



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

18 January 2021

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Adjunct Professor of Medicine: Cornell University



CAPRISA hosts a  
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Excellence in  
HIV Prevention



National  
Research  
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CAPRISA is the UNAIDS Collaborating  
Centre for HIV Research and Policy



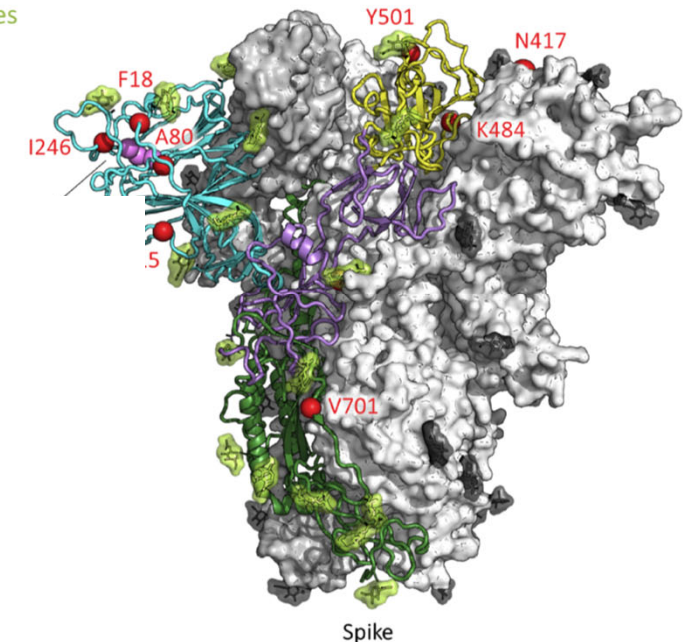
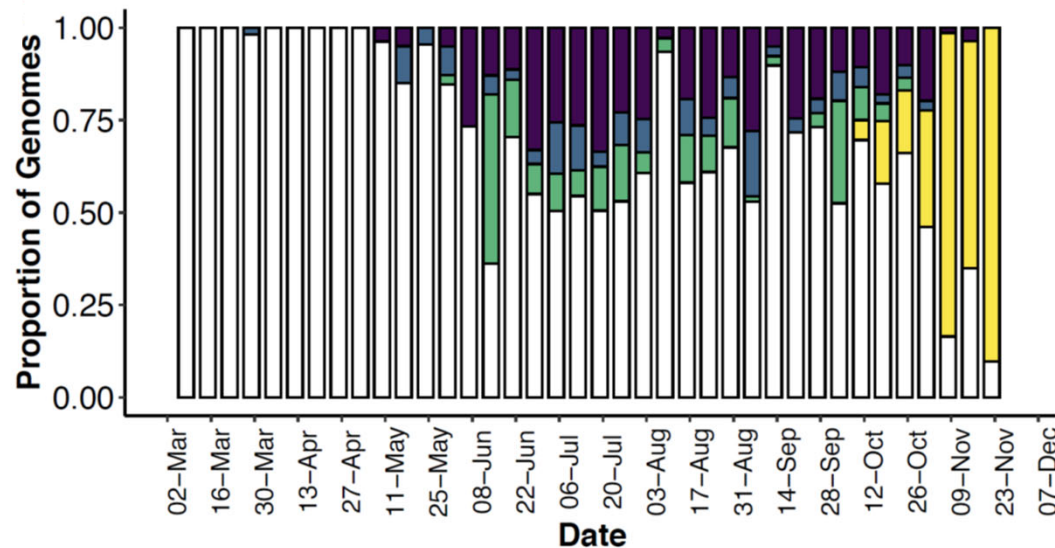
CAPRISA hosts a MRC HIV-TB Pathogenesis  
and Treatment Research Unit  
CAPRISA hosts a DoH-MRC Special Initiative  
for HIV Prevention Technology



# 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

Houriyyah Tegally<sup>1\*</sup>, Edean Wilkinson<sup>1\*</sup>, Marta Giovanetti<sup>2,3\*</sup>, Arash Iranzadeh<sup>4\*</sup>, Vagner Fonseca<sup>1,2</sup>, Jennifer Giandhari<sup>1</sup>, Deelan Doolabh<sup>5</sup>, Sureshnee Pillay<sup>1</sup>, Emmanuel James San<sup>1</sup>, Nokukhanya Msoni<sup>6</sup>, Koleka Mlisana<sup>7,8</sup>, Anne von Gottberg<sup>9,10</sup>, Sibongile Walaza<sup>9,11</sup>, Mushal Allam<sup>9</sup>, Arshad Ismail<sup>9</sup>, Thabo Mohale<sup>9</sup>, Allison J Glass<sup>10,12</sup>, Susan Engelbrecht<sup>13</sup>, Gert Van Zyl<sup>13</sup>, Wolfgang Preiser<sup>13</sup>, Francesco Petruccione<sup>14,15</sup>, Alex Sigal<sup>16,17,18</sup>, Diana Hardie<sup>19</sup>, Gert Marais<sup>19</sup>, Marvin Hsiao<sup>19</sup>, Stephen Korsman<sup>19</sup>, Mary-Ann Davies<sup>20,21</sup>, Lynn Tyers<sup>5</sup>, Innocent Mudau<sup>5</sup>, Denis York<sup>22</sup>, Caroline Maslo<sup>23</sup>, Dominique Goedhals<sup>24</sup>, Shareef Abrahams<sup>25</sup>, Oluwakemi Laguda-Akingba<sup>25,26</sup>, Arghavan Alisoltani-Dehkordi<sup>27,28</sup>, Adam Godzik<sup>28</sup>, Constantinos Kurt Wibmer<sup>9</sup>, Bryan Trevor Sewell<sup>29</sup>, José Lourenço<sup>30</sup>, Luiz Carlos Junior Alcantara<sup>2,3</sup>, Sergei L Kosakovsky Pond<sup>31</sup>, Steven Weaver<sup>31</sup>, Darren Martin<sup>4,5</sup>, Richard J Lessells<sup>1,8</sup>, Jinal N Bhiman<sup>9,10\*</sup>, Carolyn Williamson<sup>5,8,19\*</sup>, Tulio de Oliveira<sup>1,8,32\*</sup>

- S1 N-terminal domain  
Receptor binding domain  
Sub-domain 1 & 2
- S2 Fusion machinery
- Glycosylation sites



# Key questions addressed in this update

## 1. Is the 501Y.V2 variant in the 2<sup>nd</sup> 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?

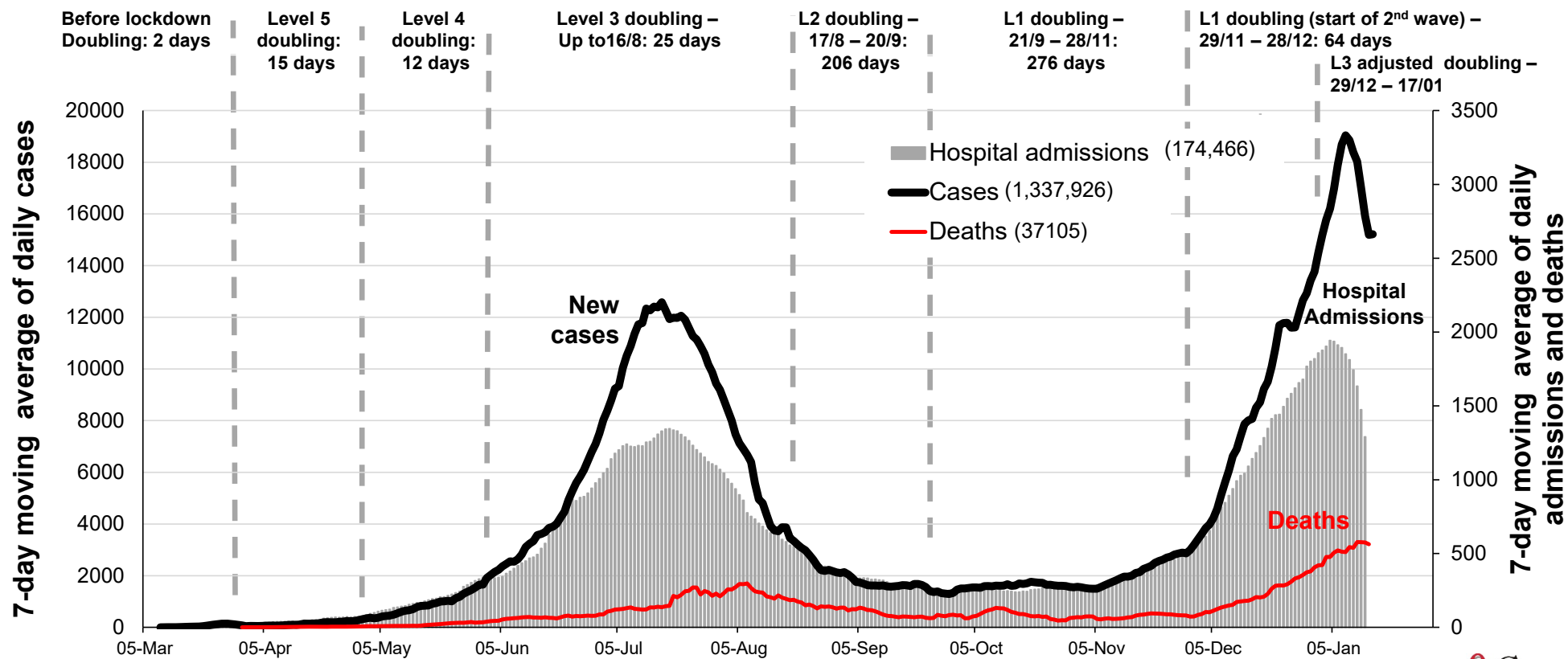
## 3. Any new evidence on whether Covid-19 vaccines are effective or not against the 501Y.V2 variant?

