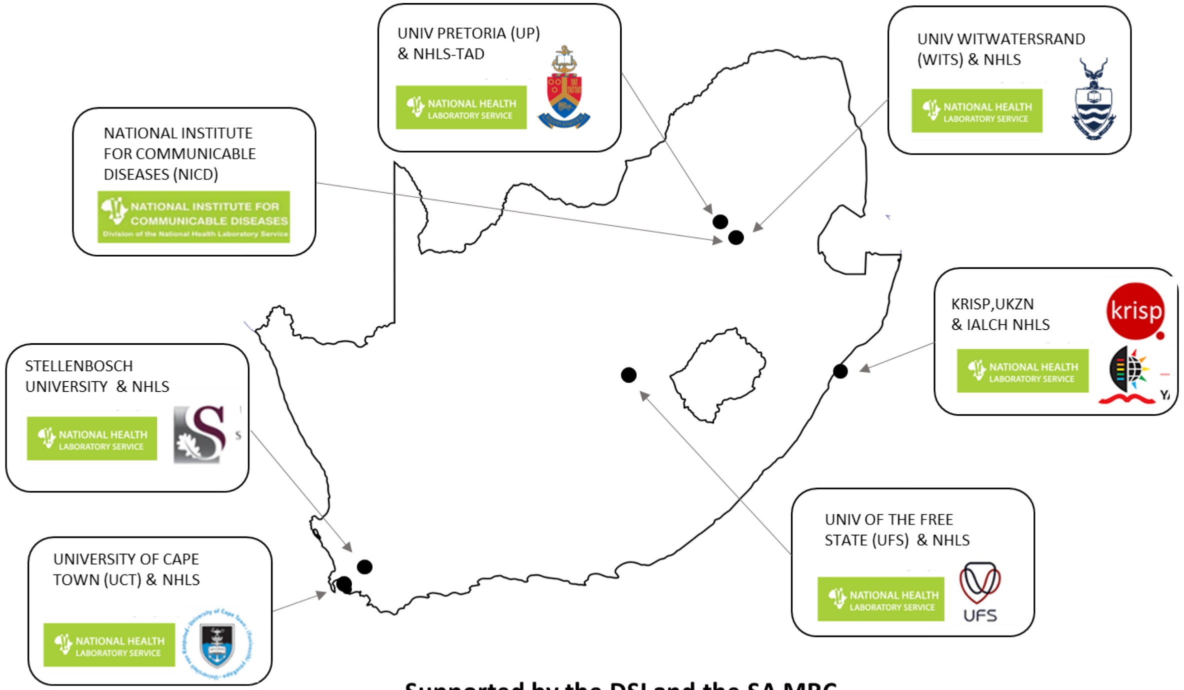
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update
25 November 2022



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)

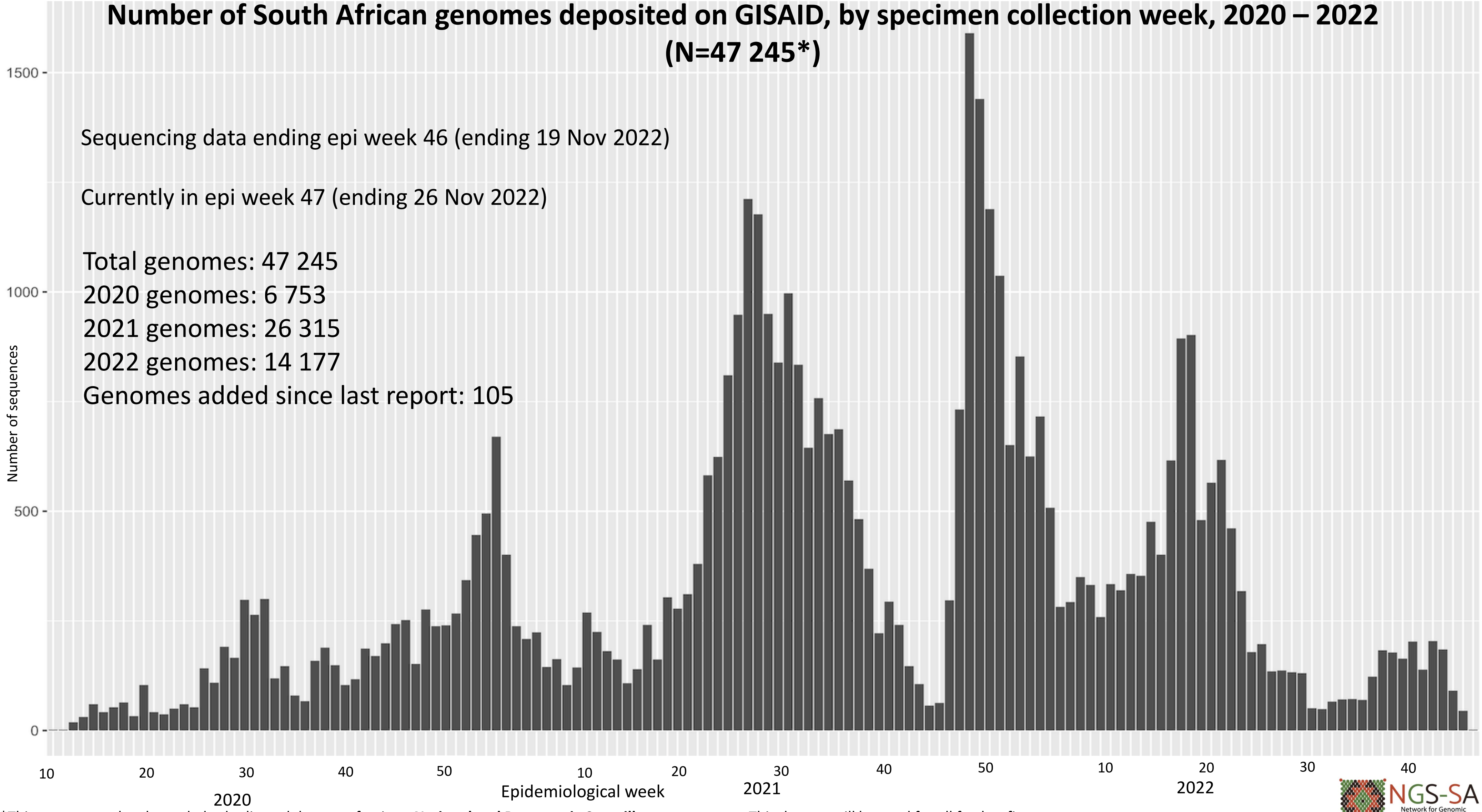
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 25 November 2022 at 15h00

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

Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022 (N=47 245*)



Sequencing data ending epi week 46 (ending 19 Nov 2022)

Currently in epi week 47 (ending 26 Nov 2022)

Total genomes: 47 245
2020 genomes: 6 753
2021 genomes: 26 315
2022 genomes: 14 177
Genomes added since last report: 105

