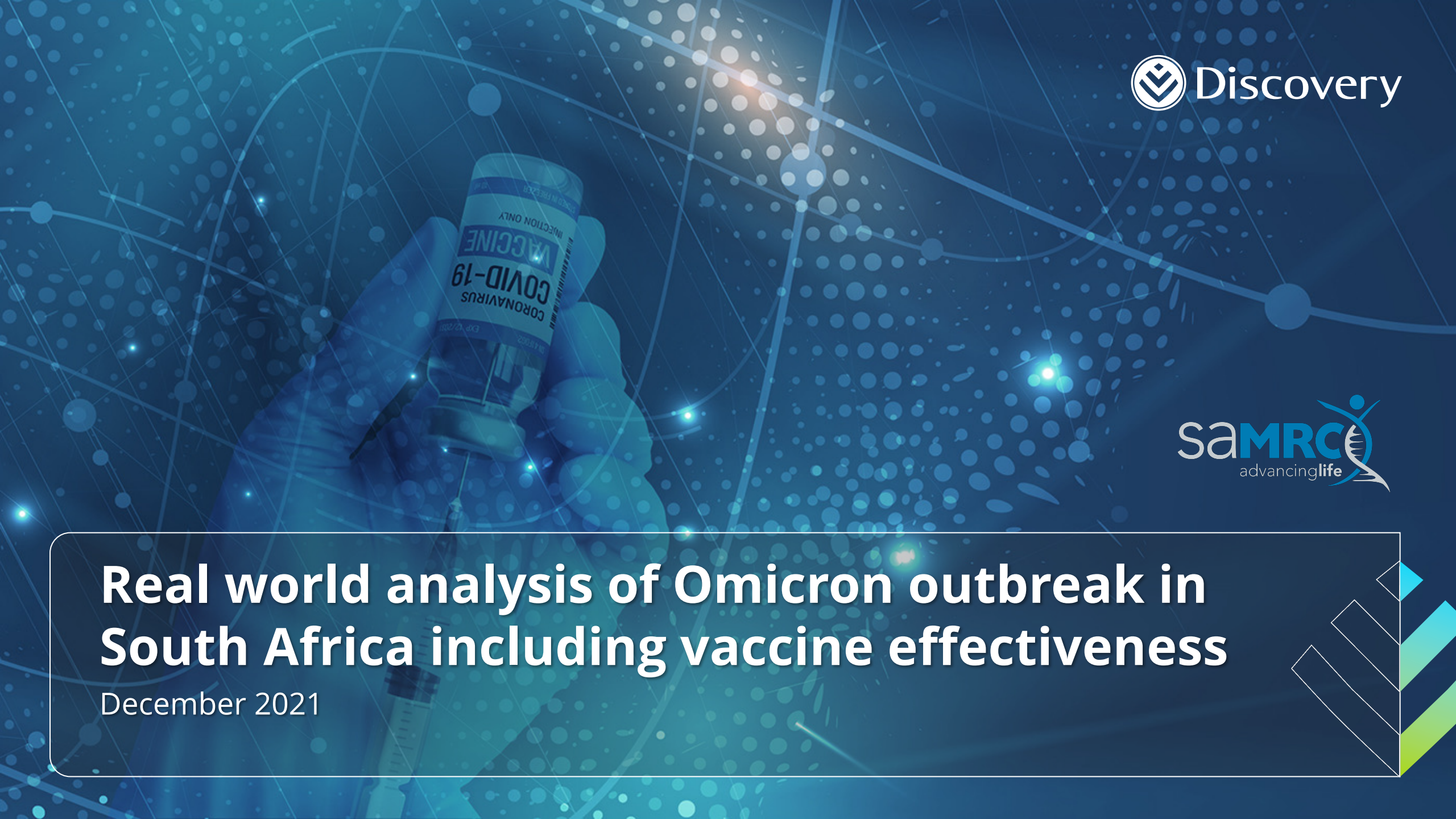


Discovery

saMRC advancinglife

Real world analysis of Omicron outbreak in South Africa including vaccine effectiveness

December 2021

Preface

SA scientists from Network for Genomic Surveillance first to announce the identification of Omicron variant.

SA is first to experience Omicron-driven outbreak commencing about 3 weeks ago.

Discovery Health has continuously shared data throughout the pandemic.

Discovery Health is in an unusual position to avail early insights given the dominance of the Omicron variant in SA, and the availability of member data spanning demographic details, clinical and pathology records and vaccination records.

The National DoH has created considerable capacity to vaccinate the South African population at scale. The insights herein support the priority of vaccination and the NDoH's existing approval of third dose Pfizer-BioNTech boosters.

Discovery Health's insights have been shared with the SA NDoH, the SA National Institute for Communicable Diseases (NICD), the US CDC, leading SA and UK scientists and others

Dataset is derived for the early period of the Omicron outbreak. Consequently these preliminary insights may change as this Covid-19 wave extends

Panel

Professor Glenda Gray

President and Chief Executive Officer, South African Medical Research Council

Shirley Collie

Chief Health Analytics Actuary, Discovery Health

Dr Ryan Noach

Chief Executive Officer, Discovery Health

Executive summary | Omicron Insights

1. Epidemiological tracking shows steep trajectory of new Covid-19 infections indicating rapid Omicron spread, but with a flatter trajectory of hospital admissions, indicating likely lower severity

2. Anecdotal observations demonstrate nuanced differences in the clinical features of Omicron both out of hospital and in hospital

3. Data indicates that the severity of Omicron is 29% lower than D614G (first) wave of Covid-19 infections in South Africa

4. Vaccine effectiveness of the double dose Pfizer-BioNTech regime:
   - Has reduced from 80% in Delta wave to 33% in Omicron wave against Covid-19 infection; and
   - Has reduced from 93% in Delta wave to 70% in Omicron wave against severe complications of Covid-19 (hospital admission)

5. The protective effect of prior infection has reduced over time, and Omicron has eroded that protective effect further

6. Children experiencing very low test-positivity rate relative to adults, and low Covid-19 admissions in absolute terms, but appear to be at 20% greater risk of hospitalisation during Omicron wave relative to D614G wave

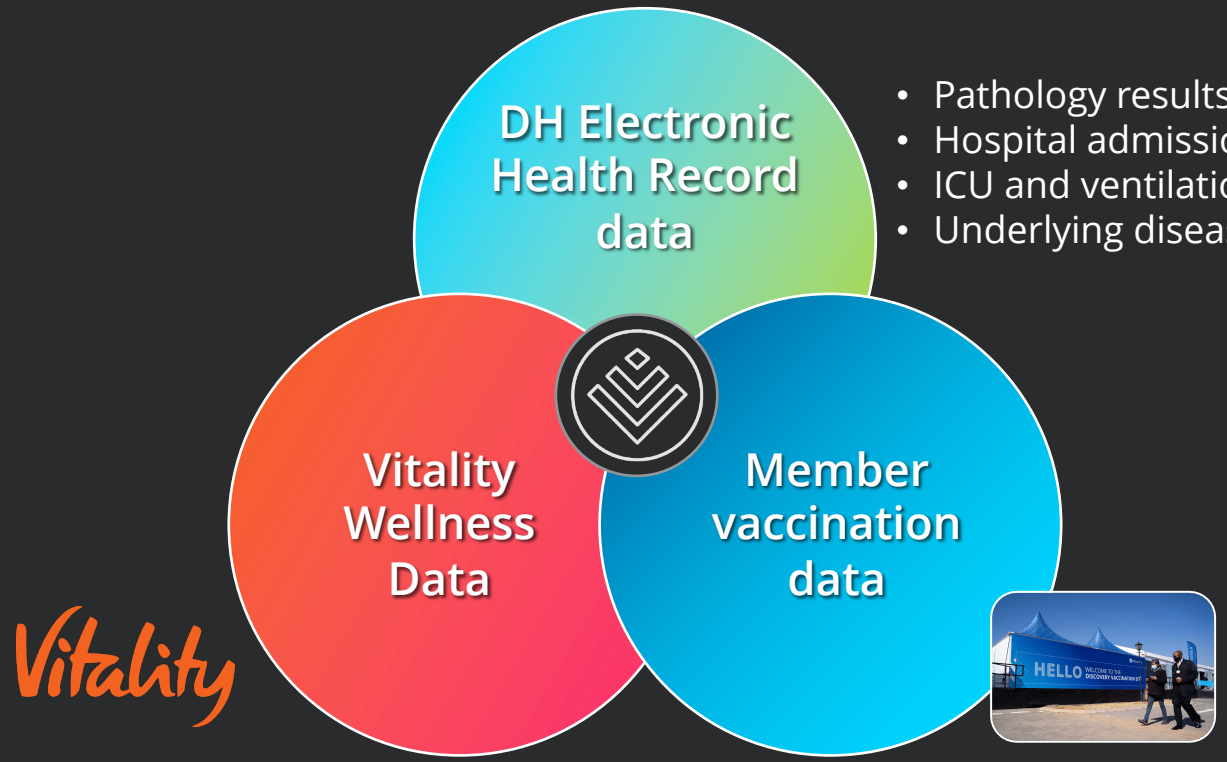
Background

Clinical and epidemiological observations

Real-world insights into vaccine effectiveness

Discovery Health (DH) is uniquely positioned to derive powerful COVID-19 insights

>3.7 million health insurance lives administered by Discovery Health



- Pathology results
- Hospital admissions
- ICU and ventilation
- Underlying disease burden

- Underlying wellness
- Physical activity
- Mobility data

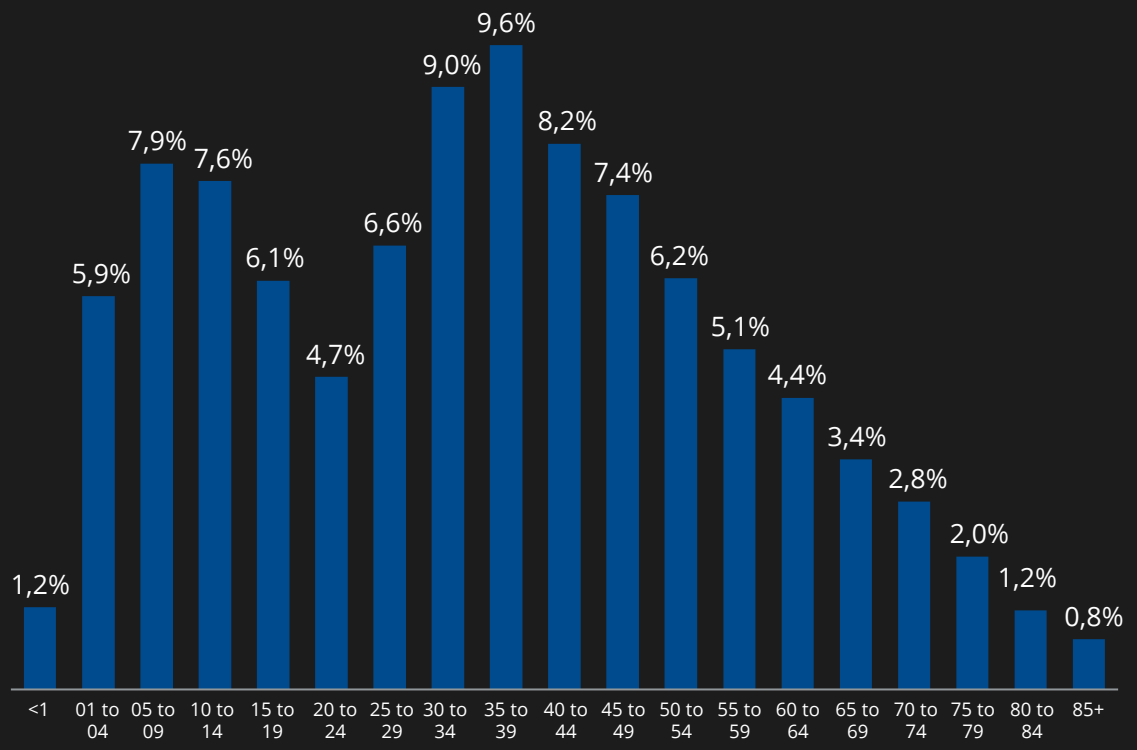
- Vaccination status
- Dose adherence
- Vaccine type

