University of Washington
Public Health Capacity Building Center

COVID-19 Clinical Update
I-TECH Videoconference September 13, 2021

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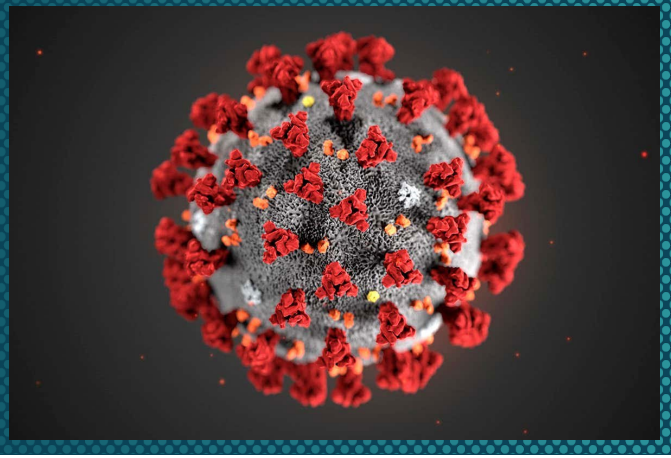


Last Updated: September 13, 2021

I-TECH
International Training and Education Center for Health

Overview

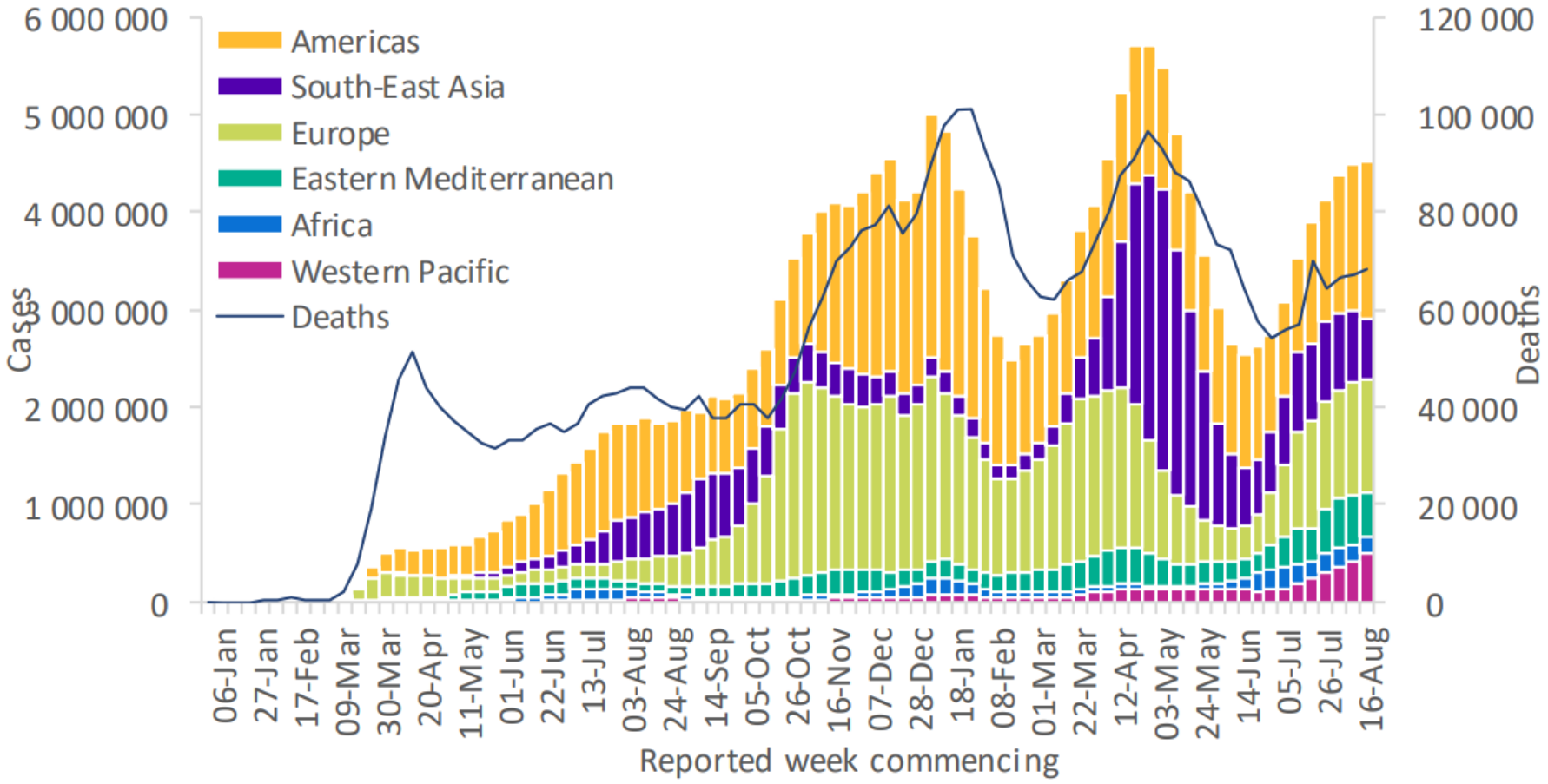
- Epidemiology
- Vaccines – Focus on Efficacy
  - Impact of Delta Variant
  - Impact of time and waning immunity

Global Trends in COVID-19 Diagnoses & Deaths

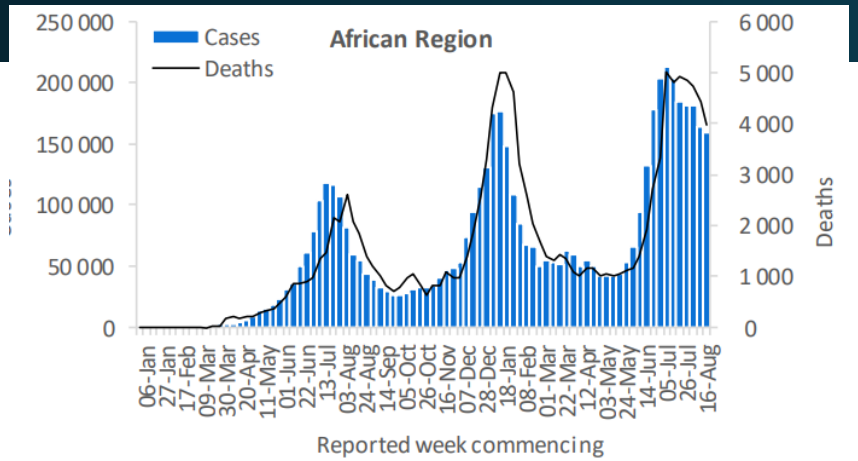
>211 Million Confirmed Cases
4.5 million cases/week

~4.4 Million Confirmed Deaths
45,000 deaths/week

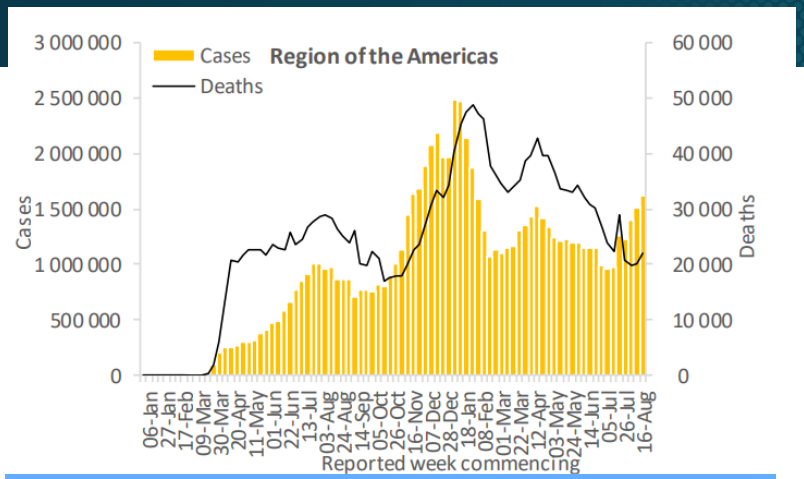
Figure 1. COVID-19 cases reported weekly by WHO Region, and global deaths, as of 22 August 2021**



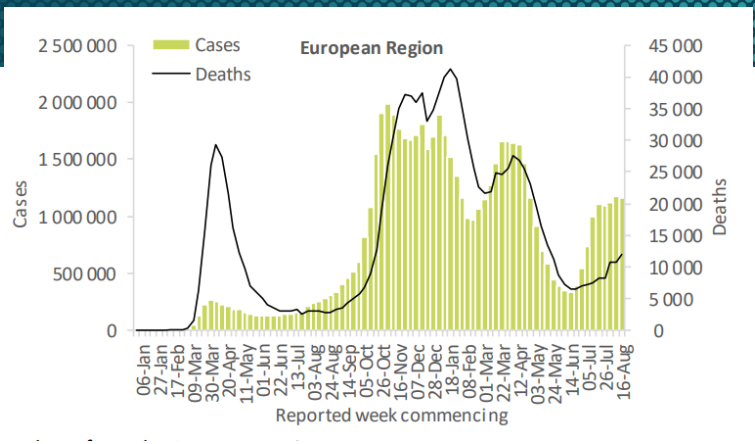
Global Trends in COVID-19 Diagnoses & Deaths



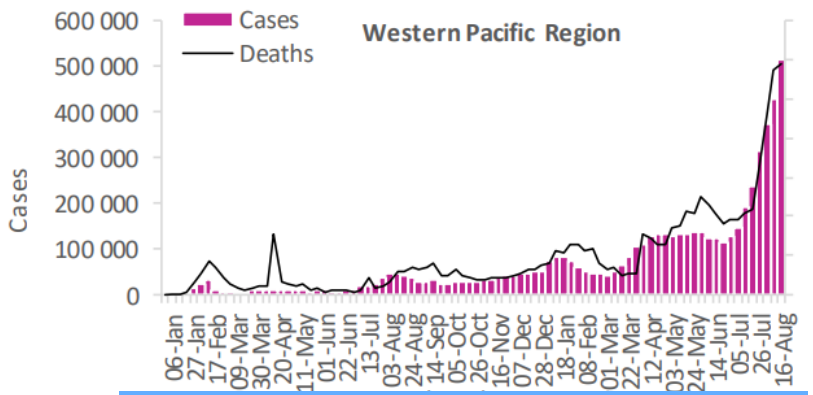
Highest Rate in Botswana, though declining



