



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 DST-NRF Centre of Excellence in HIV Prevention



National Research Foundation



CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy



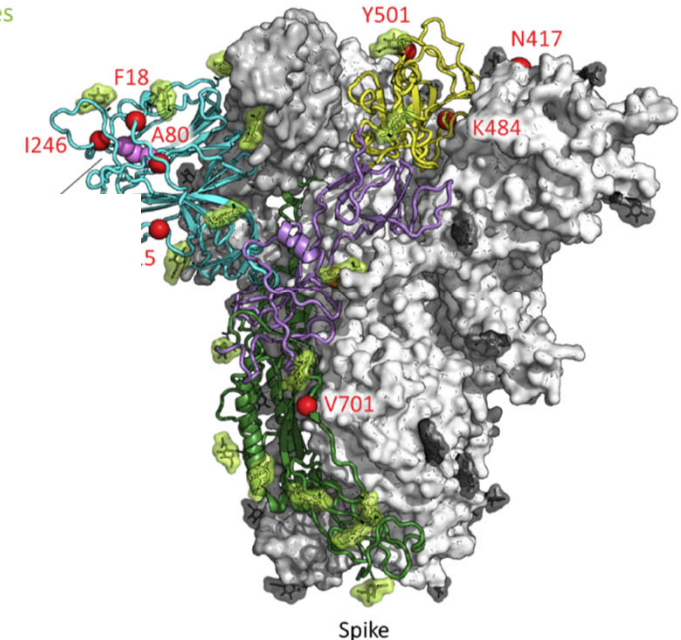
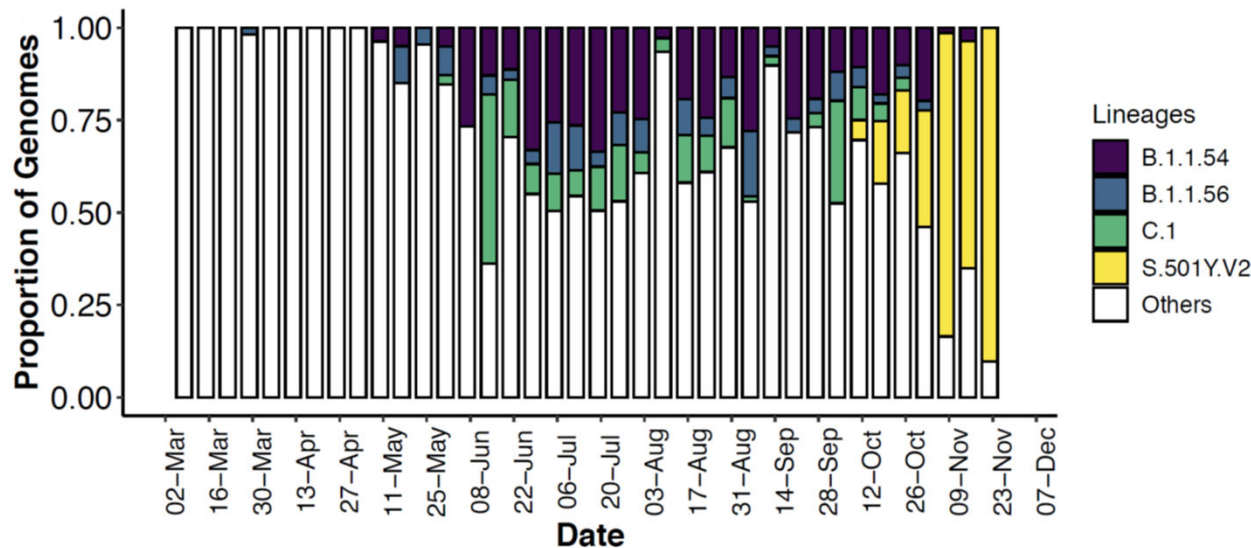
CAPRISA hosts a MRC HIV-TB Pathogenesis and Treatment Research Unit
CAPRISA hosts a DoH-MRC Special Initiative for HIV Prevention Technology



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^{1*}, Eduan Wilkinson^{1*}, Marta Giovanetti^{2,3*}, Arash Iranzadeh^{4*}, Vagner Fonseca^{1,2}, Jennifer Giandhari¹, Deelan Doolabh⁵, Sureshnee Pillay¹, Emmanuel James San¹, Nokukhanya Msoni⁶, Koleka Mlisana^{7,8}, Anne von Gottberg^{9,10}, Sibongile Walaza^{9,11}, Mushal Allam⁹, Arshad Ismail⁹, Thabo Mohale⁹, Allison J Glass^{10,12}, Susan Engelbrecht¹³, Gert Van Zyl¹³, Wolfgang Preiser¹³, Francesco Petruccione^{14,15}, Alex Sigal^{16,17,18}, Diana Hardie¹⁹, Gert Marais¹⁹, Marvin Hsiao¹⁹, Stephen Korsman¹⁹, Mary-Ann Davies^{20,21}, Lynn Tyers⁵, Innocent Mudau⁵, Denis York²², Caroline Maslo²³, Dominique Goedhals²⁴, Shareef Abrahams²⁵, Oluwakemi Laguda-Akingba^{25,26}, Arghavan Alisoltani-Dehkordi^{27,28}, Adam Godzik²⁸, Constantinos Kurt Wibmer⁹, Bryan Trevor Sewell²⁹, José Lourenço³⁰, Luiz Carlos Junior Alcantara^{2,3}, Sergei L Kosakovsky Pond³¹, Steven Weaver³¹, Darren Martin^{4,5}, Richard J Lessells^{1,8}, Jinal N Bhiman^{9,10*}, Carolyn Williamson^{5,8,19*}, Tulio de Oliveira^{1,8,32*}

- 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 2nd 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?

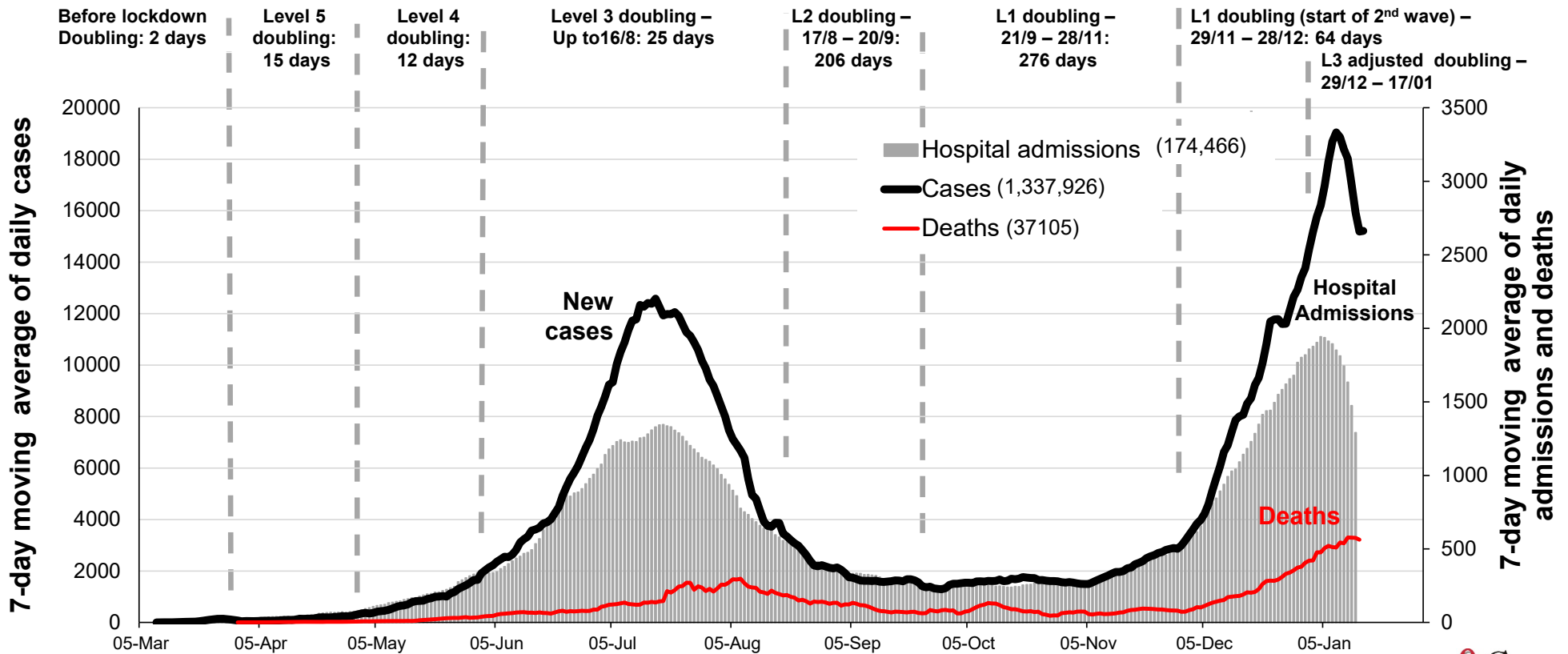
3. Any new evidence on whether Covid-19 vaccines are effective or not against the 501Y.V2 variant?

