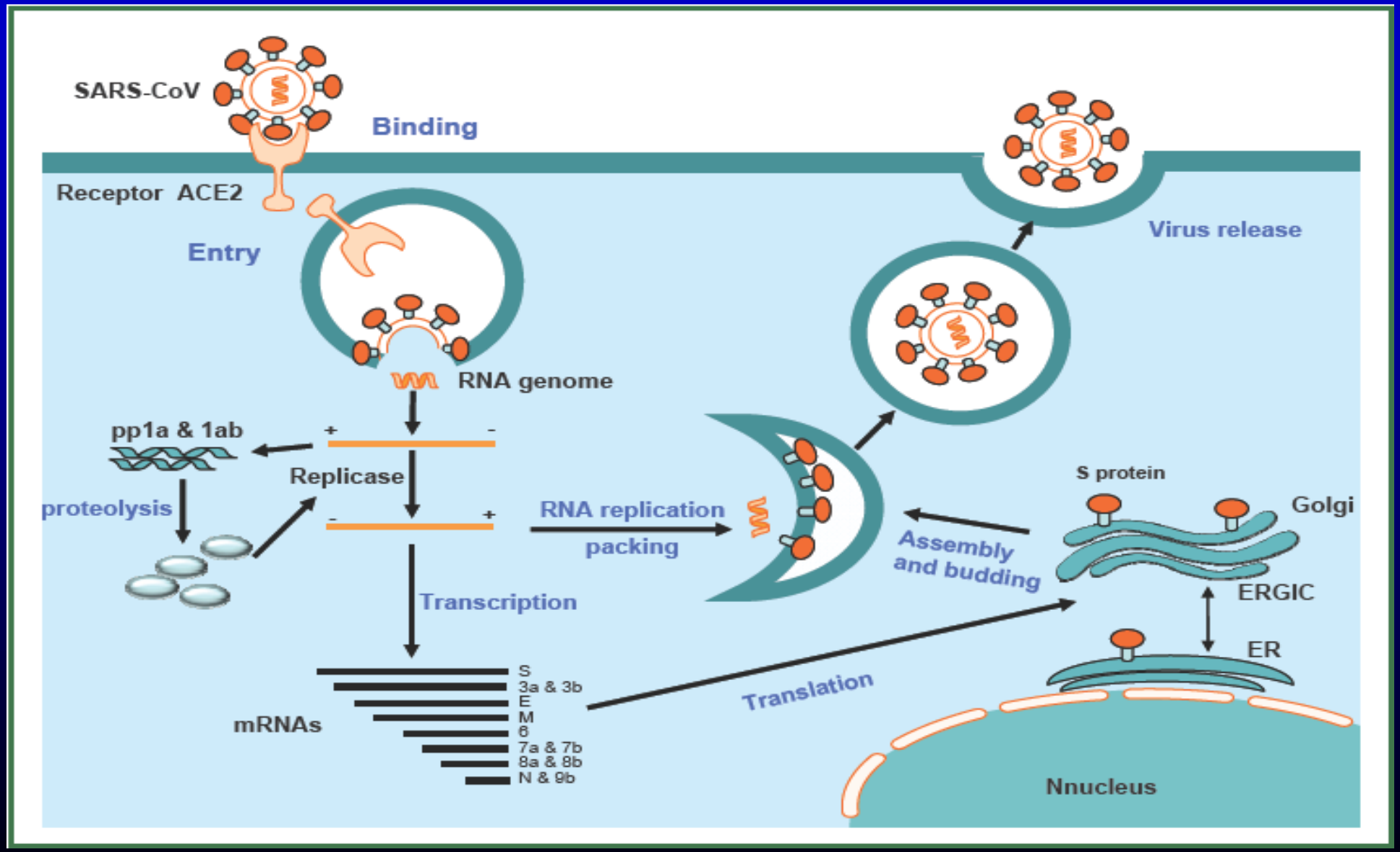
- **Pathophysiology and epidemiology of COVID-19**

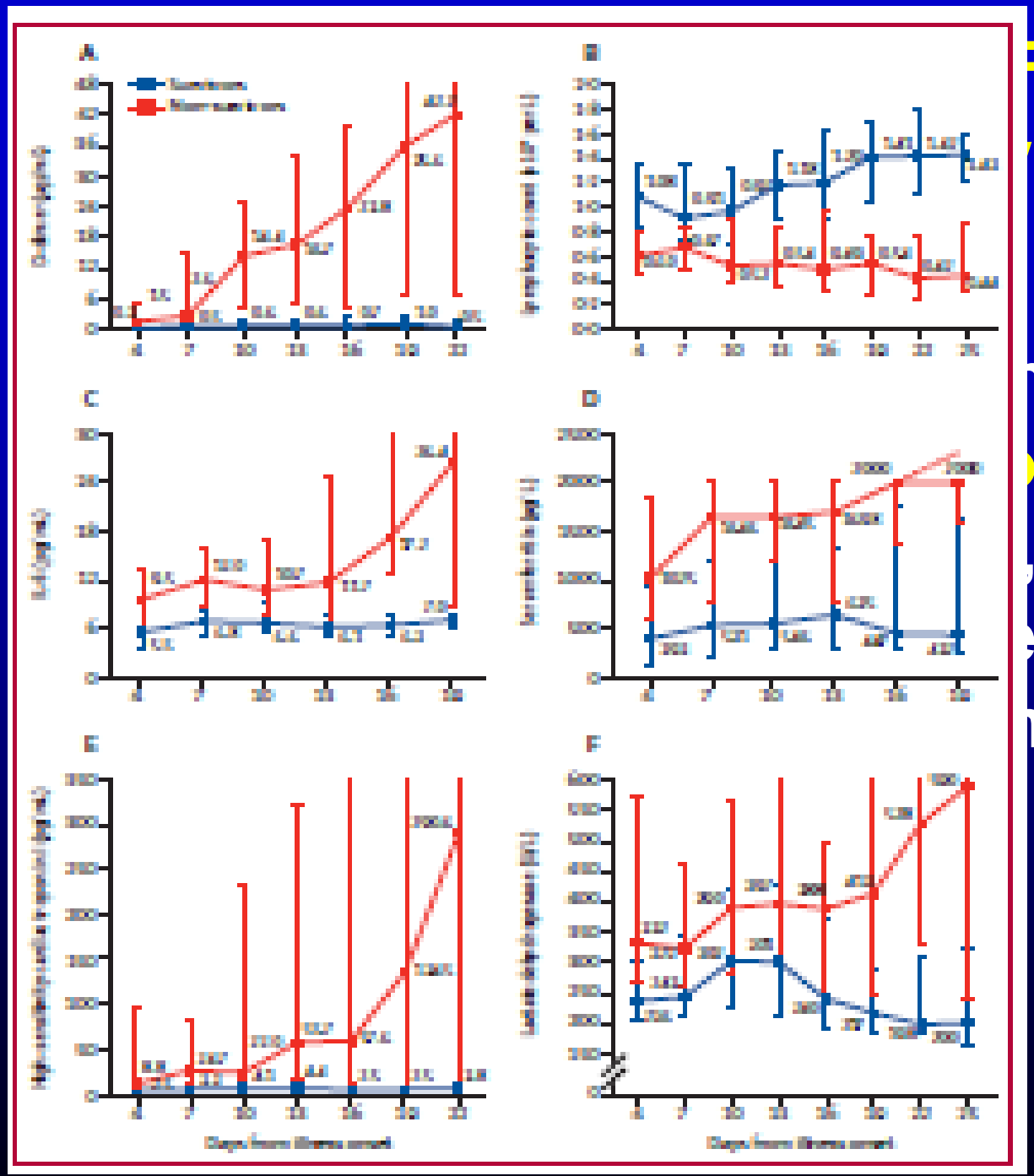


MOLECULAR PATHOGENESIS OF SARS-CoV-2 INFECTION



PATHOPHYSIOLOGY OF COVID-19
(Why does it make us sick, why does it kill?)

- COVID-19 triggers severe l***ocal and systemic inflammation*** (far worse than influenxa, more like Ebola)…”**cytokine storm**” with markedly elevated D-dimer, Ferritin, CRP, IL6, TNF, LFTs (esp LDH)…when severe, features of hemophagocytic syndrome-MAS



F COVID-19

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Zhou et al. Lancet 2020

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- **It is also *prothrombotic*, triggering local and diffuse microscopic intravascular thrombosis clotting, 50% risk DVT, MI, iCVA, PE**

PATHOPHYSIOLOGY OF COVID-19 (Why does it make us sick, why does it kill?)

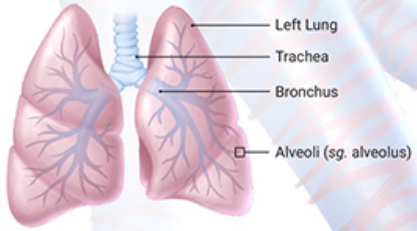
- COVID-19 triggers severe l*ocal and systemic inflammation* (far worse than influenxa, more like Ebola)…"cytokine storm" with markedly elevated d-dimer, CRP, IL6, TNF, LFTs
- It is also *prothrombotic*, triggering local and diffuse microscopic intravascular thrombosis clotting, 50% risk DVT, MI, iCVA, PE
- **Often severe *inflammation of lungs*, with *hypoxemic respiratory failure***

COVID-19

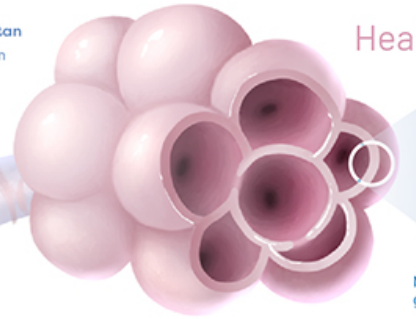
HOW DOES IT AFFECT YOU?

Designed by Avesta Rastan
www.azuravesta.com
@azuravesta
@azuraviz

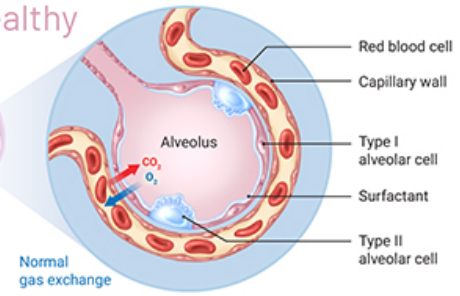
Coronavirus Disease 2019 (COVID-19) is a pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2, also called SARS-CoV-2. Despite the widespread awareness regarding COVID-19, many are still unaware about how it affects the human body.



SARS-CoV-2 starts its journey in the nose, mouth, or eyes and travels down to the alveoli in the lungs. Alveoli are tiny sacs of air where gas exchange occurs.

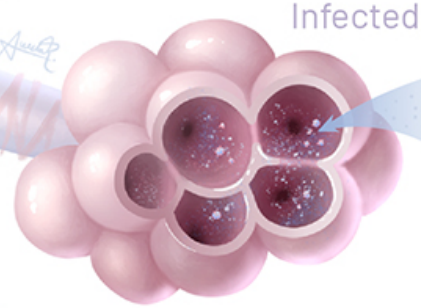


Healthy

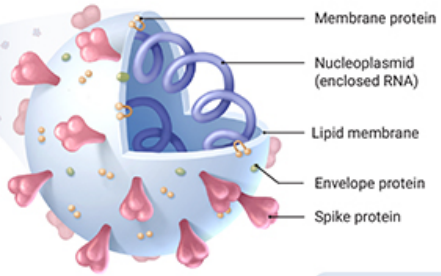


Gas Exchange

Each sac of air, or alveolus, is wrapped with capillaries where red blood cells release **carbon dioxide** (CO_2) and pick up **oxygen** (O_2). Two alveolar cells facilitate gas exchange; **Type I** cells are thin enough that the oxygen passes right through, and **Type II** cells secrete **surfactant** – a substance that lines the alveolus and prevents it from collapsing.



Infected

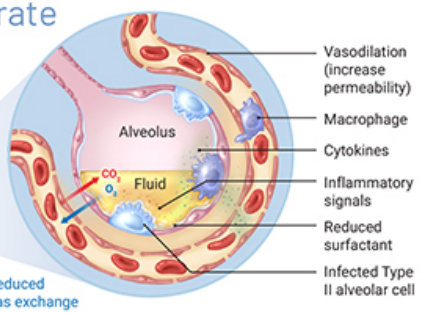


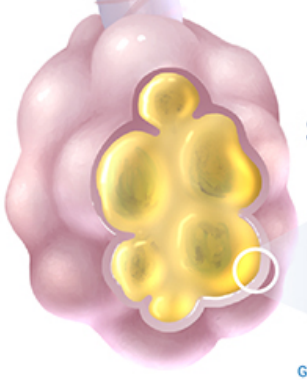
SARS-CoV-2 Structure

Viral Infection

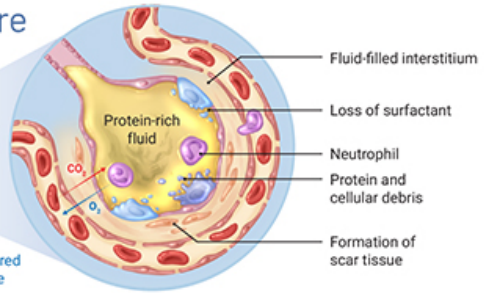
The spike proteins covering the coronavirus bind ACE2 receptors primarily on type II alveolar cells, allowing the virus to inject its RNA. The RNA "hijacks" the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host cell is destroyed in this process and the new coronaviruses infect neighbouring cells.

Moderate





Severe



Impaired Gas Exchange

When the immune system attacks the area of infection it also kills healthy alveolar cells. This results in three things that hinder gas exchange:

1) Alveolar collapse due to loss of surfactant from Type II cells
2) Less oxygen enters the blood-stream due to lack of Type I cells
3) More fluid enters the alveolus

Stay Home

Symptoms may start to show (e.g. dry cough, fever, etc.)

Pneumonia develops

Shortness of breath

Hospitalization

Dangerous for high-risk individuals; secondary infections may occur

Intensive Care (ICU)

Patients may require ventilators and life-support

Complications unrelated to COVID-19 may occur

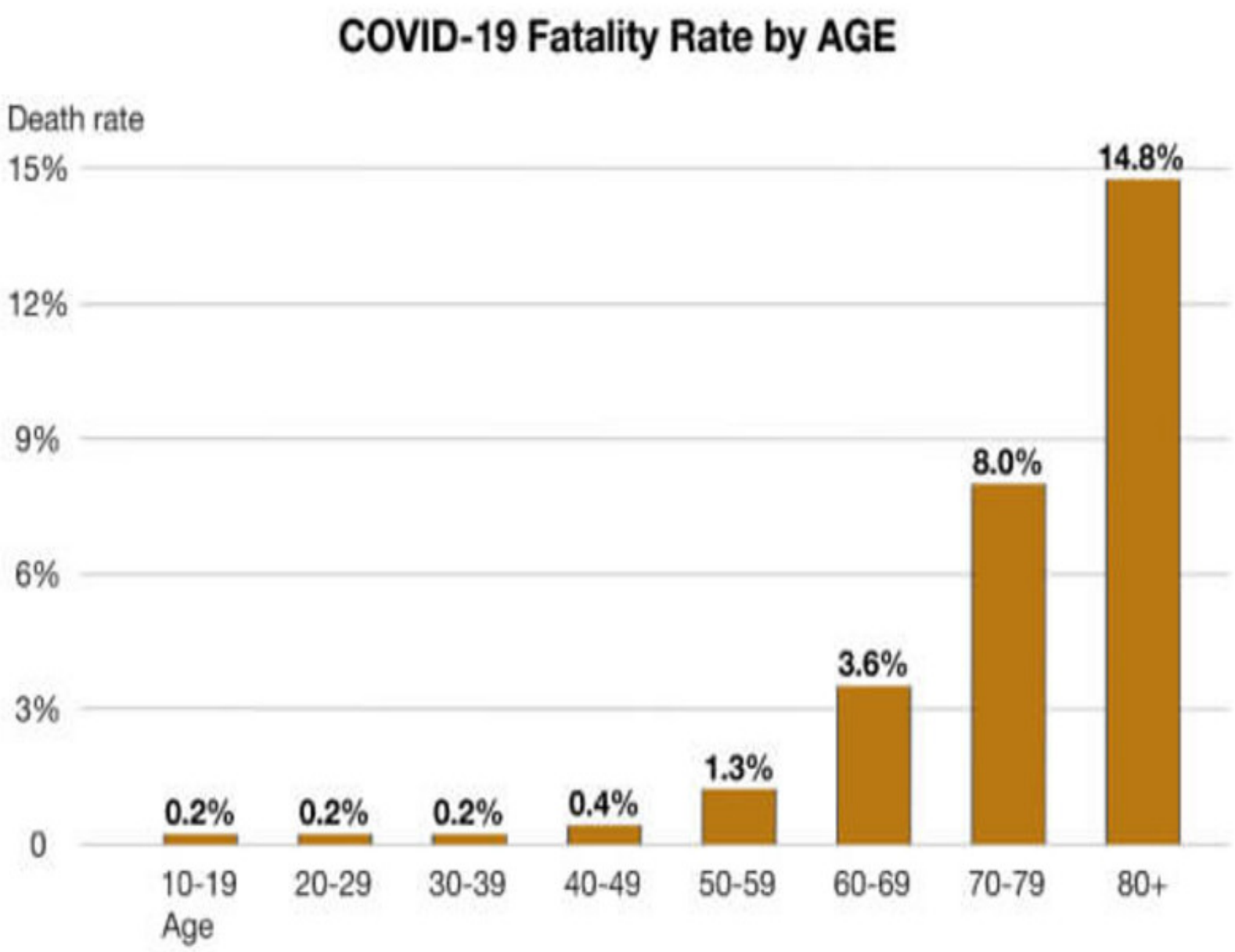
With proper care, patients may recover at any point during this process

