University of Washington
Public Health Capacity Building Center

COVID-19 Clinical Update

I-TECH Videoconference November 8, 2021

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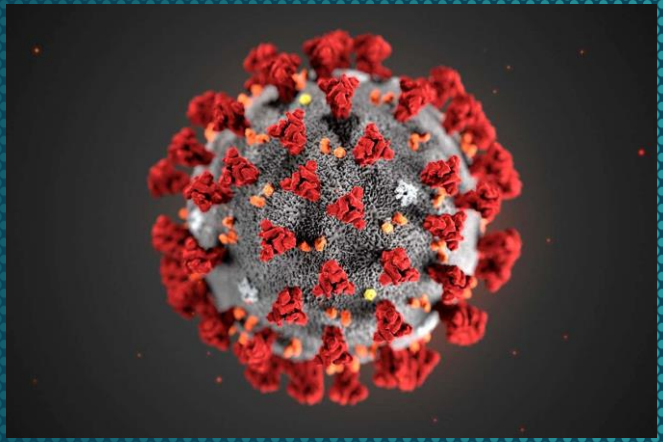


Last Updated: November 8, 2021

I-TECH
International Training and Education Center for Health

Overview

- Epidemiology & new data on HIV and COVID
- Vaccines –
  - More data on waning immunity
  - Boosters
- COVID-19 treatment
  - Sotrovimab
  - Paxlovid

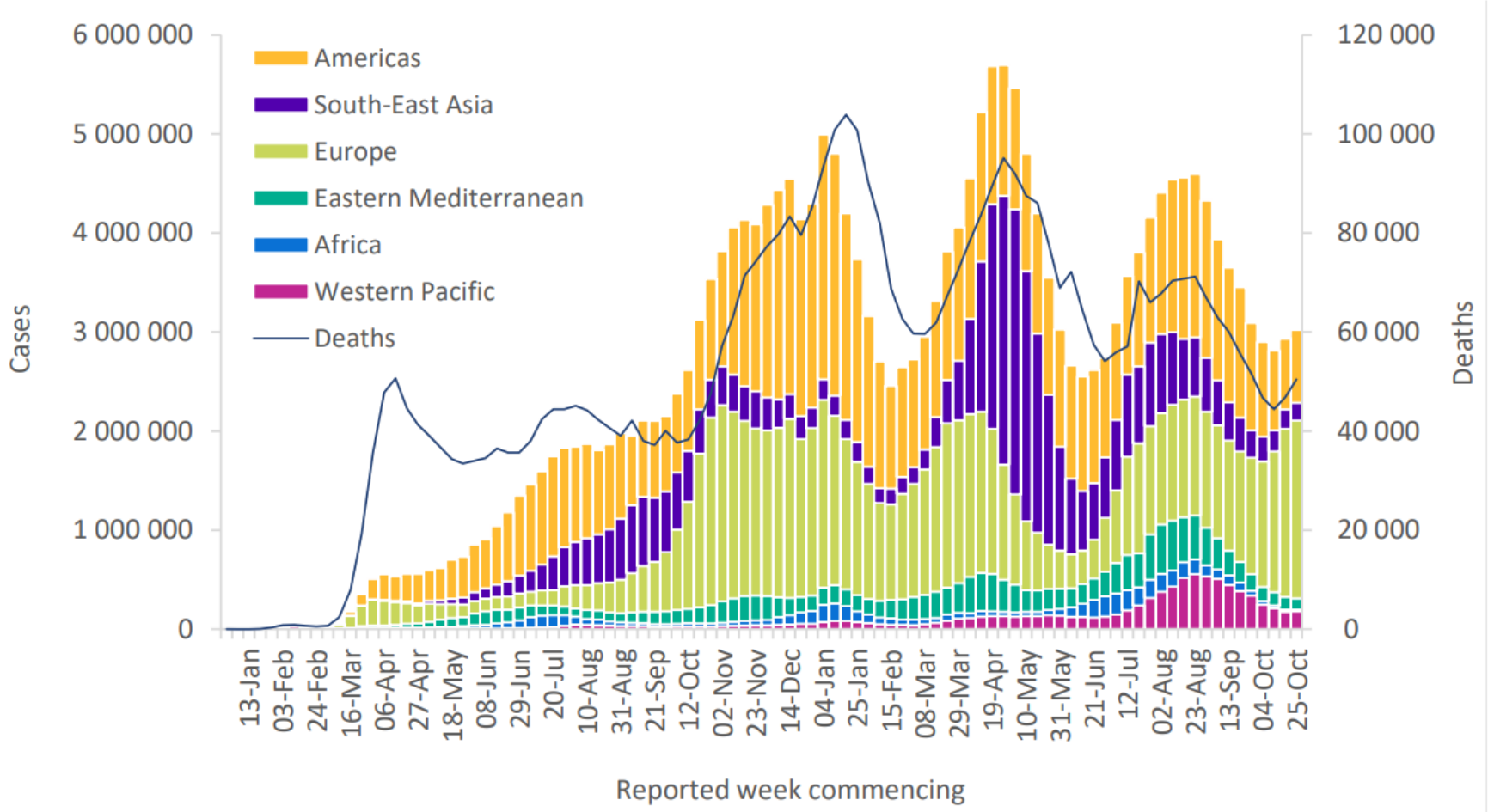
Global Trends in COVID-19 Diagnoses & Deaths

>246 Million Confirmed Cases
>3 million cases/week

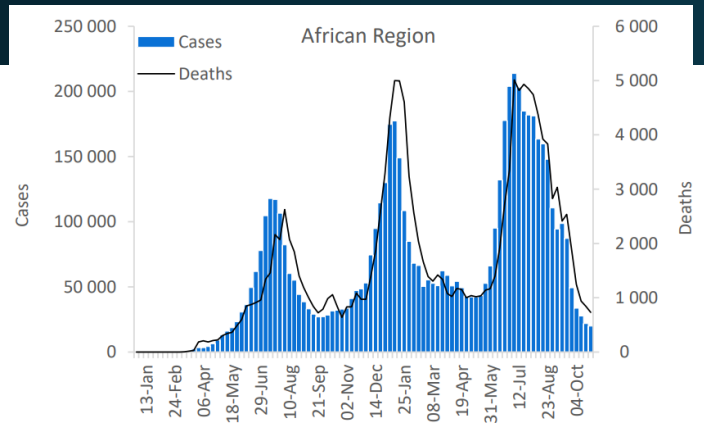
~5 Million Confirmed Deaths
>50,000 deaths/week

