Update on Covid-19 epidemic & the 501Y.V2 variant in South Africa

18 January 2021

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Member: African Task Force for Coronavirus
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Adjunct Professor of Medicine: Cornell University
Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa

Key questions addressed in this update

1. Is the 501Y.V2 variant in the 2\textsuperscript{nd} wave spreading faster?
   - Biological evidence showing that the virus binds more readily and more strongly (higher affinity) to the human cells
   - Epidemiological evidence from areas where the new variant is known to be dominant

2. Is the 501Y.V2 variant more severe?

3. Any new evidence on whether Covid-19 vaccines are effective or not against the 501Y.V2 variant?

4. Do antibodies from SA’s 1\textsuperscript{st} wave kill the 501Y.V2 variant of the 2\textsuperscript{nd} wave?

Conclusion & next steps
Covid-19 in South Africa

7-day moving average of new cases, sentinel hospital admissions and Covid-19 deaths – to 17 Jan 2021

Source of hospital admissions data: Lucille Blumberg, Richard Welch and Waasila Jassat – DATCOV, NICD
The N501Y and K417N mutations in the spike protein of SARS-CoV-2 alter the interactions with both hACE2 and human derived antibody: A Free energy of perturbation study

Filip Fratev¹, ²

- Amino acid changes lead to charge & shape alterations
- By measuring free energy perturbation (FEP), show that binding of RBD to ACE2 increasing significantly with 501 mutation
- RBD rotates 20° - approaches deeper to the binding site with ACE2 receptor

RBD = receptor-binding domain of the spike protein; ACE2 = angiotensin converting enzyme-2
Average daily tests & proportion of positive tests

Cumulative number tests 4 March - 17 January = 7,433,571

Lighter shade is an incomplete week
### Daily new cases over last 7 days/100,000 - up to 11 Jan 2021

<table>
<thead>
<tr>
<th>Province</th>
<th>Population /100,000</th>
<th>7-day ave on 1 Jan</th>
<th>29 Dec – 4 Jan</th>
<th>Cases /100,000 /day</th>
<th>7-day ave on 8 Jan</th>
<th>5 Jan – 11 Jan</th>
<th>Cases /100,000 /day</th>
<th>Increase / decrease</th>
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<tr>
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<td>952</td>
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<td>301</td>
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<tr>
<td>GP</td>
<td>152</td>
<td>3583</td>
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<td>5291</td>
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<td>+32.3%</td>
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<tr>
<td>KZN</td>
<td>113</td>
<td>4498</td>
<td>39.8</td>
<td>5088</td>
<td>45.1</td>
<td>+11.6%</td>
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</tr>
<tr>
<td>LP</td>
<td>60</td>
<td>777</td>
<td>13.0</td>
<td>1598</td>
<td>25.2</td>
<td>+51.4%</td>
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<td>MP</td>
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<td>555</td>
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<td>1112</td>
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<tr>
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<td>157</td>
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<tr>
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<td>437</td>
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<td>755</td>
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<td>3233</td>
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<tr>
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<td>14496</td>
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<td>19042</td>
<td>31.8</td>
<td>+23.9%</td>
<td></td>
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</tbody>
</table>
Daily new cases over last 7 days/100,000
- up to 18 Jan 2021

