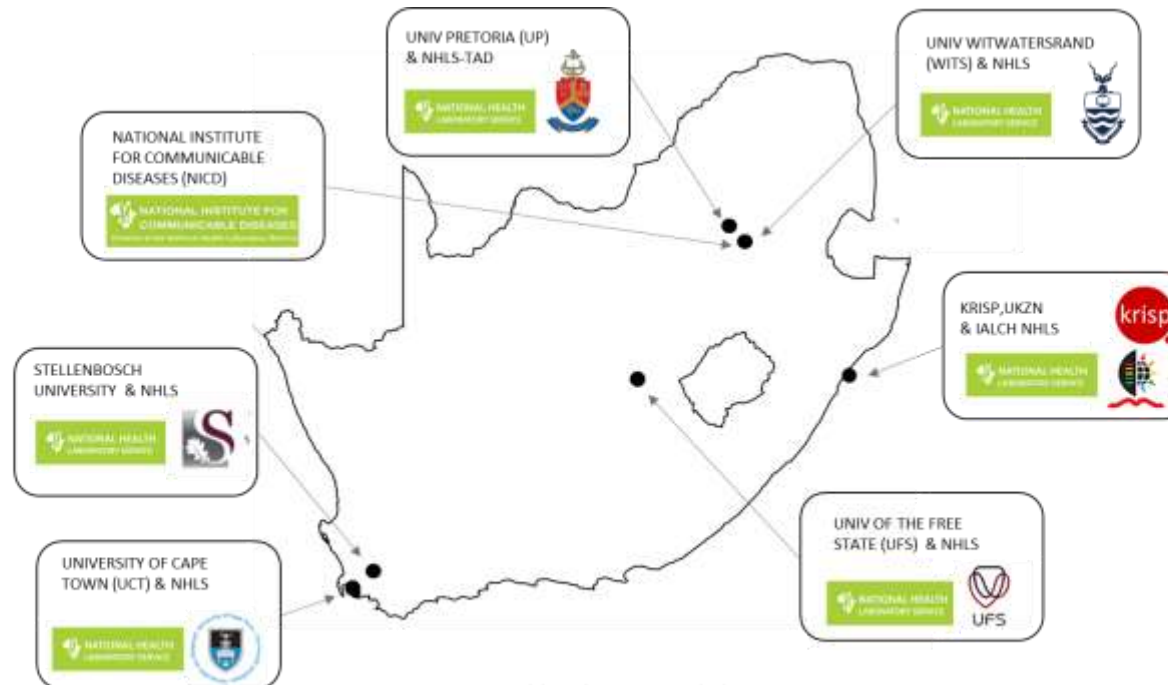


## SARS-CoV-2 Sequencing Update 21 January 2022



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](http://www.gisaid.org)) on 21 January 2022 at 08h31



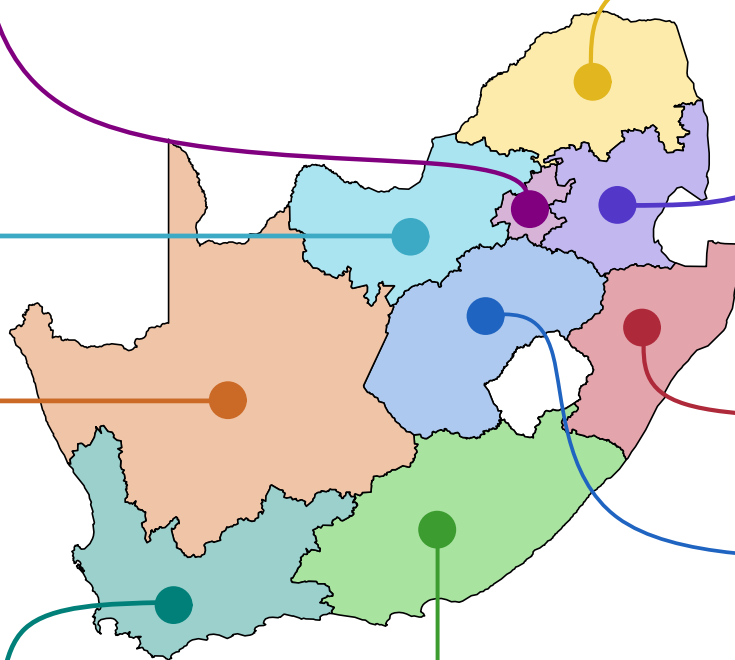
Data license: <https://www.gisaid.org/registration/terms-of-use/>

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 PMID: 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 PMID: PMC5388101

# SARS-CoV-2

## GENOMIC SURVEILLANCE epiweeks 39 (2021) - 2 (2022)



### Gauteng ↓PTP: 11.2%

Genomes Cases  
1 291 (27.9%) 231 449 (36.1%)

Genomes deposited in the last week

76 3 2 1

### North West ↓PTP: 14.0%

Genomes Cases  
273 (5.9%) 31 316 (4.9%)

Genomes deposited in the last week

68 1 1 2 4 3

### Northern Cape ↓PTP: 24.3%

Genomes Cases  
365 (7.9%) 15 226 (2.4%)

Genomes deposited in the last week

31 1 17 3

### Western Cape ↓PTP: 23.3%

Genomes Cases  
958 (20.7%) 107 965 (16.8%)

Genomes deposited in the last week

78 6 1 1

### Eastern Cape ↓PTP: 18.4%

Genomes Cases  
251 (5.4%) 48 126 (7.5%)

Genomes deposited in the last week

34 1

### Limpopo ↓PTP: 19.8%

Genomes Cases  
114 (2.5%) 23 009 (3.6%)

Genomes deposited in the last week

12 2

### Mpumalanga ↓PTP: 16.2%

Genomes Cases  
354 (7.7%) 29 123 (4.5%)

Genomes deposited in the last week

125 10 1

### KwaZulu-Natal ↓PTP: 17.1%

Genomes Cases  
783 (16.9%) 123 001 (19.2%)

Genomes deposited in the last week

74 22 2

### Free State ↓PTP: 12.8%

Genomes Cases  
234 (5.1%) 32 020 (5.0%)

Genomes deposited in the last week

89 4

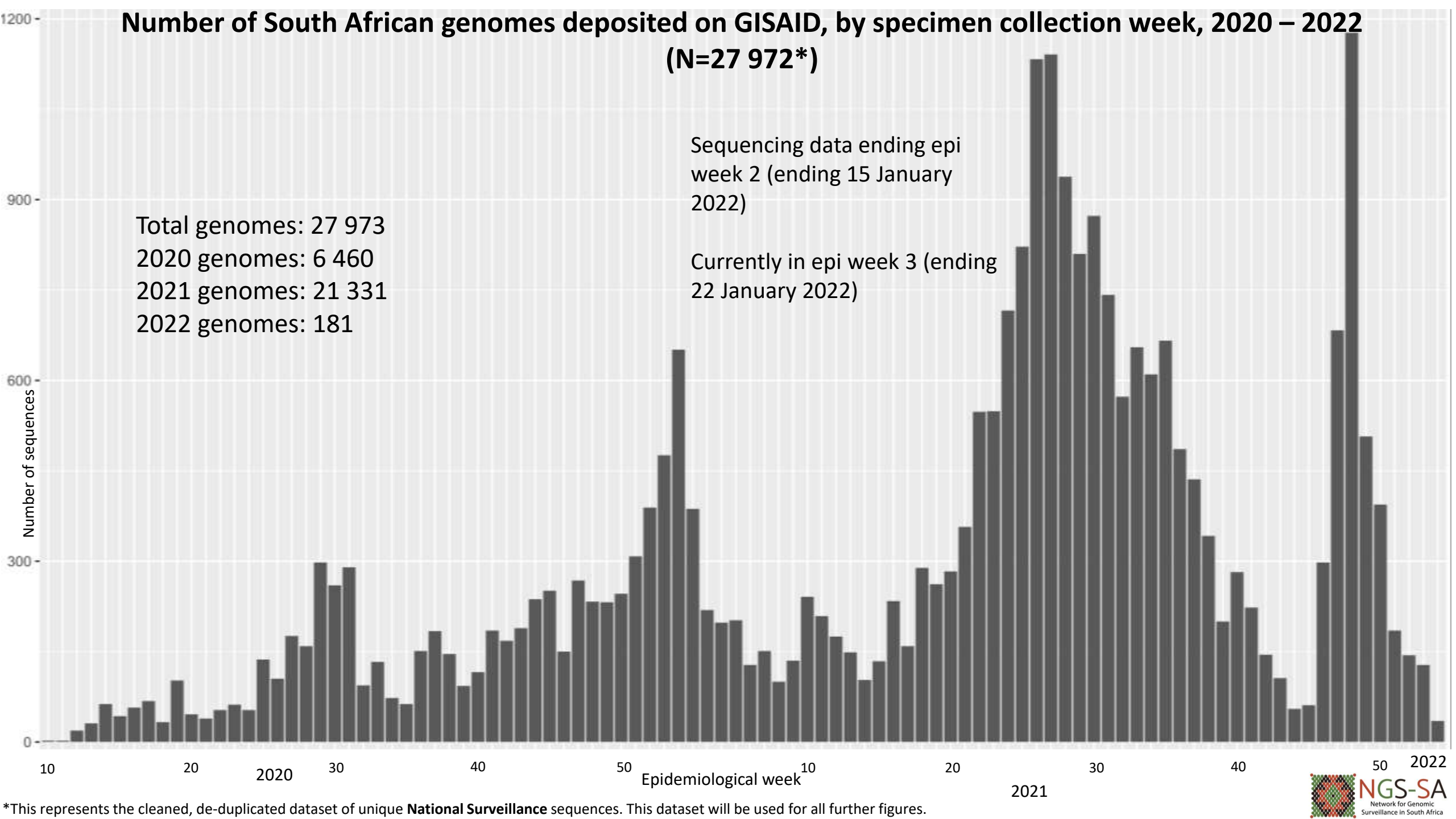
Omicron (21K) Beta (20H, V2) 20A 20C  
 Omicron (21L) Alpha (20I, V1) 20B 20D  
 Omicron (21M) Delta (21A) Unassigned  
 C.1.2 (20D) Delta (21I) Delta (21J) Cases

675 genomes deposited in the past week

Bar graphs represent genomes sequenced per epiweek, with lines representing cases by collection date (weeks 39 [2021] – 2 [2022])

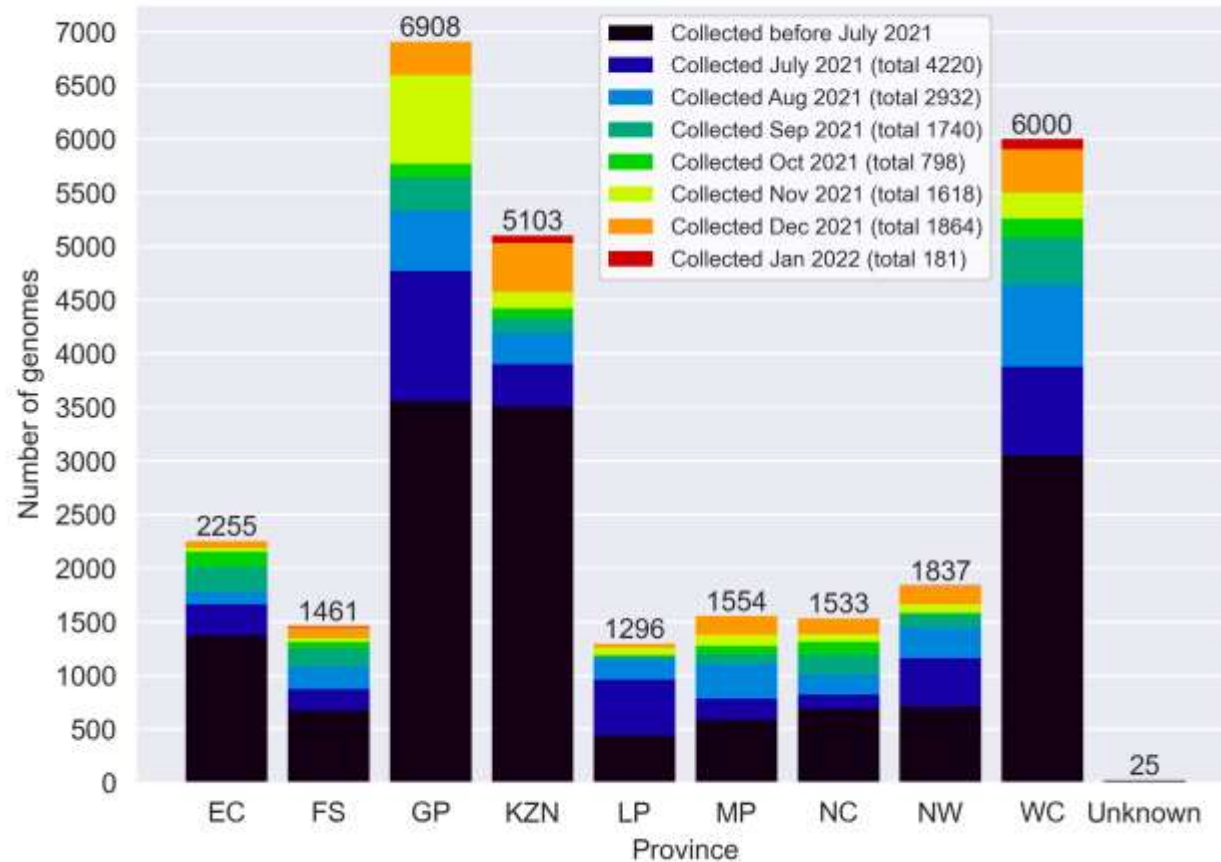
Genomes and cases presented as provincial total (percentage of national total) for epiweeks 39 (2021) – 2 (2022)