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

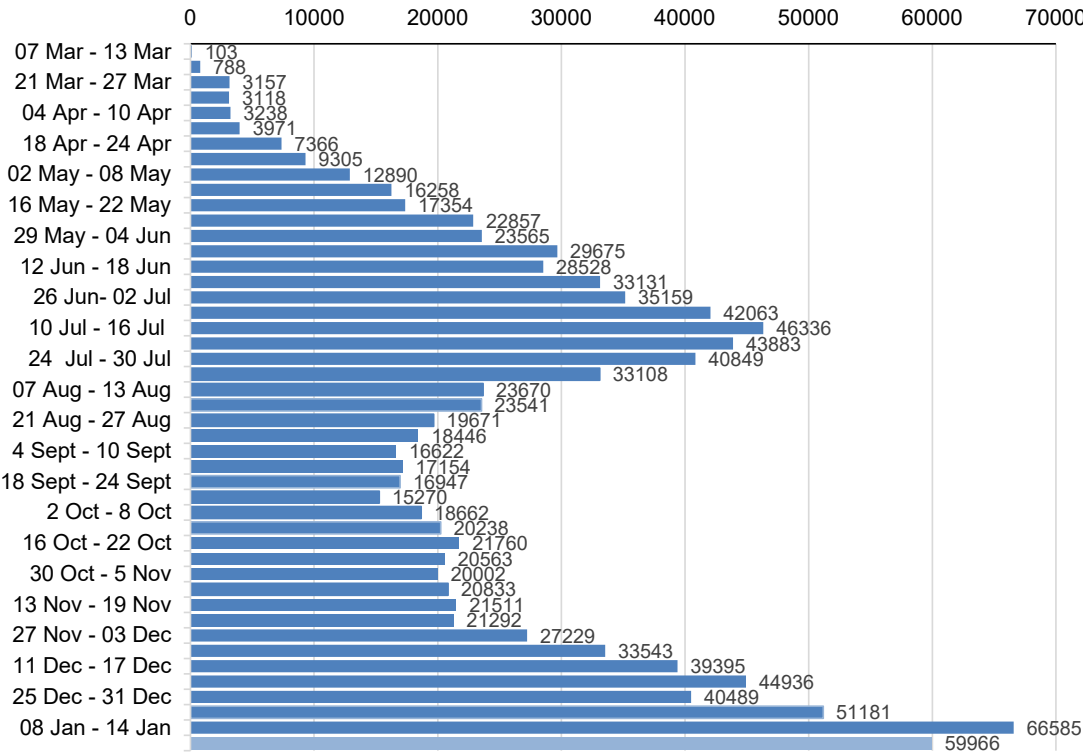
Filip Fratev^{1,2}

- **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**

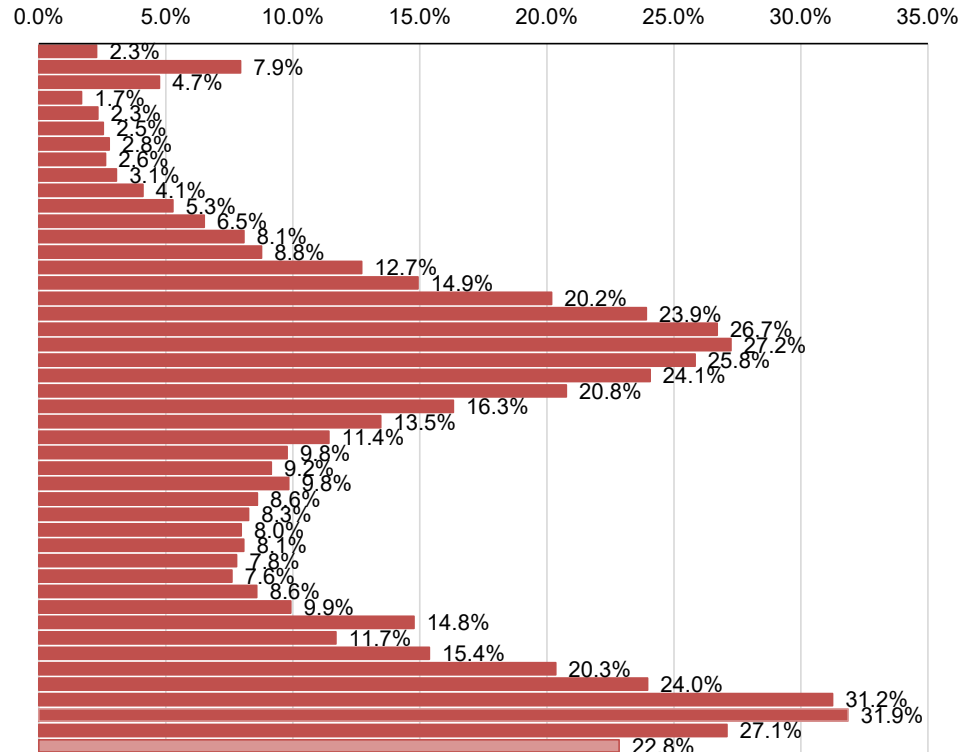
RBD = receptor-binding domain of the spike protein; ACE2 = angiotensin converting enzyme-2

