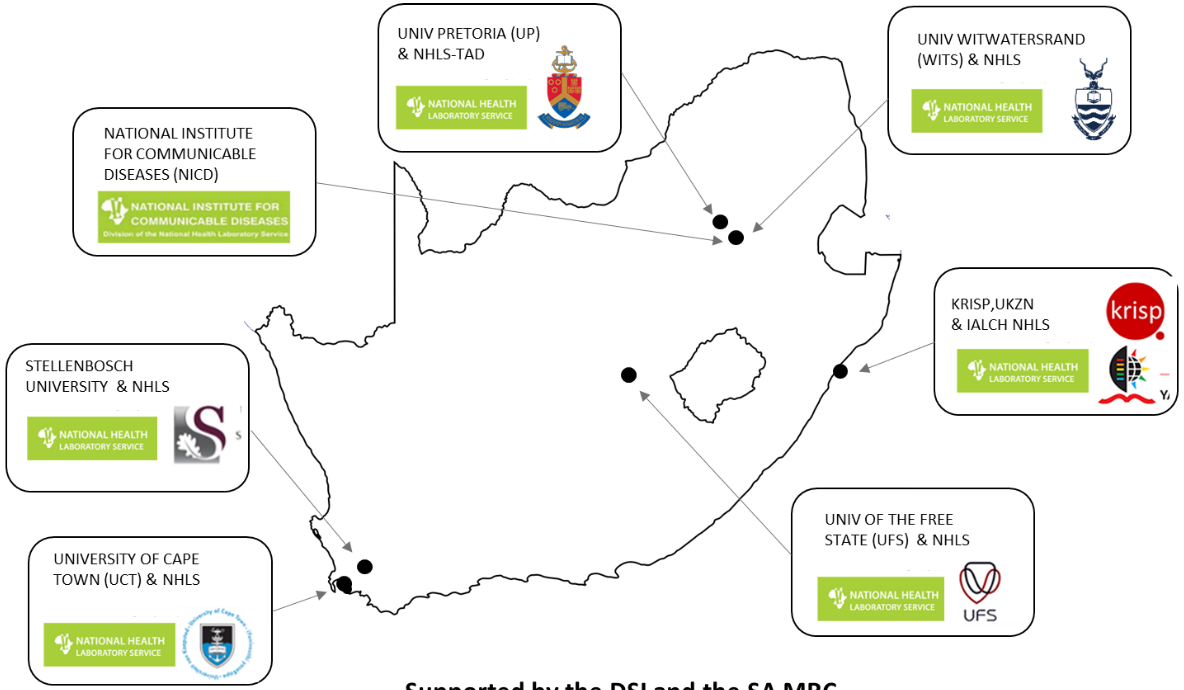
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update
18 March 2022



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Supported by the DSI and the SA MRC

Msomi N, Mlisana K, et al. Lancet Microbe 2020

Prepared by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory (NHLS) on behalf of the Network for Genomics Surveillance in South Africa (NGS-SA)

The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 18 March 2022 at 08h15

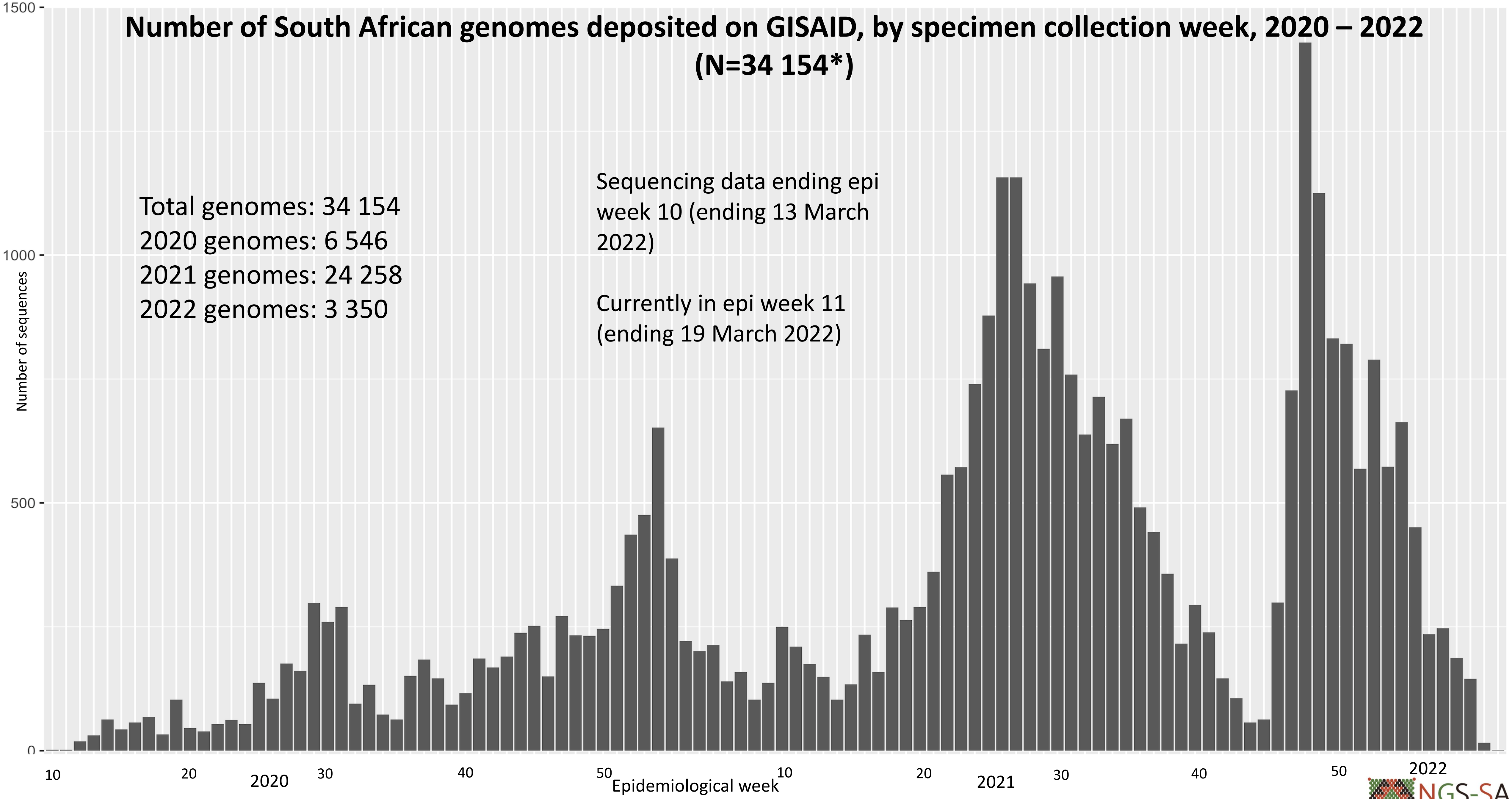
Data license: https://www.gisaid.org/registration/terms-of-use/

Elbe, S., and Buckland-Merrett, G. (2017) Data, disease and diplomacy: GISAID's innovative contribution to global health. Global Challenges, 1:33-46. DOI: 10.1002/gch2.1018 PMCID: 31565258

Shu, Y., McCauley, J. (2017) GISAID: Global initiative on sharing all influenza data – from vision to reality. EuroSurveillance, 22(13) DOI: 10.2807/1560-7917.ES.2017.22.13.30494 PMCID: PMC5388101

Case data is based on specimen collection date. Cases from https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-epidemiological-brief/
Test data gives weekly percentage testing positive rates, from https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-testing-summary/

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022 (N=34 154*)



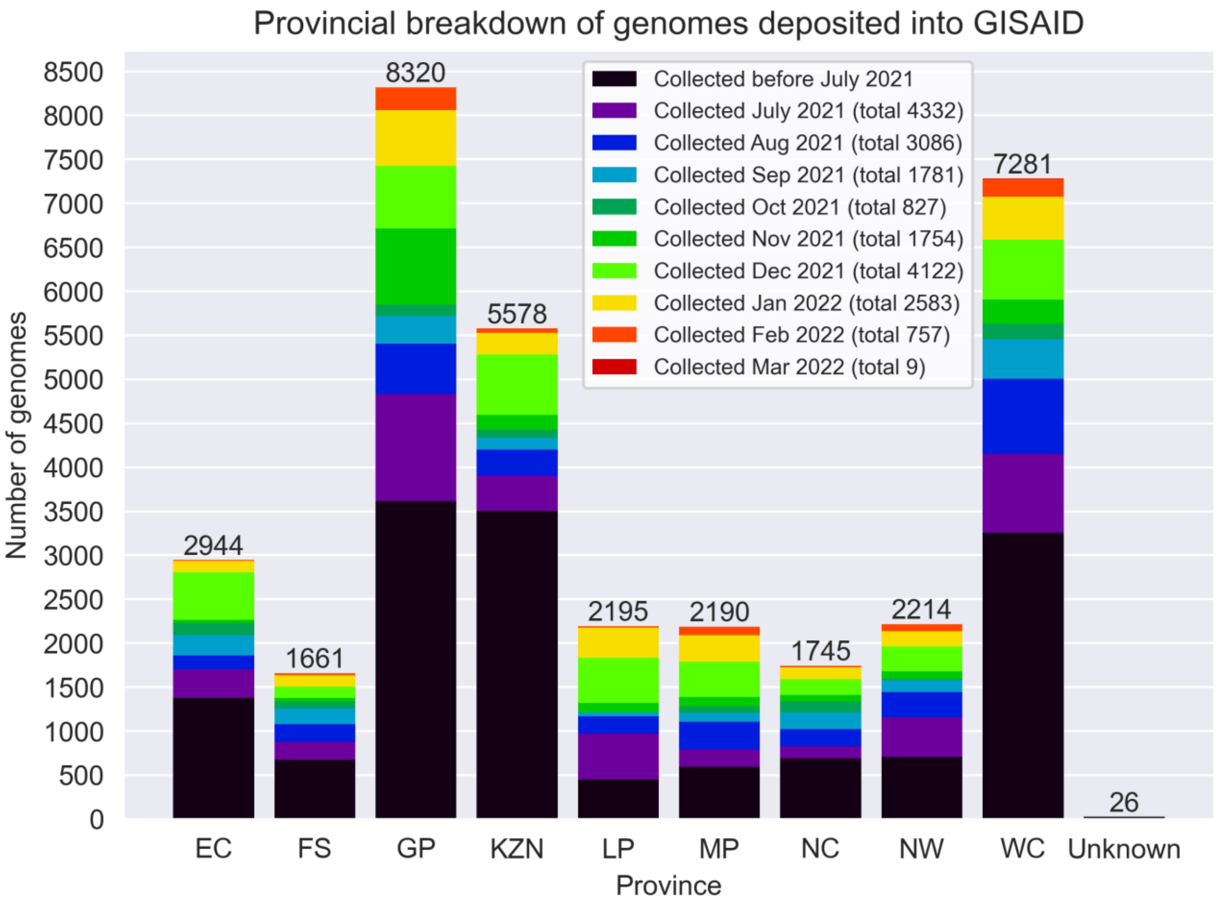
Total genomes: 34 154
2020 genomes: 6 546
2021 genomes: 24 258
2022 genomes: 3 350