Unique, real-world Covid-19 insights

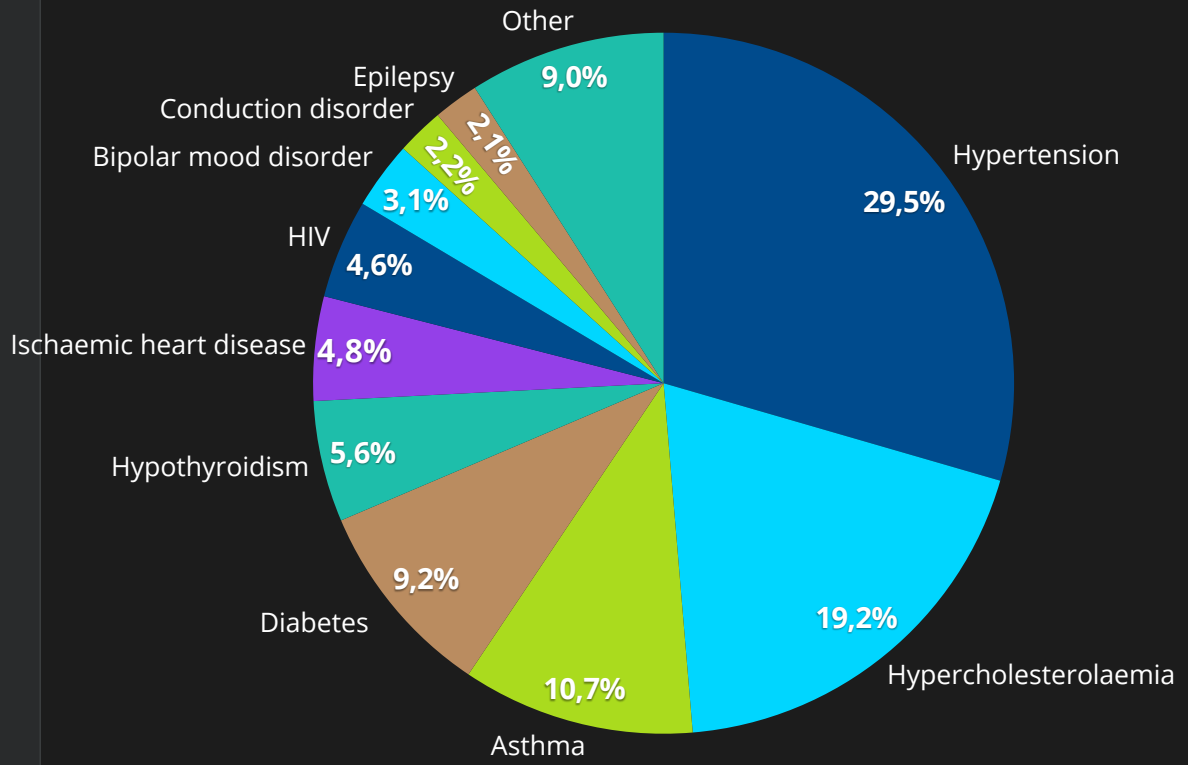
Epidemiological tracking & modelling,, resilience against severe disease, Vaccine effectiveness safety and side effects

Discovery Health beneficiaries are diverse, allowing for relevant real world insights to be derived

Data distributed widely across age groups



26% of all individuals are living with chronic illness



Source: Discovery Health Analysis

Discovery Health has extensive South Africa-specific, real-world data

10 Dec 2021

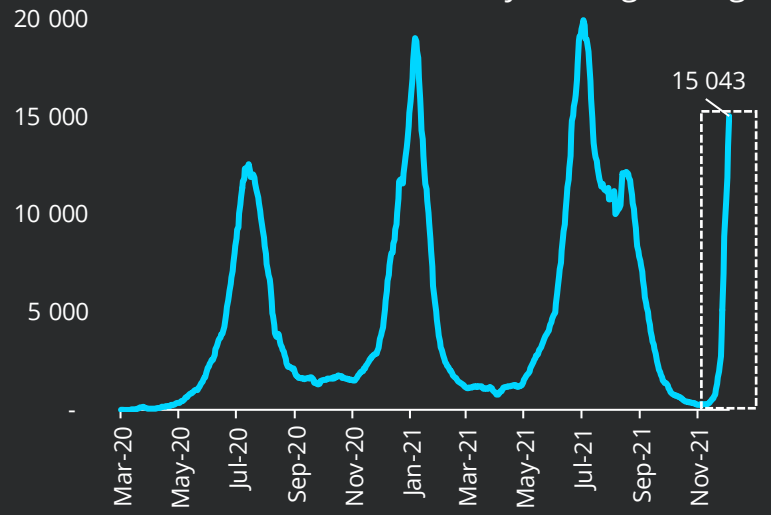
We have been tracking and codifying unique member data since the start of the pandemic

	Tests conducted	Positive cases	Active cases	Repeat cases	Recoveries	Members admitted	Deaths	Vaccines administered
DH	2,604,385	467,530	28,415	15,580	424,717	61,579	14,398	2,713,122
SA	19,912,714	3,071,064	113,060		2,867,966		90,038	26,781,642
	65.2% Testing rate	13.3% COVID proportion of DH lives	7.0% % Active	3.41% Proportion of repeat positive	90.0% Recovery rate	13.8% Proportion admitted	3.3% Case fatality rate	62.3% % Adult vaccinated
	39.9% Testing rate	456,225 Unique DH entities				9.0% Proportion readmitted	18.2% Hospital mortality rate	43.8% Proportion administered national

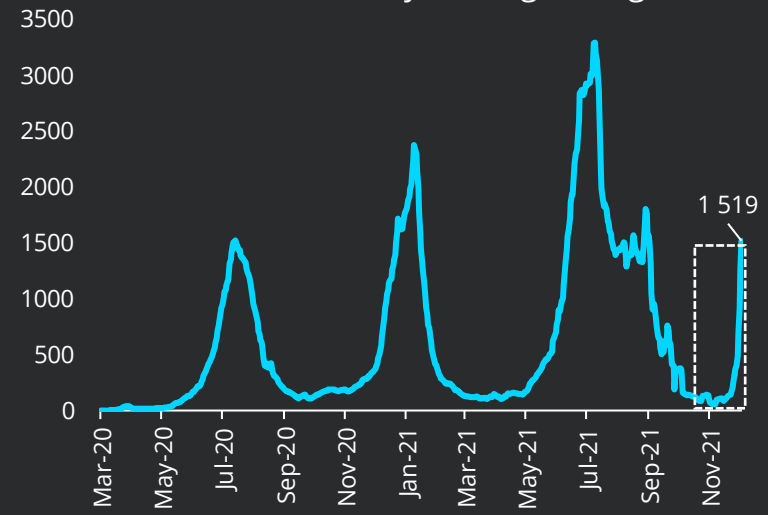
Pfizer vaccine 14 days – 99 days after second dose. Excludes data on members vaccinated in the public sector post September 2021.
Source: Discovery Health Insights https://discv.co/DiscoveryHealthInsights

SA has experienced 3 prior waves of COVID-19 and now entering a fourth wave with rapid rise in cases driven by Omicron variant

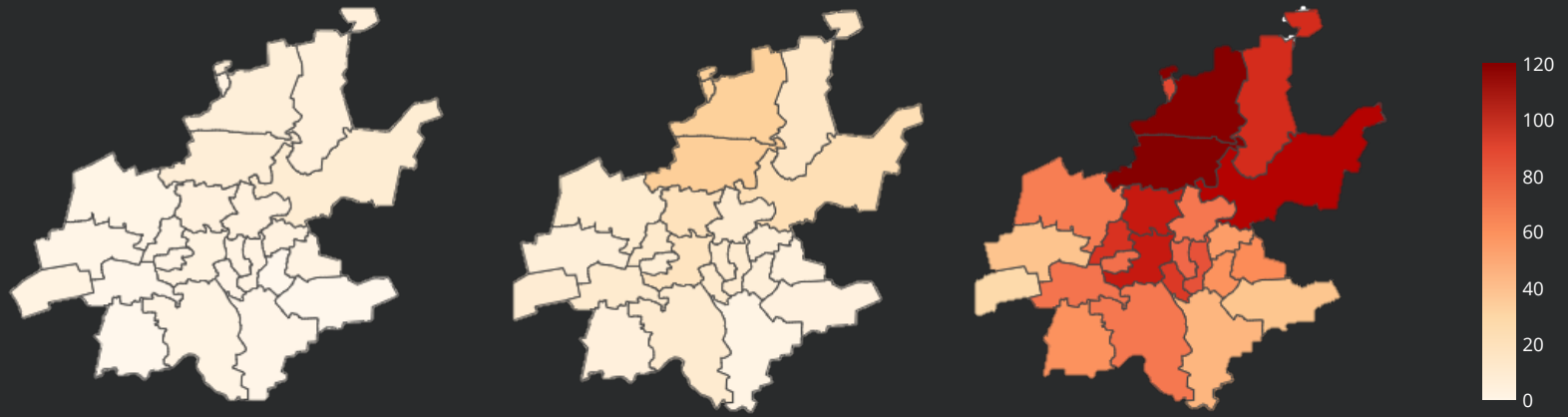
National new cases (7-day moving average)



DH new cases (7-day moving average)



Average weekly new DH cases per 100,000 lives for Gauteng (7-day moving average)



Week ending 20 Nov

Week ending 27 Nov

Week ending 4 Dec

*Gauteng Province accounts for **63%** of current COVID-19 cases nationally, and **67%** of Discovery Health cases in fourth wave*

***26%** of the national population resides in Gauteng Province. Upcoming mobility due to high migrant worker base and holiday period pose a risk of imminent spread to other provinces across South Africa*

Source: NICD, Discovery Health Analysis

Background

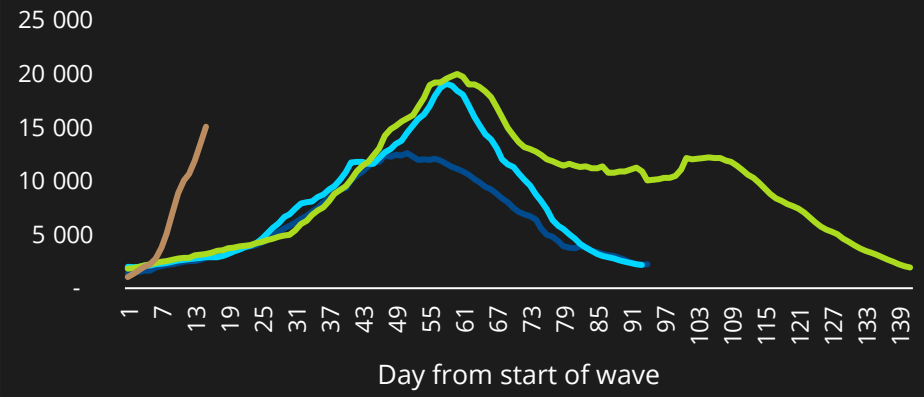
Clinical and epidemiological observations