*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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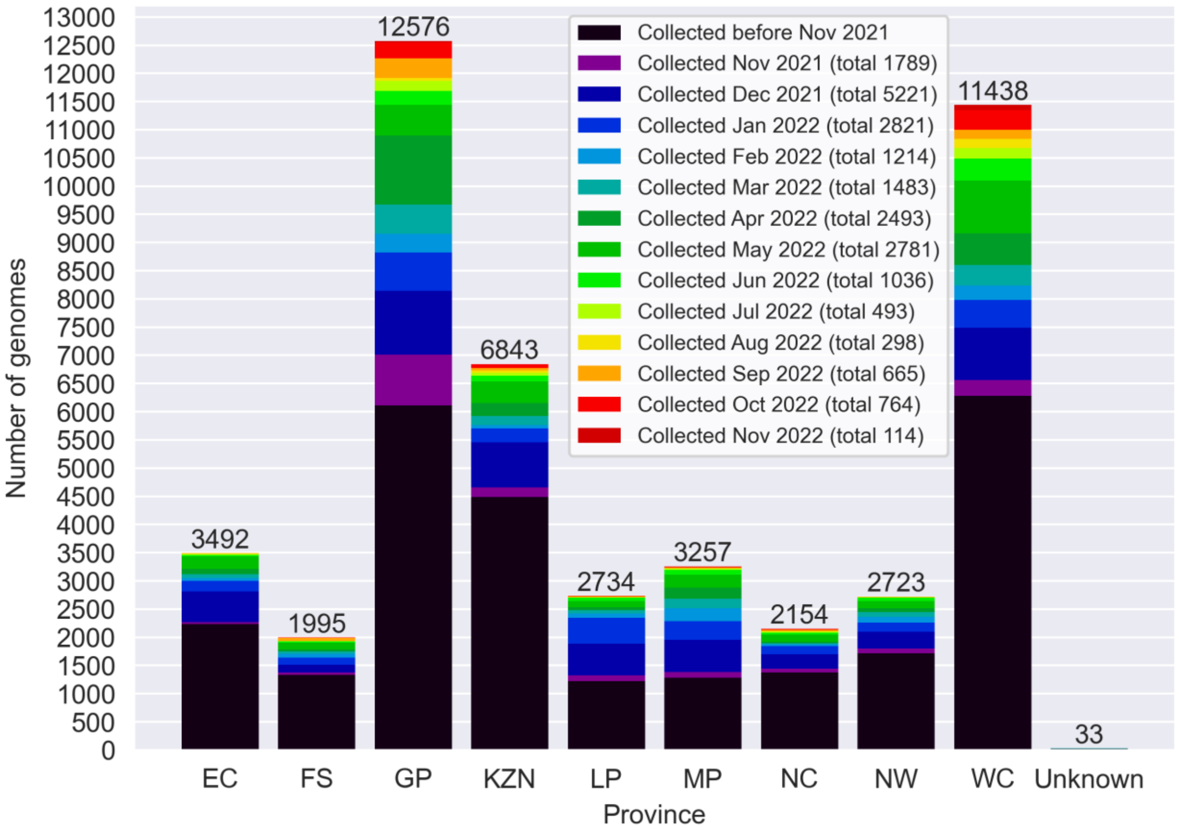
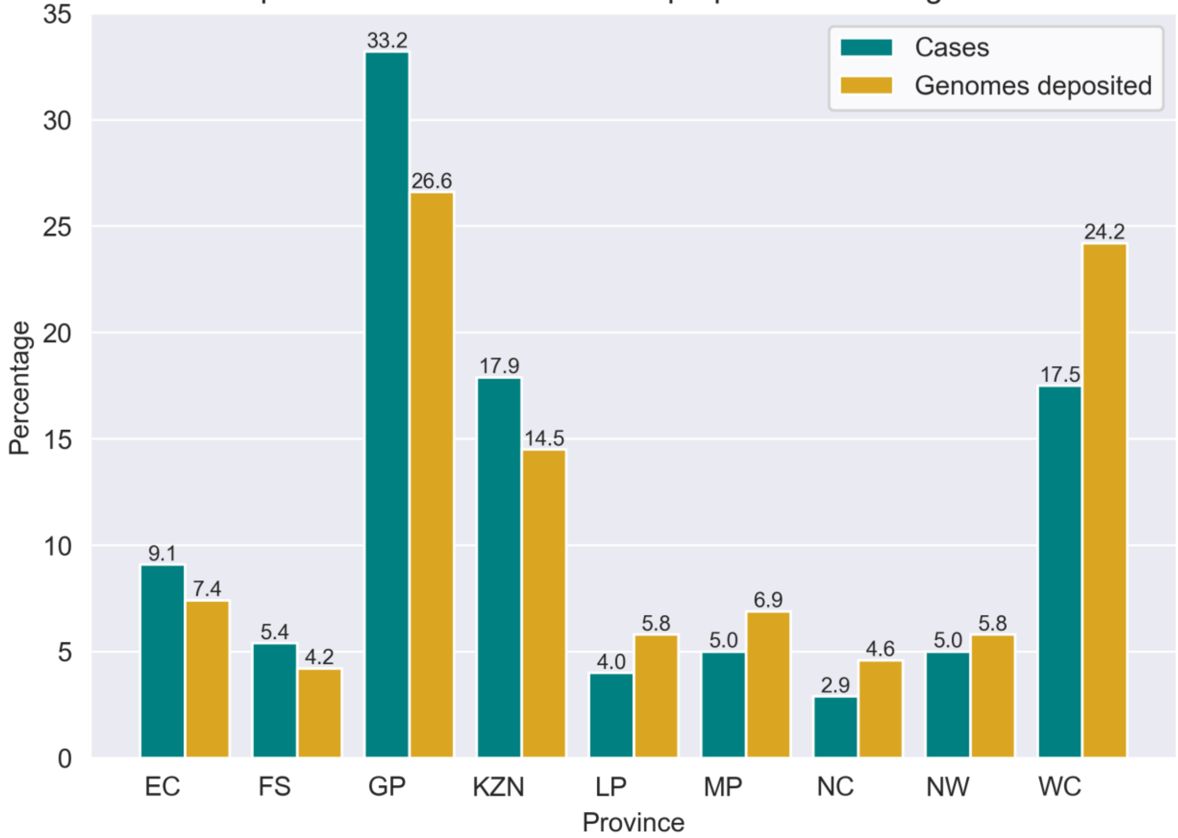
GISAID genomes vs total cases, 2020 – 2022 (N=47 245)


Provincial breakdown of genomes deposited into GISAID


Proportion of total cases versus proportion of total genomes

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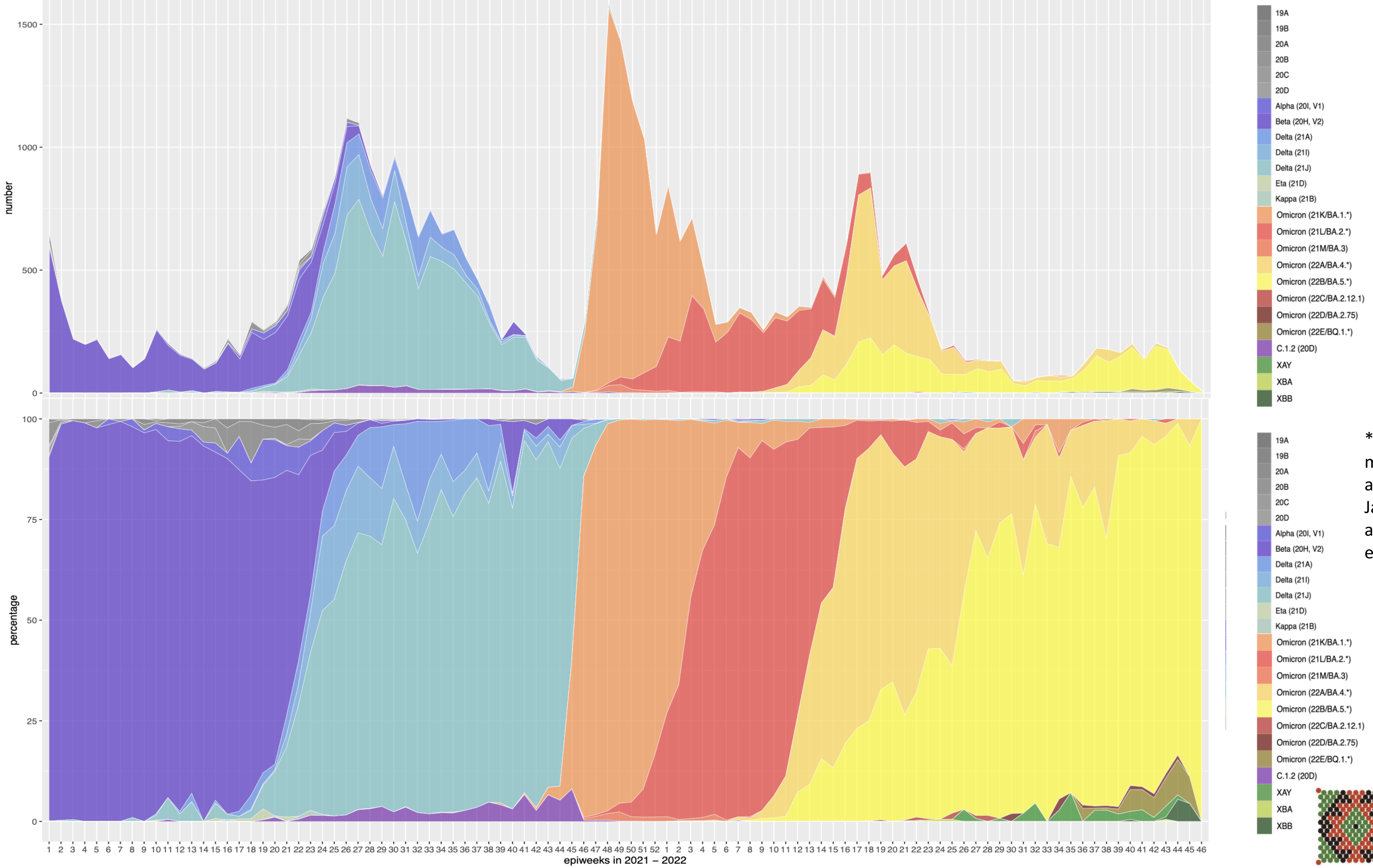
Number and percentage of clades by epiweek in South Africa, 2021 – 2022 (40 486*)



