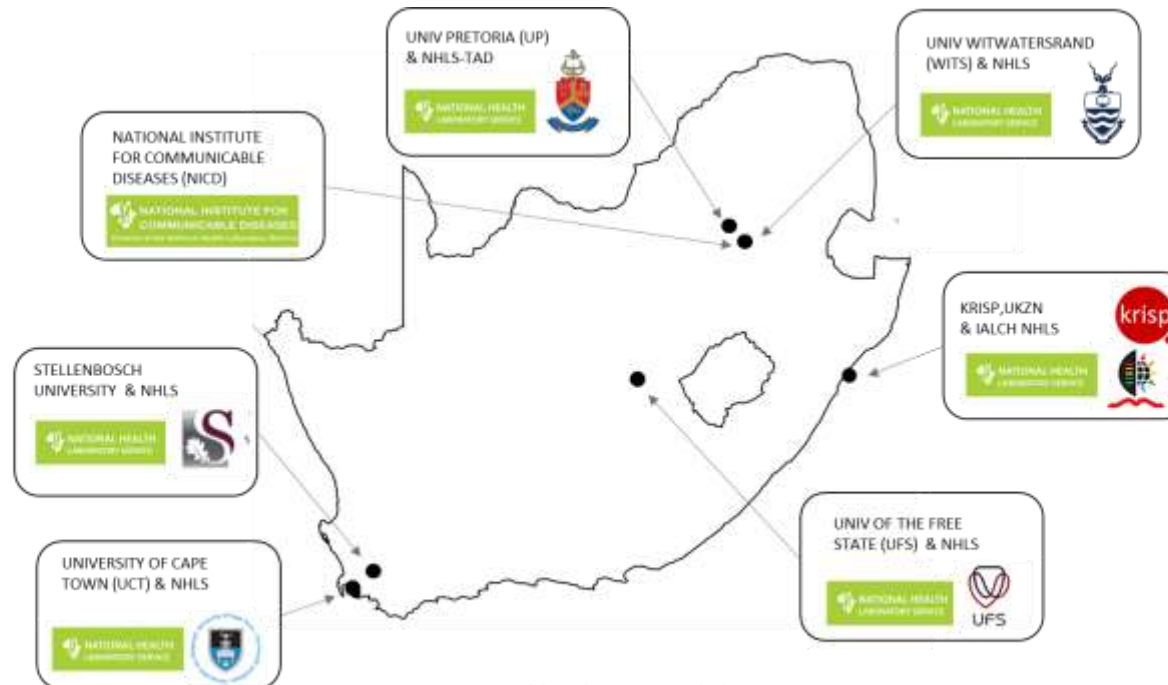


SARS-CoV-2 Sequencing Update 10 December 2021



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 10 December at 07h45



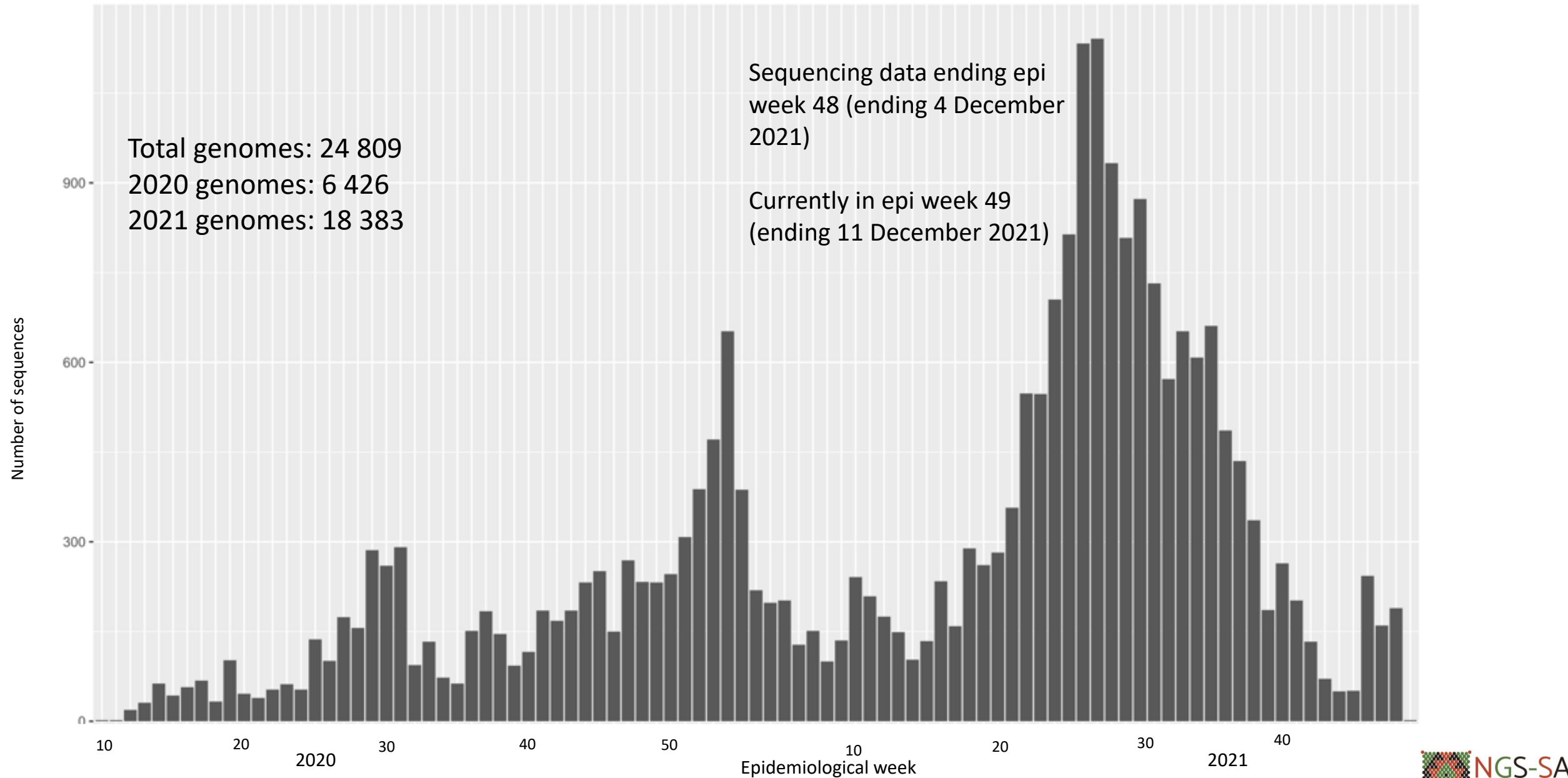
Data license: <https://www.gisaid.org/registration/terms-of-use/>

