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## Supplementary appendix

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**Supplementary material**

**Supplementary table 1.** Multivariable logistic regression analysis evaluating the association between S-gene positive infection, compared to S-gene target failure (SGTF) infection, and hospitalisation, South Africa, 1 December 2021 – 20 January 2022[a] (N=92,962)

| | | **Hospital admission[b] n/N (%)** | **Adjusted odds ratio (95% CI)** |
|---|---|---|---|
| **SARS-CoV-2 sub-lineage** | | N=95,470 | |
| | SGTF (BA.1 proxy) | 2,965/87,194 (3.4) | Ref |
| | S-gene positive (BA.2 proxy) | 295/8,276 (3.6) | 0.96 (0.85-1.09) |
| **Age group (years)** | | N=95,470 | |
| | <5 | 226/1,681 (13.4) | **7.49 (6.02-9.32)** |
| | 5-12 | 98/4,426 (2.2) | 1.16 (0.89-1.50) |
| | 13-18 | 109/5,278 (2.1) | 1.06 (0.83-1.37) |
| | 19-24 | 146/7,127 (2.1) | Ref |
| | 25-39 | 855/35,551 (2.4) | 1.19 (0.99-1.42) |
| | 40-59 | 847/30,953 (2.7) | **1.39 (1.16-1.66)** |
| | ≥60 | 979/10,454 (9.4) | **4.97 (4.12-5.94)** |
| **Sex** | | N=94,564 | |
| | Male | 1,364/42,017 (3.3) | Ref |
| | Female | 1,884/52,547 (3.6) | **1.14 (1.06-1.22)** |
| **Province** | | N=93,849 | |
| | Eastern Cape | 3/100 (3.0) | 1.35 (0.42-4.35) |
| | Free State | 78/2,126 (3.7) | **1.35 (1.01-1.82)** |

| | | | |
|---|---|---|---|
| | Gauteng | 1,517/51,745 (2.9) | **1.38 (1.14-1.66)** |
| | KwaZulu-Natal | 1,026/20,615 (5.0) | **2.16 (1.78-2.62)** |
| | Limpopo | 77/3,688 (2.1) | 1.17 (0.88-1.57) |
| | Mpumalanga | 179/4,559 (3.9) | **2.13 (1.68-2.70)** |
| | North West | 156/4,272 (3.7) | **1.95 (1.53-2.49)** |
| | Northern Cape | 33/1,203 (2.7) | 0.97 (0.65-1.44) |
| | Western Cape | 122/5,541 (2.2) | Ref |
| **Healthcare sector** | | N=95,470 | |
| | Public | 1,049/23,498 (4.5) | Ref |
| | Private | 2,211/71,972 (3.1) | **0.63 (0.58-0.68)** |
| **Re-infection[c]** | | N=95,470 | |
| | No | 3,016/86,086 (3.5) | Ref |
| | Yes | 244/9,384 (2.6) | 0.99 (0.86-1.14) |

[a] Cases followed-up for hospital admission until 10 February 2022

[b] Admission to hospital between 7 days prior to 21 days after diagnosis (specimen collection date)

[c] Re-infection was defined as an individual with at least one positive SARS-CoV-2 test >90 days prior to the current episode

**Supplementary table 2.** Multivariable logistic regression analysis evaluating the association between S gene positive infection, compared to S-gene target failure (SGTF) infection, and severe disease among hospitalised individuals with known outcome, South Africa, 1 December 2021 – 20 January 2022[a] (N=2,984)

| | | **Severe disease[a] n/N (%)** | **Adjusted odds ratio (95% CI)** |
|---|---|---|---|
| **SARS-CoV-2 sub-lineage** | | N=3,058 | |
| | SGTF (BA.1 proxy) | 929/2776 (33.5) | Ref |
| | S-gene positive (BA.2 proxy) | 86/282 (30.5) | 0.91 (0.68-1.22) |
| **Age group (years)** | | N=3,058 | |
| | <5 | 37/216 (17.1) | 0.79 (0.45-1.39) |
| | 5-12 | 8/92 (8.7) | **0.38 (0.16-0.90)** |
| | 13-18 | 18/103 (17.5) | 0.80 (0.41-1.57) |
| | 19-24 | 28/139 (20.1) | Ref |
| | 25-39 | 135/804 (16.8) | 0.83 (0.52-1.33) |
| | 40-59 | 284/790 (36.0) | **2.09 (1.33-3.31)** |
| | ≥60 | 505/914 (55.3) | **4.36 (2.77-6.85)** |
| **Sex** | | N=3,046 | |
| | Male | 473/1,275 (37.1) | Ref |
| | Female | 536/1,771 (30.3) | **0.83 (0.70-0.98)** |
| **Province** | | N=2,994 | |
| | Eastern Cape | 1/3 (33.3) | 2.21 (0.16-31.1) |
| | Free State | 28/70 (40.0) | **2.44 (1.19-5.02)** |
| | Gauteng | 509/1,384 (36.8) | **2.79 (1.72-4.55)** |
| | KwaZulu-Natal | 297/996 (29.8) | **1.78 (1.08-2.94)** |
| | Limpopo | 10/76 (13.2) | 0.81 (0.34-1.89) |

