COVID Pandemic Updates

August 5th, 2022

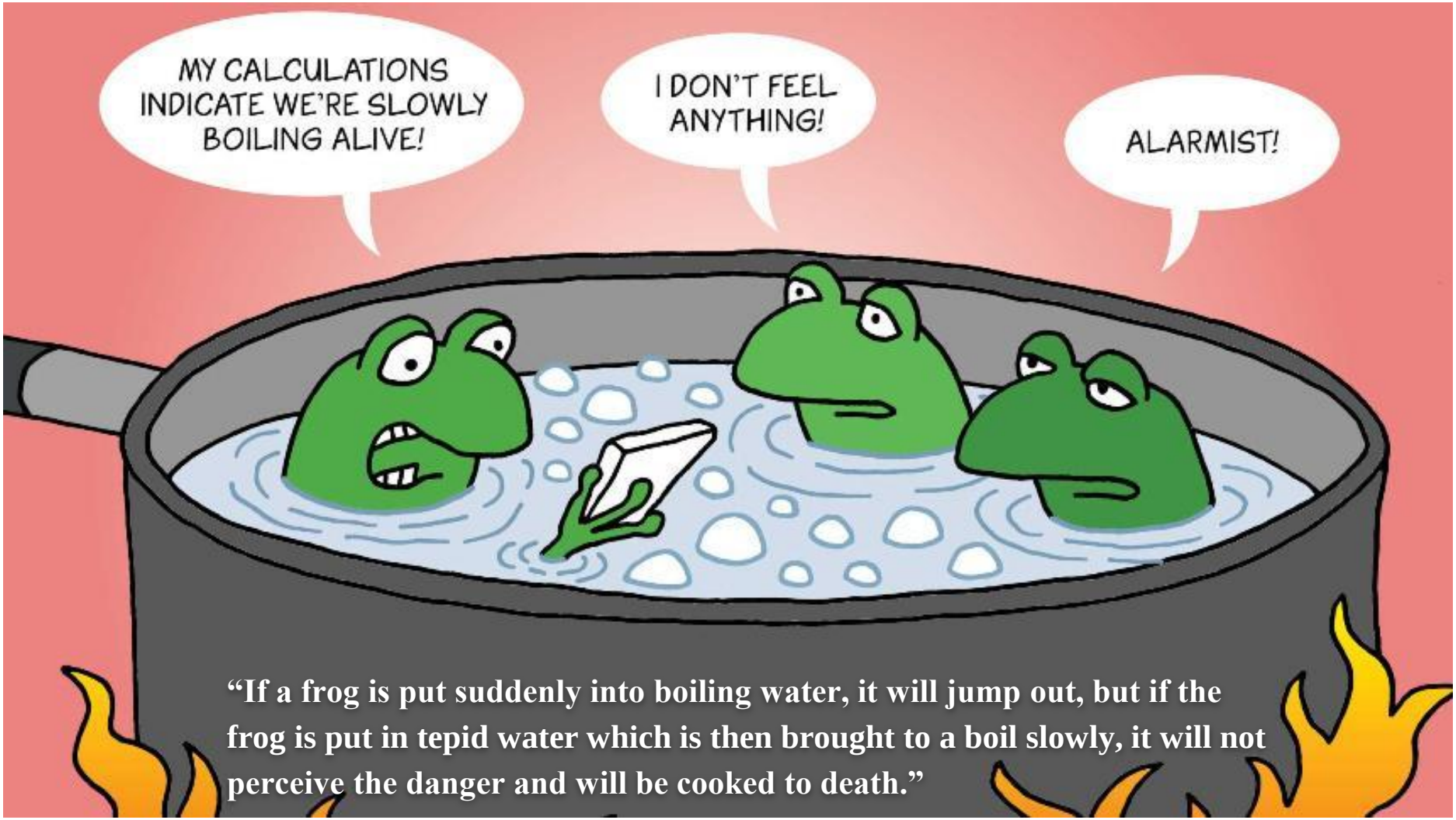
CME Program

AHMC COVID Team

Outline

8/5/2022

1. Dr. Eric Topol: COVID and the Boiling Frog



"If a frog is put suddenly into boiling water, it will jump out, but if the frog is put in tepid water which is then brought to a boil slowly, it will not perceive the danger and will be cooked to death."

Source

COVID and the Boiling Frog (1/5)

- **Dr. Eric Topol's Boiling Frog Theory may be worth reading**

(Eric Topol MD, Ground Truths; 7/18/22)

- **Currently, deaths are averaging 440/day. While COVID's death levels won't be 4,000/day again (Alpha wave), we are not adequately perceiving the threats: its fitness* is getting enhanced while our immunity walls are being built.**
- **These 2 concurrent and opposing trends are hiding the impact of the virus's evolution, and our perception of these events is similar to the boiling frog metaphor.**

***Fitness: Combination of lineage growth, Ro, and immune evasiveness**

Source: Ground Truths

COVID and the Boiling Frog (2/5)

- The virus is getting more fit as it evolves

(bioRxiv, medRxiv, Eric Topol MD, Ground Truths; 7/18/22)

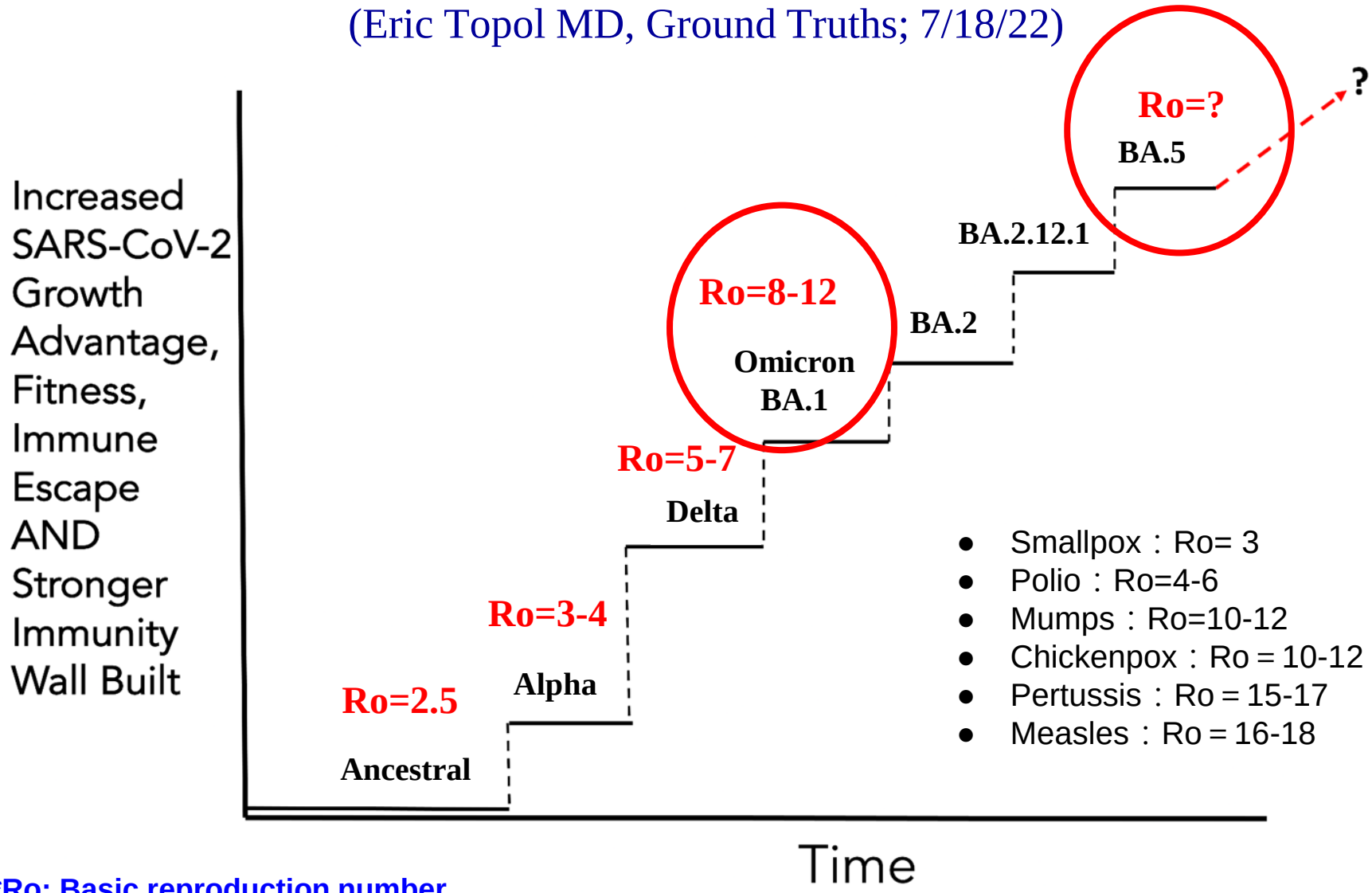
- **BA.5 has evolved to have higher immune evasion and increased infectivity.**
- **When a new variant out-competes another, those with prior infections/vaccinations can better withstand the virus.**
- **This makes us think it's "mild" and less of a threat, but the pressure being put on the virus is making it more formidable.**
- **But more viral evolution is inevitable, with mutations from IC hosts, animal spillover, and new recombinant variants.**

Source: bioRxiv, medRxiv, Ground Truths

COVID and the Boiling Frog (3/5)

- Timeline of increased infectivity (Ro) for each variant

(Eric Topol MD, Ground Truths; 7/18/22)



*Ro: Basic reproduction number

Source: Owid, CDC, Ground Truths, Vaccines Today

COVID and the Boiling Frog (4/5)

- Our immunity is being built as the virus evolves

(CDC, Eric Topol MD, Ground Truths; 7/18/22)

- **People with recent BA.1 or BA.2 infections are getting reinfected, and vaccines are unable to meaningfully block infections or spread.**
- **The latest CDC report showed the following:**

Predominant	2 doses against hospitalization	3 doses against hospitalization
BA.1	61%	85-92%
BA.2.12.1	24% ⬇	52-69% ⬇

- **VE data for BA.5 is limited, but it's waning effectiveness for current vaccines shows no sign of slowing down.**

Source: CDC, Ground Truths

COVID and the Boiling Frog (5/5)

- The future of COVID is still optimistic

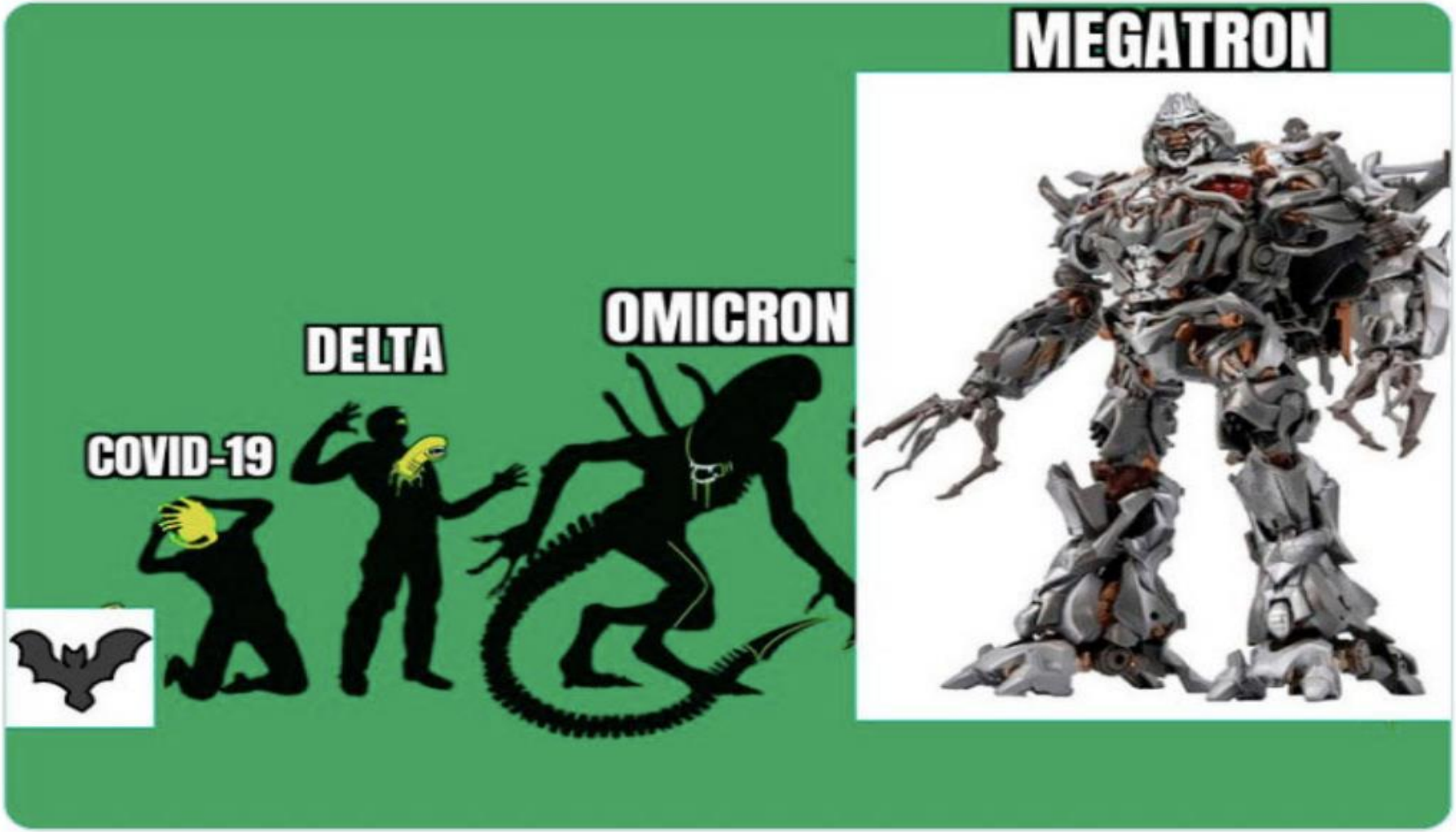
(Eric Topol MD; Ground Truths, 7/18/22)

- **COVID-19 is a much easier virus to prevail over than flu.**
- **COVID vaccines have reached 95% efficacy before; however the best flu vaccines are only 40% effective.**
- **Paxlovid is much more effective than Tamiflu, despite issues with rebound and resistance.**
- **In the future, variant-proof vaccines and nasal vaccines are our way to "turn off the heat".**
- **We know what we need to do; we're just not doing it. The boiling frog metaphor is contributing to the lack of taking action.**

Source: Ground Truths

2. Trend Analysis of Variants

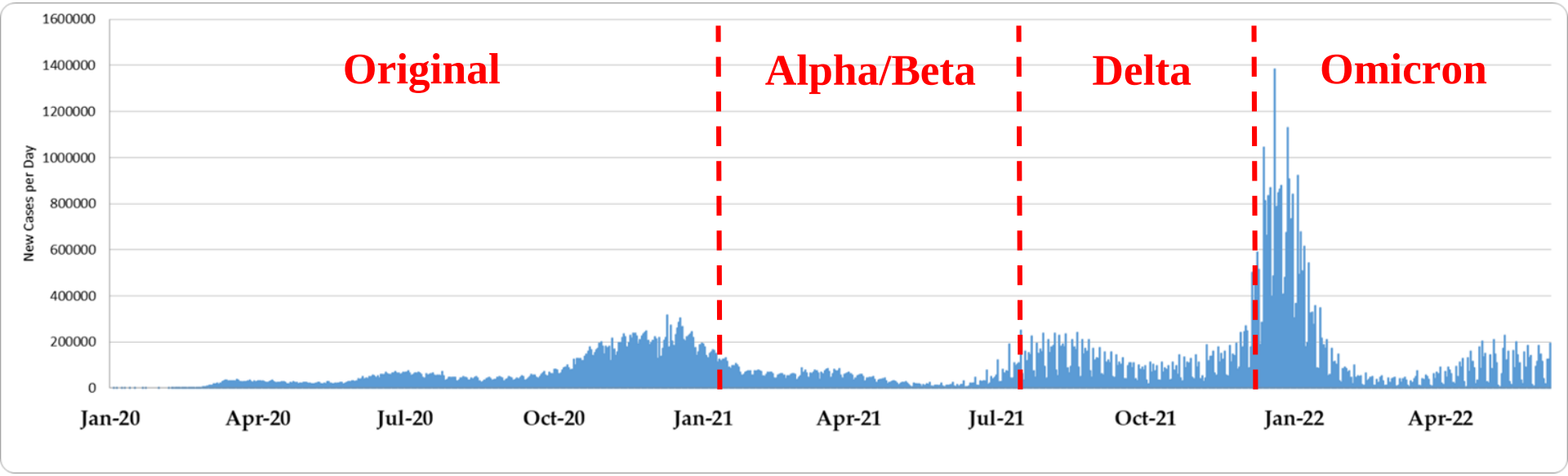
- BA.5, Reinfection, and What's Next?



Delta, Omicron, and What's Next?

