NGS-SA SARS-CoV-2 Sequencing Update

19 July 2021

Network for Genomic Surveillance South Africa (NGS-SA)

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

NATIONAL HEALTH LABORATORY SERVICE

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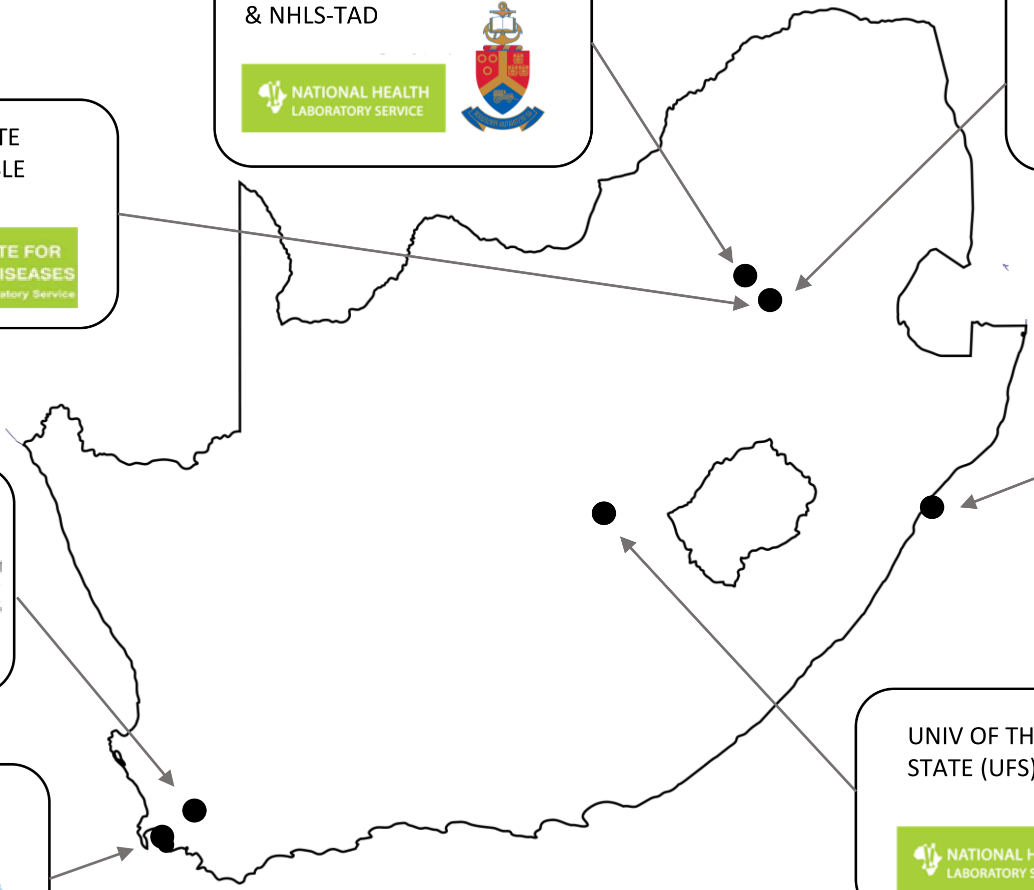
NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

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

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



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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 19 July at 09h00

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

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 B.1.351.2 B.1.351.3	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2	G/478K.V1	21A	+S:417N	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

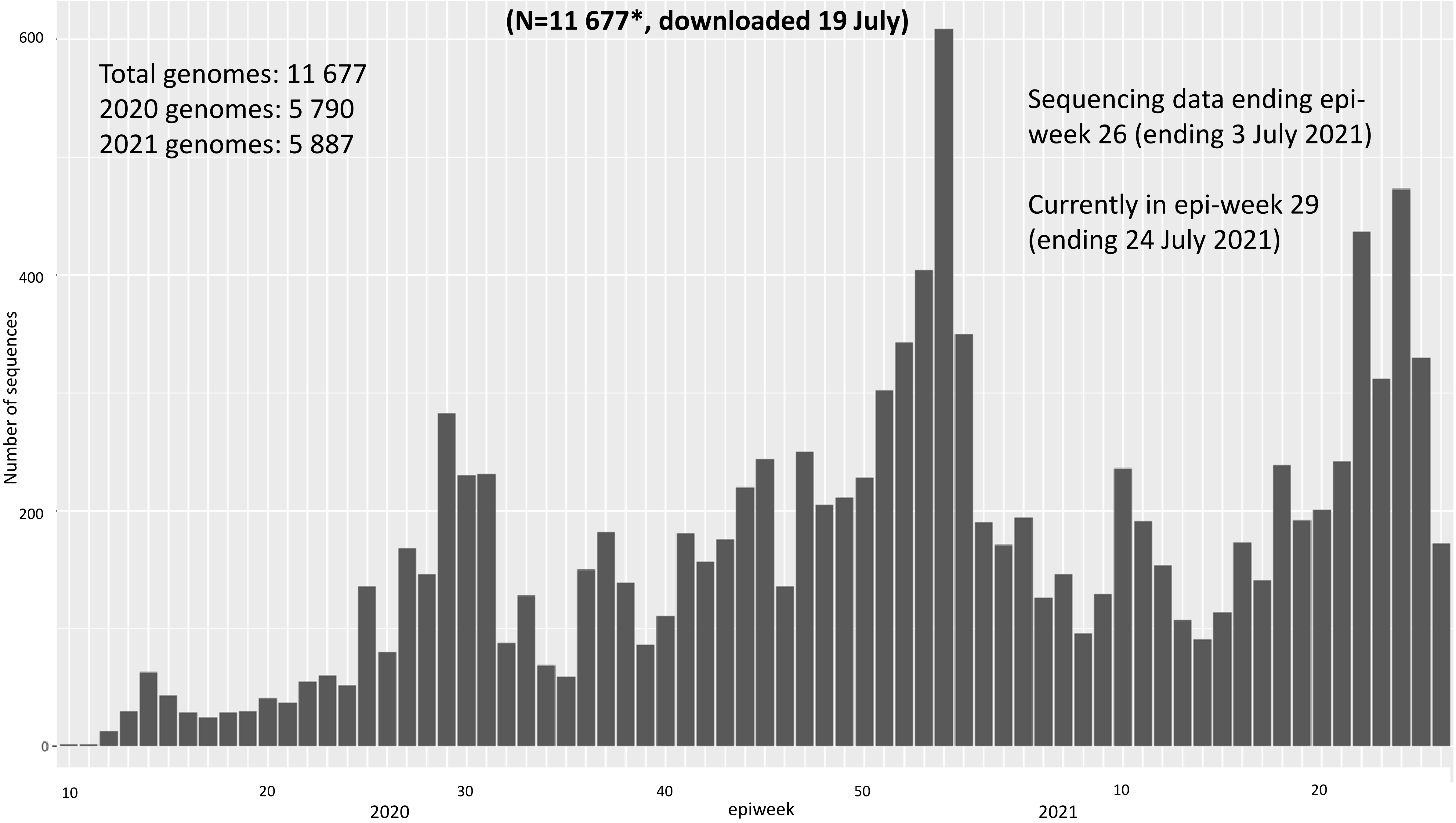
*Notable spike (S) amino acid changes under monitoring, which are currently reported in a minority of sequenced samples

Currently designated Variants of Interest (VOI)

WHO label	Pango lineages	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Eta	B.1.525	G/484K.V3	21D	Multiple countries, Dec-2020	17-Mar-2021
Iota	B.1.526	GH/253G.V1	21F	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21B	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 and 2021 (N=11 677*, downloaded 19 July)



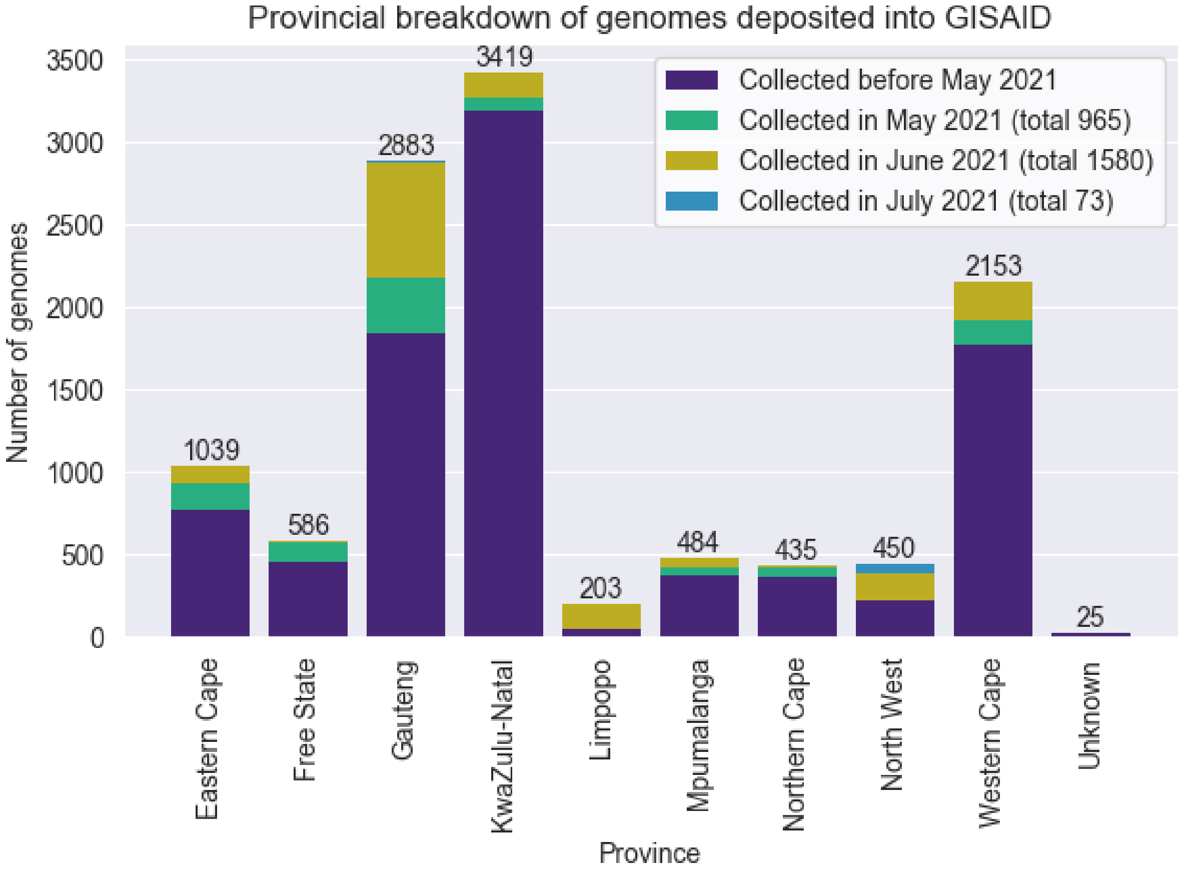
Total genomes: 11 677
2020 genomes: 5 790
2021 genomes: 5 887

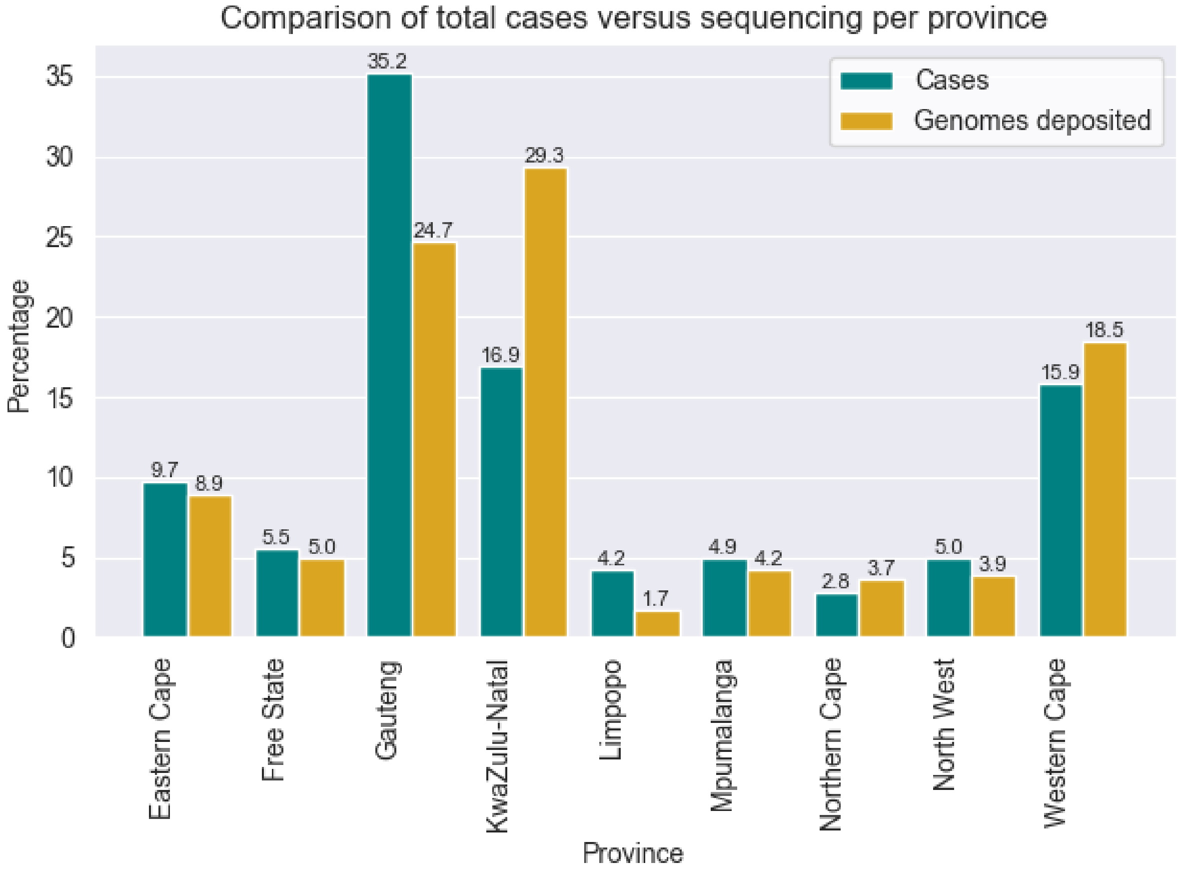
Sequencing data ending epi-week 26 (ending 3 July 2021)