## 4. Do antibodies from SA's 1<sup>st</sup> wave kill the 501Y.V2 variant of the 2<sup>nd</sup> 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**

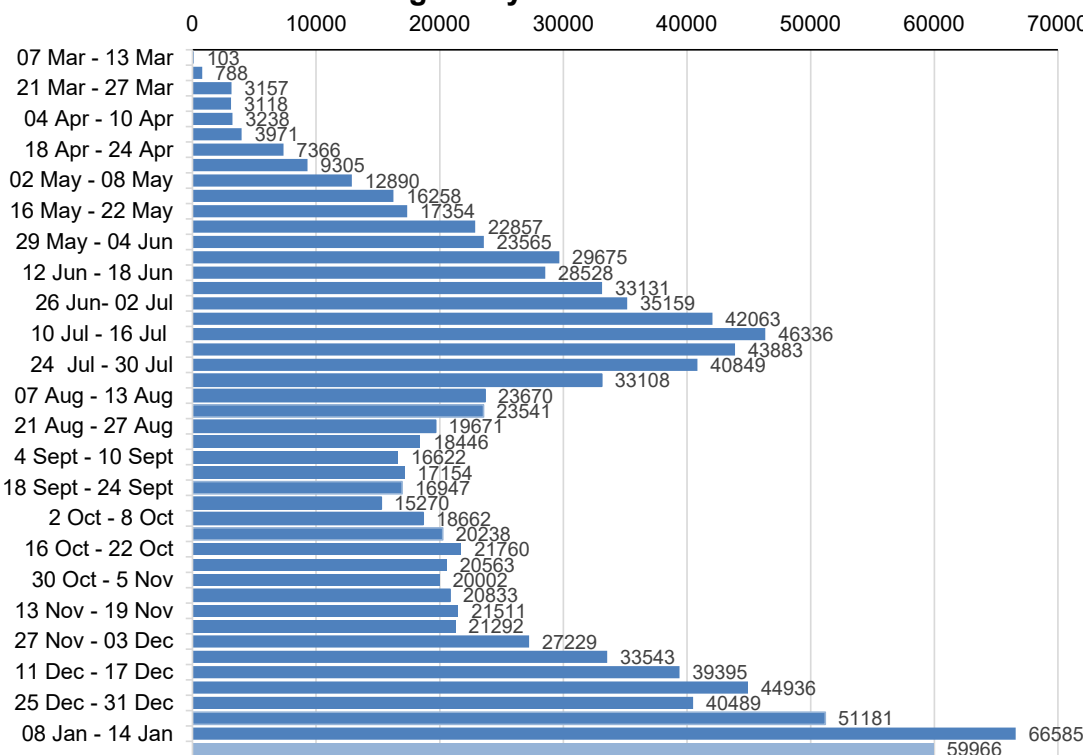
Filip Fratev<sup>1,2</sup>

- **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**

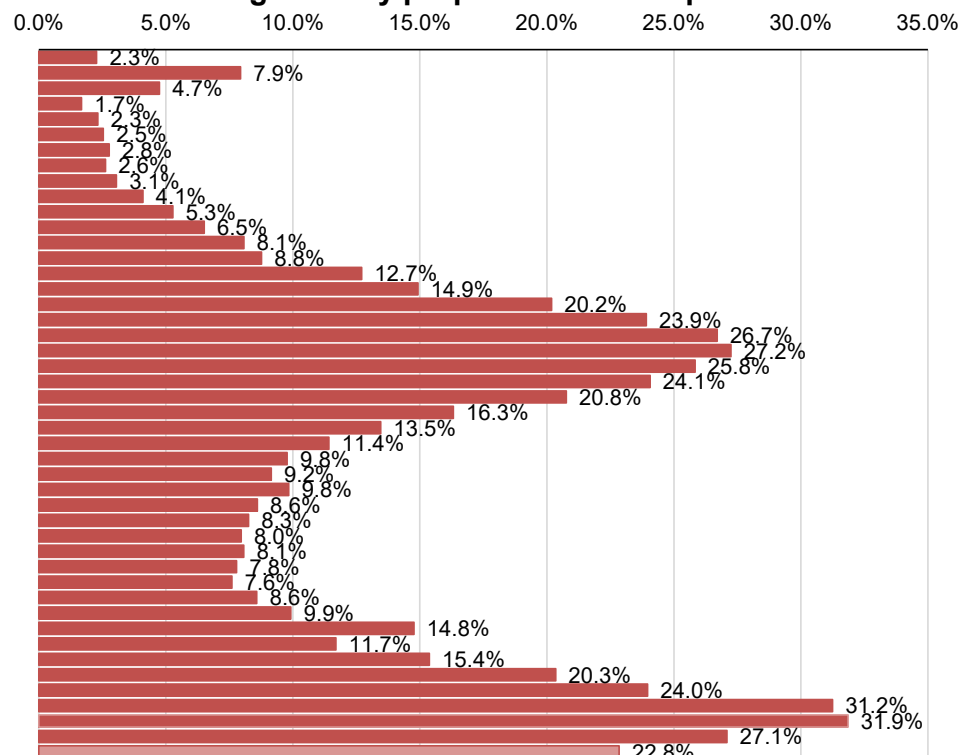
RBD = receptor-binding domain of the spike protein; ACE2 = angiotensin converting enzyme-2

