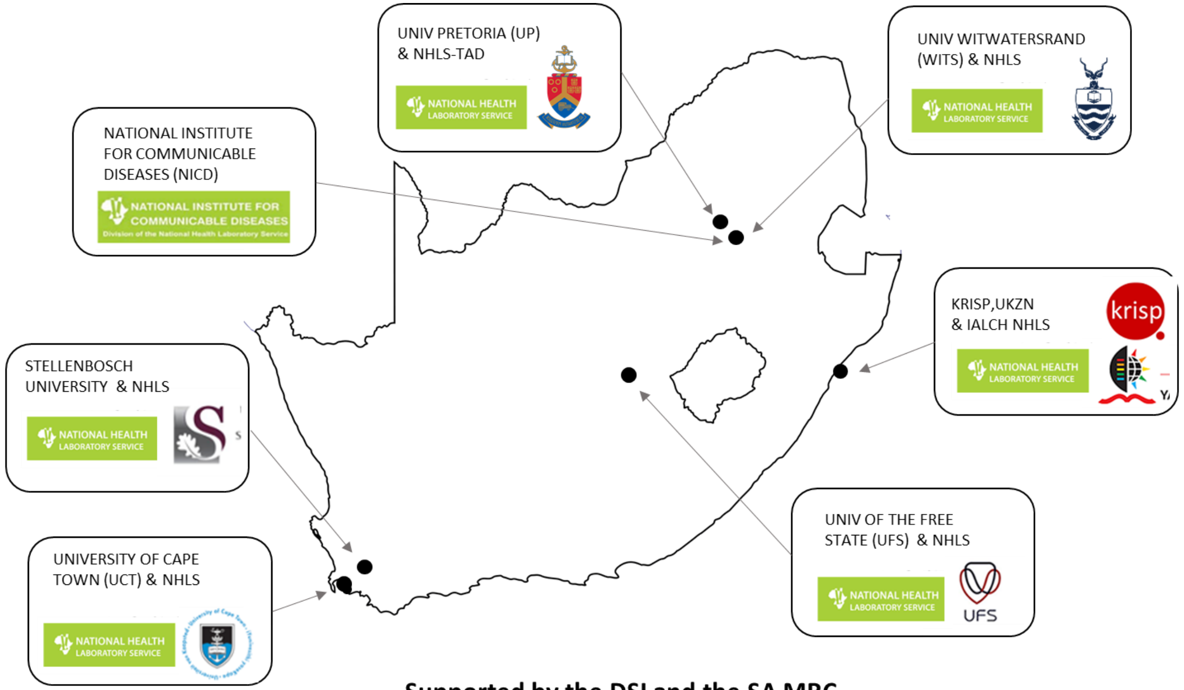
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update
09 September 2022



UNIV PRETORIA (UP) & NHLS-TAD

UNIV WITWATERSRAND (WITS) & NHLS

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES (NICD)

KRISP,UKZN & IALCH NHLS

STELLENBOSCH UNIVERSITY & NHLS

UNIV OF THE FREE STATE (UFS) & NHLS

UNIVERSITY OF CAPE TOWN (UCT) & NHLS

Supported by the DSI and the SA MRC

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

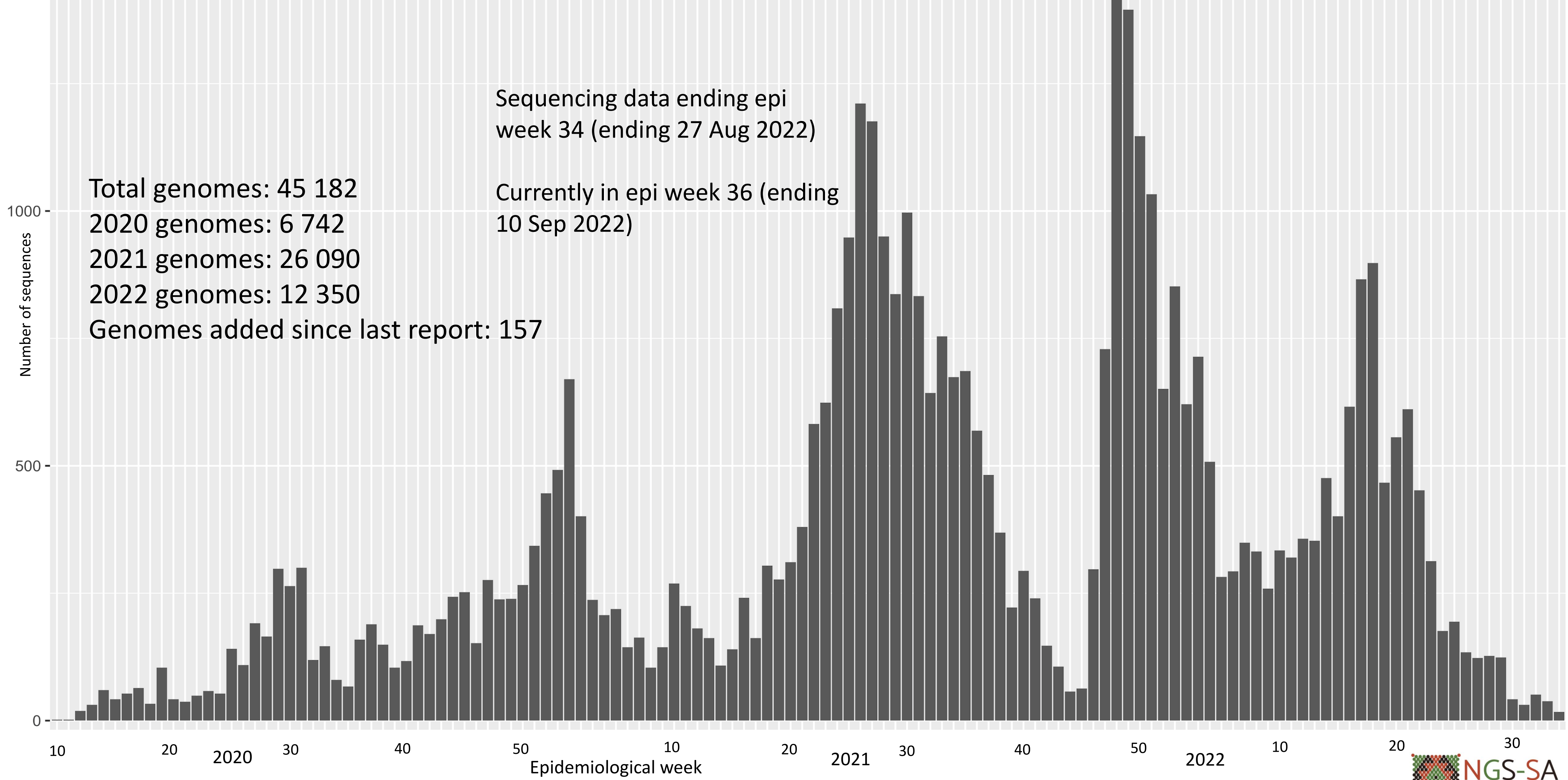
Prepared by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory (NHLS) on behalf of the Network for Genomics Surveillance in South Africa (NGS-SA)

The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 09 September 2022 at 13h34

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

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022
(N=45 182*)



Total genomes: 45 182
2020 genomes: 6 742
2021 genomes: 26 090
2022 genomes: 12 350
Genomes added since last report: 157

Sequencing data ending epi week 34 (ending 27 Aug 2022)

Currently in epi week 36 (ending 10 Sep 2022)

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

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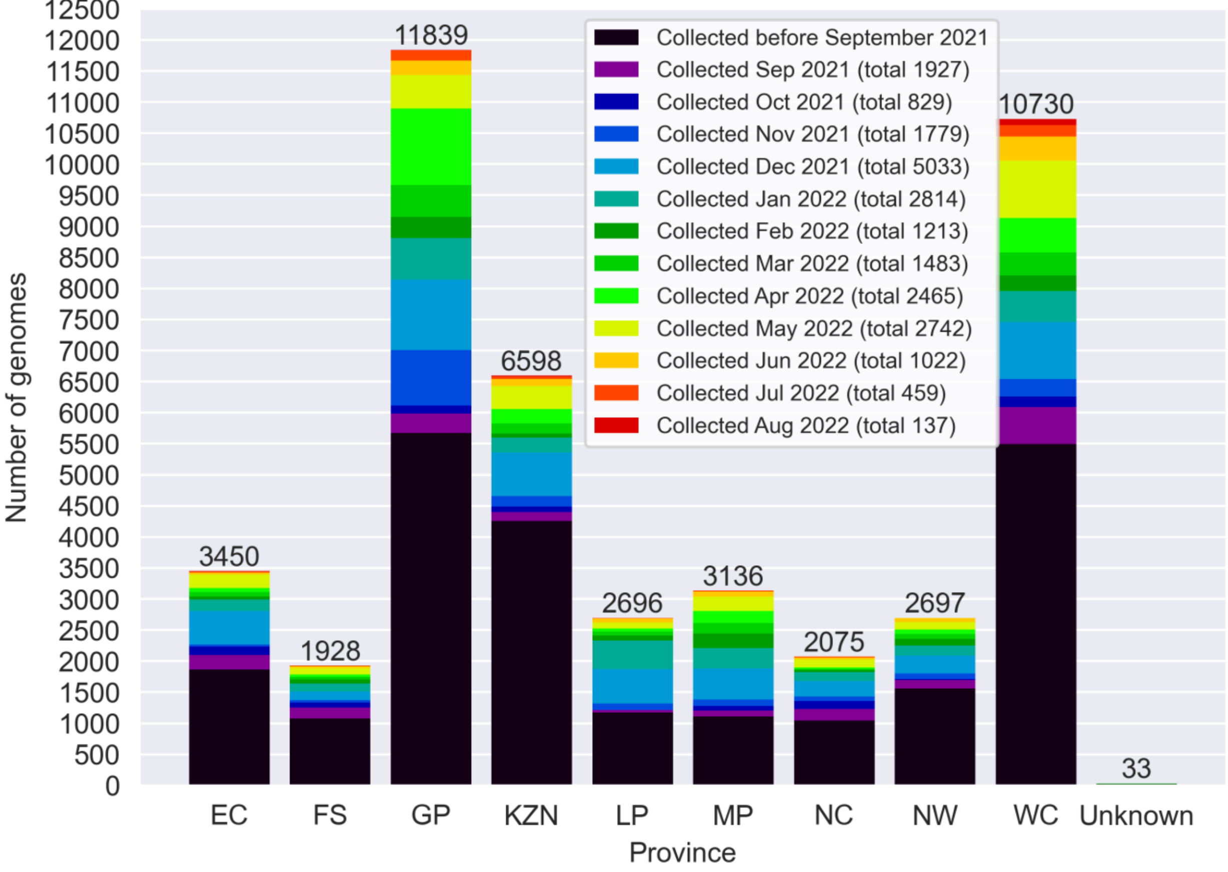
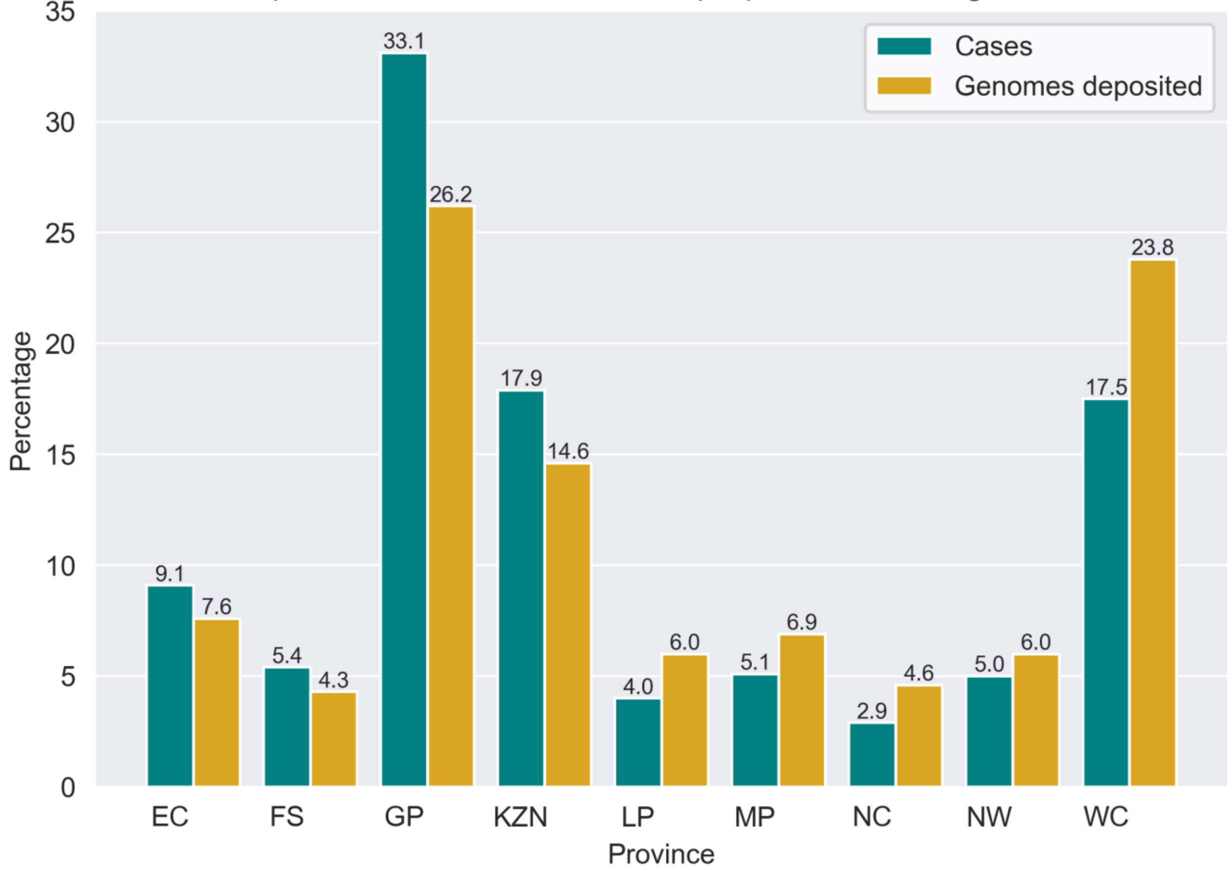
GISAID genomes vs total cases, 2020 – 2022 (N=45 182)