Increase in new cases and deaths since last month's review

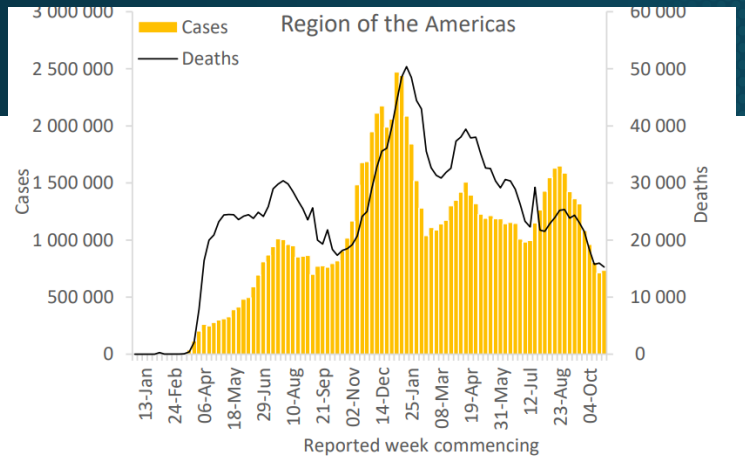
Figure 1. COVID-19 cases reported weekly by WHO Region, and global deaths, as of 31 October 2021**



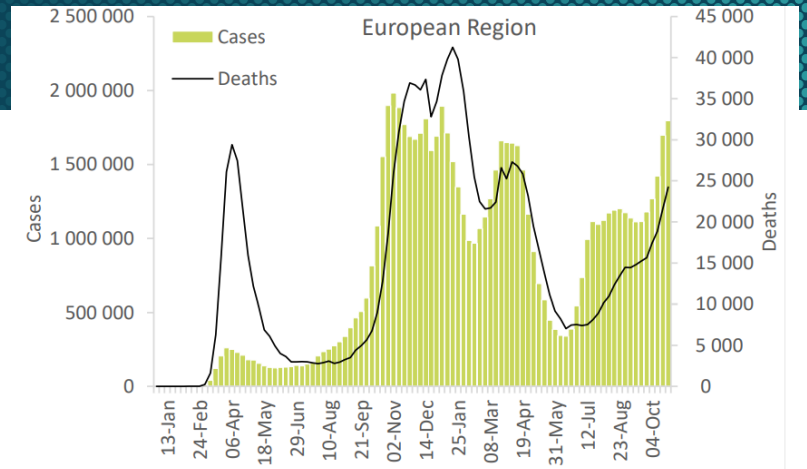
Global Trends in COVID-19 Diagnoses & Deaths



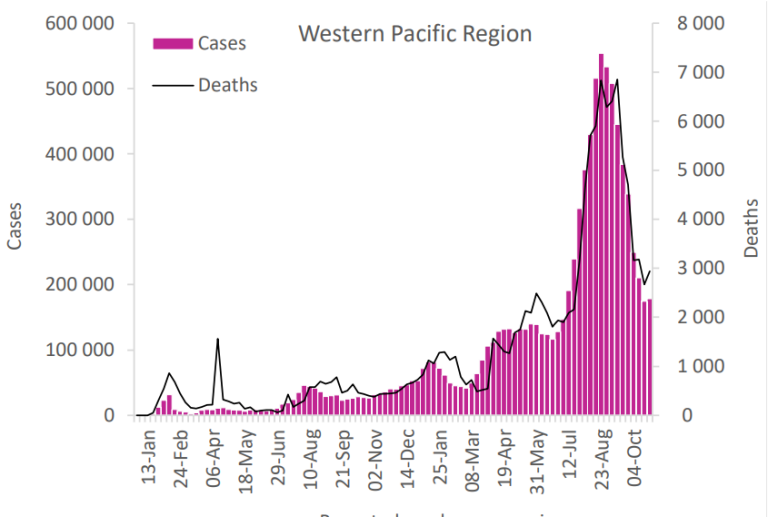
13%↓ Deaths – ↑ Cases Rwanda & Eritrea



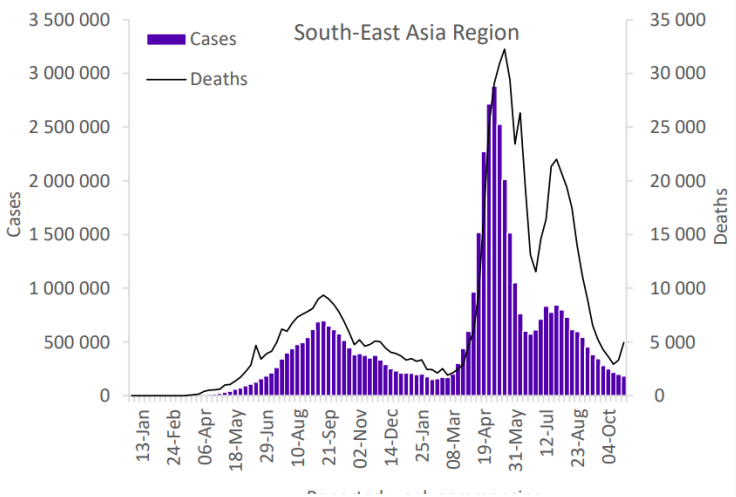
4%↓ Deaths – Slowing in decline with increases in parts Caribbean