Average daily tests & proportion of positive tests

Average daily number of tests each week



Average weekly proportion of tests positive



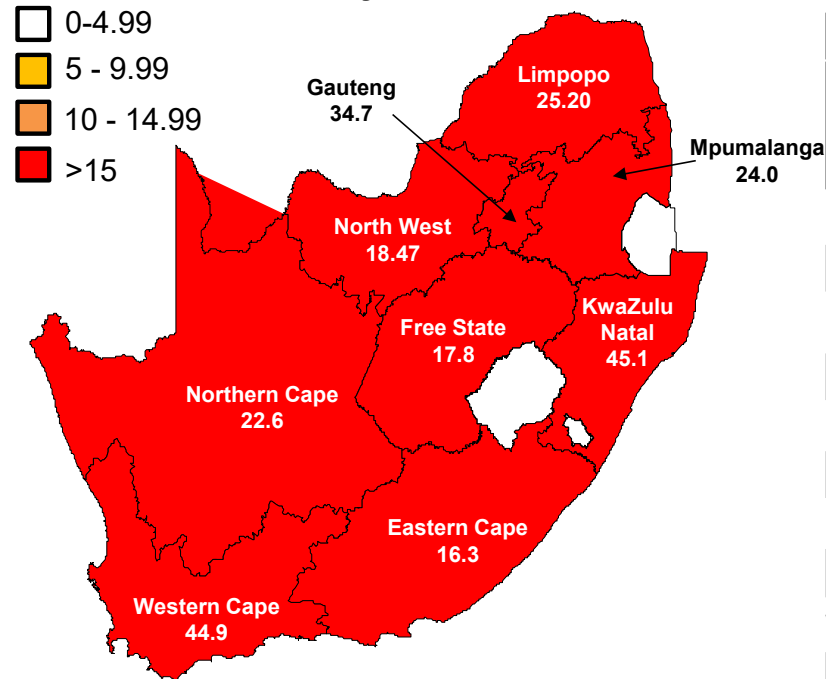
Lighter shade is an incomplete week

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

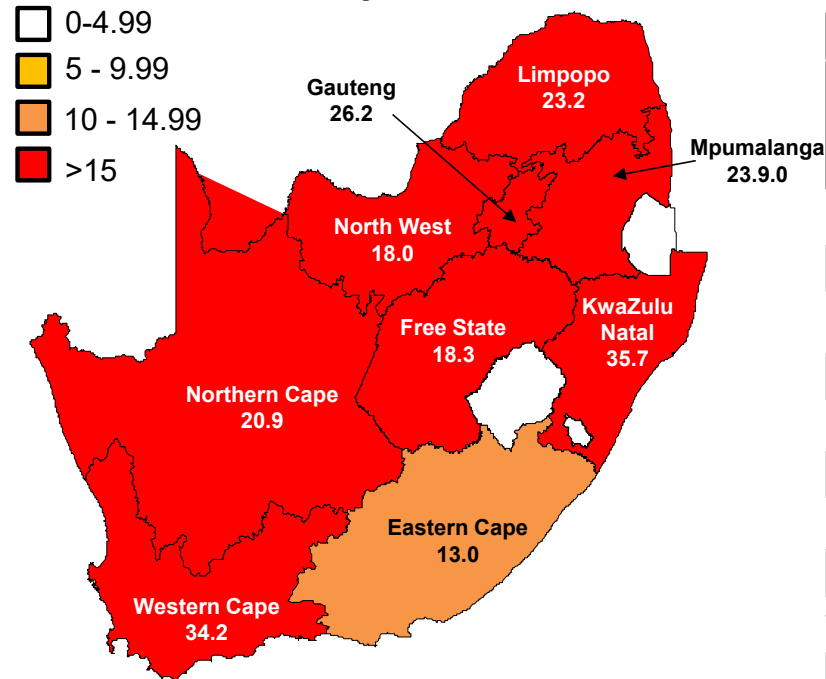


Province	Population /100,000	29 Dec – 4 Jan		5 Jan – 11 Jan		Increase / decrease
		7-day ave on 1 Jan	Cases /100,000 /day	7-day ave on 8 Jan	Cases /100,000 /day	
EC	67	952	14.8	1041	16.3	+8.5%
FS	29	301	9.2	513	17.8	+41.3%
GP	152	3583	23.6	5291	34.7	+32.3%
KZN	113	4498	39.8	5088	45.1	+11.6%
LP	60	777	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

