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

SARS-CoV-2 Sequencing Update
28 January 2022

UNIV PRETORIA (UP) & NHLS-TAD

UNIV WITWATERSRAND (WITS) & NHLS

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES (NICD)

KRISP, UKZN & IALCH NHLS

STELLENBOSCH UNIVERSITY & NHLS

UNIVERSITY OF CAPE TOWN (UCT) & NHLS

UNIV OF THE FREE STATE (UFS) & NHLS
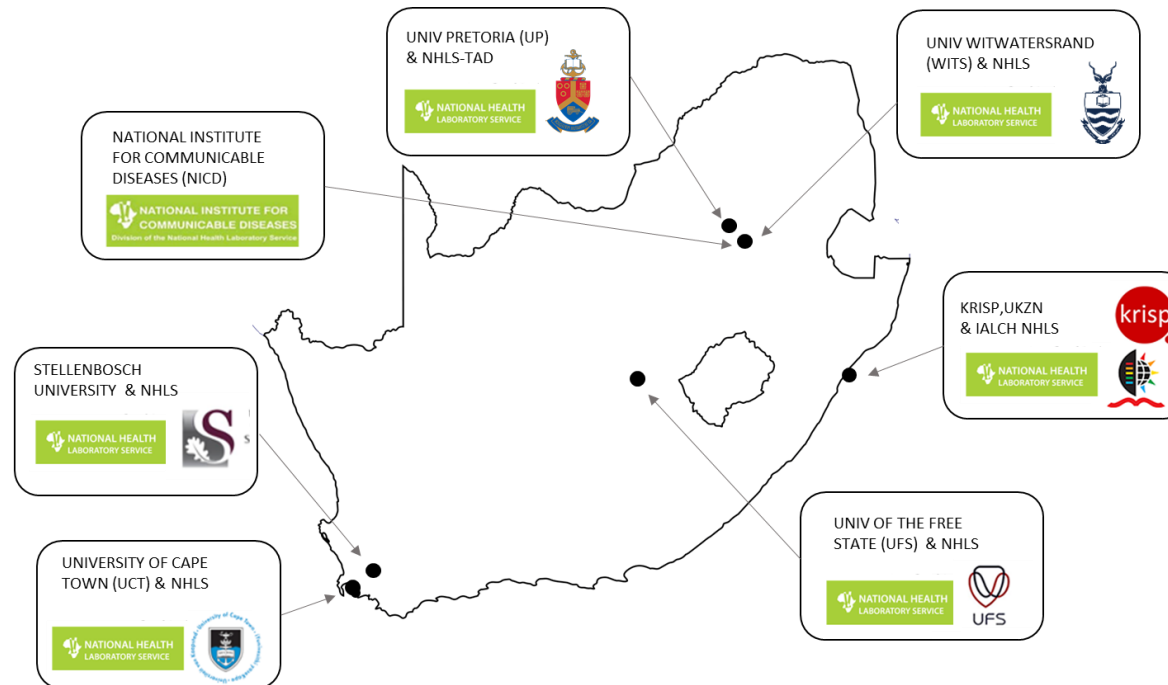
Supported by the DSI and the SA MRC
Msomi N, Mlisana K, et al. Lancet Microbe 2020

The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 28 January 2022 at 08h17

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) - 3 (2022)
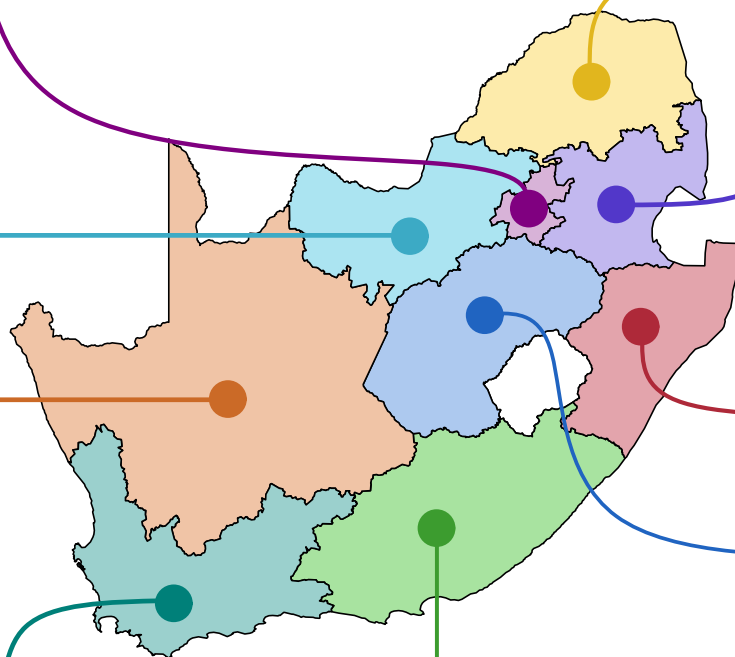
Gauteng ↓PTP: 8.7%
Genomes	Cases
1 501 (28.0%)	236 739 (35.7%)

Genomes deposited in the last week
☐ 154 ☐ 51 ☐ 3 ☐ 1 ☐ 17

North West ↑PTP: 14.5%
Genomes	Cases
286 (5.3%)	32 698 (4.9%)

Genomes deposited in the last week
☐ 12 ☐ 1

Northern Cape ↓PTP: 18.4%
Genomes	Cases
402 (7.5%)	15 964 (2.4%)

Genomes deposited in the last week
☐ 26 ☐ 2 ☐ 9 ☐ 1

Western Cape ↓PTP: 14.8%
Genomes	Cases
1 230 (22.9%)	112 516 (17.0%)

Genomes deposited in the last week
☐ 256 ☐ 16 ☐ 2 ☐ 10 ☐ 13

Limpopo ↑PTP: 24.4%
Genomes	Cases
120 (2.2%)	25 161 (3.8%)

Genomes deposited in the last week
☐ 2 ☐ 4

Mpumalanga ↑PTP: 16.2%
Genomes	Cases
393 (7.3%)	30 662 (4.6%)

Genomes deposited in the last week
☐ 34 ☐ 1 ☐ 4 ☐ 2

KwaZulu-Natal ↓PTP: 11.1%
Genomes	Cases
899 (16.8%)	126 812 (19.1%)

Genomes deposited in the last week
☐ 105 ☐ 8 ☐ 1 ☐ 1 ☐ 1

Free State ↓ PTP: 9.3%
Genomes	Cases
280 (5.2%)	33 132 (5.0%)

Genomes deposited in the last week
☐ 17 ☐ 5 ☐ 23 ☐ 1

Eastern Cape ↓PTP: 10.9%
Genomes	Cases
251 (4.7%)	49 611 (7.5%)

Genomes deposited in the last week
☐ 1

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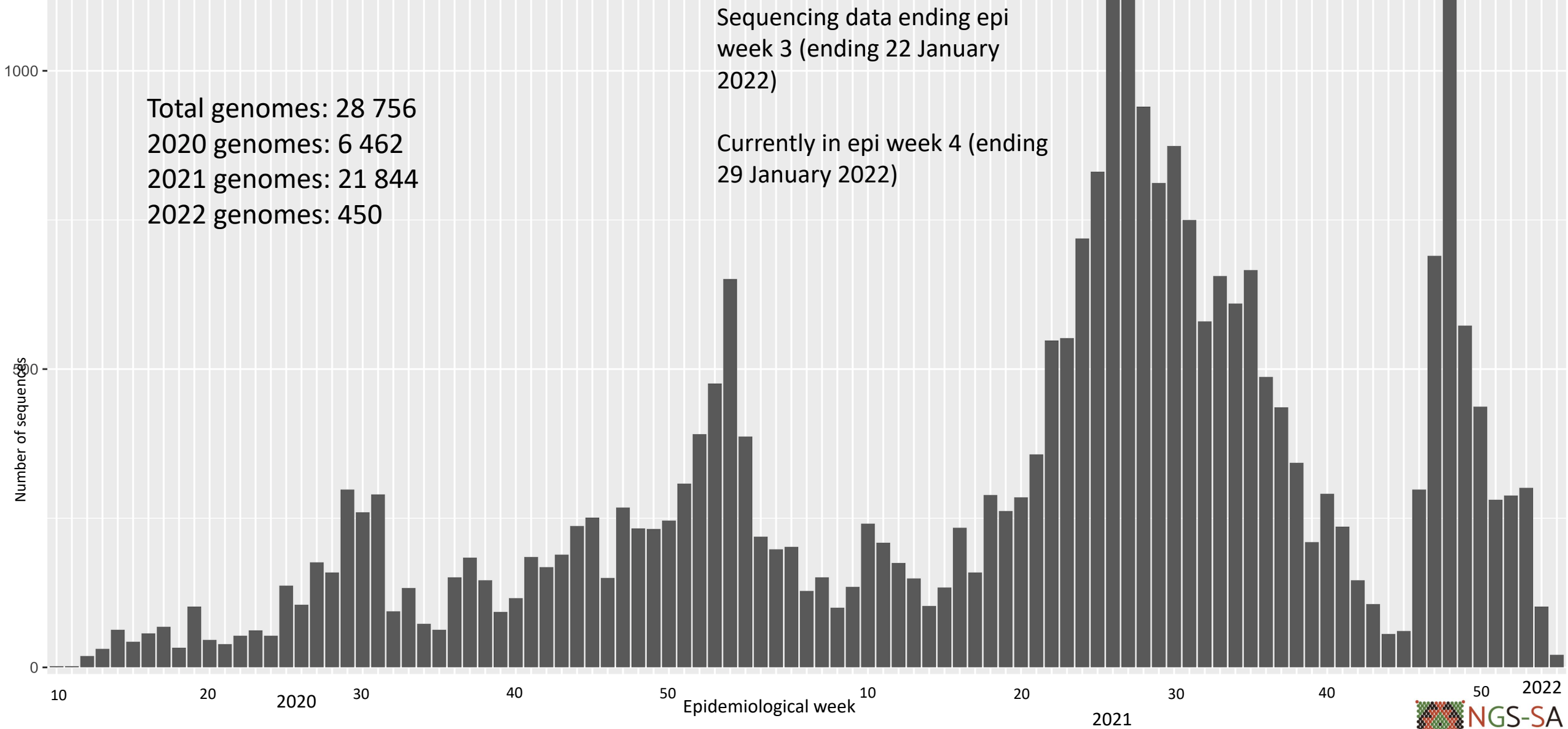- Unassigned
- Delta (21J)
- 20C
- 20D
- — Cases

784 genomes deposited in the past week

Bar graphs represent genomes sequenced per epiweek, with lines representing cases by collection date (weeks 39 [2021] – 3 [2022])
Genomes and cases presented as provincial total (percentage of national total) for epiweeks 39 (2021) – 3 (2022)
PTP: percentage testing positive in week 3 (16 Jan 2022 – 22 Jan 2022); the arrow indicates direction of change since the previous week (9 Dec 2021 – 15 Jan 2022)
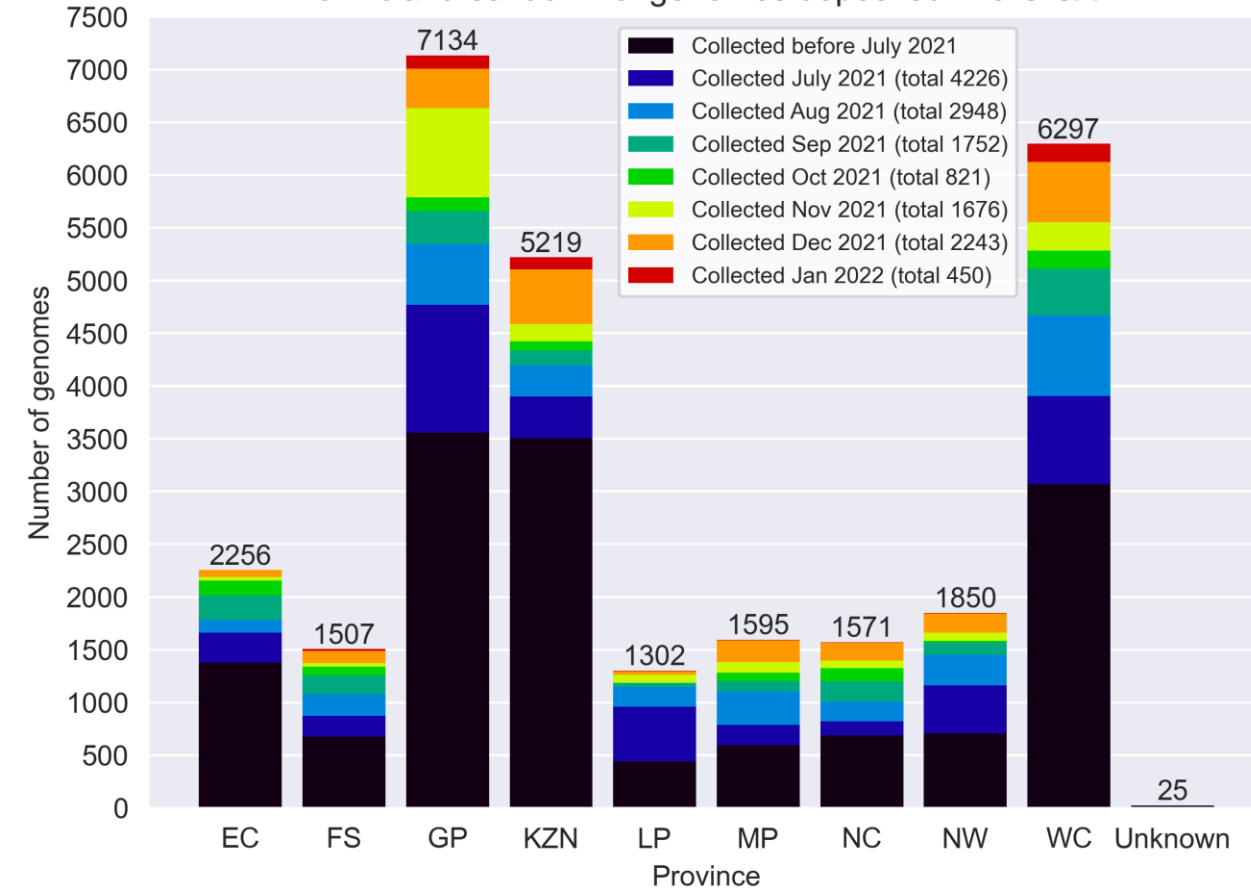
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Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022 (N=28 756*)