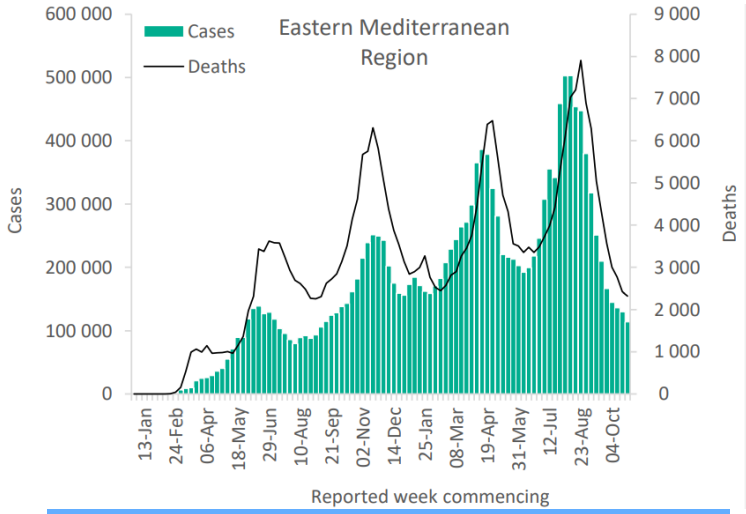
12%↑ Deaths – High in UK, Russia, Ukraine



