COVID-19 The Pandemic: What Did We Learn?

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Learning Objectives

Describe	Describe the origin theories germane to COVID-19 evolution
Review	Review the statistical data regarding the magnitude of COVID-19
Define	Define the clinical management of patients with life threatening COVID-19
Describe	Describe the learning lessons achieved from COVID-19

Origin Theories of COVID-19

- **Two main theories exist:**
  - The virus spilled over from an animal into people, most likely in a market in Wuhan, China.
  - The virus came from the Wuhan Institute of Virology and spread due to some type of laboratory accident.

What's The Scientific Belief?

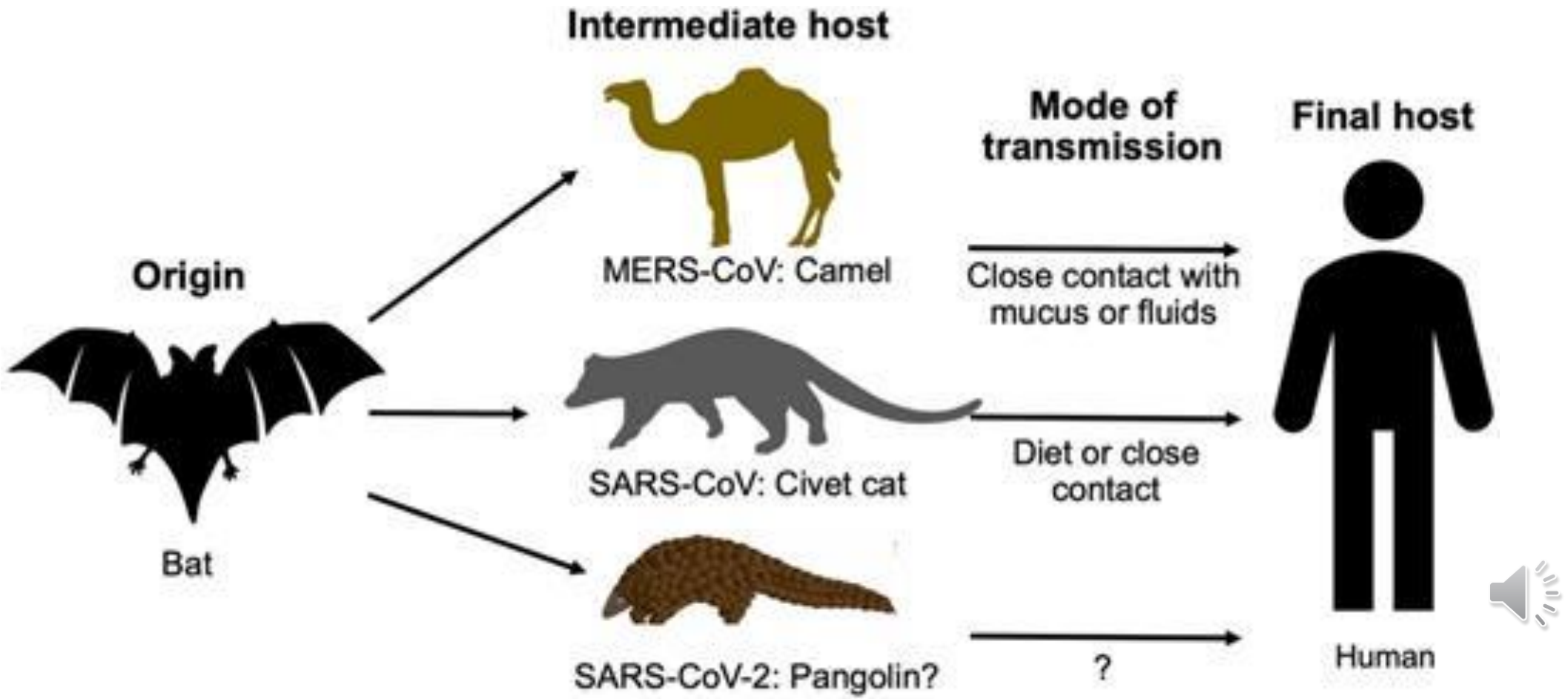
- As of June 2023, the **U.S. intelligence community** still has no consensus about the origin of SARS-CoV-2.
- Four of the eight intelligence agencies lean toward a natural origin for the virus, with "low confidence," while two of them — the DOE and the Federal Bureau of Investigation — support a lab origin, with the latter having "moderate confidence" about its conclusion.
- **Virologists** who study pandemic origins are much less divided than the U.S. intelligence community. They say there is "very convincing" data and "overwhelming evidence" pointing to an animal origin.
    - Specifically, they conclude that the coronavirus most likely jumped from a **caged wild animal** into people at the Huanan Seafood Wholesale Market, where a huge COVID-19 outbreak began in December 2019.

Zoological Theory

Photographic evidence of wild animals such as raccoon dogs and a red fox, which can be infected with and shed SARS-CoV-2, sitting in cages in the market in late 2019.

What's more, the caged animals are shown in or near a stall where scientists found SARS-CoV-2 virus on several surfaces, including on cages, carts and machines that process animals after they are slaughtered at the market.

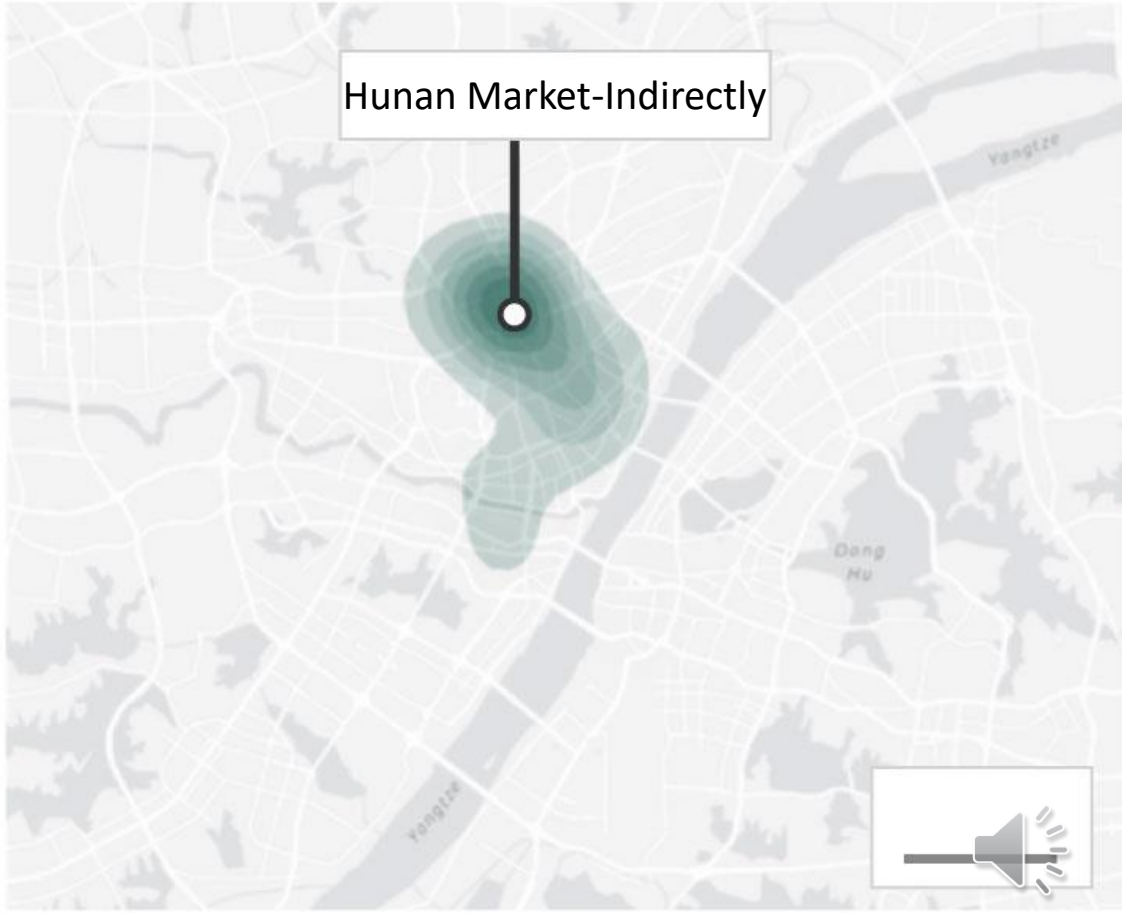
Historical Coronaviruses



Live susceptible animals were held in a stall where SARS-CoV-2 was later detected on a machine that processed animals in the market

Chinese Wet Market?

These maps show the estimated concentration of the earliest 156 cases of COVID-19 in Wuhan, China, in December 2019. The highest concentration of those cases centered on the Huanan Seafood Wholesale Market. Even for the subset of 123 individuals with no direct contact with the market, the same pattern emerged, strongly suggesting community transmission of the coronavirus began at or near the market.



- Smuggled pangolins are killed for their scales to be used in traditional Chinese medicine. They are suspected to be the world's most-trafficked mammal, apart from humans.

- Racoon Dog: The common raccoon dog, also called the Chinese or Asian raccoon dog to distinguish it from the Japanese raccoon dog, is a small, heavy-set, fox-like canid native to East Asia. Named for its raccoon-like face markings, it is most closely related to foxes

Lab Leak Theory

The Virus escaped accidentally form the Wuhan institute of Virology

May have been specimens that were found in caves from the horseshoe bat in 2013

2013 China Miners

- **The case of six miners** in China who fell ill in 2012 after being hired to clear a cave of bat guano. The Wuhan Institute of Virology was called in to investigate. Researchers from the lab tested bats from the mine for coronaviruses and found an unidentified strain resembling SARS; several bats were infected with more than one virus. That created opportunities for recombination, in which viruses undergo rapid, large-scale mutations that create new pathogens.
- Three miners died of COVID 19 like pathophysiology

The Lab Leak Hypothesis

- Wuhan Institute of Virology near the original epicenter of the Covid-19 outbreak
- Shi Zhengli, a renowned virologist at the Wuhan lab. She told Scientific American last year that she recalled being told in December 2019 about a mysterious pneumonia caused by a coronavirus spreading in the city of Wuhan and wondering if the pathogen came from her lab.
- There have been reports that researchers at the institute were performing gain-of-function experiments, where a natural virus is modified to become more virulent or to better infect humans.
- Chan also noted that the Huanan Seafood Wholesale Market in Wuhan was initially suspected as the location where a SARS-CoV-2 spillover from animals to humans occurred, but to date, no infected animal has been identified and Chinese researchers have ruled it out as the origin of the virus.


WUHAN INSTITUTE OF VIROLOGY, CAS

Top Chinese scientist concedes that Coronavirus may have leaked from Wuhan lab

Did the Virus Leak From A Lab?

- The WHO report also concludes that it's highly unlikely that the coronavirus escaped from a lab at the Wuhan Institute of Virology. Most scientists say that evidence overwhelmingly favors SARS-CoV-2 having spilled over from animals into humans, but a few have backed the idea that the virus was intentionally or accidentally leaked from a lab.
- The Wuhan researchers also said that they hadn't kept any live virus strains similar to SARS-CoV-2.
- In their discussions with the investigative team, showing that similar viruses exist in animals in China, rather than in their lab.
- They further explained that everyone in the lab has safety training and psychological evaluations, and that their physical and mental health are continuously monitored.