Sequencing data ending epi week 46 (ending 19 Nov 2022)

Currently in epi week 47 (ending 26 Nov 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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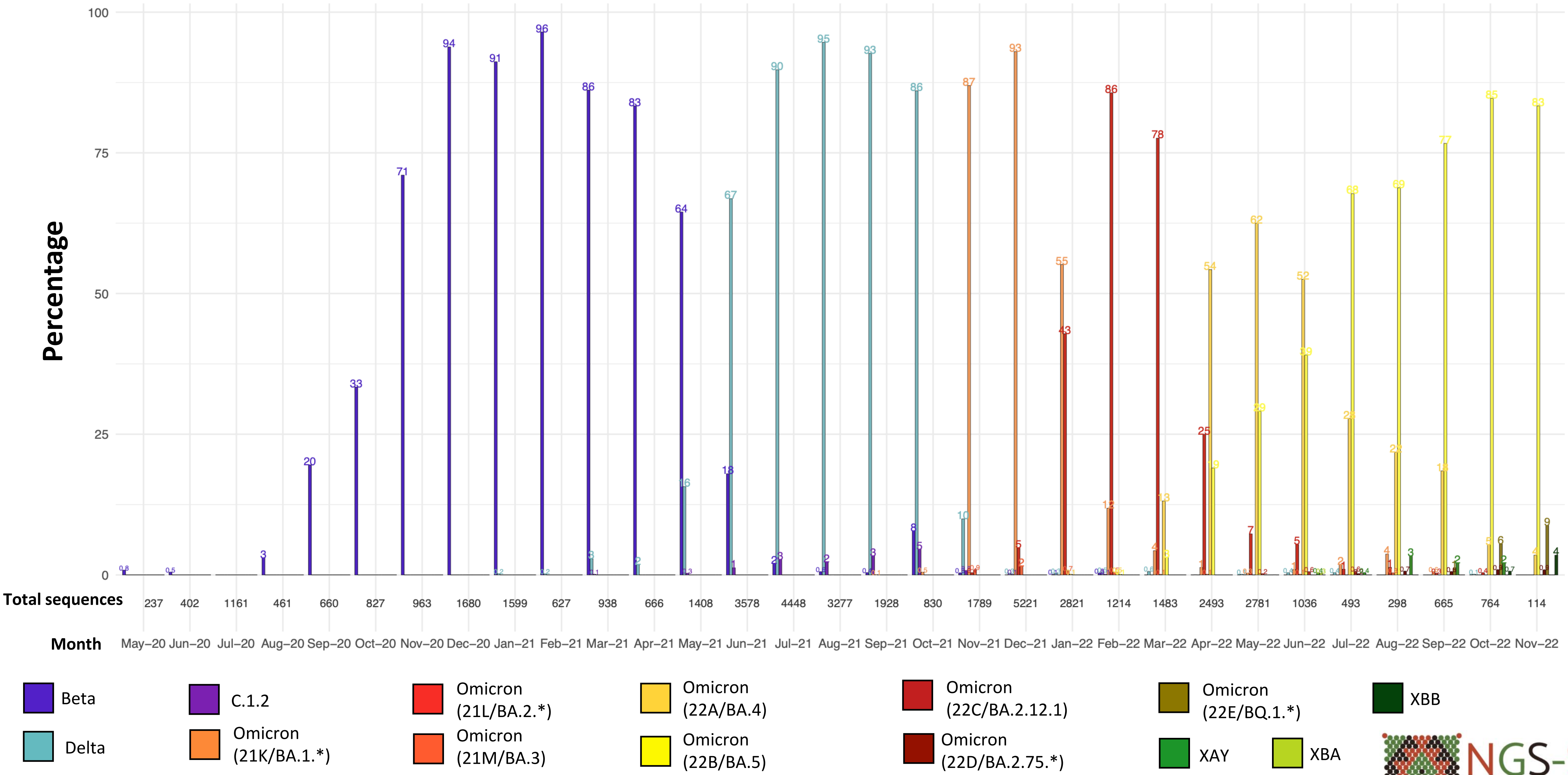
Detection Rates: Beta, Delta, C.1.2, recombinants, and Omicron



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

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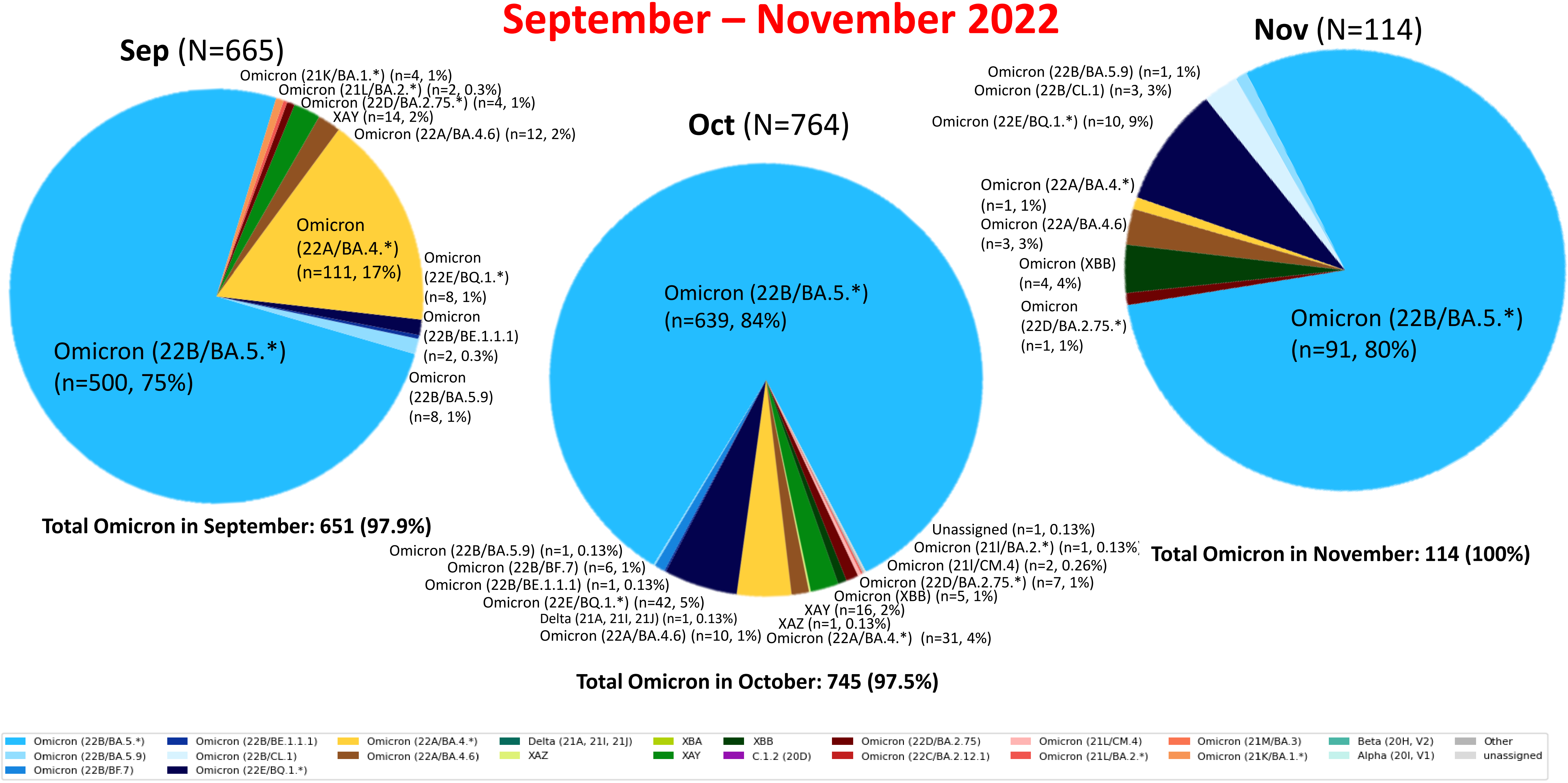
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in September – November 2022

