University of Washington
Public Health Capacity Building Center

COVID-19 Clinical Update

I-TECH Videoconference December 12, 2021

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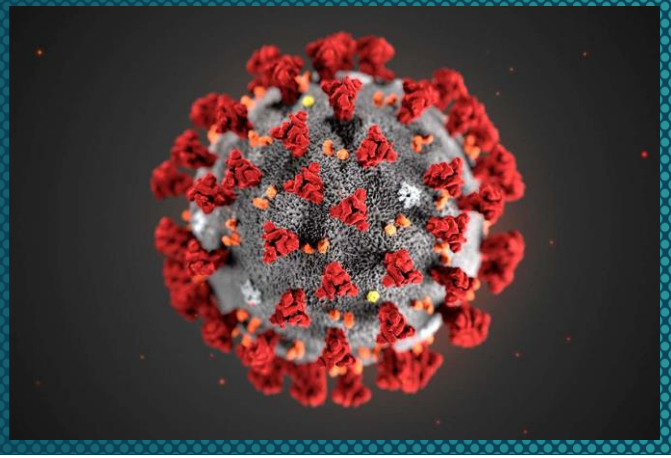


Last Updated: December 12, 2021

I-TECH
International Training and Education Center for Health

Overview

- Epidemiology
- Omicron
  - Epidemiology
  - Genetics – mechanisms of action
  - Impact on immunity
  - Disease severity

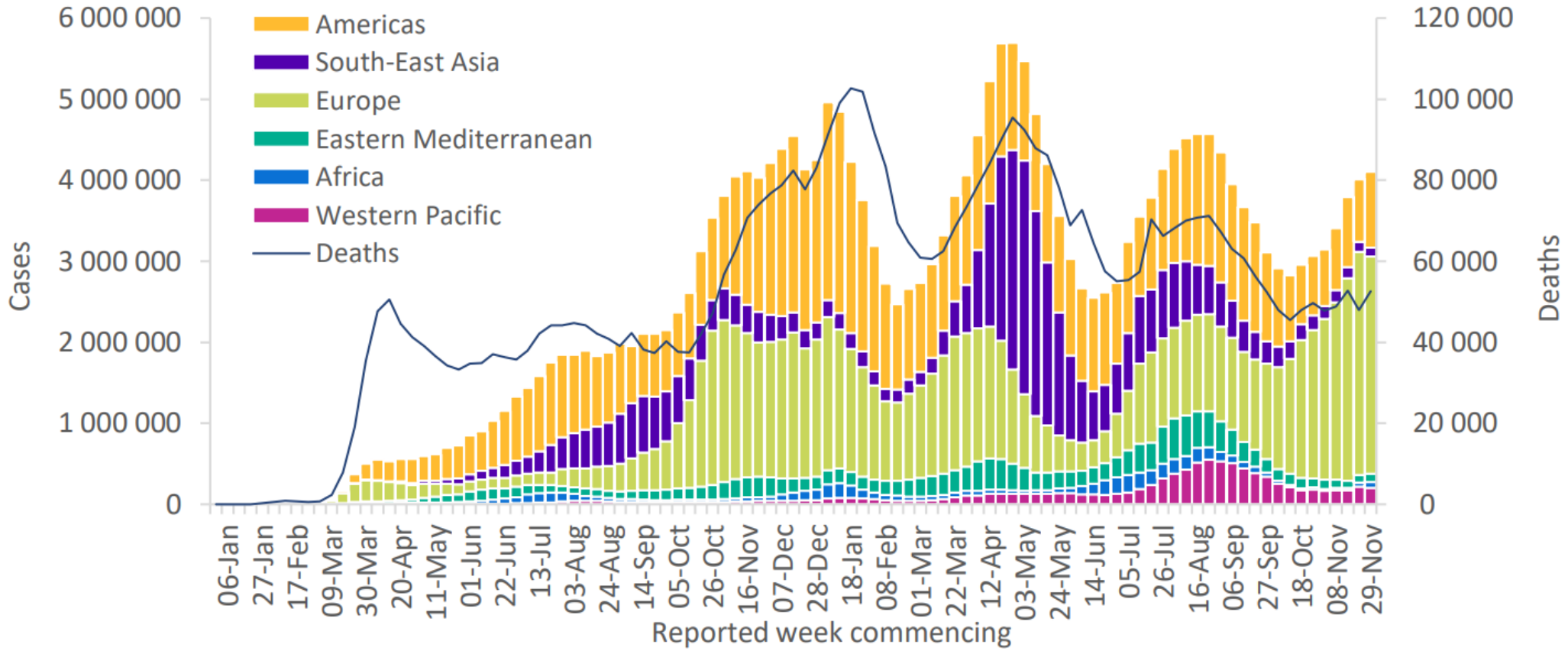
Global Trends in COVID-19 Diagnoses & Deaths

>265 Million Confirmed Cases
>4 million cases/week

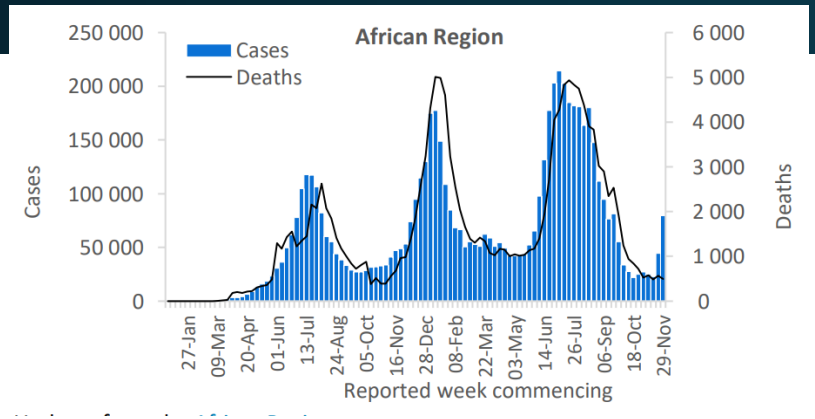
~5.2 Million Confirmed Deaths
>50,000 deaths/week

Increase in new cases with stable number of deaths since last month's review

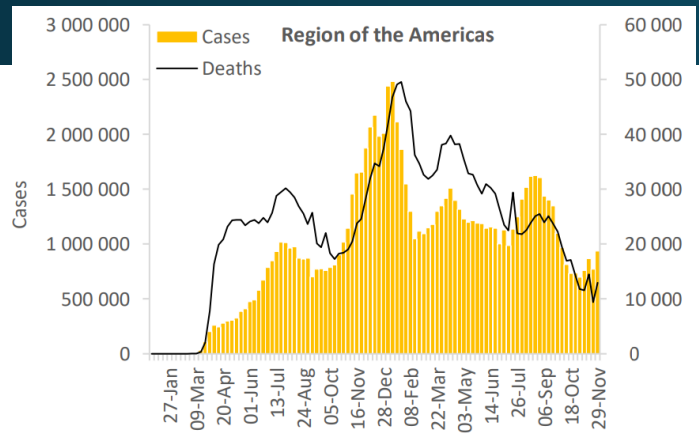
Figure 1. COVID-19 cases reported weekly by WHO Region, and global deaths, as of 5 December 2021**



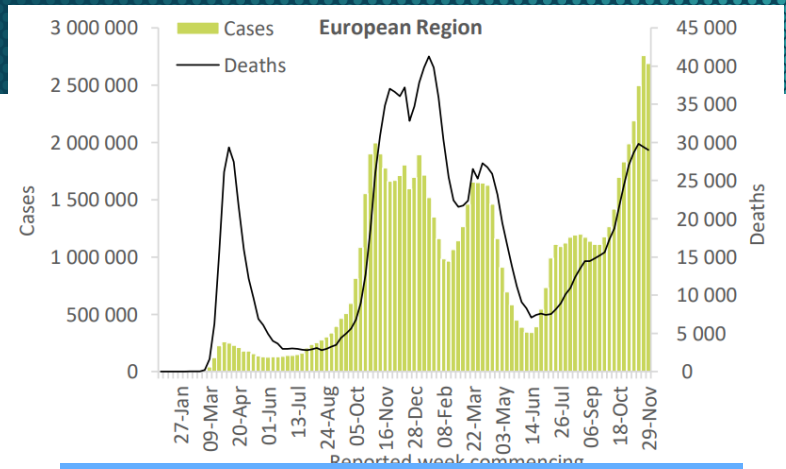
Global Trends in COVID-19 Diagnoses & Deaths



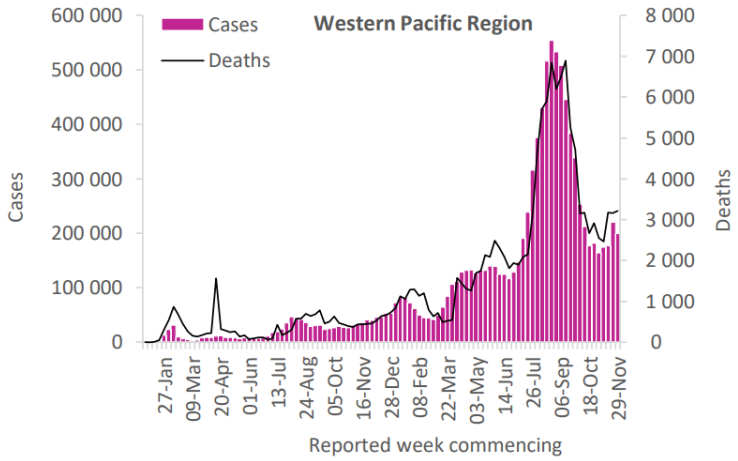
↑79% Cases with -3%↓ Deaths – Deaths ↑10% S. Africa