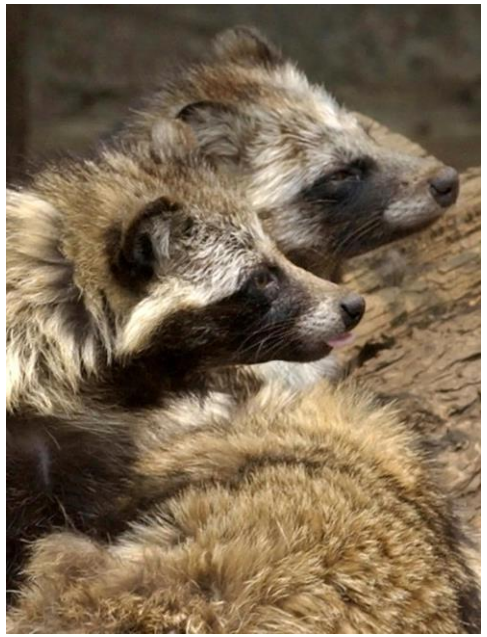
Evidence released by the intelligence community provides further proof that COVID-19 originated in a Wuhan laboratory.

- **David Feith, former Deputy Assistant Secretary of State for East Asian and Pacific Affairs, explained that the State Department's January 2021 Fact Sheet, which revealed evidence of sick researchers at the Wuhan Institute of Virology in fall 2021, is the most *"potentially probative part of the story that we are yet aware of…there was, after all, U.S. government information about a cluster of illnesses in that lab which is exactly what you would expect to happen if the origin of COVID came from a laboratory accident where a worker became ill, knowingly or not, and then took the virus out into the community."***
- **Former Director Ratcliffe issued a bombshell statement in his opening remarks that current intelligence supports the lab leak as the only credible explanation for the origination of COVID-19: *"My informed assessment, as a person with as much or more access than anyone to our government's intelligence during the initial year of the virus outbreak and pandemic onset, has been and continues to be that a lab leak is the only explanation credibly supported by our intelligence, by science and by common sense. From a view inside the IC, if our intelligence and evidence supporting a lab leak theory was placed side-by-side with our intelligence and evidence pointing to a naturally occurring "spillover" theory, the lab leak side of the ledger would be long and overwhelming while the "spillover" side would be nearly empty."***

COMMITTEE ON OVERSIGHT AND ACCOUNTABILITY

The lab leak hypothesis is bolstered, the report said, by the absence of any published evidence that SARS-CoV-2 was circulating in animals before the pandemic. Samples of virus collected on refrigerators, countertops and other surfaces at the Huanan market were genetically similar to human samples, suggesting the virus was shed by humans, not animals, it said.

But some experts said the inability to find an infected animal did not prove anything, because China shut down the market and killed all of the animals before they could be tested.



Researchers found it striking that the raccoon dog DNA came from a stall at the Huanan market that was also positive for SARS-CoV-2, the virus that causes Covid

Peter Ben Embarek, Peter Daszak and Marion Koopmans, members of the WHO team tasked with investigating the origins of COVID, at a hotel in Wuhan in 2021.

Where Did COVID Come From? We May Never Know.

- But in the three years since COVID-19 emerged, researchers have been unable to determine how it infected its first victim, triggering a pandemic that has since killed almost 7 million people, according to an official count by the World Health Organization, and many more if the tally included deaths caused by unreported infections.

- Debate intensified recently after a Chinese research team uploaded DNA evidence, swabbed from the market during the outbreak, to an international gene sequence database. The previously undisclosed data indicated the presence of wild animals in the same section of the market where the team had found SARS-CoV-2. The animals, known to be susceptible to bat viruses, included raccoon dogs, bamboo rats and porcupines.

- Although not conclusive, some scientists said the data add evidence to the theory that the virus jumped from animals to humans through what is known as “zoonotic spillover,” a source of many infectious diseases in humans.

- Others suspect the pathogen somehow leaked from a Wuhan laboratory, 27 km from the market, where researchers study bat viruses. The idea gained more traction earlier this year when the U.S. Department of Energy, with “low confidence,” in a report said that a lab leak was likely. Other U.S. agencies that have studied the matter lean toward natural spillover, although also inconclusively.

- Though it remains a mystery how the virus got to Wuhan, spillover risk has been increasing dramatically in China, including several regions within 400 km of the market. Chinese court records are replete with cases of poachers taking wildlife from risky areas, and scientists from the Wuhan lab have collected bat samples there.

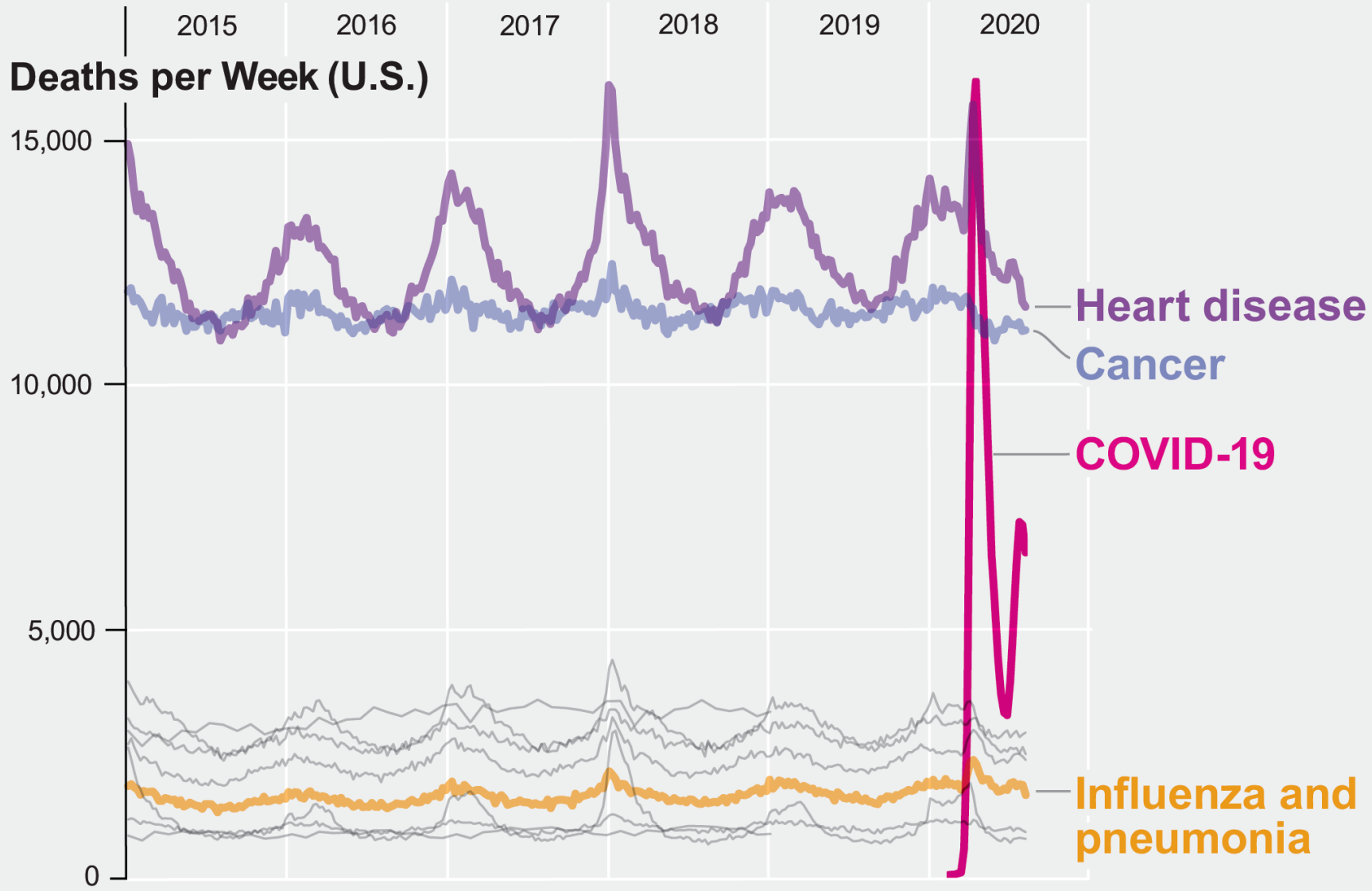
The Magnitude of COVID-19

Globally, the COVID death toll is nearing 7 million. Across all ages, on average, each person who died passed away 10 years younger than they otherwise would have. That's tens of millions of years wiped away.

In the U.S., more than 80% of deaths from the disease have been in people aged 65 and older. Underlying medical conditions and disabilities also raise the risk of severe illness and dying from COVID.

The virus is also disproportionately killing Black, Hispanic, and Indigenous people and those with less access to health care.

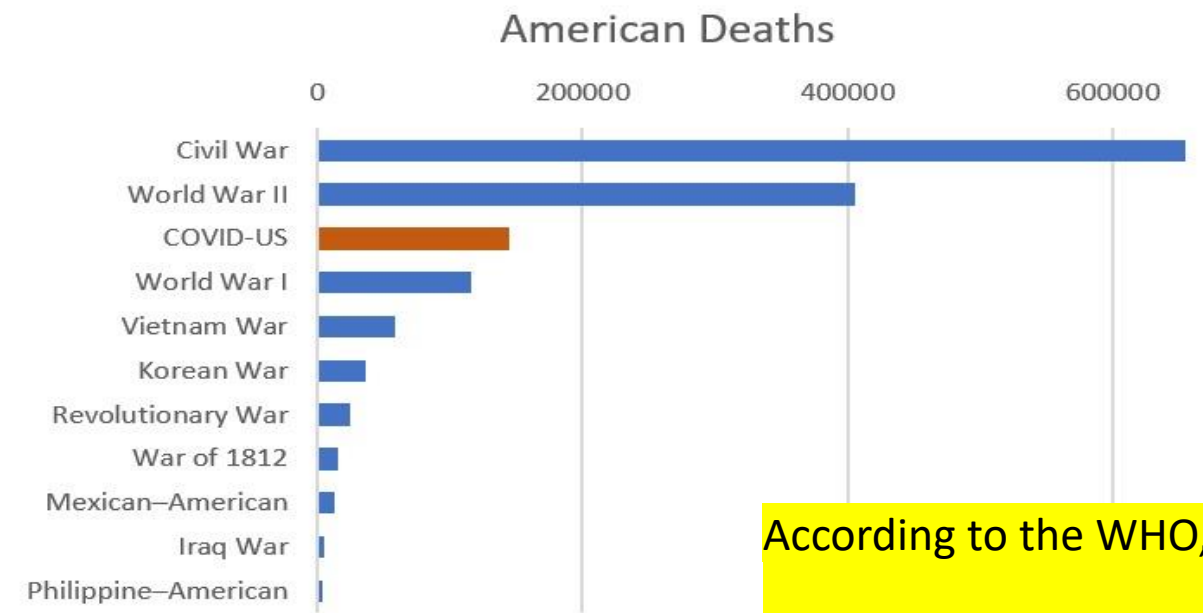
An estimated 26 million people in the U.S. living with long COVID.


