VIEW OF OMICRON FROM CAPE TOWN, SOUTH AFRICA

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OMICRON

Spreading globally and Impossible to stop

New variant classified by WHO as Variant of Concern (VoC)

First identified in South Africa 24 November

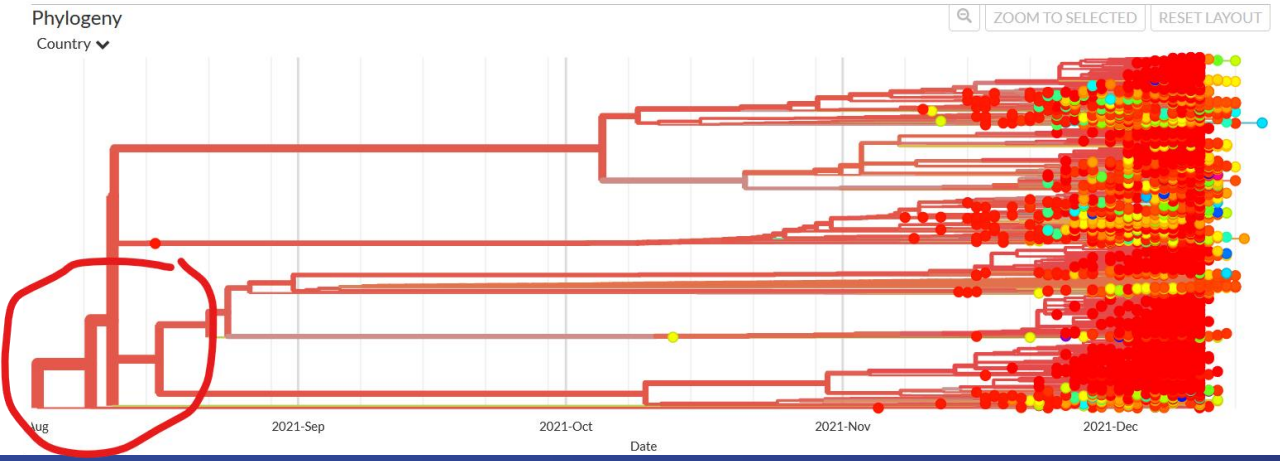
Probably been circulating since August

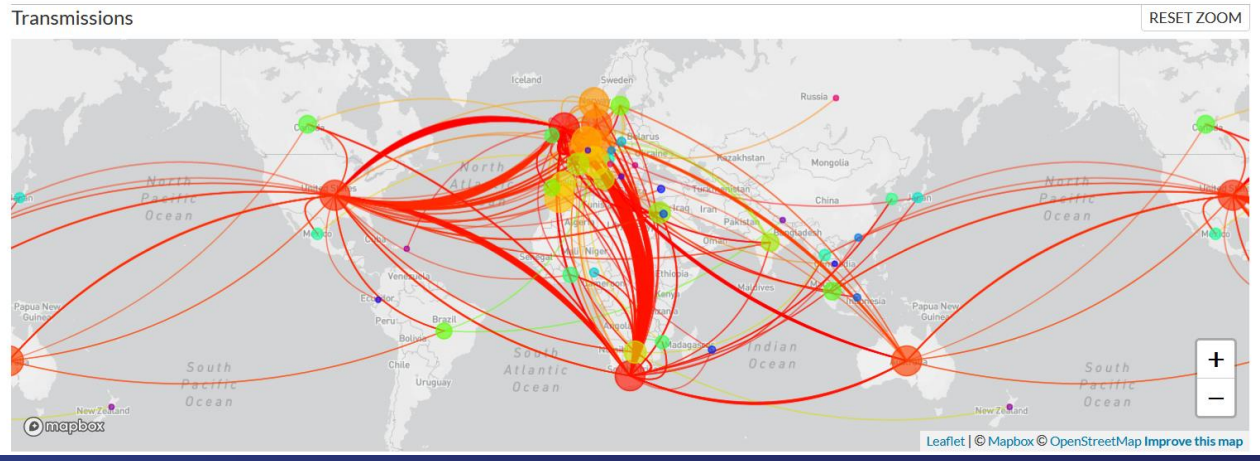
Presence grossly underestimated now in many countries (current 78 countries)

Impossible to stop globally

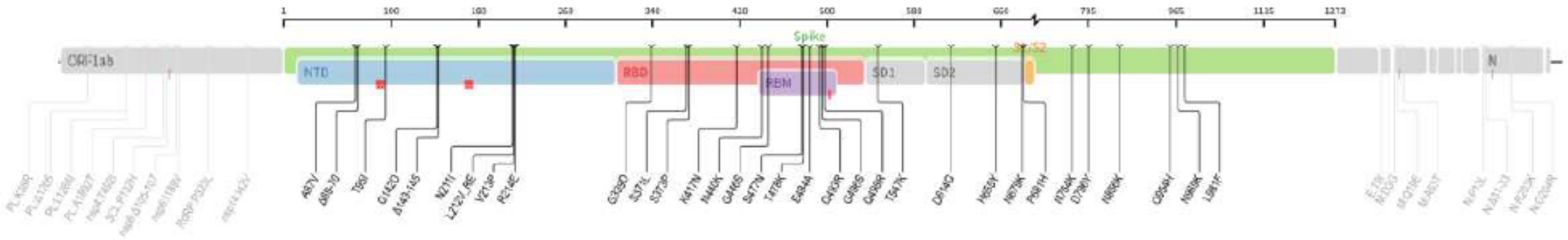
Phylodynamics of pandemic coronavirus variant VOC Omicron GRA (B.1.1.529+BA.*) first detected in Botswana/Hong Kong/South Africa

Showing 3 985 of 3 985 genomes collected between Aug 2021 and Dec 2021, last updated 2021-12-19





Omicron lineage mutation profile



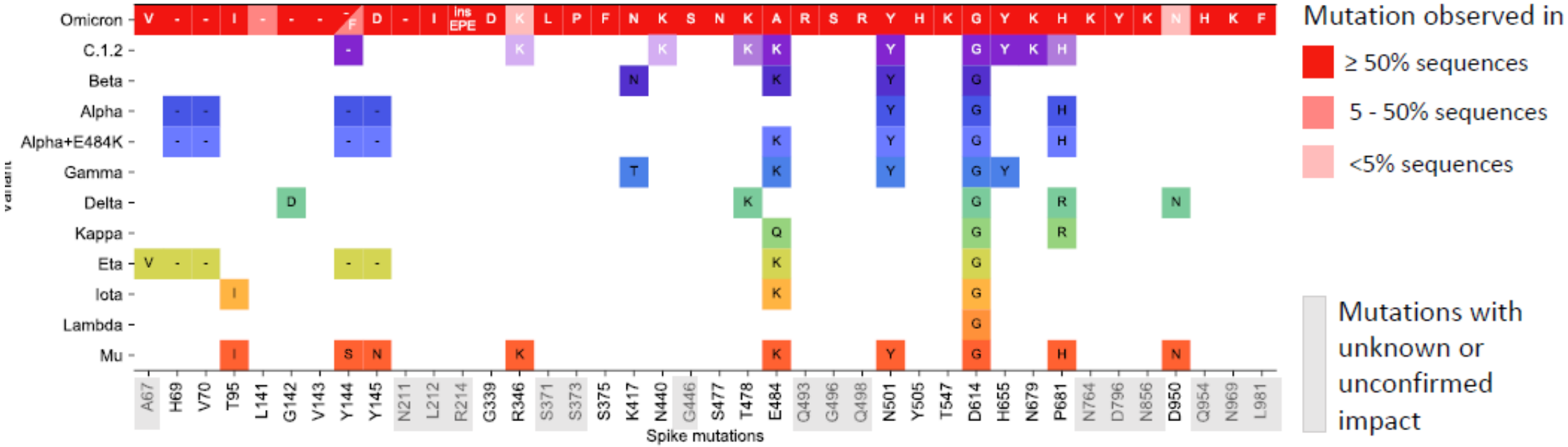
- 45-52 amino acid changes (including deletions) across the whole GENOME
  - 26-32 changes in SPIKE

- Does not possess the RdRp G671S change associated with a decrease in Ct value for Delta variants
- Does possess the Spike Δ69-70, which causes the S-Gene Target Failure (SGTF) and was previously seen in the Alpha VOC

- Nucleocapsid mutations not predicted to affect antigen rapid diagnostic tests

NGS-SA
Network for Genomic Surveillance in South Africa

Omicron spike mutations compared to other VOC/VOIs



- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - including a three amino acid insertion

This is important as we will see – it makes existing antibodies less effective

- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H

This likely makes it bond more tightly to human cell receptors – more transmissible

- Effect of most spike S2 subunit changes have not been defined

NGS-SA Network for Genomic Surveillance in South Africa

OMICRON RISK

What's the risk?

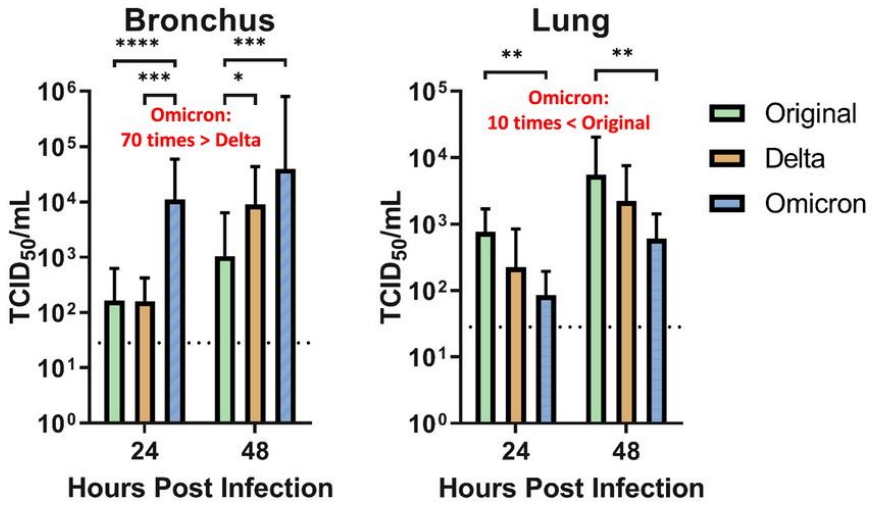
Risk = Likelihood x Severity

- Depends on context
  - levels of T-cell immunity and neutralising antibodies
  - Existing hospital pressure – NHS already stretched, SA hospitals not
  - Adherence to NPIs
  - Availability of treatment