10%↑ Deaths

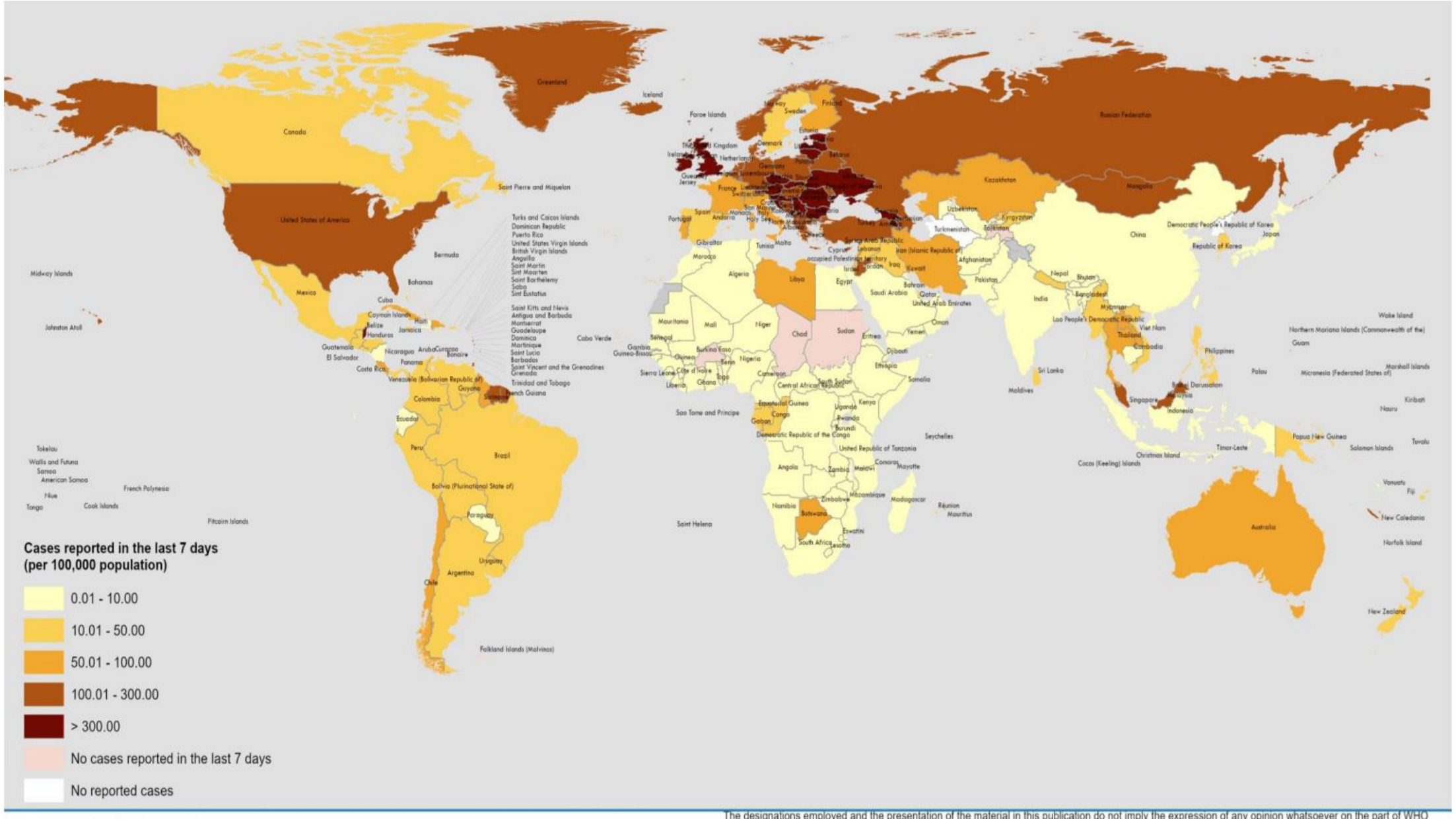


50%↑ Deaths – Case rate and deaths going in opposite directions



4%↓ Deaths – Rates very high in Iran and Iraq

COVID-19 cases/100,000 population, October 25-31, 2021



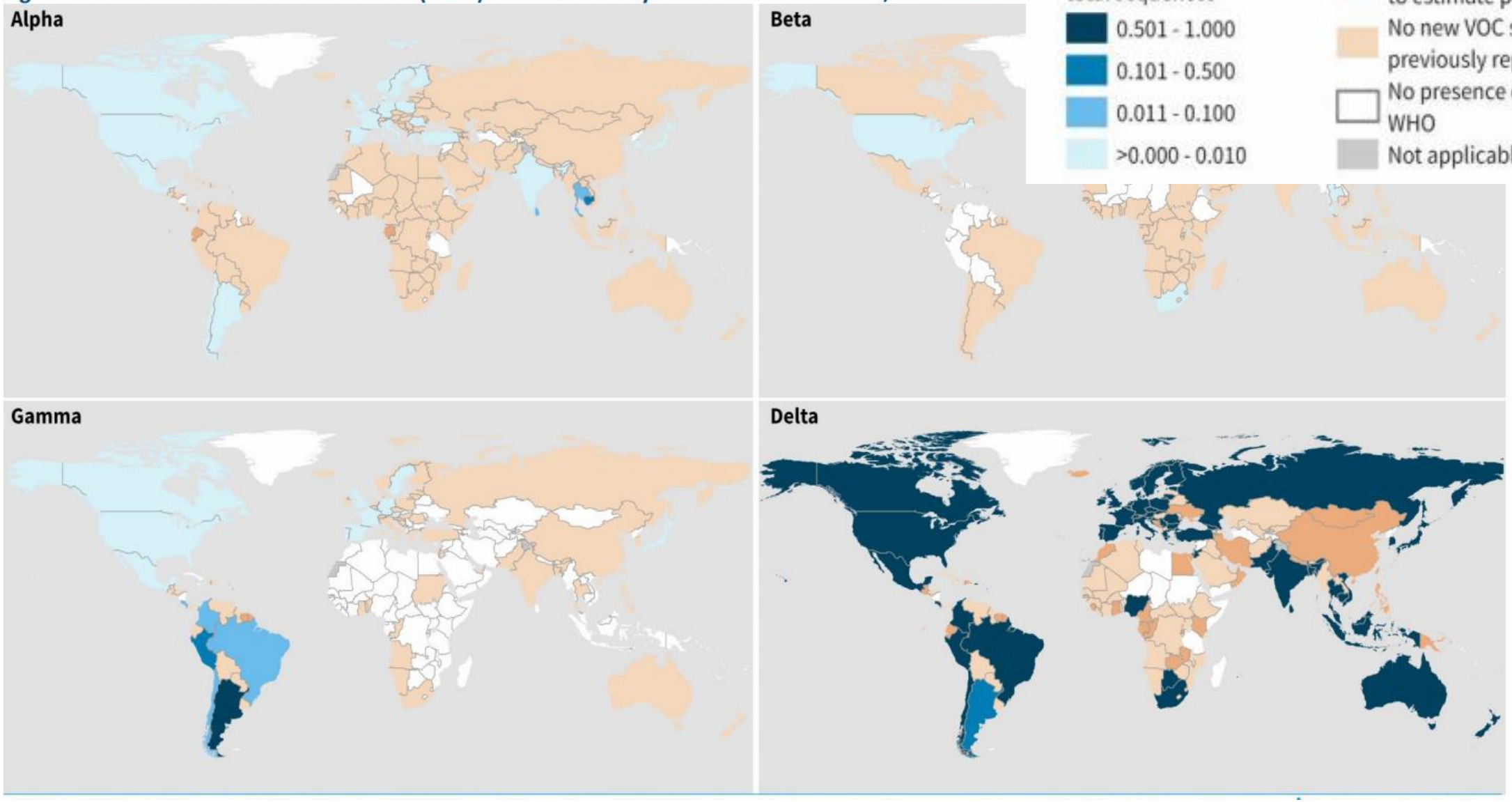
COVID-19 deaths/100,000 population, October 25-31, 2021

Data Source: World Health Organization

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed

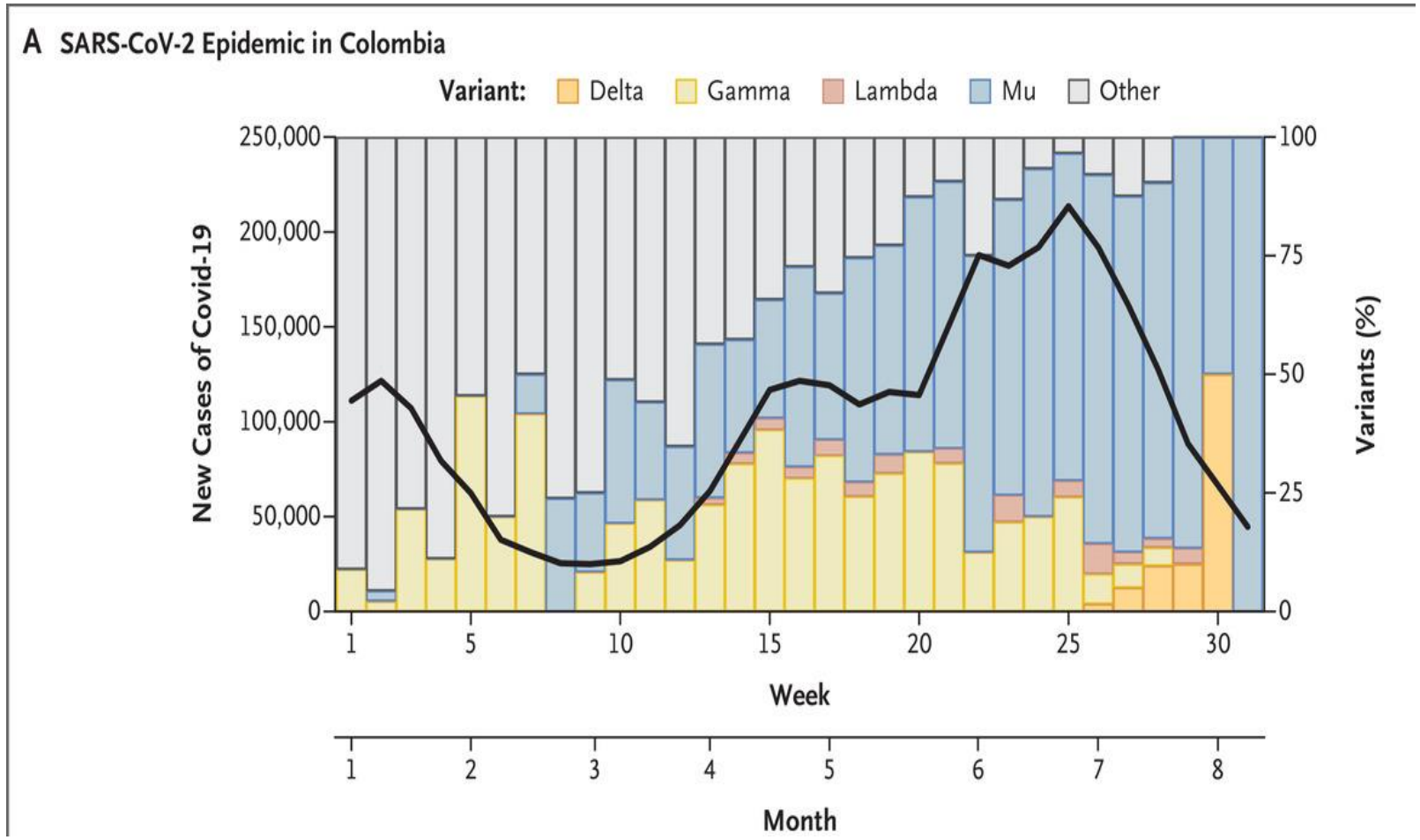
SARS-CoV-2 Variants

Figure 4. Prevalence of Variants of Concern (VOCs) in the last 60 days and historic detections, data as of 2 N