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

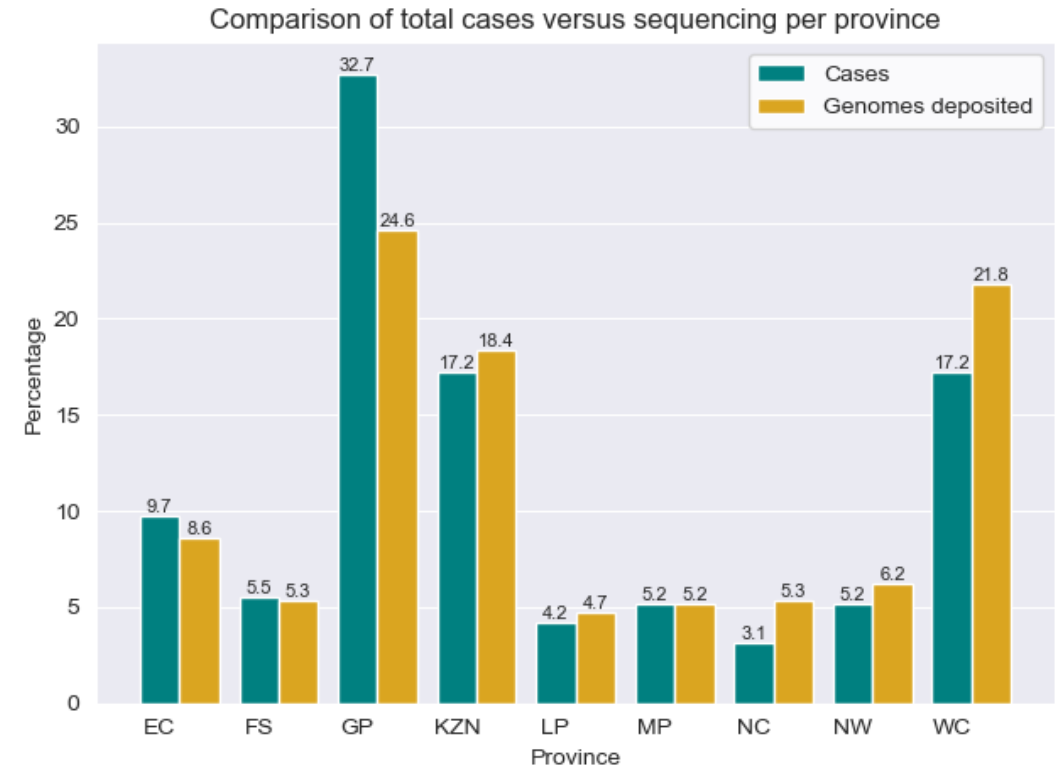
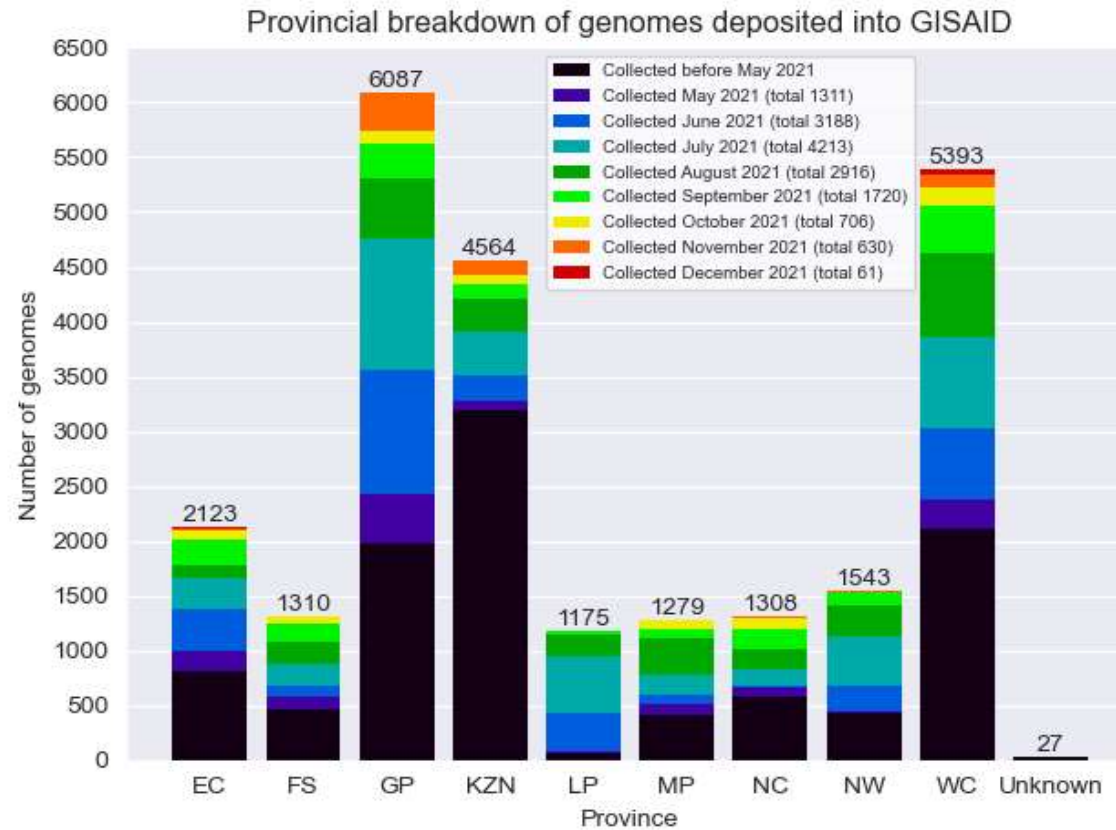
Case data is based on specimen collection date. Cases from <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-epidemiological-brief/> Test data from <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-testing-summary/>

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 and 2021 (N=24 809*)



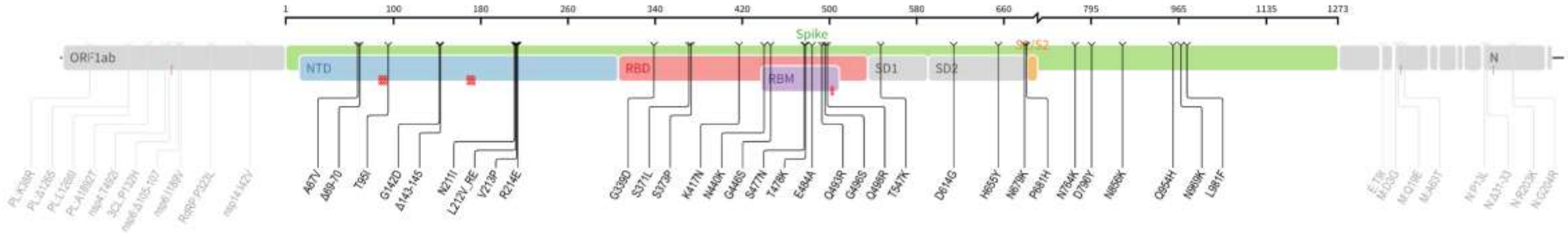
*This represents the cleaned, de-duplicated dataset of unique sequences. This dataset will be used for all further figures.

GISAID genomes vs total cases, 2020 and 2021 (N=24 809)



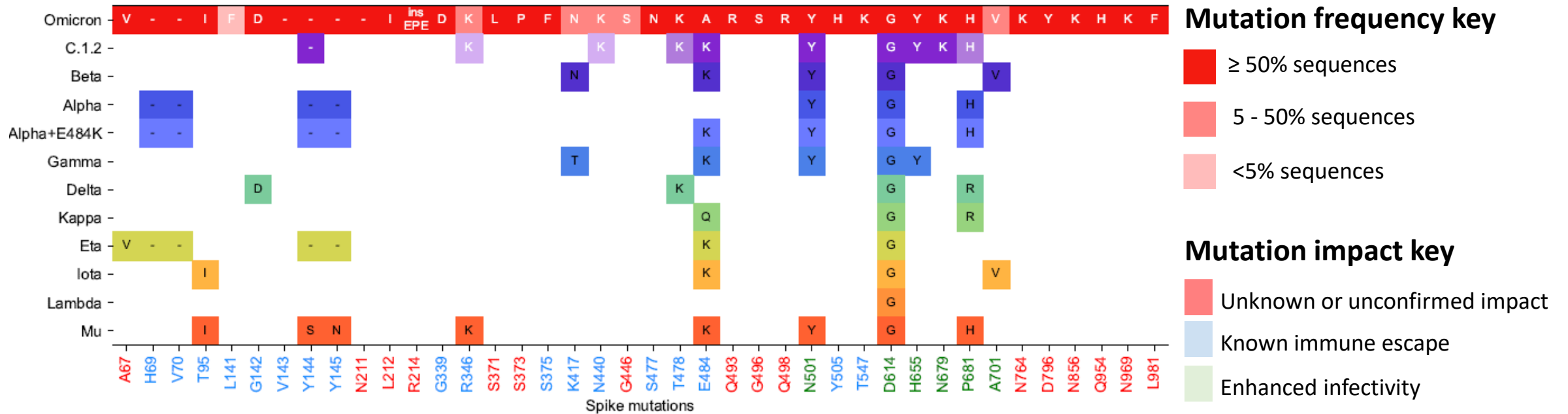
All provinces, apart from GP, KZN, NC and WC, have comparable percentage of overall cases and overall sequenced genomes. The majority of November sequencing data is from Gauteng.

Omicron lineage mutation profile



- 45-52 amino acid changes (including deletions) across the whole GENOME
 - 26-32 changes in SPIKE
- Does not possess the RdRp G671S change associated with a decrease in Ct value for Delta variants
- Does possess the Δ69-70, which causes the S-Gene Target Failure (SGTF) and was previously seen in the Alpha VOC

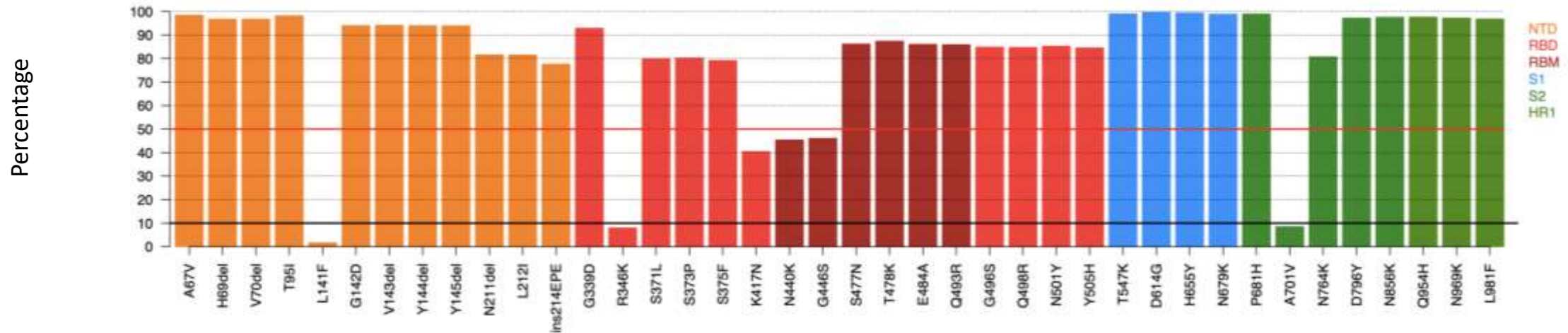
Omicron spike mutations compared to other VOC/VOIs