Source

US COVID-19 Four Waves Analysis (1/2)

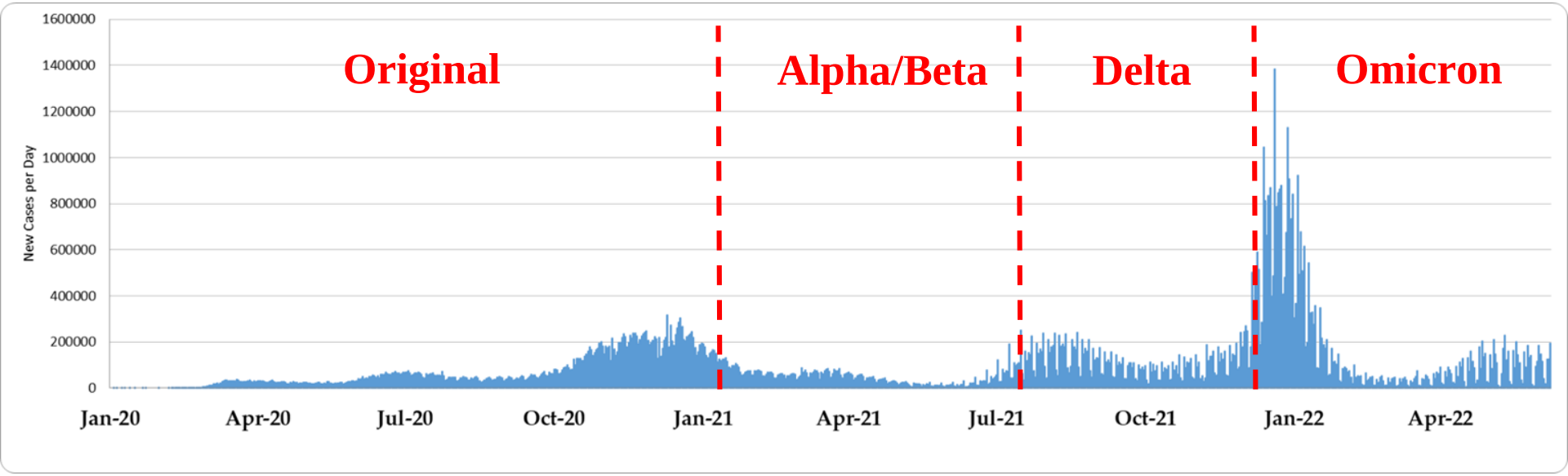


	Original 1/22/2020-2/28/2021	Alpha/Beta 3/1/2021-7/15/2021	Delta 7/16/2021-12/14/2021	Omicron 12/15/2021-present
Hospitalization %	4.46%	1.12%	2.83%	2.92%
Total Deaths	512,047	93,155	197,203	214,710
CFR	1.78%	1.78%	1.60%	1.16%
Mortality Rate**	0.15%	0.03%	0.06%	0.06%

*Ro: according to JAMA.

Data Source: Owid; Variant Period: CDC

US COVID-19 Four Waves Analysis (2/2)



	Original 1/22/2020-2/28/2021	Alpha/Beta 3/1/2021-7/15/2021	Delta 7/16/2021-12/14/2021	Omicron 12/15/2021-present
Total Cases	28,747,351	5,312,301	16,179,107	37,216,906
Incidence Rate*	8.64%	1.60%	4.86%	11.18%
Ro*	2.5	3-4	5-7	10
Full Vax %	9.00%	50.22%	62.05%	67.24%

*Incident Rate: Total cases/ total population
**Mortality Rate: Total deaths/ total population

Data Source: Owid; Variant Period: CDC

Four Waves Analysis Summary

- **Original wave has highest severity , and Omicron has highest infectivity**

(CDC, 1/28/2022)

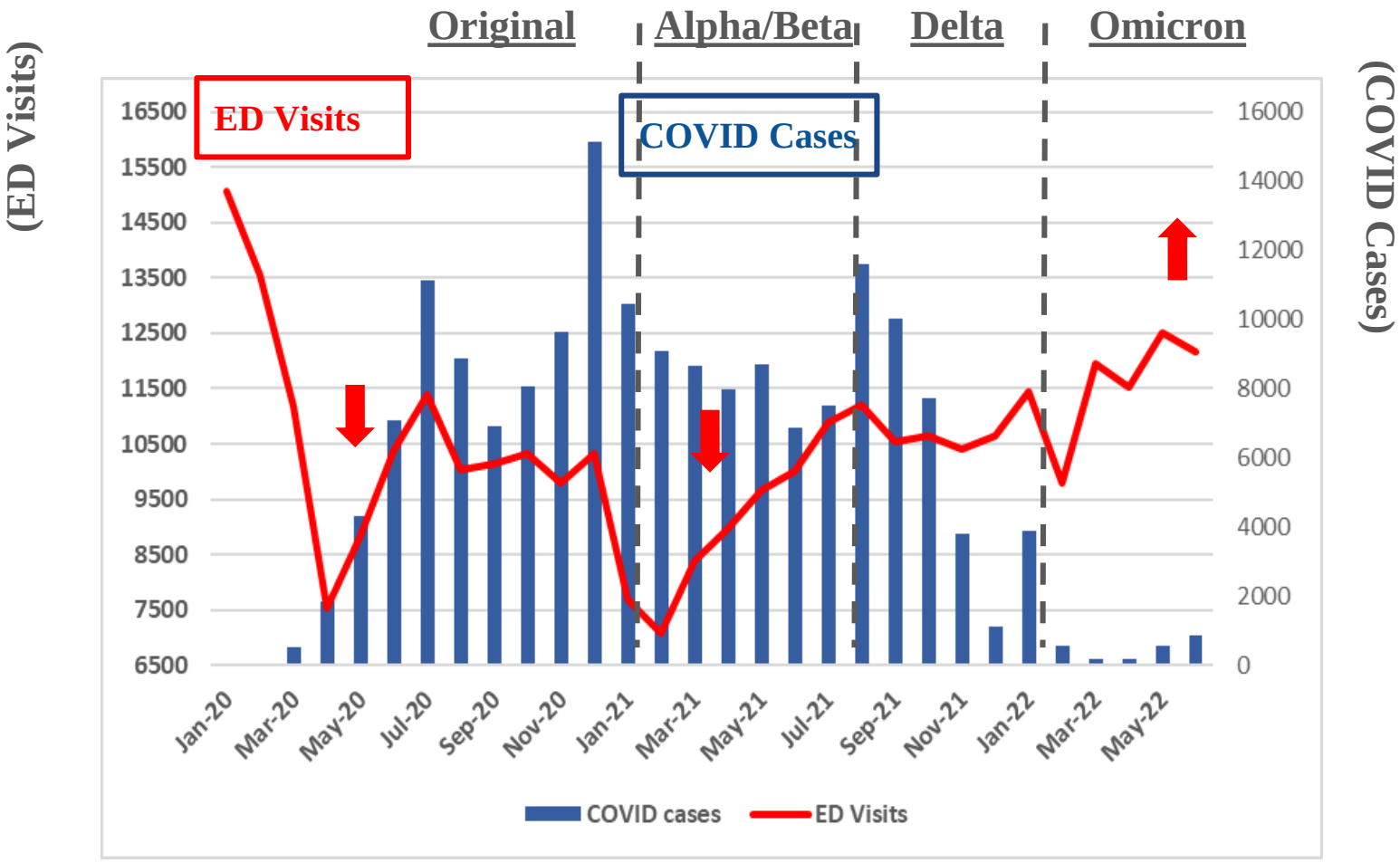
- **CDC has defined 4 waves:**
  - **Original (Wuhan) strain (1/22/2020-2/28/2021)**
  - **Alpha/Beta strain (3/1/2021-7/15/2021)**
  - **Delta strain (7/16/2021-12/14/2021)**
  - **Omicron strain (12/15/2021-present)**
- **Original wave - highest in total deaths, mortality rate, hospitalization rate, and CFR (highest severity)**
- **Omicron wave - highest in total cases, incidence rate, and Ro (highest infectivity)**
- **Fully vaccinated rate has reached 67.15% during the Omicron wave, which has impacted severity.**

Data Source: CDC

ED Visits During COVID of AHMC

- **ED visits declined for the original and Alpha waves at AHMC**
- **But ED visits increased for the Omicron wave (Boiling frog)**

(AHMC; 7/27/22)



Source: AHMC

CDC and WHO Tracker of Variants

- The only VOC listed in WHO and CDC is Omicron now

(CDC; WHO, 7/27/2022)

	CDC	WHO
Variants of Interest (VOI)	**None**	**None**
Variants of Concern (VOC)	**Omicron (B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5 lineages)**	**Omicron (B.1.1.529, BA.4, BA.5, BA.2.9.1, BA.2.11, BA.2.13)**
Variant of High Consequence (VOHC)	**None**	**None**
CDC: Variants Being Monitored (VBM) WHO: Previously Circulating Variants of Interest (VOI)	**Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), Epsilon (B.1.427, B.1.429), Eta (B.1.525), Iota (B.1.526), Kappa (B.1.617.1), Zeta (P.2), Mu (B.1.621, B.1.621.1)**	**Epsilon (B.1.427, B.1.429), Zeta (P.2), Eta (B.1.525), Theta (P.3), Iota (B.1.526), Kappa (B.1.617.1), Lambda (C.37), Mu (B.1.621)**

***BA.2.75 is still being monitored**

Source: CDC, WHO

New Variant BA.2.75: What We Know So Far

- **The new variant is being monitored, but isn't yet a VOI or VOC**

(Mayo Clinic, 7/28/2022; BioRxiv, 8/1/2022)

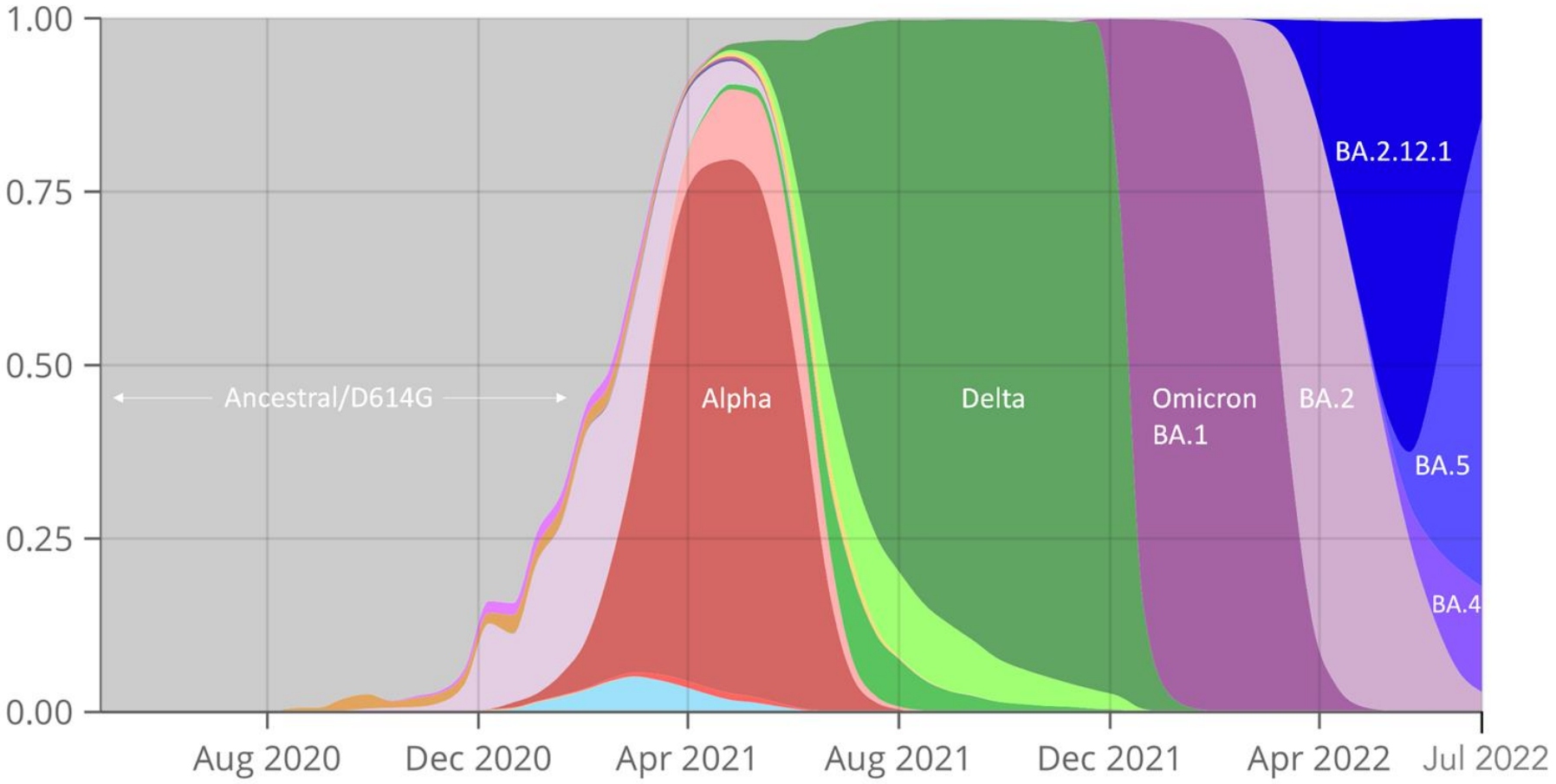
- **BA.2.75 was first detected in India in May, and is currently being monitored by WHO and CDC.**
- **A few cases have been reported in approximately 14 other countries, including the United States.**
- **What we know about BA.2.75:**
  - **More immune evasive than BA.2 (1.8-fold) and BA.2.12.1 (1.1-fold)**
  - **Not more immune evasive than BA.5/4 (0.6-fold)**
  - **More resistant to bebtelovimab (3.7-fold)**
  - **Potentially more infectious than other Omicron variants**
  - **Still unclear if it can compete with BA.5 globally**

Source: Mayo Clinic, BioRxiv

Trend of Variant Proportion in the US

- **Shifting from Ancestral to Omicron BA.5 due to infectivity and immune evasion**

(CoVariants, 7/28/2022)



Source: CoVariants

COVID-19 Variant Proportions in the US

- BA.5/BA.4 increased from 81% to 93.2% in two weeks

(CDC, 8/2/2022)

7/3/2022 – 7/9/2022	7/24/2022 – 7/30/2022

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	65.0%	62.2-67.7%
	BA.2.12.1	VOC	17.3%	15.7-19.0%
	BA.4	VOC	16.3%	14.5-18.3%
	BA.2	VOC	1.4%	1.3-1.6%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

BA.5: 65%
BA.4: 16.3%

81.3%

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	85.5%	83.8-87.0%
	BA.4	VOC	7.7%	7.0-8.5%
	BA.4.6	VOC	4.1%	3.2-5.4%
	BA.2.12.1	VOC	2.6%	2.4-2.8%
	BA.2	VOC	0.1%	0.1-0.1%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

BA.5: 85.5%
BA.4: 7.7%

93.2%

Source: CDC

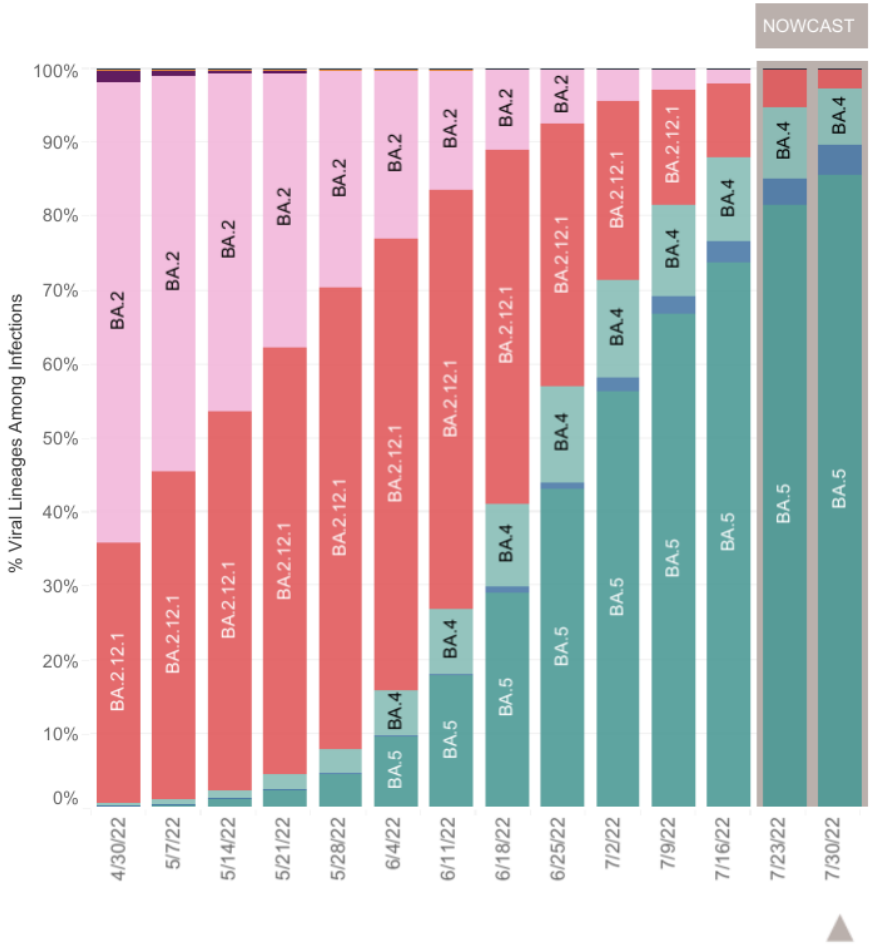
COVID-19 Variant Proportions in the US

- BA.5/BA.4 account for 93.2%

- New BA.4.6 accounts for 4.1%

(CDC, 8/2/2022)

United States: 4/24/2022 – 7/30/2022



United States: 7/24/2022 – 7/30/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	85.5%	83.8-87.0%
	BA.4	VOC	7.7%	7.0-8.5%
	BA.4.6	VOC	4.1%	3.2-5.4%
	BA.2.12.1	VOC	2.6%	2.4-2.8%
	BA.2	VOC	0.1%	0.1-0.1%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Sublineages of BA.5 are aggregated to BA.5.