Currently in epi-week 29 (ending 24 July 2021)

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

GISAID genomes vs total cases, 2020 and 2021 (N=11 677)

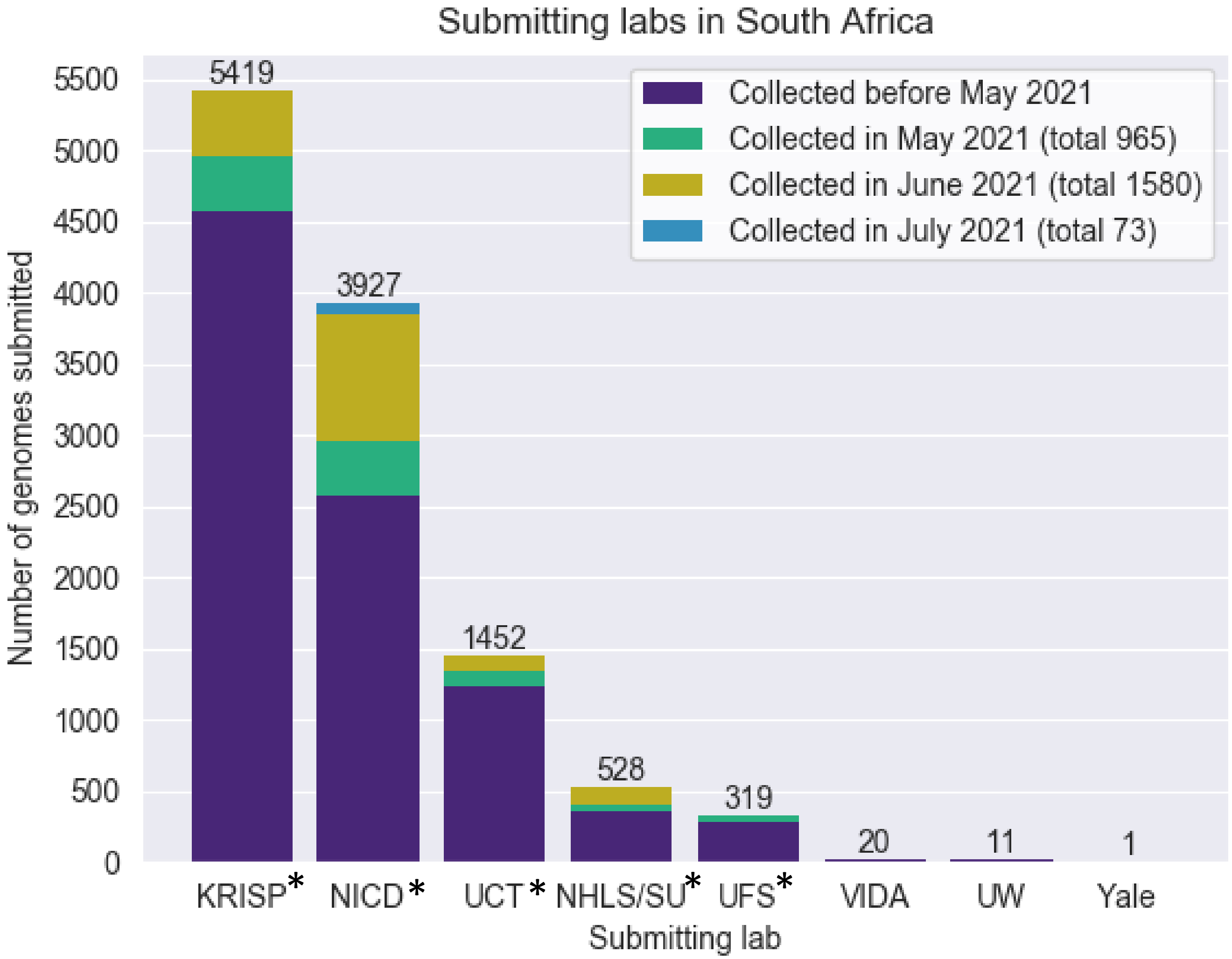




All provinces, apart from Limpopo (less), Gauteng (less) and KZN (more), have a similar percentage of cases as sequenced genomes.

Case data from https://www.nicd.ac.za/wp-content/uploads/2021/07/COVID-19-Weekly-Epidemiology-Brief-week-27-2021.pdf

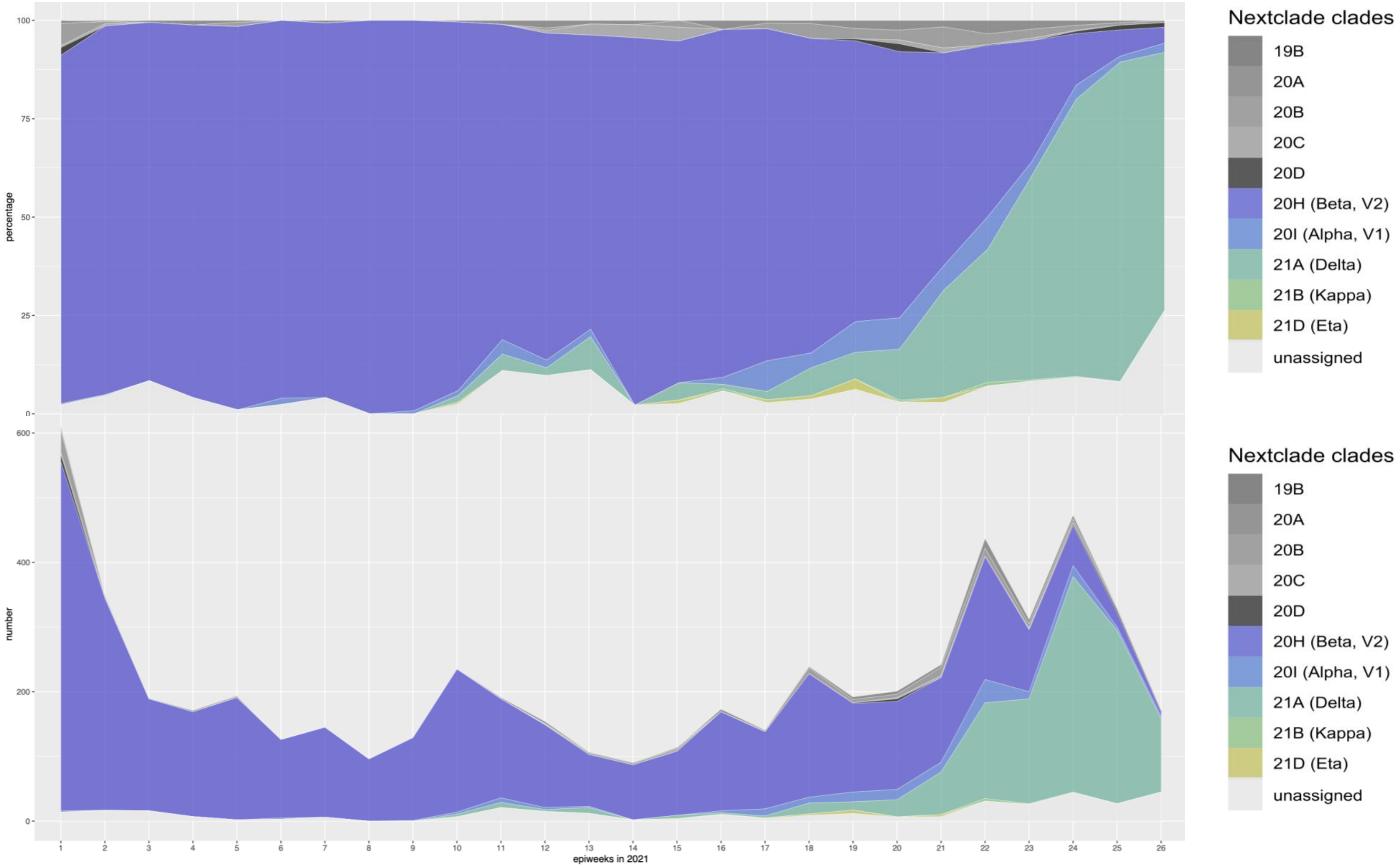
South African genomes submitted per sequencing lab, 2020 and 2021 (N=11 677)



*NGS-SA laboratories

Multiple labs from NGS-SA are contributing to the sequencing effort. Sequencing is increasing with the third wave.

Distribution and number of clades in South Africa, 2021 (N=5 887)



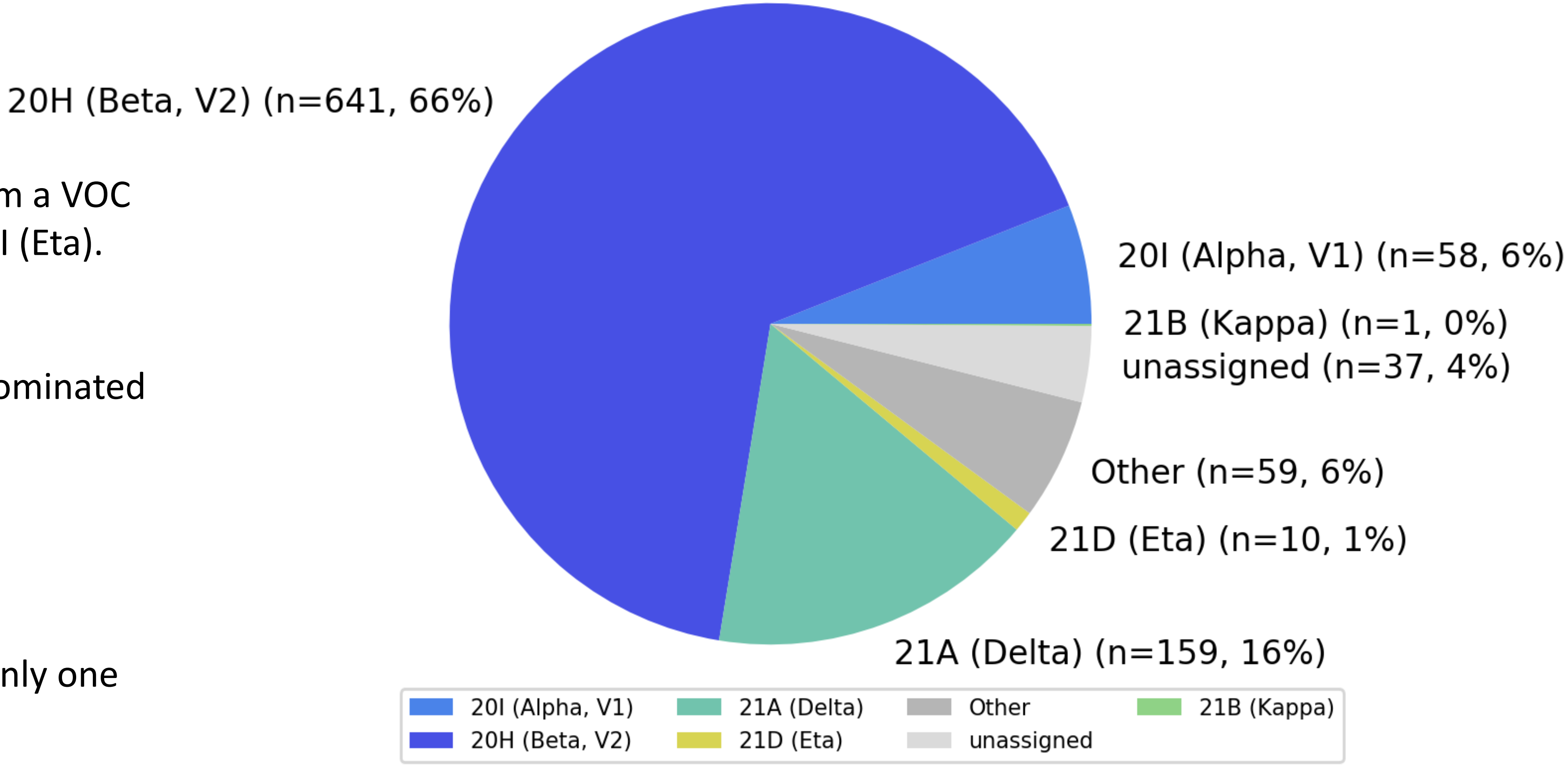
Sequencing data ending epi-week 26 (ending 3 July 2021)

Currently in epi-week 29 (ending 24 July 2021)

Alpha, Delta and Eta variant frequency increasing as of the beginning of May (epi-week 18, 2 May). Delta becoming dominant by end of June (333/473, 70% in week 24; 268/330, 81% in week 25; 75/100, 75% in week 26)

Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in May 2021 sequences, South Africa (N=965)

