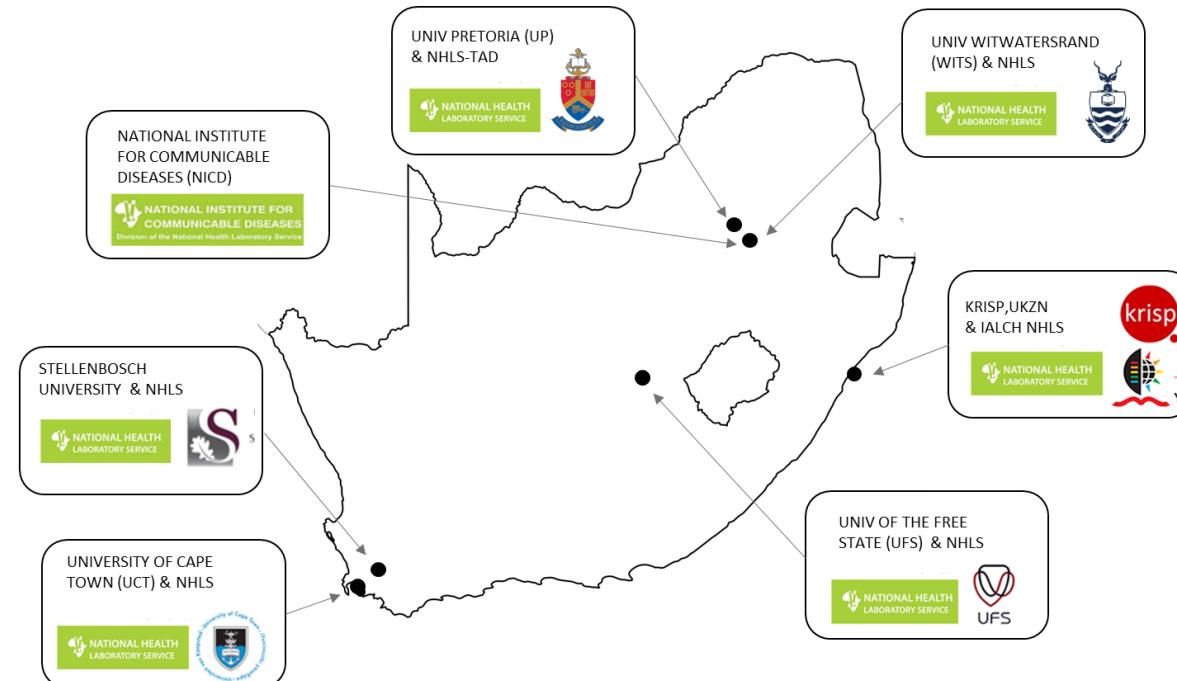


SARS-CoV-2 Sequencing Update

13 May 2022



Supported by the DSI and the SA MRC

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

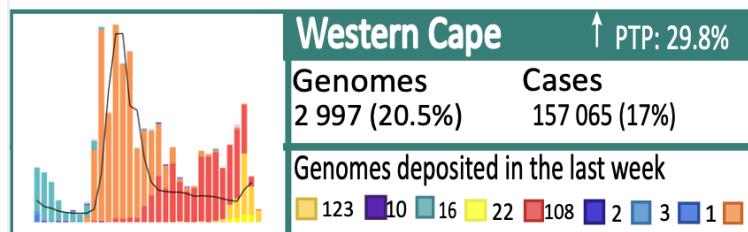
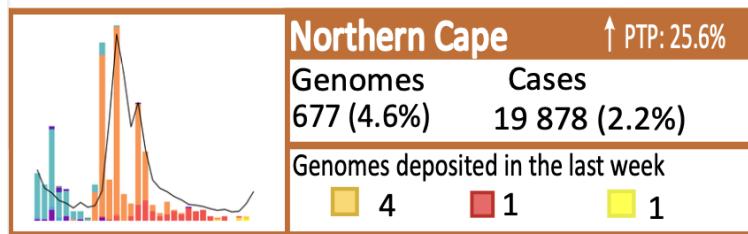
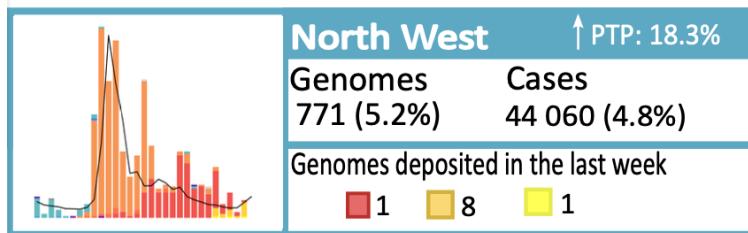
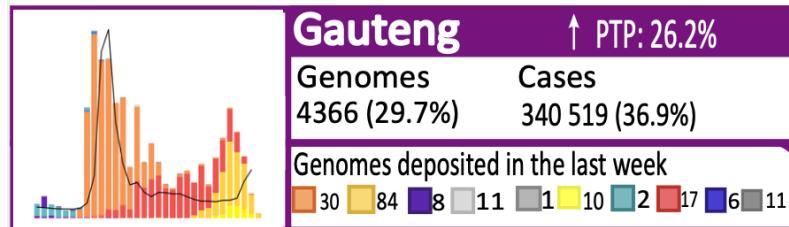
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 13 May 2022 at 08h25



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

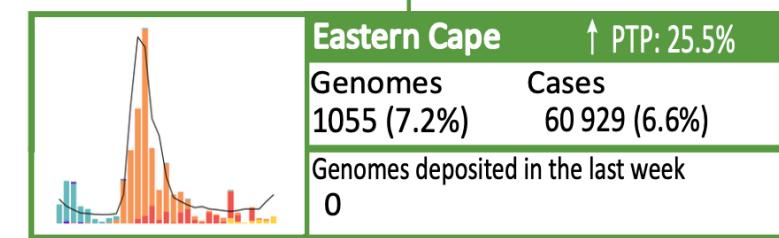
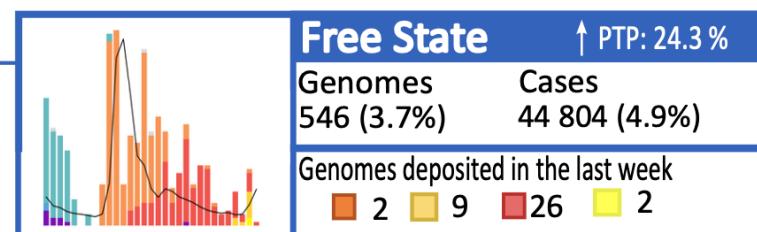
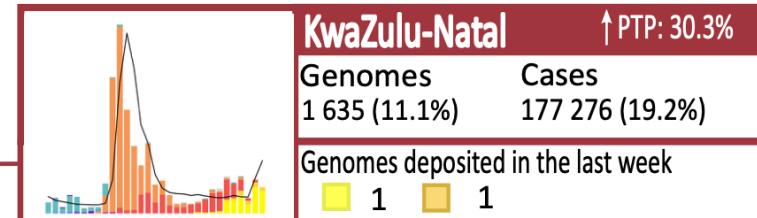
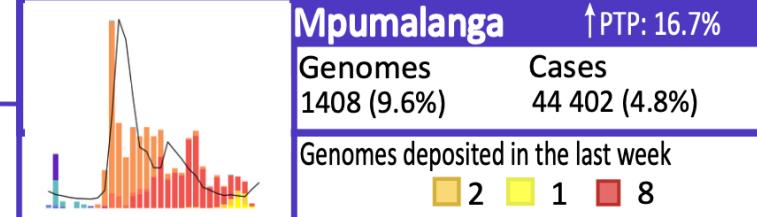
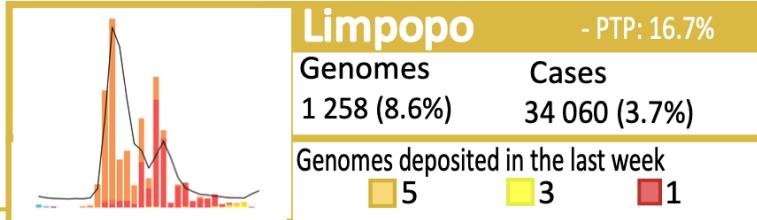
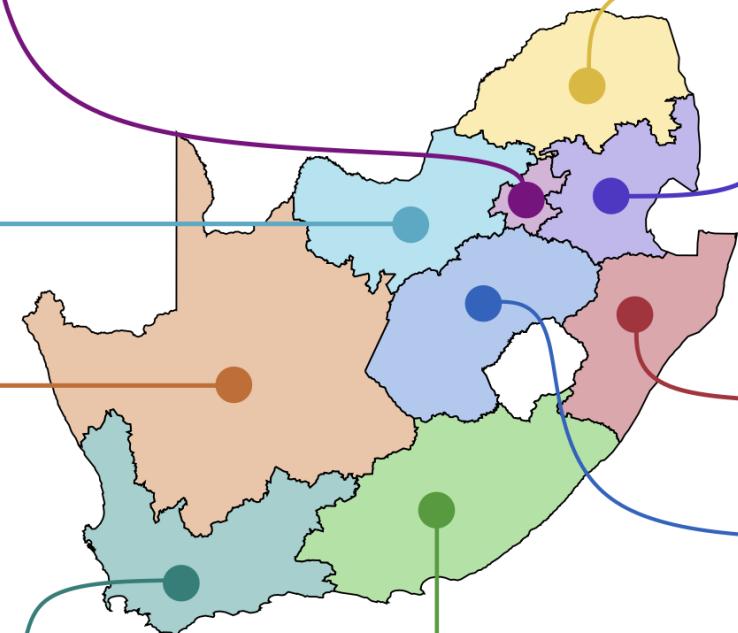
Elbe, S., and Buckland-Merrett, G. (2017) Data, disease and diplomacy: GISAID's innovative contribution to global health. *Global Challenges*, 1:33-46. DOI: 10.1002/gch2.1018 PMCID: 31565258

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



SARS-CoV-2 GENOMIC SURVEILLANCE

epiweeks 39 (2021) - 18 (2022)



Omicron (BA.1)	Beta (20H, V2)	Omicron (BA.5)	20A
Omicron (BA.1.1)	Alpha (20I, V1)	Omicron (BA.4)	20B
Omicron (BA.2)	C.1.2	20D	
Omicron (BA.3)	Delta (21A)		
	Delta (21I)	Delta (21J)	— Cases

547 genomes added since the previous report

Bar graphs represent genomes sequenced per epiweek, with lines representing cases by collection date (weeks 39 [2021] – 18 [2022])

Genomes and cases presented as provincial total (percentage of national total) for epiweeks 39 (2021) – 18 (2022)

PTP: percentage testing positive in week 18 (1 April 2022 – 7 April 2022); arrow indicates direction of change since previous week (24 Apr 2022 – 30 May 2022) if change was significant ($P < 0.05$)

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022 (N=39 463*)

Total genomes: 39 463
2020 genomes: 6 657
2021 genomes: 25 811
2022 genomes: 6 995

Sequencing data ending epi week 18 (ending 7 May 2022)

Currently in epi week 19 (ending 14 May 2022)