PTP: percentage testing positive in week 2 (9 Jan 2022 – 15 Jan 2022); the arrow indicates direction of change since the previous week (2 Jan 2021 – 8 Jan 2022)

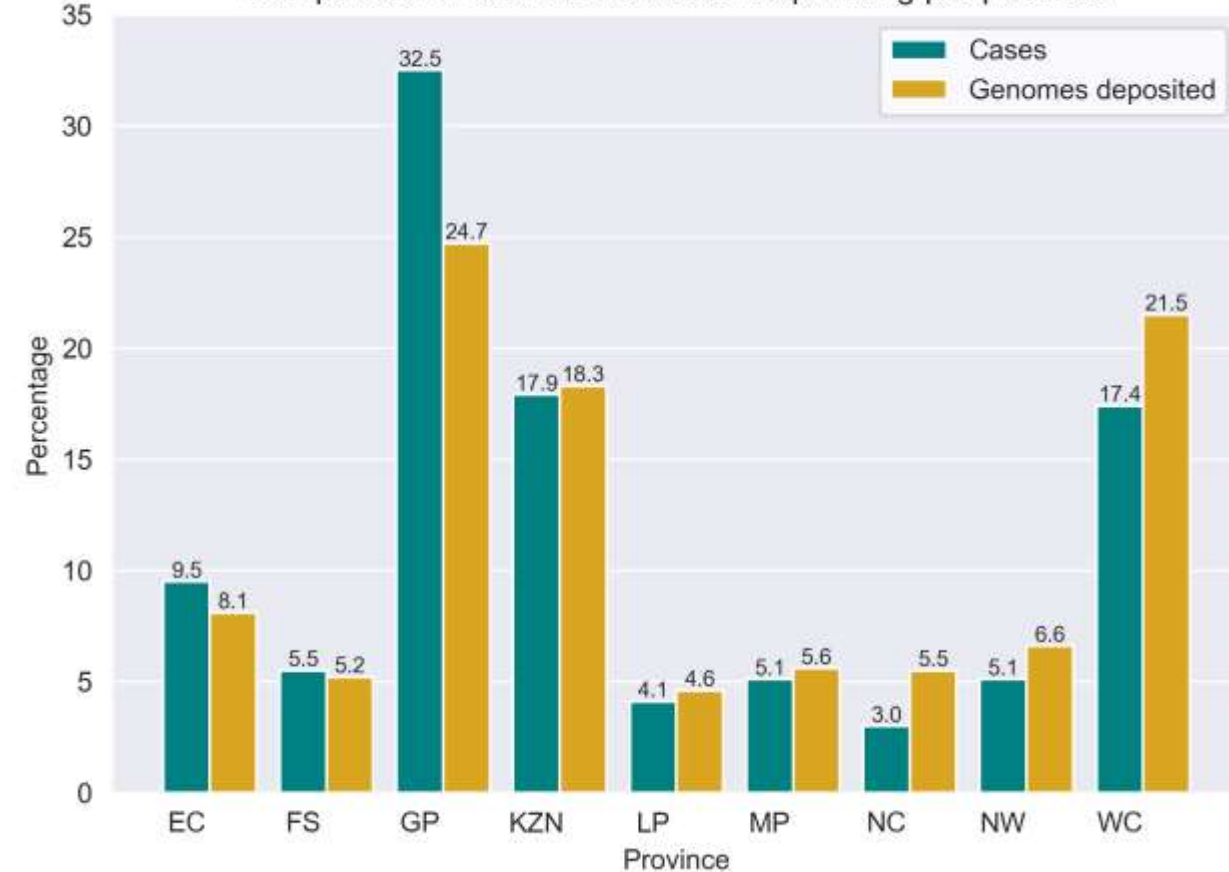


# GISAID genomes vs total cases, 2020 – 2022 (N=27 972)

Provincial breakdown of genomes deposited into GISAID



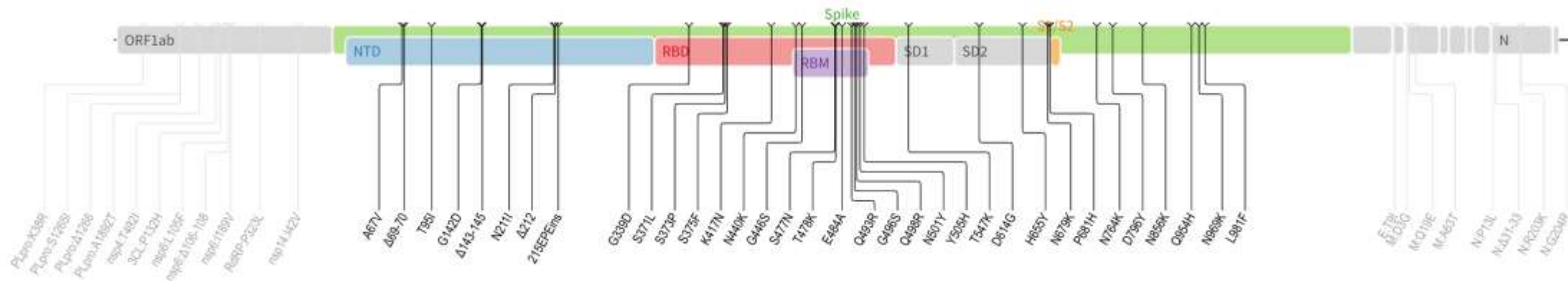
Comparison of total cases versus sequencing per province



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

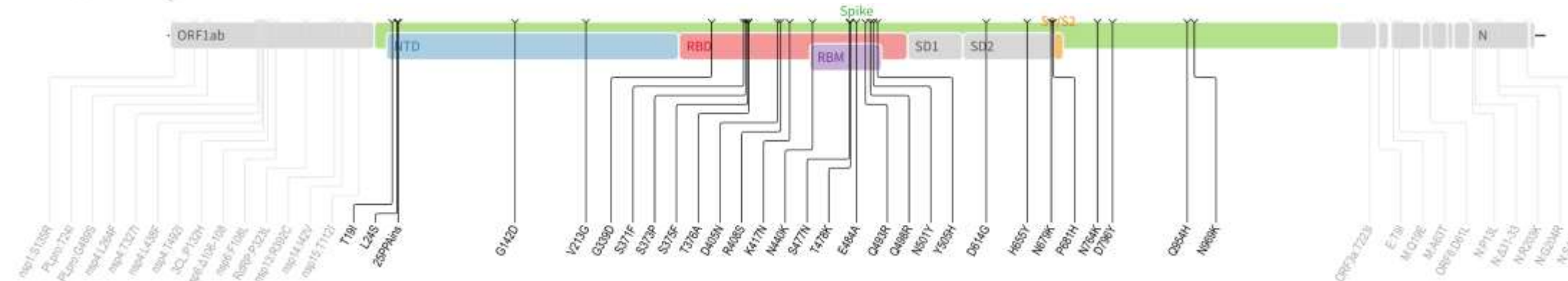
# Omicron sub-lineage spike mutation profiles

**BA.1**  
**21K**

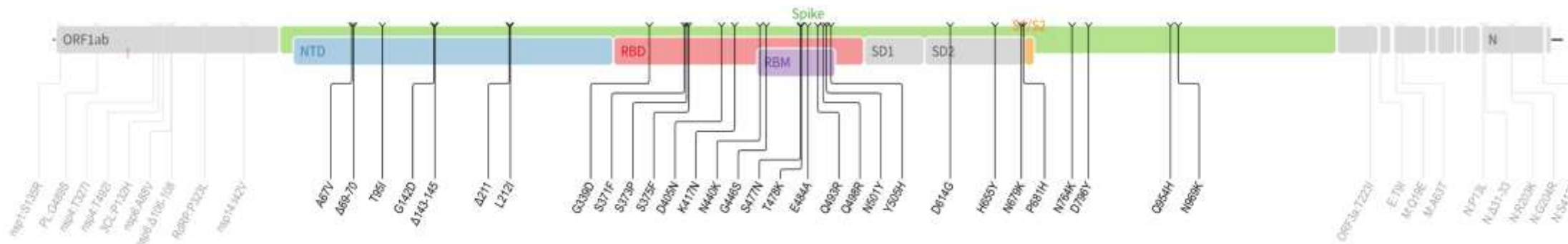


**BA.2**  
**21L**

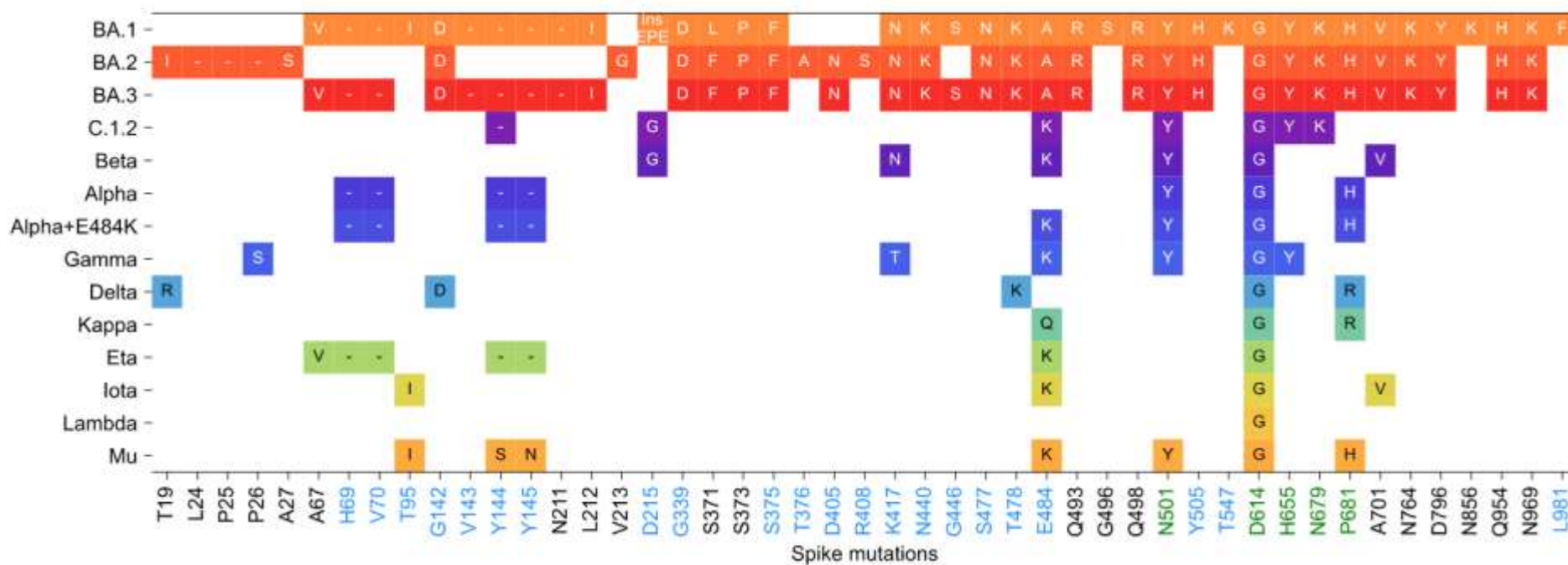
Lacks 69-70del  
Not detectable by  
S-Gene Target  
Failure



**BA.3**  
**21M**



# 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.

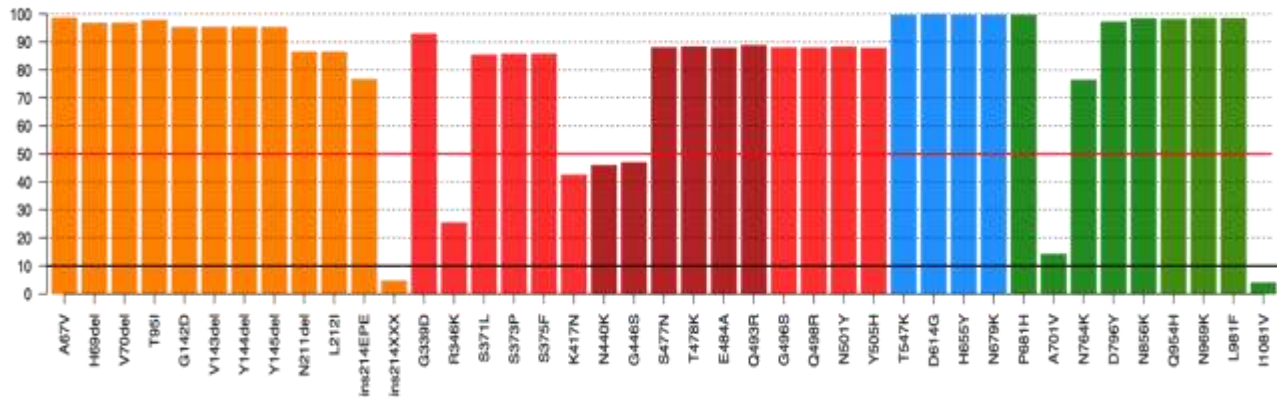
### Mutation impact key

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

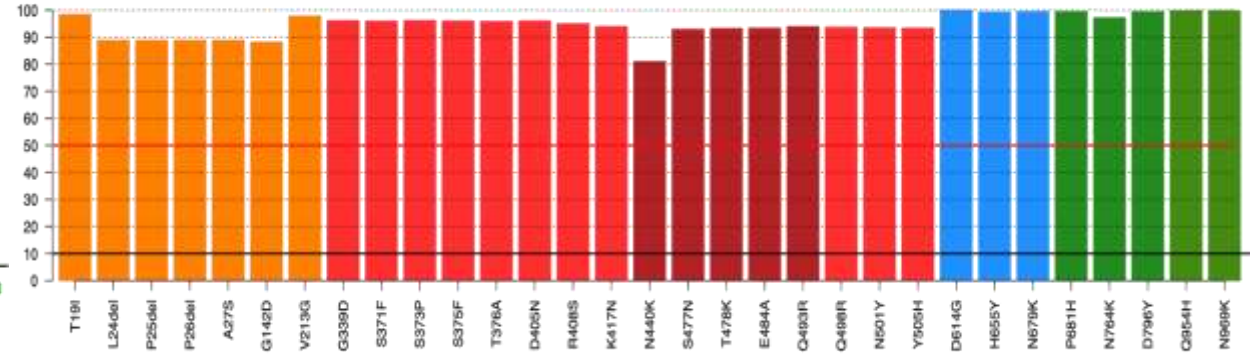
- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be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