Total genomes: 28 756
2020 genomes: 6 462
2021 genomes: 21 844
2022 genomes: 450

Sequencing data ending epi week 3 (ending 22 January 2022)
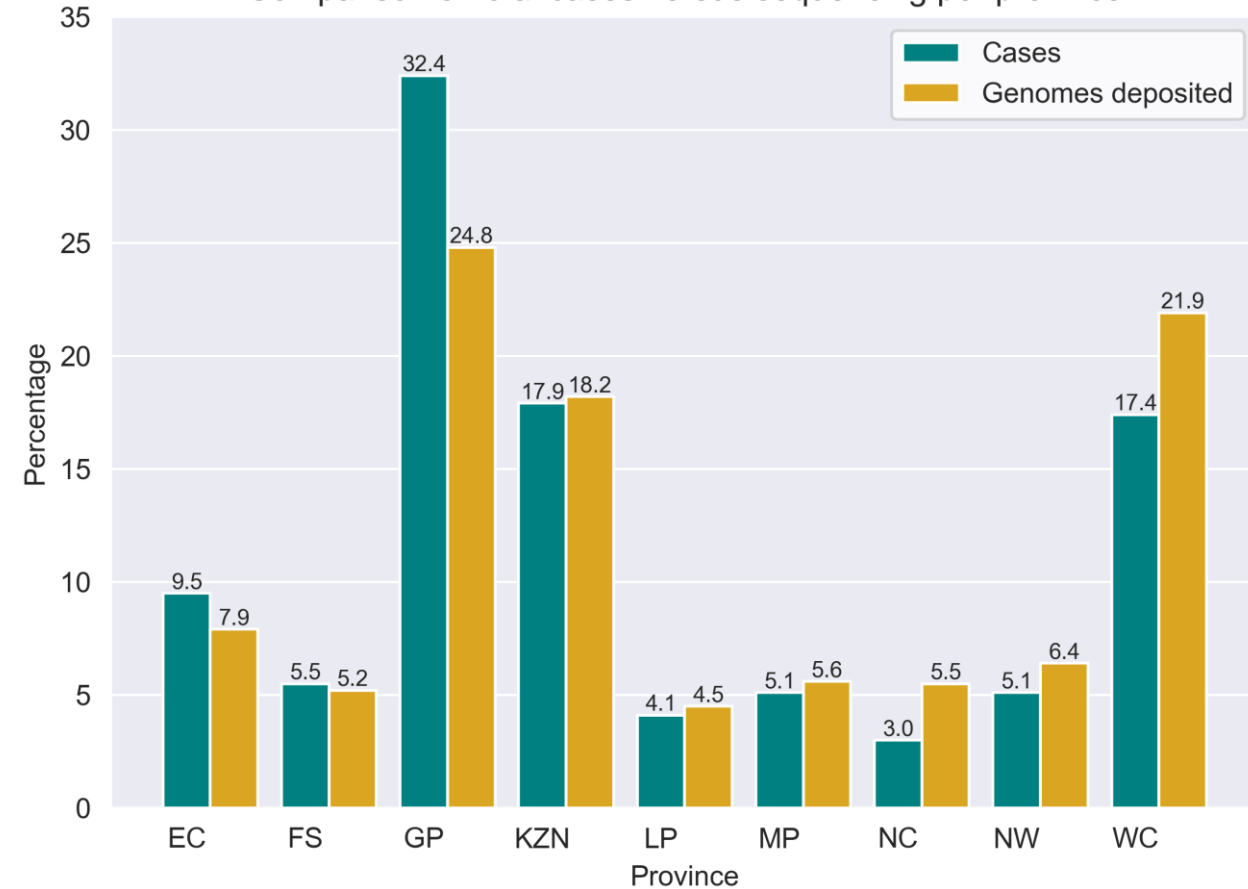
Currently in epi week 4 (ending 29 January 2022)

*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=28 756)

Provincial breakdown of genomes deposited into GISAID

Legend:
- Collected before July 2021
- Collected July 2021 (total 4226)
- Collected Aug 2021 (total 2948)
- Collected Sep 2021 (total 1752)
- Collected Oct 2021 (total 821)
- Collected Nov 2021 (total 1676)
- Collected Dec 2021 (total 2243)
- Collected Jan 2022 (total 450)

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.

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Omicron sub-lineage spike mutation profiles

BA.1 21K
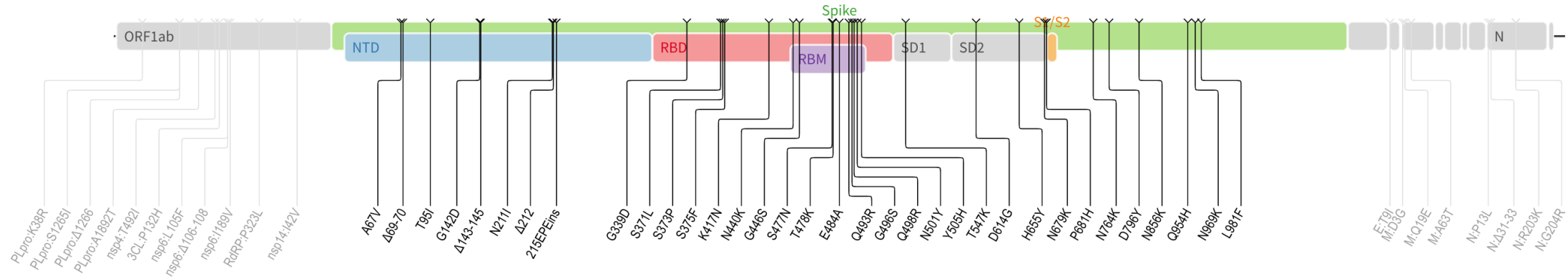
BA.2 21L

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

BA.3 21M

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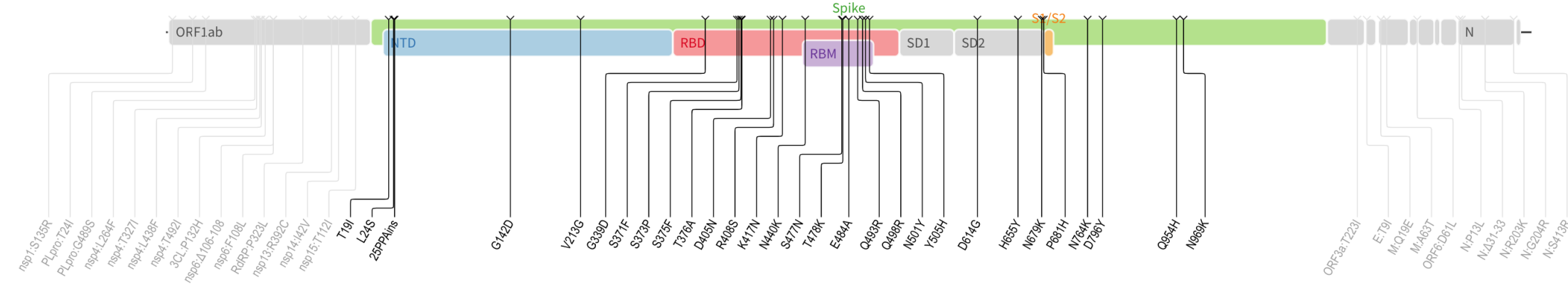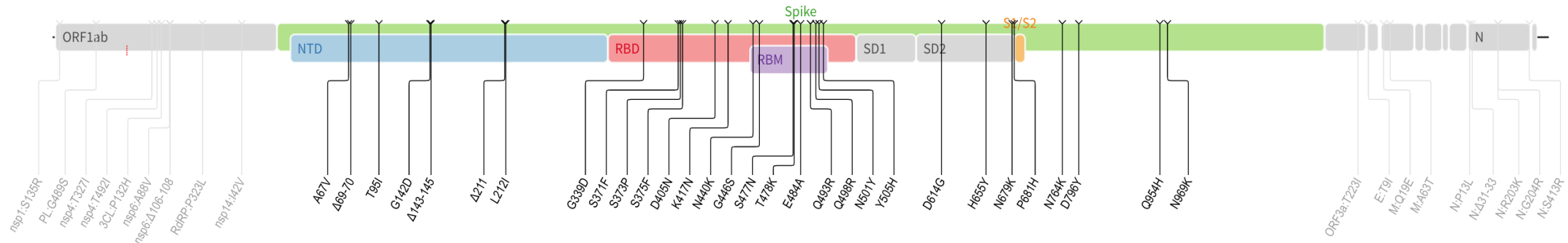
Omicron spike mutations compared to other VOC/VOIs
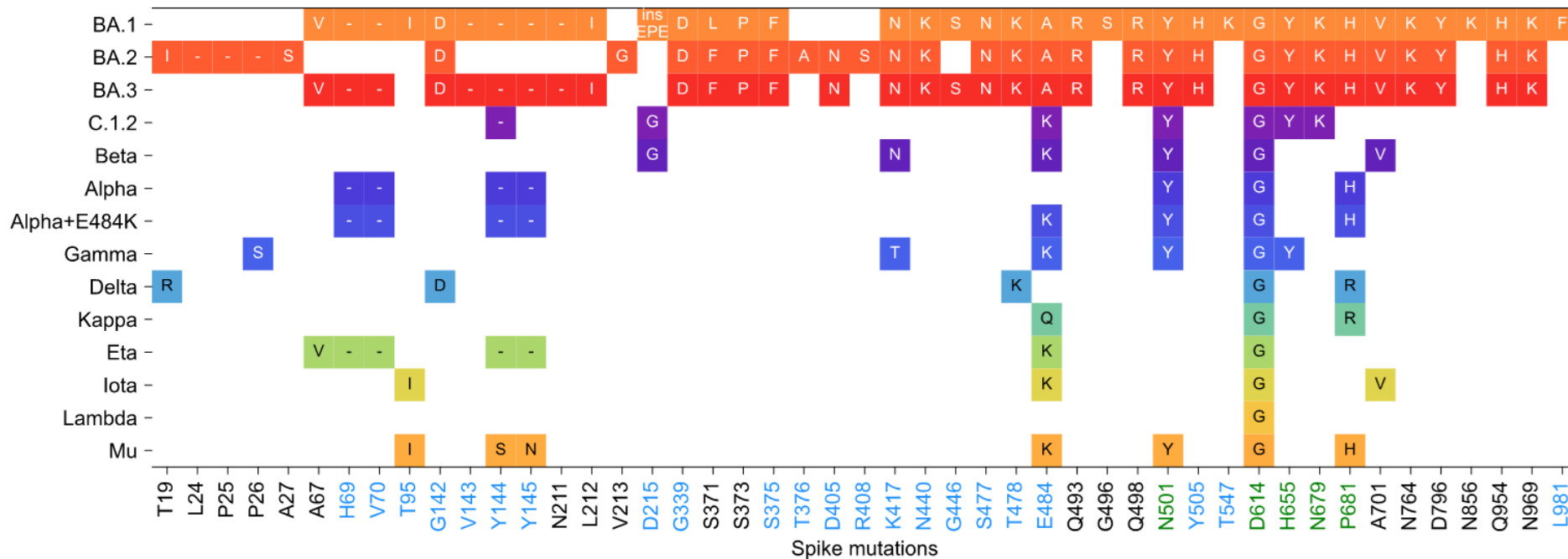
Only lineage-defining mutations are pictured here. Low prevalence mutations can be seen on the following slide.