Predominant Variant

BA.2.12.1: 2.6%

BA.5: 85.5%
BA.4: 7.7%

93.2%

BA.4.6: 4.1%

Source: CDC

BA.5 Second Highest in Confirmed Cases

- **The real number may be substantially higher due to case undercounts**

(Our World in Data, 8/1/2022)

Global Confirmed Cases (per million)

Omicron BA.5 Reinfection Risks

- 25% of new cases are reinfections in UK

- Multiple reinfections can increase risk of long COVID

(Johns Hopkins, 7/2/2022)

- **BA.5 is the most predominant variant in the US due to immunity evasion from previous infection or vaccination.**
- **In the UK, about 25% of new cases are reinfections.**
- **While BA.5 may not cause more severe disease in the acute phase, hospitalizations are rising and evidence suggests that multiple reinfections can increase the risk of long COVID and other morbidities.**

Source: Johns Hopkins

Because BA.5 and BA.4 Escape Antibodies, BA.1-Specific Booster May Not Be as Effective

(Nature, 6/17/2022)

- **Most cross-reactive neutralizing antibodies from BA.1 are escaped by BA.5/4 mutations (L452Q, L452R, and F486V).**
- **BA.1 infection can induce new clones of BA.1 antibodies, but these antibodies are escaped by BA.5/4.**
- **Results indicate that Omicron may evolve mutations to evade the humoral immunity elicited by BA.1 infection, suggesting that BA.1 boosters may not achieve broad-spectrum protection against new Omicron variants.**

Source: Nature

FDA Recommends Inclusion of Omicron BA.5 and BA.4 for Upcoming Vaccine Boosters

- New booster candidates may include BA.5/4

(FDA, 6/30/2022)

- **Preliminary Pfizer/Moderna Omicron boosters target only the original strain and BA.1, but provided 3-fold less protection against BA.5 and BA.4 compared to BA.1.**
- **So, FDA recommends that new boosters provide protection against circulating and emerging variants (BA.5/4).**
- **Both Pfizer and Moderna have said they are prepared to update their current candidates to include BA.5 and BA.4.**

Source: FDA, Pfizer

New Omicron Boosters Won't Need New Clinical Trials for Clearance

- FDA is fast tracking new booster development

(FDA, 7/1/2022)

- **Vaccine manufacturers won't need to conduct new clinical trials as they develop booster shots targeting BA.5/BA.4.**
- **FDA will use data from earlier clinical trials.**
- **FDA said that the next set of booster shots should be against the newest variants (BA.5/4) of the virus instead of just BA.1.**
- **Relying on existing data will let the FDA and vaccine makers have booster shots available sooner**

Source: FDA

Biden Administration Plans to Offer Updated Booster Shots in September

- **Expanding current 2nd booster eligibility scrapped**
- **Omicron boosters may be ready by mid-September**

(NYT, 7/28/2022)

- **FDA says those under 50 should wait to receive 2nd boosters.**
- **BA.5 boosters are expected to perform better against BA.5, although data is still preliminary.**
- **Officials at the FDA and CDC argued that the government should concentrate on the new boosters, as both Pfizer and Moderna have assured that they could deliver millions of doses by mid-September.**

Source: NYT

Q&A: BA.5 & Reinfection (1/3)

(ONS, 7/29/2022; BMJ, 7/27/2022; ZOE, 6/15/2022; Nature, 6/9/2022)

Q1. Are there any symptomatic differences for BA.5 infection?

Cough (>50%), sore throat (>45%), fatigue (>40%), fever (>30%), and muscle aches (>30%) are among the most common. Less than 20% have reported loss of smell and taste or 'brain fog' since Omicron began.

Q2. For anosmia, has long-term persistence changed with BA.5?

Persistent anosmia (loss of smell and taste) has reduced to less than 5% for all Omicron, which is lower than other variants.

Q3. Has symptomatic duration changed with BA.5?

BA.5 symptomatic duration is shorter for all Omicron (6.9 days) versus pre-Omicron (8.9 days).

Source: ONS, BMJ, ZOE, Nature

Q&A: BA.5 & Reinfection (2/3)

(MedRxiv, 7/25/2022; SSRN 7/18/2022; CDC, 8/1/2022; HHS, 8/1/2022; MedRxiv, 7/12/2022)

Q4. Is BA.5 less severe compared to previous Omicron subvariants?

Studies from Portugal and Denmark suggest that BA.5 may pose a greater risk of hospitalization compared to BA.2 (77% reduction for BA.5 vs. 93% reduction for BA.2 in vaccinated/boosted).

Q5. Will BA.5's death toll reach BA.1 levels?

With BA.5 predominating, ICUs have remained at low capacity (about 6%). Compared to BA.1, the BA.5 daily death toll is much lower (2,700 vs. 440).

Q6. Is reinfection more common with BA.5?

A Qatar study suggests those with non-Omicron prior infection have only about 15% protection against BA.5 reinfection. If the prior infection was Omicron-related, that estimate rises to 76%.

Source: MedRxiv, SSRN, CDC, HHS, MedRxiv

Q&A: BA.5 & Reinfection (3/3)

(NEJM, 7/20/2022; Research Square, 6/17/2022; Nature, 7/26/2022)

Q7. What treatment options are still effective against BA.5?

A recent study from NEJM found that nirmatrelvir (Paxlovid), molnupiravir, remdesivir, and bebtelovimab still work against BA.5.

Q8: Are there any long-term risks with BA.5 reinfections?

A recent Nature preprint concluded that 2 or more reinfections may double the risk (Reinfection HR: 1st = 1.35, 2nd = 2.11, 3rd = 3.00) for morbidity, hospitalization, and all-cause mortality.

Q9. What is the most effective way to detect a BA.5 infection?

For BA.5, a recent Nature article suggests that using rapid antigen tests may be preferable to detect if someone is infectious or not, as PCR tests can show positive results even after someone is no longer infectious.

Source: NEJM, Research Square, Nature

Detecting Infectiousness: PCR and Antigen

- **Rapid antigen tests more useful for detecting infectiousness**

(Nature; 7/26/2022; NEJM, 7/21/2022; Albert Ko, MD, 8/1/2022; Annals of Internal Medicine, 1/19/2022)

- **PCR tests are useful as a confirmatory test to see if you are sick with COVID, but are not useful to determine whether you are infectious to others.**
- **PCR tests can return positive results beyond the period of infectiousness, as they may pick up non-infectious remnants left behind after most of the live virus has been eliminated.**
- **In contrast, rapid antigen tests offer a better guide to infectiousness because they detect proteins produced by actively replicating virus.**

Source: Nature, NEJM, Annals of Internal Medicine, Albert Ko, MD

Efficacy of Monoclonal Antibodies and Antiviral Drugs Against BA.5

- **Nirmatrelvir (Paxlovid), molnupiravir, remdesivir, and bebtelovimab still work against BA.5**

(NEJM, 7/20/2022)

Monoclonal Antibodies (vs. BA.5)	Neutralizing Activity Reduction (lower is better)	Antiviral Drugs (vs. BA.5)	Virus Susceptibility (higher is better)
Imdevimab	588.4	Remdesivir	2.0
Casirivimab	>50,000	Molnupiravir	4.1
Tixagevimab	>50,000	Nirmatrelvir (Paxlovid)	4.4
Cilgavimab	56.8		
Sotrovimab	>50,000		
Bebtelovimab	3.3		

Source: NEJM

BA.5 Reinfection Risk, Hospitalization, and Vaccine Protection Compared with BA.2

- **Risk of hospitalization is greater with BA.5 vs. BA.2**
- **Prior Omicron infection with 3 doses offers protection against BA.5**

(medRxiv, 7/25/2022; SSRN, 7/18/2022)

1. Portugal study*

- **The protection against reinfection was lower in BA.5 cases when compared with BA.2 (OR=1.44)**
- **Of those infected with BA.5, booster vaccination was associated with 77% (hospitalization) and 88% (deaths) reduction, while higher risk reduction was found for BA.2 at 93% (hospitalization) and 94% (deaths)**

2. Denmark study*

- **There is high protection against BA.5 from prior Omicron infection in triple-vaccinated individuals, and similar vaccine effectiveness for BA.5 infection as BA.2**

***Portugal study with 27,702 collected samples; 4/25-6/10, 2022**

***Denmark study with 4,809 BA.5 cases and 164,369 test-negative individuals; 4/10-6/20/2022**

Source: medRxiv, SSRN

3. New Cases and Vaccines

Me tryna find my 14th booster pass for the Omicron Variant so I can buy a sandwich. (Winter 2025)

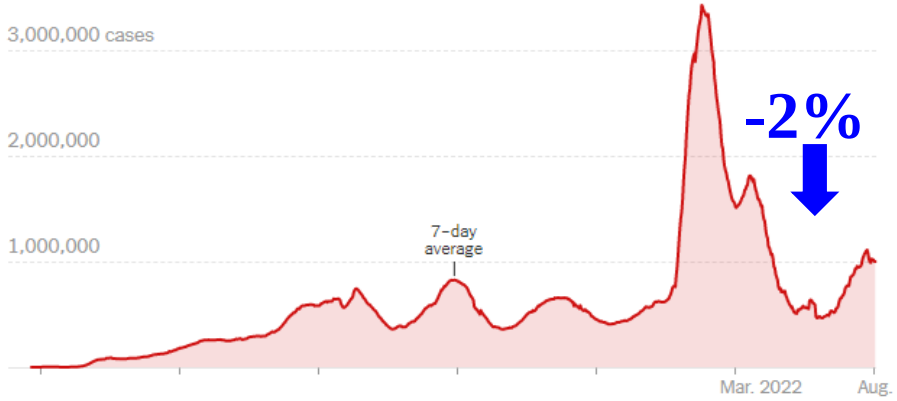
Source

Global New Cases and Deaths 14 Days Changes

-Over 12 billion vaccine doses have been administered worldwide, including more than 2 billion booster or additional doses.

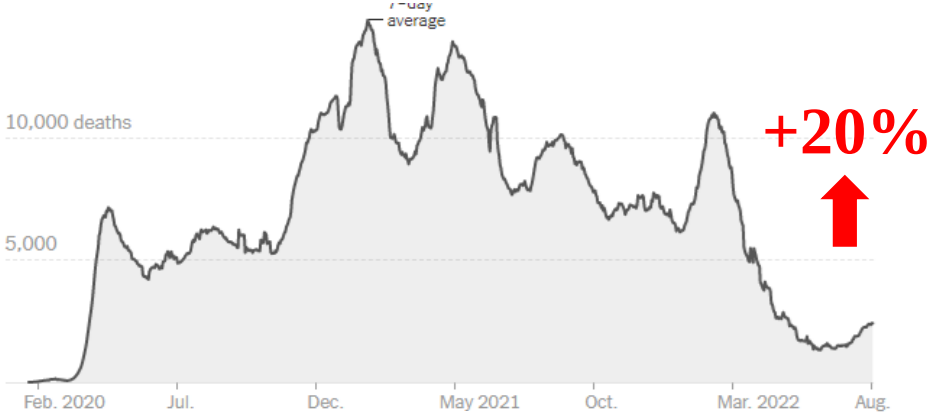
(NYT, 8/3/2022)

Cases



-2%

Deaths



+20%

Full Vaccination Rate

61.6%

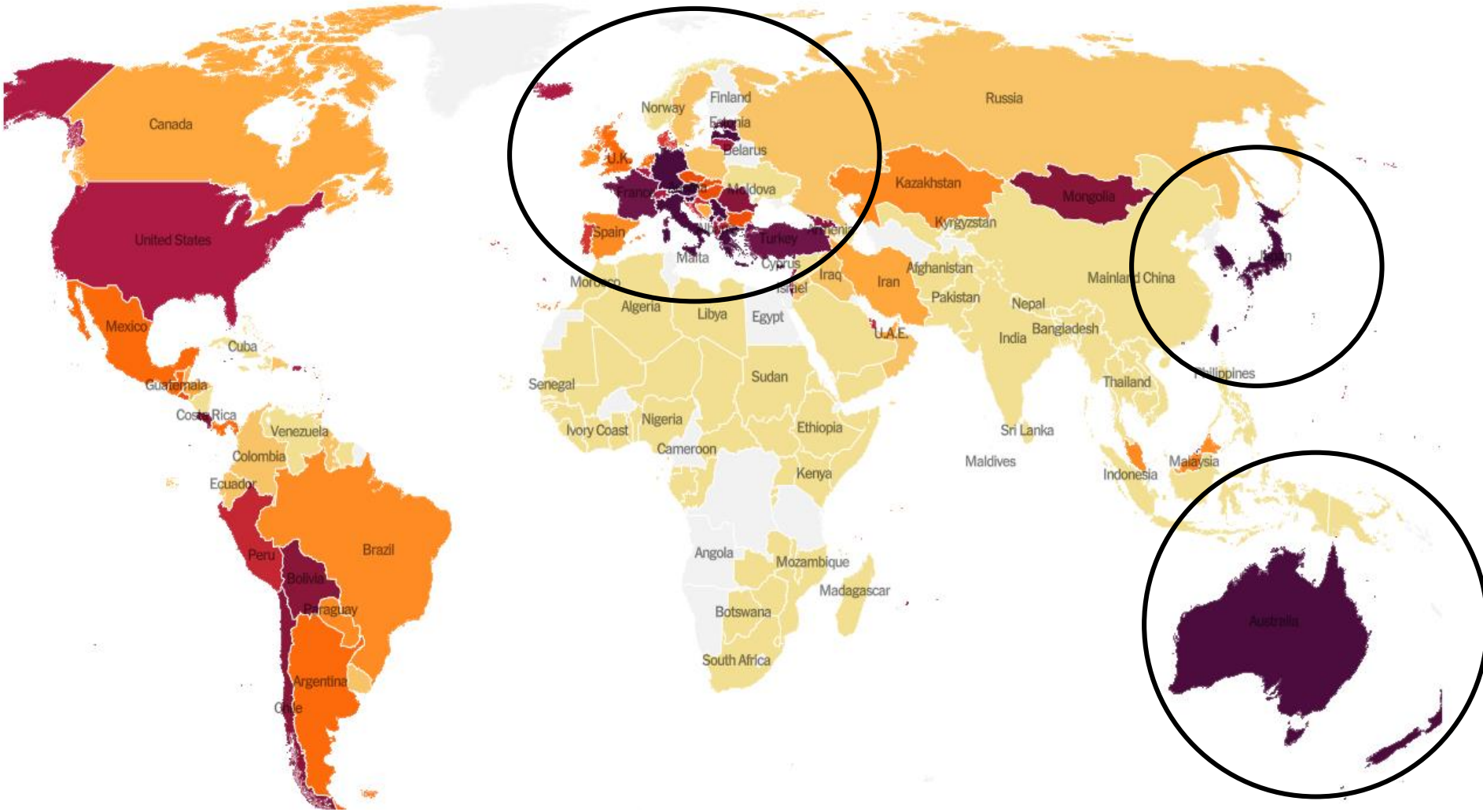
(Booster: 28.76%)

Case Fatality Rate (CFR)

0.22%

Global COVID-19 Hotspots

(NYT, 8/3/2022)



Source: NYT

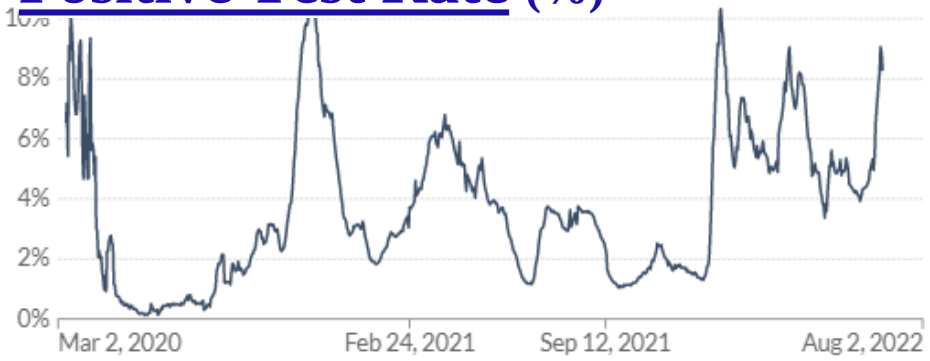
Current Trends in Greece

- New Cases: 360 cases/ 100,000
- Case Fatality Rate: 0.18%
- Fully Vaccinated: 73.08%
- Vaccine Booster Doses: 60.11%

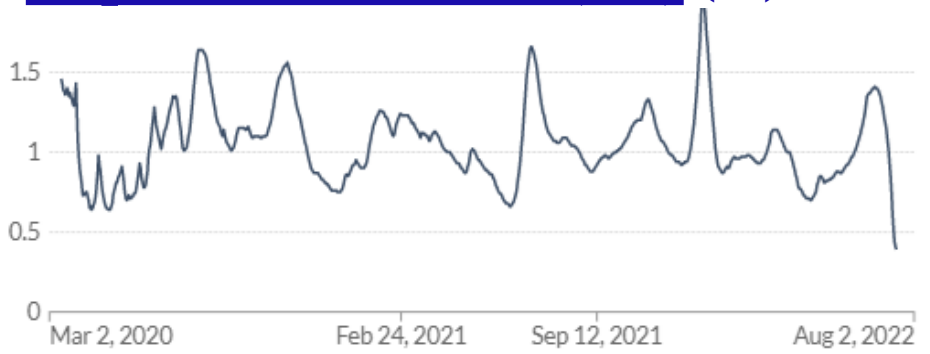
New Cases (per 1M)

New Deaths (per 1M)

Positive Test Rate (%)



Reproduction Rate (Ro) (%)



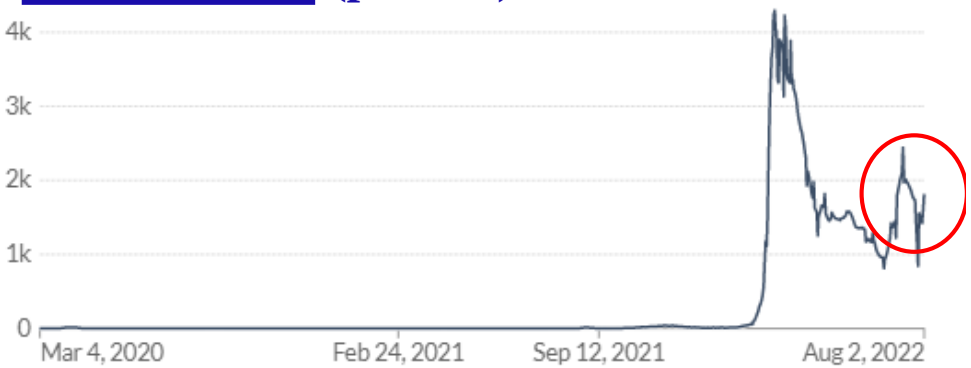
(Our World in Data, 8/3/2022)

