COVID-19 Clinical Updates: Omicron and More

USET COVID-19 ECHO Presentation

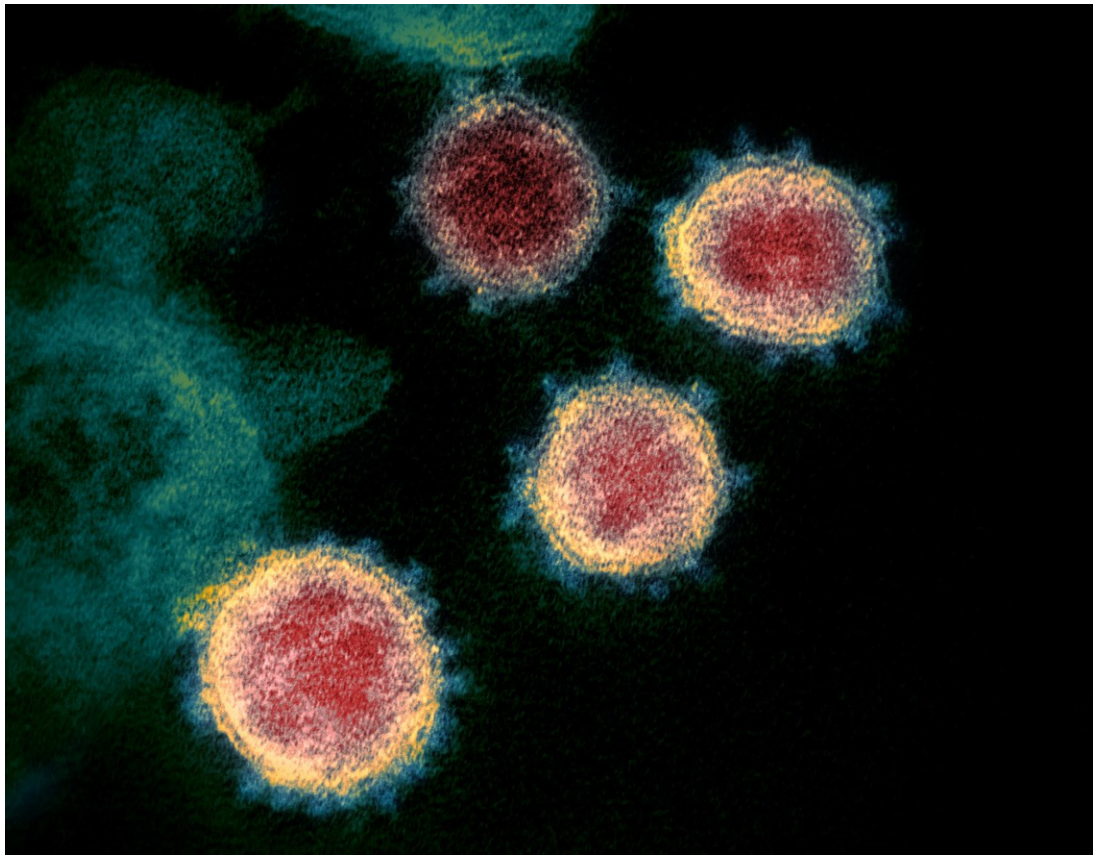
December 10, 2021

Harry J Brown, MD

USET Tribal Epidemiology Center

Because there is Strength in Unity

Day 640 of the COVID-19 Pandemic



- The Omicron Variant
- Vaccine Efficacy – Where we are after 1 year
- Molnupiravir – the antiviral we've all been waiting for???

Because there is Strength in Unity

Objectives for Today's Presentation

1) Become familiar with the current knowledge of the Omicron Variant of SARS-CoV-2
2) Be aware of some new safety and efficacy data of current Covid-19 vaccines
3) Be aware of the probable impending release of molnupiravir

Because there is Strength in Unity

Disclosures and Disclaimers

- I have no conflicts of interest
- I will be mentioning vaccine/pharmaceutical companies by name, but this does not imply endorsement of any company or product
- The opinions expressed, as well as any errors, are entirely on me
- Employed by USET and EBCI – Cherokee Indian Hospital Authority

Omicron Variant – What Do We Know?