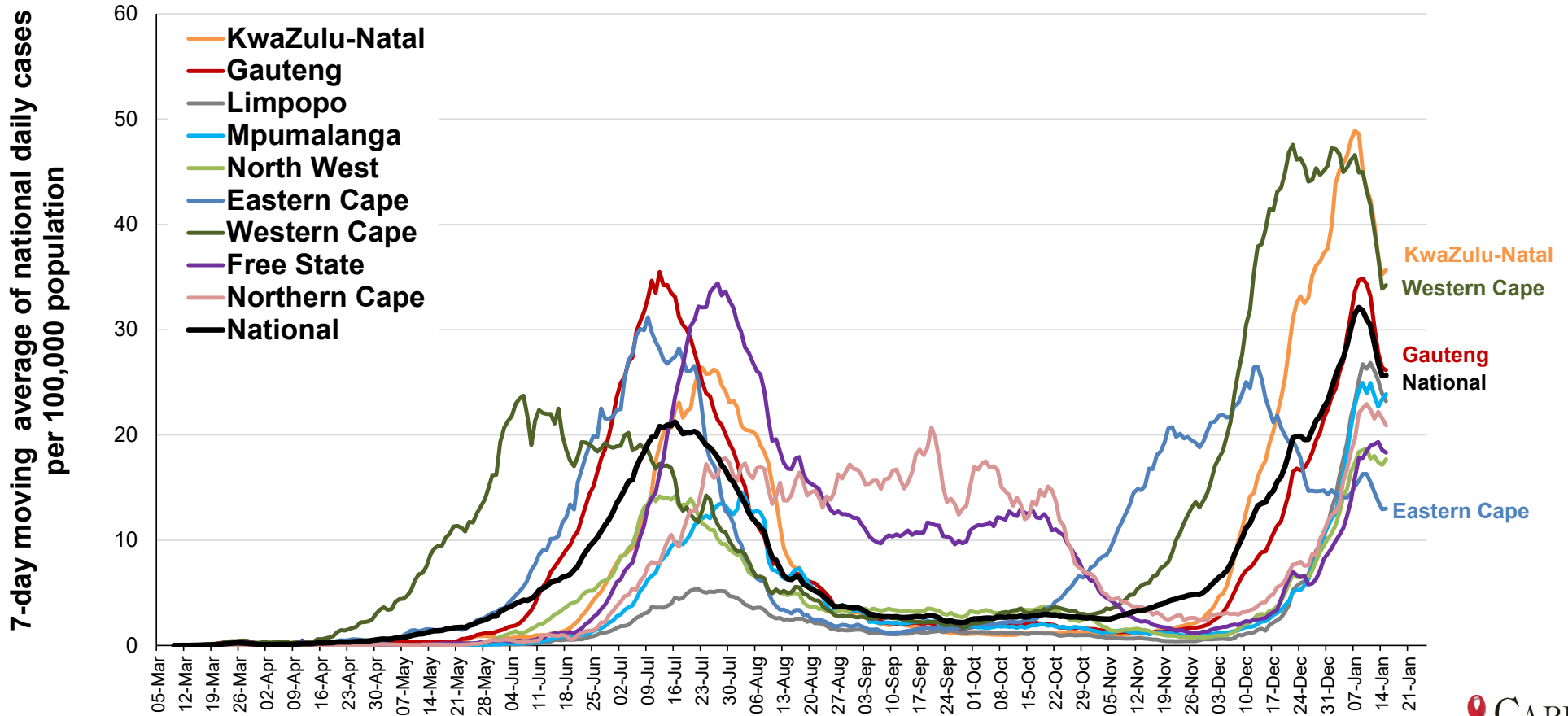
Cases /100,000 /day



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%

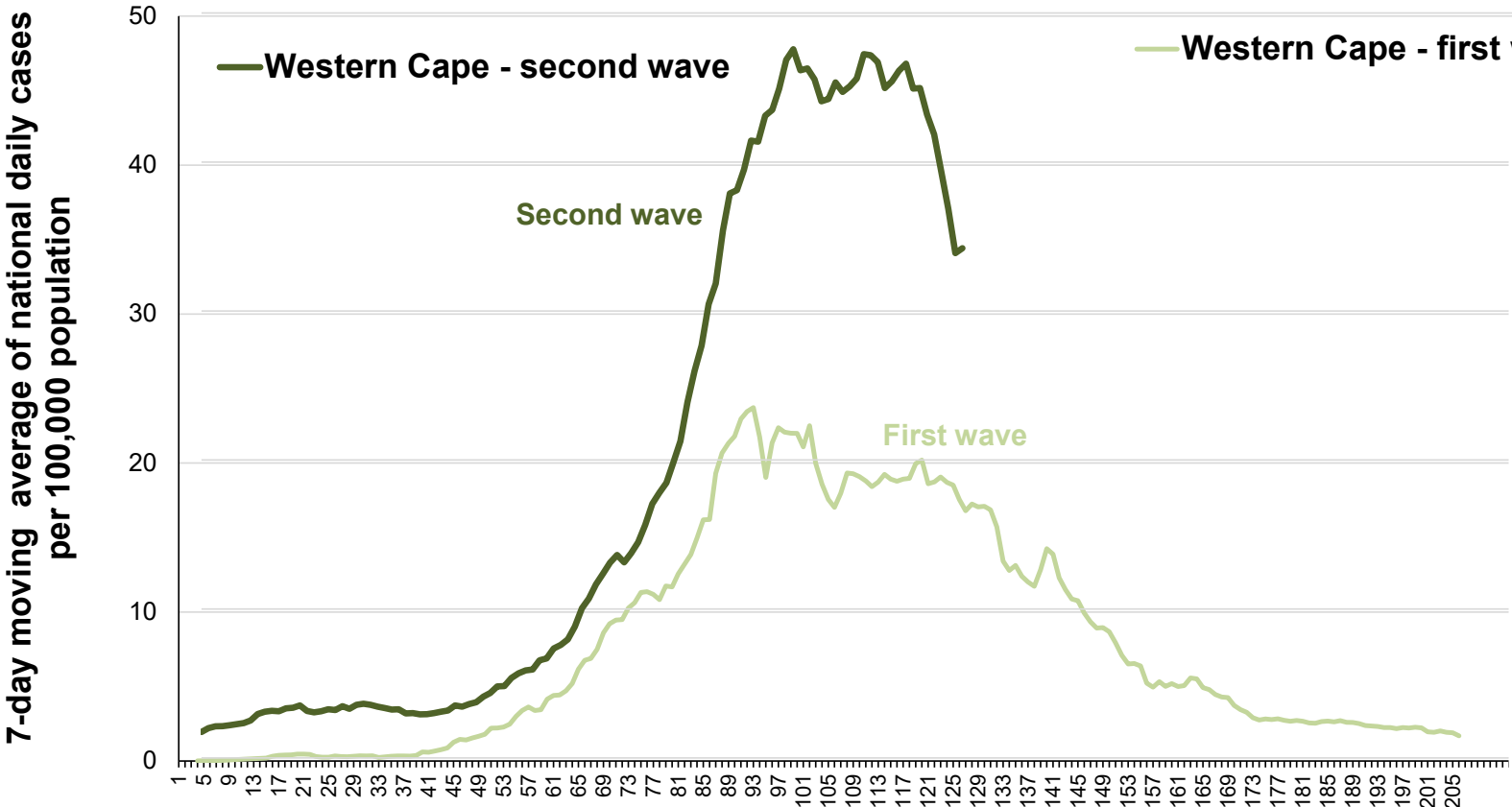
Confirmed SARS-CoV-2 cases by province

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



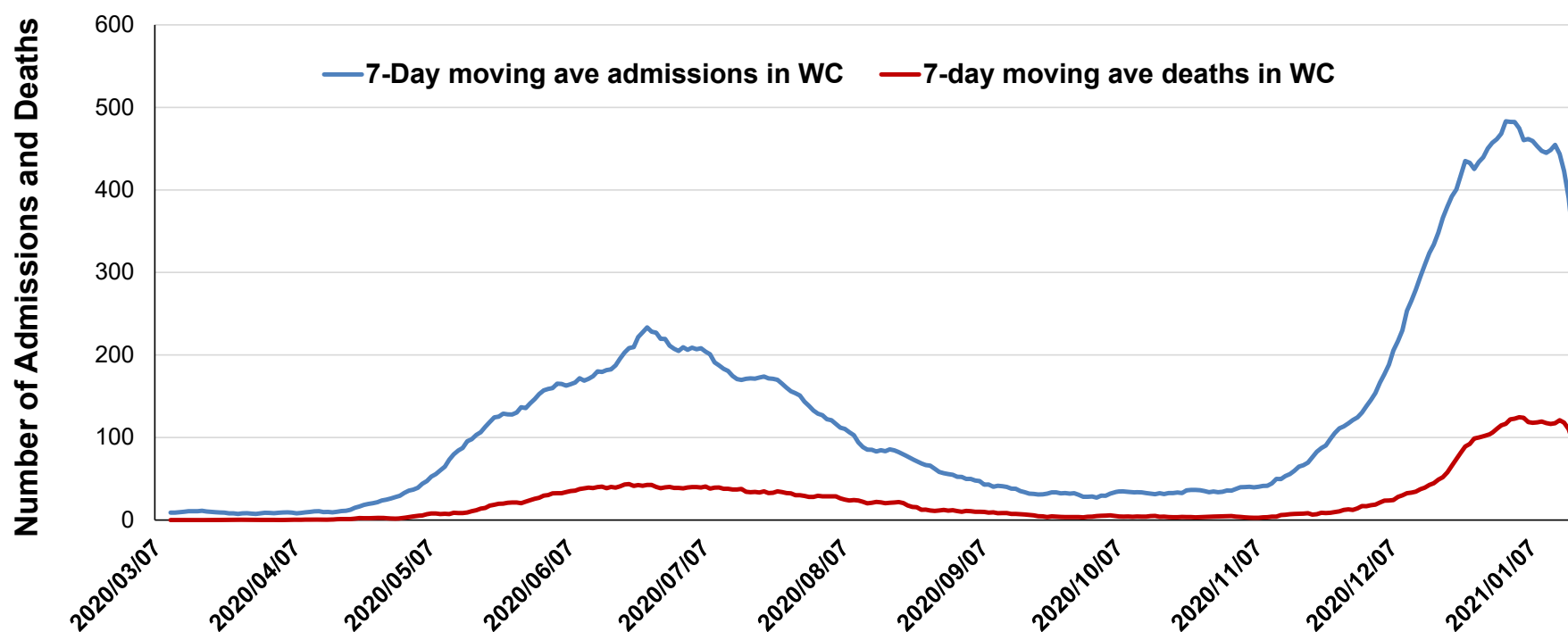
SARS-CoV-2 cases in 1st & 2nd waves in Western Cape

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



Western Cape daily hospital admissions and in-hospital deaths

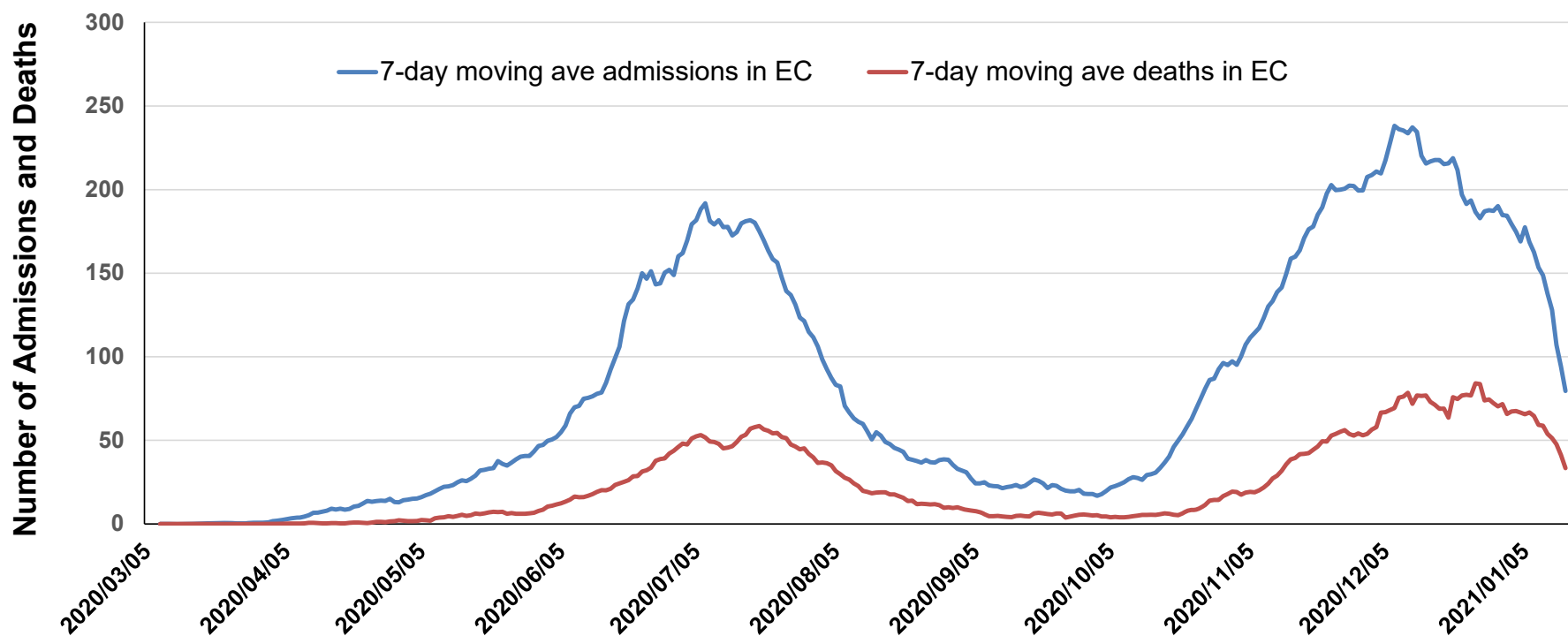
(7-day moving average up 17 January 2021)