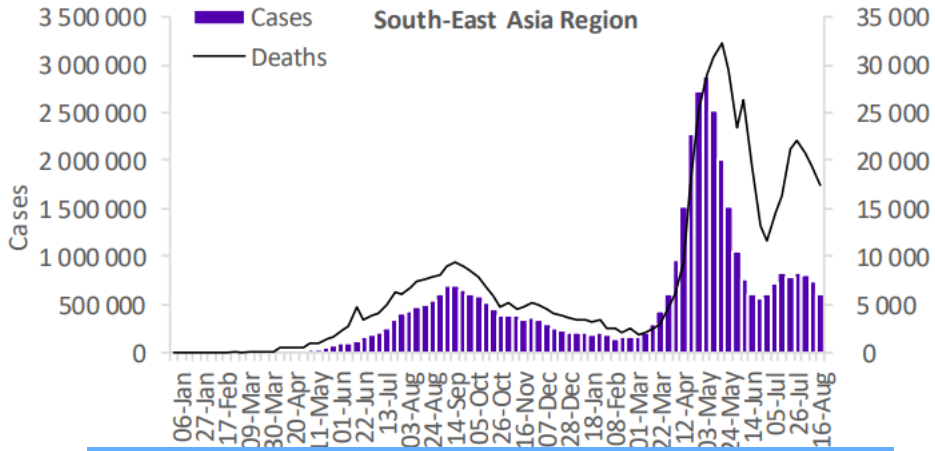
Highest rates in US, but death is higher Mexico and Brazil