WE KNOW ALMOST NOTHING FOR SURE… YET

Because there is Strength in Unity

Omicron – the latest Variant of Concern

- On Nov 24, public health authorities in South Africa reported a new SARS-CoV-2 variant to the World Health Organization (WHO)
- On Nov 26 the WHO designated this new variant as a Variant of Concern, and gave it the name of Omicron (nu and xi were skipped)
- Has a large number of mutations, including ~34 in the spike (S) gene
- Concern that it may be resistant to natural immunity, vaccine immunity, some treatments (monoclonal antibodies), and give false test results

Update on Omicron (who.int)

Mutations in Variants of Concern

Supplementary Table 3. Mutations in the spike proteins of SARS-CoV-2 variants of concern. Compared to the parental SARS-CoV-2 isolate B.1, Omicron gains additional substitutions, insertions and deletions. Amino acid substitutions already found in other variants are highlighted in red. Altered positions but with different distinct substitutions are indicated in blue.

Parental:	B.1	D614G
Alpha:	B.1.1.7	HV69-70del, Y144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H
Beta:	B.1.351	L18F, D80A, D215G, R246I, K417N, E484K, N501Y, D614G, A701V
Gamma:	P.1	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T10277I
Delta:	B.1.617.2	T19R, T95I, G142D, E156-, F157-, R158G, L452R, T478K, D614G, P681R, D950N
Omicron:	B.1.1.529	A67V, HV69-70del, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, 446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

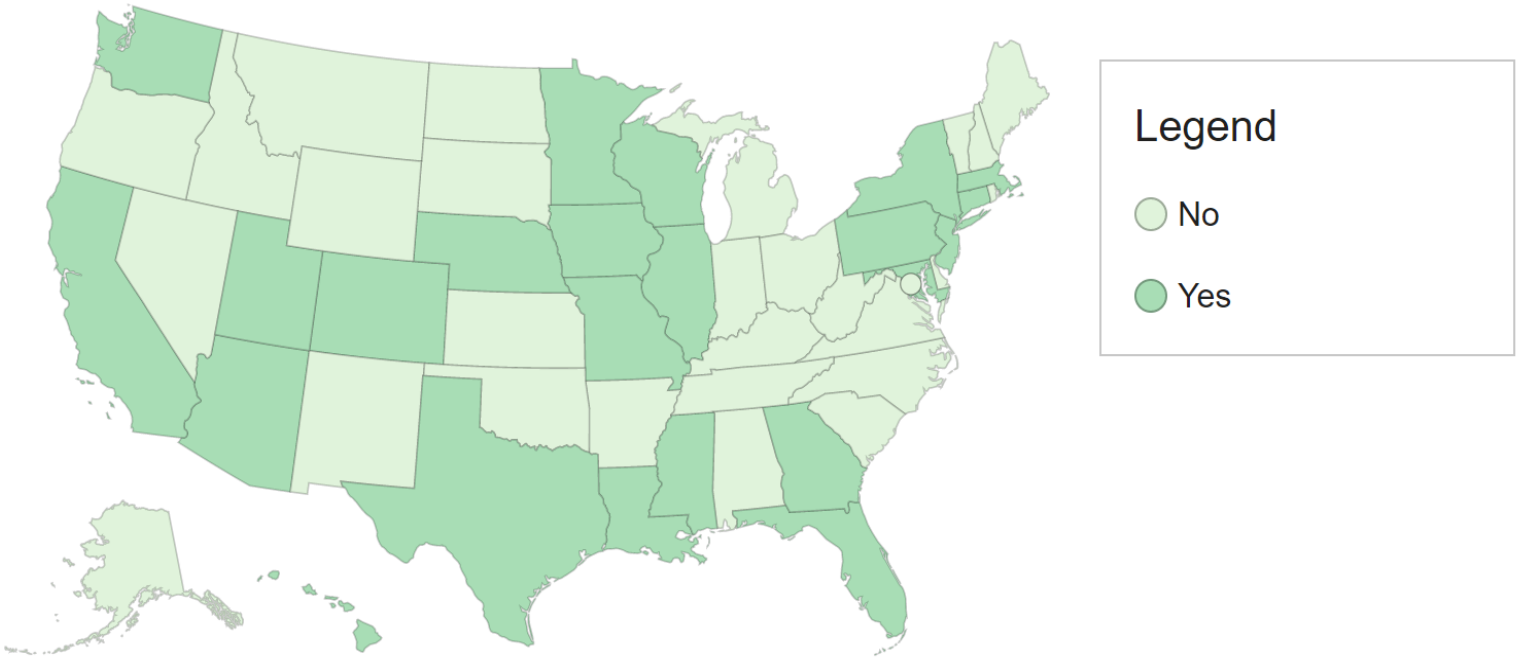
medRxiv preprint doi: https://doi.org/10.1101/2021.12.07.21267432