Immune Response

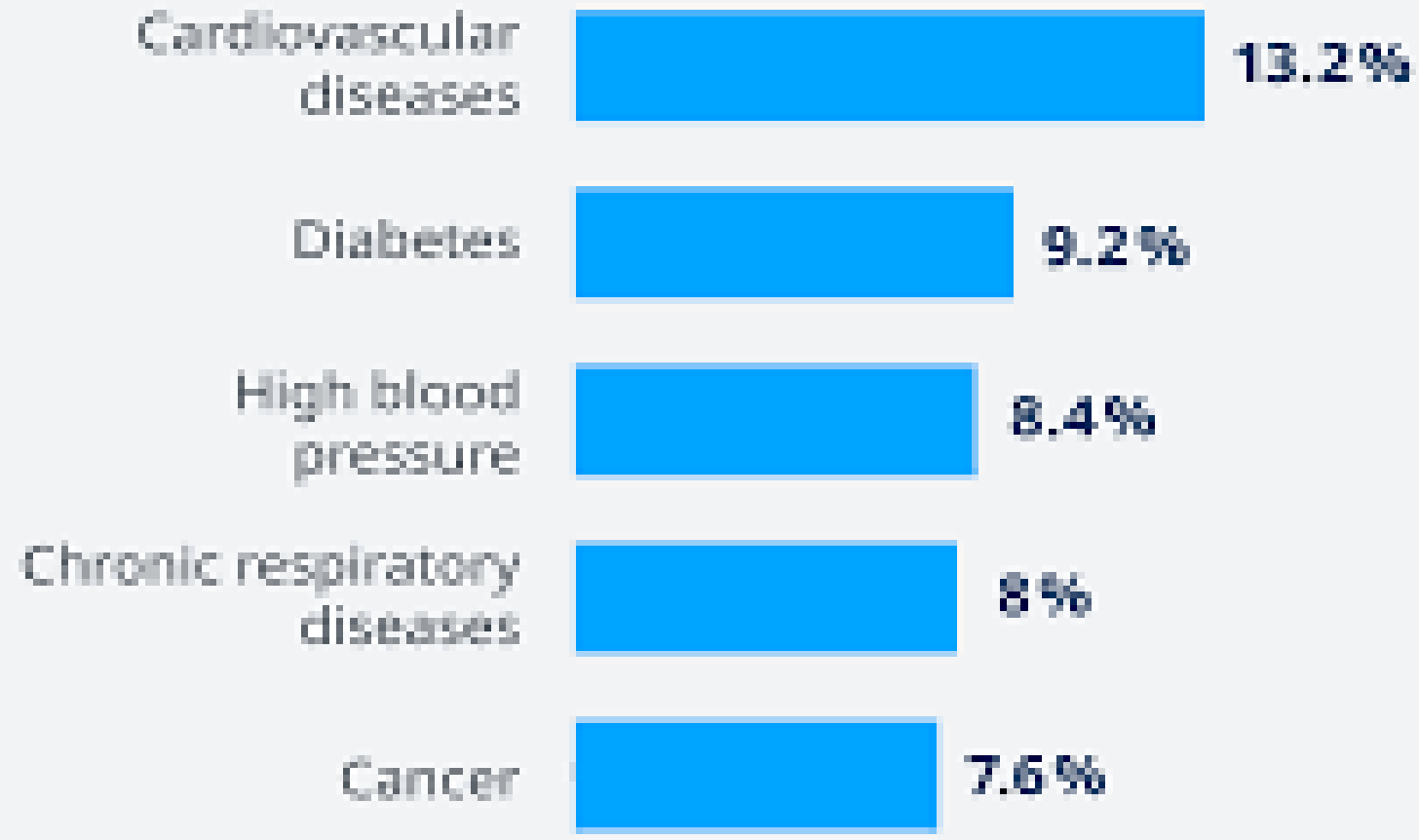
1. After infection, Type II cells release **inflammatory signals** that recruit **macrophages** (immune cells).
2. Macrophages release **cytokines** that cause vasodilation, which allows more immune cells to come to the site of injury and exit the capillary.
3. Fluid accumulates inside the alveolus.
4. The fluid dilutes the surfactant which triggers the onset of alveolar collapse, decreasing gas exchange and increasing the work of breathing.
5. **Neutrophils** are recruited to the site of infection and release Reactive Oxygen Species (ROS) to destroy infected cells.
6. Type I and II cells are destroyed, leading to the collapse of the alveolus and causing **Acute Respiratory Distress Syndrome** (ARDS).
7. If inflammation becomes severe, the protein-rich fluid can enter the bloodstream and travel elsewhere in the body, causing **Systemic Inflammatory Response Syndrome** (SIRS).
8. SIRS may lead to **septic shock** and **multi-organ failure**, which can have fatal consequences.

PATHOPHYSIOLOGY OF COVID-19
(Why does it make us sick, why does it kill?)

- COVID-19 triggers severe l*ocal and systemic inflammation* (far worse than influenxa, more like Ebola)
- It is also *prothrombotic*, triggering local and diffuse microscopic intravascular thrombosis clotting, 50% risk DVT, MI, iCVA, PE
- Ubiquitous *inflammation of lungs*, with *hypoxemic respiratory failure*
- **High risk of secondary *multi-organ injury*, especially kidneys, heart, GI tract and brain, beyond the lungs**


COVID-19 Fatality Rate by AGE
Death rate
15%
12%
9%
6%
3%
0
0.2%
0.2%
0.2%
0.4%
1.3%
3.6%
8.0%
14.8%
10-19
20-29
30-39
40-49
50-59
60-69
70-79
80+
Age

SARS-CoV-2 mortality rate after previous illness



Source: WHO | China, February 2020

Case fatality rates: COVID-19 vs. US Seasonal Flu

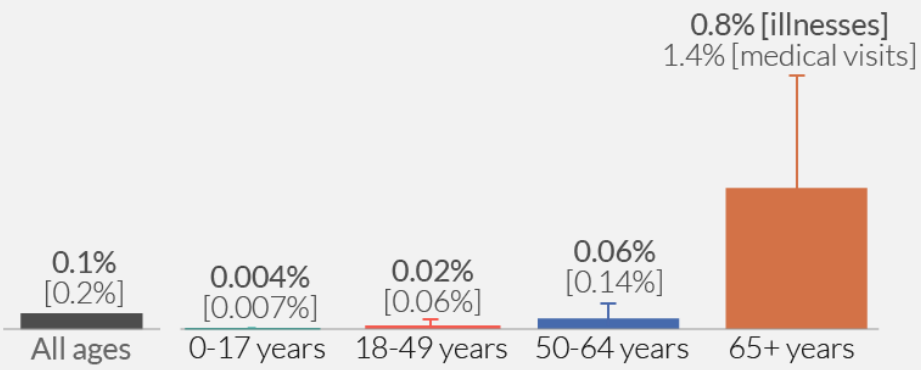
Case fatality rate (CFR) is specific to a location and time. It is calculated by dividing the total number of deaths from a disease by the number of confirmed cases.

Our World in Data

Seasonal Flu

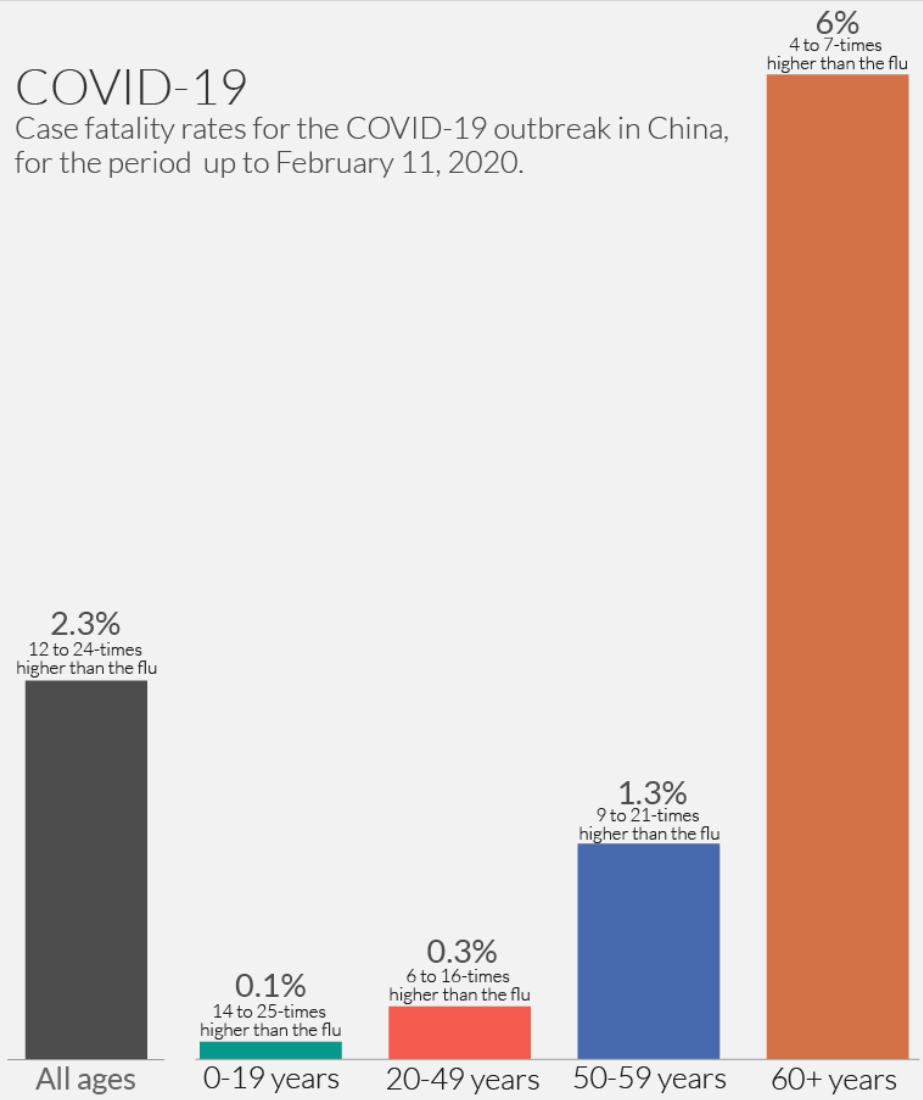
Case fatality rates for the influenza season 2018-19 in the USA.

Symptomatic cases are calculated based on models which aim to account for underreporting – figures based on medical visits are therefore also shown in square brackets, which may be a closer comparison to COVID-19 case fatality rates.



COVID-19

Case fatality rates for the COVID-19 outbreak in China, for the period up to February 11, 2020.



Data: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly.
US Influenza data is sourced from the US Centers for Disease Control and Prevention (CDC).

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

Goals*: To Understand*

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China
- The biology of coronaviruses
- Endemic human coronavirus infection
- What's new? *The 3rd Coronavirus pandemic of the 20th Century!*
- The extraordinary global spread of COVID-19 since January 2020

- **The epidemiology of COVID-19**

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **Droplet nuclei that are inhaled or swallowed**

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
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  - **Contact transmission with virus transmitted hand-to-nose or mouth**

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **Droplet nuclei** that are inhaled or swallowed
  - **Contact transmission** with virus transmitted hand-to-nose or mouth
  - **Respiratory transmission** over longer distances thought very rare, and ***respiratory precautions NOT routinely needed except with high-risk procedures generating aerosols***: CDC and WHO

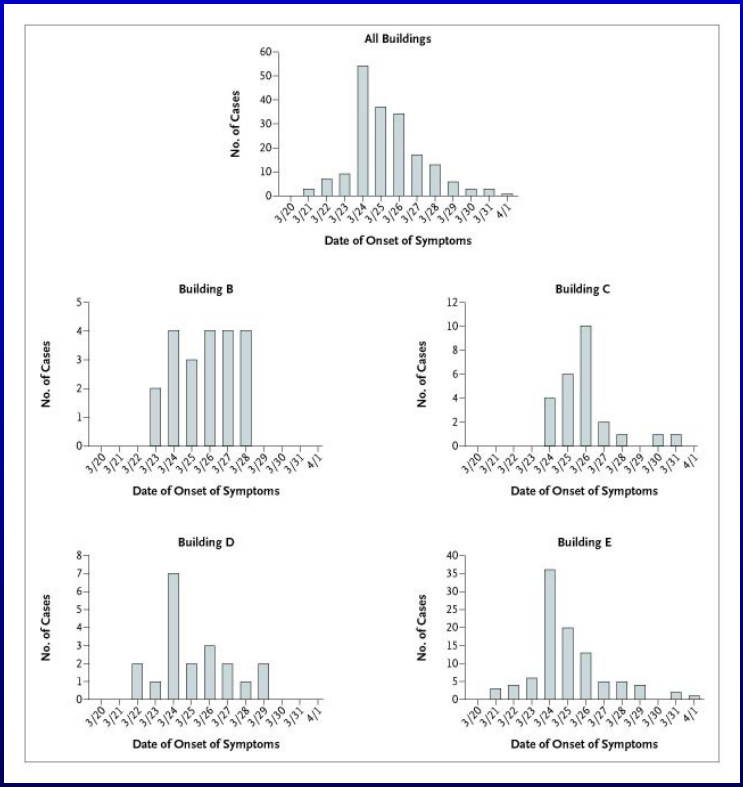
EPIDEMIOLOGY OF COVID-19

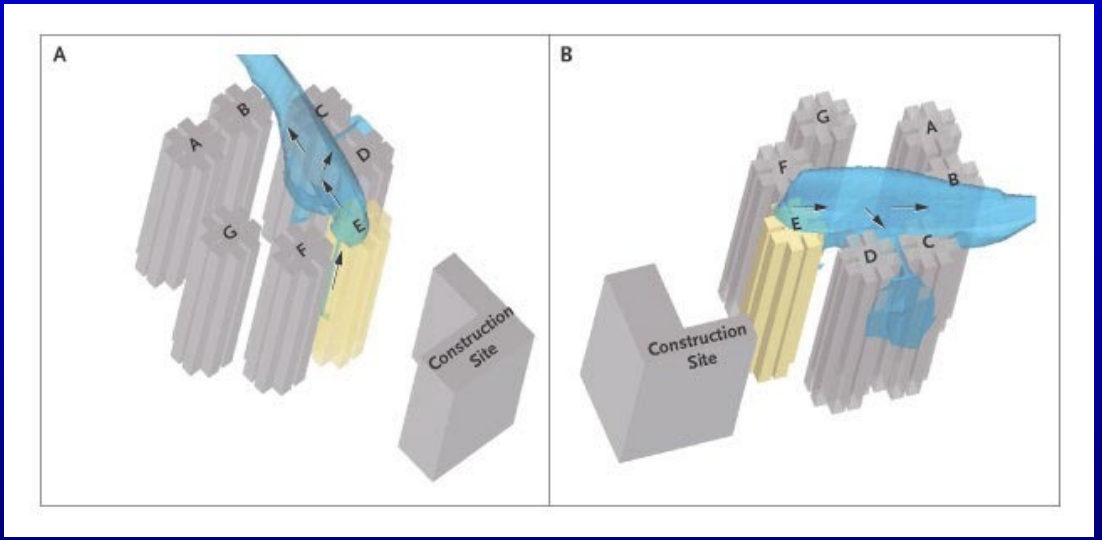
- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **There is considerable evidence that COVID-19 is transmitted through the air over longer distances (*Respiratory Transmission*):**

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **There is considerable evidence that COVID-19 is transmitted through the air over longer distances (*Respiratory Transmission*):**
    - **SARS-CoV-1 in 2003-4 shown to have capacity for distant airborne spread, Hong Metropole Kong hotel outbreak involving multiple floors, and the huge Amoy Garden housing complex outbreak, both originating from a single index cas, SARS-CoV-2 and SARS-CoV-2 biologically closely related.**

AN EXTRAORDINARY SARS-COV-1 OUTBREAK IN A HONG KONG HOUSING COMPLEX





Over 10 days, 187 cases of SARS in the huge Amoy Garden Housing complex in Hong Kong originating from from a single index case

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
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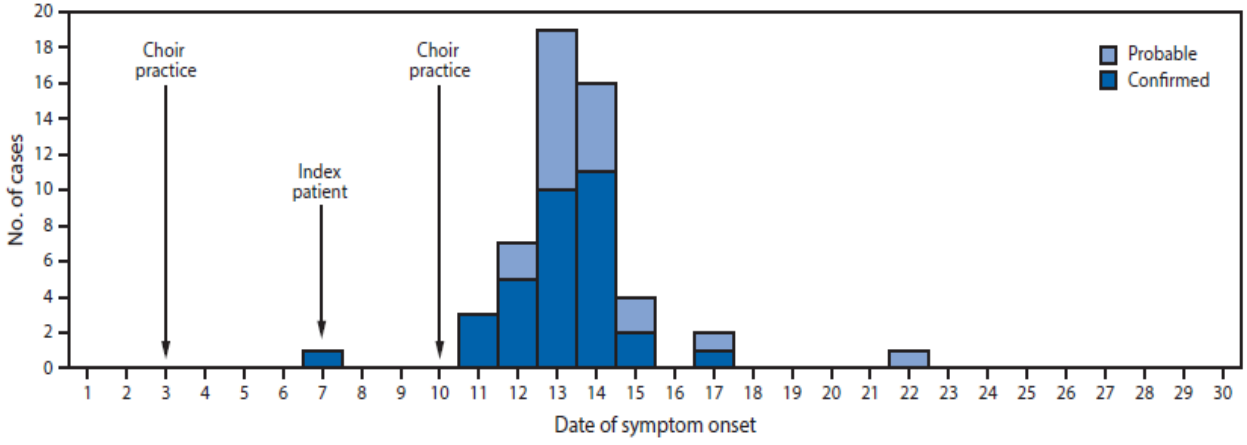
    - **Washington State choir outbreak.**

AN EXTRAORDINARY OUTBREAK OF COVID-19 IN A VERNON, WASHINGTON CHURCH CHOIR AFTER A 2 ½ HR PRACTICE

FIGURE. Confirmed* and probable† cases of COVID-19 associated with two choir practices, by date of symptom onset (N = 53) — Skagit County, Washington, March 2020