Provincial breakdown of genomes deposited into GISAID


Proportion of total cases versus proportion of total genomes

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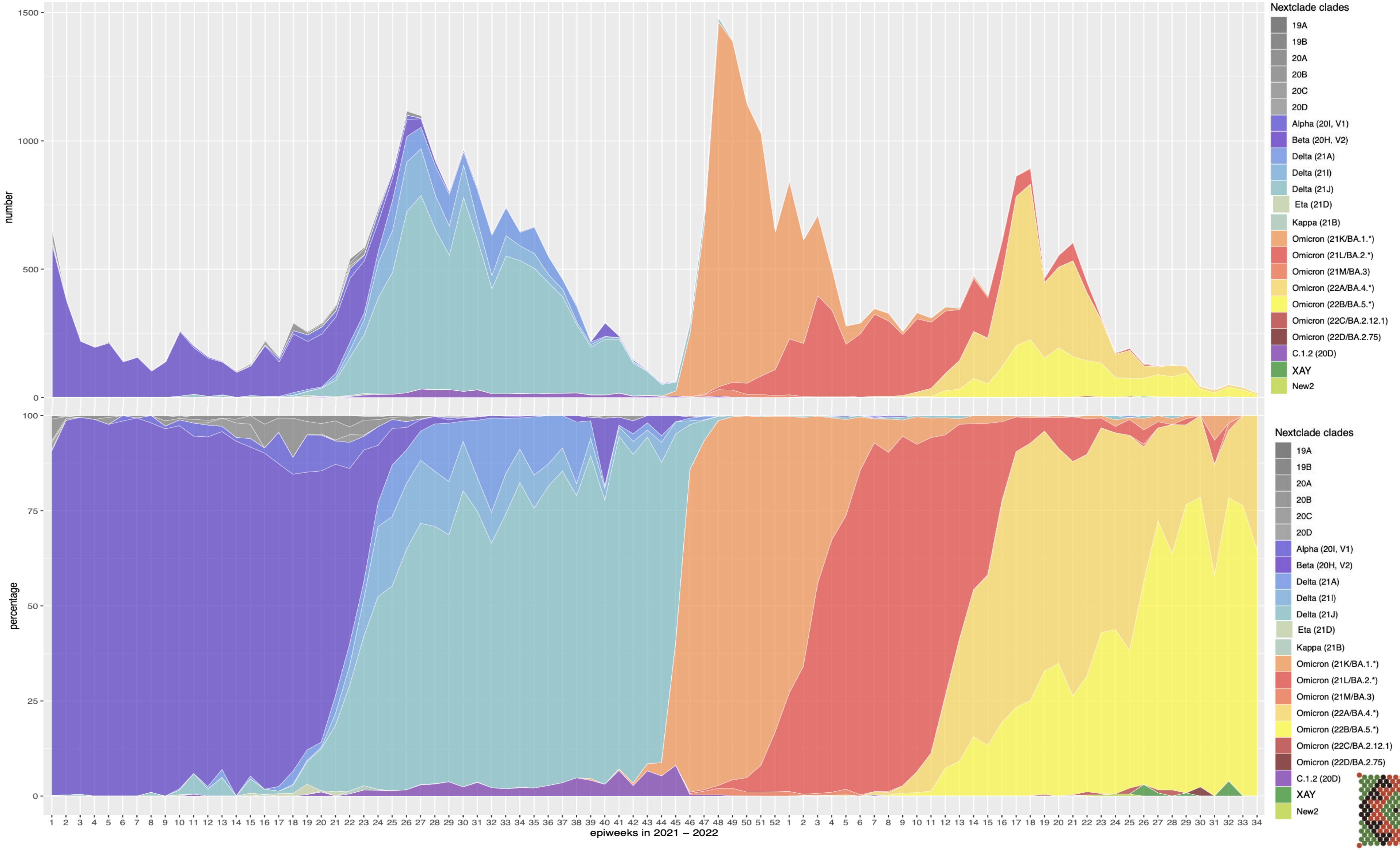
Number and percentage of clades by epiweek in South Africa, 2021 – 2022 (38 347*)



Sequencing data ending epi week 34 (ending 27 Aug 2022)

Currently in epi week 36 (ending 10 Sep 2022)

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

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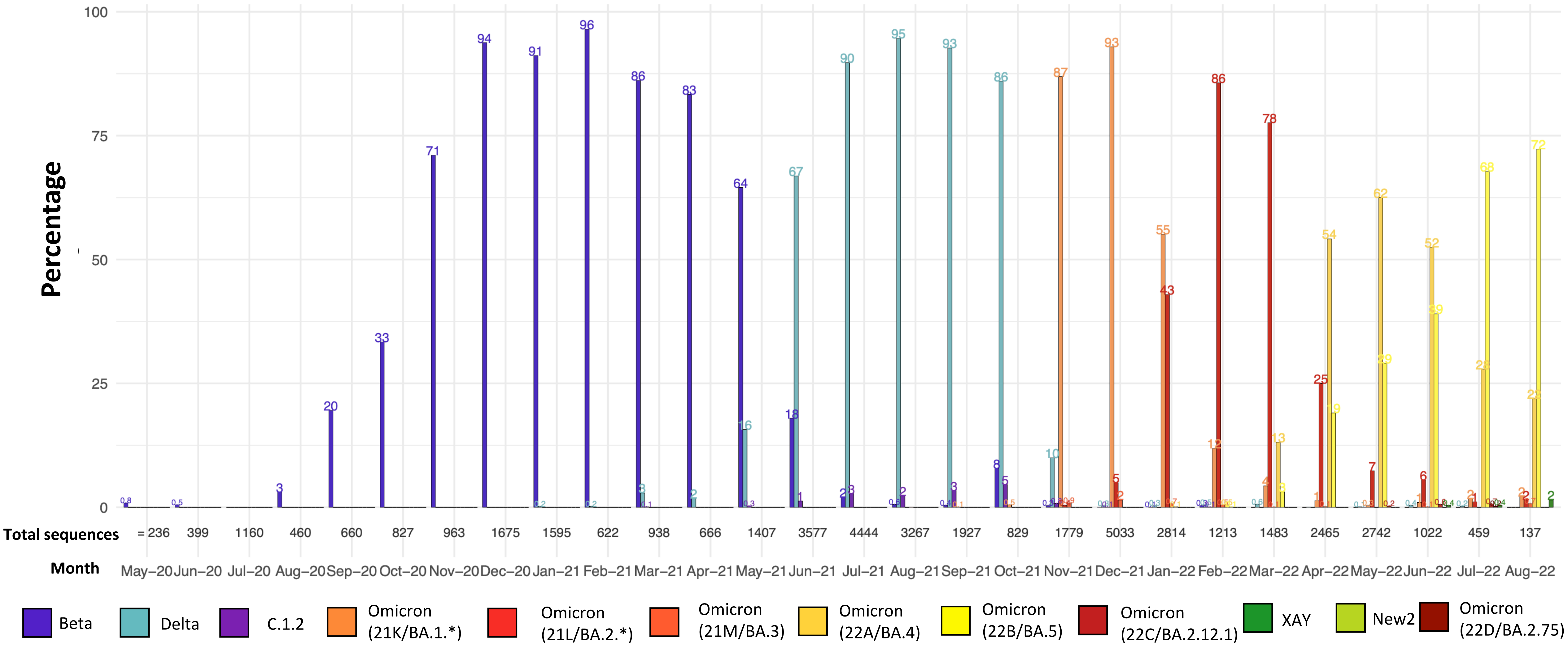
Detection Rates: Beta, Delta, C.1.2 and Omicron