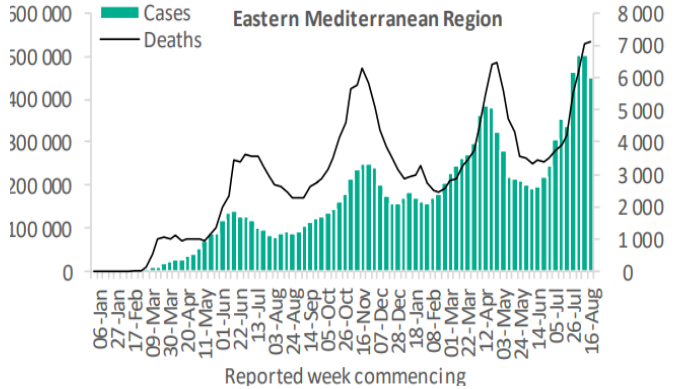
Highest rates in UK



Highest rate and death rates in Malaysia

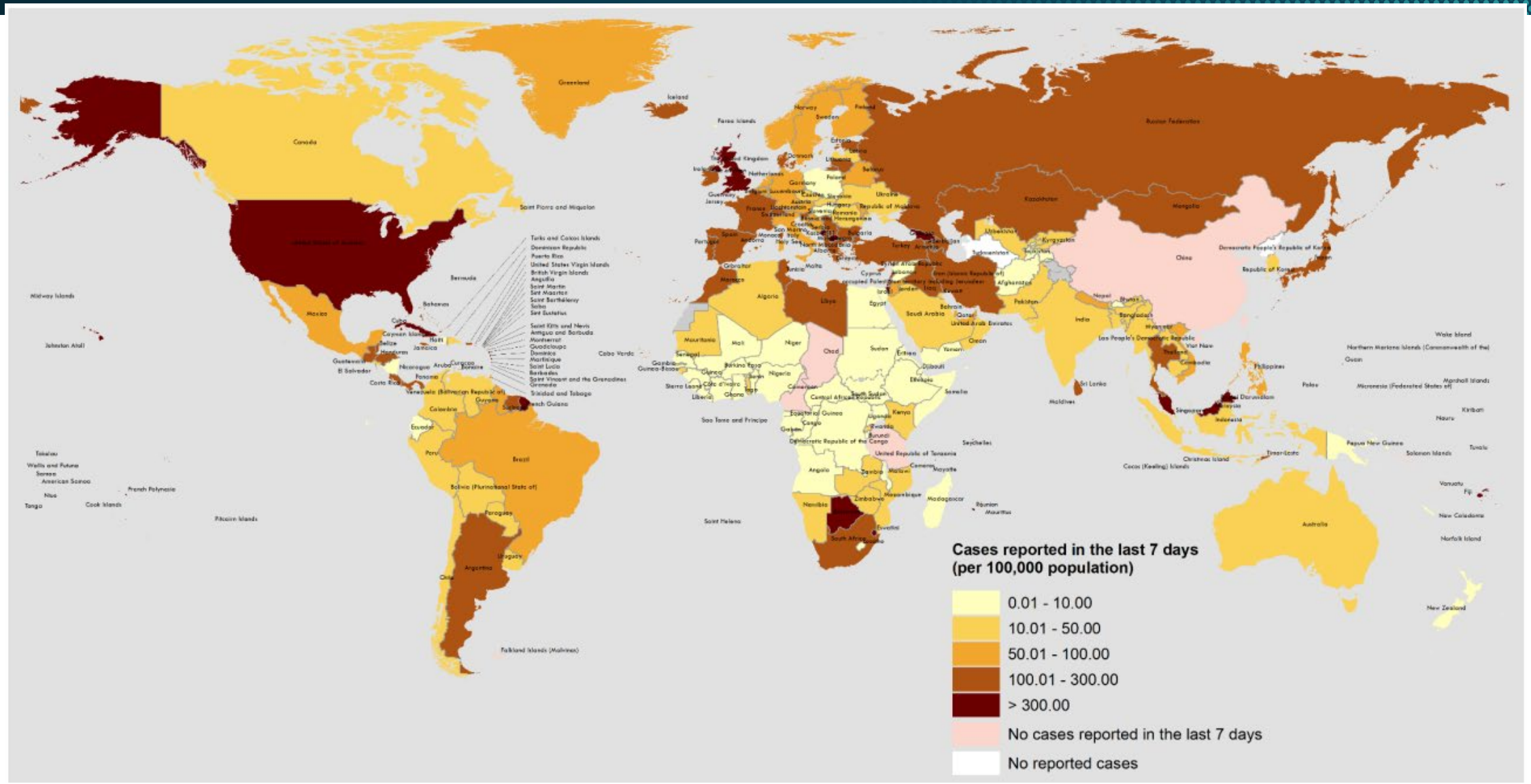


Highest rate in Thailand. Highest death rate in Indonesia

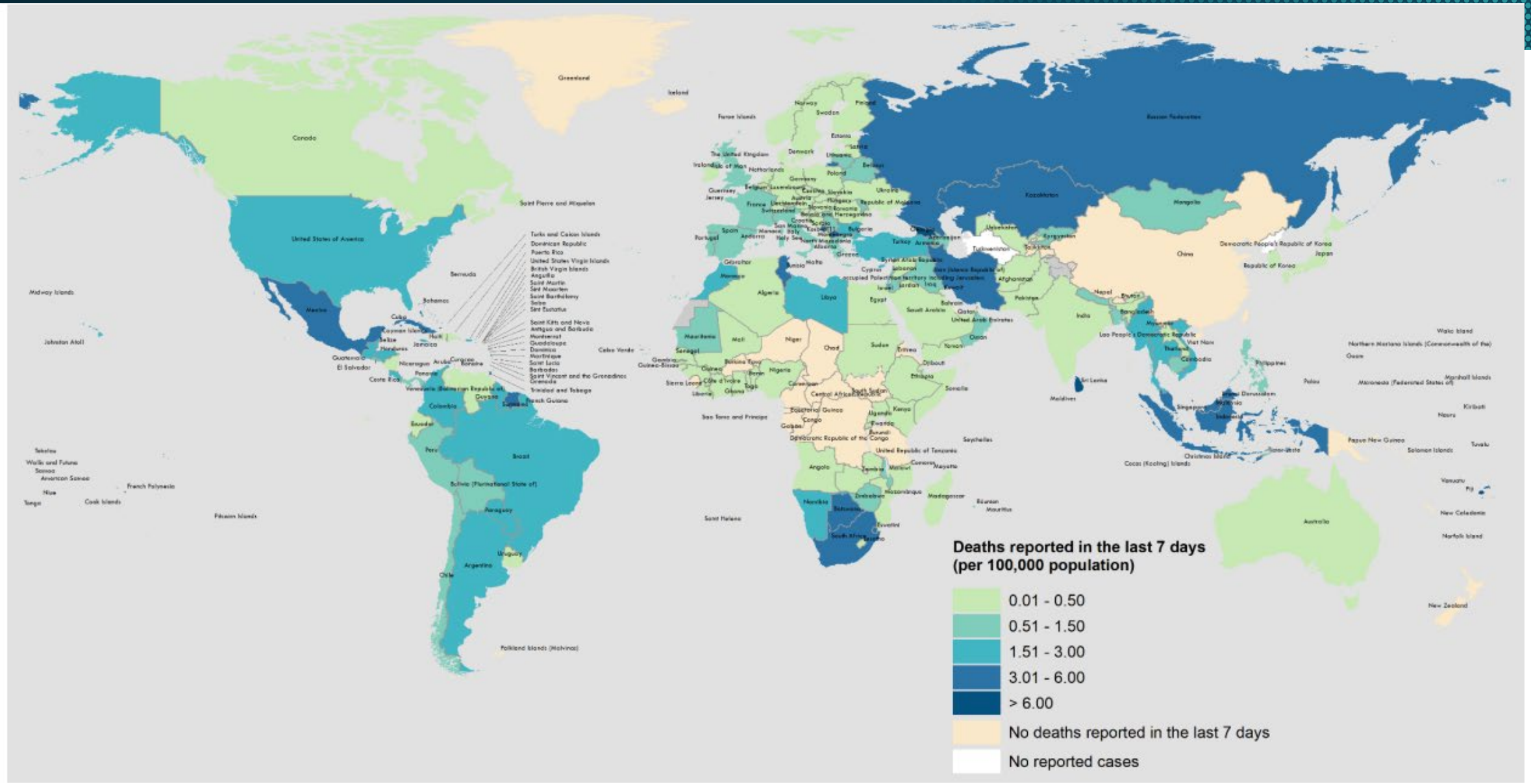


Highest rate and death rates in Iran

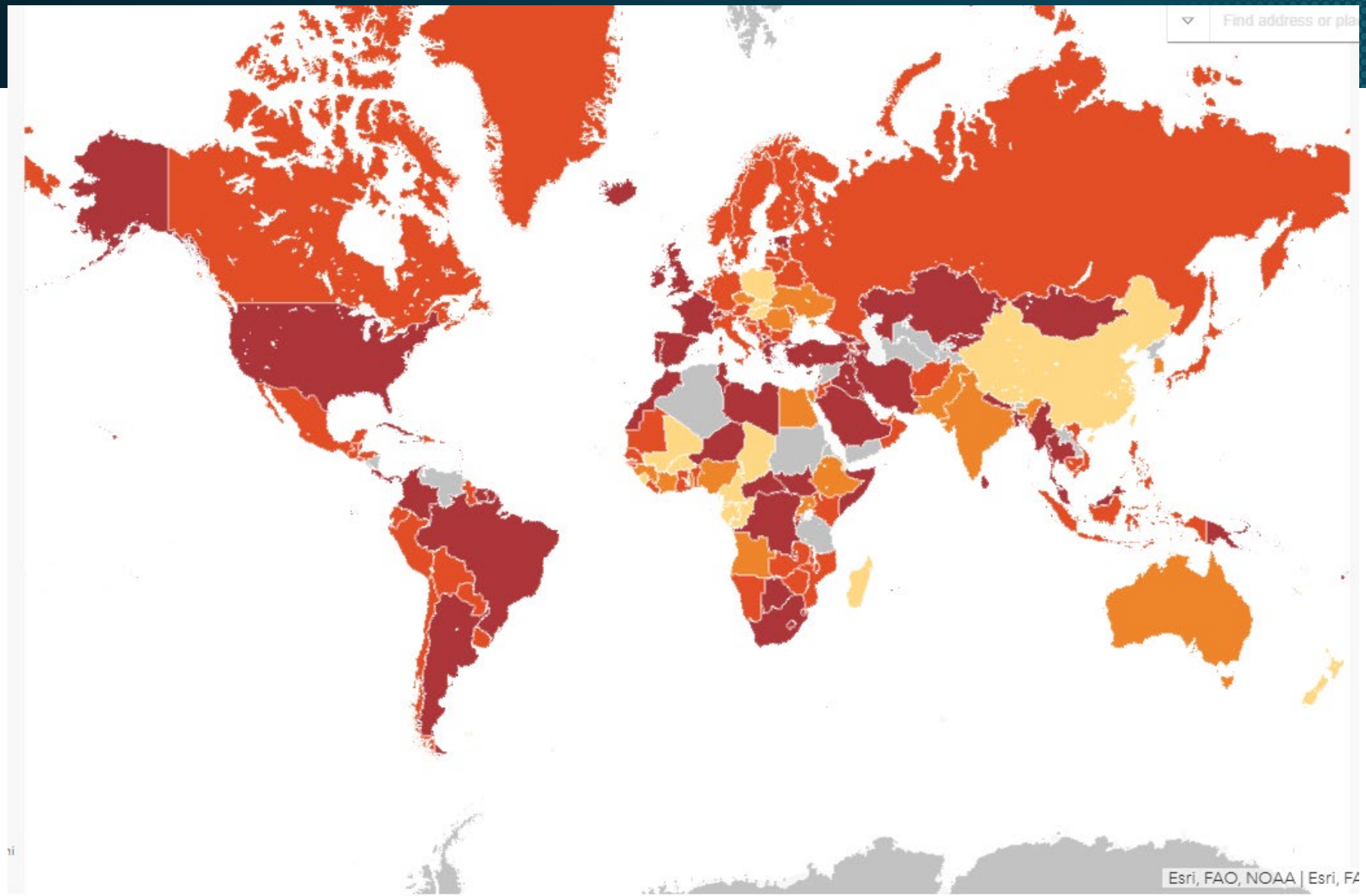
COVID-19 cases/100,000 population, 16 August – 22 August 2021



COVID-19 deaths/100,000 population, 16 August – 22 August 2021



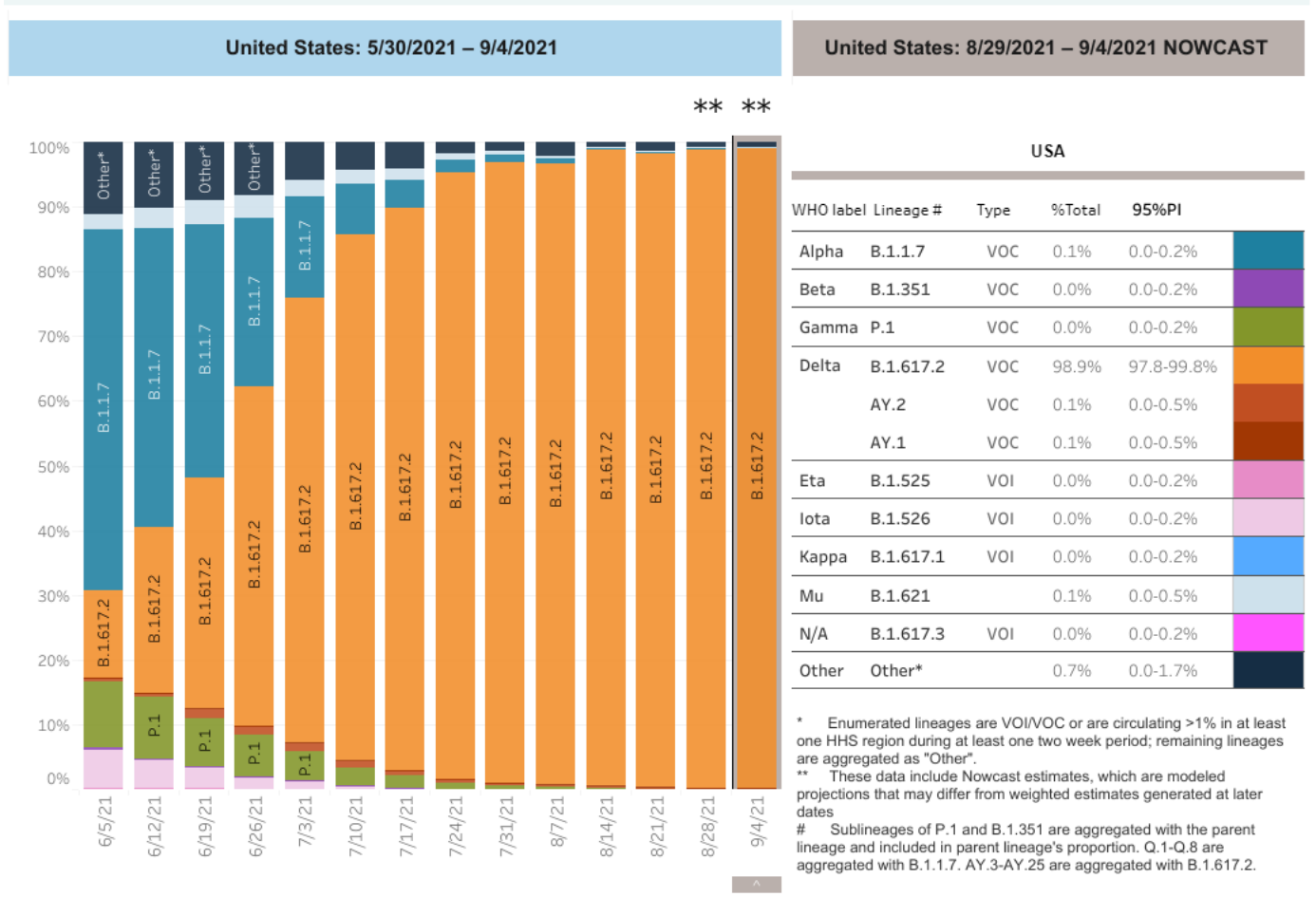
CDC COVID-19 Risk Assessment



Risk Assessment Level for COVID-19

- Level 4: COVID-19 Very High
- Level 3: COVID-19 High
- Level 2: COVID-19 Moderate
- Level 1: COVID-19 Low
- Level Unknown: COVID-19 Unknown

New CDC Variant Classification System



United States: 8/29/2021 – 9/4/2021 NOWCAST

USA

WHO label	Lineage #	Type	%Total	95%PI
Alpha	B.1.1.7	VOC	0.1%	0.0-0.2%
Beta	B.1.351	VOC	0.0%	0.0-0.2%
Gamma	P.1	VOC	0.0%	0.0-0.2%
Delta	B.1.617.2	VOC	98.9%	97.8-99.8%
	AY.2	VOC	0.1%	0.0-0.5%
	AY.1	VOC	0.1%	0.0-0.5%
Eta	B.1.525	VOI	0.0%	0.0-0.2%
Iota	B.1.526	VOI	0.0%	0.0-0.2%
Kappa	B.1.617.1	VOI	0.0%	0.0-0.2%
Mu	B.1.621		0.1%	0.0-0.5%
N/A	B.1.617.3	VOI	0.0%	0.0-0.2%
Other	Other*		0.7%	0.0-1.7%

* Enumerated lineages are VOI/VOC or are circulating >1% in at least one HHS region during at least one two week period; remaining lineages are aggregated as "Other".
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# Sublineages of P.1 and B.1.351 are aggregated with the parent lineage and included in parent lineage's proportion. Q.1-Q.8 are aggregated with B.1.1.7. AY.3-AY.25 are aggregated with B.1.617.2.

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

Vaccines

Impact of mRNA Vaccines on Household Transmission

Background: Impact of vaccines on transmission not well defined. UK data (reviewed in July) suggested ~50% decreased transmission in households following immunization.

Design: Comparison of periods before and after healthcare workers were vaccinated in UK

Population: 194,362 household members of 144,525 healthcare workers

Outcome: CoV-2 + test and hospitalization in <u>unvaccinated</u> household contacts