Because there is Strength in Unity

AND EASTERN TRIBES, INC.
Established 1969

Omicron in the US

US COVID-19 Cases Caused by the Omicron Variant



Because there is Strength in Unity

UNITED SOUTH AND EASTERN TRIBES, INC.
Established 1969

Effect on Testing for Covid-19

- Some PCR tests are affected by the Omicron Variant
- S-gene target failure, or S-gene dropout, occurs with Omicron
- Most PCR tests will still be positive, because they test for 2 or 3 genes
- Because there are so many mutations in the spike (S) gene, the result for this gene will be negative, but other genes will be detected
- Two PCR tests show complete failure:
  - Meridian Bioscience Revogene SARS-CoV-2
  - Tide Laboratories DTPM COVID-19 RT-PCR Test

SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests | FDA

S Gene Target Failure

- One common PCR test, ThermoFisher TaqPath Assay, shows S-gene "dropout"
- The overall test is still positive
- The S-gene dropout is a clue that you may be dealing with Omicron
- S-gene dropout also occurred with the Alpha Variant

SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests | FDA

Omicron and Monoclonal Antibodies

- Imdevimab-casirivimab (*REGEN-COV*) is a monoclonal antibody used for treatment and prophylaxis of high-risk individuals under an EUA
- Initial studies are showing that this monoclonal antibody combination is not effective against the Omicron variant
- Studies are ongoing

medRxiv preprint doi: https://doi.org/10.1101/2021.12.07.21267432

Omicron and Vaccines

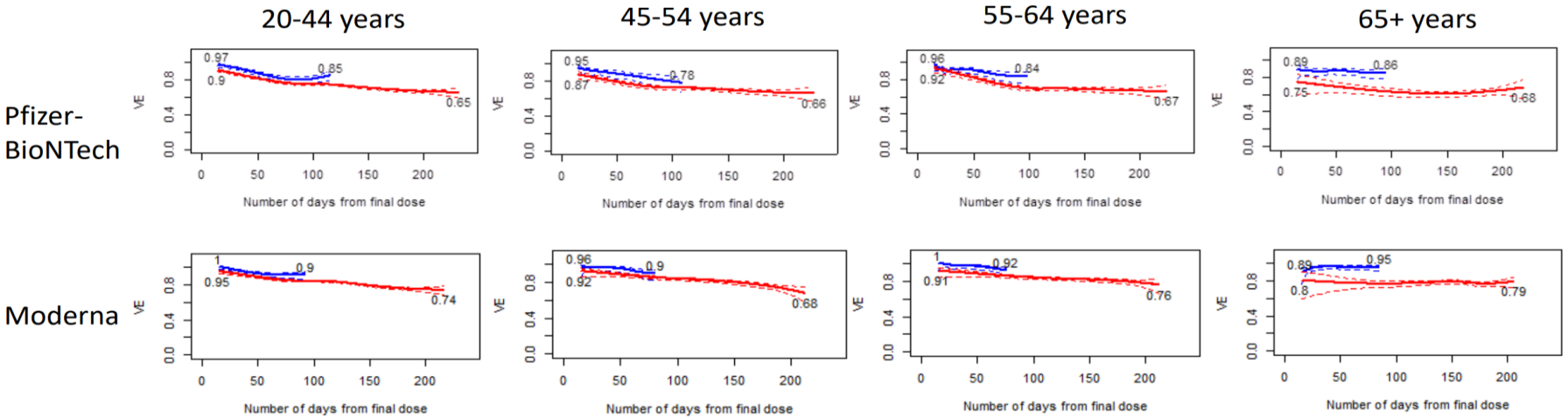
- There have been 3 preliminary studies looking at immunity to the Omicron Variant in laboratory studies (Germany, Sweden, South Africa)
- All have shown increased resistance of Omicron to vaccinated individuals
- One study showed that people with a booster dose had better protection
- “Breakthrough” cases in South Africa are reportedly mild
- Neutralizing antibodies are not the whole story

What Can We Do About It?