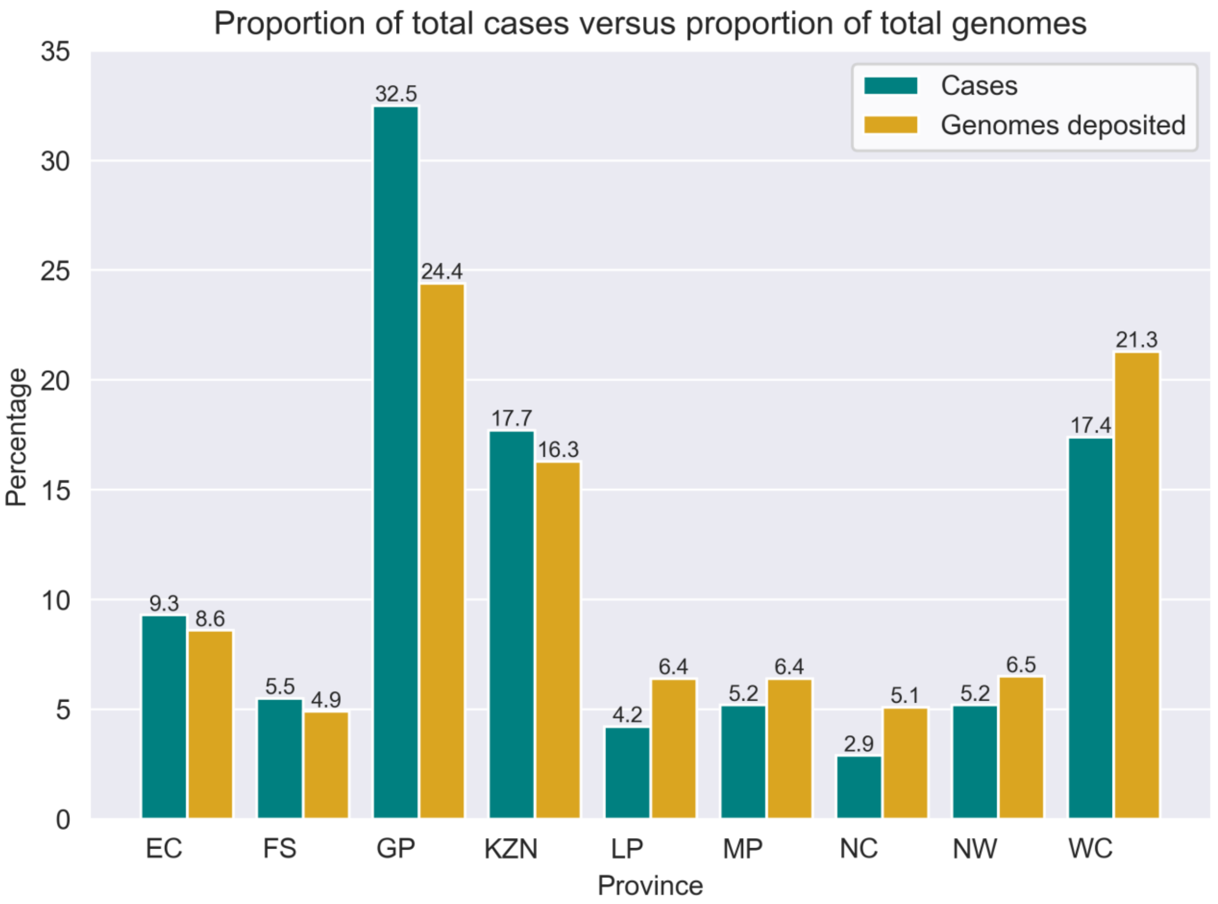
Sequencing data ending epi week 10 (ending 13 March 2022)

Currently in epi week 11 (ending 19 March 2022)

*This represents the cleaned, de-duplicated dataset of unique **National and Pneumonia Surveillance** sequences. This dataset will be used for all further figures.

GISAID genomes vs total cases, 2020 – 2022 (N=34 154)


Provincial breakdown of genomes deposited into GISAID


Proportion of total cases versus proportion of total genomes

All provinces, apart from GP, LP, NC and WC, have comparable percentages of overall cases and overall sequenced genomes.

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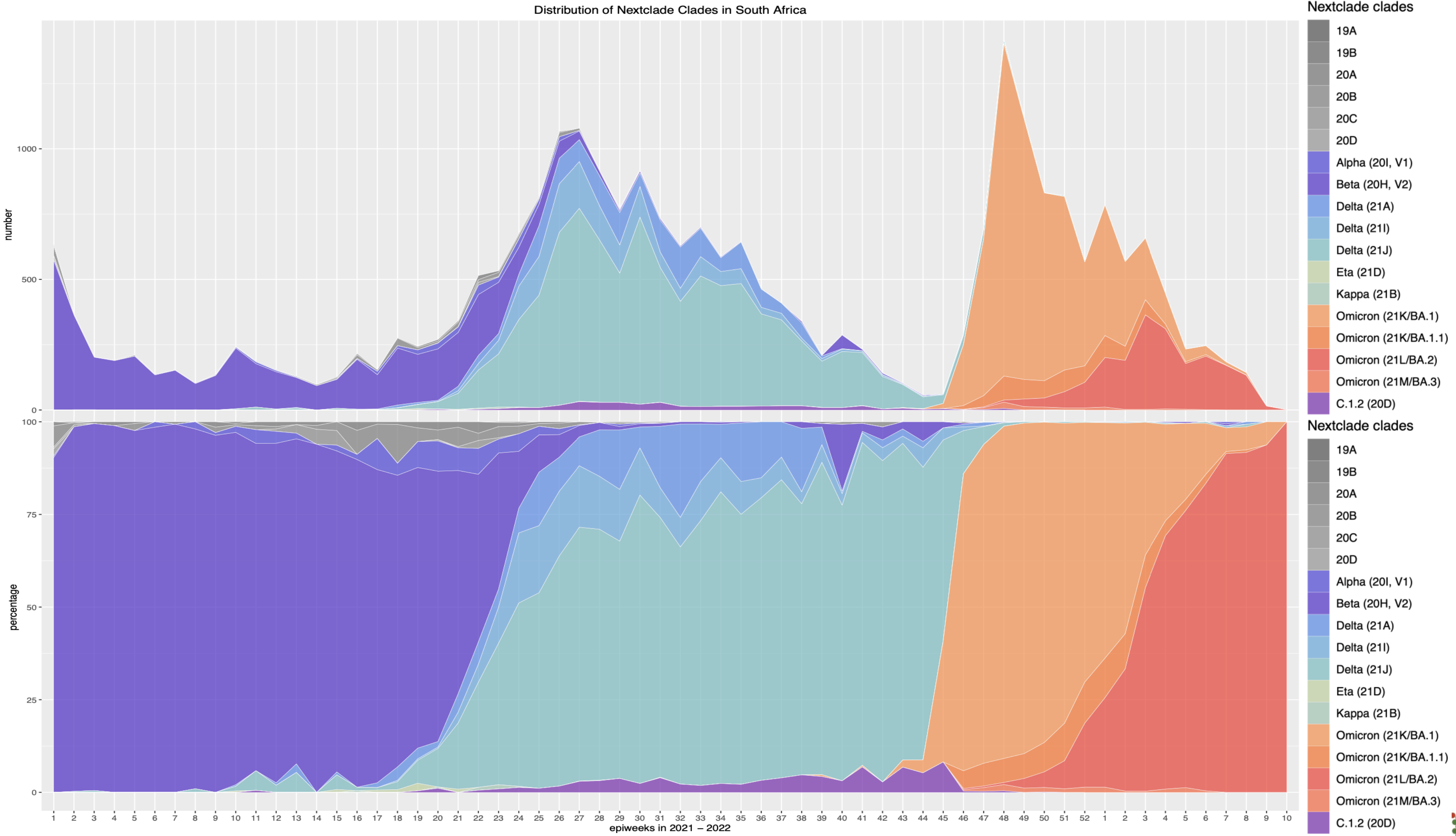
Percentage and number of clades by epiweek in South Africa, 2021 - 2022 (N=27 608)



Sequencing data ending epi week 10 (ending 12 March 2022)

Currently in epi week 11 (ending 19 March 2022)

Delta dominated in South Africa until October at >80%. Omicron has dominated from November onwards.

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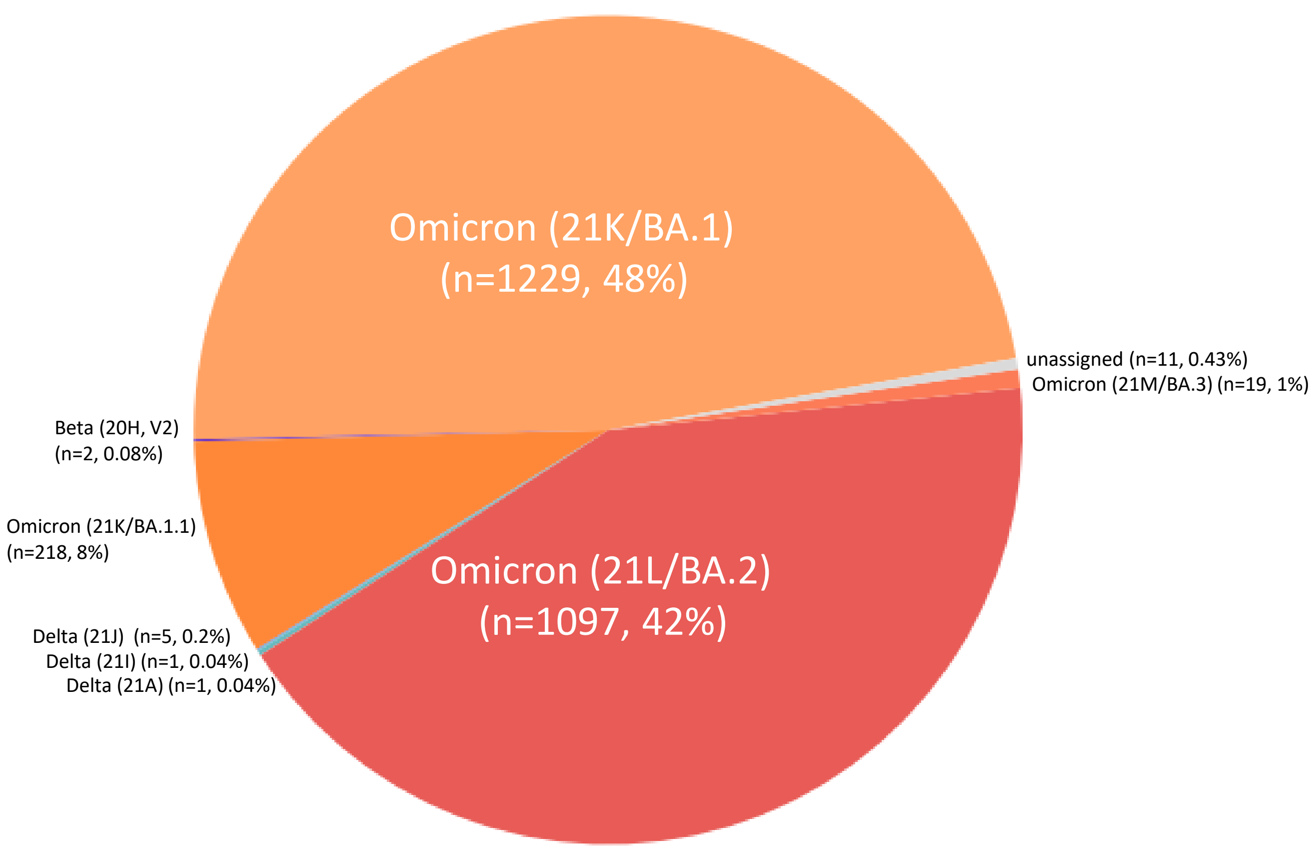
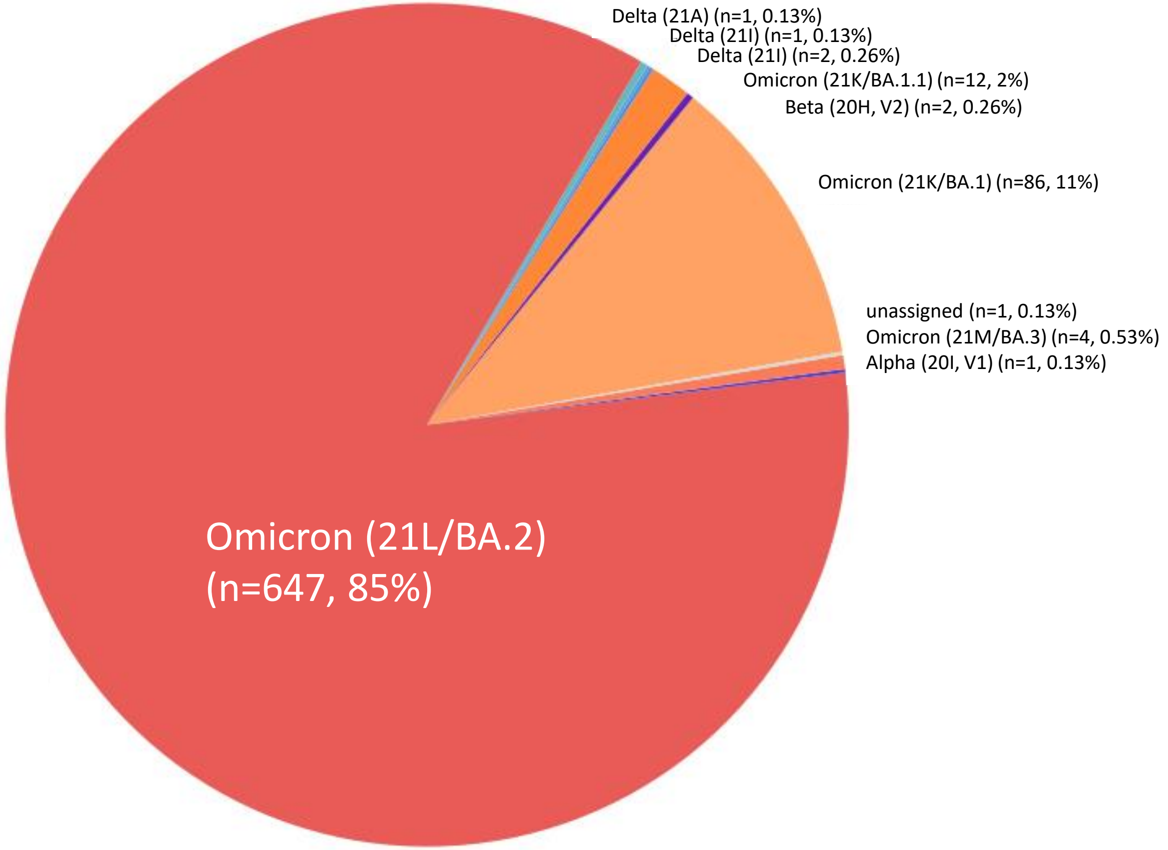
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in Jan – Feb 2022