Real-world insights into vaccine effectiveness

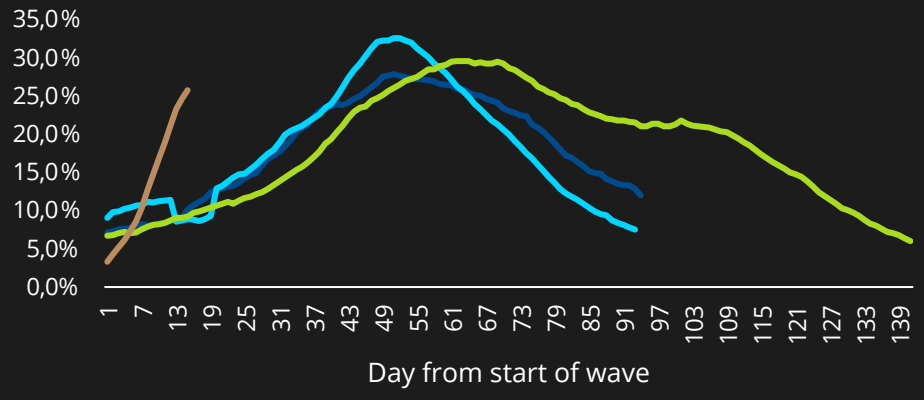
Omicron-driven fourth wave is developing at a steeper trajectory of new infections relative to prior waves

National data

SA daily cases (7-day average) by wave

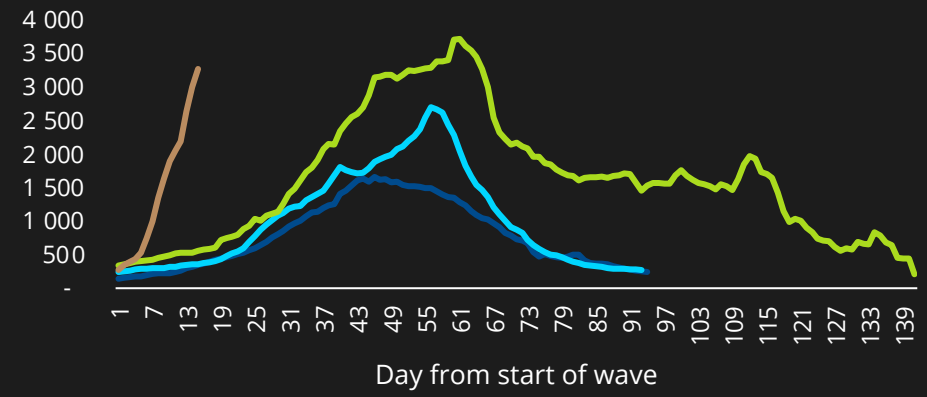


SA weekly test positivity rate by wave

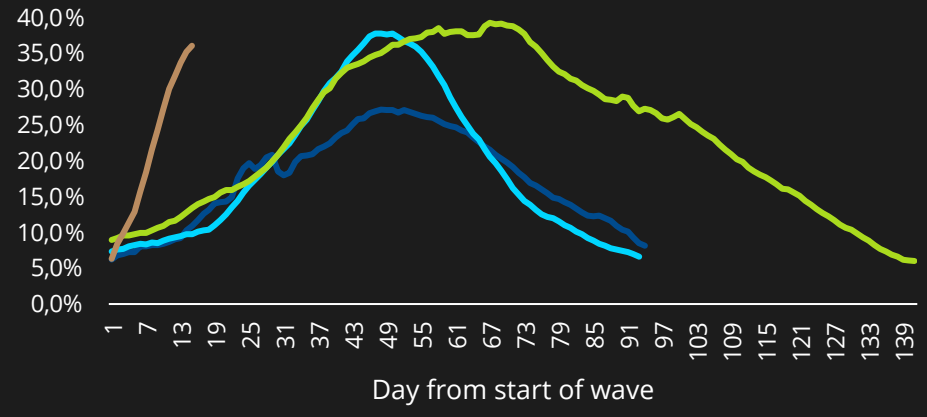


Discovery Health data

DH daily cases (7-day average) by wave



DH weekly test positivity rate by wave



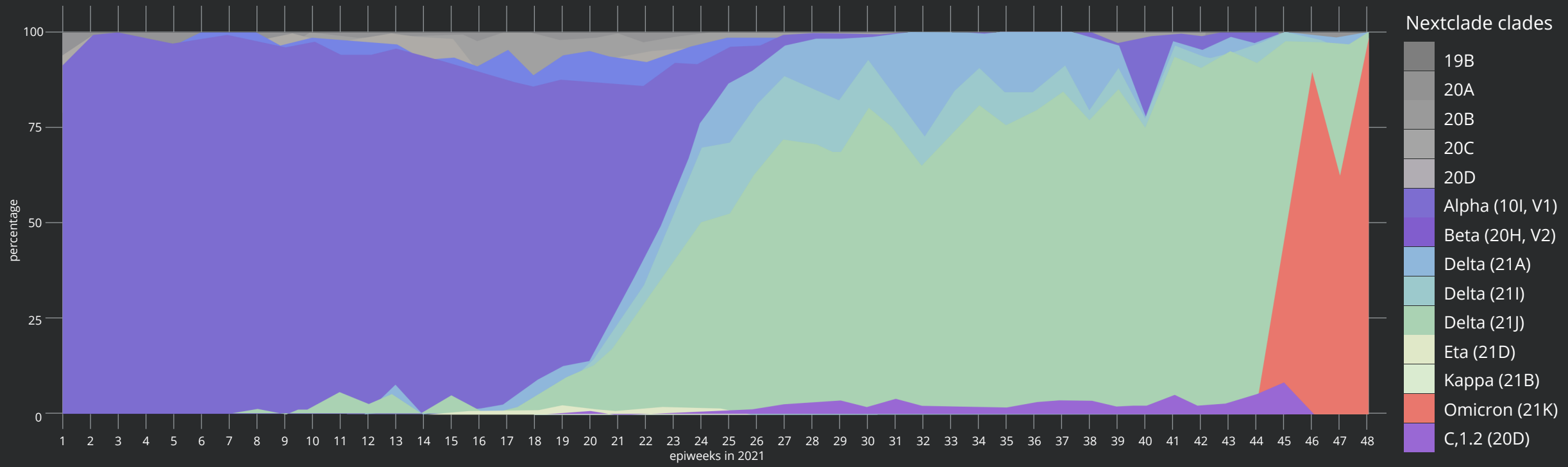
Steeper increase in new infections and test positivity rate during the first three weeks of the fourth wave **indicating highly transmissible variant with rapid community spread**

- D614G wave
- Beta wave
- Delta wave
- Omicron wave

Source: NICD, Discovery Health Analysis

Omicron variant has displaced Delta and now dominates new infections in SA

04 Dec 2021



NGS-SA
Network for Genomic Surveillance in South Africa

- Network of virology and genomic laboratories, scientists and academic institutions across South Africa
- Genomic data produced at five sequencing facilities under the guidance of more than 50 investigators and scientists
- Launched in June 2020 with support of the Department of Science and Innovation and South African Medical Research Council

Source: Network for Genomic Surveillance in South Africa

Anecdotal evidence demonstrates nuanced differences in the clinical presentation

Out-of-hospital acute care

- **Higher reinfections and breakthrough infections** than other waves, including vaccinated
- **Shorter incubation period** of 3-4 days
- **Milder illness** with reported **recoveries within 3 days**
- **Scratchy/sore throat** most common early symptom, like other waves
- Typical features include **nasal congestion, dry cough and myalgia, especially lower back pain**

Admissions

- Most **hospitalised patients** for Covid-19 related disease are **unvaccinated**
- High number of hospitalisations in Gauteng for non-Covid care, present with Covid as an **incidental finding on admission**
- **Less respiratory distress** on presentation
- Proportion of **High care and ICU admissions lower** compared to previous waves
- Significantly lower proportion of admitted patients requiring oxygen support
- Most hypoxic **patients requiring oxygenation are unvaccinated**
- **16% of ICU admissions are vaccinated** (raw data)

Intercare Leaders in Health MEDICLINIC

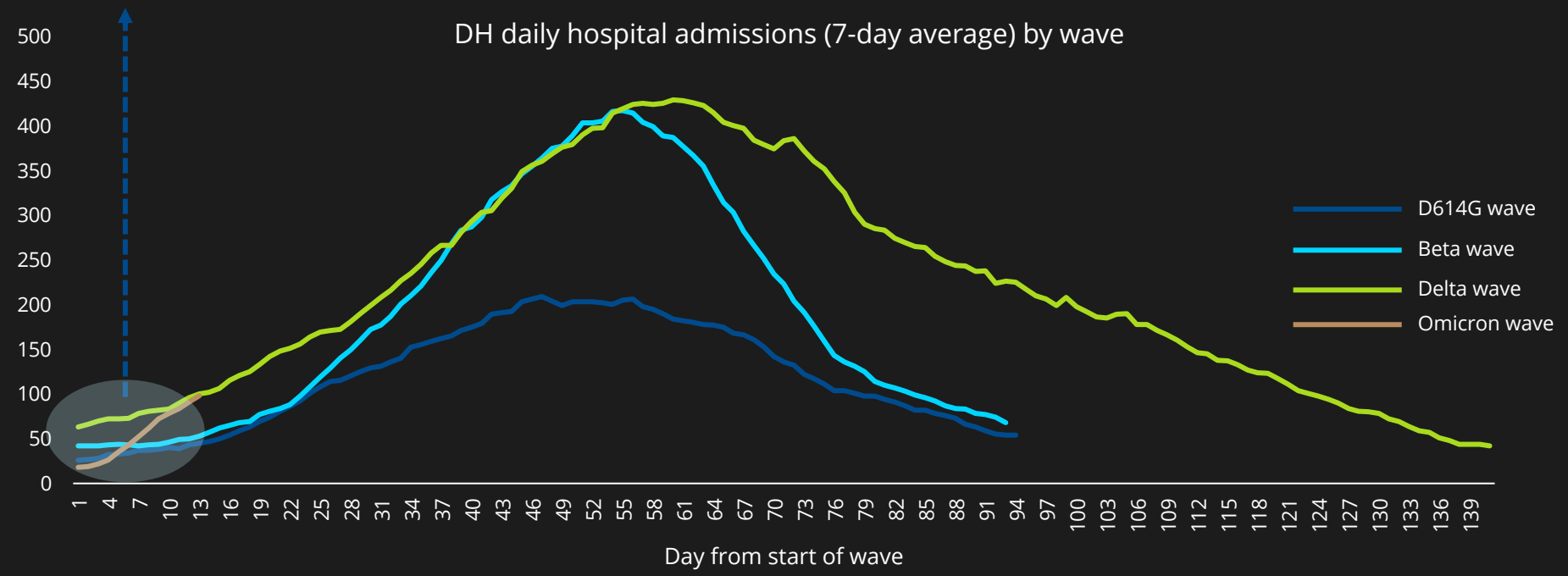
Source: Dr Gerrit De Villiers, Chief Clinical Officer of Mediclinic Southern Africa

Flatter trajectory of hospital admissions, indicating lower severity

Hospital admissions per 1,000 infections

44	131	101	38
D614G	*Beta*	*Delta*	*Omicron*

Hospital admissions by wave at 3 week snapshot



Caveats:

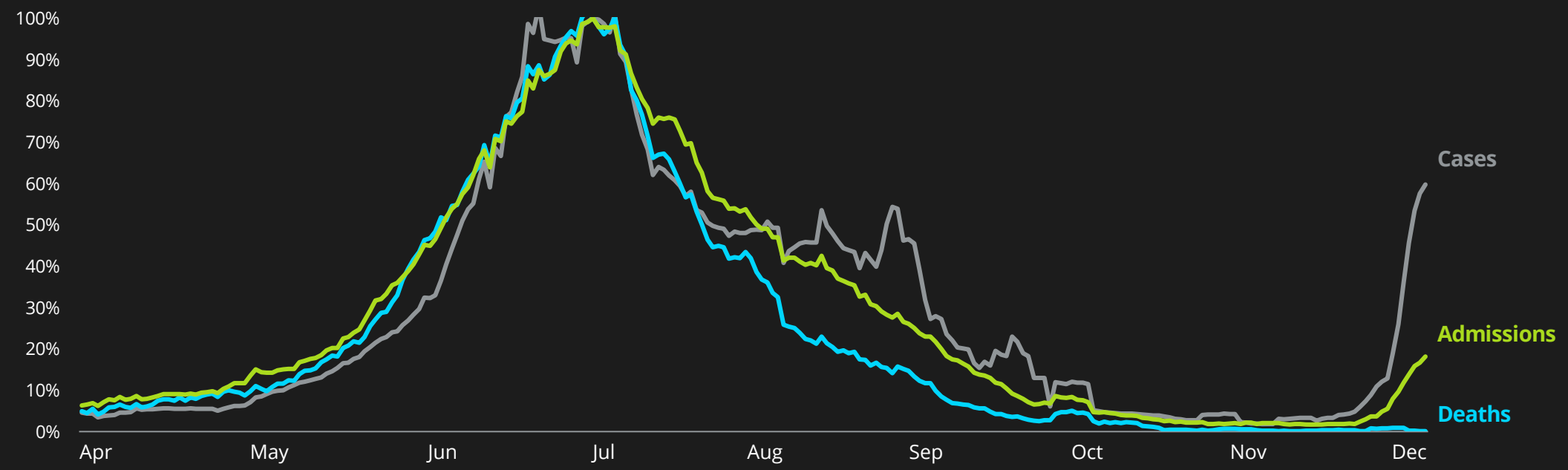
- Underlying Covid-19 antibody seroprevalence in SA population high, especially following Delta wave
- Covid-19 treatment has improved since D614G wave; especially with the introduction of dexamethasone
- Data represents the first 3 weeks of Omicron wave, caution in interpretation of hospital admissions therefore required

Source: Discovery Health Analysis

Apparent de-linking of infection curve from admission curve

Much steeper increase in new cases **during the first three weeks of the Omicron wave** compared to the Delta variant driven third wave. However, **admissions and deaths are not increasing as rapidly.**

Cases, admissions and deaths indexed to the Delta wave, each as a share of Delta peak (%)



Source: Discovery Health Analysis

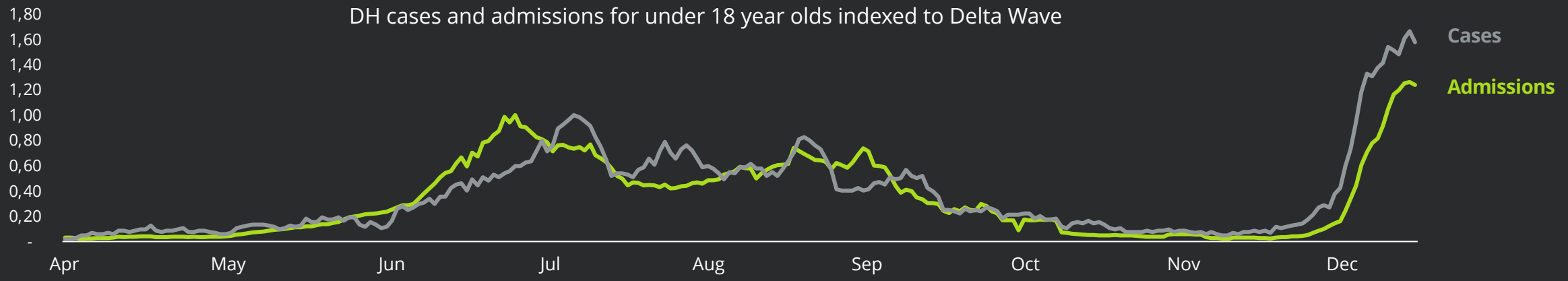
Paediatric cases and admissions appear more prevalent than prior waves, but typically present as mild cases

Paediatric out-of-hospital cases

- **Higher number of paediatric cases** testing positive relative to prior waves
- Children present with a **sore throat, nasal congestion and fever for 2-3 days**, and tend to complain of a headache
- Seems to resolve quickly with **recovery after 3 days**

Paediatric admissions

- Primary diagnoses in children on admission for Covid-19 related disease in Omicron wave are **bronchiolitis and pneumonia**
- Often with associated diarrhoea and vomiting, and dehydration
- Incidental Covid-19 diagnosis for multiple paediatric admissions, exceeding Covid-19 specific admissions

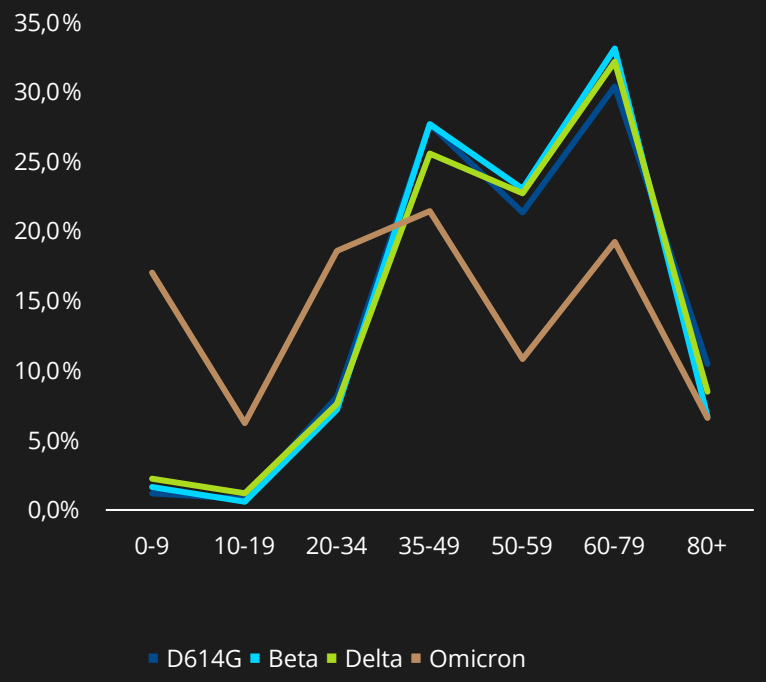


Source: Dr Gerrit De Villiers, Chief Clinical Officer of Mediclinic Southern Africa; Discovery Health Analysis

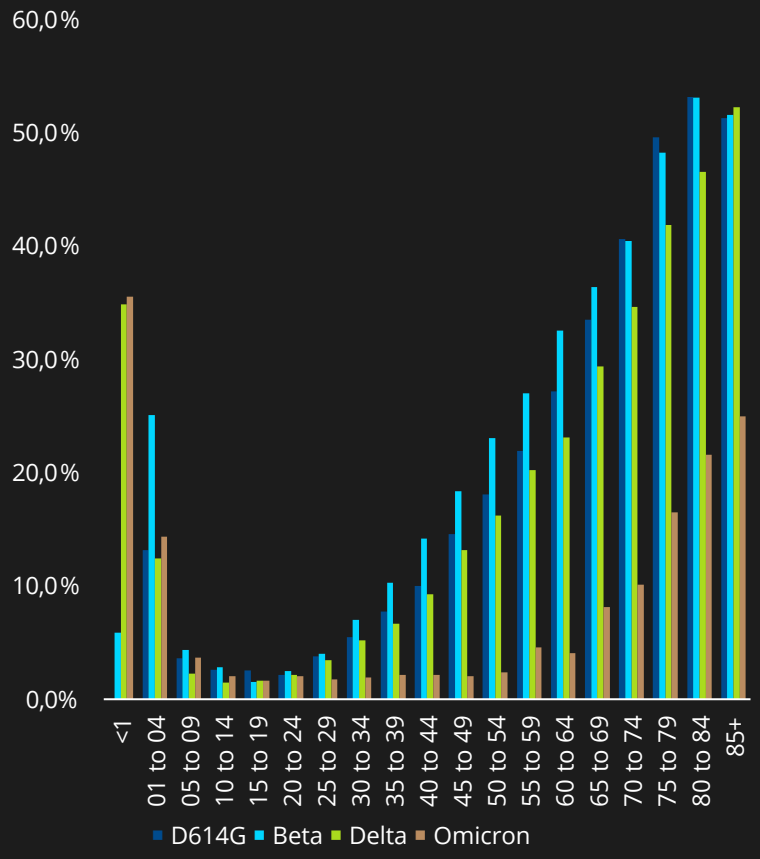
Increase in paediatric admissions, with high number of incidental Covid-19 diagnoses for unrelated admissions

Admission proportion by age band

Increase in proportion of paediatric admissions in the Omicron wave, **possibly driven by incidental Covid-19 diagnosis** on admission