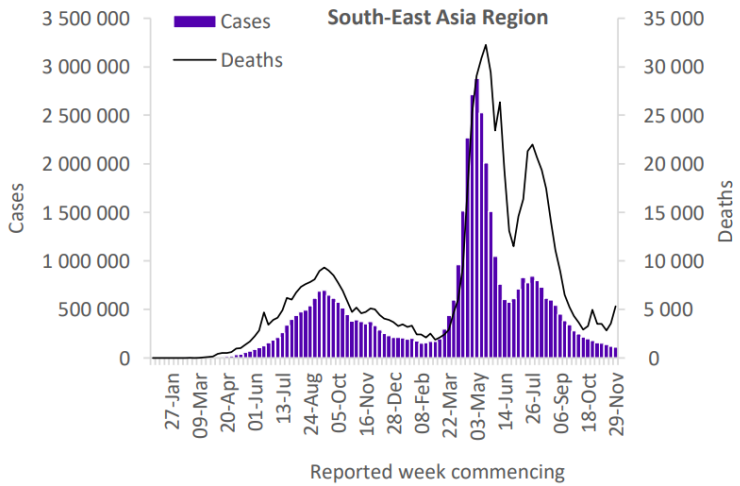
↑21% Cases with - ↑38% Deaths



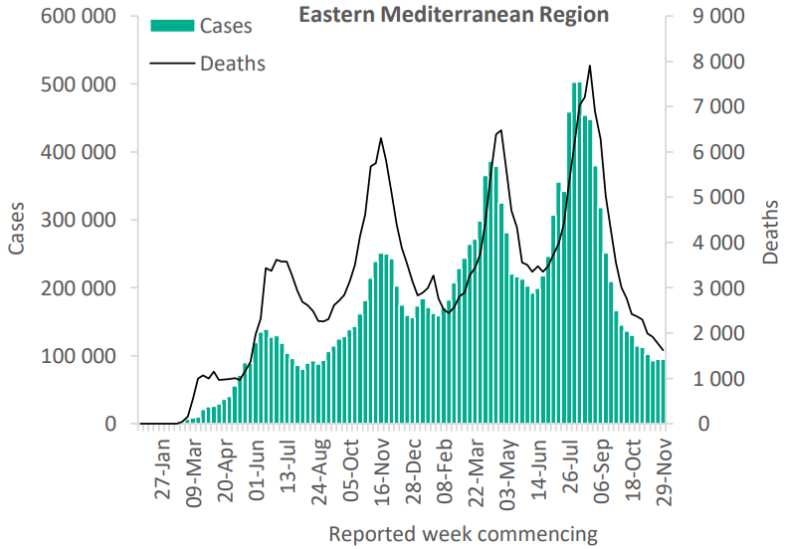
Plateau new cases & deaths following increase