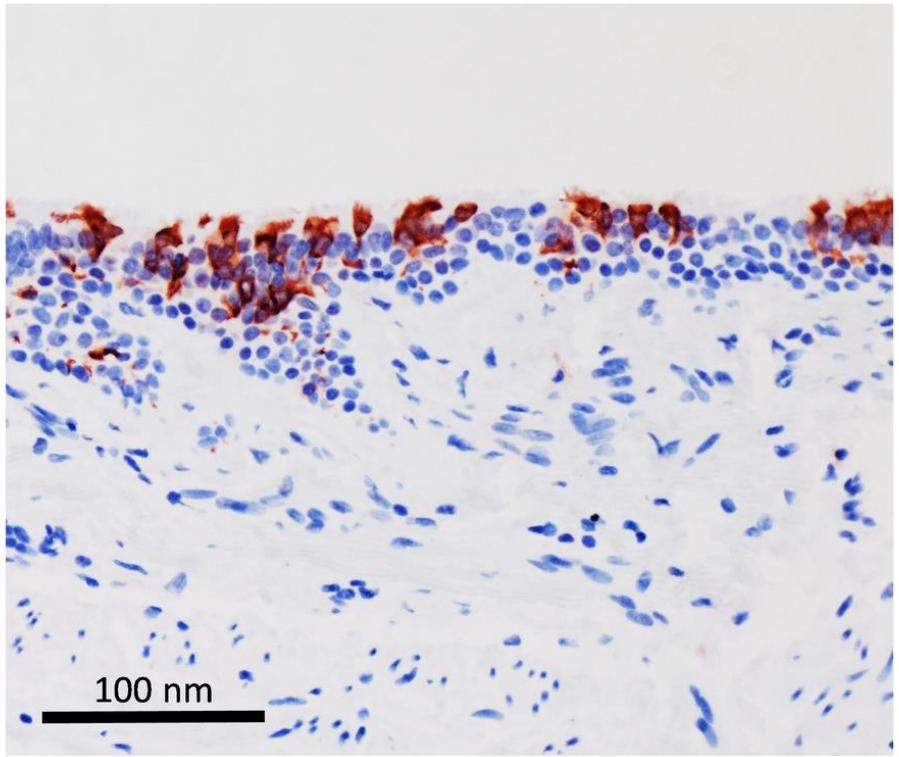
OMICRON RISK

Lab research vs epi data

Uni of Hong Kong research report



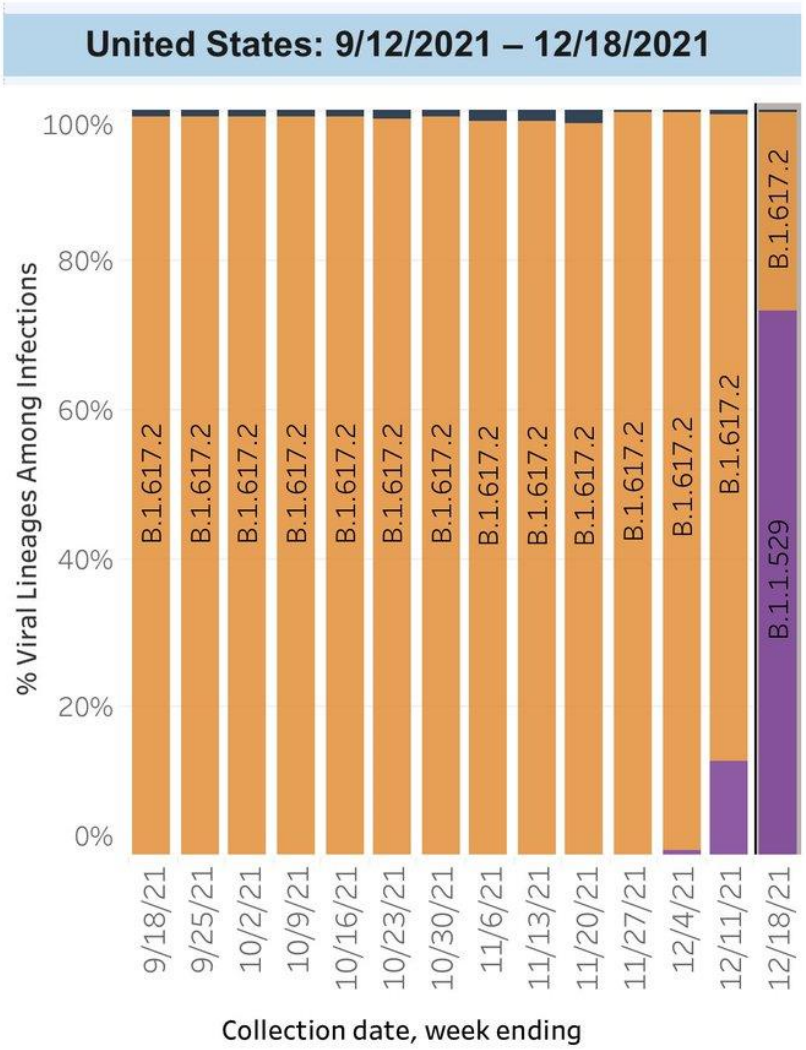
- Growth 70 times greater than ancestral in bronchus
  - more transmissible
- Growth 10 times less in lungs
  - Less severe

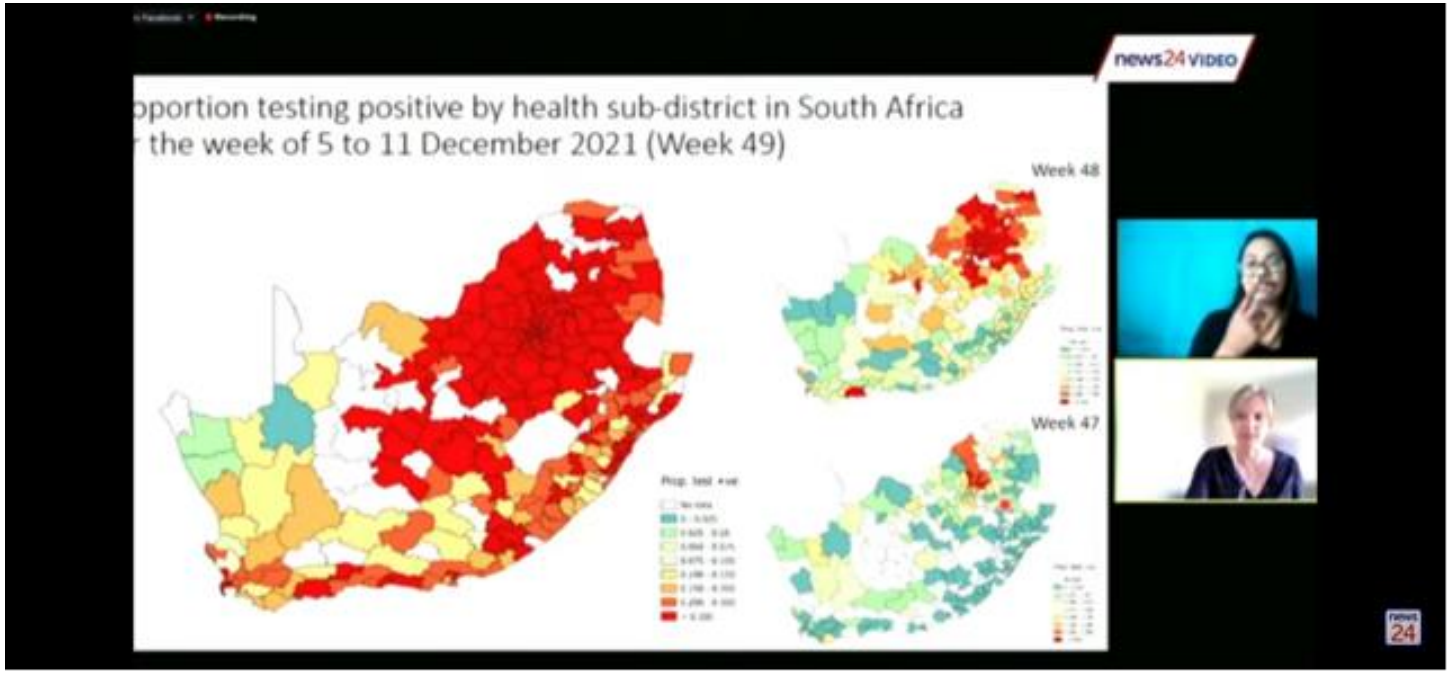


Omicron variant of SARS-CoV-2 (in red) infected human bronchus tissues.

OMICRON TRANSMISSION GLOBALLY

Unbelievably quick spread – CDC nowcast estimate for USA – took 2 to 3 weeks to outcompete delta