Within 1 week, 88% of 61 attendees developed COVID-19, 2 died

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **There is considerable evidence that COVID-19 can be transmitted through the air over longer distances (*Respiratory Transmission*):**
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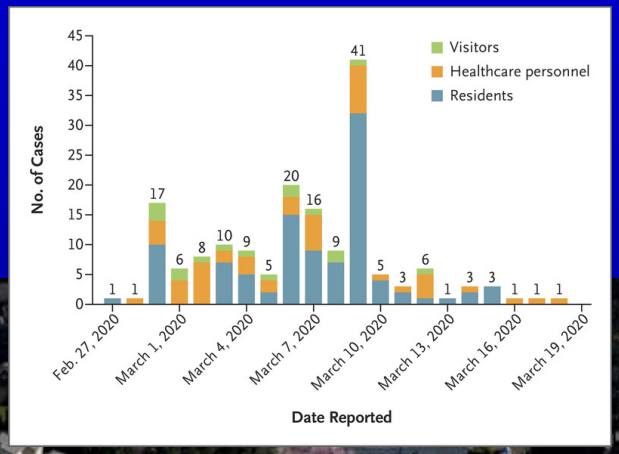
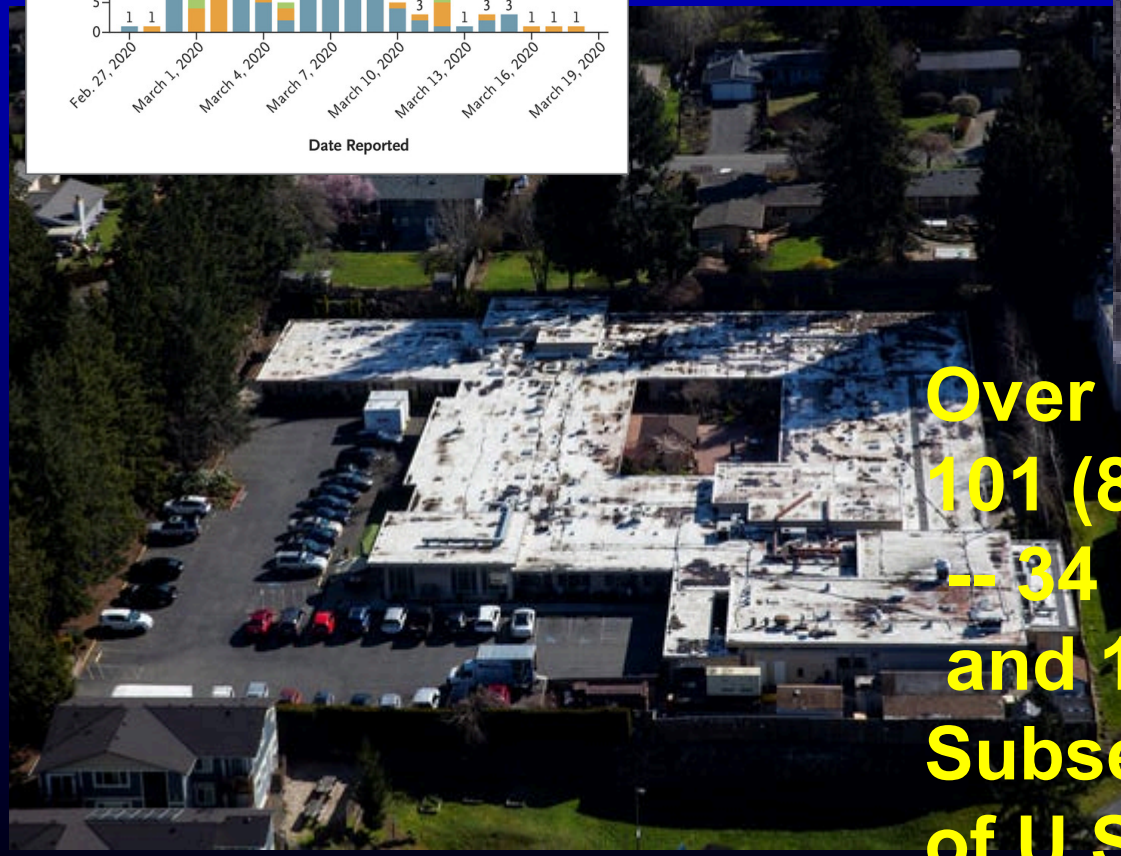
    - **Washington State choir outbreak.**
    - **Kirkland, WA, nursing home outbreak.**

AN EXTRAORDINARY COVID-19 OUTBREAK IN A KIRKLAND, WASHINGTON NURSING HOME





Over 10 days, COVID-19 in 101 (89%) of 117 residents -- 34 dying -- 50 HCWs and 16 visitors infected. Subsequently, thousands of U.S. nursing home outbreaks

EPIDEMIOLOGY OF COVID-19

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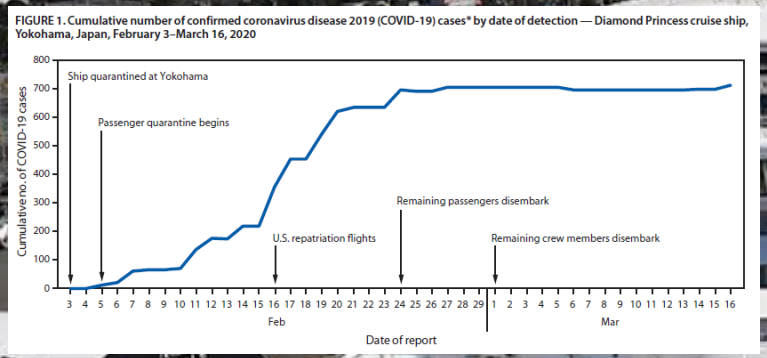
    - **Washington State choir outbreak.**
    - **Kirkland, WA, nursing home outbreak.**
    - **Diamond Princess Cruise ship outbreak.**

Overall 700 passengers became infected, 300 passengers quarantined in their cabins developed COVID-19 without any contact with the crew or other passengers



LIFE ABOARD THE QUARANTINED DIAMOND PRINCESS

EPIDEMIOLOGY OF COVID-19

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    - **Washington State choir outbreak.**
    - **Kirkland, WA, nursing home outbreak in Feb 2020.**
    - **Diamond Princess Cruise ship outbreak, SARS-CoV-2 found on multiple surfaces in guests' rooms and recovered from the air as well as air in hallways outside rooms.**
    - **The Arkansas church outbreak**

AN EXTRAORDINARY CHURC OUTBREAK OF COVID-19

Of 92 attendees at an Arkansas church service, 35 (38%) acquired COVID-19 from two minimally symptomatic members, 3 died, 26 additional citizens in the community became secondarily infected

EPIDEMIOLOGY OF COVID-19

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **There is considerable evidence that COVID-19 is transmitted through the air over longer distances (*Respiratory Transmission*):**
    - SARS-CoV-1 in 2003-4 shown to have capacity for distant airborne spread, huge Hong Kong Metropole Hotel hotel outbreak involving multiple floors,
      and the huge Amoy Gardens housing complex outbreak, ARS-CoV-2 and SARS-CoV-2 biologically closely related.
    - Washington State choir outbreak.
    - Kirkland, WA, nursing home outbreak in Feb 2020.
    - Diamond Princess Cruise ship outbreak, SARS-CoV-2 found on multiple surfaces in guests' rooms and recovered from the air as well as air
      in hallways outside rooms.
    - The Arkansas church outbreak
    - **The recovery of SARS-CoV-2 from air and multiple surfaces in infected patients' hospital rooms but also outside hallways and viable in air for >5 hrs**

“239 Experts With One Big Claim: The Coronavirus Is Airborne”

NEW YORK TIMES
JULY 4, 2020

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China
- The biology of coronaviruses
- Endemic human coronavirus infection
- What's new? *The 3rd Coronavirus pandemic of the 20th Century!*
- The extraordinary global spread of COVID-19 since January 2020
- Pathophysiology and epidemiology of COVID-19
- **Clinical features of COVID-19 and laboratory diagnosis**

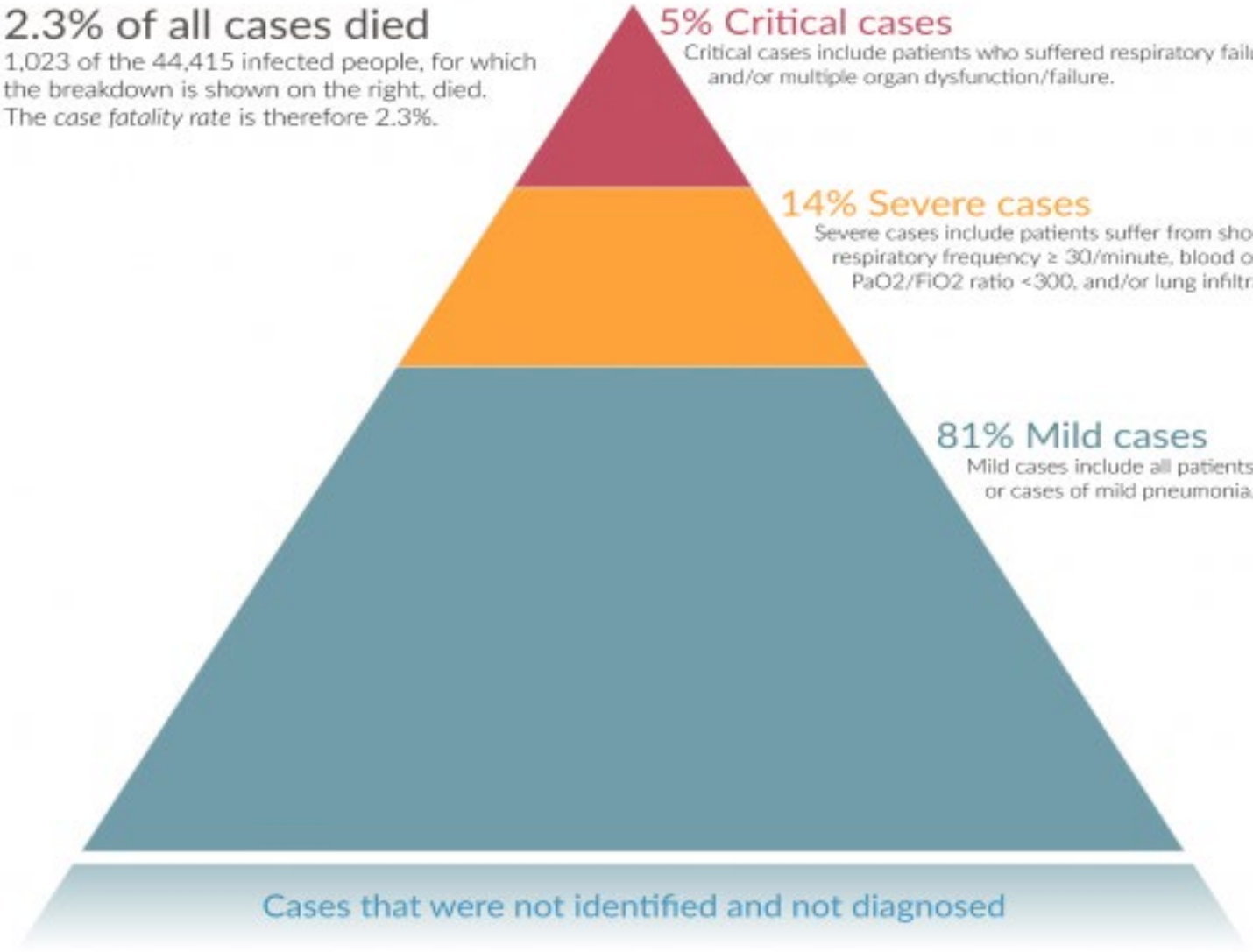
Coronavirus [COVID-19]: the severity of diagnosed cases in China

Descriptions of 44,415 confirmed cases of COVID-19 nationwide in China.
Included are confirmed cases in the early period of the outbreak of the disease up to February 11, 2020.

Our World in Data

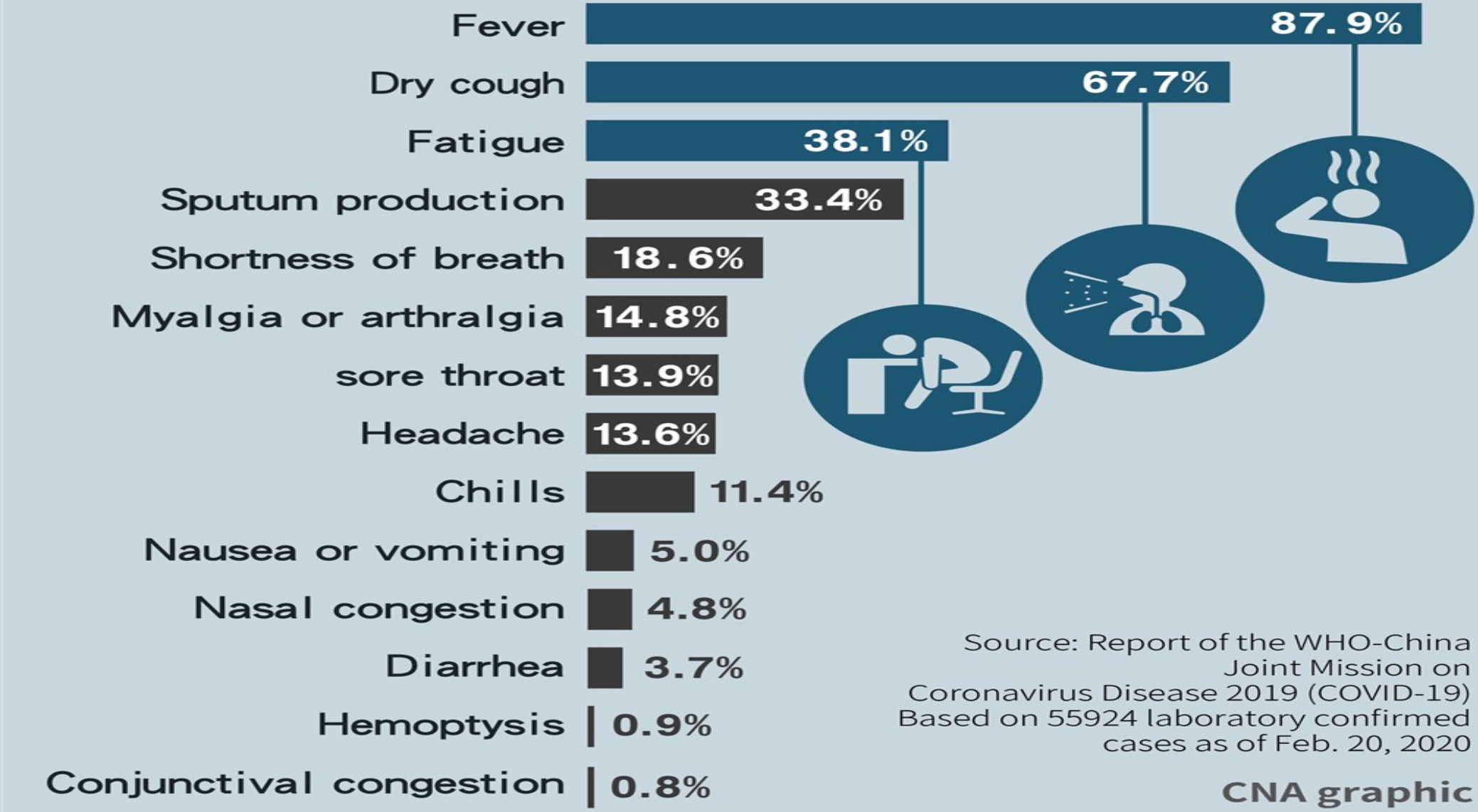
2.3% of all cases died

1,023 of the 44,415 infected people, for which the breakdown is shown on the right, died.
The *case fatality rate* is therefore 2.3%.



Data source: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. *Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020.* China CDC Weekly. Case counts: 36,160 mild cases; 6,168 severe cases; 2,087 critical cases.