Source: Shah A. NEJM 202

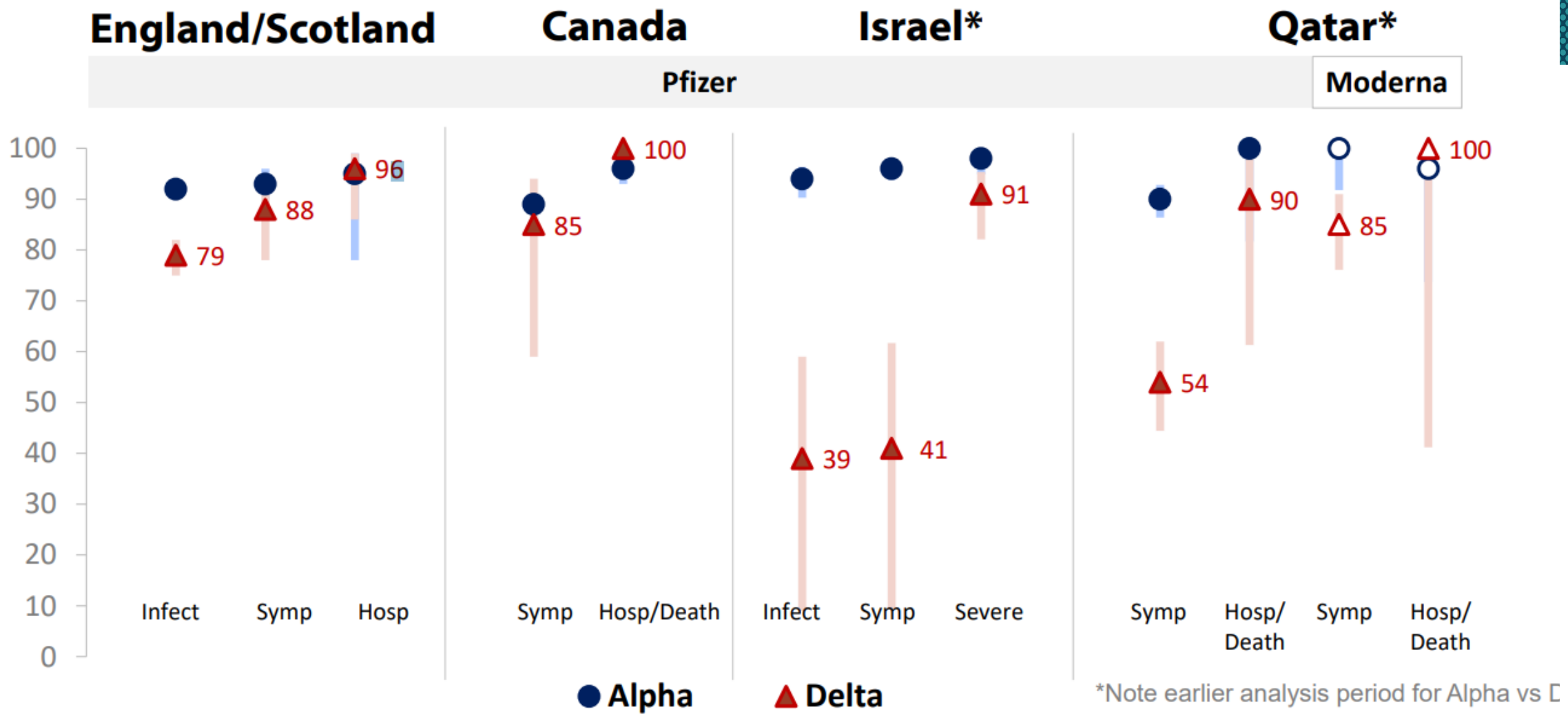
Table 1. Effect of Vaccination of Health Care Workers on Documented Covid-19 Cases and Hospitalizations in Health Care Workers and Their Households.*

Variable	Health Care Workers			Household Members		
	Unvaccinated Period	Period Beginning 14 Days after First Dose	Hazard Ratio (95% CI)	Unvaccinated Period	Period Beginning 14 Days after First Dose	Hazard Ratio (95% CI)
Cases†						
No. of patients	144,525	109,074		194,362	148,366	
No. of events	3191	1152		2037	1086	
Mean person-time — days	40	45		41	45	
Rate per 100 person-yr	20.13	8.51		9.40	5.93	
Comparison of rates per 100 person-yr						
Unadjusted model			0.51 (0.48–0.55)			0.74 (0.67–0.82)
Model 1			0.52 (0.49–0.56)			0.73 (0.66–0.81)
Model 2			0.55 (0.51–0.59)			0.75 (0.68–0.83)
Model 3			0.45 (0.42–0.49)			0.71 (0.63–0.78)
Model 4‡			0.45 (0.42–0.49)			0.70 (0.63–0.78)
Hospitalizations						
No. of patients	144,525	111,081		194,362	149,689	
No. of events	158	19		111	64	
Mean person-time — days	41	45		41	45	
Rate per 100 person-yr	0.97	0.14		0.51	0.35	
Comparison of rates per 100 person-yr						
Unadjusted model			0.16 (0.10–0.27)			0.83 (0.58–1.17)
Model 1			0.16 (0.10–0.27)			0.81 (0.57–1.15)
Model 2			0.17 (0.10–0.29)			0.86 (0.61–1.23)
Model 3			0.15 (0.09–0.26)			0.77 (0.53–1.10)
Model 4‡			0.16 (0.09–0.27)			0.77 (0.53–1.10)

Successive Models adjust for increasing number covariates

Successive Models adjust for increasing number covariates

Pfizer & Moderna 2-Dose Effectiveness for Alpha vs. Delta



Sheikh et al. Lancet (2021): https://doi.org/10.1016/S0140-6736(21)01358-1; Lopez Bernal et al. medRxiv preprint; https://doi.org/10.1101/2021.05.22.21257658; Stowe et al. PHE preprint: https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZlEig/view/479607266; Nasreen et al.medRxiv preprint: https://doi.org/10.1101/2021.06.28.21259420; Haas et al Lancet (2021): https://doi.org/10.1016/S0140-6736(21)00947-8 ; Israel MOH: https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_two-dose-vaccination-data.pdf Abu-Radad and Butt. NEJM (2021); Chemaitelly et al. Nature Med (2021): Tang et al medRxiv

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-13/04-COVID-Scobie-508.pdf

Changing Vaccine Effectiveness

Background: Numerous studies have suggested that the effectiveness of mRNA vaccines against the delta variant is diminished. Relative impact on different mRNA vaccines uncertain.
Design & Population: Retrospective cohort study two cohorts of ~25,000 (vaccinated & unvaccinated) adults wit no h/o SAR-CoV2 matched for demographics, date vaccination, h/o PCT testing in the Mayo Health System, MN, USA. Comparison VE 2 vaccines in 5 states of Mayo System
Outcome: Vaccine effectiveness against infection & hospitalization.

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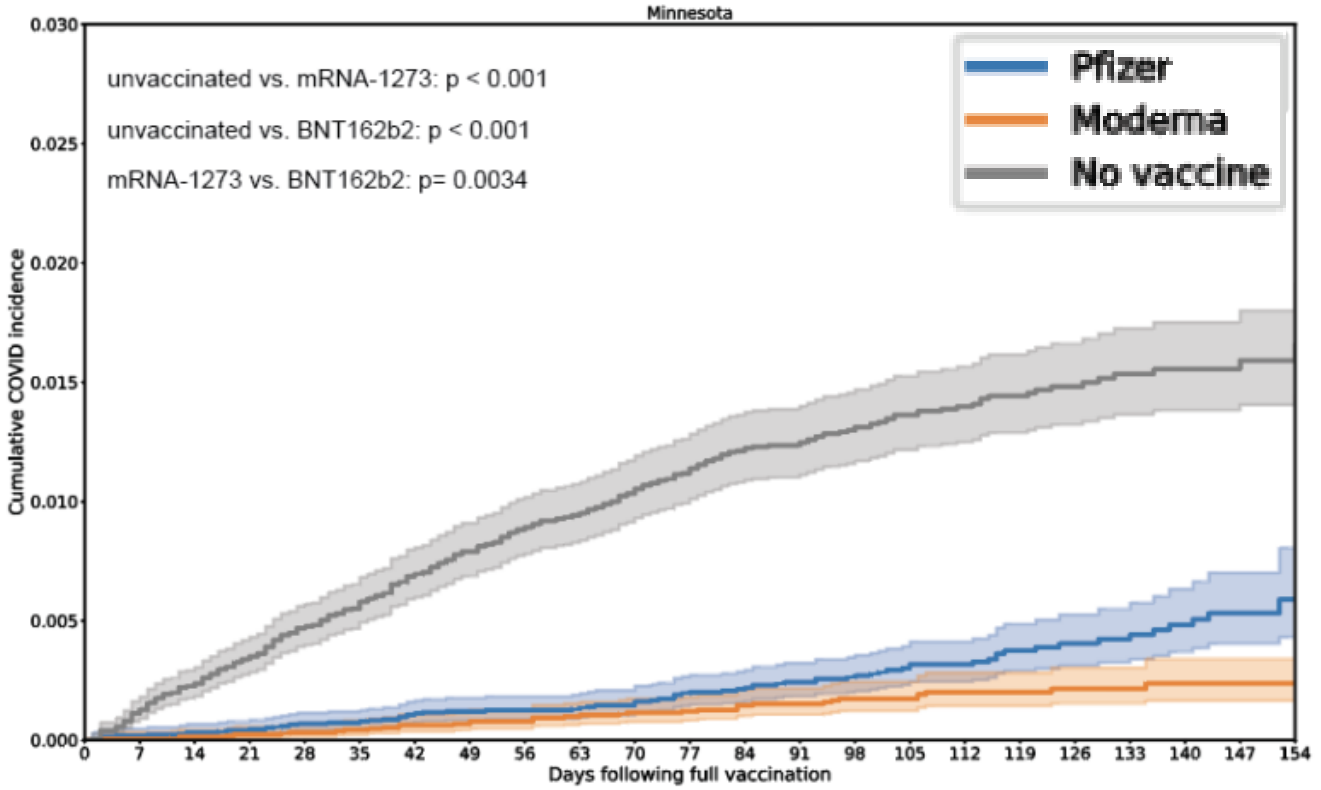
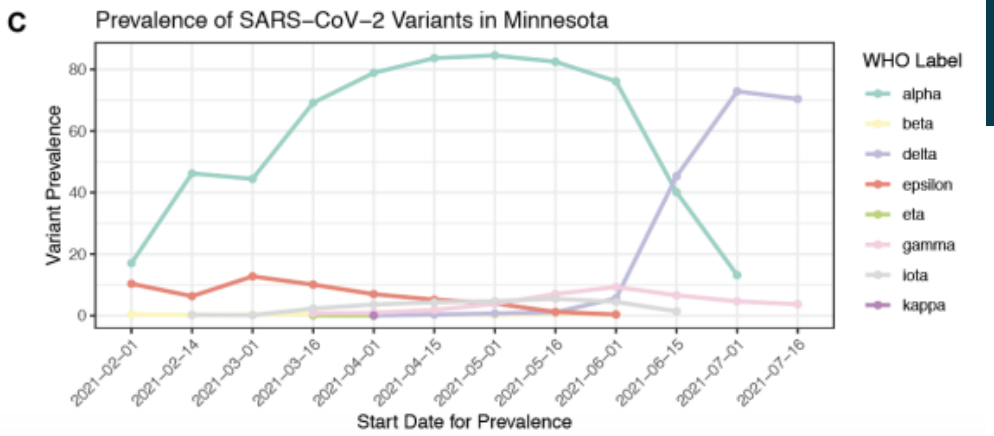
Comparison of cumulative incidence of SARS-CoV-2 infection between propensity-matched individuals in Minnesota