- The use of well-fitting masks
- Cover coughs and sneezes
- Good hand hygiene
- Physical distancing and avoiding crowded spaces, especially indoors
- Improved ventilation of indoor spaces
- Getting vaccinated, including booster doses for anyone who is due for one

Vaccine Efficacy Over Time

VE against symptomatic infection by age group and time since vaccination in pre-Delta and Delta periods



Pre-Delta (March 13–May 29) with 95% CIs in dotted lines
Delta (July 18–August 31) with 95% CIs in dotted lines

The presented (fitted) curves are truncated on the day with ≤10 cases observed beyond it to avoid presenting wide confidence bounds.

- VE is lower during Delta
- VE wanes during both periods
- Curves similar across age groups
- For ≥65, VE lower than for other age groups soon after vaccination, no clear trend over time since vaccination

UNITED SOUTH AND EASTERN TRIBES, INC.
Established 1969
Because there is Strength in Unity

mRNA Vaccine Safety - Myocarditis

Myocarditis in Israel

Reported after Pfizer-BioNTech COVID-19 vaccine, December 2020-October 10, 2021

	Age (years)	Post-dose 1 Rate per 100,000	Post-dose 2 Rate per 100,000	Post-dose 3 Rate per 100,000	Number of 3rd dose delivered
Females	12-15	0	0.6	0	279
	16-19	0	0.9	0	97,807
	20-24	0.4	2.5	0	141,910
	25-29	0	0.4	0	130,283
	≥30	0.1	0.3	0	1,542,142
Males	12-15	0.5	6.6	0	292
	16-19	1.2	16.1	5.2	96,238
	20-24	2.2	10.3	3.6	139,015
	25-29	1.2	8.4	0.7	133,650
	≥30	0.5	1.7	0.4	1,448,745

Rates of myocarditis after a third dose appear to fall **between** rates seen after **dose 1** and **dose 2**

As reported by Israel at FDA's VRBPAC meeting. Slides here: https://www.fda.gov/media/153086/download .

UNITED SOUTH AND EASTERN TRIBES, INC. Established 1969

Risks and Benefits of Booster Doses

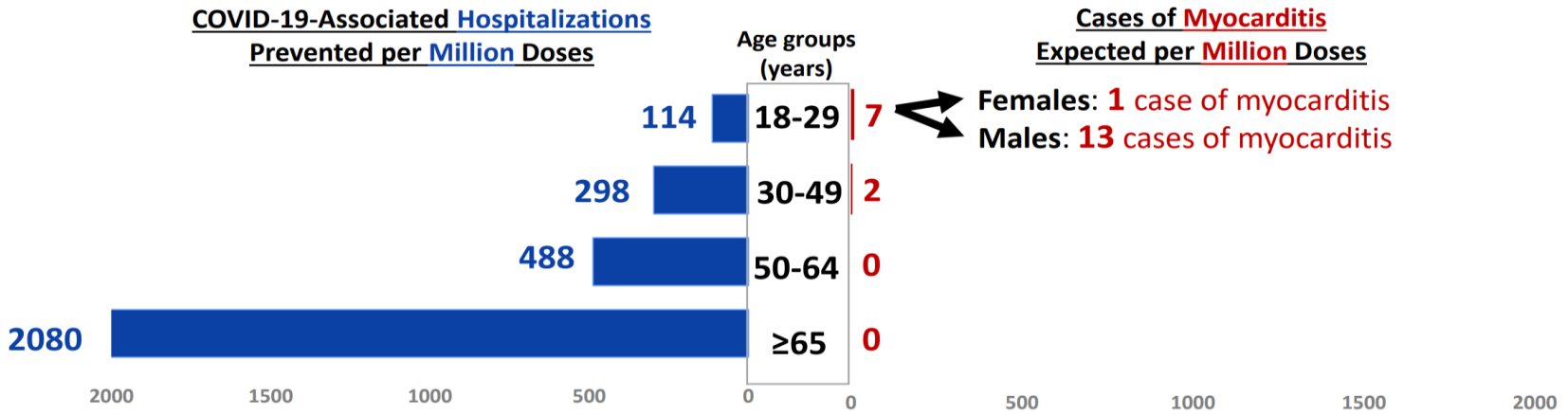
Benefits and risks after Pfizer-BioNTech COVID-19 booster dose

*For every **million** doses of vaccine given*

Scenario:

- VE for hospitalization averaged from four platforms[1]
- Boost to 95% VE for hospitalization
- **Myocarditis risk equivalent to risk after 1st and 2nd dose averaged**