Mu Variant

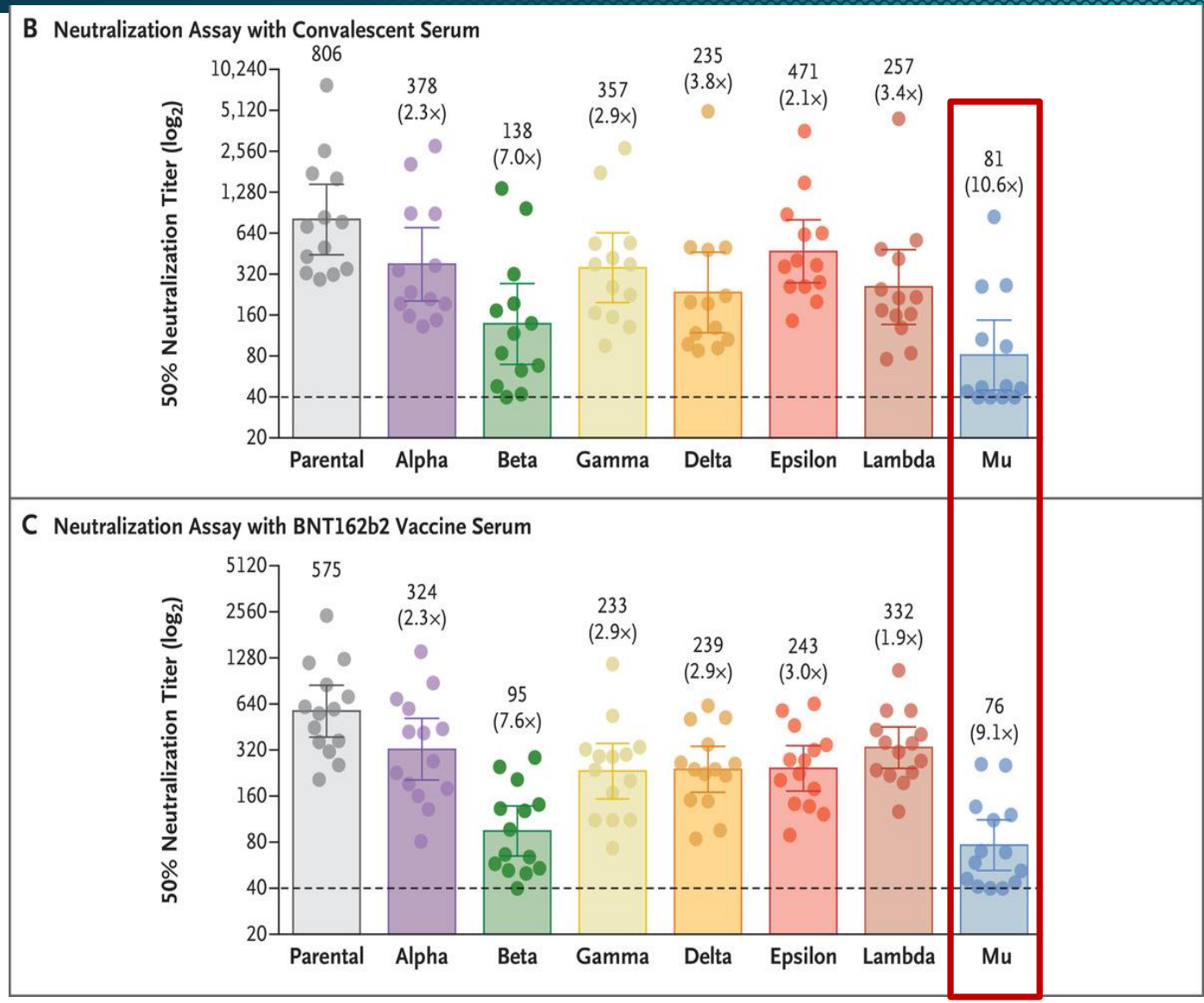
Background: Mu initially seen in Columbia in January 2021. Now in 39 countries. Includes numerous mutations seen in prior variants.
Design: Virus neutralization experiment using pseudovirus with Mu spike and serum from 13 people infected April-Sept 2020 & 14 vaccinated with Pfizer
Outcome: *In vitro* neutralization



Source: Uriu K. NEJM 2021

Mu Variant

- Antibody neutralization of Mu was 9.1-10.6X lower than the initial SARS-CoV2 using both convalescent serum and serum from Pfizer vaccine recipients



Source: Uriu K. NEJM 2021

Household Transmission in Vaccinated Persons

Background: Waning immunity and DOVID evolution may affect vaccine protection
Design: Cohort study of household contacts to COVID-19
Population: 162 index cases & 231 contacts swabbed daily for 20 days
Outcome: Secondary attack rate in household contacts by index case and contact vaccine status

RESULTS

- Secondary attack rate (SAR) was 38% in unvaccinated and 26% in vaccinated contacts (p=0.14)
  - Consistent with 34% vaccine efficacy
- Time from 2nd dose of vaccine longer in infected than uninfected household contacts (p=0.001)
  - Consistent with waning of immunity
- SAR did not vary by index case vaccine status nor did if vary with time since index case received last vaccine
  - Breakthrough infections are comparably infectious as infections in unvaccinated index cases
- Viral decline rate was faster in vaccinated delta index cases than in unvaccinated delta cases, alpha variant cases, or pre-alpha variant cases
  - Vaccination led to fast clearance in cases - ~3 days vaccinated delta vs. pre-alpha