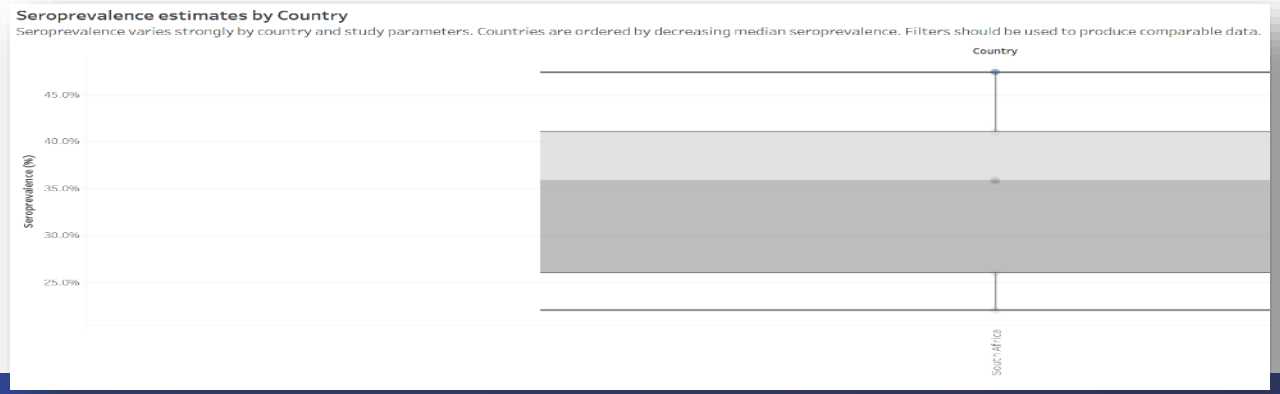


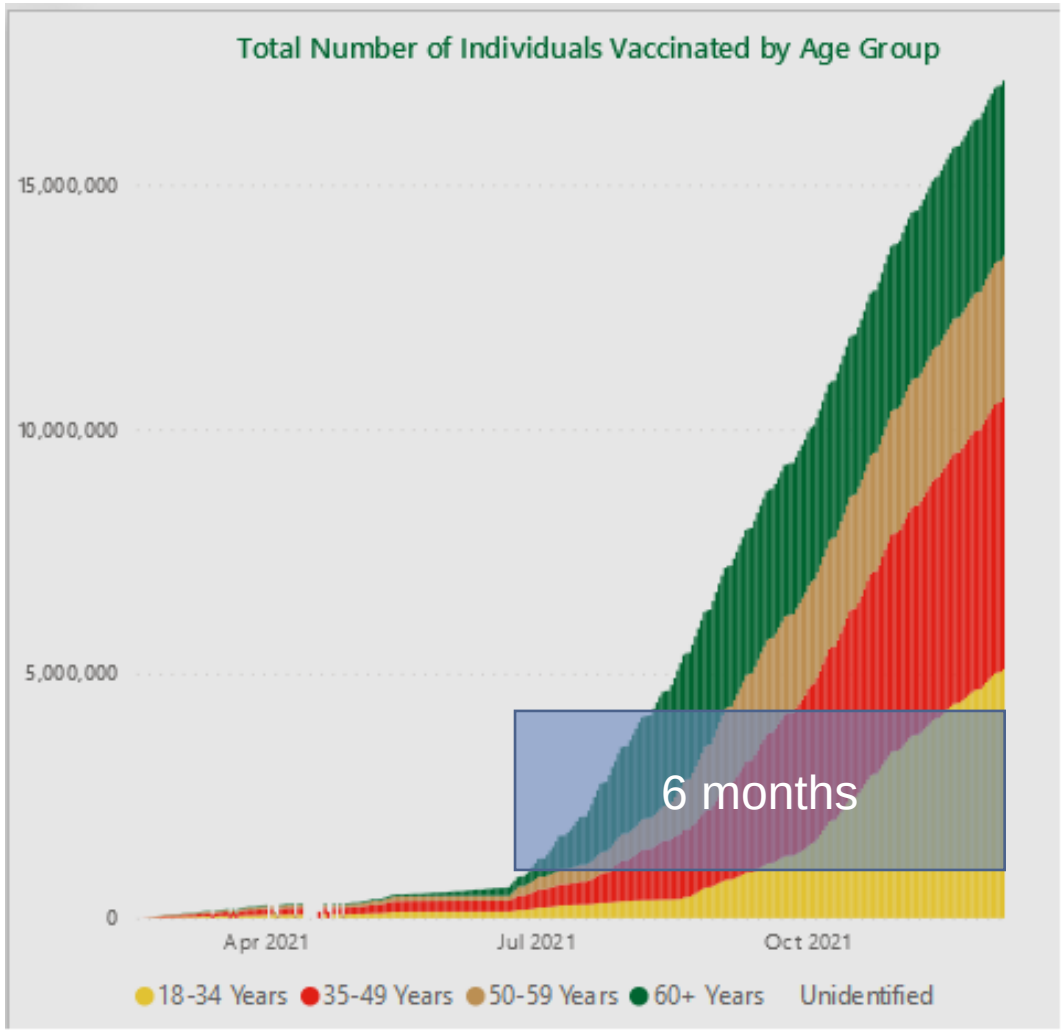


OMICRON TRANSMISSION IN SOUTH AFRICA

High levels of immunity in South Africa

- 15 Jan to 15 May 2021
  - 17,000 blood donors in national survey
  - 47% prevalence of covid antibodies
  - BEFORE delta wave
- Most people vaccinated within 6 months
- Estimated 80% with antibodies to COVID-19 now

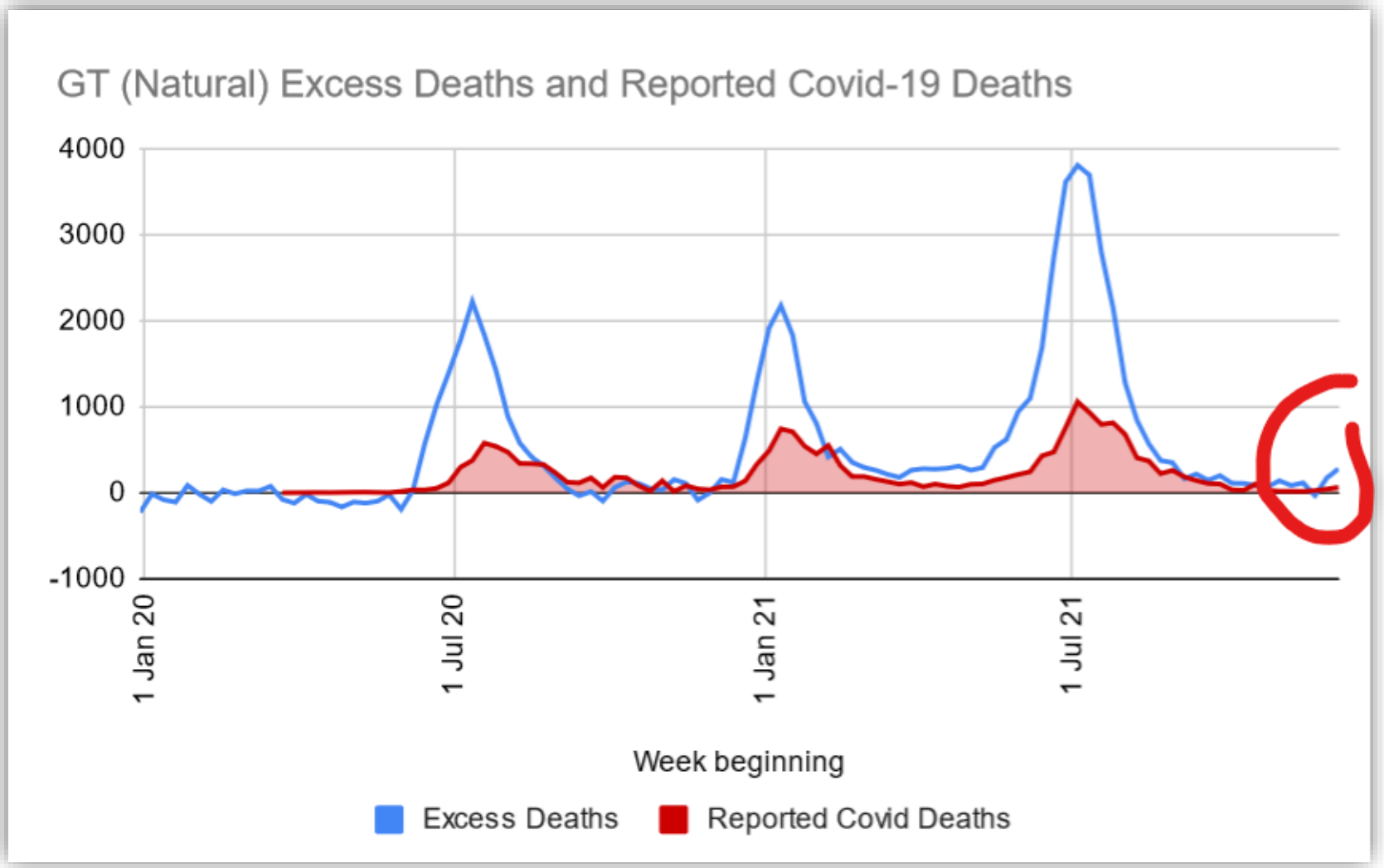




OMICRON TRANSMISSION

Highly transmissible – spreading though population with high levels of immunity (vaccine and natural infection acquired)

- Doubling time in ramp up 1.5 to 2 days
- Infecting 3 to 6 times as many people as delta
- 2.4 (SA*) to 5.4 times (UK**) greater risk of reinfection compared to previous variants
- Death rates only slightly increased
- Note- highly immune population in South Africa



South African Medical Research Council – 20 Dec for Gauteng Province

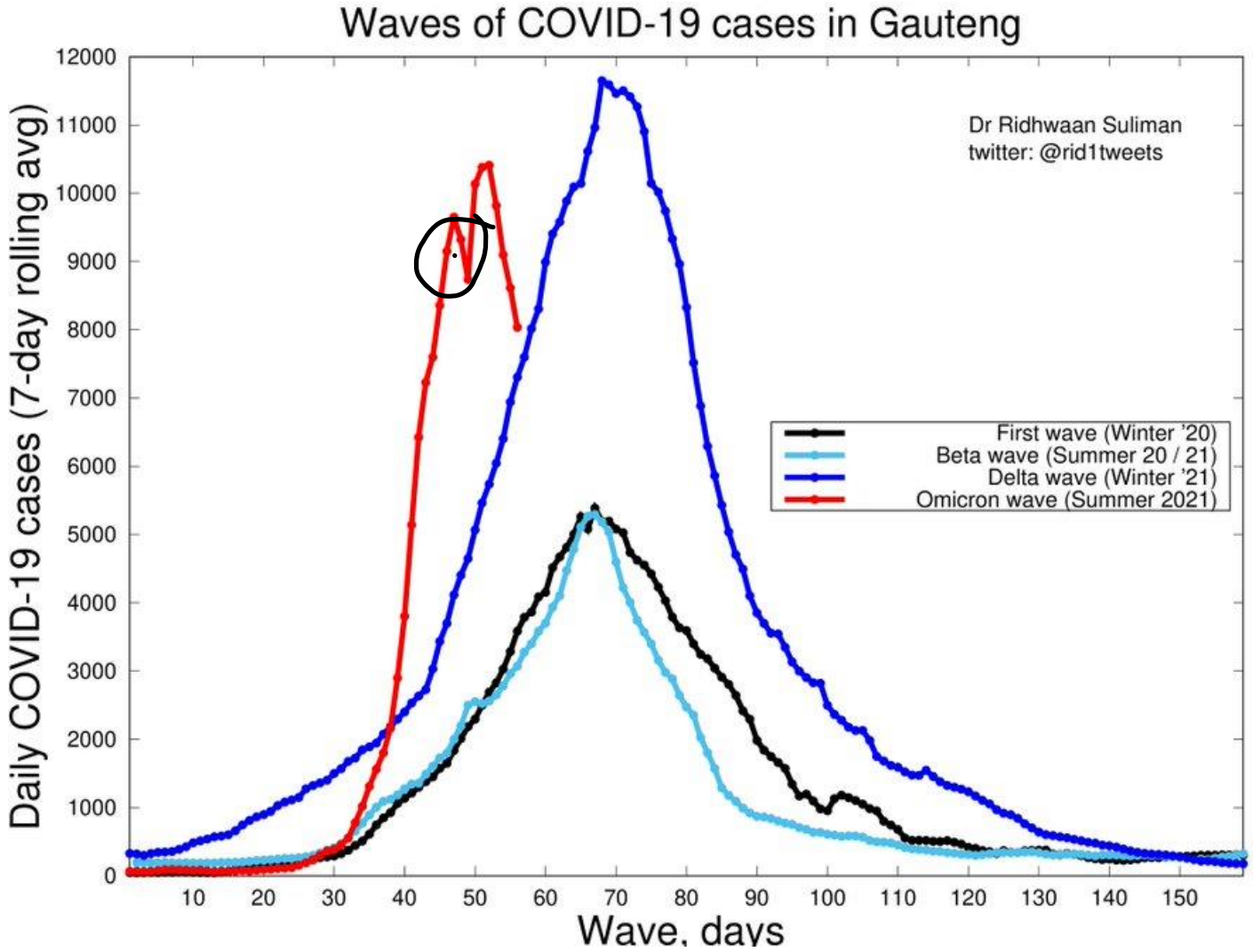
*Pulliam et al, 2 Dec 21
** Imperial College Report 49