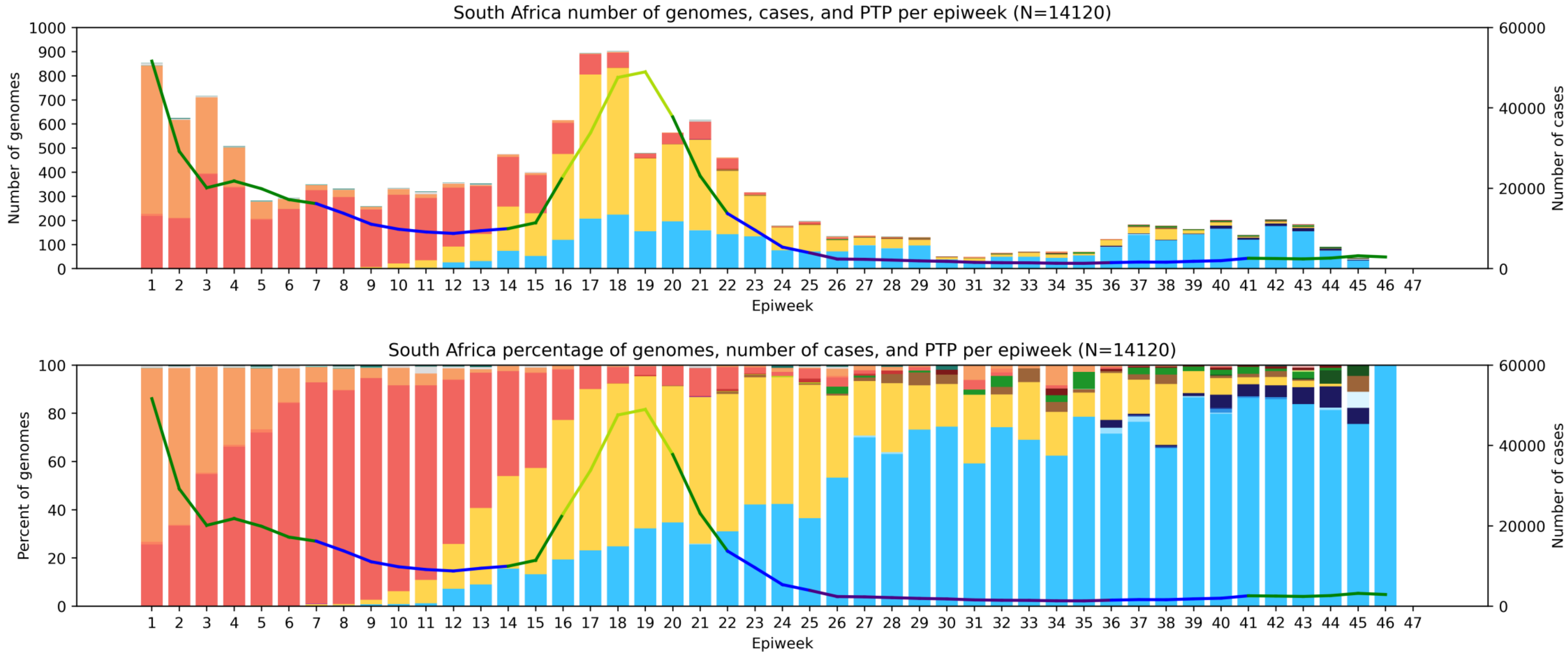


Total Omicron in September: 651 (97.9%)

Total Omicron in October: 745 (97.5%)

Total Omicron in November: 114 (100%)

South Africa, 2022, n = 14 120*



Clade key (bar graph)

- XBB
- XAY
- XBA
- Omicron (21K/BA.1.*)
- Omicron (21L/BA.2.*)
- Omicron (21L/CM.4)
- Omicron (22C/BA.2.12.1)
- Omicron (22D/BA.2.75)
- Omicron (21M/BA.3)
- Omicron (22A/BA.4.*)
- Omicron (22A/BA.4.6)
- Cases
- Omicron (22B/BA.5.*)
- Omicron (22B/BF.7)
- Omicron (22B/BA.5.9)
- Omicron (22B/BE.1.1.1)
- Omicron (22B/CL.1)
- Omicron (22E/BQ.1.*)
- C.1.2 (20D)
- Beta (20H, V2)
- Alpha (20I, V1)
- Delta (21A, 21I, 21J)
- 20B
- 20A
- unassigned
- XAZ

Weekly percentage testing positive key (line graph)

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

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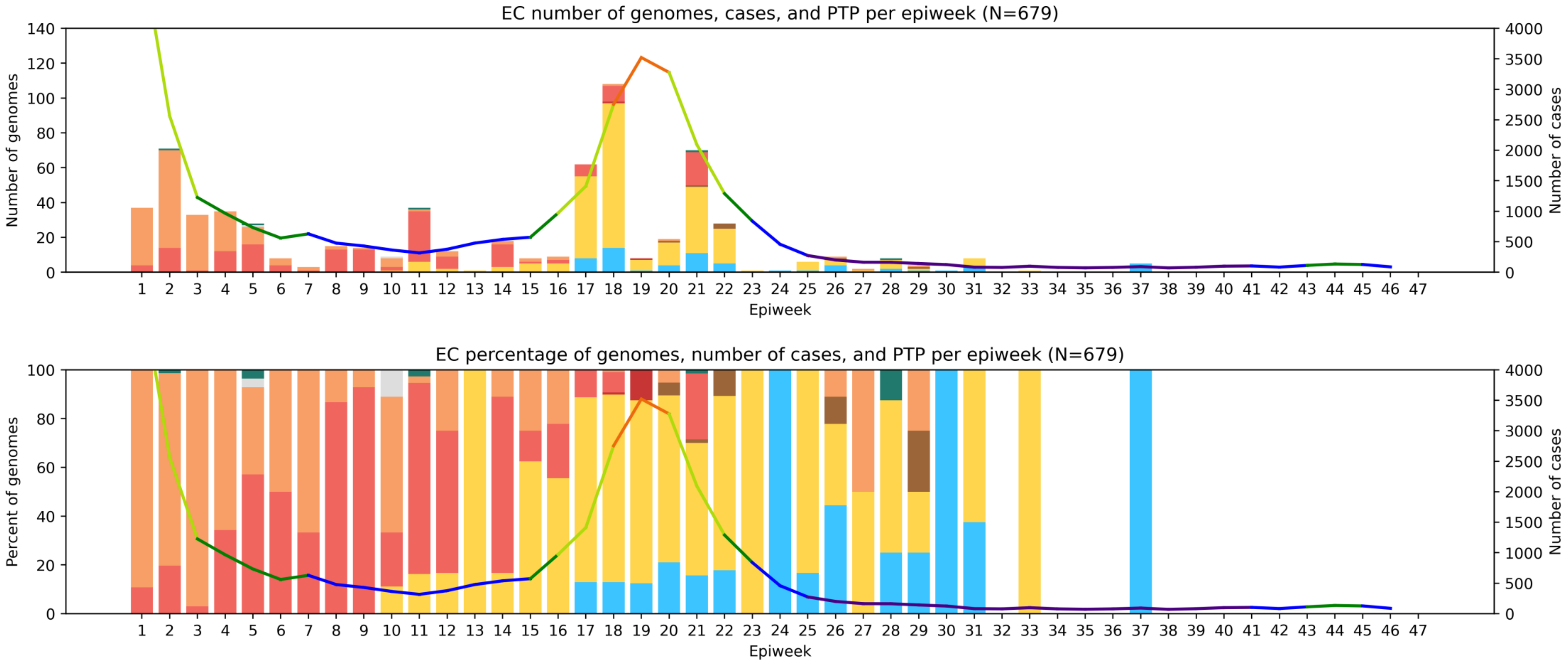
*Excludes sequences missing collection dates. Lineages of particular interest (currently WHO Omicron subvariants under monitoring) are separate from the main clade groupings.