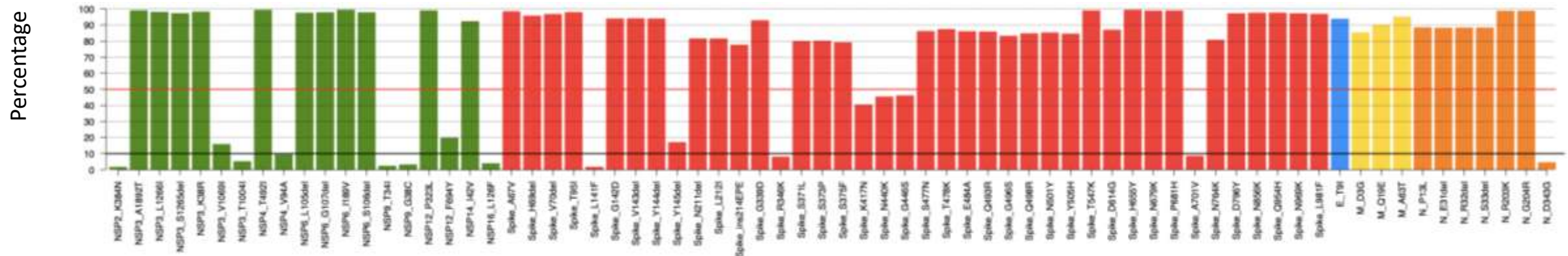
- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
 - including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
 - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be linked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

Mutational profile of Omicron sequences

Frequency of Spike SNVs for Omicron (n = 1522)



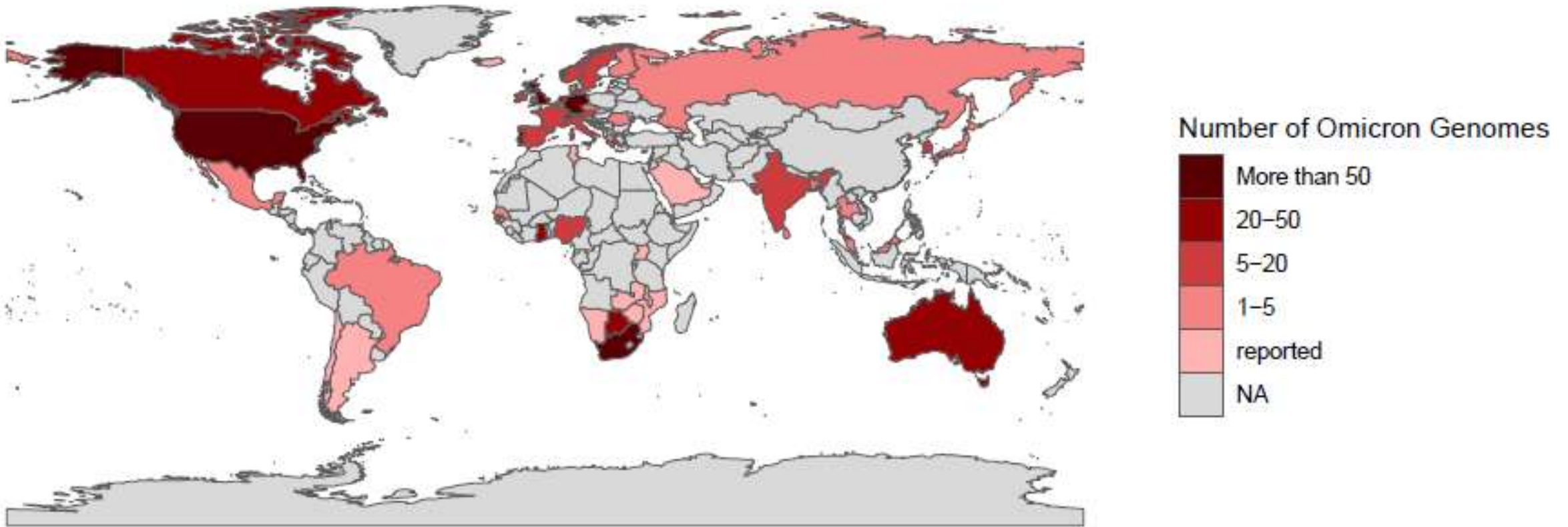
Frequency of whole genome SNVs for Omicron (n = 1522)



Mutational profile of Omicron is largely shared amongst all sequences. Low mutation frequencies for N417N, N440K, G446S and N764K are most likely a result of poor coverage due to primer drop off.

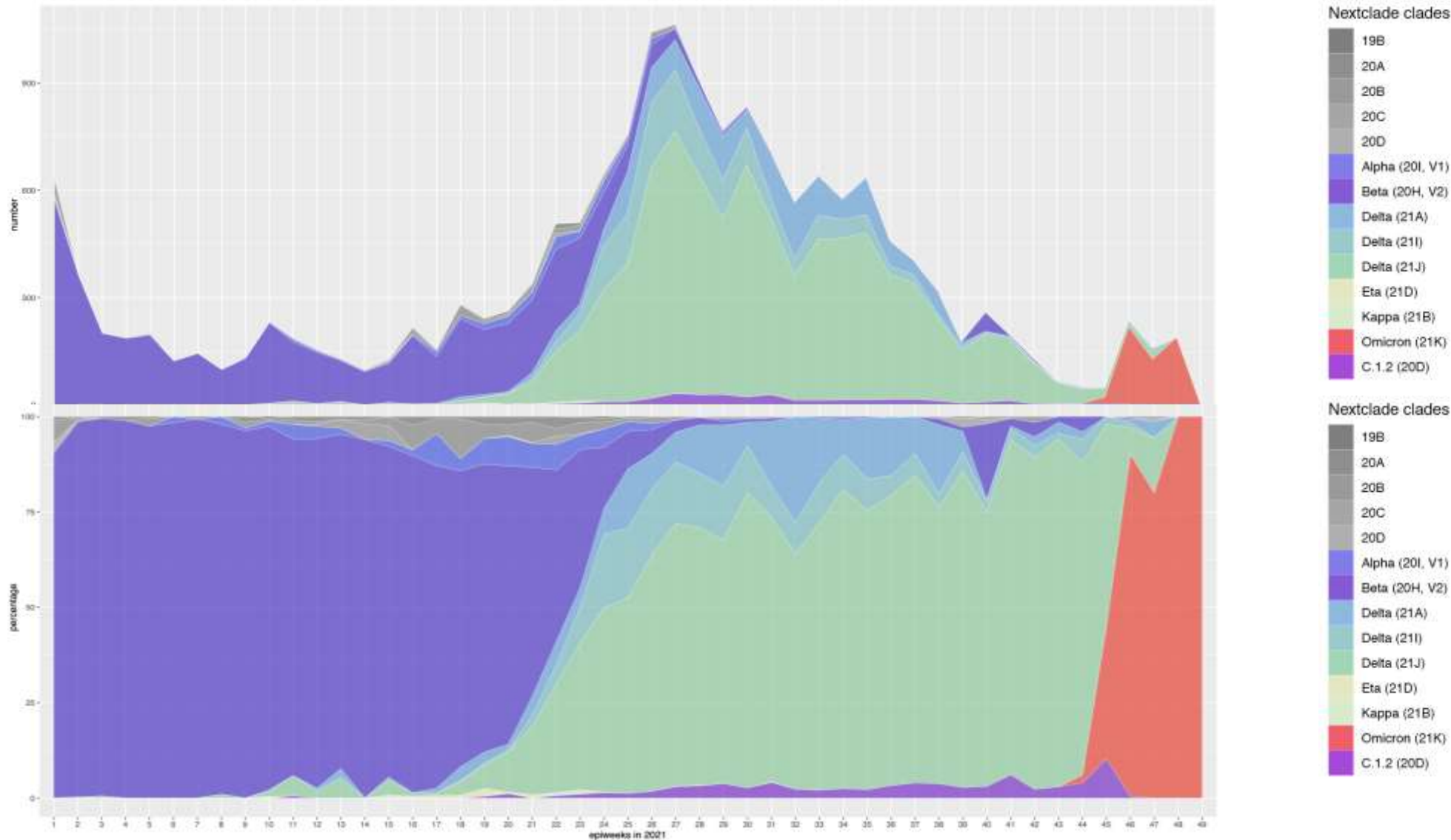
Omicron global prevalence

Detection of Omicron Globally (countries = 56; n = 1556)



Omicron has been detected in 56 countries across the globe (detections based on GISAID).