Typical symptoms of COVID-19



Source: Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) Based on 55924 laboratory confirmed cases as of Feb. 20, 2020

CNA graphic

LAB DIAGNOSIS COVID-19

- **Culture**

  IMPRACTICAL, *HAZARDOUS FOR LAB WORKERS*

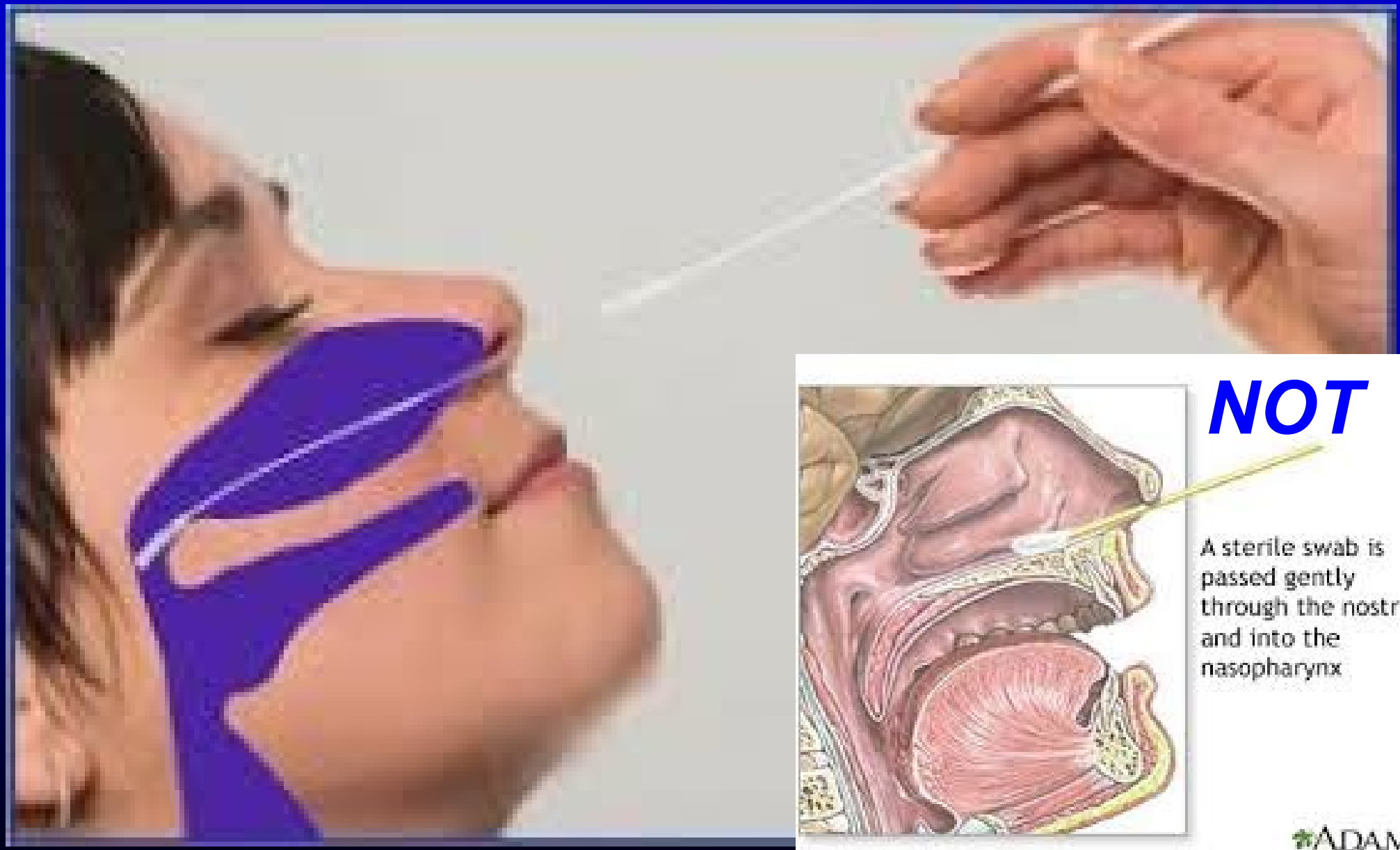
LAB DIAGNOSIS COVID-19

- **Culture**

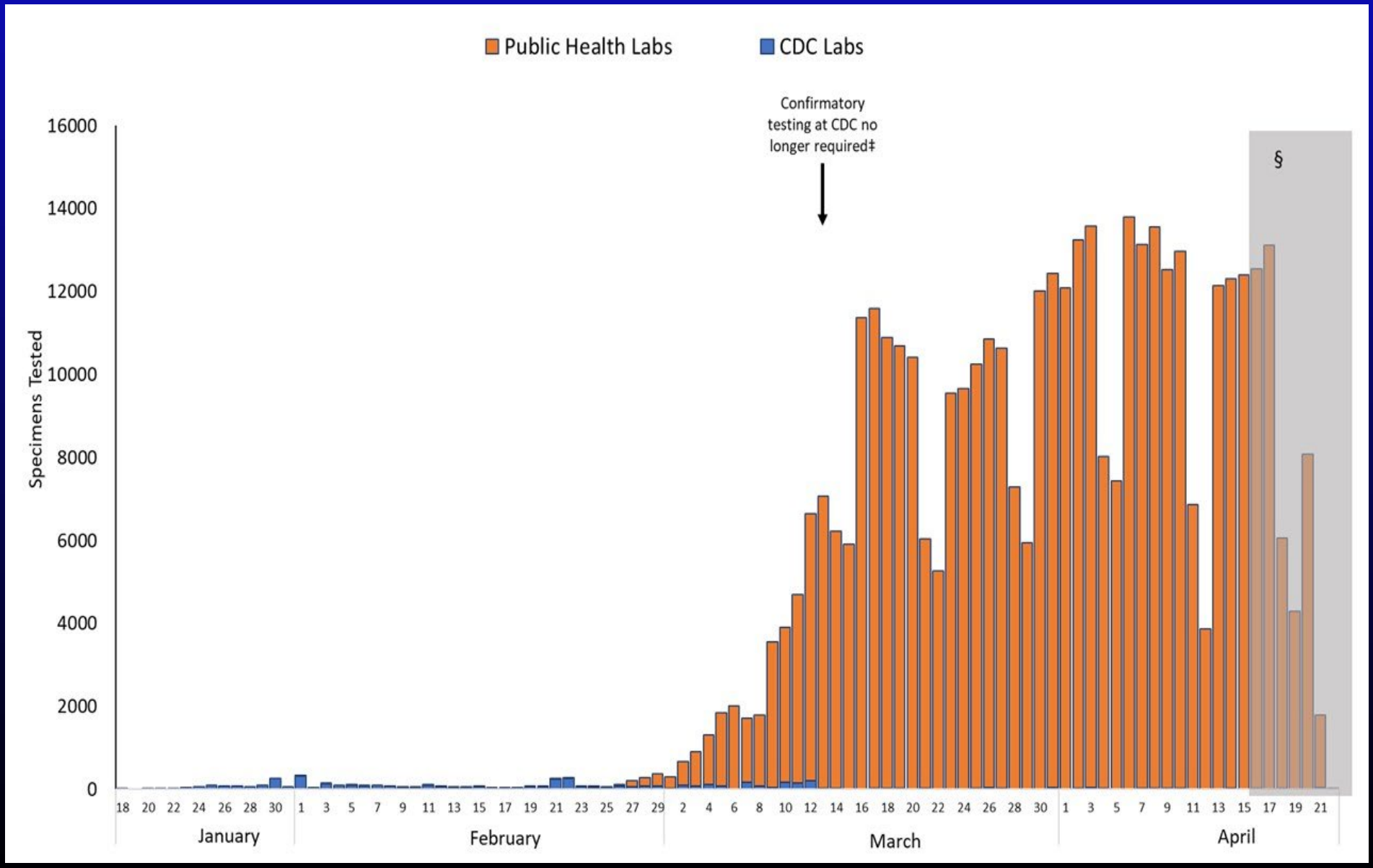
  IMPRACTICAL, *HAZARDOUS FOR LAB WORKERS*

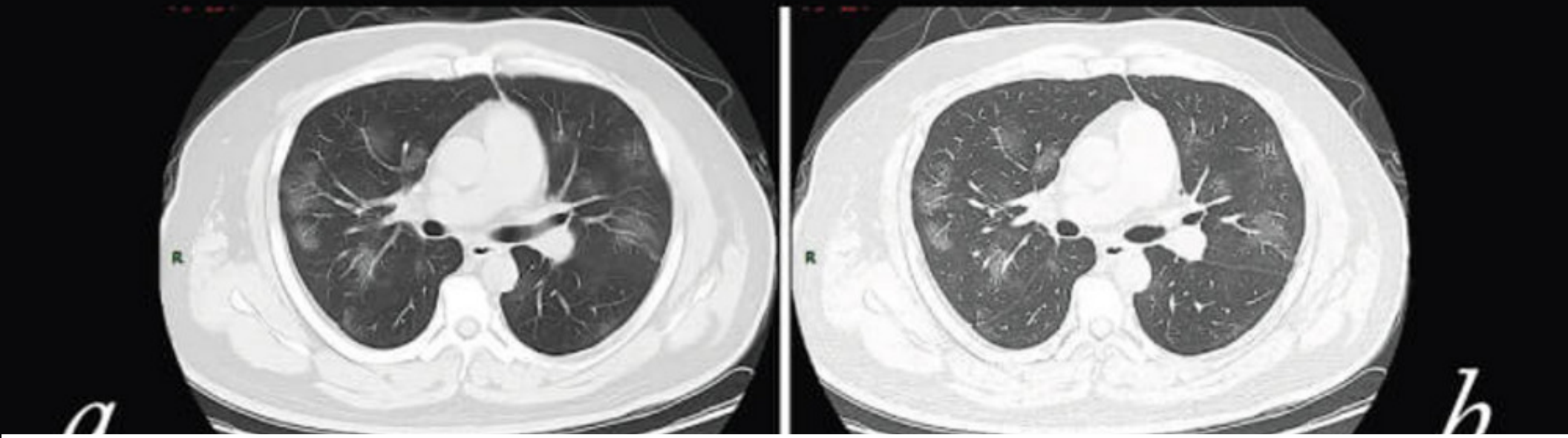
- **Real-time RT-PCR (the best, the gold standard)**

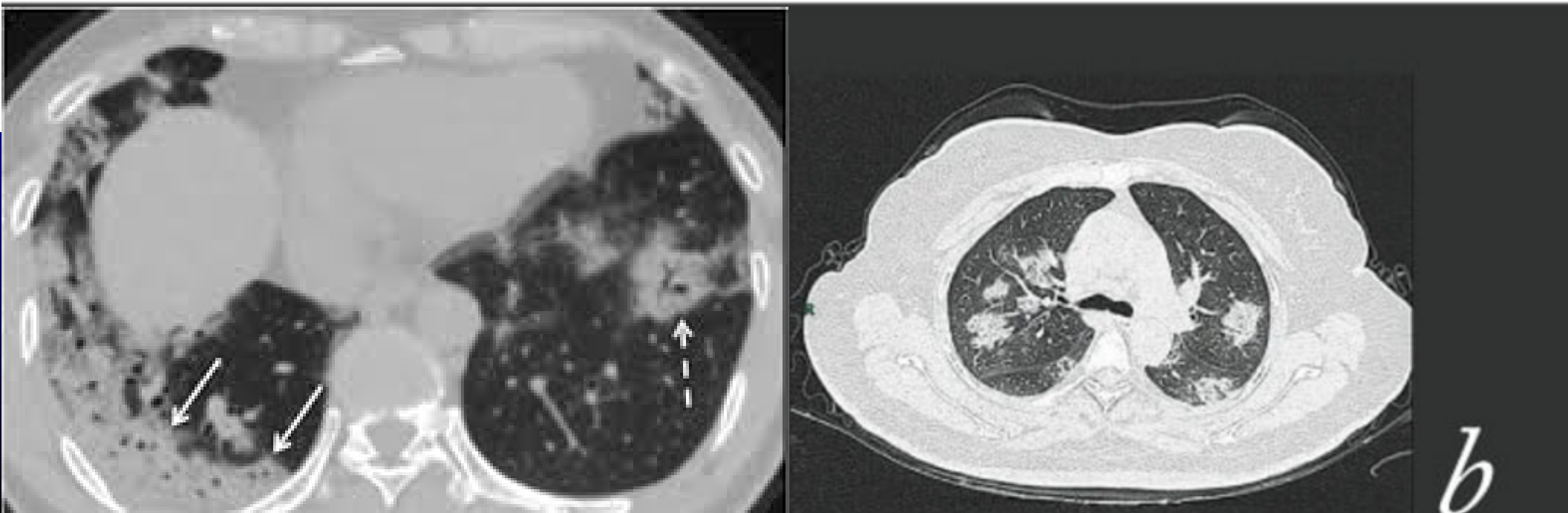
A Proper Nasopharyngeal Swabbing for PCR



COVID-19 PCR TESTING IN THE U.S.




a
b


b

LAB DIAGNOSIS COVID-19

- **Culture**

  IMPRACTICAL, *HAZARDOUS FOR LAB WORKERS*

- **Real-time RT-PCR** (the best, the gold standard)

  REPEAT THE PCR IF THE FIRST TEST IS NEGATIVE BUT THE CLINICAL PICTURE IS SUSPICIOUS…

  then >95% sensitive & specific…being adapted for saliva

LAB DIAGNOSIS COVID-19

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- **Antigen Tests**

  POOR SENSITIVITY, POORLY STANDARDIZED

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  then >95% sensitive & specific

- **Antigen Tests**

  POOR SENSITIVITY, POORLY STANDARDIZED

- **Antibody tests (serology) IgM and IgG**

  Positive ~5 d (IgM) and ~14 d (IgG) illness.

  ACCURACY UNPROVEN, *POSITIVE SEROLOGY MANDATES PCR TO R/O ACTIVE INFECTION*,

  MAINLY USEFUL FOR POPULATION STUDIES

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China
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- Pathophysiology and epidemiology of COVID-19
- Clinical features of COVID-19 and its laboratory diagnosis
- **Management of COVID-19. Is there a role for antiviral or antinflammatory therapy?**

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, **HOME QUARANTINE**

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, HOME QUARANTINE

- IF SYMPTOMATIC AND ILL, HOSPITALIZE:

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, **HOME QUARANTINE**
- IF SYMPTOMATIC AND ILL, HOSPITALIZE:
  - **R/O alternative cause of symptoms,**

    eg, r/o *co-infection, especially bacterial CAP, CHF and/or decompensation of COPD*

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, **HOME QUARANTINE**
- IF SYMPTOMATIC AND ILL, HOSPITALIZE:
  - R/O alternative cause symptoms, eg, *co-infection*
  - **Monitor SpO2 continuously**

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, **HOME QUARANTINE**

- IF SYMPTOMATIC AND ILL, HOSPITALIZE:
  - R/O alternative cause symptoms, eg, *co-infection*
  - Monitor SpO2 continuously
  - ***ISOLATION***, droplet nuclei, contact and, if possible, respiratory isolation in a dedicated HEPA-filtered COVID-19 Unit

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, **HOME QUARANTINE**

- IF SYMPTOMATIC AND ILL, HOSPITALIZE:
  - R/O alternative cause symptoms, eg, *co-infection*
  - Monitor SpO2 continuously
  - ISOLATION, droplet nuclei, contact and, if possible, respiratory in a dedicated COVID-19 Unit or ICU
  - If no contraindication, ***ANTICOAGULATE***

MANAGEMENT OF COVID-19

- If hospitalization NOT indicated, *HOME QUARANTINE* with self-monitoring of SpO2
- IF SYMPTOMATIC AND ILL, *HOSPITALIZE*:
  - ISOLATION, droplet nuclei, contact and, if possible, respiratory in a dedicated COVID-19 Unit or ICU
  - R/O alternative cause symptoms, eg, *co-infection*
  - Monitor SpO2 continuously
  - If no contraindication, *ANTICOAGULATE*
  - ***ANTI-VIRAL THERAPY + DEXAMETHASONE***


QUEEN BEGS HARRY:
DIVORCE MEGHAN & SAVE OUR FAMILY
NATIONAL ENQUIRER
MIRACLE PILL AND KITCHEN TREATMENTS THAT WORK!
CORONAVIRUS CURES FINALLY FOUND!
Warning! Surgical masks SPREAD INFECTION!
WORLDWIDE DEATHS 3,254
AMERICAN DEATHS 11 AND COUNTING
NATIONAL ENQUIRER
Better Homes & Gardens

POTENTIAL CANDIDATES FOR ANTIVIRALTHERAPY FOR COVID-19

A number of drugs have *in vitro* activity against SARS-CoV and SARS-CoV-2 or may prove effective in modulating the severe SIRS:

- Lopinavir-ritonavir
- Hydroxychloroquine with/without Azithro
- Ramdesivir
- Favipiravir, Umifenivir
- Brilacidin
- Kevzara
- Camestat mesylate

Biologics

- Corticosteroids
- Colchicine
- Convalescent plasma
- Monoclonal Ab
- G-CSF
- Interferon alpha/beta
- Tocilizumab
- JAK 2 inhibitors

TWO (OF 4) NEGATIVE RCTs OF HYDROXYCHLOROQUINE FOR PREVENTION OR TREATMENT OF COVID-19

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 6, 2020 VOL. 383 NO. 6

A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19

D.R. Boulware, M.F. Pullen, A.S. Bangdiwala, K.A. Pastick, S.M. Lofgren, E.C. Okafor, C.P. Skipper, A.A. Nascene, M.R. Nicol, M. Abassi, N.W. Engen, M.P. Cheng, D. LaBar, S.A. Lother, L.J. MacKenzie, G. Drobot, N. Marten, R. Zarychanski, L.E. Kelly, I.S. Schwartz, E.G. McDonald, R. Rajasingham, T.C. Lee, and K.H. Hullsiek

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19

A.B. Cavalcanti, F.G. Zampieri, R.G. Rosa, L.C.P. Azevedo, V.C. Veiga, A. Avezum, L.P. Damiani, A. Marcadenti, L. Kawano-Dourado, T. Lisboa, D.L.M. Junqueira, P.G.M. de Barros e Silva, L. Tramujas, E.O. Abreu-Silva, L.N. Laranjeira, A.T. Soares, L.S. Echenique, A.J. Pereira, F.G.R. Freitas, O.C.E. Gebara, V.C.S. Dantas, R.H.M. Furtado, E.P. Milan, N.A. Golin, F.F. Cardoso, I.S. Maia, C.R. Hoffmann Filho, A.P.M. Kormann, R.B. Amazonas, M.F. Bocchi de Oliveira, A. Serpa-Neto, M. Falavigna, R.D. Lopes, F.R. Machado, and O. Berwanger, for the Coalition Covid-19 Brazil I Investigators*

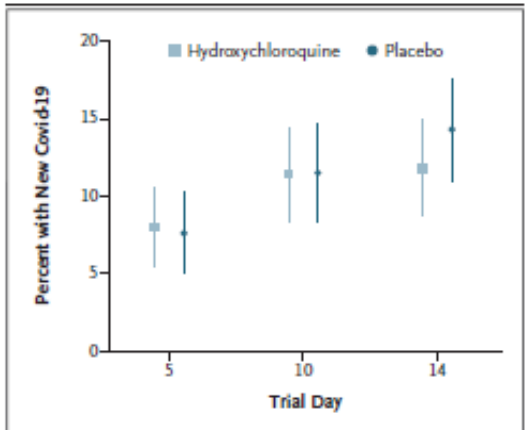


Figure 2. Cumulative Incidence of Illness Compatible with Coronavirus Disease (Covid-19).

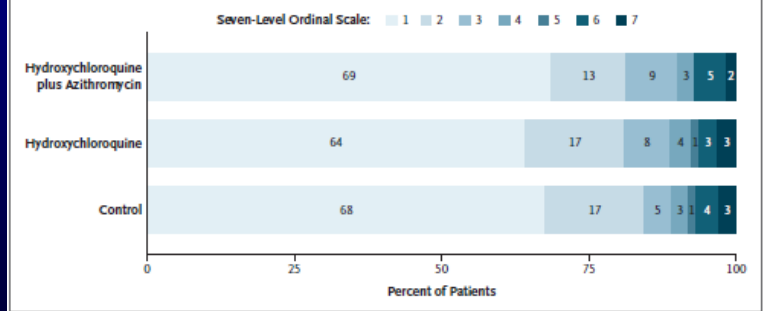


Figure 1. Status of Patients on Day 15.