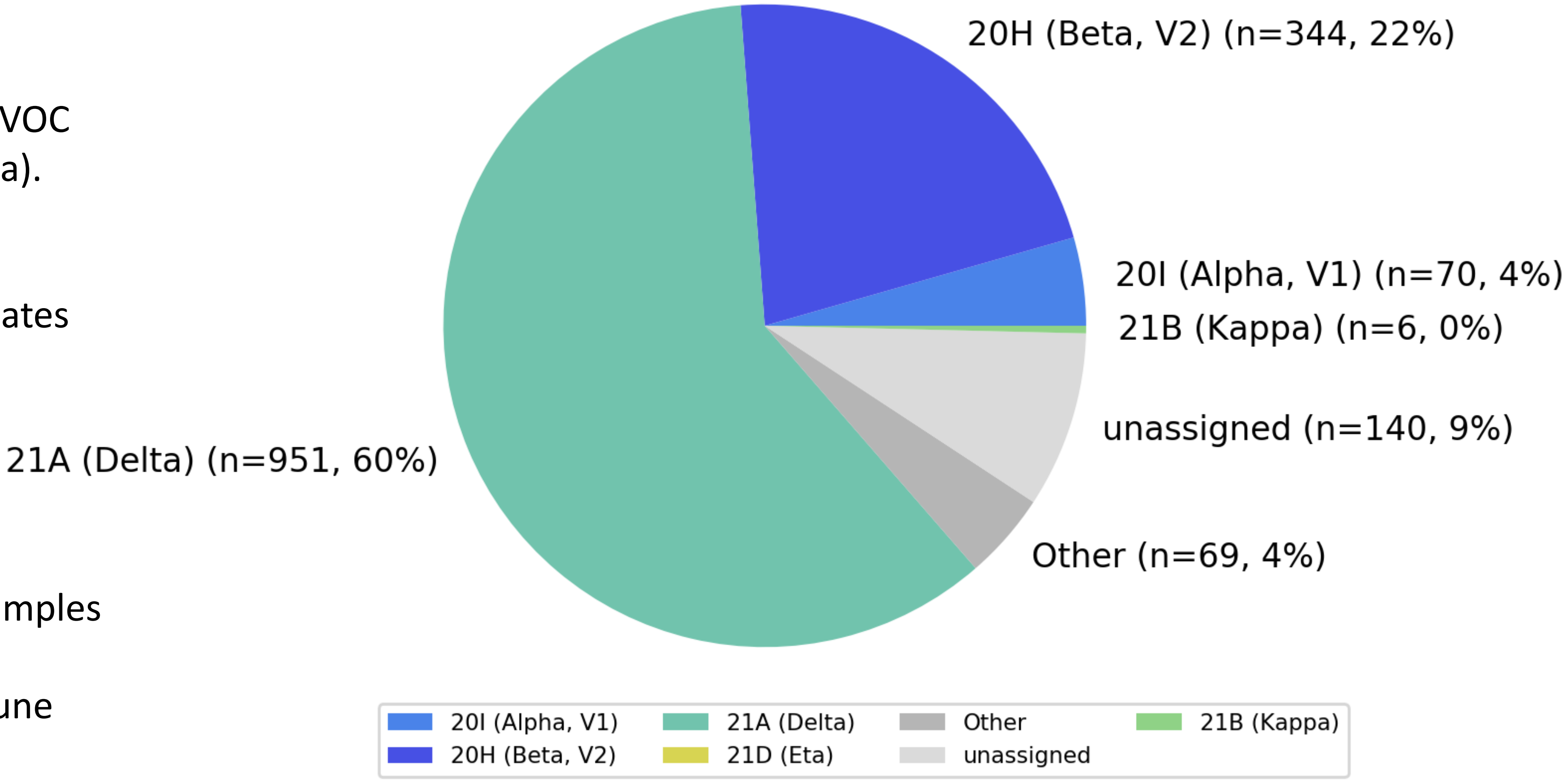
- 90% of sequences are from a VOC (Alpha, Beta, Delta) or VOI (Eta).
- Greater than 10%
  - Beta variant (66%) dominated
  - Delta (16%)
- Less than 10%
  - Alpha (6%).
  - Eta (VOI, 1%)
  - Kappa is present in only one sample (0.001%).



Beta variant dominated in May in South Africa

Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in June 2021 sequences, South Africa (N=1 580)

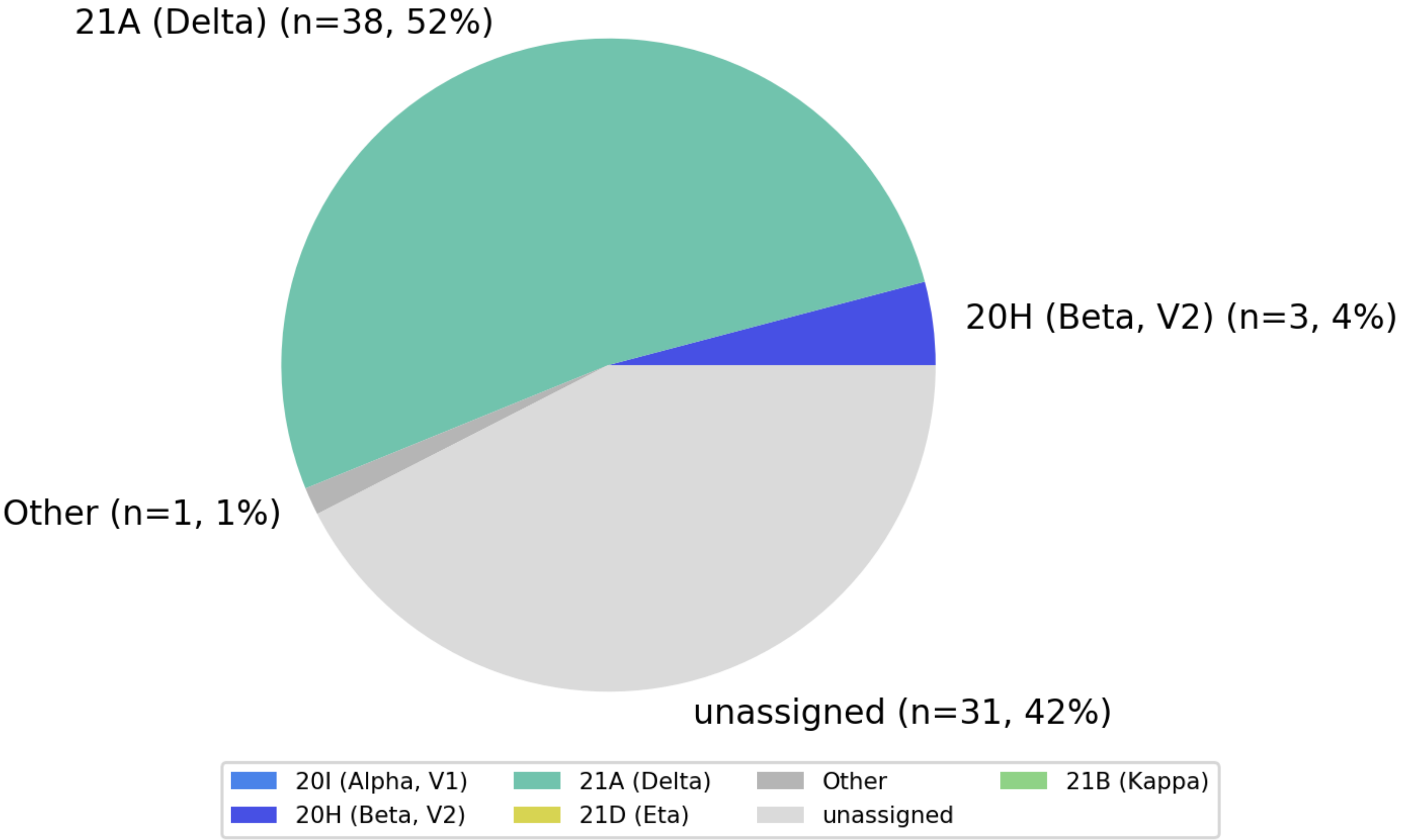
- 87% of sequences are from a VOC (Alpha, Beta, Delta) or VOI (Eta).
- Greater than 10%
  - Delta variant now dominates (60%)
  - Beta variant (22%)
- Less than 10%
  - Alpha (4%).
  - Kappa is present in six samples (0.004%).
  - Eta not yet detected in June



Delta variant dominated in June in South Africa

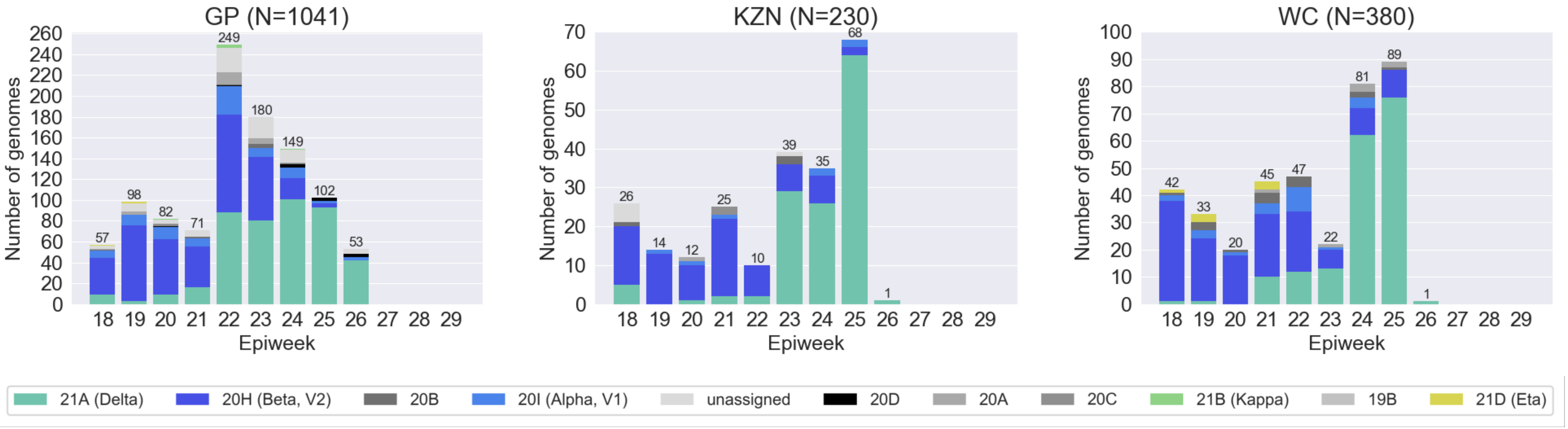
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in July 2021 sequences, South Africa (N=73)

- 69% of sequences are from a VOC (Beta, Delta)
- Greater than 10%
  - Delta variant now dominates (52%)
- Less than 10%
  - Beta (4%).
- More high quality data is required to establish variant dominance and diversity



Delta variant appears to dominate in July in South Africa so far, but more high quality sequence data is required to confirm this

Genomes sequenced from specimens collected in May and June 2021 from KwaZulu-Natal, Gauteng, Western Cape Provinces



Gauteng

- Delta is present in early weeks (May) and increases in proportion in later weeks (June)
- Eta detected in May but is not present in June. Kappa detected in May and early June

KwaZulu-Natal

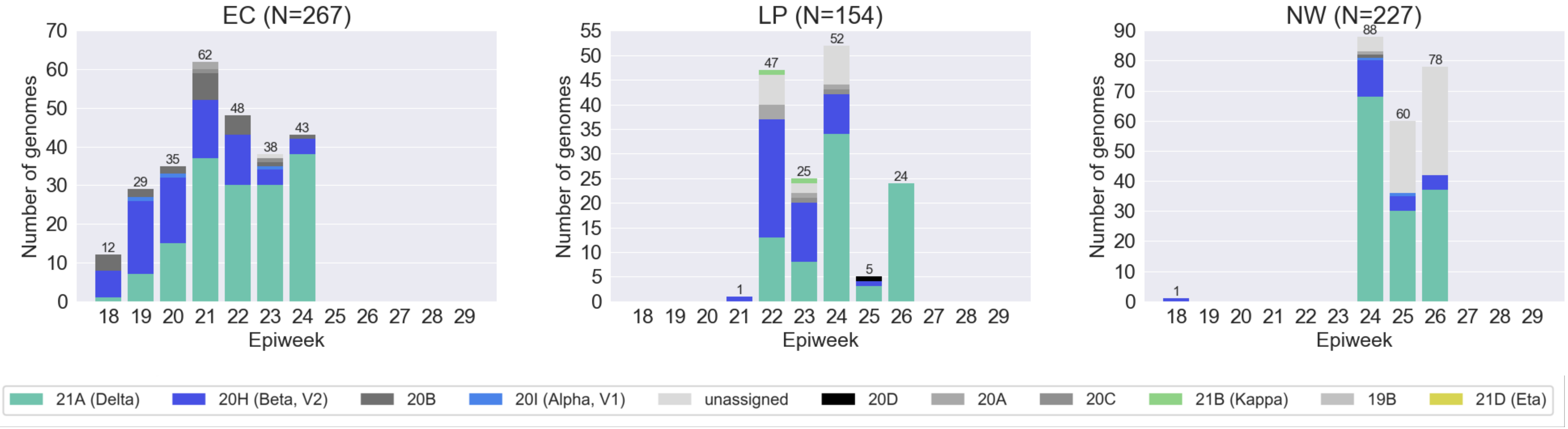
- Delta is present in early weeks (May) and increases in proportion later weeks (June)
- Eta was not detected

Western Cape

- Beta dominates until week 22, when Delta increases and rapidly dominates (early June)
- Eta is detected in higher numbers than in GP and KZN, but not detected in most recent weeks

Beta dominates in all provinces in May, however following its detection in week 18, Delta rapidly begins to dominate in all three provinces by mid-June

Genomes sequenced from specimens collected in May and June 2021 from Eastern Cape, Limpopo and North-West Provinces



Eastern Cape

- Delta detected in early May and rapidly increases to predominate by end of May
- Alpha detected at low frequency in May and only once in June

Limpopo

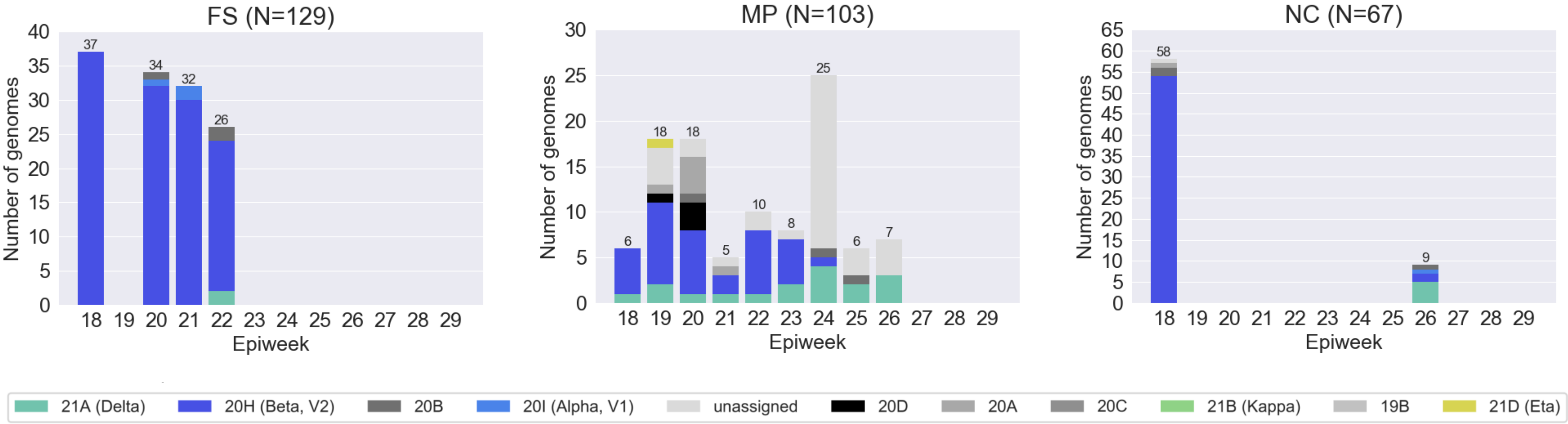
- Delta detected at the end of May and predominates by early June
- Kappa detected at low frequency in May and early June