2015
2016
2017
2018
2019
2020
Deaths per Week (U.S.)
15,000
10,000
5,000
0
Heart disease
Cancer
COVID-19
Influenza and pneumonia

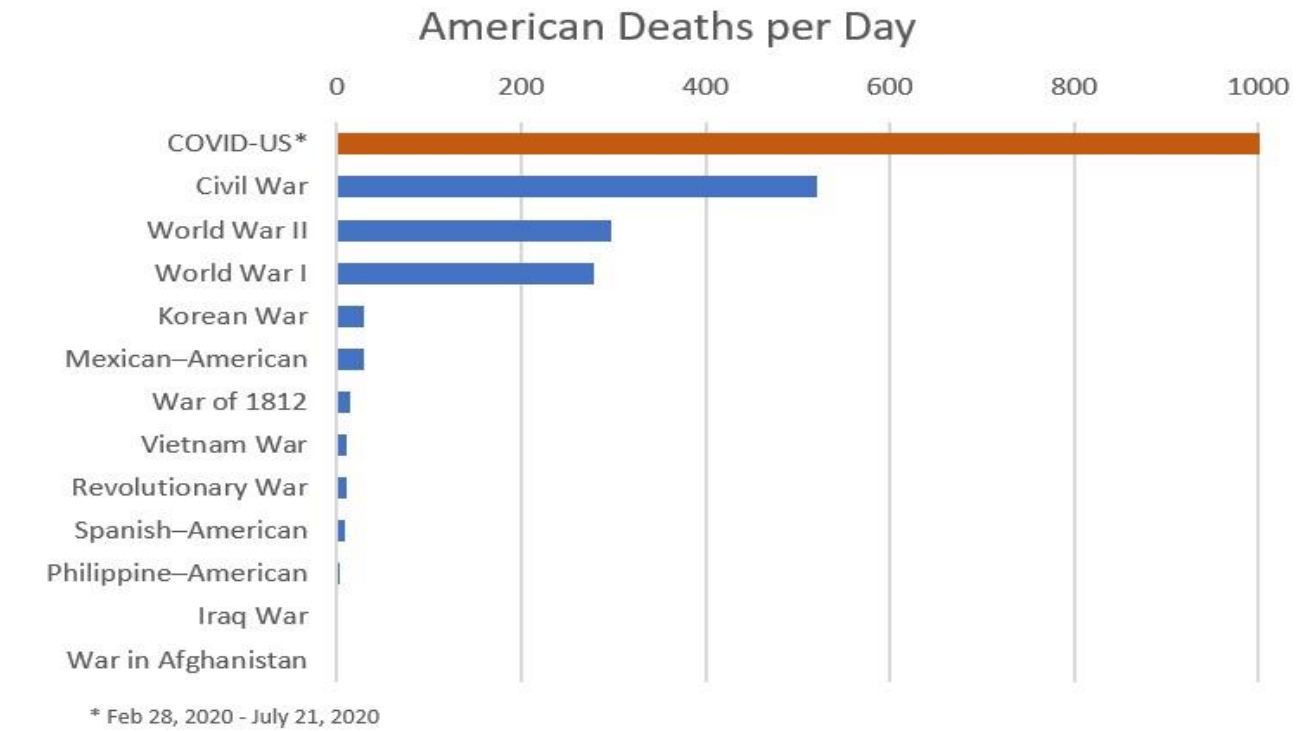
Historic Drop in Life Expectancy

More than 1.1 million Americans have died from COVID over the past 3 years, and experts say the official numbers are likely underestimated due to errors in death certificate reporting. Although deaths have waned from earlier in the pandemic, the disease has become the fourth leading cause of death in the U.S. after heart disease, cancer, and "unintentional injury" such as drug overdoses.

By the end of 2021, Americans overall were dying 3 years sooner, on average, than they were before the pandemic, with life expectancy dropping from 79 years to 76 years, the largest decline in a century.



According to the WHO, an estimated 336.8 million life-years were lost globally



Novel coronavirus (COVID-19) de

statista.com/statistics/1093256/novel-coronavirus-2019ncov-deaths-worldwide-by-country/

statista

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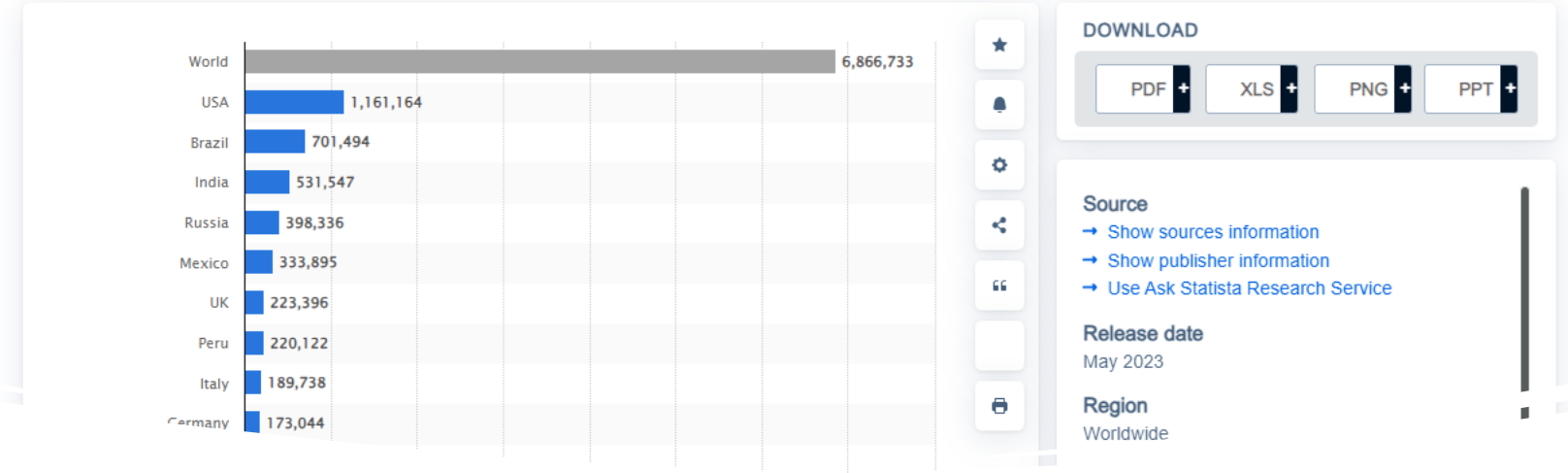
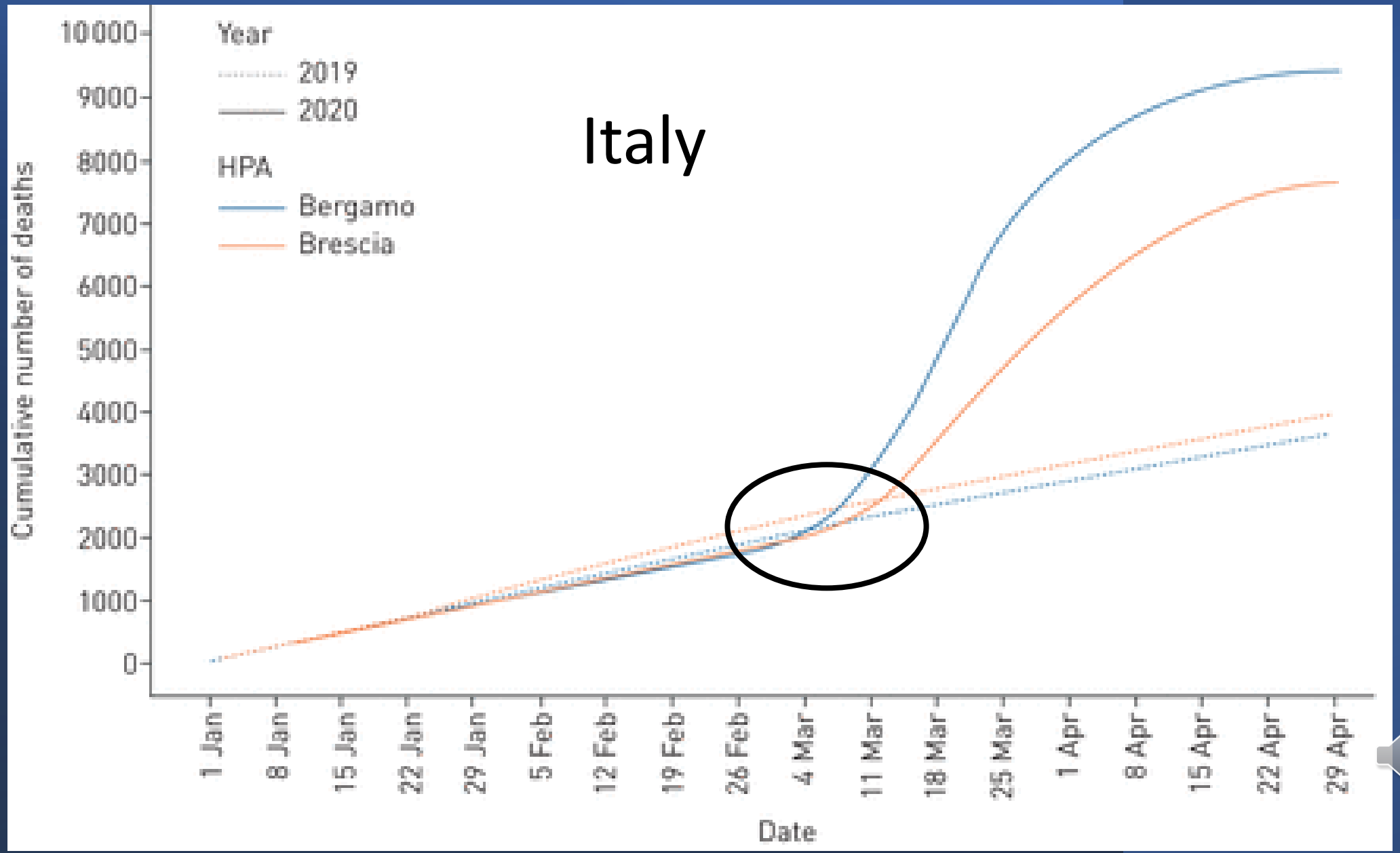
Health, Pharma & Medtech › State of Health

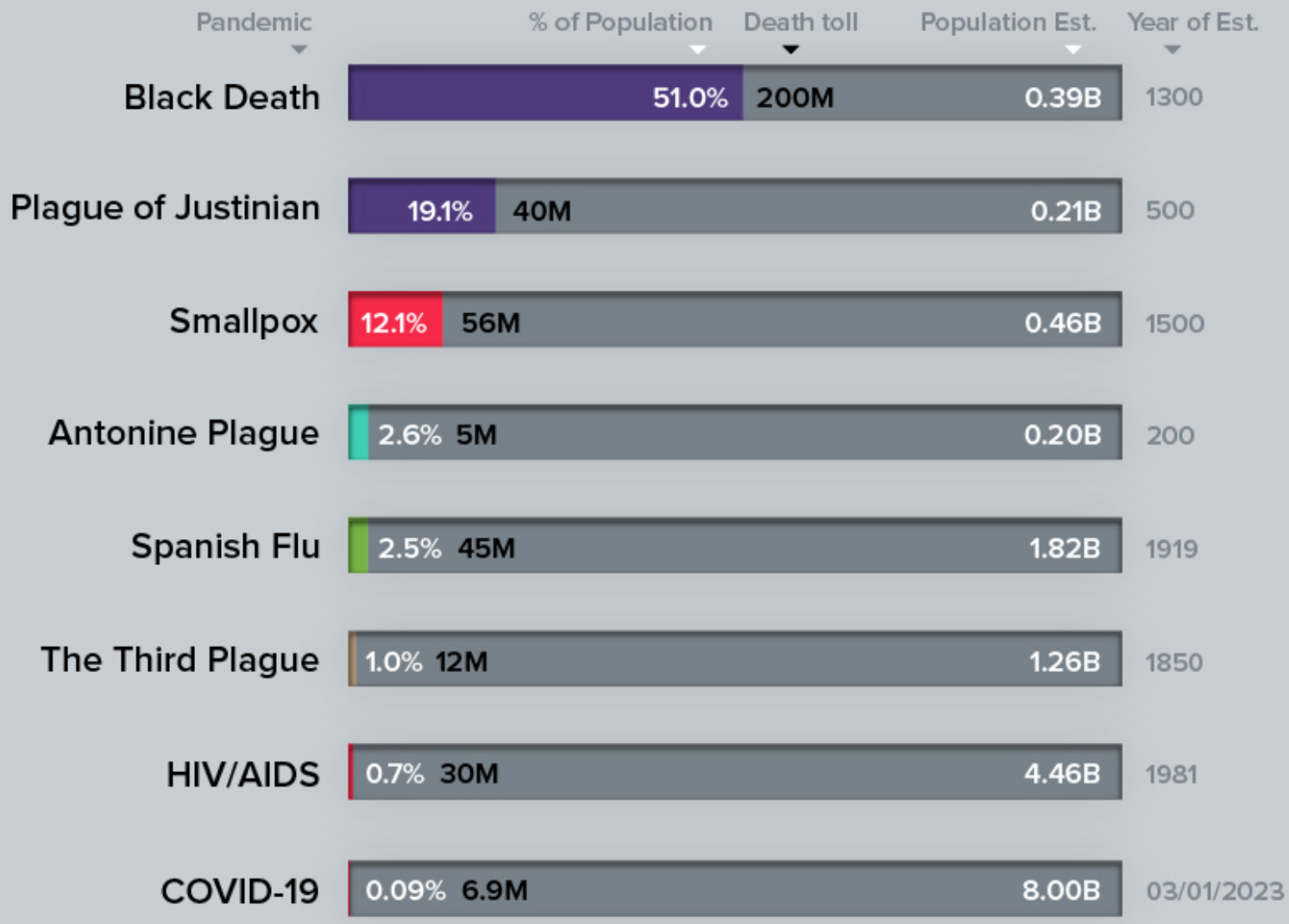
Number of novel coronavirus (COVID-19) deaths worldwide as of May 2, 2023, by country and territory