Age Group	VE for hospitalization
18 – 29 years	90.7%
30 – 49 years	90.2%
50 – 64 years	91.1%
≥65 years	85.1%



1. Scobie et al., COVID-NET, VISION, IVY Network
COVID-NET hospitalization rates from the week of August 21, 2021; Myocarditis rates from VAERS data through August 18, 2021

UNITED SOUTH AND EASTERN TRIBES, INC. Established 1969

Because there is Strength in Unity

Vaccines – Take Home Points

- Booster doses are now for everyone 16 and older
  - 16 and 17 year olds now eligible for Pfizer-BioNTech booster dose
  - For mRNA vaccines, give booster 6 months after 2nd dose
  - For J&J/Janssen, give booster 2 months after 2nd dose
- Booster doses will give the best protection against Omicron
- 71.5% of the US population now “fully vaccinated” (95% of 65+ yrs)
- Almost 50 million people have now gotten booster doses

UNITED SOUTH AND EASTERN TRIBES, INC.
Established 1969

Because there is Strength in Unity

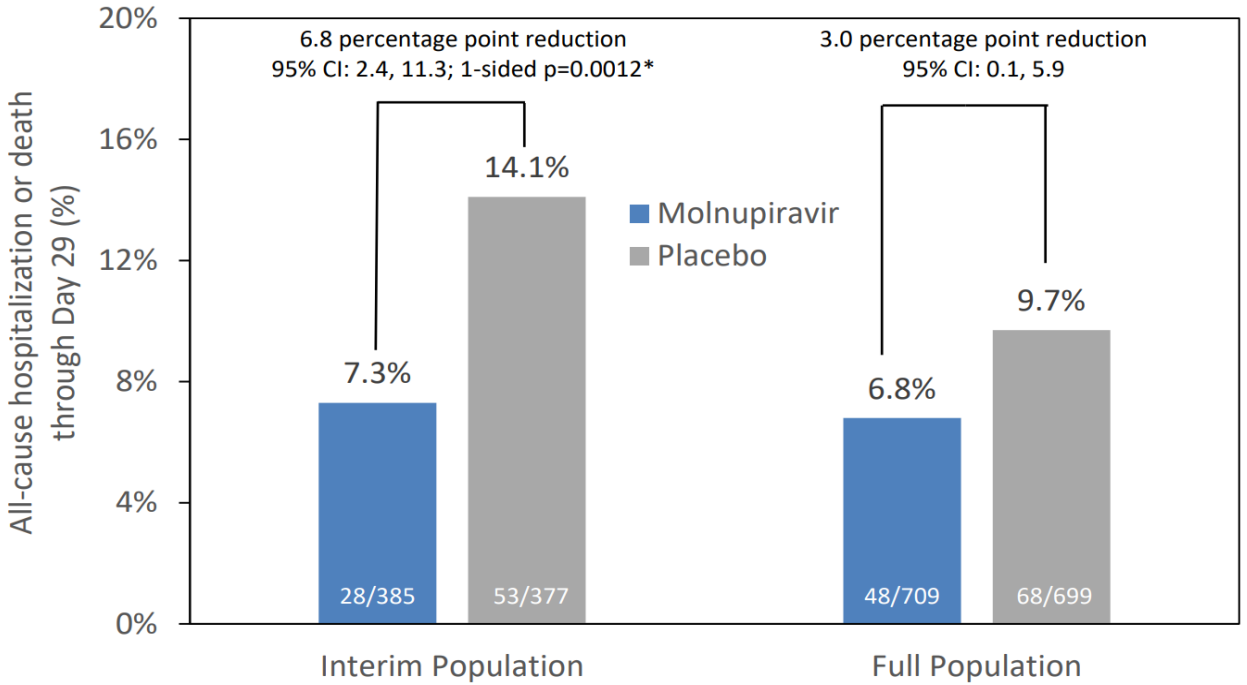
Molnupiravir – a new antiviral

- Molnupiravir is an antiviral drug developed by Ridgeway Biotherapeutics in partnership with Merck
- Works by causing replication mistakes in SARS-CoV-2
- Oral drug
- Only works within 5 days of onset of symptoms
- Dose: 800 mg every 12 hours for 5 days
- UK approved use on Nov 4
- FDA advisory panel voted for EUA (13-10 vote) on Nov 30

Molnupiravir Clinical Trials

- Trial in hospitalized patients discontinued due to lack of effectiveness
- Outpatient trial done in multiple countries
- Total trial involved about 1400 participants
- Within 5 days of onset of symptoms
- Unvaccinated, high risk individuals
- Initial results promising: ~50% reduction in hospitalization & death
- Final results less effective: ~30% reduction in hospitalization & death
- Overall death prevention good, but small numbers

Molnupiravir Clinical Trial Outcome



* Met the pre-specified interim assessment stopping boundary (1-sided p-value <0.0092)
Formal statistical testing was not performed for the full population assessment, because statistical significance was demonstrated at the interim population assessment. The nominal 1-sided p-value was 0.0218.