Source: Sanganayagam A. Lancet ID 2021

More Data on Waning Immunity from mRNA Vaccines

Background: Several studies have reported waning of vaccine-induced COVID-19 immunity
Design: Analysis of open-label phase of Moderna trial comparing COVID-19 incidence July-August 2021 among early and late vaccinees (placebo group in initial trial)
Population: ~26,000 persons
Outcome: COVID-19 incidence & severe disease

Early vaccinees Late vaccinees

Table 1. Covid-19 Cases and Incidence Rates after Receipt of the Second Dose of mRNA-1273 Vaccine, from July 1 to August 27, 2021.*

Covid-19 Cases and Age Group	mRNA-1273e Group (N=14,746)			mRNA-1273p Group (N=11,431)			Difference in Incidence Rates (95% CI)
	no. of cases	*no. of person-yr*	*incidence rate per 1000 person-yr*	*no. of cases*	*no. of person-yr*	*incidence rate per 1000 person-yr*	%
All cases	162	2102	77.1	88	1796	49.0	36.4 (17.1 to 51.5)
Age 18 to <65 yr	136	1558	87.3	68	1289	52.8	39.6 (18.6 to 55.5)
Age ≥65 yr	26	544	47.8	20	507	39.5	17.4 (–53.9 to 56.3)
Severe cases	13	2102	6.2	6	1796	3.3	46.0 (–52.4 to 83.2)
Age 18 to <65 yr	7	1558	4.5	4	1289	3.1	30.9 (–171.7 to 85.2)
Age ≥65 yr	6	544	11.0	2	507	3.9	64.2 (–100.2 to 96.5)

Difference greater in younger people - unanticipated

Source: Baden LR. NEJM 2021

CDC Booster Guidance

IF YOU RECEIVED

Pfizer-BioNTech or Moderna

You are eligible for a booster if you are:

- 65 years or older
- Age 18+ who live in long-term care settings
- Age 18+ who have underlying medical conditions
- Age 18+ who work or live in high-risk settings

When to get a booster:
At least 6 months after your second shot

Which booster should you get?
Any of the COVID-19 vaccines authorized in the United States

IF YOU RECEIVED

Johnson & Johnson's Janssen

You are eligible for a booster if you are:
18 years or older

When to get a booster:
At least 2 months after your shot

Which booster should you get?
Any of the COVID-19 vaccines authorized in the United States

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html

UK Booster Guidance

Who can get a COVID-19 booster vaccine

Booster vaccine doses will be available on the NHS for people most at risk from COVID-19 who have had a 2nd dose of a vaccine at least 6 months ago.

This includes:

- people aged 50 and over
- people who live and work in care homes
- frontline health and social care workers
- people aged 16 and over with a health condition that puts them at high risk of getting seriously ill from COVID-19
- people aged 16 and over who are a main carer for someone at high risk from COVID-19
- people aged 16 and over who live with someone who is more likely to get infections (such as someone who has HIV, has had a transplant or is having certain treatments for cancer, lupus or rheumatoid arthritis)

Which COVID-19 vaccine will I get?

Most people will be offered a booster dose of the Pfizer/BioNTech vaccine or Moderna vaccine.

This means your booster dose may be different from the vaccines you had for your 1st and 2nd doses.

Some people may be offered a booster dose of the Oxford/AstraZeneca vaccine if they cannot have the Pfizer/BioNTech or Moderna vaccine.

https://www.nhs.uk/conditions/coronavirus-covid-19/coronavirus-vaccination/coronavirus-booster-vaccine/

Pfizer mRNA Vaccine Efficacy in Children 5-11

Background: In the U.S., COVID-19 vaccines are not approved for use in children under 12