# Spike mutational profile of Omicron sequences

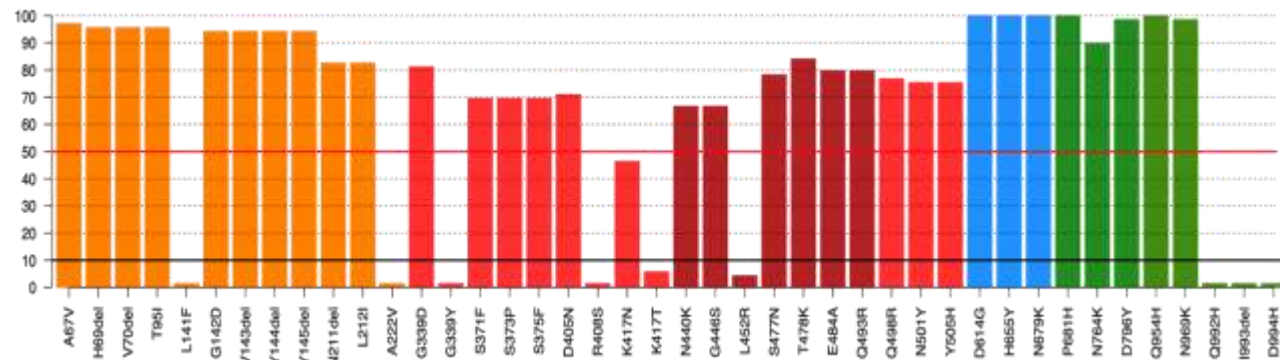
Frequency of Spike SNVs for BA.1 (n=462258)



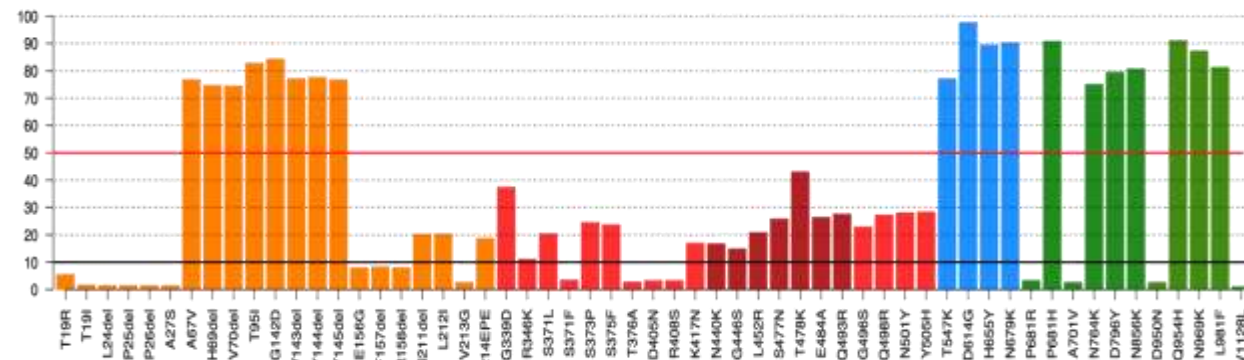
Frequency of Spike SNVs for BA.2 (n=8985)



Frequency of Spike SNVs for BA.3 (n=69)



Frequency of Spike SNVs for B.1.1.529 (n=3123)

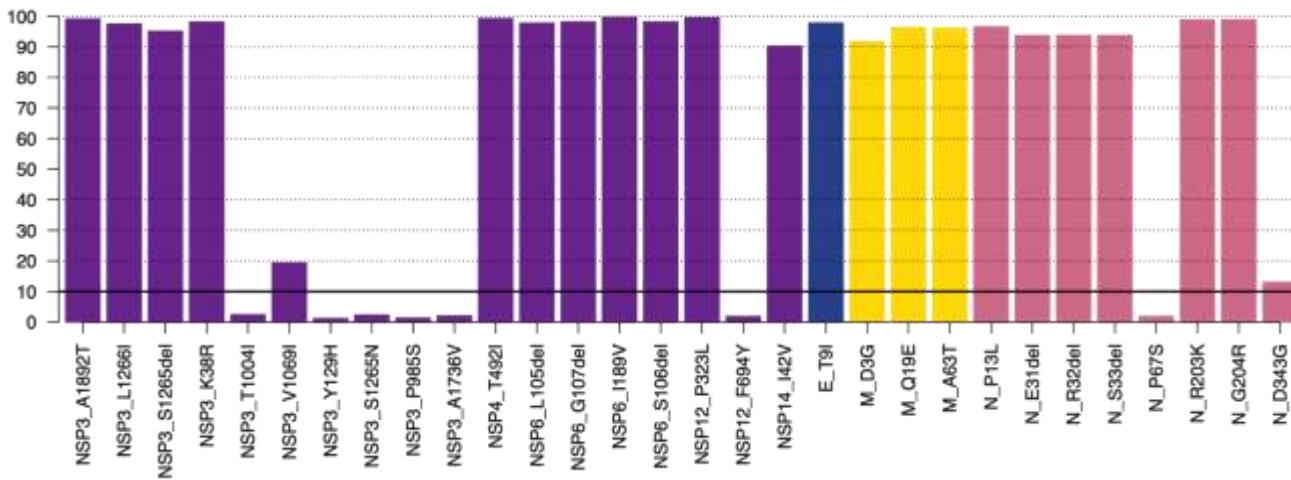


B.1.1.529 includes low-quality sequences that are missing data, so the frequency of these mutations cannot be considered fully reliable estimates.

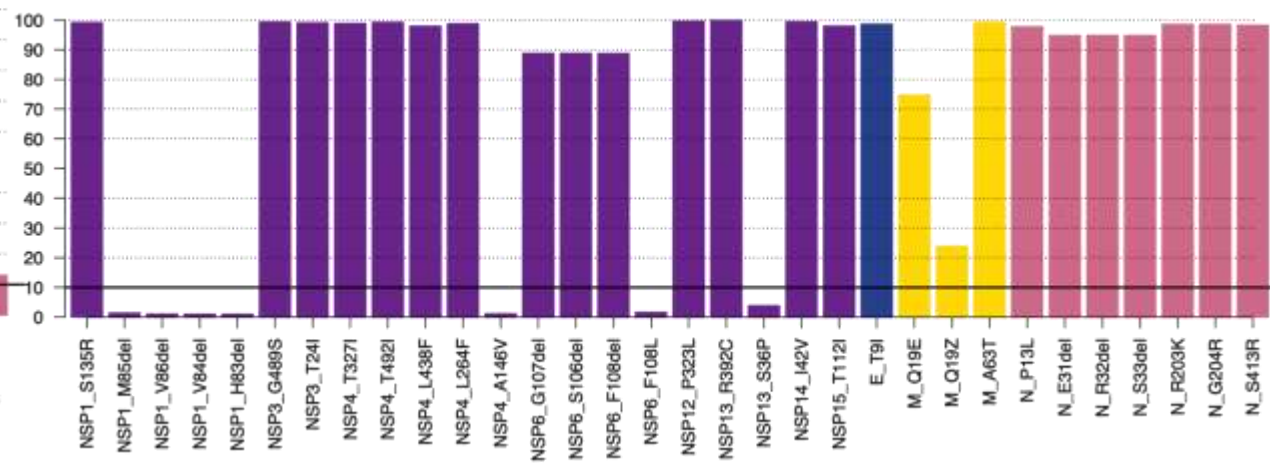
Low mutation frequencies for N417N, N440K, G446S and N764K are most likely a result of poor coverage due to primer drop off. There are significant differences in insertions and deletions amongst sub-lineages. BA.2 has lowest spike diversity of all Omicron sub-lineages.

# Mutational profile of Omicron sequences

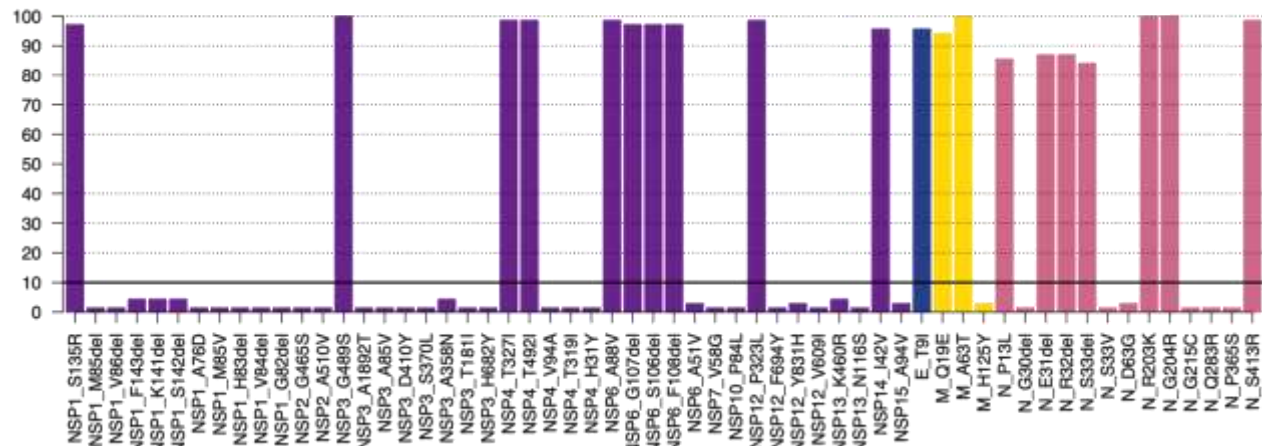
Frequency of whole genome SNVs for BA.1 (n=462258)



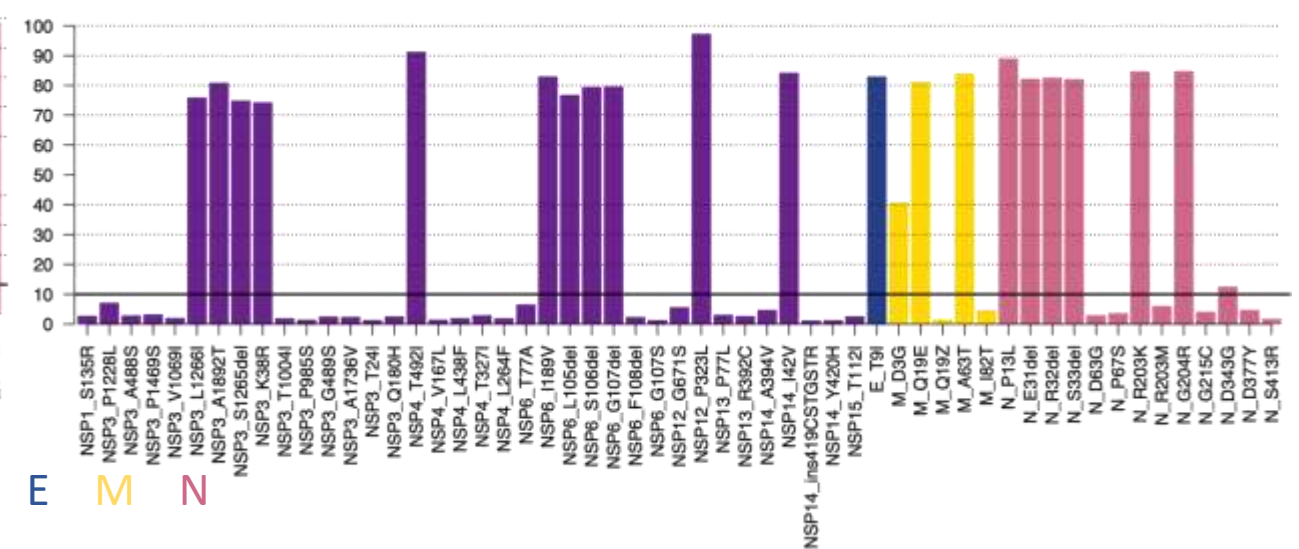
Frequency of whole genome SNVs for BA.2 (n=8985)



Frequency of whole genome SNVs for BA.3 (n=69)



Frequency of whole genome SNVs for B.1.1.529 (n=3123)