North-West

- Delta detected at high proportion in June, but additional earlier time points required for sequencing

Delta variant dominating in Eastern Cape, Limpopo and North-West Provinces

Genomes sequenced from specimens collected in May and June 2021 from Free State, Mpumalanga and Northern Cape Provinces



Free State

- Delta has been detected at low frequency in June
- Recent sequences are required to determine whether Delta has begun to dominate

Mpumalanga

- Delta detected throughout May and June, however increased specimen numbers required to estimate predominance of a particular variant

Northern Cape

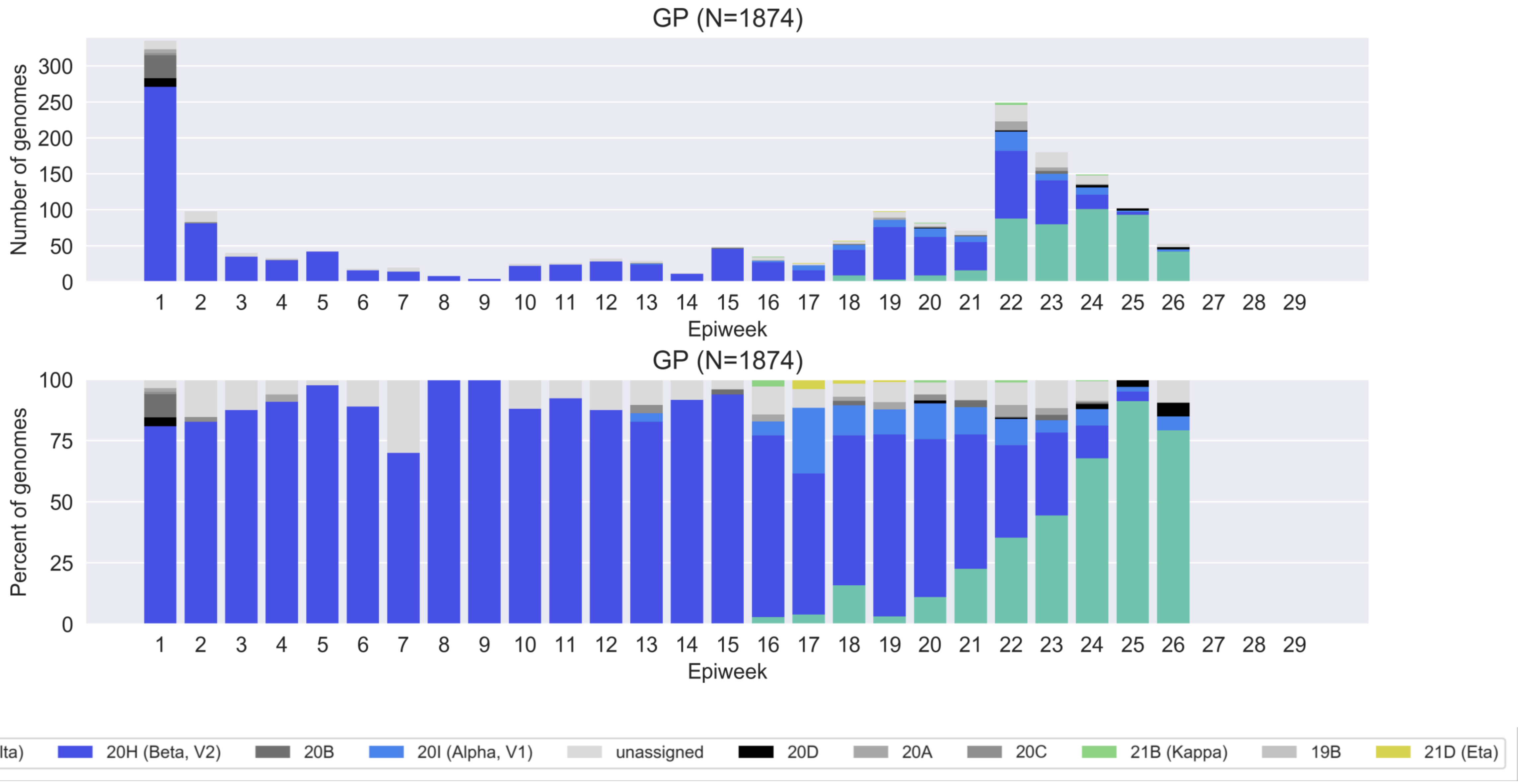
- Delta was detected in March (not shown, see later slides) in Northern Cape, but the Beta variant continued to cause a significant number of infections
- Delta again detected at most recent time point, but more sequences are required to establish prevalence levels

Recent data is required from these provinces to estimate the dominance of Delta

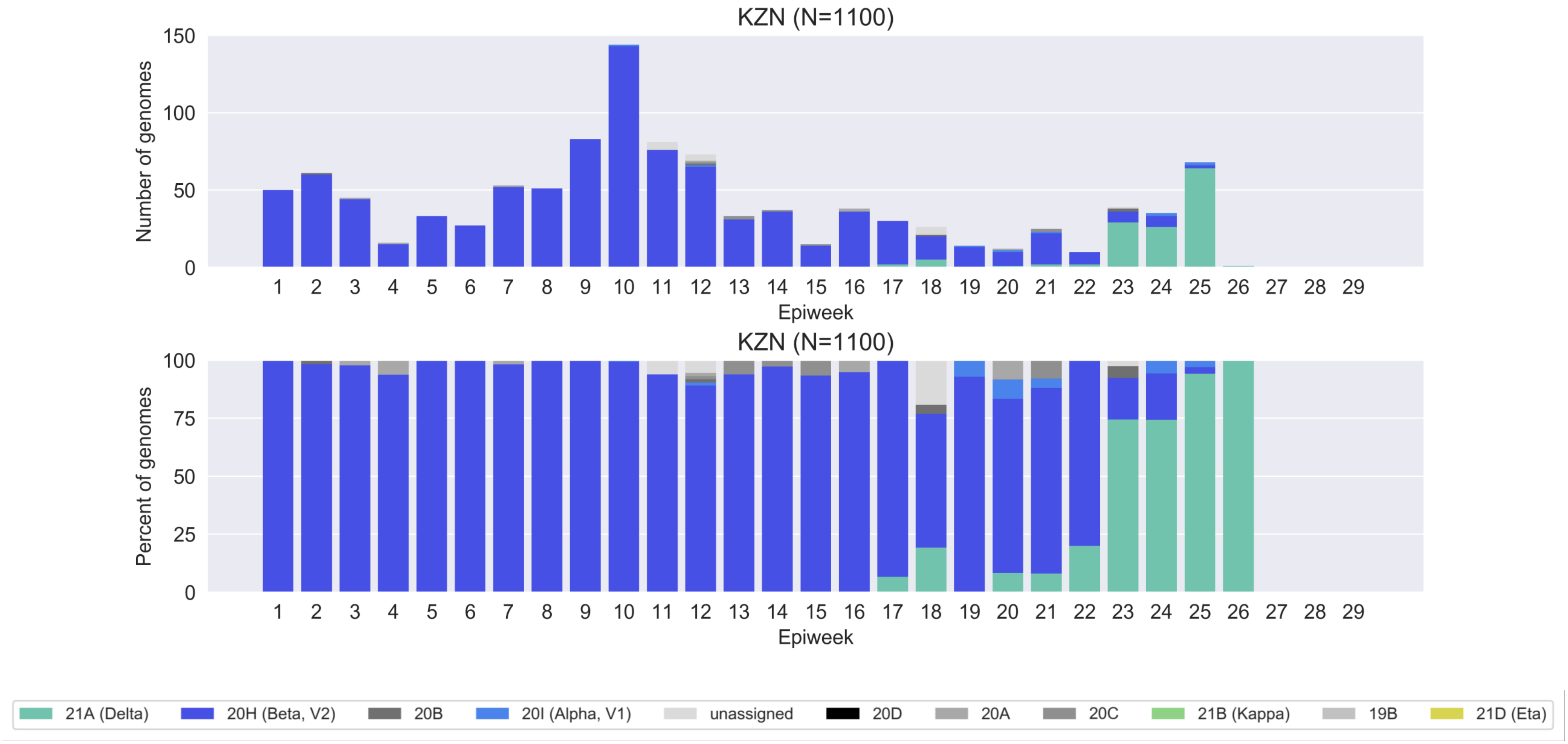
SARS-CoV-2 clade distribution per province