Proportion and number of clades by epiweek in South Africa, 2021 (N= 18 383)



Sequencing data
ending epi week 48
(ending 4
December 2021)

Currently in epi
week 49 (ending 11
December 2021)

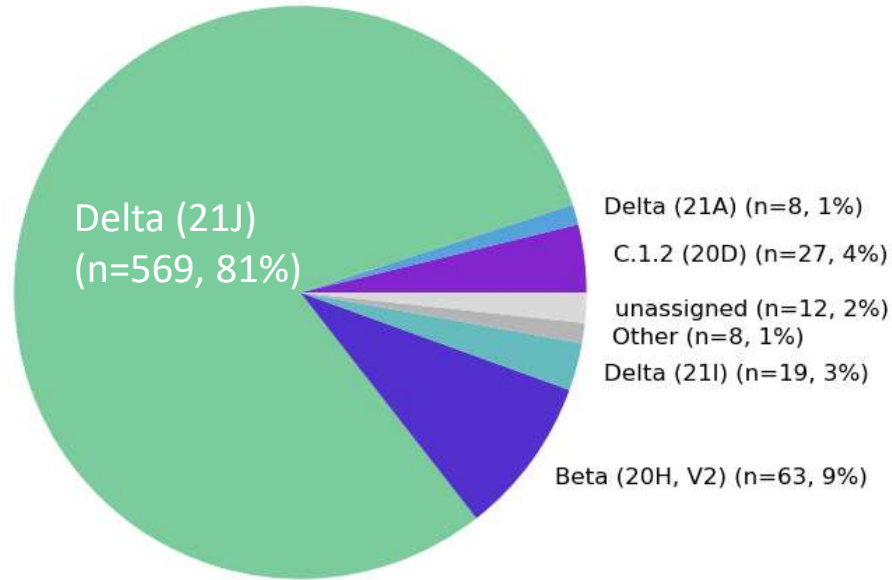
Delta dominated South Africa's third wave with >80% frequency in October, with C.1.2 detection remaining <4%.
Omicron appears to dominate November sequencing data but sequencing is ongoing to determine its prevalence.

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

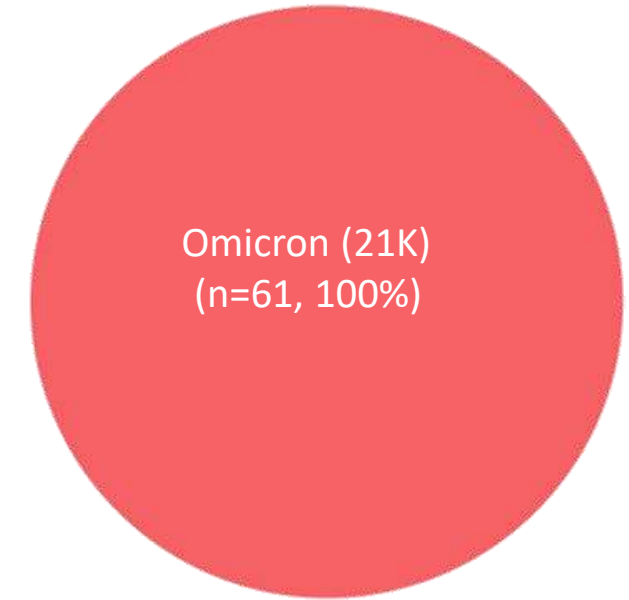
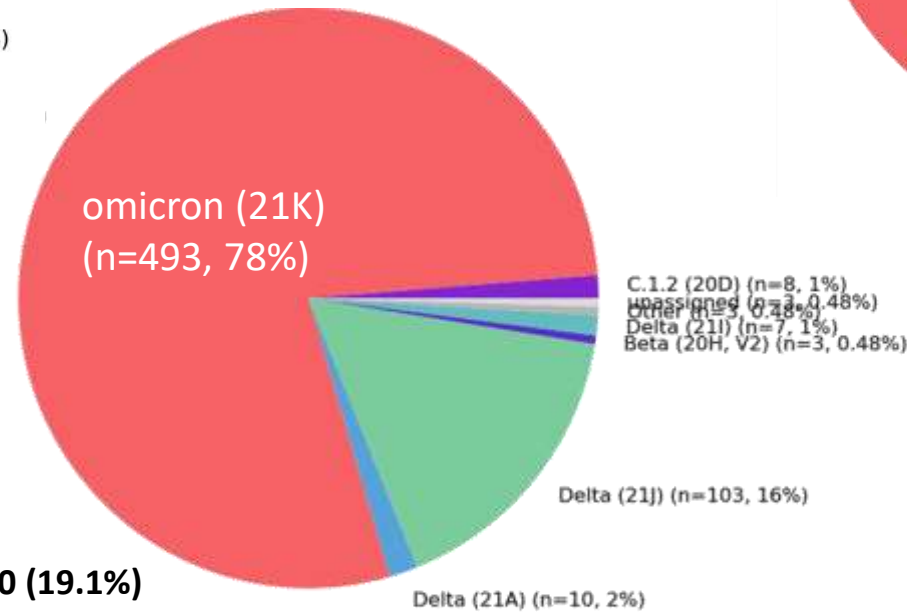
October (N=706)

October – December 2021

December (N=61)



November (N=630)



Total Delta in Oct: 596 (84.4%)

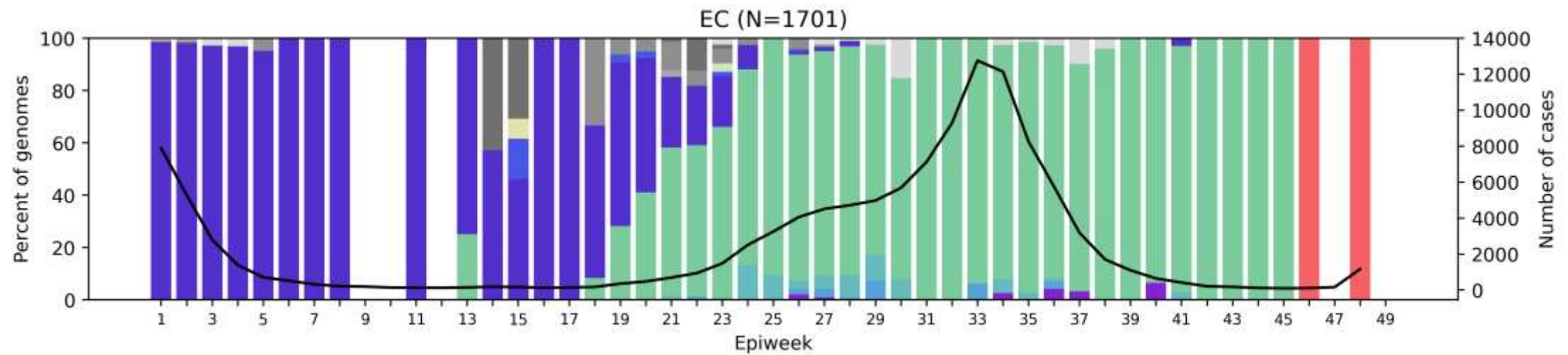
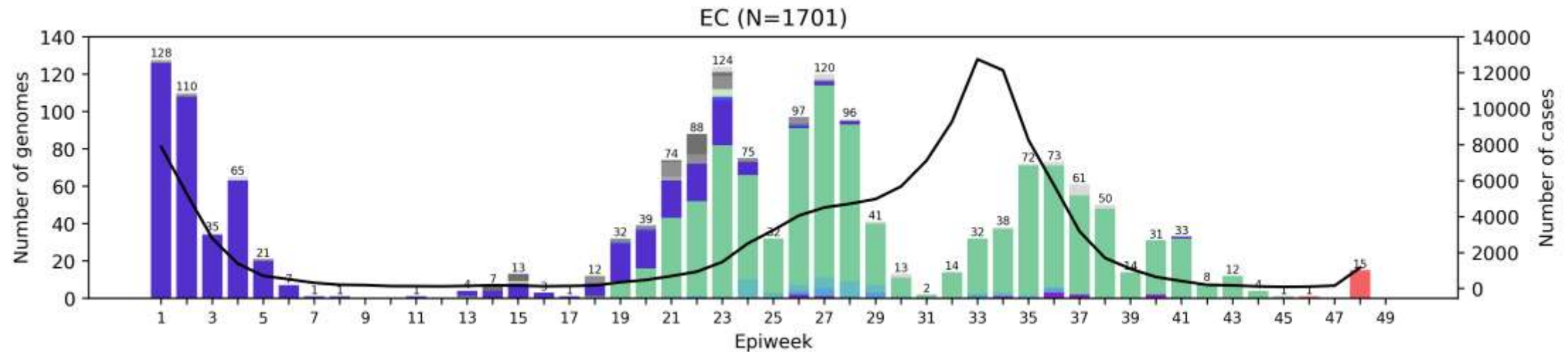
Total omicron in Dec: 61 (100%)

Total Delta in Nov: 120 (19.1%)

Legend: Omicron (21K) C.1.2 (20D) Beta (20H, V2) Alpha (20I, V1) Delta (21A) Delta (21I) Delta (21J) Kappa (21B) Eta (21D) Other unassigned