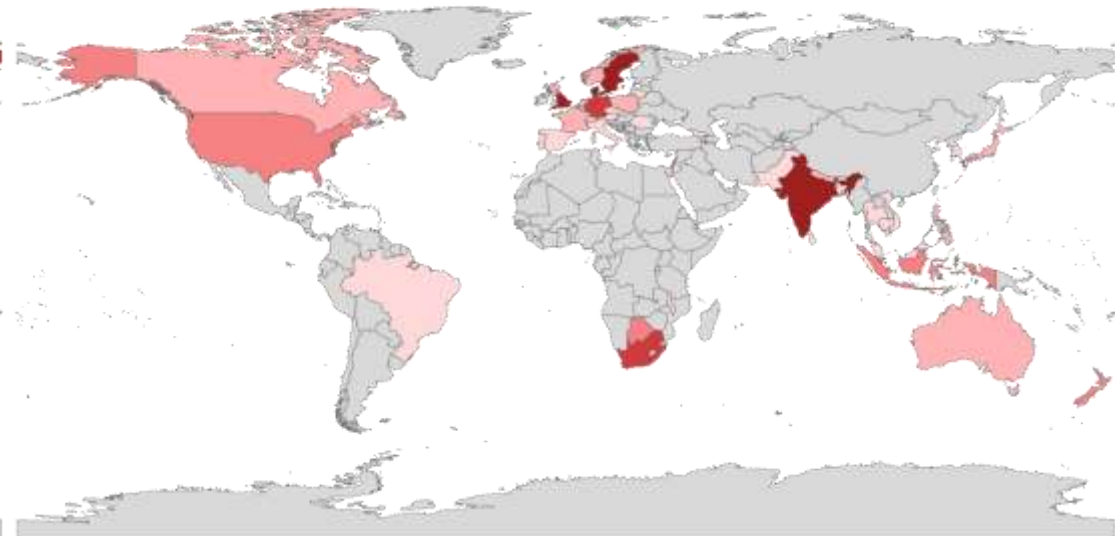
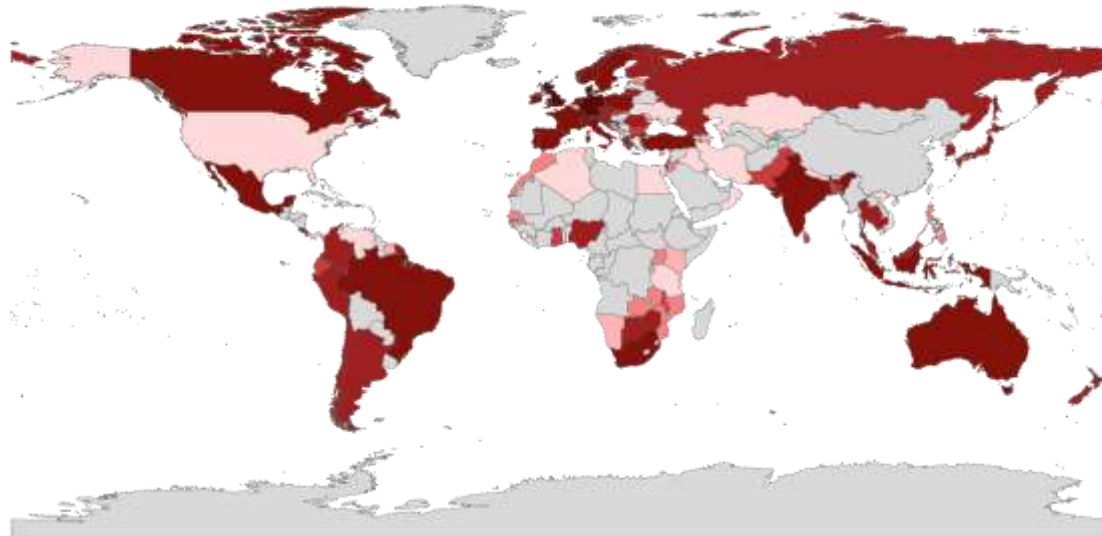
ORF1a/b E M N

Non-spike mutational profile of Omicron varies between sub-lineages, especially within ORF1a/b. Most defining E, M and N mutations are shared. BA.1 appears to be the least diverse of the sub-lineages.

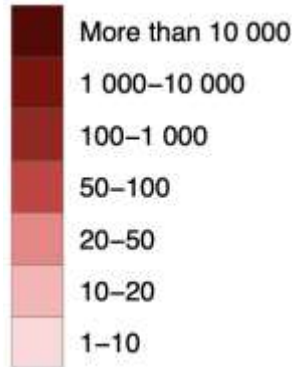
# Omicron global prevalence

Detection of BA.1 Globally (countries = 128; n = 466258)

Detection of BA.2 Globally (countries = 49; n = 8985)

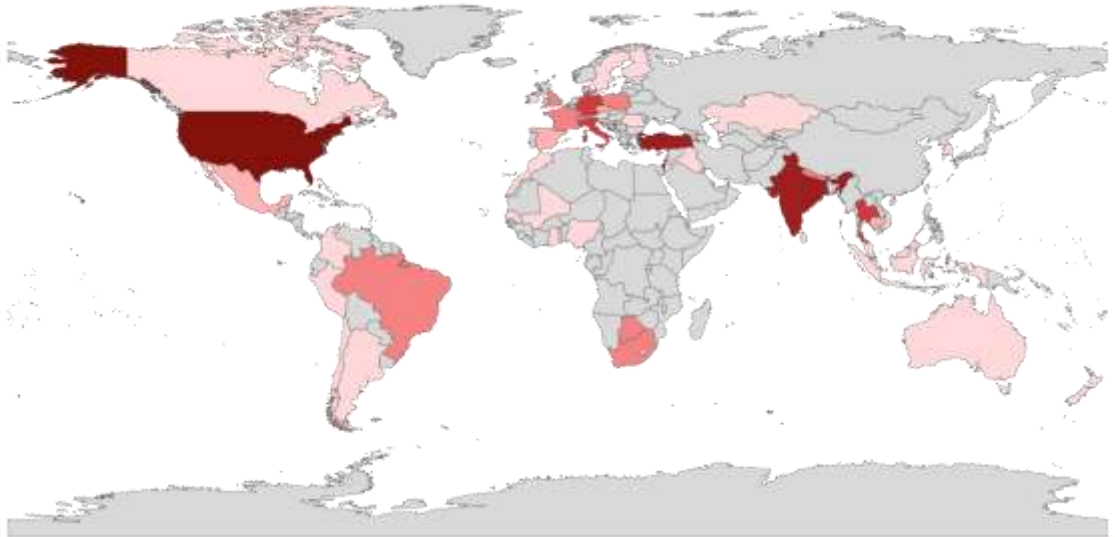
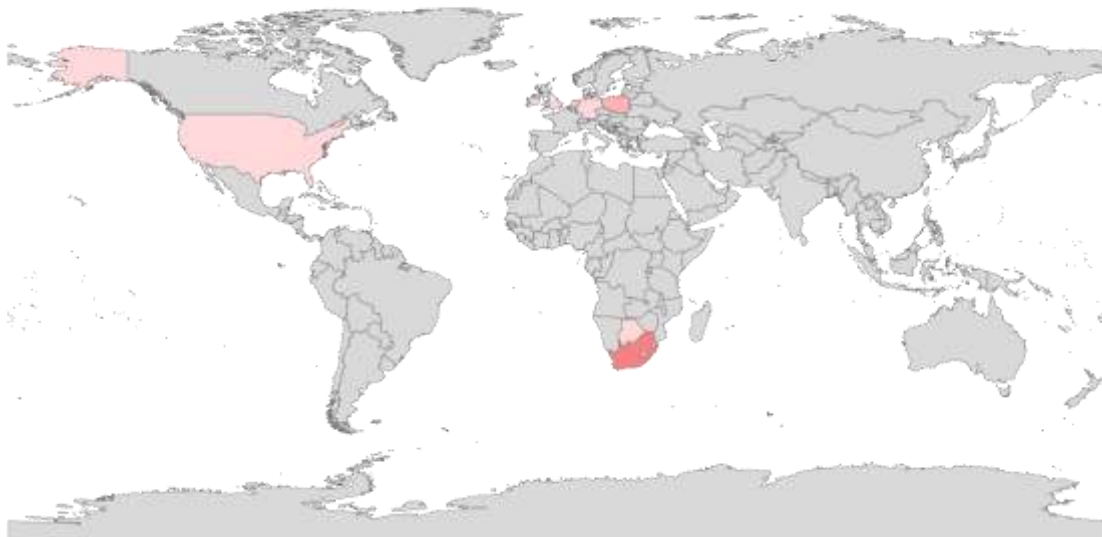


Number of  
Omicron genomes



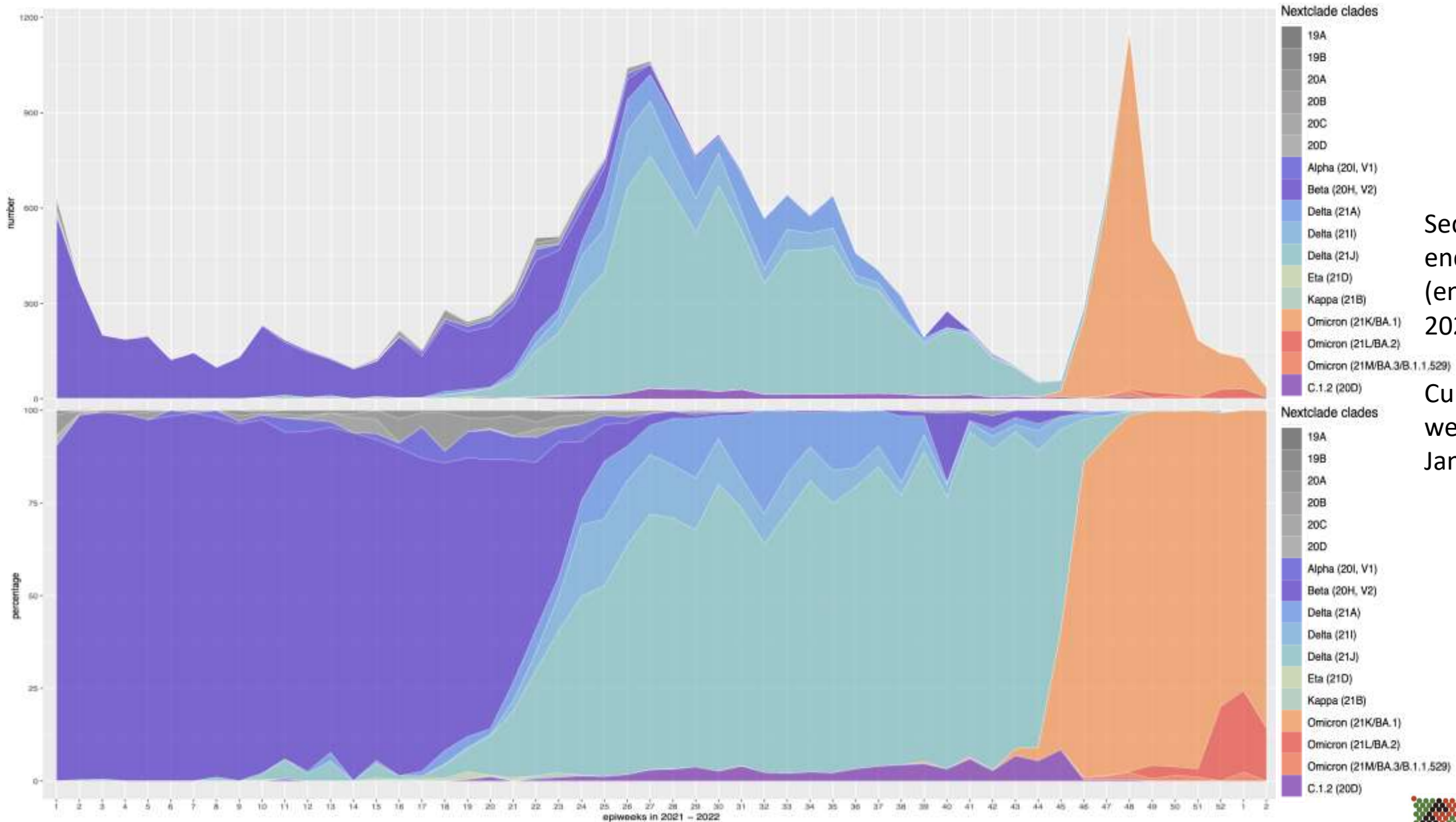
Detection of BA.3 Globally (countries = 9; n = 69)

Detection of B.1.1.529 Globally (countries = 63; n = 3145)



Omicron has been detected in 145 countries across the globe (detections based on GISAID).