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

Eastern Cape daily hospital admissions and in-hospital deaths

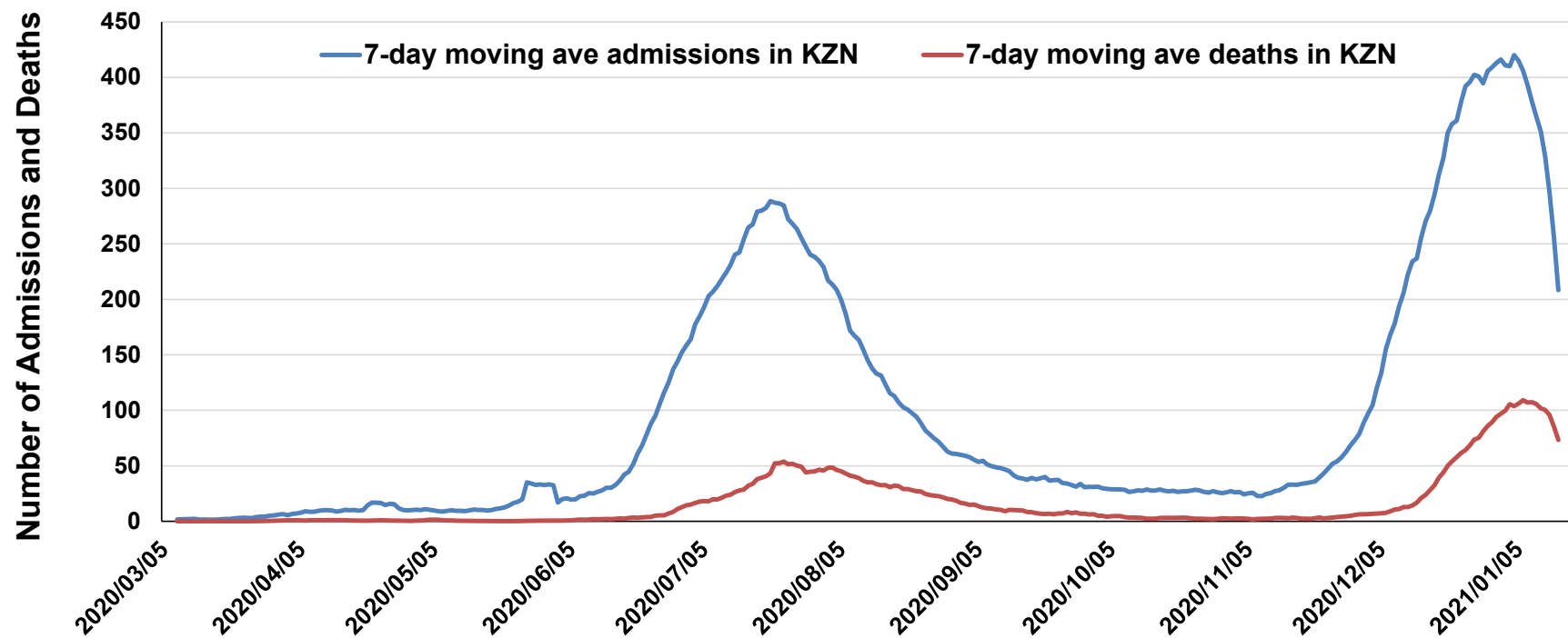
(7-day moving average up 17 January 2021)



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

KwaZulu-Natal daily hospital admissions and in-hospital deaths

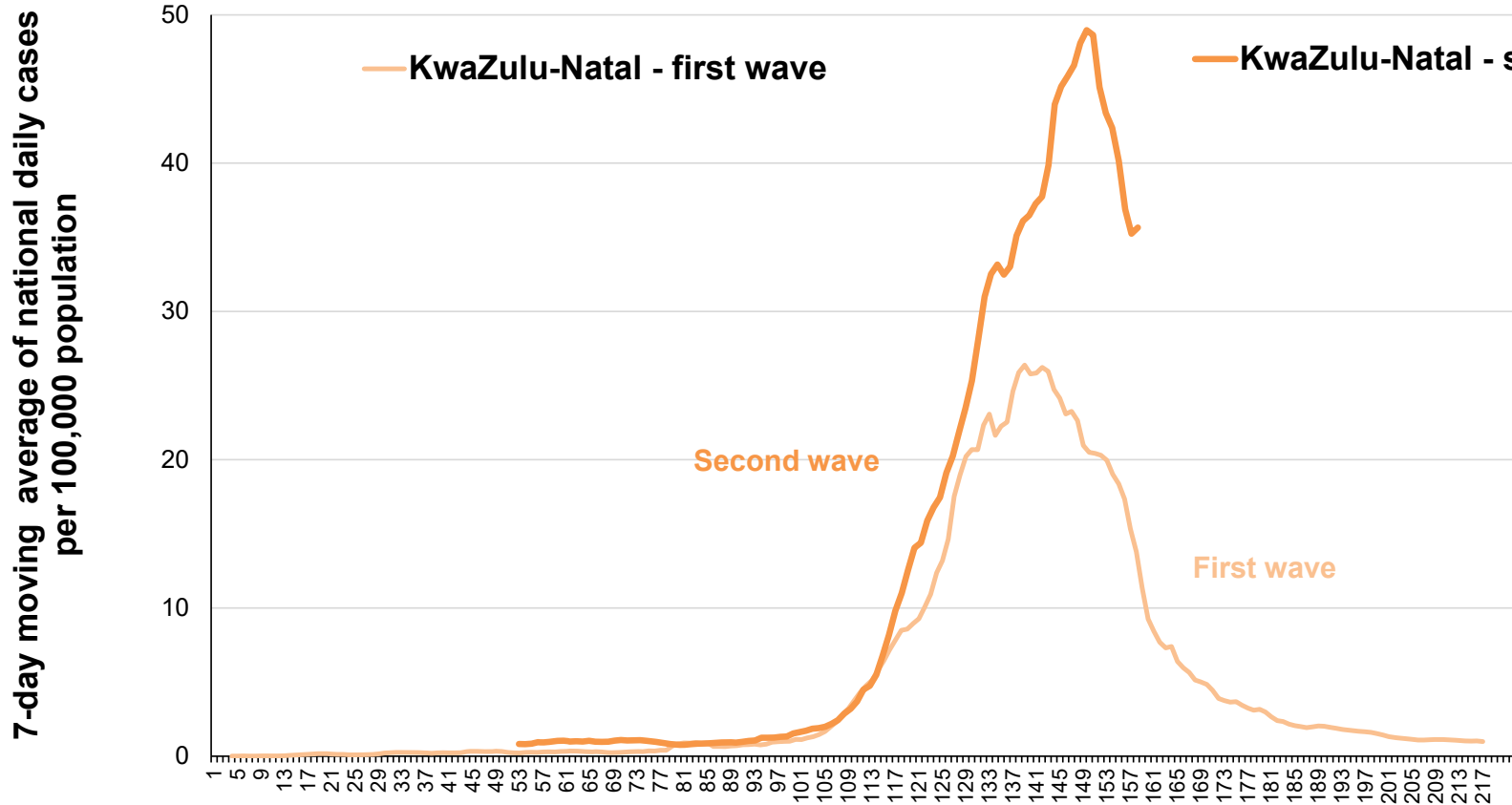
(7-day moving average up 17 January 2021)



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

SARS-CoV-2 cases in 1st & 2nd wave in KwaZulu-Natal

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

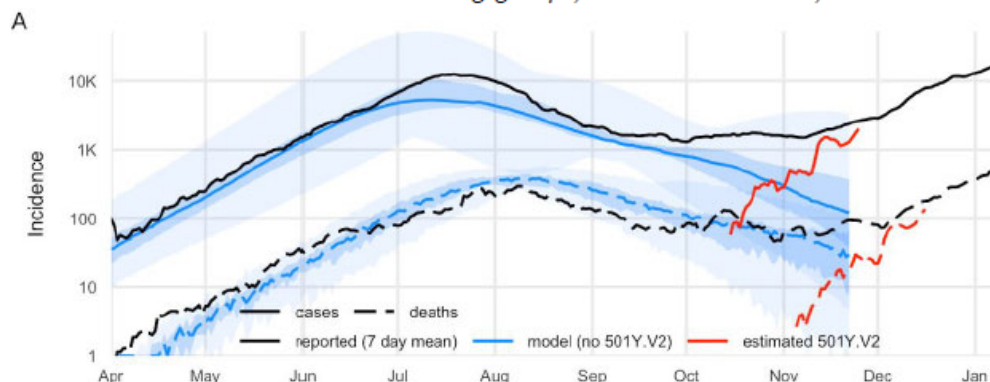


How much faster is it spreading in SA's 2nd wave?