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

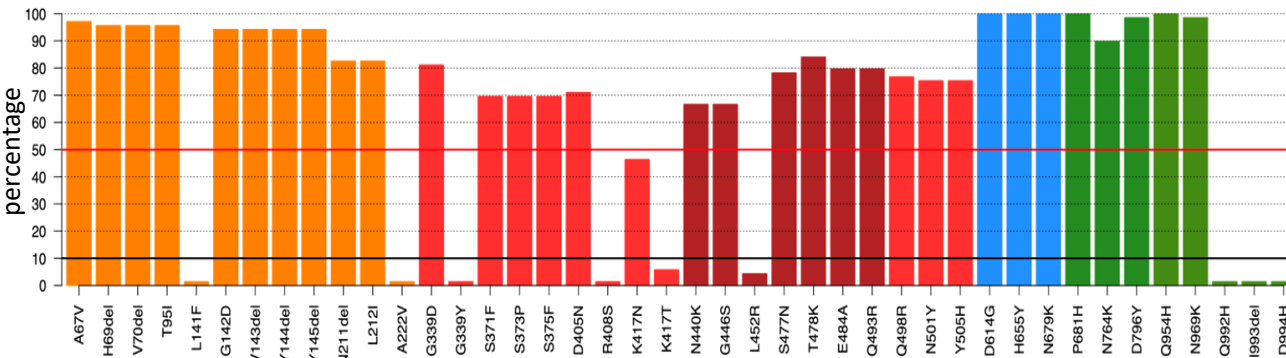# Spike mutational profile of Omicron sequences*

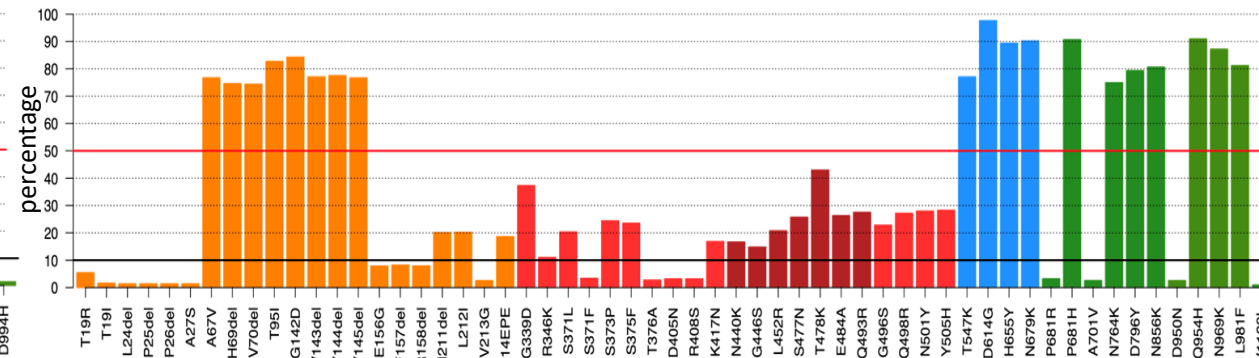Frequency of Spike SNVs for BA.1 (n=462258)
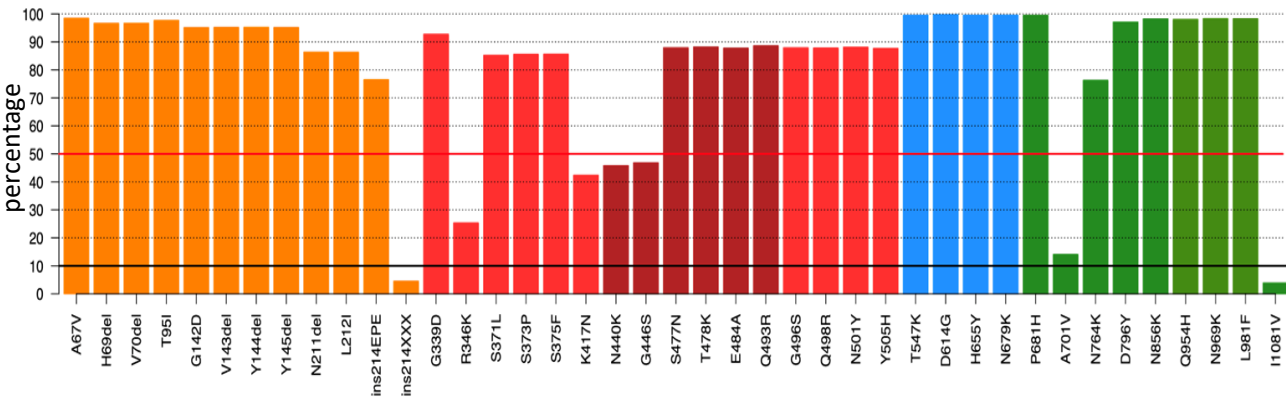
Frequency of Spike SNVs for BA.2 (n=8985)
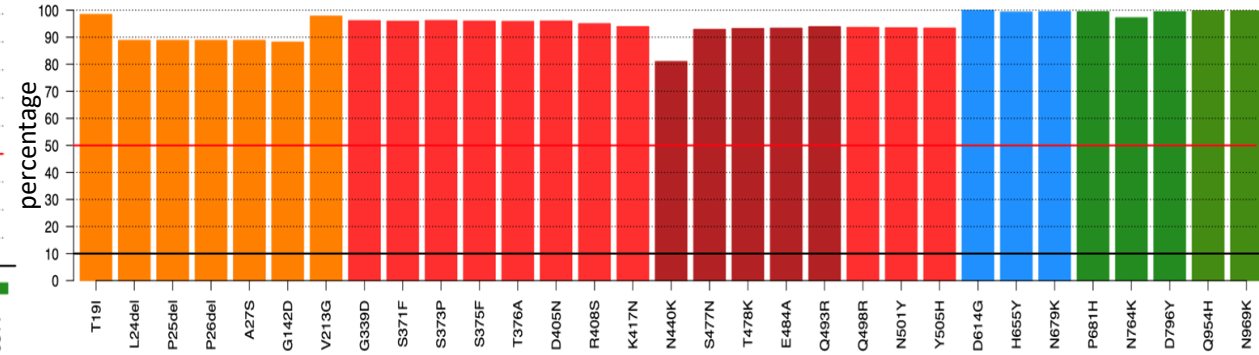
Frequency of Spike SNVs for BA.3 (n=69)

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.

NTD   **RBM**   **RBD**   **S1**   **S2**
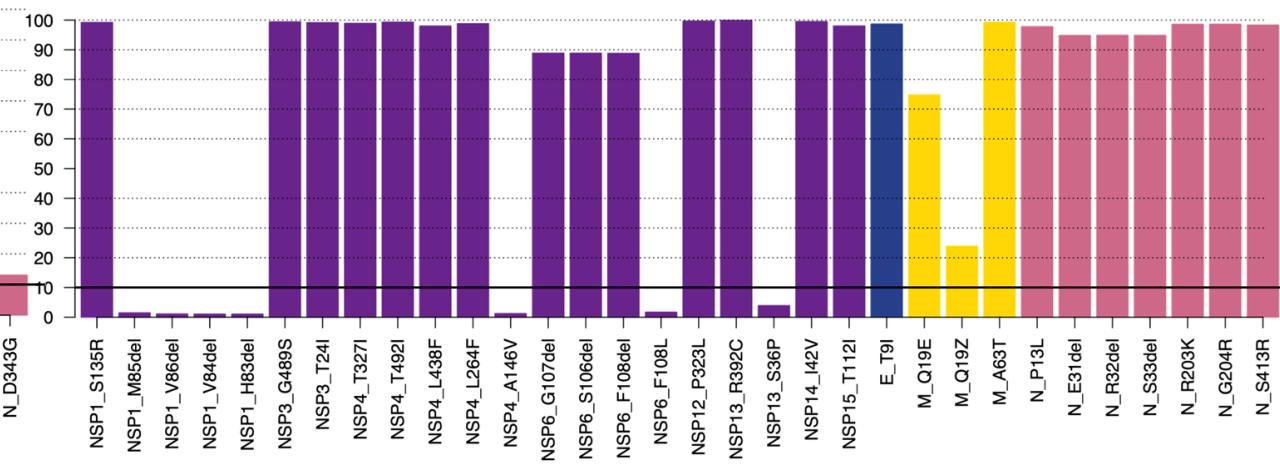
*as of data on GISAID 21 Jan 2022, 09h31

Low mutation frequencies for K417N, N440K and G446S are most likely a result of poor coverage due to primer drop off. There are significant differences in the presence and prevalence of insertions and deletions amongst sub-lineages. BA.2 has lowest spike diversity of all Omicron sub-lineages.

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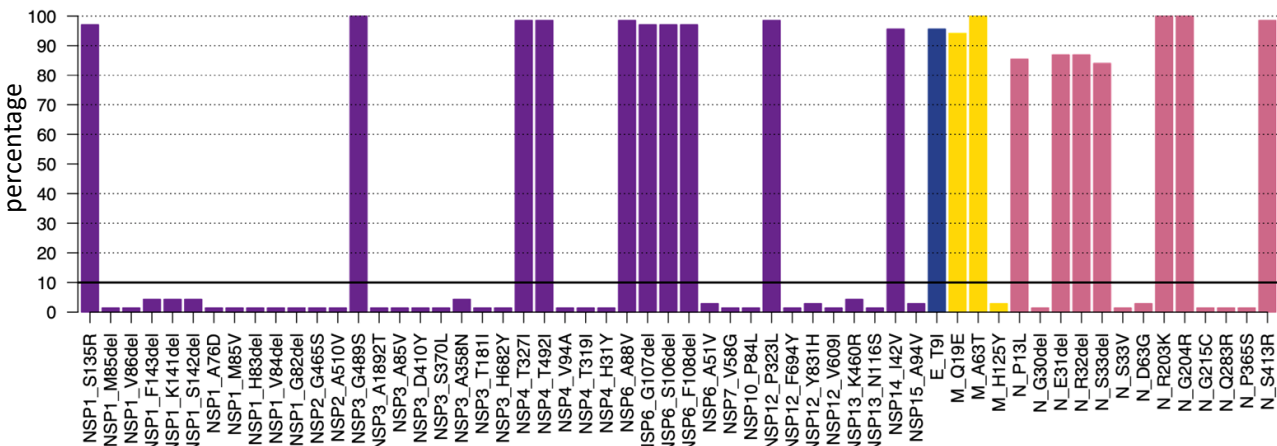# Mutational profile of Omicron sequences*

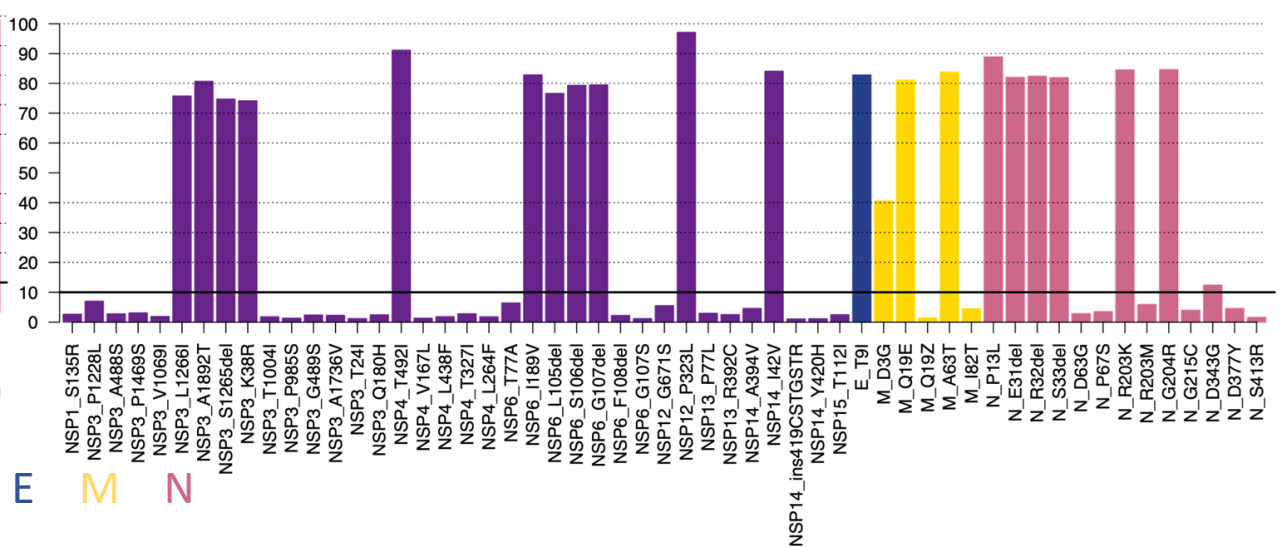Frequency of whole genome SNVs for BA.1 (n=462258)
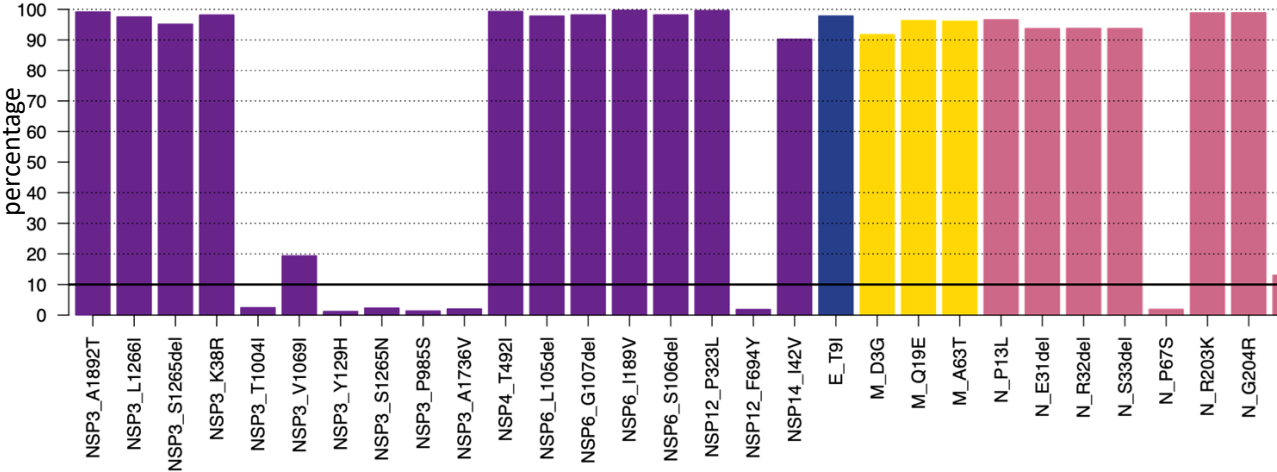
Frequency of whole genome SNVs for BA.2 (n=8985)

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

*as of data on GISAID 21 Jan 2022, 09h31

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.
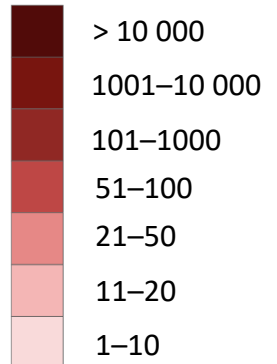
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Omicron global prevalence*