January (N=2583)



Total Omicron in Jan: 2544 (98.5%)

February (N=757)



Total Omicron in Feb: 745 (98.4%)

🟧 Omicron (21K) 🟥 Omicron (21M) 🟪 Beta (20H, V2) 🟦 Delta (21A) 🟦 Delta (21I) 🟦 Delta (21J) 🟩 Kappa (21B) 🟩 Eta (21D) ⬜ Other ⬜ unassigned
🟥 Omicron (21L) 🟪 C.1.2 (20D) 🟦 Alpha (20I, V1)

Omicron dominated in January (98.5%, 2544/2583) and February (98.4%, 745/757). BA.2 increased in prevalence throughout January and was dominant in February.

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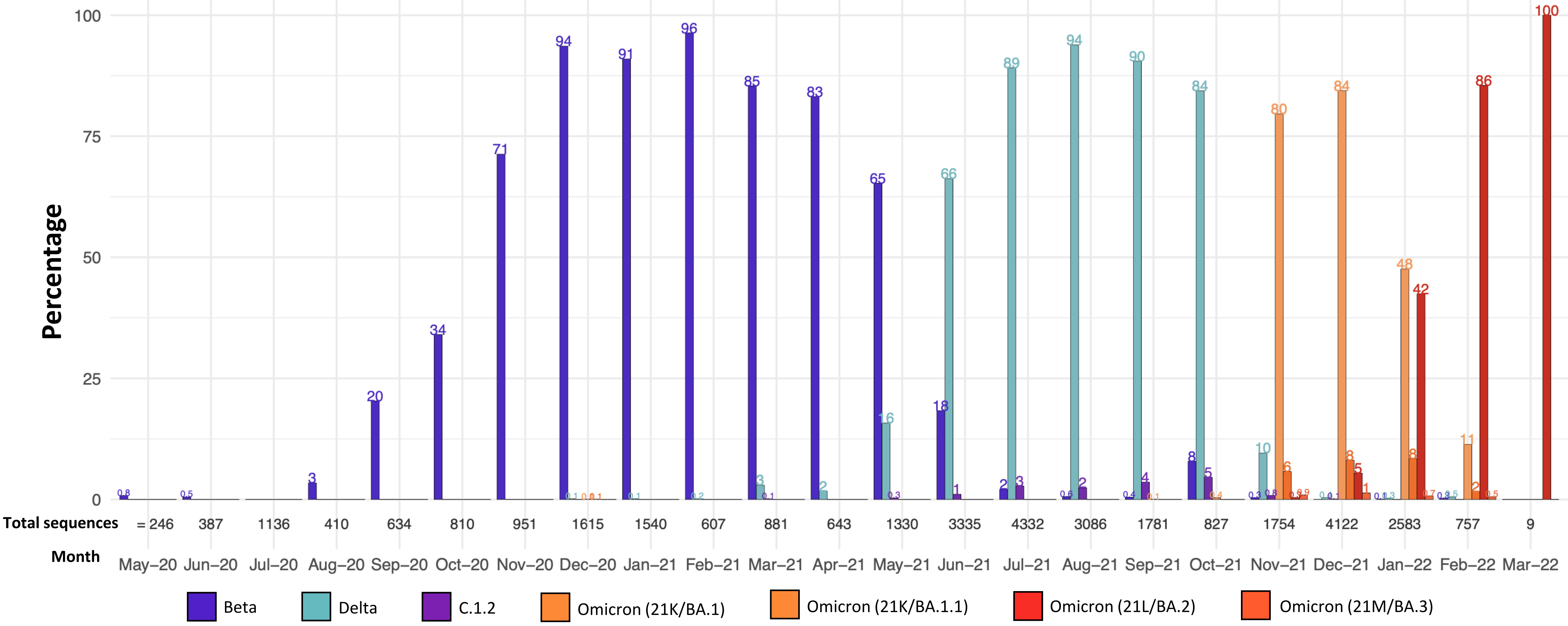
Detection Rates: Beta, Delta, C.1.2 and Omicron

Detection rates of variants being monitored in South Africa*



*Bars represent percentage prevalence of variant for the month; total sequences collected for the month are given below

Omicron has been dominant since November (>80% in November, >98% in December, January and February).
BA.2 has increased in frequency, making up 42% of genomes in January and 86% in February.
BA.3 continues to be present at low levels.

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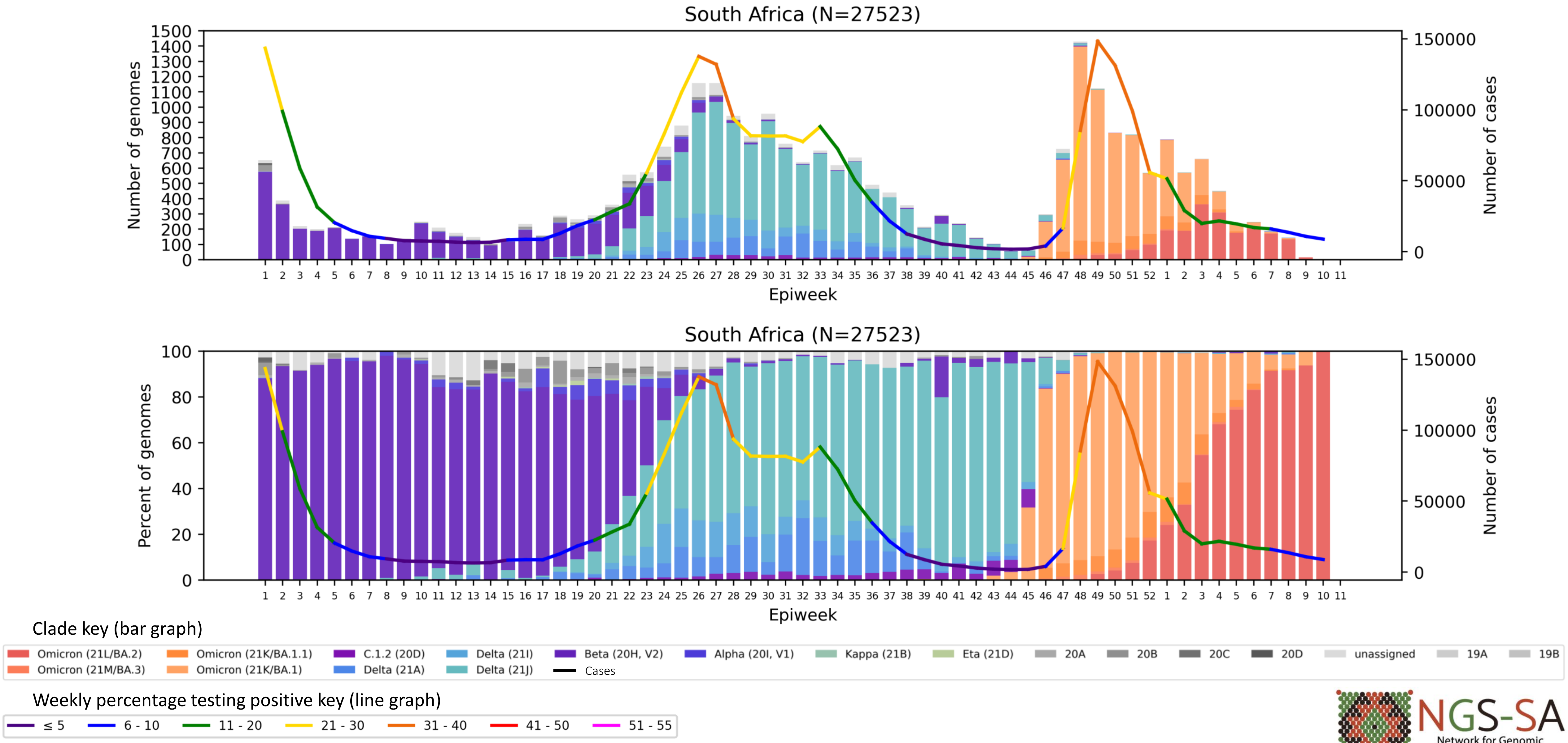
South Africa, 2021-2022, n = 27523*



*Excludes sequences missing collection dates, as well as those collected January 1st and 2nd 2021 as they are part of epiweek 53 of 2020.