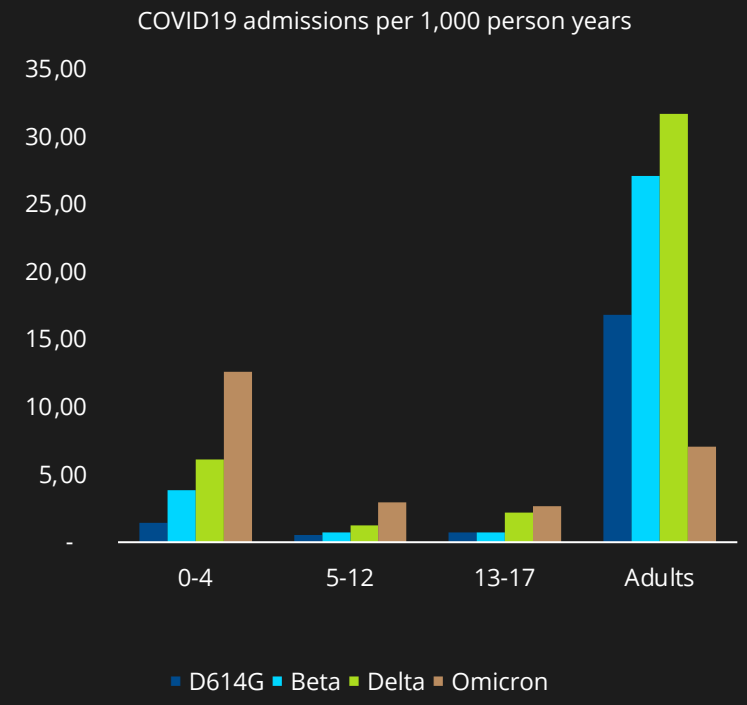


Admission rate by age band



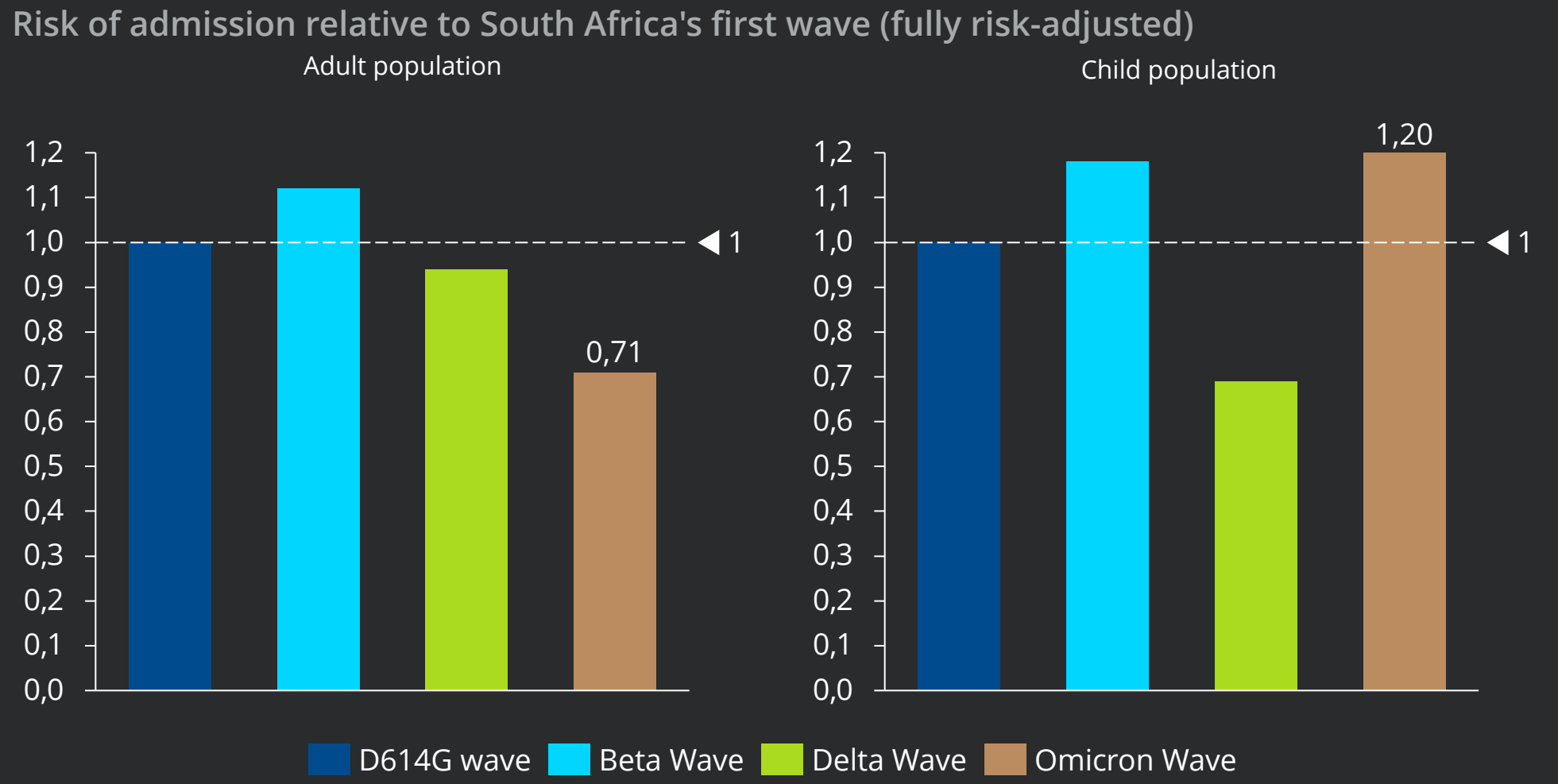
Admission risk by age band

To date, **children under age 5** have experienced **higher admission risk** than adults



Source: Discovery Health Analysis

Risk-adjusted, Omicron may pose risk of increased severity to children under 18 years of age; very early data which should be carefully followed; low risk in absolute terms



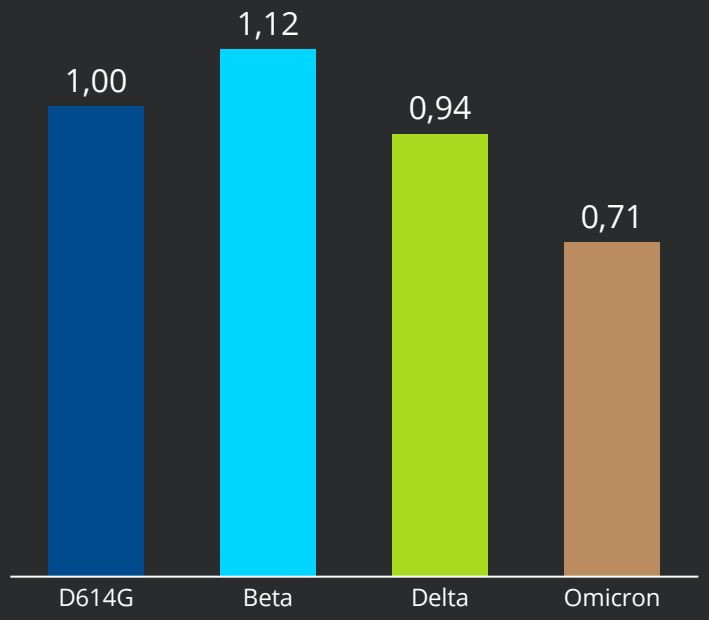
29% average lower admission risk relative to D614G wave. Children, to date, have had a 20% higher risk of admission

Assessed using a Cox proportional hazard model allowing for days since PCR collection date, age, sex, number of documented risk factors, vaccination status and documented prior infection*
To be submitted for peer review and publication
Source: Discovery Health Insights https://discv.co/DiscoveryHealthInsights

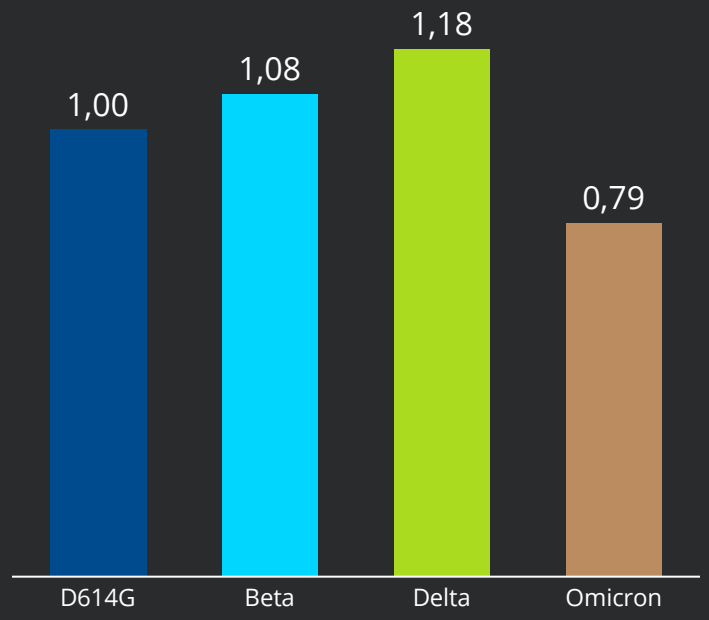
Risk-adjusted data correlates with anecdotal evidence demonstrating lower severity in current Omicron wave than previous waves

Adults are experiencing **29% lower admission risk of Covid-19 admissions** relative to the **D614G** wave. Those who are hospitalised also have a **lower admission acuity** and a **lower propensity to be admitted to ICU**, relative to prior waves

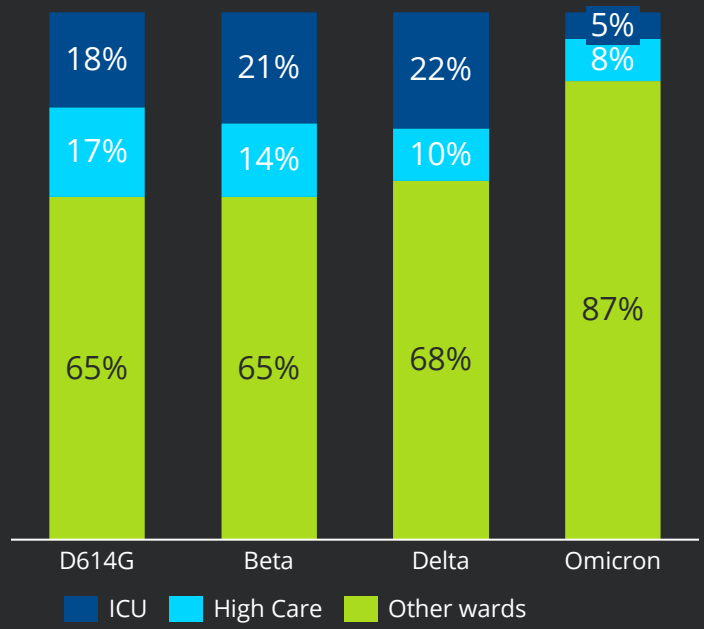
Admission risk indexed to the first wave