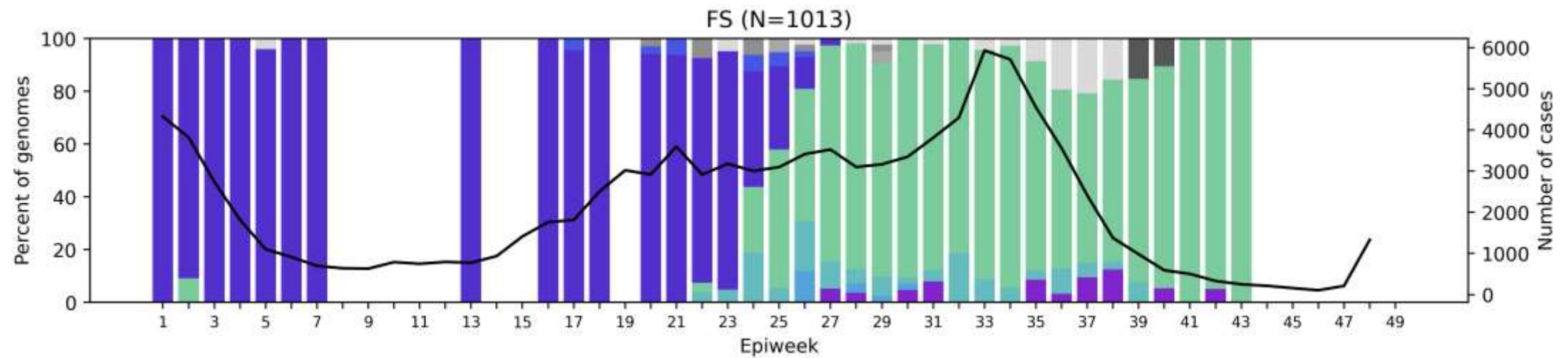
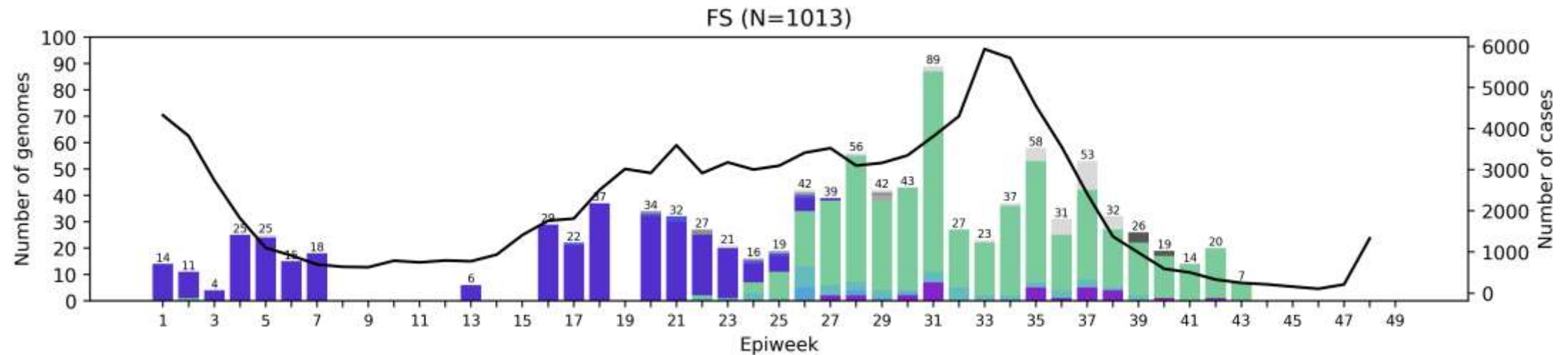
The Delta variant dominated in October in South Africa with >80% frequency.
Omicron was first detected in South Africa in November comprising 78% (493/630) of sequences.

Eastern Cape Province, 2021, n =1701



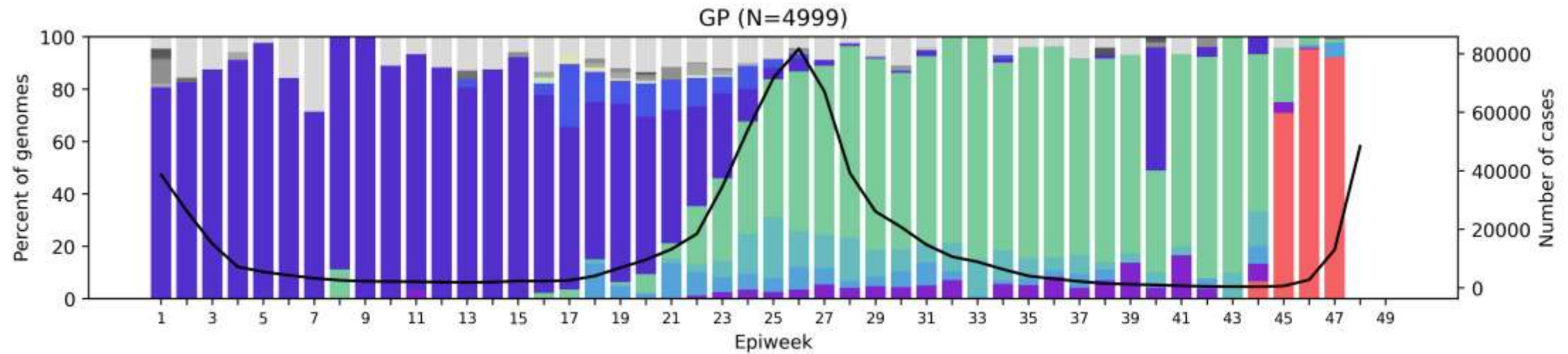
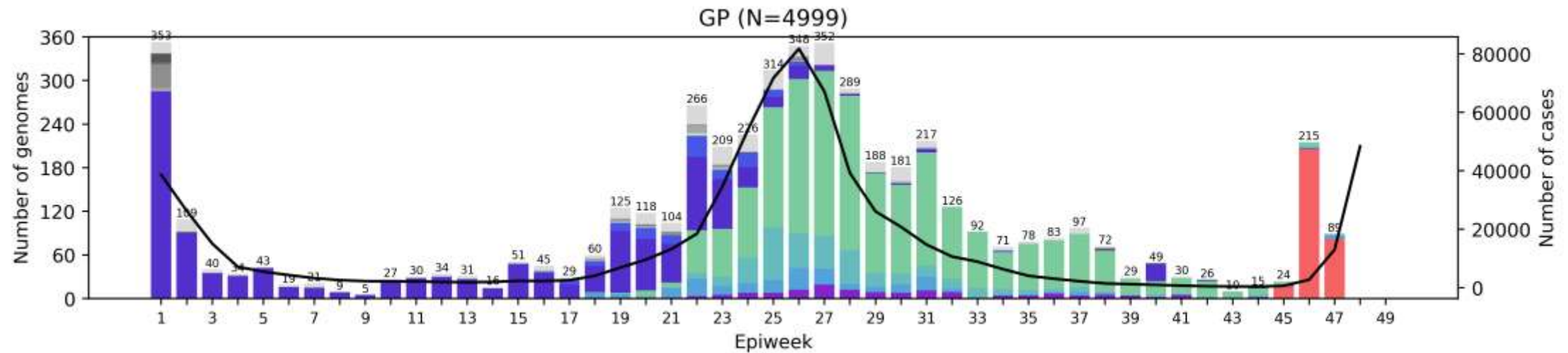
— cases — Omicron (21K) — C.1.2 (20D) — Delta (21A) — Delta (21I) — Delta (21J) — Beta (20H, V2) — Alpha (20I, V1) — Kappa (21B) — Eta (21D) — 20A — 20B — 20C — 20D — unassigned — 19B

Free State Province, 2021, n = 1013



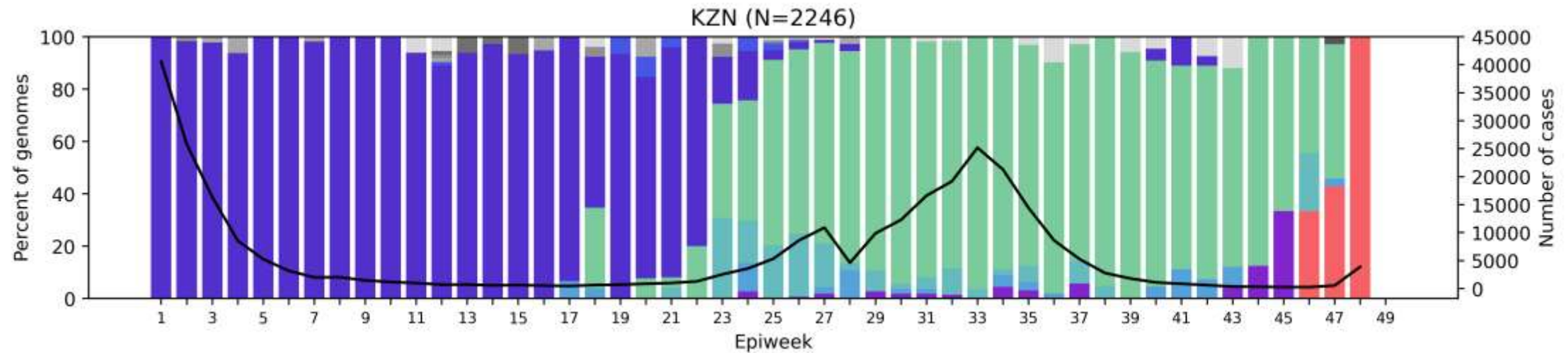
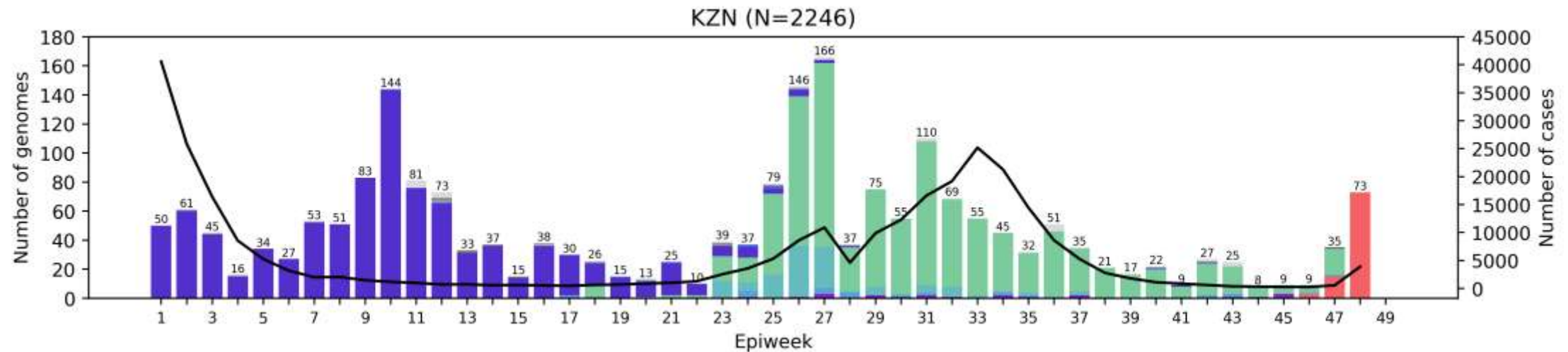
— cases Omicron (21K) C.1.2 (20D) Delta (21A) Delta (21I) Delta (21J) Beta (20H, V2) Alpha (20I, V1) Kappa (21B) Eta (21D) 20A 20B 20C 20D unassigned 19B