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

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

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

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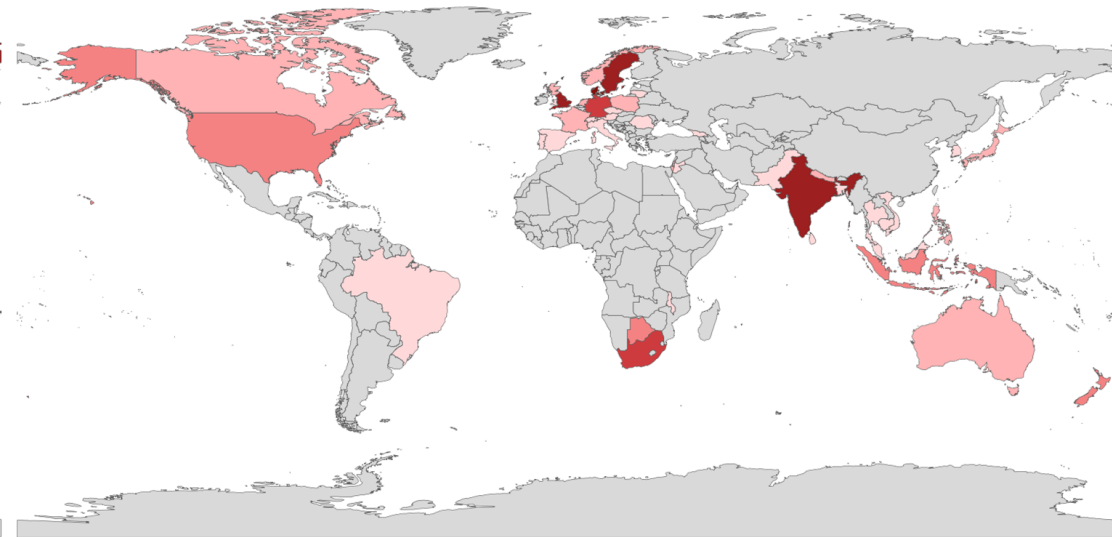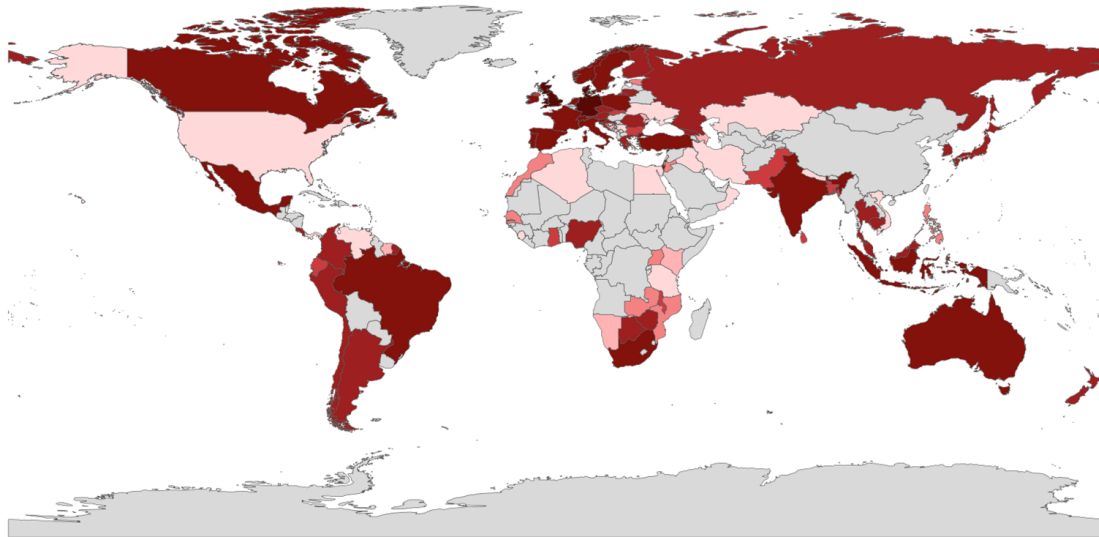
Number of Omicron genomes

> 10 000

1001–10 000

101–1000

51–100

21–50

11–20

1–10
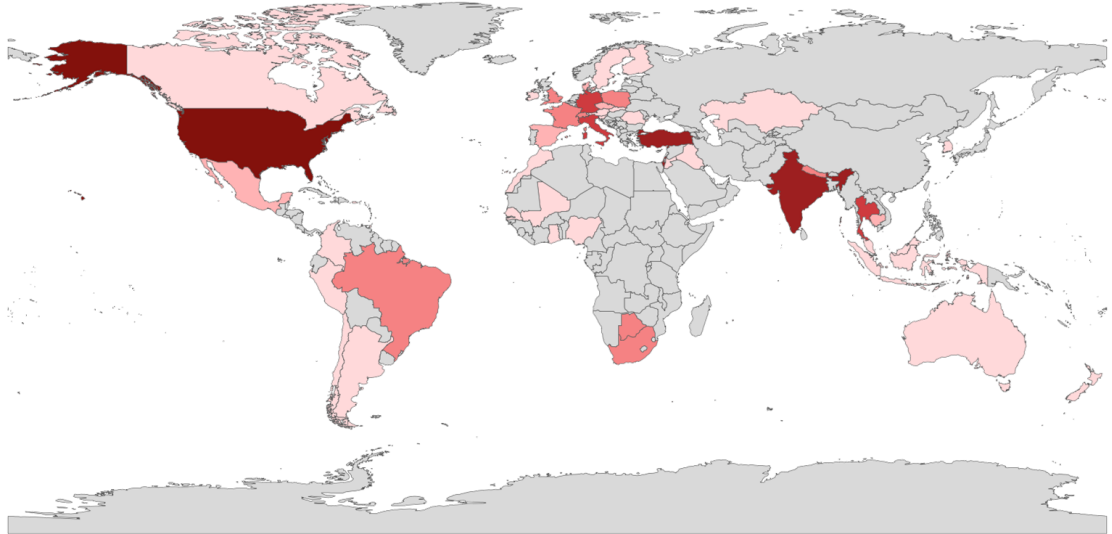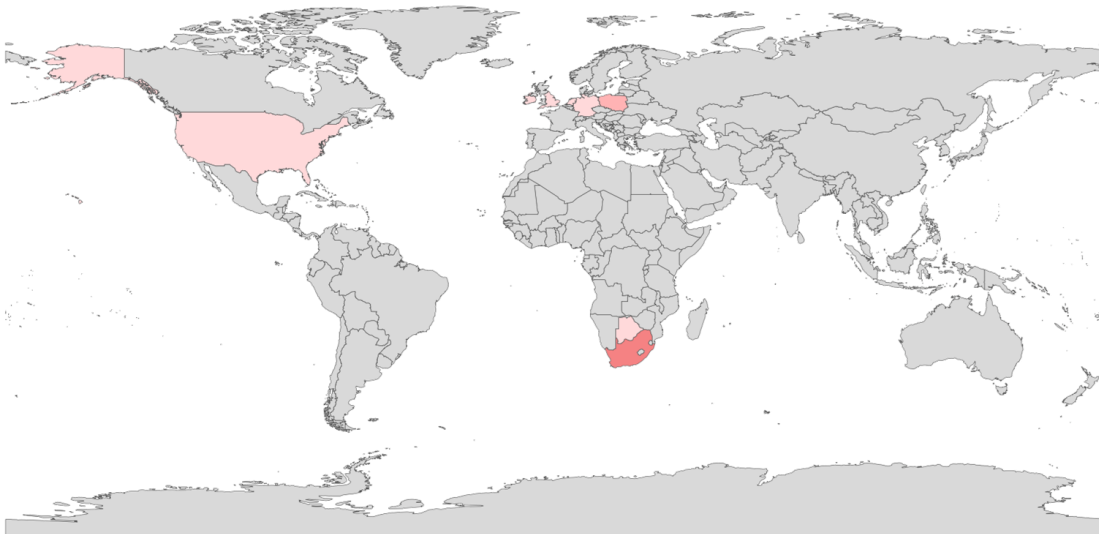
*as of data on GISAID 21 Jan 2022, 09h31

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

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Proportion and number of clades by epiweek in South Africa, 2021 - 2022 (N=22 294)
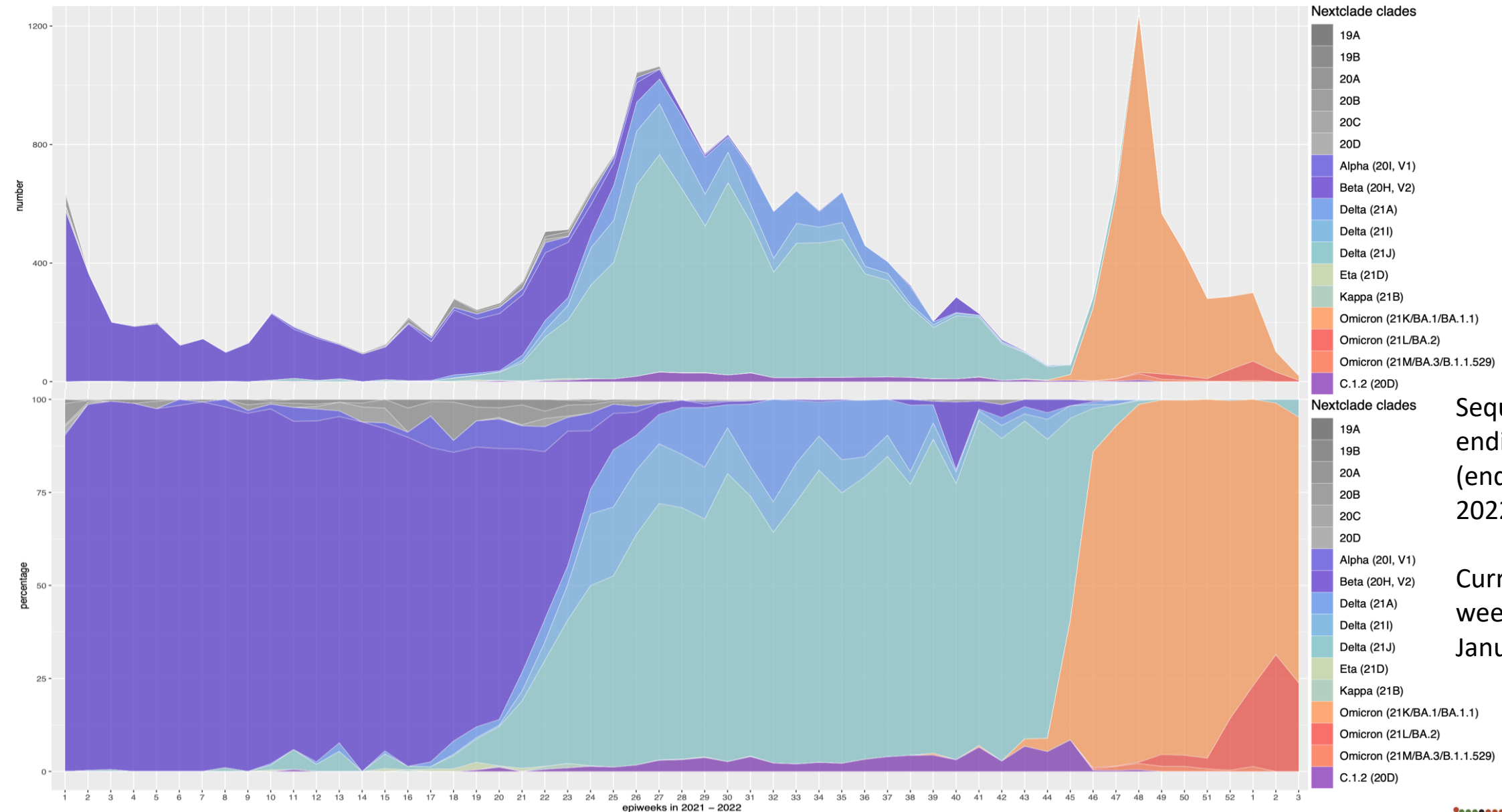
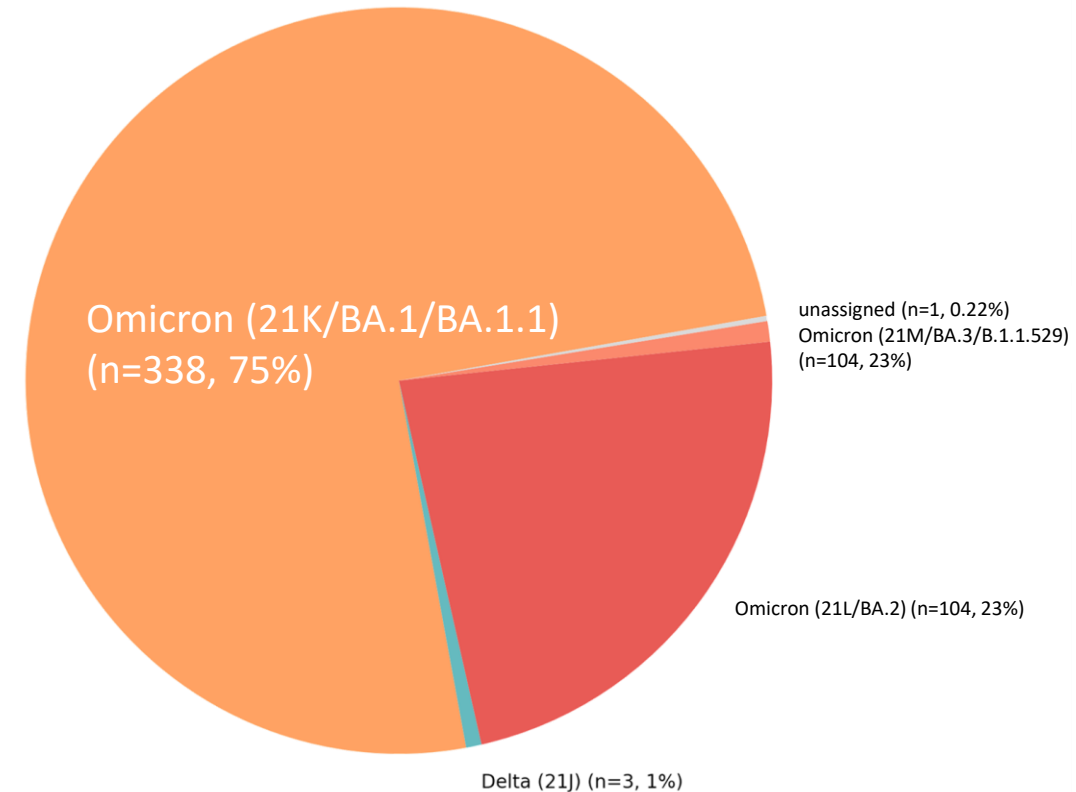**Delta dominated in South Africa until October at >80%. Omicron dominated November and December at >95%.**