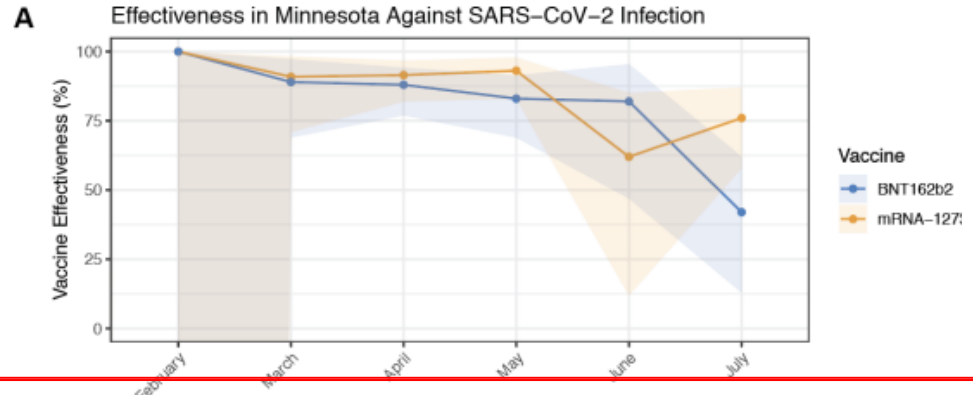


	VE Infection	VE Hospitalization
Pfizer	76%	85%
Moderna	86%	92%

Changing Vaccine Effectiveness

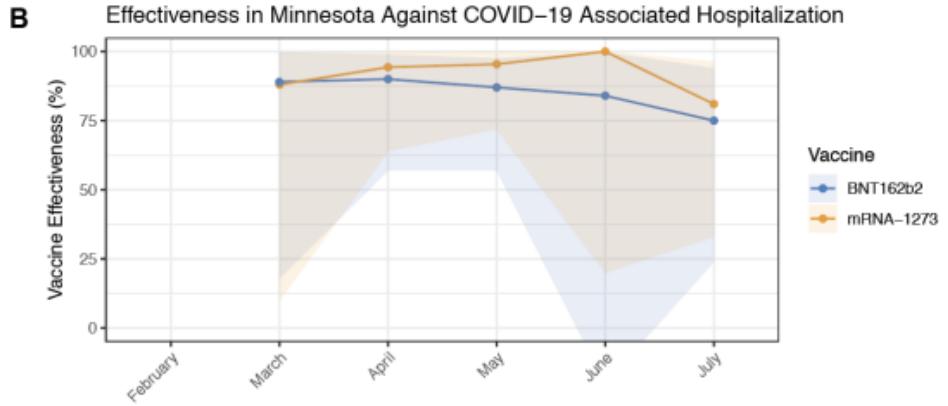


Delta Becomes Dominant June-July



VE July
-Pfizer 42%
-Moderna 76%

Moderna vs. Pfizer
IRR 0.56 (0.36-0.83)



VE July
-Pfizer 75%
-Moderna 81%
Moderna vs. Pfizer
IRR 0.57 (0.17-0.1.7)

Comparison IRR SARS-CoV2 Infection Moderna vs Pfizer Vaccines, 5 States

Timing Vaccination & Time Period	IRR Moderna vs. Pfizer
1-7 days after 2nd dose (entire period)	1.1 (0.16-2.2)
≥14 days after 2nd dose (entire period)	0.5 (0.39-0.64)
≥14 days after 2nd dose (July Only)	0.44 (0.32-0.6)

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Waning Vaccine-Induced Immunity: Israel

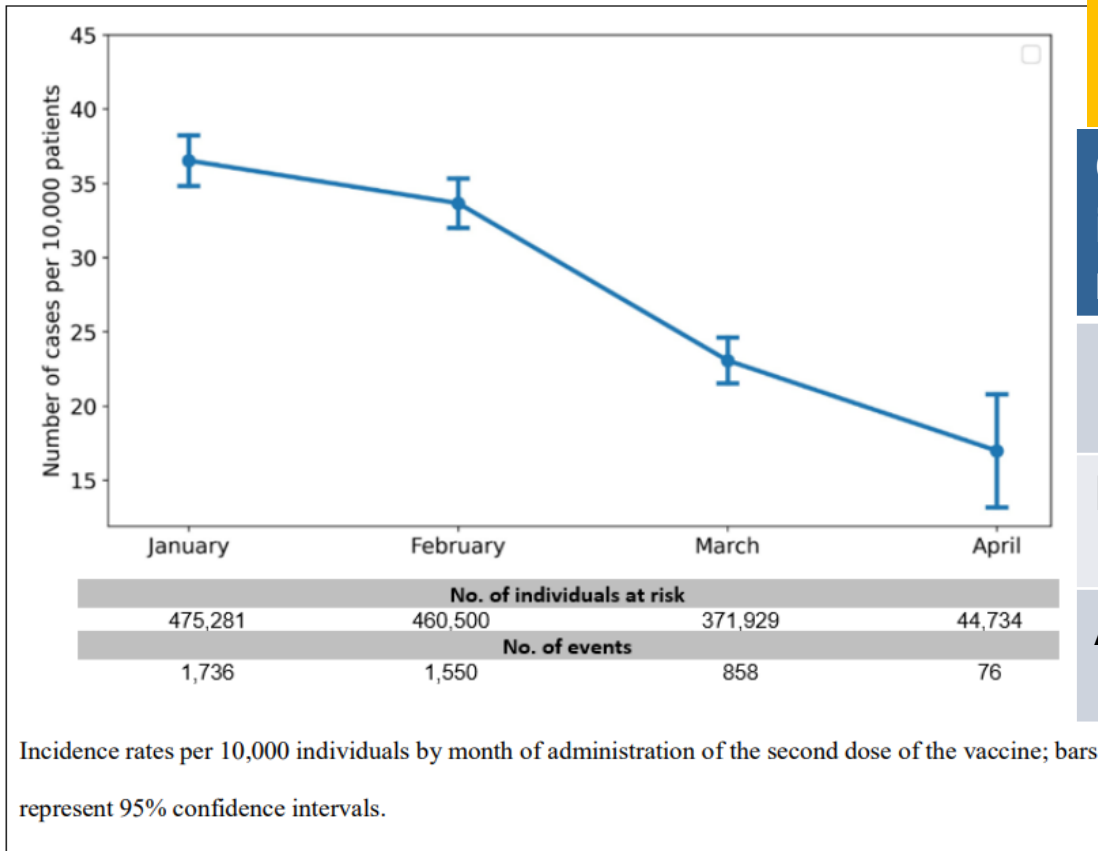
Background: Israel instituted mass immunization with Pfizer vaccine in 12/20 with >100-fold ↓ in cases. A resurgent epidemic June 2020 (>95% Delta). Uncertain role for waning immunity vs. Delta variant.

Data & Population: ~1.3 million Vaccinated Maccabi Healthcare Systems (MHS) patients with no h/o SARS-CoV2

Design: Retrospective cohort study persons receiving care through Maccabi Healthcare Systems (an HMO).

Outcome: SARS-CoV2 June 1-July 27, 2021

Incidence SARS-CoV-2 6/1/21-7/27/21, by Time of 2nd Vaccine Dose



Incidence rates per 10,000 individuals by month of administration of the second dose of the vaccine; bars represent 95% confidence intervals.

Risk of SARS-CoV-2 Among Persons Vaccinated in January 2021 vs. Feb-March

Comparison month	OR (95% CI)
Feb	**1.33** (1.21-1.46)
March	**1.65** (1.44-1.89)
April	**2.26** (1.70-3.01)

Mizrahi B. MedRxiv 2021

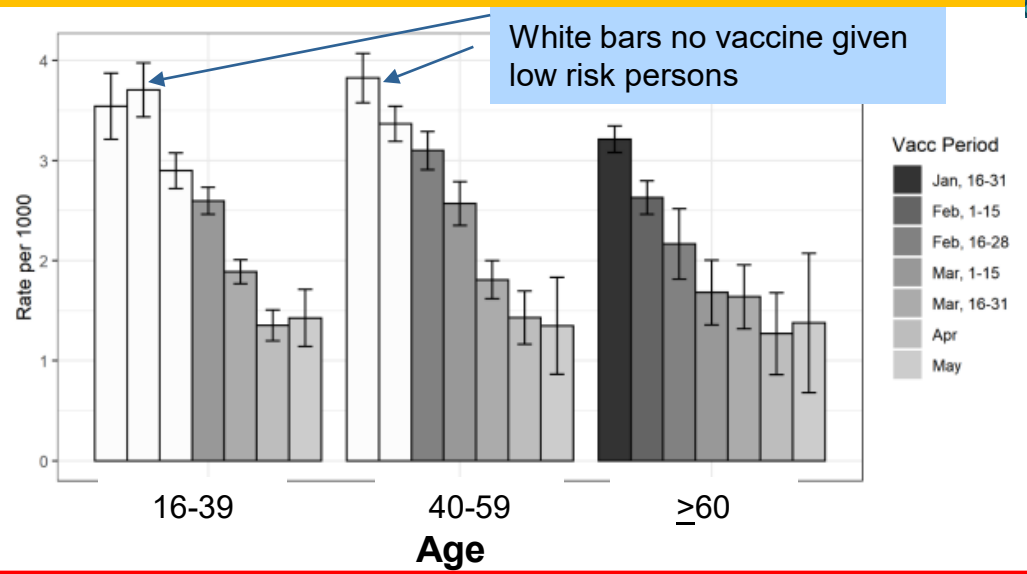
Waning Vaccine-Induced Immunity: Israel

Background: Israel instituted mass immunization with Pfizer vaccine in 12/20 with >100-fold ↓ in cases. A resurgent epidemic occurred in June 2020 (>95% Delta). Uncertain role for waning immunity vs. Delta variant.
Data & Population: All PCR+ cases in Israel July 11-31 among ~5 million vaccinated persons
Design: Comparison of rates of infection and severe infection among persons vaccinated at different times.
Outcome: SARS-CoV2 infection or Severe COVID

Goldberg Y. MedRxiv 2021

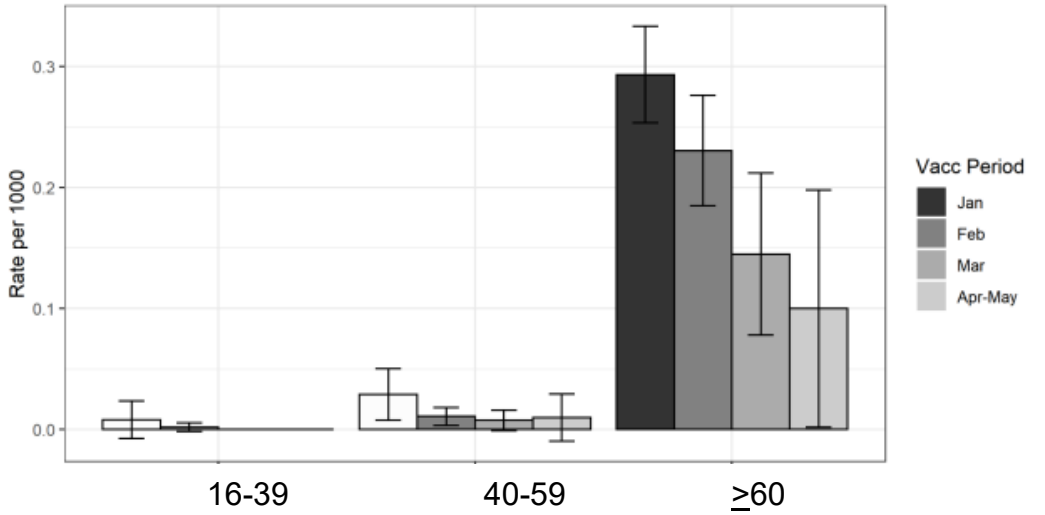
Rate SARS-CoV-2 July 11-31, 2021by Time of 2nd Vaccine Dose & Age

Rates lower in more recently vaccinated



Rate Severe SARS-CoV-2 July 11-31, 2021

Rates severe disease very low in younger people, but lower in more recently vaccinated elderly



Waning Vaccine-Induced Immunity: Israel
Multivariate Analysis

Protection against SARS-CoV2 and Severe COVID-19 compared to persons vaccinated January 16-31, by age group.