Number of sequences

1500

1000

500

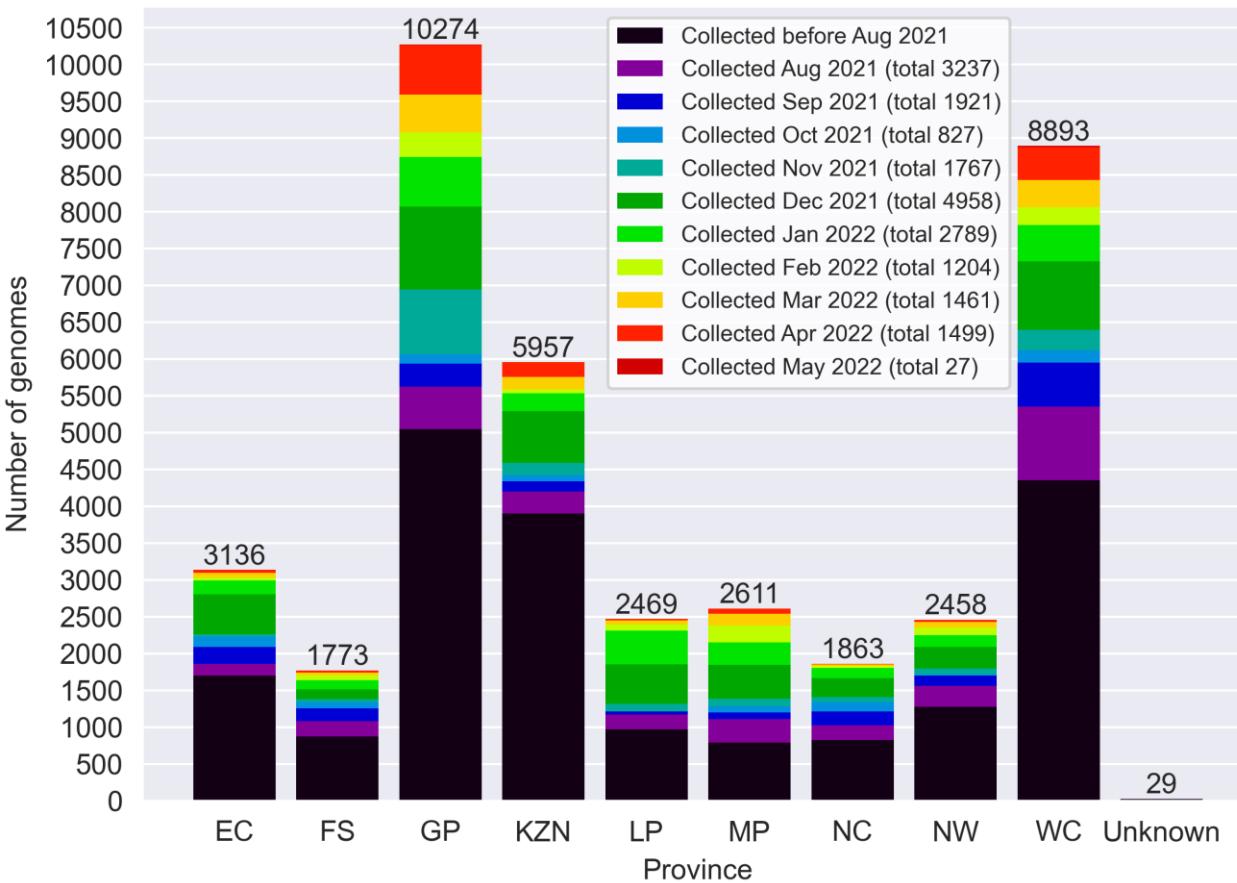
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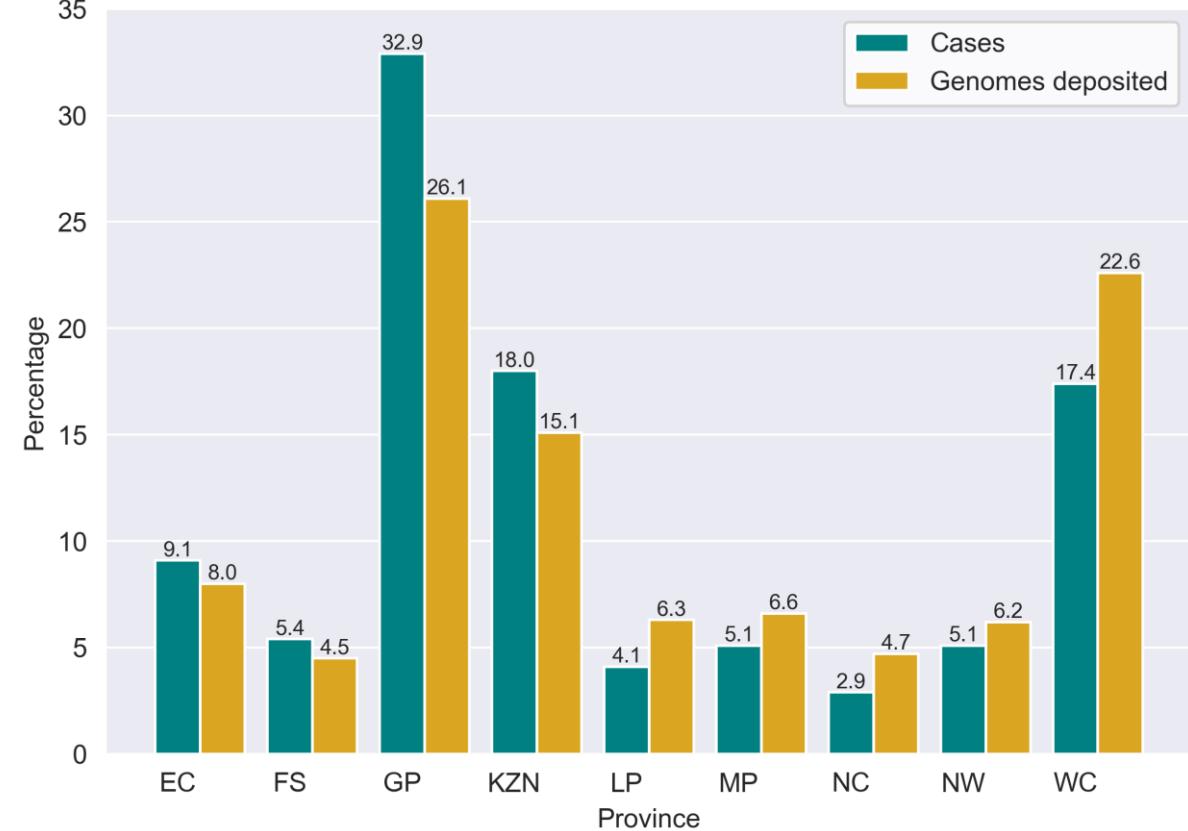
*This represents the cleaned, de-duplicated dataset of unique National and Pneumonia Surveillance sequences. This dataset will be used for all further figures.

GISAID genomes vs total cases, 2020 – 2022 (N= 39 463)

Provincial breakdown of genomes deposited into GISAID

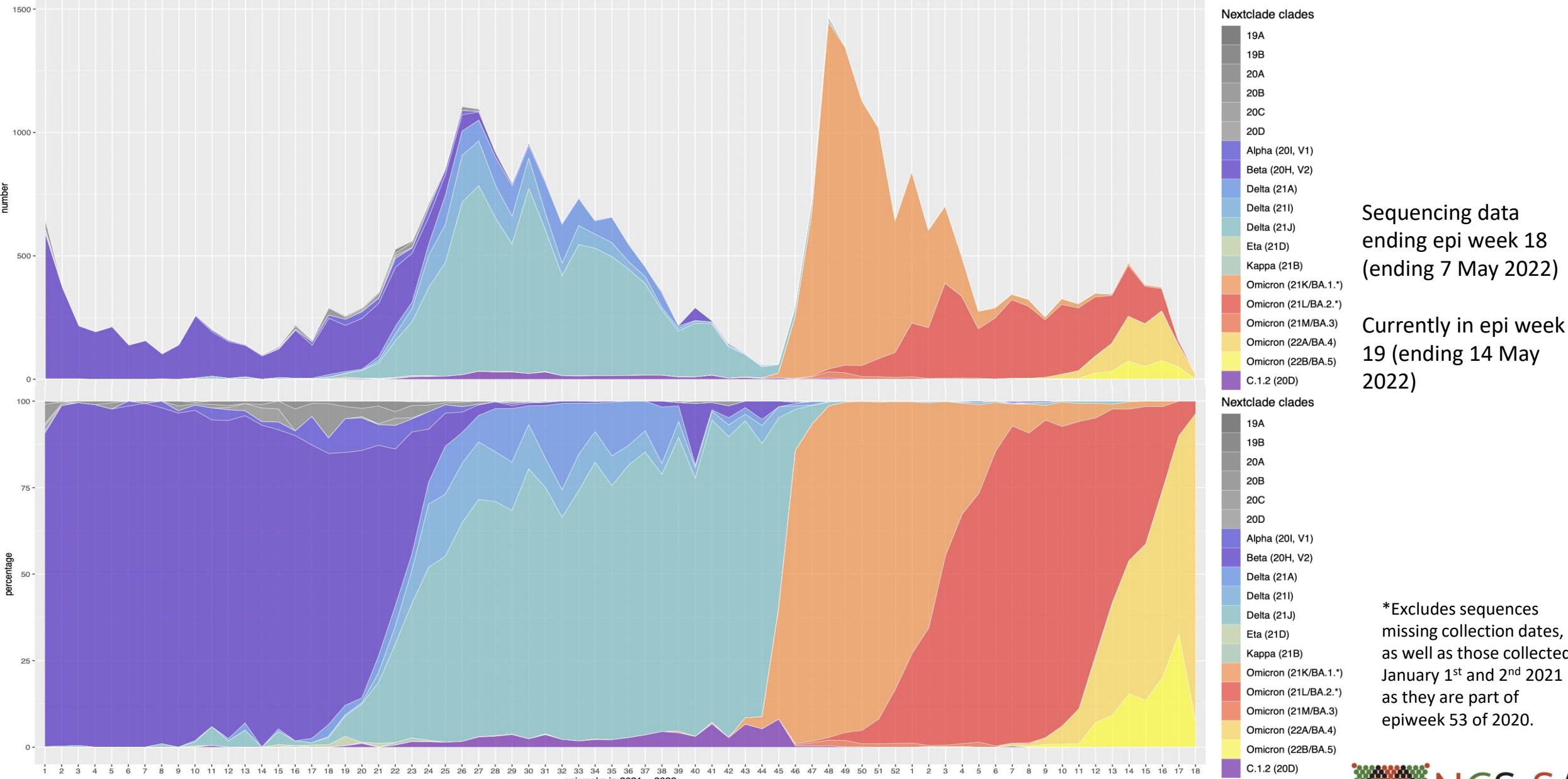


Proportion of total cases versus proportion of total genomes



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

Number and percentage of clades by epiweek in South Africa, 2021 – 2022 (32 719*)



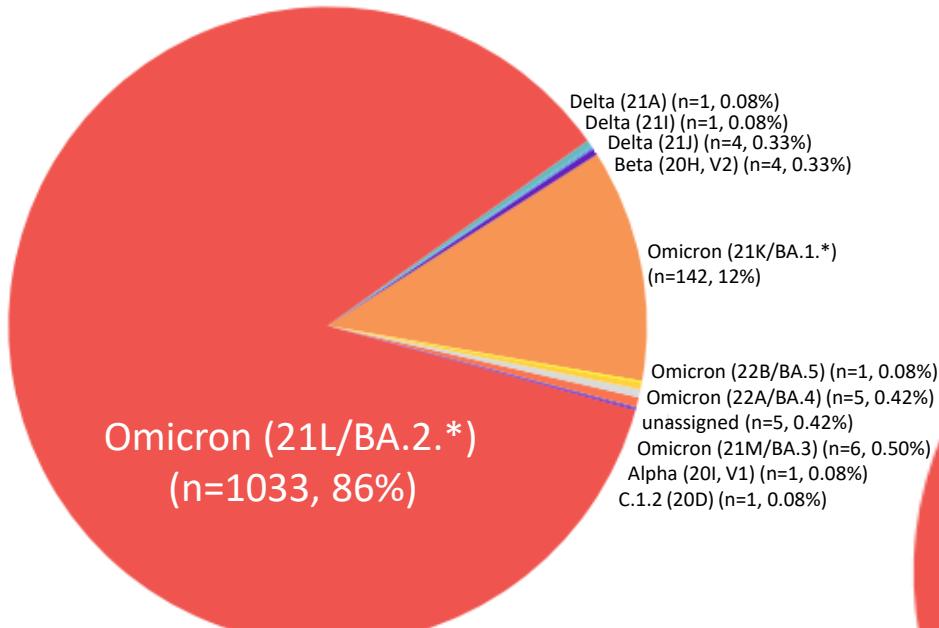
*Excludes sequences missing collection dates, as well as those collected January 1st and 2nd 2021 as they are part of epiweek 53 of 2020.