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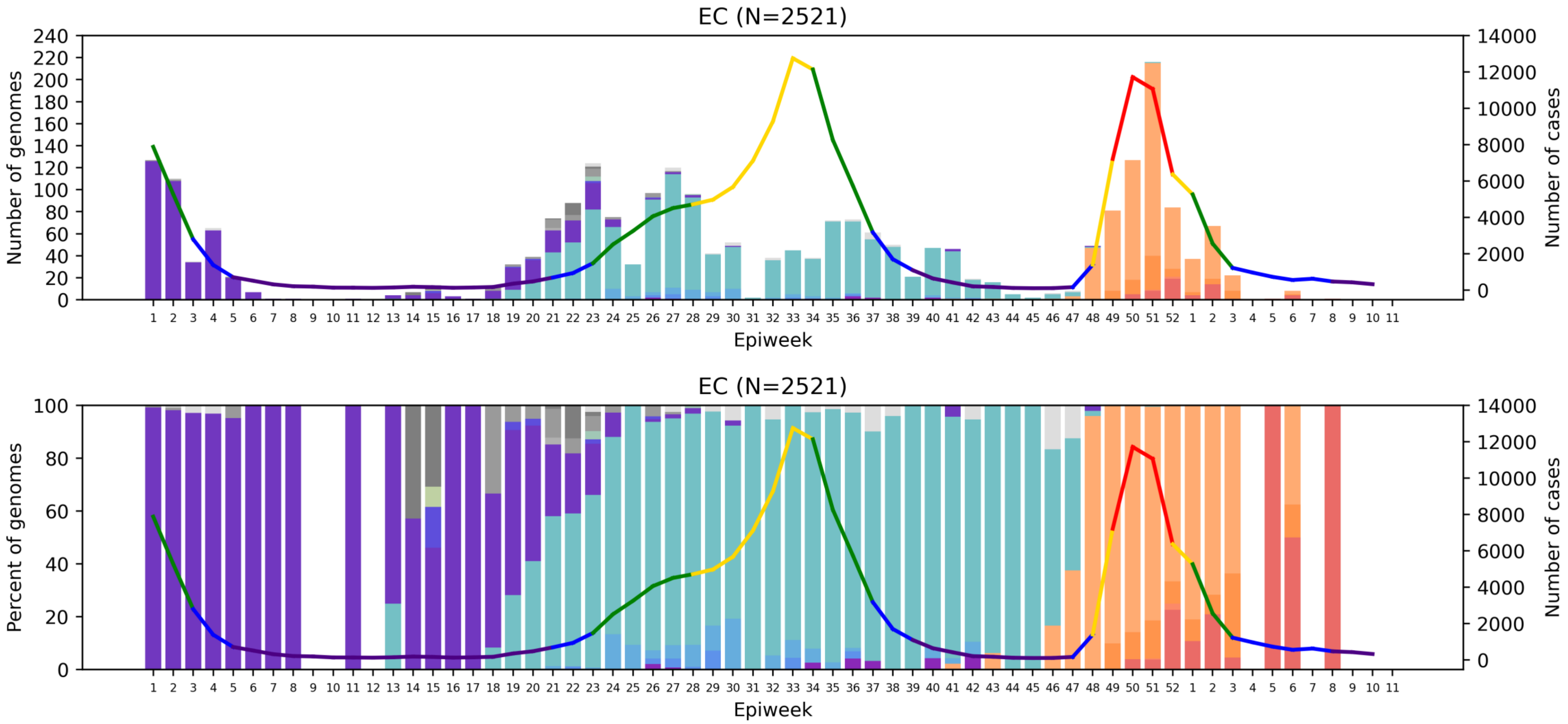
Eastern Cape Province, 2021-2022, n = 2521



Clade key (bar graph)

- Omicron (21L/BA.2)
- Omicron (21M/BA.3)
- Omicron (21K/BA.1.1)
- Omicron (21K/BA.1)
- C.1.2 (20D)
- Delta (21A)
- Delta (21I)
- Delta (21J)
- Beta (20H, V2)
- Cases
- Alpha (20I, V1)
- Kappa (21B)
- Eta (21D)
- 20A
- 20B
- 20C
- 20D
- unassigned
- 19A
- 19B

Weekly percentage testing positive key (line graph)

- ≤ 5
- 6 - 10
- 11 - 20
- 21 - 30
- 31 - 40
- 41 - 50
- 51 - 55

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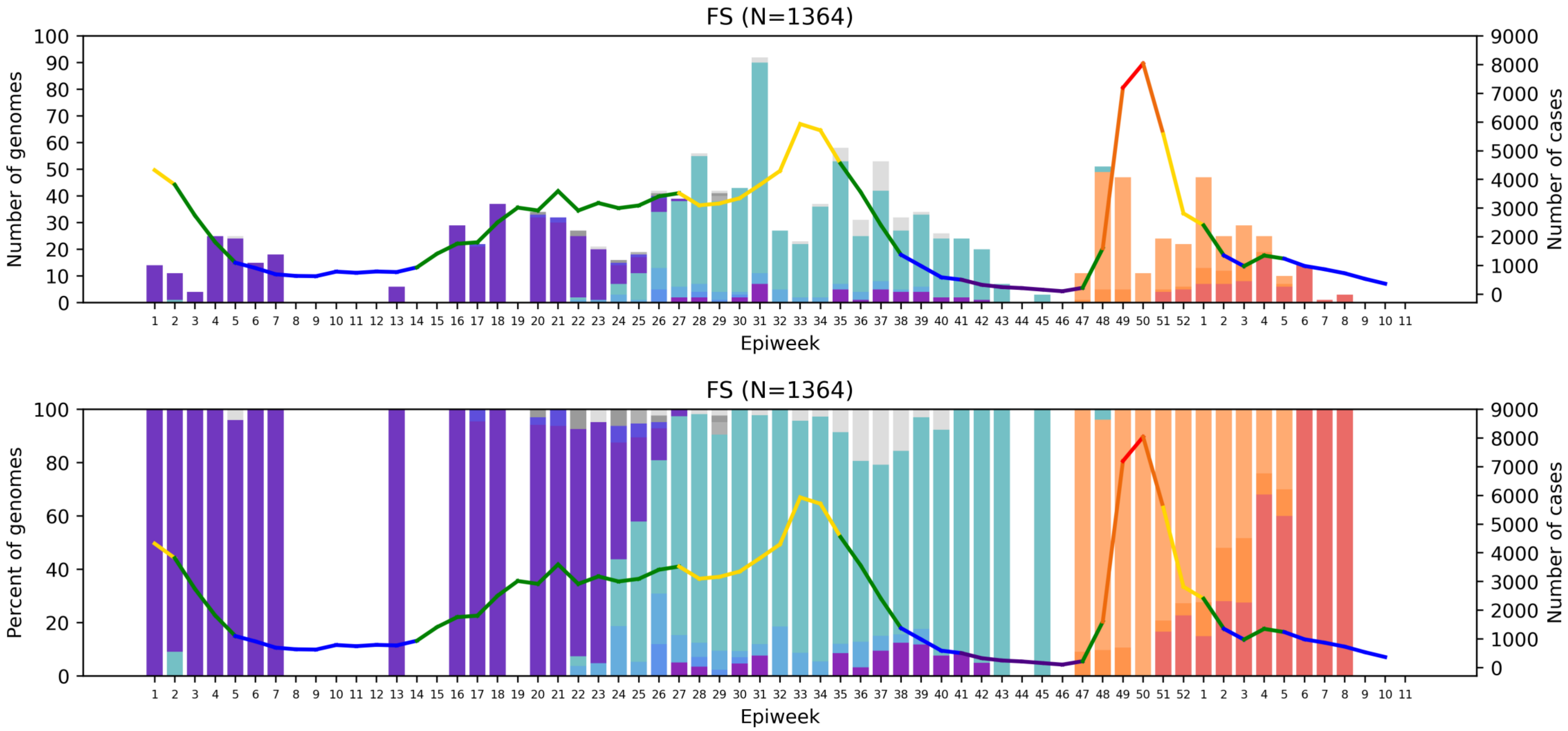
Free State Province, 2021-2022, n = 1364



Clade key (bar graph)

- ▬ Omicron (21L/BA.2)
- ▬ Omicron (21M/BA.3)
- ▬ Omicron (21K/BA.1.1)
- ▬ Omicron (21K/BA.1)
- ▬ C.1.2 (20D)
- ▬ Delta (21A)
- ▬ Delta (21I)
- ▬ Delta (21J)
- ▬ Beta (20H, V2)
- ▬ Cases
- ▬ Alpha (20I, V1)
- ▬ Kappa (21B)
- ▬ Eta (21D)
- ▬ 20A
- ▬ 20B
- ▬ 20C
- ▬ 20D
- ▬ unassigned
- ▬ 19A
- ▬ 19B

Weekly percentage testing positive key (line graph)

- ▬ ≤ 5
- ▬ 6 - 10
- ▬ 11 - 20
- ▬ 21 - 30
- ▬ 31 - 40
- ▬ 41 - 50
- ▬ 51 - 55

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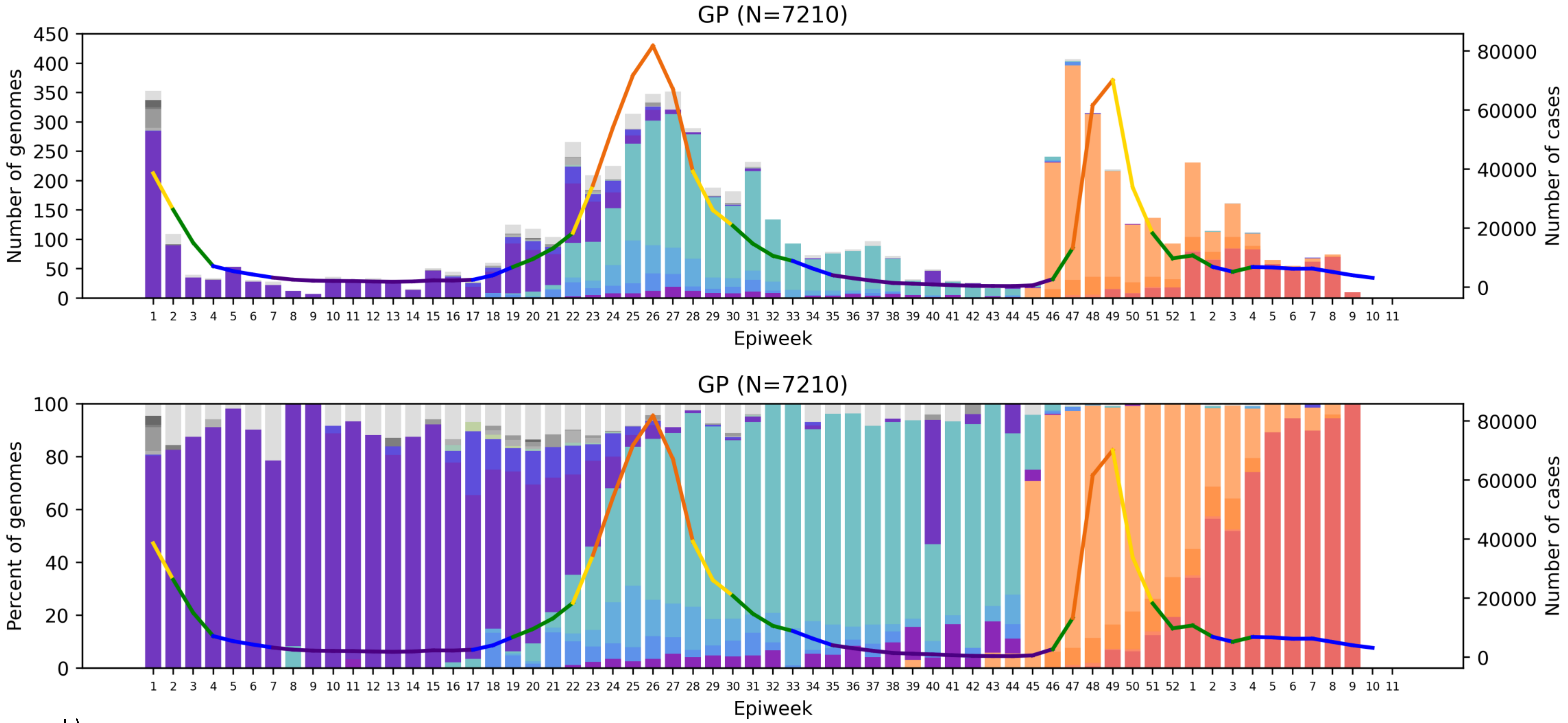
Gauteng Province, 2021-2022, n = 7210