Detection rates of variants being monitored in South Africa



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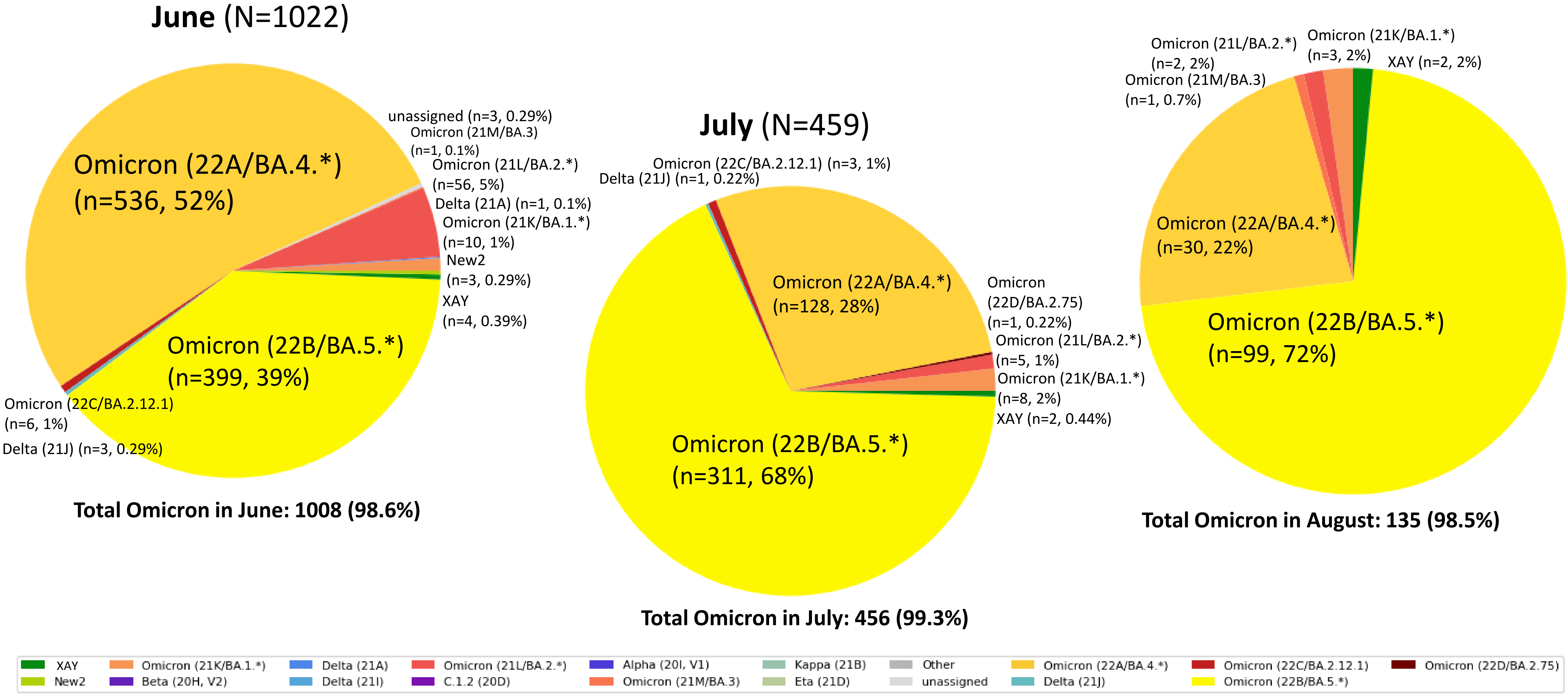
*Bars represent percentage prevalence of variant for the month; total number sequences collected for the month are given below the bar

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

June – August 2022



June (N=1022)

Total Omicron in June: 1008 (98.6%)

July (N=459)

Total Omicron in July: 456 (99.3%)

August (N=137)

Total Omicron in August: 135 (98.5%)

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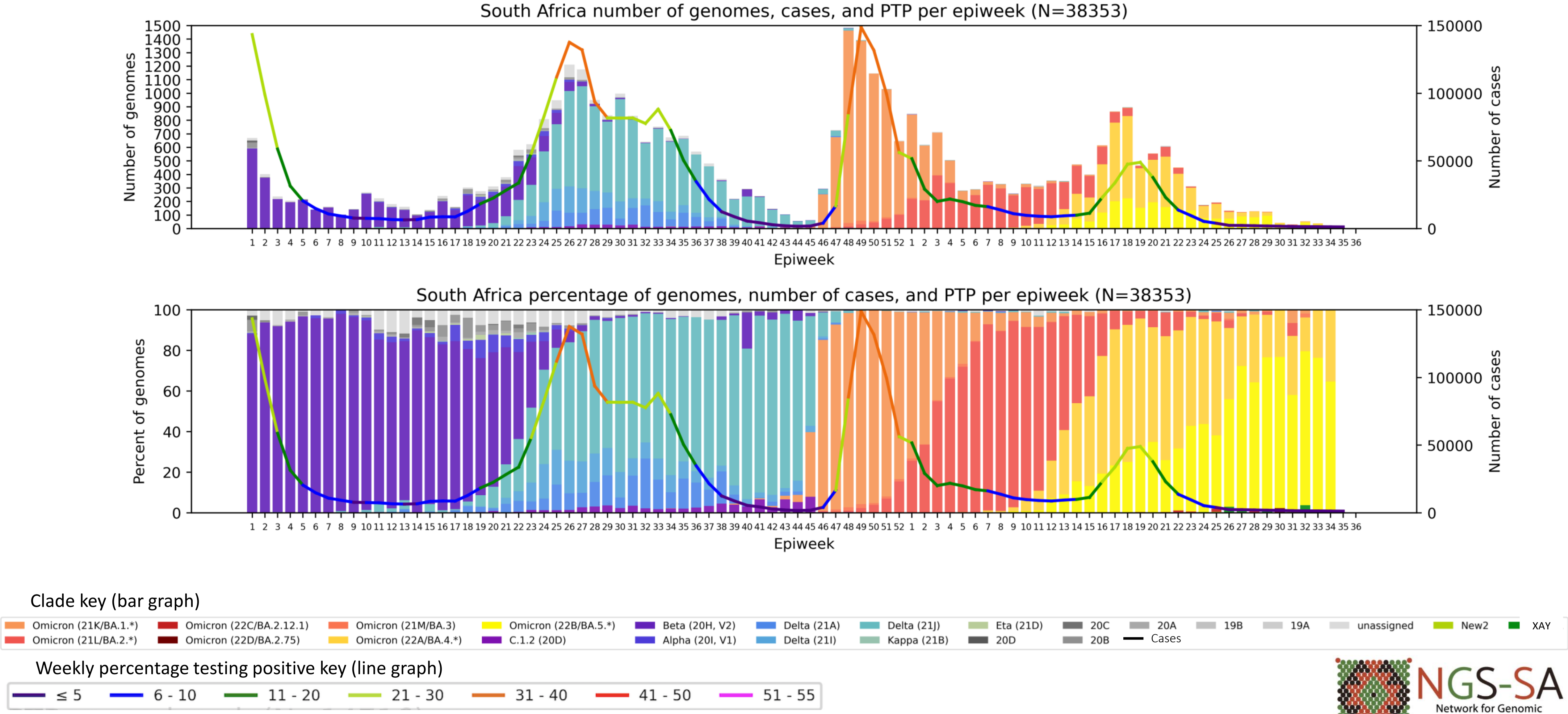
South Africa, 2021-2022, n = 38 353*



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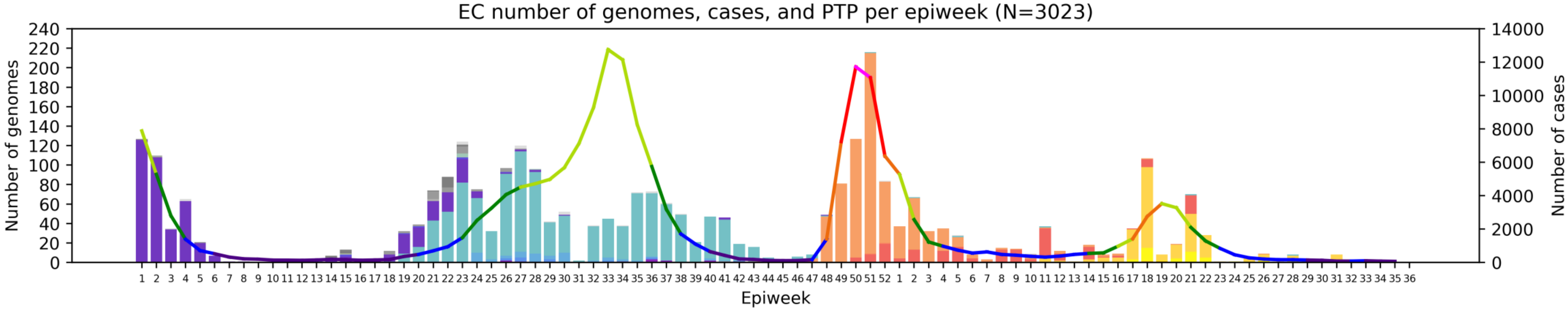
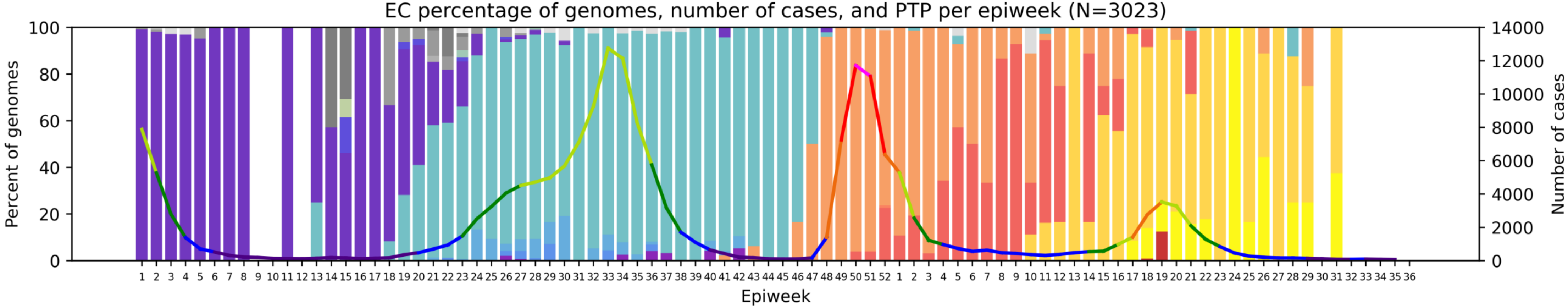
*Excludes sequences missing collection dates, as well as those collected January 1st and 2nd 2021 as they are part of epiweek 53 of 2020.