OMICRON TRANSMISSION

Explosive spread in highly immune population – immune escape and very transmissible

- **Immune escape**
- **Incredibly transmissible**

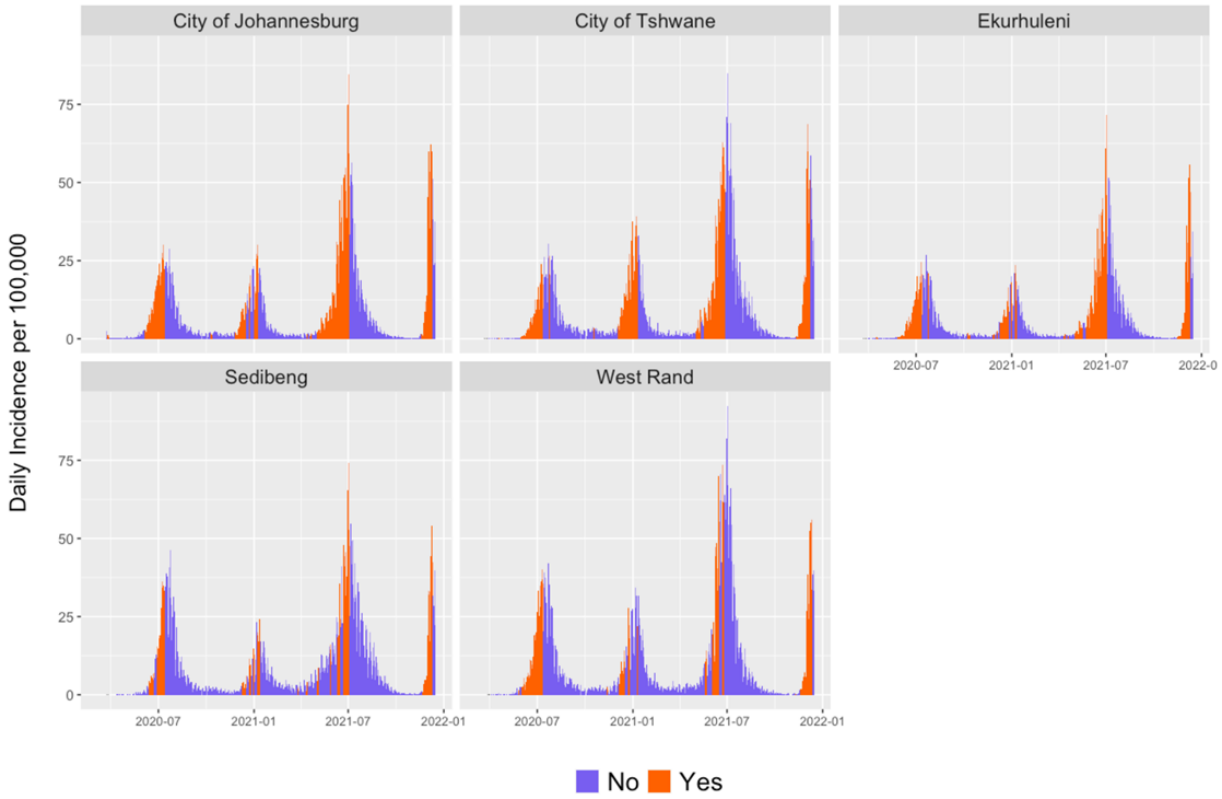
Note: Ignore the slight downward trend that suggests it may have peaked. One needs to understand the data limitations – testing and reported hospital and case data has limitations – reporting date different to collecting date, and PCR and antigen tests reported differently with delays in some cases – don't just look at reported numbers and take them at face value – they really need an expert to interpret properly

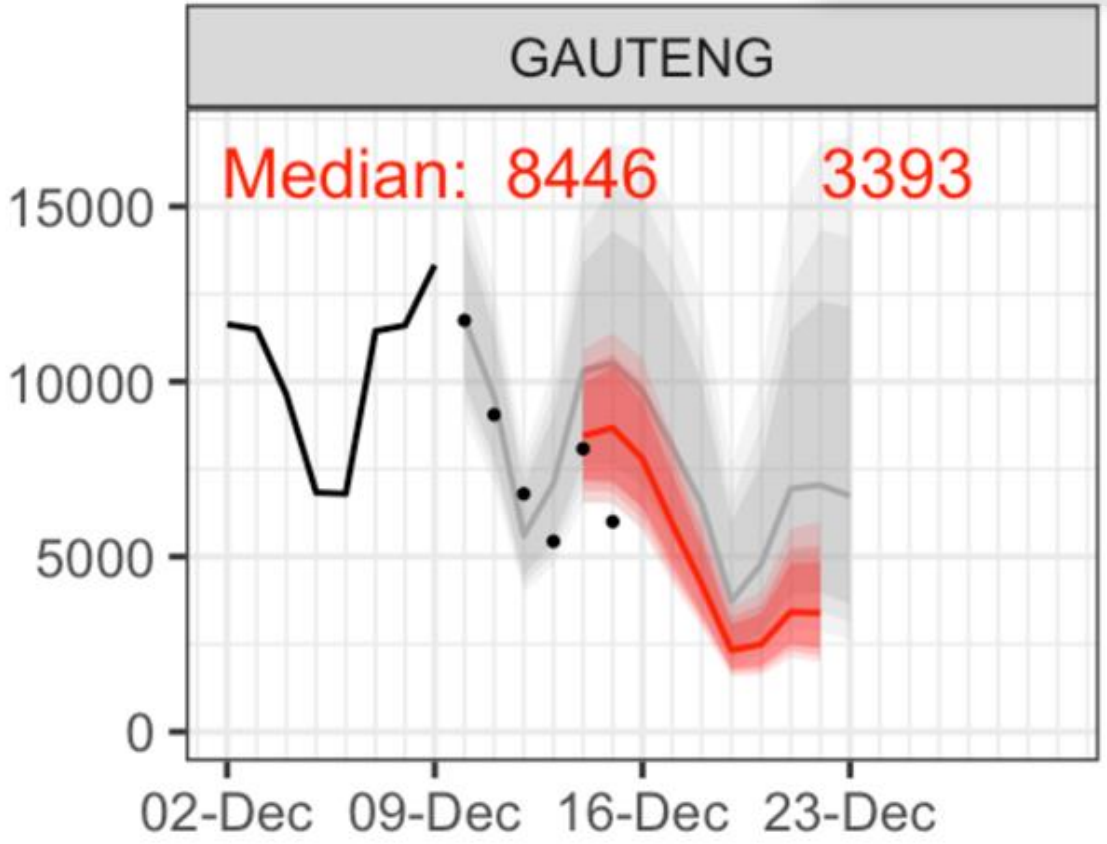


GAUTENG PROVINCE OVER THE PEAK?

Estimated Rt fallen from 2.6 to 1.05

no uptick in the 7 day moving average for reported cases across all districts for the last 5 days at least (data reported to 15 Dec





SOUTH AFRICAN COVID-19 MODELLING CONSORTIUM
Epidemic Explorer - Open Access

OMICRON SEVERITY - GAUTENG

Information from health authorities at media conference on Friday 17 Dec

- The health authorities and NICD indicated on Friday that:
  - Hospital testing practices have not changed (so no bias)
  - Many admissions are incidental positives
  - Most admissions are mild and short duration (we heard the previous week the duration of hospital stay for COVID-19 and decreased from 8.5 days down to around 3.5 days)
  - Most admissions are unvaccinated
  - Paediatric admissions are mostly for non-respiratory problems
  - The in-hospital case fatality rate and oxygen utilisation is much lower (see graphs that follow)

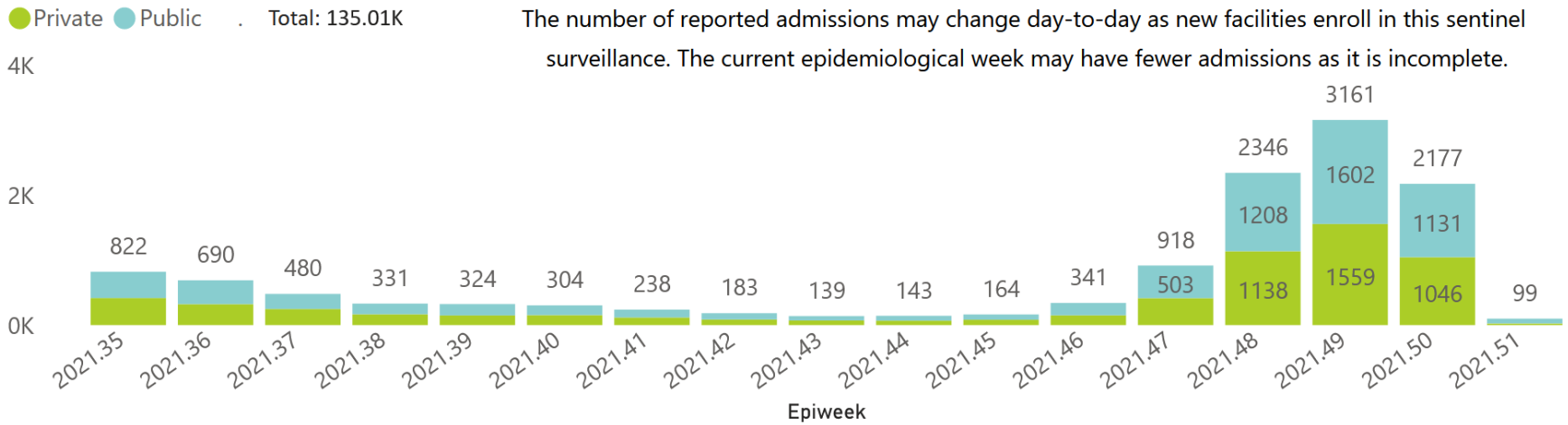
OMICRON SEVERITY - GAUTENG

Hospital data from DATCOV data – NICD. Disregard latest Epi week (50) as data incomplete