<table>
<thead>
<tr>
<th>Province</th>
<th>Population /100,000</th>
<th>7-day ave on 8 Jan</th>
<th>Cases /100,000 /day</th>
<th>7-day ave on 15 Jan</th>
<th>Cases /100,000 /day</th>
<th>Increase / decrease</th>
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</thead>
<tbody>
<tr>
<td>EC</td>
<td>67</td>
<td>1041</td>
<td>16.3</td>
<td>873</td>
<td>13.0</td>
<td>-19.2%</td>
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<tr>
<td>FS</td>
<td>29</td>
<td>513</td>
<td>17.8</td>
<td>529</td>
<td>18.3</td>
<td>+3.1%</td>
</tr>
<tr>
<td>GP</td>
<td>152</td>
<td>5291</td>
<td>34.7</td>
<td>4084</td>
<td>26.2</td>
<td>-29.6%</td>
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<tr>
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<td>4175</td>
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<td>-21.9%</td>
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<tr>
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<td>1351</td>
<td>23.2</td>
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<tr>
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<td>294</td>
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<tr>
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<td>755</td>
<td>18.4</td>
<td>726</td>
<td>18.0</td>
<td>-4.0%</td>
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<td>WC</td>
<td>68</td>
<td>3075</td>
<td>44.9</td>
<td>2342</td>
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<td>25.7</td>
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</tr>
</tbody>
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Confirmed SARS-CoV-2 cases by province
(7-day moving average cases per 100,000 population – up to 17 January 2021)
SARS-CoV-2 cases in 1\textsuperscript{st} & 2\textsuperscript{nd} waves in Western Cape

(7-day moving average cases per 100,000 population – up to 17 January)
Western Cape daily hospital admissions and in-hospital deaths
(7-day moving average up 17 January 2021)

Analysis: Amanda Brewer; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD
Eastern Cape daily hospital admissions and in-hospital deaths

(7-day moving average up 17 January 2021)

Analysis: Amanda Brewer; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD
KwaZulu-Natal daily hospital admissions and in-hospital deaths
(7-day moving average up 17 January 2021)

Analysis: Amanda Brewer; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD
SARS-CoV-2 cases in 1\textsuperscript{st} & 2\textsuperscript{nd} wave in KwaZulu-Natal

(7-day moving average cases per 100,000 population – up to 17 January)
How much faster is it spreading in SA’s 2nd wave?

- Days to reach 100,000 cases in the 1st & 2nd wave:
  - Western Cape: 50% faster 107 vs 54 days
  - KwaZulu-Natal: 39% faster 54 vs 33 days

- Caveats: confounding by behaviour, testing, reporting, etc

501Y.V2 is 50% more transmissible than previous variants
Assumes minimal reinfection levels

Source: Cheryl Baxter, CAPRISA
How does 501Y.V2 compare with B.1.1.7 variant?

- Comparing SARS-CoV-2 prevalence, Covid-19 hospital admissions, hospital & ICU bed occupancy in areas with high & low variant prevalence
- The B.1.1.7 variant with the sole RBD mutation at position 501 is 56% more transmissible than pre-existing variants
- No evidence of more severe disease
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2. Is the 501Y.V2 variant more severe?

3. Any new evidence on whether Covid-19 vaccines are effective or not against the 501Y.V2 variant? *Not yet! Working on it*

4. Do antibodies from SA’s 1st wave kill the 501Y.V2 variant of the 2nd wave?

Conclusion & next steps
Is 501Y.V2 associated with increased admissions?

• When the Western Cape and KwaZulu-Natal reached 100,000 cases in 1\textsuperscript{st} & 2\textsuperscript{nd} wave the admission rate (per 1000 reported cases) was:

  Western Cape: 159 vs 147  (15,942 vs 14,796)
  KwaZulu-Natal: 110 vs 106  (11,042 vs 10,632)

• Caveats: confounding by reporting, age, lag, etc

Analysis: Cheryl Baxter, CAPRISA; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD
Admission disease profile in WC similar in both waves

Wave period

Early wave 1:  
<1 June 2020  
1968 admissions

Late wave 1:  
1 Jun - 31 Aug 2020  
7128 admissions

Between waves:  
1 Sep – 15 Oct 2020  
666 admissions

Wave 2  
≥ 16 Oct 2020  
3968 admissions

No notable difference admitted (or deceased) patients for the different wave periods.