Eastern Cape Province, 2021-2022, n = 3023

Genomes added since last report: 12*





Clade key (bar graph)

🟧 Omicron (21K/BA.1.*)
🟥 Omicron (21L/BA.2.*)
🟥 Omicron (22C/BA.2.12.1)
🟫 Omicron (22D/BA.2.75)
🟧 Omicron (21M/BA.3)
🟨 Omicron (22A/BA.4.*)
🟨 Omicron (22B/BA.5.*)
🟪 C.1.2 (20D)
🟪 Beta (20H, V2)
🟦 Alpha (20I, V1)
🟦 Delta (21A)
🟦 Delta (21I)
🟦 Delta (21J)
🟩 Kappa (21B)
🟩 Eta (21D)
⬛ 20D
⬛ 20C
⬜ 20B
⬜ 20A
⬜ 19B
⬜ 19A
⬜ unassigned
🟩 New2
🟩 XAY

Weekly percentage testing positive key (line graph)

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

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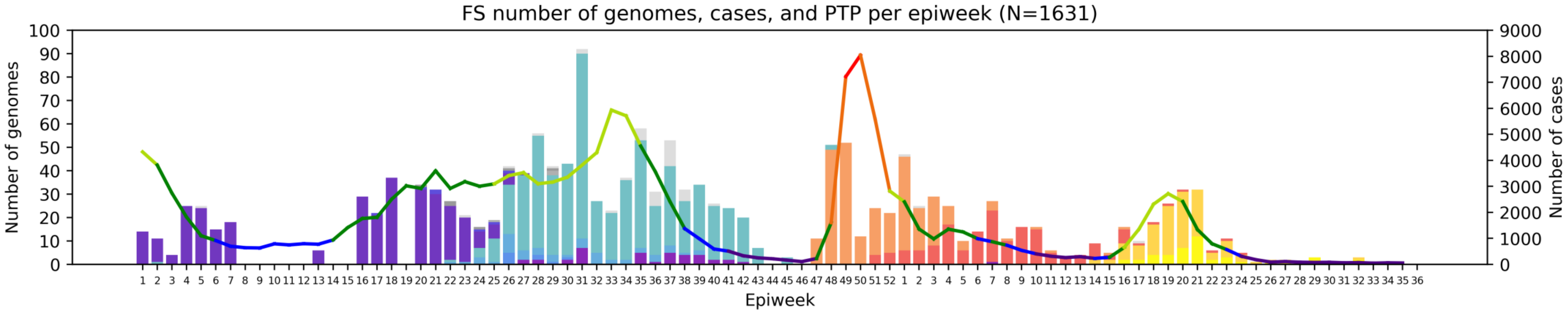
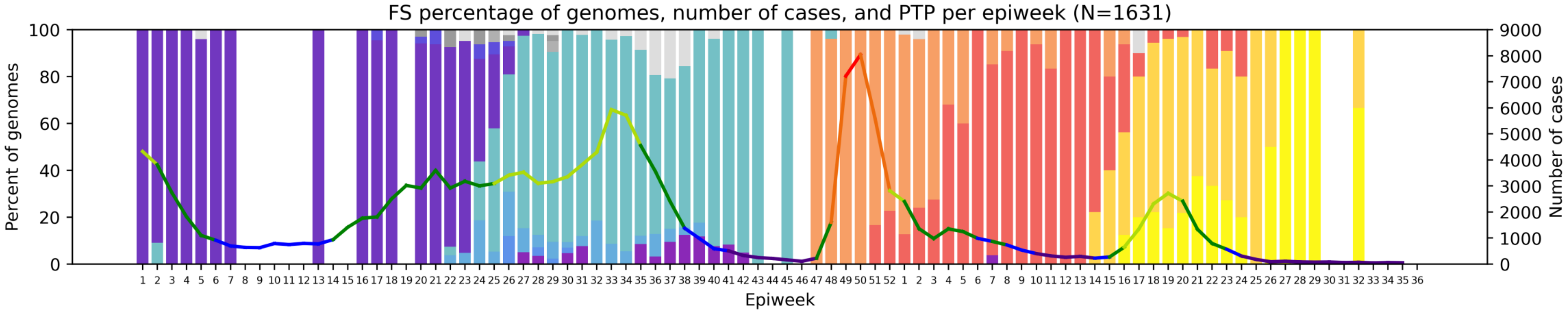
*May include genomes from 2020 which are not pictured here and are not included in the slide total.

Free State Province, 2021-2022, n = 1631

Genomes added since last report: 4*


FS number of genomes, cases, and PTP per epiweek (N=1631)


FS percentage of genomes, number of cases, and PTP per epiweek (N=1631)

Clade key (bar graph)

- Omicron (21K/BA.1.*)
- Omicron (21L/BA.2.*)
- Omicron (22C/BA.2.12.1)
- Omicron (22D/BA.2.75)
- Omicron (21M/BA.3)
- Omicron (22A/BA.4.*)
- Omicron (22B/BA.5.*)
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- Delta (21J)
- Kappa (21B)
- Eta (21D)
- 20D
- 20C
- 20B
- 20A
- 19B
- 19A
- unassigned
- New2
- XAY

Weekly percentage testing positive key (line graph)

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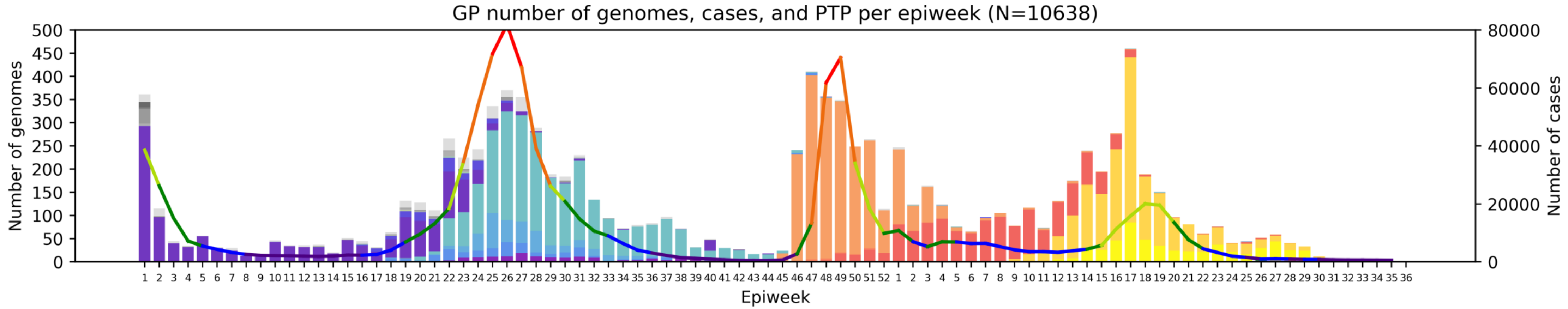
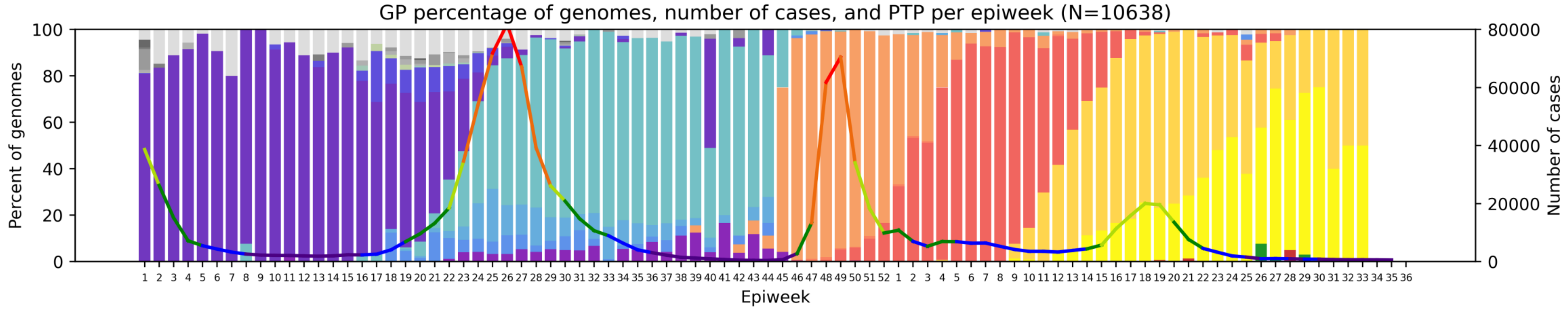
Gauteng Province, 2021-2022, n = 10 638

Genomes added since last report: 61*



GP number of genomes, cases, and PTP per epiweek (N=10638)



GP percentage of genomes, number of cases, and PTP per epiweek (N=10638)

Clade key (bar graph)

- Omicron (21K/BA.1.*)
- Omicron (21L/BA.2.*)
- Omicron (22C/BA.2.12.1)
- Omicron (22D/BA.2.75)
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- 20C
- 20B
- 20A
- 19B
- 19A
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Weekly percentage testing positive key (line graph)

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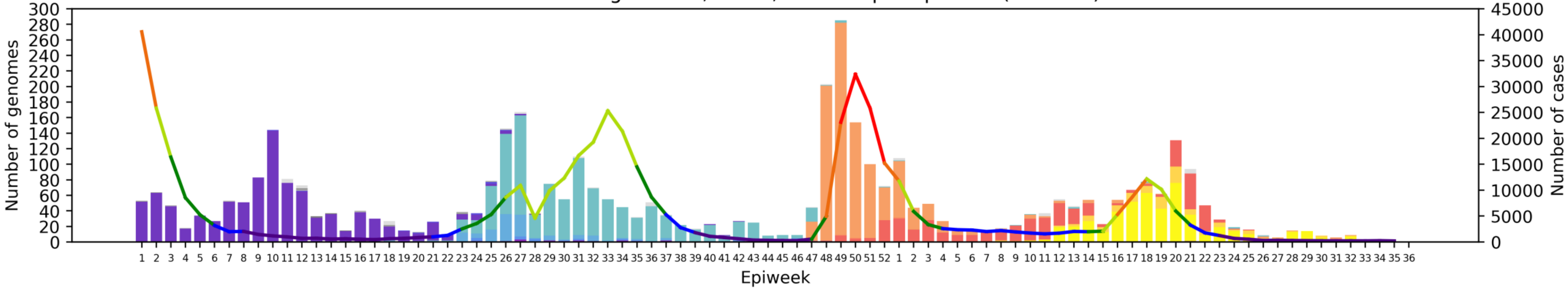
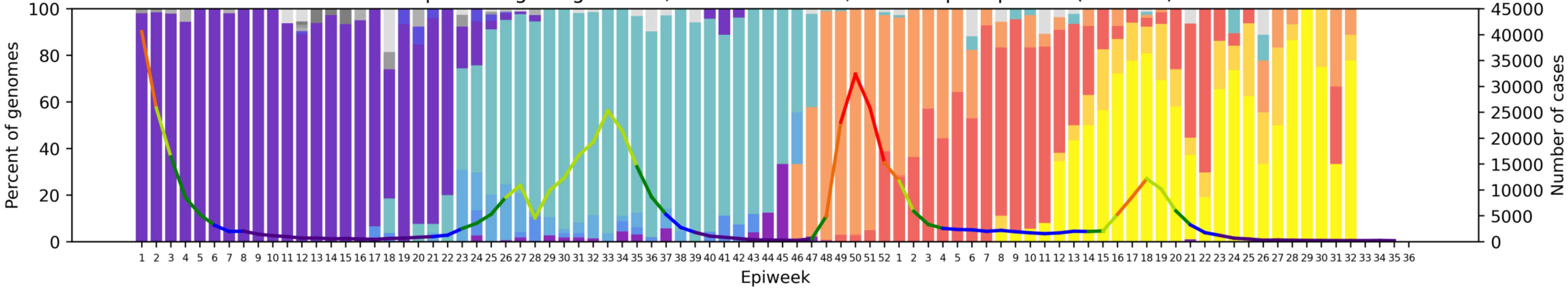
KwaZulu-Natal Province, 2021-2022, n = 4243

Genomes added since last report: 2*

KZN number of genomes, cases, and PTP per epiweek (N=4243)



KZN percentage of genomes, number of cases, and PTP per epiweek (N=4243)



Clade key (bar graph)