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

Carl AB Pearson^{1,2}, Timothy W Russell¹, Nicholas G Davies¹, Adam J Kucharski¹, CMMID
COVID-19 working group¹, W John Edmunds¹, Rosalind M Eggo¹.



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

- 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

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. Davies¹, 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**

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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 1st & 2nd 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

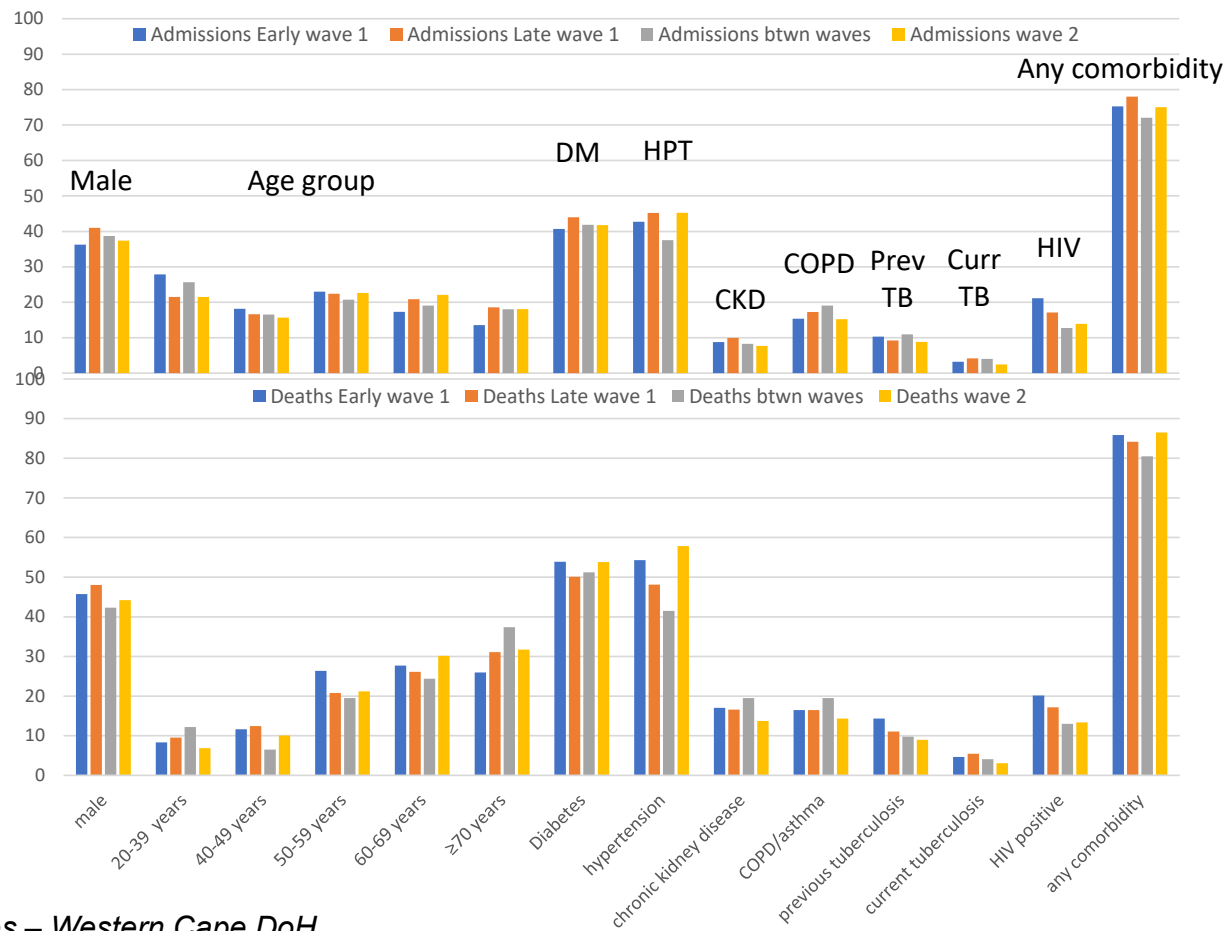
Wave period

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”

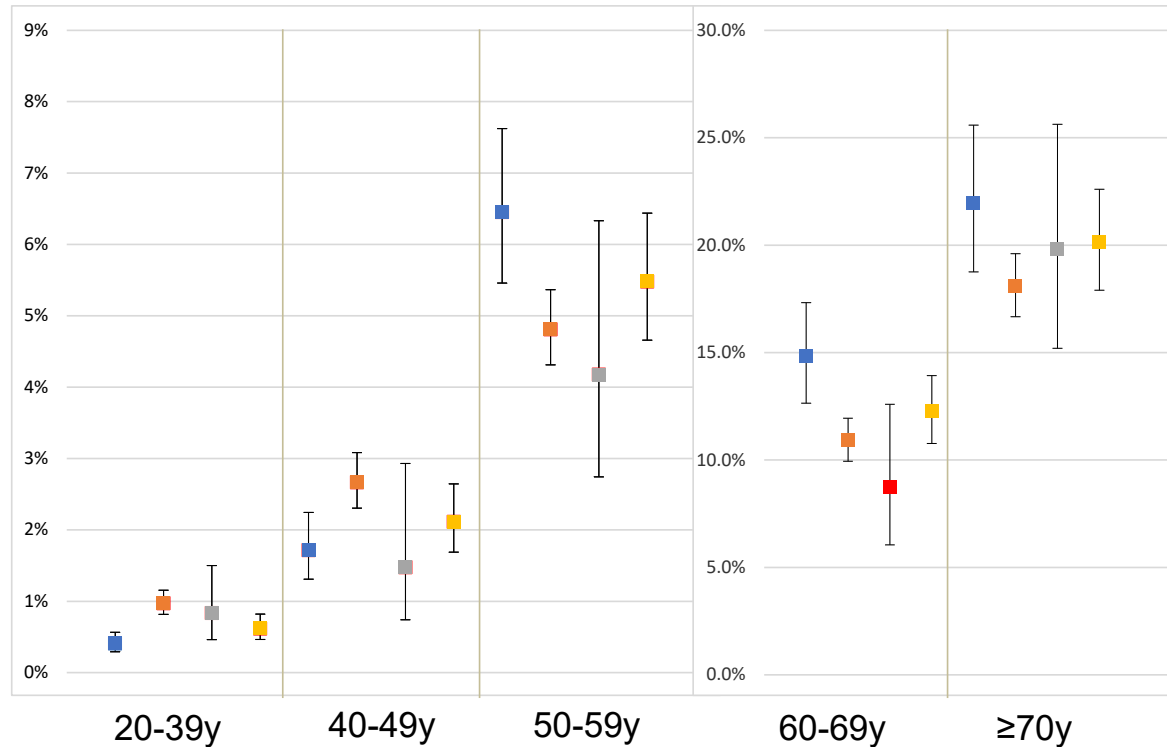
Wave period from L-R

Early wave 1:
<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”