# Average daily tests & proportion of positive tests

Average daily number of tests each week



Average weekly proportion of tests positive



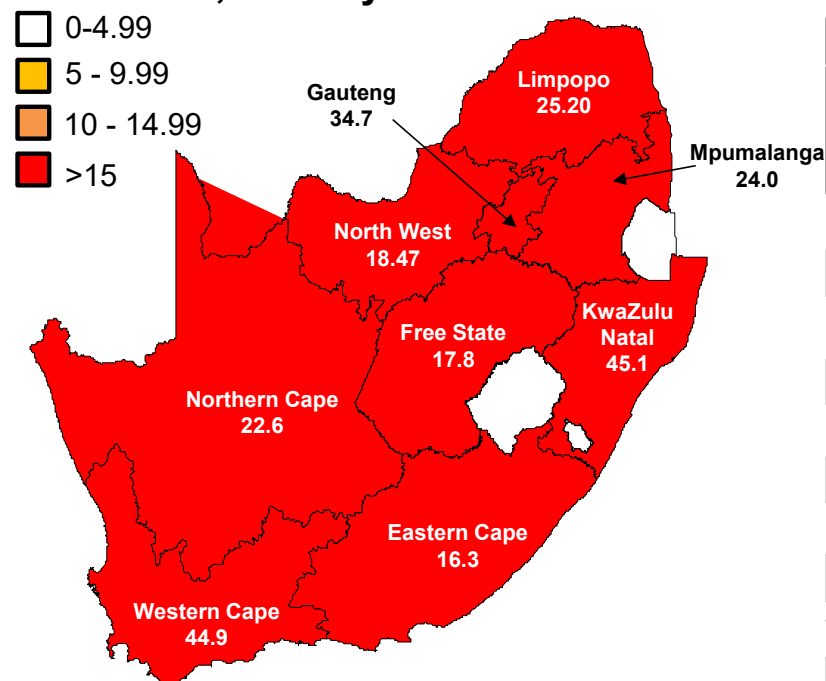
Lighter shade is an incomplete week

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

# Daily new cases over last 7 days/100,000

## - up to 11 Jan 2021

### Cases /100,000 /day

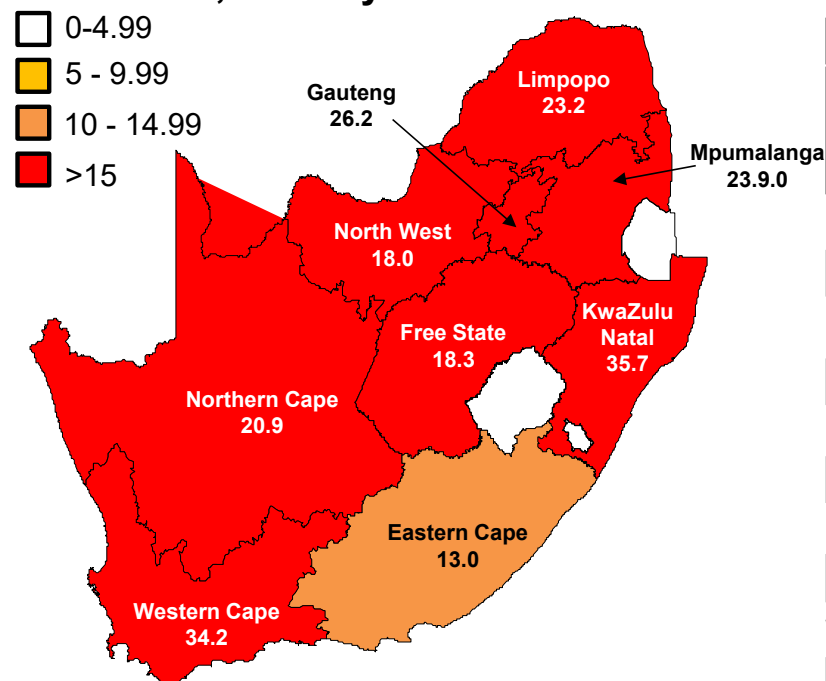


Province	Population /100,000	29 Dec – 4 Jan		5 Jan – 11 Jan		Increase / decrease
		7-day ave on 1 Jan	Cases /100,000 /day	7-day ave on 8 Jan	Cases /100,000 /day	
EC	67	952	14.8	1041	16.3	+8.5%
FS	29	301	9.2	513	17.8	+41.3%
GP	152	3583	23.6	5291	34.7	+32.3%
KZN	113	4498	39.8	5088	45.1	+11.6%
LP	60	777	13.0	1598	25.2	+51.4%
MP	46	555	12.1	1112	24.0	+50.1%
NC	13	157	12.4	285	22.6	+44.9%
NW	41	437	10.7	755	18.4	+42.1%
WC	68	3233	47.2	3075	44.9	-4.9%
National	580	14496	24.2	19042	31.8	+23.9%

# Daily new cases over last 7 days/100,000

## - up to 18 Jan 2021

### Cases /100,000 /day

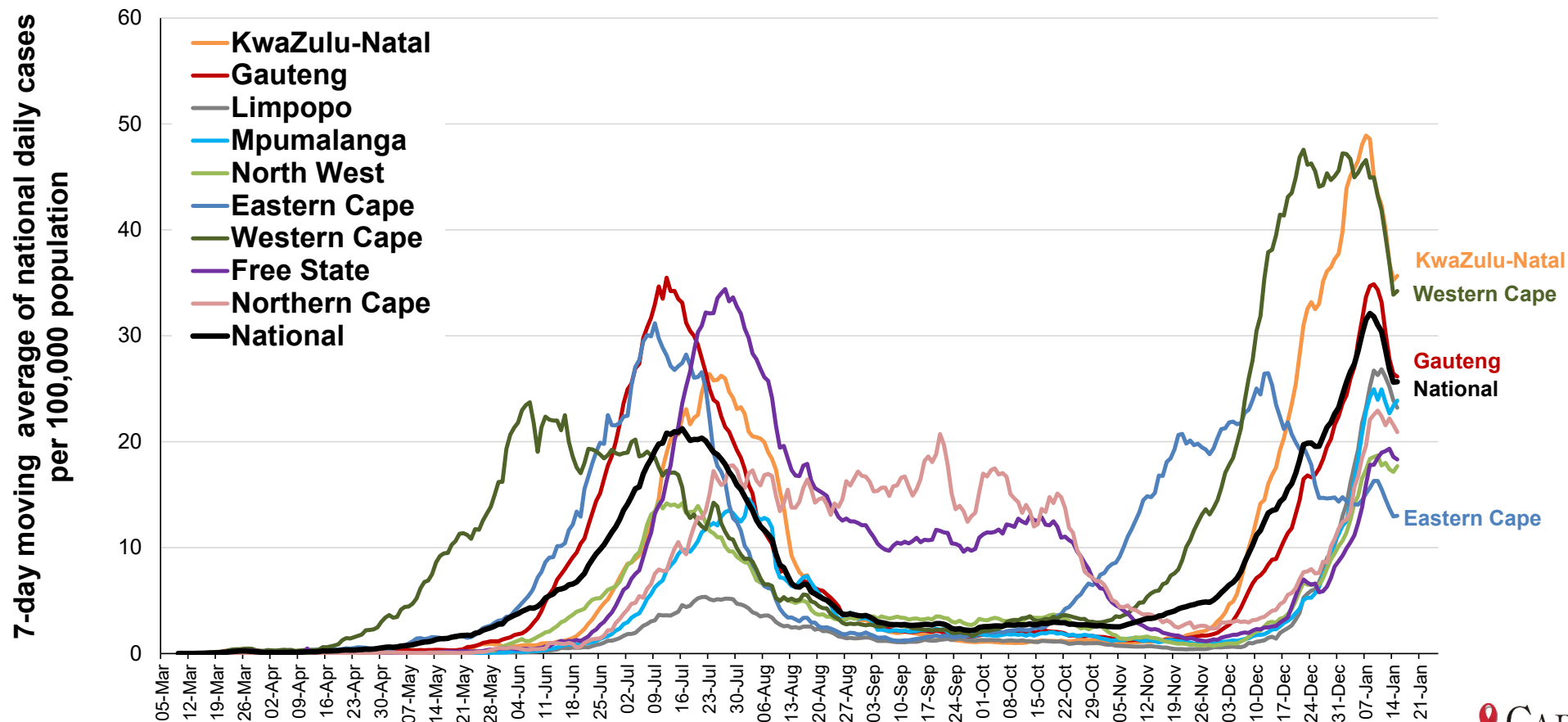


Province	Population /100,000	5 Jan – 11 Jan		12 Jan – 18 Jan		Increase / decrease
		7-day ave on 8 Jan	Cases /100,000 /day	7-day ave on 15 Jan	Cases /100,000 /day	
EC	67	1041	16.3	873	13.0	-19.2%
FS	29	513	17.8	529	18.3	+3.1%
GP	152	5291	34.7	4084	26.2	-29.6%
KZN	113	5088	45.1	4175	35.7	-21.9%
LP	60	1598	25.2	1351	23.2	-18.3%
MP	46	1112	24.0	1097	23.9	-1.37%
NC	13	285	22.6	294	20.9	+3.2%
NW	41	755	18.4	726	18.0	-4.0%
WC	68	3075	44.9	2342	34.2	-31.3%
National	580	19042	31.8	15214	25.7	-25.2%



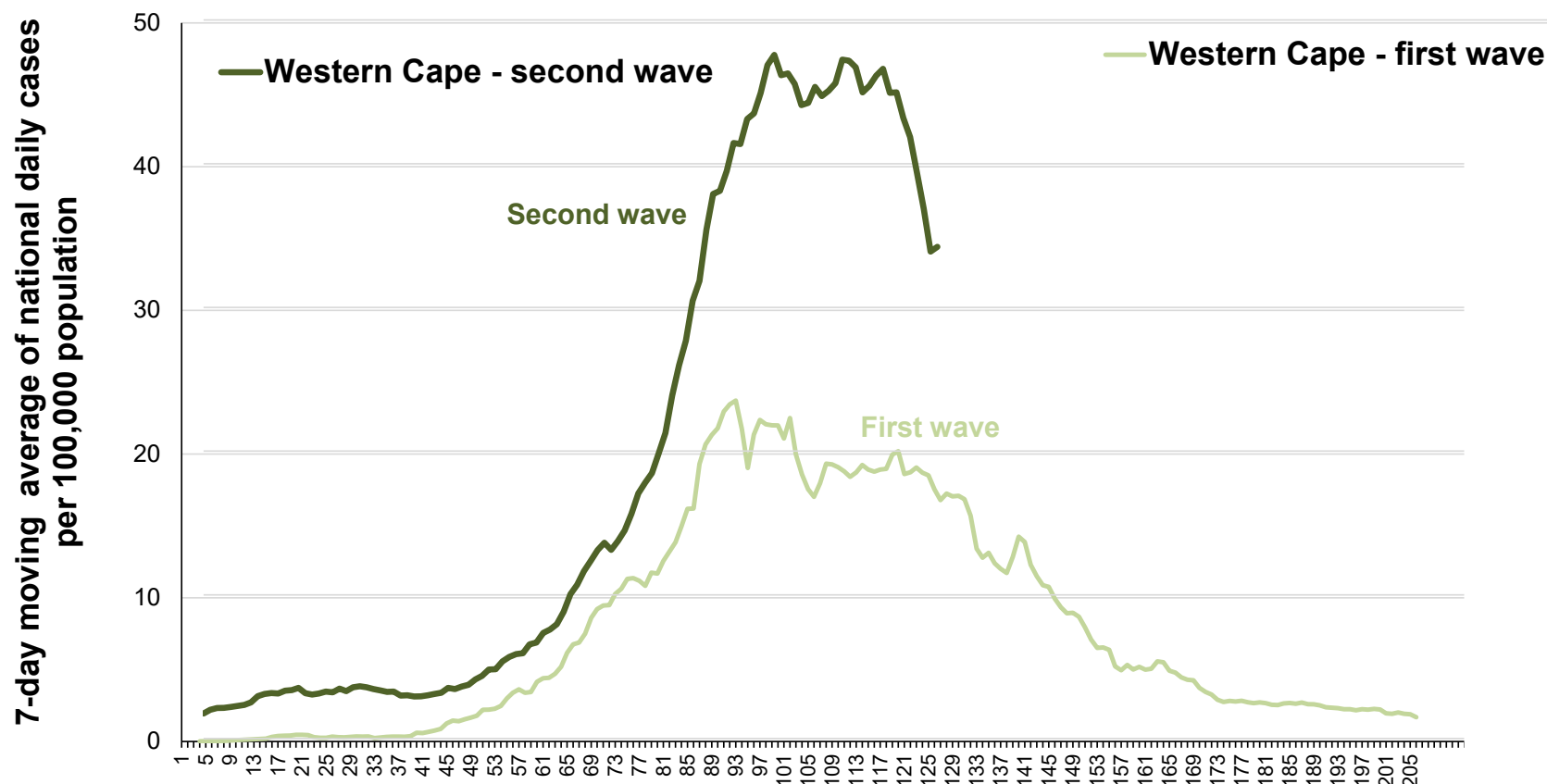
# Confirmed SARS-CoV-2 cases by province