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

Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in

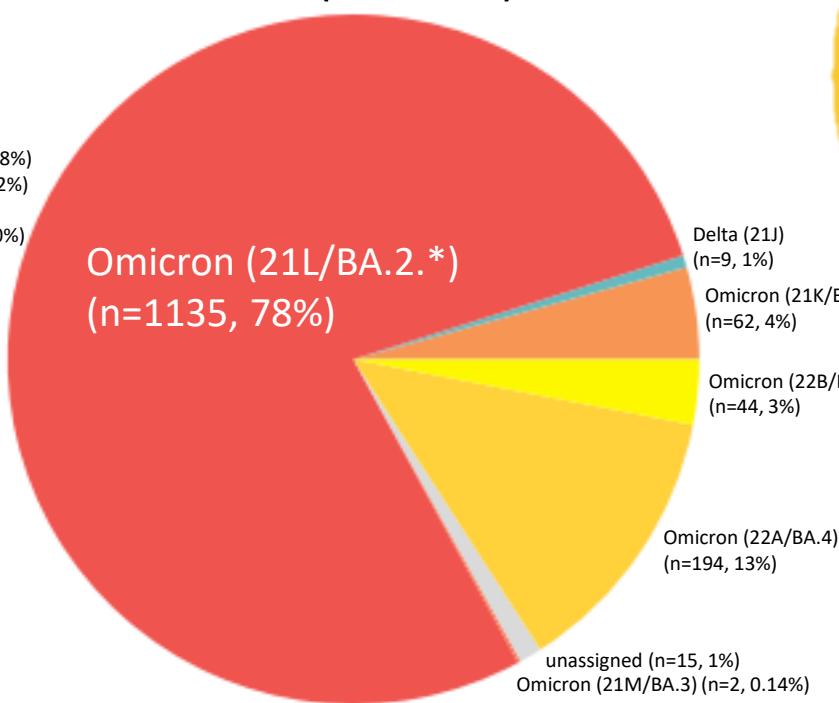
Feb – Apr 2022

February (N=1204)



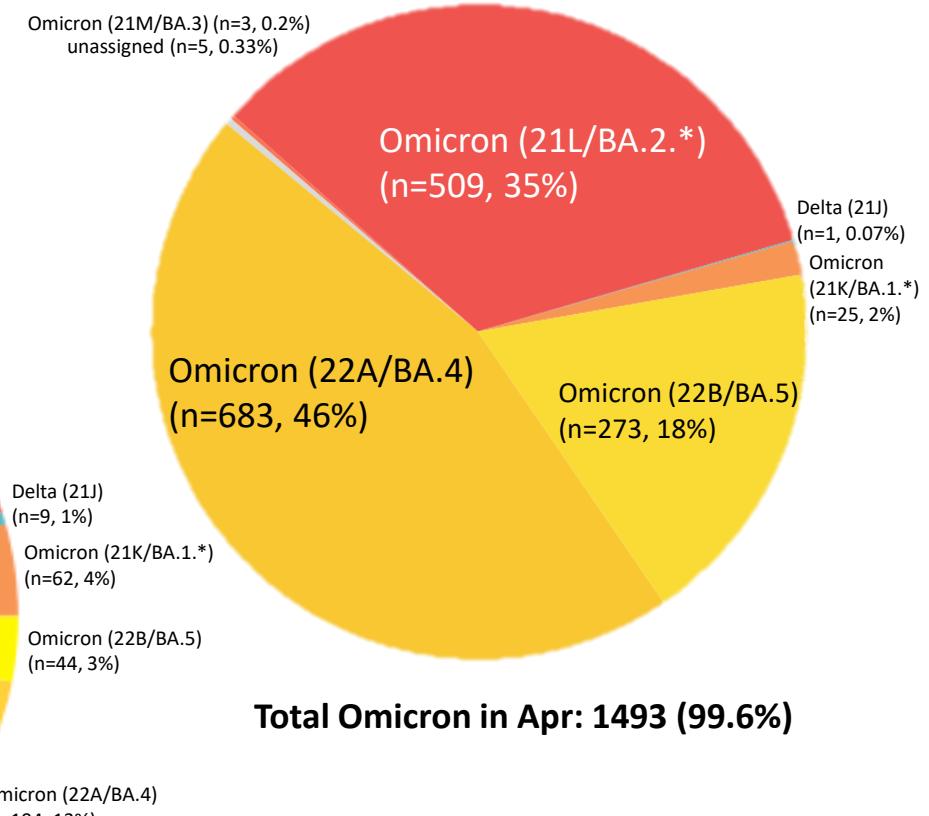
Total Omicron in Feb: 1187 (98.6%)

March (N=1461)

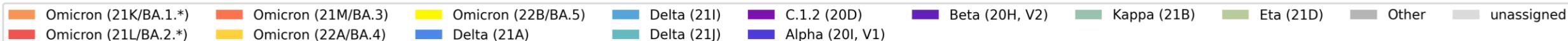


Total Omicron in Mar: 1437 (98.4%)

April (N=1499)



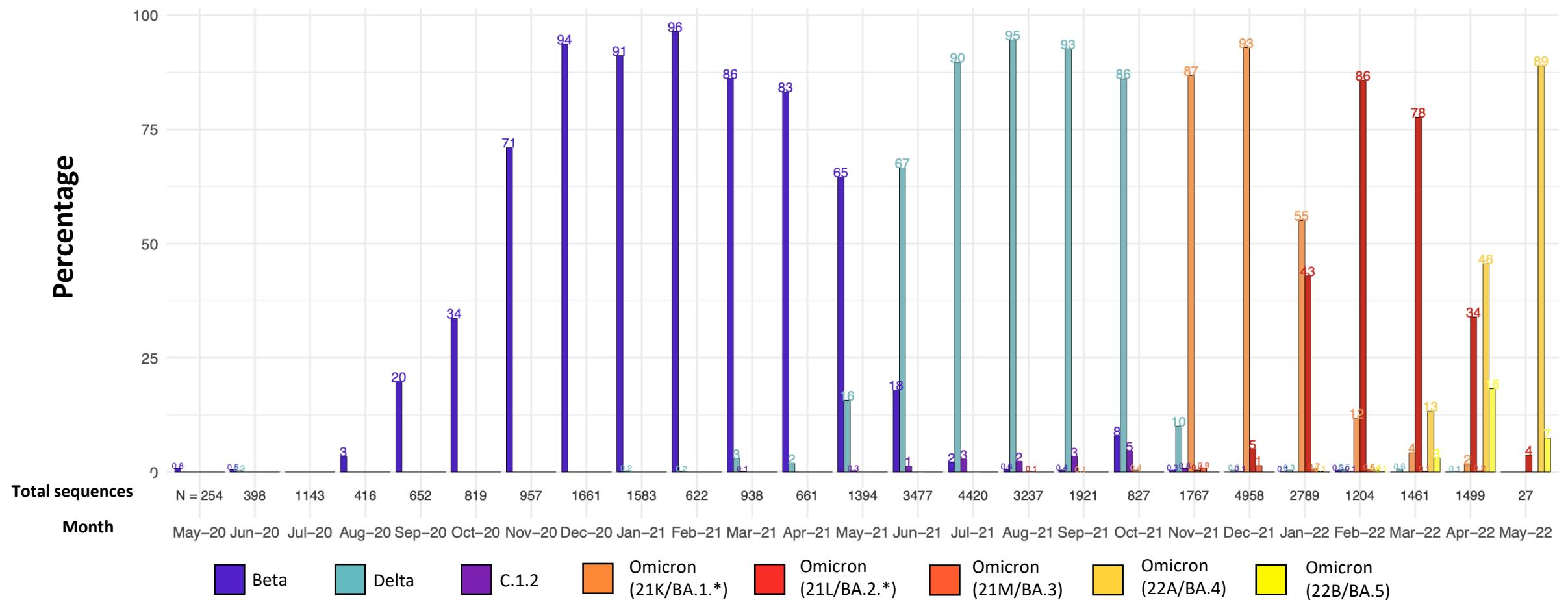
Total Omicron in Apr: 1493 (99.6%)



Omicron dominated in February (98.6%, 1187/1204), March (98.4%, 1437/1461) and April (99.6%, 1493/1499). BA.2 was dominant in February and March. BA.4 and BA.5 together were dominant in April.

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

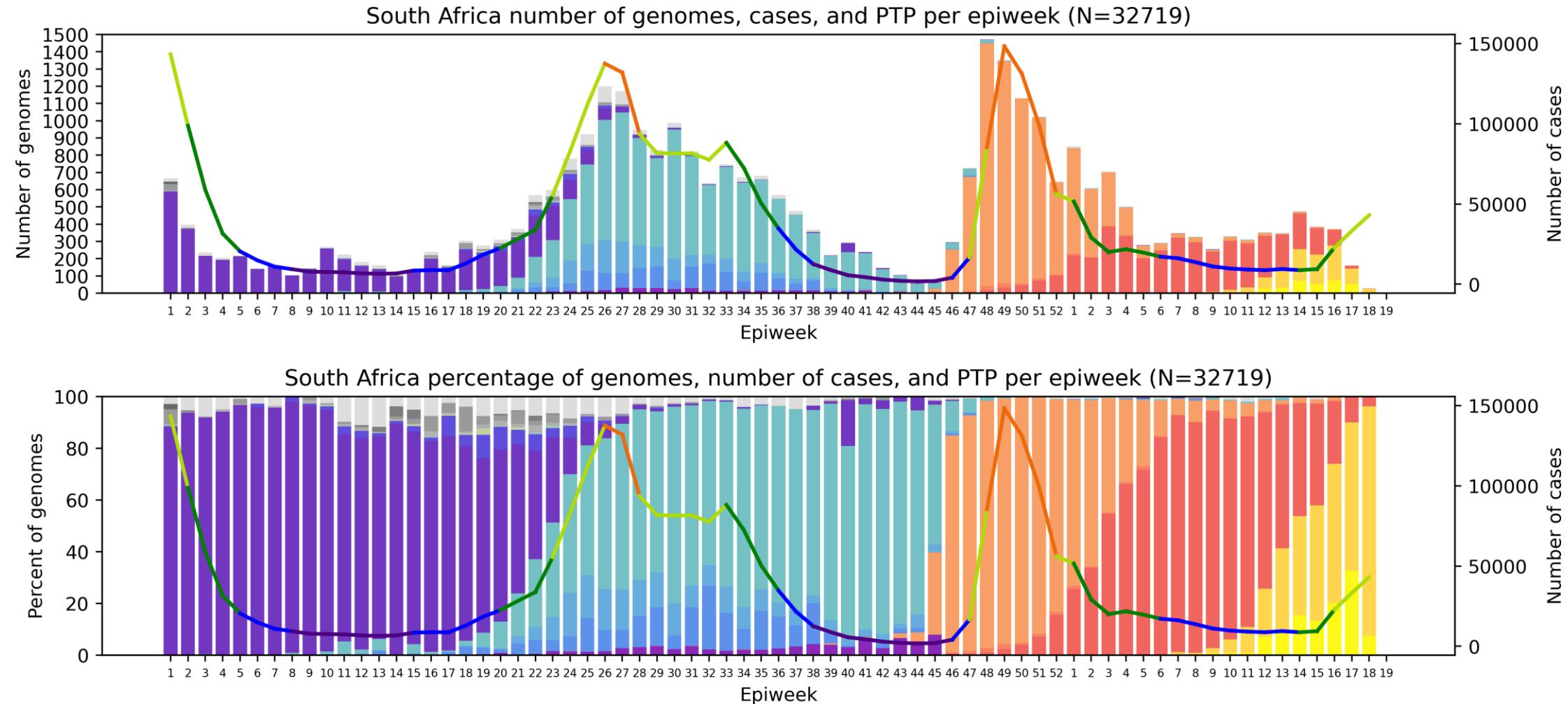
Detection rates of variants being monitored in South Africa



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

Omicron has been dominant since November (>85% in November, >98% in December – May).
BA.2 made up 43% of genomes in January, 86% in February, 78% in March and 34% in April. BA.4 and BA.5 together dominated in April, at 46% and 18% respectively, and appear to be dominant in May.