Source: Our World in Data, NYT

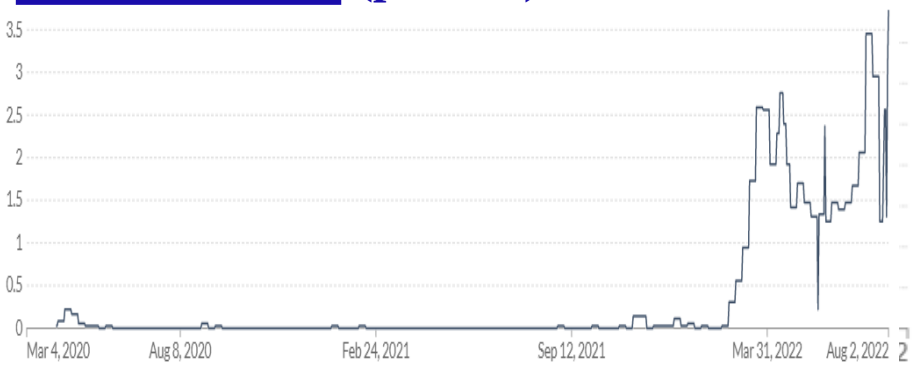
Current Trends in New Zealand

- New Cases: 182 cases/ 100,000
- Case Fatality Rate: 0.21%
- Fully Vaccinated: 80.46%
- Vaccine Booster Doses: 59.99%

New Cases (per 1M)



New Deaths (per 1M)



Reproduction Rate (Ro) (%)

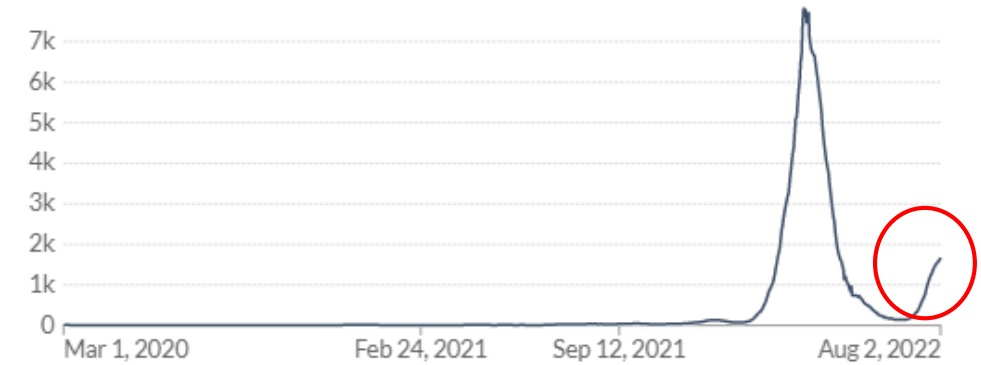
(Our World in Data, 8/3/2022)

Source: Our World in Data, NYT

Current Trends in South Korea

- New Cases: 167 cases/ 100,000
- Case Fatality Rate: 0.04%
- Fully Vaccinated: 86.15%
- Vaccine Booster Doses: 75.76%

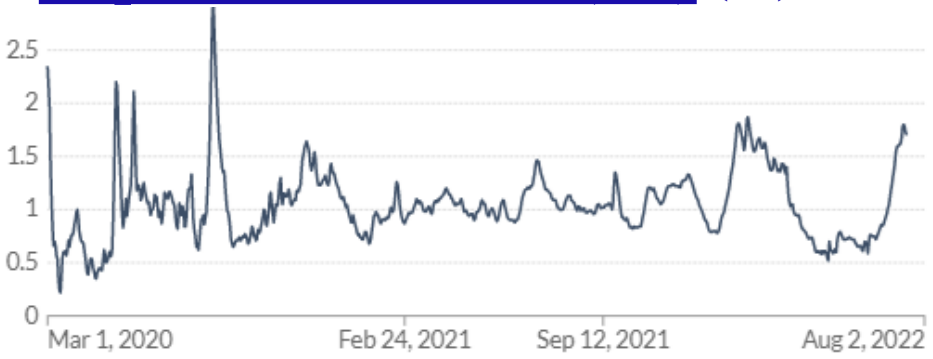
New Cases (per 1M)



New Deaths (per 1M)

Positive Test Rate (%)

Reproduction Rate (Ro) (%)



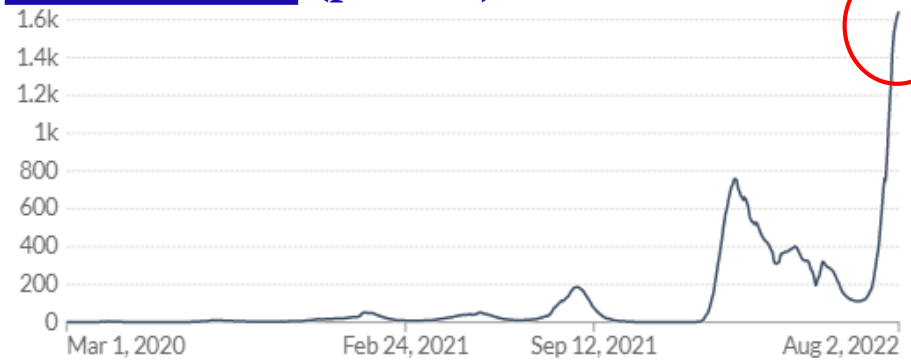
(Our World in Data, 8/3/2022)

Source: Our World in Data, NYT

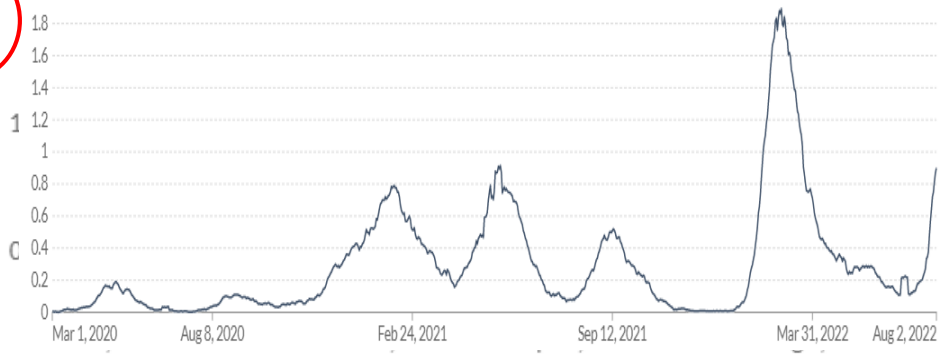
Current Trends in Japan

- New Cases: 164 cases/ 100,000
- Case Fatality Rate: 0.08%
- Fully Vaccinated: 82.27%
- Vaccine Booster Doses: 74.06%

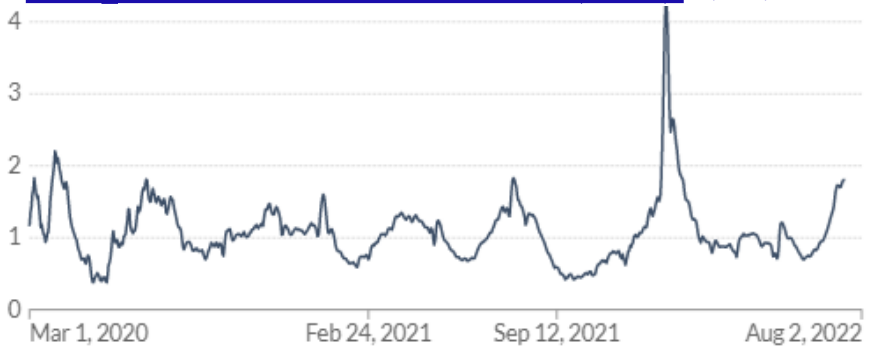
New Cases (per 1M)



New Deaths (per 1M)



Reproduction Rate (Ro) (%)



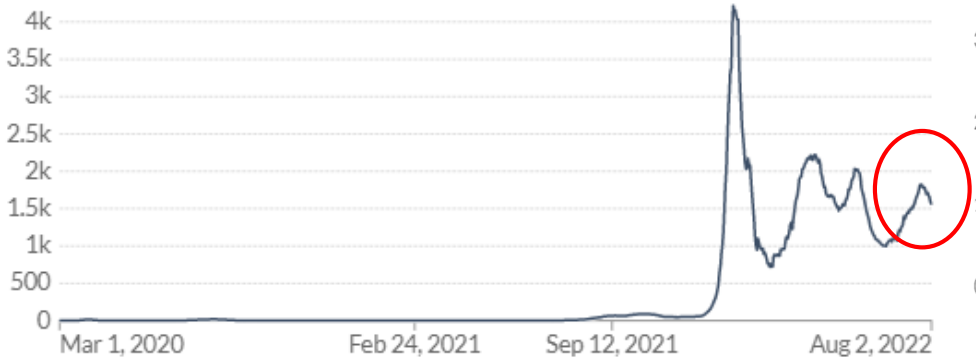
(Our World in Data, 8/3/2022)

Source: Our World in Data, NYT

Current Trends in Australia

- New Cases: 155 cases/ 100,000
- Case Fatality Rate: 0.19%
- Fully Vaccinated: 83.85%
- Vaccine Booster Doses: 54.44%

New Cases (per 1M)



New Deaths (per 1M)

Positive Test Rate (%)

Reproduction Rate (Ro) (%)

(Our World in Data, 8/3/2022)

Source: Our World in Data, NYT

Current Trends in Singapore

- New Cases: 134 cases/ 100,000
- Case Fatality Rate: 0.06%
- Fully Vaccinated: 91.68%
- Vaccine Booster Doses: 77.95%

New Cases (per 1M)

New Deaths (per 1M)

Positive Test Rate (%)

Reproduction Rate (Ro) (%)

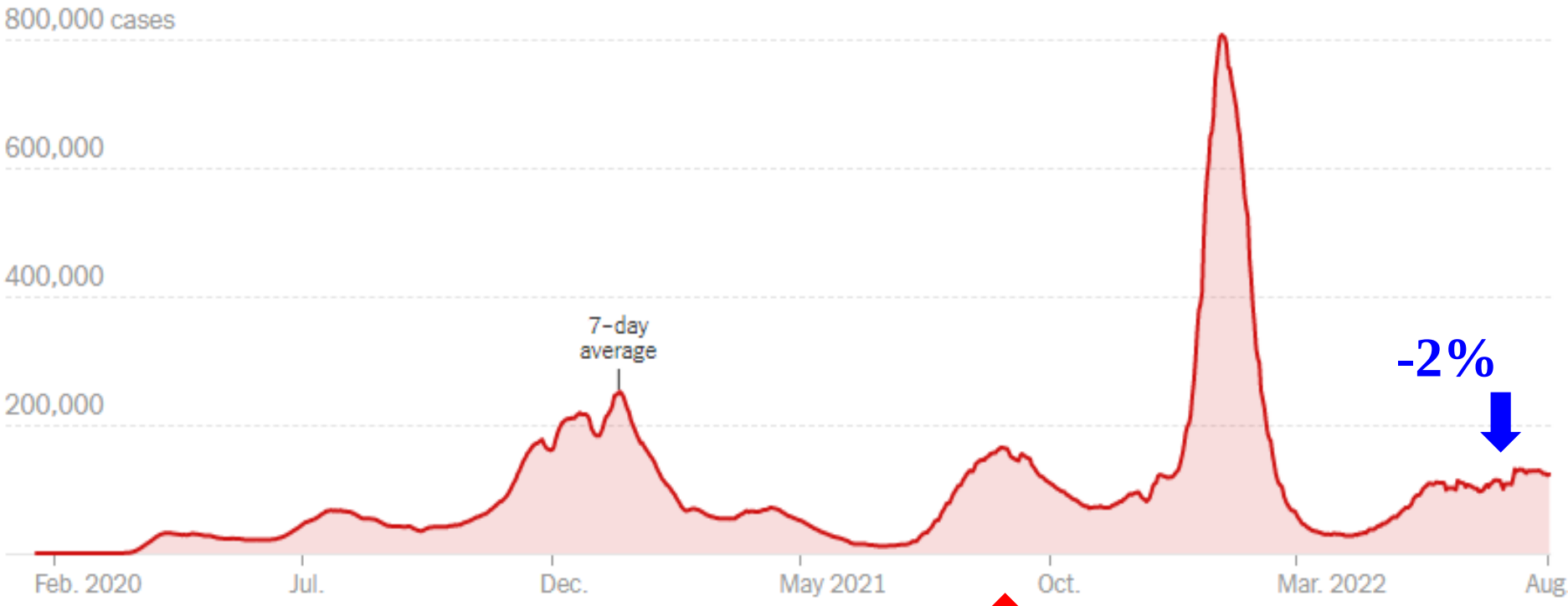
(Our World in Data, 8/3/2022)

Source: Our World in Data, NYT

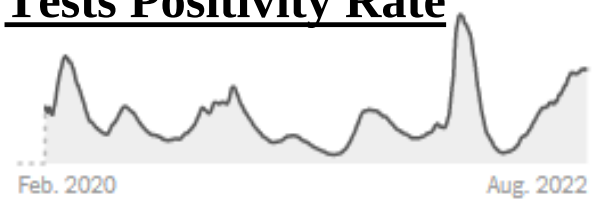
US Trend and 14-Day Change

(NYT, 8/3/2022)

Cases

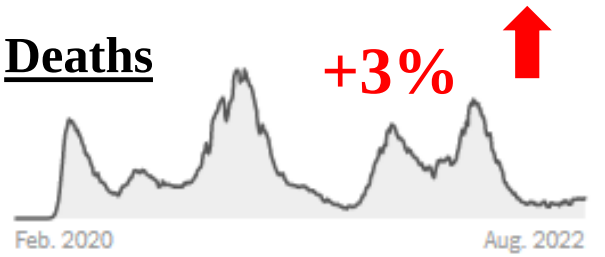


Tests Positivity Rate



Hospitalizations +4%

Deaths +3%



Source: NYT

Top 10 US States with Highest Daily New Cases

(NYT, 8/3/2022)

#	States	Daily New Cases	Test Positivity	Fully Vaccinated	14 Days Change
1	California	16,617	16%	73%	-22% ↓
2	Texas	11,614	29%	63%	-4% ↓
3	Florida	10,279	23%	68%	-7% ↓
4	New York	6,650	13%	78%	-10% ↓
5	North Carolina	4,828	24%	63%	29% ↑
6	Illinois	4,430	13%	69%	3% ↑
7	Ohio	4,268	18%	59%	22% ↑
8	Georgia	4,017	25%	56%	88% ↑
9	New Jersey	3,576	13%	77%	-1% ↓
10	Pennsylvania	3,528	16%	70%	25% ↑

Source: NYT (Cases); NYT (Vaccines)

Hospital Utilizations in the US

- **6.25% inpatient beds and 6.65% ICU beds in use for COVID**

(HHS, 8/3/2022)

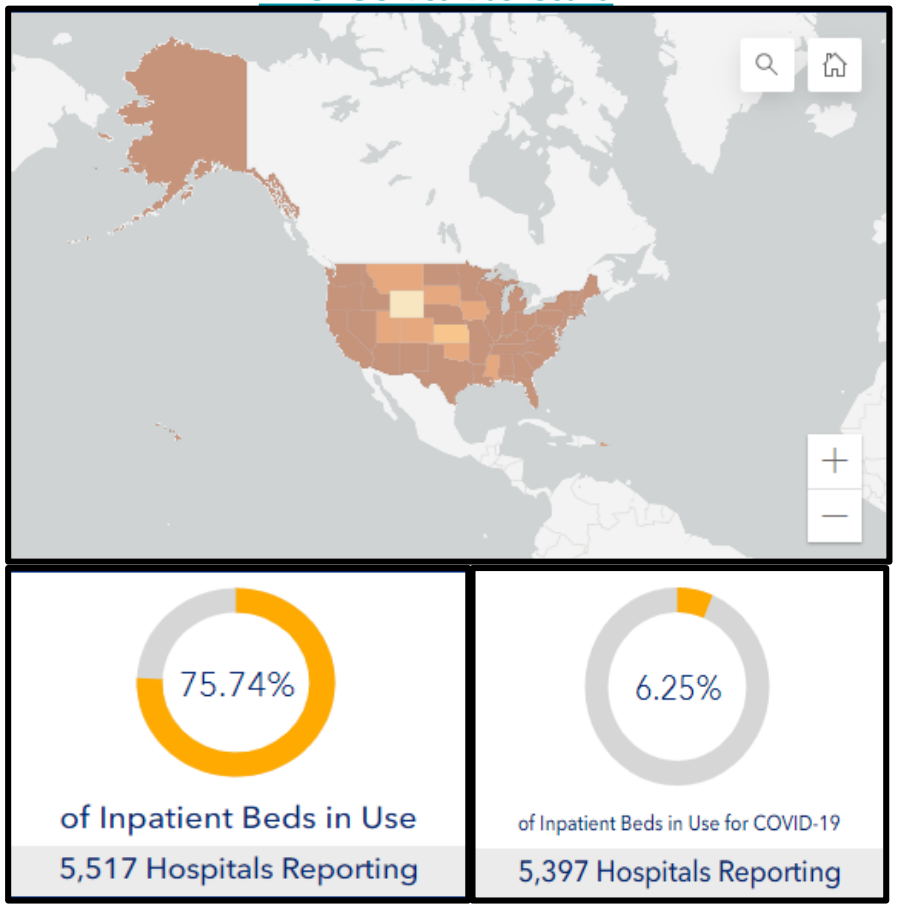
ICU Bed Use

- **71.59% ICU beds in use**
  (5,516 Hospitals Reporting)
- **6.65% ICU beds in use for COVID-19 (7/15: 6.02%)**
  (5,396 Hospitals Reporting)

Inpatient Bed Use

- **75.74% inpatient beds in use**
  (5,517 Hospitals Reporting)
- **6.25% Inpatient beds in use for COVID-19 (7/15: 5.49%)**
  (5,397 Hospitals Reporting)