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

December (N=2243)

Omicron (21K/BA.1/BA.1.1)
(n=2113, 94%)

Beta (20H, V2) (n=1, 0.04%)
unassigned (n=6, 0.27%)
Omicron (21M/BA.3/B.1.1.529) (n=30, 1%)
C.1.2 (20D) (n=3, 0.13%)
Omicron (21L/BA.2) (n=80, 4%)
Delta (21J) (n=9, 0.4%)
Delta (21I) (n=1, 0.04%)
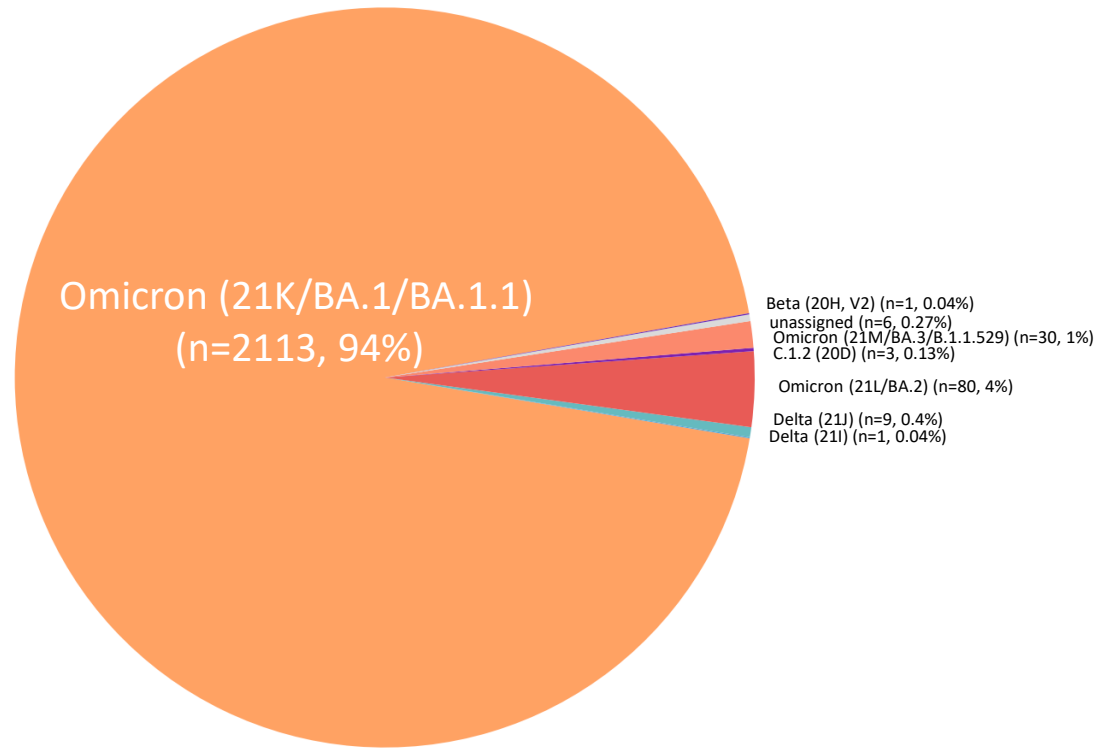
Total Omicron in Dec: 2223 (99.1%)

January (N=450)

Omicron (21K/BA.1/BA.1.1)
(n=338, 75%)

unassigned (n=1, 0.22%)
Omicron (21M/BA.3/B.1.1.529)
(n=104, 23%)

Omicron (21L/BA.2) (n=104, 23%)

Delta (21J) (n=3, 1%)

Total Omicron in Jan: 446 (99.1%)

Legend:
- 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)
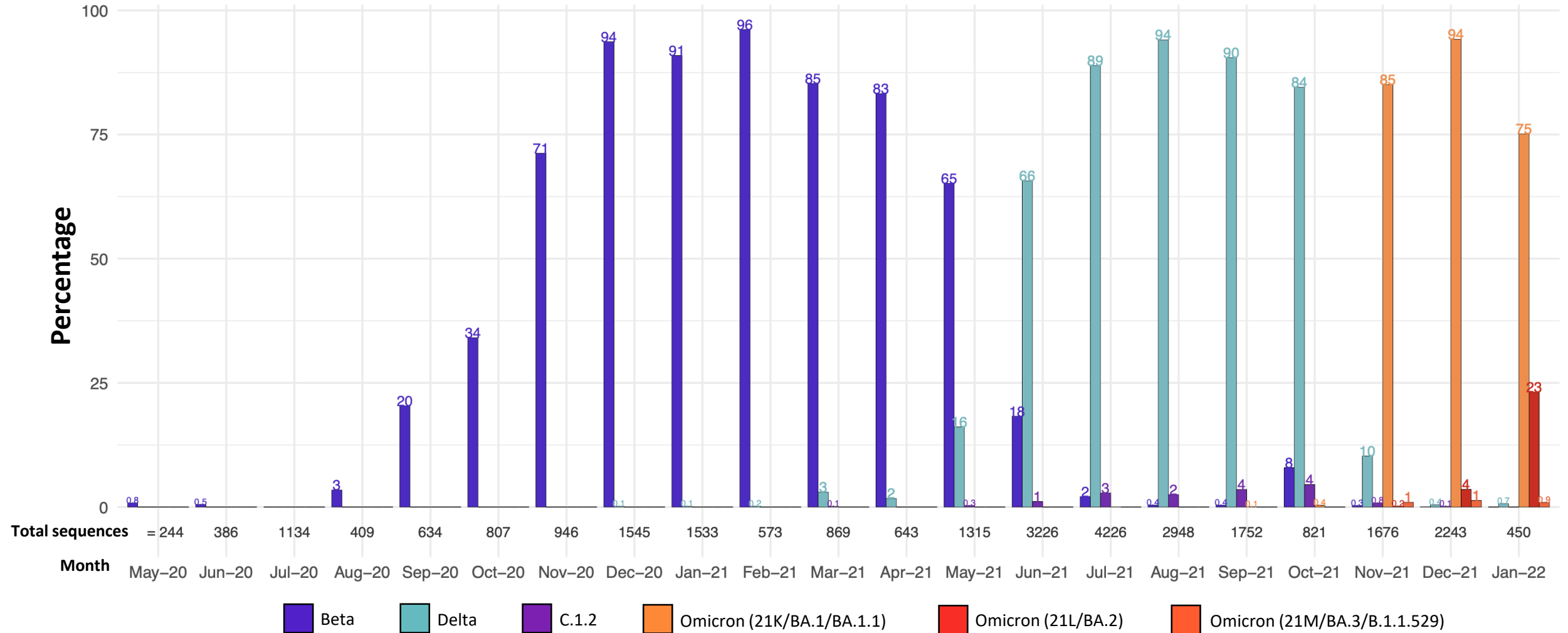
Omicron dominated in December (99%, 2223/2243). Omicron appears to continue dominating in January (99%, 446/450), with BA.2 increasing in prevalence.

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

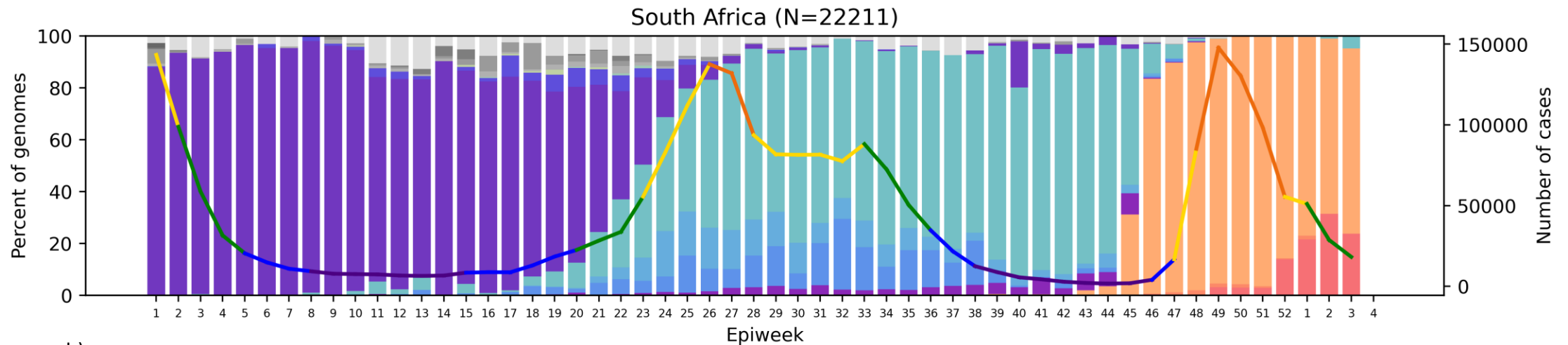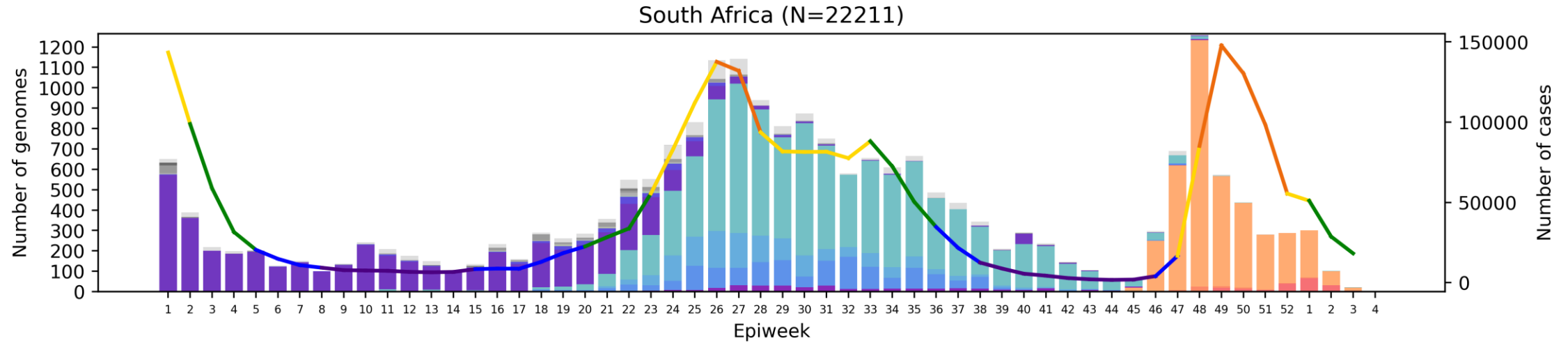Detection rates of variants being monitored in South Africa*

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

**C.1.2, Beta and Delta detection has remained low since November 2021.
Omicron has been dominant since November (>80% in November, >98% in December and January). BA.2 has increased in frequency in January, now making up 23% of genomes.**
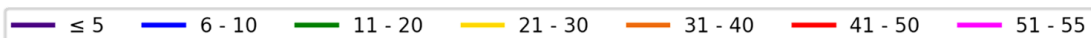
South Africa, 2021-2022, n = 22211*

South Africa (N=22211)

Clade key (bar graph)

Omicron (21L) | Omicron (21K) | Delta (21A) | Delta (21J) | Beta (20H, V2) | Alpha (20I, V1) | Kappa (21B) | Eta (21D) | 20A | 20B | 20C | 20D | unassigned | 19A | 19B
Omicron (21M) | C.1.2 (20D) | Delta (21I) | Cases

Weekly proportion 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 = 1834

Clade key (bar graph)

Omicron (21L)   Omicron (21K)   Delta (21A)   Delta (21J)   Beta (20H, V2)   Alpha (20I, V1)   Kappa (21B)   Eta (21D)   20A   20B   20C   20D   unassigned   19A   19B

Omicron (21M)   C.1.2 (20D)   Delta (21I)   Cases

Weekly proportion testing positive key (line graph)