- Omicron (21K/BA.1.*)
- Omicron (21L/BA.2.*)
- Omicron (22C/BA.2.12.1)
- Omicron (22D/BA.2.75)
- Omicron (21M/BA.3)
- Omicron (22A/BA.4.*)
- Omicron (22B/BA.5.*)
- C.1.2 (20D)
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- Delta (21J)
- Kappa (21B)
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- 20B
- 20A
- 19B
- 19A
- unassigned
- New2
- XAY

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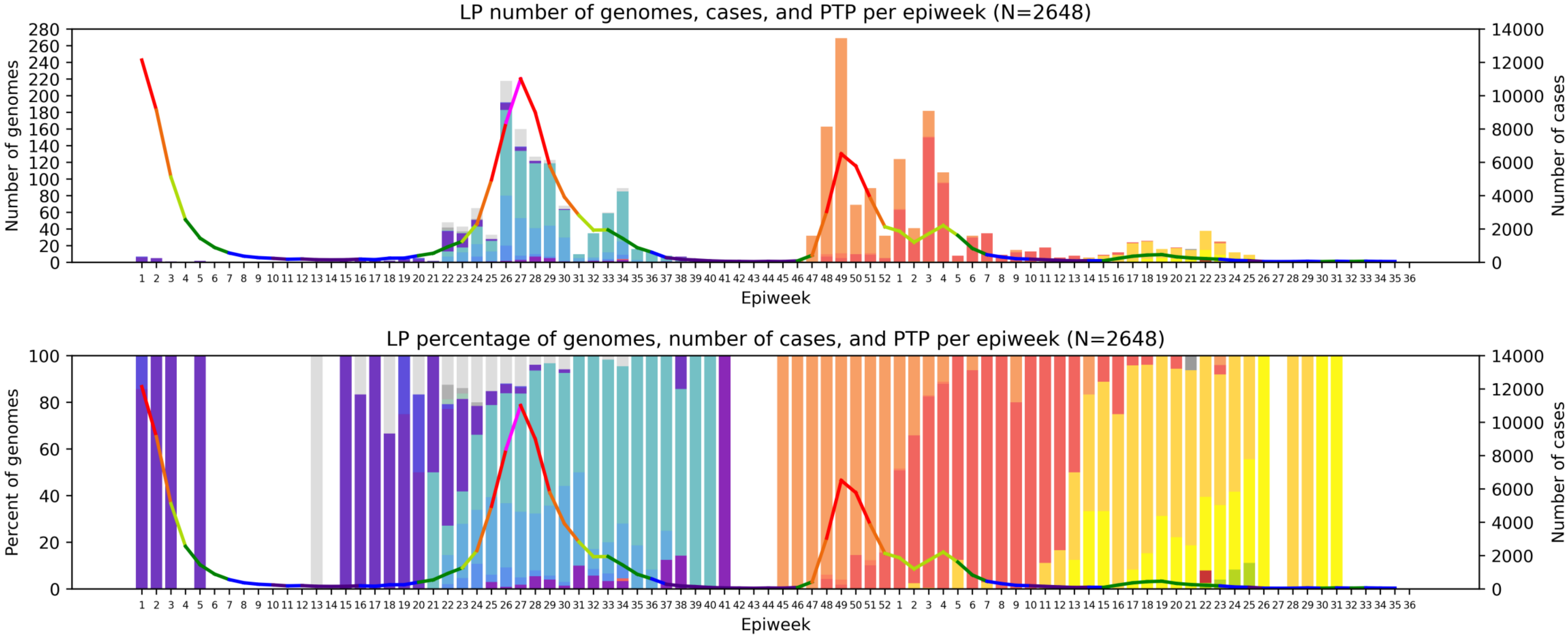
Limpopo Province, 2021-2022, n = 2648

Genomes added since last report: 14*



Clade key (bar graph)

- 🟧 Omicron (21K/BA.1.*)
- 🟥 Omicron (21L/BA.2.*)
- 🟥 Omicron (22C/BA.2.12.1)
- 🟫 Omicron (22D/BA.2.75)
- 🟧 Omicron (21M/BA.3)
- 🟨 Omicron (22A/BA.4.*)
- 🟨 Omicron (22B/BA.5.*)
- 🟪 C.1.2 (20D)
- 🟪 Beta (20H, V2)
- 🟦 Alpha (20I, V1)
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- ⬛ 20D
- ⬛ 20C
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- ⬜ unassigned
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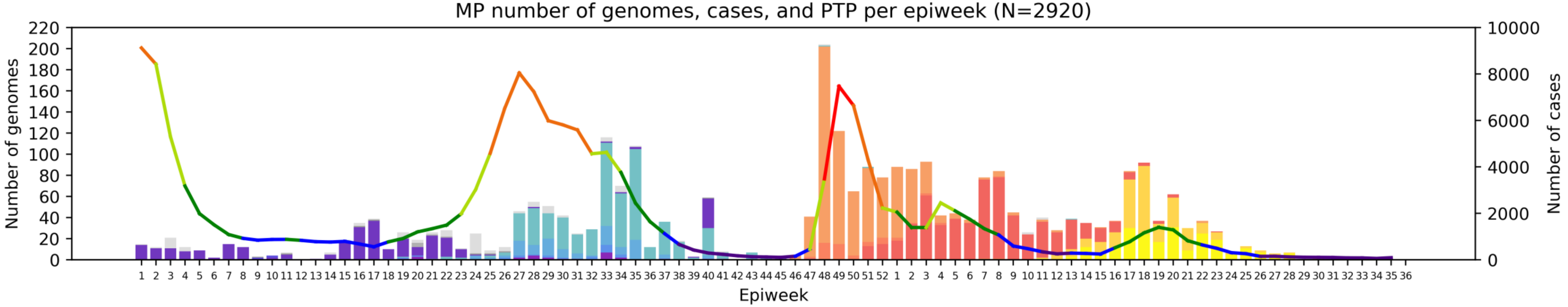
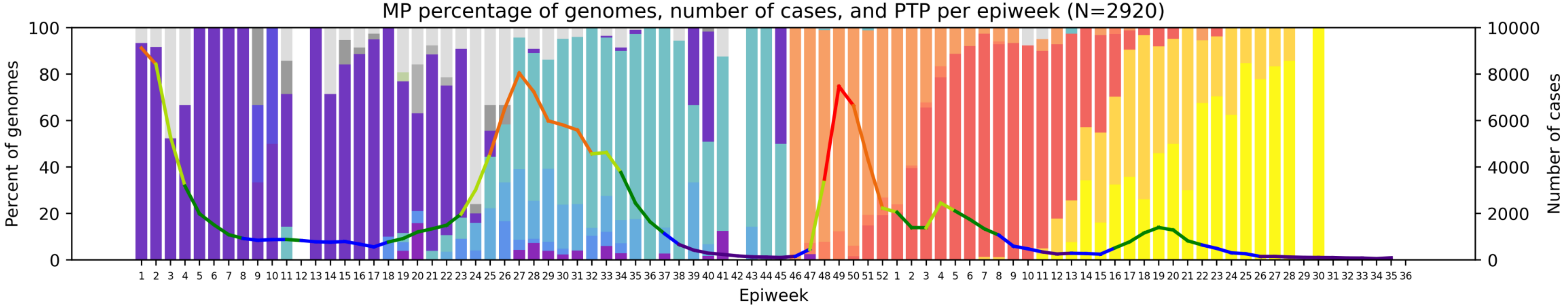
Mpumalanga Province, 2021-2022, n = 2920

Genomes added since last report: 28*


MP number of genomes, cases, and PTP per epiweek (N=2920)


MP percentage of genomes, number of cases, and PTP per epiweek (N=2920)

Clade key (bar graph)

- Omicron (21K/BA.1.*)
- Omicron (21L/BA.2.*)
- Omicron (22C/BA.2.12.1)
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- 20C
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Weekly percentage testing positive key (line graph)

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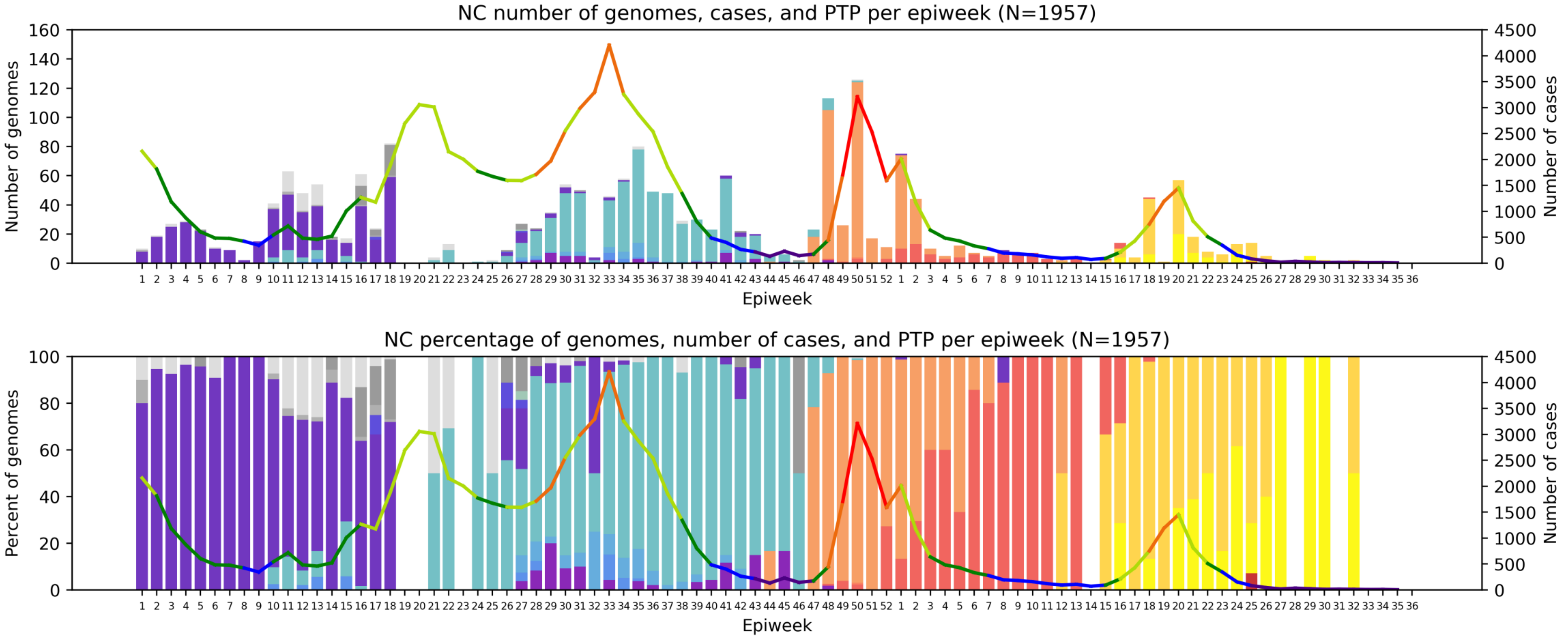
Northern Cape Province, 2021-2022, n = 1957

Genomes added since last report: 2*


NC number of genomes, cases, and PTP per epiweek (N=1957)

NC percentage of genomes, number of cases, and PTP per epiweek (N=1957)

Clade key (bar graph)