- By April 26, 2023, more than 104 million U.S. COVID-19 cases, 6 million related hospitalizations, and 1.1 million COVID-19–associated deaths were reported to CDC and summarized on CDC's COVID Data Tracker.


Italy
Year
2019
2020
HPA
Bergamo
Brescia
Cumulative number of deaths
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
1 Jan
8 Jan
15 Jan
22 Jan
29 Jan
5 Feb
12 Feb
19 Feb
26 Feb
4 Mar
11 Mar
18 Mar
25 Mar
1 Apr
8 Apr
15 Apr
22 Apr
29 Apr
Date

[DEATH TOLL AS A PERCENT OF THE POPULATION]



Globally, as of 6:07pm CEST, 31 May 2023, there have been:
-767,364,883 confirmed cases of COVID-19,
-including 6,938,353 deaths, reported to WHO.

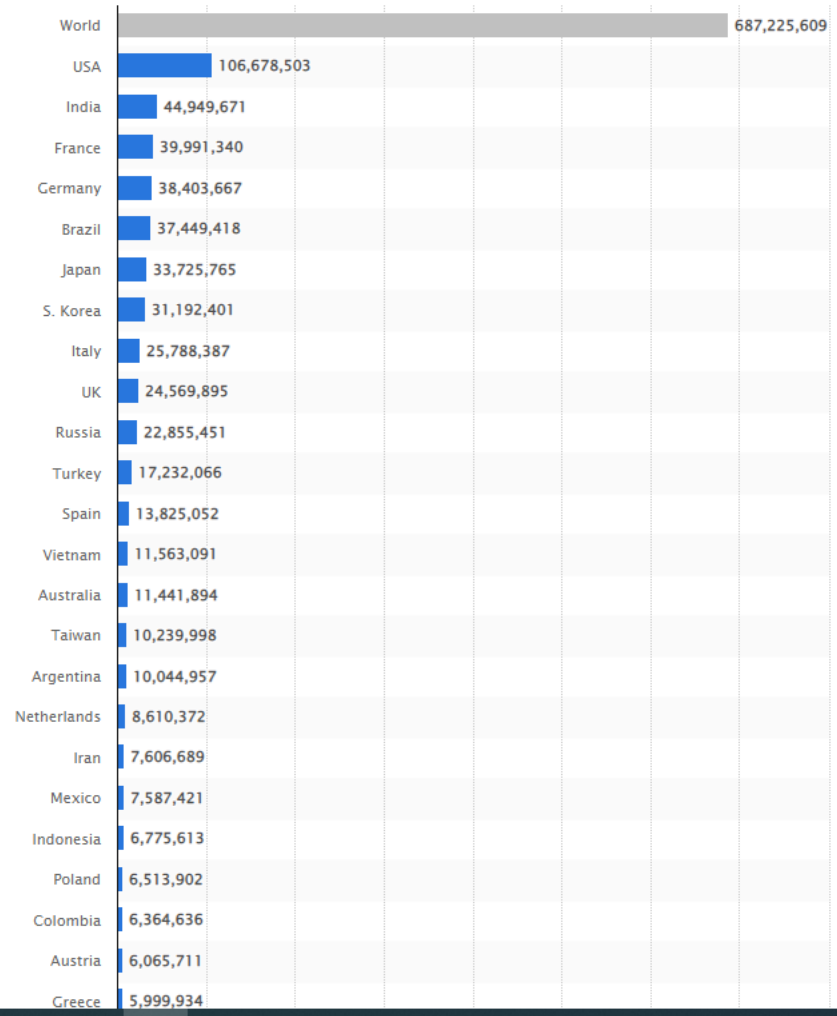
As of 29 May 2023, a total of 13,356,281,548 vaccine doses have been administered.

Five

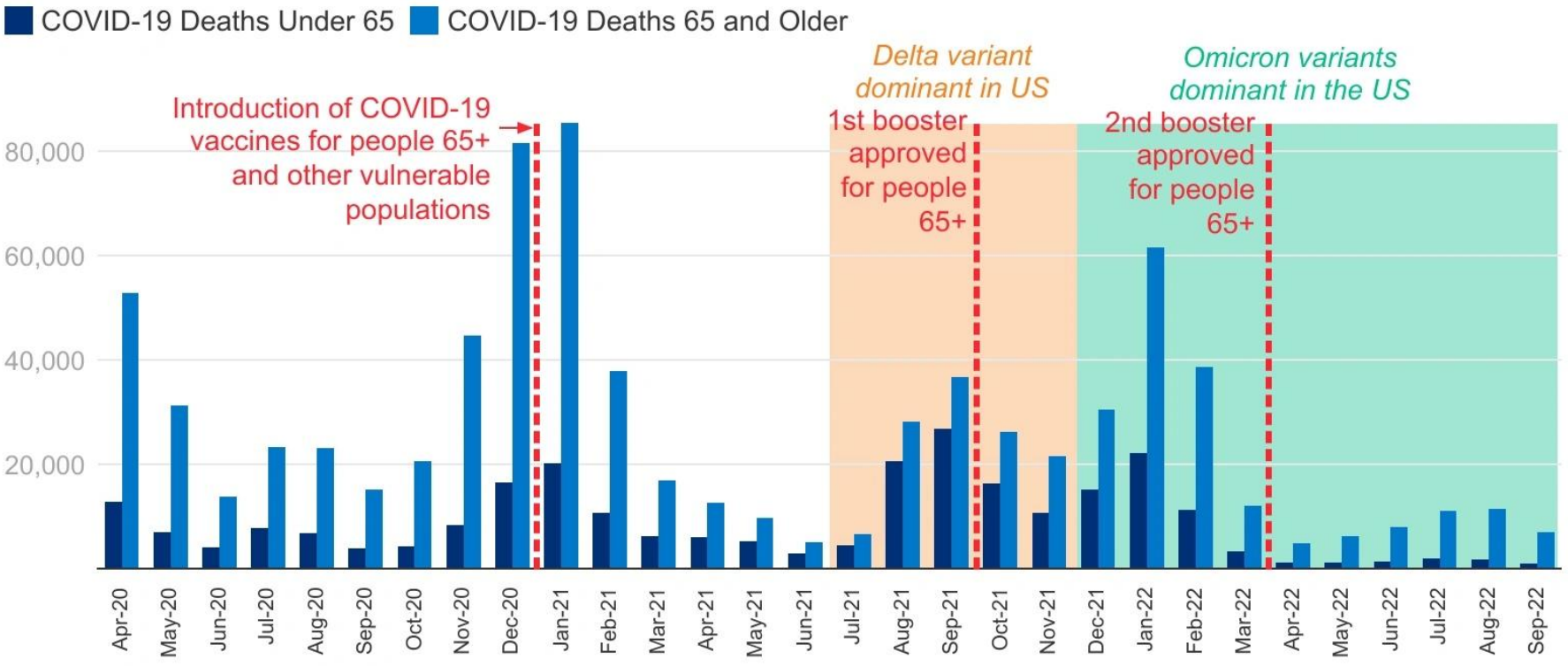
Number of named variants of concern

SARS-CoV-2 evolves and changes as it spreads over time, which has sometimes given rise to new “variants of concern”, or genetic changes in the virus with potentially harmful implications for public health. Since the original version of the virus emerged, WHO has identified 5 different variants of concern: Alpha, Beta, Gamma, Delta, and Omicron (the dominant global variant now in circulation).

Number of coronavirus (COVID-19) cases worldwide as of May 2, 2023, by country or territory



Deaths Due to COVID-19 Rose Faster for Older than Younger Adults in the Summer of 2022

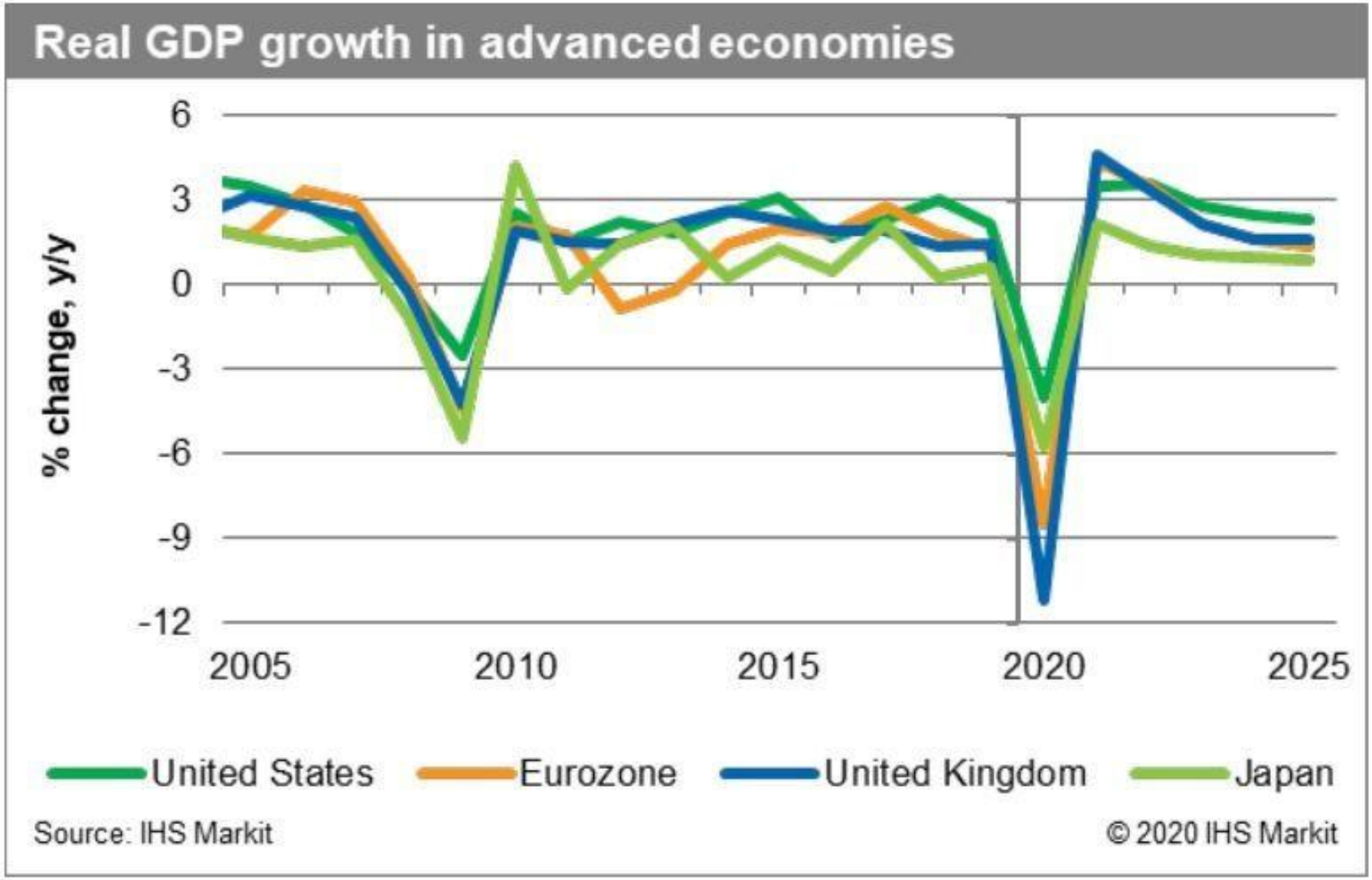


SOURCE: KFF analysis of CDC Provisional COVID-19 Death Counts by Sex and Age, as of the week ending October 1, 2022.