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

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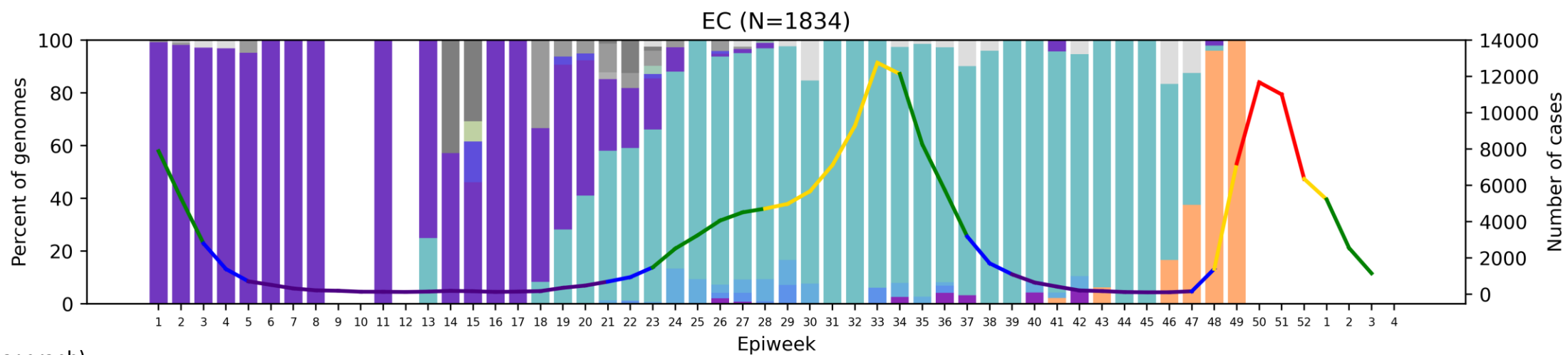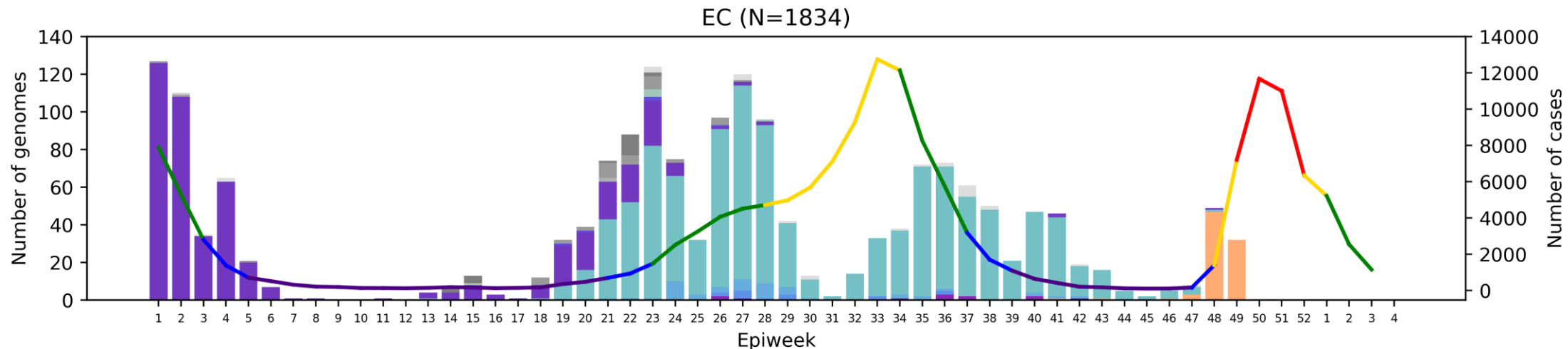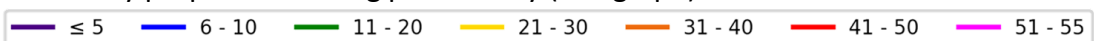
Free State Province, 2021-2022, n = 1210

FS (N=1210)

FS (N=1210)

Clade key (bar graph)

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

Weekly proportion testing positive key (line graph)

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

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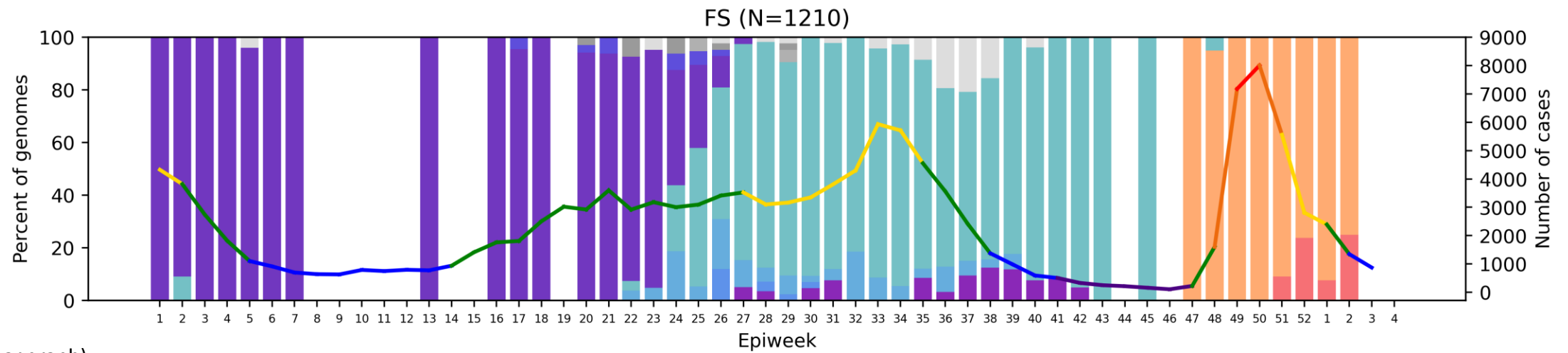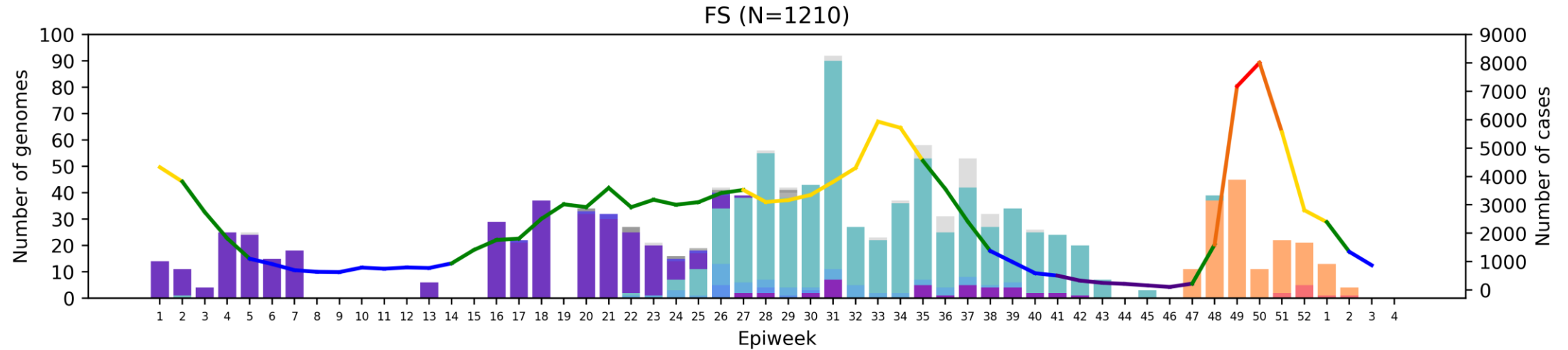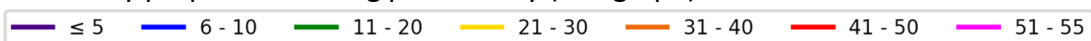
Gauteng Province, 2021-2022, n = 6040
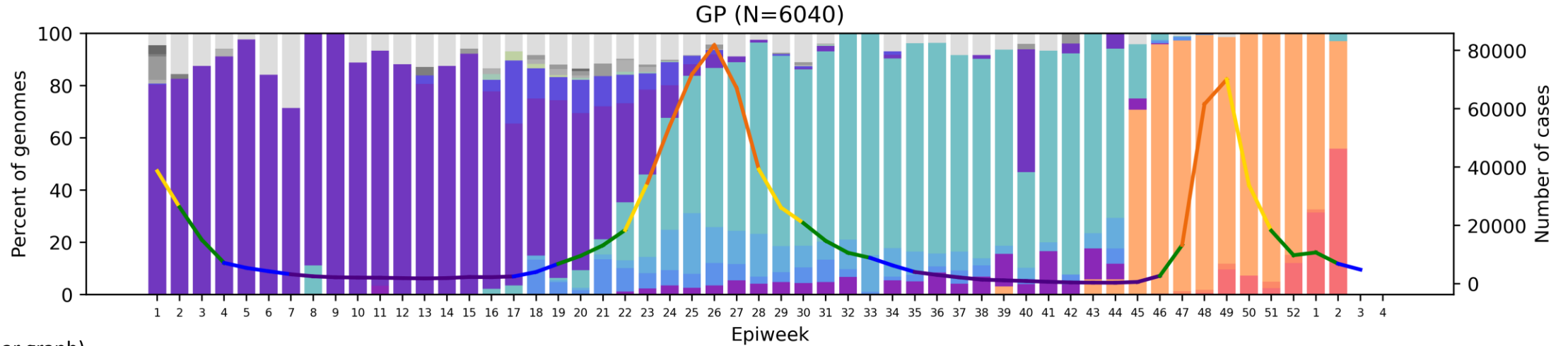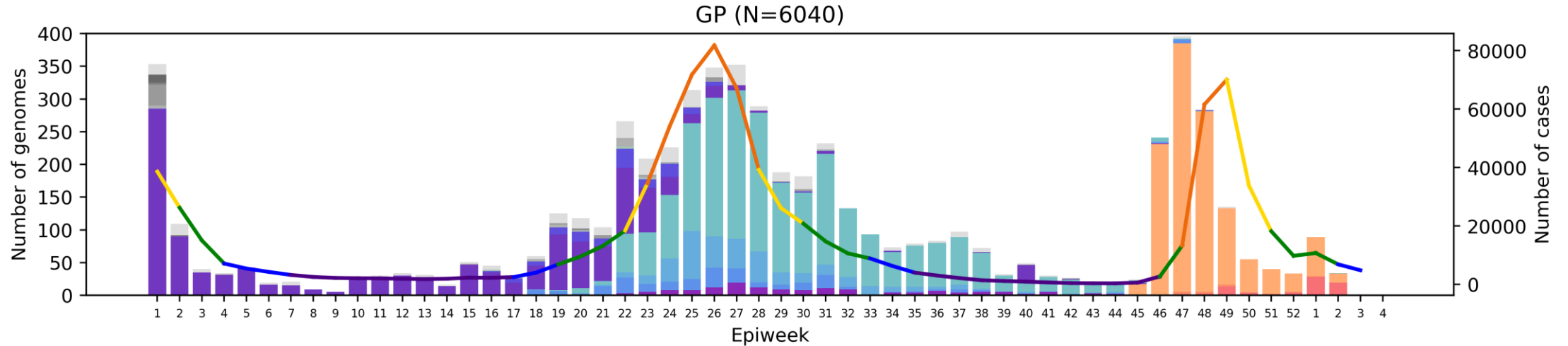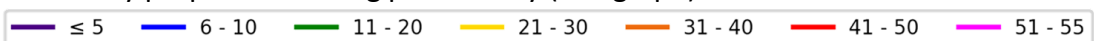
KwaZulu-Natal Province, 2021-2022, n = 2911

KZN (N=2911)

Clade key (bar graph)

Omicron (21L) · Omicron (21K) · Delta (21A) · Delta (21J) · Beta (20H, V2) · Alpha (20I, V1) · Kappa (21B) · Eta (21D) · 20A · 20B · 20C · 20D · unassigned · 19A · 19B

Omicron (21M) · C.1.2 (20D) · Delta (21I) · Cases

Weekly proportion testing positive key (line graph)