Case mix of Covid 19 admissions indexed to the first wave

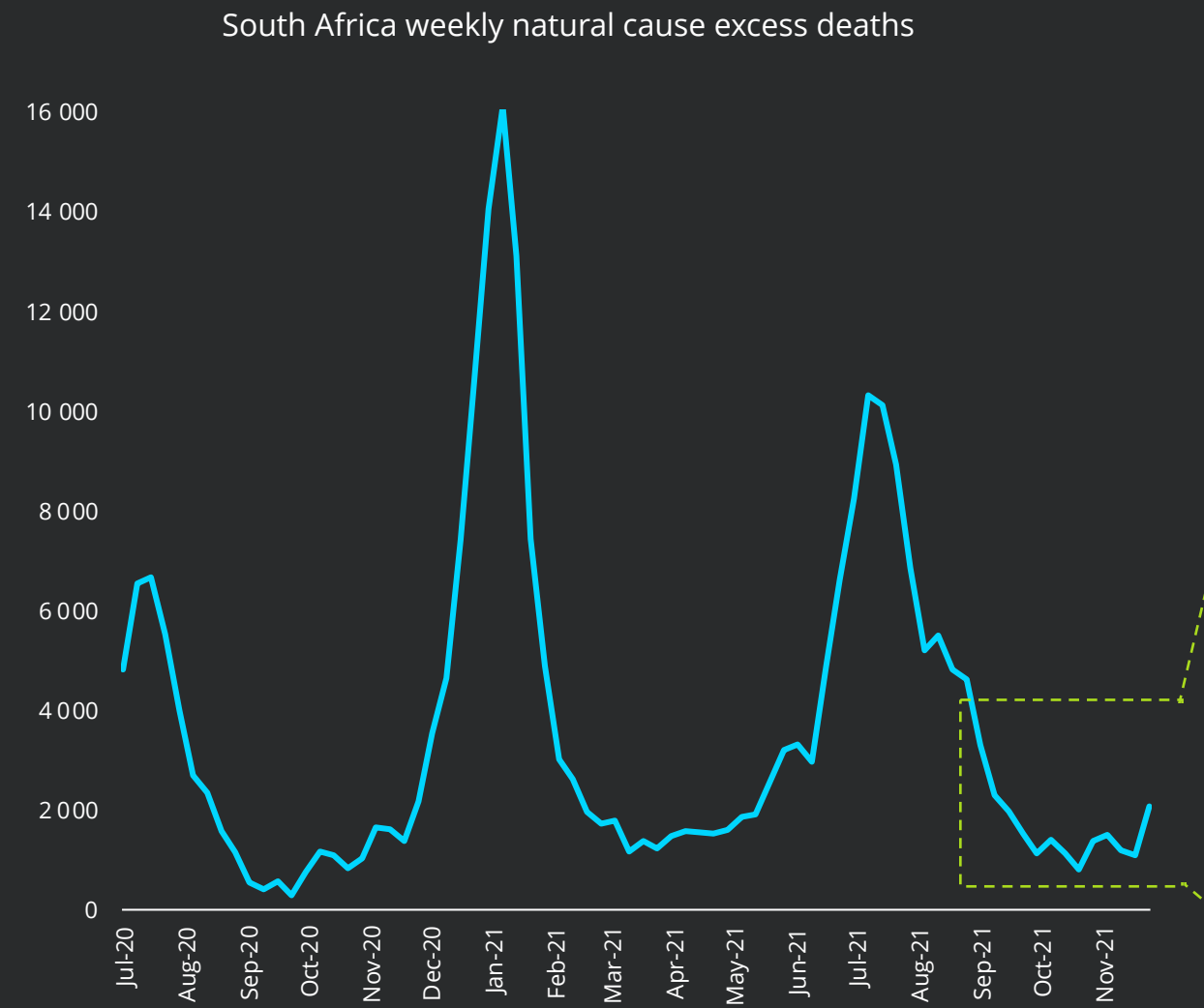


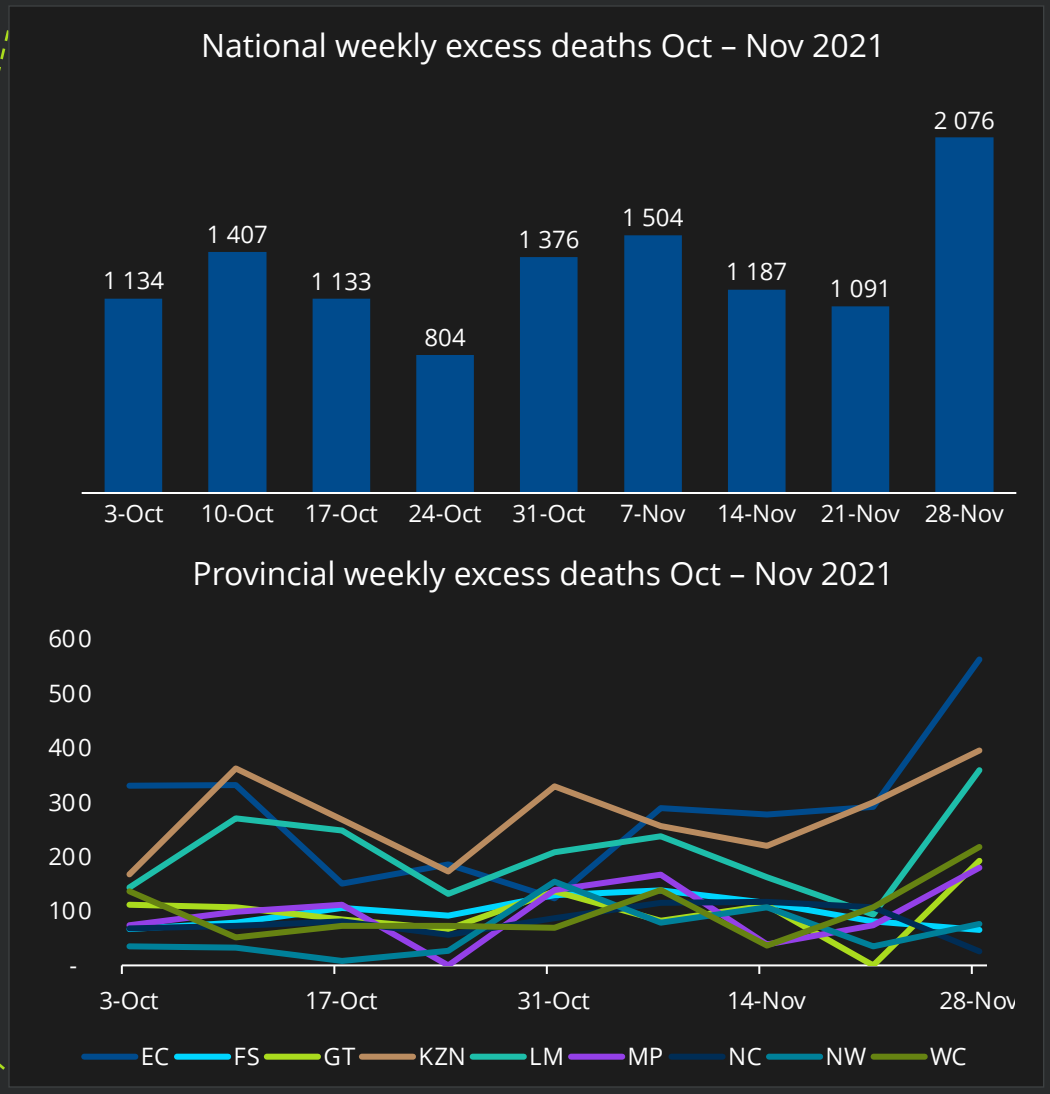
Proportion of admissions in High care and ICU by wave



Assessed using a Cox proportional hazard model allowing for days since PCR collection date, age, sex, number of documented risk factors, vaccination status and documented prior infection*
To be submitted for peer review and publication
Source: Discovery Health Data

Although national excess natural deaths increased in the last week of Nov, excess natural deaths are still significantly lower than previous waves





Source: South African Medical Research Council excess natural deaths report

Background

Clinical and epidemiological observations

Real-world insights into vaccine effectiveness

Rapid timeline of Omicron research following identification by SA scientists; accelerated severity & vaccine effectiveness insights through DH collaboration with SAMRC

Less than 3 weeks

24 November	First report of B.1.1.529 from South African scientists
26 November	WHO designates Omicron a variant of concern
27 November	South African clinicians note mildness of cases relative to prior variants Moderna and Pfizer announce plans for Omicron-specific vaccine
2 December	250% increase in re-infection for Omicron relative to prior variants in South Africa *(Juliet Pulliam et al)*
7 December	4 lab neutralisation studies pre-print published with ~40% reduction in neutralization *(Sigal et al, Ciesek et al, Sheward et al, Pfizer-BioNTech study)*
10 December	First report of clinical vaccine effectiveness for 2 shots and boosters, 3-fold household transmission contact transmission vs Delta *(UKHSA)*
Today	First real world study at scale on Pfizer-BioNTech vaccine effectiveness. Pre-print published by Discovery Health and the South African Medical Research Council

Source: Adapted from Eric Topol twitter, with addition in blue

Omicron vaccine effectiveness study parameters

1 Sep – 7 Dec 2021 study duration

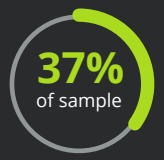
211,610 Covid-19 PCR test results for adult population

Pre-Omicron Period

1 September to 31 October 2021

Proxy Omicron Period

15 November to 7 December 2021



Sensitivity 1

SGTF positive test results from Lancet Laboratories

Sensitivity 2

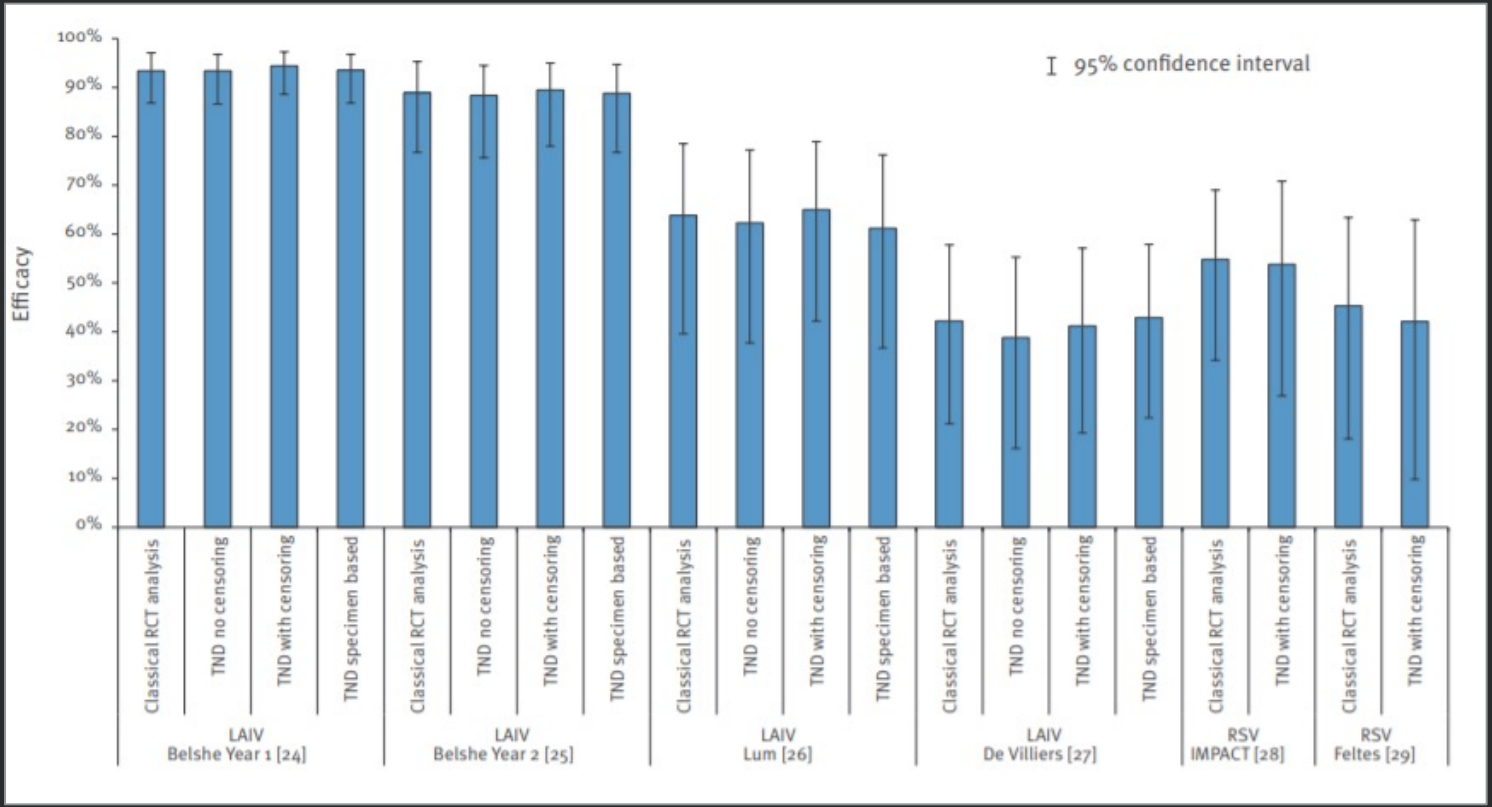
Gauteng PCR tests

Sensitivity 3

PCR test results amongst symptomatic admitted patients

Omicron vaccine effectiveness study methodology: Test negative design

Method used globally on pathology surveillance data to assess annual influenza vaccine effectiveness

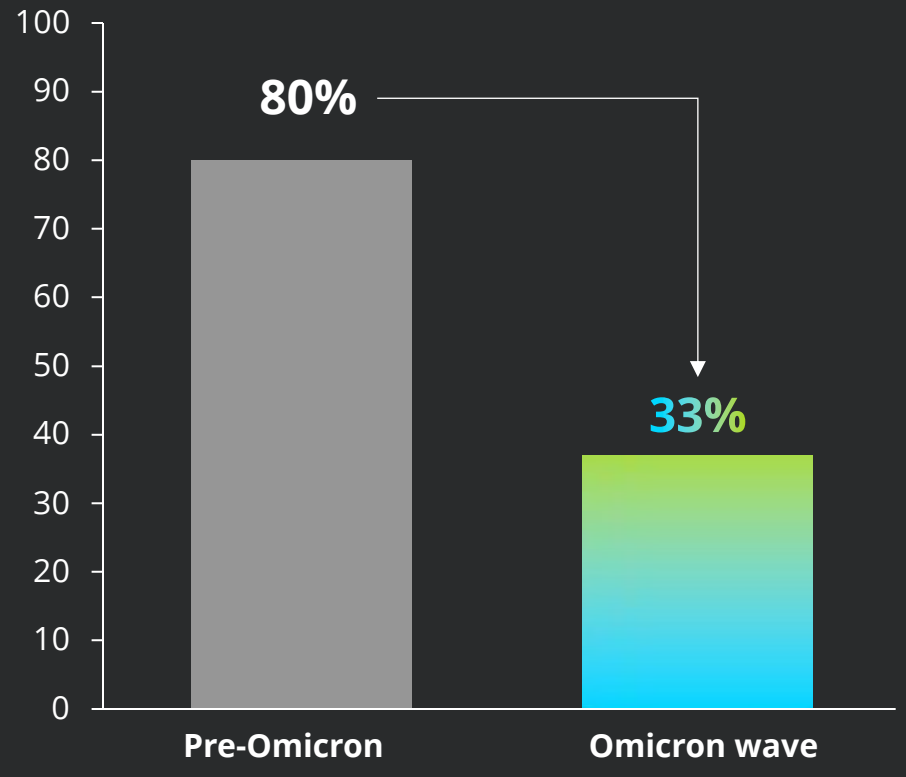


- Method is generalisable to other specific respiratory conditions provided vaccination does not have clinical efficacy for other respiratory conditions
- Methodology implicitly adjusts for biases due to health-seeking behaviour
- Efficacy estimates and associated confidence intervals are consistent with randomized control studies
- A number of publications have used a test-negative design for real world Covid-19 vaccine effectiveness studies