- 🟧 Omicron (21K/BA.1.*)
- 🟥 Omicron (21L/BA.2.*)
- 🟥 Omicron (22C/BA.2.12.1)
- 🟥 Omicron (22D/BA.2.75)
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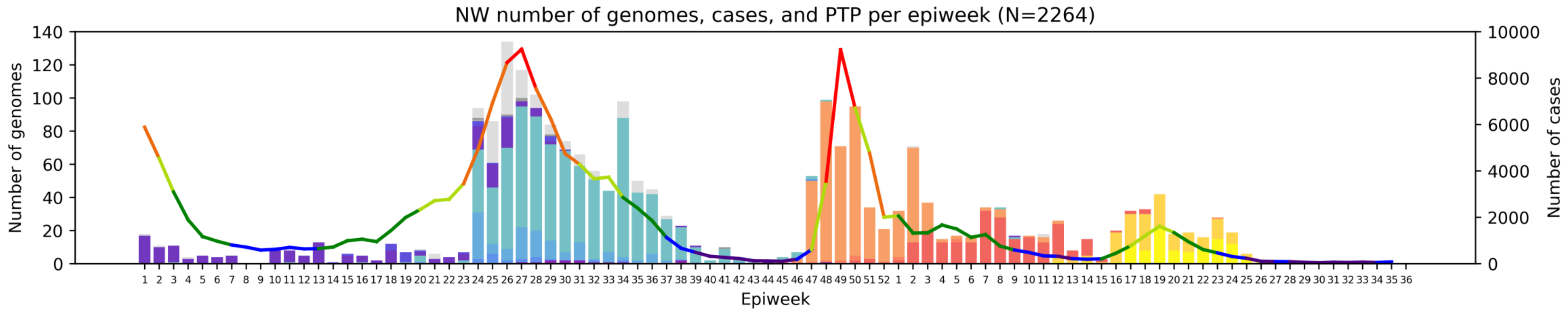
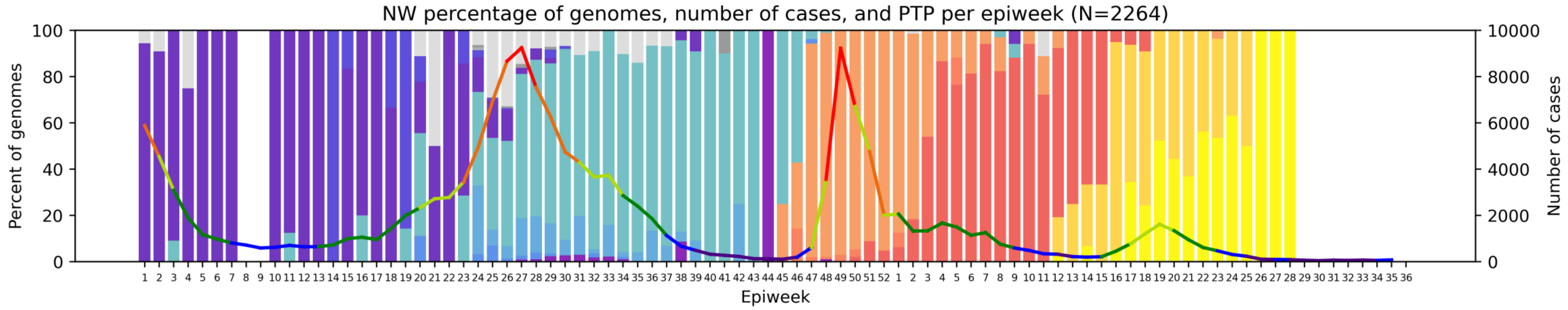
North West Province, 2021-2022, n = 2264

Genomes added since last report: 6*


NW number of genomes, cases, and PTP per epiweek (N=2264)


NW percentage of genomes, number of cases, and PTP per epiweek (N=2264)

Clade key (bar graph)

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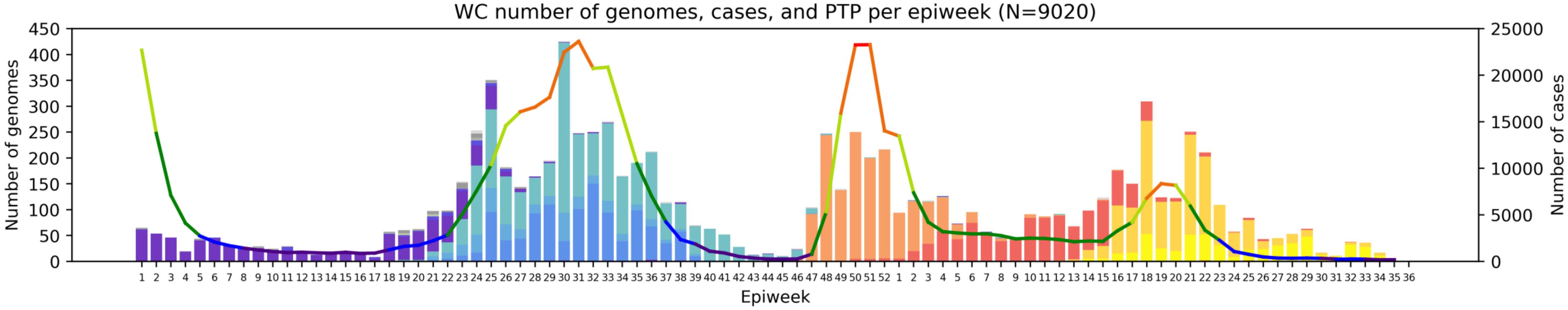
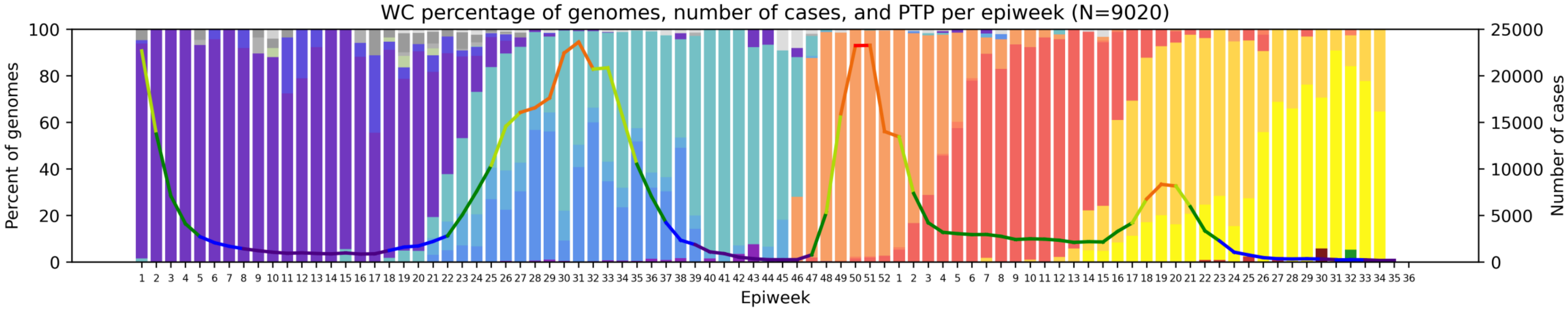
Western Cape Province, 2021-2022, n = 9020

Genomes added since last report: 28*


WC number of genomes, cases, and PTP per epiweek (N=9020)


WC percentage of genomes, number of cases, and PTP per epiweek (N=9020)

Clade key (bar graph)

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Summary

- **Sequencing update**
  - All provinces have sequences for June and July. Only the Eastern Cape and North West do not have August data.
  - Omicron dominated in June (99%) and July (99%), with BA.4 and BA.5 dominant.
  - In August Omicron makes up 99% of sequences, with BA.5 dominant (72%).
- **N=12 sequences with novel mutational profile**
  - The New1 cluster (n = 8, predominantly from Gauteng) has been designated “XAY” while New2 cluster’s numbers (n = 4) are still too low for designation[1].
  - No new sequences detected since the previous report.
- **Variant of Concern Omicron in South Africa**
  - Dominates 2022 sequencing data at >98% of genomes.
  - While BA.1 was the predominant lineage in January (55%), BA.2 dominated in February (86%) and March (78%).
  - Omicron lineages BA.4 and BA.5 were dominant in April (73%), May (91%), June (91%), July (96%) and August (94%).
  - BA.2.12.1 was detected in South Africa at low prevalence in May, June and July (<1%)
  - BA.2.75 was detected for the first time in South Africa in July (n=1).
- Low frequency of previously circulating variants such as Delta still detected in recent data.

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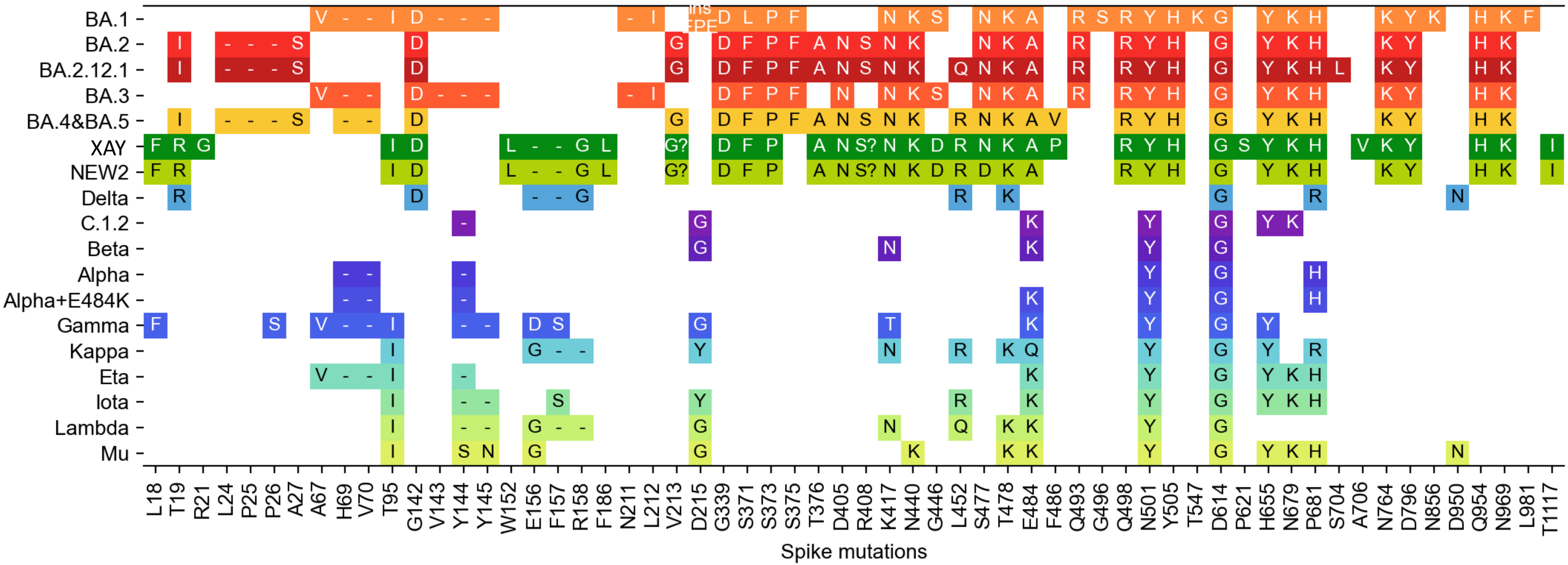
[1] https://github.com/cov-lineages/pango-designation/issues/844