South Africa, 2021-2022, n = 32719*



Clade key (bar graph)

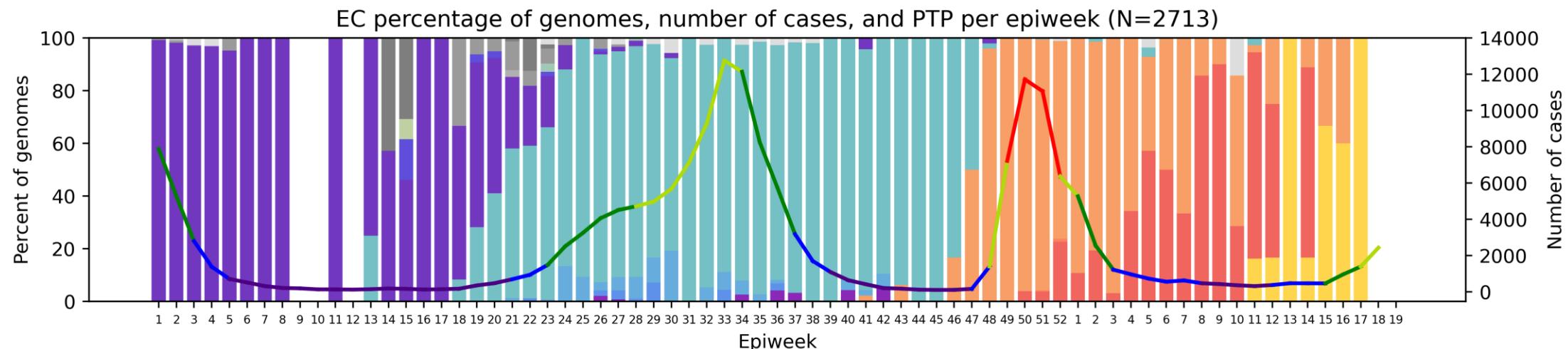
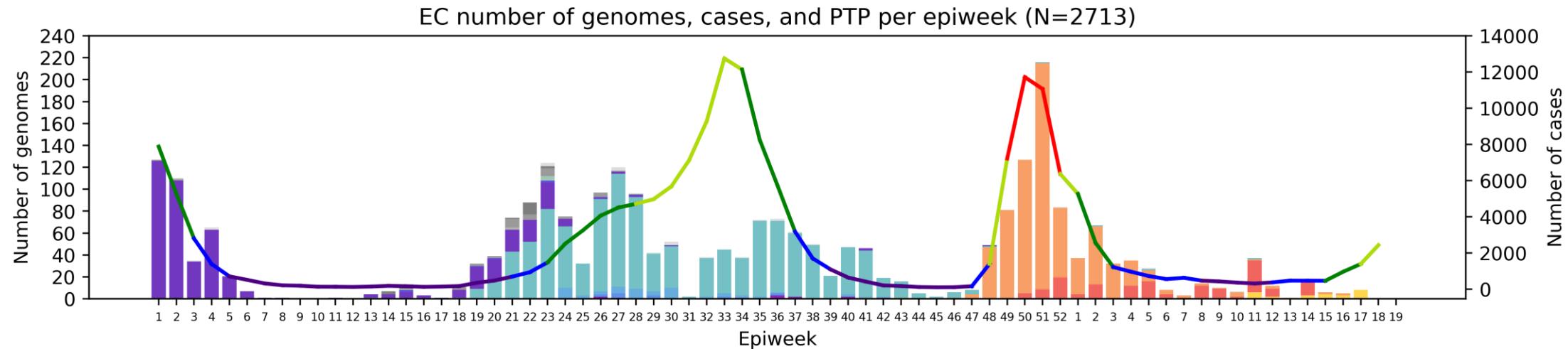
Omicron (21K/BA.1,*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2,*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)	Delta (21)									

Weekly percentage testing positive key (line graph)

≤ 5	6 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 55
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*Excludes sequences missing collection dates, as well as those collected January 1st and 2nd 2021 as they are part of epiweek 53 of 2020.

Eastern Cape Province, 2021-2022, n = 2713



Clade key (bar graph)

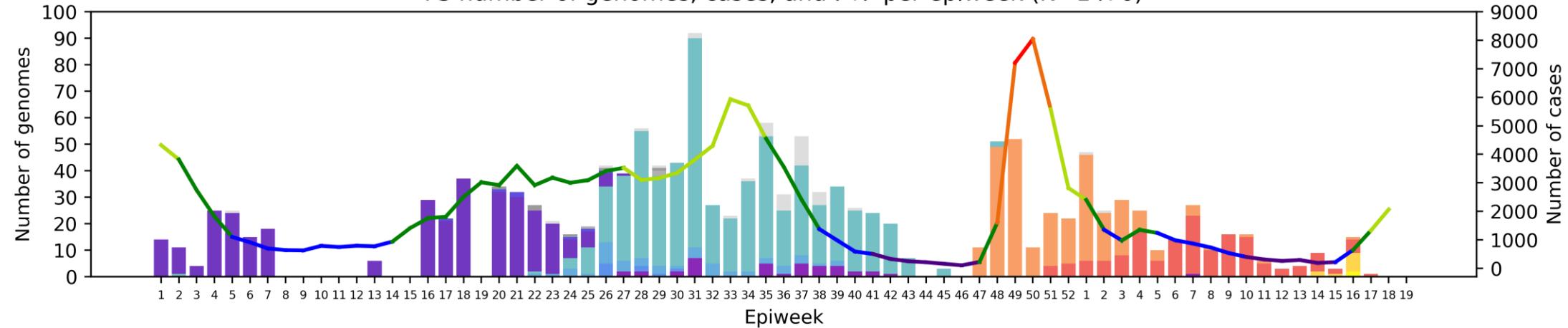
Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2.*)	Omicron (21L/BA.2.*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)	Delta (21)	Delta (21)	Delta (21)	Delta (21)	Delta (21)	Delta (21)	Delta (21)	Delta (21)	Delta (21)

Weekly percentage testing positive key (line graph)

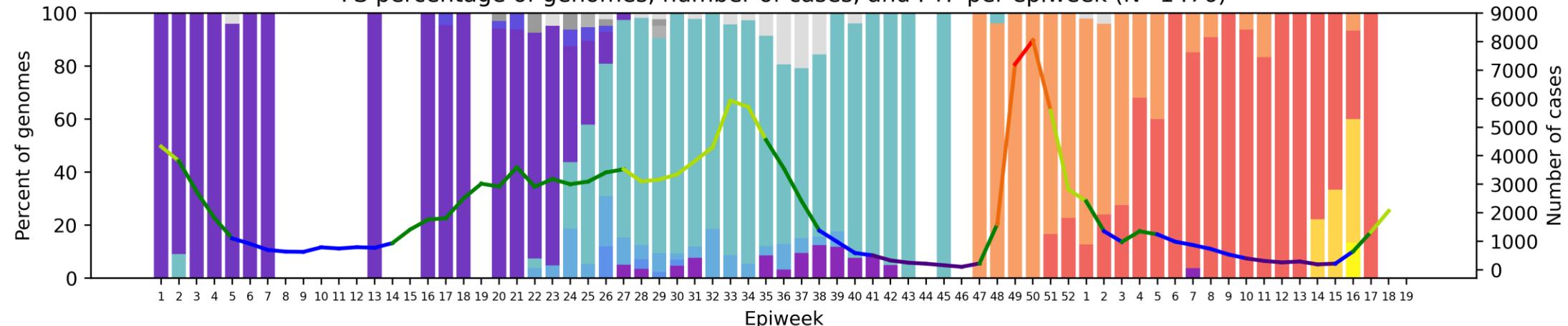
≤ 5	6 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 55
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Free State Province, 2021-2022, n = 1476

FS number of genomes, cases, and PTP per epiweek (N=1476)



FS percentage of genomes, number of cases, and PTP per epiweek (N=1476)



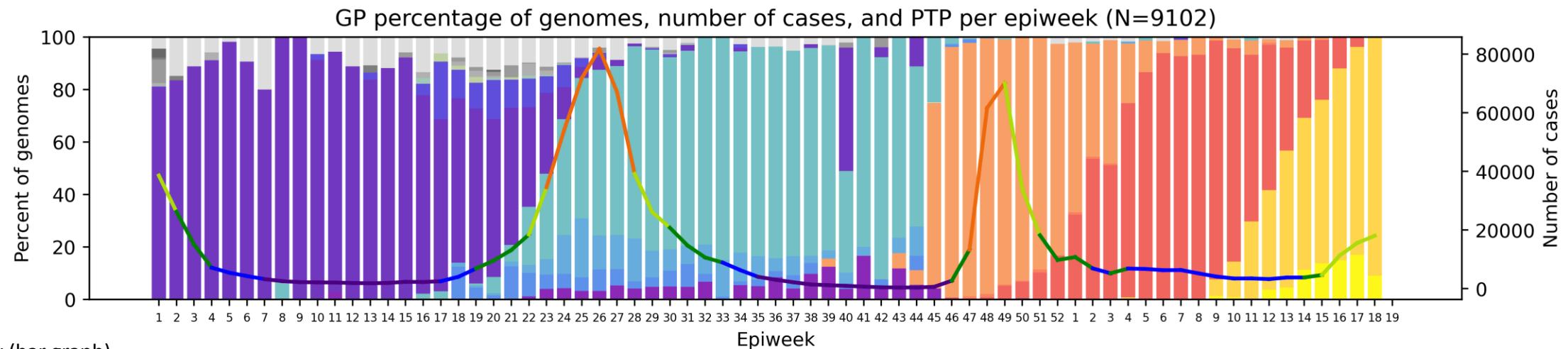
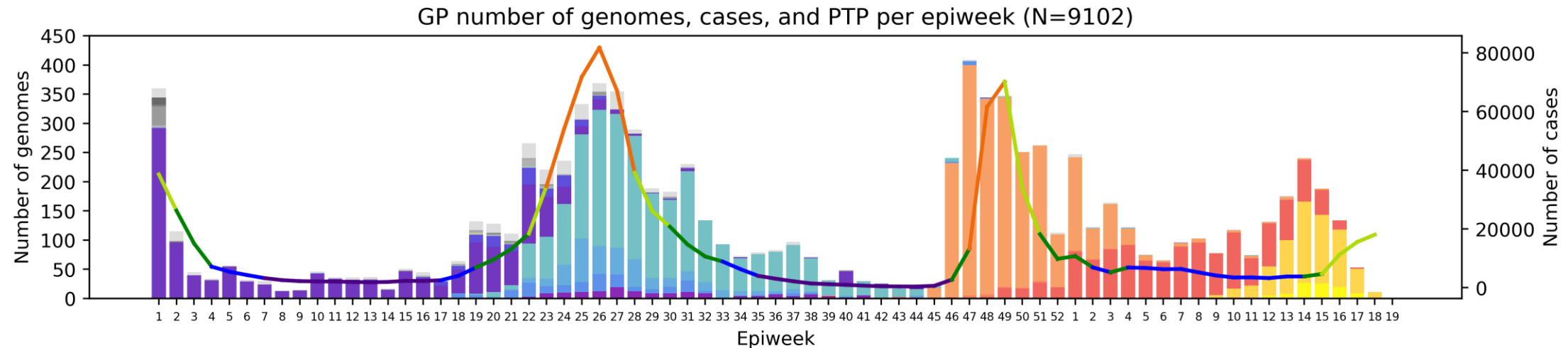
Clade key (bar graph)

Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2.*)	Omicron (21L/BA.2.*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)									

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 = 9102



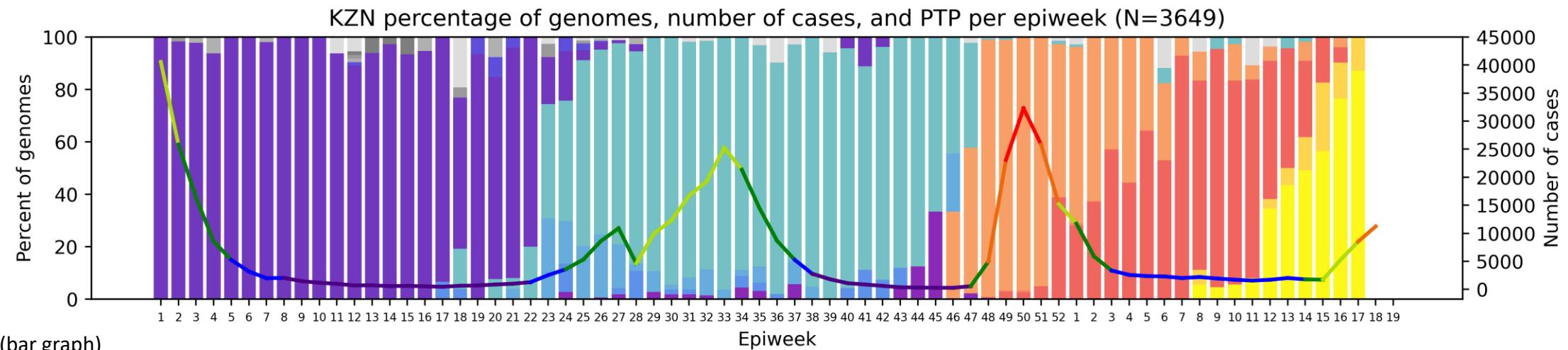
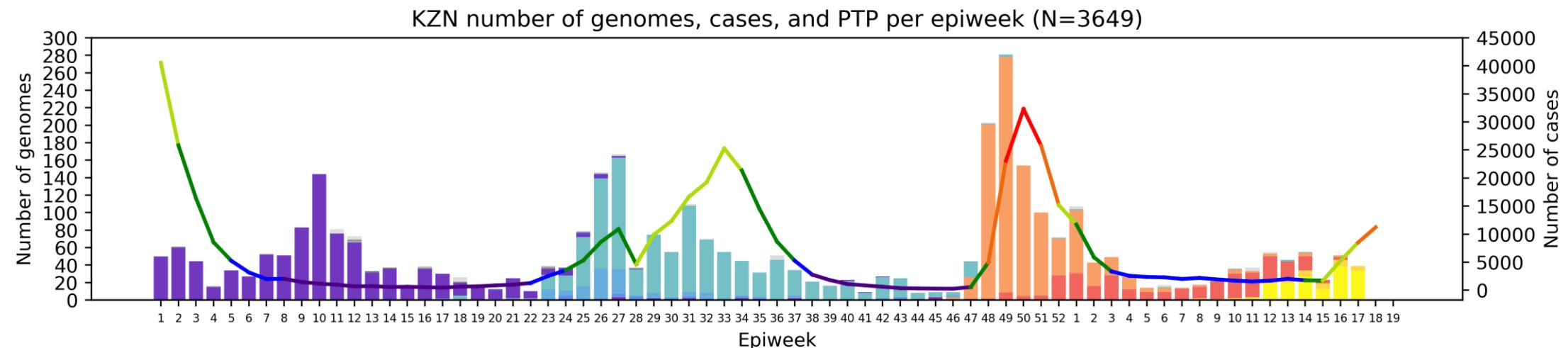
Clade key (bar graph)

Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2.*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)										

Weekly percentage testing positive key (line graph)

≤ 5	6 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 55
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KwaZulu-Natal Province, 2021-2022, n = 3649



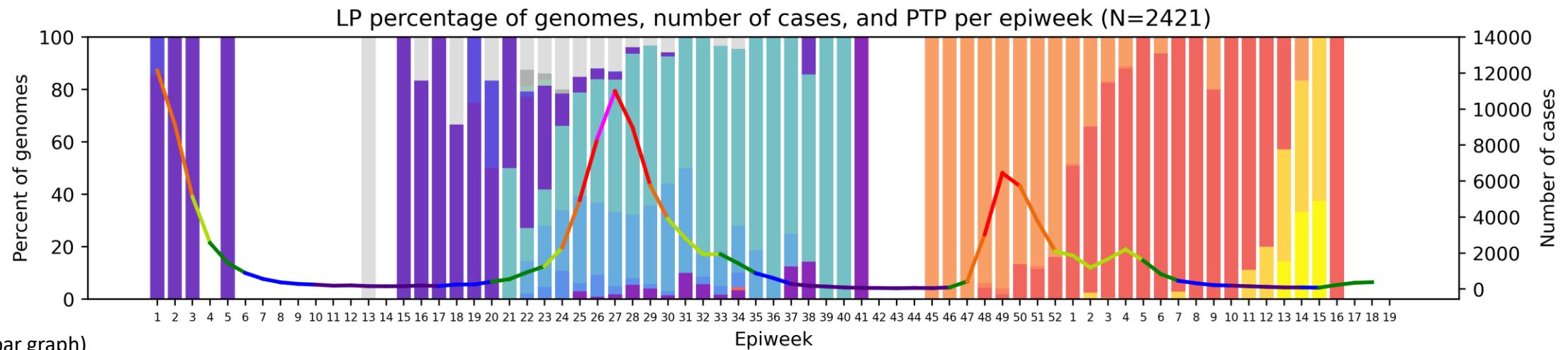
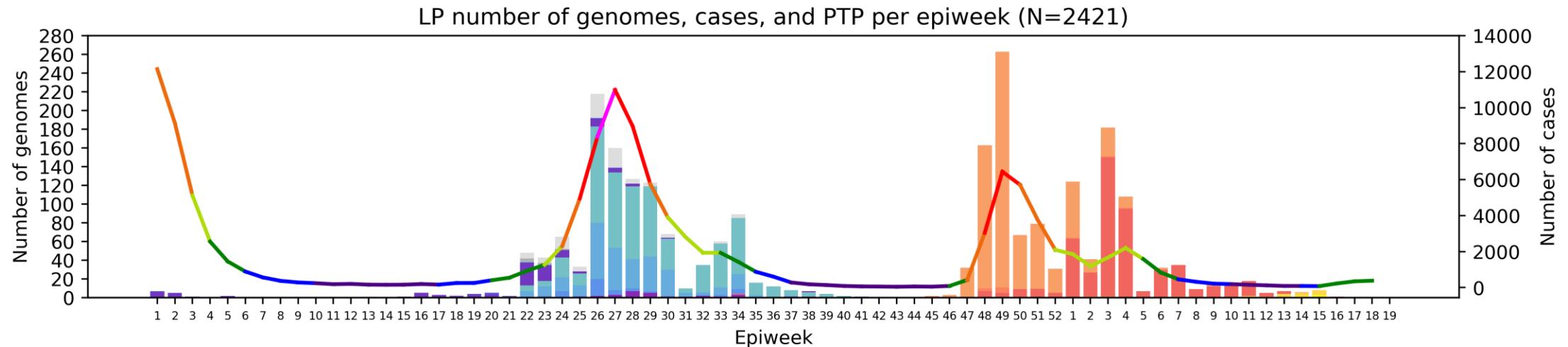
Clade key (bar graph)

Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2.*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)	Delta (21)			20D	20C	20B	20A	19B	19A	

Weekly percentage testing positive key (line graph)

≤ 5	6 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 55
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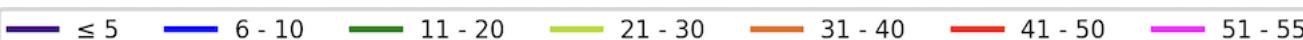
Limpopo Province, 2021-2022, n = 2421



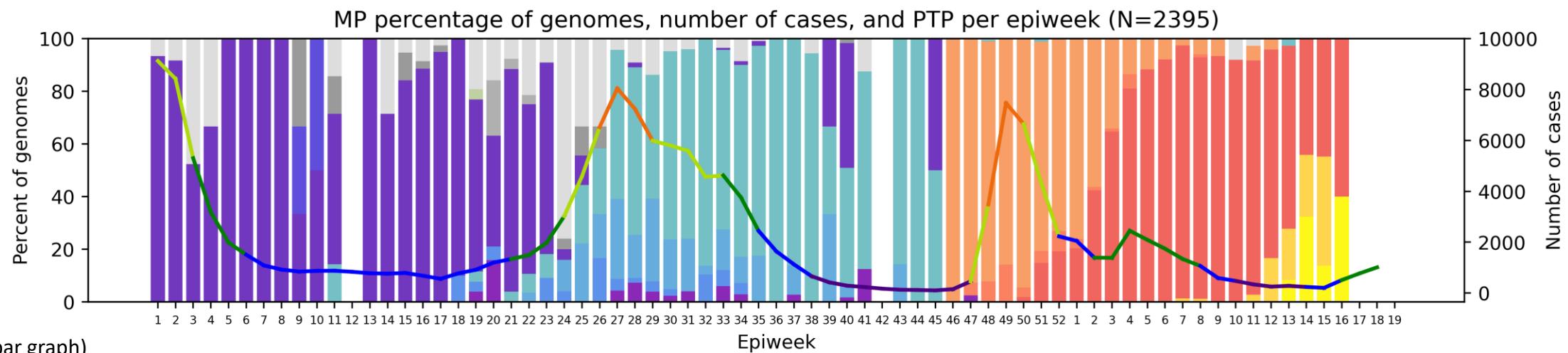
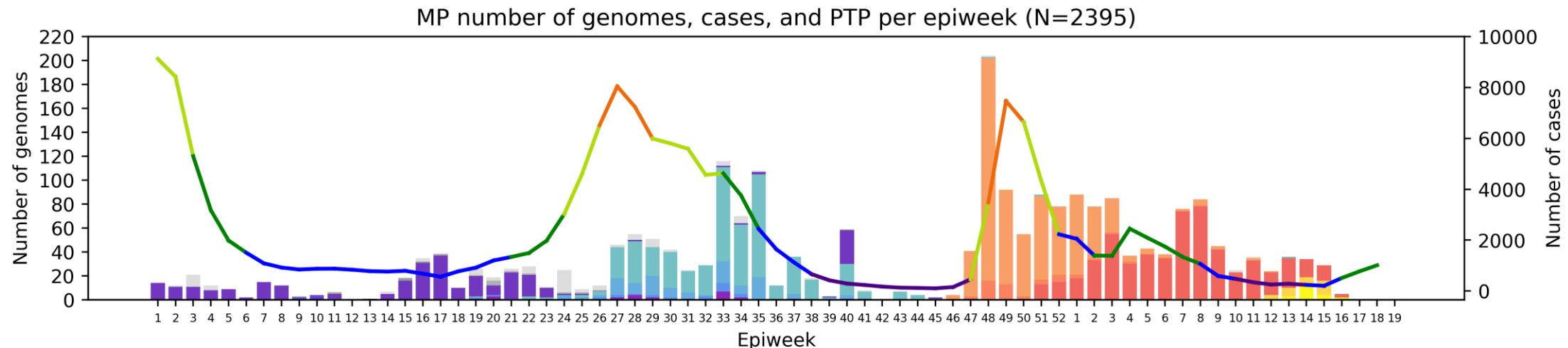
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