The primary outcome was clinical status evaluated at 15 days according to a seven-level ordinal scale. The scores on the scale were defined as follows: a score of 1 indicated not hospitalized with no limitations on activities; 2, not hospitalized but with limitations on activities; 3, hospitalized and not receiving supplemental oxygen; 4, hospitalized and receiving supplemental oxygen; 5, hospitalized and receiving oxygen supplementation administered by a high-flow nasal cannula or noninvasive ventilation; 6, hospitalized and receiving mechanical ventilation; and 7, death. The percentages shown have been rounded to whole numbers.

RANDOMIZED MULTICENTER CLINICAL TRIALS OF RAMDESIVIR FOR TREATMENT OF COVID-19

Wang et al. *Lancet* 2020

- No. patients 237
- Mean time to clinical improvement
  21 d vs 23 d
  P = NS
- Mortality (%) at 28 days
  14% vs 13%
  P = NS

Beigel et al. *NEJM* 2020

- No. patients 1059
- Mean time to clinical improvement
  11 d vs 15 d
  P < 0.001
- Mortality at 28 days
  7.1% vs 11.9%
  P = 0.06

Effectiveness of convalescent plasma therapy in severe COVID-19 patients

Kai Duan[a,b,1], Bende Liu[c,1], Cesheng Li[d,1], Huajun Zhang[e,1], Ting Yu[f,1], Jieming Qu[g,h,i,1], Min Zhou[g,h,i,1], Li Chen[j,1], Shengli Meng[b], Yong Hu[d], Cheng Peng[e], Mingchao Yuan[k], Jinyan Huang[l], Zejun Wang[b], Jianhong Yu[d], Xiaoxiao Gao[e], Dan Wang[k], Xiaoqi Yu[m], Li Li[b], Jiayou Zhang[b], Xiao Wu[d], Bei Li[e], Yanping Xu[g,h,i], Wei Chen[b], Yan Peng[d], Yeqin Hu[b], Lianzhen Lin[d], Xuefei Liu[g,h,i], Shihe Huang[b], Zhijun Zhou[d], Lianghao Zhang[b], Yue Wang[d], Zhi Zhang[b], Kun Deng[d], Zhiwu Xia[b], Qin Gong[d], Wei Zhang[d], Xiaobei Zheng[d], Ying Liu[d], Huichuan Yang[a], Dongbo Zhou[a], Ding Yu[a], Jifeng Hou[n], Zhengli Shi[e], Saijuan Chen[l], Zhu Chen[l,2], Xinxin Zhang[m,2], and Xiaoming Yang[a,b,2]

[a]China National Biotec Group Company Limited, 100029 Beijing, China; [b]National Engineering Technology Research Center for Combined Vaccines, Wuhan Institute of Biological Products Co. Ltd., 430207 Wuhan, China; [c]First People's Hospital of Jiangxia District, 430200 Wuhan, China; [d]Sinopharm Wuhan Plasma-derived Biotherapies Co., Ltd, 430207 Wuhan, China; [e]Key Laboratory of Special Pathogens, Wuhan Institute of Virology, Center for Biosafety Mega-Science, Chinese Academy of Sciences, 430071 Wuhan, China; [f]WuHan Jinyintan Hospital, 430023 Wuhan, China; [g]Department of Respiratory and Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; [h]National Research Center for Translational Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; [i]Institute of Respiratory Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; [j]Clinical Research Center, Department of Gastroenterology, Ruijin Hospital North, Shanghai Jiao Tong University School of Medicine, 200018 Shanghai, China; [k]Wuhan Blood Center, 430030 Wuhan, China; [l]State Key Laboratory of Medical Genomics, Shanghai Institute of Hematology, National Research Center for Translational Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; [m]Research Laboratory of Clinical Virology, Ruijin Hospital and Ruijin Hospital North, National Research Center for Translational Medicine, Shanghai Jiao Tong University School of Medicine, 200025 Shanghai, China; and [n]National Institute for Food and Drug Control of China, 102629 Beijing, China

Contributed by Zhu Chen, March 18, 2020 (sent for review March 5, 2020; reviewed by W. Ian Lipkin and Fusheng Wang)

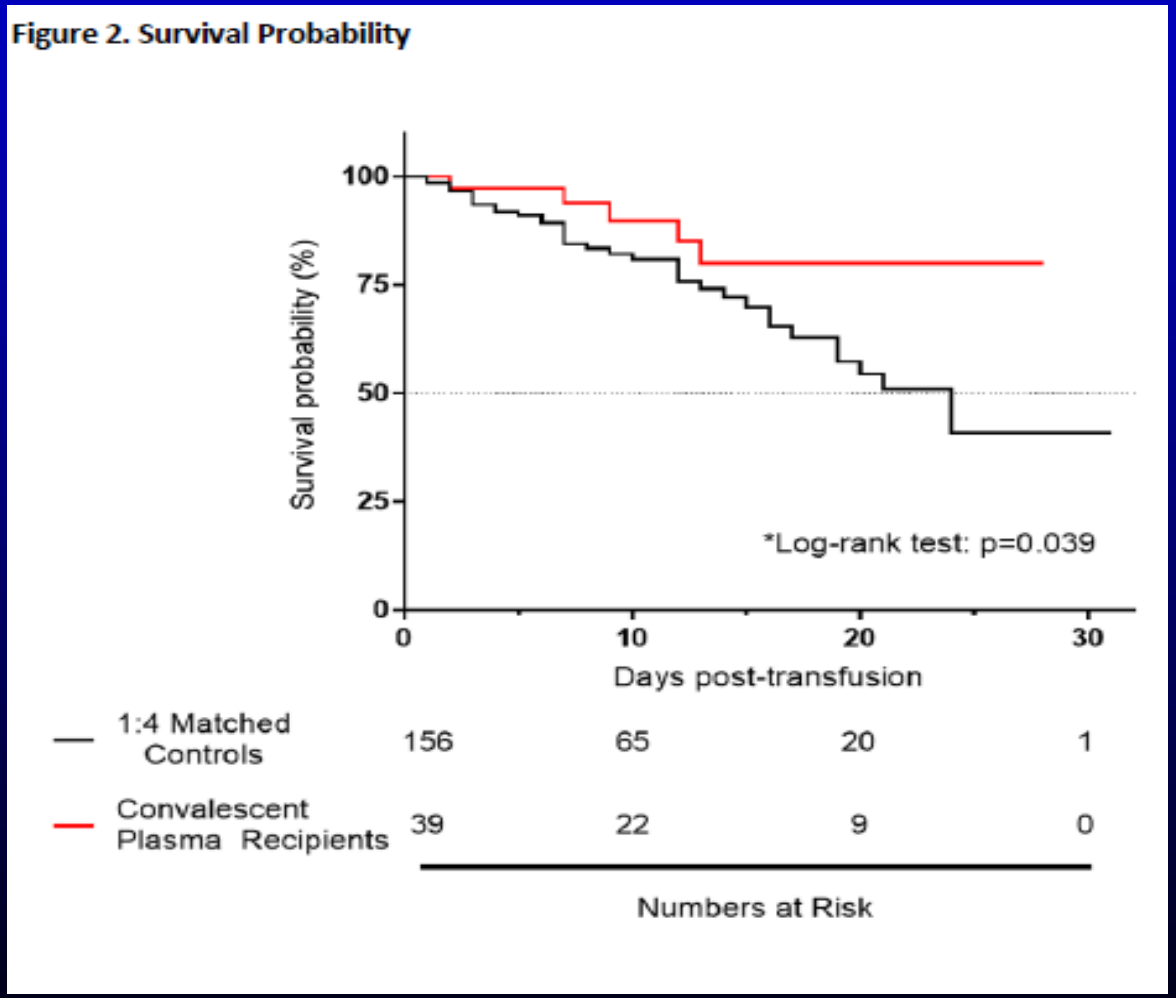
Currently, there are no approved specific antiviral agents for novel coronavirus disease 2019 (COVID-19). In this study, 10 severe patients confirmed by real-time viral RNA test were enrolled prospectively. One dose of 200 mL of convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640 was transfused to the patients as an addition to maximal supportive care and antiviral agents. The primary endpoint was the safety of CP transfusion. The second endpoints were the improvement of clinical symptoms and laboratory parameters within 3 d after CP transfusion. The median time from onset of illness to CP transfusion was 16.5 d. After CP transfusion, the level of neutralizing antibody increased rapidly up to 1:640 in five cases, while that of the other four cases maintained at a high level (1:640). The clinical symptoms were significantly improved along with increase of oxyhemoglobin saturation within 3 d. Several parameters tended to improve as compared to pretransfusion, including increased lymphocyte counts (0.65×10^9/L vs. 0.76×10^9/L) and decreased C-reactive protein (55.98 mg/L vs. 18.13 mg/L). Radiological examinations showed varying degrees of absorption of lung lesions within 7 d. The viral load was undetectable after transfusion in seven patients who had previous viremia. No severe adverse effects were observed. This study showed CP therapy was well tolerated and could potentially improve the clinical outcomes through neutralizing viremia in severe COVID-19 cases. The opti-

ritonavir (4, 5). Although remdesivir was reported to possess potential antiviral effect in one COVID-19 patient from the United States, randomized controlled trials of this drug are ongoing to determine its safety and efficacy (6). Moreover, the corticosteroid treatment for COVID-19 lung injury remains controversial, due to delayed clearance of viral infection and complications (7, 8). Since the effective vaccine and specific antiviral medicines are unavailable, it is an urgent need to look

Significance

COVID-19 is currently a big threat to global health. However, no specific antiviral agents are available for its treatment. In this work, we explore the feasibility of convalescent plasma (CP) transfusion to rescue severe patients. The results from 10 severe adult cases showed that one dose (200 mL) of CP was well tolerated and could significantly increase or maintain the neutralizing antibodies at a high level, leading to disappearance of viremia in 7 d. Meanwhile, clinical symptoms and paraclinical criteria rapidly improved within 3 d. Radiological examination showed varying degrees of absorption of lung lesions within 7 d. These results indicate that CP can serve as a

Case-Control Study of Convalescent Plasma in Severe COVID-19



Liu et al 2020

TWO *NEGATIVE RANDOMIZED* CLINICAL TRIALS OF CONVALESCENT PLASMA FOR COVID-19

- Li L, Zhang W, Hu Y, et al.
  Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial.
  JAMA. 2020;324(5):460-470.

- Arvind Gharbharan, C.E. Jordans, Corine Geurtsvan Kessel et al.
  Convalescent Plasma for COVID-19. A randomized clinical trial 2020. doi: *https://doi.org/10.1101/2020.07.01.20139857*

RANDOMIZED MULTI-CENTER CLINICAL TRIAL OF DEXAMETHASONE FOR COVID-19

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19 A Meta-analysis

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

Respiratory Support at Randomization	Dexamethasone	Usual Care	Rate Ratio (95% CI)
	no. of events/total no. (%)		
Invasive mechanical ventilation	95/324 (29.3)	283/683 (41.4)	0.64 (0.51–0.81)
Oxygen only	298/1279 (23.3)	682/2604 (26.2)	0.82 (0.72–0.94)
No oxygen received	89/501 (17.8)	145/1034 (14.0)	1.19 (0.91–1.55)
All Patients	**482/2104 (22.9)**	**1110/4321 (25.7)**	**0.83 (0.75–0.93)**
			P<0.001

Chi-square trend across three categories: 11.5

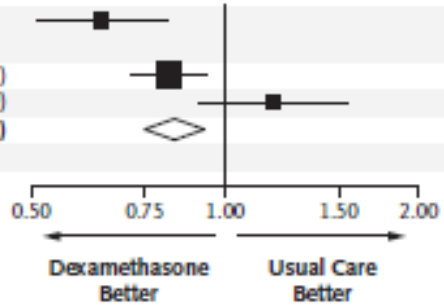
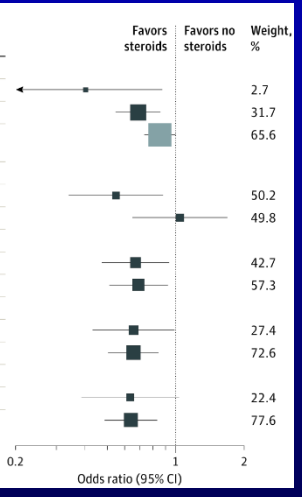


Figure 3. Effect of Dexamethasone on 28-Day Mortality, According to Respiratory Support at Randomization.

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

Subgroup	No. of deaths/total No. of patients: Steroids	No steroids	Odds ratio (95% CI)	Weight, %
Invasive mechanical ventilation (IMV)				
No (I^2 = 0%)	14/70	28/74	0.41 (0.19-0.88)	2.7
Yes (I^2 = 44.1%)	208/608	397/951	0.69 (0.55-0.86)	31.7
Oxygen treatment without IMV (RECOVERY)	298/1279	682/2604	0.86 (0.73-1.00)	65.6
Taking vasoactive medication				
No (I^2 = 0%)	51/184	68/184	0.55 (0.34-0.88)	50.2
Yes (I^2 = 0%)	76/169	74/158	1.05 (0.65-1.69)	49.8
Age, y				
≤60 (I^2 = 0%)	72/338	141/483	0.67 (0.48-0.94)	42.7
>60 (I^2 = 49.7%)	150/339	284/541	0.69 (0.51-0.93)	57.3
Sex				
Female (I^2 = 0%)	60/202	106/286	0.66 (0.43-0.99)	27.4
Male (I^2 = 14.7%)	162/476	319/739	0.66 (0.51-0.84)	72.6
Symptomatic, d				
≤7 (I^2 = 69.1%)	51/130	99/211	0.63 (0.39-1.04)	22.4
>7 (I^2 = 0%)	139/418	293/693	0.64 (0.49-0.83)	77.6



MY APPROACH TO THE MANAGEMENT OF COVID-19 IN THE TLC AND THE eICU

If hospitalized and require O2:

- **ANTICOAGULATE (LMWH, unfract Heparin drip or Apixaban)**
- **RAMDESIVIR, DEXAMETHASONE,CONVALESCENT PLASMA (?),**
- **Strive to avert intubation/ mechanical ventilation with HFnc O2→BiPAP**
- **But if rising FIO2 requirements and/or ↑WOB, INTUBATE, COMMENCE CMV WITH OPTIMAL TITRATED PEEP**
- **For severe hypoxemia, VOLITIONAL PRONE MV → SEDATE → NEUROMUSCULAR BLOCKADE (cisatracurium) WITH PRONE CMV → NO (or inhaled prostacycline)**
- ***PATIENCE*, *give the patient time to improve*, continue to look for alternative causes hypoxemia, PE, VAP, CHF**

UWHC eICU COVID-19 ventilated ICU patient survival is ~80%

SARS-CoV-2 and COVID-19

Dealing with a Reprise of 1918

Goals*: To Understand*

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China
- The biology of coronaviruses
- Endemic human coronavirus infection
- What's new? *The 3rd Coronavirus pandemic of the 20th Century!*
- The extraordinary global spread of COVID-19 since January 2020
- Pathophysiology and epidemiology of COVID-19
- Clinical features of COVID-19 and its laboratory diagnosis
- Management of COVID-19. Is there any role for antiviral therapy?
- **The challenge of protecting healthcare providers**

PROTECTING HEALTHCARE PROVIDERS AND OTHER UNINFECTED PATIENTS

- Like the SARS pandemic of 2003, *there has been an extraordinary high rate of infection of healthcare providers (HCPs) in the COVID-19 pandemic, over 3000 Chinese, 10,000 Italian, thousands of other European and over 10,000 U.S. HCPs, 1% have died*.

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- WHY?
  - Undiagnosed COVID-19, no precautions employed.
  - Shortages of PPE, especially masks and gloves
  - Understaffing and exhaustion, get careless
  - Inadequate policies that fail to cover all routes of infection
  - Community-acquired infection

PROTECTING HEALTHCARE PROVIDERS AND OTHER UNINFECTED PATIENTS

MECHANISMS OF TRANSMISSION OF SARS-CoV-2:

– If COVID-19 can spread by *Respiratory Transmission*:

- Single room, whenever possible a **NEGATIVE-PRESSURE designated ISOLATION ROOM** with separate roofline exhaust.

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- Gloves, full-sleeve gown, face shield and N95 RESPIRATOR or PAPR when entering the room.

  Great care when removing PPE, followed by 20-sec HAND HYGIENE.