KFF

An economist explains what COVID-19 has done to the global economy

- COVID-19 has caused an economic shock three times worse than the 2008 financial crisis.
- Europe and emerging markets have been hit hard economically; China has escaped a recession.
- But the worst could be behind us, and a greener economy could emerge after the pandemic.


Real GDP growth in advanced economies
% change, y/y
6
3
0
-3
-6
-9
-12
2005
2010
2015
2020
2025
United States
Eurozone
United Kingdom
Japan
Source: IHS Markit
© 2020 IHS Markit

The Clinical Management of Life Threatening COVID

- Ventilator settings
- Provide low TV ventilation:
- AC with TV target 6 mL/kg IBW
- PEEP/FiO2: PEEP 10 to 15 cm H2O to start
- Titrate oxygen to target PaO2 55 to 80/SpO2 88 to 96 for most patients
- Plateau pressure <30 cm H2O
- ARDSNet provides a guide to PEEP and FiO2 titration; refer to UpToDate text for details.
- Prone ventilation
- Suggest prone positioning should low TV ventilation fail (eg, P/F ratio <150 mmHg × 12 hours, FiO2 requirement ≥0.6, requirement for PEEP ≥5 cm H2O)
- Advise daily prone position for 12 to 16 hours/day
- Need experienced staff; ensure that ETT and vascular access remain secured when turning
- Effects of prone ventilation typically seen over 4 to 8 hours; improvements continue the longer it is used.

Ventilator Management

Ventilator settings

- Provide low TV ventilation:
- AC with TV target 6 mL/kg IBW
- PEEP/FiO2: PEEP 10 to 15 cm H2O to start

Titrate oxygen to target PaO2 55 to 80/SpO2 88 to 92 for most patients

Plateau pressure <30 cm H2O

ARDSNet provides a guide to PEEP and FiO2 titration

Prone Positioning

- Prone ventilation
- Suggest prone positioning should low TV ventilation fail
  - (eg, P/F ratio <150 mmHg × 12 hours, FiO2 requirement ≥0.6, requirement for PEEP ≥8 cm H2O)
- Advise daily prone position for 12 to 16 hours/day
- Need experienced staff; ensure that ETT and vascular access remain secured when turning
- Effects of prone ventilation typically seen over 4 to 8 hours; improvements continue the longer it is used.

Rescue Therapies

- For patients who fail prone ventilation (eg, P/F ratio <150 mmHg while prone), may consider the following interventions:
- Recruitment maneuvers and high PEEP strategies
- Trial of inhaled pulmonary vasodilators such as inhaled NO/epoprostenol
- Neuromuscular blockade for patients with refractory hypoxemia (eg, P/F ratio <100 mmHg) or ventilator dyssynchrony
- ECMO as a last resort; however, ECMO is not universally available

- There are no prospective trials of pulmonary vasodilators in COVID-19. However, a meta-analysis of mostly small, retrospective trials did not show improved outcomes. A Cochrane review of 13 trials evaluated the use of inhaled nitric oxide in patients with ARDS who did not have COVID-19 and found no reduction in mortality. Because the review showed a transient benefit for oxygenation, it is reasonable to attempt using inhaled nitric oxide as a rescue therapy in patients with COVID-19 and severe ARDS after other options have failed. However, if the use of nitric oxide does not improve a patient's oxygenation, it should be tapered quickly to avoid rebound pulmonary vasoconstriction, which may occur when nitric oxide is discontinued after prolonged use.

- The Panel recommends using, as needed, intermittent boluses of neuromuscular blocking agents (NMBAs) or a continuous NMBA infusion to facilitate protective lung ventilation.
- Rationale

- Although the use of NMBAs in patients with ARDS reduces ventilator dyssynchrony, a large multicenter trial across several ICUs reported no significant difference in mortality between patients who received deep sedation and continuous NMBA infusion and patients who received a usual-care approach of lighter sedation without routine NMBAs.

Oxygen Delivery

- Several studies have informed clinical practice on the optimal oxygen delivery system for patients with COVID-19 and acute hypoxemic respiratory failure.

- A randomized study of 711 patients with COVID-19 in 34 intensive care units (ICUs) in France compared HFNC oxygen delivery to oxygen delivery through a nonrebreather mask. The patients had acute respiratory failure with a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) ≤200 mm Hg.5 The mean FiO_2 was 0.58 in both arms. Although the difference between arms for the primary endpoint of 28-day mortality was not statistically significant (10% in the HFNC oxygen arm vs. 11% in the conventional oxygen arm [absolute difference -1.2%; 95% CI, -5.8% to 3.4%; P = .60]), the intubation rate was significantly lower in the HFNC oxygen arm than in the conventional oxygen arm.

- Unless a contraindication exists, most Panel members would switch to HFNC oxygen delivery for patients with respiratory failure who do not require mechanical ventilation but have worsening hypoxemia or increased work of breathing despite receiving conventional oxygen at flow rates up to 10 L/min.

NIV vs HFNC

For patients with COVID-19 and acute hypoxemic respiratory failure who do not respond to conventional oxygen therapy, HFNC oxygen is preferred over NIV.

No studies directly compare HFNC oxygen with mask-delivered NIV in patients with COVID-19; therefore, this guidance is based on an unblinded clinical trial in patients without COVID-19 who had acute hypoxemic respiratory failure.6 Study participants were randomized to receive HFNC oxygen, conventional oxygen therapy, or NIV.
The patients in the HFNC oxygen arm had more ventilator-free days (mean 24 days) than those in the conventional oxygen therapy arm (mean 22 days) or the NIV arm (mean 19 days; P = 0.02). In addition, the conventional oxygen therapy arm (HR 2.01; 95% CI, 1.01–3.99) and the NIV arm (HR 2.50; 95% CI, 1.31–4.78) had higher 90-day mortality than the HFNC oxygen arm.

In the subgroup of patients with severe hypoxemia (those with PaO2/FiO2 ≤200 mm Hg), the HFNC oxygen arm had a lower intubation rate than the conventional oxygen therapy arm and the NIV arm (HR 2.07 and 2.57, respectively).

The trial's findings were corroborated by a meta-analysis of 8 trials with 1,084 participants that assessed the effectiveness of oxygenation strategies.7 Compared to NIV, HFNC oxygen reduced the rate of intubation (OR 0.48; 95% CI, 0.31–0.73) and ICU mortality (OR 0.36; 95% CI, 0.20–0.63).

Awake Prone Positioning in Nonmechanically Ventilated Adults

- **Recommendations:**
- For adults with persistent hypoxemia who require HFNC oxygen and for whom endotracheal intubation is not indicated, the Panel recommends a trial of awake prone positioning .

- The Panel recommends against the use of awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation.

- The study enrolled 1,126 patients between April 2, 2020, and January 26, 2021, and the intention-to-treat analysis included 1,121 patients.21 Of the 564 patients who underwent awake prone positioning, 223 (40%) met the composite primary endpoint of intubation or death within 28 days of enrollment. Among the 557 patients who received standard care, 257 (46%) met the primary endpoint (relative risk 0.86; 95% CI, 0.75−0.98). The incidence of intubation by Day 28 was lower in the awake prone positioning arm than in the standard care arm (HR for intubation 0.75; 95% CI, 0.62−0.91). There was no difference in 28-day mortality between the awake prone positioning arm and the standard care arm (HR for mortality 0.87; 95% CI, 0.68−1.11).

- During the first 14 days of the study, the median daily duration of awake prone positioning was 5.0 hours (IQR 1.6–8.8 hours).21 However, the median daily duration varied from 1.6 hours to 8.6 hours across the individual trials. Longer daily durations for awake prone positioning were associated with treatment success by Day 28.

PEEP

The Panel recommends using a higher positive end-expiratory pressure (PEEP) strategy over a lower PEEP strategy.

PEEP is beneficial in patients with ARDS because it prevents alveolar collapse, improves oxygenation, and minimizes atelectrauma, a source of ventilator-induced lung injury.

A meta-analysis of individual patient data from the 3 largest trials that compared lower and higher levels of PEEP in patients with COVID-19 found that less ICU mortality and in-hospital mortality was associated with higher levels of PEEP in those with moderate (PaO2/FiO2 100–200 mm Hg) and severe (PaO2/FiO2 <100 mm Hg) ARDS.22

Although there is no clear standard for a high level of PEEP, a conventional threshold is >10 cm H2O. Recent reports have suggested that, in contrast to patients with ARDS not caused by COVID-19, some patients with moderate or severe ARDS due to COVID-19 have normal static lung compliance. In these patients, high levels of PEEP may cause harm by compromising hemodynamics and cardiovascular performance.

These seemingly contradictory observations suggest that patients with COVID-19 and ARDS are a heterogeneous population, and assessments for responsiveness to high levels of PEEP should be individualized based on oxygenation, P-V tools, transpulmonary monitoring, and lung compliance.

COVID-19 Patients with Asthma Fare Better than Those with COPD

COVID-19 severity was increased in patients with COPD and decreased in those with asthma, eosinophilia, and non-eosinophilic asthma, independent of clinical confounders. These findings suggest that COVID-19 severity may be influenced by intrinsic immunologic factors in patients with airway diseases, such as T2 inflammation.”

COPD have a 11% mortality compared to 3% with Asthma

What Did We Learn?