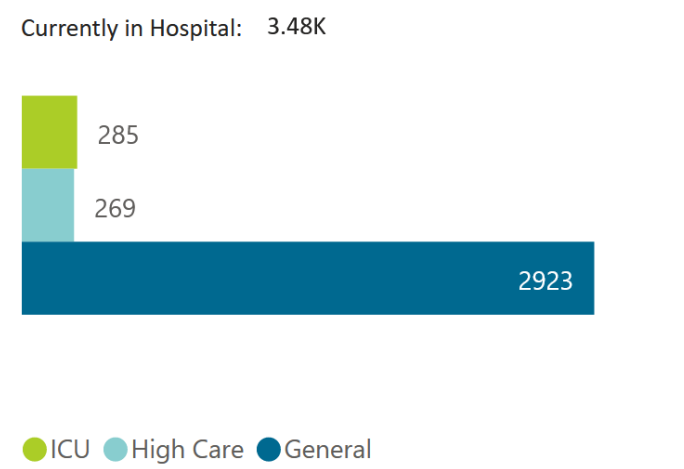
health
Department:
Health
REPUBLIC OF SOUTH AFRICA

The number of reported admissions may change day-today as enrolled facilities back-capture historical data.
The Western Cape government has been unable to provide daily data on patients who are on oxygen or ventilated.
The data below refer to admitted patients who test positive for SARS-CoV-2 on PCR or antigen tests.

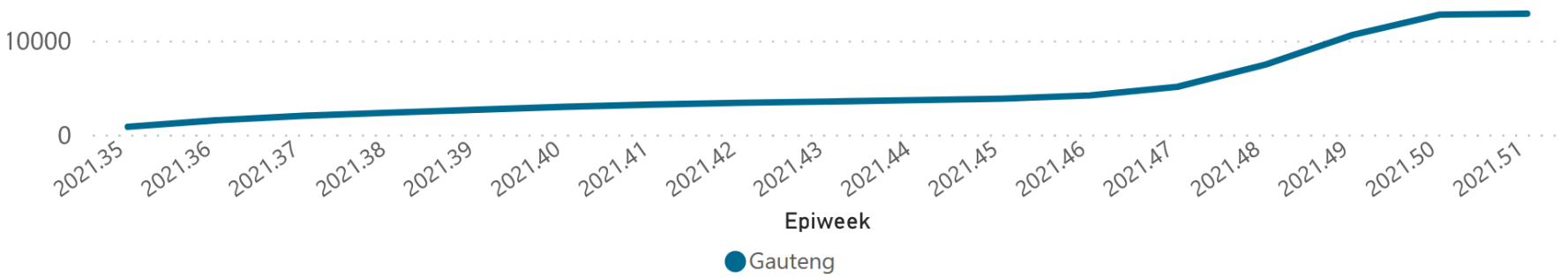
Hospital admissions of COVID-19 cases, by health sector, by epidemiological week