Note: different y-axis for age ≥60 years

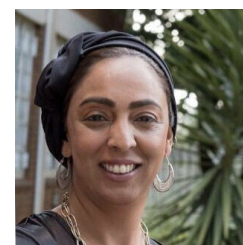
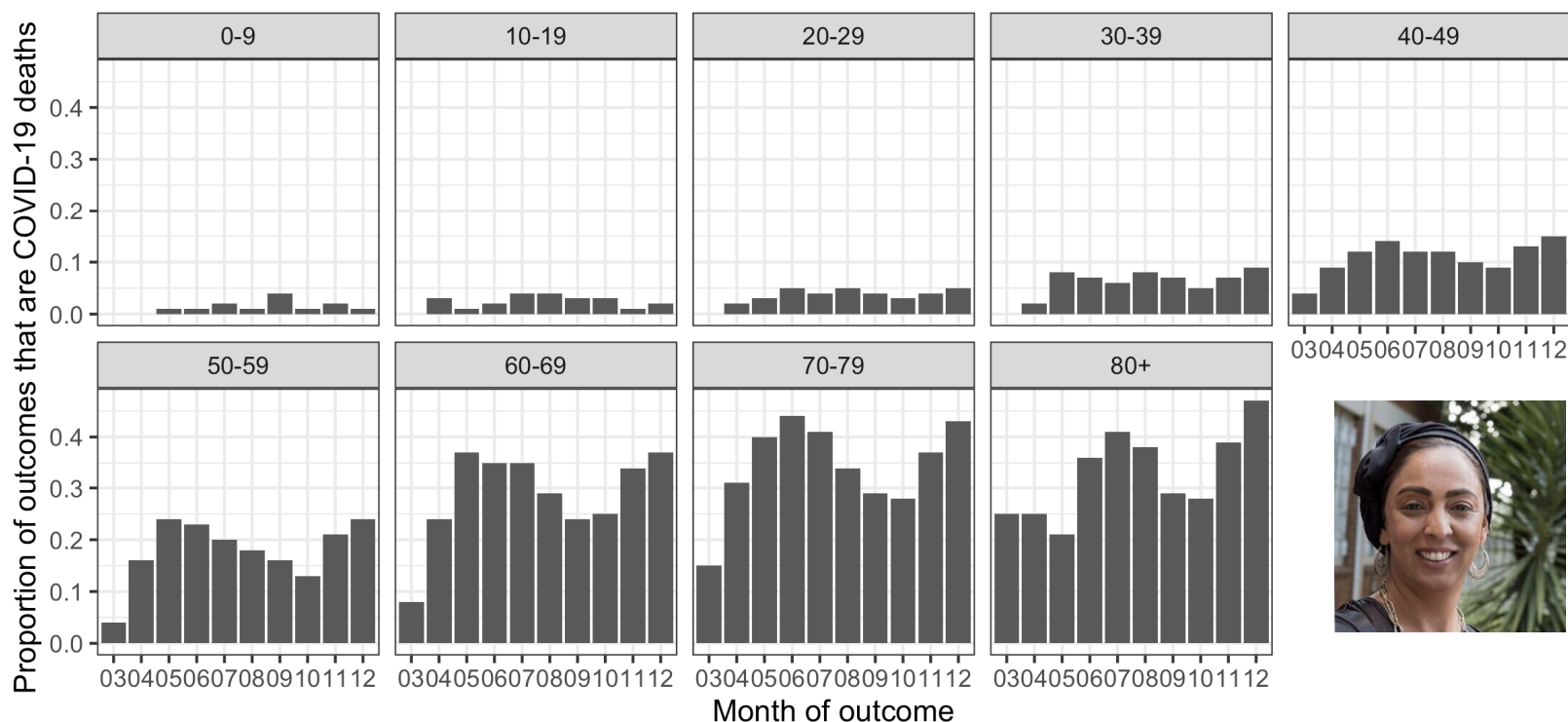
No difference in mortality by age group between waves