Eastern Cape Province, 2022, n = 679

Genomes added since last report: 0*


EC number of genomes, cases, and PTP per epiweek (N=679)

EC percentage of genomes, number of cases, and PTP per epiweek (N=679)

Clade key (bar graph)

- ■ XBB
- ■ XAY
- ■ XBA
- ■ Omicron (21K/BA.1.*)
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- ■ Omicron (21L/CM.4)
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- ■ Omicron (22A/BA.4.*)
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- ■ 20A
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Weekly percentage testing positive key (line graph)

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

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

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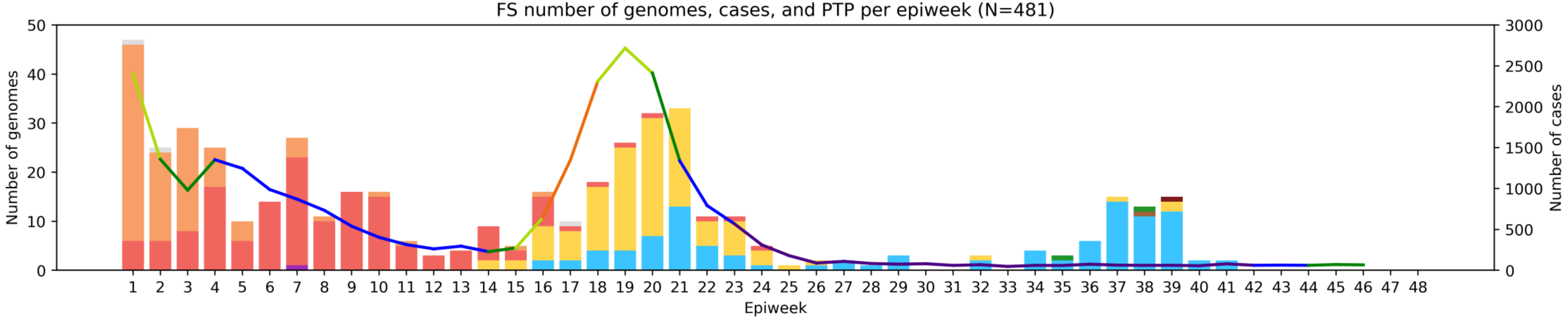
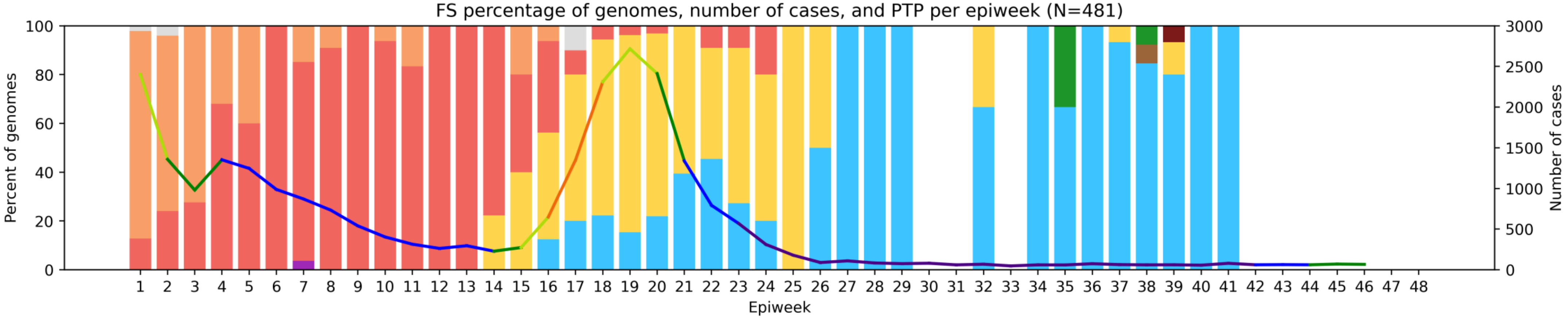
Free State Province, 2022, n = 481

Genomes added since last report: 0*





Clade key (bar graph)

- 🟩 XBB
- 🟩 XAY
- 🟩 XBA
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- 🟦 Omicron (22B/BE.1.1.1)
- ⬜ Omicron (22B/CL.1)
- ⬛ Omicron (22E/BQ.1.*)
- 🟪 C.1.2 (20D)
- 🟩 Beta (20H, V2)
- 🟩 Alpha (20I, V1)
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- ⬜ 20B
- ⬜ 20A
- ⬜ unassigned
- 🟨 XAZ

Weekly percentage testing positive key (line graph)

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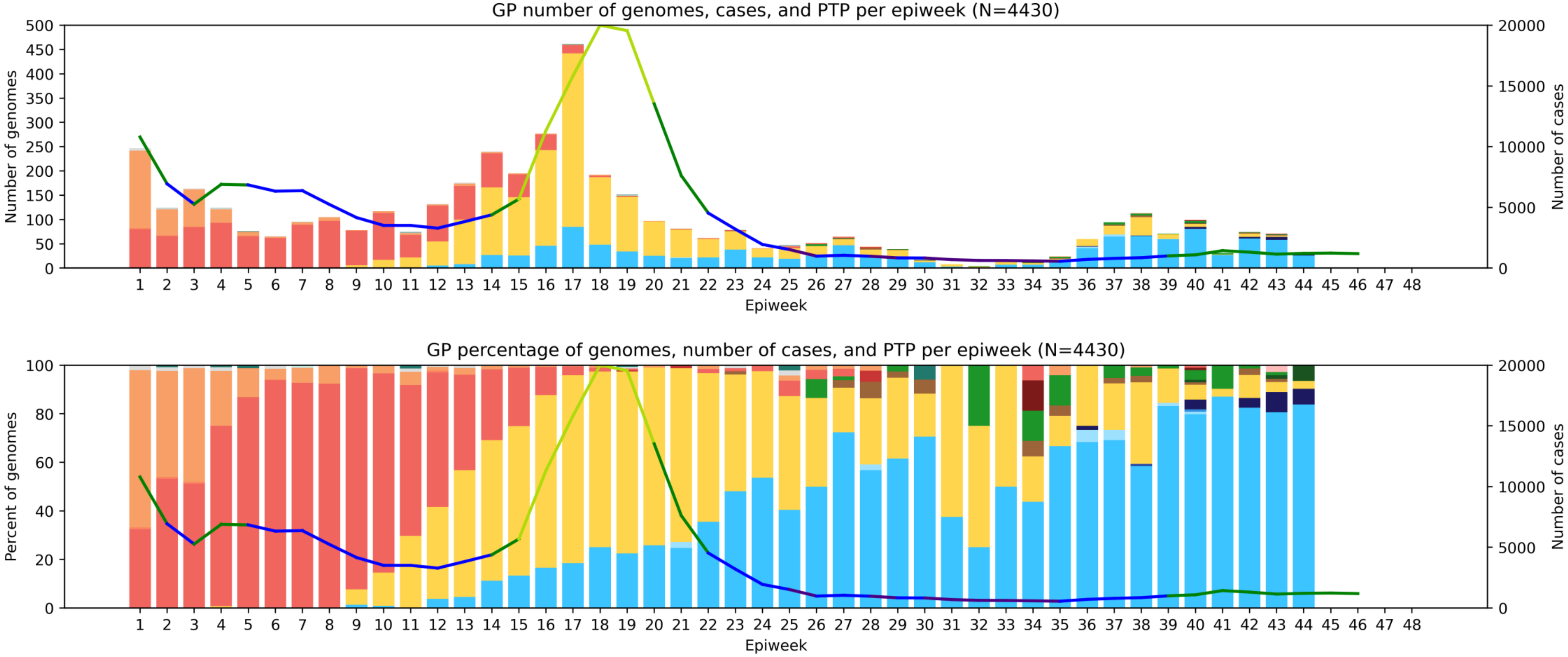
Gauteng Province, 2022, n = 4430

Genomes added since last report: 24*



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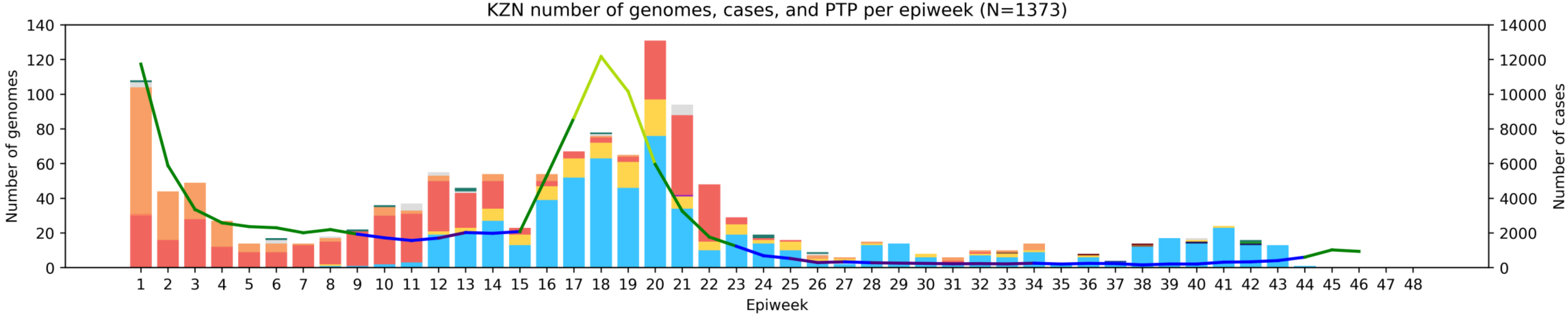
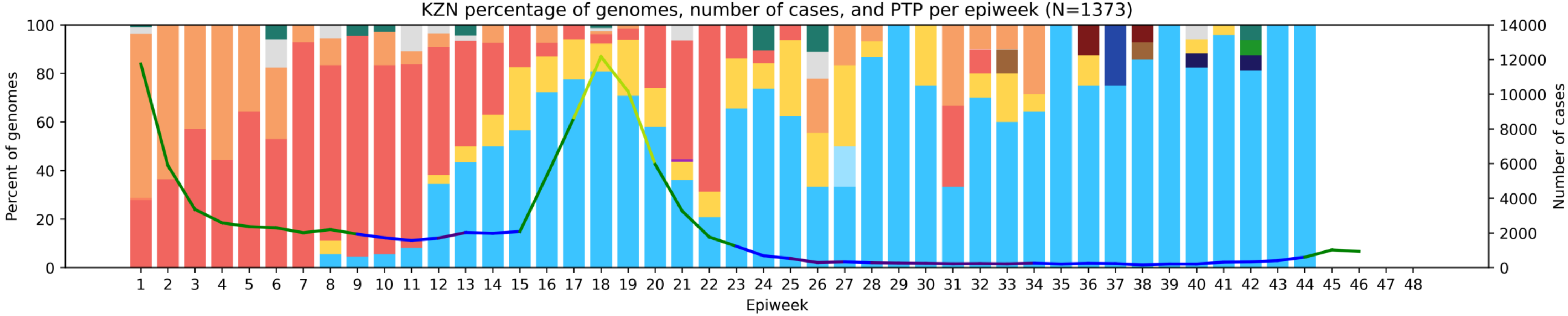
KwaZulu-Natal Province, 2022, n = 1373