Although COVID-19 cases and associated hospitalizations have decreased in recent months, COVID-19 remains an ongoing public health challenge

Updated public health tracking* will keep you informed about COVID-19

Hospital admissions	track →	Spread in communities + severity of illness
Death certificates	track →	Severity of illness
Emergency department visits	track →	Early signs of spread
Genomic sequencing	tracks →	New variants

Check COVID.cdc.gov to know when to take action

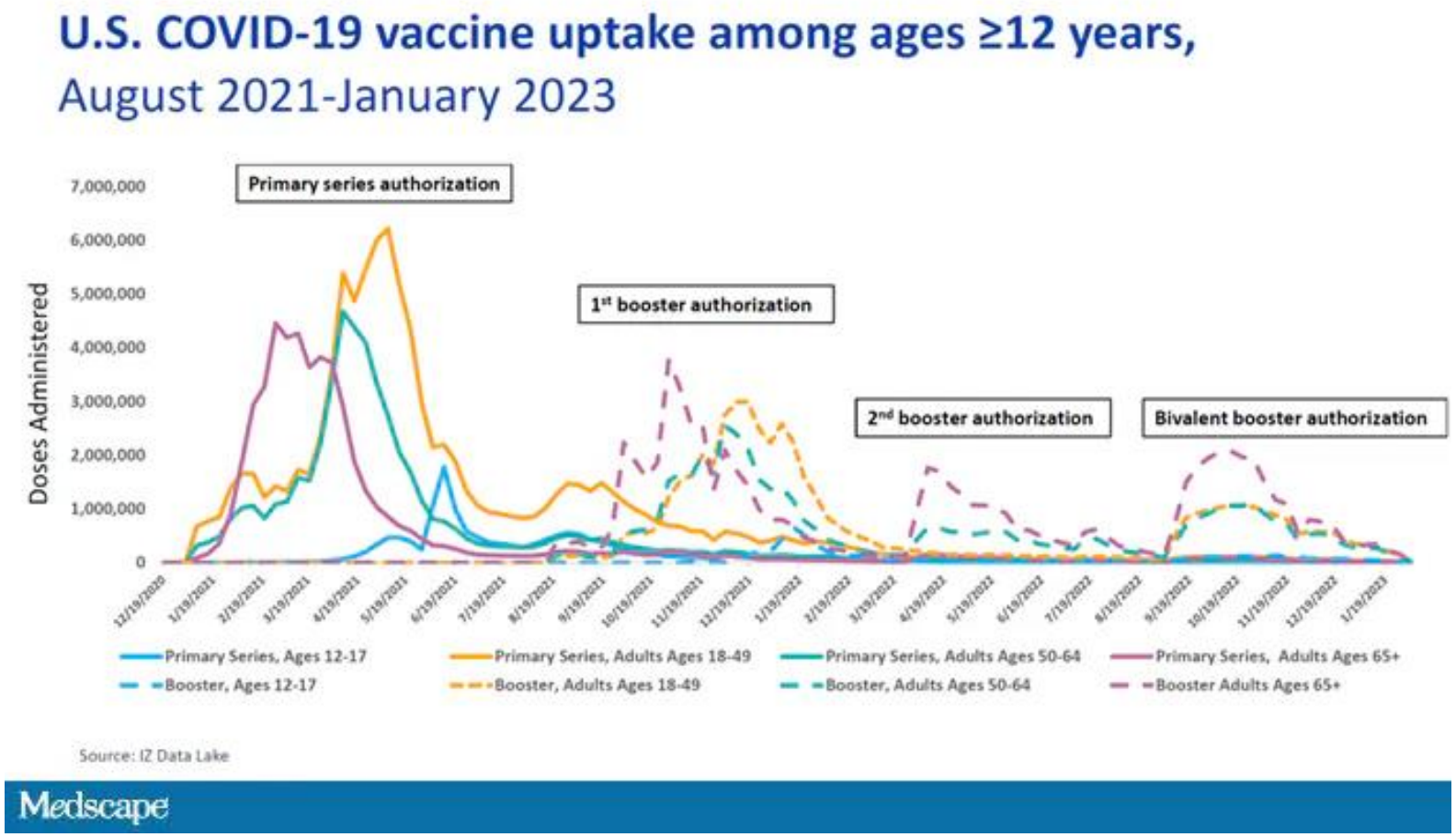
*To account for changes in available data after the end of the U.S. Public Health Emergency declaration

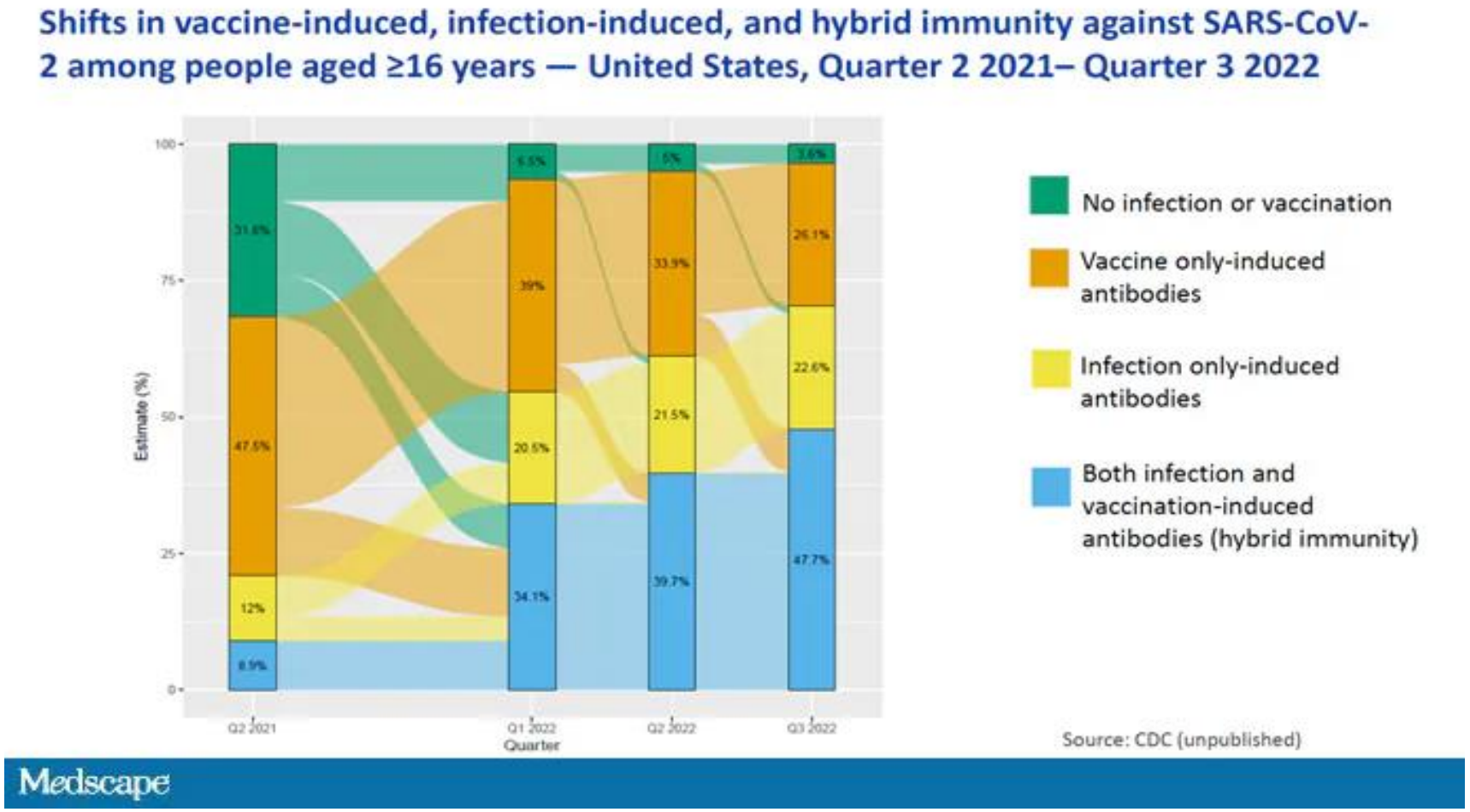
bit.ly/mm7219e1

MAY 5, 2023

MMWR

US Vaccine Administration





What you can see is that by quarter three of 2022, just 3.6% of people who had blood drawn at a commercial laboratory had no evidence of infection or vaccination. In other words, almost no one was totally naive. Then 26% of people had never been infected — they only have vaccine antibodies — plus 22% of people had only been infected but had never been vaccinated. And then 50% of people had both. So there's a tremendous amount of existing immunity out there.

CDC Study: Nearly All Americans Had Some Level of COVID-19 Immunity by Last Fall

- The research found that 96% of blood donation samples had antibodies against the coronavirus from vaccination, infection or hybrid immunity.
- About 23% were from infection alone and 26% were from vaccination alone. Nearly 48% had hybrid immunity – a number that's only expected to grow as the coronavirus continues to circulate.
- Hybrid immunity, or the combination of protection from vaccination and infection, is believed to be higher and longer lasting than protection from either source on its own.

WHO Recommends New COVID Shots Should Target Only XBB Variants

- New formulations should aim to produce antibody responses to the XBB.1.5 or XBB.1.16 variants, the advisory group said, adding that other formulations or platforms that achieve neutralizing antibody responses against XBB lineages could also be considered.

- The group suggested no longer including the original COVID-19 strain in future vaccines, based on data that the original virus no longer circulates in human beings and shots targeting the strain produce "undetectable or very low levels of neutralizing antibodies" against currently circulating variants.

- In late March, WHO had revised its COVID vaccination recommendations and suggested healthy children and adolescents might not necessarily need a shot, but older and high-risk groups should get a booster between six and 12 months after their last vaccine.

COVID ICU Patients Reach Zero for First Time Since Oct. 2020 in central New York May 30 2023

For the first time in 952 days, COVID Intensive Care Unit hospitalizations reached zero in Central New York, according to New York State Department of Health data.

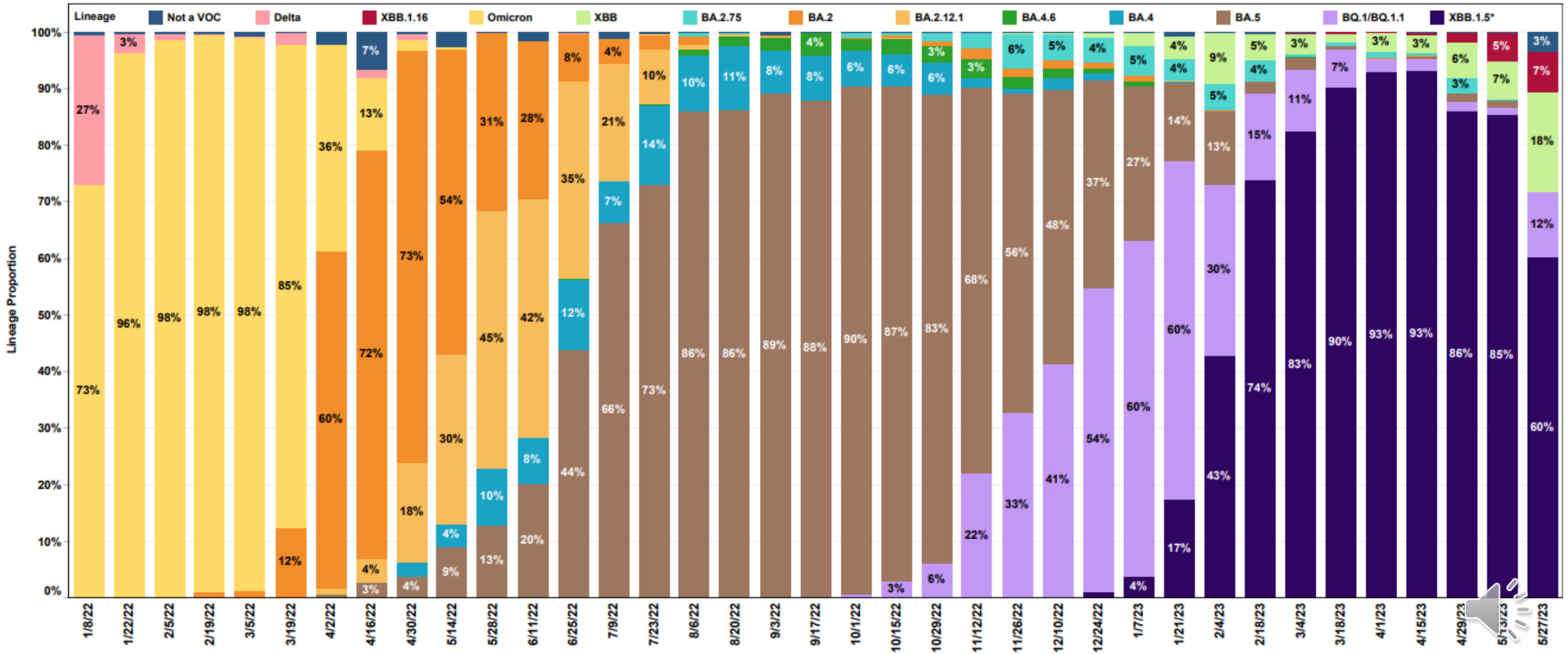
Despite the Global Emergency Order being lifted by the World Health Organization and the United States following suit in the past month by lifting its public health emergency — New York has continued to compile hospital data, allowing for a clear picture of the toll COVID still has in communities.