HHS ICU Bed Dashboard

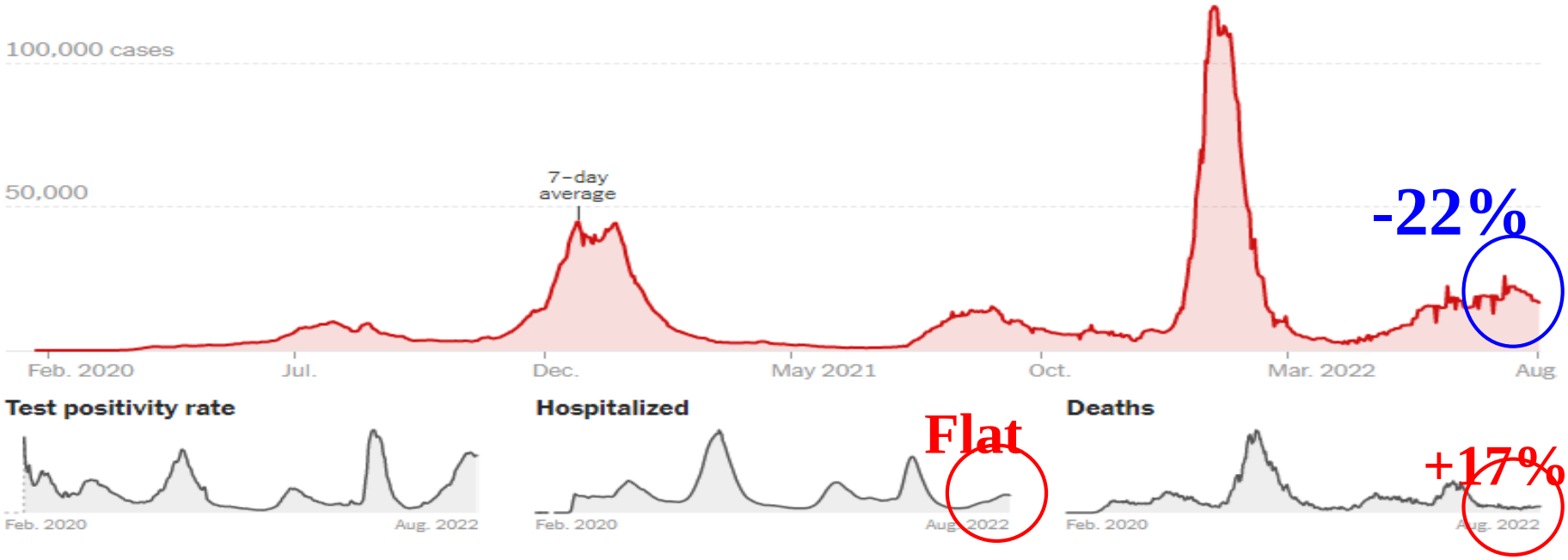


Source: HHS

California New Cases Trend

- Decrease in cases (22%) amd increase in death (17%) in the past 14 days

(NYT, 8/3/2022)



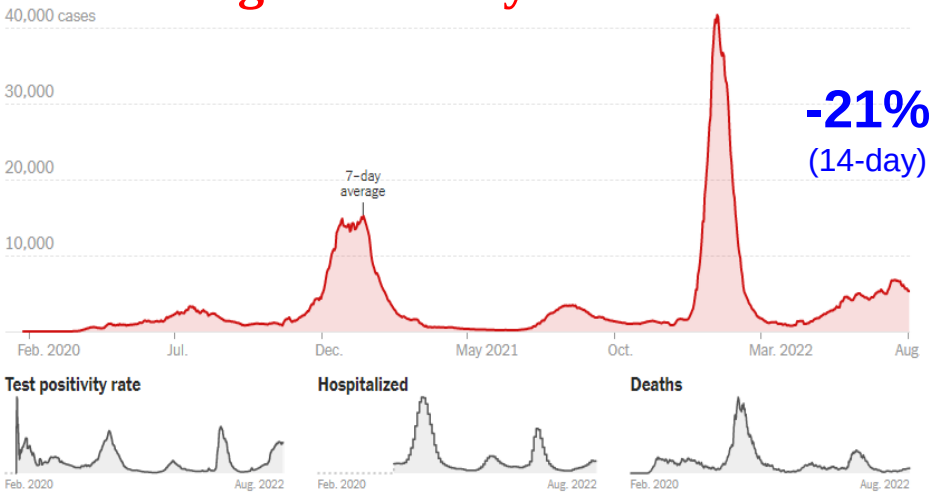
	DAILY AVG. ON AUG. 2	14-DAY CHANGE	TOTAL REPORTED
Cases	16,617	−22%	10,757,986
Test positivity	16%	—	—
Hospitalized	5,012	Flat	—
In I.C.U.s	535	+7%	—
Deaths	42	+17%	93,734

Source: NYT

90-Day County Trends in AHMC Service Area

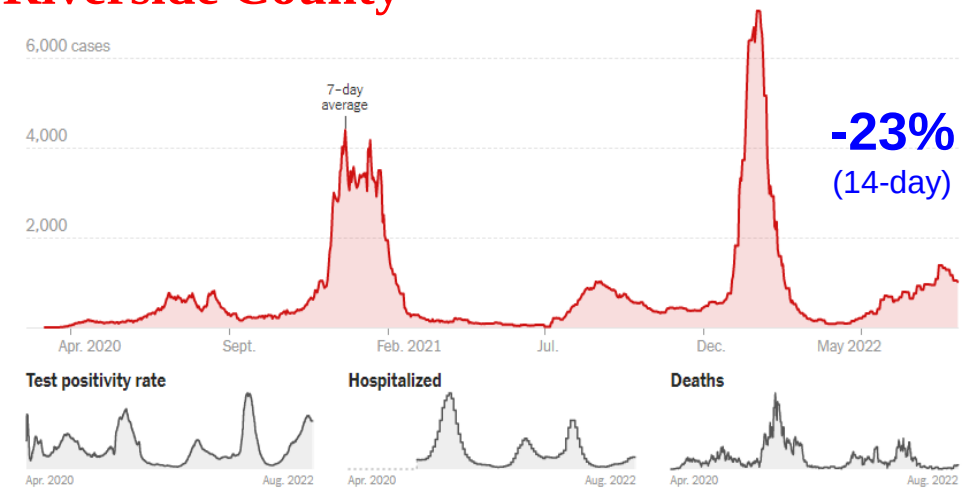
(NYT, 8/3/2022)

Los Angeles County



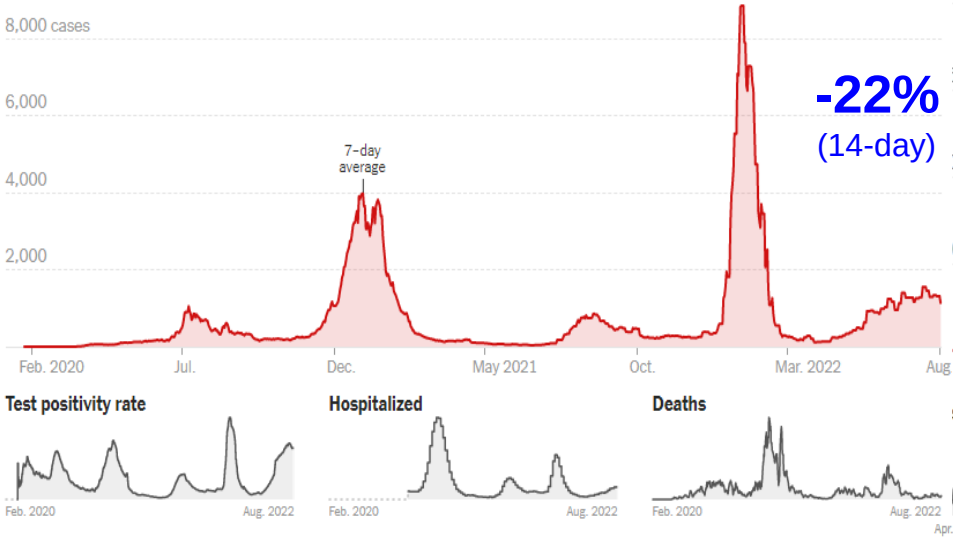
-21%
(14-day)

Riverside County



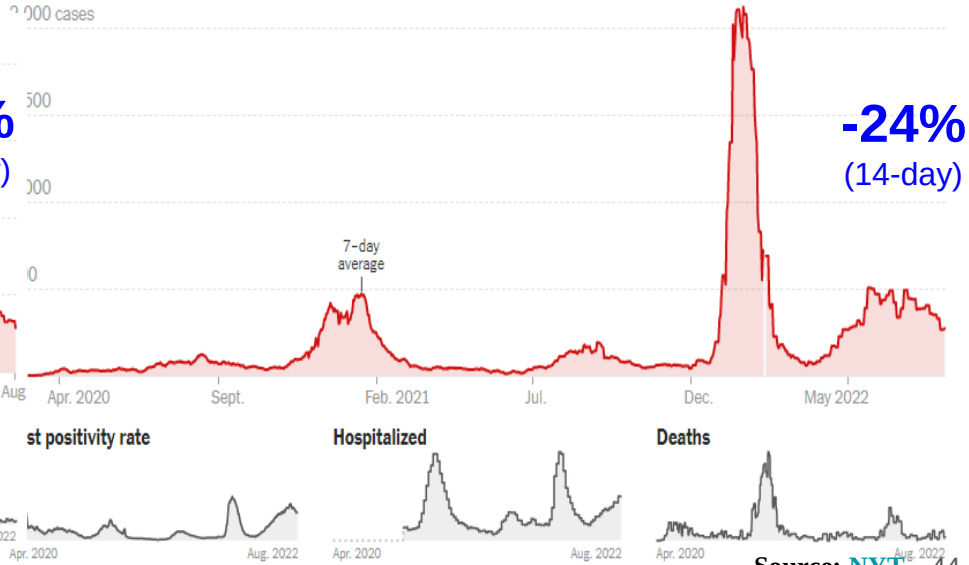
-23%
(14-day)

Orange County



-22%
(14-day)

San Mateo County

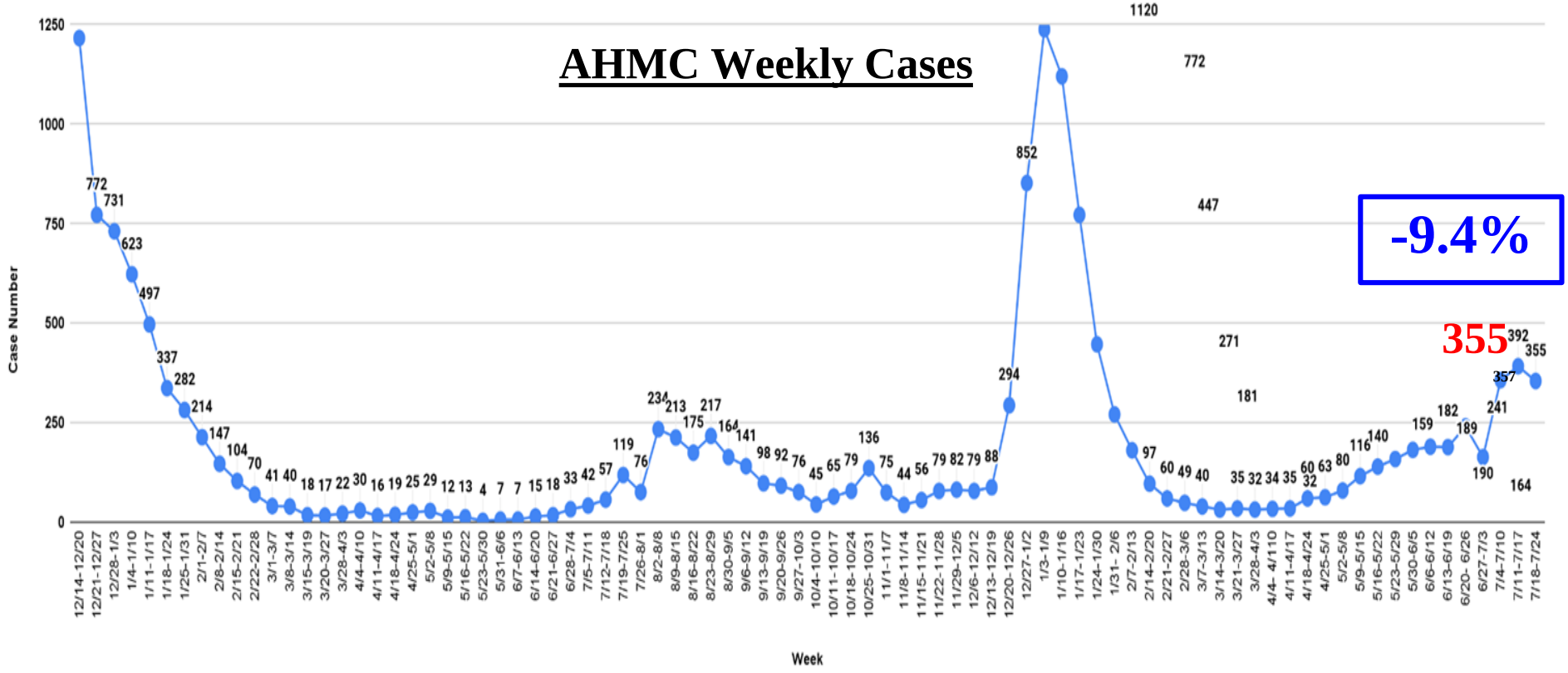


-24%
(14-day)

Source: NYT

AHMC Weekly Cases

(Data as of 8/2/2022)



Approved/EUA COVID-19 Vaccines

- Novavax received EUA on July 13, 2022

(CDC, 7/14/2022)

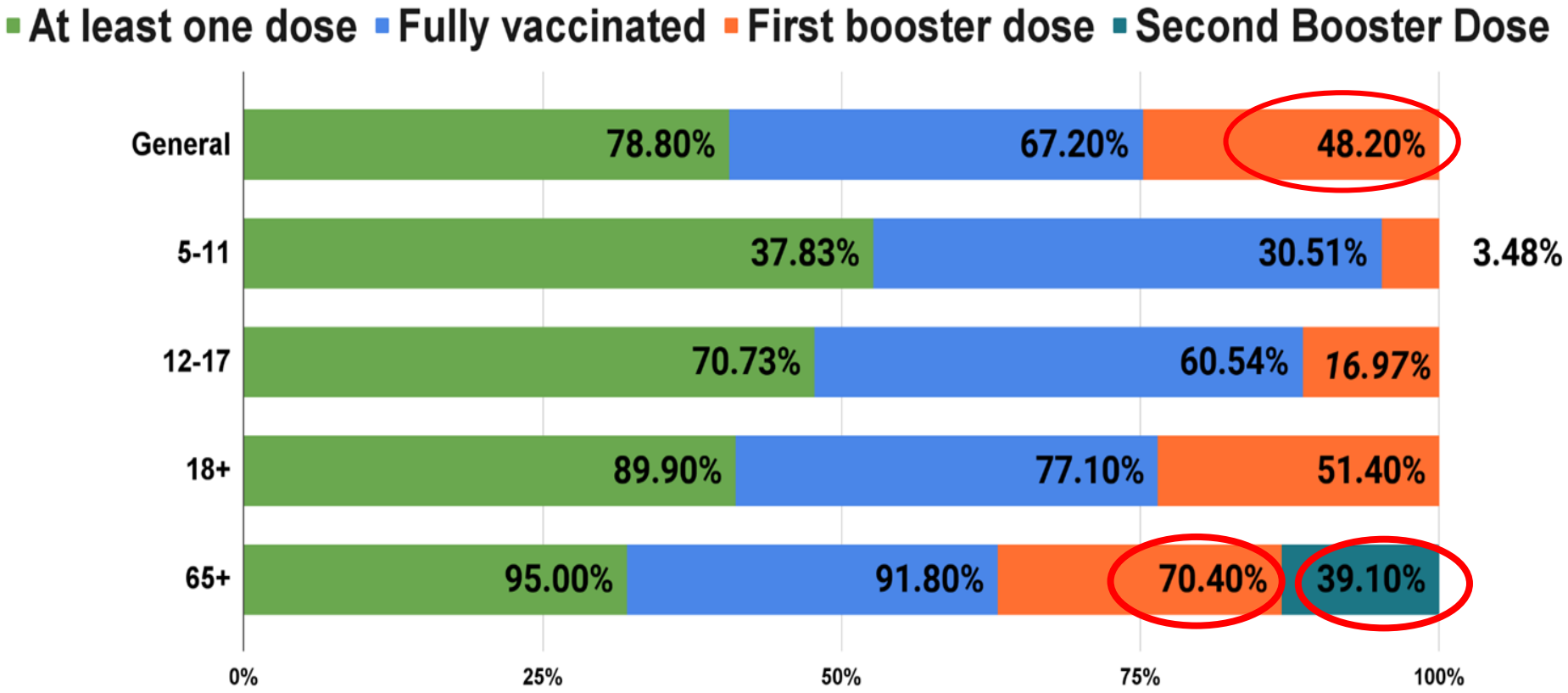
	Pfizer (mRNA)	Moderna (mRNA)	Janssen (Modified cold virus)	Novavax (Stabilized form of spike protein)
First Approved	Aug 23, 2021	Dec 18, 2021	Feb 27, 2021	Jul 13, 2022
6 mos-4 yrs (Pfizer) 6 mos-5 yrs (Moderna)	YES	YES	No	No
5-11 years (Pfizer) 6-11 years (Moderna)	YES	YES	No	No
12-17 years	YES	YES	No	No
18+ years	YES	YES	YES	YES
1 Booster	• Everyone age 5 years and older		No	No
2 Boosters	• Adults ages 50 years and older • People ages 12 years and older who are moderately or severely immunocompromised		No	No

CDC; WebMD

COVID-19 Vaccinations in the US

- 1st booster uptake is 48.2% for all and 70.4% in 65+ y/o
- 2nd booster uptake is 39.1% in 65+ y/o

(CDC, 8/4/2022)