Increasing protection among more recently vaccinated on multivariate analysis

OUTCOME = Positive SARS-CoV-2 PCR test

Age	FebA	FebB	MarA	MarB	Apr	May
16-39	0.9 [0.8, 1]	1.2 [1, 1.3]	1.3 [1.1, 1.4]	1.5 [1.4, 1.7]	2 [1.7, 2.3]	2 [1.6, 2.5]
40-59	1.1 [1, 1.1]	1.1 [1, 1.2]	1.2 [1.1, 1.4]	1.6 [1.4, 1.8]	1.9 [1.6, 2.4]	2.3 [1.6, 3.3]
60+	1.1 [1.1, 1.2]	1.3 [1.1, 1.5]	1.6 [1.3, 2]	1.6 [1.3, 2]	2.1 [1.5, 2.9]	2.1 [1.2, 3.4]

OUTCOME = Severe COVID-19

Age	Feb	Mar
40-59	2.2 [0.8, 6.1]	2.8 [0.7, 10.9]
60+	1.2 [0.9, 1.5]	1.7 [1.0, 2.7]

Adjusted for week infection, # prior PCR tests, demographic group (Jewish, Arab, ultra-orthodox), gender

Findings Consistent with Waning Immunity with Time from Immunization Over ~6 months

Vaccine Effectiveness Remained High Among Younger People

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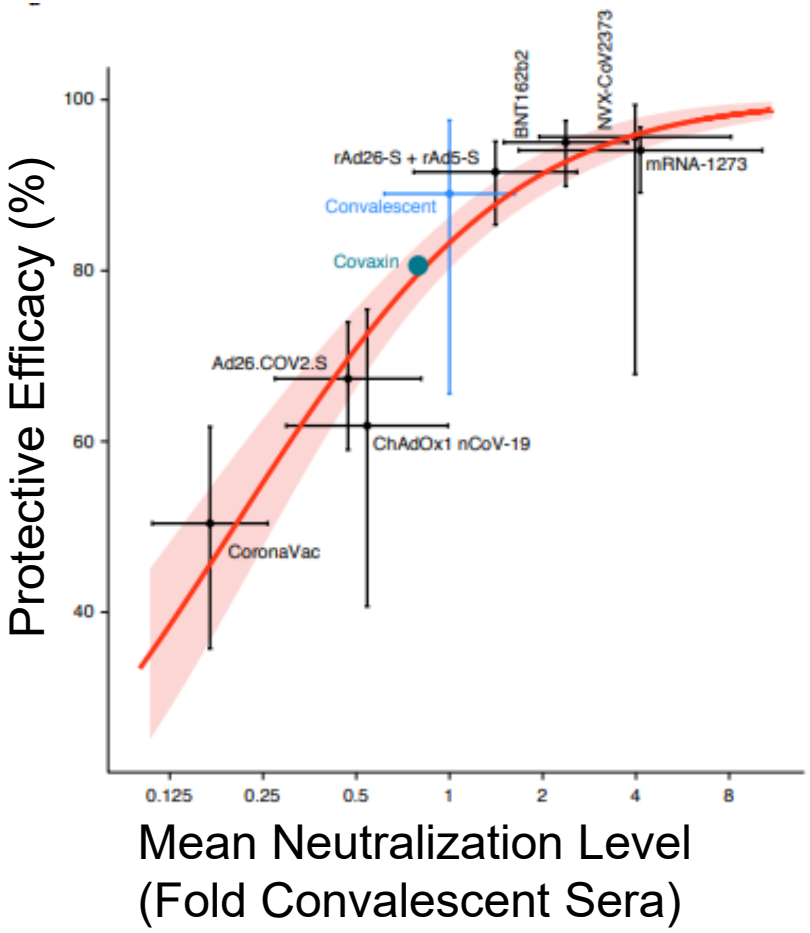
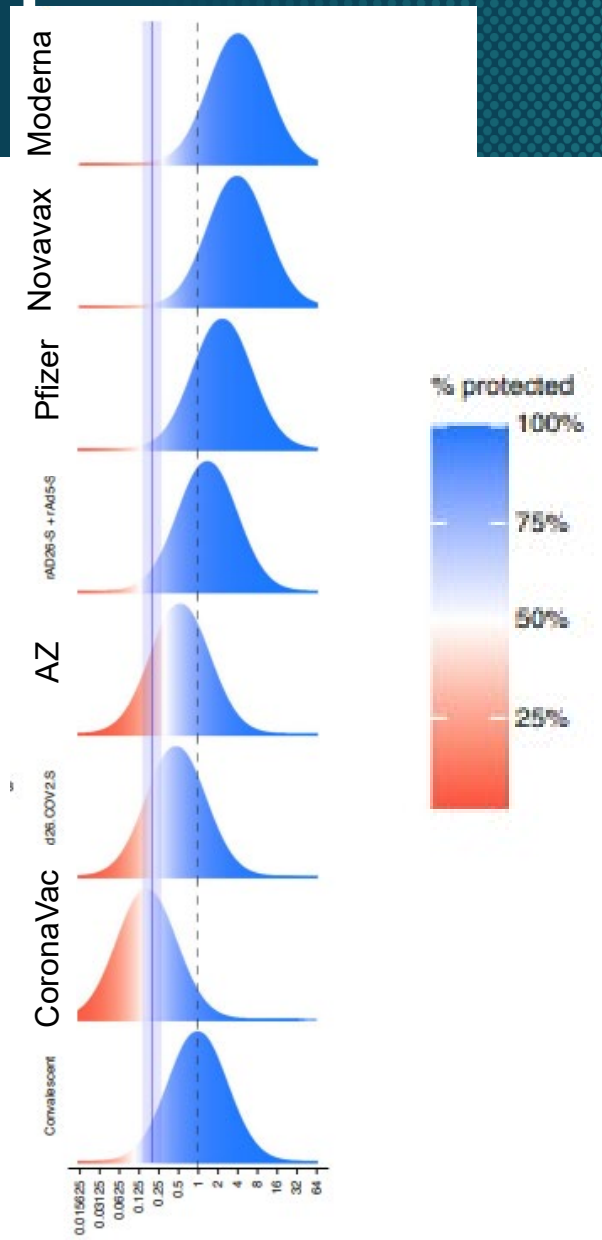
Association of Antibody Response with Protection

Relationship of Mean Antibody Neutralization Level and Observed Protective Efficacy in COVID-19 Vaccine Trials



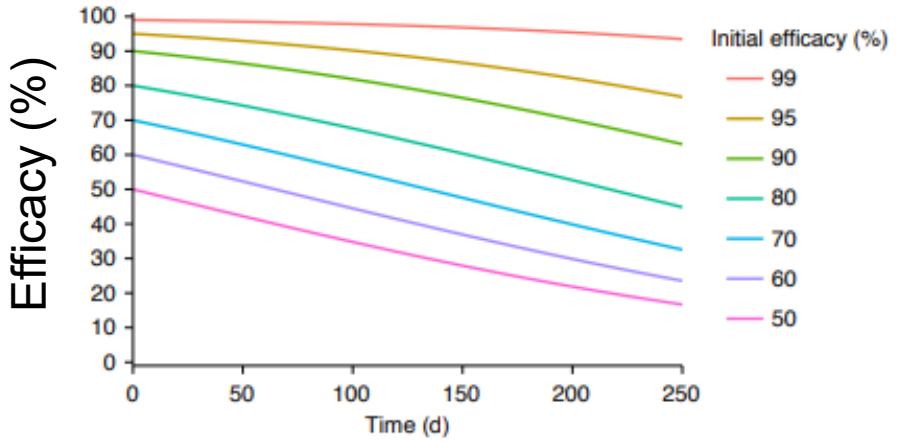


Relationship of Mean Antibody Neutralization Level and Observed Protective Efficacy in COVID-19 Vaccine Trials

Khoury DS. Nature Med 2021

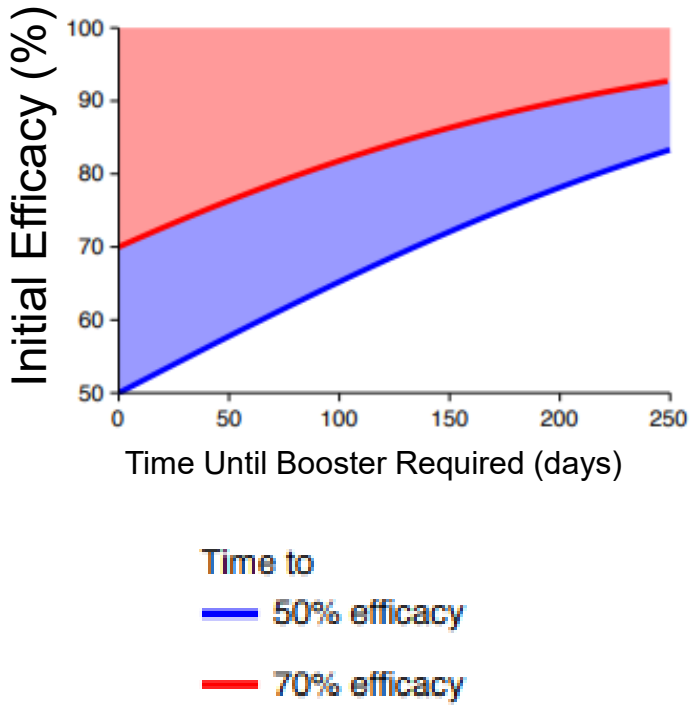
Estimated Decay in Vaccine Efficacy Based, Time to Need for Booster, and Impact of Variants on Efficacy