South Africa 2021

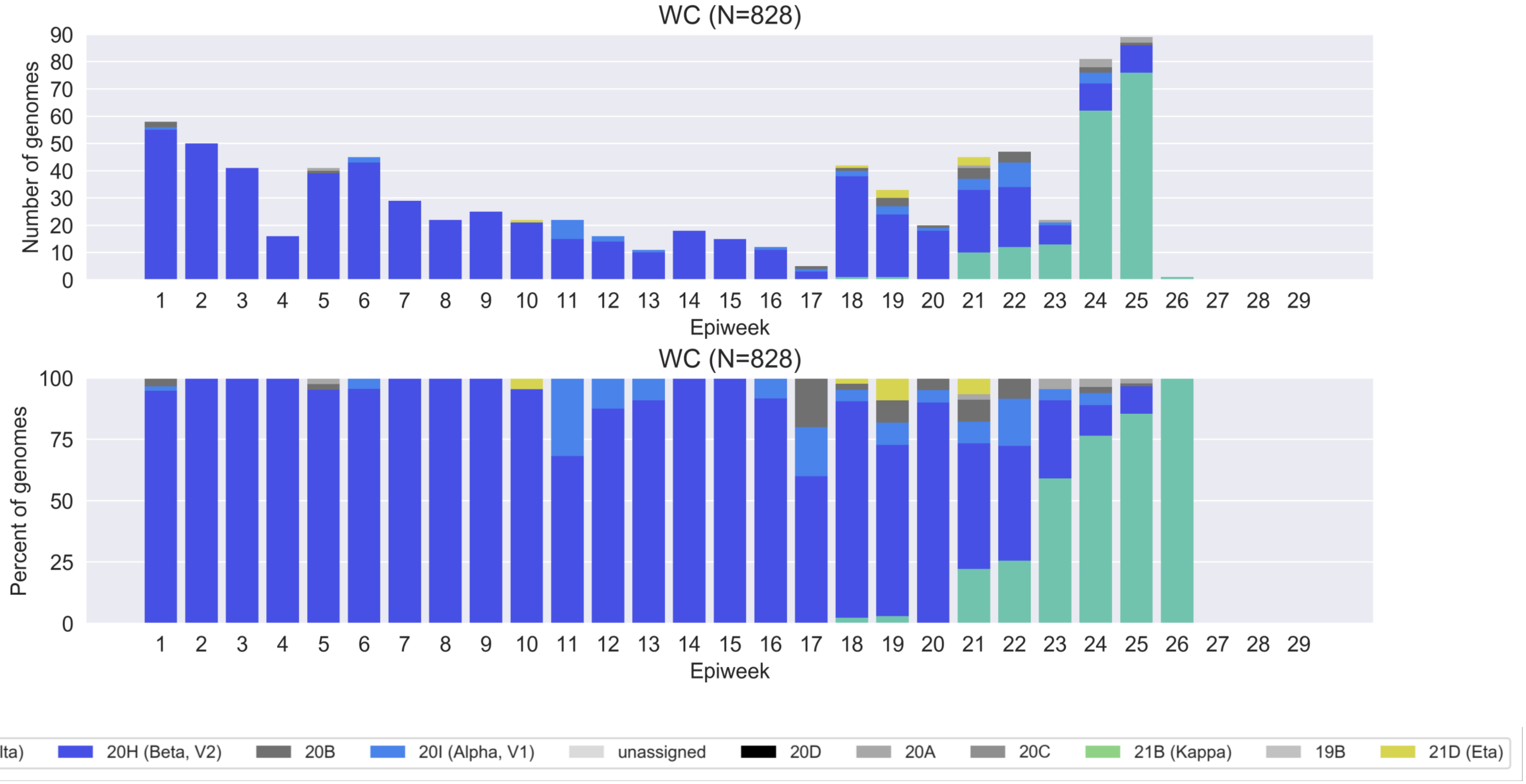
Gauteng Province, 2021, n = 1 874



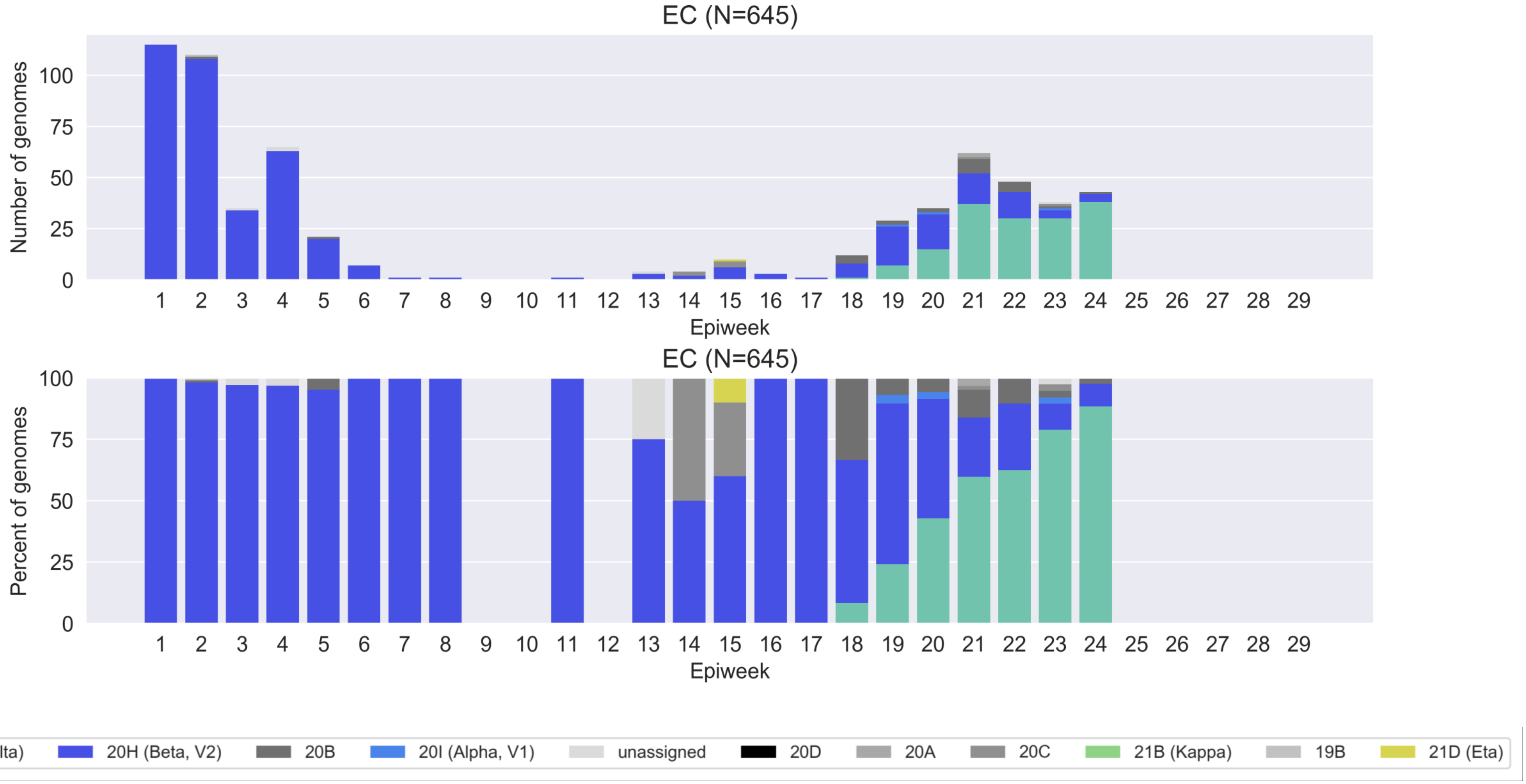
KwaZulu-Natal Province, 2021, n = 1 100



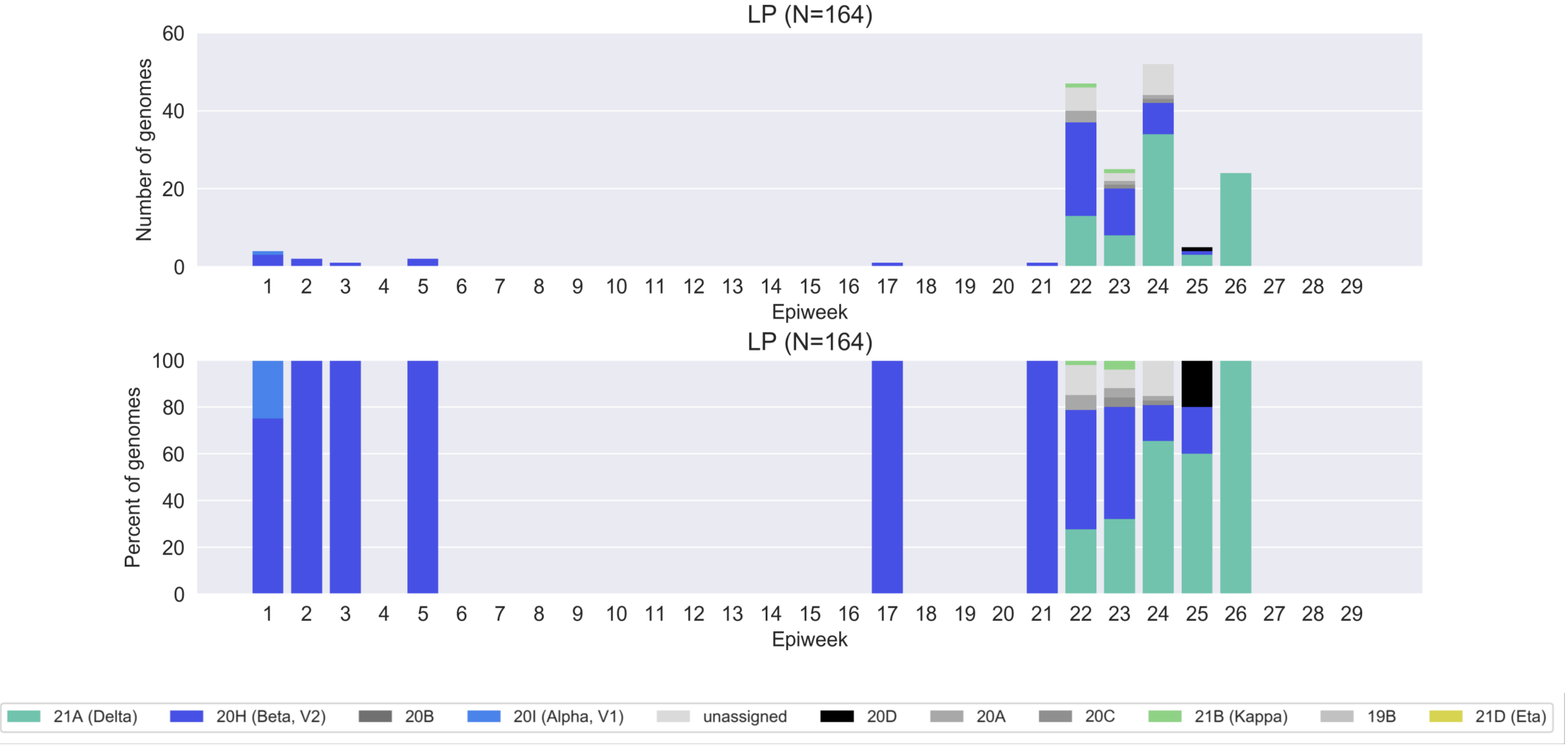
Western Cape Province, 2021, n = 828



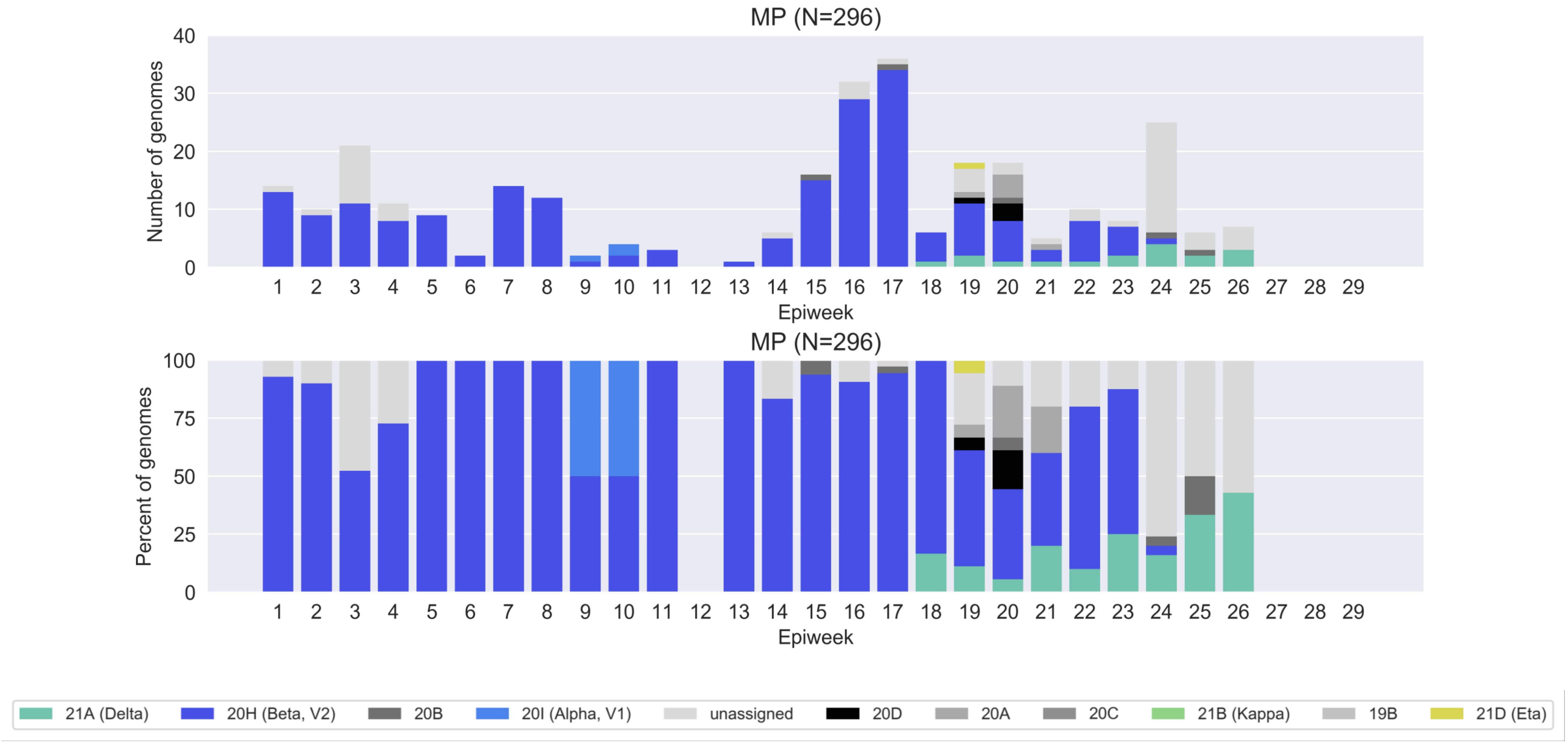
Eastern Cape Province, 2021, n = 645



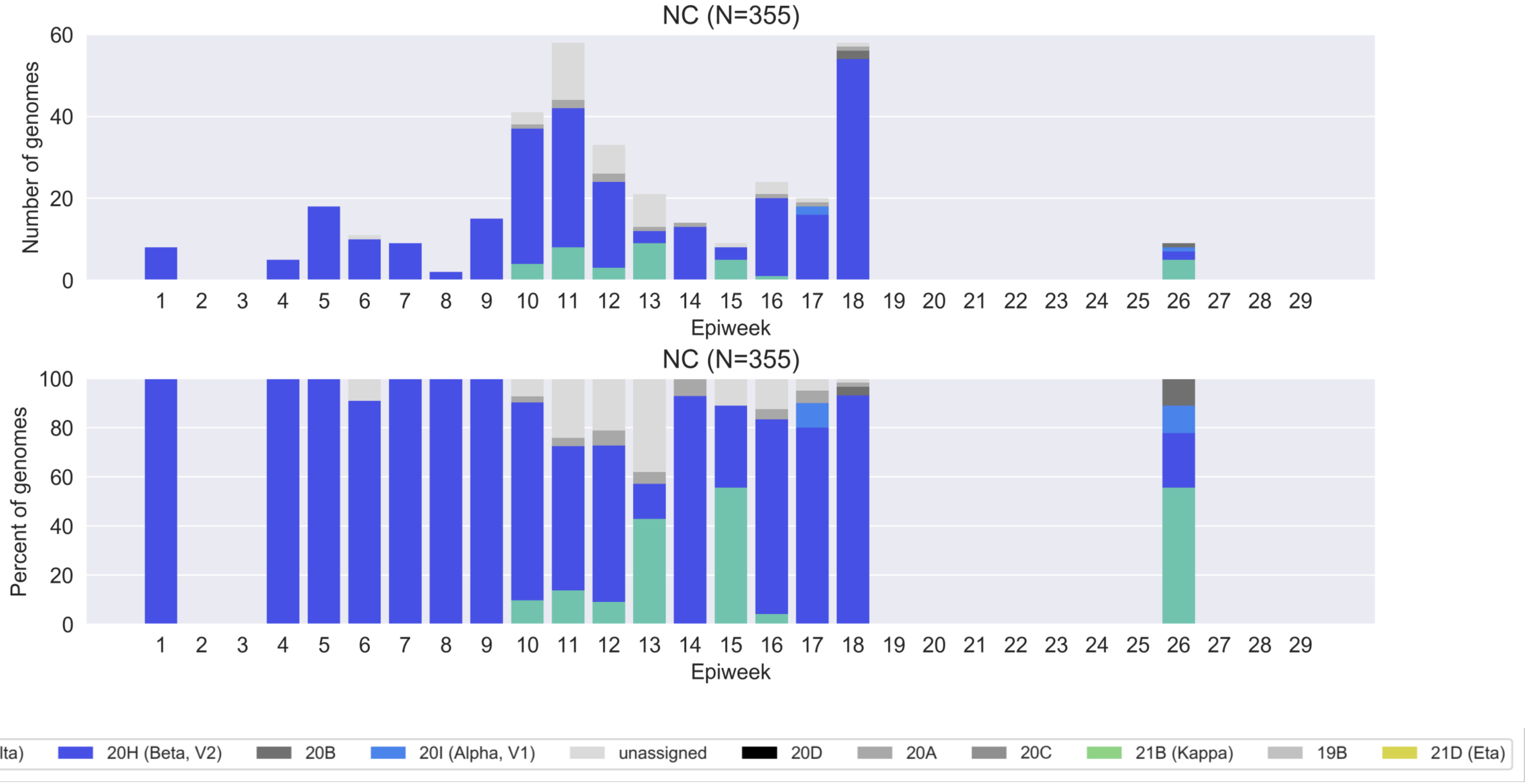
Limpopo Province, 2021, n = 164



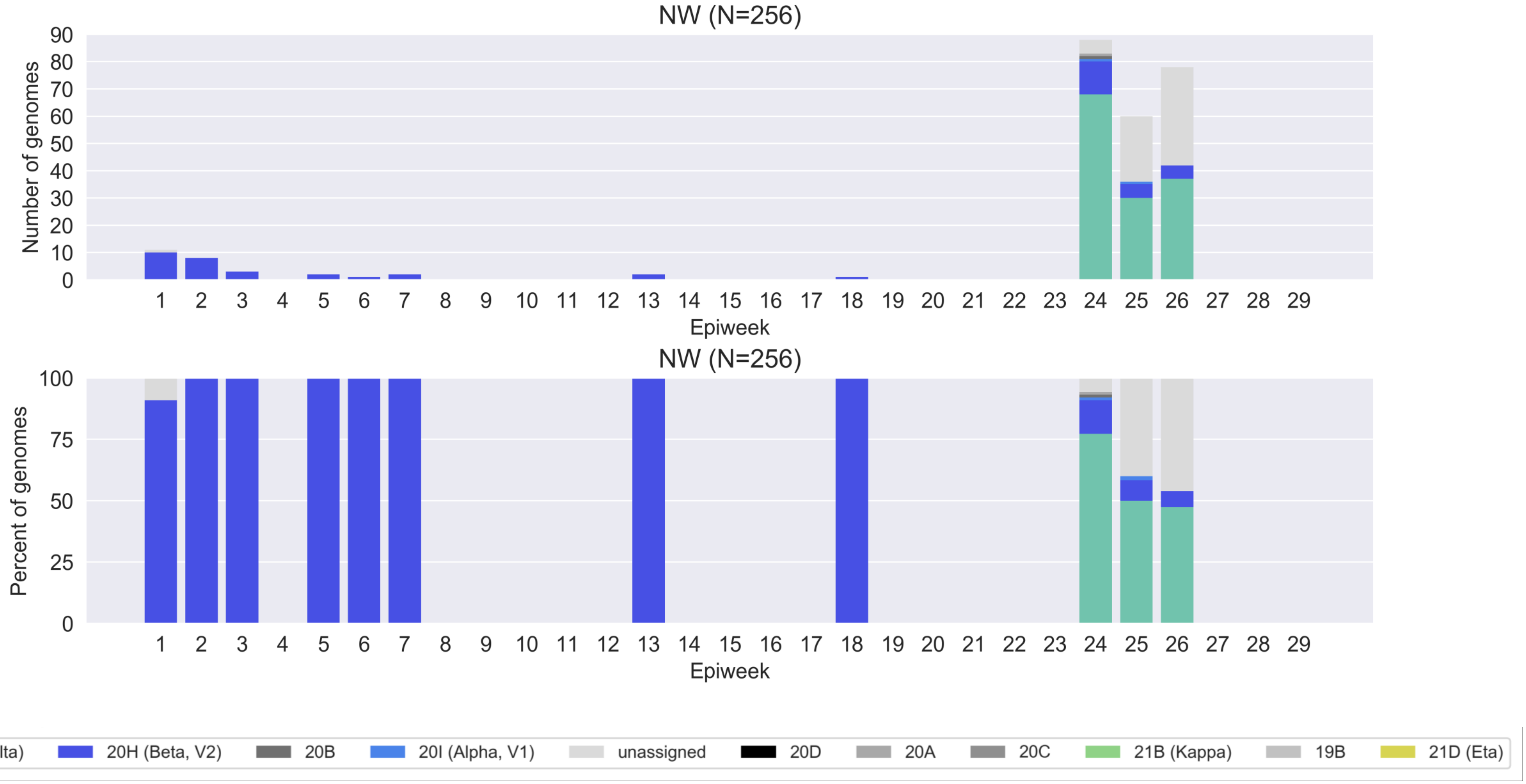
Mpumalanga Province, 2021, n = 296