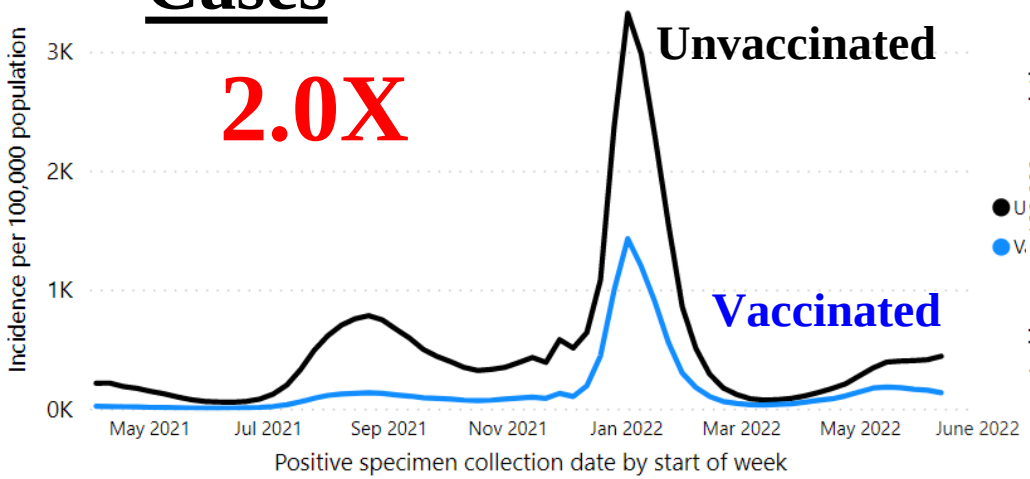


Source: CDC

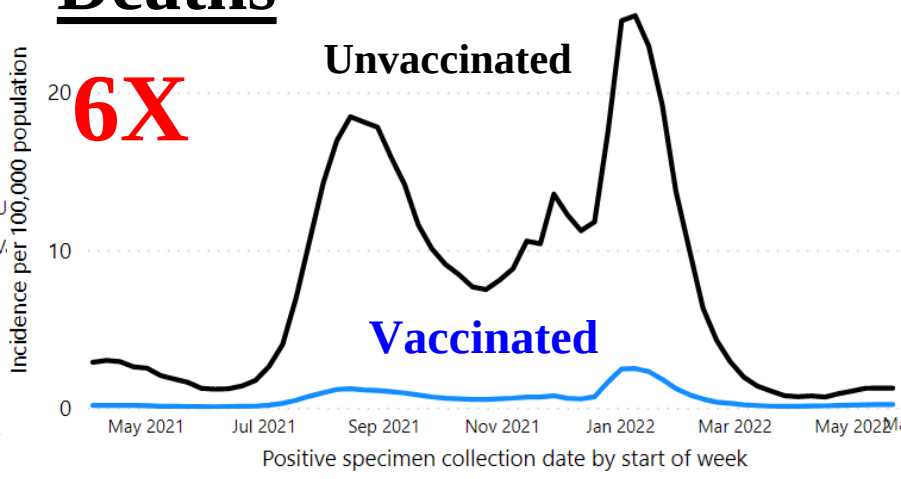
Rates of Case, Death, and Hospitalization by Vaccination Status

(CDC, 8/3/2022)

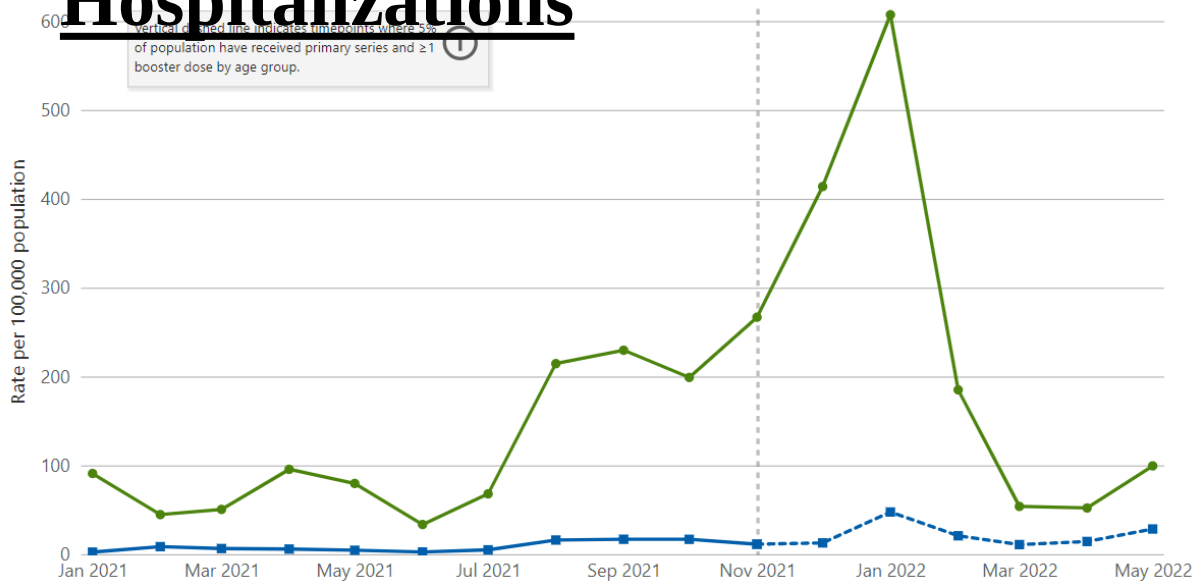
Cases



Deaths



Hospitalizations



Source: CDC

Effectiveness of 2, 3, or 4 Vaccine Doses Among Immunocompetent Adults

- **COVID vaccine efficacy waned as Omicron mutated**

(CDC MMWR, 7/15/2022)

mRNA Vaccine	Time	Dominant	Vaccine Effectiveness
1st or 2nd Doses	December 2021 - March 2022	BA.1	61%
	March 2022 - June 2022	BA.2 / BA.2.12.1	24%
3rd Dose	-	BA.1	92%
	-	BA.2.12.1	69%
4th doses	Late March 2022	BA.2 / BA.2.12.1	80%

Source: CDC

Novavax Vaccine

(CDC, 7/20/2022)

- **Clinical Trials: 90% efficacy***
- **Number of Shots: 2 doses in the primary series, given 3–8 weeks apart.**
- **People who are moderately or severely immunocompromised should also receive 2 doses, given 3 weeks apart.**
- **Booster Shot: Novavax COVID-19 vaccine is not authorized for use as a booster dose.**
- **Type of Vaccine: Protein subunit**
- **Does NOT Contain: Eggs, preservatives, latex, metals**

*** Clinical trials during pre-Omicron period**

The Types of COVID Vaccines and Other Vaccines

(HHS, 12/20/2021)

Other Vaccines	Other Diseases	COVID-19
Inactive vaccines	Hepatitis A, Flu, Polio	Sinopharm, Sinovac, COVAXIN
Live-attenuated vaccines	MMR, Rotavirus, Smallpox, Chickenpox, Yellow Fever	None
Messenger RNA (mRNA) vaccines	None	Pfizer-BNT, Moderna
Subunit, Recombinant Vaccines	Hepatitis B, Haemophilus influenzae type b, HPV, whooping cough, Pneumococcal disease, Meningococcal disease, Shingles	Novavax
Toxoid Vaccines	Diphtheria, Tetanus	None
Viral Vector Vaccines	Clinical trial: Zika, flu & HIV……	Janssen (J&J), Oxford-AstraZeneca (AZ)

Source: HHS

EMA Adding Anaphylaxis Warning Label for Novavax

- A few cases of anaphylaxis have been reported so far

(ContagionLive, 7/15/2022)

- **The EMA is adding a warning label on the Novavax vaccine for anaphylaxis, paraesthesia, and hypoaesthesia.**
- **Several cases of anaphylaxis have been reported spontaneously with use of Novavax.**
- **A total of 1094 cases of spontaneous side effects were reported from EU/EEA countries with zero fatalities. These side effects are not necessarily related to or caused by the vaccine**
- **According to the EMA, about 216,000 doses of Novavax vaccines had been administered in adults in the EU since June 26, 2022.**

Source: ContagionLive

5 Studies: Reduction in Mortality for a 4th Dose (vs. 3rd Dose) in Ages 50+ to 80+

- 4th dose shows much higher protection than 3rd dose

(NEJM, Nature, The Lancet, CDC, CID; 2022)

Place and Age Group	Protection of 4th Dose vs 3rd Dose	Variant Period	Source
Israel; Age 60+	74% vs. death 68% vs. hospitalization	Omicron B.1.1.529	NEJM; April 28, 2022
Israel; Age 60+	78% vs. death 64% vs. hospitalization	Omicron B.1.1.529	Nature; April 25, 2022
Sweden; Age 80+	60% reduced all-cause mortality	Omicron	The Lancet; July 13, 2022
United States; Age 50+	4-fold reduction in mortality	Omicron BA.2 and BA.2.12.1	CDC, 2022
Israel; Median Age 80	50% reduction need of ventilation or death	Omicron B.1.1.529	Clinical Infectious Diseases; June 20, 2022

Source: NEJM, Nature, The Lancet, CDC, Clinical Infectious Diseases

Pfizer Vaccine Effectiveness (VE) against Omicron in Children (5-11 y/o)

- 82.7% effective at preventing hospitalization

(NEJM, 7/20/22)

- **Study**
  - **A national cohort study from 1/21/2022 through 4/8/2022 (Omicron).**
  - **Analyzed data of 255,936 children (5-11 y/o) in Singapore.**
- **Results**
  - **Partially vaccinated children: VE was 13.6% against all infections, 24.3% against PCR-confirmed infection, and 42.3% against COVID hospitalization.**
  - **Fully vaccinated children: VE was 36.8% against all infections, 65.3% against PCR-confirmed infection, and 82.7% against COVID hospitalization.**

Source: NEJM

The Future of Vaccines

- 3 directions: bivalent, universal, nasal

(FDA, 6/30/2022; Wired, 7/26/22)

(1) Bivalent vaccines (Ancestral and BA. 4/5)

FDA have advised to add an Omicron BA.5/4 spike protein component to the current vaccine, to be used starting in early to mid-fall 2022.

(1) Universal vaccines (targeting all coronaviruses)

A vaccine that would target the entire coronavirus family, including merbecoviruses (MERS), embecoviruses (common colds), and sarbecoviruses (COVID and SARS).

Source: FDA, Wired

The Future of Vaccines

- **3 directions: bivalent, universal, nasal**
(NIH, 6/16/2022)

(3) Antiviral Nasal Sprays

- **NIAID have developed a nasal spray. It has the potential to treat and prevent COVID infection**
- **The researchers picked four compounds and tested in human lung and colon cells**
- **The most promising compound is N-0385. It stopped infection and was suitable for use as a nasal spray**
- **Intramuscular injections generate systemic immunity, but little or no immune response in the nose**

Source: NIH 1, 2

12 Nasal Spray Vaccines are in Development

- 4 nasal sprays are in phase 3 clinical trials

(The Scientist, June 2022)

- **Around the world, more than a dozen IN delivered COVID-19 vaccines have entered clinical trials, and they run from adenovirus-vectored genes for viral antigens to recombinant protein–based formulations to live attenuated SARS-CoV-2**

Bharat Biotech: BBV154	**Phase 2/3 trial**
Gamaleya National Center of Epidemiology and Microbiology: Sputnik V	**reported success of small clinical trials**
University of Hong Kong, Xiamen University, and Beijing Wantai Biological Pharmacy: DelNS1-2019-nCoV-RBD-OPT1	**Phase 3 trial**
Razi Vaccine and Serum Research Institute: Razi Cov Pars	**Phase 3 trial**
Codagenix: CoviLiv	**Phase 2/3 trial**
Center for Genetic Engineering and Biotechnology (CIGB): Mambisa	**Phase 1/2 trial**
Icahn School of Medicine at Mount Sinai: NDV-HXP-S	**Phase 2 trial**
CanSino Bio and Beijing Institute of Biotechnology: Convidecia	**Phase 1/2 trial**
AstraZeneca: Vaxzevria	**Phase 1 trial**
Meissa Vaccines: MV-014-212 (Spun off from work at Emory University)	**Phase 1 trial**
CyanVac: CVXGA1 (Spun off from work at the University of Georgia and the University of Iowa)	**Phase 1 trial**
Tetherex Pharmaceuticals: SC-Ad6-1	**Phase 1 trial**

The Scientist

4. Updates on Treatments and Studies

Source

Updated NIH Guidelines (1/2)
Therapeutic Management of Nonhospitalized Adults

(Updated 5/31/2022)

Does not Require Hospitalization or Supplemental Oxygen	• **Prefered Therapy (in order)**
	  ○ **Paxlovid (Ritonavir-boosted nirmatrelvir) (Alla)**
	  ○ **Remdesivir (Blla)**

	• **Alternative Therapy (only when preferred therapies are not available)**
	  ○ **Bebtelovimab (Clll)**
	  ○ **Molnupiravir (Clla)**

*** Sotrovimab is no longer authorized for use in US**

Source: NIH

Updated NIH Guidelines (2/2)
Therapeutic Management of Hospitalized Adults
(Updated 5/31/2022)

	Recommendations for Antiviral or Immunomodulator Therapy	Recommendations for Anticoagulation Therapy
Hospitalized but does not require supplemental oxygen	• Recommends against the use of dexamethasone (AIIa) or other corticosteroids • Insufficient evidence for routine use of remdesivir (may be appropriate for high risk pt)	For pts without evidence of VTE • Prophylactic dose of heparin, unless contraindicated (AI)
Hospitalized and requires supplemental oxygen	Remdesivir for pts who require minimal supplemental oxygen (BIIa) • Dexamethasone + Remdeivir (BIIb) • Dexamethasone (BI)	For non-pregnant pts with D-dimer level > ULN* who are not increased bleeding risk • Therapeutic dose of heparin (CIIa) For other pts • Prophylactic dose of heparin unless contraindicated (AI)

*ULN : upper limits of normal

Source: NIH

Paxlovid and Severe COVID Outcomes During the Omicron Surge

- **67% reduction in hospitalization; 81% reduction in mortality**

(Research Square, 6/1/22)

- **Earlier Pfizer clinical trials showed the effectiveness of Paxlovid against Delta, but not Omicron.**
- **Israel study: Participants were age ≥40, with confirmed Omicron infection, and considered at high-risk for progression.**
- **Paxlovid had a 67% reduction in hospitalizations and an 81% reduction in mortality in patients ≥65 years.**
- **No significant benefit in avoidance of severe outcomes was shown in younger adults.**

Source: Research Square

FDA Authorizes Pharmacists to Prescribe Paxlovid

(JAMA, 7/19/2022)

- **The FDA revised the EUA for Paxlovid, allowing state-licensed pharmacists to prescribe the medication.**
- **The revision was made to allow for expanded access to timely treatment for patients.**
- **Physicians, advanced practice registered nurses(NP), physician assistants(PA), and pharmacists are now all authorized to prescribe Paxlovid.**

Source: JAMA

Both Biden and Fauci Had Paxlovid Rebound

Biden tested positive on July 21st. After completing a five-day course of Paxlovid, he tested negative for COVID-19 after 5 days, then tested positive again on July 30th (4th day).

After finishing a 5-day course of Paxlovid, Fauci tested negative on antigen tests for 3 days in a row. On the 4th day, he reverted back to positive.

Source: Statnews, abc news

COVID-19 Rebound Rate after Paxlovid and Molnupiravir during January-June 2022

(medRxiv, 6/21/2022)

- **Paxlovid Rebound Rates:**

Rebound Rates	Infection	COVID-19 Symptoms	Hospitalization
7-day	3.53%	2.31%	0.44%
30-day	5.40%	5.87%	0.77%

- **Molnupiravir Rebound Rates:**

Rebound Rates	Infection	COVID-19 Symptoms	Hospitalization
7-day	5.86%	3.75%	0.84%
30-day	8.59%	8.21%	1.39%

Source: medRxiv

Paxlovid Prevalence and Rebound Guidelines

(CDC, 5/24/22 ; MedRxiv, 6/21/2022 ; NEJM, 6/21/2022)

- **Prevalence:**
  - **The 7-day and 30-day COVID rebound rates after Paxlovid treatment were 3.53% and 5.40%.**
  - **Some experts stated that the rebound rate was underestimated.**
- **There is currently no evidence that additional treatment for COVID is needed for rebound.**
- **Those with COVID rebound advised to follow CDC's guidance on isolation. Patients should reisolate for at least 5 days, and should wear a mask for 10 days after rebound symptoms begin.**

Source: MedRxiv, NEJM

COVID Mutations Will Cause Drug Resistance to Paxlovid

(bioRxiv, 6/29/2022)

- **66 prevalent main protease (Mpro) mutations were located at the nirmatrelvir binding site. 11 mutants showed enzymatic activity and resistance to nirmatrelvir**
- **All 66 Mpro mutants are naturally occurring COVID mutations that could potentially affect the efficacy of Paxlovid.**
- **Continuous prescription of Paxlovid might likely increase the frequency of these pre-existing drug resistant mutants.**
- **It remains to be understood whether these mutants impair the fitness of viral replication and transmission.**

Source: bioRxiv

Q&A: Evusheld (1/2)

- **The only preventive treatment for COVID infection**
- **For immunocompromised or those who can't be vaccinated**

(JAMA, 7/25/22)

Q1. What is Evusheld?

- **Evusheld is a combination of 2 monoclonal antibodies (tixagevimab-cilgavimab) that bind to the spike protein of the virus to prevent it from infecting human cells.**

Q2. When can Evusheld be given and who is eligible?

- **Evusheld is not a treatment for COVID-19 and should not be given to patients who are already infected. Administration should be deferred until at least 2 weeks after vaccination.**

Q3. How is Evusheld given?

- **By 2 separate consecutive IM injections during a single session. Individuals are observed on site for at least 1 hour after injection. Evusheld is currently given every 6 months at no cost.**

Source: JAMA

Q&A: Evusheld (2/2)

- **The only preventive treatment for COVID infection**
- **For immunocompromised or those who can't be vaccinated**

(JAMA, 7/25/22)

Q4. How effective is Evusheld against COVID-19?