Source: Mary-Ann Davies – Western Cape DoH
Risk of dying in the Western Cape public sector by age and “wave period”

Wave period from L-R

**Early wave 1:**
<1 June 2020

**Late wave 1:**
1 Jun - 31 Aug 2020

**Between waves:**
1 Sep – 15 Oct 2020

**Wave 2**
≥ 16 Oct 2020

Kaplan-Meier probability of death among known public sector adult cases by 30 days since diagnosis by age & “wave period”

No difference in mortality by age group between waves

Source: Mary-Ann Davies – Western Cape DoH
Covid-19 in-hospital monthly case-fatality-ratio by age group shows little change across waves

5 March 2020 - 9 January 2021

Analysis: Juliet Pulliam from SACEMA; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD
Expected & actual all-cause deaths during Covid-19

Source: Bradshaw D, et al
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4. Do antibodies from SA’s 1st wave kill the 501Y.V2 variant of the 2nd wave?

Conclusion & next steps
Source: https://ssrn.com/abstract=3725763 & Dejnirattisai W. The antigenic anatomy of SARS-CoV-2 receptor binding domain, 2020 (Pre-print)
Immune responses target 2 main areas of the spike protein:

- Receptor-binding domain (RBD)
- N-terminal domain

Source: https://ssrn.com/abstract=3725763 & Dejnirattisai W. The antigenic anatomy of SARS-CoV-2 receptor binding domain, 2020 (Pre-print)
hACE2 Contact sites

Source: https://ssrn.com/abstract=3725763 & Dejnirattisai W. The antigenic anatomy of SARS-CoV-2 receptor binding domain, 2020 (Pre-print)
Convalescent sera from 4 patients were not able to neutralize viruses with a 484 mutation, which alters the charge & shape of the RBD.

Source: [https://ssrn.com/abstract=3725763](https://ssrn.com/abstract=3725763) & Dejnirattisai W. The antigenic anatomy of SARS-CoV-2 receptor binding domain, 2020 (Pre-print)
Note: These are all antibody binding studies – they do not factor in T-cell immunity, which is also likely to play an important role in preventing reinfection.

Study of convalescent sera from 44 South Africans infected in first wave, >90% showed reduced immunity & 48% had complete immune escape to 501Y.V2.
Should this information change vaccine approach?

- No, not at this stage. Vaccines like Pfizer & Moderna are among most effective vaccines we have for any disease.
- They achieve an important goal – reduce clinical illness & hospitalisation.
- There are many unknowns - will take long to resolve and answer fully:
  1. Are they free of long-term side effects?
  2. Do they prevent asymptomatic infection?
  3. Do they prevent viral spread from vaccinees?
  4. Do they work against new variants?
- Vaccine rollout is not going to be easy or quick – mammoth logistical task that needs all hands on deck to vaccinate at least HCWs, elderly, and patients with hypertension, diabetes and cancer.....
What have we learnt from this update on the 501Y.V2 variant?

• With some caveats – unpublished data, data quality, etc
• Virus is spreading (~50%) faster in 2nd wave than 1st wave in SA’s coastal provinces where the 501Y.V2 variant is known to be dominant
• Current data suggests that new variant is not more severe
• Published convalescent serum studies suggest natural antibodies less effective – viral escape facilitated by 484, 501 & N-terminal mutations
• Vaccine antibodies are different – may or may not be impacted
• No empiric evidence yet on whether vaccines are effective against the 501Y.V2 variant – studies are underway

*Note:* variant is called “501Y.V2” & not “South African” variant just like “SARS-CoV-2” is not called “China virus”. Many variants in the world.
“The pandemic has exposed the paradox that while we are more connected, we are also more divided….

“To come out of this crisis better, we have to recover the knowledge that as a people we have a shared destination. The pandemic has reminded us that no one is saved alone. What ties us to one another is what we commonly call solidarity. Solidarity is more than acts of generosity, important as they are; it is the call to embrace the reality that we are bound by bonds of reciprocity. On this solid foundation we can build a better, different, human future.”

- Pope Francis, head of the Catholic Church