Clade key (bar graph)

- Omicron (21L/BA.2)
- Omicron (21M/BA.3)
- Omicron (21K/BA.1.1)
- Omicron (21K/BA.1)
- C.1.2 (20D)
- Delta (21A)
- Delta (21I)
- Delta (21J)
- Beta (20H, V2)
- Cases
- Alpha (20I, V1)
- Kappa (21B)
- Eta (21D)
- 20A
- 20B
- 20C
- 20D
- unassigned
- 19A
- 19B

Weekly percentage testing positive key (line graph)

- ≤ 5
- 6 - 10
- 11 - 20
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- 41 - 50
- 51 - 55

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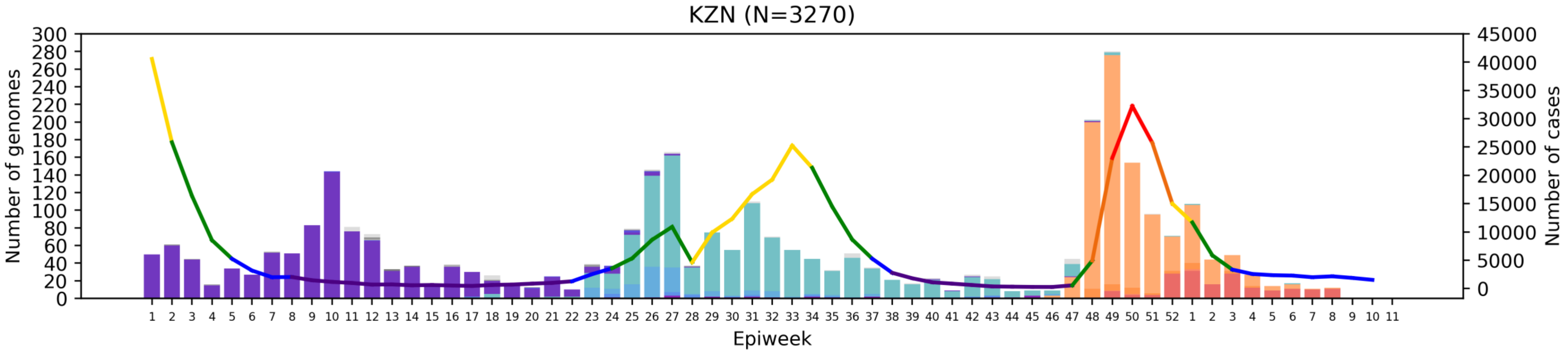
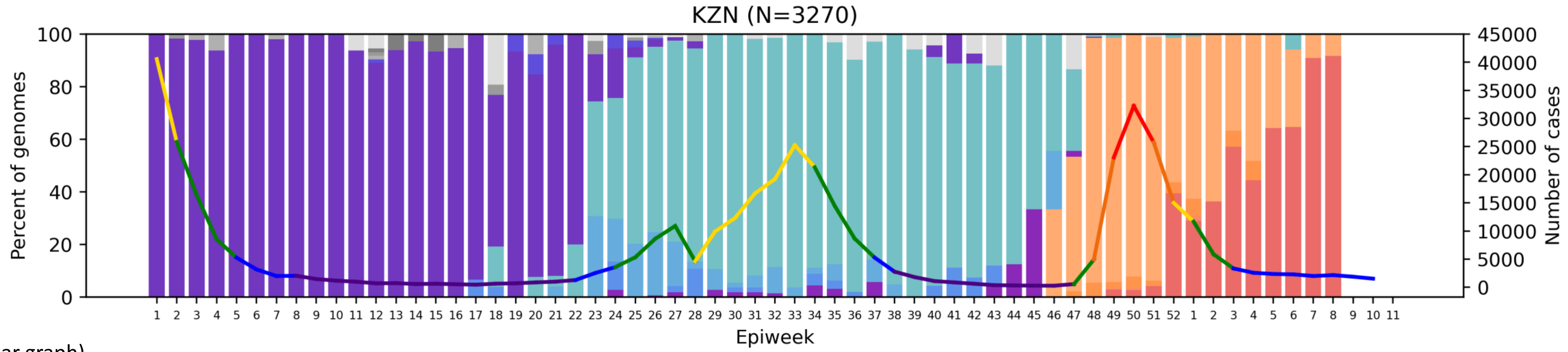
KwaZulu-Natal Province, 2021-2022, n = 3270





Clade key (bar graph)

- Omicron (21L/BA.2)
- Omicron (21M/BA.3)
- Omicron (21K/BA.1.1)
- Omicron (21K/BA.1)
- C.1.2 (20D)
- Delta (21A)
- Delta (21I)
- Delta (21J)
- Beta (20H, V2)
- Cases
- Alpha (20I, V1)
- Kappa (21B)
- Eta (21D)
- 20A
- 20B
- 20C
- 20D
- unassigned
- 19A
- 19B

Weekly percentage testing positive key (line graph)

- ≤ 5
- 6 - 10
- 11 - 20
- 21 - 30
- 31 - 40
- 41 - 50
- 51 - 55

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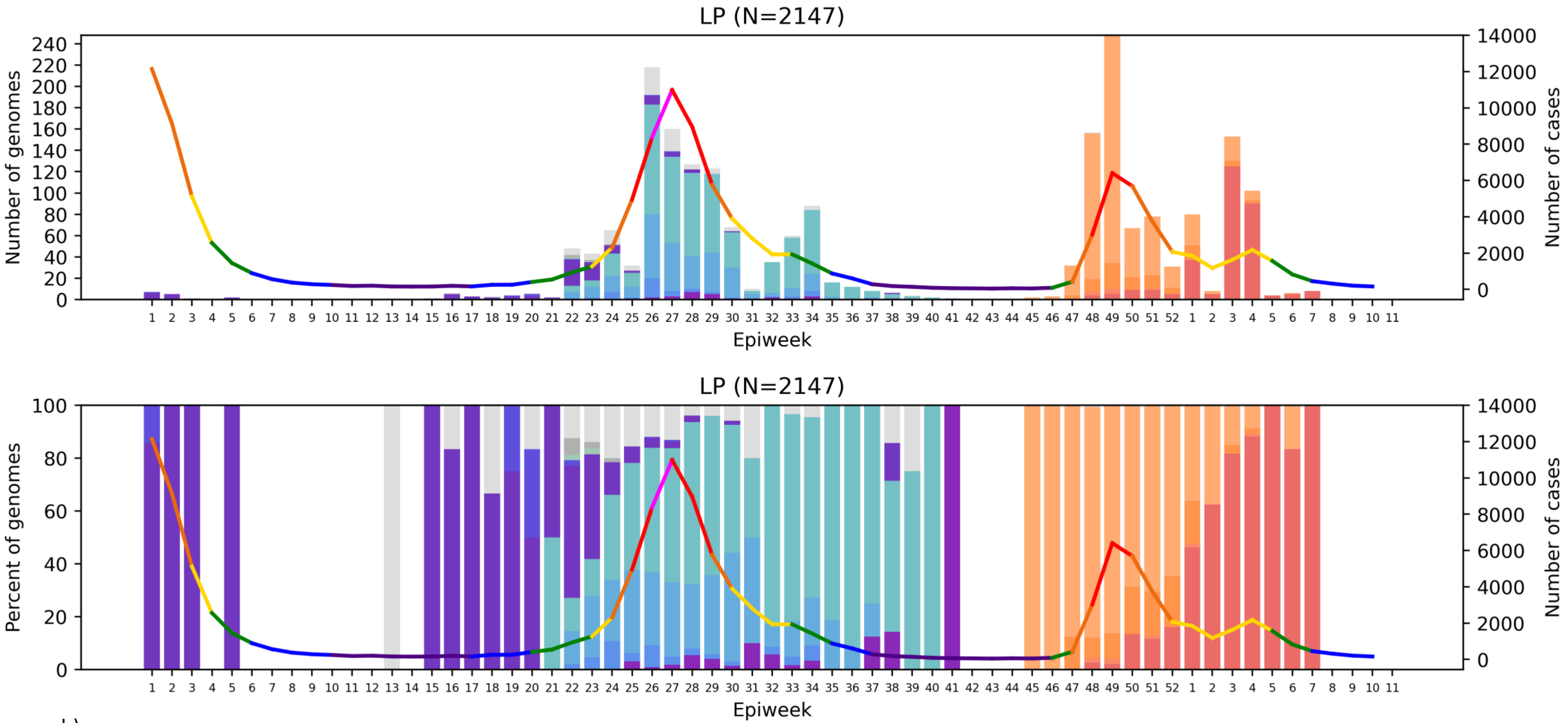
Limpopo Province, 2021-2022, n = 2147



Clade key (bar graph)

- ▬ Omicron (21L/BA.2)
- ▬ Omicron (21M/BA.3)
- ▬ Omicron (21K/BA.1.1)
- ▬ Omicron (21K/BA.1)
- ▬ C.1.2 (20D)
- ▬ Delta (21A)
- ▬ Delta (21I)
- ▬ Delta (21J)
- ▬ Beta (20H, V2)
- — Cases
- ▬ Alpha (20I, V1)
- ▬ Kappa (21B)
- ▬ Eta (21D)
- ▬ 20A
- ▬ 20B
- ▬ 20C
- ▬ 20D
- ▬ unassigned
- ▬ 19A
- ▬ 19B

Weekly percentage testing positive key (line graph)