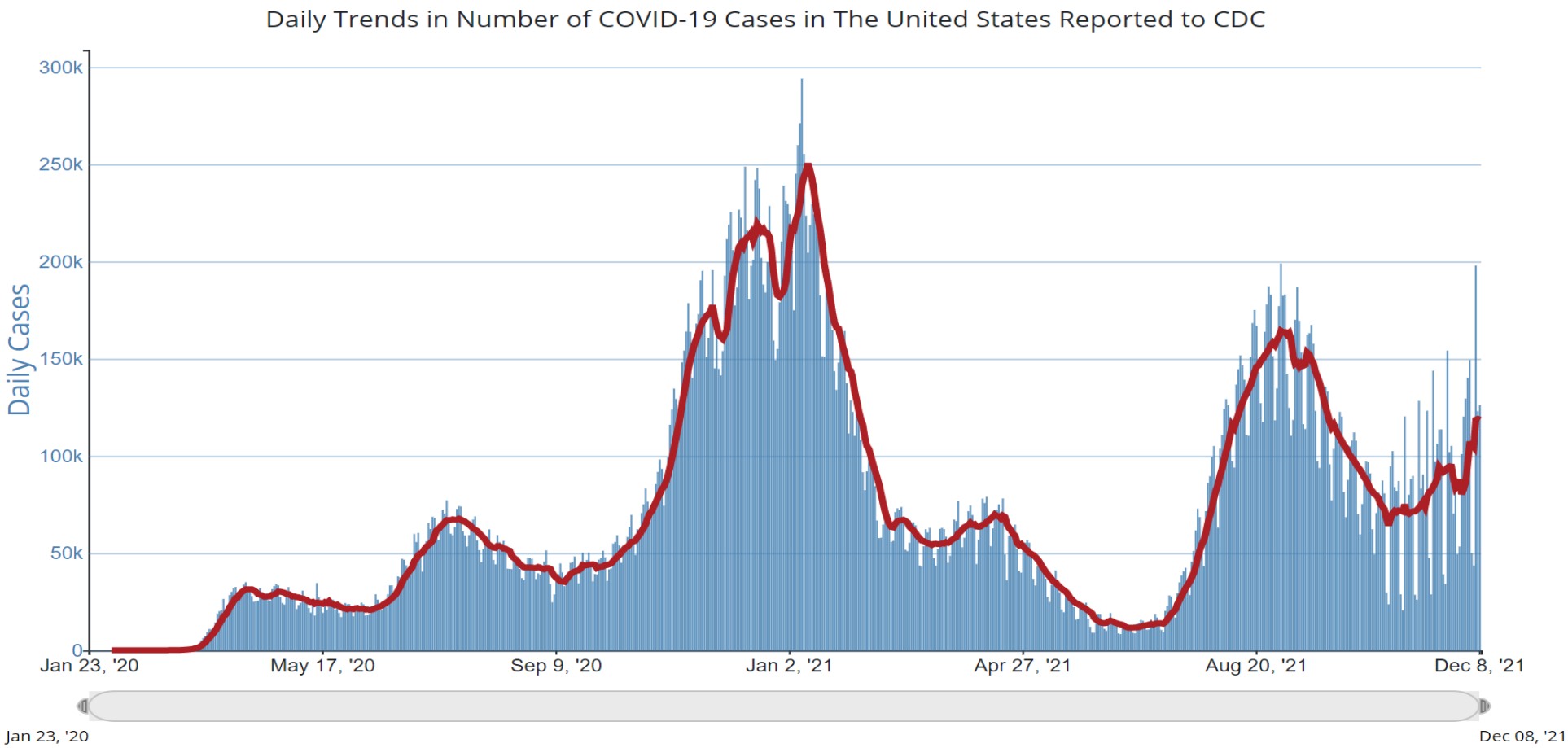
www.fda.gov

Because there is Strength in Unity

Molnupiravir Concerns

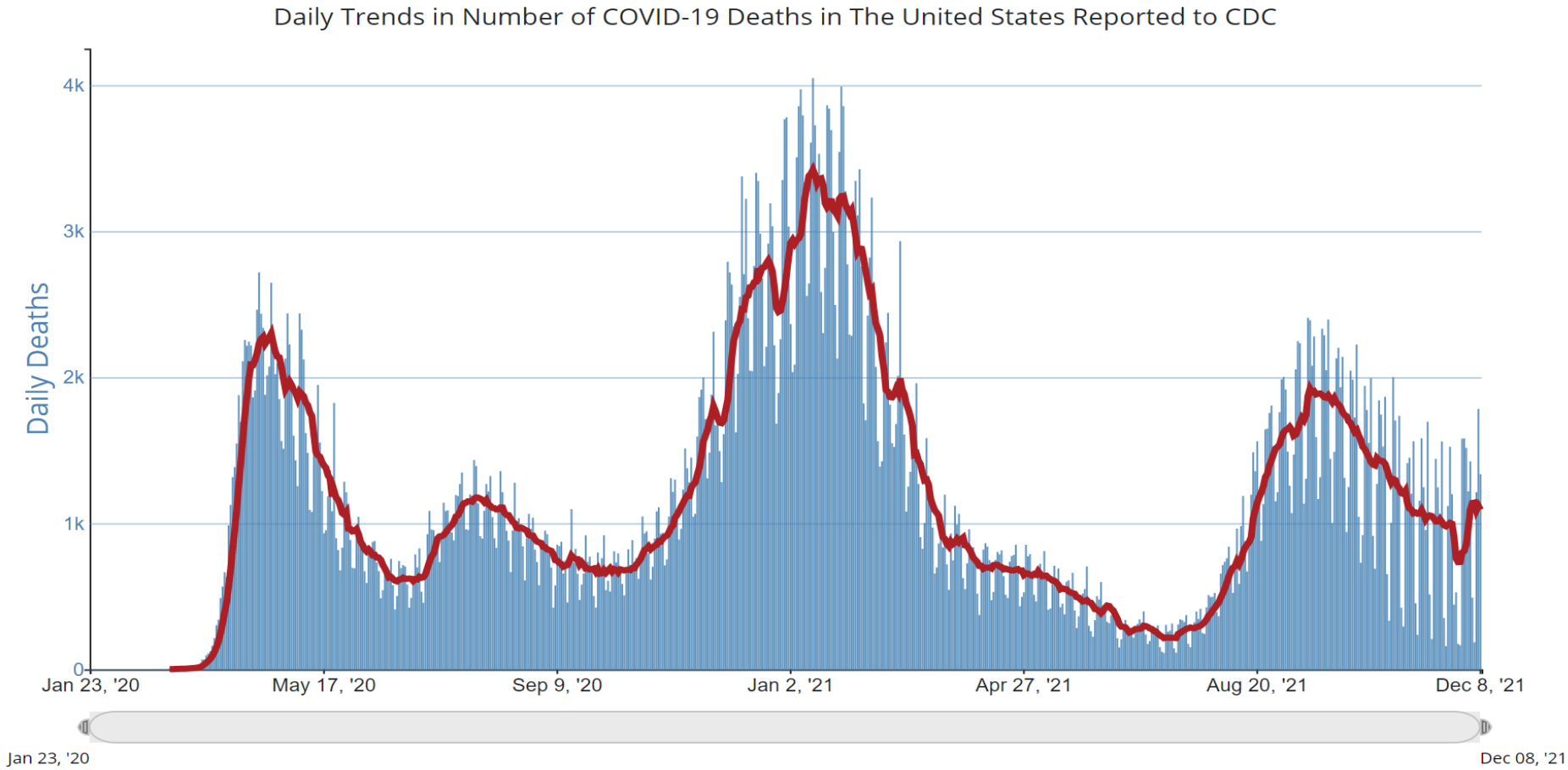
- Bone and cartilage toxicity – don't give to under 18
- Embryofetal toxicity – don't give in pregnancy
- Bone marrow toxicity in dogs – not seen in human trials
- Mutagenicity (potential to cause cancer) – considered low
- Potential for enhanced viral evolution
- Bottom line – may be helpful for high-risk individuals if given early, and is probably safe at human dose and short course

Where are we headed?