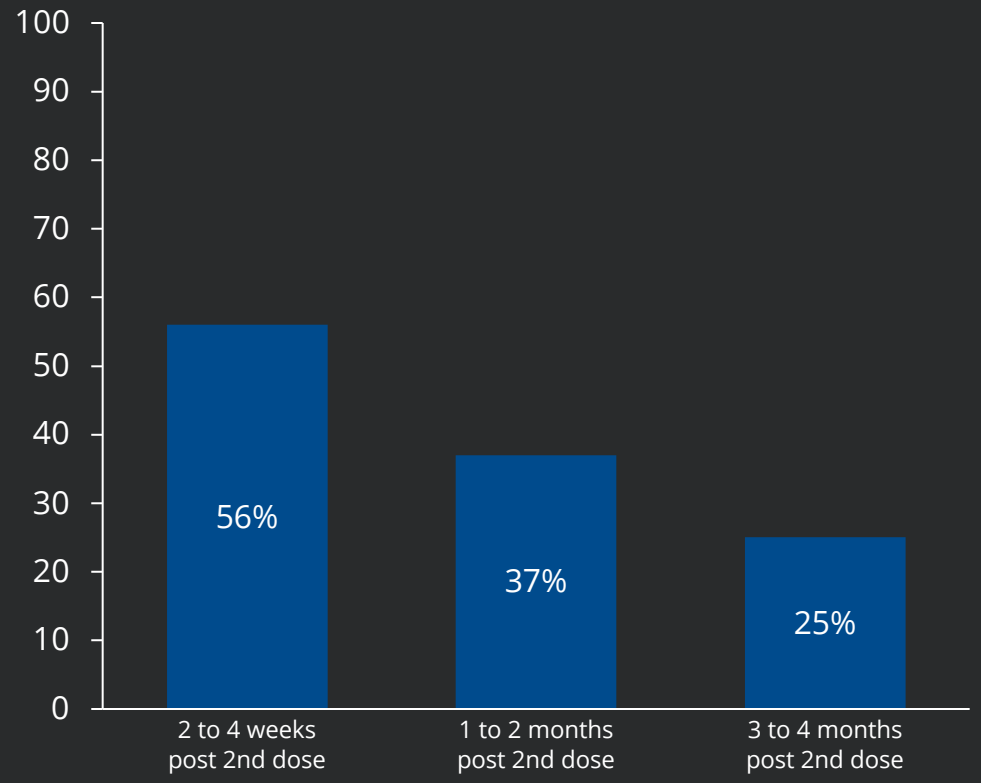
De Serres G, Skowronski DM, Wu XW, Ambrose CS. The test-negative design: validity, accuracy and precision of vaccine efficacy estimates compared to the gold standard of randomised placebo-controlled clinical trials . Euro Surveill. 2013;18(37):pii=2058

Pfizer-BioNTech vaccine 33% effective in reducing Omicron-related infection

Real-world Pfizer vaccine effectiveness against infection



Waning effectiveness against infection over time

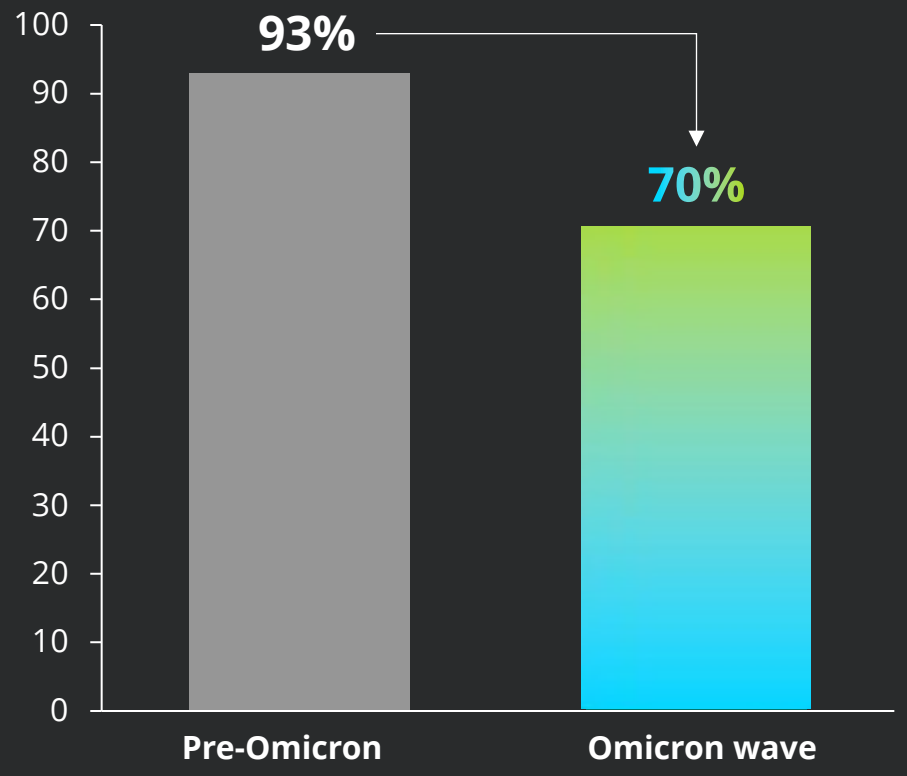


Omicron has materially reduced vaccine effectiveness against new infections, potentially compounded by waning durability

*To be submitted for peer review and publication
Authors have no conflicts of interest direct or in kind
Source: Discovery Health Insights https://discv.co/DiscoveryHealthInsights

Pfizer-BioNTech vaccine 70% effective in reducing Omicron-related hospital admissions

Real-world Pfizer-BioNTech vaccine effectiveness against hospital admission

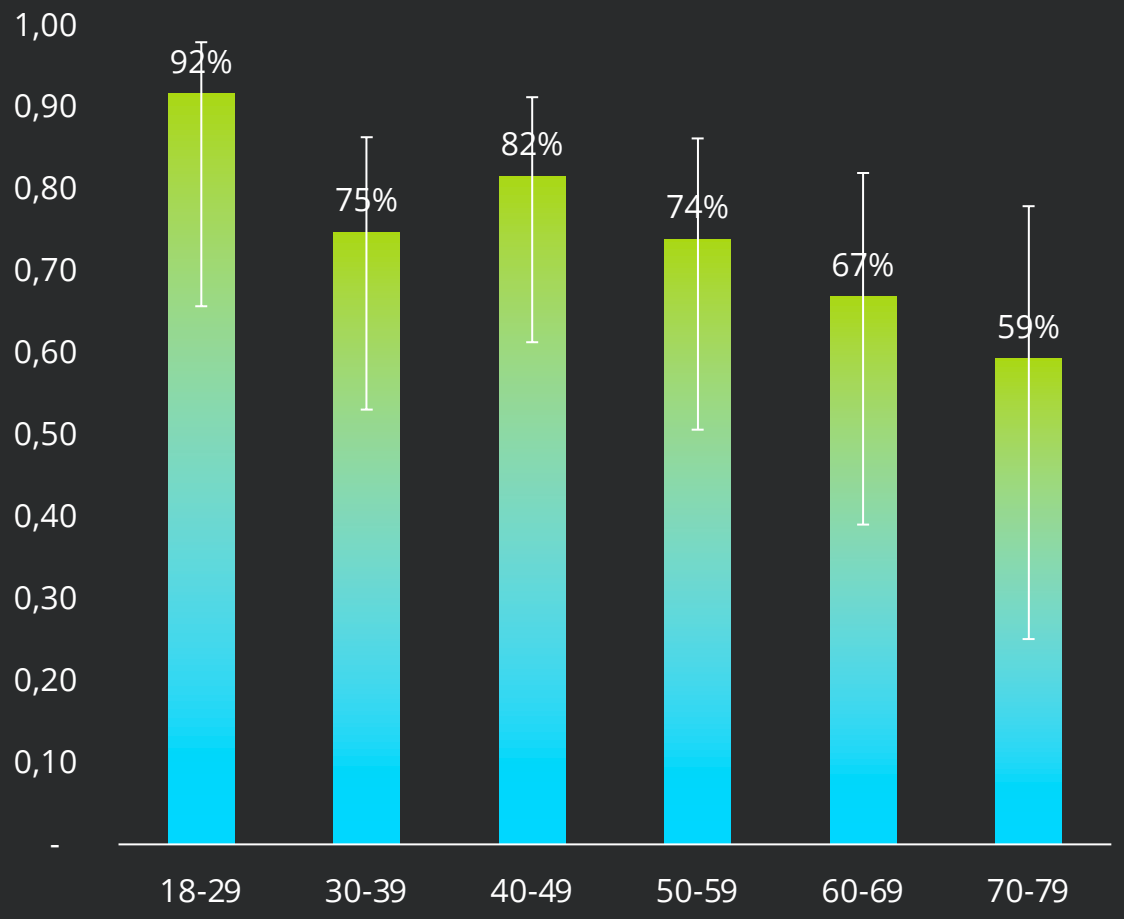


Real world effectiveness of the Pfizer-BioNTech vaccine against hospital admission has reduced from 93% in the Delta (pre-Omicron) wave to 70% in the Omicron wave, continuing to provide substantial protection against hospital admission