- — ≤ 5
- — 6 - 10
- — 11 - 20
- — 21 - 30
- — 31 - 40
- — 41 - 50
- — 51 - 55

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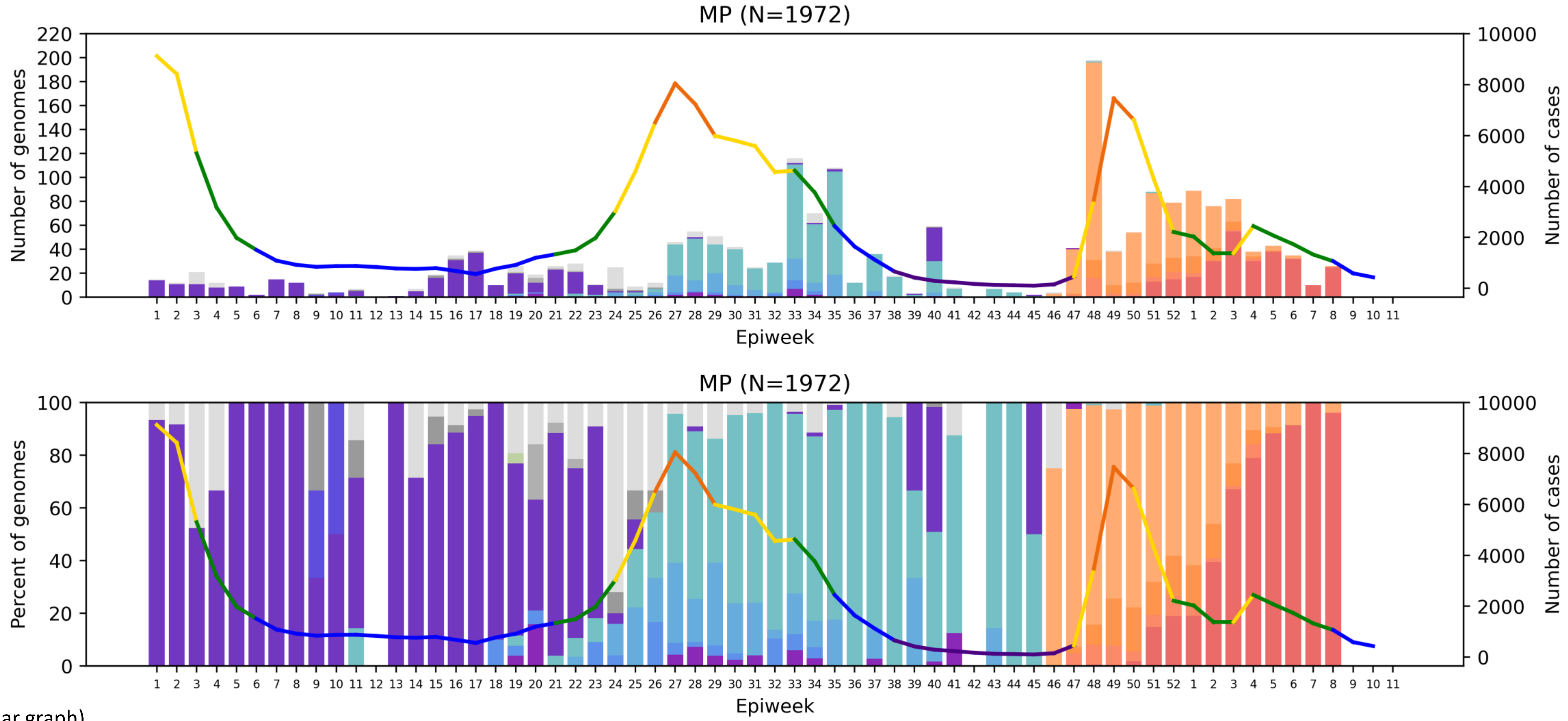
Mpumalanga Province, 2021-2022, n = 1972



Clade key (bar graph)

- ▬ Omicron (21L/BA.2)
- ▬ Omicron (21M/BA.3)
- ▬ Omicron (21K/BA.1.1)
- ▬ Omicron (21K/BA.1)
- ▬ C.1.2 (20D)
- ▬ Delta (21A)
- ▬ Delta (21I)
- ▬ Delta (21J)
- ▬ Beta (20H, V2)
- — Cases
- ▬ Alpha (20I, V1)
- ▬ Kappa (21B)
- ▬ Eta (21D)
- ▬ 20A
- ▬ 20B
- ▬ 20C
- ▬ 20D
- ▬ unassigned
- ▬ 19A
- ▬ 19B

Weekly percentage testing positive key (line graph)

- — ≤ 5
- — 6 - 10
- — 11 - 20
- — 21 - 30
- — 31 - 40
- — 41 - 50
- — 51 - 55

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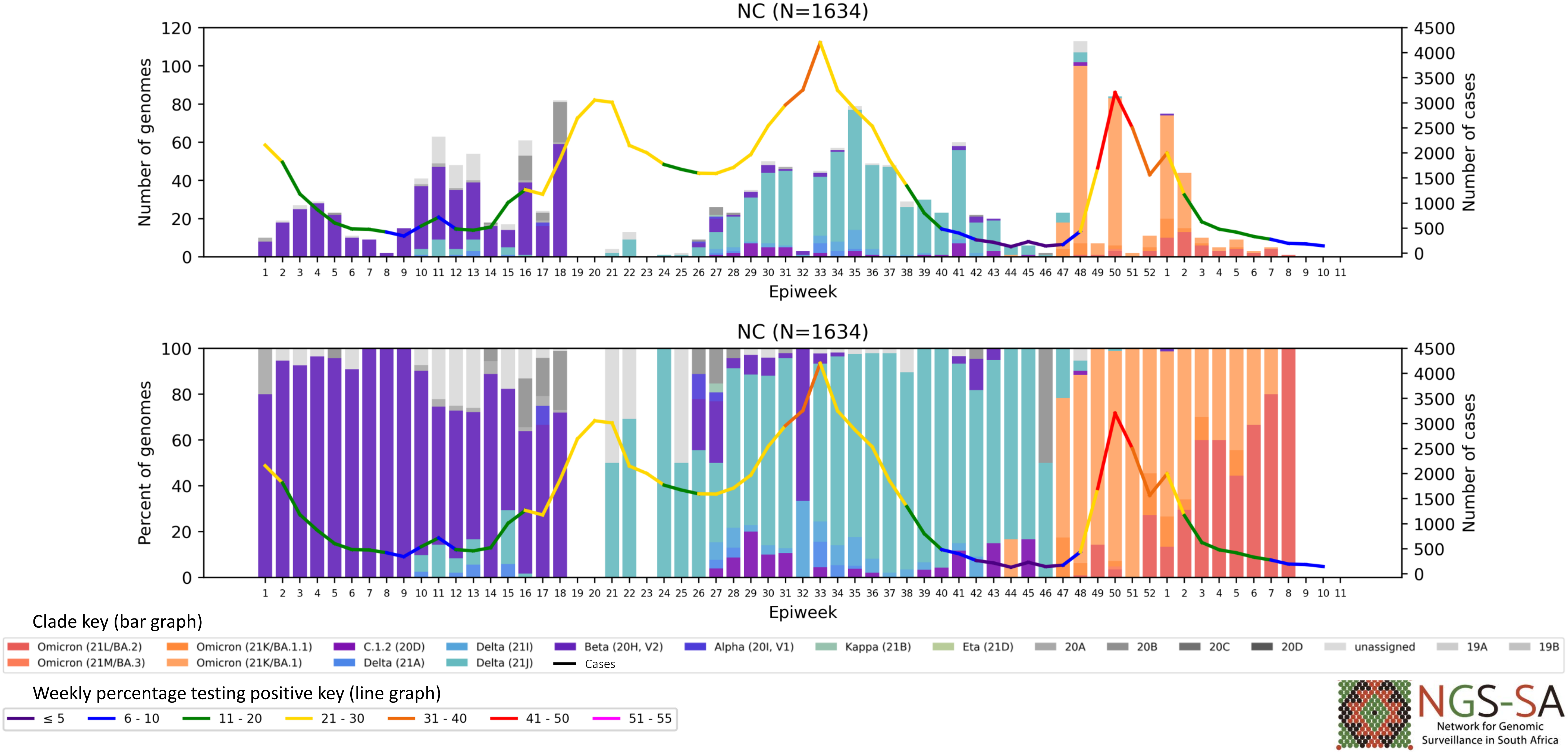
Northern Cape Province, 2021-2022, n = 1634



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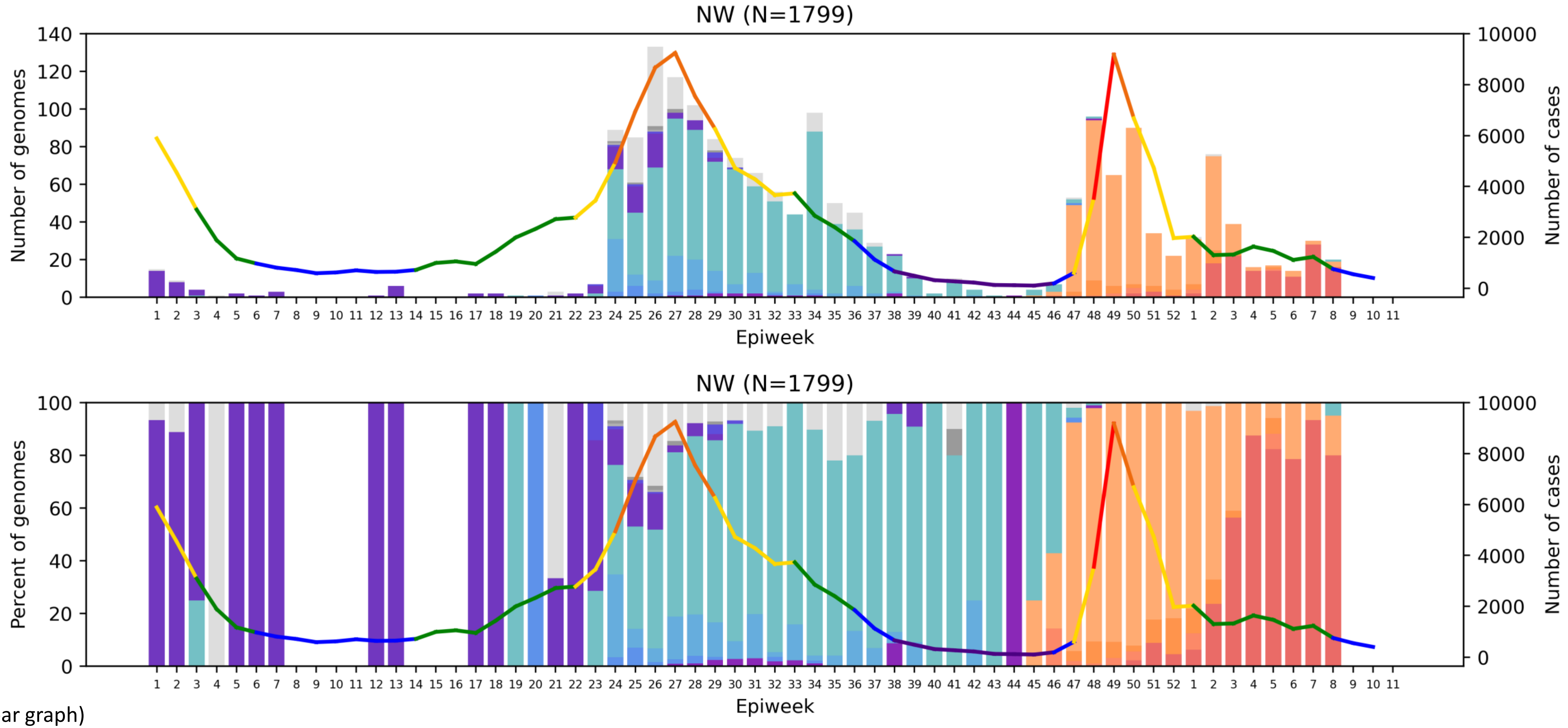
North West Province, 2021, n = 1799



Clade key (bar graph)

🟥 Omicron (21L/BA.2)
🟥 Omicron (21M/BA.3)
🟧 Omicron (21K/BA.1.1)
🟧 Omicron (21K/BA.1)
🟪 C.1.2 (20D)
🟦 Delta (21A)
🟦 Delta (21I)
🟦 Delta (21J)
🟪 Beta (20H, V2)
— Cases
🟦 Alpha (20I, V1)
🟩 Kappa (21B)
🟩 Eta (21D)
⬛ 20A
⬛ 20B
⬛ 20C
⬛ 20D
⬜ unassigned
⬜ 19A
⬜ 19B

Weekly percentage testing positive key (line graph)