# Proportion and number of clades by epiweek in South Africa, 2021 - 2022 (N=21 512)



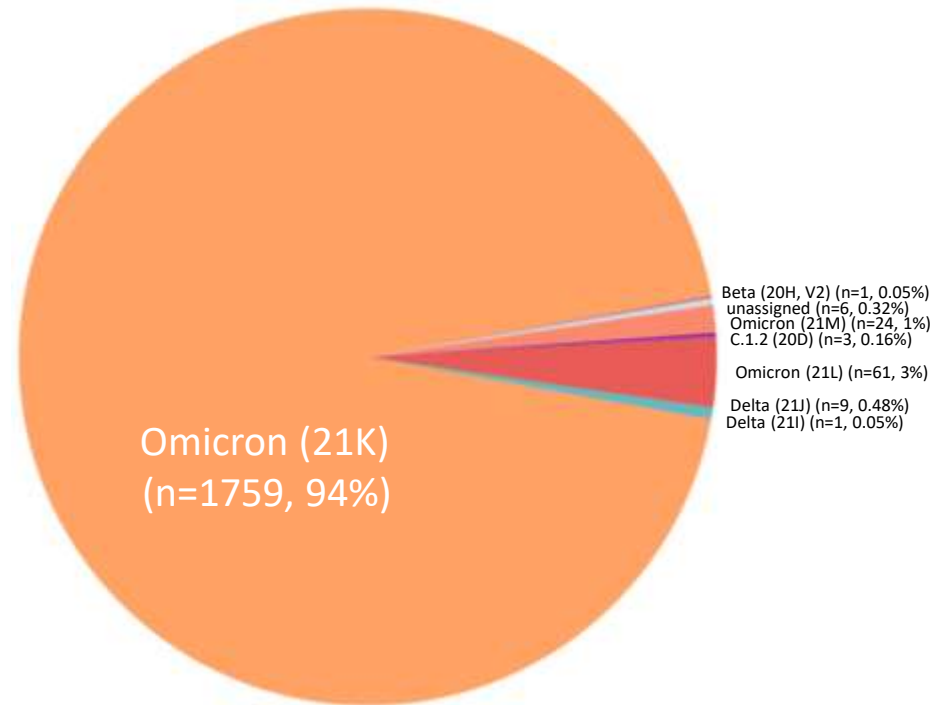
Sequencing data  
ending epi week 2  
(ending 15 January  
2022)

Currently in epi  
week 3 (ending 22  
January 2022)

Delta dominated in South Africa until October at >80%. Omicron dominated November and December at >95%.

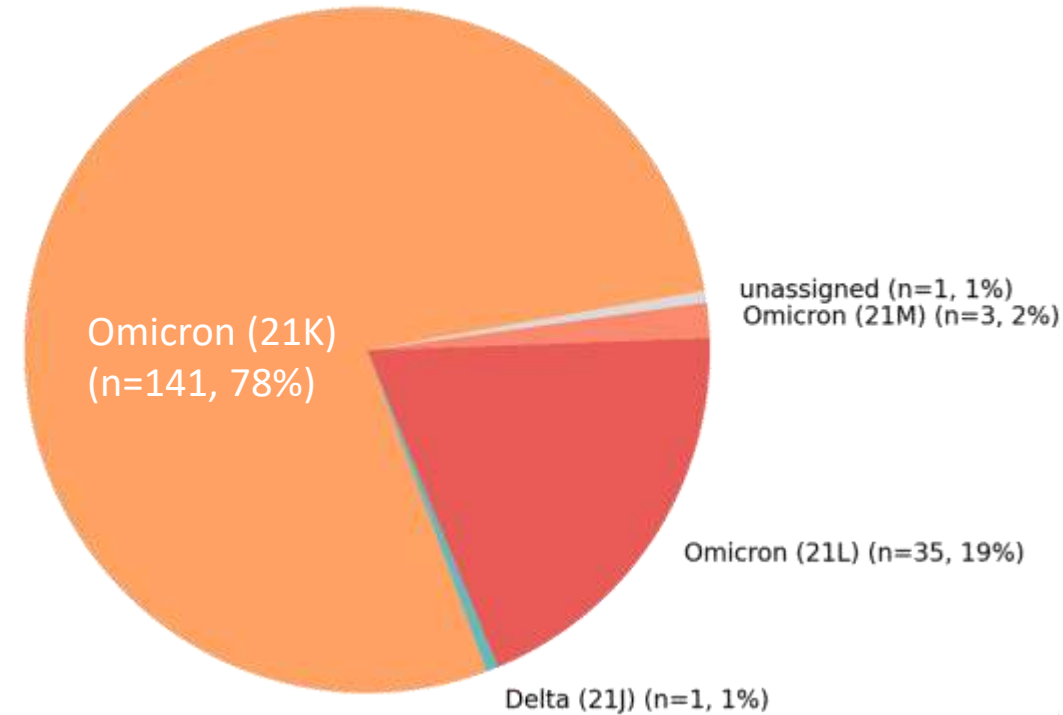
# Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in Dec 2021 – Jan 2022

December (N=1864)



Total Omicron in Dec: 1844 (98.9%)

January (N=181)



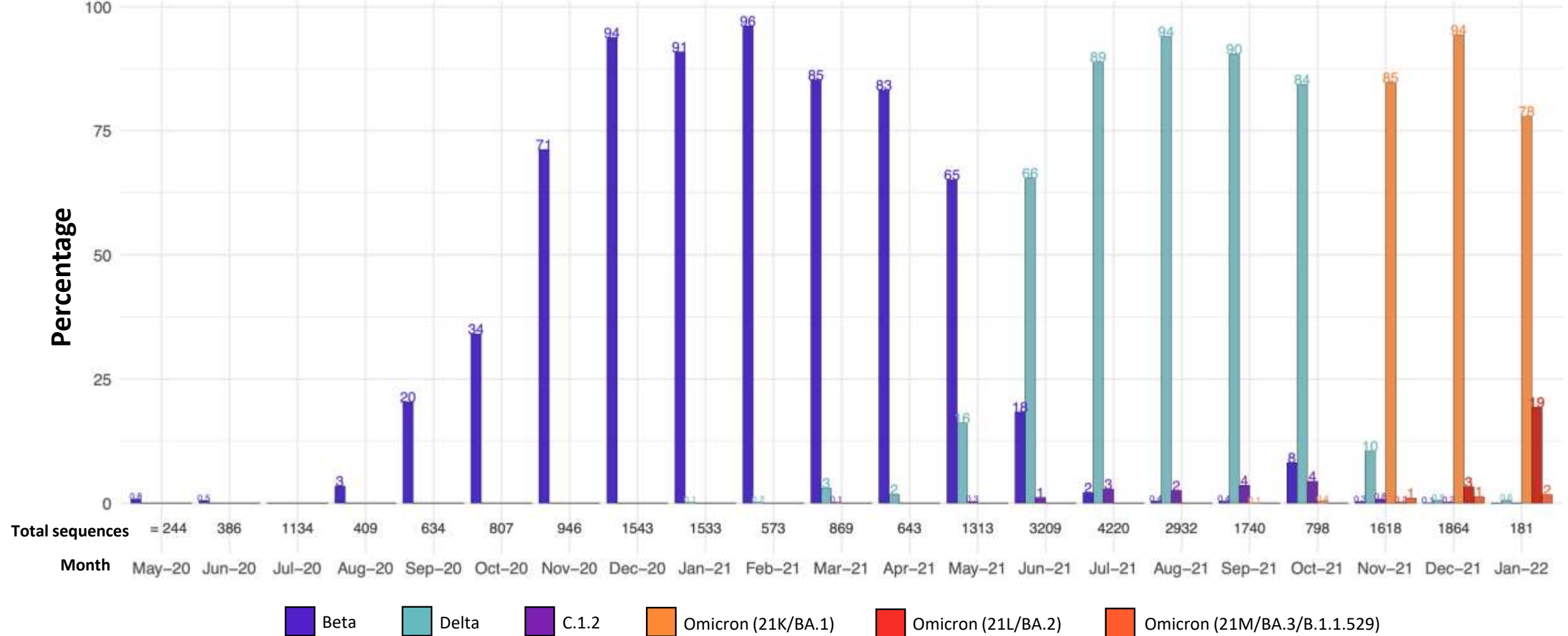
Total Omicron in Jan: 179 (98.9%)



Omicron dominated in December (99%, 1844/1864). Omicron appears to continue dominating in January (98%, 179/181), although more sequencing data is needed to confirm this trend and the BA.2 increase.

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

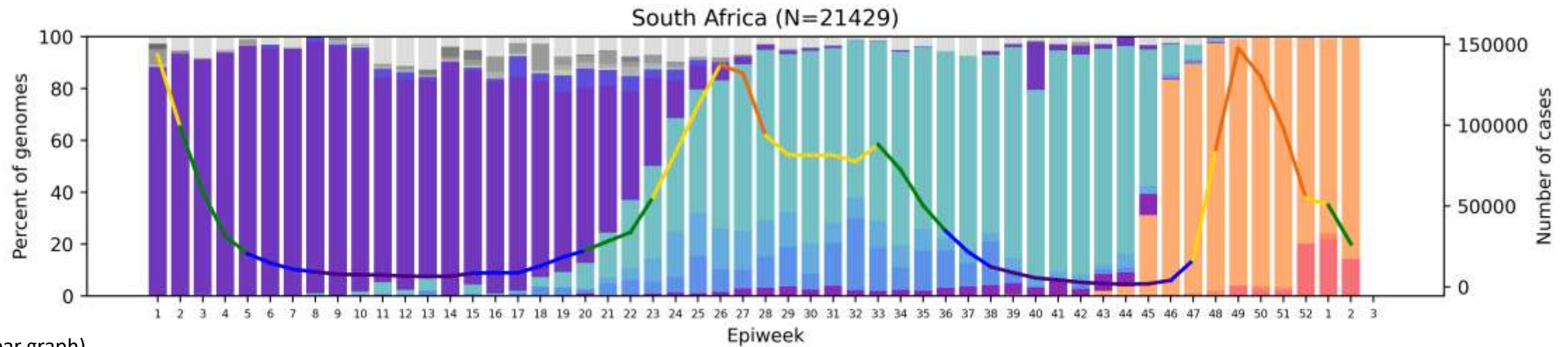
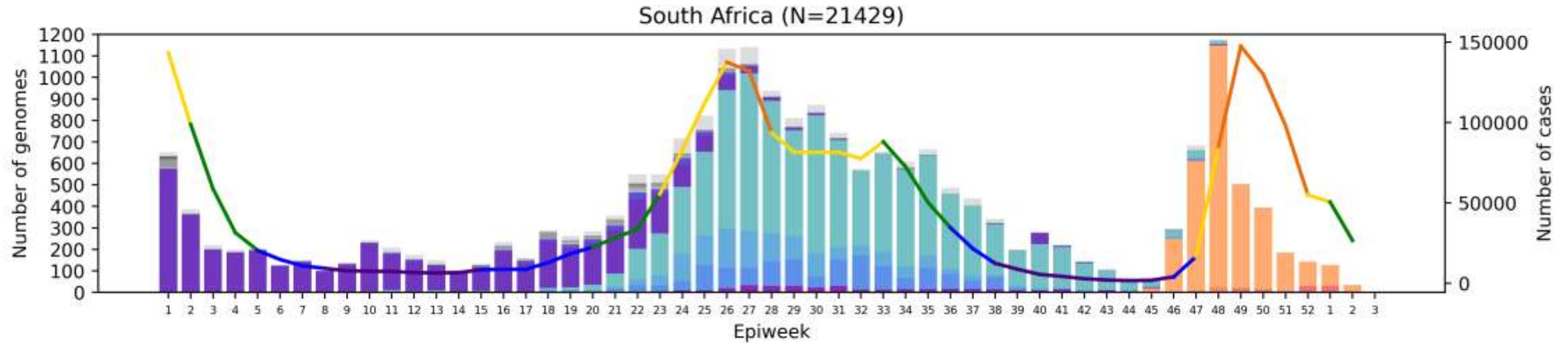
Detection rates of variants being monitored in South Africa\*



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

**C.1.2 has been detected at  $\leq 4\%$  of sequences monthly since May 2021.**  
**Beta prevalence increased slightly in October but has since remained at low levels in November and December.**  
**Omicron has been dominant since November ( $>80\%$  in November,  $>98\%$  in December and January).**

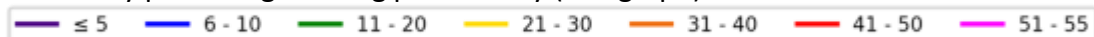
# South Africa, 2021-2022, n = 21429\*



Clade key (bar graph)

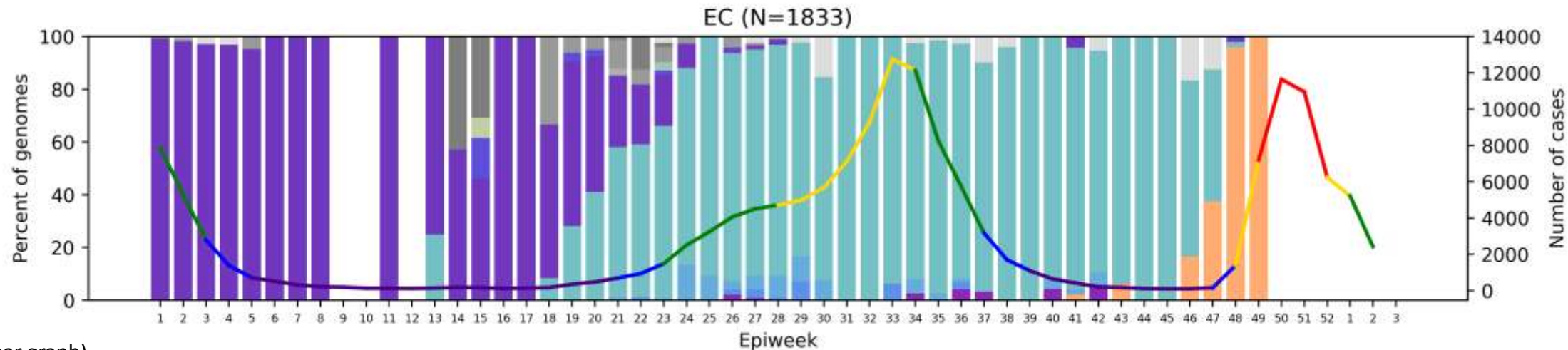
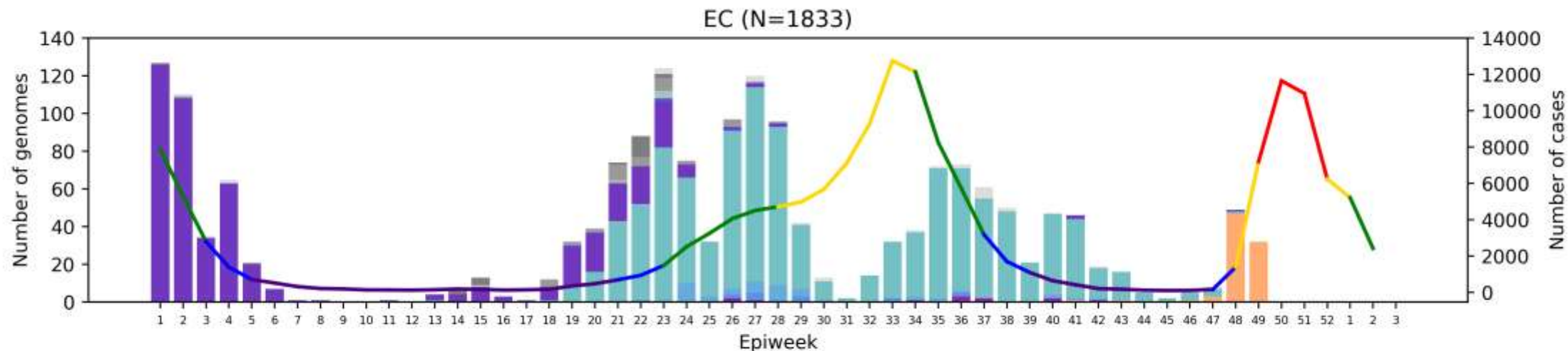


Weekly percentage testing positive key (line graph)



\*Excludes sequences collected January 1<sup>st</sup> and 2<sup>nd</sup> (2021) as they fall under epiweek 53 of 2020, as well as those without complete collection dates.