Estimated Vaccine Efficacy Over Time Based on Initial Efficacy*

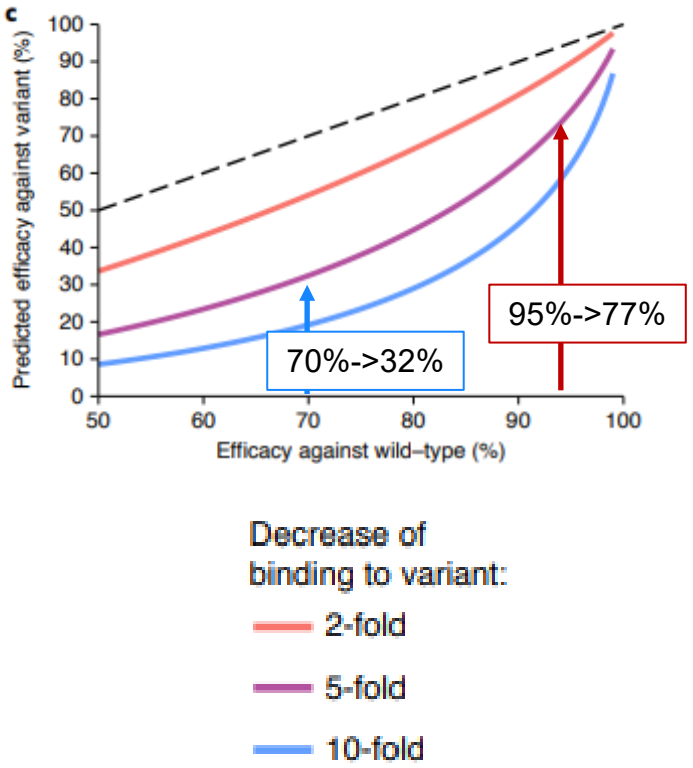


*Based on decline in neutralizing Ab assuming constant relationship to Ab to efficacy

Time for Efficacy to Drop to 50% or 70% Based on Initial Efficacy



Predicted Efficacy Against Variants Based on Observed Decrease in Neutralization

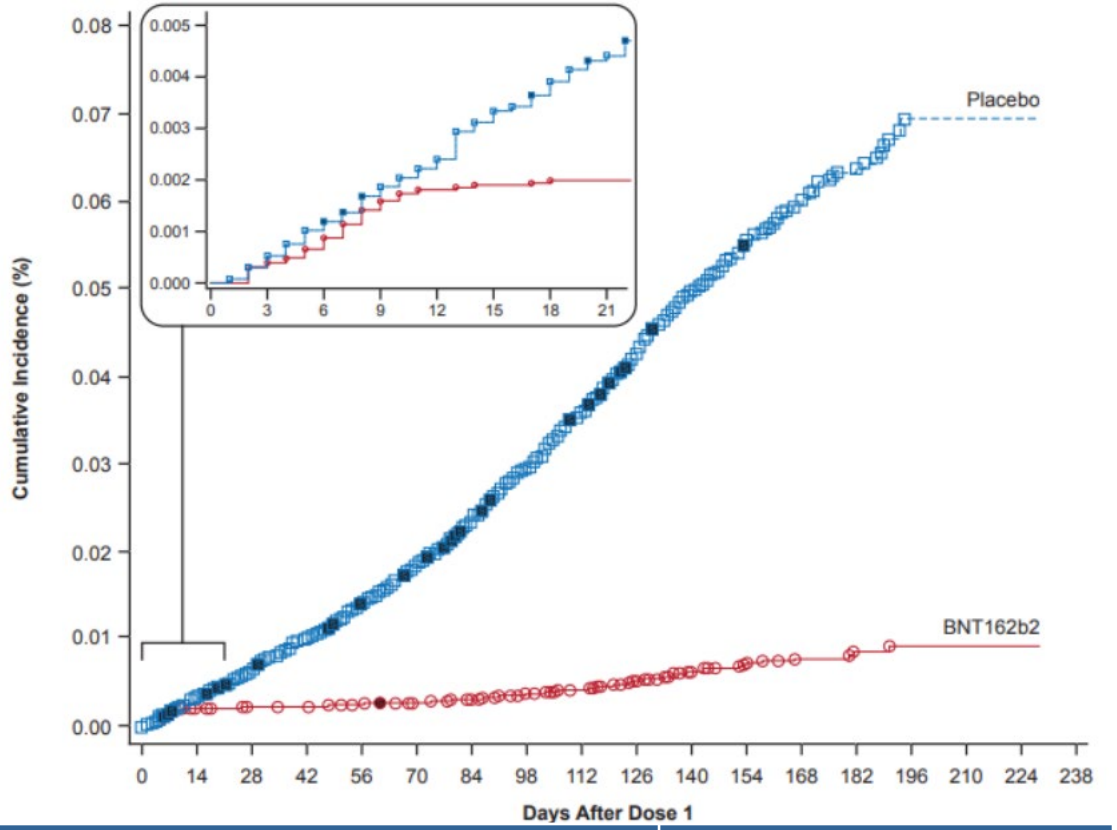


Khoury DS. Nature Med 2021

Waning Vaccine-Induced Immunity: Randomized Trial Data

Background: Long-term vaccine effectiveness of COVID-19 vaccines uncertain.
Data & Population: 44,165 age >16 and 2,264 age 14-15 participating in a RCT of Pfizer vaccine
Design: 6-month follow-up on vaccine effectiveness and safety – cases through March 13, 2021.
Outcome: PCR+ SARS-CoV2 infection ≥7 days post 2nd vaccine

Cumulative Incidence SARS-CoV2



	Vaccine Efficacy
≥7 days to <2 months after 2nd dose	**96.2%** (93.3-98.1)
≥2 months to <4 months after 2nd dose	**90.1%** (86.6-92.9)
≥4 months after 2nd dose	**83.7%** (74.7-89.9)

Vaccine Remains Efficacious at 6 months
Some Evidence Declining Immunity
Pre-Delta Variant

Thomas SJ. MedRxiv 2021

Sinovac (Coronavac) Antibody Response

Background: Antibody response may be a good correlate of immunity. The duration of immunity following immunization is uncertain.
Population: 185 Thai healthcare workers who completed 2 doses of Sinovac (SV) or AstraZeneca (AZ) vaccine.
Design: Prospective cohort study. Ab levels measured at 4 weeks and 12 weeks (SV only) using surrogate viral neutralization test
Outcome: Seroconversion and Ab levels

Seroconversion Among Thai HCWs at 4 Weeks post 2nd Dose Vaccine

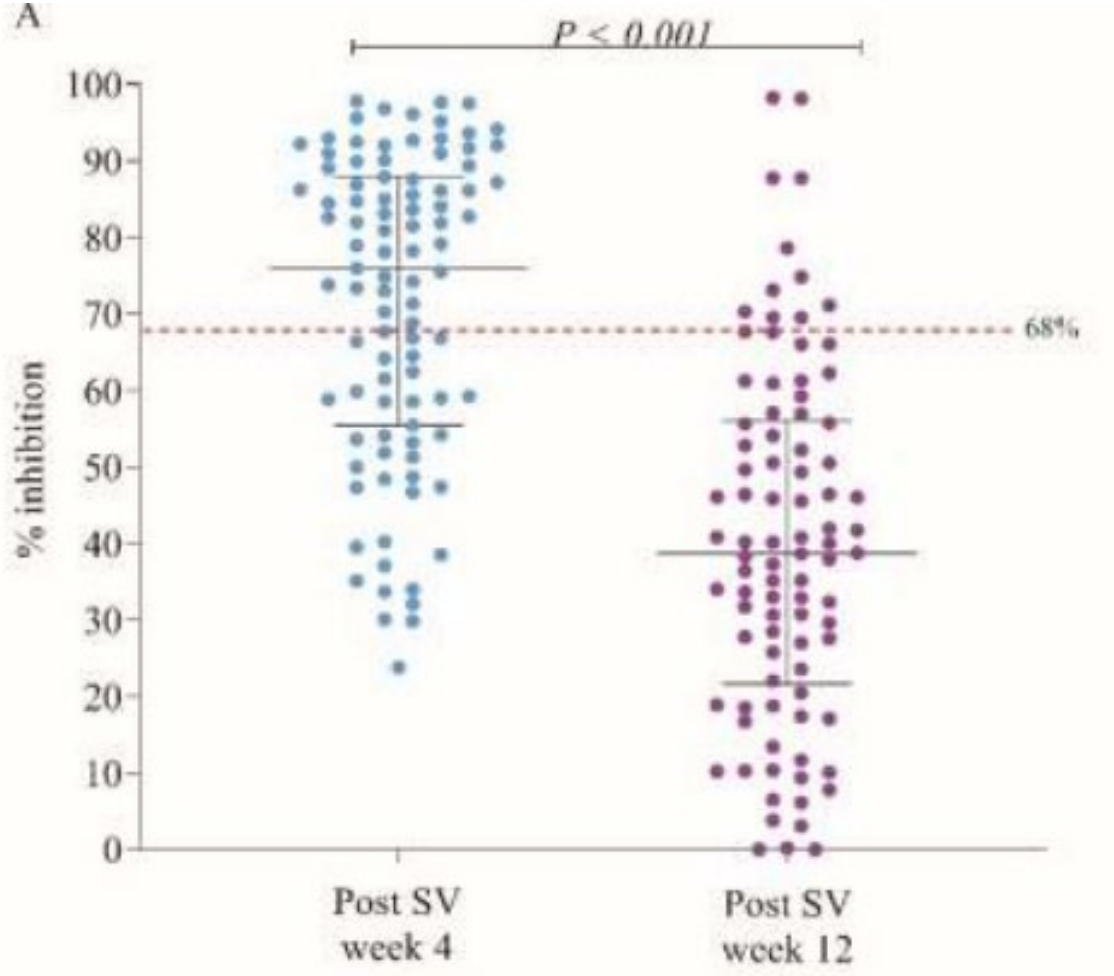
	Sinovac (N=94)	AZ (N=91)	Mild COVID19 (N=58)	COVID19 Pneumonia (N=53)
% Inhibition ≥68%*	60.6%	85.6%	69%	92%
% Inhibition ≥80%**	45.7%	70.3%	51.7%	86.8%
SARS-CoV2 total antibody ≥132 U/ml+	71.3%	100%	34.5%	83%

*Definition serocoverstion **Surrogate for efficacy against variants of concern. +High titer per US FDA

Jantarabenjakul W . MedRxiv 2021

Sinovac (Coronavac) Antibody Response

- Among Sinovac recipients, antibody levels declined between 4 and 12 weeks
- Only 12% met author's criteria for immunity at 12 weeks