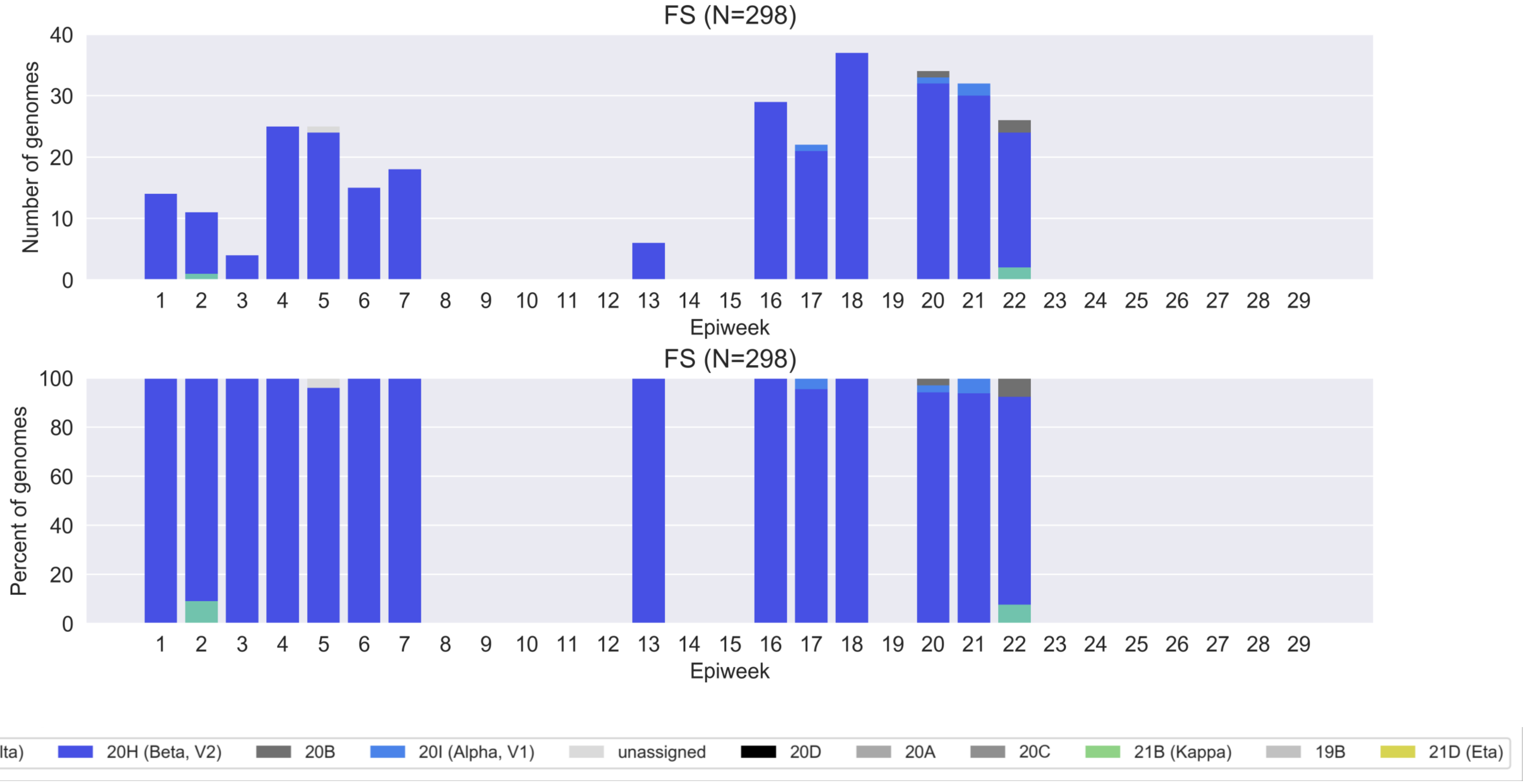
Northern Cape Province, 2021, n = 355



North West Province, 2021, n = 256



Free State Province, 2021, n = 298

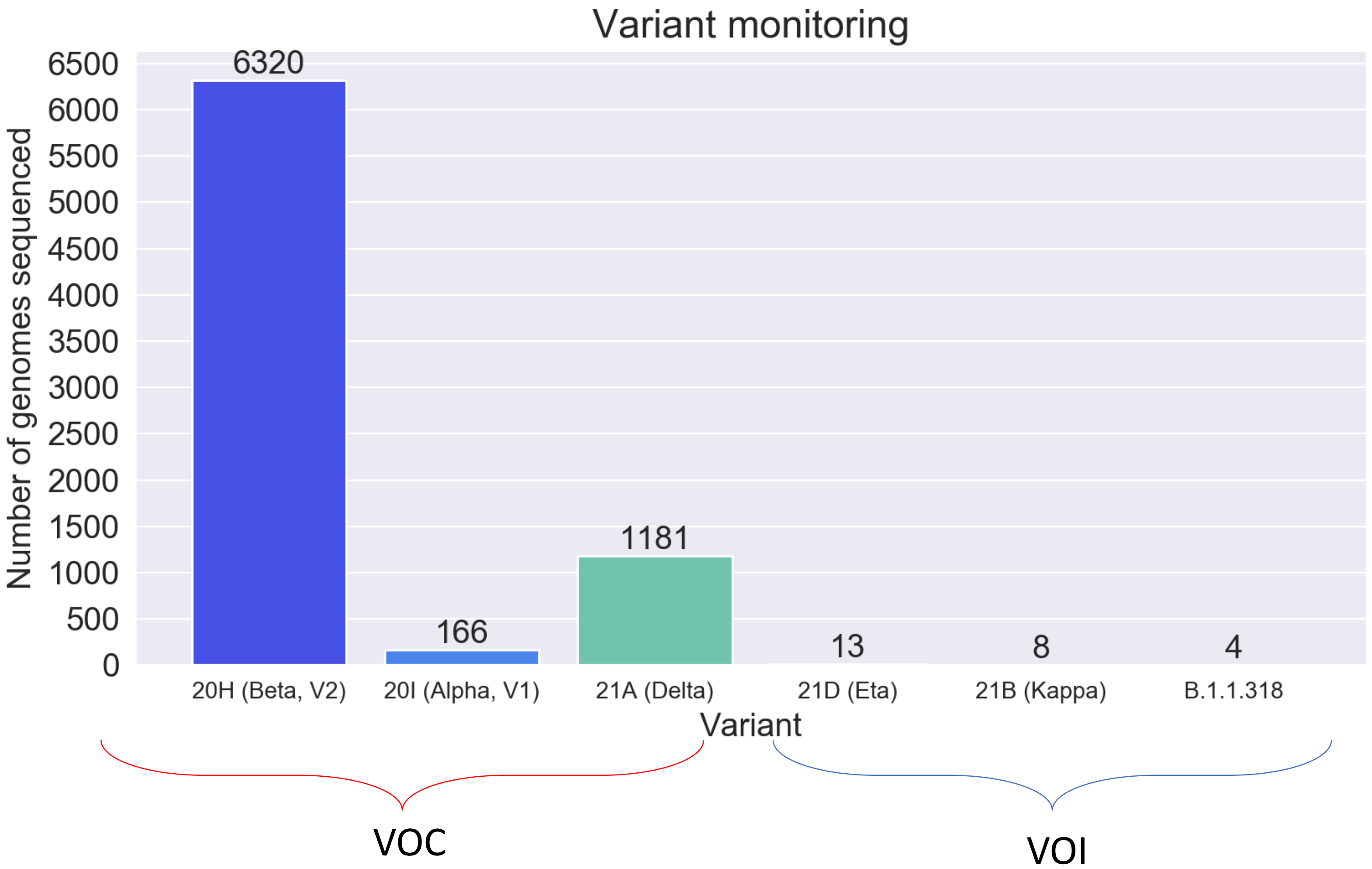


Monitoring mutations in SARS-CoV-2 lineages

South Africa 2021

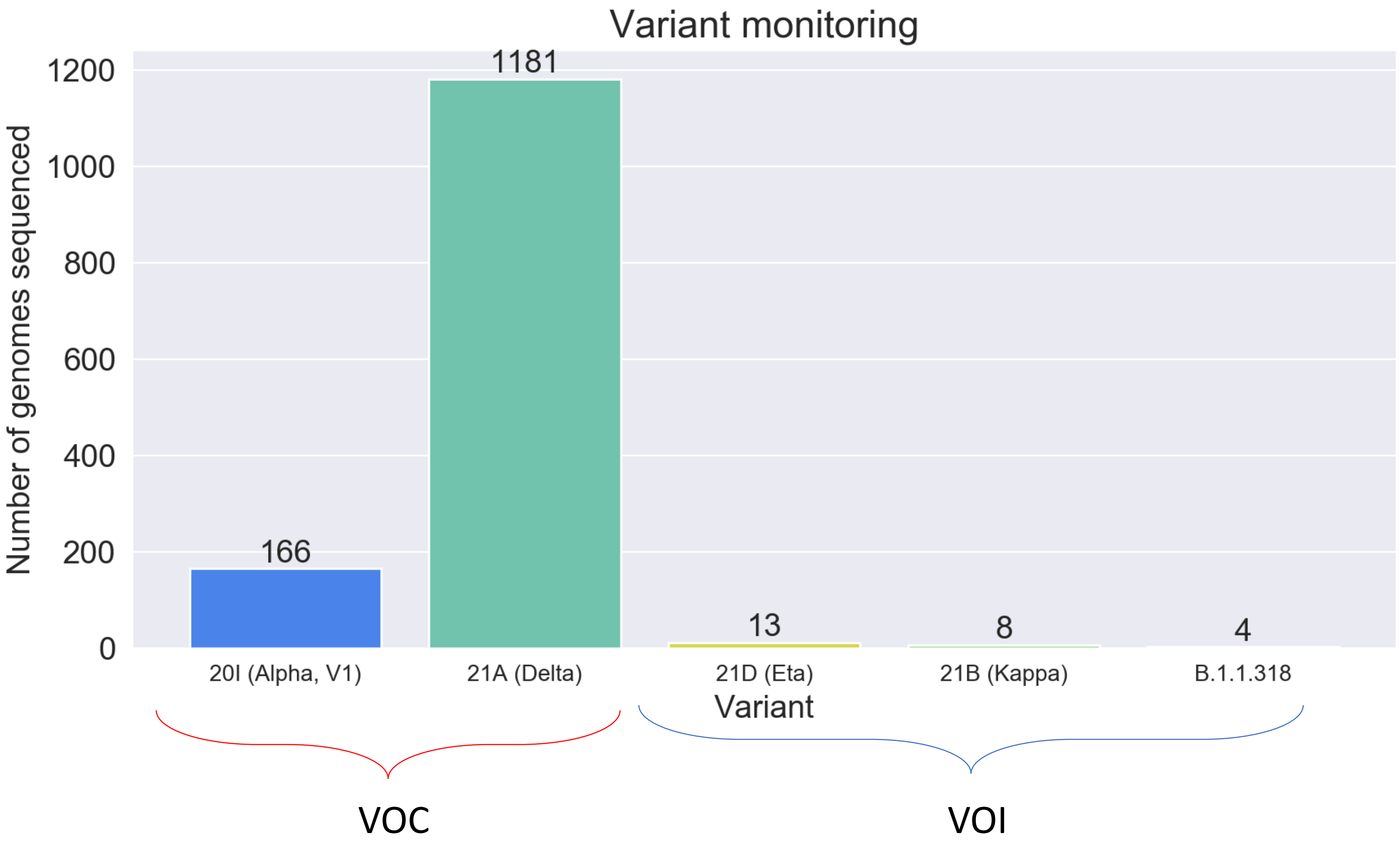
Monitoring VOCs and VOIs in South Africa (N=7 692, 66% of all sequences)

(2020 – 2021)



Variant monitoring has detected a number of VOCs and VOIs. Within these, no unusual mutations have yet been detected.