Source: Mary-Ann Davies – Western Cape DoH

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

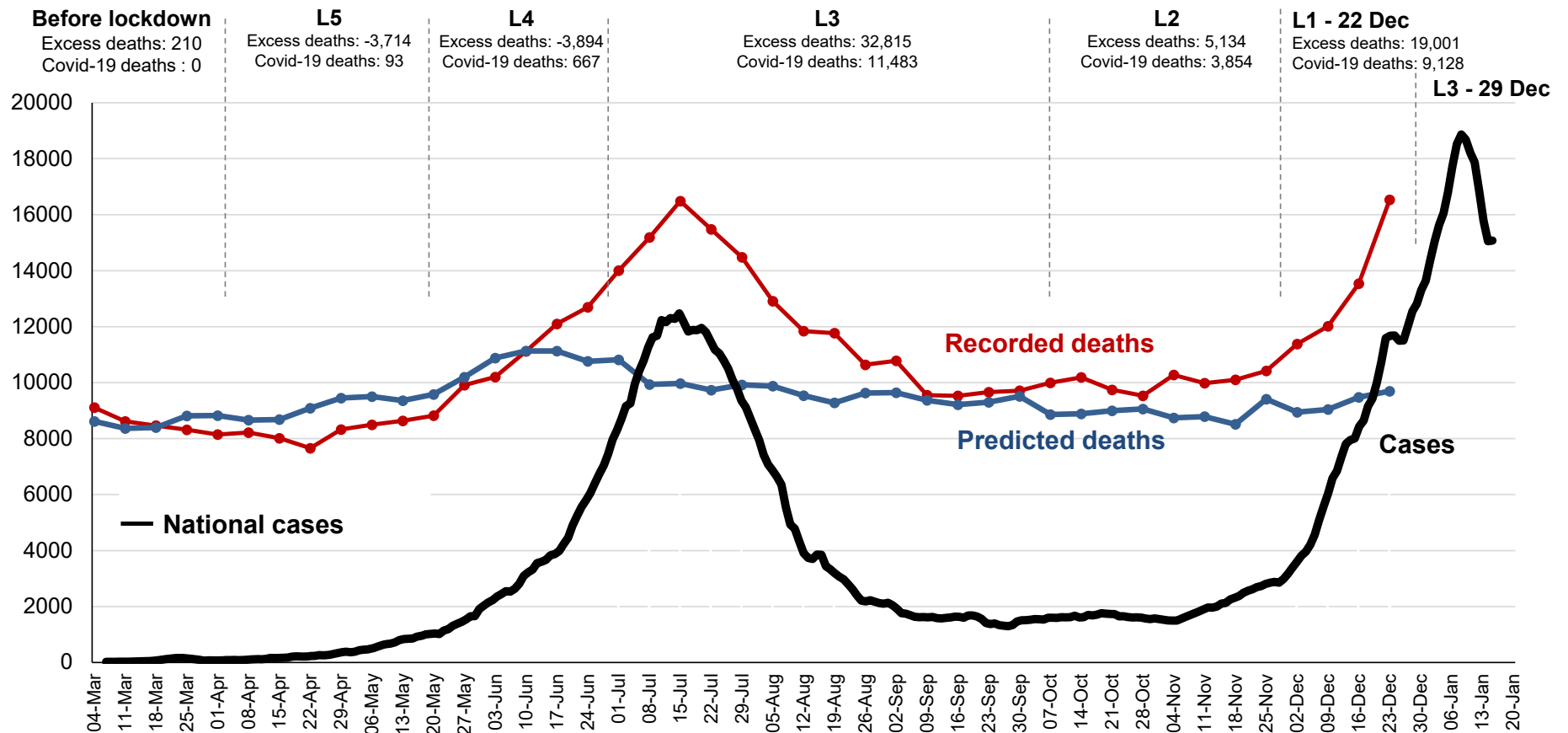
5 March 2020 - 9 January 2021

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



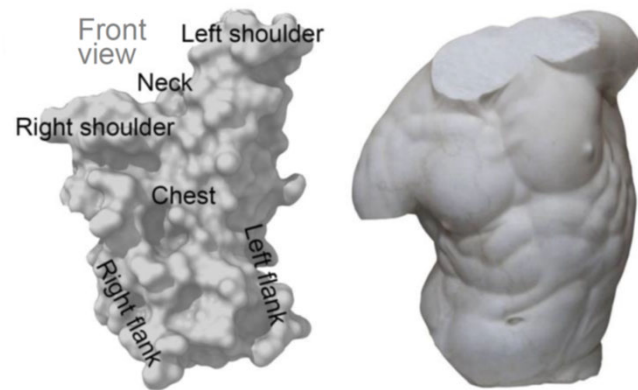
Source: Bradshaw D, et al



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

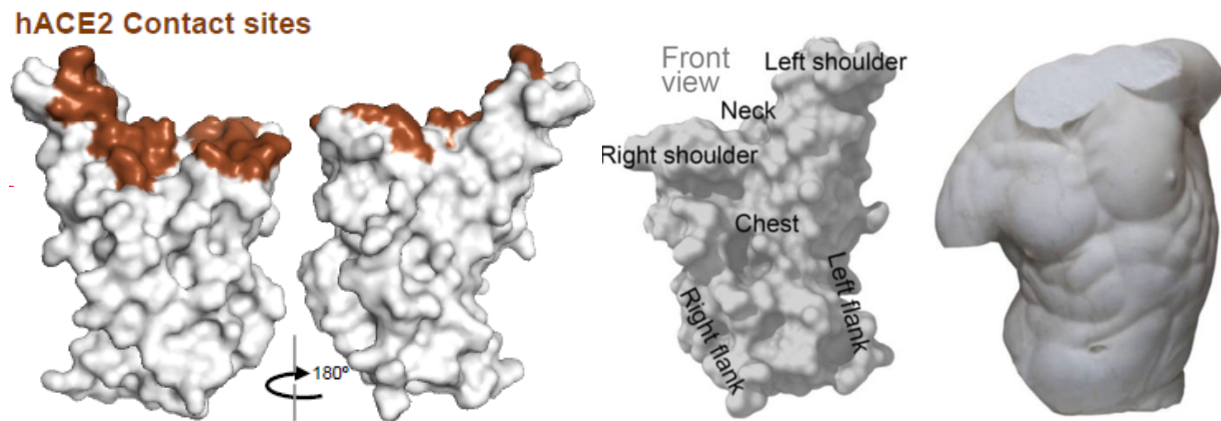
Conclusion & next steps



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

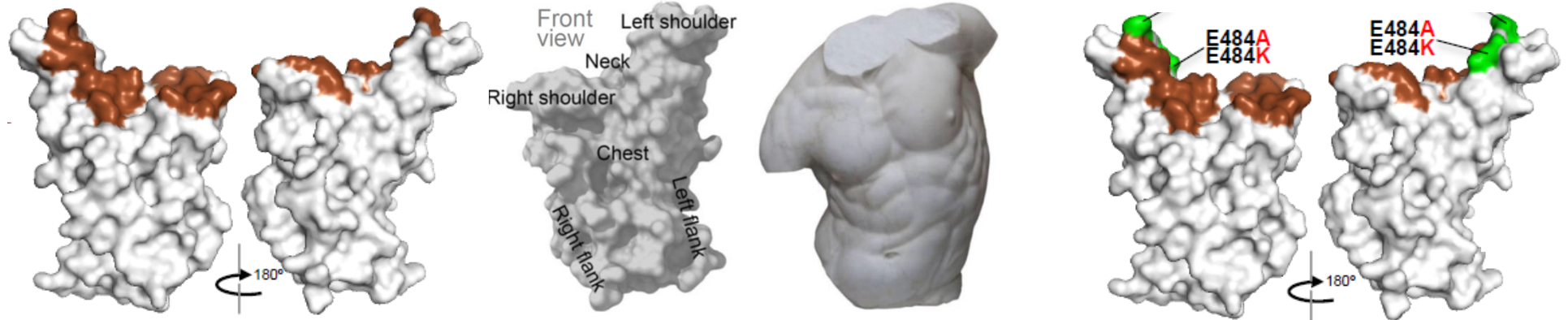
Immune responses target 2 main areas of the spike protein:

- 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)

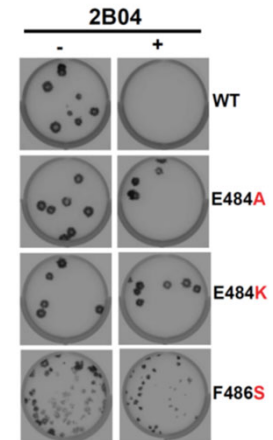
hACE2 Contact sites



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

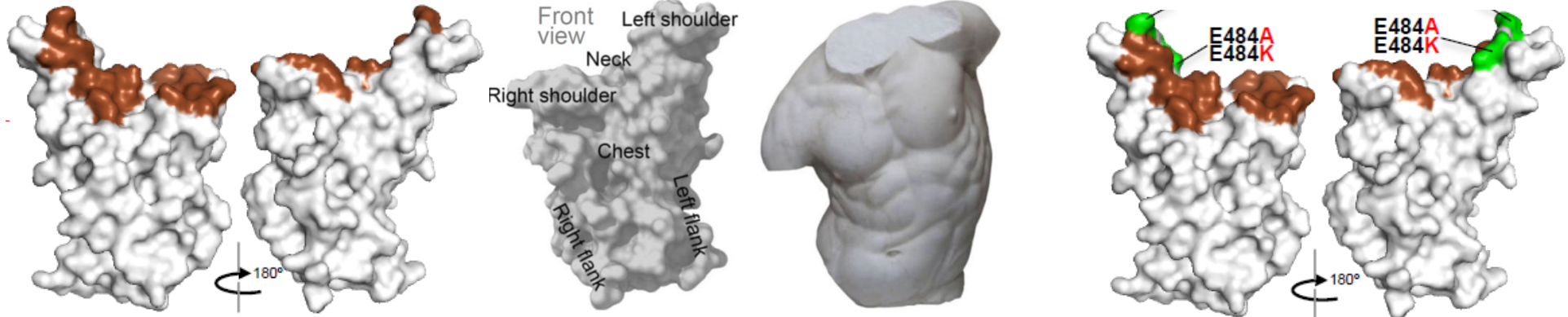
Landscape analysis of escape variants identifies SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization

Zhuoming Liu^{1,6}, Laura A. VanBlargan^{2,6}, Paul W. Rothlauf^{1,3}, Louis-Marie Bloyet¹, Rita E. Chen^{2,4}, Spencer Stumpf¹, Haiyan Zhao⁴, John M. Errico⁴, Elitza S. Theel⁵, Ali H. Ellebedy^{1,4}, Daved H. Fremont⁴, Michael S. Diamond^{1,2,4,*}, and Sean P. J. Whelan^{1,7*}



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

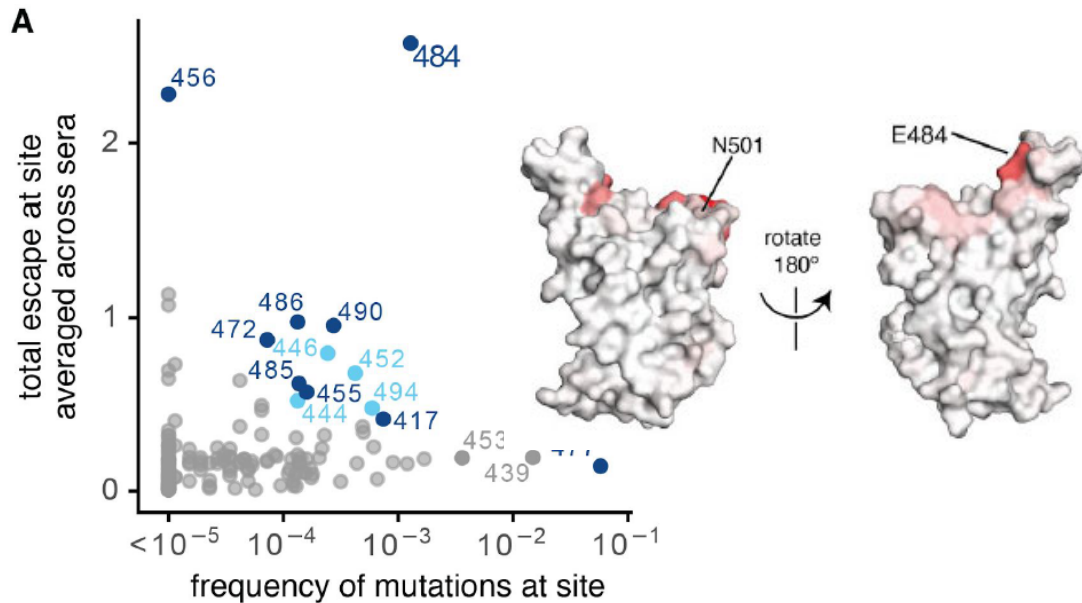
hACE2 Contact sites



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^{1,2}, Andrea N. Loes^{1,3}, Katharine H.D. Crawford^{1,2}, Tyler N. Starr^{1,3}, Keara D. Malone¹, Helen Y. Chu⁴, Jesse D. Bloom^{1,3,#}



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 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 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