Plateauing cases & deaths

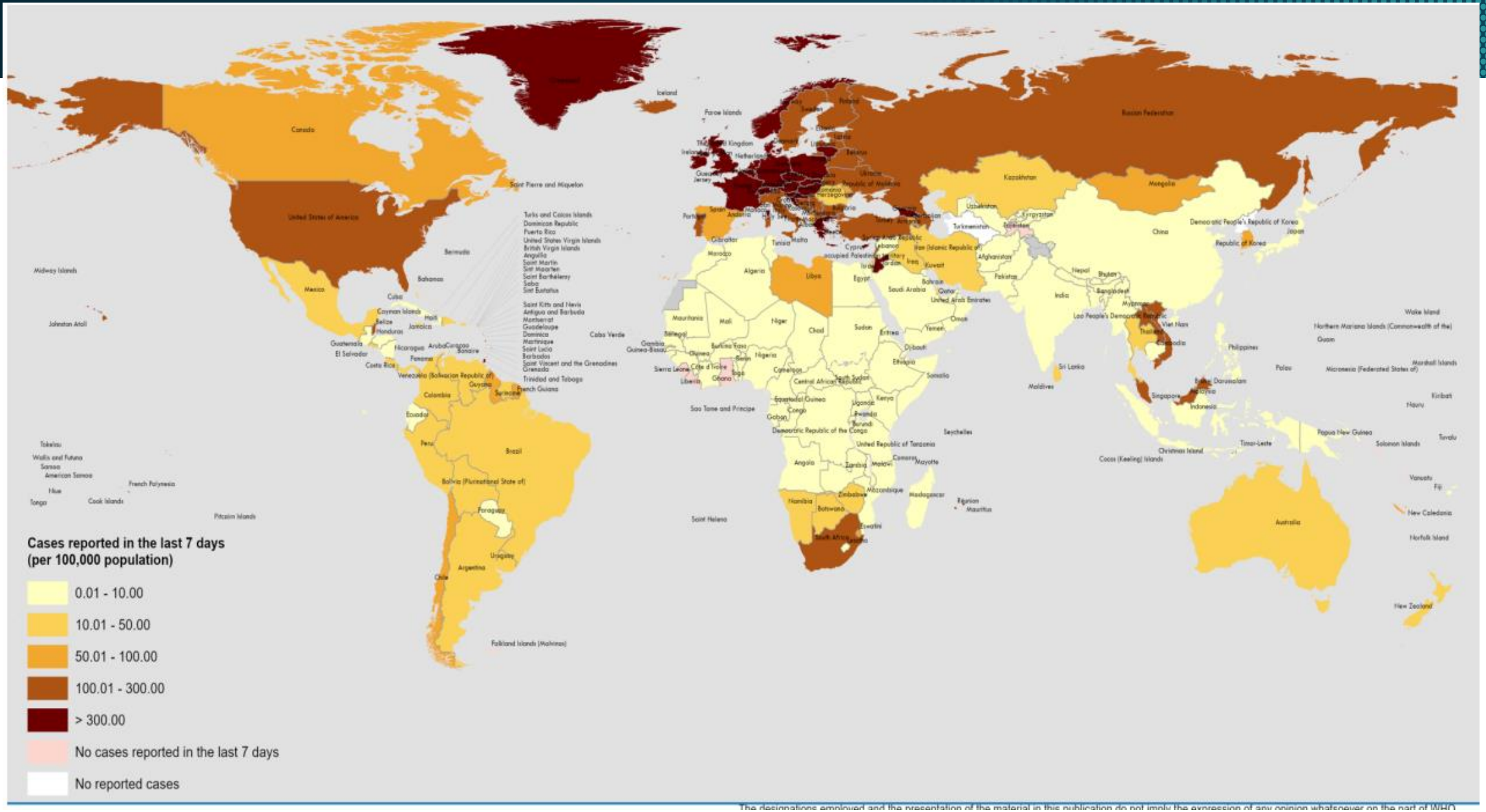


10%↓ Cases ↑49 Deaths



0%↓ Cases -8% Deaths

COVID-19 cases/100,000 population, November 29-December 5

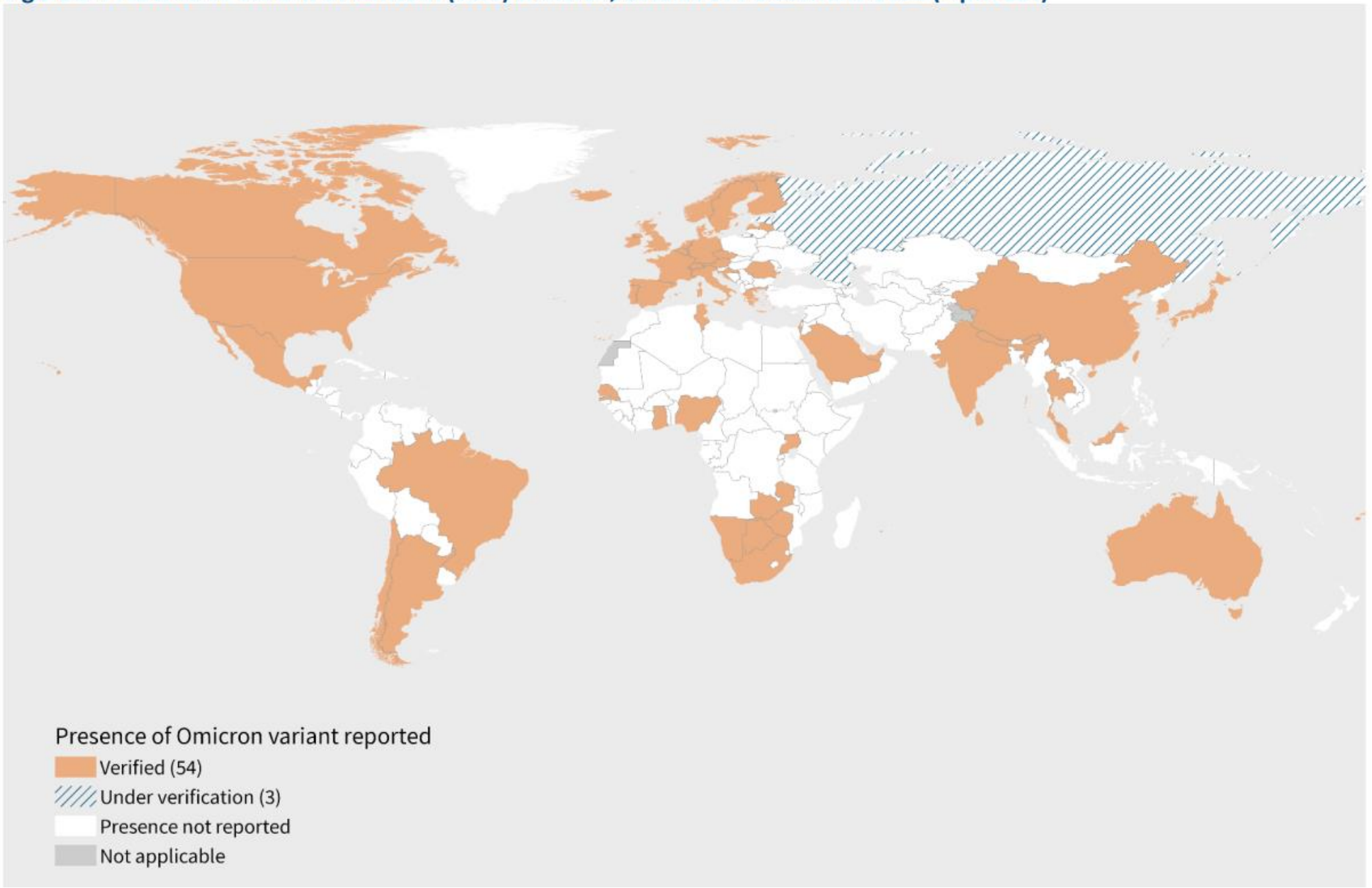


COVID-19 deaths/100,000 population, November 29-December 5

Omicron (B1.1529) Variant Timeline

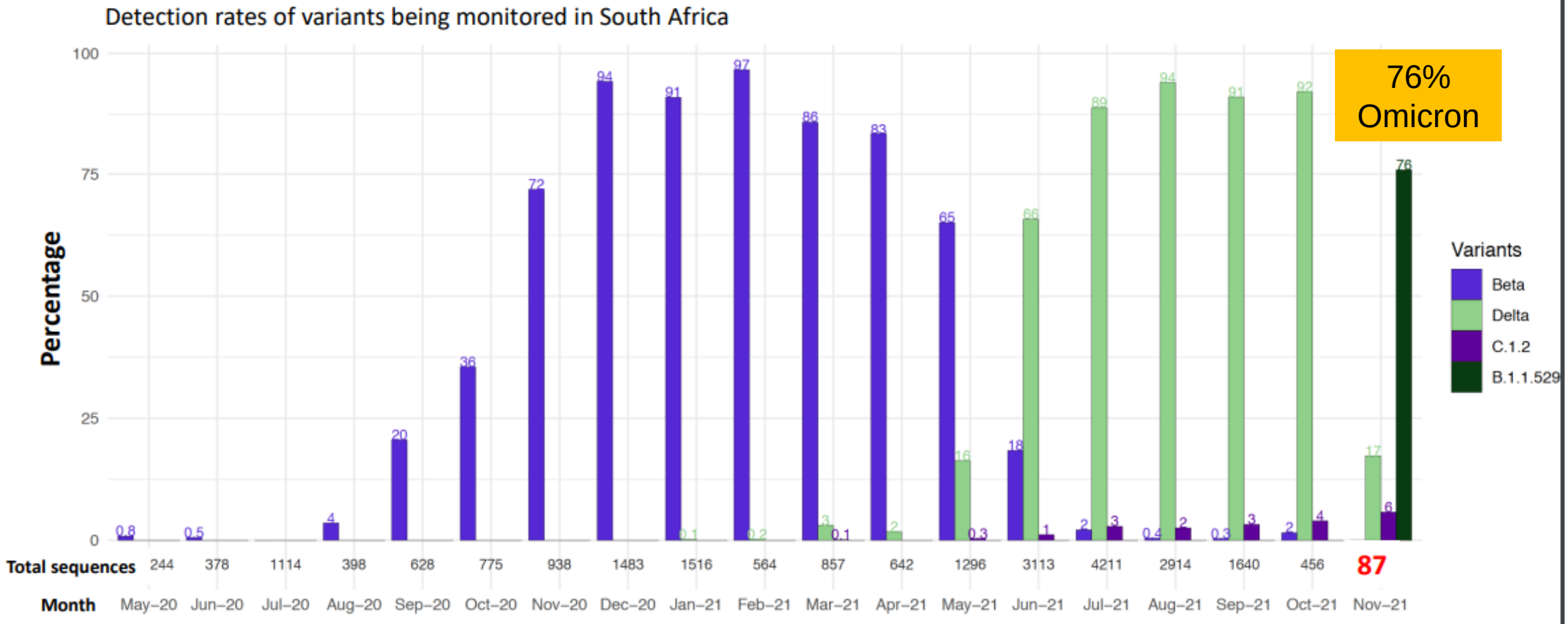
- November 11 & 14, 2021 – Specimens collected in Botswana and South Africa that are subsequently identified as Omicron
- November 24 – Variant reported to WHO
- November 26 – Omicron defined as VOC
  - Increase in cases in South Africa concurrent with detection of new variant
  - Large number of genetic substitutions suggest potential for increased transmission and reduced antibody neutralization

Figure 5. Presence of Variant of Concern (VOC) Omicron, data as of 7 December 2021 (4 pm CET)



Omicron (B1.1529) Trends in South Africa

Detection Rates: Beta, Delta, C.1.2 and B.1.1.529

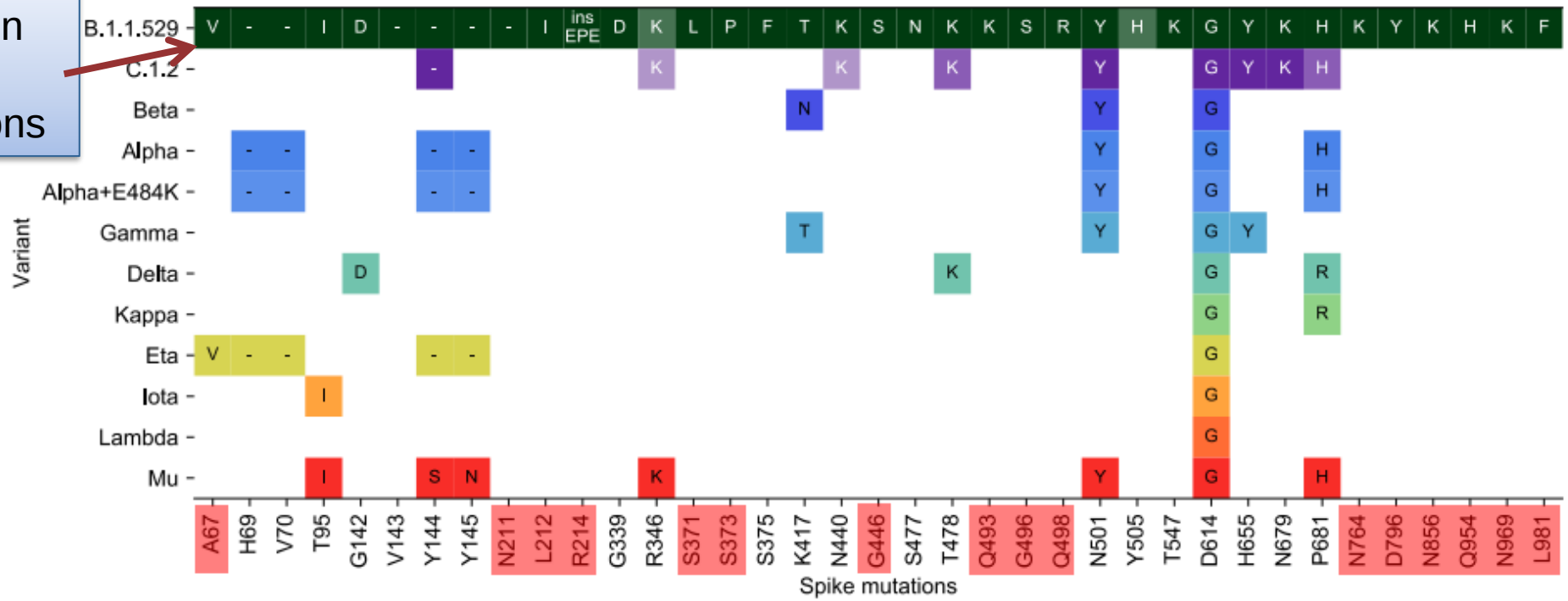


C.1.2 has been detected at ≤ 6% of sequences monthly.
B.1.1.529 was first detected in South Africa on November 14th. It makes up 76% (n=66/87) of November sequences released on GISAID.