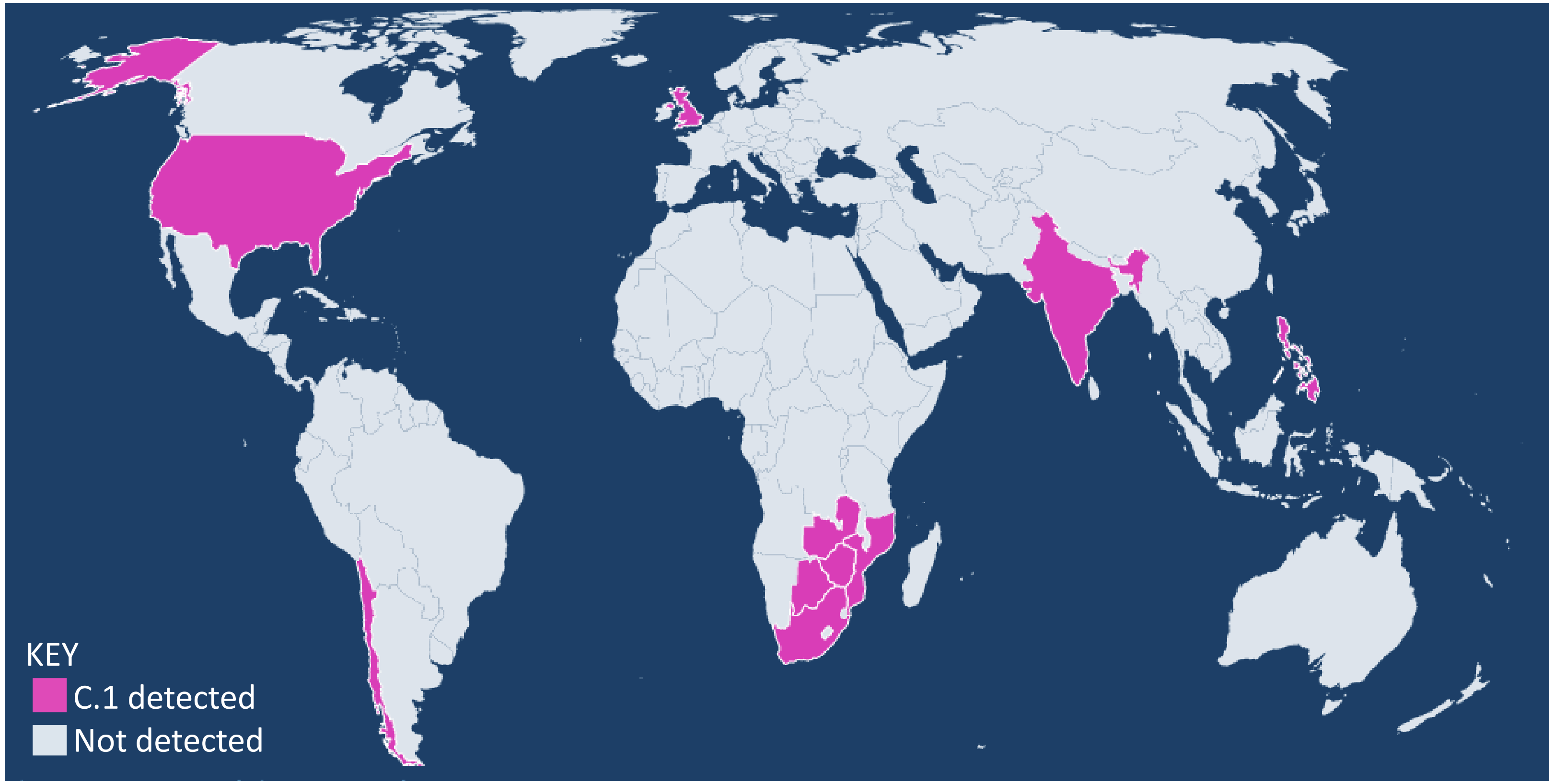
Monitoring VOCs and VOIs in South Africa (excluding 20H, Beta; 2020 – 2021)



Variant monitoring has detected a number of VOCs and VOIs. Within these, no unusual mutations have yet been detected. Lambda variant not yet detected.

C.1 evolution in South Africa

C.1 global distribution



https://outbreak.info/situation-reports?pango=c.1

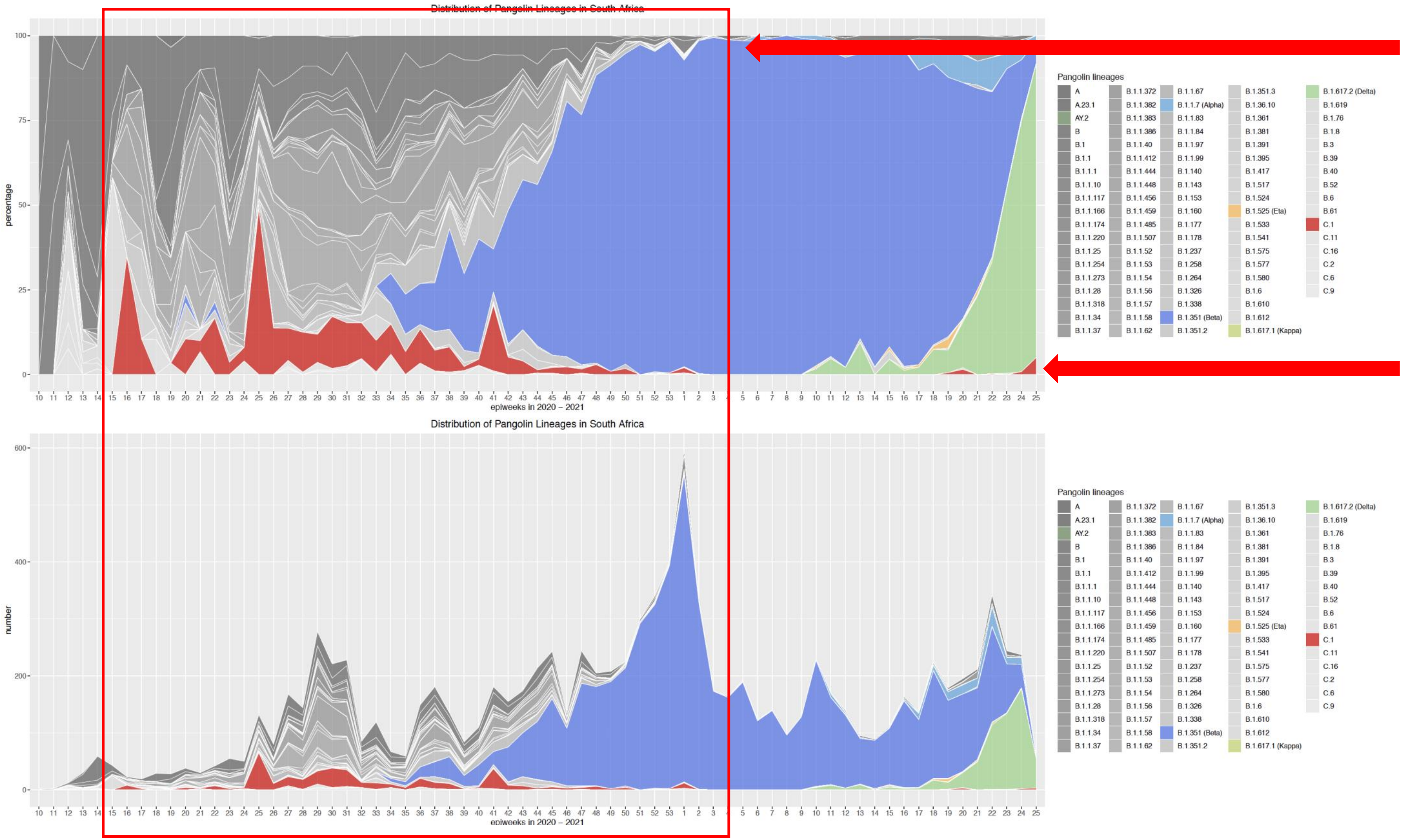
Globally, N=422 (according to GISAID as of 12pm, 8 July).

Of these, 391 (93%) sequences are from South Africa (C1 was first detected in South Africa – Tegally 2021 Nat Med).

The majority of SA sequences were collected in 2020. In 2021, 18 C.1 sequences have been detected. 8 in January, 4 in May, 6 in June.

The 10 sequences detected since May 2021 (6 in GP, 3 in LP, 1 in MP) possess a number of unusual mutations, some of which are found in the three VOCs present in SA (Alpha, Beta, Delta)

C.1 frequency in South Africa



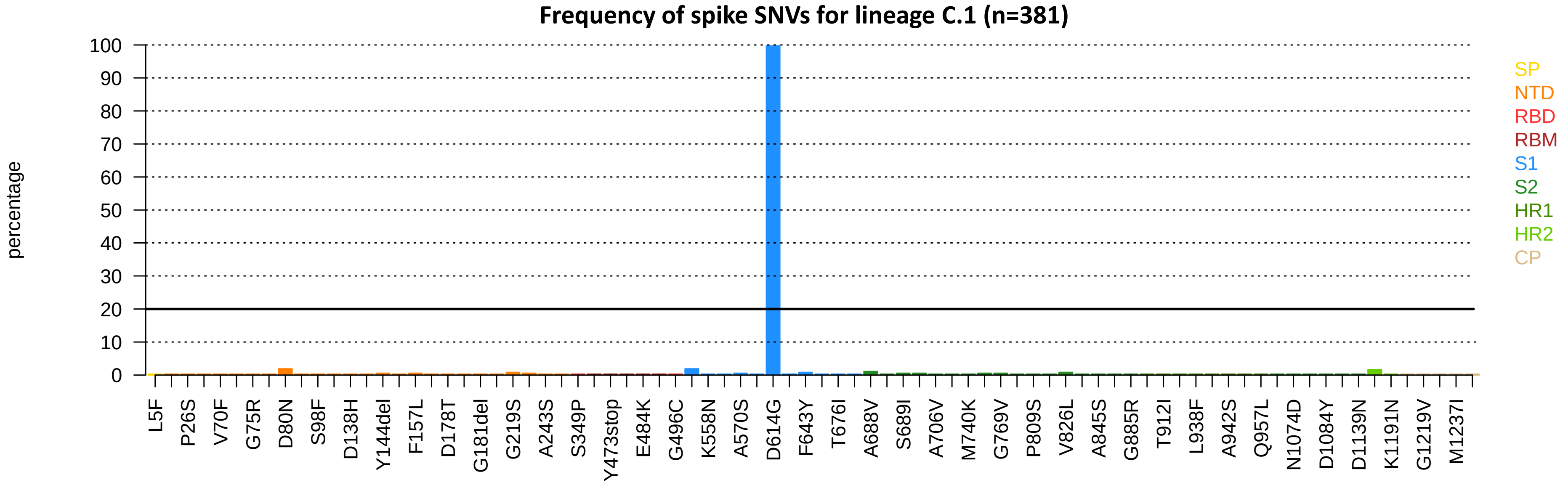
C.1 seen before in SA during the first wave and part of the second

But this C.1 is not that same as the previous lineage!

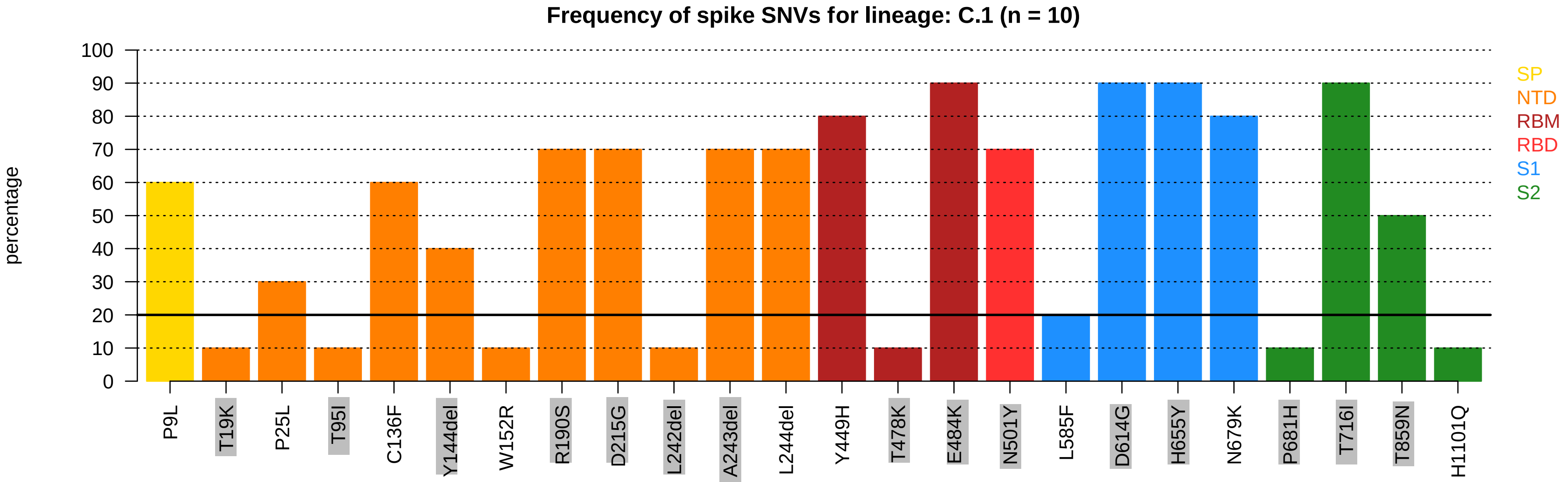
C.1 spike mutation prevalence: 2020 vs May and June 2021

- Significant increase in the number of spike mutations in the C.1 lineage
- Many of these are present in other variants of concern or variants of interest (grey shading)
- Functional studies are currently underway