MEDICAL MASKS FOR COVID-19

"Spatter Mask"

Surgical Mask

N95 Respirator Mask

PAPRs


WWW.NEWS.CN

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- **Minimize entries into patient rooms,** tele-round

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- *UNIVERSAL MASKING, FACE-SHIELDS 24/7v*of ALL hospital and clinic personnel (surgical masks).
- **STRINGENT LIMITATIONS ON VISITORS** (in essence, patients who are dying)

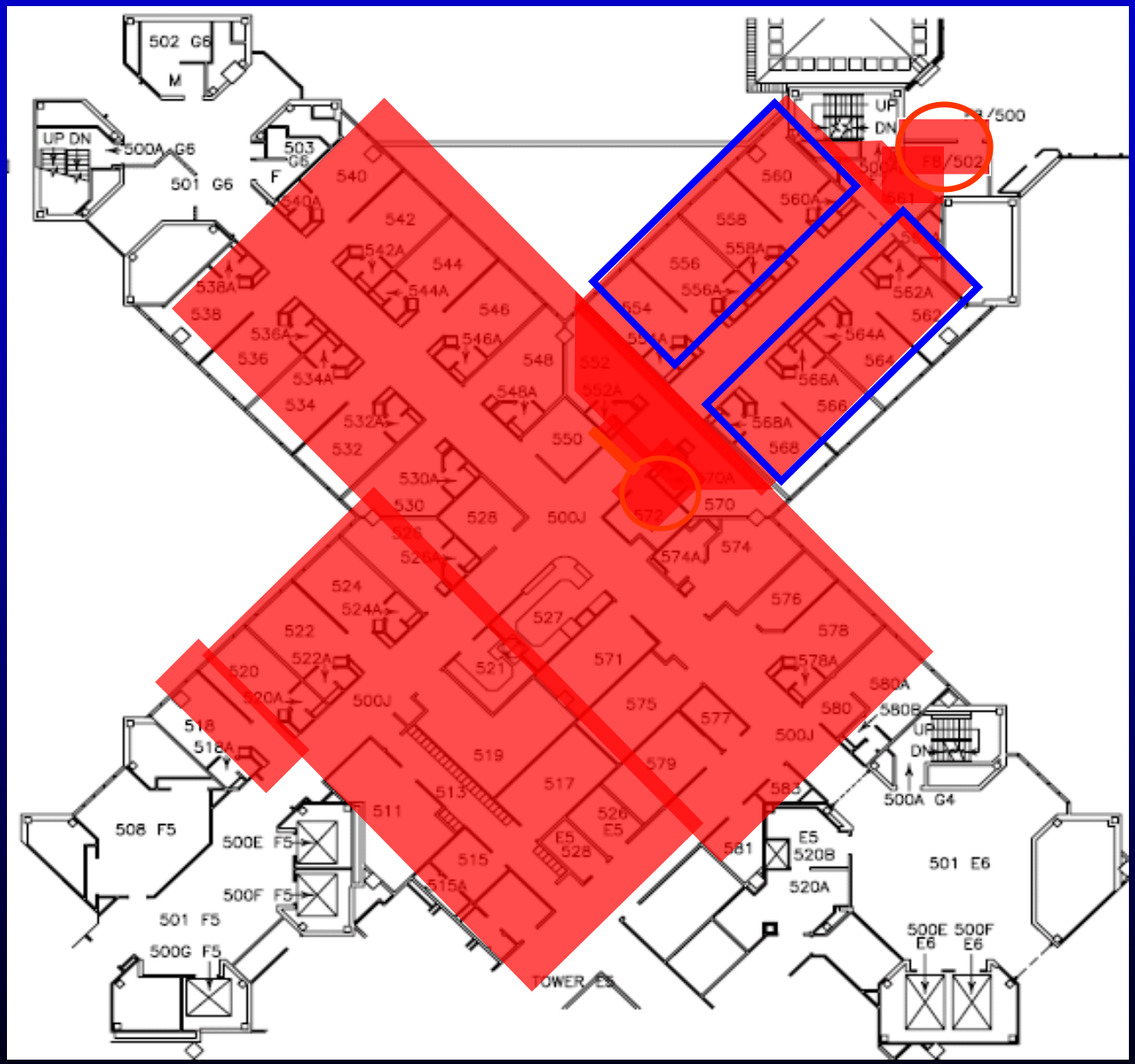
PROTECTING HEALTHCARE PROVIDERS AND OTHER UNINFECTED PATIENTS

- **MECHANISMS OF TRANSMISSION OF SARS-CoV-2:**
  - **If COVID-19 can spread by *Respiratory Transmission*:**
    - Single room, whenever possible a NEGATIVE-PRESSURE designated ISOLATIO ROOM with roofline exhaust.
    - Gloves, full-sleeve gown and N95 RESPIRATOR MASK or PAPR when entering the room. Great care when removing PPE, followed by 20-sec HAND HYGIENE.
    - UNIVERSAL MASKING of all HCPs (surgical mask) and GLOVING throughout work day.
    - **COHORT NURSING, ideally a DEDICATED COVID-19 UNIT.**

A 36-bed Emerging Pathogens Unit
University of Wisconsin Hospital and Clinics

- We have undertaken major renovation of an inpatient medical units (F6/5) as an Emerging Pathogens surge capacity unit for emergent use.

A 36-bed Emerging Pathogens Unit
University of Wisconsin Hospital and Clinics



Rapid installation of hallway doors creats 10-bed cohort unit.

Nurses Station, IT and Pharmacy self-contained.

Eight rooms fitted for self-contained ICU, with capacity for monitoring and mechanical ventilation.

Entire unit has separate roofline exhaust, can be set at negative pressure.

A 36-bed Emerging Pathogens Unit
University of Wisconsin Hospital and Clinics

- In anticipation of the need to provide ICU care to these patients but still derive the benefit of cohorting and res[iratory containment,

  8 rooms have been equipped for ICU use:

  ventilator-capable, monitor-capable, with extra power outlets for additional equipment.

A 36-bed Emerging Pathogens Unit
University of Wisconsin Hospital and Clinics

- The availability of this unit will enable us to cohort up to 36 potentially contagious patients in a single controlled location.

- Cohorting of dedicated staff in this unit will minimize exposures of HCWs and other hospital patients to a potentially virulent, contagious pathogen.

A 36-bed Emerging Pathogens Unit
University of Wisconsin Hospital and Clinics

- These rooms are *not* currently used for ICU care and will only be activated in an emergency where containment of a dangerous, virulent pathogen is an essential priority.

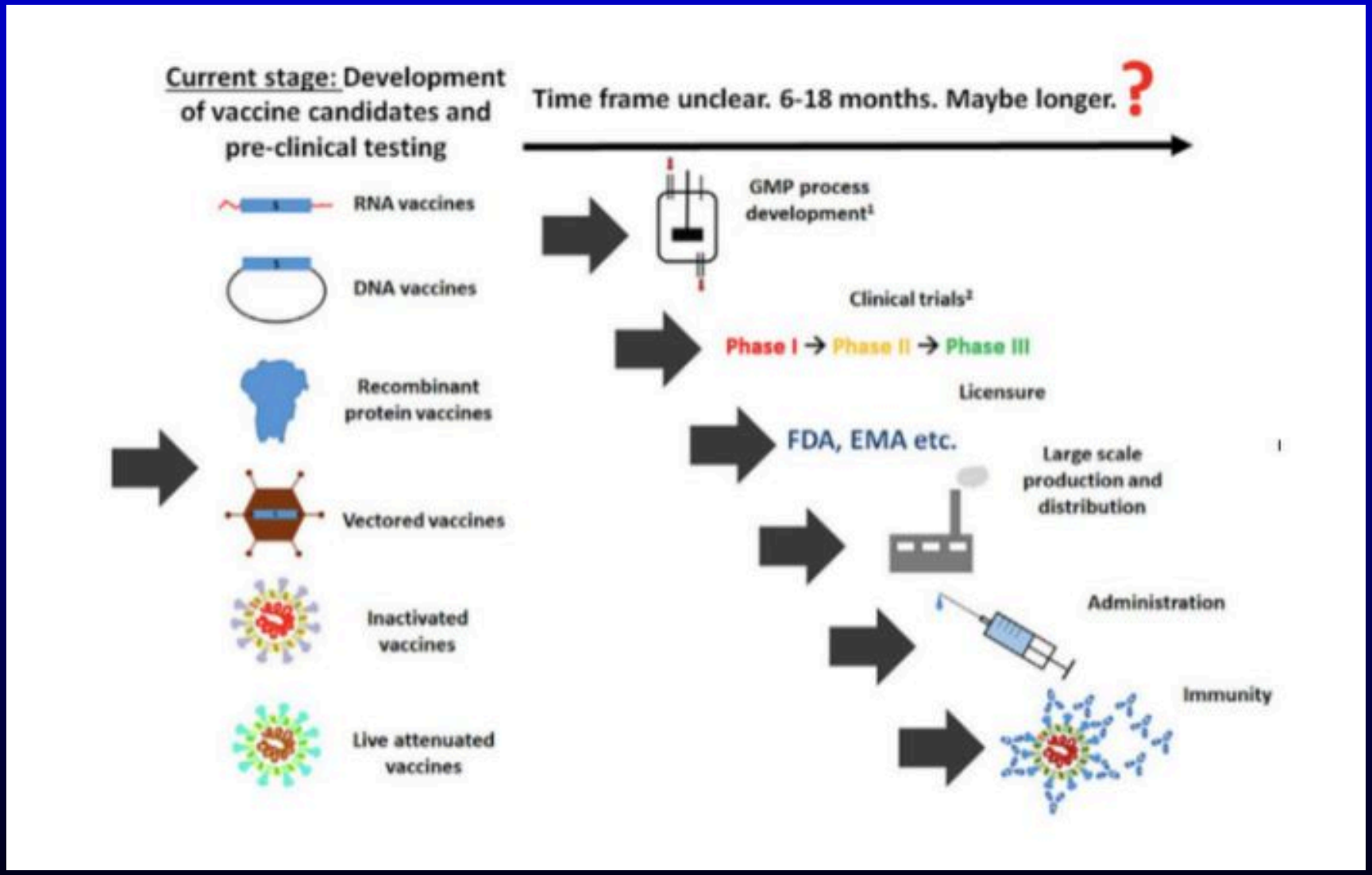
- Activation of the surge capacity EID Unit will be initiated only in a declared public health emergency, in coordination with the Wisconsin Division of Health.

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

- An outbreak of SARS-like Coronavirus Infection in Wuhan, China
- The biology of coronaviruses
- Endemic human coronavirus infection
- What's new? *The 3rd Coronavirus pandemic of the 20th Century!*
- The extraordinary global spread of COVID-19 since January 2020
- Pathophysiology and epidemiology of COVID-19
- Clinical features of COVID-19 and its laboratory diagnosis
- Management of COVID-19. Is there any role for antiviral therapy?
- The challenge of protecting healthcare providers and other patients
- **Prevention of COVID-19 and prospects for a vaccine**

A COVID-19 VACCINE



CONTROL OF COVID-19 IN THE POPULATION

- **A VACCINE**

As of April 2020, Phase I studies of 5 vaccine candidates were launched:

- **mRNA-1273: The NIH-NIAID has collaborated with Moderna to develop an RNA vaccine which encodes a spike protein of the coronavirus and on 16 March 2020, the human study in Seattle began.**
- **Ad5-nCoV: A recombinant adenovirus vaccine manufactured by CanSino Biologics Inc. in China began recruiting subjects in Wuhan in March 2020.[1]**
- **ChAdOx1 nCoV-19: The Jenner Institute at Oxford has also developed an adenovirus vaccine and begun recruitment in March 2020.**

>100 other groups, companies actively developing a vaccine, at least 6 in Phase 3 clinical trials.

CONTROL OF COVID-19 IN THE POPULATION

- **A VACCINE**

  As of April 2020, Phase I studies of 5 vaccine candidates initiated:

IT IS NOT GOING TO BE EASY, ESPECIALLY SINCE MULTIPLE CORONAVIRUS VACCINES FOR ANIMALS HAVE FAILED TO DATE, AS HAVE EXPERIMENTAL VACCINES FOR SARS AND MERS.

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THE EARLIEST WE MIGHT HAVE EFFICACY DATA IS NOVEMBER, MORE LIKELY JANUARY 2021.

Figure

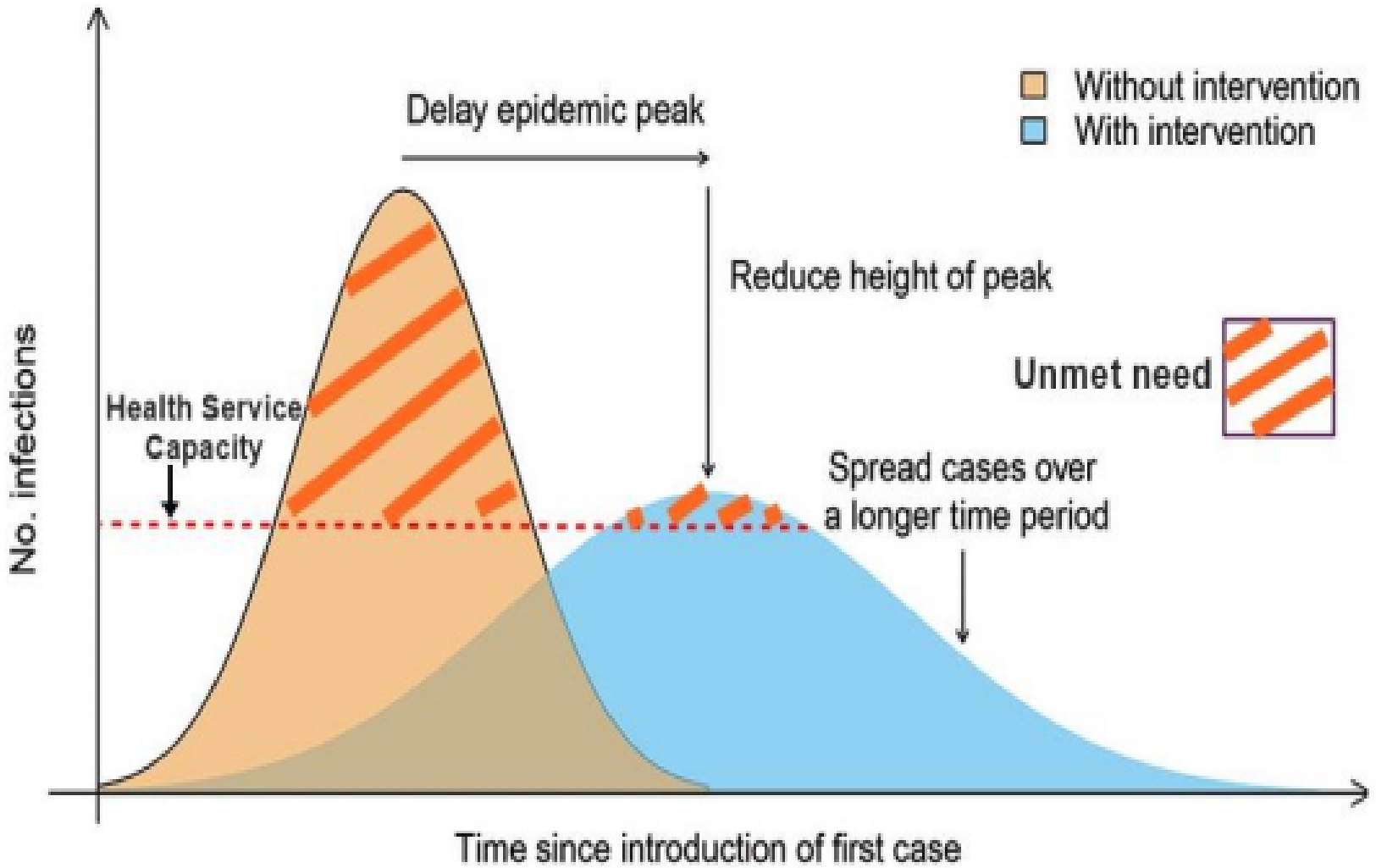


Figure 1: Intended impact of enhanced hygiene and social distancing measures on the COVID-19 pandemic adapted from Fong.[8]

CONTROL OF COVID-19 IN THE POPULATION

- **EPIDEMIOLOGIC (MITIGATION) MEASURES:**

  In the population:

  Home quarantining the population (except for "essential" occupations)

  Social distancing and limiting the size of groups

  Working from home

Source: Government o

Scientists measure the intensity of an infectious disease by its reproduction number **(R_0)**.

R_0: the average number of people a sick person will infect

For **COVID-19**, this has been estimated at **2.5**

Source

To illustrate the potential of social distancing, **the following assumptions are made:**

There is a direct linear correlation between **social exposure** and **R_0**

5 Days

The median incubation period of **COVID-19** is approximately five days—after this period, a person will experience symptoms and self quarantine

With these in mind, here's how distancing measures can control the spread of the disease:

REDUCING SOCIAL EXPOSURE BY 75%

DAY 1

1 Person

DAY 5

0.625 People **INFECTED**

DAY 30

2.5 People **INFECTED**

With these in mind, here's how distancing measures can control the spread of the disease:

REDUCING SOCIAL EXPOSURE BY 75%

1 Person

0.625 People
INFECTED

2.5 People
INFECTED

REDUCING SOCIAL EXPOSURE BY 50%

1 Person

1.25 People
INFECTED

15 People
INFECTED

INFECTED

NO SOCIAL DISTANCING MEASURES IN PLACE

DAY 1

INFECTS

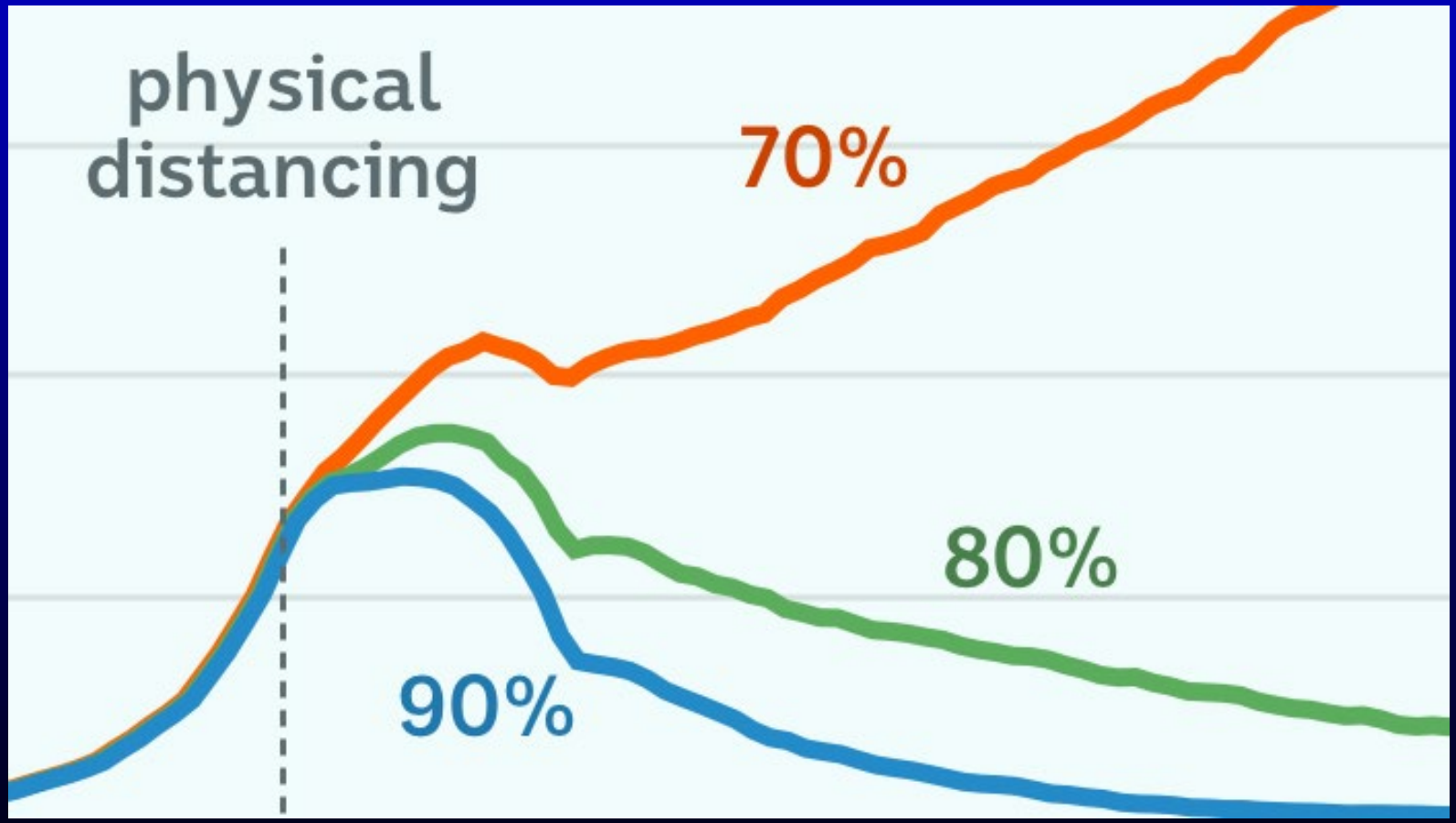
1 Person

DAY 5

2.5 People
INFECTED

406 People
INFECTED
IN 30 DAYS

THE EFFECTIVENESS OF MITIGATION STRATEGIES IS TOTALLY DEPENDENT ON THE DEGREE OF ITS ACCEPTANCE AND PRACTICE BY THE PUBLIC