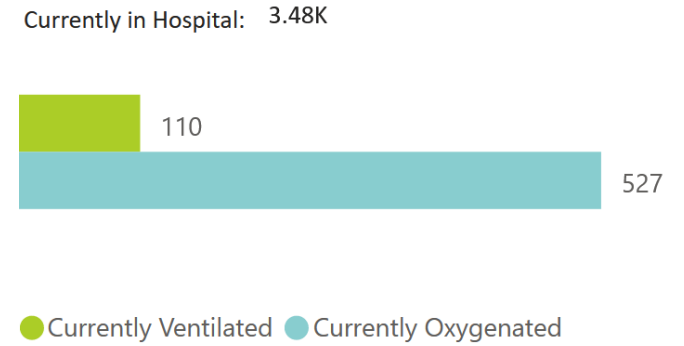
Ward of currently admitted patients



Cumulative reported admissions by province, by epidemiological week

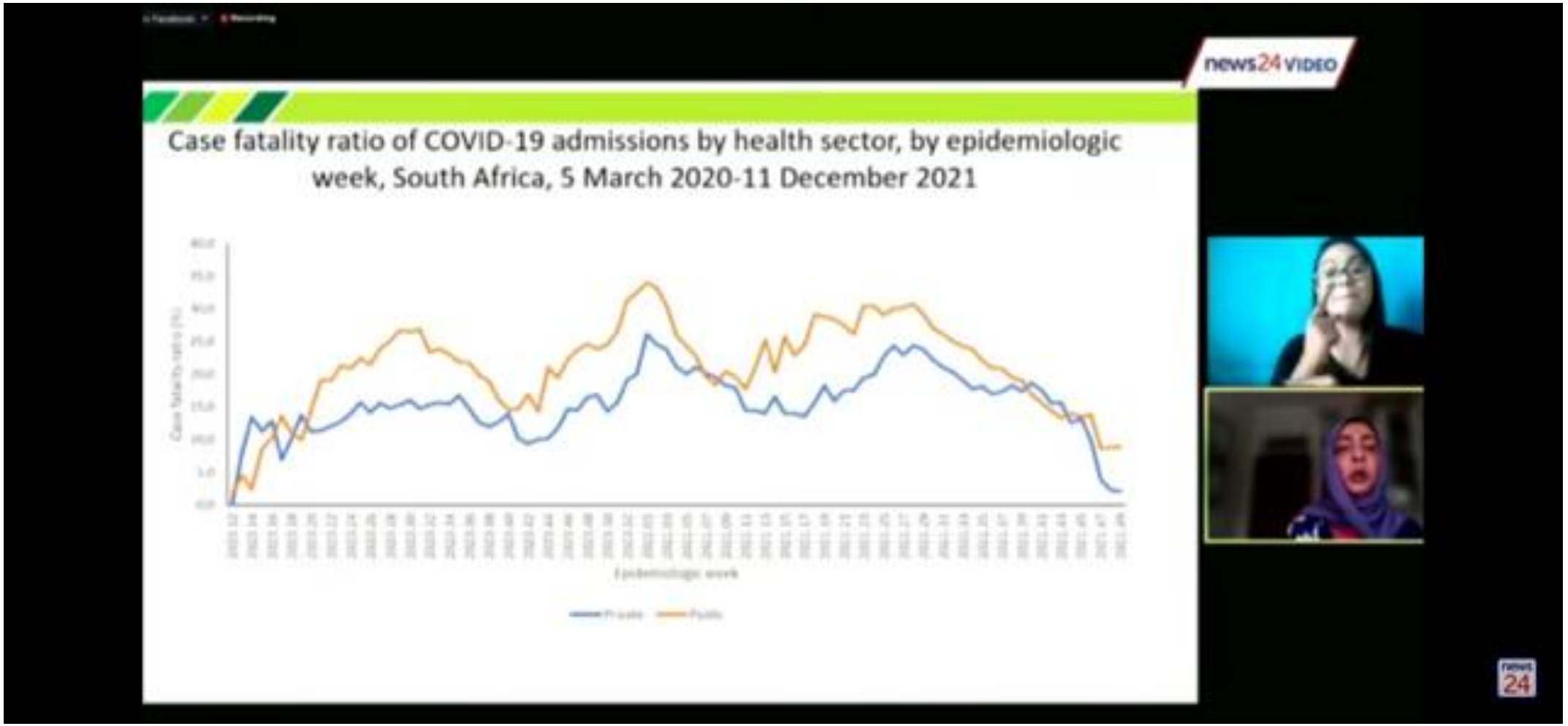


Interventions for currently admitted patients



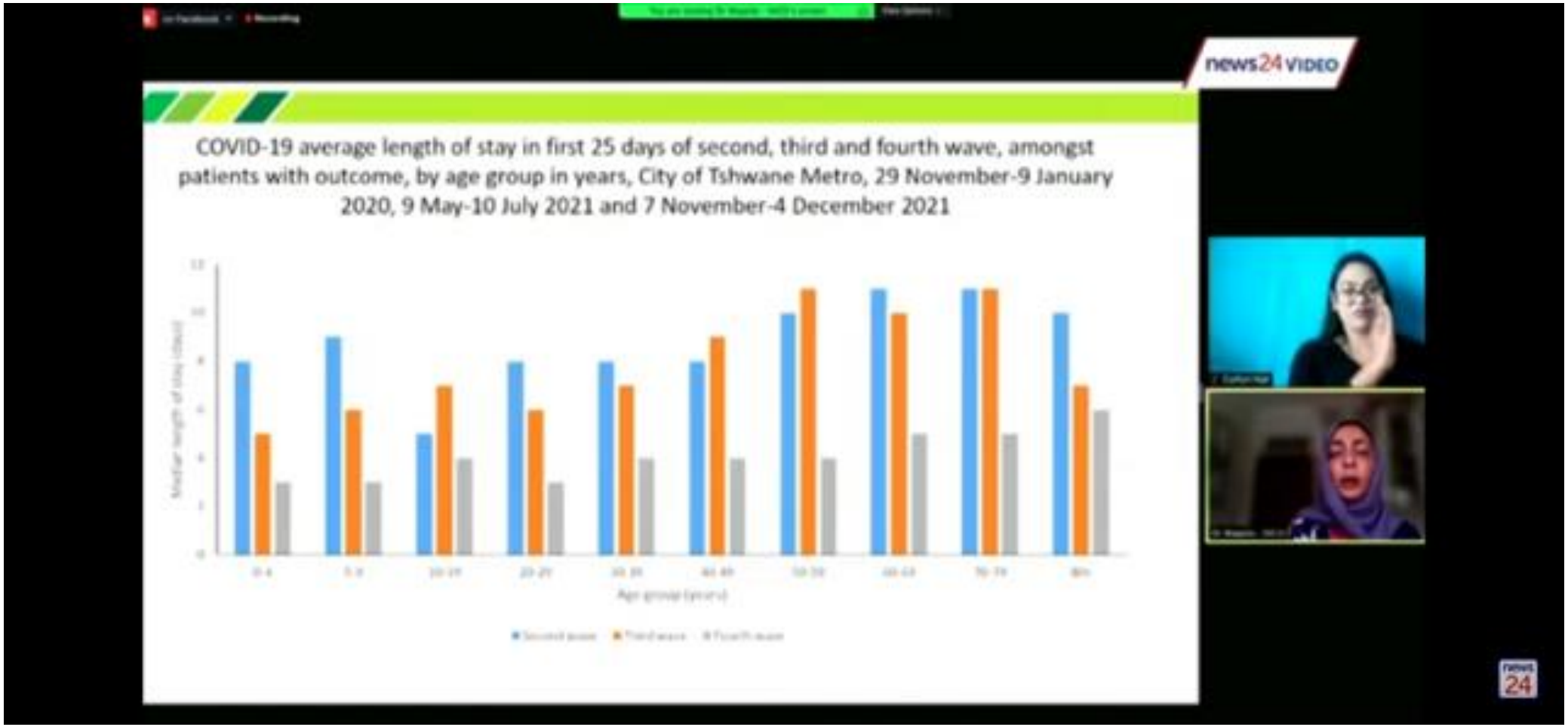
OMICRON SEVERITY

Case fatality ratio for hospital admissions much lower



OMICRON SEVERITY

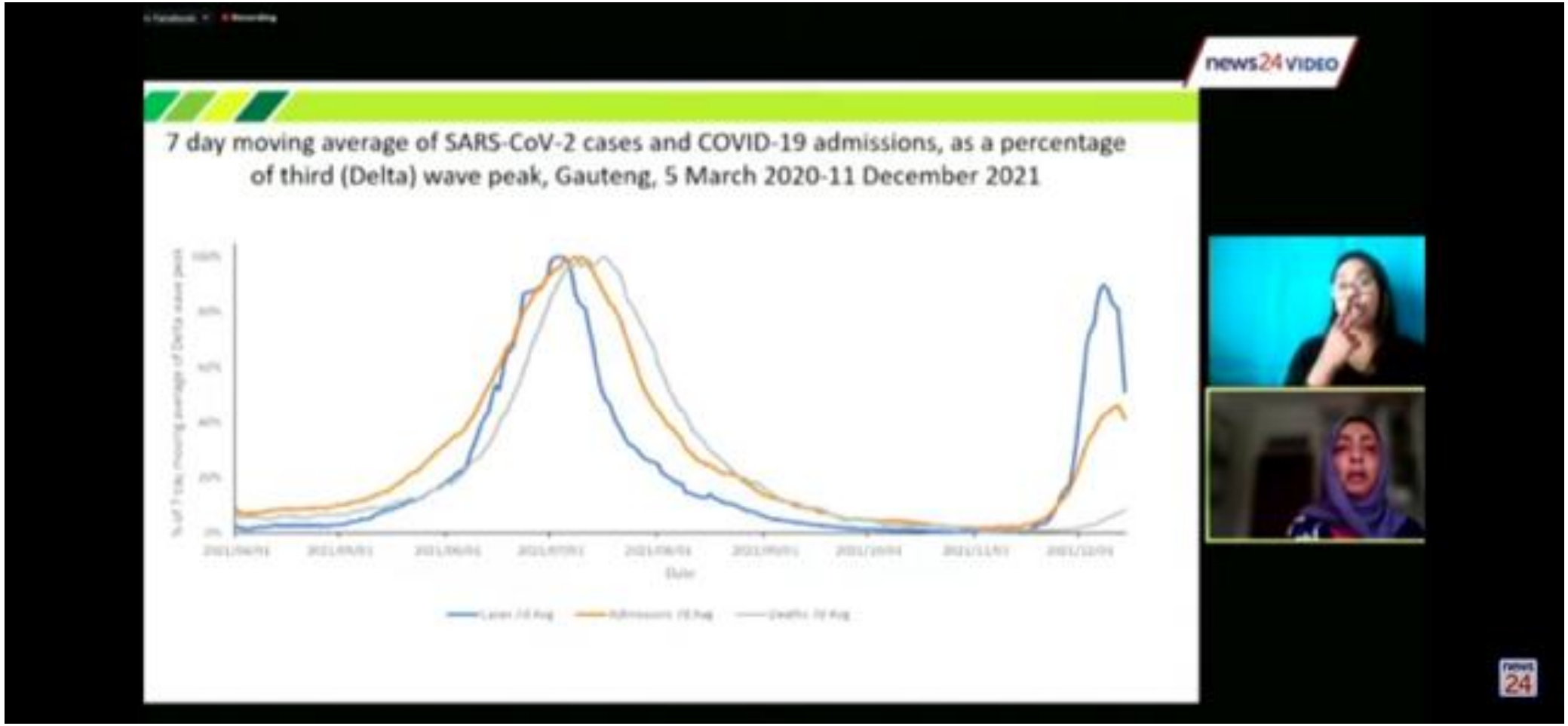
Av length of hospital stay has dropped a lot



OMICRON SEVERITY

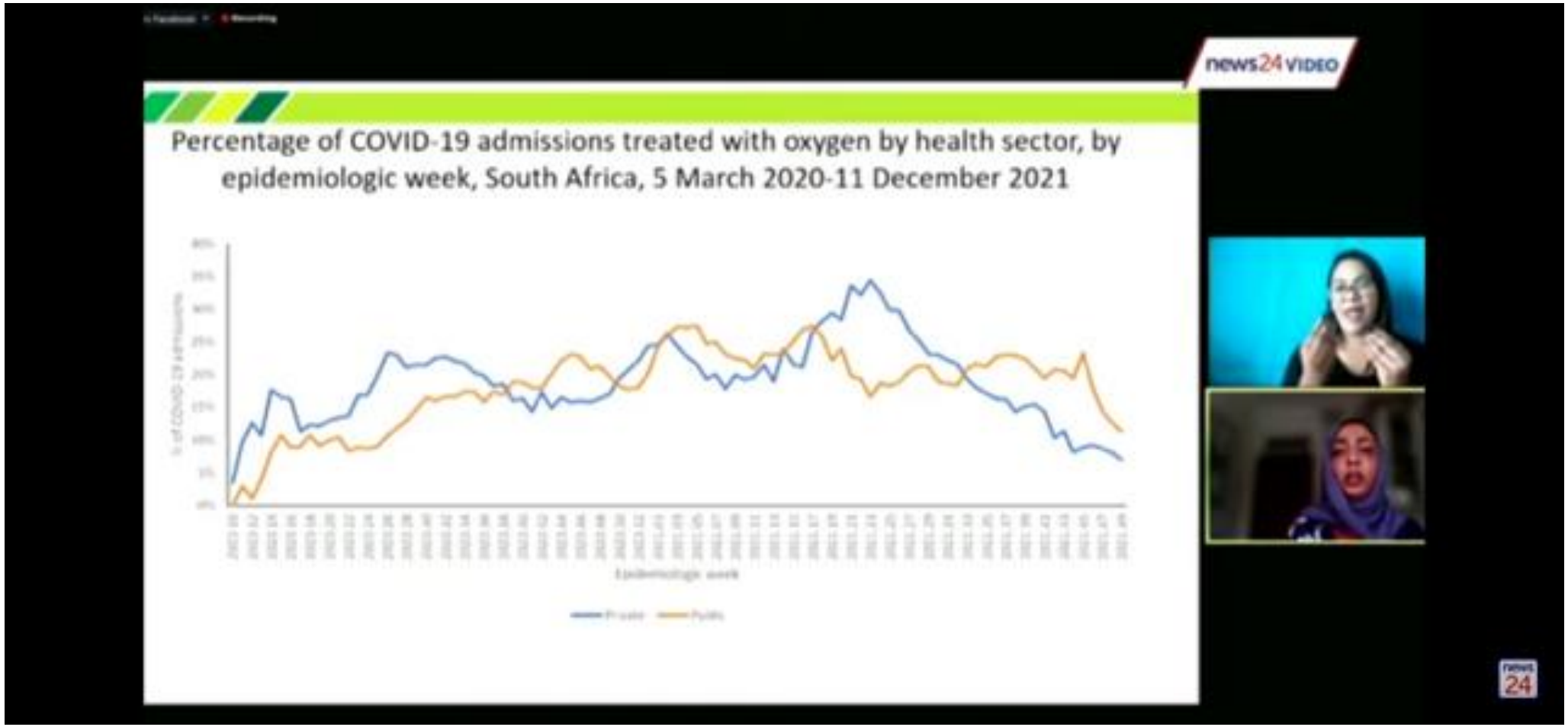
This graph is excellent and shows the % of COVID-19 cases (blue), admissions (orange) and deaths (grey) compared to the 3rd wave Delta peak (100%) as a 7 day moving average.

The uncoupling is striking here – deaths are just so much lower than previous.



