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

December 2021
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.

DH Electronic Health Record data:
- Pathology results
- Hospital admissions
- ICU and ventilation
- Underlying disease burden

Vitality Wellness Data:
- Underlying wellness
- Physical activity
- Mobility data

Member vaccination 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

>3.7 million health insurance lives administered by Discovery Health
Discovery Health beneficiaries are diverse, allowing for relevant real world insights to be derived.

**Data distributed widely across age groups**

- Less than 1: 1.2%
- 1 to 4: 5.9%
- 5 to 9: 7.9%
- 10 to 14: 7.6%
- 15 to 19: 6.1%
- 20 to 24: 4.7%
- 25 to 29: 6.6%
- 30 to 34: 9.0%
- 35 to 39: 9.6%
- 40 to 44: 8.2%
- 45 to 49: 7.4%
- 50 to 54: 6.2%
- 55 to 59: 5.1%
- 60 to 64: 4.4%
- 65 to 69: 3.4%
- 70 to 74: 2.8%
- 75 to 79: 2.0%
- 80 to 84: 1.2%
- 85+: 0.8%

**26% of all individuals are living with chronic illness**

- Hypertension: 29.5%
- Asthma: 19.2%
- Hypercholesterolaemia: 10.7%
- Diabetes: 9.2%
- Other: 9.0%
- Bipolar mood disorder: 7.4%
- Conduction disorder: 6.6%
- Epilepsy: 4.8%
- Ischaemic heart disease: 4.6%
- HIV: 4.6%
- Hypothyroidism: 4.5%
- Conduction disorder: 2.1%

Source: Discovery Health Analysis
Discovery Health has extensive South Africa-specific, real-world data. We have been tracking and codifying unique member data since the start of the pandemic.

<table>
<thead>
<tr>
<th>Tests conducted</th>
<th>Positive cases</th>
<th>Active cases</th>
<th>Repeat cases</th>
<th>Recoveries</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,604,385</td>
<td>467,530</td>
<td>28,415</td>
<td>15,580</td>
<td>424,717</td>
</tr>
<tr>
<td>19,912,714</td>
<td>3,071,064</td>
<td>113,060</td>
<td></td>
<td>2,867,966</td>
</tr>
</tbody>
</table>

- **65.2%** Testing rate
- **13.3%** COVID proportion of DH lives
- **7.0%** % Active
- **3.41%** Proportion of repeat positive
- **90.0%** Recovery rate

<table>
<thead>
<tr>
<th>Members admitted</th>
<th>Deaths</th>
<th>Vaccines administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>61,579</td>
<td>14,398</td>
<td>2,713,122</td>
</tr>
</tbody>
</table>

- **13.8%** Proportion admitted
- **3.3%** Case fatality rate
- **62.3%** % Adult vaccinated

- **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.

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.

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.

Source: NICD, Discovery Health Analysis
Omicron variant has displaced Delta and now dominates new infections in SA

- 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)

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

<table>
<thead>
<tr>
<th>Wave</th>
<th>Admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>D614G</td>
<td>44</td>
</tr>
<tr>
<td>Beta</td>
<td>131</td>
</tr>
<tr>
<td>Delta</td>
<td>101</td>
</tr>
<tr>
<td>Omicron</td>
<td>38</td>
</tr>
</tbody>
</table>

Hospital admissions by wave at 3 week snapshot

DH daily hospital admissions (7-day average) by wave

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

- **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**

- **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

**DH cases and admissions for under 18 year olds indexed to Delta Wave**

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

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

> 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.

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.

Source: Discovery Health Insights  [https://discv.co/DiscoveryHealthInsights](https://discv.co/DiscoveryHealthInsights)

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

<table>
<thead>
<tr>
<th>Wave</th>
<th>D614G</th>
<th>Beta</th>
<th>Delta</th>
<th>Omicron</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,00</td>
<td>1,12</td>
<td>0,94</td>
<td>0,71</td>
</tr>
</tbody>
</table>

Case mix of Covid 19 admissions indexed to the first wave

<table>
<thead>
<tr>
<th>Wave</th>
<th>D614G</th>
<th>Beta</th>
<th>Delta</th>
<th>Omicron</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,00</td>
<td>1,08</td>
<td>1,18</td>
<td>0,79</td>
</tr>
</tbody>
</table>

Proportion of admissions in High care and ICU by wave

<table>
<thead>
<tr>
<th>Wave</th>
<th>ICU</th>
<th>High Care</th>
<th>Other wards</th>
</tr>
</thead>
<tbody>
<tr>
<td>D614G</td>
<td>18%</td>
<td>65%</td>
<td>65%</td>
</tr>
<tr>
<td>Beta</td>
<td>17%</td>
<td>65%</td>
<td>21%</td>
</tr>
<tr>
<td>Delta</td>
<td>22%</td>
<td>68%</td>
<td>10%</td>
</tr>
<tr>
<td>Omicron</td>
<td>5%</td>
<td>87%</td>
<td>8%</td>
</tr>
</tbody>
</table>

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.
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

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

Source: Adapted from Eric Topol twitter, with addition in blue
## Omicron vaccine effectiveness study parameters

<table>
<thead>
<tr>
<th>Study Duration</th>
<th>Covid-19 PCR test results for adult population</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Sep – 7 Dec 2021</td>
<td>211,610</td>
</tr>
</tbody>
</table>

### Study Parameters

**Pre-Omicron Period**
- 1 September to 31 October 2021
- 63% of sample

**Proxy Omicron Period**
- 15 November to 7 December 2021
- 37% of sample

**Sensitivity 1**
- SGTF positive test results from Lancet Laboratories
- 45% of sample

**Sensitivity 2**
- Gauteng PCR tests
- 55% of sample

**Sensitivity 3**
- PCR test results amongst symptomatic admitted patients
- 8% of sample
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
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](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**

- 18-29: 93%
- 30-39: 75%
- 40-49: 82%
- 50-59: 74%
- 60-69: 67%
- 70-79: 59%

**Vaccine effectiveness by comorbidity during Omicron period**

- Diabetes: 68%
- Hypertension: 69%
- Hypercholesterolemia: 63%
- Ischemic Heart Disease: 64%

*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.

<table>
<thead>
<tr>
<th></th>
<th>Odds of reinfection - Omicron period</th>
<th>Odds of reinfection Sept/Oct 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>D614G</td>
<td>0.73</td>
<td>0.29</td>
</tr>
<tr>
<td>Beta</td>
<td>0.59</td>
<td>0.27</td>
</tr>
<tr>
<td>Delta</td>
<td></td>
<td>0.48</td>
</tr>
</tbody>
</table>

*To be submitted for peer review and publication, Pre-Omicron period refers to September - October
Source: Discovery Health Insights [https://discv.co/DiscoveryHealthInsights](https://discv.co/DiscoveryHealthInsights)
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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
Real world analysis of omicron outbreak in South Africa including vaccine effectiveness

December 2021