- **Evusheld has been shown to substantially decrease the risk of developing symptomatic infection for up to 6 months after use. Efficacy against BA.5 is somewhat reduced (NEJM).**

Q5. What are the possible side effects of Evusheld?

- **Allergic reactions can occur during or after administration, including serious cardiac events. People who have had severe reactions to COVID-19 vaccines are at higher risk.**

Source: JAMA

Underestimation of COVID Infection

(CBS, Face the Nation; 4/10/2022; Health Affairs, 2/11/2022)

- **Scott Gottlieb (former FDA commissioner)**
  - **Cases dramatically being undercounted (likely only 1/7 or 1/8 infections accounted for)**
- **3 reasons: changes in testing behavior, lack of public interest, and underfunded local public health departments**
- **UK's Test and Trace program showed only 14% of rapid tests results were reported**
- **Together, these factors create a perfect storm of misleading case counts and hospitalizations**

Source: Scott Gottlieb, HealthAffairs

COVID Forecasts Are Becoming Less Reliable

- **More at-home testing may be contributing to less reliable case data**

(FiveThirtyEight, MedRxiv; June-July 2022)

- **More use of at-home rapid tests and less use of lab-based PCR tests are causing case data to become less reliable.**
- **PCR tests are automatically reported, but the majority of at-home test results go unreported to health authorities.**
- **A recent study that analyzed case counts in NYC during the BA.2/BA.2.12.1 surge estimated that the true case counts can be anywhere up to 29-fold higher than official numbers.**

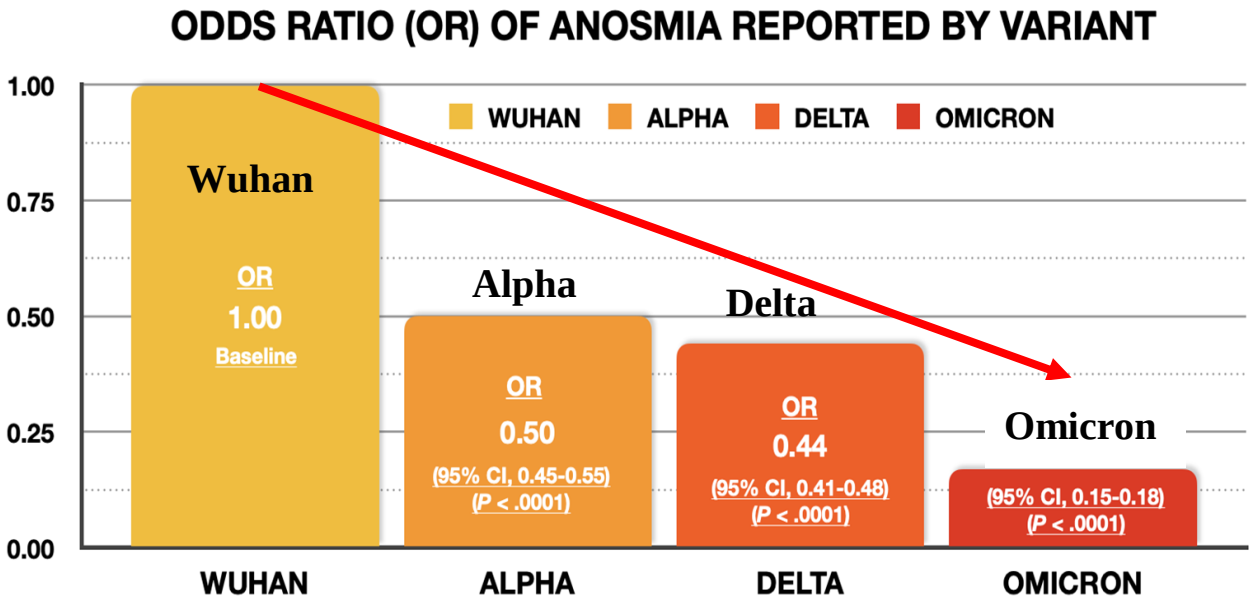
Source: FiveThirtyEight, MedRxiv

Reported Cases of Loss of Smell and Taste Decreasing with Each New Variant

- New variants have significantly lower chance of causing anosmia
  - Anosmia still affects those infected early in the pandemic

(Nature, 6/9/2022)

- **Smell/taste disruption becoming less common as COVID evolves.**
- **Compared to the Wuhan strain, the odds ratio for anosmia was 0.50 for Alpha, 0.44 for Delta, and 0.17 for Omicron.**



Source: Nature

Meta-Analysis: How Long Does Loss of Smell and Taste After COVID Last?

- Less than 5% have persistence after 6 months

(BMJ; 7/27/22)

- **18 studies (3699 patients) from 4180 records.**
- **Approximately less than 5% have persistence after 6 months.**

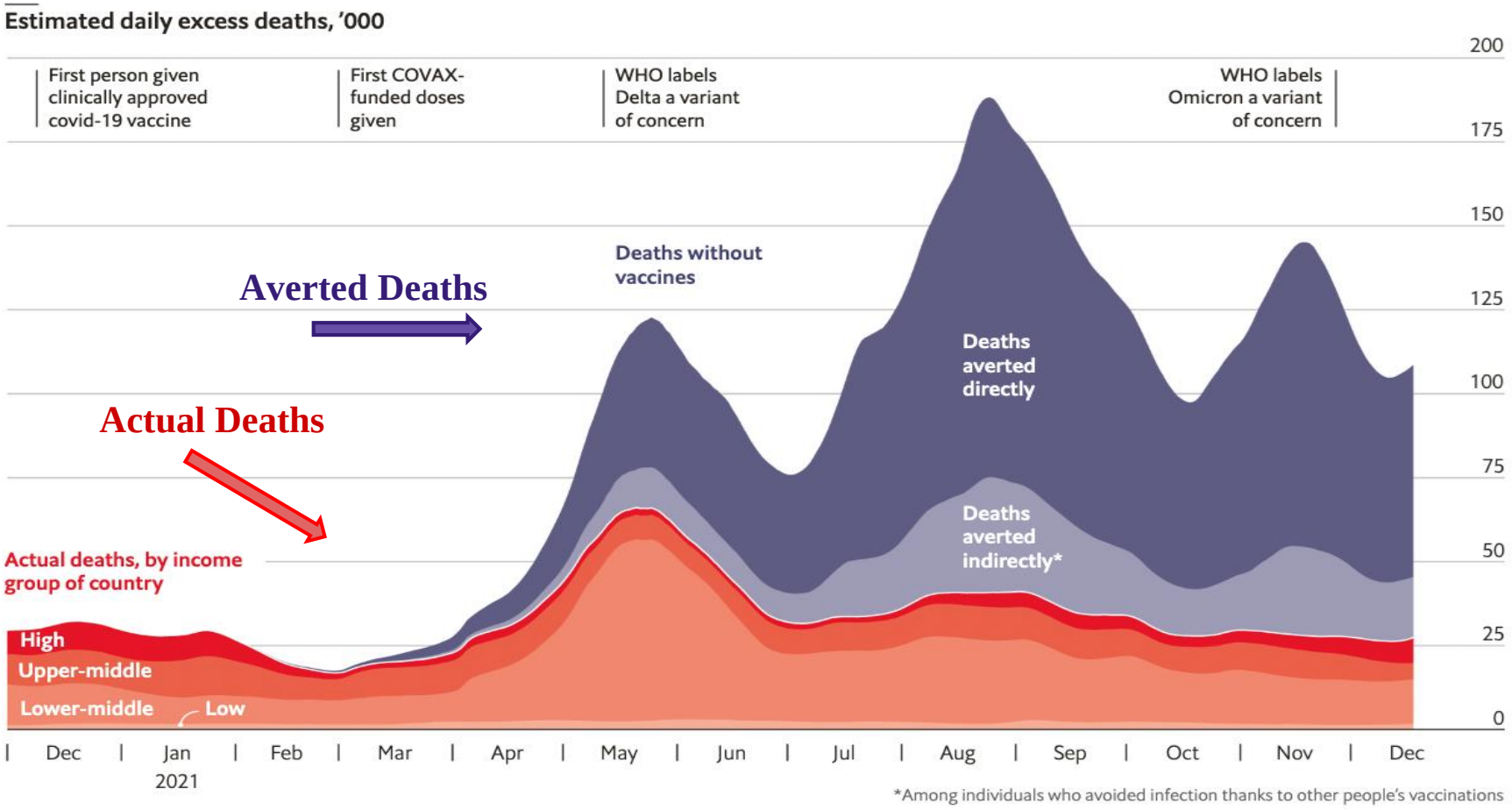
% of Patients Who Recovered	Dysfunction Recovery Time Period			
	30 Days	60 Days	90 Days	180 Days
Smell	74.1%	85.8%	90.0%	95.7%
Taste	78.8%	87.7%	90.3%	98.0%

Source: BMJ

Vaccines Saved an Estimated 20 Million Lives During Their First Year

- Global reduction of 63% in total deaths

(The Lancet, The Economist; June-July 2022)



Source: The Lancet, The Economist

5. Impact of Long COVID

- Future Problems Following COVID Infection

Source

Long COVID: Aiming for a Consensus

- Definitions and durations still being evaluated

- WHO : 3 months / CDC : ≥ 4 weeks

(The Lancet, 5/4/2022)

Term Used		Duration	Definition
Post-COVID-19 condition	WHO	At least 2 months, usually 3 months	Post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection
Ongoing symptomatic COVID-19	NICE (UK)*	4-12 weeks	Signs and symptoms of COVID-19
Post-COVID-19 syndrome	NICE (UK)*	> 12 weeks	Signs and symptoms that develop during or after an infection consistent with COVID-19
Post-COVID conditions	CDC (US)	≥ 4 weeks	An umbrella term for the wide range of physical and mental health consequences experienced by some patients
Post-acute sequelae of SARS CoV-2 infection (PASC)	NIH (US)	Still being evaluated	Persistent or new symptoms after COVID-19 infection
Post-acute COVID-19 syndrome (PACS)		>3 weeks	Persistent or new sequelae present after severe, mildly symptomatic or asymptomatic SARS-CoV-2 infection

*NICE:The National Institute for Health and Care Excellence (UK)

Source: The Lancet, PH Ontario

NIH's 2 Perspectives of Long COVID

(JAMA Network, 8/3/2022)

- **Post-COVID-19 Conditions (PCC) - WHO/CDC**

  A broad term that captures illness due to direct and indirect effects of the virus. Equivalent to Long COVID.

- **Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) - NIH**

  A more specific term to capture the direct effects of the virus. Used more in the medical research community.

- **An estimated 4.3 million to 9.7 million US adults have new long-term symptoms as a result of COVID infection.**

Source: JAMA Network

What's Long COVID?

(NIH, 5/16/2022; ONS, 7/29/2022; CDC, 5/5/2022)

- **Long COVID definition: (NIH)**

  "Long COVID is marked by wide-ranging symptoms, including shortness of breath, fatigue, fever, headaches, "brain fog" and other neurological problems. Such symptoms can last for many months or longer

- **Most common syptoms: (ONS)**

  The most common symptoms were fatigue (56%), shortness of breath (31%), loss of smell (22%) and muscle ache (21%).

- **Can vaccines protect against long COVID?**

  Vaccines may reduce, but not eliminate, the risk of Long COVID.

Source: NIH, ONS, CDC

Long COVID in Vaccinated vs. Unvaccinated
- Large studies suggest vaccines reduce long COVID

(NYT, 4/26/2022; Nature, 5/25/2022; The Lancet, 8/4/2022)

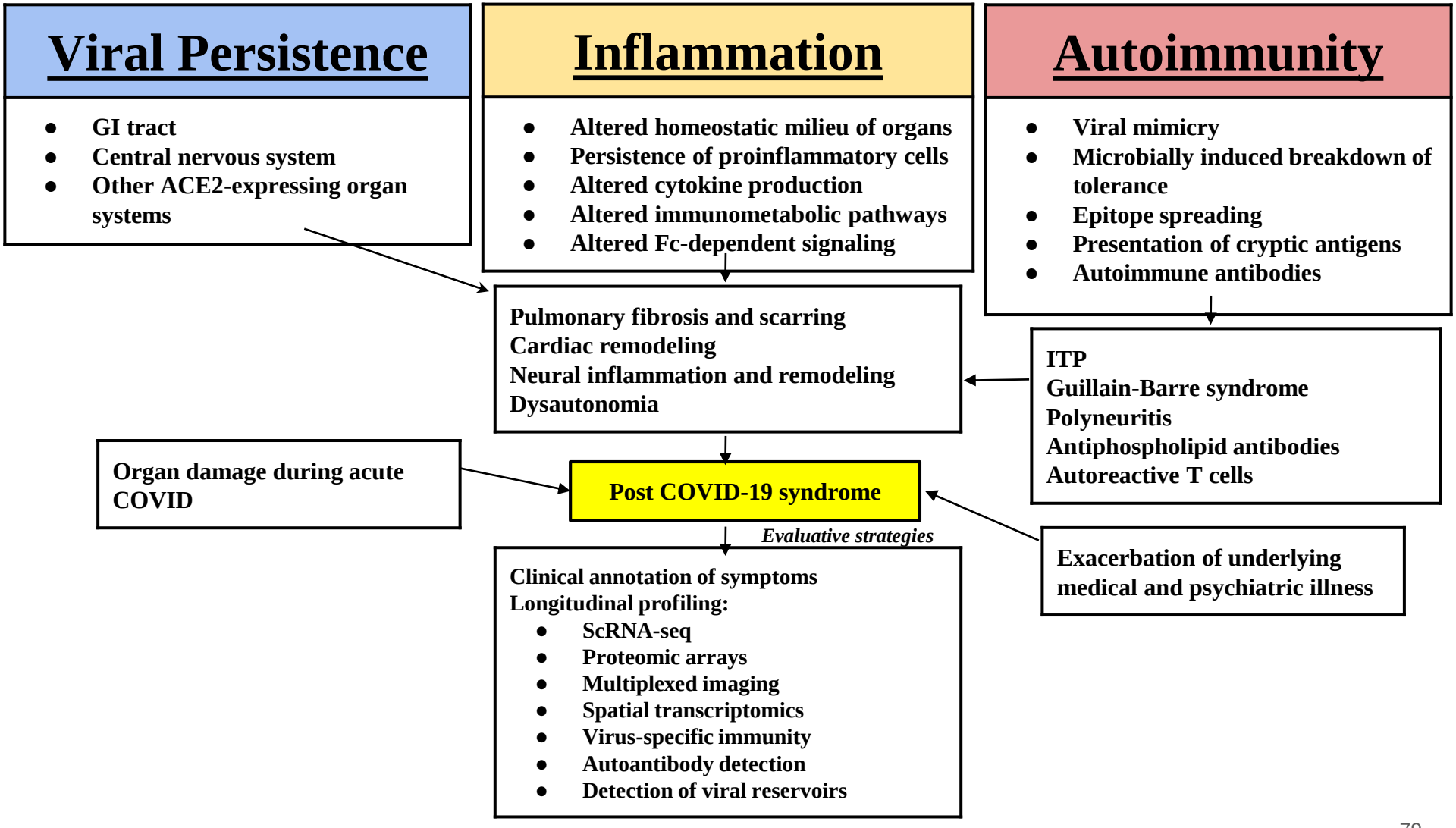
- **The Lancet: 12.7% of COVID patients developed Long Covid (3.7% to 9.8% fully vaccinated). Vaccinated showed slightly lower risk of developing Long Covid symptoms.**
- **Nature: Vaccinated had a 15% lower risk than the unvaccinated of having symptoms six months later.**
- **Britain studies: One found a 50% lower risk and another found a 41% of lingering symptoms among vaccinated patients.**
- **US study with 240,000 patients: Those receiving 1+ dose before their infection were 10-14% as likely to report two or more symptoms of long Covid (12-20 weeks later).**
- **Israel study: People who received 2 doses of vaccine had 54-82% lower risk than unvaccinated patients to report having 7 of the 10 most common long-term symptoms.**

Source: NYT, Nature, The Lancet

Putative Mechanisms and Diagnostic Strategies for Patients with Post-COVID-19 Syndromes

- Three possible mechanisms of Long COVID

(Nature Immunology, 2/1/2022)



Source: Nature Immunology

Post–COVID Conditions Among Adult COVID Survivors (1/2)

- **20-25% of people 18+ may experience long COVID**

(CDC, 5/24/2022)

- **COVID patients have twice the risk of uninfected people to develop respiratory symptoms and lung problems.**
- **Chance of COVID survivors getting at least one long COVID condition as a result of previous infection:**
  - **~20% of those aged 18–64 years**
  - **~25% of those aged ≥ 65 years**

Source: CDC

Post–COVID Conditions Among Adult COVID Survivors (2/2)

- 9 Systems 26 post-COVID condition risks

(CDC, 5/24/2022)

Cardiovascular	Pulmonary	Renal	Hemolytic & Vascular	GI
Acute MI, cardiac dysrhythmias, cardiovascular disease, heart failure, myocarditis	Acute pulmonary embolism, respiratory symptoms, asthma	Renal failure, chronic kidney disease	Thromboembolic event, cerebrovascular disease, coagulation and hemorrhagic	Gastrointestinal and esophageal

Neurologic	Mental Health	Musculoskeletal	Endocrine
Neurologic conditions Smell and taste Disturbances	Mood disorders Other mental conditions Anxiety and fear Sleeping disorders Substance-related disorders	Malaise and fatigue Muscle disorders Musculoskeletal pain	Diabetes type 2 Diabetes type 1

Source: CDC

Long COVID Symptoms in Positive Children Aged 0-14 Years Old

- **1 out of 3 experienced at least one long-term symptom**

(The Lancet, 6/22/2022)

- **Study:**
  - **National, cross-sectional study in Denmark (44,000 kids)**
  - **Children who had history of COVID in all age groups (0-14 y/o) reported a higher prevalence (4-66%) of long COVID symptoms**
- **Common symptoms varied by age group:**

Age group	Common Symptoms
0 - 3 y/o	mood swings, rashes, stomach aches
4 - 11 y/o	memory and concentration issues
12 - 14 y/o	fatigue, mood swings, memory and concentration

Source: The Lancet

6. Monkeypox Updates

Squirrels are the most important carrier.