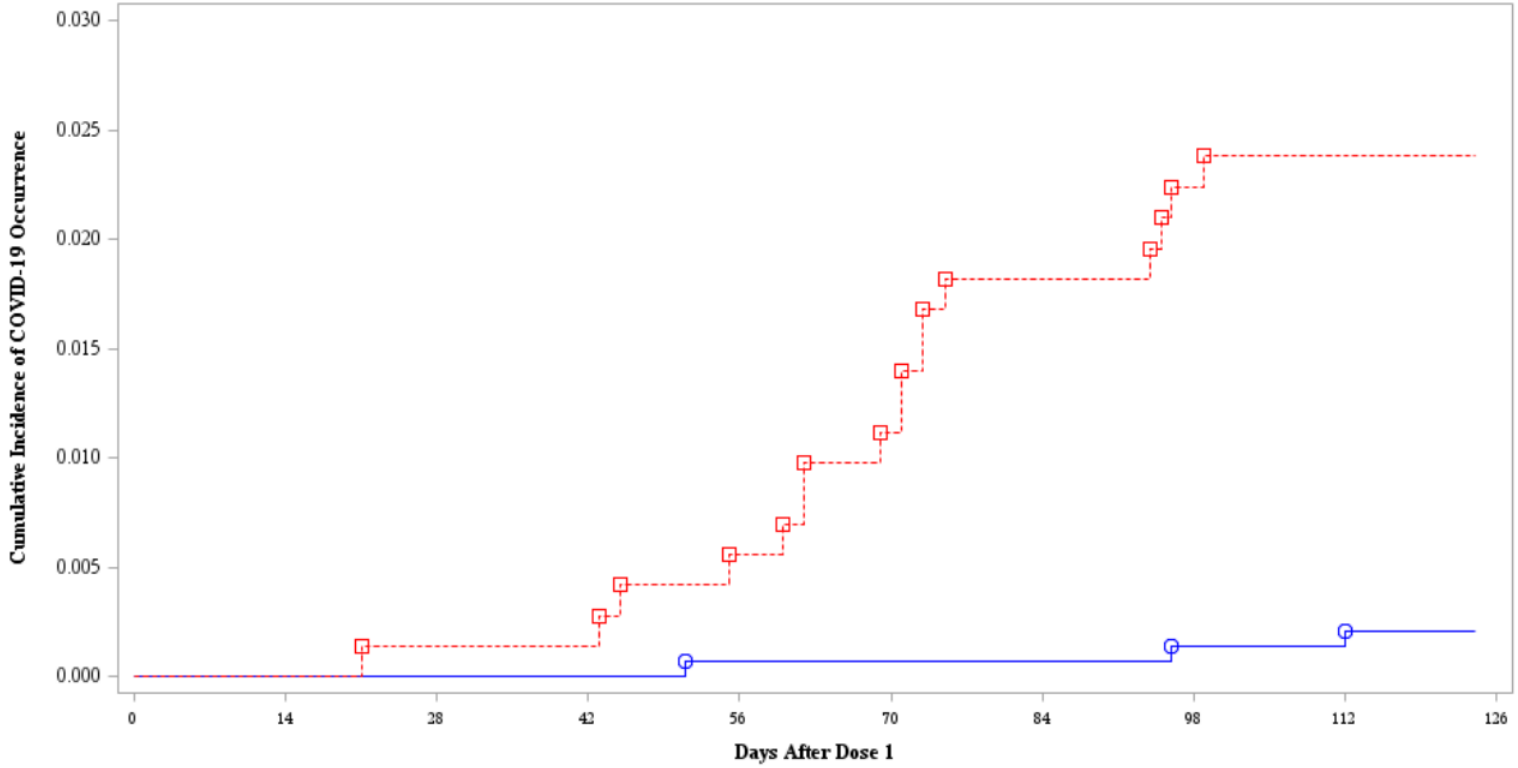
Intervention: 2 10ug dose 3 weeks apart

Design: Analysis of open-label phase of Moderna trial comparing COVID-19 incidence July-August 2021 among and large vaccinees

Population: ~2250 children ages 5-<12 years (1518 vaccine recipients)

Outcome: COVID-19 >7 days after 2nd dose

Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1 – Phase 2/3 Initial Enrollment Group – 5 to <12 Years of Age – Dose 1 All-Available Efficacy Population



Vaccine efficacy 90.9%

No cases myocarditis, hospitalization, or death

https://www.fda.gov/media/153409/download

Pfizer mRNA Vaccine: Risk & Benefits
Model 1 Million Children – 6 Months

	Prevented Cases	Prevented Hospitalizations	Prevented Deaths	Excess Myocarditis Cases	Excess Myocarditis hospitalizations	Excess Myocarditis Deaths
Incidence 9/21	45,773	192	1	106	58	0
Peak incidence	54,345	250	1	106	58	0
Low incidence	2,639	21	0	106	58	0
9/21 Incidence – 90% VE	58,851	241	1	106	58	0
High death rate – CDC tracker	45,773	192	3	106	58	0
Scenario 1 – 50% myocarditis risk	45,773	192	1	53	29	0

https://www.fda.gov/media/153447/download

COVID-19 Vaccination in Children: Guidelines

CDC

- **≥12 years** – **2 doses** Pfizer vaccine 21 days apart
- **Ages 5-11**
  - 1/3 dose vaccine
  - 2 doses 21 days apart
- Vaccines other than Pfizer not currently recommended

UK

- **Ages 12-15 years** – **Single** dose Pfizer vaccine
- 2nd dose recommended if
  - Child lives with someone at high risk for infection
  - Child has a condition that places them at high risk for COVID-19

Norway, Hong Kong also using a single dose

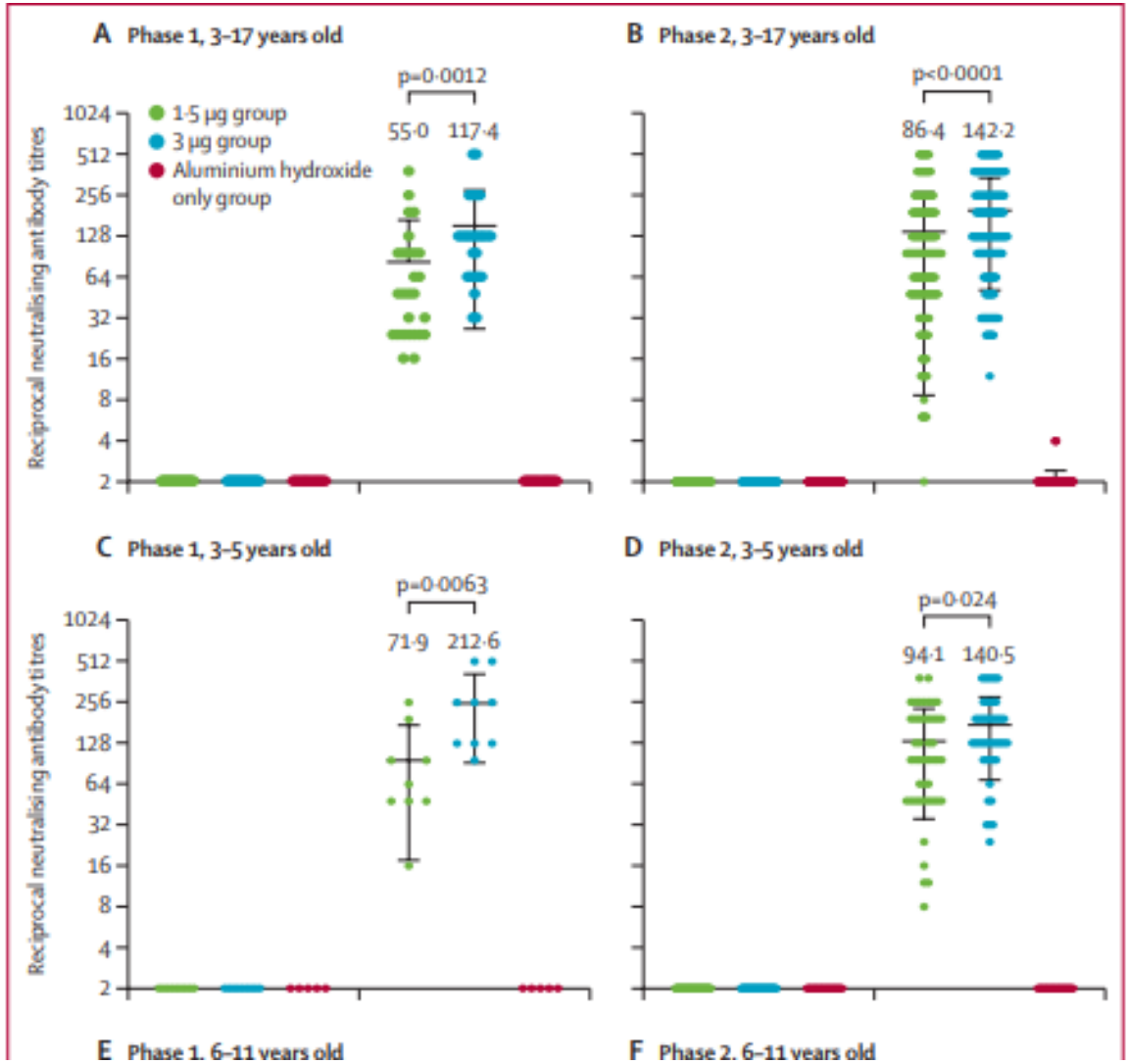
Discussion of vaccine in children
https://www.nytimes.com/2021/10/06/health/covid-vaccine-children-dose.html