Genomes added since last report: 0*





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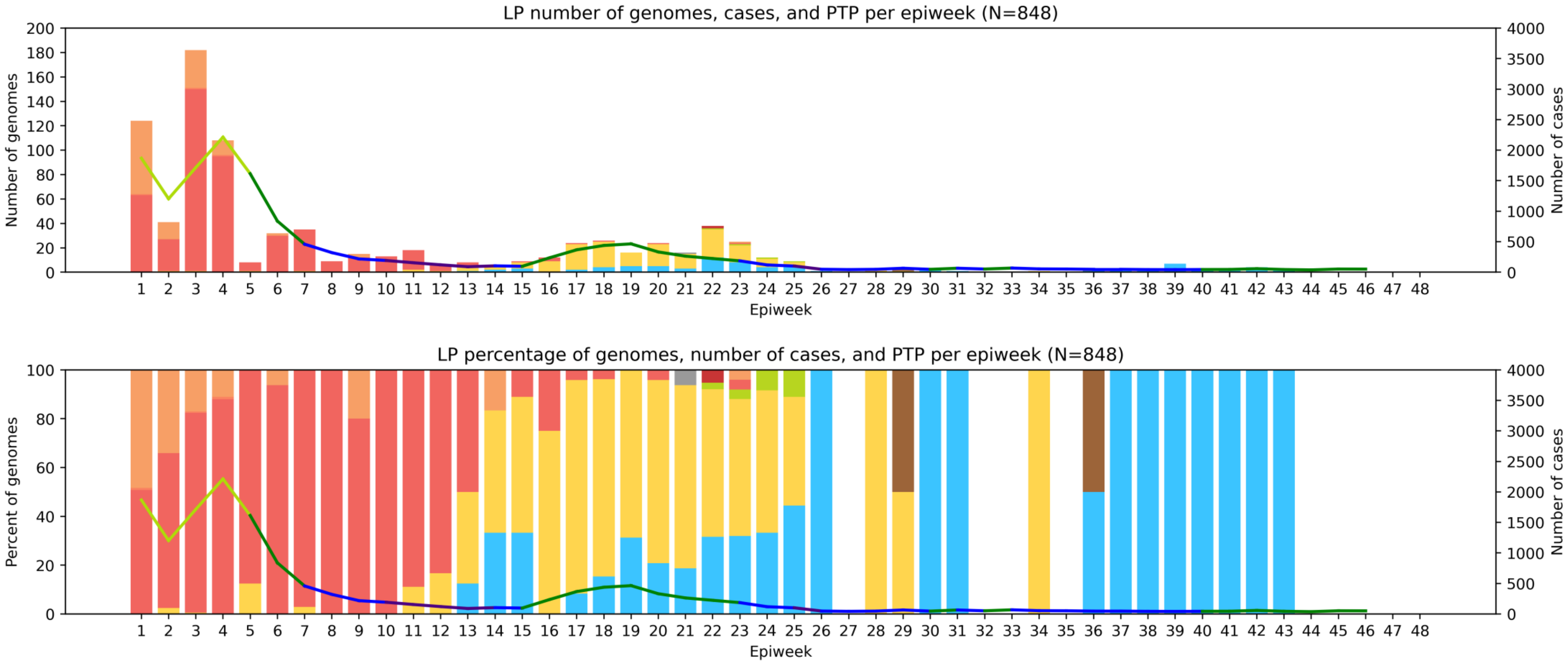
Limpopo Province, 2022, n = 848

Genomes added since last report: 0*



Clade key (bar graph)

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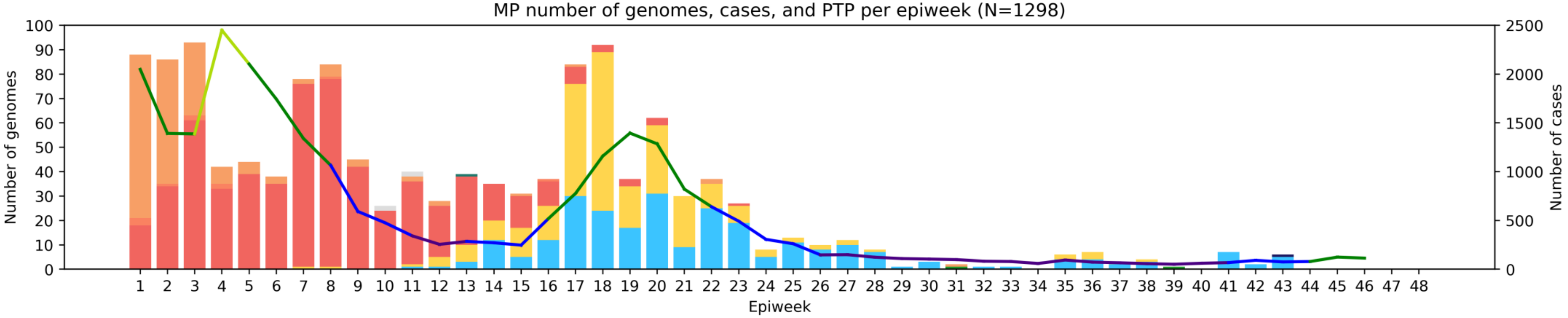
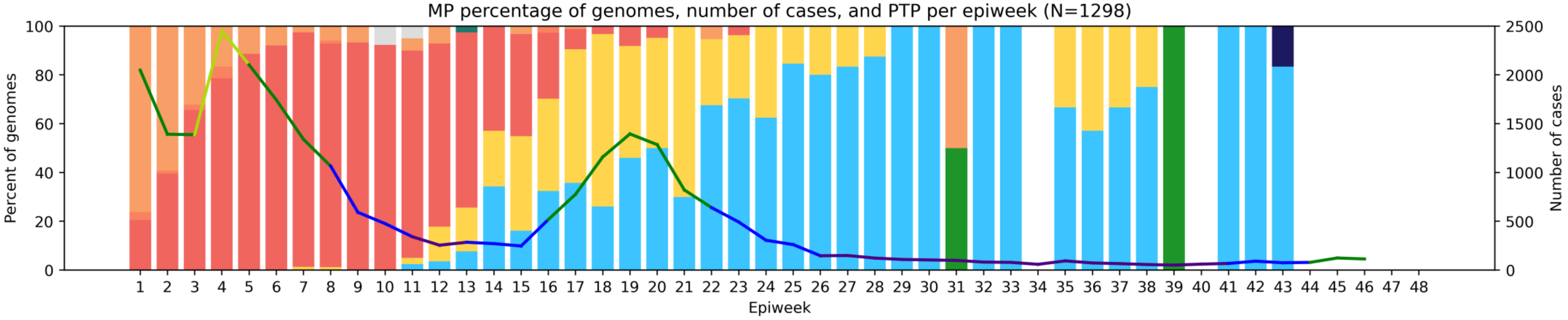
Mpumalanga Province, 2022, n = 1298