NGS-SA
Network for Genomic Surveillance in South Africa

B.1.1.529 spike mutations compared to other VOC/VOIs

Omicron 26-32 mutations



Mutations with unknown or unconfirmed impact

- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined

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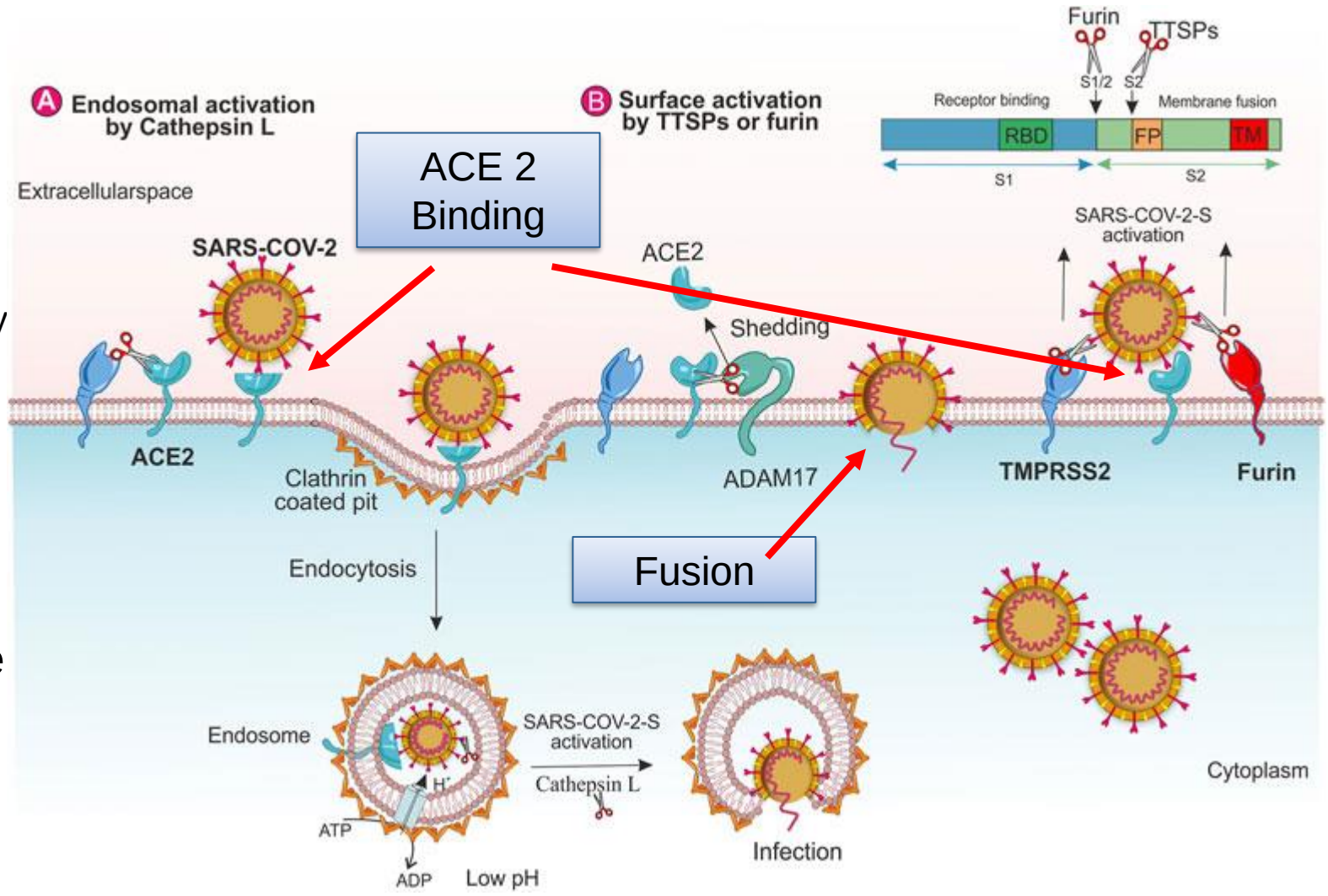
Omicron (B1.1529): Genetics

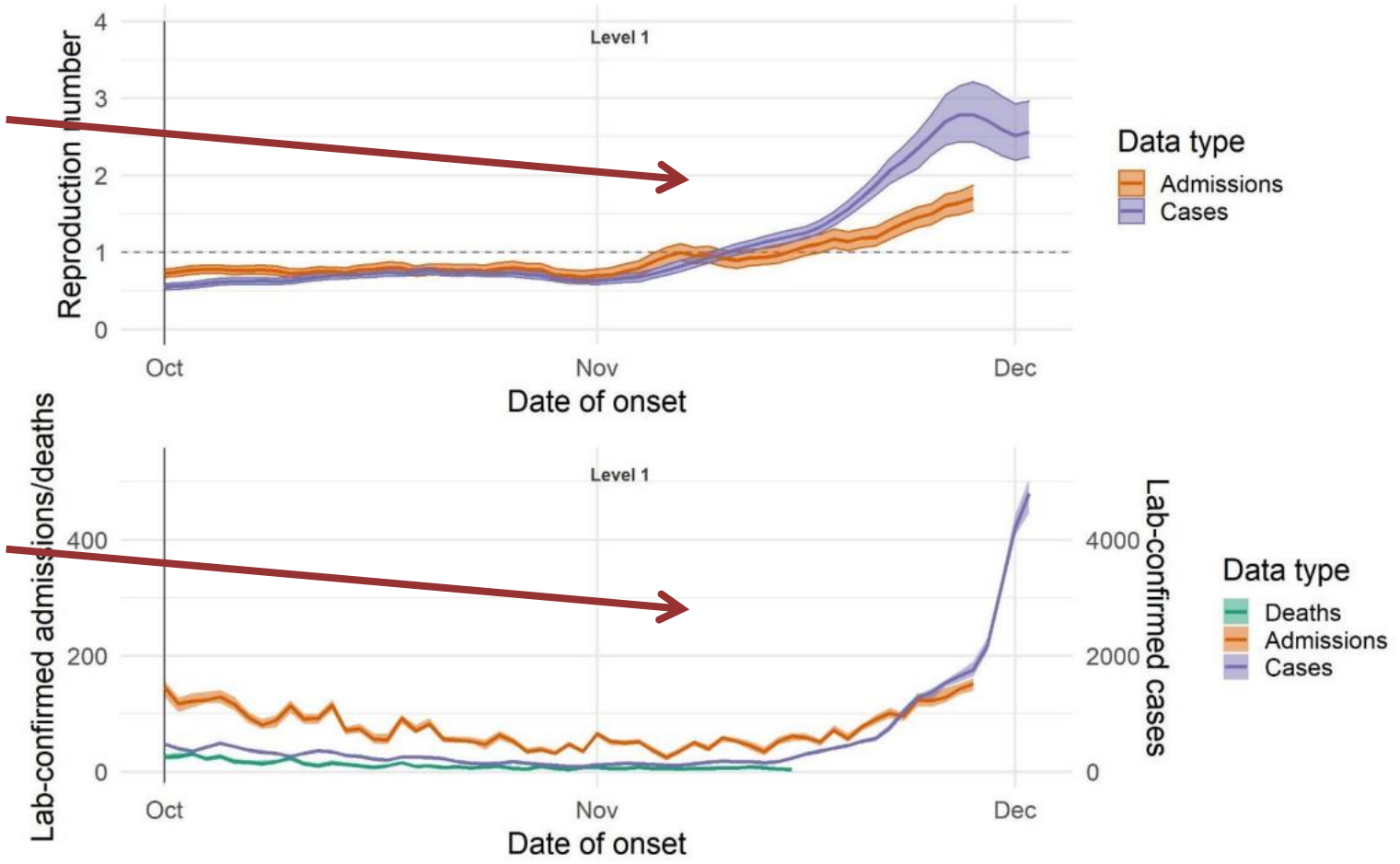
- Virus enters cells via 2 pathways
  - Endocytosis
  - Cell surface entry
- Spikes have 2 domains
  - S1 – receptor binding ACE2
    - Omicron binds ACE2 more efficiently
  - S2 – membrane fusion for viral entry – primed by proteolytic cleavage
    - Cleavage leads to conformational changes that release the S2 fusion peptide for insertion into the cell membrane
    - Mutations may make this fusion more efficient



Rising Effective Reproductive Number (R) in South Africa
Data Through December 4, 2021

Estimated R based on admissions and reported cases
- Big increase in November

Number of cases, admissions and deaths

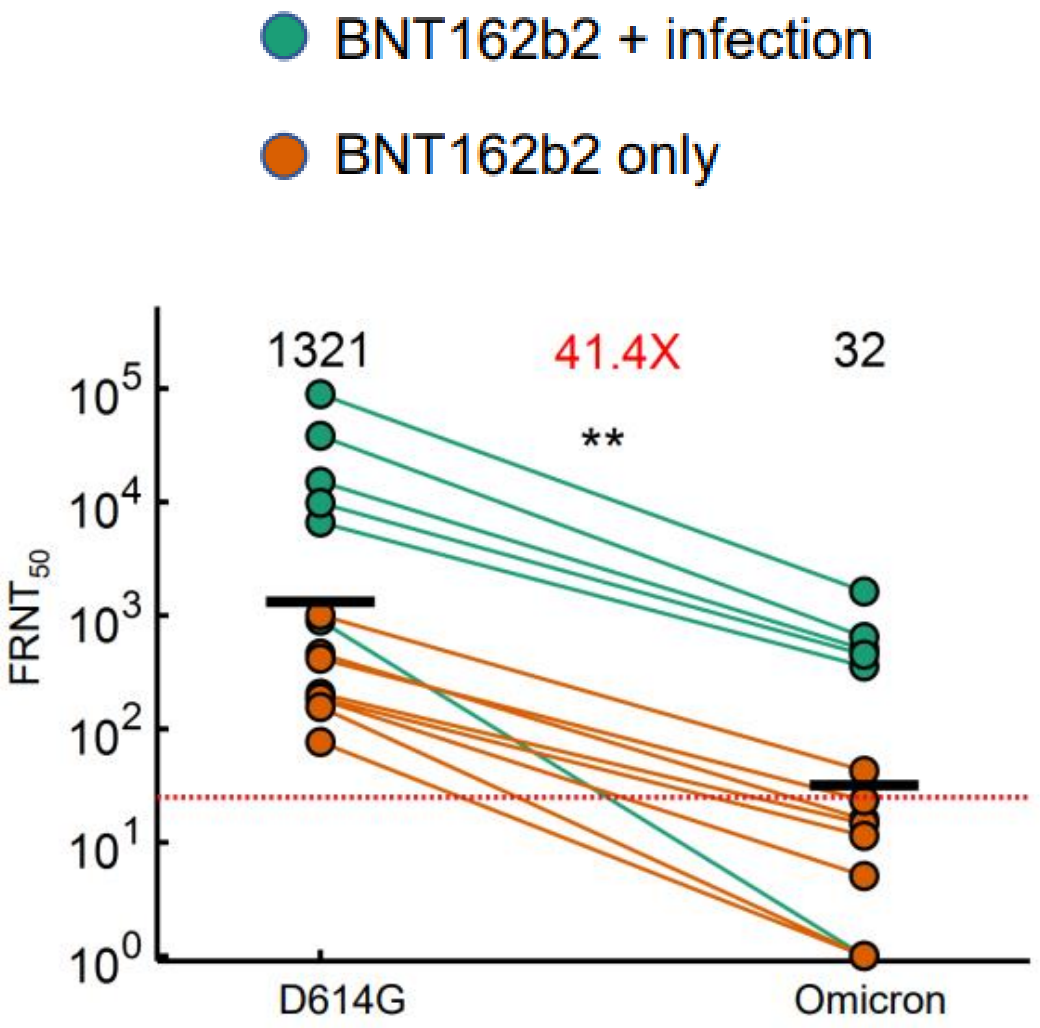


https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/covid-19-special-reports/the-initial-and-daily-covid-19-effective-reproductive-number-in-south-africa/