(7-day moving average cases per 100,000 population – up to 17 January 2021)



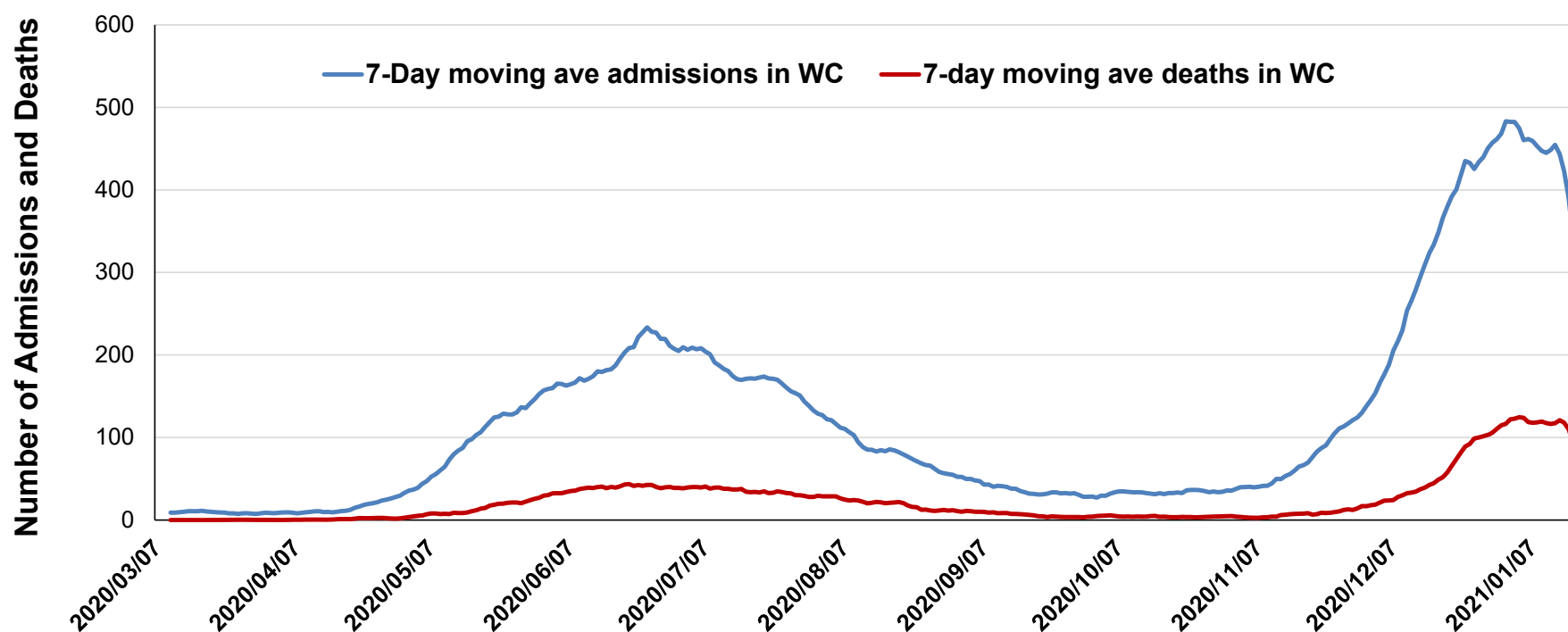
# SARS-CoV-2 cases in 1<sup>st</sup> & 2<sup>nd</sup> waves in Western Cape

(7-day moving average cases per 100,000 population – up to 17 January)



# Western Cape daily hospital admissions and in-hospital deaths

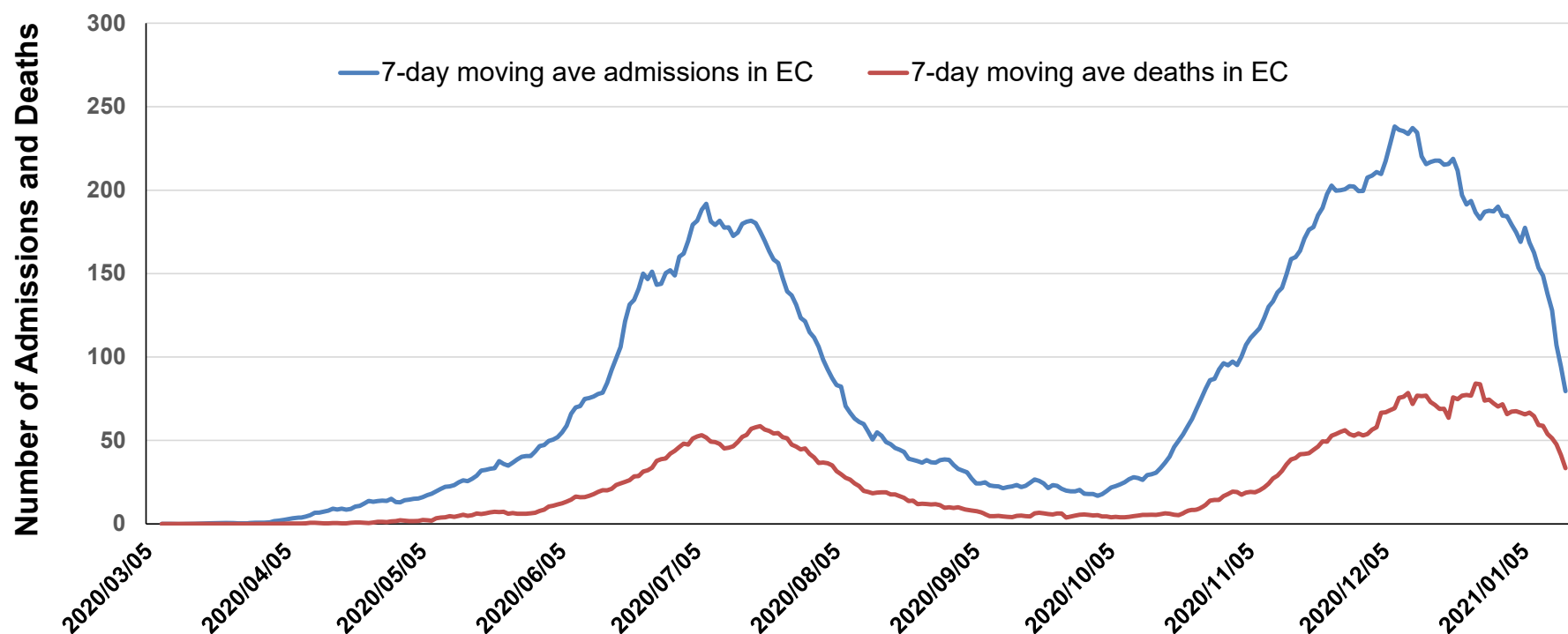
(7-day moving average up 17 January 2021)