Genomes added since last report: 0*





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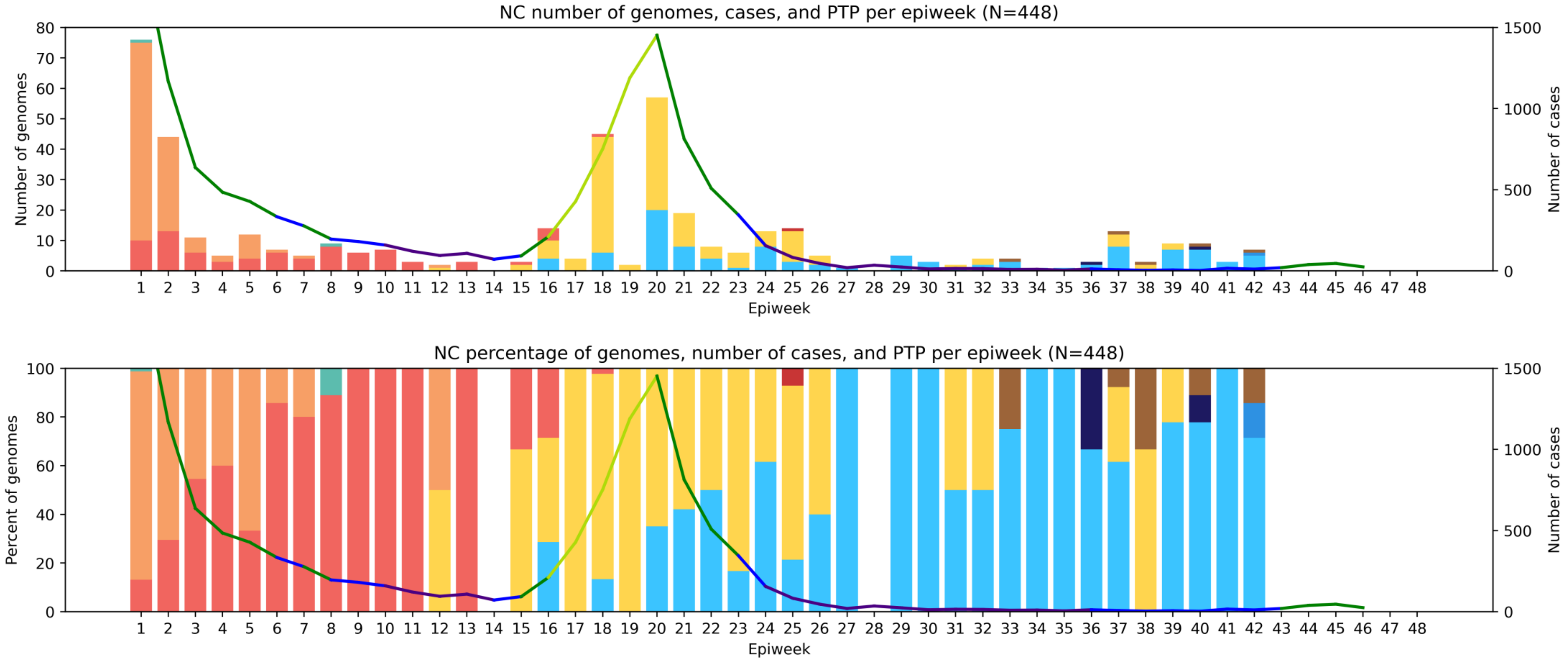
Northern Cape Province, 2022, n = 448

Genomes added since last report: 0*



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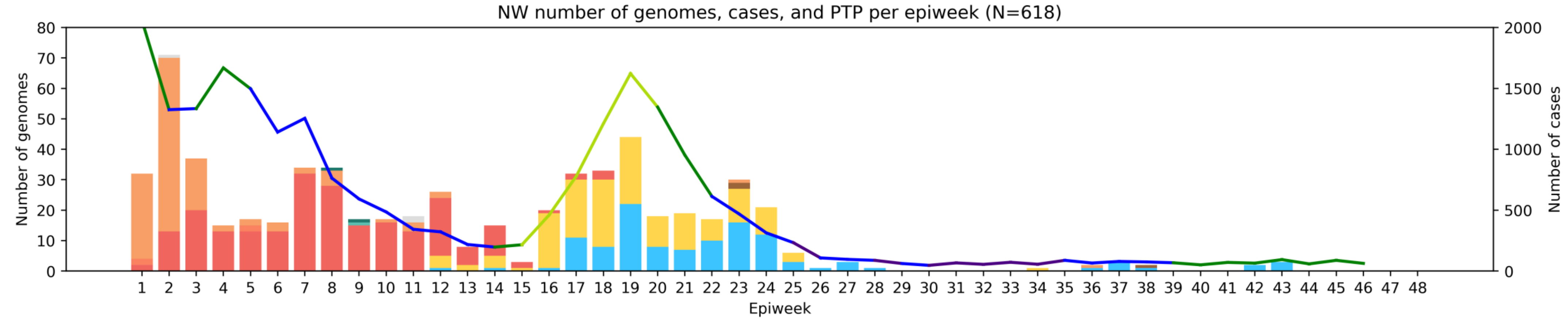
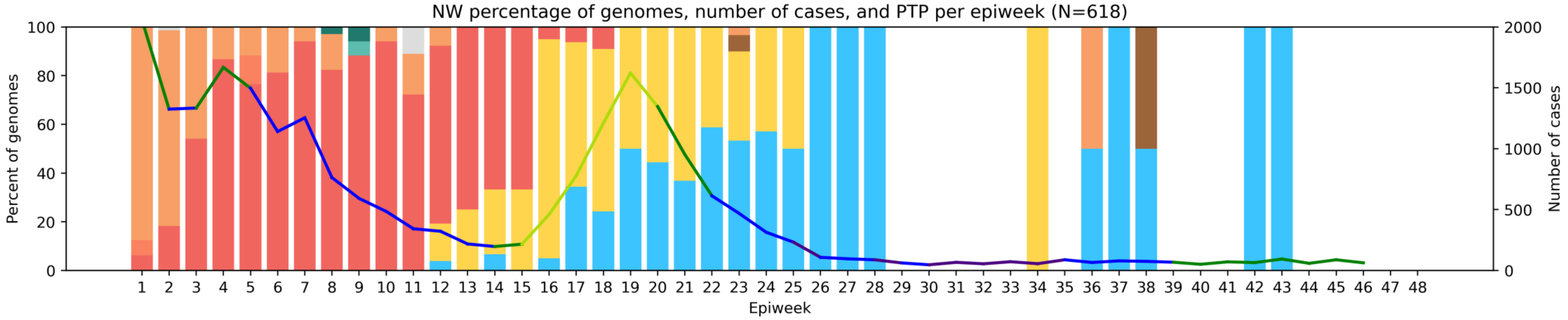
North West Province, 2022, n = 618

Genomes added since last report: 0*





Clade key (bar graph)

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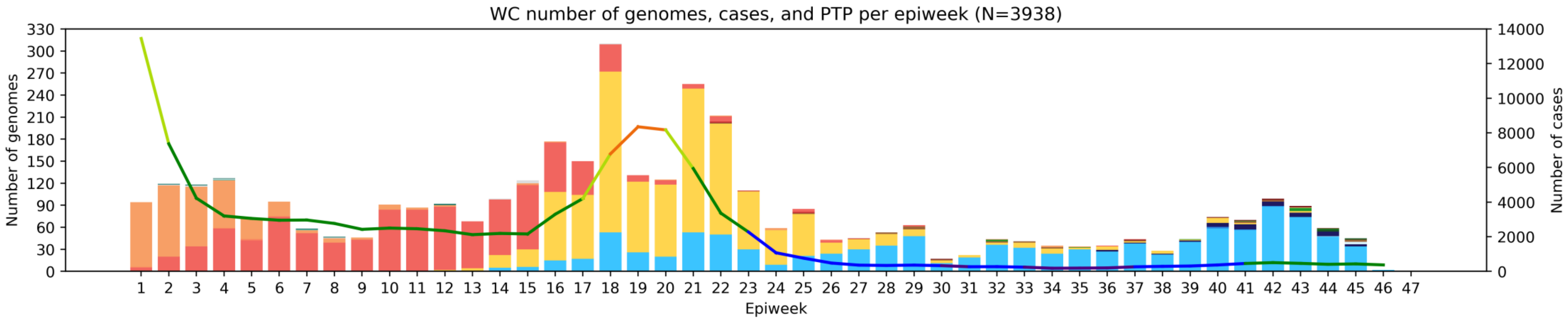
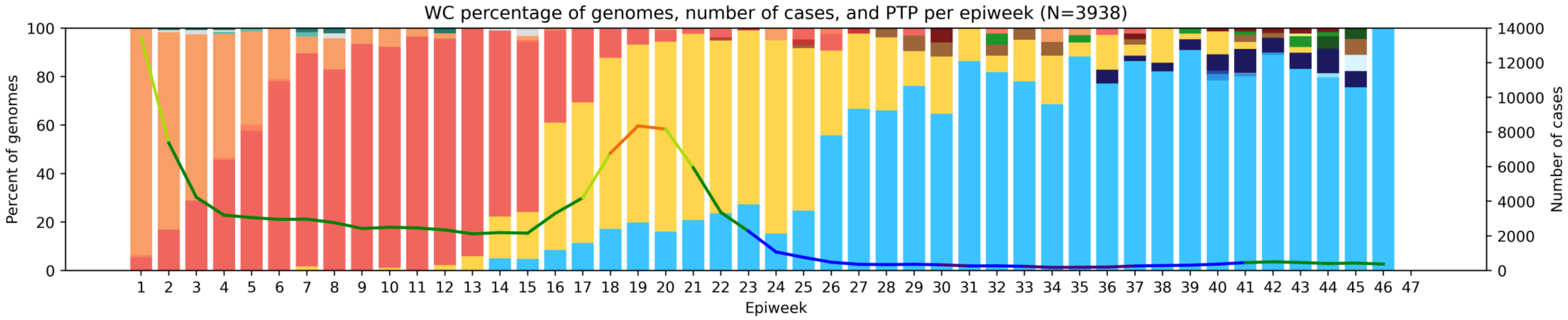
Western Cape Province, 2022, n = 3938