Antibody Neutralization: Omicron

Background: Extent to which Omicron may evade immunity induced by prior infection with another variant of vaccine-induced immunity uncertain
Design: Viral neutralization assay
Population: Sera 12 Pfizer vaccine recipients, 6 with a history of D614G infection
Outcome: Viral neutralization comparing D614G vs. omicron

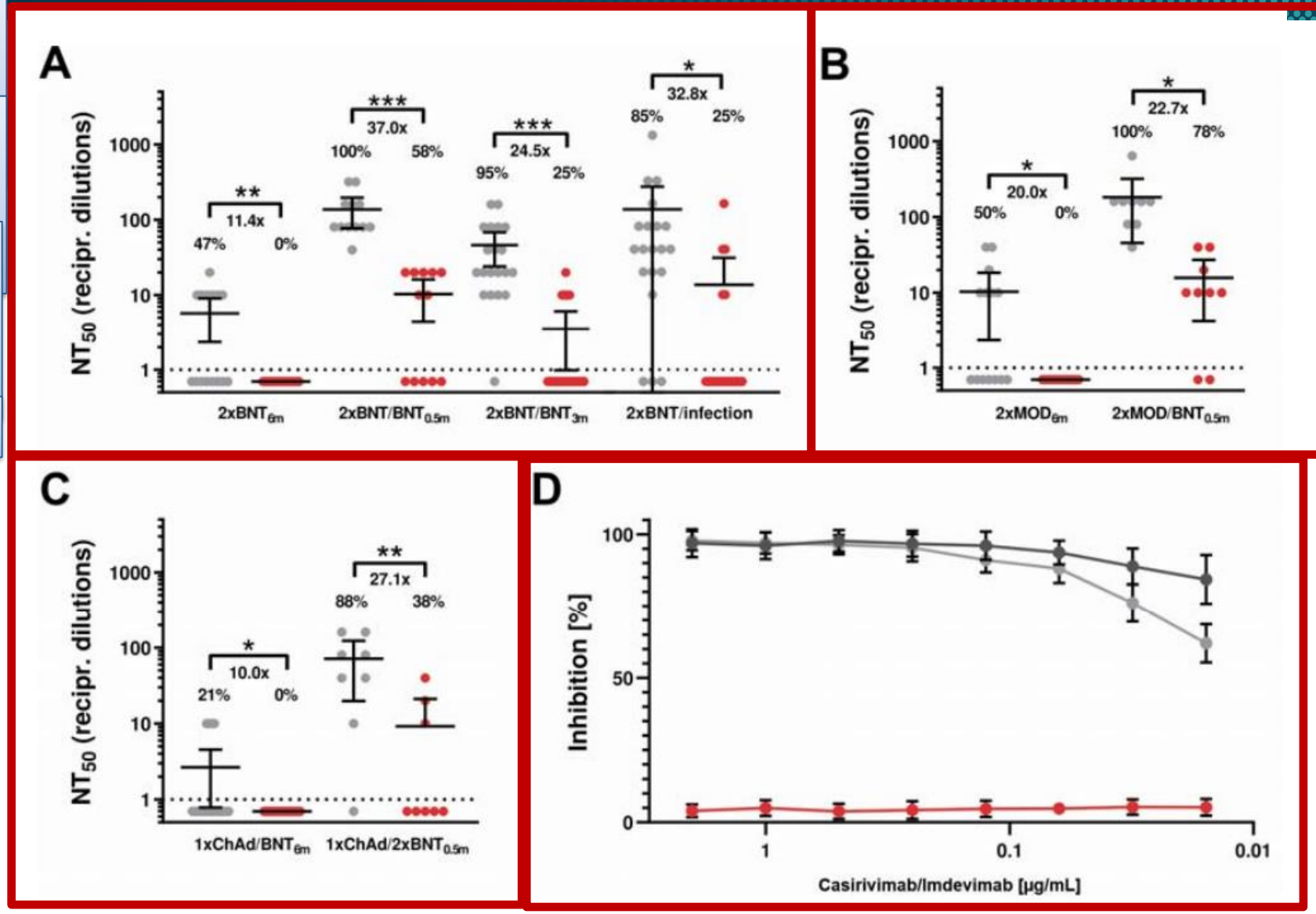
- 41-fold reduction in titer with Omicron
- People with prior infections mostly retained high levels of antibody neutralization



Source: Cele S. MedRxiv 2021

Antibody Neutralization: Omicron

- No neutralization in 2x Pfizer recipients
- No neutralization in 2x Moderna recipients
- Lower but some neutralization with
- No neutralization AstraZeneca/Pfizer
- Lower but some neutralization with Pfizer booster (3rd dose)
- No neutralization with mAb recipients
  - 2 Astrazenica vaccine recipients
  - Inhibition mAB (imdevimab & casirivimab)



Source: Wilhelm A. MedRxiv 2021

Vaccine Effectiveness
Pfizer Press Release

- Sera from persons receiving 2 doses of Pfizer - 25-fold reduction in neutralization against Omicron compared to wild-type SARS-CoV-2
- Third dose (1 month after third dose) leads to neutralization similar to that achieved with 2 doses (3 weeks after 2nd dose) against wildtype
  - Also increased CD8+ T cells against spike protein
- 80% epitopes on spike protein recognized by CD8+ T cells not affected by Omicron mutations
- Company developing vaccine against omicron variant – can be available in March
- Pfizer plans to produce 4 billion doses in 2022

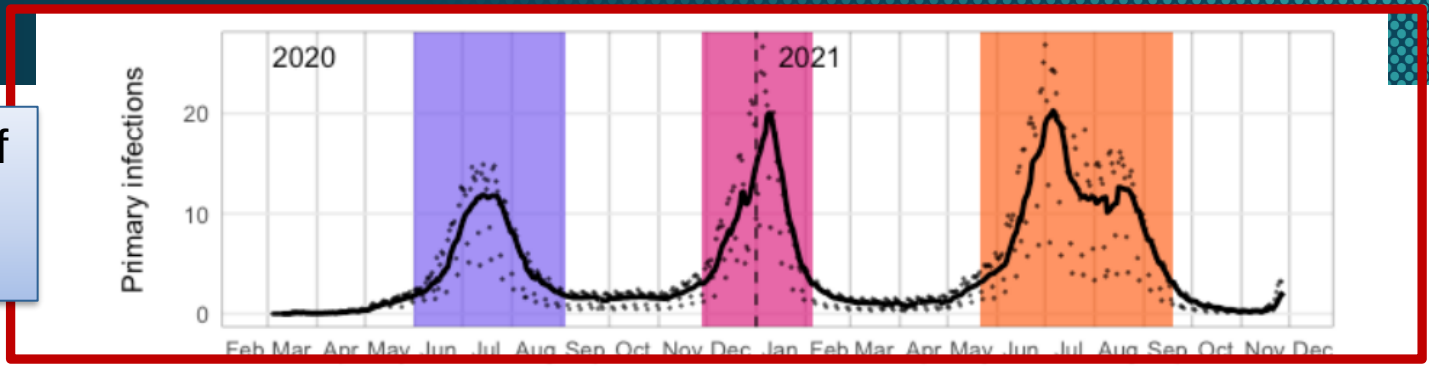
https://investors.biontech.de/news-releases/news-release-details/pfizer-and-biontech-provide-update-omicron-variant
https://www.samrc.ac.za/news/tshwane-district-omicron-variant-patient-profile-early-features