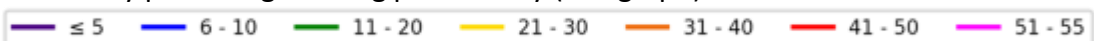
# Eastern Cape Province, 2021-2022, n = 1833



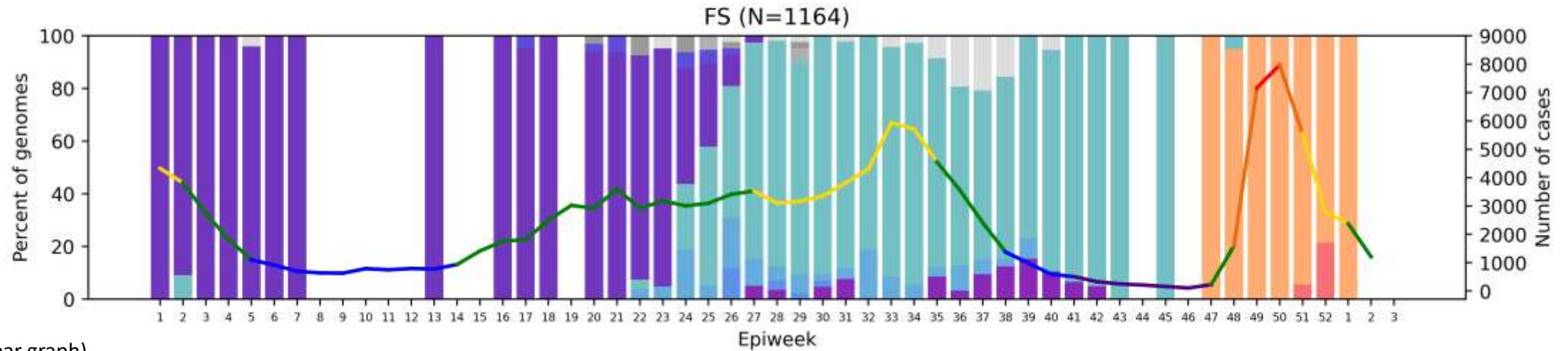
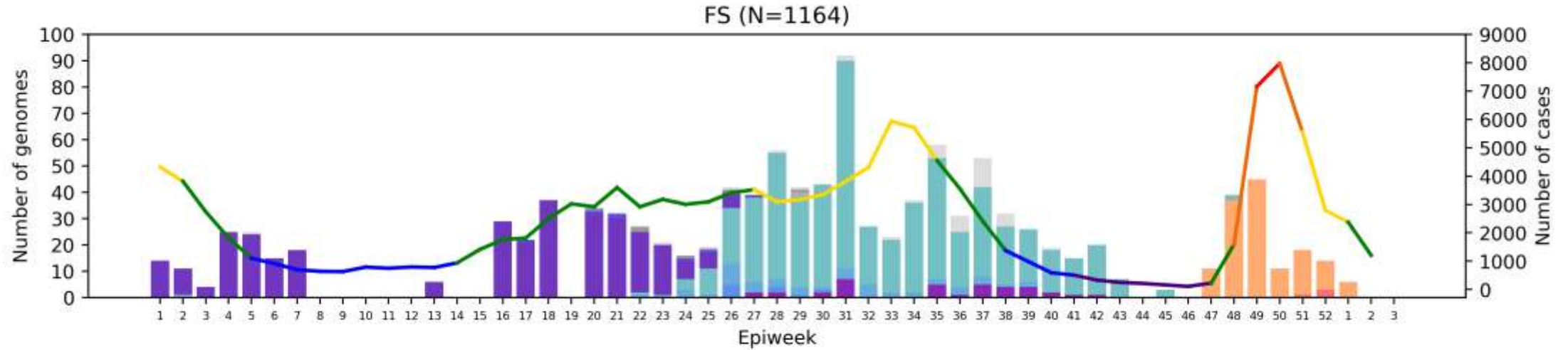
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



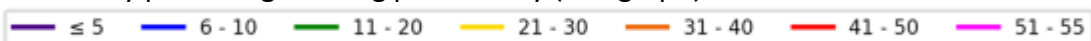
# Free State Province, 2021-2022, n = 1164



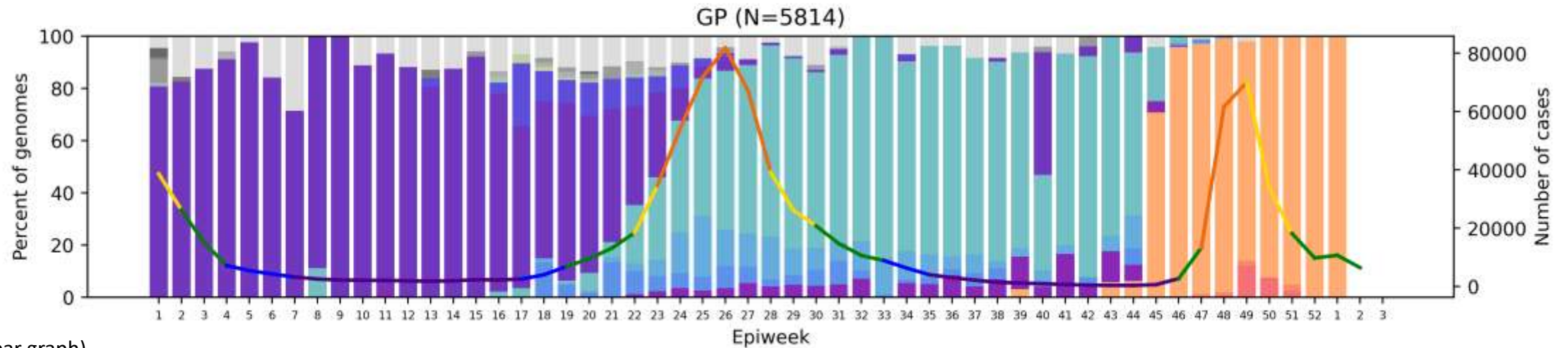
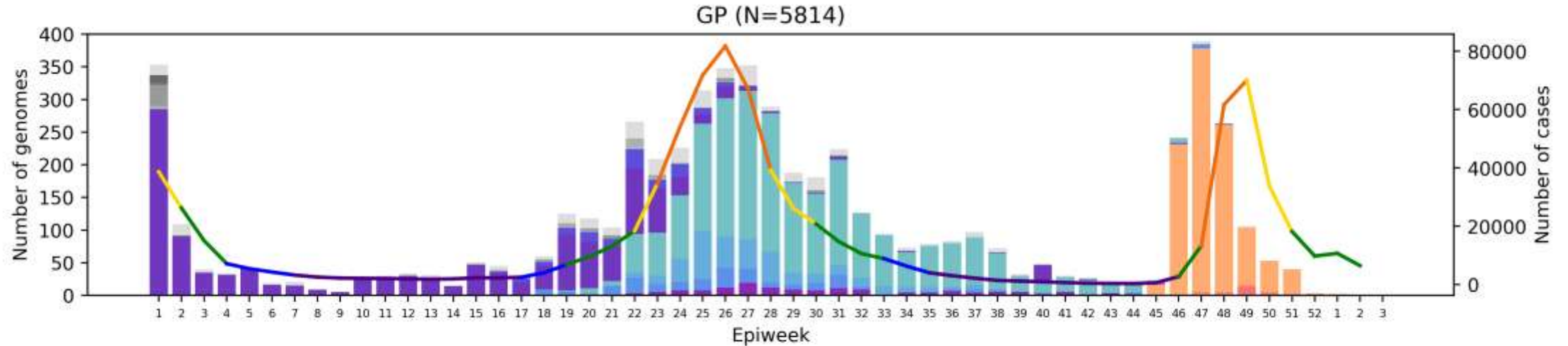
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



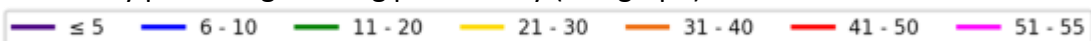
# Gauteng Province, 2021-2022, n = 5814



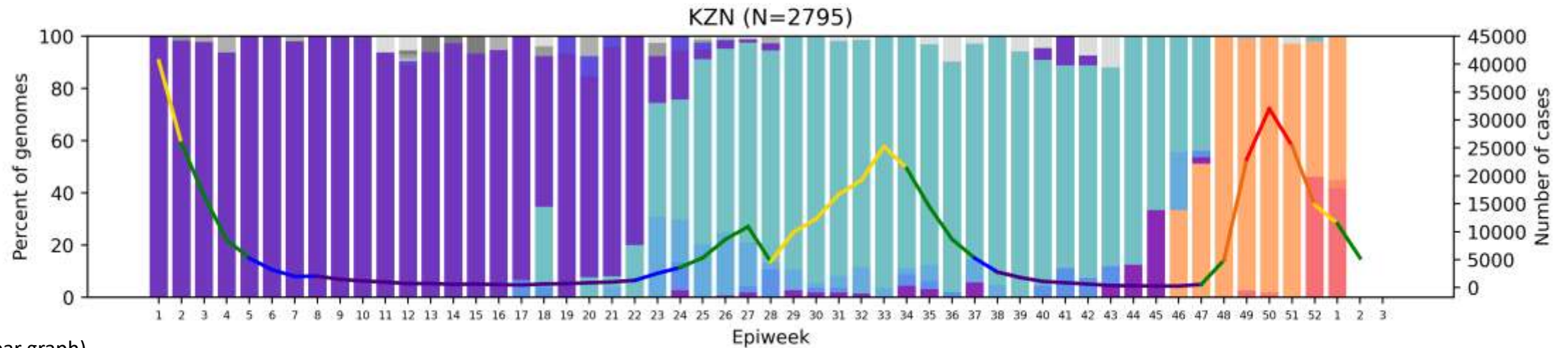
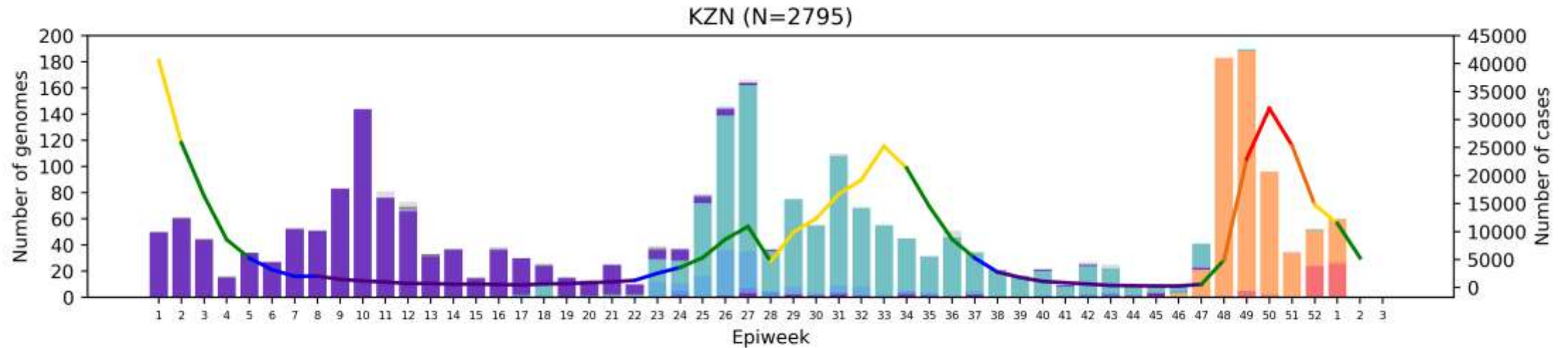
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



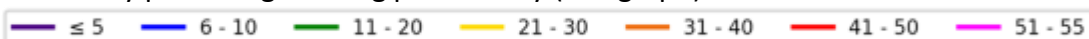
# KwaZulu-Natal Province, 2021-2022, n = 2795