Spike protein mutation* profile of Variants of Interest and Concern



	L18	T19	R21	L24	P25	P26	A27	A67	H69	V70	T95	G142	V143	Y144	Y145	W152	E156	F157	R158	F186
BA.1								V	-	-	I	D	-	-	-					
BA.2		I		-	-	-	S					D								
BA.2.12.1		I		-	-	-	S					D								
BA.3								V	-	-		D	-	-	-					
BA.4&BA.5		I		-	-	-	S		-	-		D								
XAY	F	R	G								I	D				L	-	-	G	L
NEW2	F	R									I	D				L	-	-	G	L
Delta		R										D					-	-	G	
C.1.2														-						
Beta																				
Alpha									-	-				-						
Alpha+E484K									-	-				-						
Gamma	F					S		V	-	-	I			-	-		D	S		
Kappa											I						G	-	-	
Eta								V	-	-	I			-						
Iota											I			-	-			S		
Lambda											I			-	-		G	-	-	
Mu											I			S	N		G			

	N211	L212	V213	D215	G339	S371	S373	S375	T376	D405	R408	K417	N440	G446	L452	S477	T478	E484	F486	Q493
BA.1	-	I		ins EPE	D	L	P	F				N	K	S		N	K	A		R
BA.2			G		D	F	P	F	A	N	S	N	K			N	K	A		R
BA.2.12.1			G		D	F	P	F	A	N	S	N	K		Q	N	K	A		R
BA.3	-	I			D	F	P	F		N		N	K	S		N	K	A		R
BA.4&BA.5			G		D	F	P	F	A	N	S	N	K		R	N	K	A	V	
XAY			G?		D	F	P		A	N	S?	N	K	D	R	N	K	A	P	
NEW2			G?		D	F	P		A	N	S?	N	K	D	R	D	K	A		
Delta															R		K			
C.1.2				G														K		
Beta				G								N						K		
Alpha																				
Alpha+E484K																		K		
Gamma				G								T						K		
Kappa				Y								N			R		K	Q		
Eta																		K		
Iota				Y											R			K		
Lambda				G								N			Q		K	K		
Mu				G									K				K	K		

	G496	Q498	N501	Y505	T547	D614	P621	H655	N679	P681	S704	A706	N764	D796	N856	D950	Q954	N969	L981	T1117
BA.1	S	R	Y	H	K	G		Y	K	H			K	Y	K		H	K	F	
BA.2		R	Y	H		G		Y	K	H			K	Y			H	K		
BA.2.12.1		R	Y	H		G		Y	K	H	L		K	Y			H	K		
BA.3		R	Y	H		G		Y	K	H			K	Y			H	K		
BA.4&BA.5		R	Y	H		G		Y	K	H			K	Y			H	K		
XAY		R	Y	H		G	S	Y	K	H		V	K	Y			H	K		I
NEW2		R	Y	H		G		Y	K	H			K	Y			H	K		I
Delta						G				R						N				
C.1.2			Y			G		Y	K											
Beta			Y			G														
Alpha			Y			G				H										
Alpha+E484K			Y			G				H										
Gamma			Y			G		Y												
Kappa			Y			G		Y		R										
Eta			Y			G		Y	K	H										
Iota			Y			G		Y	K	H										
Lambda			Y			G														
Mu			Y			G		Y	K	H						N				

- 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

*Only mutations present in Omicron, Delta, or the new SGTP sequences are pictured

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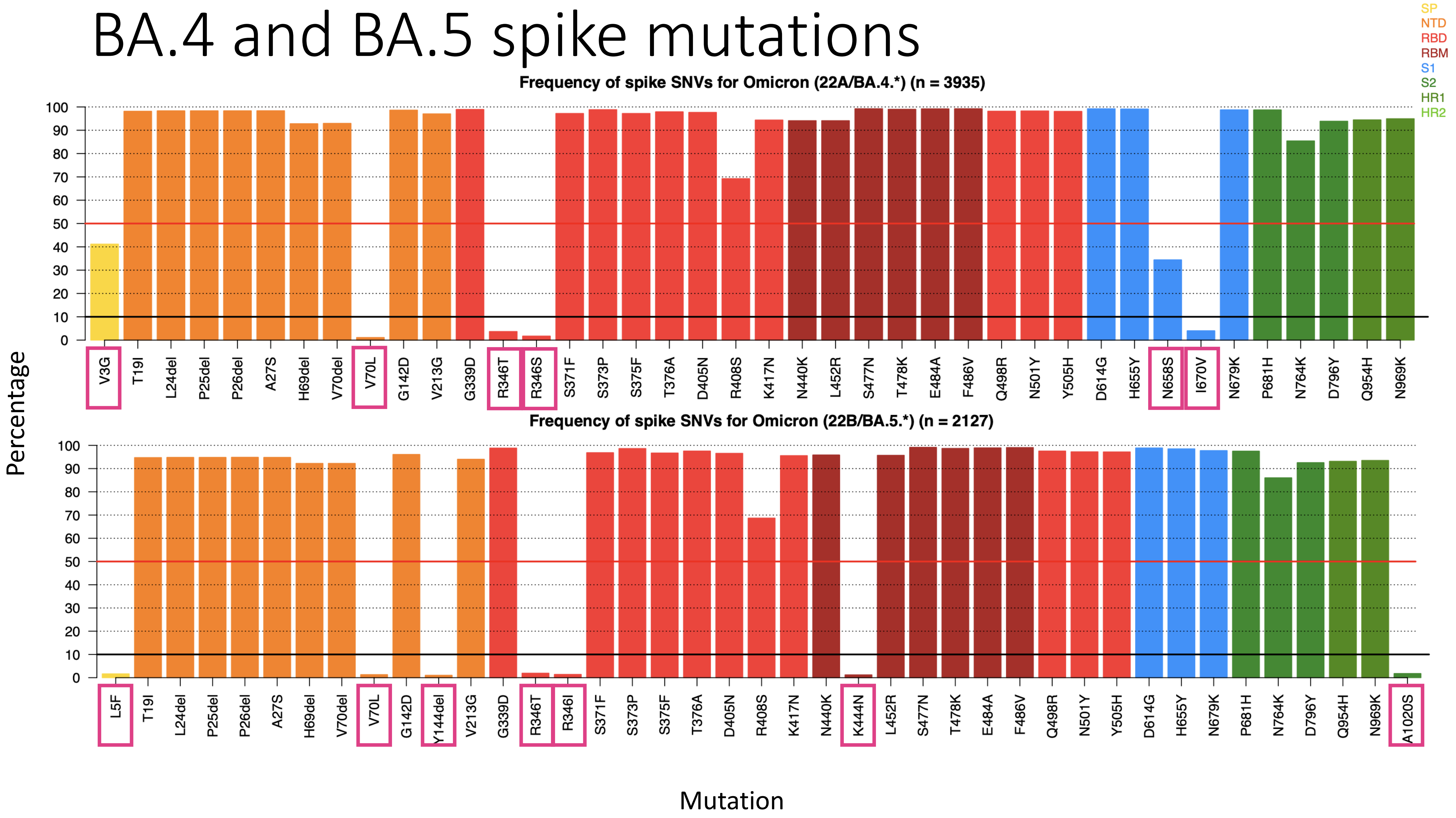
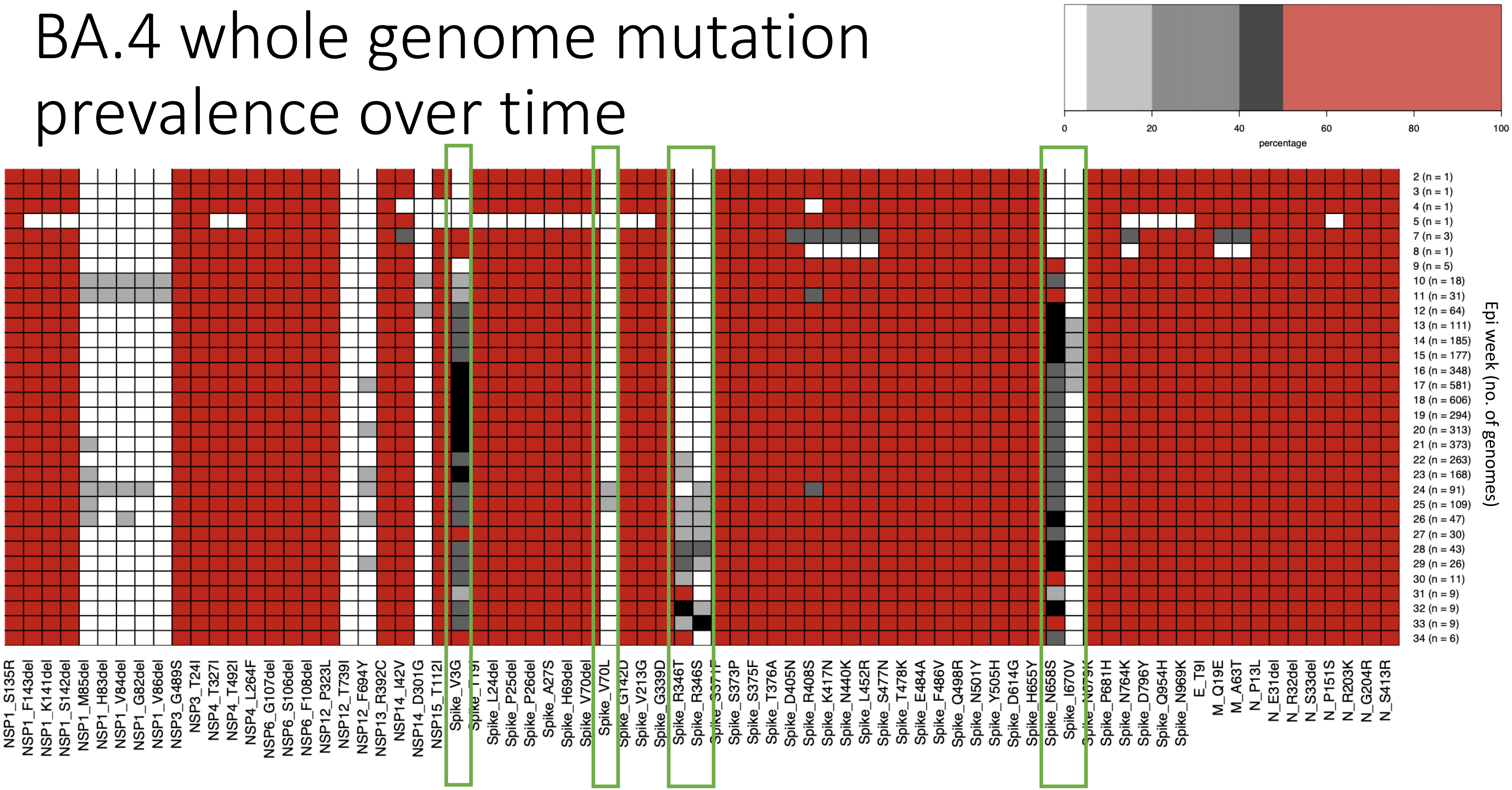
BA.4 and BA.5 spike mutations