— ≤ 5
— 6 - 10
— 11 - 20
— 21 - 30
— 31 - 40
— 41 - 50
— 51 - 55

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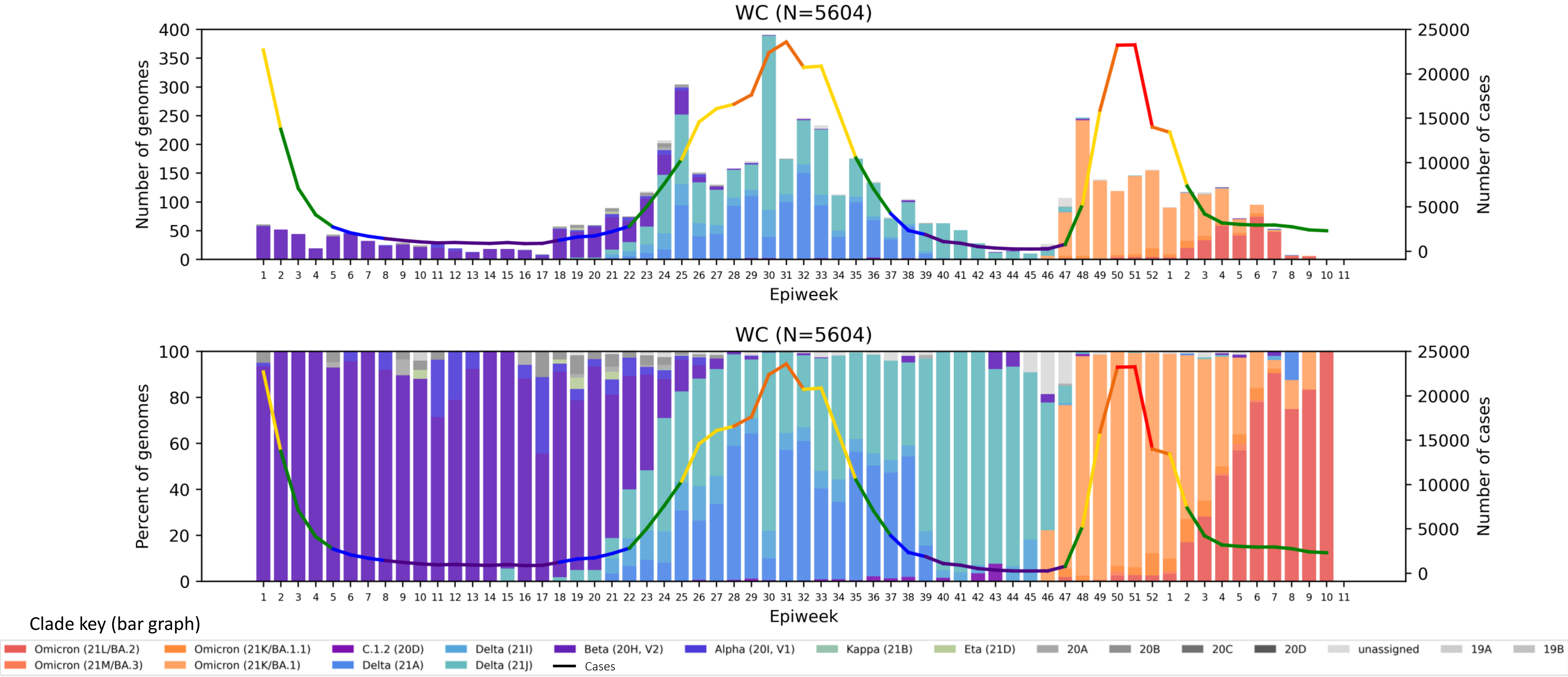
Western Cape Province, 2021-2022, n = 5604



Weekly percentage testing positive key (line graph)

≤ 5	6 - 10
11 - 20	21 - 30
31 - 40	41 - 50
51 - 55	

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Summary

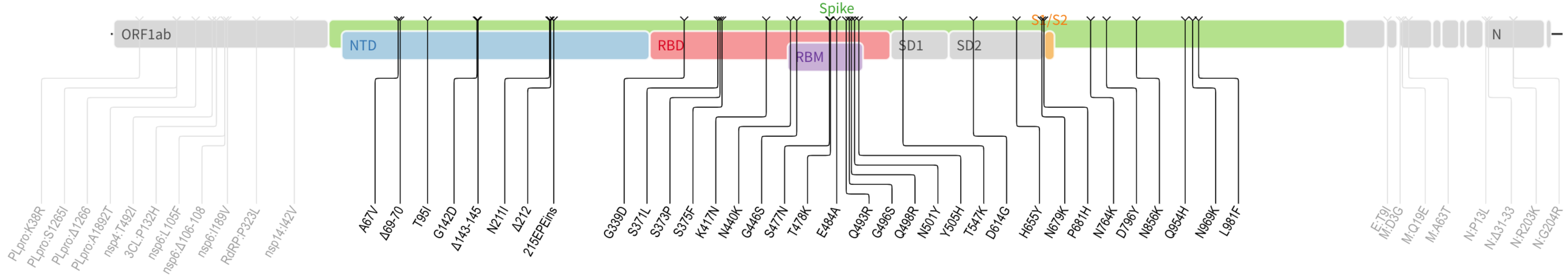
- **Variant of Concern Omicron**
  - Detected in at least 153 countries and dominating globally
  - Split into different lineages based on different mutational profiles. Predominant lineages currently BA.1 (21K), BA.1.1 (21K, BA.1+spike R346K), BA.2 (21L), BA.3 (21M). More lineages are being assigned but defining mutations are not yet available.

  - South Africa (detected in all provinces):
    - Dominated December, January and February sequencing data at >98% of genomes
    - While BA.1 was the predominant sub-lineage in December (84%) and January (48%), the proportion of BA.2 increased from 5% in December and 42% in January to 86% in February
    - BA.3 continues to be detected at low levels

- Low frequency of currently and previously circulating variants such as Delta and Beta still detected in recent data

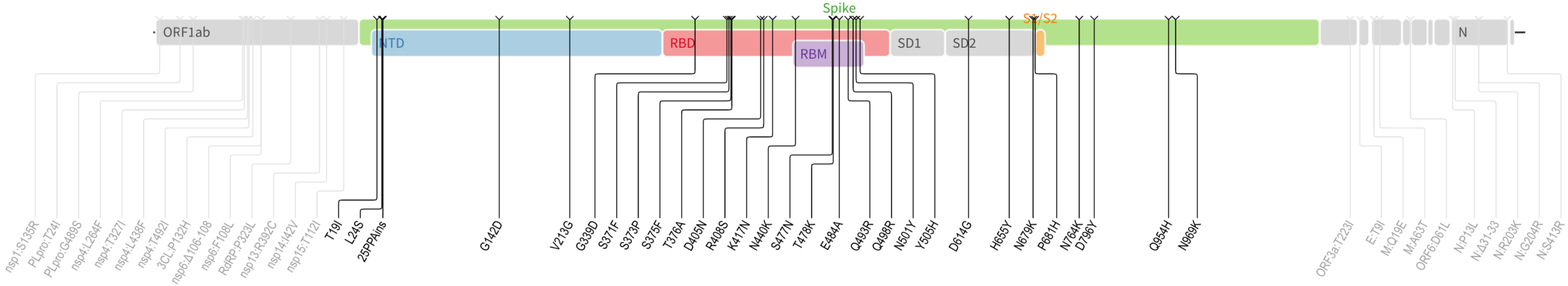
Omicron sub-lineage spike mutation profiles

BA.1
21K

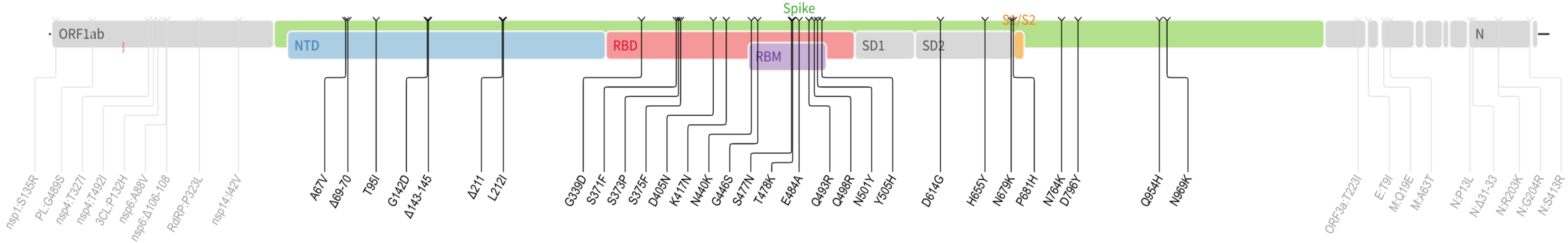


BA.2
21L

Lacks 69-70del
Not detectable by
S-Gene Target
Failure



BA.3
21M



Lineage definitions based on https://github.com/cov-lineages/pango-designation/issues/367
Images from https://covdb.stanford.edu/page/mutation-viewer/

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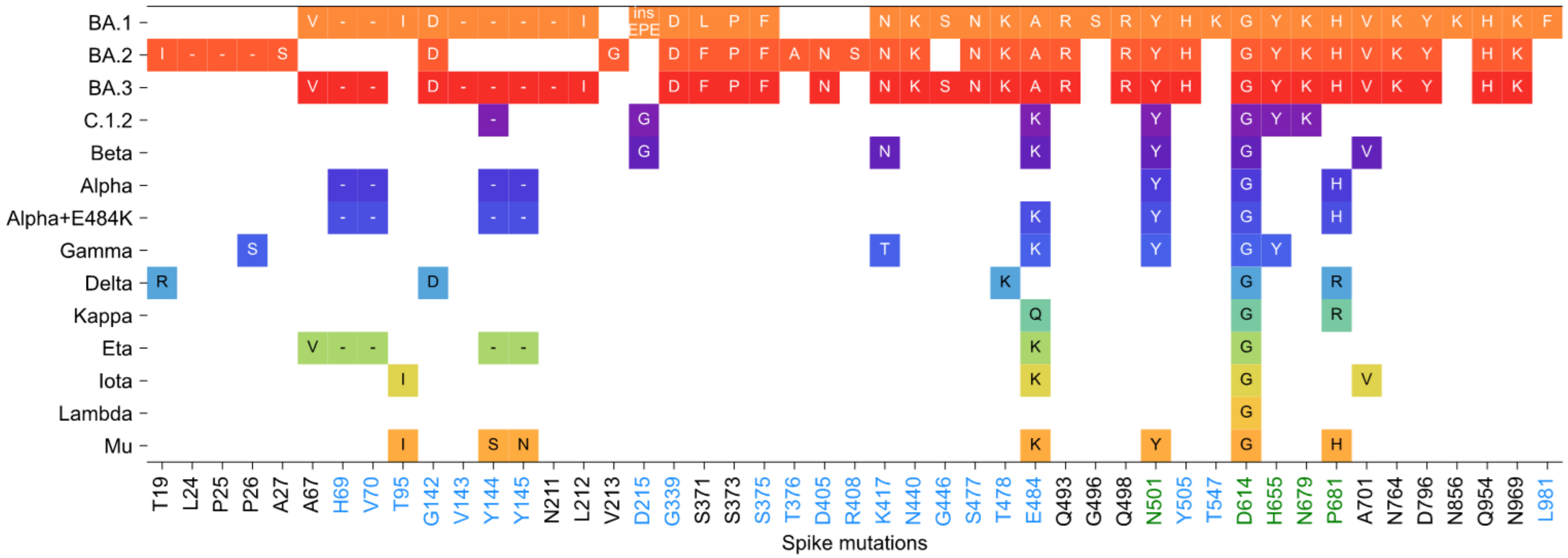
Omicron spike mutations compared to other VOC/VOIs