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

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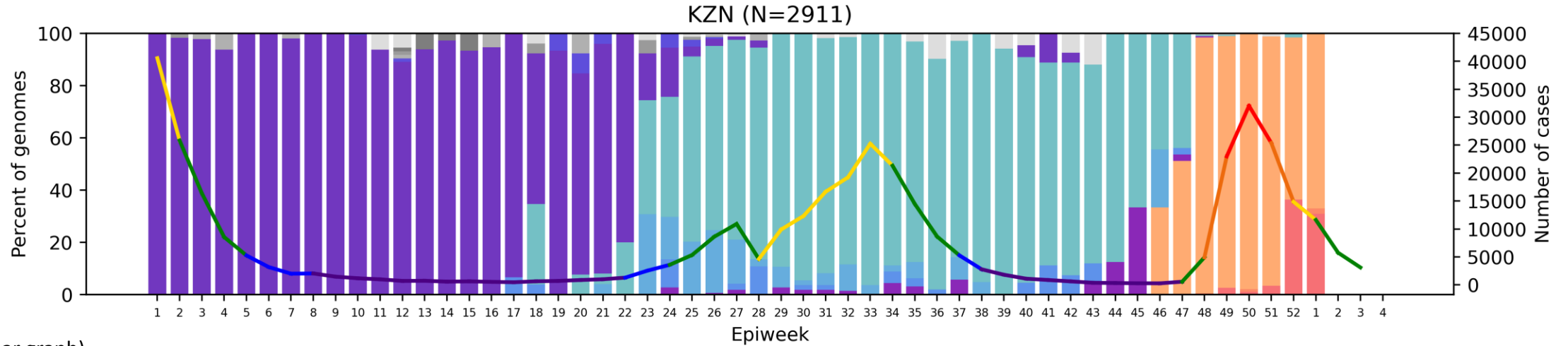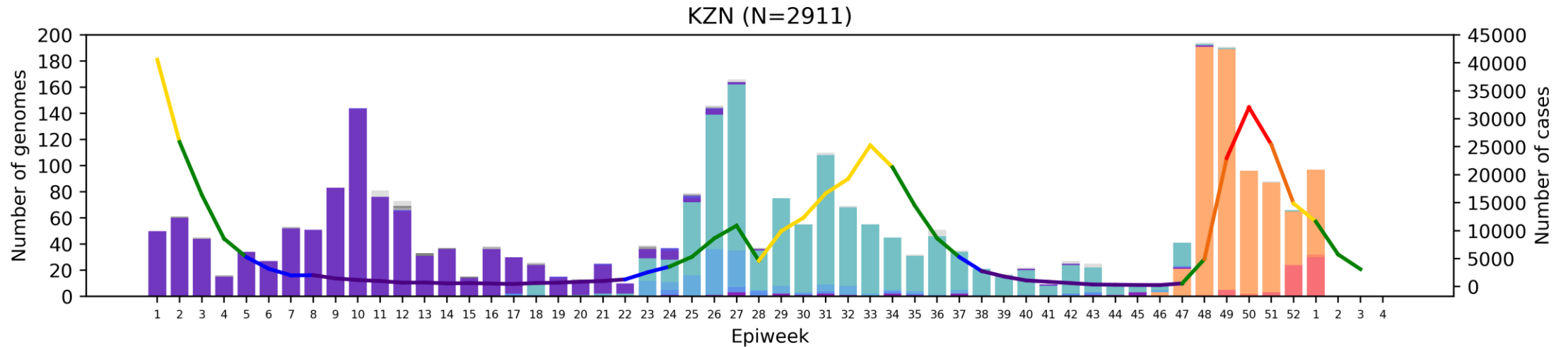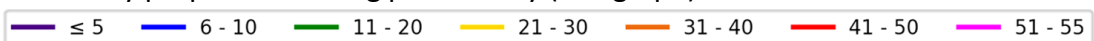
Limpopo Province, 2021-2022, n = 1254
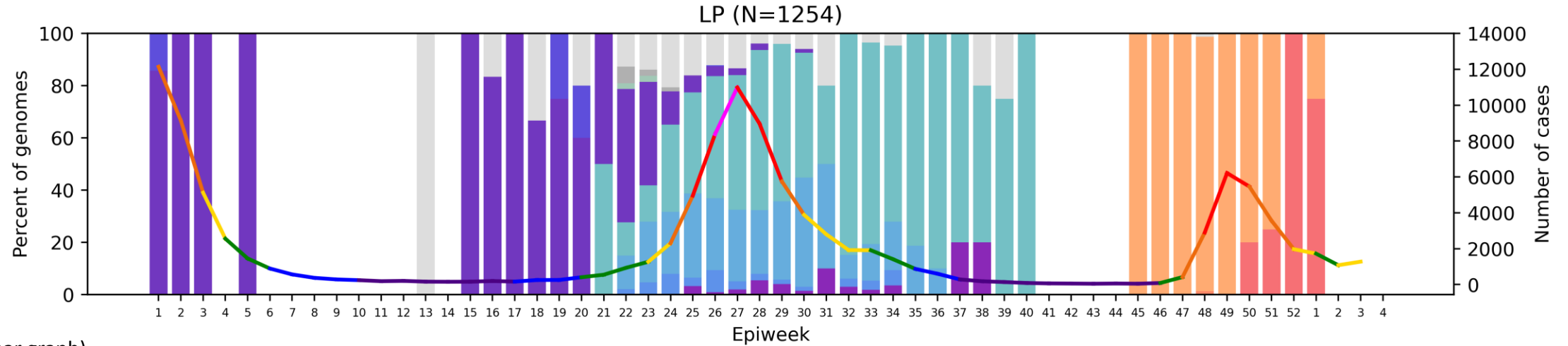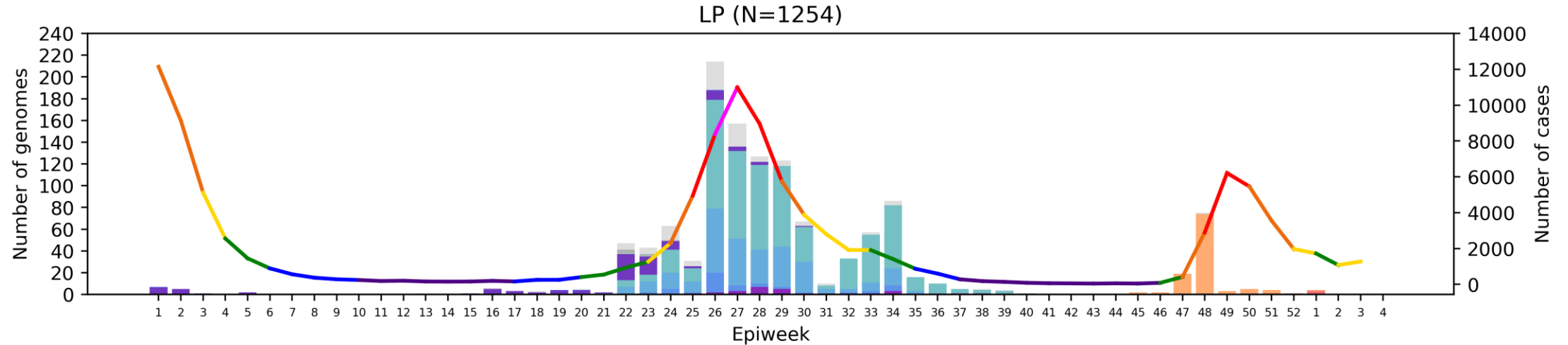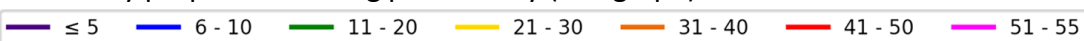
Mpumalanga Province, 2021-2022, n = 1377

MP (N=1377)

MP (N=1377)

Clade key (bar graph)

Omicron (21L)	Omicron (21K)	Delta (21A)	Delta (21J)
Omicron (21M)	C.1.2 (20D)	Delta (21I)	Cases

Beta (20H, V2) · Alpha (20I, V1) · Kappa (21B) · Eta (21D) · 20A · 20B · 20C · 20D · unassigned · 19A · 19B

Weekly proportion testing positive key (line graph)

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

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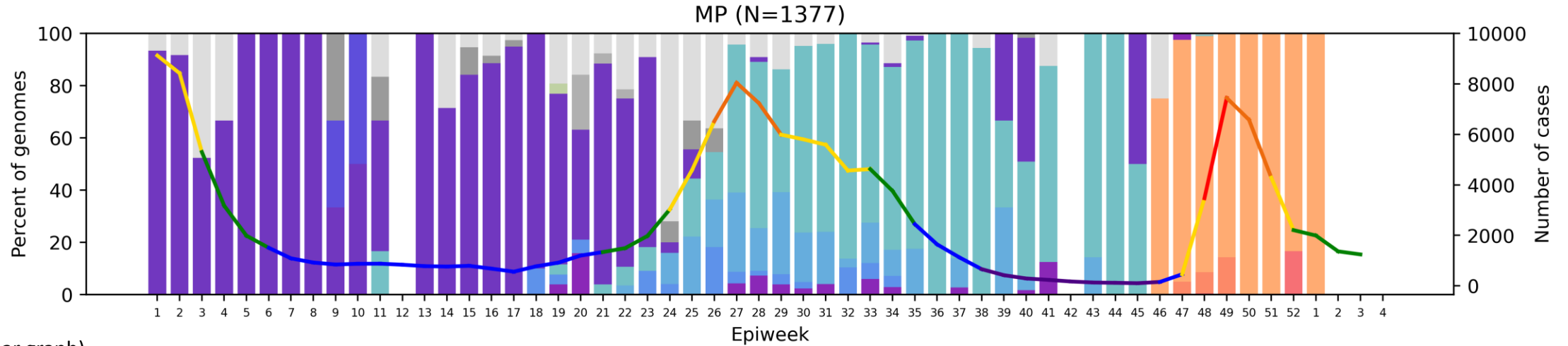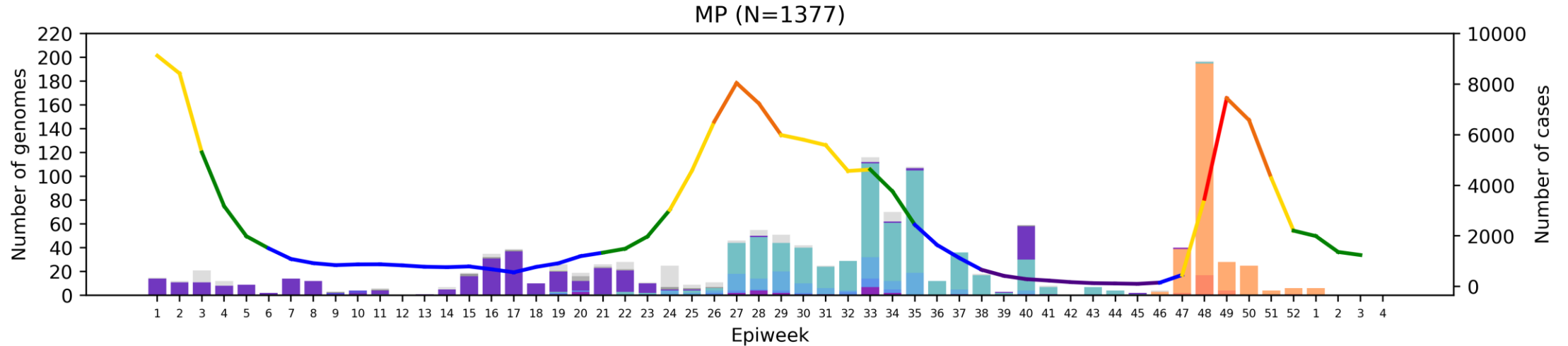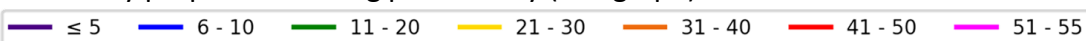
Northern Cape Province, 2021-2022, n = 1467

NC (N=1467)

NC (N=1467)

Clade key (bar graph)

Omicron (21L) — Omicron (21K) — Delta (21A) — Delta (21J) — Beta (20H, V2) — Alpha (20I, V1) — Kappa (21B) — Eta (21D) — 20A — 20B — 20C — 20D — unassigned — 19A — 19B
Omicron (21M) — C.1.2 (20D) — Delta (21I) — Cases

Weekly proportion testing positive key (line graph)