Mpumalanga Province, 2021-2022, n = 2395



Clade key (bar graph)

█ Omicron (21K/BA.1.*)
 █ Omicron (21M/BA.3)
 █ Omicron (22B/BA.5)
 █ Beta (20H, V2)
 █ Delta (21A)
 █ Delta (21J)
 █ Kappa (21B)
 █ Eta (21D)
 █ 20D
 █ 20C
 █ 20B
 █ 20A
 █ 19B
 █ 19A
 █ unassigned

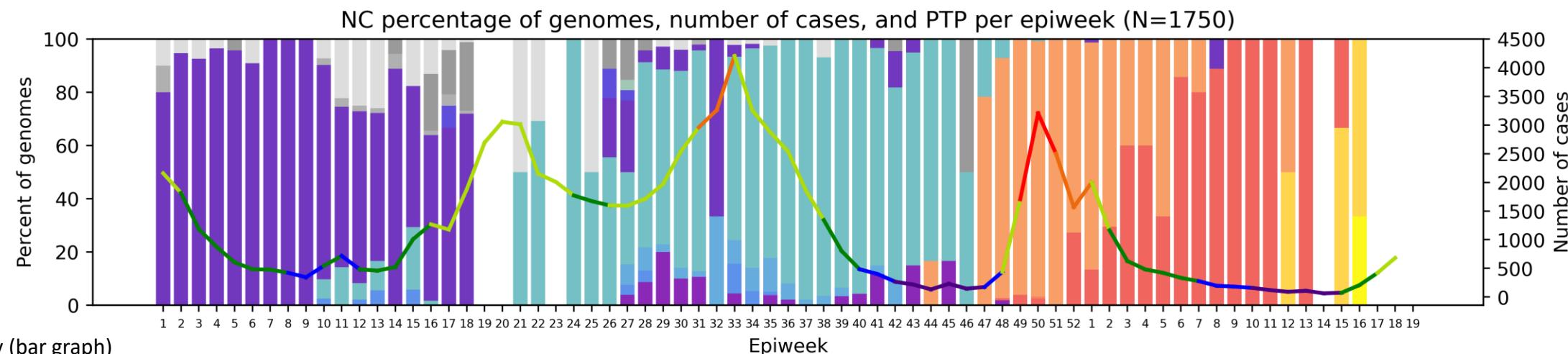
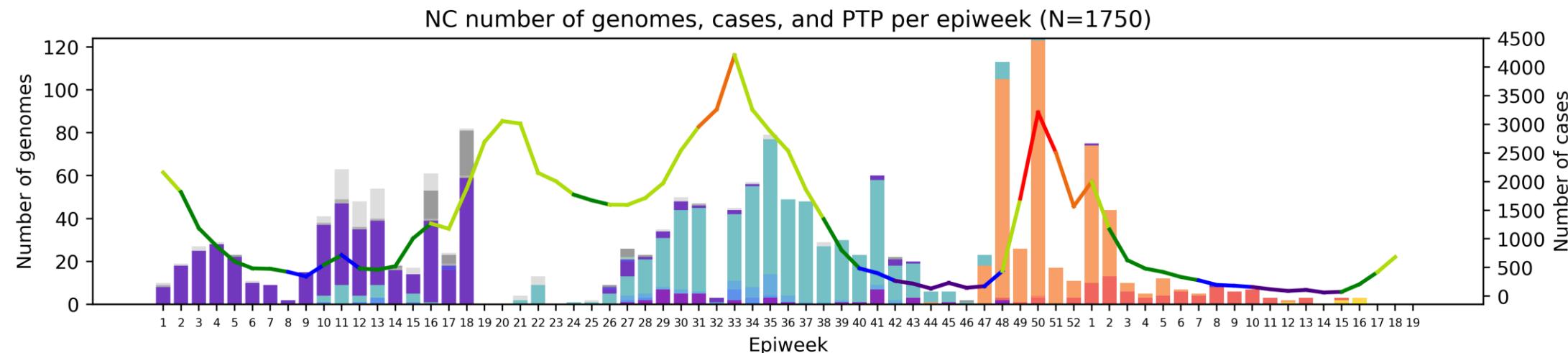
█ Omicron (21L/BA.2.*)
 █ Omicron (22A/BA.4)
 █ C.1.2 (20D)
 █ Alpha (20I, V1)
 █ Delta (21I)
 █ Cases

Weekly percentage testing positive key (line graph)

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



Northern Cape Province, 2021-2022, n = 1750



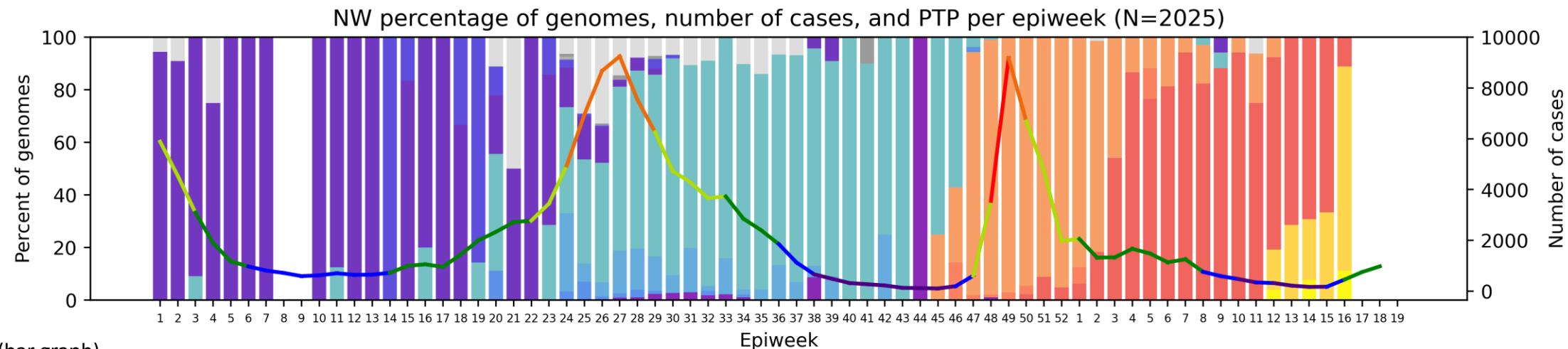
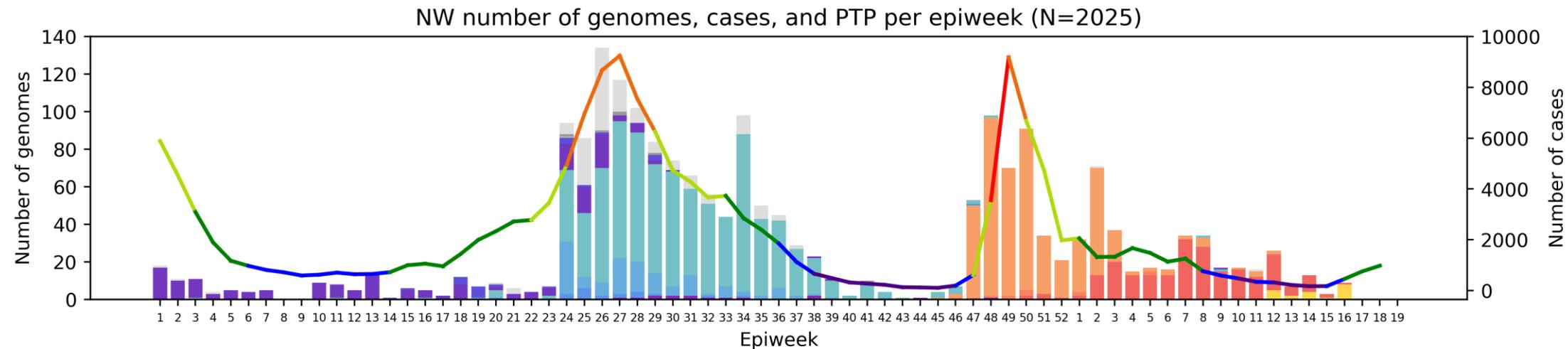
Clade key (bar graph)

Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	19B	19A	unassigned
Omicron (21L/BA.2.*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)	Delta (21)								

Weekly percentage testing positive key (line graph)

≤ 5	6 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 55
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North West Province, 2021-2022, n = 2025



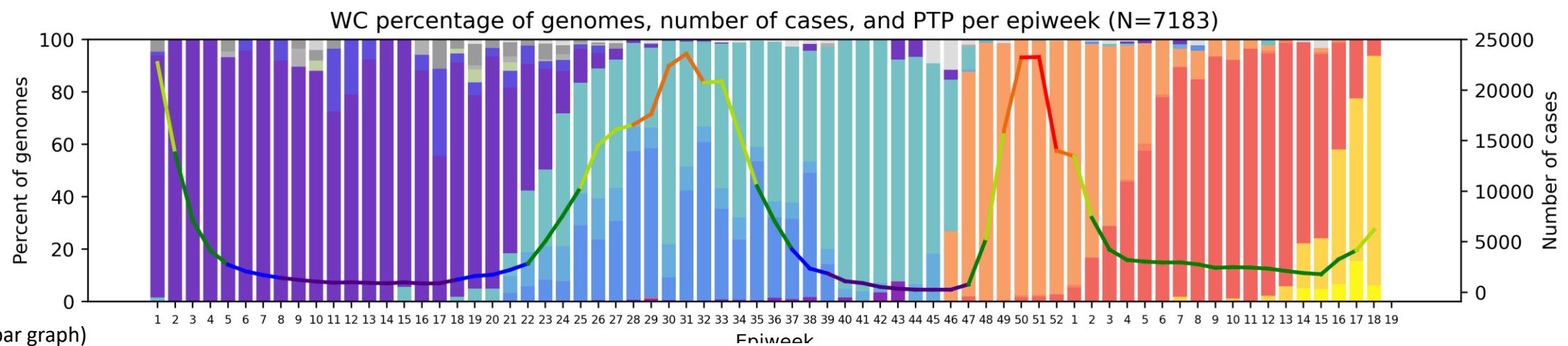
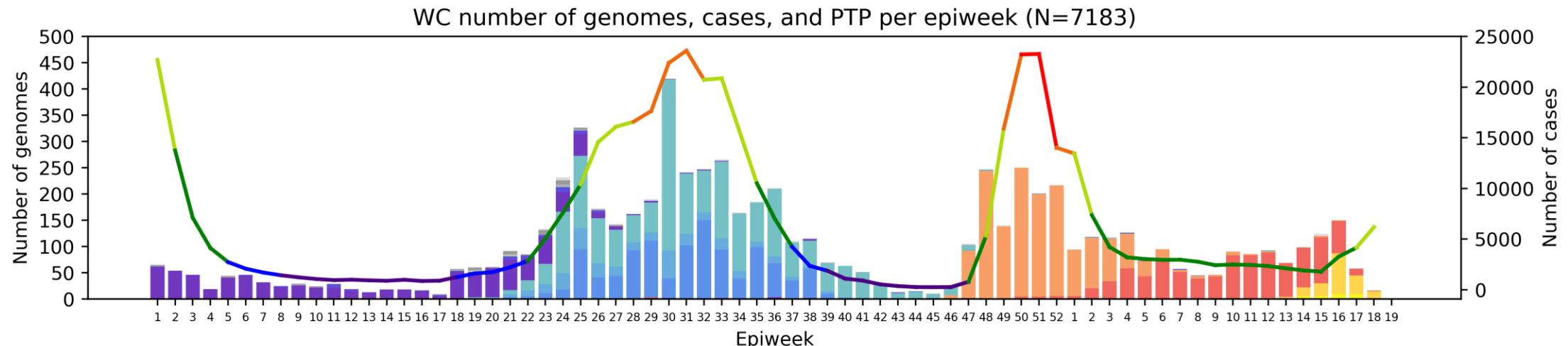
Clade key (bar graph)

Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2.*)		Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)			20D	20C	20B	20A	19B	19A	

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 = 7183



Clade key (bar graph)

Omicron (21K/BA.1.*)	Omicron (21M/BA.3)	Omicron (22B/BA.5)	Beta (20H, V2)	Delta (21A)	Delta (21J)	Kappa (21B)	Eta (21D)	20D	20C	20B	20A	19B	19A	unassigned
Omicron (21L/BA.2.*)	Omicron (22A/BA.4)	C.1.2 (20D)	Alpha (20I, V1)	Delta (21I)	Delta (21)			20D	20C	20B	20A	19B	19A	

Weekly percentage testing positive key (line graph)

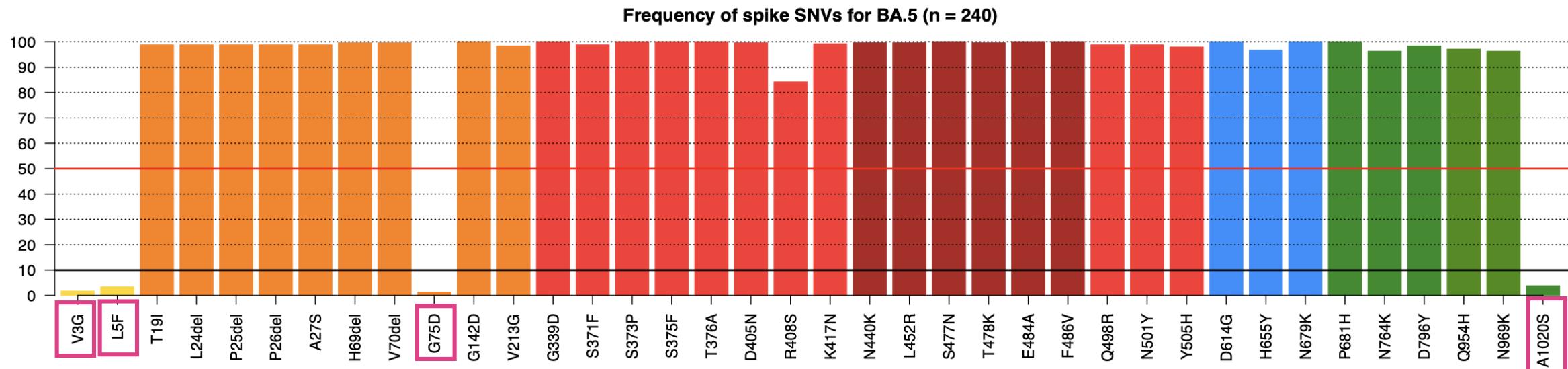
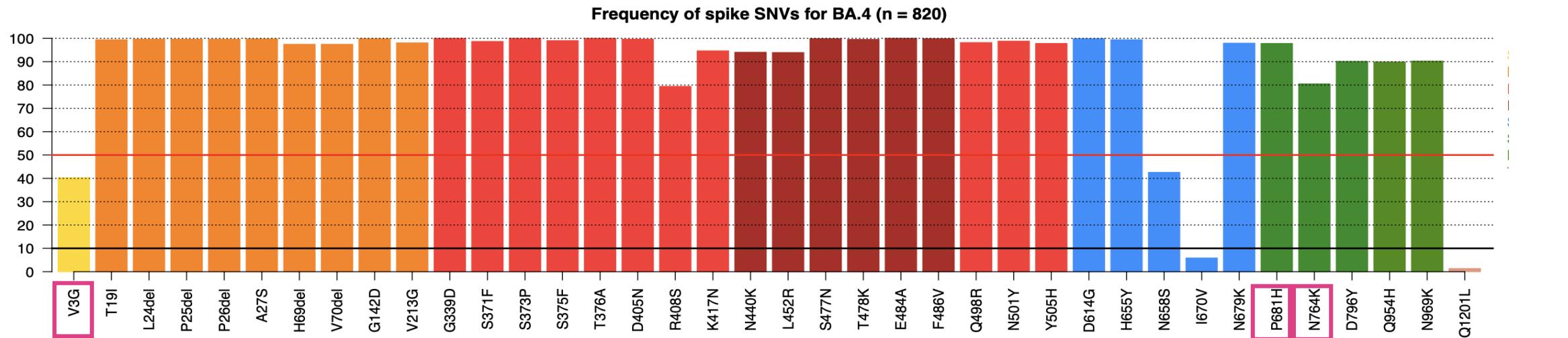
≤ 5	6 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 55
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Summary

- **Variant of Concern Omicron in South Africa**
 - Dominates 2022 sequencing data at >98% of genomes.
 - While BA.1 (and sub-lineages) was the predominant lineage in January (55%), BA.2 dominated in February (86%) and March (78%).
 - Omicron lineages BA.4 and BA.5 increased in prevalence in March (16%), and together are dominant in April (64%).
 - BA.4 and BA.5 make up 96% of May sequences, but more data is needed to determine prevalence.
 - BA.3 continues to be detected at low levels.
- NGS-SA teams are monitoring sequencing data for recombinants.
- Low frequency of previously circulating variants such as Delta still detected in recent data.