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- **EPIDEMIOLOGIC MEASURES:**

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  Working from home

  Closing schools, holding instruction on-line

  Masking in public


PLEASE TAKE
2 1
MASK HOME
PER DAY !
Wash Hands
before
Masking

UNIVERSAL MASKING IN PUBLIC

- **Masking in public clearly reduces spread:**

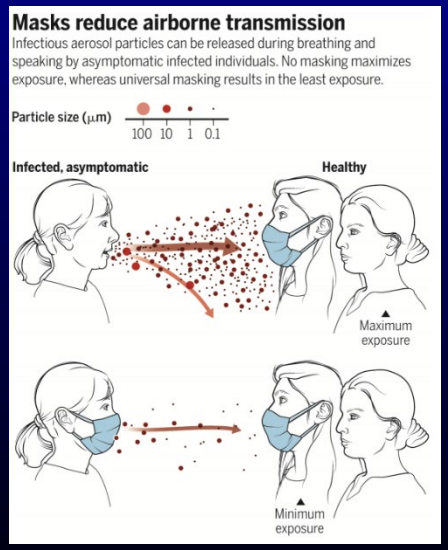
Not masking a lot

Growth of covid-19, by country or region
First 60 days after reaching 30 confirmed cases

Region/ country	Total cases	Avg. daily growth rate, %	Measures taken
Beijing	558	4.7	Lockdown, masks
Hong Kong	989	5.6	Masks
Japan	4,618	6.9	Masks
S. Korea	10,635	10.3	Masks
Germany	158,758	14.5	Lockdown
France	164,589	15.0	Lockdown
Britain	171,253	15.2	Lockdown
America	903,882	17.7	Lockdown

Sources: De Kai et al.; Johns Hopkins University CSSE; *The Economist*

The Economist



- **The question, might medical masking, even N95 masking, reduce spread much more effectively?**

Masking may be the Most Effective Community Measure for Preventing Spread of COVID-19

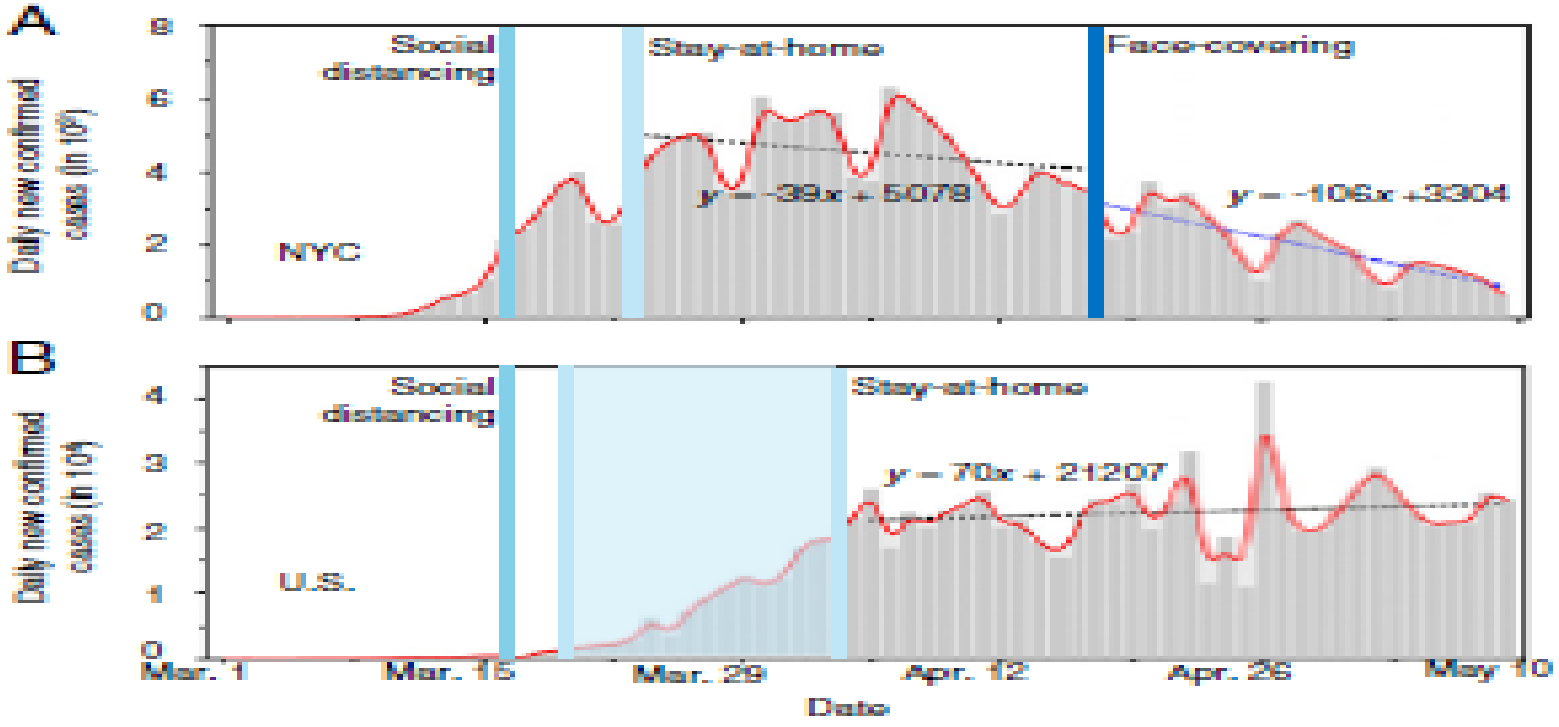


Fig. 3. Contrasting the trends of new infections between NYC and the United States. Daily new confirmed infections in (*A*) NYC and (*B*) the United States. The dotted lines represent linear fitting to the data between April 17 and May 9 in NYC and between April 4 and May 9 in the United States. In *B*, the number in NYC was subtracted from that in the United States. The vertical lines label the dates for social distancing, stay-at-home orders, and mandated face-covering.

Zhang et al. *PNAS* 2020

By Wei Lyu and George L. Wehby

Community Use Of Face Masks And COVID-19: Evidence From A Natural Experiment Of State Mandates In The US

DOI: 10.1377/hlthaff.2020.00818
HEALTH AFFAIRS 39,
NO. 8 (2020): 1–7

ABSTRACT **State policies mandating public or community use of face masks or covers in mitigating novel coronavirus disease (COVID-19) spread are hotly contested. This study provides evidence from a natural experiment on effects of state government mandates in the US for face mask use in public issued by 15 states plus DC between April 8 and May 15. The research design is an event study examining changes in the daily county-level COVID-19 growth rates between March 31, 2020 and May 22, 2020. Mandating face mask use in public is associated with a decline in the daily COVID-19 growth rate by 0.9, 1.1, 1.4, 1.7, and 2.0 percentage-points in 1–5, 6–10, 11–15, 16–20, and 21+ days after signing, respectively. Estimates suggest as many as 230,000–450,000 COVID-19 cases possibly averted By May 22, 2020 by these mandates. The findings suggest that requiring face mask use in public might help in mitigating COVID-19 spread. [*Editor's Note: This Fast Track Ahead Of Print article is the accepted version of the peer-reviewed manuscript. The final edited version will appear in an upcoming issue of* Health Affairs.]**

Wei Lyu is a research associate in the Department of Health Management and Policy, College of Public Health, University of Iowa, in Iowa City, Iowa.

George L. Wehby (george-wehby@uiowa.edu) is a professor in the Department of Health Management and Policy, College of Public Health, University of Iowa, and a research associate at the National Bureau of Economic Research.

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In the population:

Home quarantining the population (except for "essential" occupations)

Social distancing and limiting the size of groups

Working from home

Closing schools, holding instruction on-line

Masking in public, NOT touching face AMAP

In hospitals:

Dedicated COVID-19 Units, negative-pressure isolation rooms

PPE including N95 respirators for bedside care and Universal masking

Daily symptom and fever screening of all HCPs

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In Nursing homes:

- Restricting visitors
- Testing of all newly-admitted and symptomatic residents
- Close monitoring of HCPs, excluding if symptomatic, until tested

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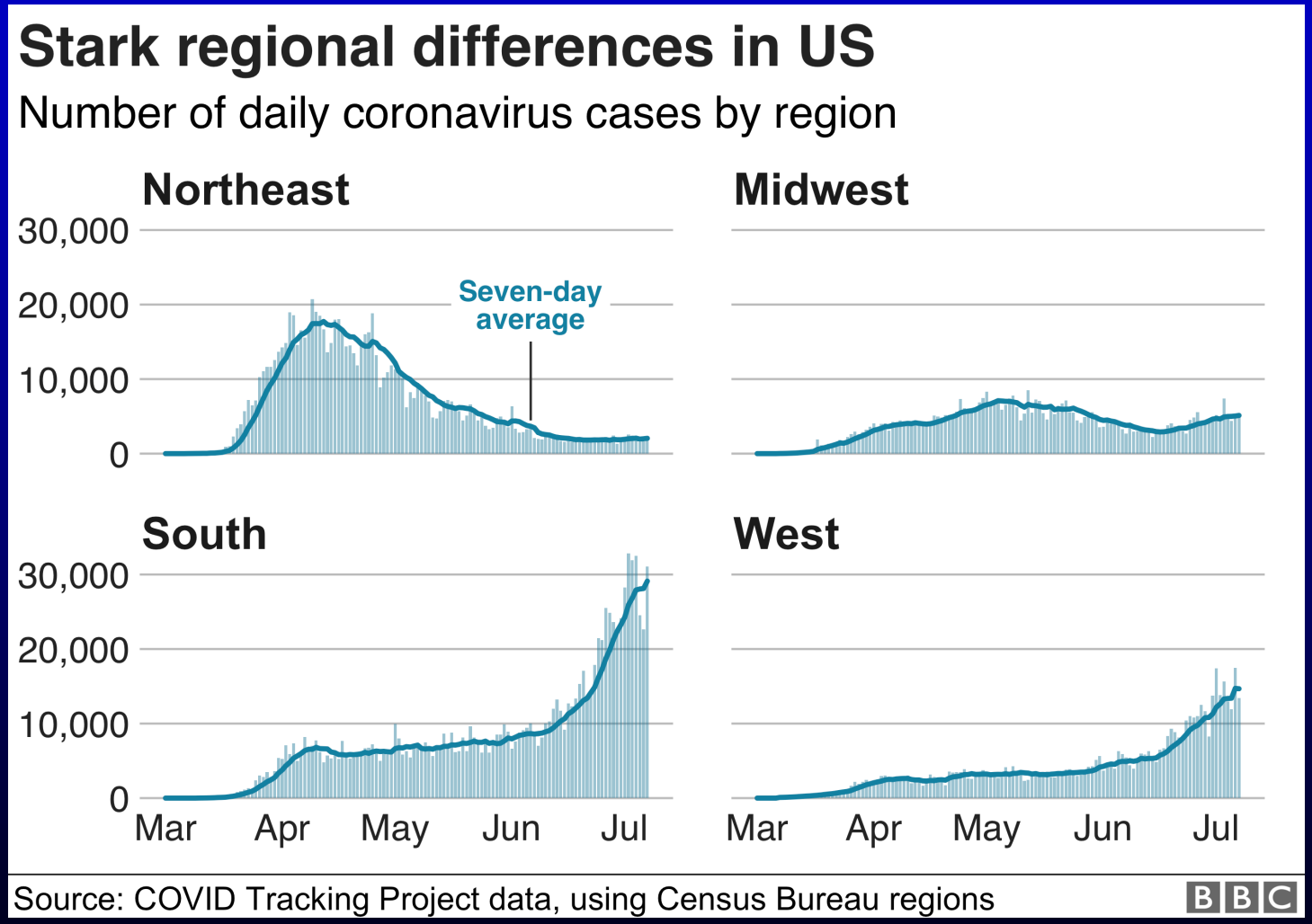
On Return to the Workplace

- Daily symptom and fever screening of all HCPs
- "Social distancing"
- Medical masks, N95s or PAPRs for HCWs, meat/poultry processors
- Possibly, PCR screening prior to return to the workplace and weekly

VARYING SUCCESS OF U.S. REGIONS IN CONTROL OF COVID-19



CONTROL OF COVID-19 IN THE POPULATION

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Testing of **all admisions** to Hospitals and Nursing Homes.

Massive widespread testing of well persons to detect silent infection
in order to place in essential stringent quarantine and to expeditiously trace their contacts to quarantine them .
In China, Hong Kong, S. Korea, Singapore ALL infected persons detected on surveillance testing are segregated in camps or hospitals until they are no longer infectious.

Testing of exposed HCWs to detect silent infection and quarantine.

Testing of all newly admitted and symptomatic nursing home residents, if infected remove from NH and test all other residents

SARS-CoV-2 and COVID-19

Nine Months into the Pandemic of 2020

Goals*: To Understand*

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- **You haven't seen anything yet!**

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- **Air travel and protecting oneself from COVID-19**

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- **Take earliest or latest flight, least likely to be filled, sit in the back where there are usually fewer people.**
- **Fly *Delta,* only airline consistently separating passengers in every other seat.**