Analysis: Amanda Brewer; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD

# Eastern Cape daily hospital admissions and in-hospital deaths

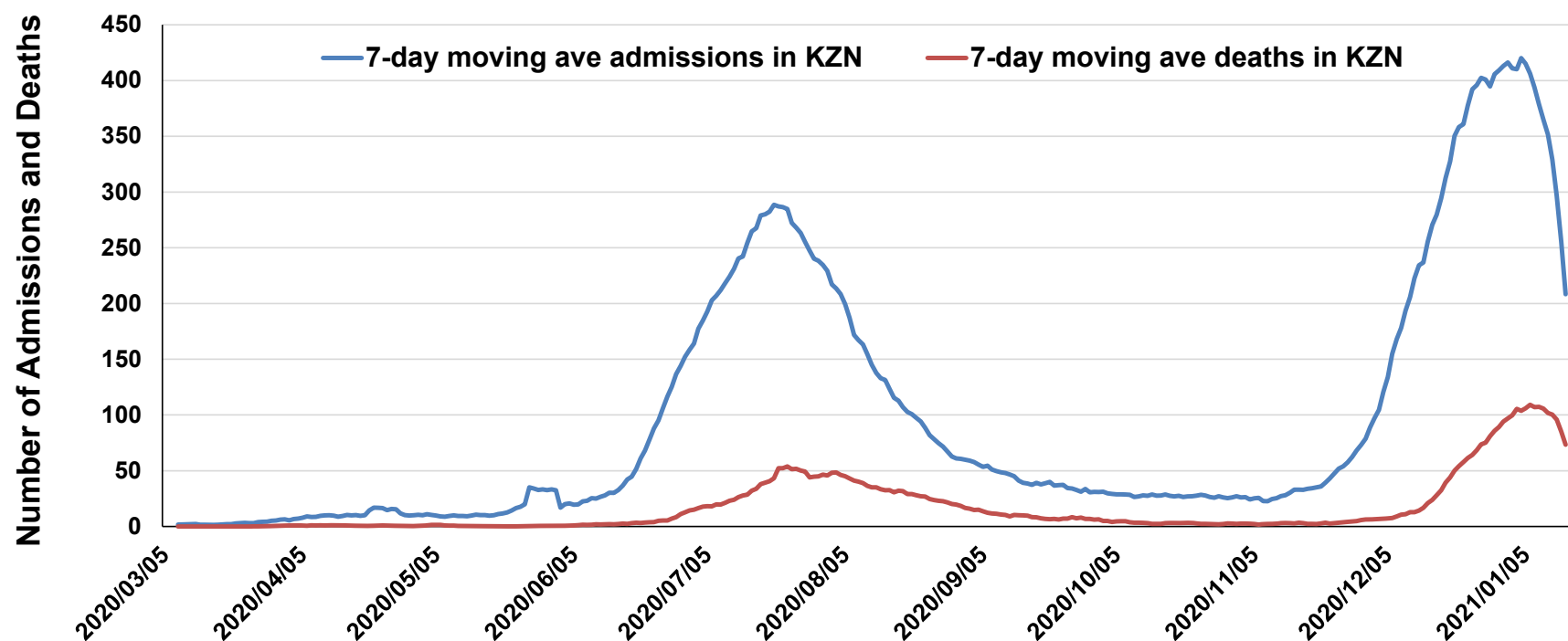
(7-day moving average up 17 January 2021)



Analysis: Amanda Brewer; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD

# KwaZulu-Natal daily hospital admissions and in-hospital deaths

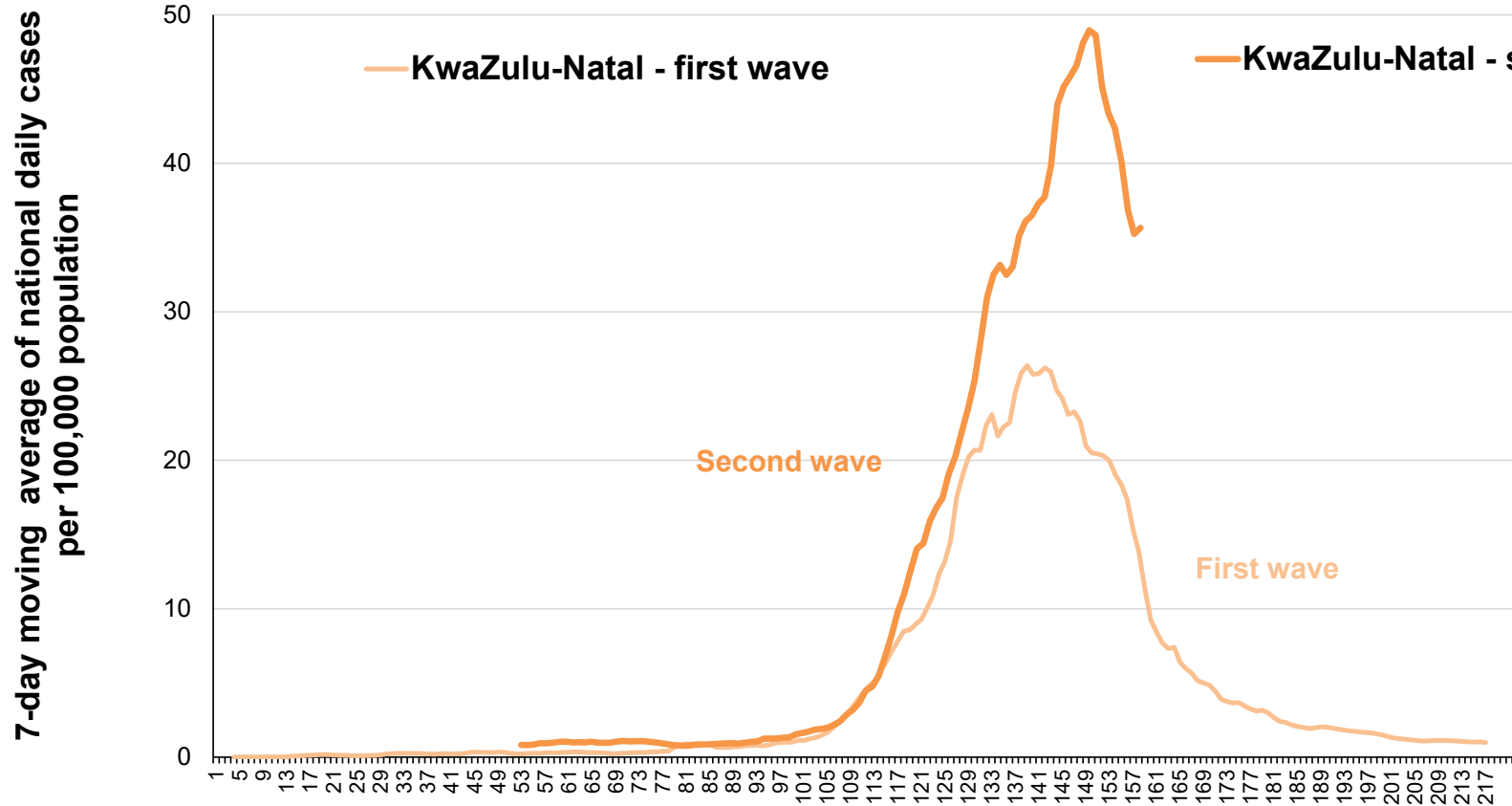
(7-day moving average up 17 January 2021)



Analysis: Amanda Brewer; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD

# SARS-CoV-2 cases in 1<sup>st</sup> & 2<sup>nd</sup> wave in KwaZulu-Natal

(7-day moving average cases per 100,000 population – up to 17 January)

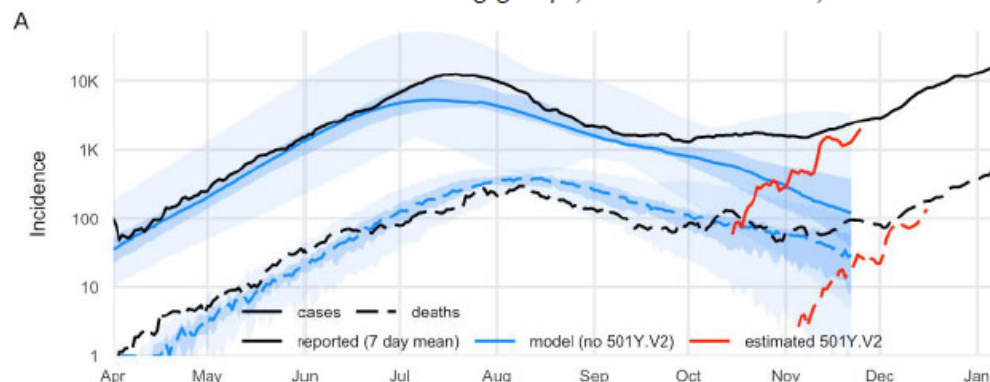


# How much faster is it spreading in SA's 2<sup>nd</sup> wave?



## Estimates of severity and transmissibility of novel South Africa SARS-CoV-2 variant 501Y.V2

Carl AB Pearson<sup>1,2</sup>, Timothy W Russell<sup>1</sup>, Nicholas G Davies<sup>1</sup>, Adam J Kucharski<sup>1</sup>, CMMID COVID-19 working group<sup>1</sup>, W John Edmunds<sup>1</sup>, Rosalind M Eggo<sup>1</sup>.