Gauteng Province, 2021, n = 4999



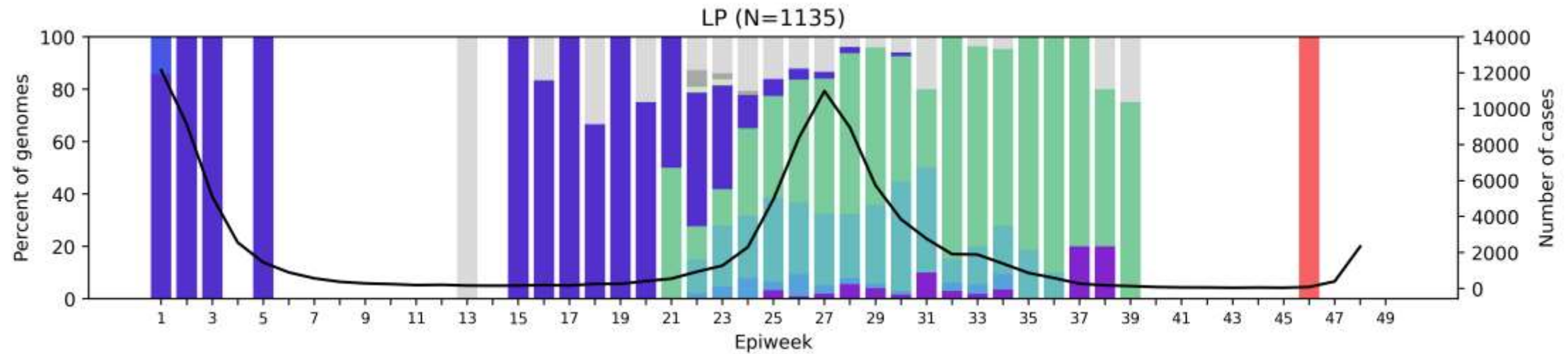
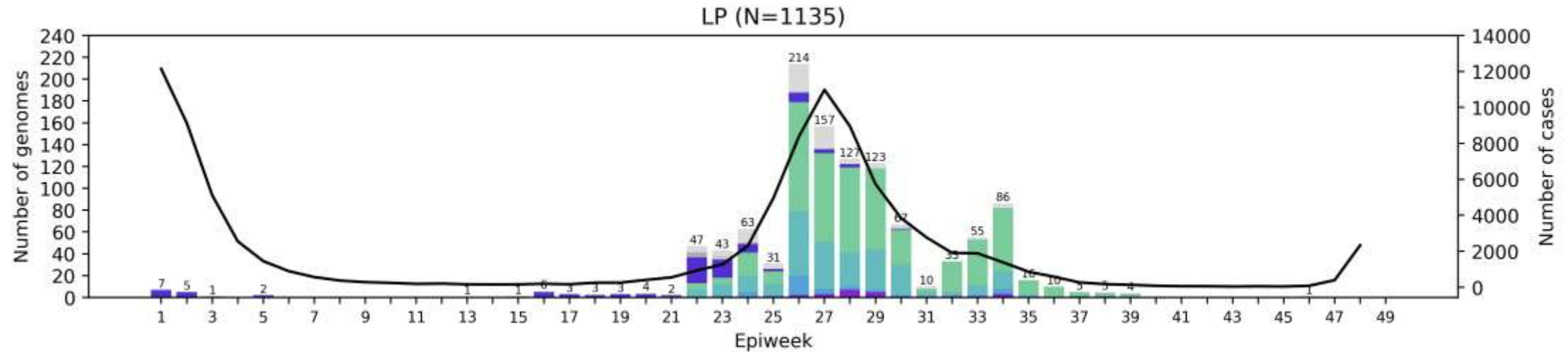
— cases Omicron (21K) C.1.2 (20D) Delta (21A) Delta (21I) Delta (21J) Beta (20H, V2) Alpha (20I, V1) Kappa (21B) Eta (21D) 20A 20B 20C 20D unassigned 19B

KwaZulu-Natal Province, 2021, n = 2246



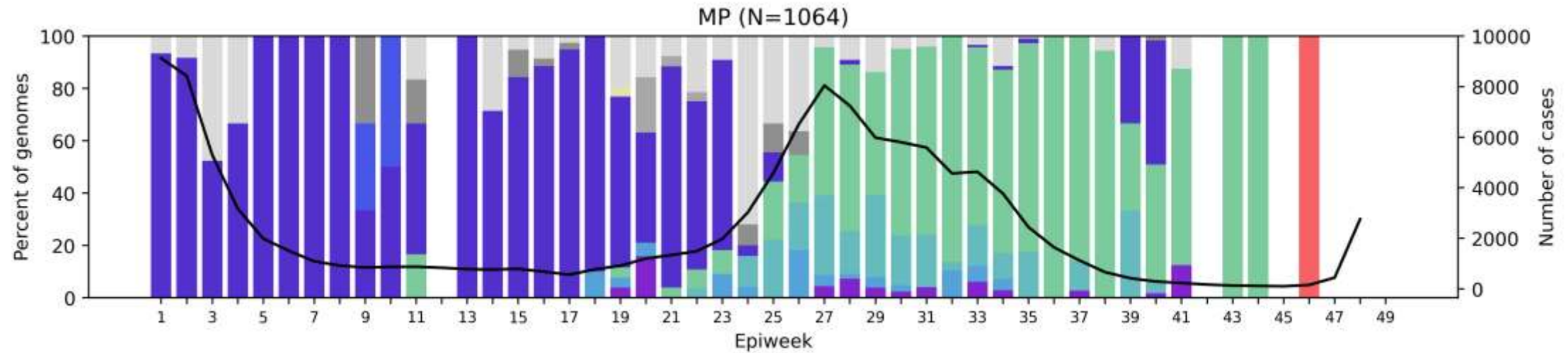
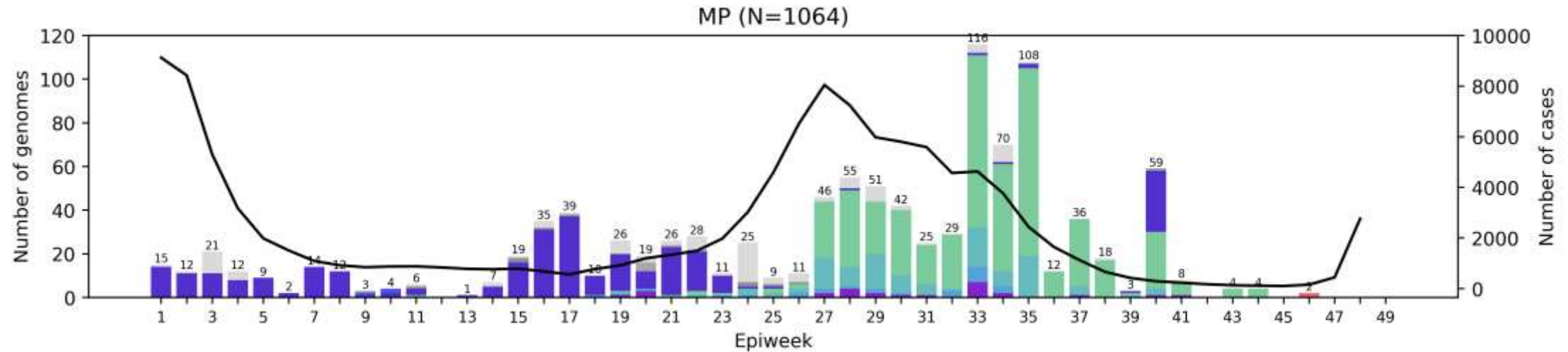
— cases Omicron (21K) C.1.2 (20D) Delta (21A) Delta (21I) Delta (21J) Beta (20H, V2) Alpha (20I, V1) Kappa (21B) Eta (21D) 20A 20B 20C 20D unassigned 19B