	T19	L24	P25	P26	A27	A67	H69	V70	T95	G142	V143	Y144	Y145	N211	L212	V213	D215	G339	S371	S373	S375	T376	D405	R408
BA.1						V	-	-	I	D	-	-	-	-	I		ins EPE	D	L	P	F			
BA.2	I	-	-	-	S					D						G		D	F	P	F	A	N	S
BA.3						V	-	-		D	-	-	-	-	I			D	F	P	F		N	
C.1.2												-					G							
Beta																	G							
Alpha							-	-				-	-											
Alpha+E484K							-	-				-	-											
Gamma				S																				
Delta	R									D														
Kappa																								
Eta						V	-	-				-	-											
Iota									I															
Lambda																								
Mu									I			S	N											

	K417	N440	G446	S477	T478	E484	Q493	G496	Q498	N501	Y505	T547	D614	H655	N679	P681	A701	N764	D796	N856	Q954	N969	L981
BA.1	N	K	S	N	K	A	R	S	R	Y	H	K	G	Y	K	H	V	K	Y	K	H	K	F
BA.2	N	K		N	K	A	R		R	Y	H		G	Y	K	H	V	K	Y		H	K	
BA.3	N	K	S	N	K	A	R		R	Y	H		G	Y	K	H	V	K	Y		H	K	
C.1.2						K				Y			G	Y	K								
Beta	N					K				Y			G				V						
Alpha										Y			G			H							
Alpha+E484K						K				Y			G			H							
Gamma	T					K				Y			G	Y									
Delta					K								G			R							
Kappa						Q							G			R							
Eta						K							G										
Iota						K							G				V						
Lambda													G										
Mu						K				Y			G			H							

Only lineage-defining mutations are pictured here. Low prevalence mutations can be seen on the following slide.

Mutation impact key

- ⬛ Unknown or unconfirmed impact
- 🟦 Known/predicted immune escape
- 🟩 Enhanced infectivity

- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be linked to immune escape

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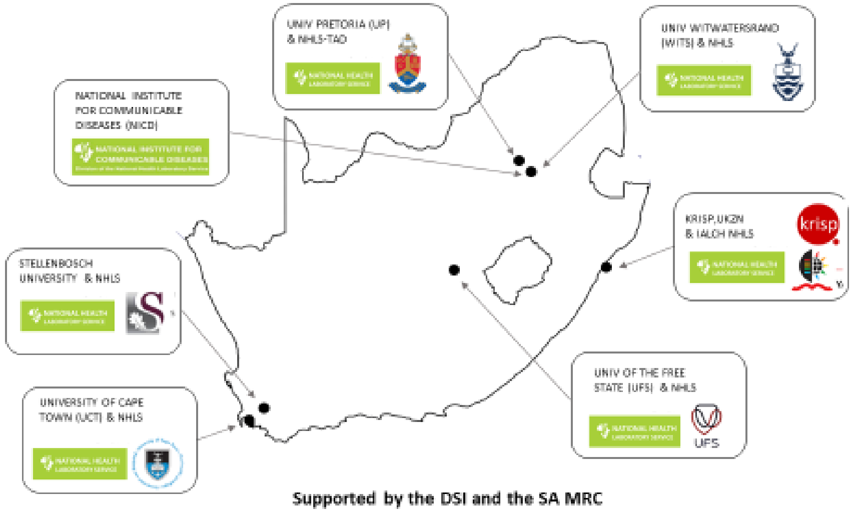

Supported by the DSI and the SA MRC

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science & innovation
Department:
Science and Innovation
REPUBLIC OF SOUTH AFRICA

UFS

saMRC advancinglife

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

EDCTP

This project (RIA2020EF-3030) is part of the EDCTP2 programme supported by the European Union"

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INYUVESI YAKWAZULU-NATALI

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Kamela Mahlakwane
Mathilda Claassen
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Dr Kerusha Govender
Dr Pravi Moodley
Dr Aabida Khan
Dr Lili Gounder
Dr Kerri Francois
Dr Cherise Naicker
Dr Joedene Chetty

Dr Neli Ngcaba
Dr Tshepiso Mosito
Mr Malcolm Ellapen
Mr Kubendran Reddy
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Eduan Wilkinson
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Sureshnee Pillay
Emmanuel James San

AHRI
Alex Sigal
Sandile Cele
Willem Hanekom

University of Cape Town, NHLS & Western Cape Government

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Theuns Jacobs
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UCT, IDM and CIDRI-Africa
Deelan Doolabh
Arash Iranzadeh
Lynn Tyers
Innocent Mudau
Nokuzola Mbhele
Fezokuhle Khumalo
Thabang Serakge
Bruna Galvão
Arghavan Alisoltani (U. California)

Robert Wilkinson
Darren Martin
Nicola Mulder
Wendy Burgers
Ntobeko Ntusi
Rageema Joseph
Sean Wasserman
Linda Boloko

Zoonotic arbo and respiratory virus program Centre for Viral Zoonoses Department Medical Virology/ NHLS Tshwane Academic division University of Pretoria

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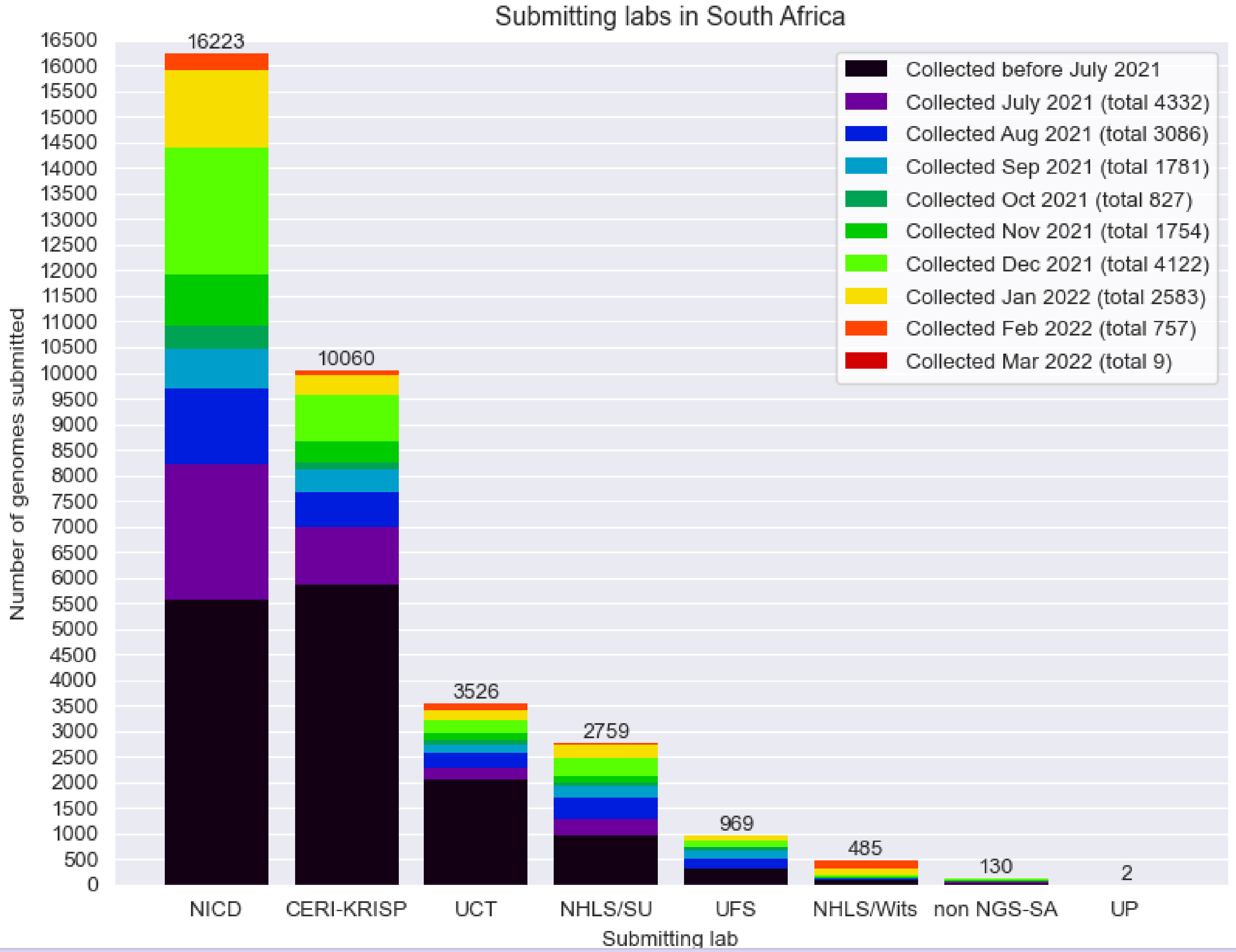
South African genomes submitted per submitting lab, 2020 - 2022 (N=34 154)



NGS-SA Labs

CERI: Centre for Epidemic Response and Innovation

KRISP: KZN Research Innovation and Sequencing Platform

NICD: National Institute for Communicable Diseases

NHLS: National Health Laboratory Service

SU: Stellenbosch University

UCT: University of Cape Town

UFS: University of the Free State

UP: University of Pretoria

Multiple labs from NGS-SA and collaborating public and private laboratories are contributing to sequencing, both as originating and as submitting (pictured here) laboratories.

NGS-SA
Network for Genomic
Surveillance in South Africa

Currently circulating Variants of Concern (VOC)

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:K417N +S:K484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GR/484A	21K	+S:R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 18 March 2022

•Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.

° Only found in a subset of sequences

Previously circulating Variants of Concern

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	United Kingdom, Sep-2020	VOC: 18-Dec-2020 Previous VOC: 09-Mar-2022
Beta	B.1.351	GH/501Y.V2	20H (V2)	South Africa, May-2020	VOC: 18-Dec-2020 Previous VOC: 09-Mar-2022
Gamma	P.1	GR/501Y.V3	20J (V3)	Brazil, Nov-2020	VOC: 11-Jan-2021 Previous VOC: 09-Mar-2022

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 18 March 2022

- Includes all descendant lineages. See the cov-lineages.org and the Pango network websites for further details.

Submission of routine specimens for sequencing

- representative of multiple geographic regions (provinces/districts/health facilities) from individuals of
  - all ages
  - over as many time periods during the SARS-CoV-2 epidemic in South Africa
- requested that testing laboratories in both the private and public sectors, submit respiratory samples to their closest NGS-SA sequencing laboratory on a routine basis (ideally every week) as follows, depending on the capacity of the testing laboratory:
  - All positives samples should be sent every week (NGS-SA laboratory will perform random sampling as described below) **OR**
  - A weekly selection of approximately 10%-20% of randomly selected positive samples should be sent every week. Number of selected samples will depend on the size of laboratory and how many other laboratories are drained by the submitting laboratory.

Submission of special interest specimens for sequencing

In addition to routine samples mentioned above, please send specimens separately to above and clearly marked if:

- Suspected vaccine breakthrough (≥14 days after vaccine), especially if hospitalised and clinically severe
- Suspected re-infection (≥90 days after previous episode), especially if hospitalised and clinically severe
- Prolonged shedding with high SARS-CoV-2 viral loads (i.e. Ct values less than 30 for more than 1 month post-primary diagnosis) in immunocompromised individuals
- Possible animal-to-human transmission
- Suspected cases of importation from another country, especially countries known to harbour SARS-CoV-2 variants of concern or countries with little available information
- Clusters of “unusual” cases (e.g., in terms of disease presentation, patient groups affected, etc.)