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

- Days to reach 100,000 cases in the 1<sup>st</sup> & 2<sup>nd</sup> wave:
  - Western Cape: **50% faster** 107 vs 54 days
  - KwaZulu-Natal: **39% faster** 54 vs 33 days
- Caveats: confounding by behaviour, testing, reporting, etc

Source: Cheryl Baxter, CAPRISA

# How does 501Y.V2 compare with B.1.1.7 variant?



## Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England

Nicholas G. Davies<sup>1</sup>, Rosanna C. Barnard\*, Christopher I. Jarvis\*, Adam J. Kucharski\*, James Munday\*, Carl A. B. Pearson\*, Timothy W. Russell\*, Damien C. Tully\*, Sam Abbott, Amy Gimma, William Waites, Kerry LM Wong, Kevin van Zandvoort, CMMID COVID-19 Working Group, Rosalind M. Eggo, Sebastian Funk, Mark Jit, Katherine E. Atkins, W. John Edmunds

- **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**



# Key questions addressed in this update

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- 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? *Not yet! Working on it*

## 4. Do antibodies from SA's 1<sup>st</sup> wave kill the 501Y.V2 variant of the 2<sup>nd</sup> wave?

Conclusion & next steps

# Is 501Y.V2 associated with increased admissions?

- When the Western Cape and KwaZulu-Natal reached 100,000 cases in 1<sup>st</sup> & 2<sup>nd</sup> 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

# Admission disease profile in WC similar in both waves

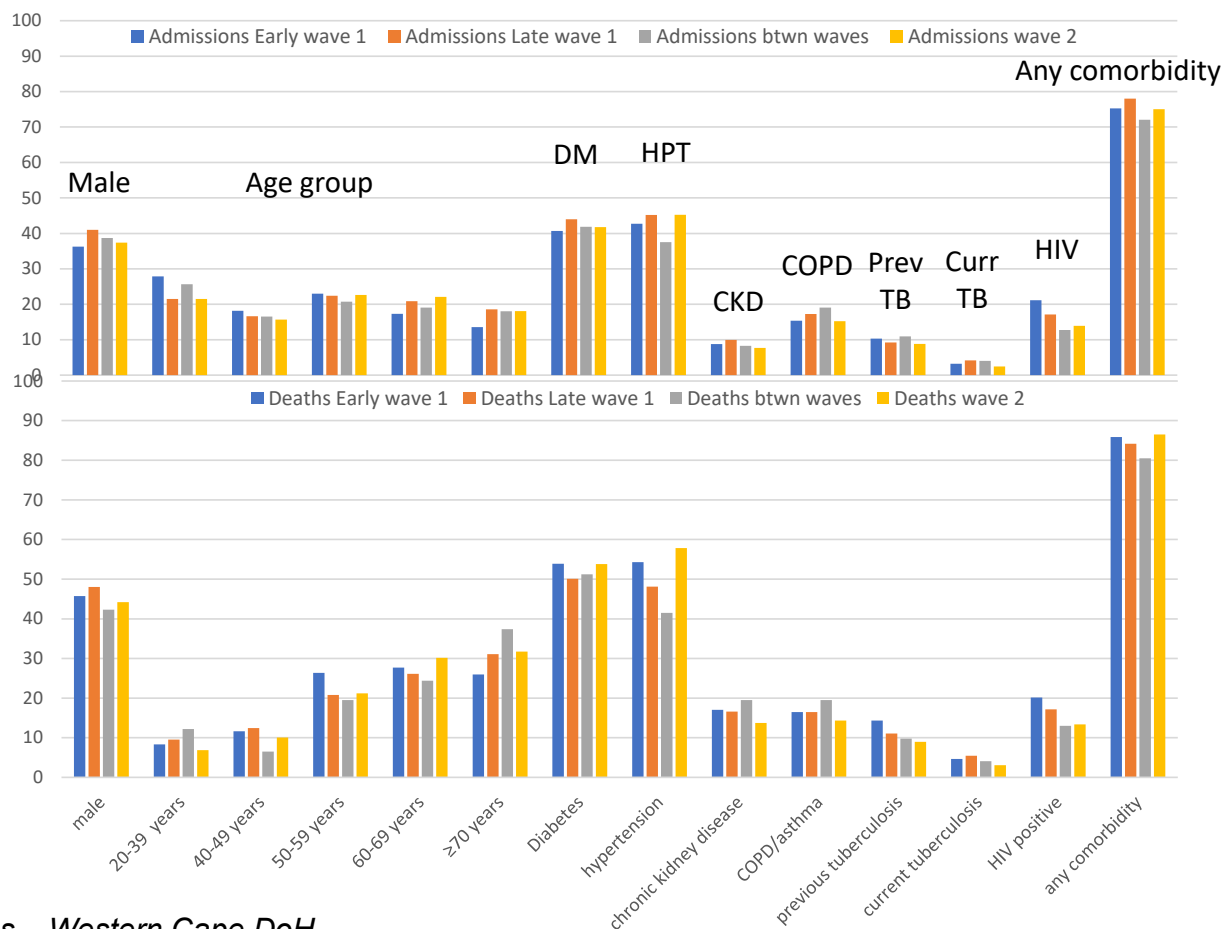
## Wave period

**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”

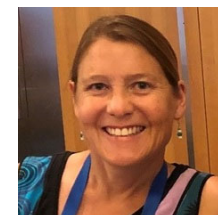
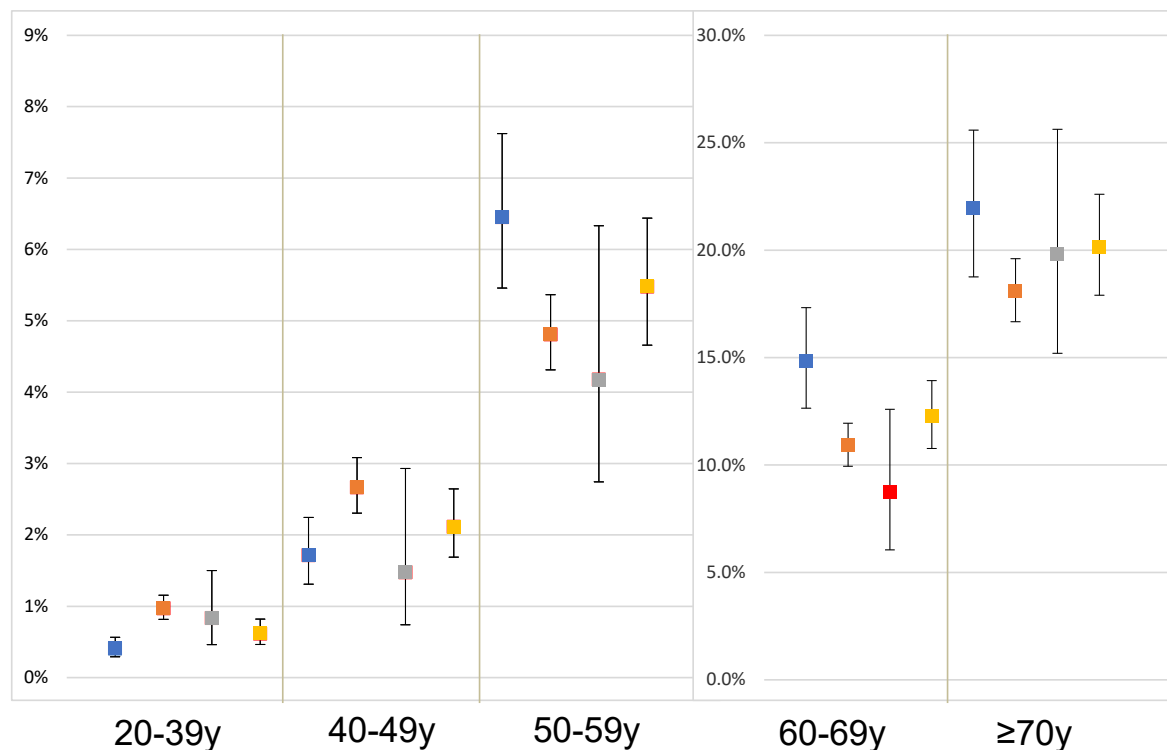
Wave period from L-R

**Early wave 1:**  
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**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”**