Limpopo Province, 2021, n = 1135



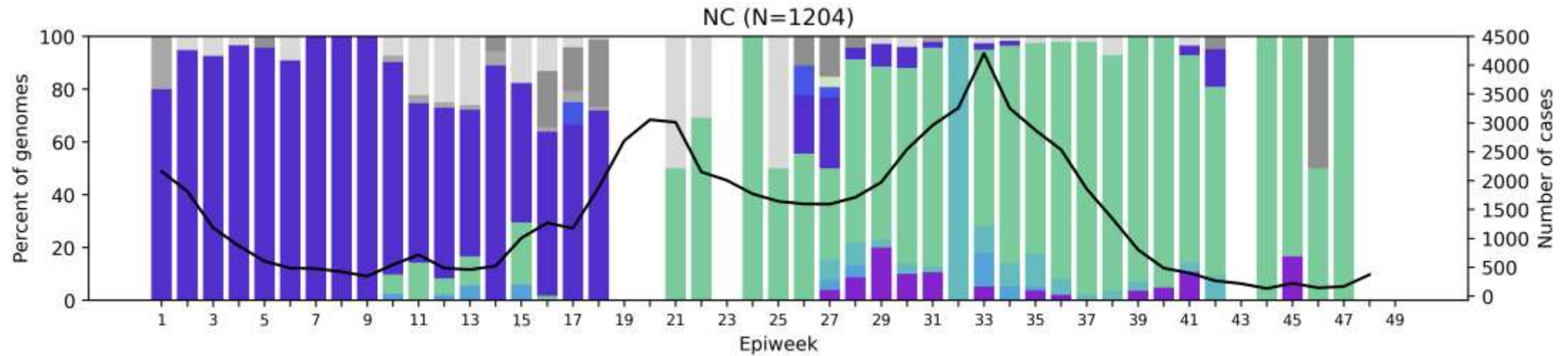
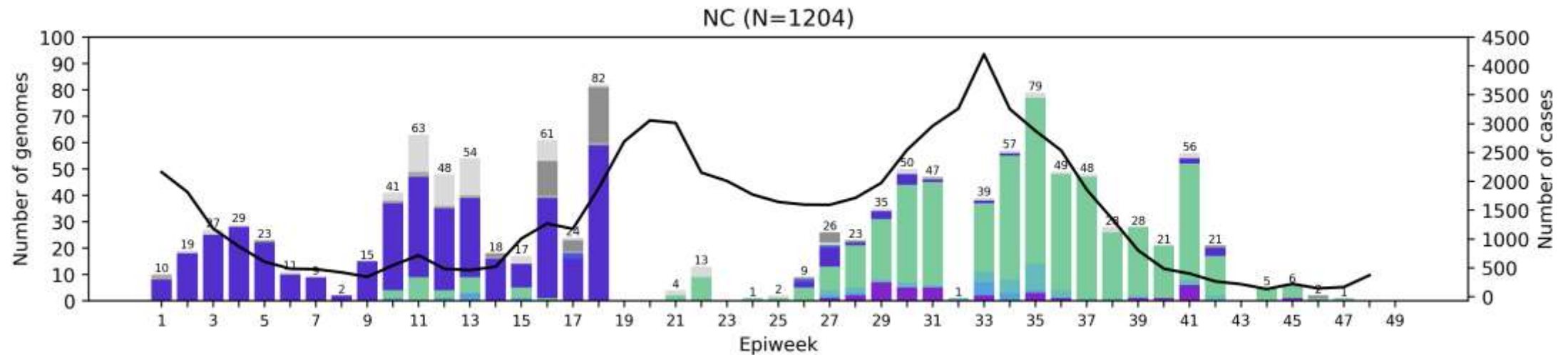
— cases Omicron (21K) C.1.2 (20D) Delta (21A) Delta (21I) Delta (21J) Beta (20H, V2) Alpha (20I, V1) Kappa (21B) Eta (21D) 20A 20B 20C 20D unassigned 19B

Mpumalanga Province, 2021, n = 1064



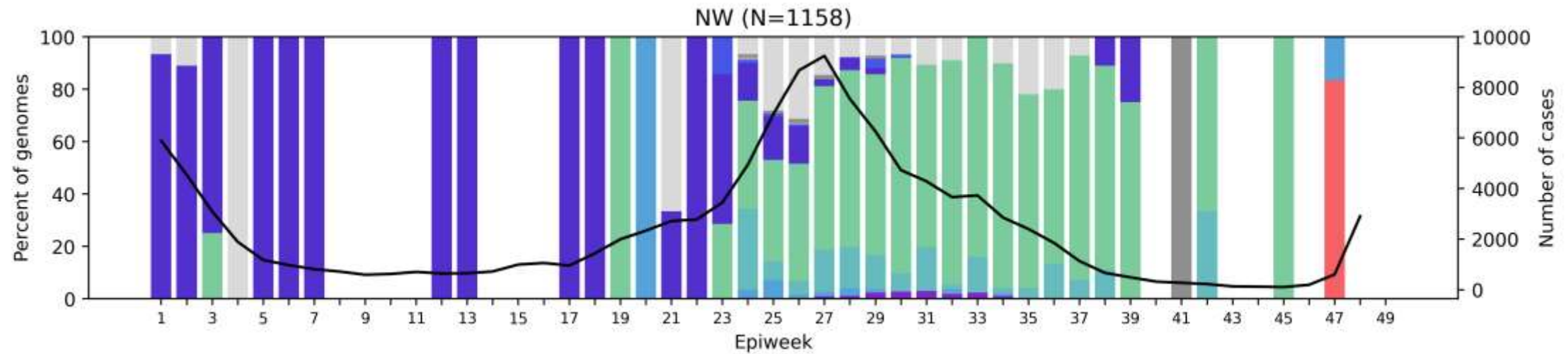
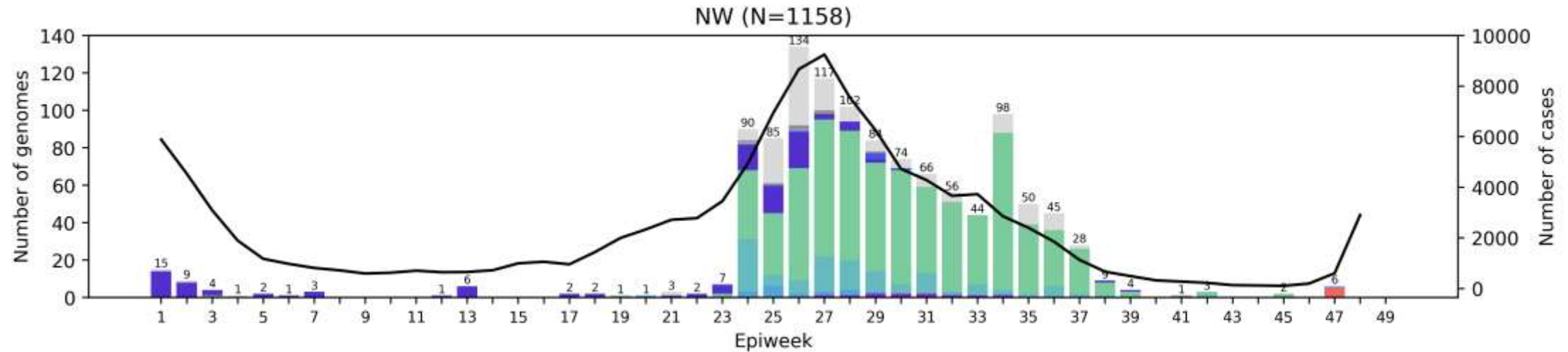
— cases Omicron (21K) C.1.2 (20D) Delta (21A) Delta (21I) Delta (21J) Beta (20H, V2) Alpha (20I, V1) Kappa (21B) Eta (21D) 20A 20B 20C 20D unassigned 19B