Across the entire state, there are currently 63 patients in the ICU.
Central New York is the only region out of New York's ten regions without a COVID ICU patient currently.

Nebraska SARS-CoV-2 Wastewater Surveillance Genomic Report

Updated 5/26/2023

Statewide Wastewater Sequencing Results: Proportions by Lineage | By Specimen Collection Date, Since January-2022



Sewer Data Says Ohio Person Has Had COVID for 2 Years

- Scientists think that a person in Ohio who has been infected with COVID-19 for 2 years is shedding thousands of times more of the virus than normal, according to wastewater monitoring data. The strain of the virus appears to be unique.
- The infected person lives in Columbus, works at a courthouse in a nearby county, and has gut health problems. The county where the person works has a population of just 15,000 people but had record COVID wastewater levels in May, The Columbus Dispatch reported. The unique COVID strain that Johnson is researching was the only COVID strain found in Fayette County's wastewater. This person was shedding thousands of times more material than a normal person ever would," Johnson told the Dispatch. "I think this person isn't well…I'm guessing they have GI issues."

- Monitoring wastewater for COVID-19 is only used to inform public health officials of community levels and spread of the virus. People with COVID are not tracked down using such information.

Deer spread COVID to Humans multiple times, new research suggests

- Americans have transmitted COVID-19 to wild deer hundreds of times, an analysis of thousands of samples collected from the animals suggests, and people have also caught and spread mutated variants from deer at least three times.
- Scientists analyzed 8,830 samples collected from wild white-tailed deer across 26 states and Washington, D.C., from November 2021 to April 2022, to study the COVID variants that had infected 282 of them.
- A total of 109 "independent spillover events" were identified, matching viruses spotted in deer to predecessors it likely descended from in previously infected humans.
- Overall, this study demonstrated that frequent introductions of new human viruses into free-ranging white-tailed deer continued to occur, and that SARS-CoV-2 VOCs were capable of persisting in white-tailed deer even after those variants became rare in the human population," the study's authors wrote.

Three had mutations that match a distinctive pattern of first spilling over from a human to deer, and then later another so-called "spillback" from deer back into humans. Two of these spillback variants were in North Carolina and one was in Massachusetts.

An investigation with the Centers for Disease Control and Prevention was able to track down three people who were infected by a variant with this hallmark deer mutation, as well as a handful of zoo lions who were also infected by the same strain. None of the humans said they had close contact with either deer or the zoo.

It could potentially serve as a long-term so-called "reservoir species" to harbor the virus as it mutates adaptations to spread among deer.

Deer regularly interact with humans and are commonly found in human environments — near our homes, pets, wastewater, and trash.

Neuroinflammation After COVID-19 With Persistent Depressive and Cognitive Symptoms

- Several days to months after acute symptoms abate, there is a high prevalence of depressive symptoms with or without cognitive impairment, ranging from approximately 15% after wild-type SARS-CoV-2 exposure in unvaccinated persons to approximately 5% in triple-vaccinated persons exposed to Delta or Omicron variants.
- Many of these symptoms, such as motor slowing, low motivation and energy, and short-term memory impairment may persist for months to years.
- Hence, depressive symptoms with or without other cognitive symptoms, after an acute episode of mild to moderate COVID-19 illness, hereinafter termed COVID-DC, is a major public health problem.
- Gliosis may be consequent to inflammation, injury, or both, particularly in the ventral striatum and dorsal putamen, which may explain some persistent depressive and cognitive symptoms, including slowed motor speed, low motivation or energy, and anhedonia, after initially mild to moderate COVID-19 illness.

Long COVID 'Brain Fog' Confounds Doctors, but New Research Offers Hope

- Brain fog is among the most common symptoms of long COVID, and also one of the most poorly understood.
- A reported 46% of those diagnosed with long COVID complain of brain fog or a loss of memory. Many clinicians agree that the term is vague and often doesn't truly represent the condition.
- That, in turn, makes it harder for doctors to diagnose and treat it. There are no standard tests for it, nor are there guidelines for symptom management or treatment.
- it makes more sense to call brain fog a brain impairment or an acquired brain injury (ABI) because it doesn't occur gradually. COVID damages the brain and causes injury. For those with long COVID who were previously in the intensive care unit and may have undergone ventilation, hypoxic brain injury may result from the lack of oxygen to the brain.

Treatments for brain fog:
may include speech, cognitive, and occupational therapy as well as meeting with a neuropsychiatrist for treatment of the mental and behavioral disorders that may result.

Jackson said that while many patients aren't functioning cognitively or physically at 100%, they can make enough strides that they don't have to give up things such as driving and, in some cases, their jobs.

Chronic fatigue and poor sleep are both commonly reported symptoms of long COVID that negatively affect brain function. Sleep disturbances, cardiac problems, dysautonomia, and emotional distress could also affect the way the brain functions post COVID. Finding the right treatment requires identifying all the factors contributing to cognitive impairment.

Although brain disorders such as Alzheimer's disease and other forms of dementia are marked by a slow decline, ABI occurs more suddenly and may include a loss of executive function and attention.

Cognitive Deficits in Some COVID-19 Long-haulers Likened to Aging a Decade

- Conducted by experts from King's College London, the study, published in eClinicalMedicine, aimed to investigate the impact of COVID-19 infection on cognitive abilities through two rounds of online testing held in 2021 and 2022. Over 3,000 participants from the COVID Symptom Study Biobank study were involved, undergoing evaluation in 12 cognitive tasks assessing memory, attention, reasoning, processing speed, and motor control.

- Notably, those participants who had endured virus-related symptoms for 12 weeks or more displayed the most significant decline in test scores due to COVID-19. The adverse effect on their test accuracy was comparable in magnitude to that of a 10-year increase in age.

- Interestingly, no substantial improvement was observed in the test scores during the nine-month interval between the two rounds of testing. By the time of the second round, participants had, on average, almost two years since their initial COVID-19 infection.

One in Five Doctors With Long COVID Can No Longer Work: Survey

- Crippling symptoms, lost careers, and eroded incomes: This is the harsh reality for doctors suffering with long COVID, according to the first major survey of physicians with the condition.
- Doctors responding to the BMA survey reported a wide range of long COVID symptoms, including fatigue, headaches, muscular pain, nerve damage, joint pain, and respiratory problems.
- Among the survey's key findings, 60% of doctors said long COVID has affected their ability to carry out day-to-day tasks on a regular basis. Almost 1 in 5 (18%) said they were no longer able to work, while fewer than 1 in 3 (31%) were working full time. This compares to more than half (57%) of respondents working full time before the onset of their COVID illness — a decline of 46%.

COVID Could Impair Men's Sperm for Months

- A COVID infection can reduce sperm count and hinder the ability of sperm to swim for at least 3 months, according to European researchers.
- The researchers were surprised that the effects lasted beyond the usual 78 days it takes for the body to make new sperm, even in people who weren't seriously ill. "We assumed that semen quality would improve once new sperm were being generated, but this was not the case," researcher Rocio Núñez-Calonge, PhD, a reproduction expert and professor in Spain, said in a statement.
- "We do not know how long it might take for semen quality to be restored, and it may be the case that COVID has caused permanent damage, even in men who suffered only a mild infection.“
- Compared to pre-infection samples, post-COVID semen volume was down 20%, sperm concentration was down nearly 27%, sperm count was down nearly 38%, and the number of live sperm was down 5%.

Did you get COVID but never feel sick? New study hints at why

- A new study published Wednesday in the scientific journal Nature suggests people with a specific version of a gene were far more likely to experience an asymptomatic infection than those without.
- The relevant set of genes is known as the human leukocyte antigen, or HLA.
- And if a person had two copies of the HLA-B*15:01 version of this gene — one from each parent — "they were 8½ times more likely to have remained asymptomatic,“
- The lab data show that the T cells of people with this version of the HLA gene managed to recognize these pieces of SARS-CoV-2 and react in a protective manner.
- After previous skirmishes with other run-of-the-mill, non-pandemic coronaviruses — the culprits behind the common cold — people with this version of this gene somehow developed the tools to better armor themselves against the pandemic strain of the coronavirus that began spreading in late 2019. There are four strains of seasonal coronaviruses that are typically responsible for 15% to 30% of respiratory tract infections annually. Folks with this B*15:01, for whatever reason, some of them have this preexisting immunity after exposure to seasonal cold viruses that happens to be just remarkably effective at dealing with the virus" that causes COVID-19.
- Having this version of the gene "is the key element to having this very effective preexisting immunity,"

US Has New Dominant COVID Variant Called EG.5

- Called "Eris" among avid COVID trackers, the strain EG.5 now accounts for 17% of all U.S. COVID infections, according to the latest CDC estimates. That's up from 12% the week prior.
- EG.5 is a descendant of the XBB strains that have dominated tracking lists in recent months. It has the same makeup as XBB.1.9.2 but carries an extra spike mutation, according to a summary published by the Center for Infectious Disease Research and Policy at the University of Minnesota.
- The spike protein is the part of the virus that allows it to enter human cells. But there's no indication so far that EG.5 is more contagious or severe than other recent variants.
- The CDC said that current vaccines protect against the variant.

COVID-19 Hospitalizations and Deaths on the Rise

- COVID-19 hospitalizations rose by 19% last week and COVID deaths by 21%, according to figures from the CDC.
- More than half the states, 26, had a "substantial increase" in hospital admissions.
- This has been the pattern for the past three years and may be where COVID may settle to: a smaller swell in the summer and a larger increase in cases in the late fall and winter.

Lessons Learned: Yale Medical Community

- Lesson 1: Masks are useful tools
- Lesson 2: Telehealth might become the new normal
- Lesson 3: Vaccines are powerful tools
- Lesson 4: Everyone is not treated equally, especially in a pandemic
- Lesson 5: We need to take mental health seriously
- Lesson 6: We have the capacity for resilience
- Lesson 7: Community is essential—and technology is too
- Lesson 8: Sometimes you need a dose of humility

Lesson 1: Masks are useful tools

- Not everyone practiced preventive measures such as mask wearing, maintaining a 6-foot distance, and washing hands frequently.
- Many people have learned a whole lot about respiratory pathogens and viruses, and how they spread from one person to another, and that sort of old-school common sense—you know, if you don't feel well—whether it's COVID-19 or not—you don't go to the party. You stay home!!!!

Lesson 2: Telehealth might become the new normal

- While there are still problems for which you need to see a doctor in person, the pandemic introduced a new urgency to what had been a gradual switchover to platforms like Zoom for remote patient visits.

- More doctors also encouraged patients to track their blood pressure at home, and to use at-home equipment for such purposes as diagnosing sleep apnea and even testing for colon cancer.

Lesson 3: Vaccines are powerful tools

- Vaccines really are worth getting, many individuals who had COVID-19 and experienced lingering symptoms, including chronic headaches.
- Some don’t like the idea of vaccine side effects. Many had vaccine side effects and had COVID-19 side effects, but many say nothing compares to the having the actual illness.