Coronavac in Children 3-17

Background: Limited data on COVID-19 vaccines in children
Intervention: 2 dose 28 days apart
Design: Phase 1/2 trial
Population: 72 (phase I) and 480 (phase 2) children in China
Outcome: Immunogenicity and safety

Vaccine immunogenic - >97% vaccinated developed antibody – all 3-5 year olds

Vaccine was safe – common local reactions, fatigue, fever



Source: Han B. Lancet ID 2021

Coronavac in Children 3-17

WORLD • COVID-19

China to Start Vaccinating Children Over 3 Years Old as COVID-19 Cases Spread

A medical worker administers a dose of a COVID-19 vaccine to a boy in Shanghai's Xuhui District on Sept. 3, 2021. Liu Ying—Xinhua/ Getty Images

- Coronavac also being used in children ≥6 years in Chile, Cambodia, and Indonesia

Moderna in Children 3-17
Press Release October 25, 2021

- Moderna currently approved in the US only for persons age 18 and over
- Trial children ages 12-17 – TeenCOVE
  - 3,732 participants
  - Vaccine efficacy 100% - press release in May, 2021
  - FDA asked for more safety data in face of concerns related to myocarditis
- Trial 4,753 children 6-11 – 2 x 50ug dose 28 days apart
  - 99.3% seroconversion
  - No data on myocarditis in press release
- Trial children 6 months to 5 years ongoing

https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-top-line-data-phase-23-study-covid-19

Sotrovimab: A New Monoclonal

Background: Sotrovimab is a pan-sarbecovirus monoclonal antibody-targets a highly conserved epitope unassociated with ACE2 receptor binding (unlike many other monoclonals)
Design: Interim analysis RCT
Population: 583 people with symptomatic COVID-19 with >1 risk for severe disease (obesity, age >60, DM, heart disease) within 5 days of symptom onset
Outcome: Hospitalization or death

Adverse events similar in treatment and placebo groups

Table 2. Efficacy Outcomes through Day 29 (Intention-to-Treat Population).*

Outcome	Sotrovimab (N = 291)	Placebo (N = 292)
Primary outcome		
Hospitalization for >24 hr for any cause or death from any cause — no. (%)	3 (1)	21 (7)
Hospitalization for >24 hr for any cause	3 (1)	21 (7)
Death from any cause	0	1 (<1)†
Alive and not hospitalized — no. (%)	284 (98)	270 (92)
Data missing — no. (%)		
All patients with missing data	4 (1)	1 (<1)
Patients with missing data because of withdrawal of consent before receipt of sotrovimab or placebo	3 (1)	1 (<1)
Relative risk reduction (97.24% CI)	85 (44–96)	—
P value	0.002	—
Other clinical outcomes‡		
Emergency department visit or hospitalization for any cause or death from any cause — no. (%)	6 (2)	28 (10)
Emergency department visit for any cause§	2 (<1)	8 (3)
Hospitalization for any cause	4 (1)¶	21 (7)‖
Death from any cause	0	1 (<1)†
Emergency department visit without hospitalization, or hospitalization for <24 hr for any cause — no. (%)**	3 (1)	7 (2)
Severe or critical progression — no. (%)††	2 (<1)	19 (7)
Low-flow nasal cannula or face mask	2 (<1)	11 (4)
Nonrebreather mask, high-flow nasal cannula, or noninvasive ventilation	0	5 (2)
Invasive mechanical ventilation	0	2 (<1)
Death from any cause	0	1 (<1)
Admission to ICU for any cause — no. (%)	0	5 (2)

Paxlovid (PF-07321332/ritonavir) – Interim Analysis

Background: There is a need for COVID-19 treatments, particularly orally administered drugs. Paxlovid is a SARS-CoV-2-3CL protease inhibitor
Design: RCT
Population: 774 non-hospitalized persons with COVID-19 at high risk for severe disease within 3 days of symptom onset – interim analysis
Outcome: Hospitalization or death through day 28

	Hospitalization or Death	Death
Paxlovid	3/389 (0.8%)	0
Placebo	27/385 (7%)	7
	P<0.0001 89% Risk Reduction	

- Similar results of persons treated within 5 days of symptom onset
- Similar adverse events in treatment and placebo groups

https://investors.pfizer.com/investor-news/press-release-details/2021/Pfizers-Novel-COVID-19-Oral-Antiviral-Treatment-Candidate-Reduced-Risk-of-Hospitalization-or-Death-by-89-in-Interim-Analysis-of-Phase-23-EPIC-HR-Study/default.aspx

Summary

- **Epidemiology**
  - Some resurgence of epidemic
  - Continued evolution – Mu varient
- **Vaccines**
  - Vaccine-induced immunity wanes over time – not a new story
  - Evolving consensus supporting boosters – undermines equity
  - New pediatric indications for immunization
- **New treatments**
  - Sotrovimab – very effective
  - Paxlovid – 2nd oral therapy -

Questions and Comments