Northern Cape Province, 2021, n = 1204



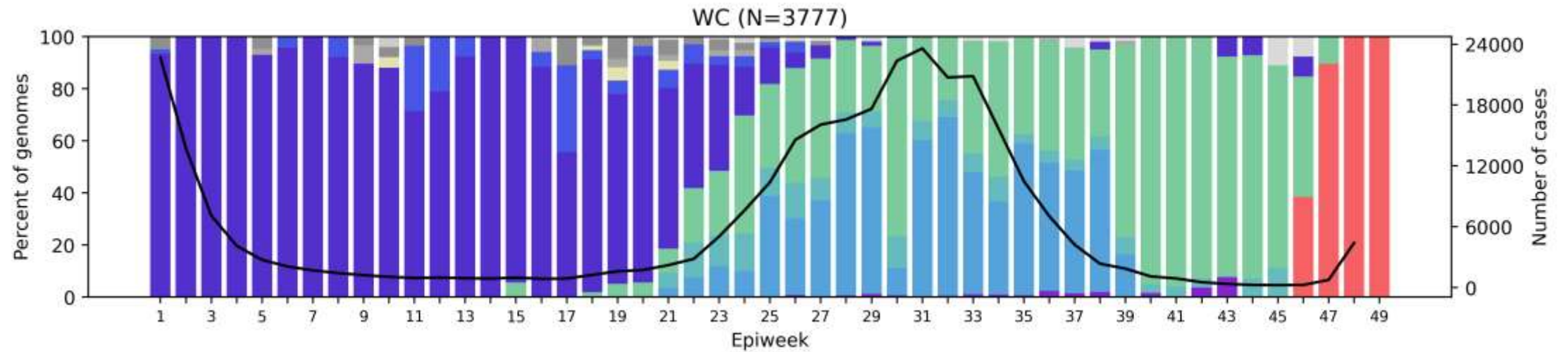
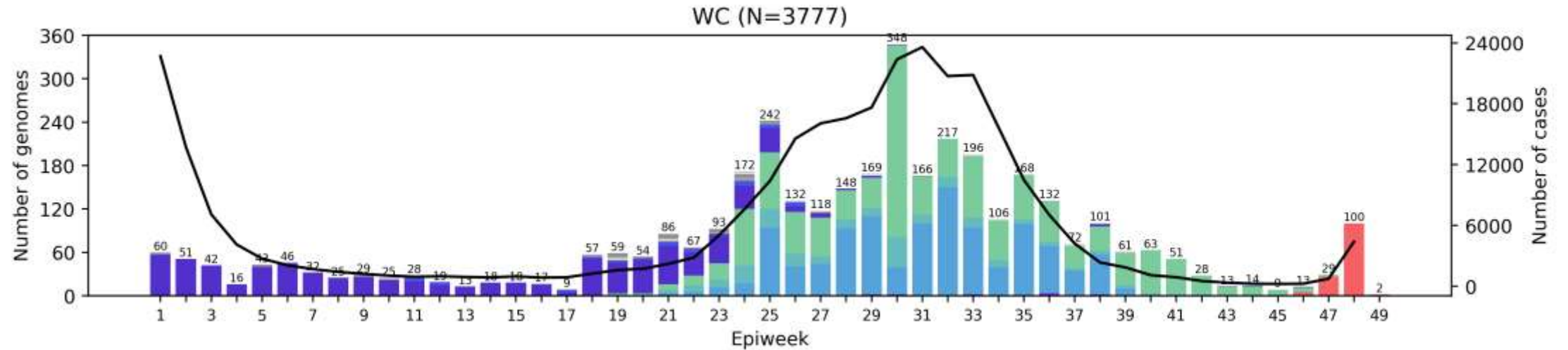
— cases Omicron (21K) C.1.2 (20D) Delta (21A) Delta (21I) Delta (21J) Beta (20H, V2) Alpha (20I, V1) Kappa (21B) Eta (21D) 20A 20B 20C 20D unassigned 19B

North West Province, 2021, n = 1158



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

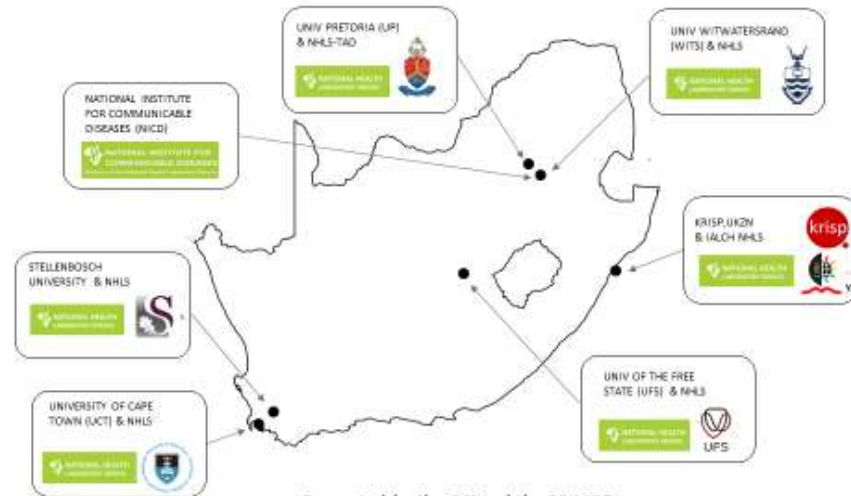
Western Cape Province, 2021, n =3777



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

Summary

- New B.1.1.529 (21K) lineage has been designated Variant of Concern Omicron
 - Current earliest detection in South Africa: 8 November, Gauteng
 - Omicron dominates November sequencing data at 78% of genomes (n=493/630). Sequencing is ongoing to determine prevalence of Omicron in other provinces.
 - Omicron has now been detected in 56 countries worldwide
- Delta variant dominated in all provinces until end October
 - The Delta sub-lineages varied by province
- C.1.2 lineage detected in all provinces of South Africa with prevalence of <4% of genomes per month



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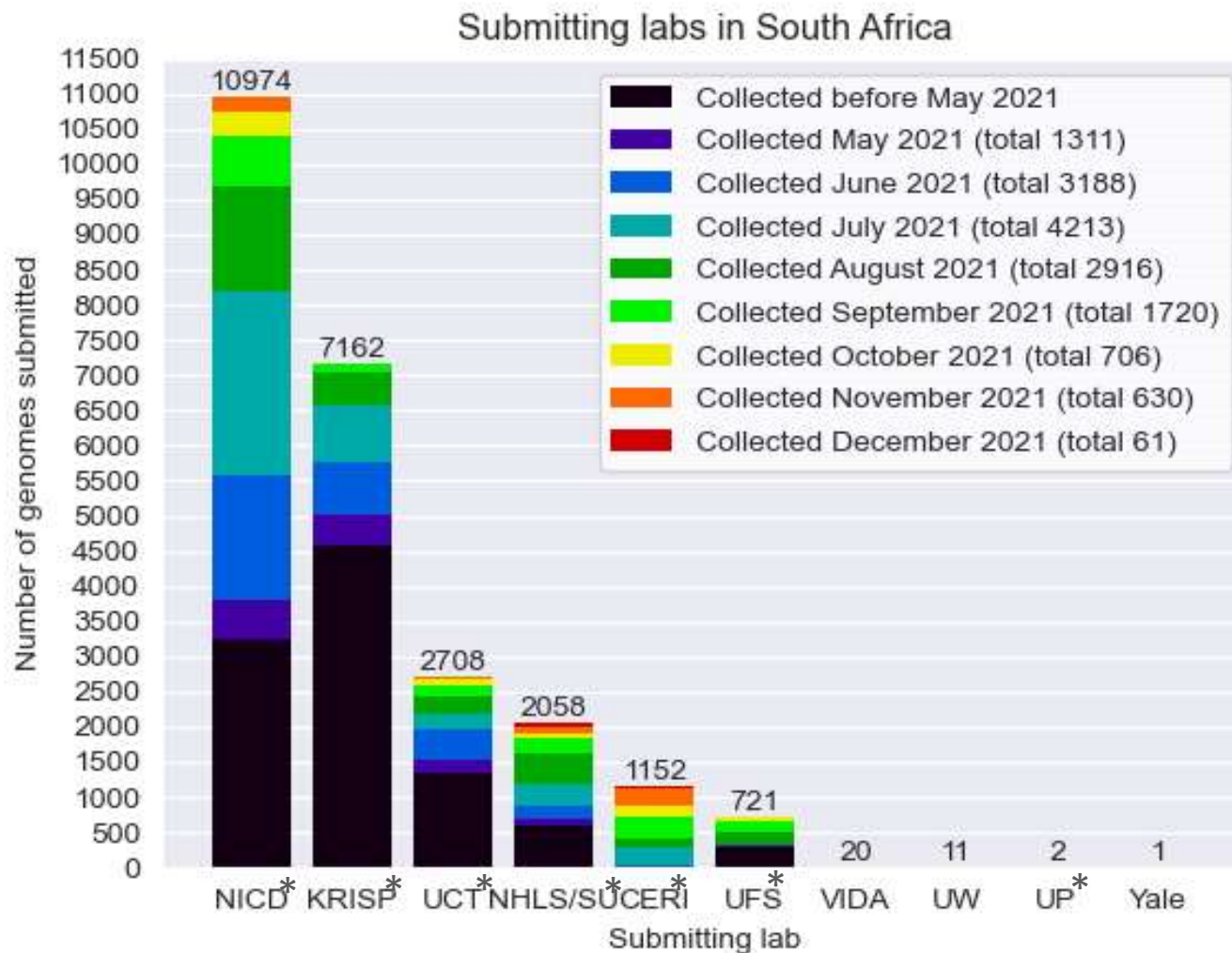
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South African genomes submitted per submitting lab, 2020 and 2021 (N=24 809)



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

*NGS-SA laboratories

Multiple labs from NGS-SA and collaborating private laboratories are contributing to the sequencing effort.

Variants of Concern (VOC)

WHO label	Pango lineages ⁺	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	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GR/484A	21K	-	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> accessed 10 December 2021

*Notable spike (S) amino acid changes under monitoring, which are currently reported in a minority of sequenced samples

⁺Includes all descendant lineages.

[#]Includes all Q.* lineages in the PANGO nomenclature system.

[§]Includes all AY.* lineages in the PANGO nomenclature system.

Currently designated Variants of Interest (VOI)

WHO label	Pango* lineages	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 10 December 2021

* Includes all descendant lineages.

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.)