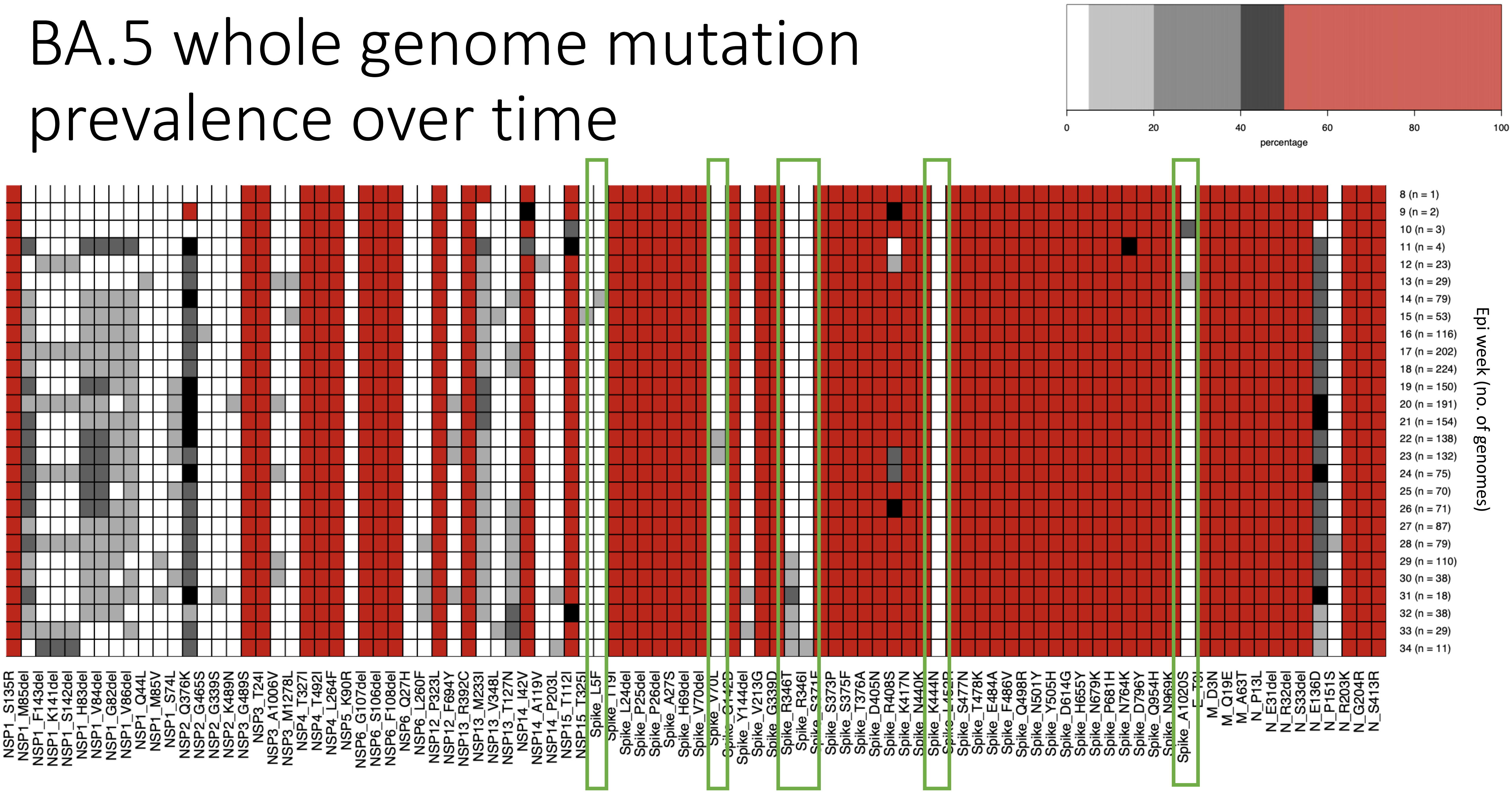

Frequency of spike SNVs for Omicron (22A/BA.4.*) (n = 3935)

Frequency of spike SNVs for Omicron (22B/BA.5.*) (n = 2127)

BA.4 whole genome mutation prevalence over time



BA.5 whole genome mutation prevalence over time



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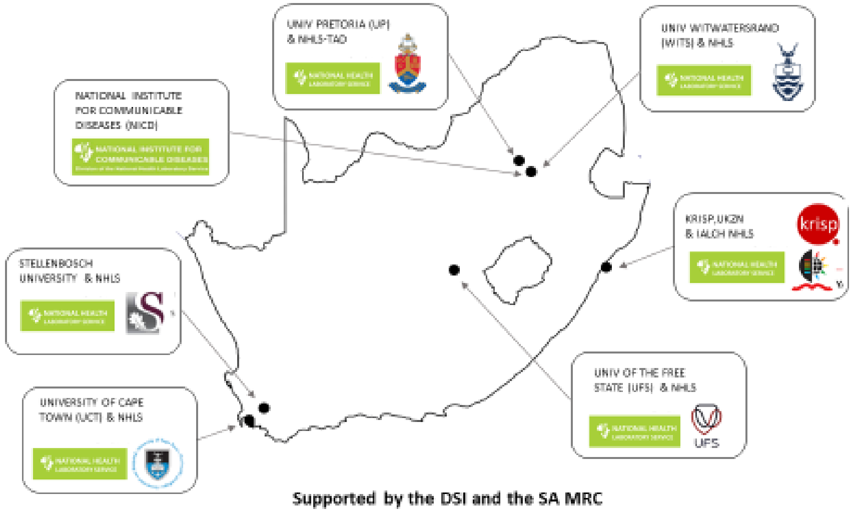

Supported by the DSI and the SA MRC

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

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This project has received funding from the European Union's Horizon Europe Research and Innovation Actions under grant No. 101046041

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Funders:
GIZ/BMBF: African Network for Improved diagnostics and epidemiology of common and emerging infectious agents (ANDEMIA)
G7 Global Health fund, Robert Koch Institute, Dr Fabian Leendertz

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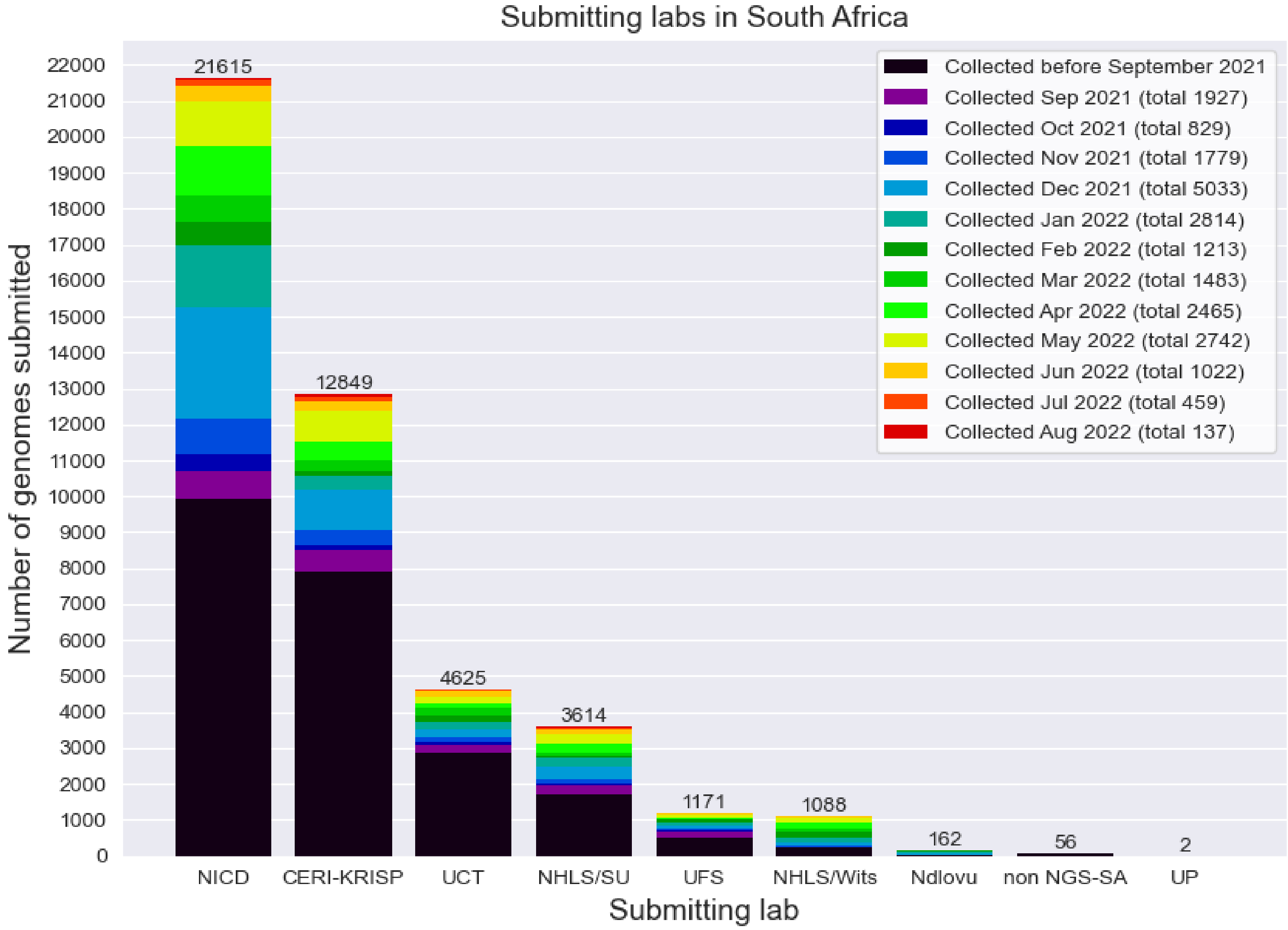
South African genomes submitted per submitting lab, 2020 - 2022 (N=45 182)



NGS-SA Labs

CERI: Centre for Epidemic Response and Innovation

KRISP: KZN Research Innovation and Sequencing Platform

NDLOVU: Ndlovu Research Laboratories

NICD: National Institute for Communicable Diseases

NHLS: National Health Laboratory Service

SU: Stellenbosch University

UCT: University of Cape Town

UFS: University of the Free State

UP: University of Pretoria

Multiple labs from NGS-SA and collaborating public and private laboratories are contributing to sequencing, both as originating and as submitting (pictured here) laboratories.

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Currently circulating Variants of Concern (VOC)

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Omicron*	B.1.1.529	GR/484A	21K, 21L, 21M, 22A, 22B, 22C, 22D	+S:R346K +S:L452X +S:F486V	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

* Includes BA.1, BA.2, BA.3, BA.4, BA.5 and descendent lineages. It also includes BA.1/BA.2 circulating recombinant forms such as XE. WHO emphasizes that these descendant lineages should be monitored as distinct lineages by public health authorities and comparative assessments of their virus characteristics should be undertaken.

° Only found in a subset of sequences

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 12 August 2022

Previously circulating Variants of Concern

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	United Kingdom, Sep-2020	VOC: 18-Dec-2020 Previous VOC: 09-Mar-2022
Beta	B.1.351	GH/501Y.V2	20H (V2)	South Africa, May-2020	VOC: 18-Dec-2020 Previous VOC: 09-Mar-2022
Gamma	P.1	GR/501Y.V3	20J (V3)	Brazil, Nov-2020	VOC: 11-Jan-2021 Previous VOC: 09-Mar-2022
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021 Previous VOC: 7-Jun-2022

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

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 12 August 2022

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.)