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SARS-CoV-2 and COVID-19

Dealing with a Reprise of 1918

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- The extraordinary global spread of COVID-19 since January 2020
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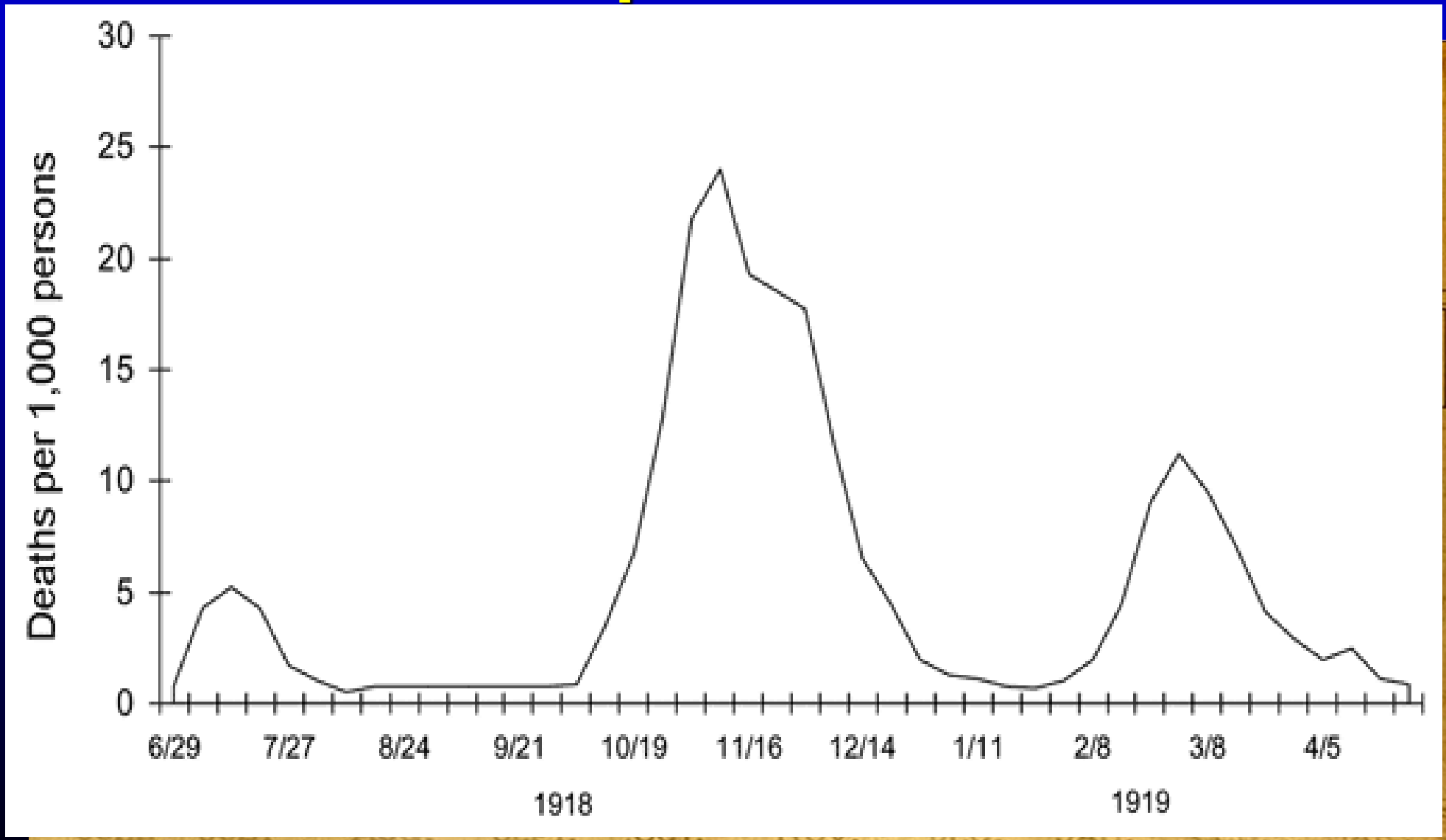
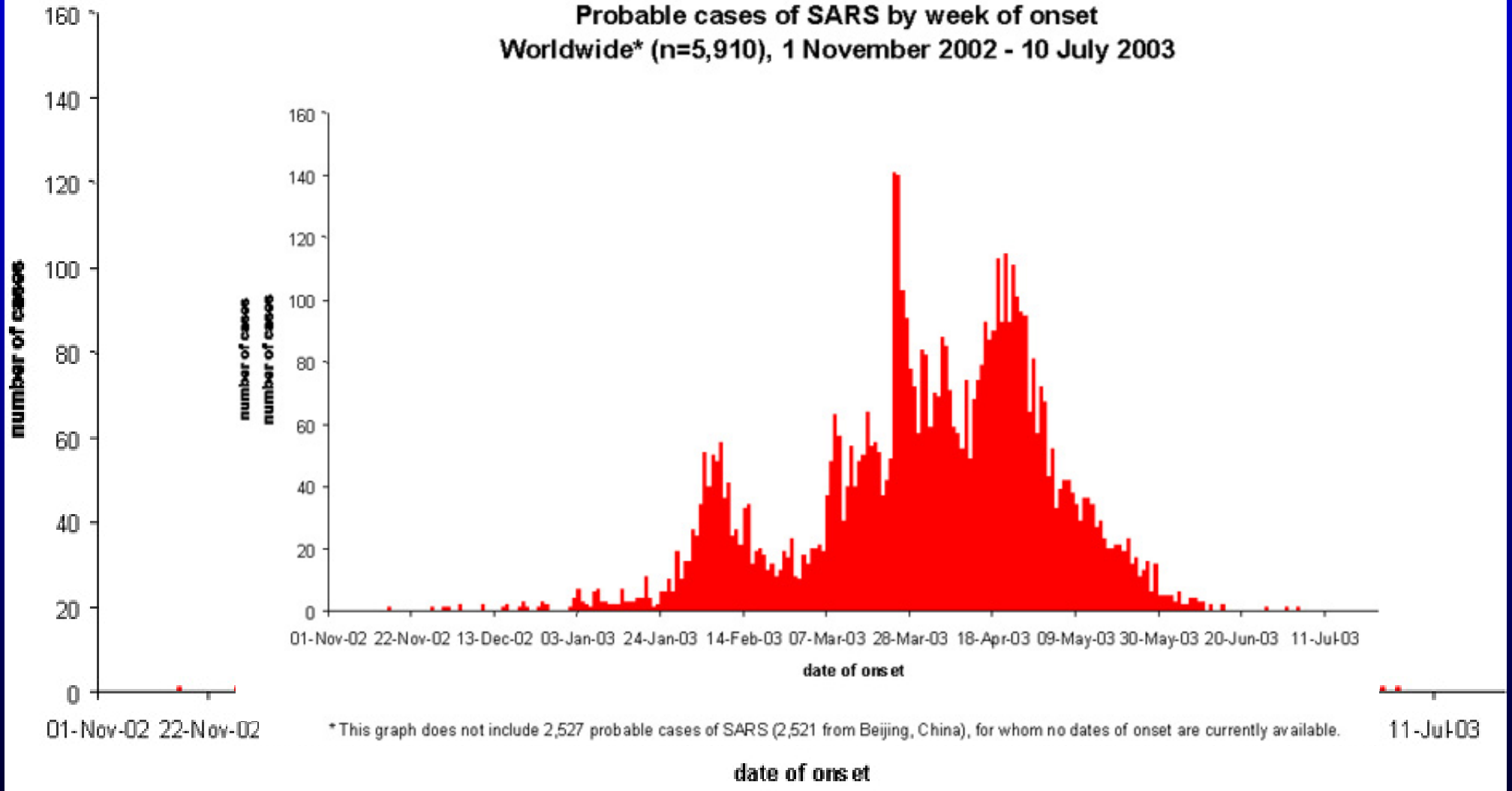
- Management of COVID-19. Is there any role for antiviral therapy?
- The challenge of protecting healthcare providers
- Prevention of COVID-19 and prospects for a vaccine

- **What does the future hold? What have we learned?**

The 3 Waves of the Great Influenza Epidemic of 1918

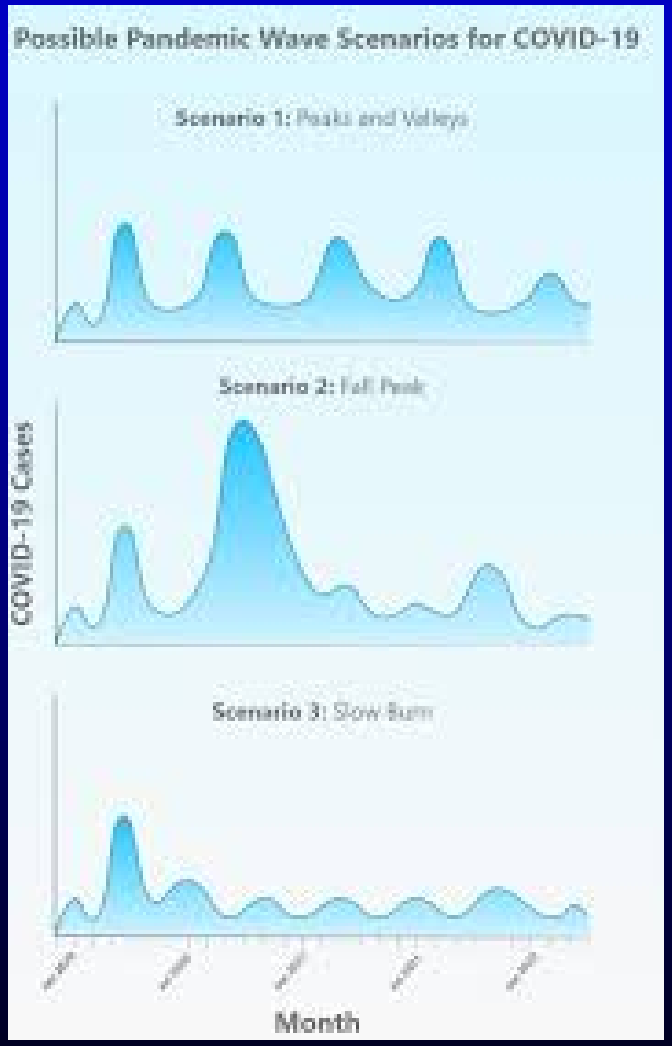


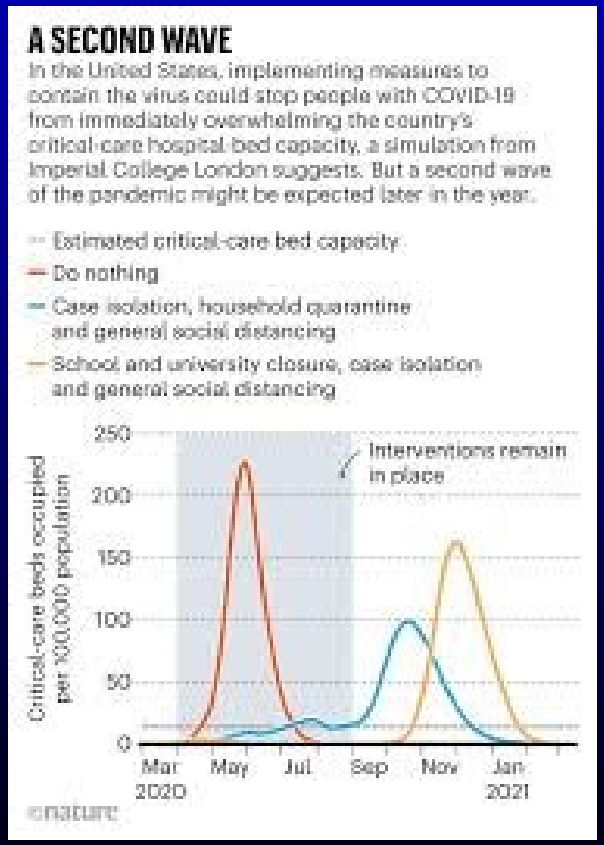
Probable cases of SARS by week of onset
Worldwide* (n=5,910), 1 November 2002 - 10 July 2003

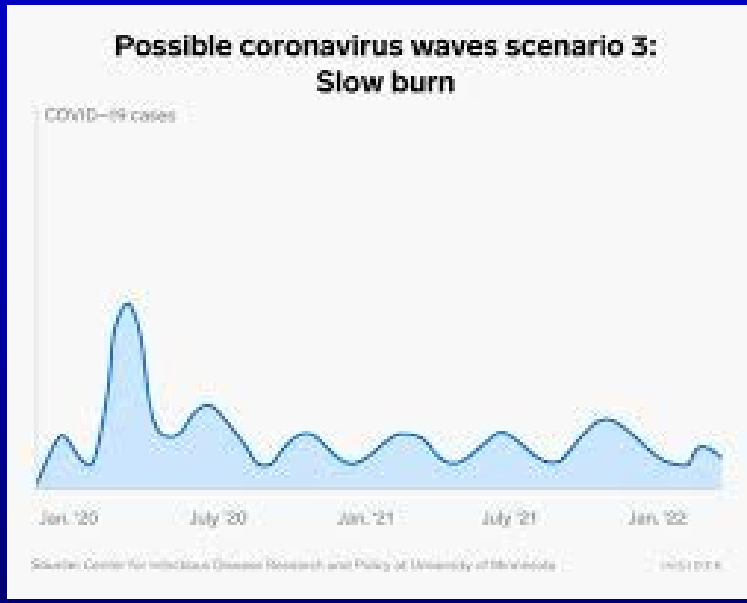


* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

PREDICTIONS ON COVID-19







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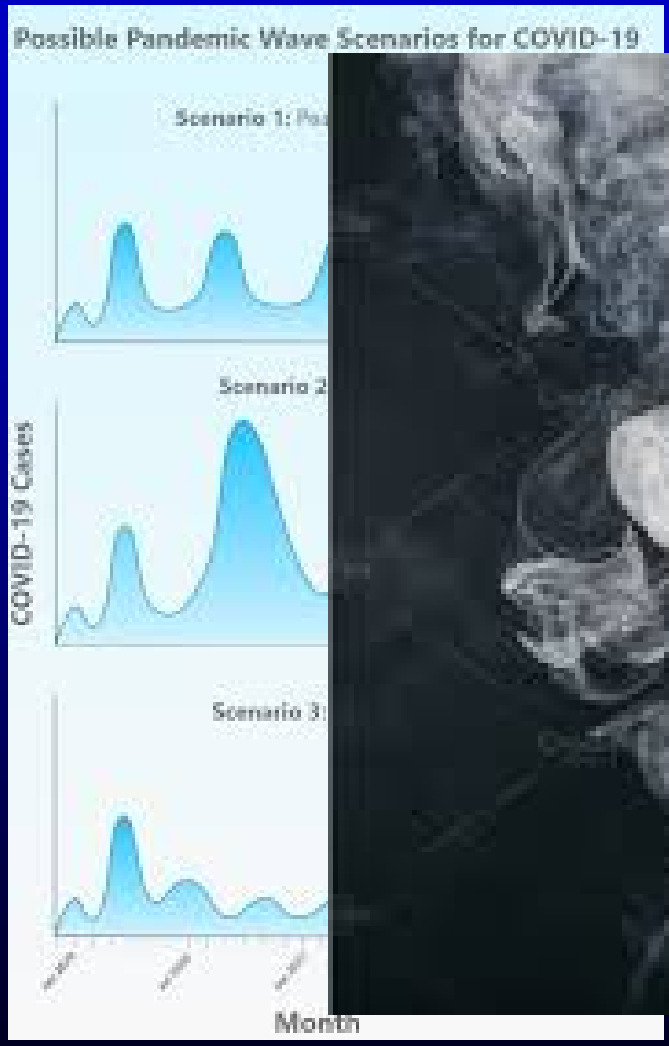
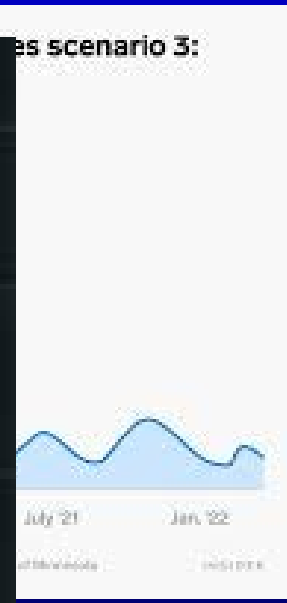




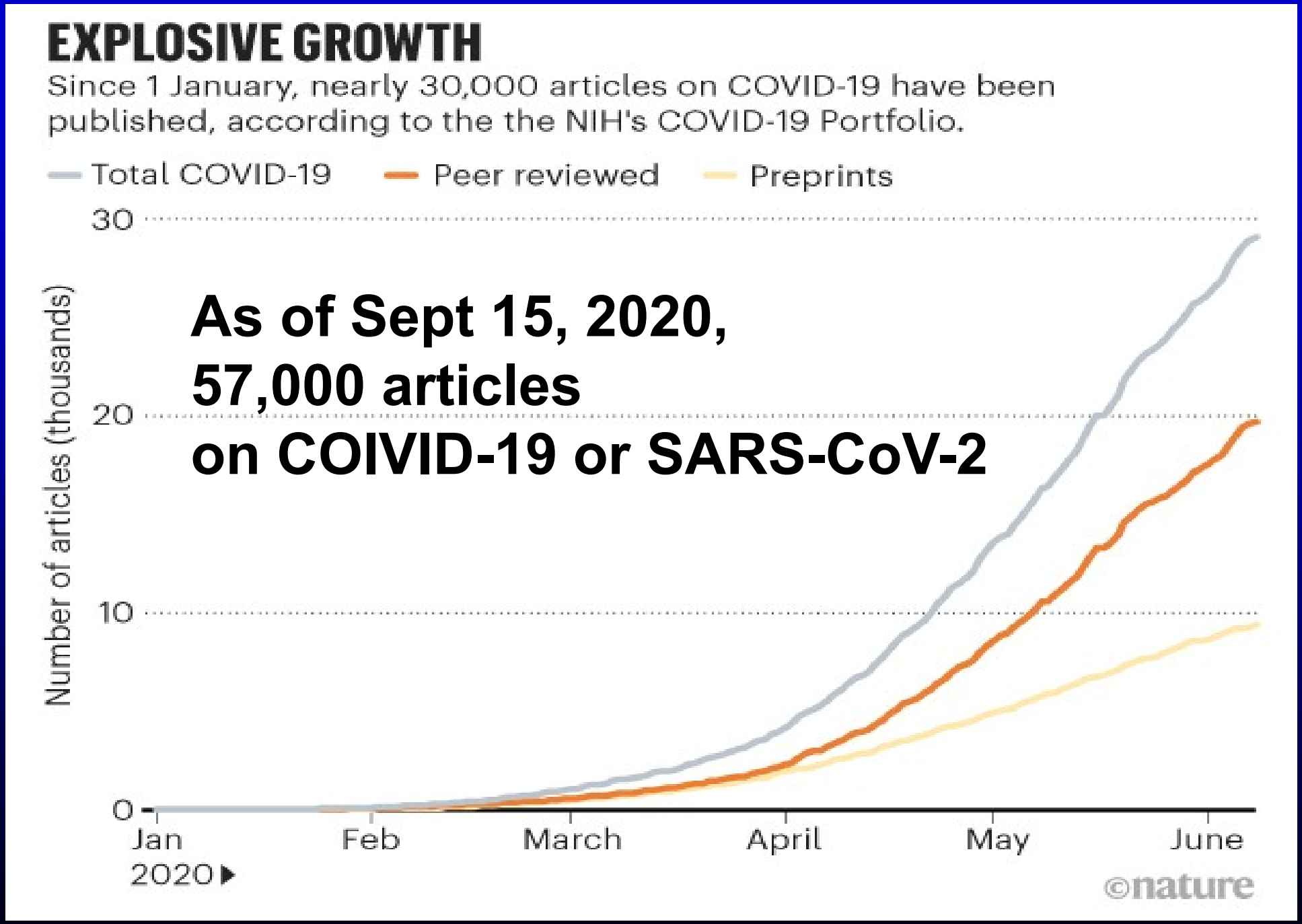
IMPACT OF THE COVID-19 PANDEMIC ON THE U.S. ECONOMY

The COVID-19 pandemic has caused the biggest blow to the US economy since the Great Depression:

- **The GDP fell at a 32.9% annualized rate, the deepest decline since records began back in 1947.**
- **30.2 million Americans were receiving unemployment checks in the week ending July 11.**
- **The initial bipartisan fiscal stimulus package added 3+ trillion dollars to the National Debt.**

WE HAVE LEARNED MUCH ABOUT SARS-CoV-2 AND HOW TO PREVENT AND MANAGE COVID-19

WHAT ELSE HAVE WE LEARNED FROM THE COVID-9 PANDEMIC?


EXPLOSIVE GROWTH
Since 1 January, nearly 30,000 articles on COVID-19 have been published, according to the the NIH's COVID-19 Portfolio.
Total COVID-19
Peer reviewed
Preprints
30
20
10
0
Number of articles (thousands)
As of Sept 15, 2020,
57,000 articles
on COIVID-19 or SARS-CoV-2
Jan
2020
Feb
March
April
May
June
©nature

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University of Wisconsin School of Medicine and Public Health