**Note: different y-axis  
for age ≥60 years**

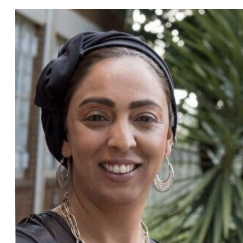
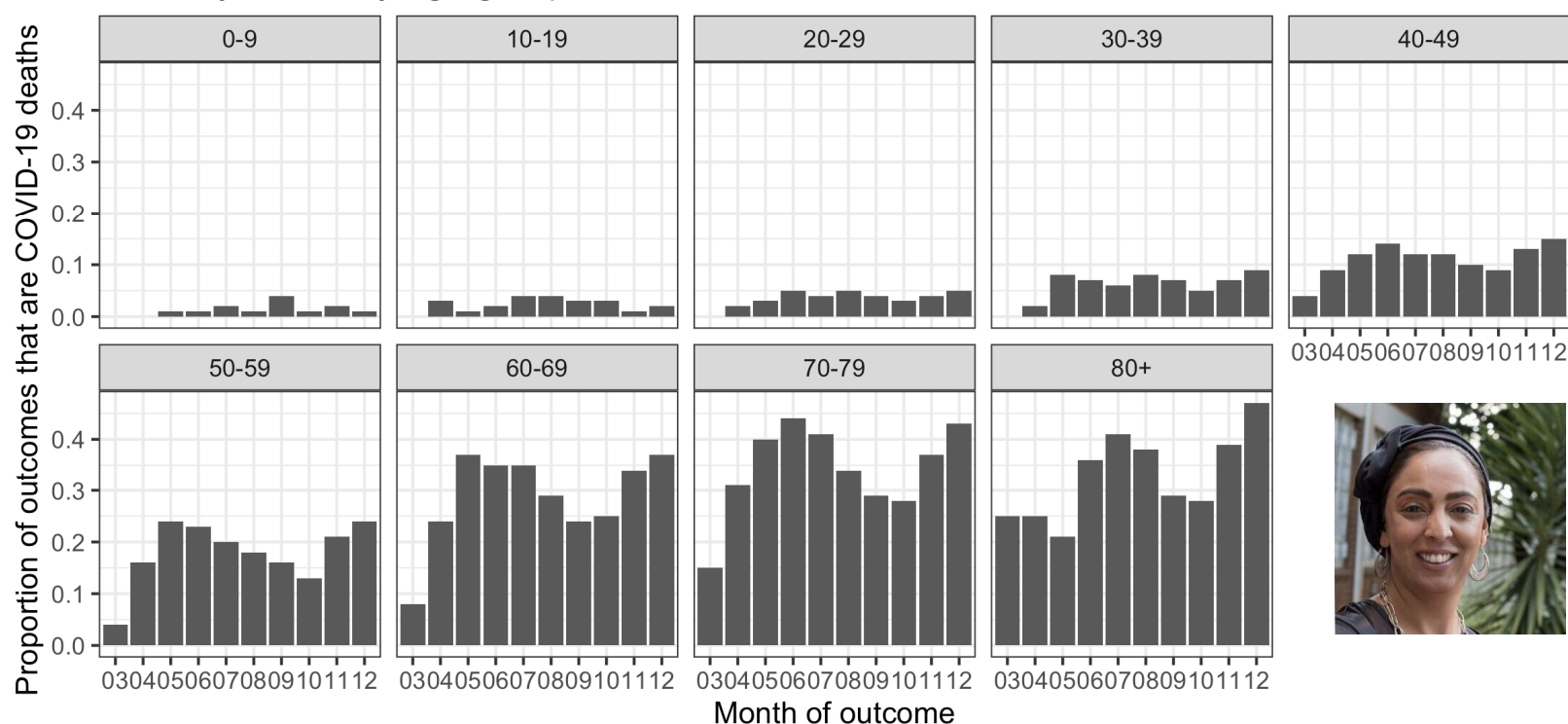
**No difference in mortality by age group between waves**

Source: Mary-Ann Davies – Western Cape DoH

# Covid-19 in-hospital monthly case-fatality-ratio by age group shows little change across waves

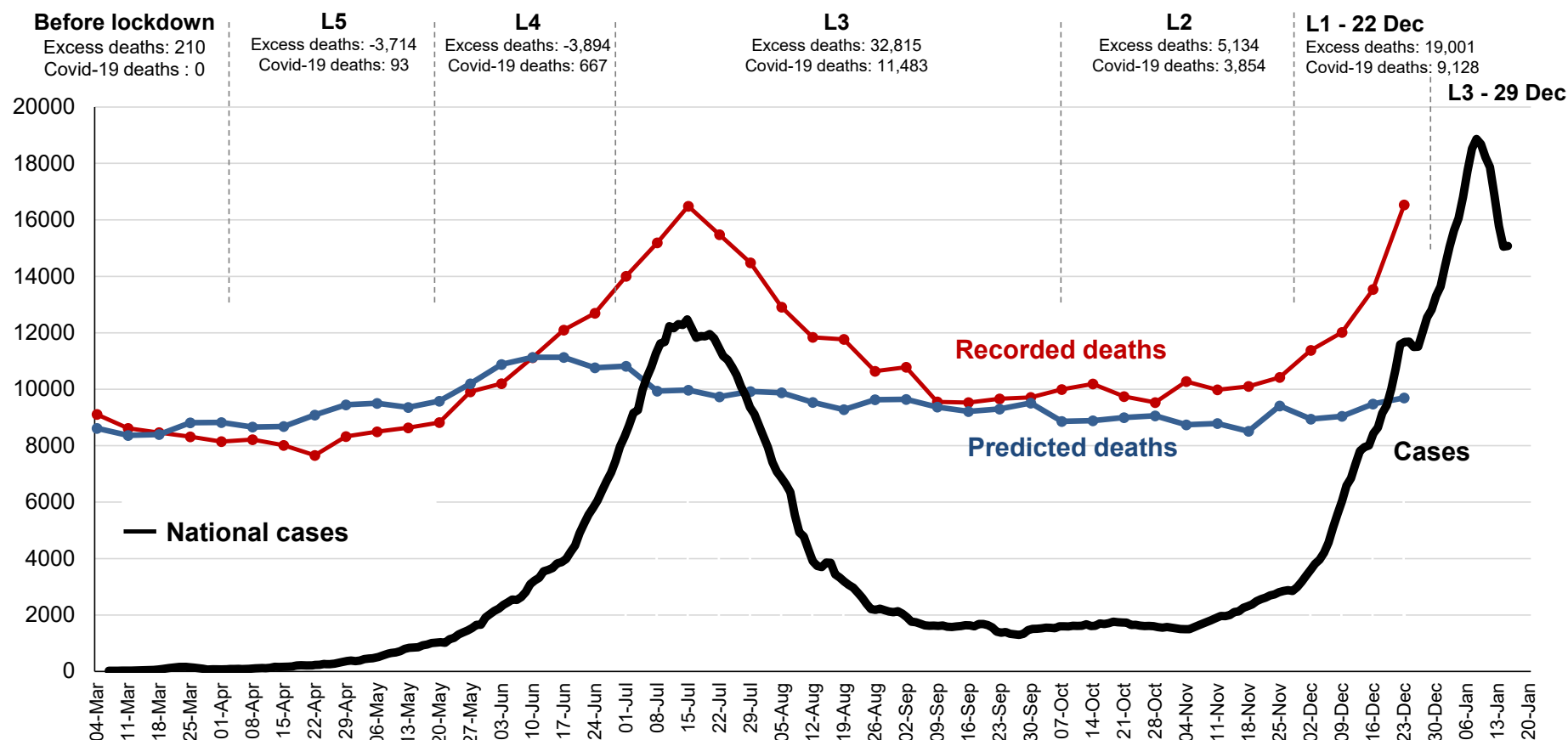
5 March 2020 - 9 January 2021

Mortality trends by age group



Analysis: Juliet Pulliam from SACEMA; Data source: Lucille Blumberg, Waasila Jassat & Richard Welch – DATCOV, NICD

# Expected & actual all-cause deaths during Covid-19



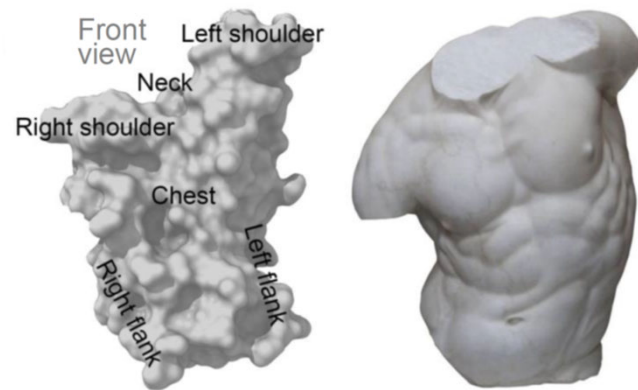
Source: Bradshaw D, et al



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**Conclusion & next steps**

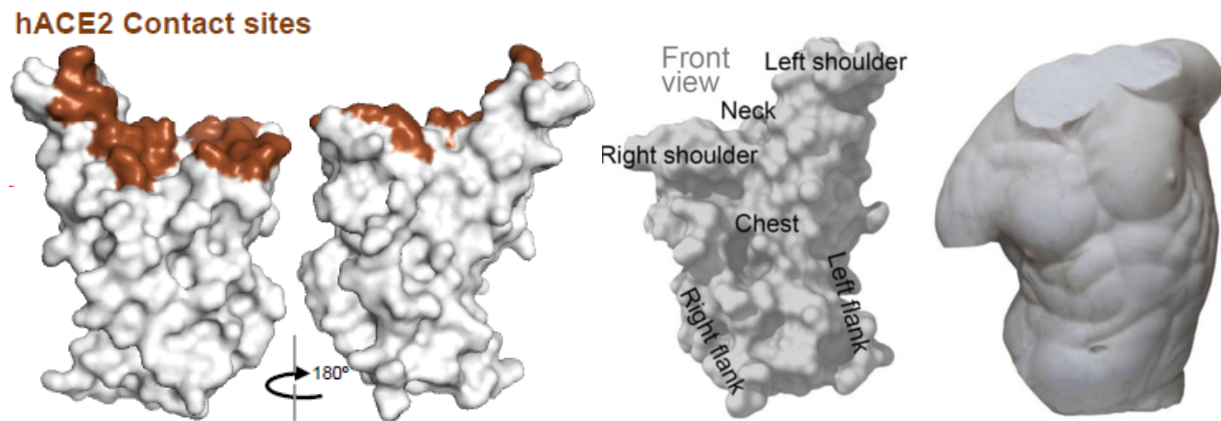


Source: <https://ssrn.com/abstract=3725763> & Dejnirattisai W. The antigenic anatomy of SARS-CoV-2 receptor binding domain, 2020 (Pre-print)