| | | | |
|---|---|---|---|
| | Mpumalanga | 56/173 (32.4) | **2.07 (1.13-3.77)** |
| | North West | 33/144 (22.9) | 1.56 (0.83-2.95) |
| | Northern Cape | 26/31 (83.9) | **12.43 (4.10-37.63)** |
| | Western Cape | 27/117 (23.1) | Ref |
| **Co-morbidity[c]** | | N=3,058 | |
| | Absent | 636/2,244 (28.3) | Ref |
| | Present | 379/814 (46.6) | **1.52 (1.25-1.84)** |
| **Healthcare sector** | | N=3,058 | |
| | Public | 377/965 (39.1) | Ref |
| | Private | 638/2093 (30.5) | 0.86 (0.70-1.07) |
| **Days between diagnosis and admission** | | N=3,058 | |
| | 1-7 days before diagnosis | 96/251 (38.3) | Ref |
| | 0-6 days after diagnosis | 803/2,496 (32.2) | 0.82 (0.60-1.11) |
| | 7-21 days after diagnosis | 116/311 (37.3) | 0.96 (0.65-1.41) |
| **Re-infection[d]** | | N=3,058 | |
| | No | 963/2,831 (34.0) | Ref |
| | Yes | 52/227 (22.9) | 0.77 (0.54-1.11) |
| **SARS-CoV-2 vaccination[e]** | | N=3,058 | |
| | No | 178/437 (40.7) | Ref |
| | Yes | 43/169 (25.4) | **0.52 (0.33-0.82)** |
| | Unknown | 794/2,452 (32.4) | **0.75 (0.57-0.98)** |

[a] Cases followed-up for in-hospital outcome until 10 February 2022

[b] Severe disease defined as a hospitalised patient meeting at least one of the following criteria: admitted to ICU, received oxygen treatment, ventilated, received extracorporeal membrane oxygenation (ECMO), experienced acute respiratory distress syndrome (ARDS) and/or died

[c] Co-morbidity defined as ≥1 of the following conditions: hypertension, diabetes, chronic cardiac disease, chronic kidney disease, asthma, chronic obstructive pulmonary disease (COPD), malignancy, HIV, and active or past tuberculosis

[d] Re-infection was defined as an individual with at least one positive SARS-CoV-2 test >90 days prior to the current episode

[e] Vaccination defined as ≥1 dose of SARS-CoV-2 vaccine (Johnson & Johnson / Pfizer-BioNTech)

**Supplementary table 3.** Comparison of clinical severity components by Omicron sub-lineage, among hospitalised individuals with known outcome, South Africa, 1 December 2021 – 20 January 2022[a] (N=3,058)

| | Omicron sub-lineage | | P-value[b] |
|---|---|---|---|
| | **SGTF (BA.1 proxy)** | **S-gene positive (BA.2 proxy)** | |
| | n (%) | n (%) | |
| **Severity component** | N=2776 | N=282 | |
| ICU admission | 252 (9.1) | 26 (9.2) | 0.937 |
| Oxygen treatment | 636 (22.9) | 58 (20.6) | 0.371 |
| Ventilated | 53 (1.9) | 4 (1.4) | 0.562 |
| Received ECMO | 0 (0.0) | 0 (0.0) | N/A |
| ARDS | 32 (1.2) | 2 (0.7) | 0.499 |
| Died | 242 (8.7) | 20 (7.1) | 0.353 |

SGTF: S-gene target failure, ICU: intensive care unit, ECMO: extracorporeal membrane oxygenation, ARDS: acute respiratory distress syndrome

[a] Cases followed-up for in-hospital outcome until 10 February 2022

[b] Pearson's Chi-squared test

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