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

NGS-SA
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Surveillance in South Africa
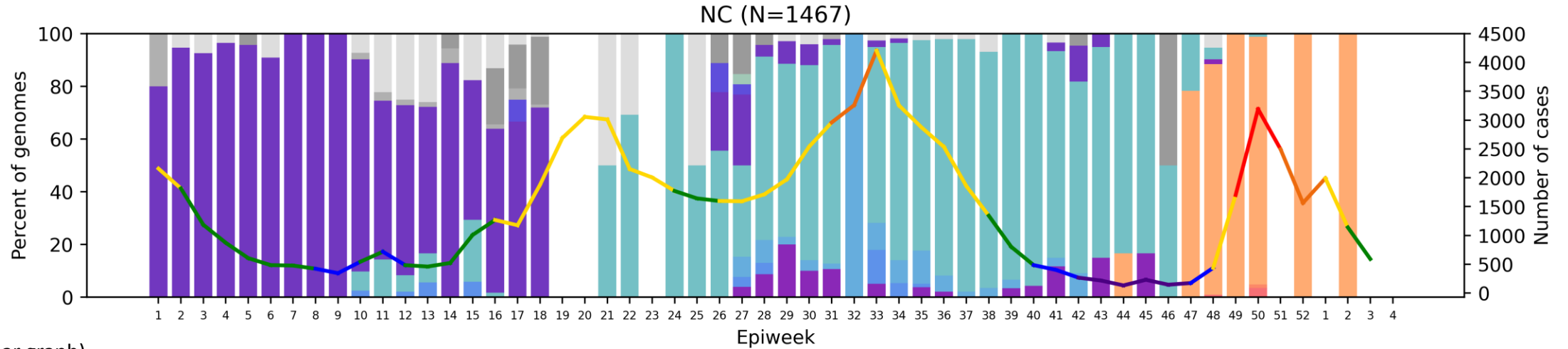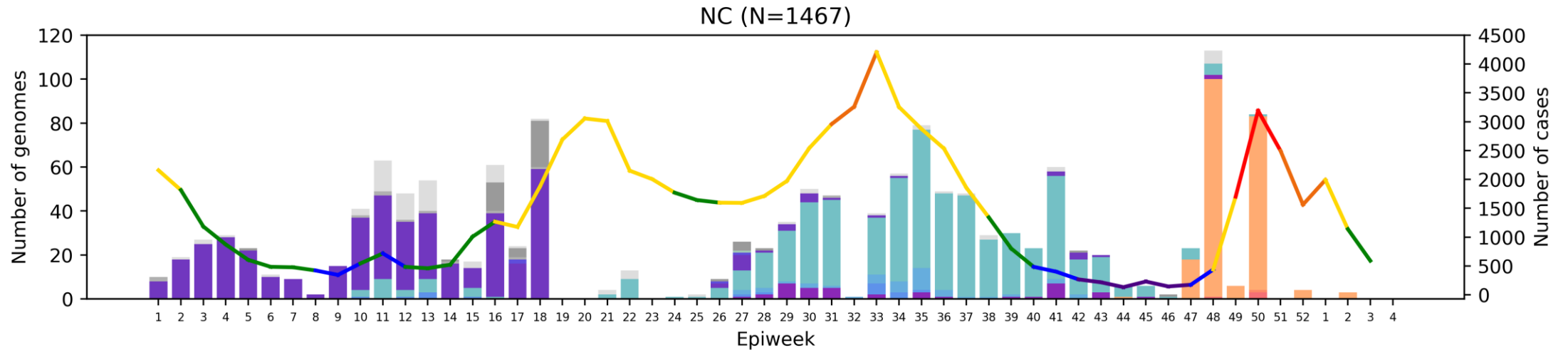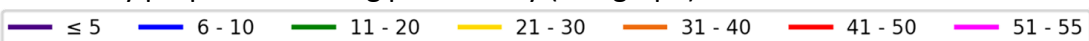
North West Province, 2021, n = 1435
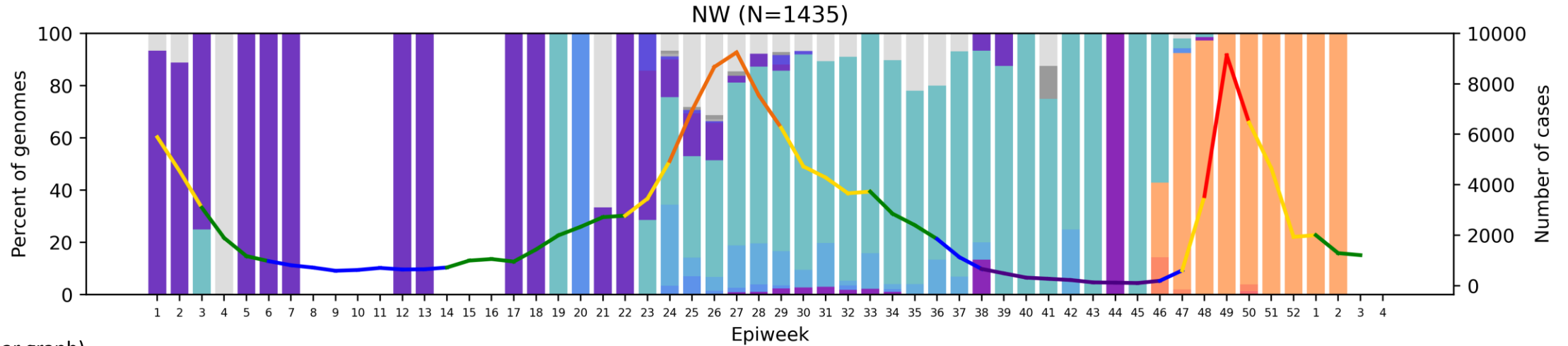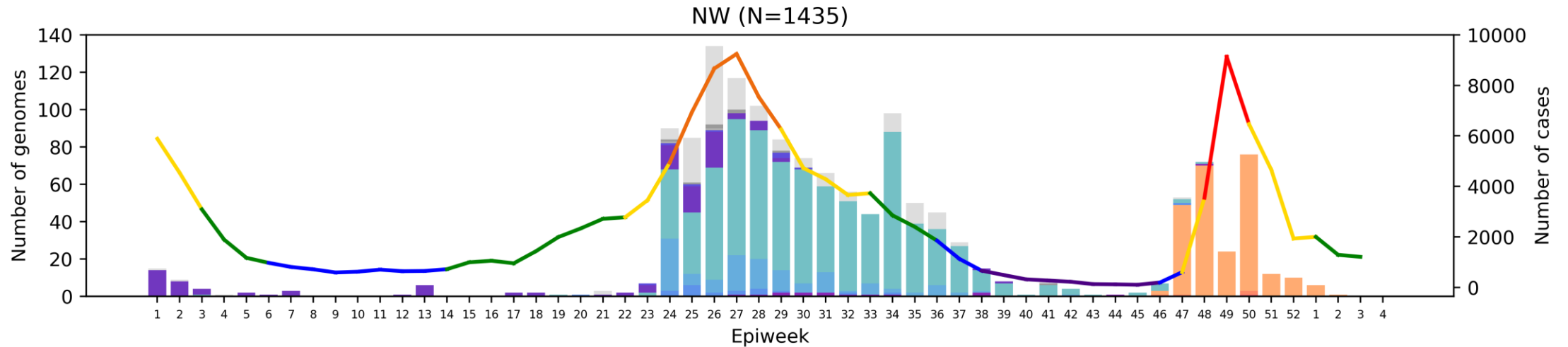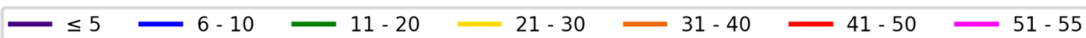
Western Cape Province, 2021-2022, n = 4681

WC (N=4681)

WC (N=4681)

Clade key (bar graph)

Omicron (21L) | Omicron (21K) | Delta (21A) | Delta (21J) | Beta (20H, V2) | Alpha (20I, V1) | Kappa (21B) | Eta (21D) | 20A | 20B | 20C | 20D | unassigned | 19A | 19B
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≤ 5 | 6 - 10 | 11 - 20 | 21 - 30 | 31 - 40 | 41 - 50 | 51 - 55

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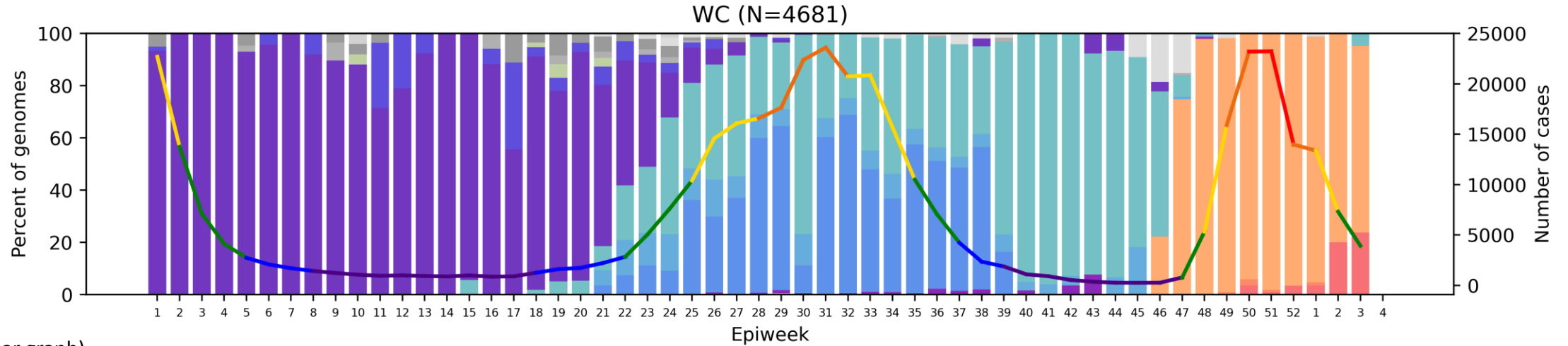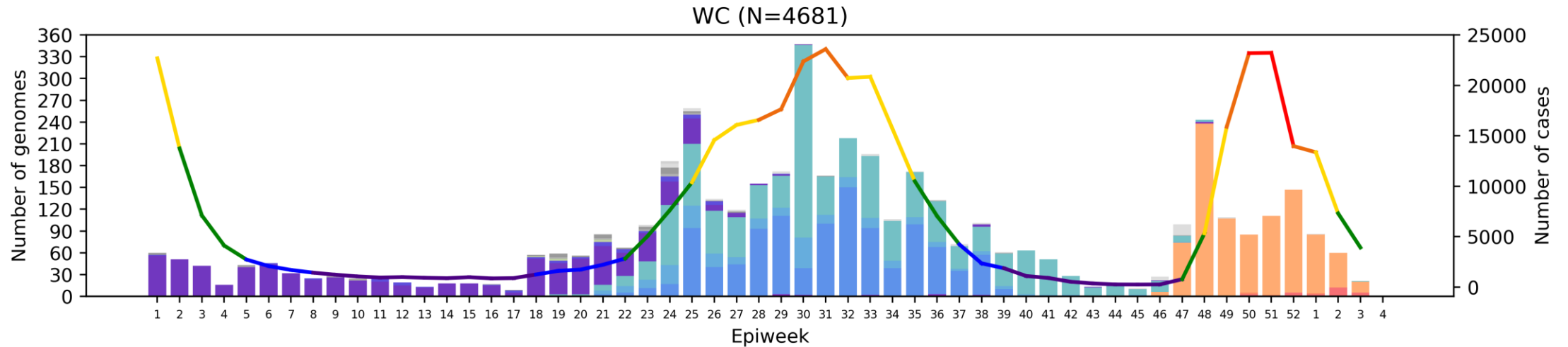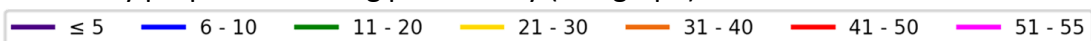
Summary

- **Variant of Concern Omicron**
  - Detected in at least 145 countries and dominating globally
  - Split into five lineages based on different mutational profiles: BA.1 (21K), BA.1.1 (21K, BA.1+spike R346K), BA.2 (21L), BA.3 (remains in 21M as does not meet requirements for new clade), B.1.1.529 (parent lineage, 21M)

  - South Africa (detected in all provinces):
    - Dominated December sequencing data at 99% of genomes (n=2223/2243)
    - Sequence data for January shows continued dominance of Omicron (n=446/450)
    - BA.1 dominant in SA, with BA.2 increase recently observed and to be confirmed by additional data
      - BA.2 makes up 23% (n=104/450) of sequences in January.
      - BA.2 has increased in recent epiweeks in the Free State, Gauteng, KwaZulu-Natal, Limpopo and the Western Cape.
- Low frequency of previously circulating variants such as Delta and C.1.2 still detected in recent data

Supported by the DSI and the SA MRC

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Funders:
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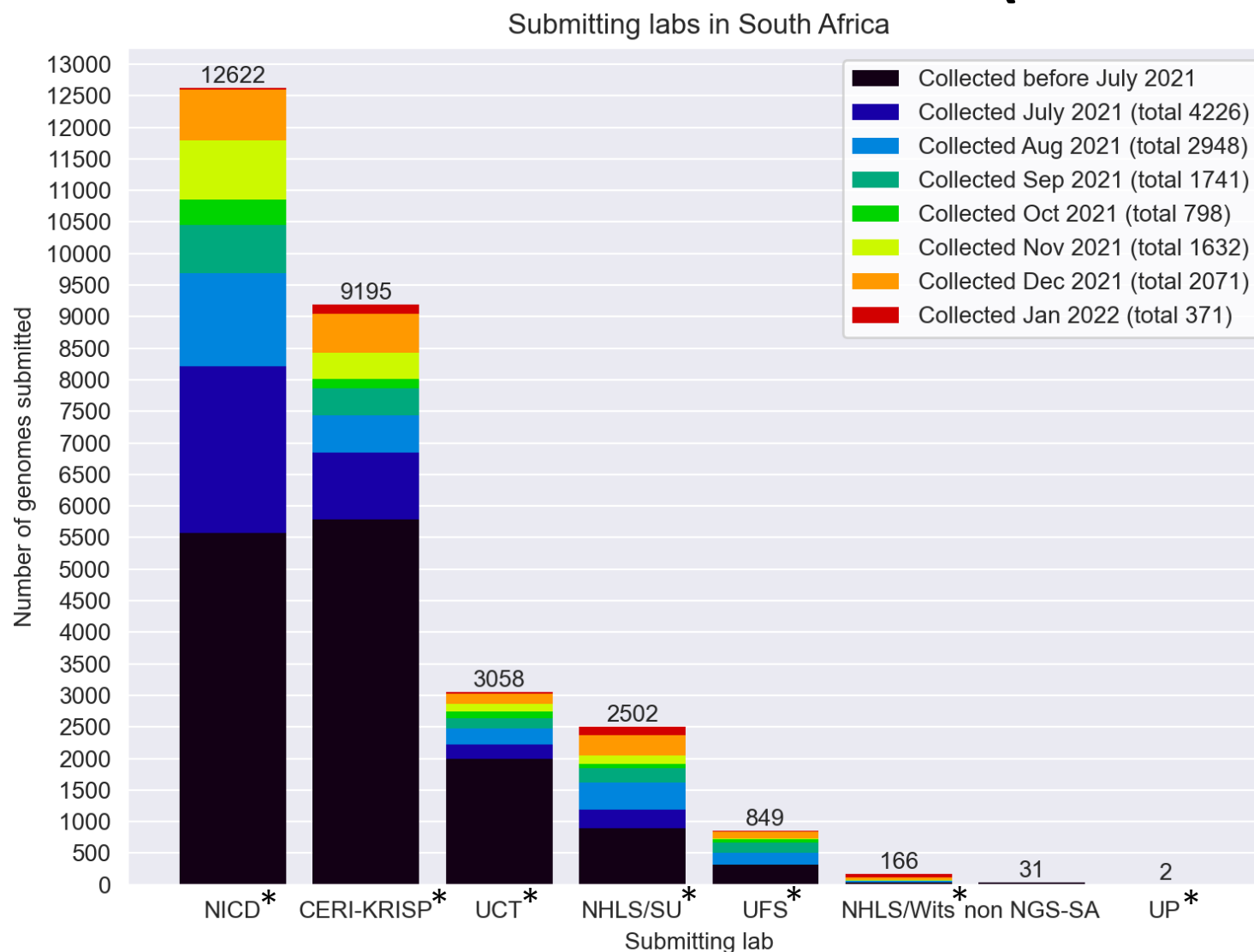

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South African genomes submitted per submitting lab, 2020 - 2022 (N=28 756)

Submitting labs in South Africa

Legend:
- Collected before July 2021
- Collected July 2021 (total 4226)
- Collected Aug 2021 (total 2948)
- Collected Sep 2021 (total 1741)
- Collected Oct 2021 (total 798)
- Collected Nov 2021 (total 1632)
- Collected Dec 2021 (total 2071)
- Collected Jan 2022 (total 371)

Y-axis: Number of genomes submitted
X-axis: Submitting lab

Bar values: NICD* 12622, CERI-KRISP* 9195, UCT* 3058, NHLS/SU* 2502, UFS* 849, NHLS/Wits non NGS-SA 166, 31, UP* 2

*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 (≥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.)