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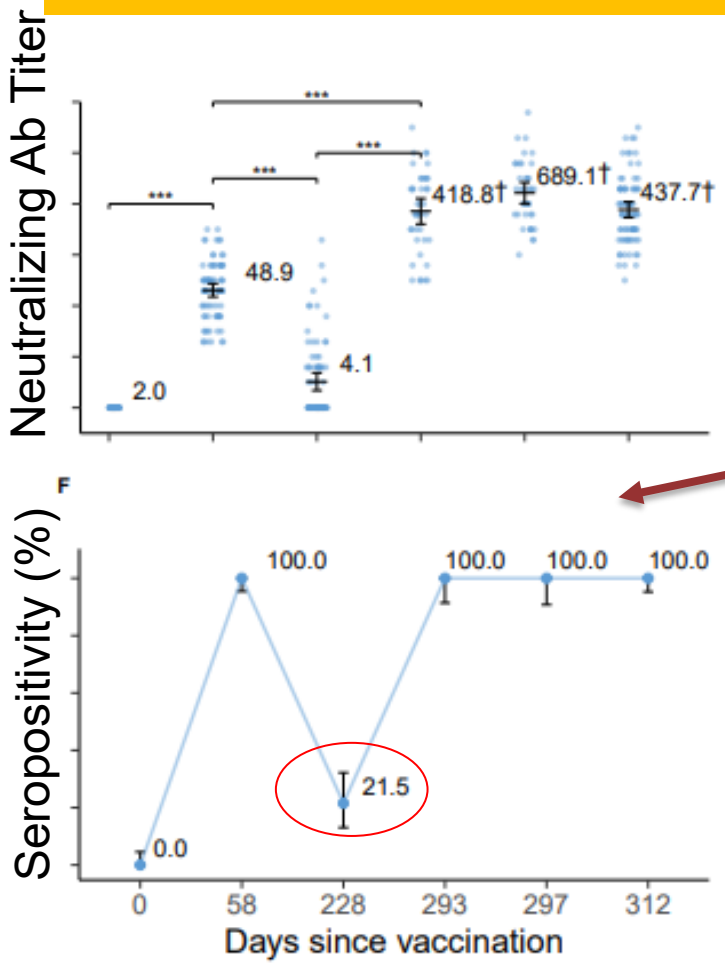
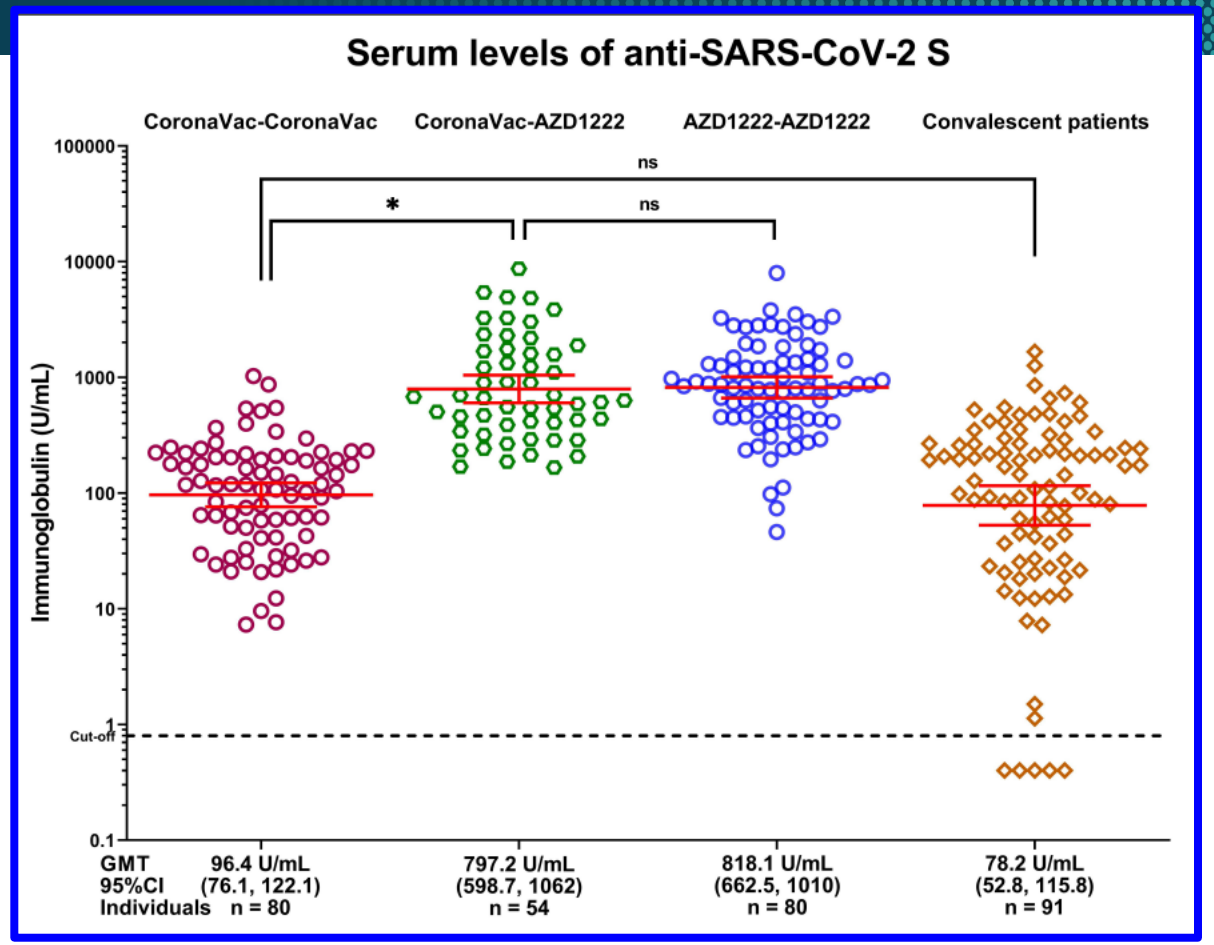
Sinovac (Coronavac) Antibody Response: Boosters

Phase 1/2 RCT Data Follow-up



- Seropositivity declined to 21.5% at 6 months
- 3rd dose was well tolerated and immunogenic

- Coronavac followed by AZ led to higher levels of antibody than 2 doses Coronvac (uncertain when levels measured)



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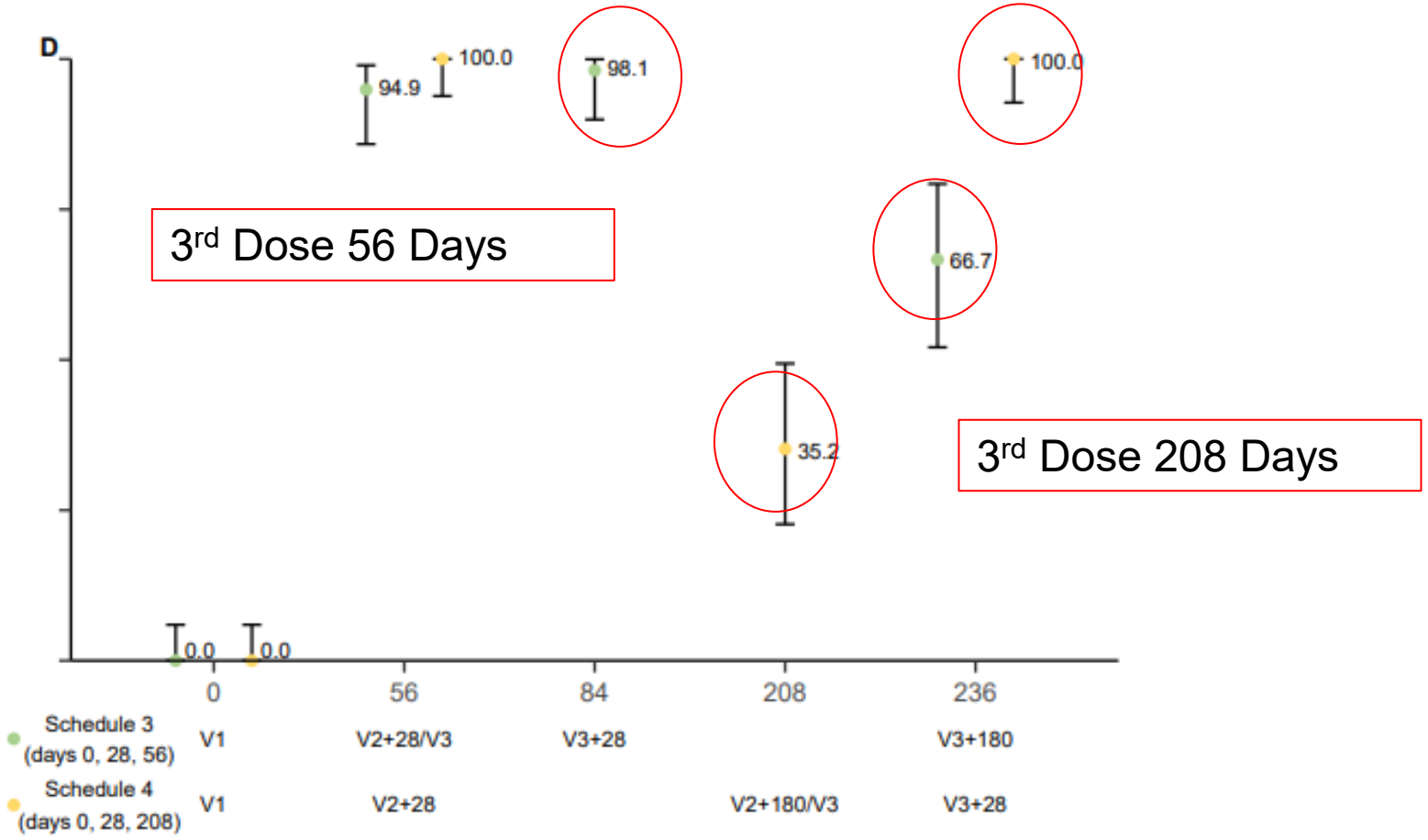
Yorsaeng R. MedRxiv 2021

Sinovac (Coronavac) Antibody Response: Boosters

- 3rd immunization at 56 or 208 days increased ab levels



Pan H. MedRxiv 2021

Summary

- **Epidemiology** – 3rd-4th Wave Around the World
- **Vaccines**
  - Vaccine-induced immunity wanes over time (evident in months not years)
  - Immunity from the least effective vaccines likely wanes faster
  - People with lower levels of antibody (e.g., elderly) will become more vulnerable faster
  - Efficacy lower with some variants (e.g., Delta)
  - Impact less on severe disease than infection – vaccines still work!
- How should this impact vaccine policy?
  - Some people will need boosters
  - Boosters in high-income nations could exacerbate global disparities in vaccine access
  - Political pressure to protect the population in high-income nations is likely to be insurmountable
  - Highlights the need to increase vaccine production

Questions and Comments