Reinfection with Omicron: South Africa

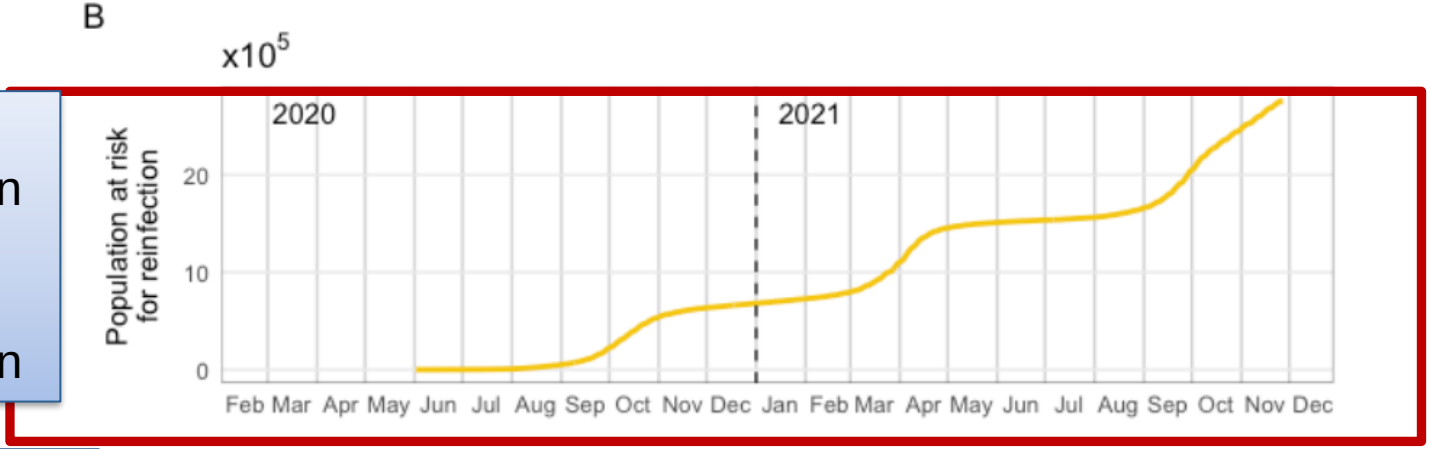
Background: Extent to which Omicron may evade immunity induced by prior infection with another variant of vaccine-induced immunity uncertain
Design: Retrospective analysis surveillance data South Africa
Population: 2,796,982 people with lab-confirmed SARS-CoV-2 90 days prior to 11/27/21.
Outcome: Reinfection - Sequential positive tests ≥90 days apart – time varying relati hazard primary vs reinfection

Source: Pulliam JRC. MedRxiv 2021

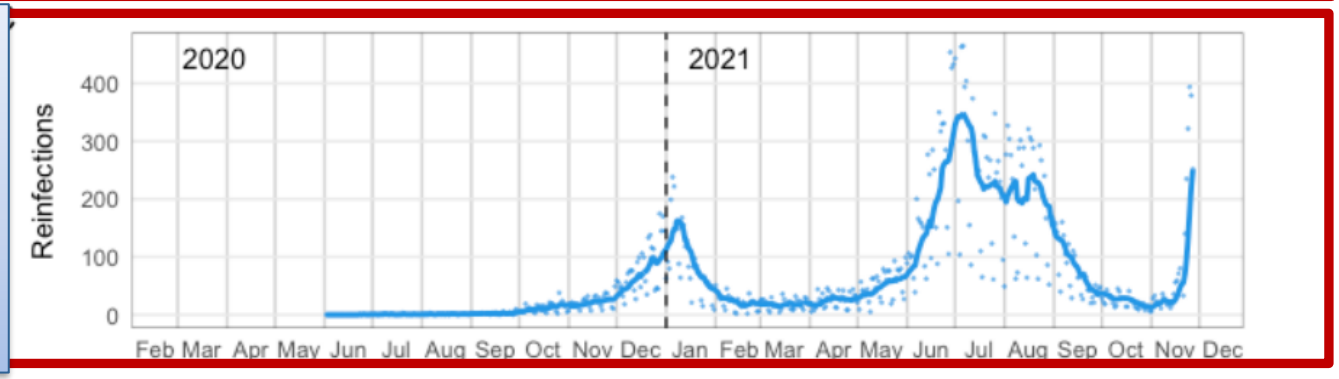
3 waves of primary infection



Growing population of people at risk for reinfection



Reinfections -Big jump in reinfections with relatively small ↑ primary infection

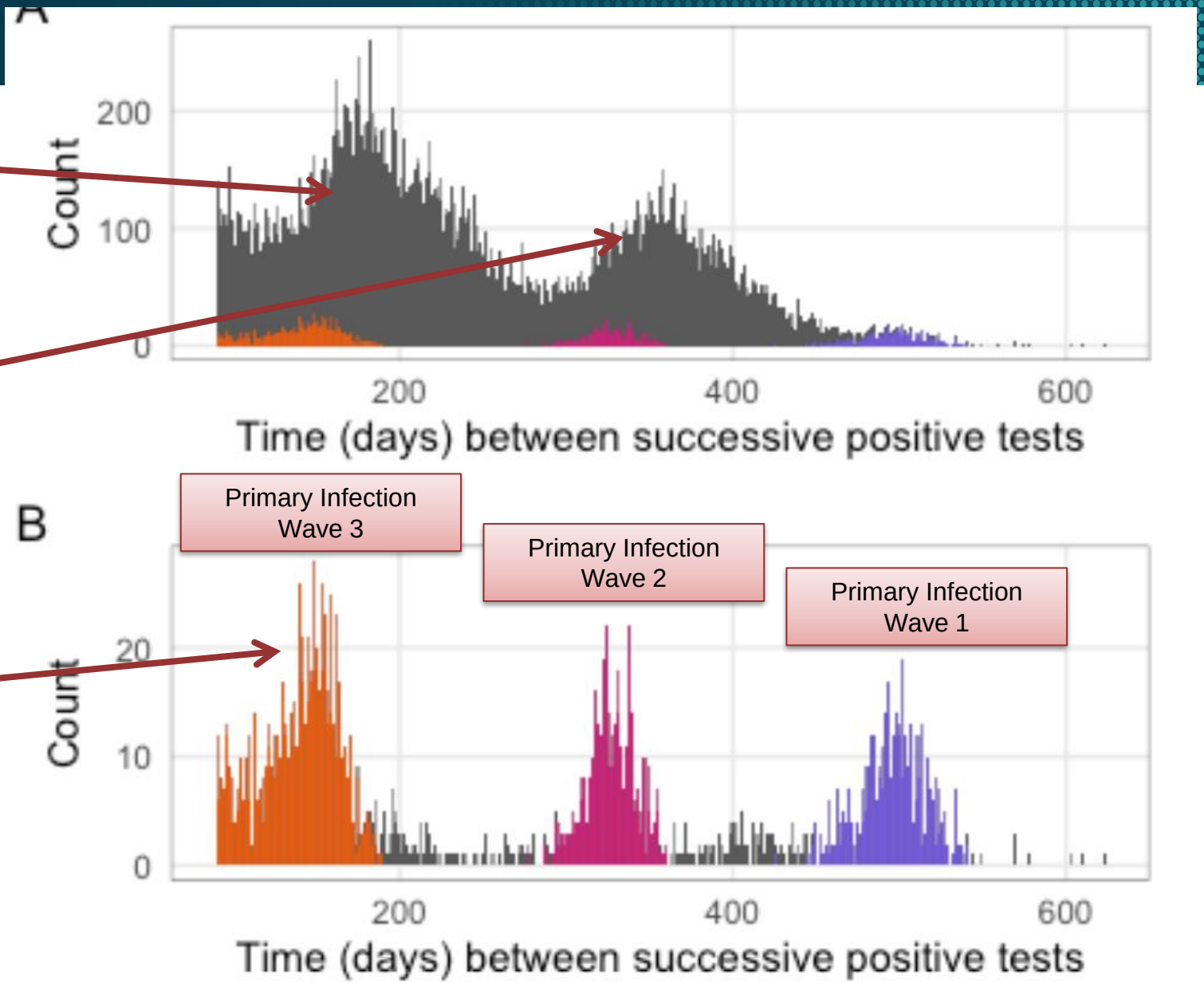


Reinfection with Omicron: South Africa

Infection in wave 1 and reinfected in wave two, or infected in wave 2 and reinfected in wave 3

Infection in wave 1 and reinfected in wave 3

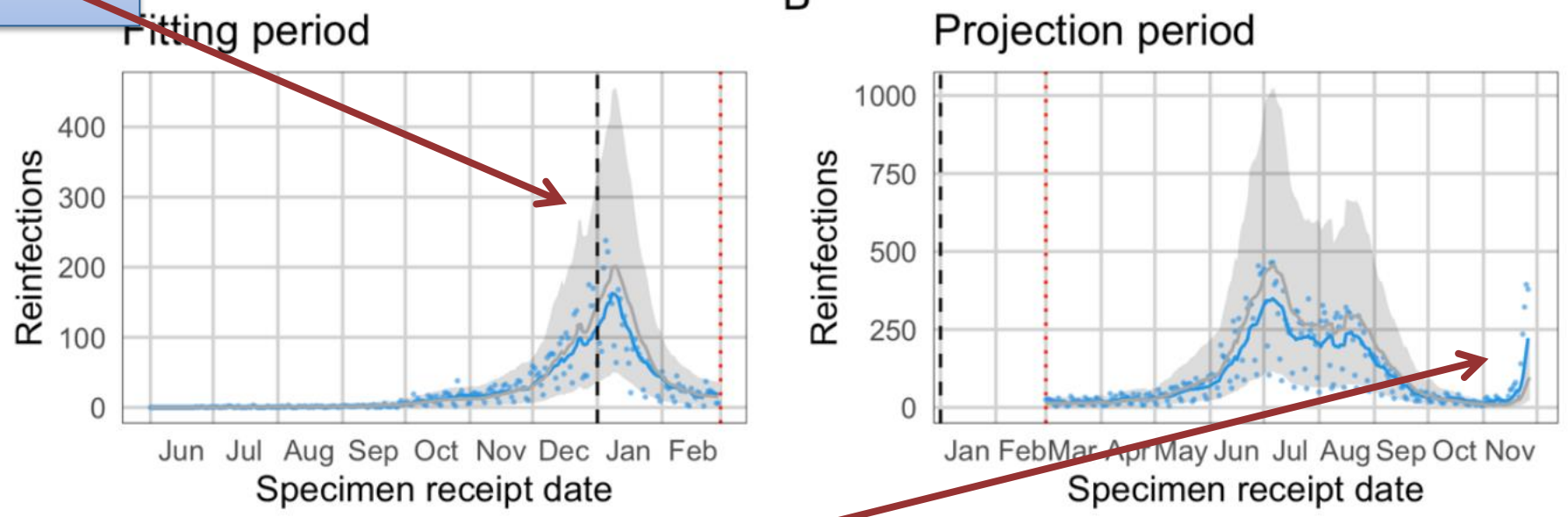
Reinfections Since November 1, 2021
Infection in wave 3 and reinfected in period of omicron