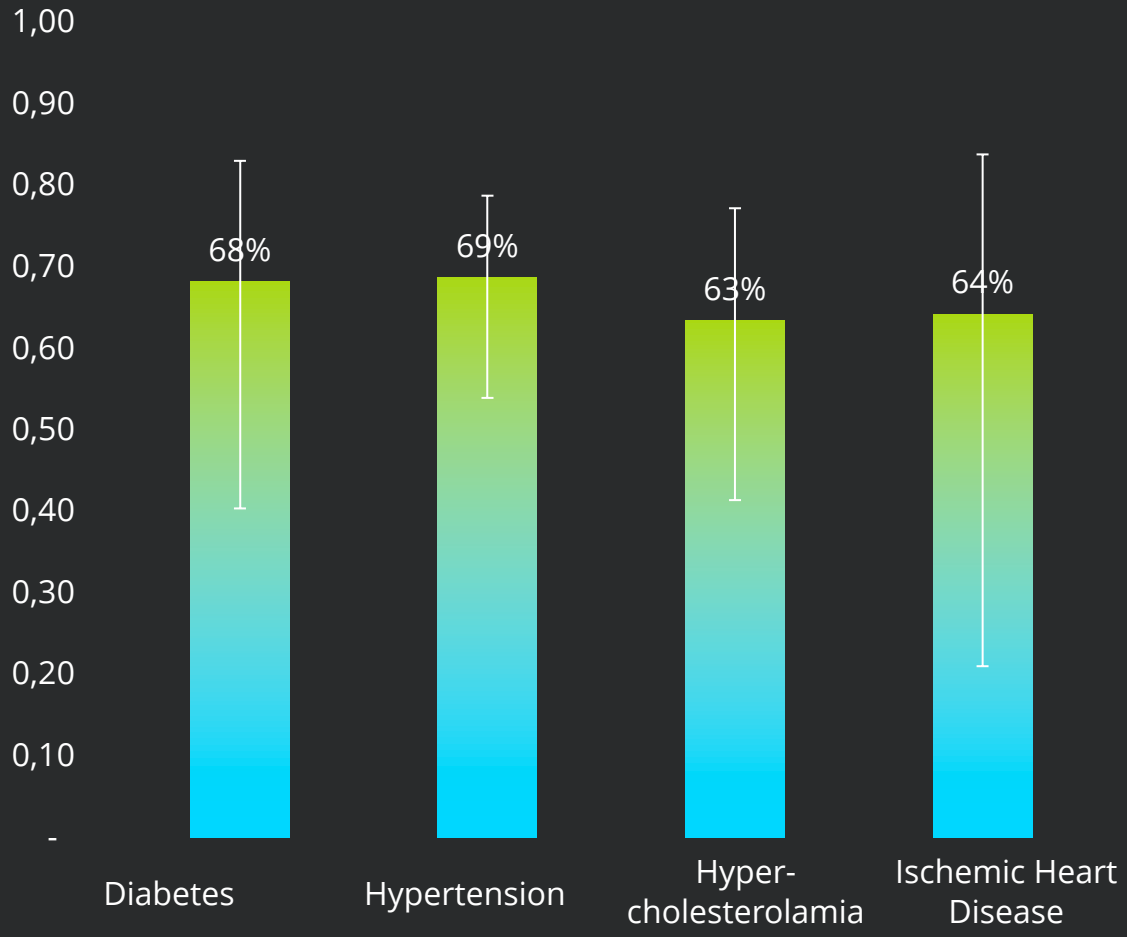
* Submitted for peer review and publication with the NEJM
Authors have no conflicts of interest direct or in kind
Source: Discovery Health analysis of Pfizer-BioNTech effectiveness

Vaccine effectiveness retracts slightly with increasing age but is maintained across various comorbidities – durability impact confounding

Vaccine effectiveness by age during Omicron period

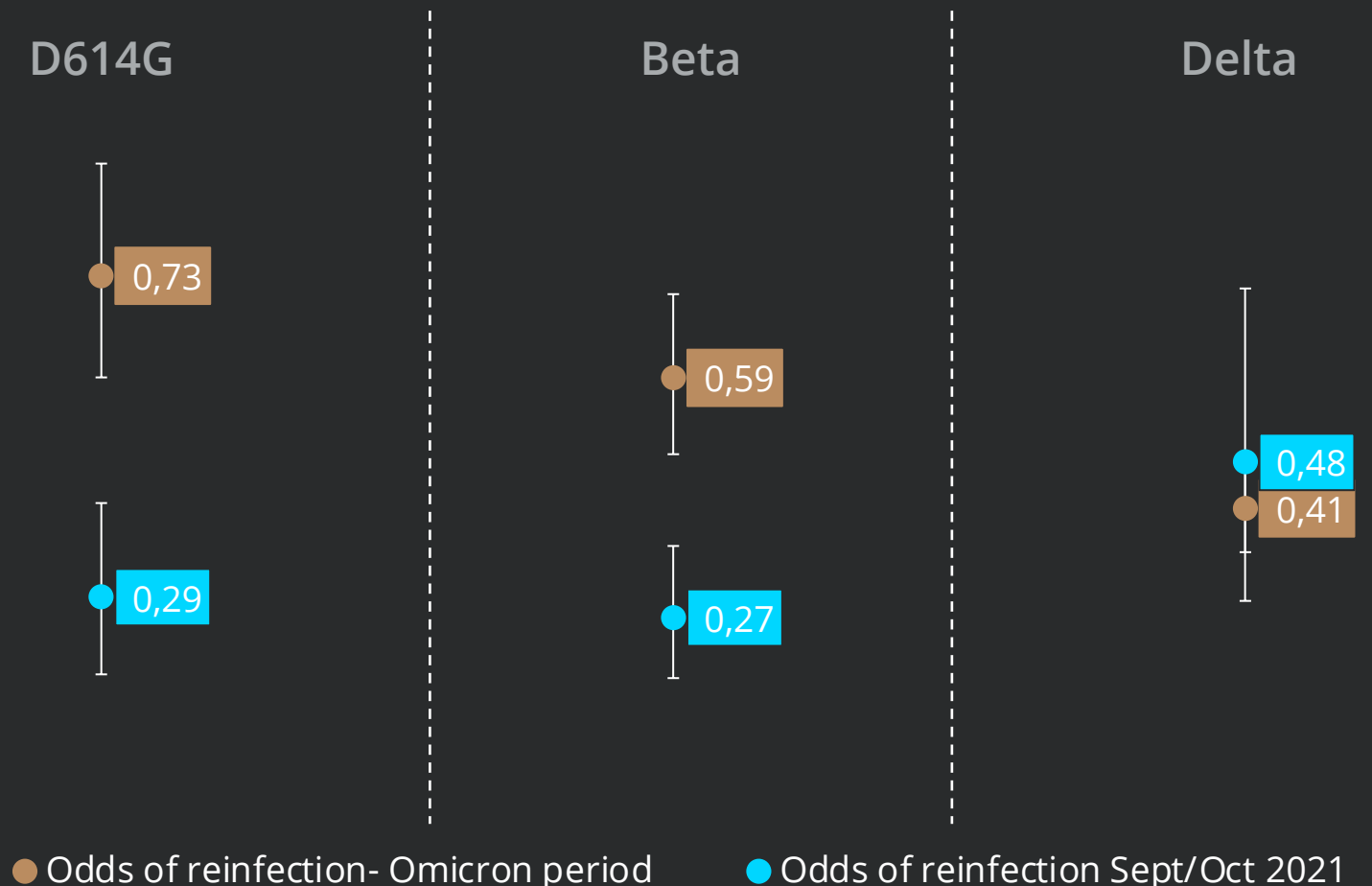


Vaccine effectiveness by comorbidity during Omicron period



*To be submitted for peer review and publication
Authors have no conflicts of interest direct or in kind
Source: Discovery Health analysis of Pfizer-BioNTech effectiveness

Although prior infection confers reduced risk of re-infection, this is diminished against Omicron re-infection



The protective effect of prior infection has reduced over time, and Omicron has eroded that protective effect further

*To be submitted for peer review and publication, Pre-Omicron period refers to September - October
Source: Discovery Health Insights https://discv.co/DiscoveryHealthInsights

Acknowledgements

Discovery

Shirley Collie, Jared Champion, Lizelle Steenkamp, Sameera Haneef, Matt Zylstra, Tommy Chen, Michael Cohen, Ismail Rasool, Thishen Govender

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

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NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
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NGS-SA
Network for Genomic Surveillance in South Africa

krisp

Dr Richard Lessels
Tulio de Oliveira

PATHOLOGISTS
LANCET
LABORATORIES
Key to Diagnostic Excellence

Hendrik van de Venter
John Sole

Conclusion| Omicron Insights

1. Apparent 29% lower severity based on early data (in high seroprevalence population) and supported by anecdotal clinical feedback

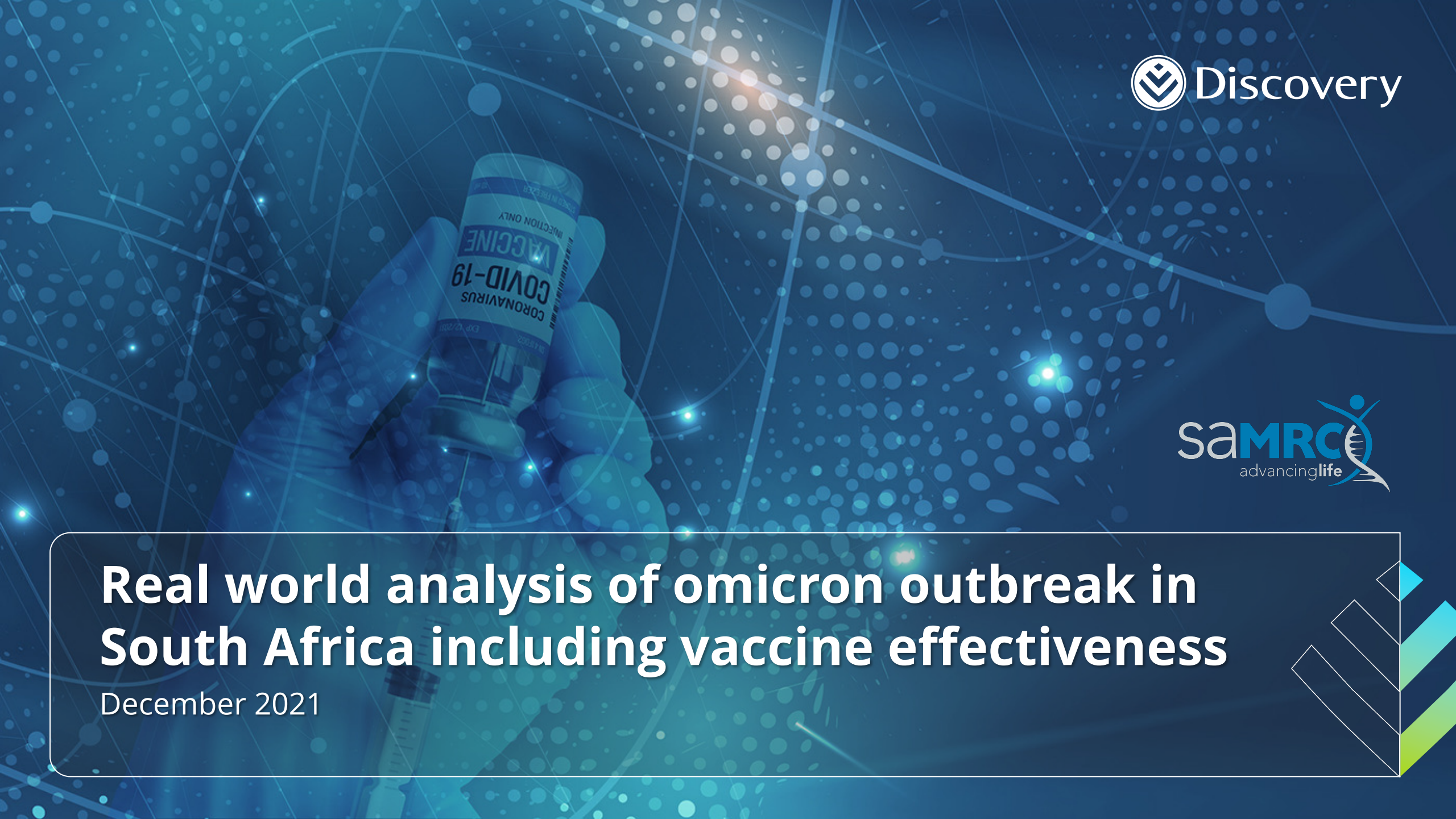
2. Vaccination remains single most important intervention to mitigate against severe Covid-19, with double dose of Pfizer-BioNTech vaccine showing 70% effectiveness in reducing risk of hospitalisation

3. Vaccine effectiveness against infection is materially reduced, with high numbers of breakthrough infections in vaccinated individuals

4. The protective effect of prior infection has reduced over time, and Omicron has eroded that protective effect further, with high re-infection rates in previously Covid-19 positive individuals

5. Notwithstanding the lower severity, health systems could still be over-run by the sheer volume of cases, considering Omicron's rapid community spread

6. Children experiencing very low test positivity rate relative to adults, and low Covid-19 admissions in absolute terms, but appear to be at 20% greater risk of hospitalisation during Omicron wave relative to D614G wave



Discovery

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Real world analysis of omicron outbreak in South Africa including vaccine effectiveness

December 2021