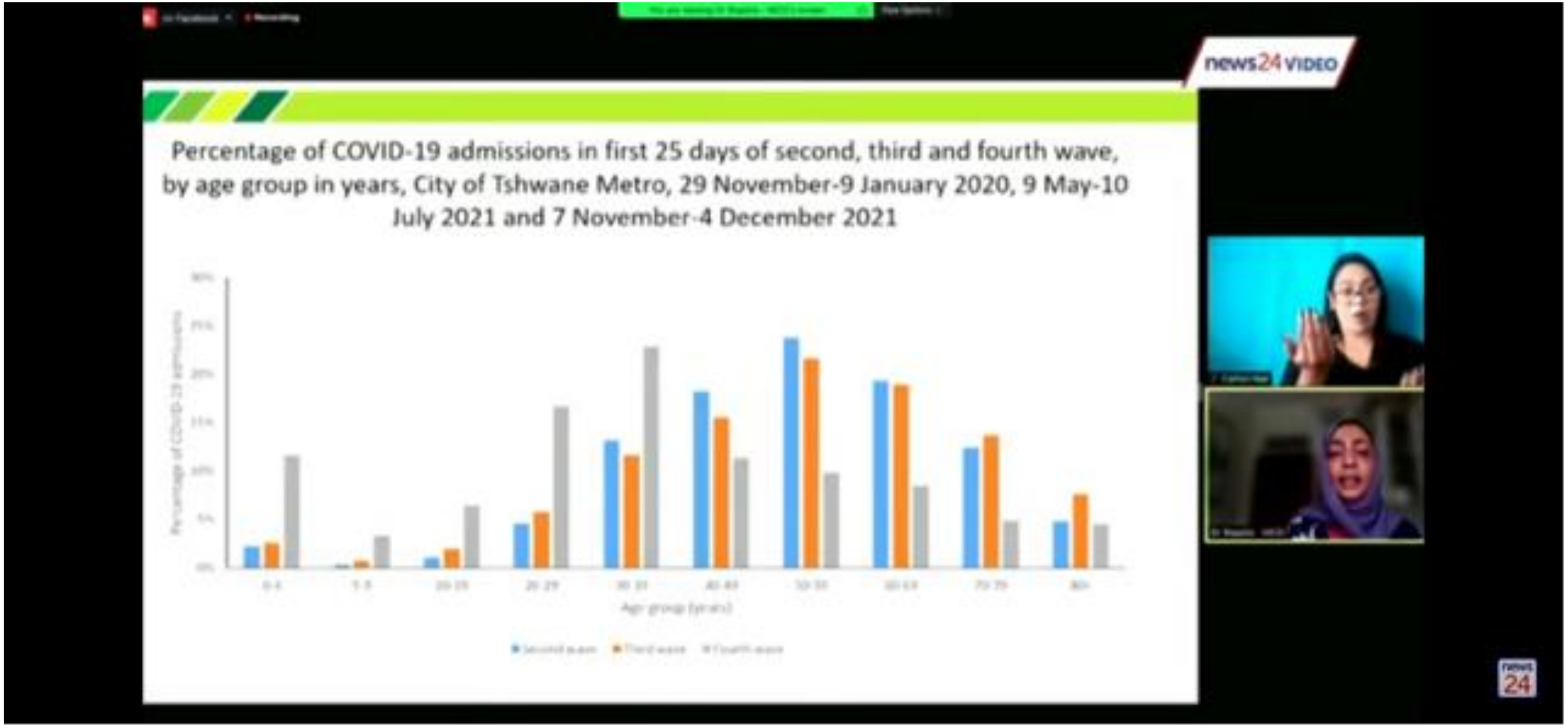
OMICRON SEVERITY

Oxygen use has dropped for hospital admissions

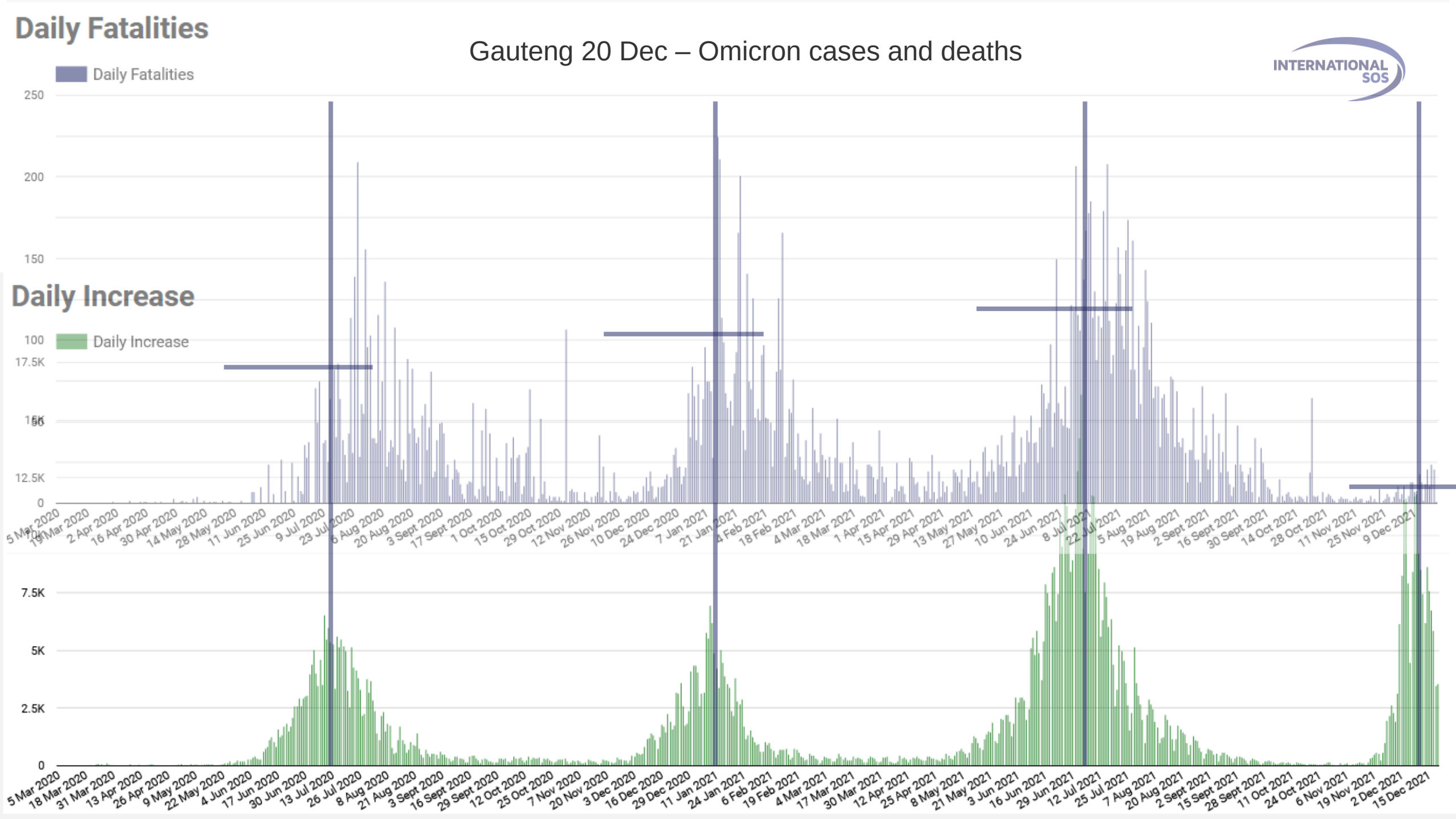


OMICRON SEVERITY

Younger age groups being admitted



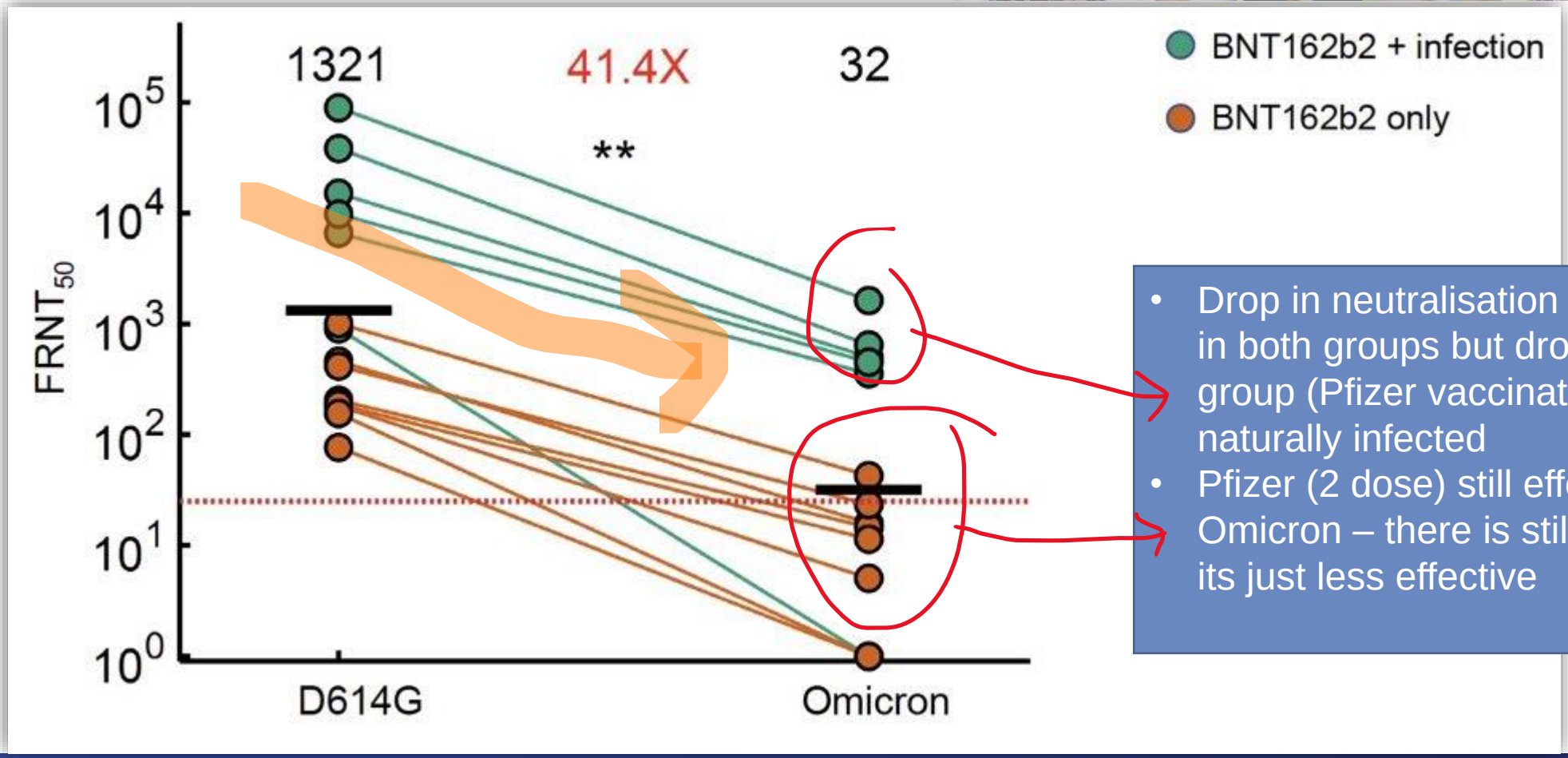
Gauteng 20 Dec – Omicron cases and deaths



NEUTRALISATION RESULTS

Early data from Alex Sigal lab in Durban, South Africa

Sigallab



- Drop in neutralisation of Omicron virus in both groups but drop lower in green group (Pfizer vaccinated (2 dose) and naturally infected
- Pfizer (2 dose) still effective against Omicron – there is still neutralisation – its just less effective

AND FROM GERMANY

Lab from Sandra Ciesek

- Moderna, Pfizer and AZ vaccines
- Boosters work really well to protect from infection
- Remember infection vs hospitalisation – what is being measured?
- These results measures drop in virus neutralisation in a laboratory situation – a better measure of protection from INFECTION
- They do not measure cellular immunity which is highly correlated with protection from hospitalisation
- **Vaccines still work very well to protect against hospitalisation its just they lose some protection against infection with Omicron**