Source: Pulliam JRC. MedRxiv 2021

Reinfection with Omicron: South Africa Comparison of Projections

Predicted reinfections (grey line) based on the number primary infections (blue line) closely match – risk of reinfection is constant through waves 1-3



Recent trends in reinfection diverge from prior experience – much higher than predicted – suggests immune escape

Source: Pulliam JRC. MedRxiv 2021

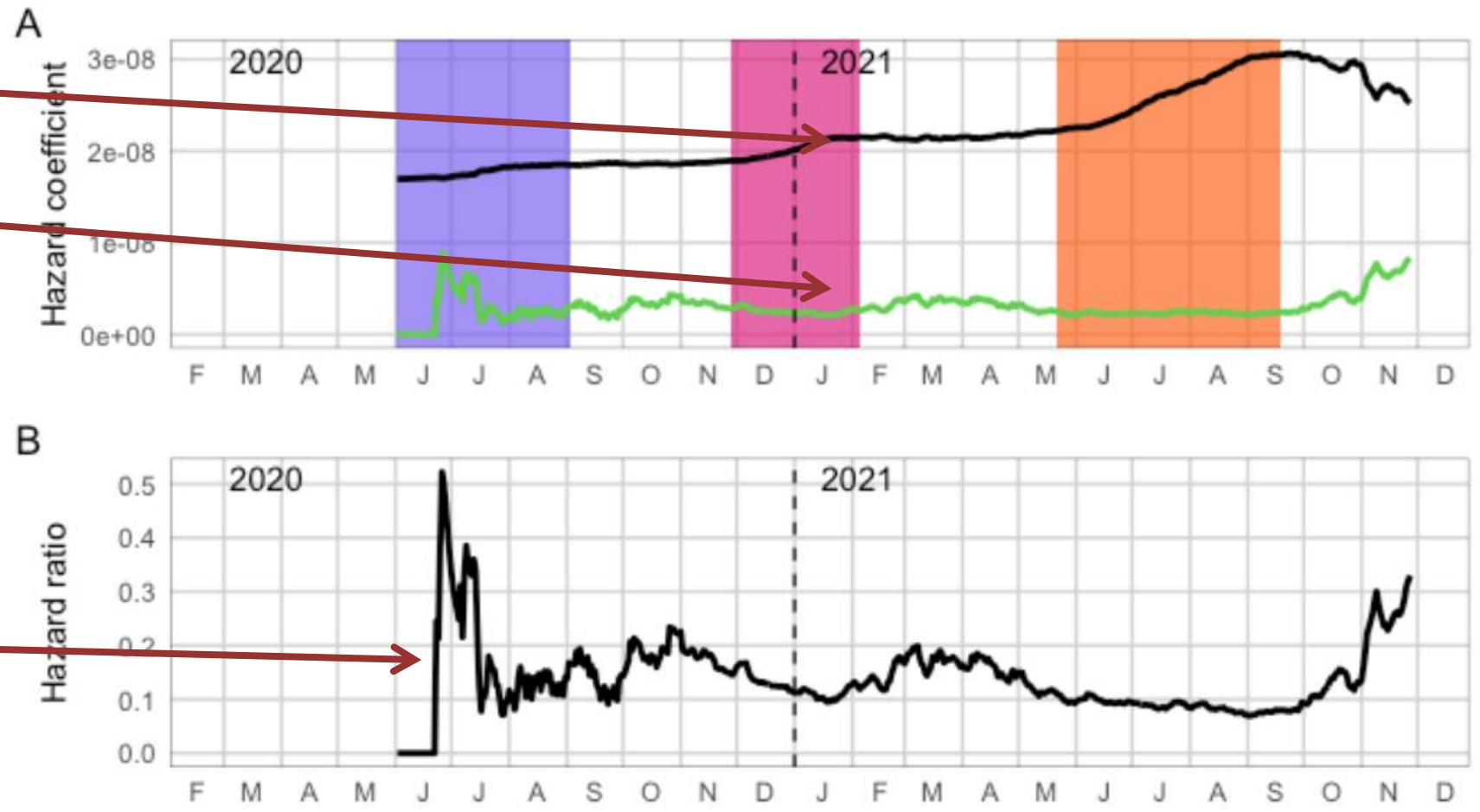
Reinfection with Omicron: South Africa

Empirical estimate of time-varying infection and reinfection Hazards

Primary infection

Reinfection

Hazard ratio primary vs reinfection
- Relative hazard rising since November



Source: Pulliam JRC. MedRxiv 2021

Reinfection with Omicron: South Africa

Empirical estimate of time-varying infection and reinfection Hazards

- No evidence of immune escape with Beta and Delta variants
  - Infection provided ~84% protection from reinfection during subsequent wave
  - *In vitro* neutralization studies suggest that there may be immune escape from Beta and Delta – data not consistent
  - Suggests that Beta and Delta waves were driven by increased transmissibility, not immune escape
- Omicron appears to be different

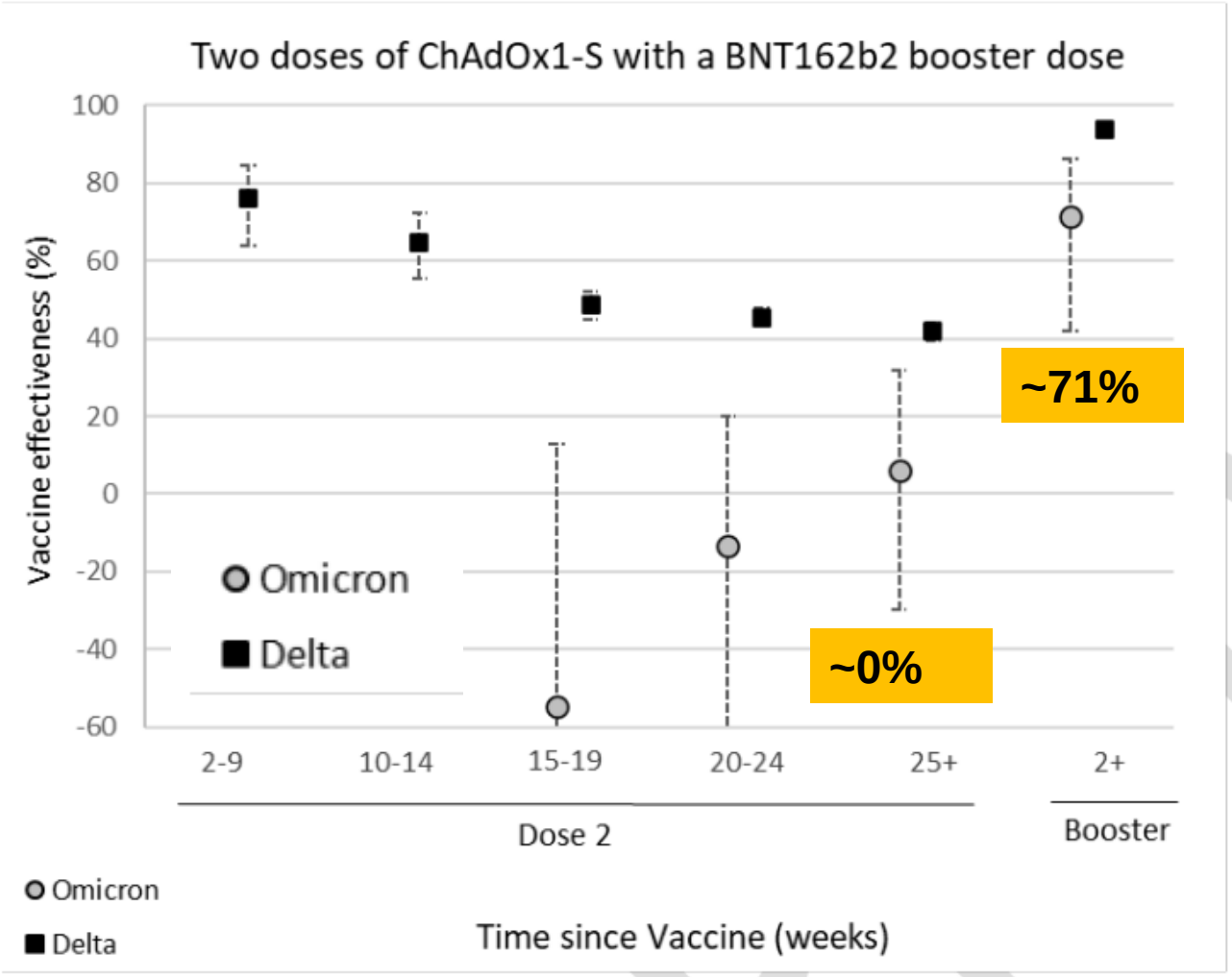
Source: Pulliam JRC. MedRxiv 2021

Vaccine Effectiveness Against Omicron: UK

Background: Vaccine effectiveness against Omicron unknown
Design: Test negative control
Population: Symptomatic persons with PCR tests Oct 16-Dec. 6.
Outcome: Symptomatic COVID-19 with Omicron – Omicron based on S-gene target failure

Cases
- 581 symptomatic Omicron cases
- 56,439 Delta
- 130,869 PCR negative controls

Vaccine Effectiveness (AZ)
- No protection from AstraZeneca against Omicron after 15 weeks
- Booster with Pfizer leads to 71% protection