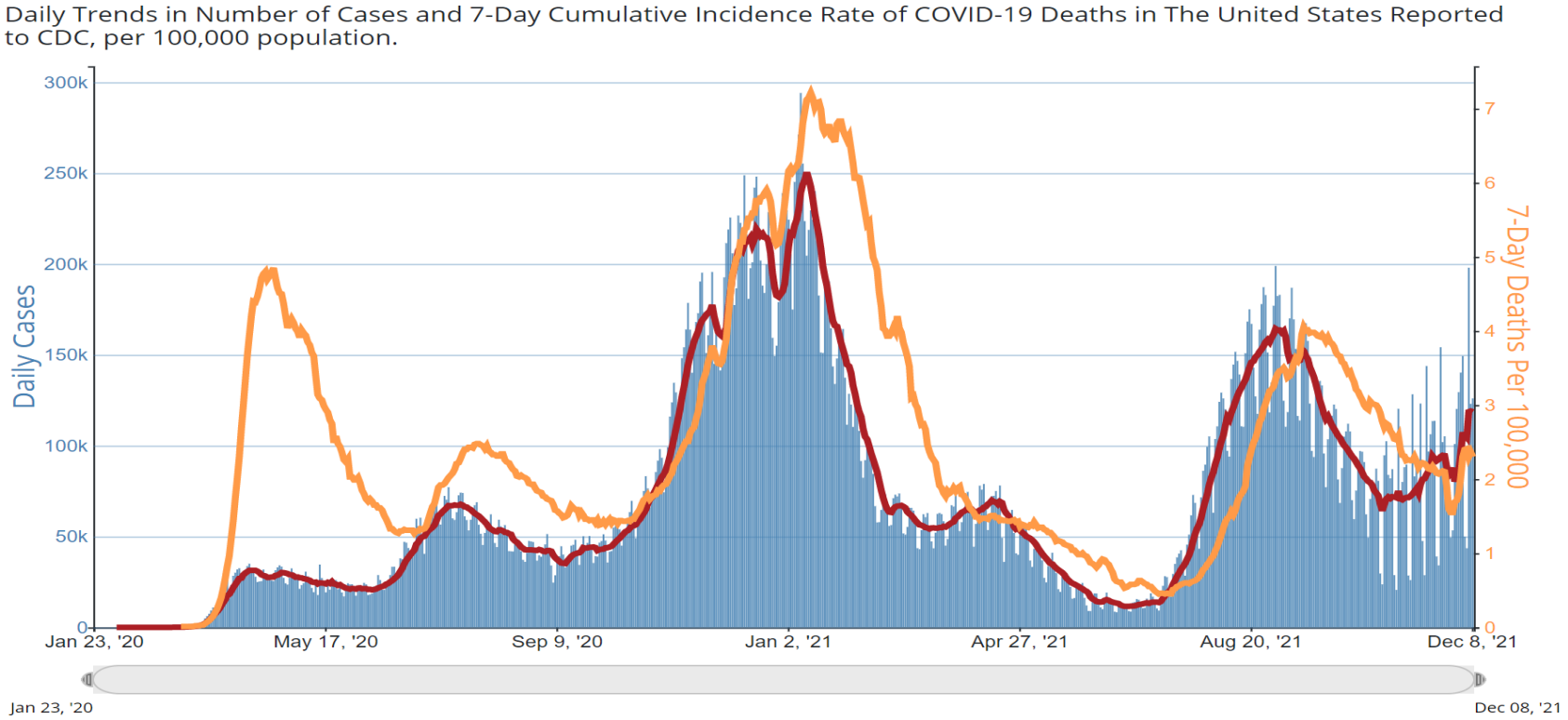
Because there is Strength in Unity

Daily Deaths in the US



Because there is Strength in Unity

Daily Cases and Deaths in the US



Because there is Strength in Unity

Take Home Points/Summary

- Omicron is here – it may be more transmissible, it is probably somewhat resistant to vaccines and monoclonal antibodies
- Booster doses of vaccines are now indicated for everyone 16 and over
- Booster doses are thought to be beneficial against Omicron
- Winter is coming!
- Get vaccinated for influenza if you haven't already
- Molnupiravir may be modestly helpful for high risk patients
- **Public health measures are still important!**

Thanks for your time and attention

Have a nice weekend!

Questions?

Harry J Brown

Medical Epidemiologist

USET Tribal Epidemiology Center

hbrown@usetinc.org

615-917-7526

Because there is Strength in Unity