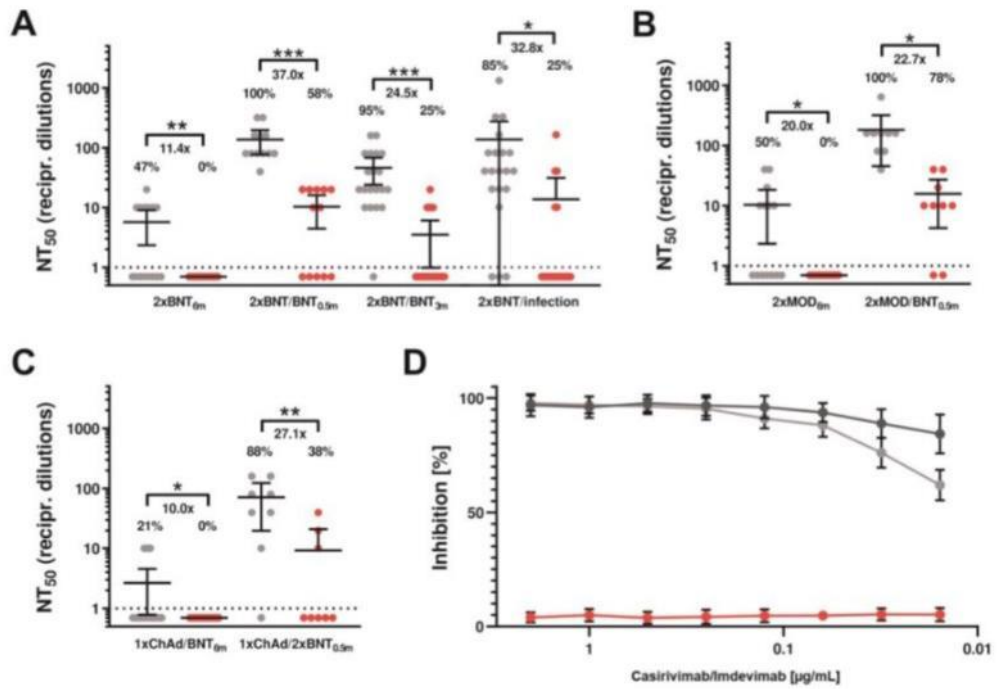


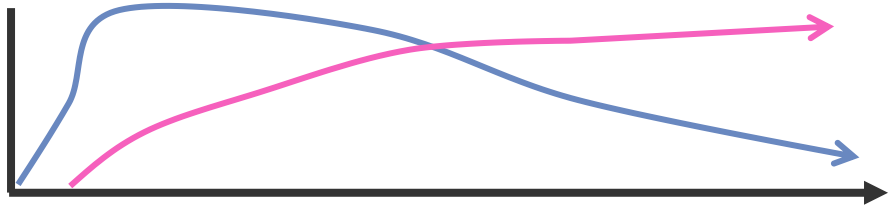
Figure 1 - Antibody-mediated neutralization efficacy against authentic SARS-CoV-2 variants Delta and Omicron. Values represent reciprocal dilutions of SARS-CoV-2 variants Delta (grey) and Omicron (red) micro-neutralization titers resulting in 50% virus neutralization (NT_{50}). **A)** Neutralization assays were performed using serum samples obtained from individuals double BNT162b2 vaccinated (2xBNT). Sera from additionally BNT162b2 boosted individuals were sampled 0.5 month (2xBNT/$BNT_{0.5m}$) or 3 month (2xBNT/BNT_{3m}) as well as sera from double BNT162b2 vaccinated and SARS-CoV-2 infected individuals (2xBNT/infection). **B)** Neutralization assays with sera from double mRNA-1273 vaccinated (2xMOD) and additionally BNT162b2 boosted (2xMOD/$MOD_{0.5m}$). **C)** Neutralization titers for sera from heterologous ChAdOx1 and BNT162b2 vaccinated (1xChAd/1x$BNT_{0.5m}$) and BNT162b2 boosted (1xChAd/2x$BNT_{0.5m}$) individuals. The x-fold reduction was determined using the difference between NT_{50} values for Delta and Omicron. Only Delta neutralizing samples were considered for the calculation. Negative titers were handled as 1. The percentages indicate the relative number of sera that achieved a measurable titer. Information regarding the sera donors (sex, age, antibody titers test and sampling dates) are summarized in in the Supplementary Appendix. **D)** Neutralization efficacy of monoclonal antibodies imdevimab and casirivimab against SARS-CoV-2 Omicron (red), B (dark grey), and Delta (grey). The indicated concentrations of mAbs casirivimab and imdevimab were applied in a 1:1 ratio. Mean values of two technical replicates per sample are depicted with 95% confidence intervals and SD. All experiments were verified using a second SARS-CoV-2 strain (Supplementary Table 4). Statistical significance compared to Delta was calculated by two-tailed, paired student's t-tests. Asterisks indicate p-values as * ($p < 0.05$), ** ($p < 0.01$), and *** ($p < 0.001$).

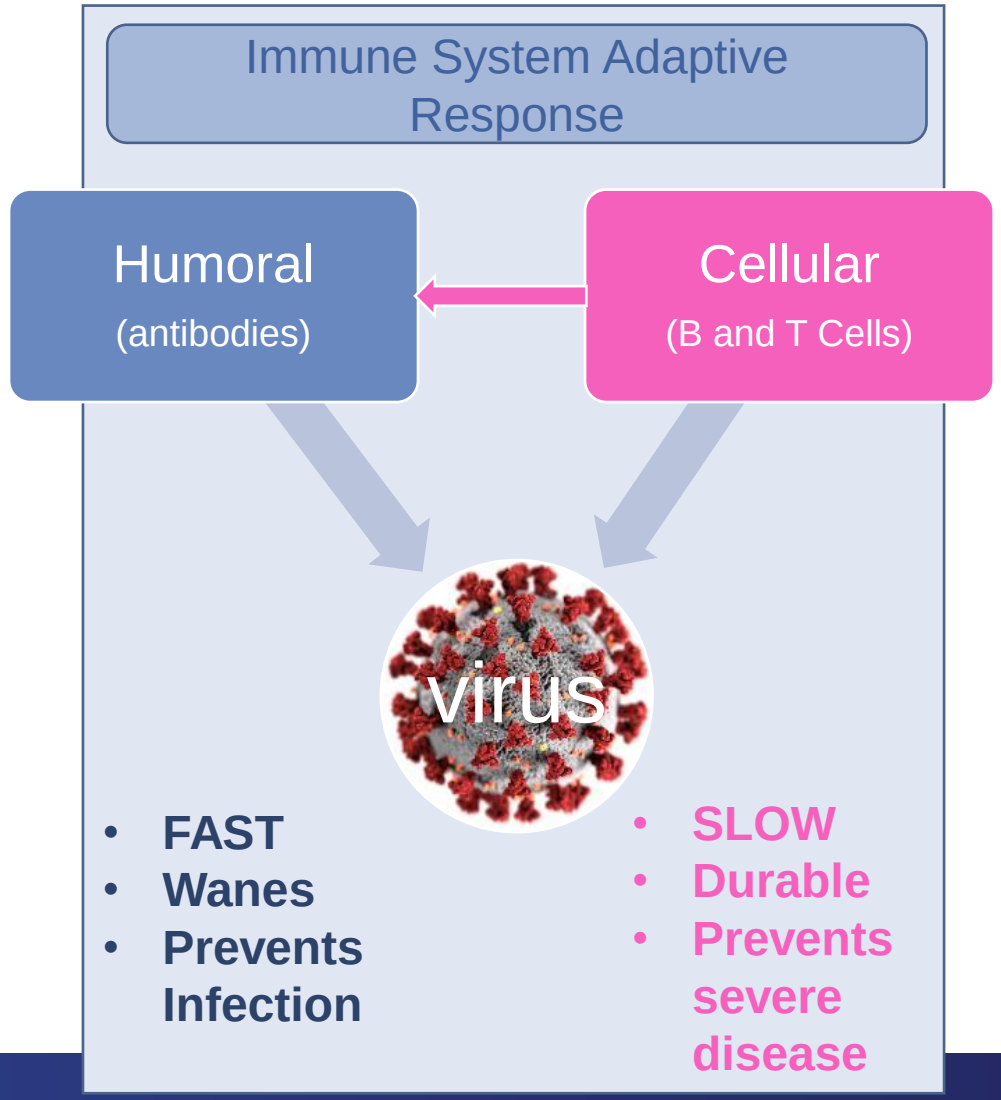
IMMUNITY

Naturally acquired versus vaccine induced immunity

- Antibodies protect against infection
- Immune cells protect against hospitalisation and death
- Naturally acquired immunity tends to be more variable
- Vaccine induced immunity is more predictable
- Best protection is vaccination on top of naturally acquired infection

- Note: when I talk about “vaccines” I am referring to Pfizer, Moderna, AZ and J&J vaccines only as the data for the Russian and Chinese developed vaccines is less transparent





IMPLICATIONS FOR BUSINESS

Explosive spread but milder disease

1. It will spread rapidly through workforce despite vaccination and prior infection
2. Vaccination will still slow spread and will definitely protect from severe disease
3. Absenteeism rates will climb rapidly (example: 1 – 20/30% in just 2 weeks)
4. Suppliers may declare Force Majeur

Supply chain disruption + absenteeism = business continuity risk

1. Review BCPs and check pinchpoints
2. Secure additional labour if appropriate
3. Set up biobubbles in key teams
4. Communicate early with suppliers and check contracts
5. Review testing and screening programs – antigen tests still work but less sensitive

IMPLICATIONS FOR BUSINESS

Explosive spread but milder disease

1. Vaccine scepticism may increase due to doubts over vaccine effectiveness
2. COVID-19 fatigue leads to less adherence to rules
3. Xmas season leads to large social gatherings

Insufficient vaccination + socialising = superspreader events

1. Vaccine messaging is key and remains tricky – need to be clear and understand science
2. Avoid superspreader events
3. Ventilation is absolutely critical
4. Working from home should be considered
5. Vaccine mandates – consider carefully and how to verify

IMPLICATIONS FOR BUSINESS

Explosive spread but milder disease

1. Countries introduce travel bans
2. Travel bans difficult to predict as largely political decisions devoid of science
3. PCR and antigen testing leads to delay or disruption to travel if test positive
4. Countries may introduce lockdowns

Travel becomes precarious and risk unpredictable

1. Reconsider travel policies – business critical?
2. Check Intl. SOS website and app regularly before travel
3. If worried call the Intl. SOS assistance centre just prior to travel as the situation is so fluid
4. Plan for delays