Lesson 4: Everyone is not treated equally, especially in a pandemic

- Racial and ethnic minority groups especially have had disproportionately higher rates of hospitalization for COVID-19 than non-Hispanic white people in every age group, and many other groups faced higher levels of risk or stress.
- These groups ranged from working mothers who also have primary responsibility for children, to people who have essential jobs, to those who live in rural areas where there is less access to health care.
- Often these were the last groups to get health care access and vaccines.

Lesson 5: We need to take mental health seriously

- The CDC reports that the percentage of adults who reported symptoms of anxiety of depression in the past 7 days increased from 36.4 to 41.5 % from August 2020 to February 2021.
- Other reports show that having COVID-19 may contribute, too, with its lingering or long COVID symptoms, which can include “foggy mind,” anxiety, depression, and post-traumatic stress disorder.

Lesson 6: We have the capacity for resilience

- People have practiced self-care in a multitude of ways during the pandemic as they were forced to adjust to new work schedules, change their gym routines, and cut back on socializing.
- Many started seeking out new strategies to counter the stress.

Lesson 7: Community is essential—and technology is too

- Many of us have become aware of how much we need other people—many have managed to maintain their social connections, even if they had to use technology to stay connected, but even that type of community has helped people.

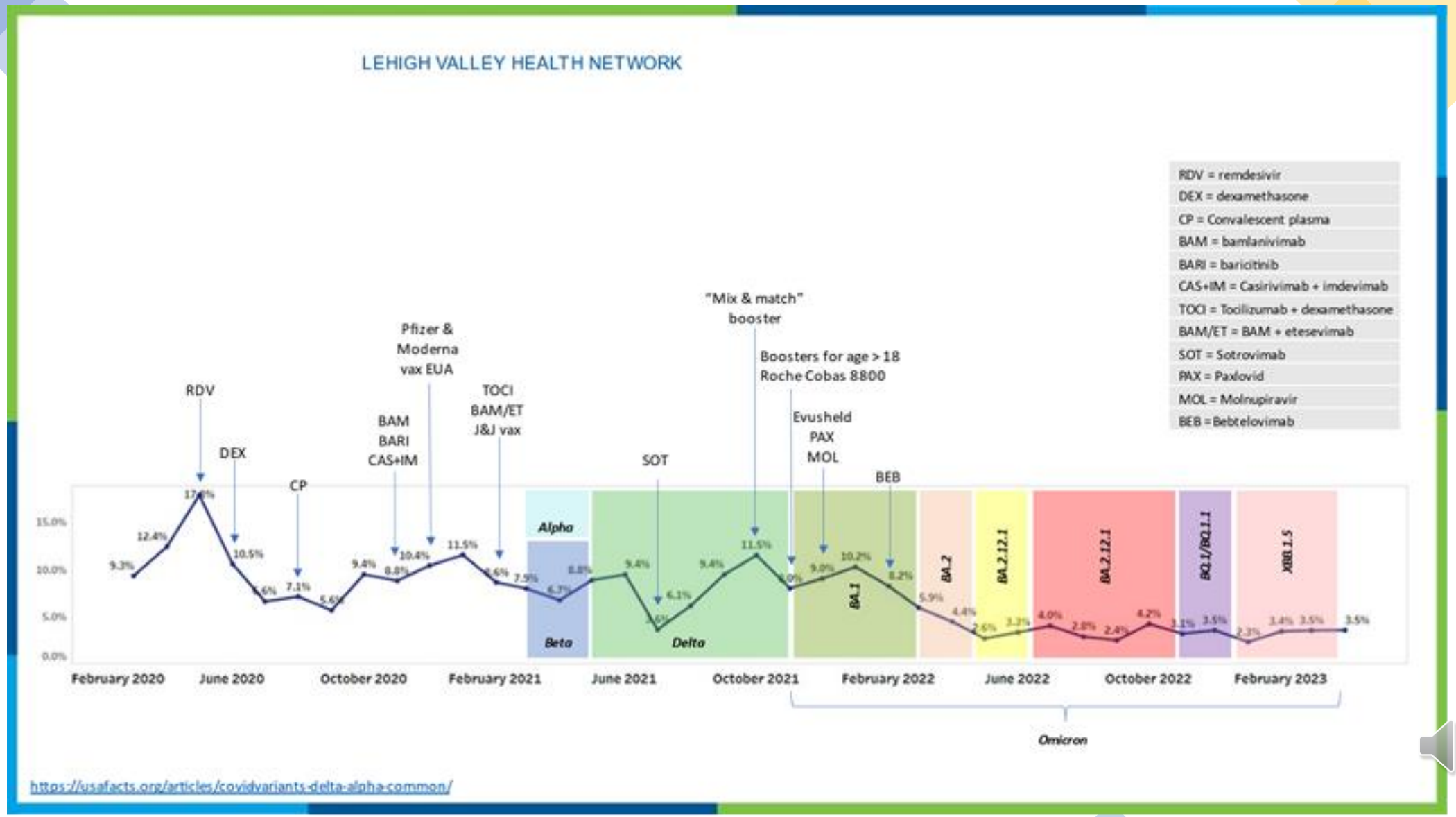
- Even people who aren't necessarily friends or family are important. Dr. Juthani recalled how she encouraged her mail carrier to sign up for the vaccine, soon learning that the woman's mother and husband hadn't gotten it either. "They are all vaccinated now," Dr. Juthani says. "So, even by word of mouth, community is a way to make things happen."

- But loneliness has been found to suppress the immune system and be a precursor to some diseases, he adds. "Even for introverted folks, the smallest circle is preferable to no circle at all:☺

Lesson 8: Sometimes you need a dose of humility

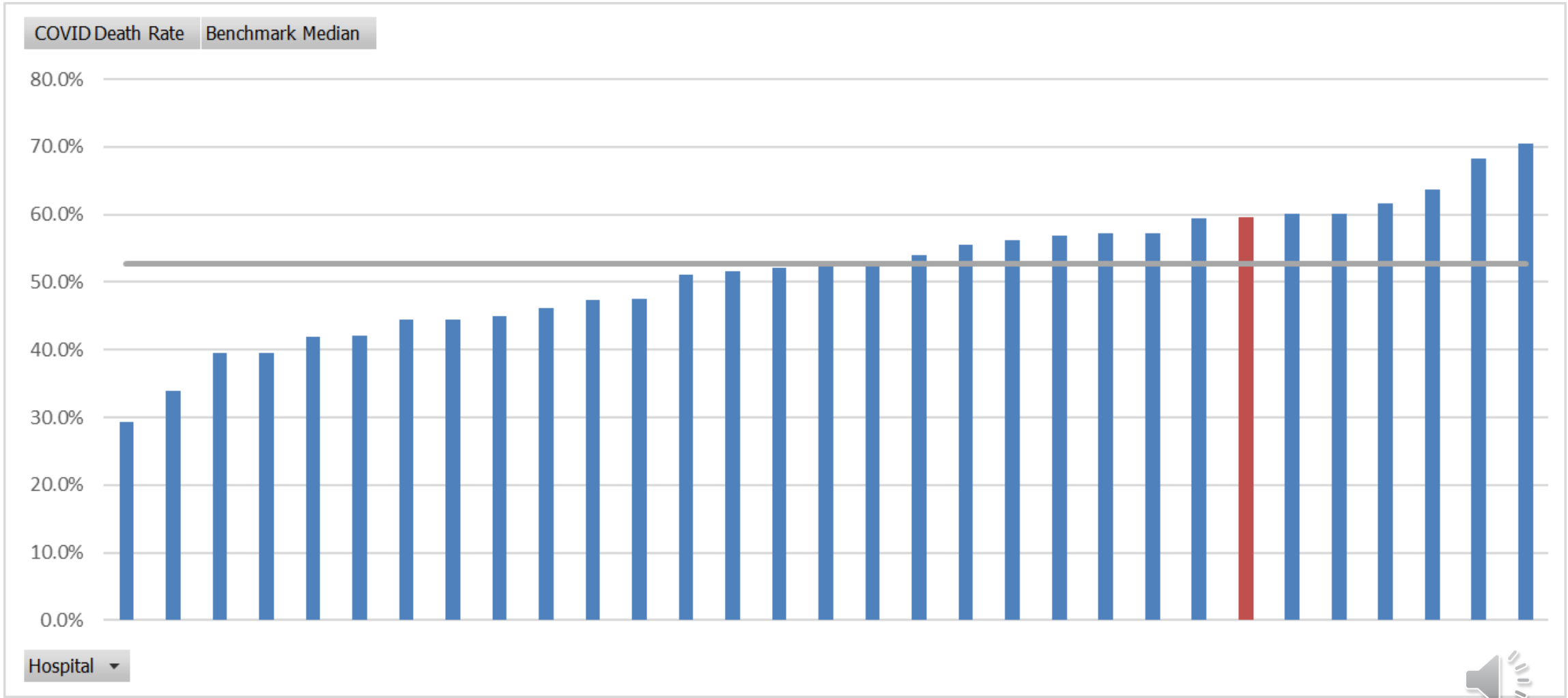
- As infectious disease doctors, we were resident experts at the beginning of the pandemic because we understand pathogens in general, and based on what we've seen in the past, we might say there are certain things that are likely to be true," Dr. Juthani says. "But we've seen that we must take these pathogens seriously. We know that COVID-19 is not the flu.
- All these strokes and clots, and the loss of smell and taste that have gone on for months are things that we could have never known or predicted. So, you must have respect for the unknown and respect science, but also try to give scientists the benefit of the doubt," she says.

- "We have been doing the best we can with the knowledge we have, in the time that we have it," Dr. Juthani says. "I think most of us have had to have the humility to sometimes say, 'I don't know. We're learning as we go.'"


LEHIGH VALLEY HEALTH NETWORK
RDV = remdesivir
DEX = dexamethasone
CP = Convalescent plasma
BAM = bamlanivimab
BARI = baricitinib
CAS+IM = Casirivimab + imdevimab
TOCI = Tocilizumab + dexamethasone
BAM/ET = BAM + etesevimab
SOT = Sotrovimab
PAX = Paxlovid
MOL = Molnupiravir
BEB = Bebtelovimab
RDV
DEX
CP
BAM
BARI
CAS+IM
Pfizer &
Moderna
vax EUA
TOCI
BAM/ET
J&J vax
SOT
"Mix & match"
booster
Boosters for age > 18
Roche Cobas 8800
Evusheld
PAX
MOL
BEB
Alpha
Beta
Delta
BA.1
BA.2
BA.2.12.1
BA.2.12.1
BQ.1/BQ.1.1
XBB.1.5
15.0%
10.0%
5.0%
0.0%
February 2020
June 2020
October 2020
February 2021
June 2021
October 2021
February 2022
June 2022
October 2022
February 2023
Omicron
https://usafacts.org/articles/covidvariants-delta-alpha-common/

- Mechanical Ventilation Outcomes
- July 31 2023

Site	Total Ventilated Pt.	Liberation	Expired	Still Ventilated
Muhl	214	85	129	0
CC	644	287	357	0
LVH-H	76	33	43	0
LVH-P	132	44	88	0
LVH-S	38	11	27	0
Total	1104	460 (41.2)	644(58.8)	0


COVID Death Rate
Benchmark Median
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
Hospital

Conclusion

The origin of the COVID-19 virus remains a mystery

The magnitude of the COVID-19 virus was enormous and still evolving

The clinical management of the ICU COVID-19 patient was speared by evidence-based practices

Lessons learned from the pandemic will be far reaching in magnitude.

Ending Thoughts/Questions