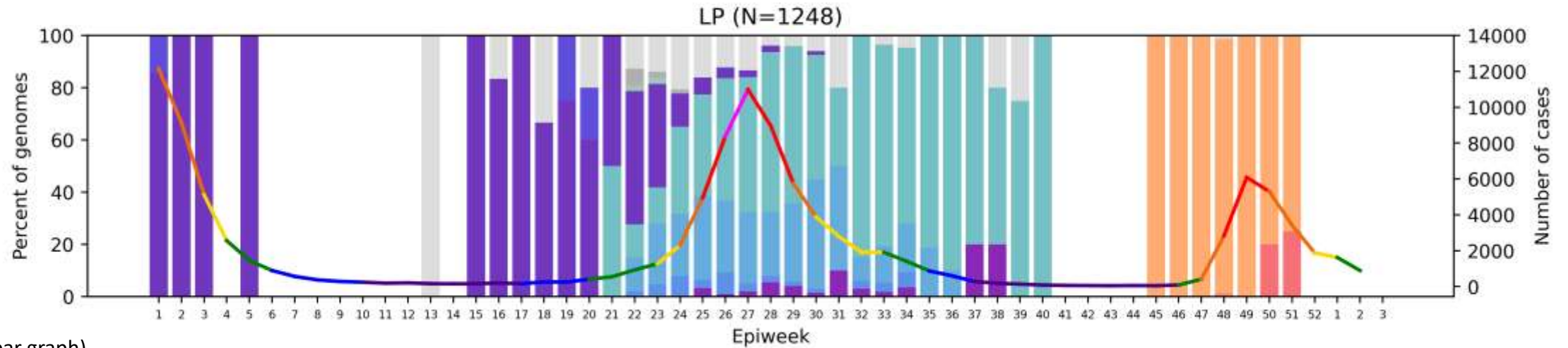
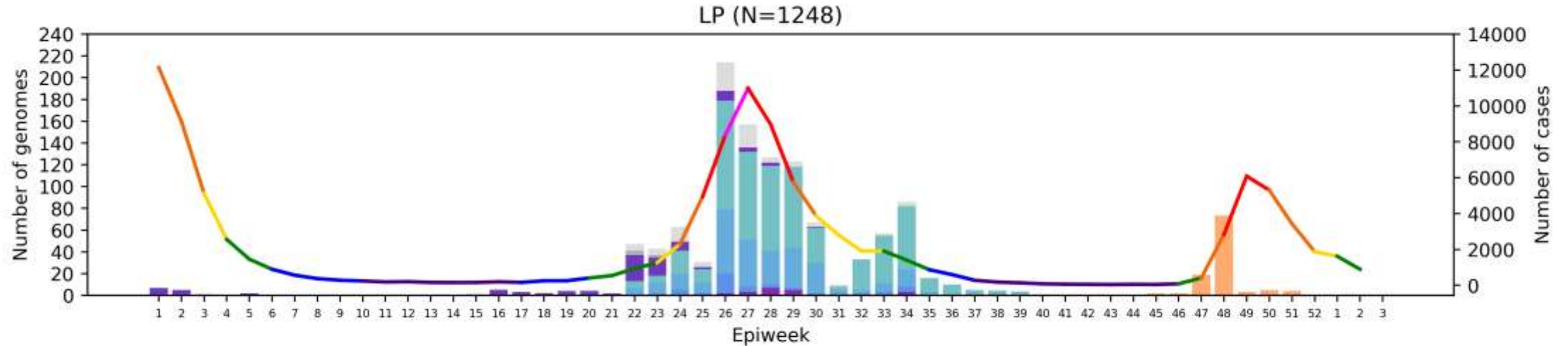
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



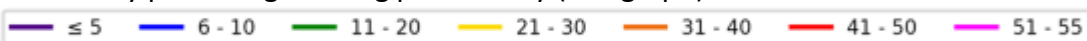
# Limpopo Province, 2021-2022, n = 1248



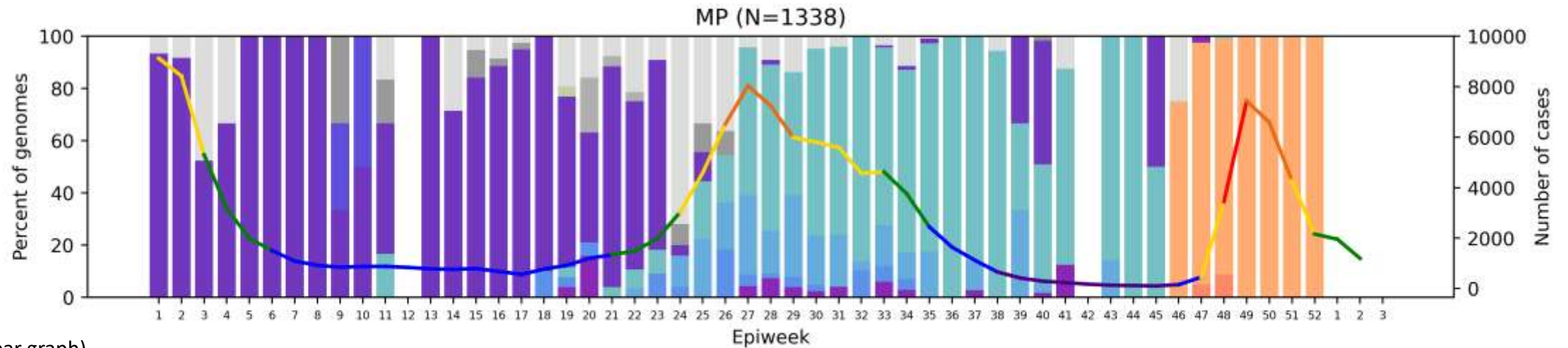
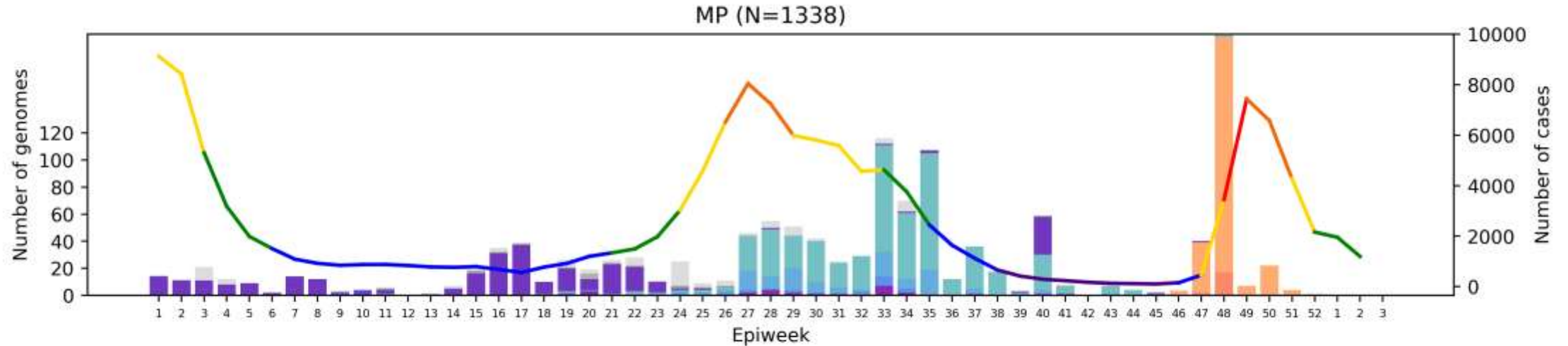
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



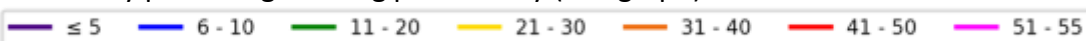
# Mpumalanga Province, 2021-2022, n = 1338



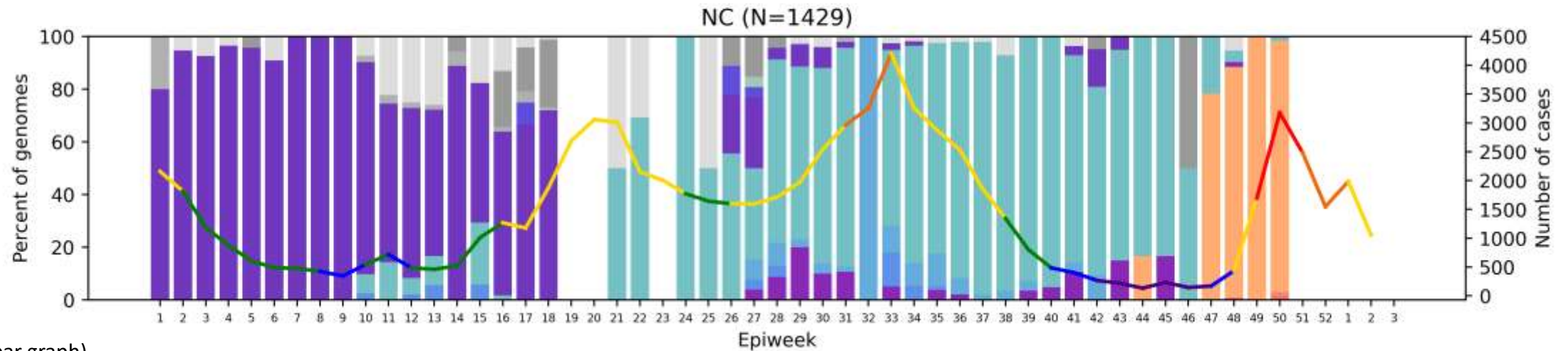
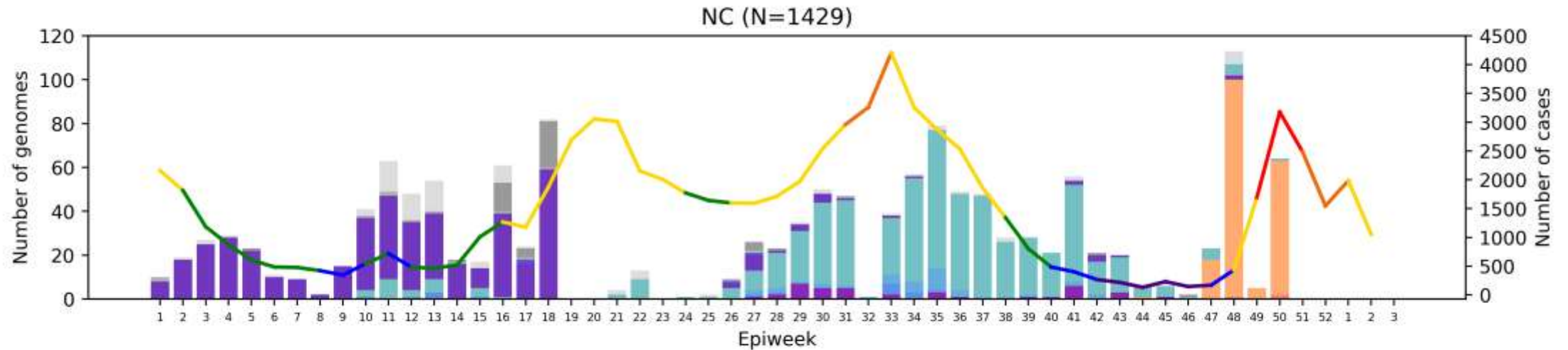
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



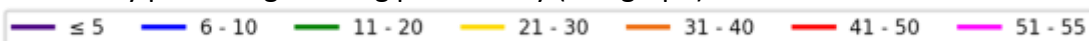
# Northern Cape Province, 2021-2022, n = 1429



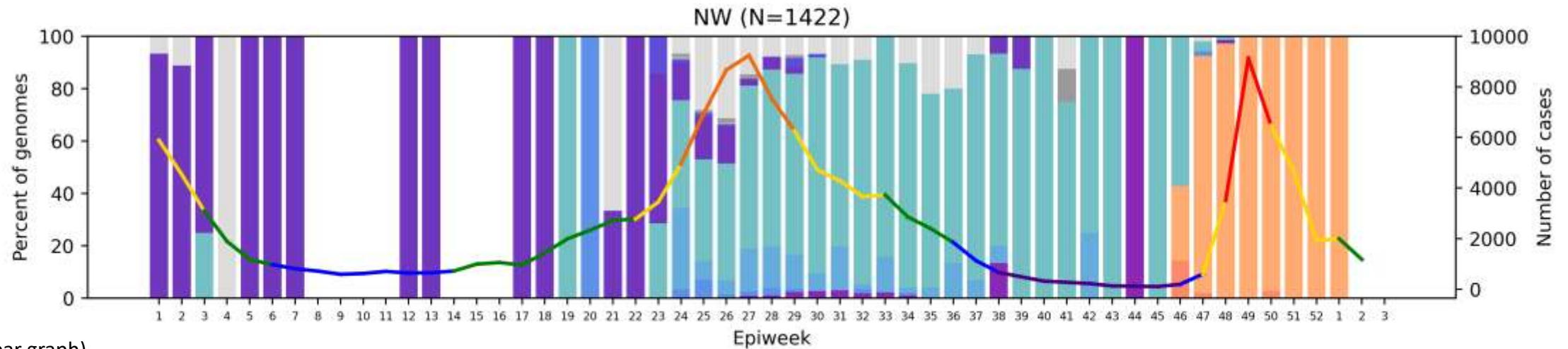
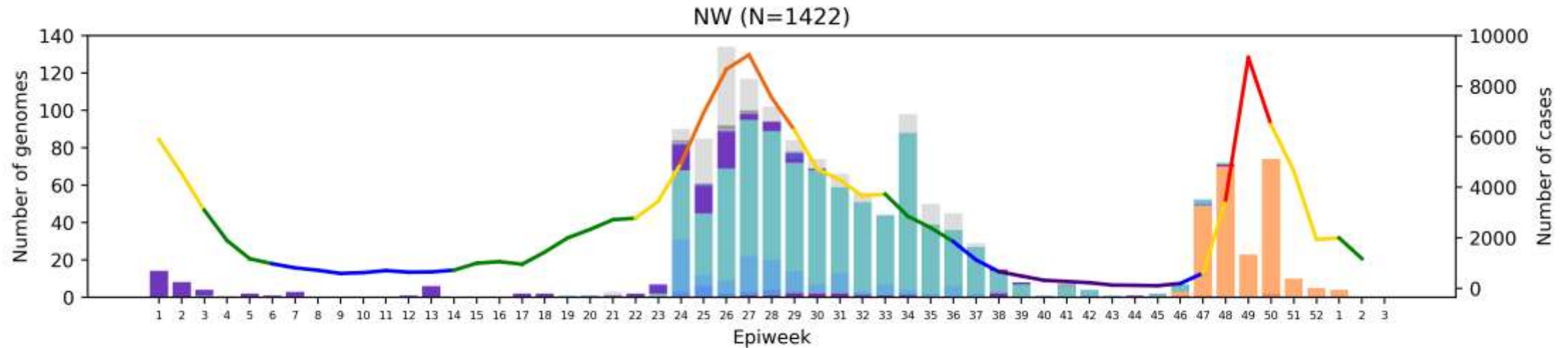
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