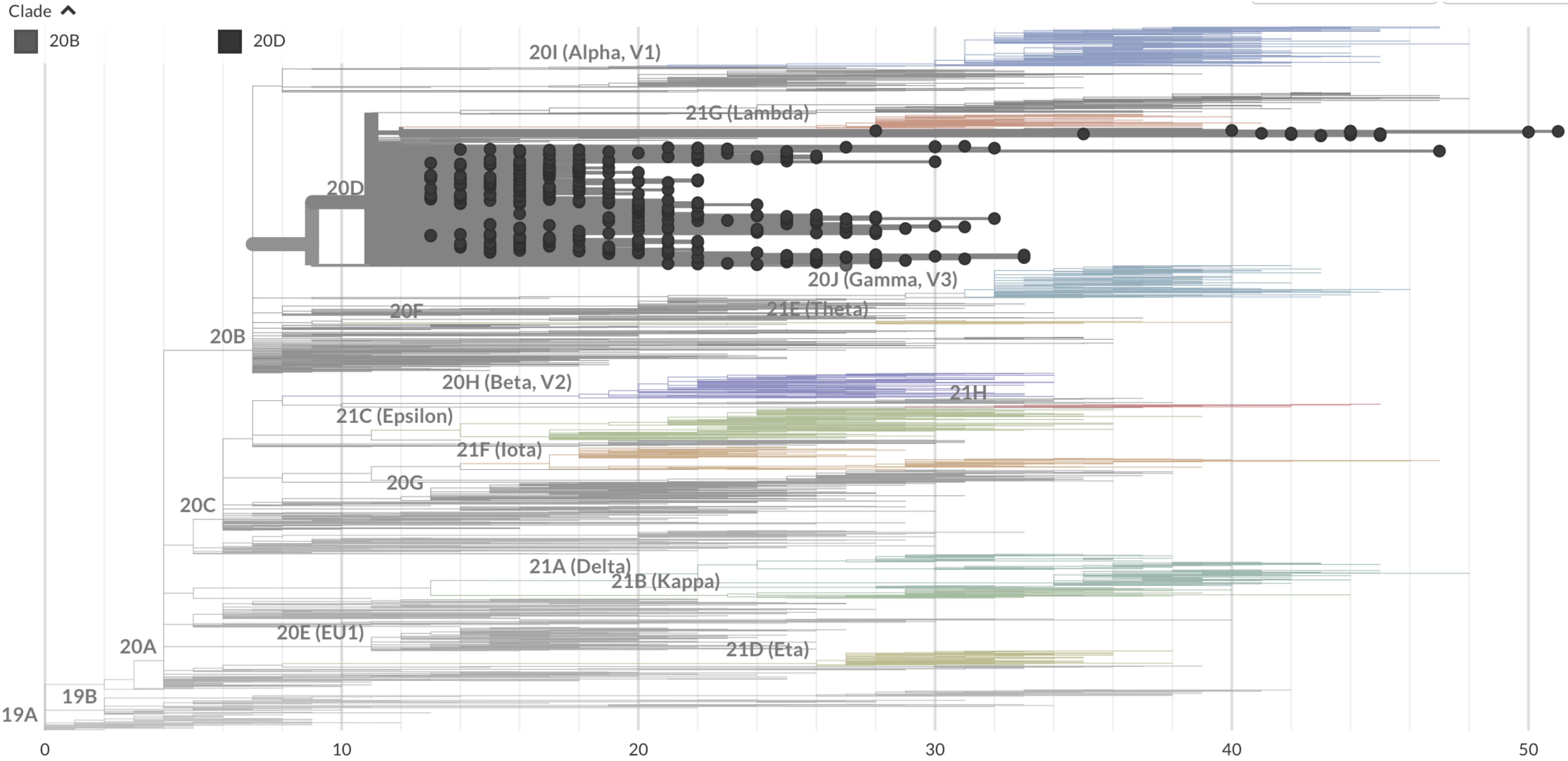
Mutation profile of C.1 in 2020 and January 2021



Mutation profile of C.1 in May and June 2021

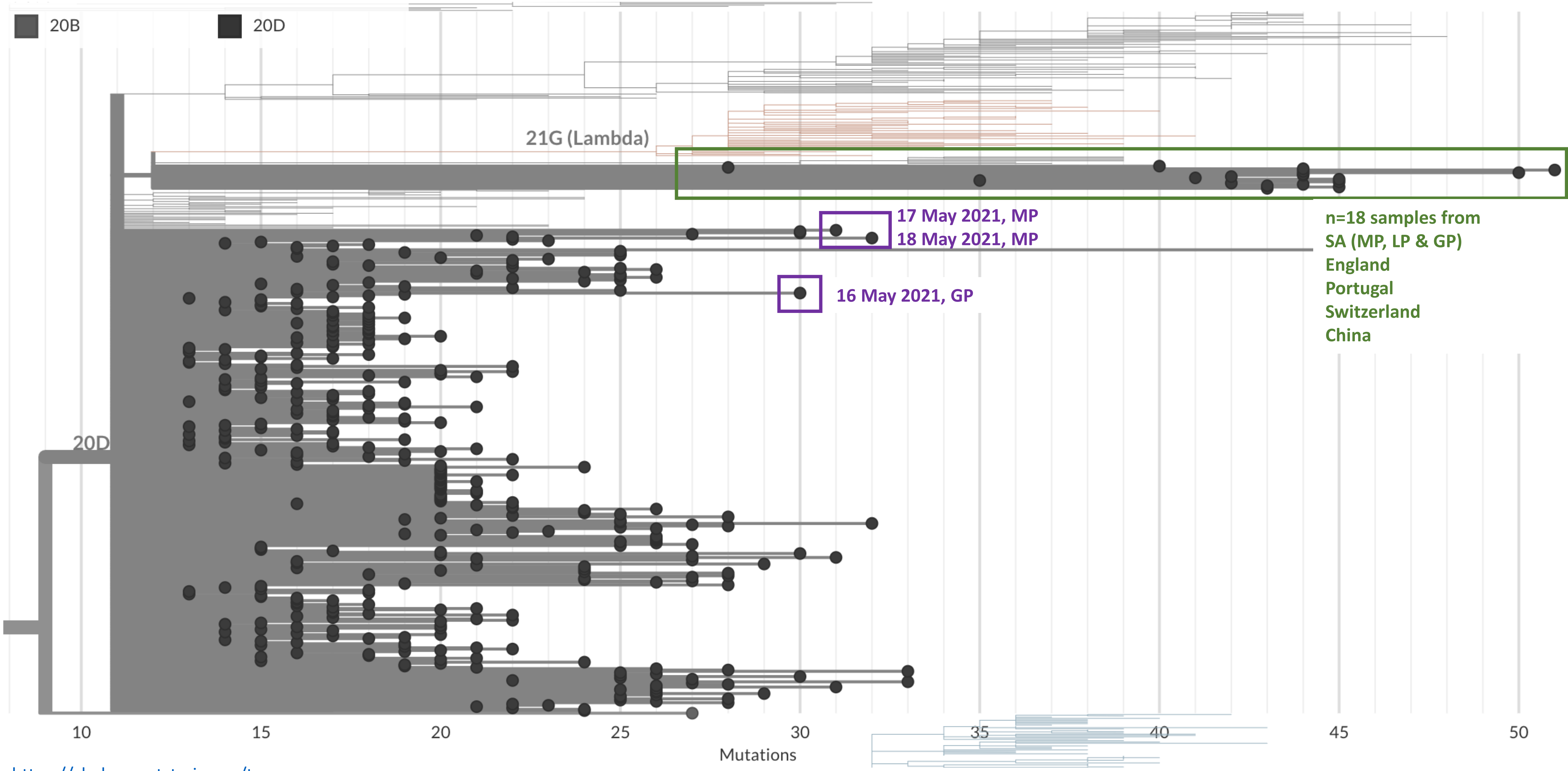


Global set of C.1 samples (N=387 as of 19 July) within nextclade global tree



https://clades.nextstrain.org/tree

Divergence between older and recent C.1 sequences



17 May 2021, MP
18 May 2021, MP

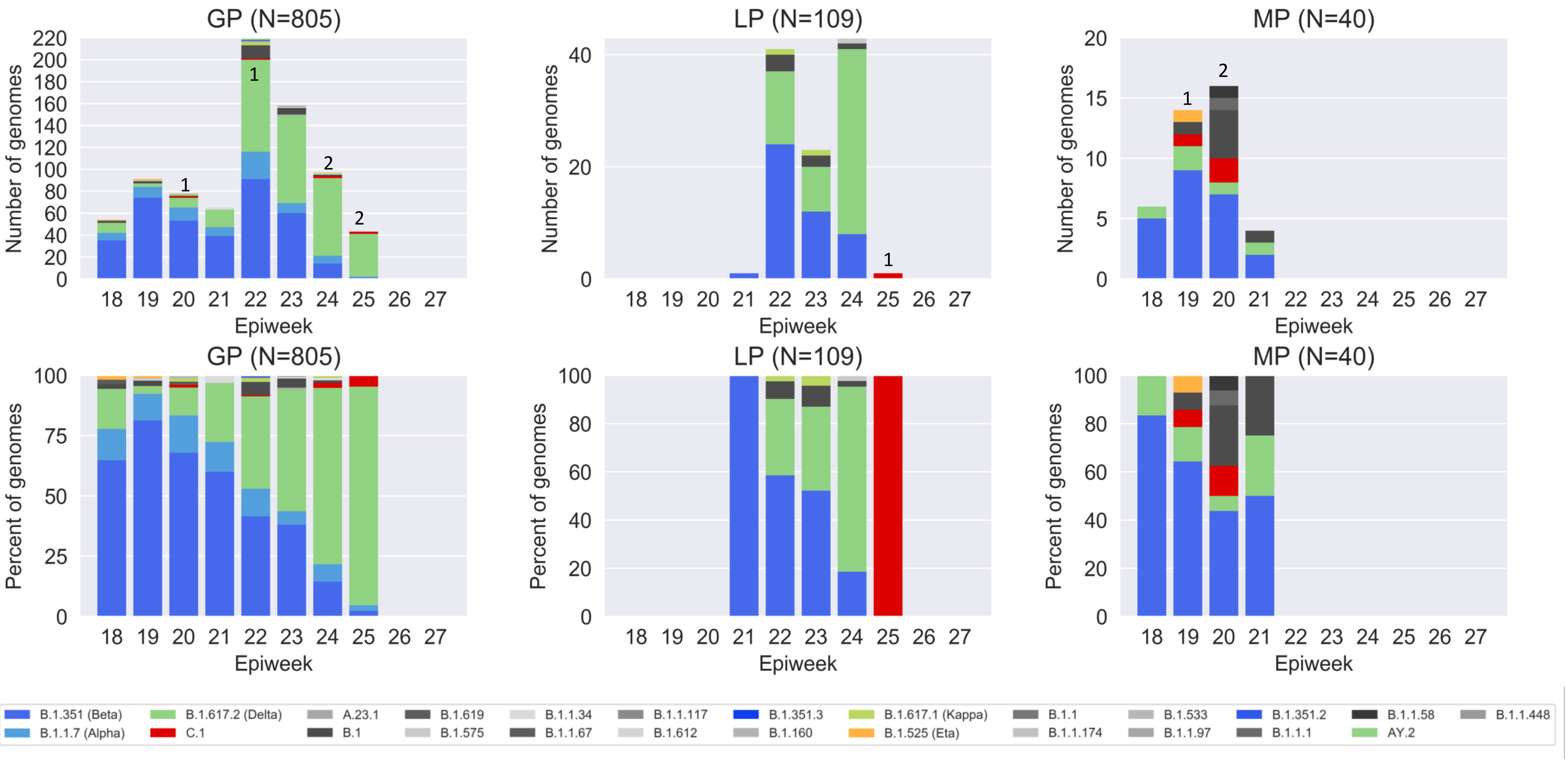
16 May 2021, GP

n=18 samples from
SA (MP, LP & GP)
England
Portugal
Switzerland
China

https://clades.nextstrain.org/tree

C.1 in May and June 2021 by epiweek

Total number of C.1 for each epiweek indicated above bar



Summary

- In June, Delta increases significantly and dominates in most provinces where recent data available.
- Delta remains dominant in July, but additional sequencing data required to confirm these estimates.
- Variant diversity appears to have decreased with the dominance of Delta.
- C.1 lineage, which was a dominant lineage prior to Beta dominance, has developed some concerning mutations (n=15 sequences).
  - Functional testing in progress (neutralization sensitivity and competition experiments)
  - Alerts to the WHO VEWG

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COVID Incident Management Team

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science & technology
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Science and Technology
REPUBLIC OF SOUTH AFRICA

AFRICA CDC
Centres for Disease Control and Prevention
Safeguarding Africa's Health

NRF National Research Foundation

saMRC advancinglife

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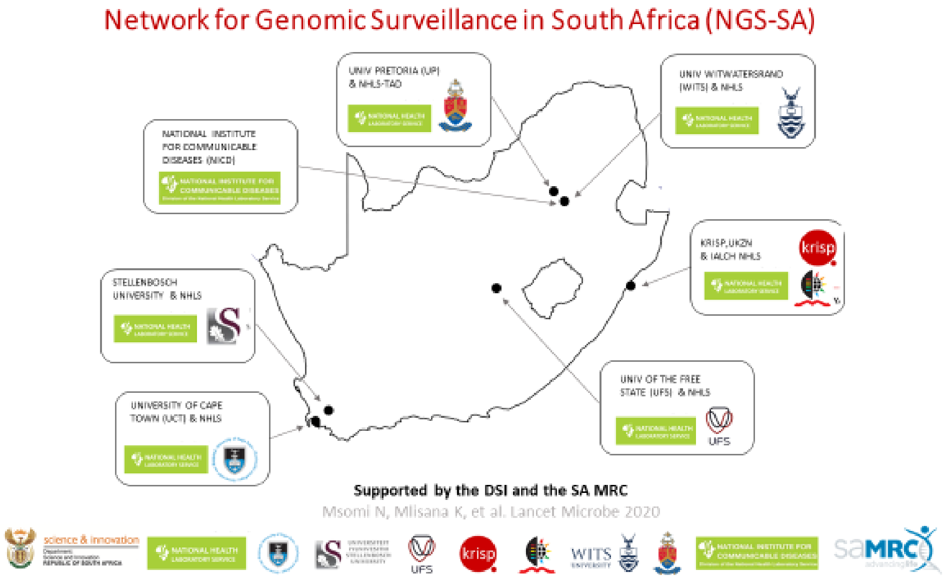
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

The Fleming Fund

Multi-institute, multi-disciplinary NGS team



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

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Simnikiwe Mayaphi
Terry Marshall
Warren Lowman
Zinhle Makatini

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 the NICD (or 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 (NICD 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.)