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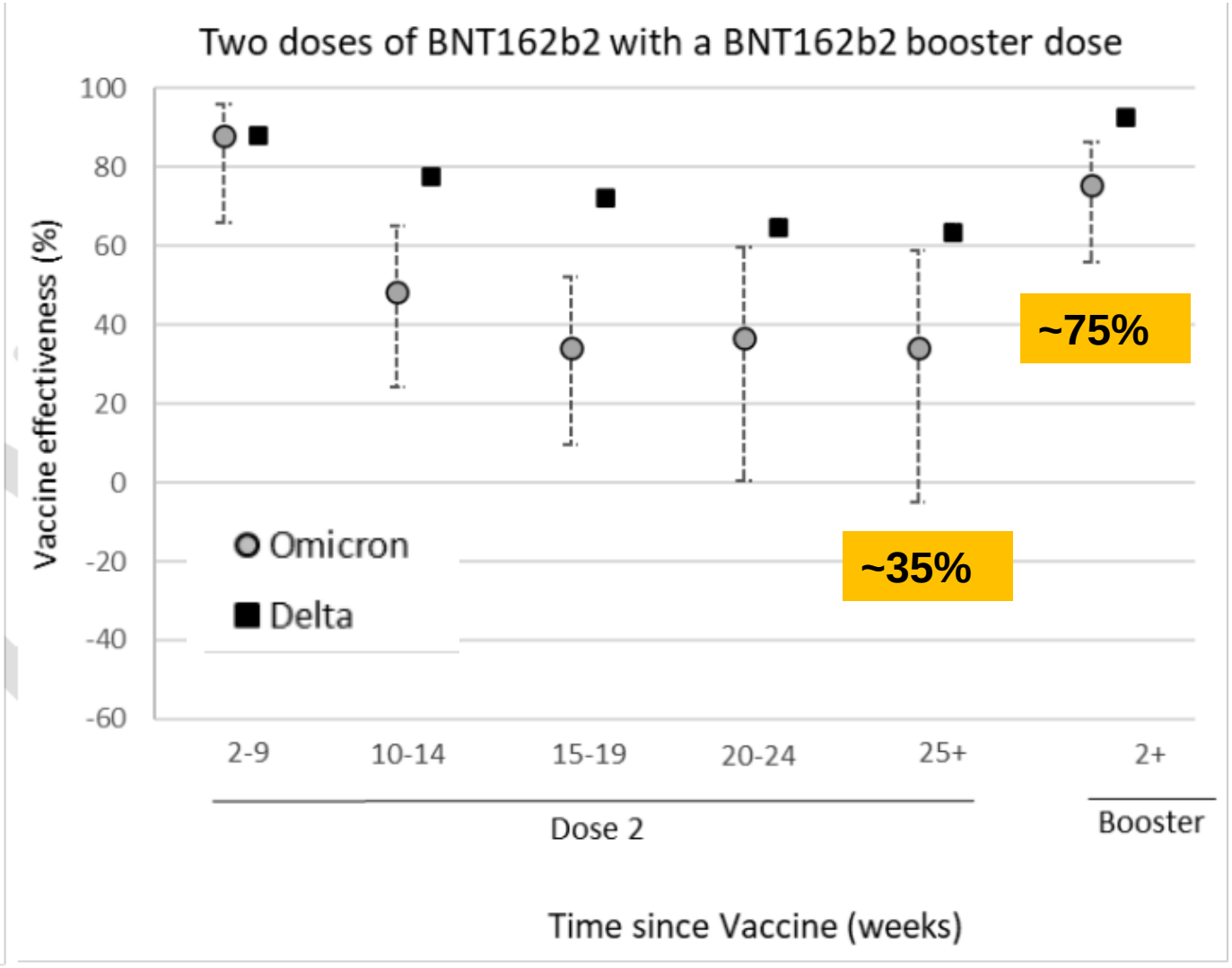
Vaccine Effectiveness Against Omicron: UK

Vaccine Effectiveness (Pfizer)

- VE 88% at 2-9 weeks, dropping to 34-37% at week 15 after second dose
- Booster with Pfizer leads to 75% protection

Conclusions

- Concerning data on VE
- AZ recipients were different than Pfizer recipients (first vaccinated included older persons) – residual confounding
- Data support boosters
- **No data on severe disease!**



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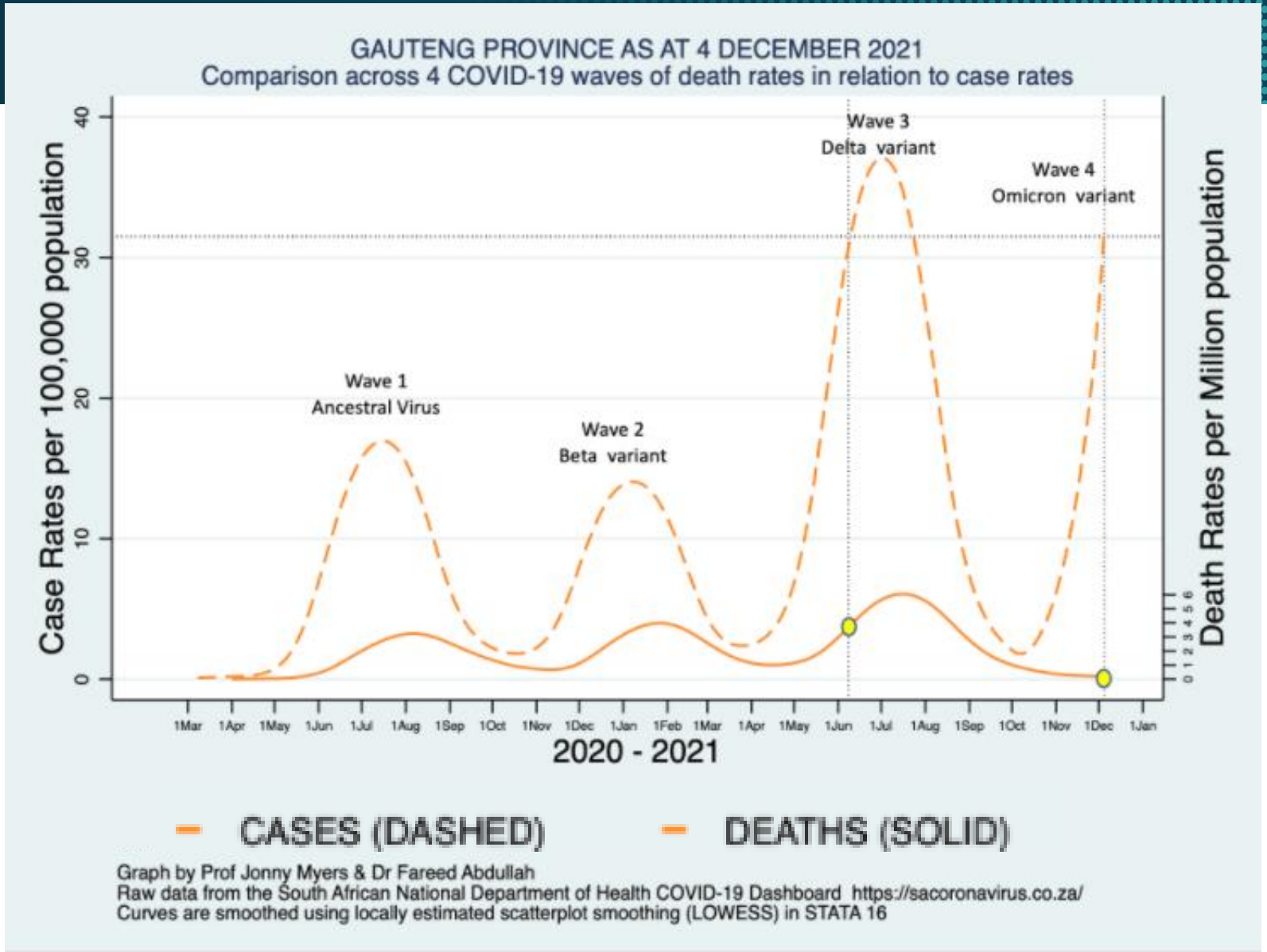
Omicron and Immunity: Conclusions

- Consistent laboratory data, evidence of increased rates of reinfection, and a small vaccine effectiveness study all suggest that natural and vaccine-induced immunity are diminished against Omicron
  - Lab data focus on antibody, not cell mediated immunity
- Magnitude of decrease and impact on severe disease unclear
- Existing evidence supports that idea that a booster will improve immunity against Omicron

Disease Severity Omicron: South Africa

- Rise in number of cases in Gauteng, South Africa not accompanied by increase in number of deaths
- No clear increase in number of admissions for severe COVID
- **Very early data** – lag in time to death



https://www.samrc.ac.za/news/tshwane-district-omicron-variant-patient-profile-early-features

- “And yet as the Omicron variant demonstrates, the pandemic is from far over. Persistent vaccine inequity has allowed this to happen.”

Tedros Adhanom Ghebreyesus

Summary

- **Epidemiology**
  - Rapid emergence and spread of Omicron – most dramatic in southern Africa
  - Extent to which high reproductive number reflects the high transmissibility of Omicron vs. the virus' ability to evade immunity is uncertain
- **Clinical**
  - Very limited data suggest that Omicron may be less pathogenic than Delta
    - Too early to draw firm conclusions on this
  - However, if the number of cases increases dramatically, even if the risk of severe disease per infection is lower the total number of deaths may still increase
- **Vaccines**
  - Vaccine-induced immunity, known to wane over time, substantially less with Omicron
  - Additional data supporting booster shots - all boosters with mRNA vaccines

Questions and Comments