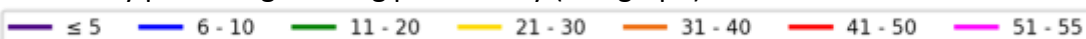
# North West Province, 2021, n = 1422



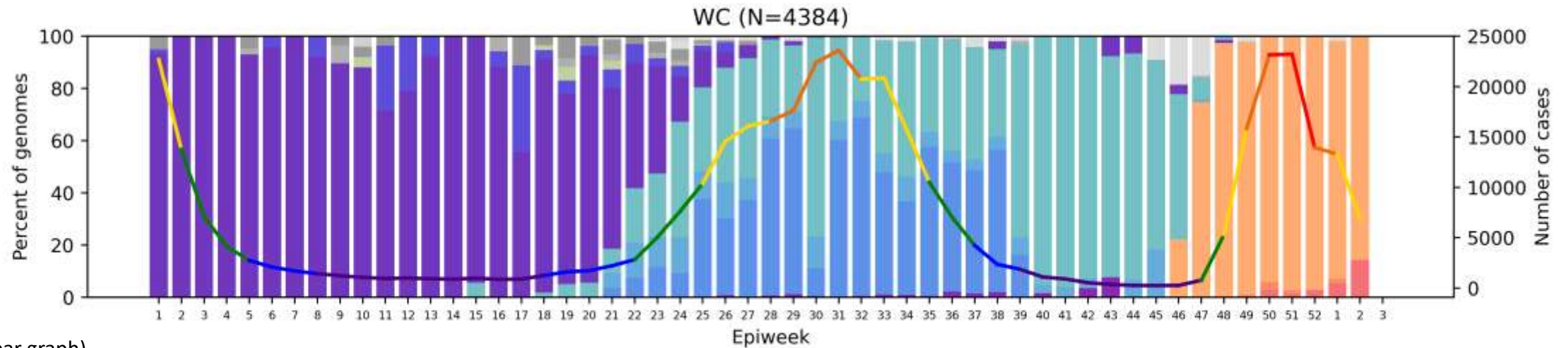
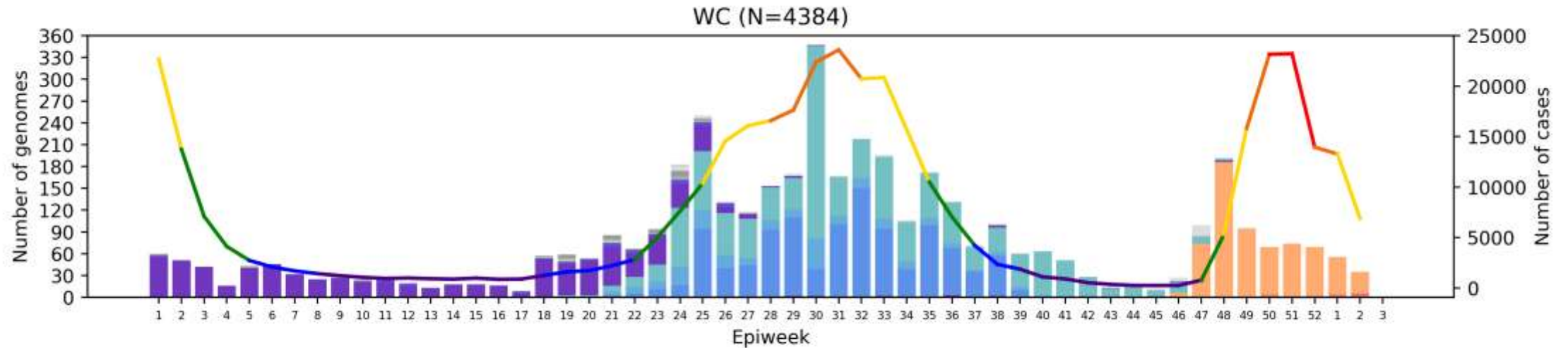
Clade key (bar graph)



Weekly percentage testing positive key (line graph)



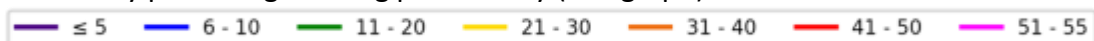
# Western Cape Province, 2021-2022, n = 4384



Clade key (bar graph)

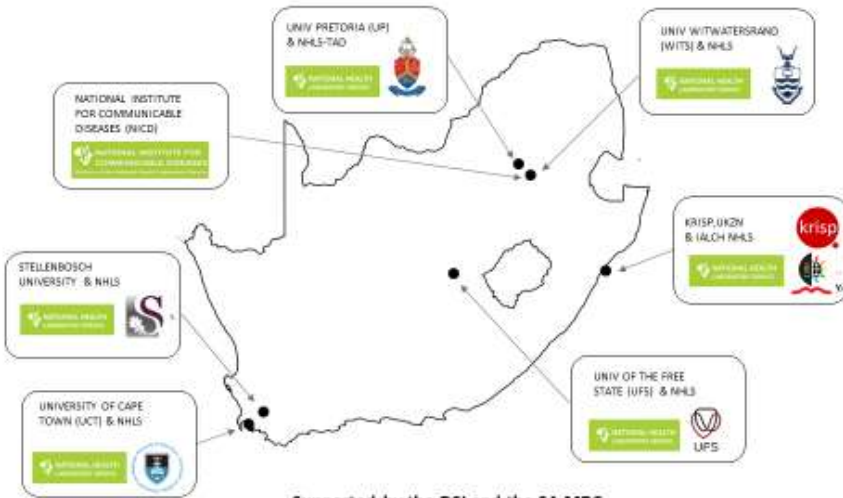


Weekly percentage testing positive key (line graph)



# Summary

- **Variant of Concern Omicron**
  - Detected in 145 countries and dominating globally
  - Split into four lineages based on different mutational profiles: BA.1 (21K), BA.2 (21L), BA.3 (remains in 21M as does not meet requirements for new clade), B.1.1.529 (parent lineage, 21M)
    - New sub-lineage has been designated: BA.1.1. This contains lineage-defining BA.1.1 + spike:R346K
- South Africa (detected in all provinces):
  - Dominated December sequencing data at 99% of genomes (n=1844/1864)
  - Limited sequence data for January shows continued dominance of Omicron (n=179/181)
  - BA.1 dominant in SA, with BA.2 increase recently observed and to be confirmed by additional data
    - BA.2 makes up 20% (n=29/144) of sequences in epiweek 53 of 2021, 22% (n=28/128) epiweek 1 of 2022, and 14% (n=5/35) sequences in epiweek 2.
- Low frequency of previously circulating variants such as Delta and C.1.2 still detected in recent data



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KWAZULU-NATAL  
INYUVESI  
YAKWAZULU-NATALI



EDCTP

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Gert van Zyl  
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The COVID-19 Bench team

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Richard Lessels  
Houriiyah Tegally  
Eduan Wilkinson  
Jennifer Giandhari  
Sureshnee Pillay  
Emmanuel James San



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



**ZARV research program/UP**  
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Michaela Davis (MSc, intern medical scientist)



**NHLS Tshwane**  
Prof Simnikiwe Mayaphi (HOD)

**Funders:**  
GIZ/BMBF: African Network for Improved  
diagnostics and epidemiology of common and  
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G7 Global Health fund, Robert Koch Institute, Dr  
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## National Institute for Communicable Diseases



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**NICD Groups**  
NICD COVID-19 response team  
NICD SARS-CoV-2 Sequencing  
Group

**Sequencing Core Facility**  
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Thokozani Mkhize  
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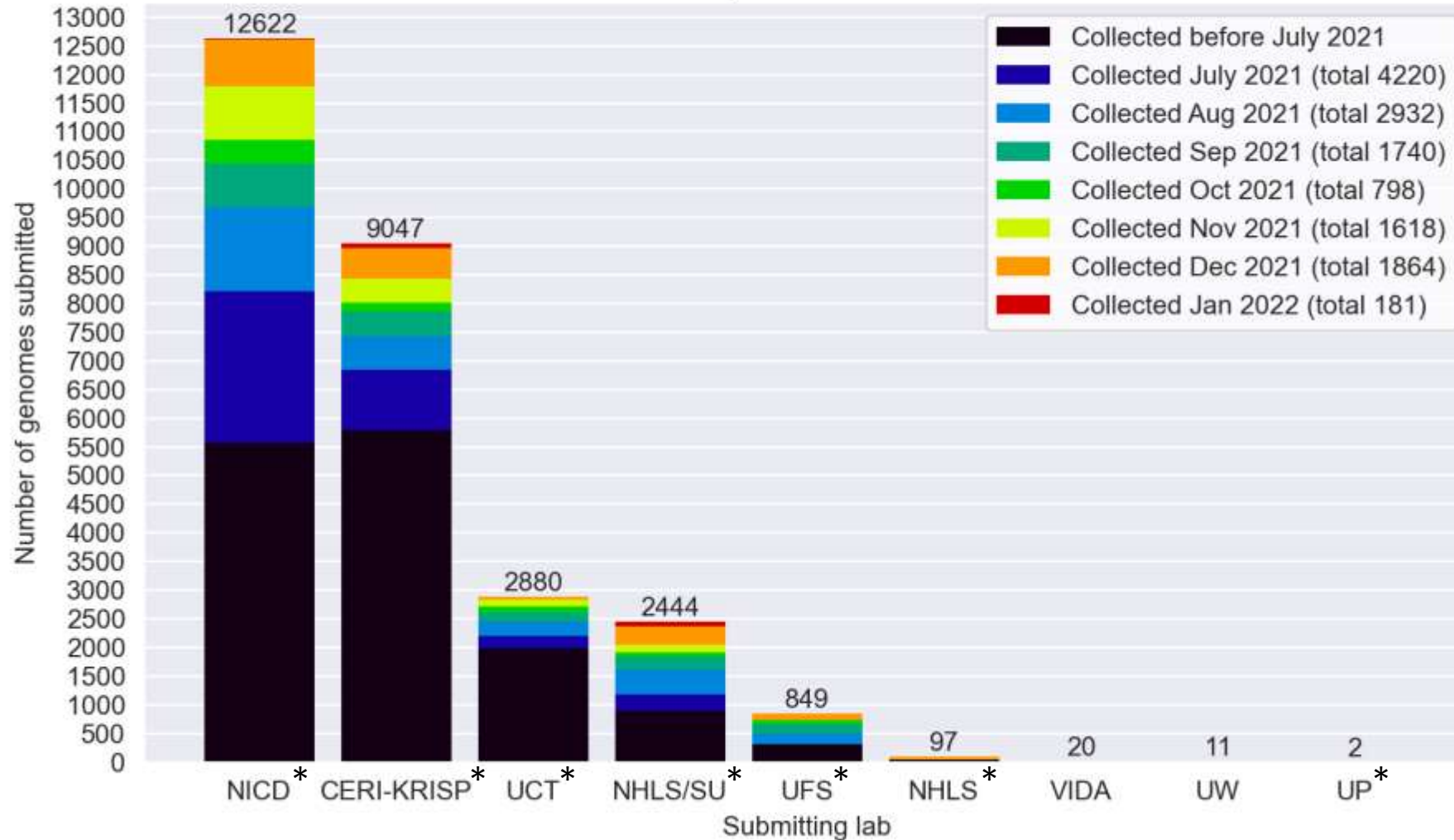
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# South African genomes submitted per submitting lab, 2020 and 2021 (N=27 972)

Submitting labs in South Africa



## \*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.

# Variants of Concern (VOC)

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A	+S:417N +S:E484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GRA	21K, 21L, 21M	+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 14 January 2022

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

\* See TAG-VE statement issued on 26 November 2021

° Only found in a subset of sequences

# Currently designated Variants of Interest (VOI)

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.631	GH	21H	Colombia, Jan-2021	30-Aug-2021

<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> accessed 17 December 2021

\* 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 ( $\geq 14$  days after vaccine), especially if hospitalised and clinically severe
- Suspected re-infection ( $\geq 90$  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.)