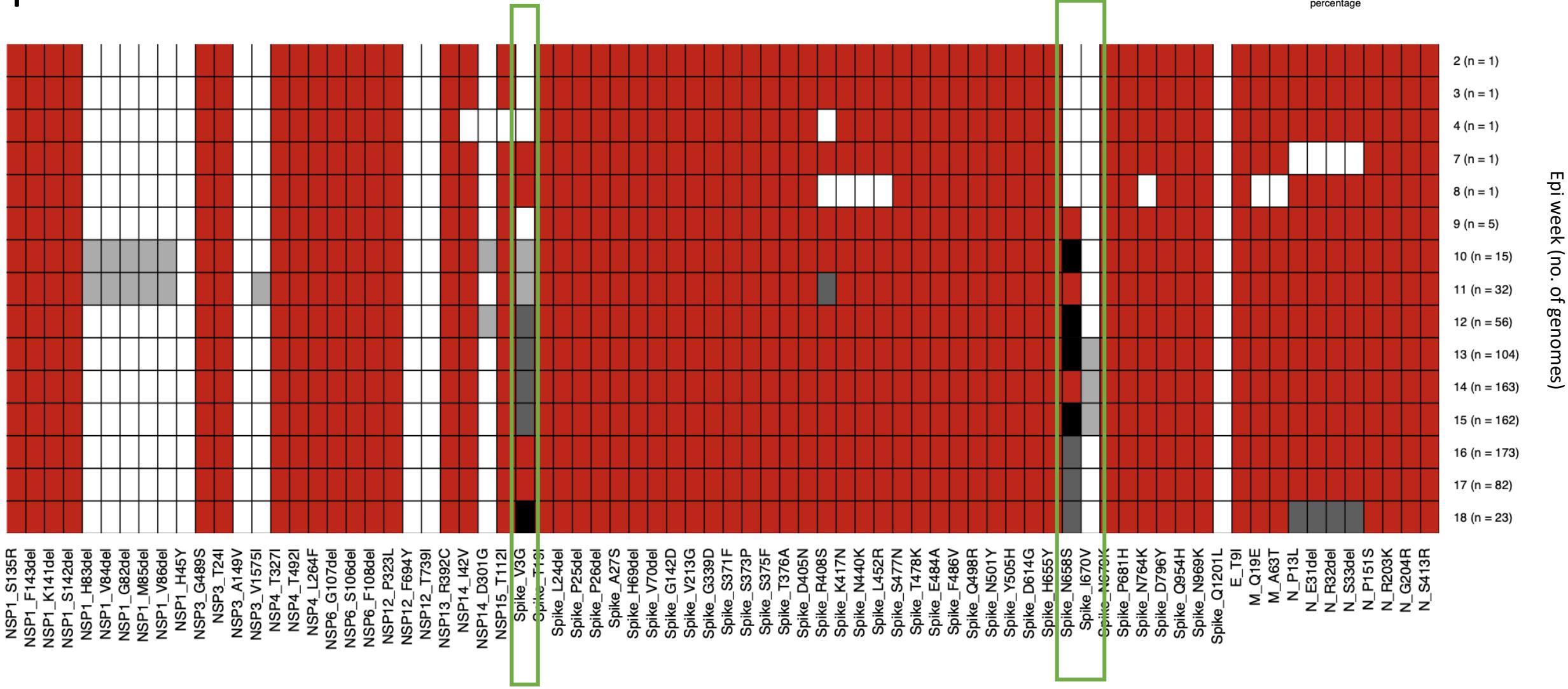
BA.4 and BA.5 spike mutations

Percentage

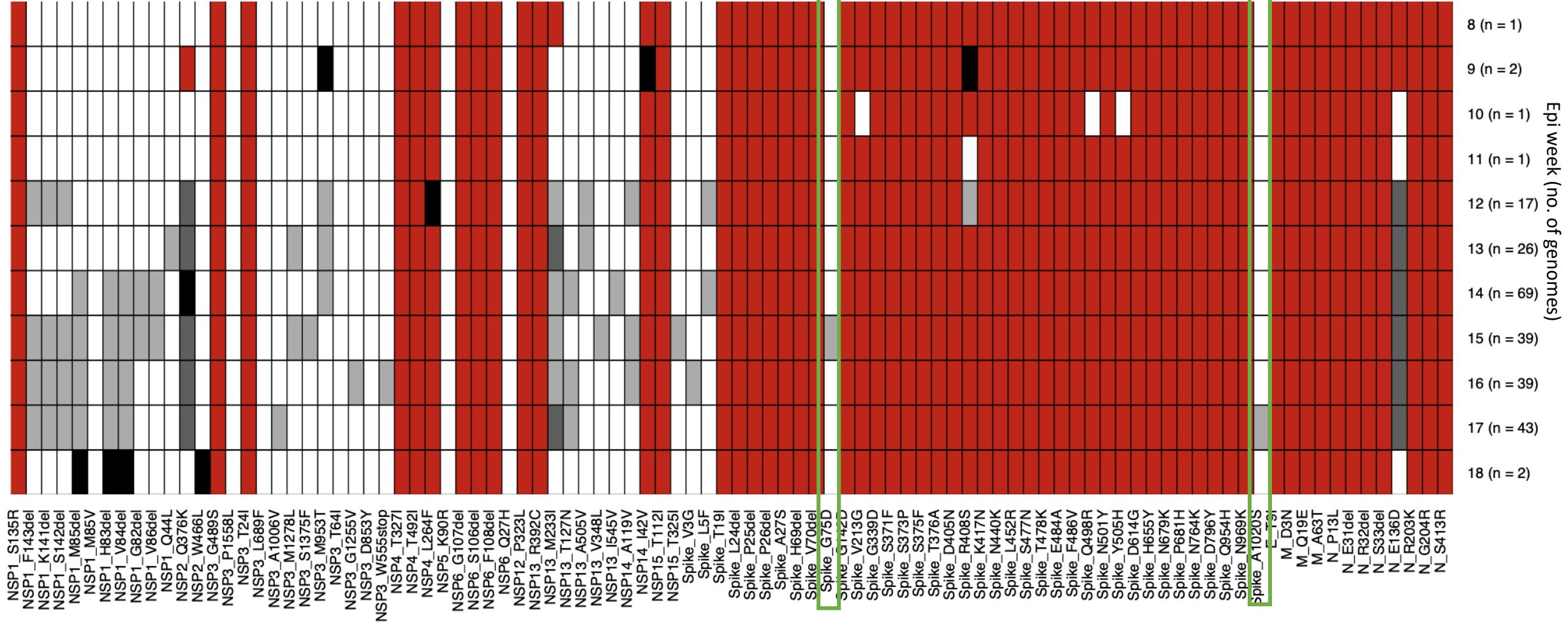
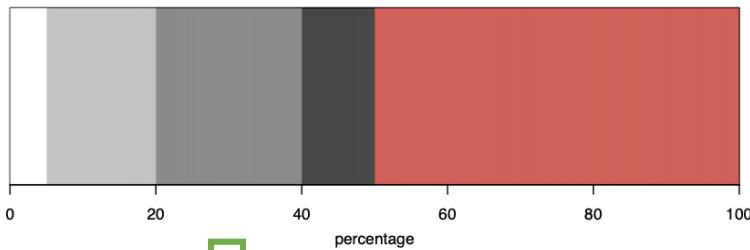


Mutation

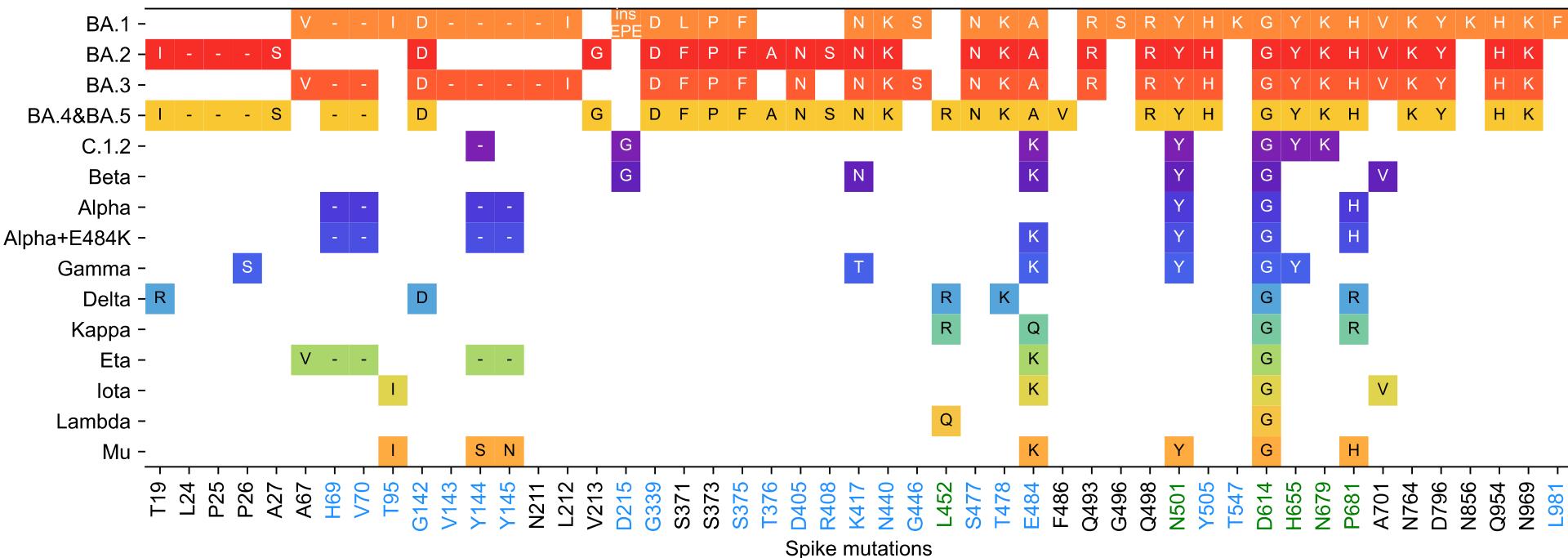
BA.4 whole genome mutation prevalence over time



BA.5 whole genome mutation prevalence over time



Omicron spike mutations compared to other VOC/VOIs

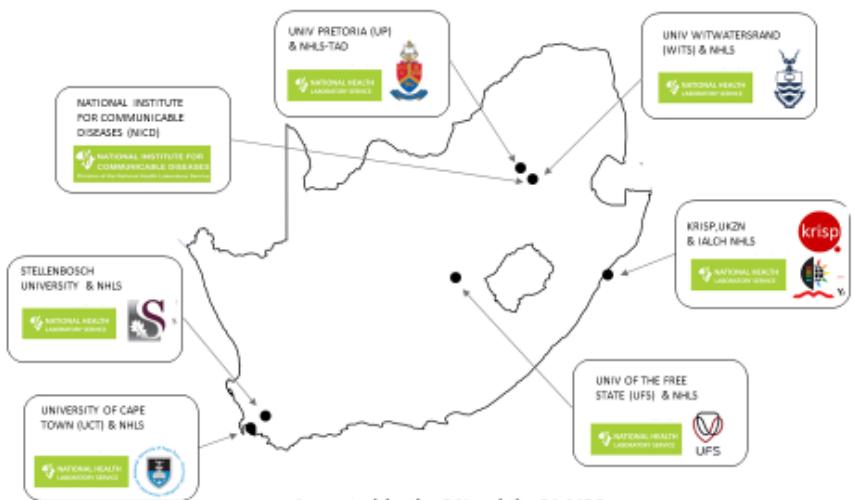


Only lineage-defining mutations are pictured here. Low prevalence mutations can be seen on the following slide.

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



Supported by the DSI and the SA MRC



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



University of Stellenbosch & NHLS Tygerberg Virology



Susan Engelbrecht
Wolfgang Preiser
Gert van Zyl
Tongai Maponga
Bronwyn Kleinhans
Shannon Wilson
Karabo Phadu
Tania Stander
Kamela Mahlakwane
Mathilda Claassen
Diagnostic laboratory staff

University of Cape Town, NHLS & Western Cape Government



NHLS-UCT

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Diana Hardie
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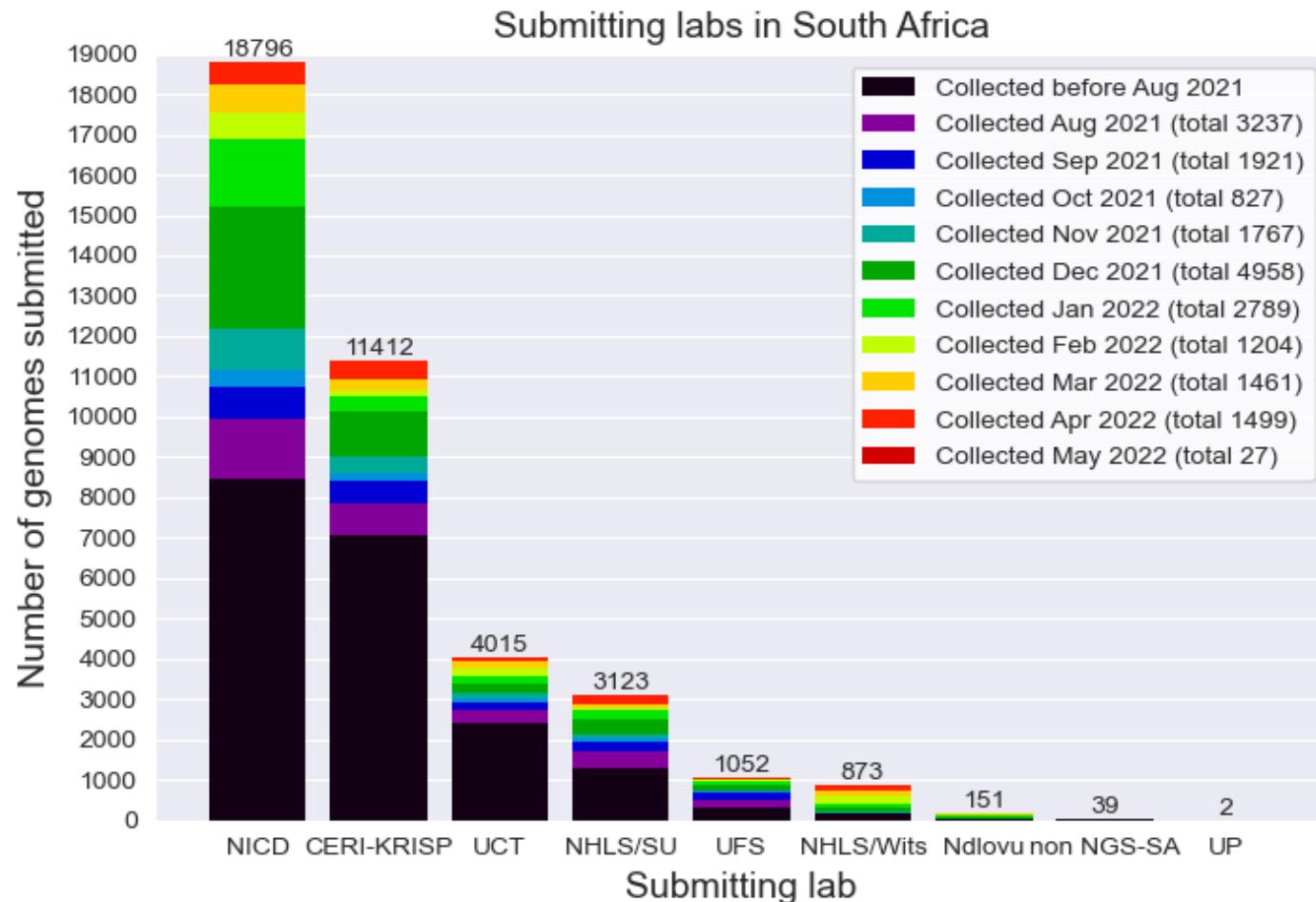
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South African genomes submitted per submitting lab, 2020 - 2022 (N=39 463)



NGS-SA Labs

CERI: Centre for Epidemic Response and Innovation

KRISP: KZN Research Innovation and Sequencing Platform

NDLOVU: Ndlovu Research Laboratories

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.

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.)