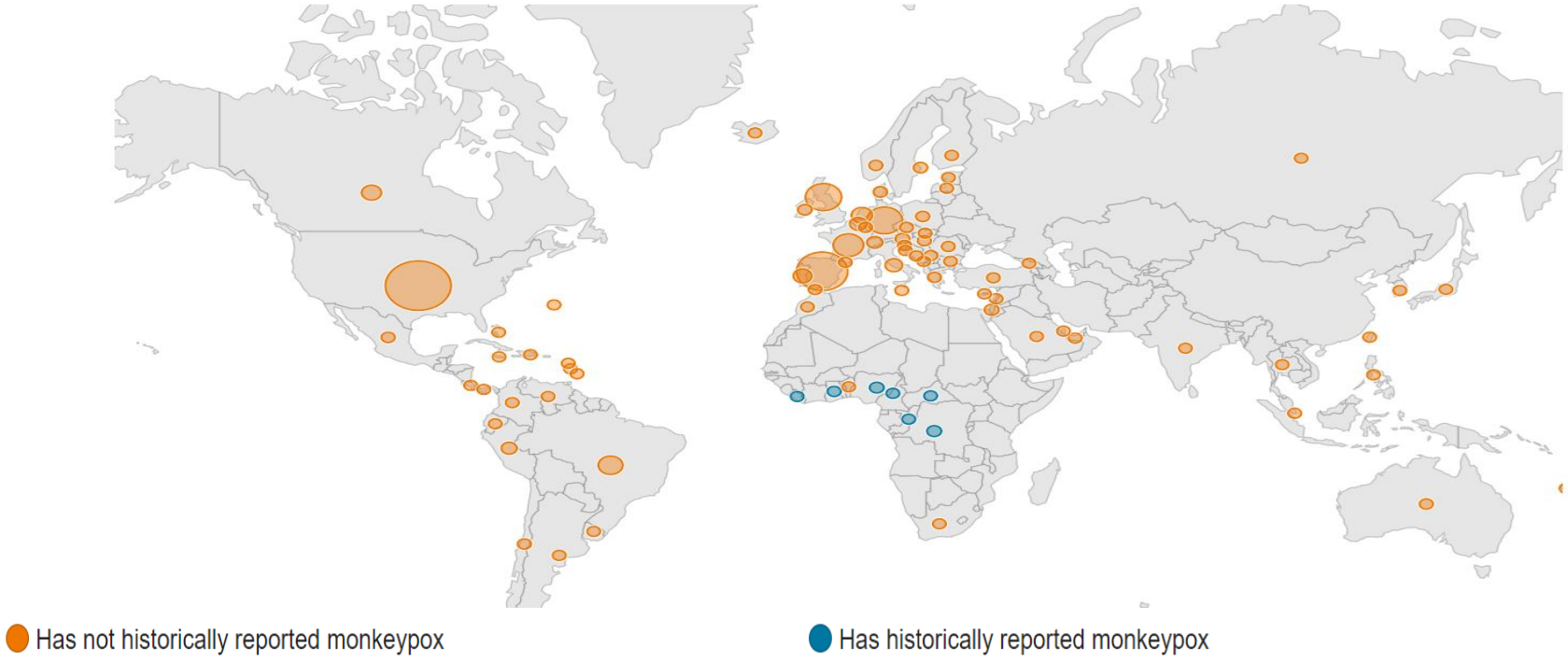
\ “Monkeypox has nothing to do with us!!” /

WHO Declared Global Monkeypox Outbreak as a Public Health Emergency of International Concern (PHEIC)

(WHO; CDC, 8/4/2022)

- **26,864 cases in 88 countries (8/4/22)**
- **6,617 confirmed cases in US (8/4/22)**

Source: CDC, WHO



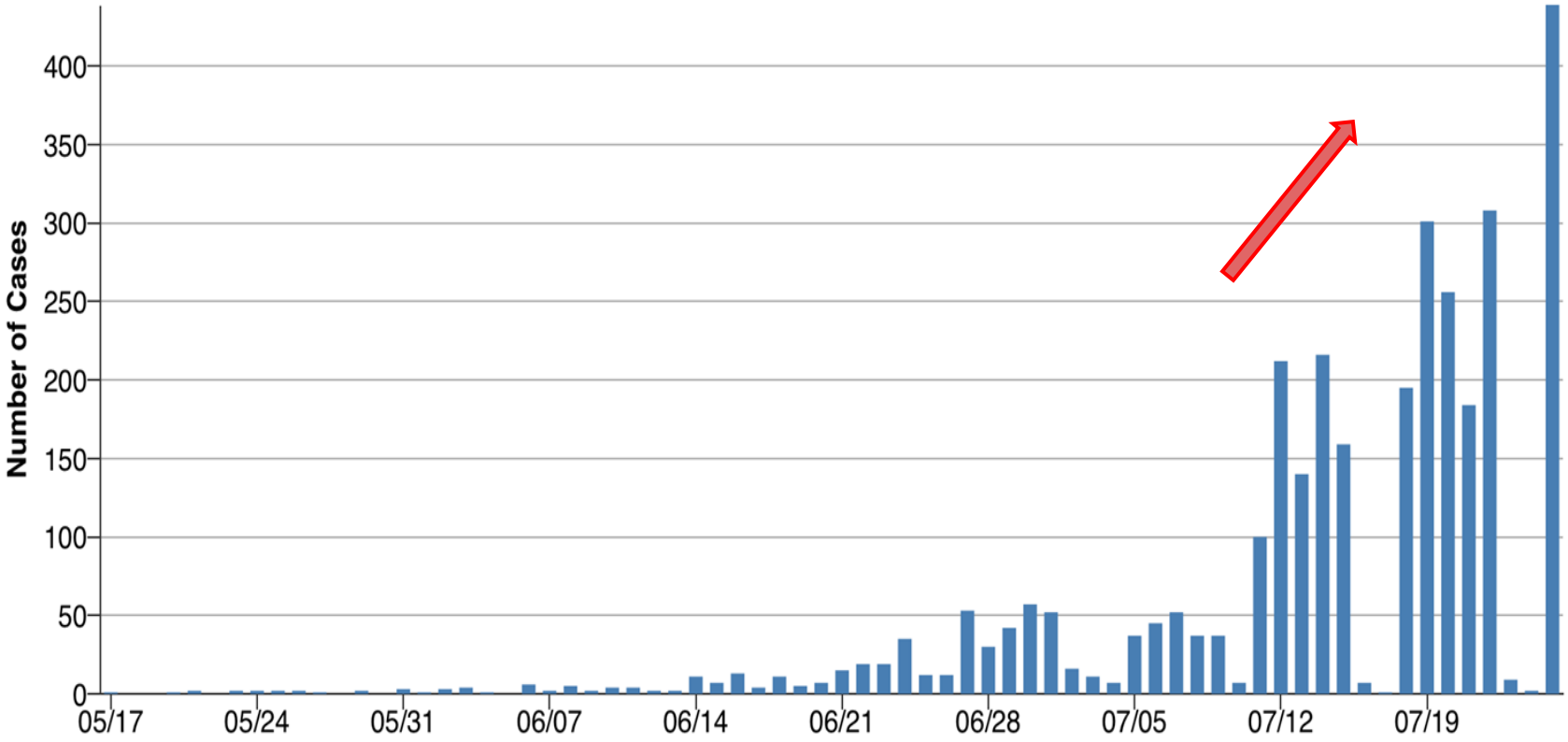
* **PHEIC definition:**

- **Serious, sudden, unusual or unexpected**
- **Carries implications for public health beyond the affected State's national border**
- **May require immediate international action**

US Monkeypox Cases Trends

(CDC, 8/4/2022)

- **Total confirmed cases in US: 6,617 (8/4/22)**



Source: CDC

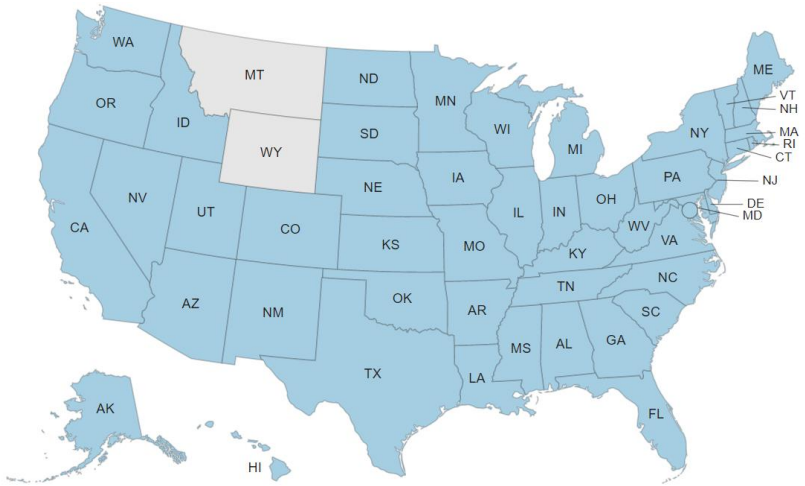
Biden Administration Declares Monkeypox a Public Health Emergency in the US

(CNBC, 8/1/2022; BHR, 8/4/2022; CNN, 8/4/2022)

- **US declared monkeypox a public health emergency as cases near 7,000.**

- **California, New York, and Illinois account for 46% of all confirmed cases.**

- **New York is the epicenter of the outbreak in the U.S., with 1,666 confirmed cases as of Thursday (8/4/2022).**



Source: CNBC, BHR, CNN

Biden Administration's Monkeypox Outbreak Response

(White House, 6/28/2022, 8/2/2022)

- **First phase of the strategy aims to rapidly deploy vaccines in the most affected communities and mitigate the spread.**
  - **Scaling and Delivering Vaccines to Mitigate New Infections: has made 1.1 million doses of vaccines to states and cities**
  - **Making Testing Easier : has expanded testing capacity from 6,000 tests per week to over 80,000 tests per week.**
  - **Activating Community Leaders and Stakeholders : share information on what the virus is, how to treat it, and which communities are most at risk.**

Source: WhiteHouse (1) , WhiteHouse (2)

7 PHEIC Declarations

(JTM, 8/12/2020; WHO, 7/23/2022)

PHEIC	Date of Declaration	Date of Undeclaration
H1N1	4/25/2009	8/10/2010
Poliovirus	5/5/2014	Remains a PHEIC
Ebola	8/8/2014	3/29/2016
Zika	2/1/2016	11/18/2016
Ebola	7/17/2019	6/26/2020
COVID-19	1/30/2020	Remains a PHEIC
Monkeypox	7/23/2022	Remains a PHEIC

Source: JTM , WHO

How Does Monkeypox Progress?

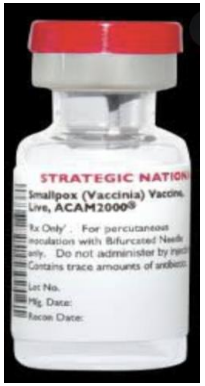
- The illness typically lasts 2-4 weeks

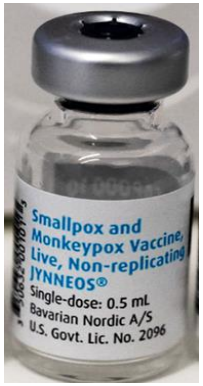
Source: CDC, icliniq

Enanthem	Macules	Papules
Onset	1~2 days	1~2 days
		
Vesicles	**Pustules**	**Scabs**
1~2 days	5~7 days	7~14 days
		

Vaccines To Prevent Monkeypox

(CDC, 7/28/2022, 6/2/2022)





- **ACAM2000 and JYNNEOS (WHO approved) are vaccines approved by FDA to prevent smallpox.**

  The immune response takes 14 days after the 2nd dose of JYNNEOS and 4 weeks after the ACAM2000 dose for maximal development.

- **Receiving Vaccine After Exposure to Monkeypox Virus**

  CDC recommends vaccine be given within 4 days from date of exposure to prevent onset of disease. If given 4–14 days after date of exposure, vaccination may reduce the symptoms, but may not prevent disease.

- **Revaccination After Exposure**

  Persons exposed to monkeypox and who have not received the smallpox vaccine within the last 3 years, should consider getting vaccinated.

Source: CDC 1, 2

5 Children Tests Positive for Monkeypox in US

- 5 children have tested positive for monkeypox in the U.S. since July

(Fox News, 8/3/2022)

- **4 of the 5 children are U.S. citizens, with 2 in California and 2 in Indiana.**
- **The 5th case was an infant but not an U.S. resident.**
- **CDC has warned that young children may be at an increased risk of more severe monkeypox cases.**
- **The cut-off age for severe risk is 8 years old**

Source: Fox News

TPOXX (Tecovirimat) for Treatment of Monkeypox

- Expanded Access and may shorten illness duration

(FDA, 7/29/2022; CDC, 7/26/2022)

- **Permitted through CDC under FDA authority (Expanded Access).**
- **There are currently no human data for efficacy of TPOXX.**

Efficacy

- **Animal studies: TPOXX shown to decrease the chance of dying from infections with orthopoxviruses when given early in disease course.**
- **People: Efficacy has been limited to drug levels in blood and a few case studies; suggested that TPOXX may shorten the duration of illness and viral shedding.**

Source: FDA, CDC

Monkeypox Q&A

(WHO, 7/12/2022; CDC, 6/24/2022)

- **Can people get seriously ill or die from monkeypox?**

  Newborn babies, children, and people with underlying immune deficiencies may be at risk of more serious symptoms and death from monkeypox (1% to 10% of infected have died).

- **How long is the incubation period of monkeypox?**

  The incubation period is roughly 1-2 weeks. The development of initial symptoms (e.g., fever, malaise, headache, weakness, etc.) marks the beginning of the prodromal period. The illness typically lasts 2-4 weeks.

Source: WHO, CDC

How to Prevent Getting Monkeypox

(CDC, 7/29/022)

- **Avoid close, skin-to-skin contact with people who have a rash that looks like monkeypox.**
- **Avoid contact with objects and materials that a person with monkeypox has used.**
- **Wash hands often with soap and water or use an alcohol-based hand sanitizer, especially before eating or touching face and after use the bathroom.**

Source: CDC

Can Monkeypox Spread Through The Air? (1/2)

(Snopes, 8/3/2022)

- **Possible to transmit and contract monkeypox through respiratory secretions, but most often spread through direct contact with an infected person's rash, scabs, or body fluids.**
- **Airborne transmission involves a different mechanism than that found in transmission via respiratory secretions.**
  - **Airborne transmission occurs when small virus particles are suspended in the air for long periods of time (as was the case with COVID-19).**
- **However, respiratory secretions drop out of the air quickly, and there have been no reported cases via airborne transmission for monkeypox so far.**

Source: Snopes

Can Monkeypox Spread Through The Air? (2/2)

- NO mask requirements for monkeypox, but close contacts should consider wearing masks

(medRxiv, 7/21/2022; NYT, 6/7/2022)

- **UK study found significant contamination in isolation facilities and potential for aerosolization of monkeypox.**
- **CDC removed the mask recommendation from the monkeypox travel notices because it caused confusion.**
- **CDC says that in countries where monkeypox is spreading, household contacts and health care workers should consider wearing masks. That guideline also applies to other people who may be in close contact with a person who has been confirmed with monkeypox.**

Source: medRxiv, NYT

Summary

1. *BA.5 accounts for 85.5% of current cases in the U.S. and has the highest immune evasion and infectivity of all variants.*
2. *Global cases are beginning to plateau. Bivalent, nasal, and universal vaccines may be the future to combat new variants.*
3. *Paxlovid is still the most effective treatment, but rebound and resistance need to be closely monitored.*
4. *Long COVID is the most important late impact of the disease; multiple reinfections (e.g. BA.5) may increase the risk.*
5. *Monkeypox is a global emergency; U.S. declared a public health emergency. CA/NY/IL account for 46% of U.S. cases.*

Thank You!

Source

8/4/22 CME Q&A and Discussion (1)

- **Alhambra Hospital Medical Center (Iris): Gave an update on COVID inpatient and reported one Monkeypox case in the ER. Monkeypox turnaround time 2-4 days per lab. CDPH allocates Monkeypox vaccine.**
- **Garfield Medical Center: Reported that most COVID cases were with mild symptoms and continued testing all patients.**
- **Dr. Joseph Kuei: Shared some COVID outpatient perspectives, and the need to evaluate how sick the patient is first, while considering drug-drug interactions and/or side effects of Paxlovid.**
- **Dr. Deepthi Jayasekara: Shared the use/drug-drug interaction/side effect of Paxlovid and suggested monitoring patients for 3-5 days before jumping into Paxlovid. He also mentioned the new booster may be available in September.**
- **Dr. John Huang: Suggested further studies on immunity (B and T cell). He also suggested in-depth studies on differences between PCR and rapid antigen testing.**

8/4/22 CME Q&A and Discussion (2)

Evusheld

- **Dr. Deepthi discussed the use of Evusheld, a combo monoclonal antibody, to be given to specific populations. For the unvaccinated, Evusheld remains a good option.**

Monkeypox

- **CDC removed travel mask requirements for Monkeypox in June, but Dr. Chiu suggested that household contacts and health care workers might consider wearing masks (see Slides #95, #96).**

PCR/Antigen Testing

- **Dr. Chiu cited a Nature paper (7/26/2022) suggesting that rapid antigen tests may be more useful for detecting infectiousness (see Slide #28), but PCR tests are still useful as a confirmatory test.**
- **Dr. Edward Chen suggested using PCR and antigen testing together. For high-risk patients, Dr. Basil recommended using antigen tests.**

Rebound Phenomenon

- **Dr. Deepthi: for asymptomatic, no additional treatment is needed; for symptomatic, follow CDC isolation guidelines (see Slide #65).**
- **Dr Deepthi agreed with Dr. Chiu that "the COVID cocktail" is probably the future direction.**