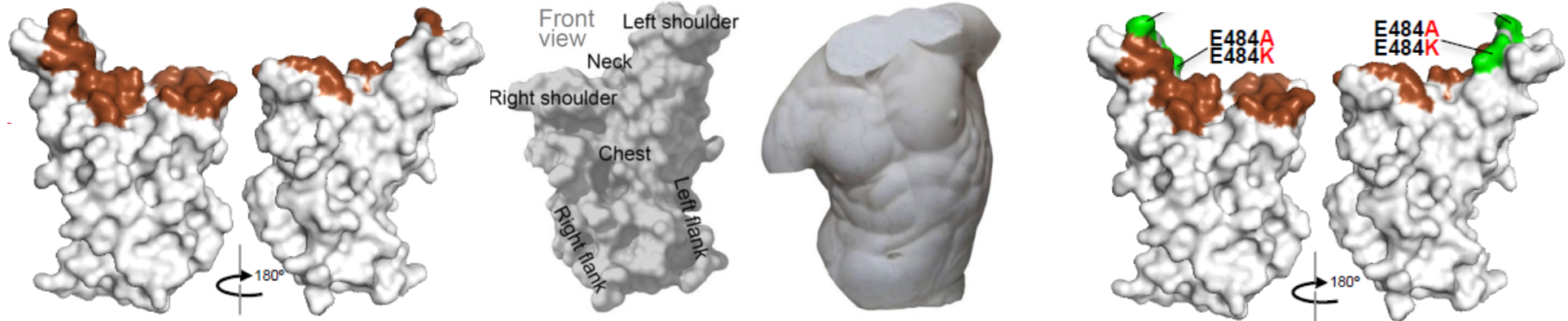
## Immune responses target 2 main areas of the spike protein:

- 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)

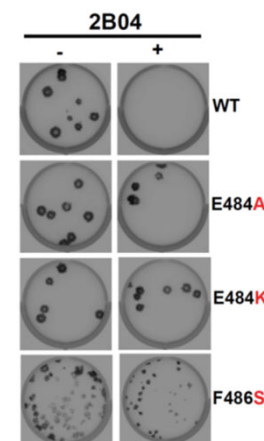
### hACE2 Contact sites



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

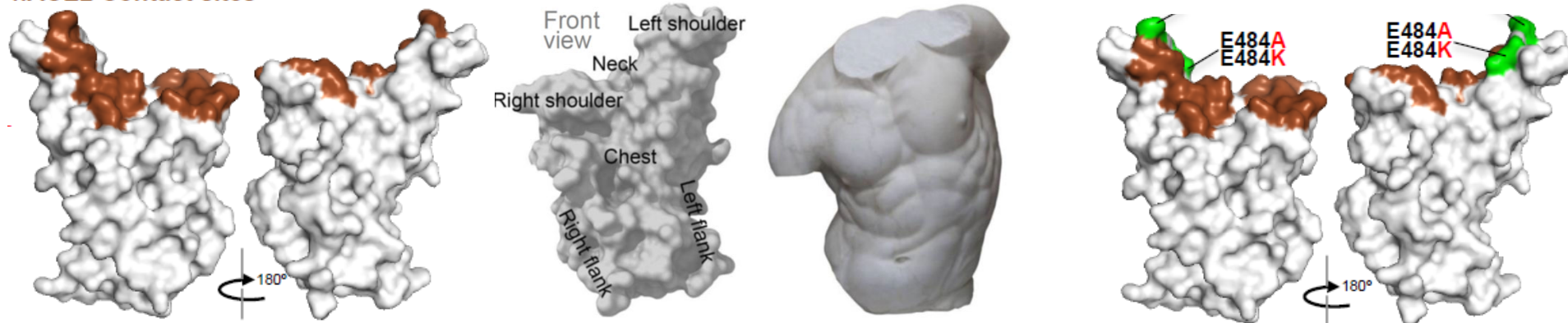
**Landscape analysis of escape variants identifies SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization**

Zhuoming Liu<sup>1,6</sup>, Laura A. VanBlargan<sup>2,6</sup>, Paul W. Rothlauf<sup>1,3</sup>, Louis-Marie Bloyet<sup>1</sup>, Rita E. Chen<sup>2,4</sup>, Spencer Stumpf<sup>1</sup>, Haiyan Zhao<sup>4</sup>, John M. Errico<sup>4</sup>, Elitza S. Theel<sup>5</sup>, Ali H. Ellebedy<sup>1,4</sup>, Daved H. Fremont<sup>4</sup>, Michael S. Diamond<sup>1,2,4,\*</sup>, and Sean P. J. Whelan<sup>1,7\*</sup>



**Convalescent sera from 4 patients were not able to neutralize viruses with a 484 mutation, which alters the charge & shape of the RBD**

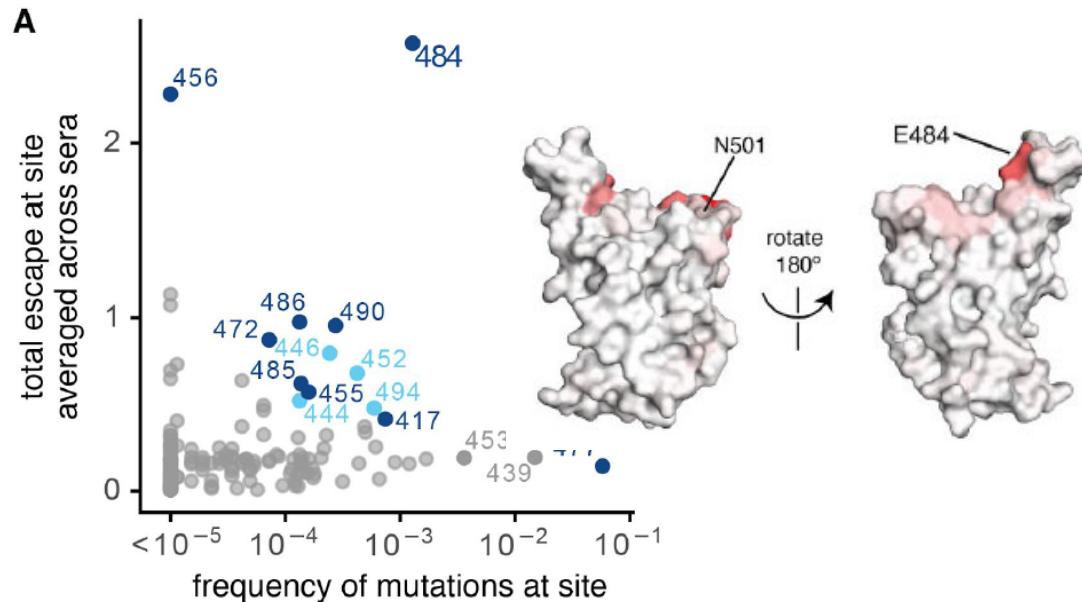
**hACE2 Contact sites**



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

# Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies

Allison J. Greaney<sup>1,2</sup>, Andrea N. Loes<sup>1,3</sup>, Katharine H.D. Crawford<sup>1,2</sup>, Tyler N. Starr<sup>1,3</sup>, Keara D. Malone<sup>1</sup>, Helen Y. Chu<sup>4</sup>, Jesse D. Bloom<sup>1,3,#</sup>



**E484 mutations reduced antibody binding in 9 of 11 convalescent serum samples, with some sera >10-fold reduction in neutralization**

**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 2<sup>nd</sup> wave than 1<sup>st</sup> 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 New York Times**

## **Pope Francis: A Crisis Reveals What Is in Our Hearts**

To come out of this pandemic better than we went in, we must let ourselves be touched by others' pain.



**“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**





**Dr Richard Lessels**

Senior Infectious Diseases Specialist,  
based at the KwaZulu-Natal Research  
Innovation & Sequencing Platform



**Prof Penny Moore**

DSI/NRF South African Research  
Chair of Virus-Host Dynamics at WITS  
and the NICD



**Prof Alex Sigal**

Virologist at the Africa Health Research  
Institute and a Research Group Leader  
at the Max Planck Institute



**Prof Koleka Mlisana**

Executive Manager of Academic  
Affairs, Research & Quality  
Assurance at the National Health  
Laboratory Services



**Prof Mary-Ann Davies**

Public Health Medicine Specialist  
responsible for epidemiology and  
surveillance in the Western Cape  
Department of Health



**Dr Waasila Jassat**

Medical doctor and public health  
medicine specialist. She heads the  
DATCOV Hospital Surveillance for  
COVID-19 at NICD



**Prof Willem Hanekom**

Leading TB and vaccines expert  
who leads the Africa Health  
Research Institute



**Prof Tulio de Oliveira**

Bioinformatician who directs the  
KwaZulu-Natal Research and  
Innovation Sequencing Platform at  
UKZN