Genomes added since last report: 81*

WC number of genomes, cases, and PTP per epiweek (N=3938)



WC percentage of genomes, number of cases, and PTP per epiweek (N=3938)



Clade key (bar graph)

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- XAY
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Weekly percentage testing positive key (line graph)

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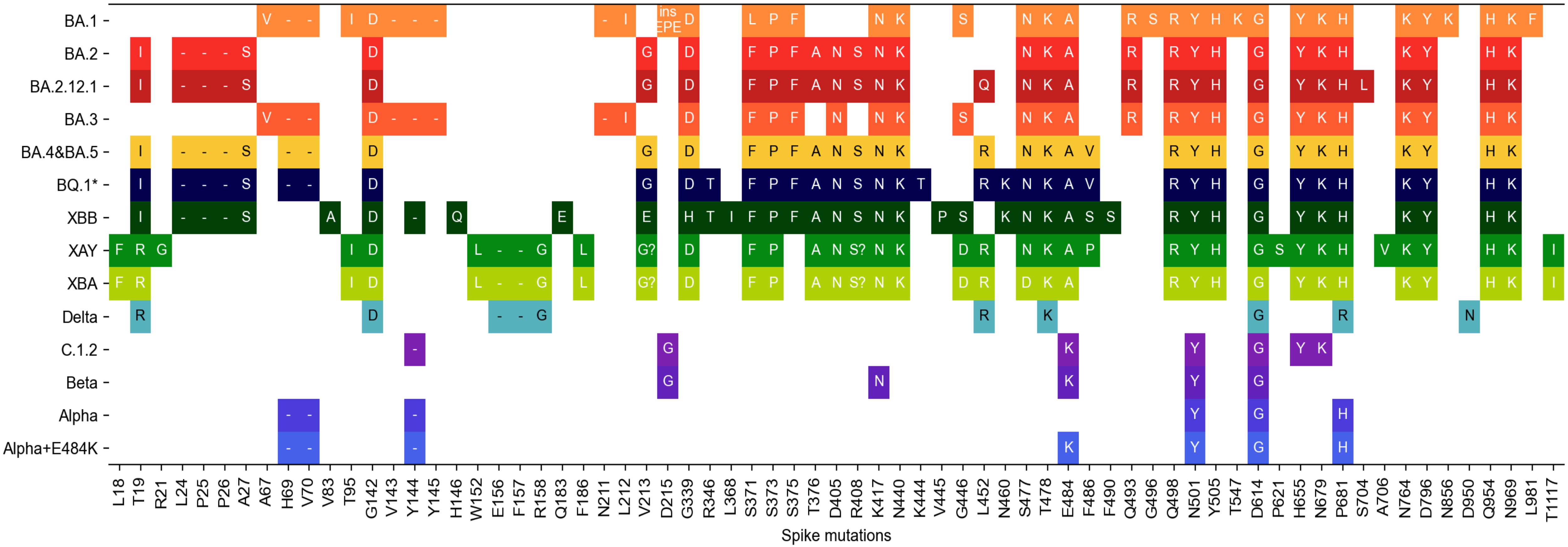
Summary

- **Sequencing update**
  - All provinces have sequences for September and all provinces, except the Eastern Cape, have sequences for October.
  - Gauteng and the Western Cape have sequences for November.
- **Variant of Concern Omicron in South Africa**
  - Omicron continued to dominate in September (98%), October (98%), and currently makes up 100% of November sequences.
  - Omicron BA.5 and sub-lineages were dominant in September (78%), October (90%) and currently make up 92% of November data.
  - BA.2.75.* has been detected in July through November at a low prevalence (≤4%).
  - XAY continues to be detected at a low prevalence (≤3%)
    - XAY has also been detected in Denmark (n=30), Israel (n=2), the USA (n=2), England (n=1), Italy (n=1), and Sweden (n=1)
  - BQ.1 and sub-lineages have been detected in September, October and November
    - September (1%) – BQ.1*: n=1 in the Northern Cape, n=6 in the Western Cape, n=1 in Gauteng
    - October (5%) – BQ.1*: n=2 in KwaZulu-Natal, n=14 in Gauteng, n=24 in the Western Cape, n=1 in the Northern Cape, n=1 in the Mpumalanga
    - November (9%) – BQ.1*: n=9 in the Western Cape and n=1 in Gauteng
  - XBB has been detected in South Africa in October (n=5) and November (n=4)
- Delta detected at low frequency until July, and once in October.

Spike protein mutation* profile of Variants of Interest and Concern



	L18	T19	R21	L24	P25	P26	A27	A67	H69	V70	V83	T95	G142	V143	Y144	Y145	H146	W152	E156	F157	R158
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								
BQ.1*		I		-	-	-	S		-	-			D								
XBB		I		-	-	-	S				A		D		-		Q				
XAY	F	R	G									I	D					L	-	-	G
XBA	F	R										I	D					L	-	-	G
Delta		R											D						-	-	G
C.1.2															-						
Beta																					
Alpha									-	-					-						
Alpha+E484K									-	-					-						

	Q183	F186	N211	L212	V213	D215	G339	R346	L368	S371	S373	S375	T376	D405	R408	K417	N440
BA.1			-	I		ins EPE	D			L	P	F				N	K
BA.2					G		D			F	P	F	A	N	S	N	K
BA.2.12.1					G		D			F	P	F	A	N	S	N	K
BA.3			-	I			D			F	P	F		N		N	K
BA.4&BA.5					G		D			F	P	F	A	N	S	N	K
BQ.1*					G		D	T		F	P	F	A	N	S	N	K
XBB	E				E		H	T	I	F	P	F	A	N	S	N	K
XAY		L			G?		D			F	P		A	N	S?	N	K
XBA		L			G?		D			F	P		A	N	S?	N	K
Delta																	
C.1.2						G											
Beta						G										N	
Alpha																	
Alpha+E484K																	

	K444	V445	G446	L452	N460	S477	T478	E484	F486	F490	Q493	G496	Q498	N501	Y505	T547	D614
BA.1			S			N	K	A			R	S	R	Y	H	K	G
BA.2						N	K	A			R		R	Y	H		G
BA.2.12.1				Q		N	K	A			R		R	Y	H		G
BA.3			S			N	K	A			R		R	Y	H		G
BA.4&BA.5				R		N	K	A	V				R	Y	H		G
BQ.1*	T			R	K	N	K	A	V				R	Y	H		G
XBB		P	S		K	N	K	A	S	S			R	Y	H		G
XAY			D	R		N	K	A	P				R	Y	H		G
XBA			D	R		D	K	A					R	Y	H		G
Delta				R			K										G
C.1.2								K						Y			G
Beta								K						Y			G
Alpha														Y			G
Alpha+E484K								K						Y			G

	P621	H655	N679	P681	S704	A706	N764	D796	N856	D950	Q954	N969	L981	T1117
BA.1		Y	K	H			K	Y	K		H	K	F	
BA.2		Y	K	H			K	Y			H	K		
BA.2.12.1		Y	K	H	L		K	Y			H	K		
BA.3		Y	K	H			K	Y			H	K		
BA.4&BA.5		Y	K	H			K	Y			H	K		
BQ.1*		Y	K	H			K	Y			H	K		
XBB		Y	K	H			K	Y			H	K		
XAY	S	Y	K	H		V	K	Y			H	K		I
XBA		Y	K	H			K	Y			H	K		I
Delta				R						N				
C.1.2		Y	K											
Beta														
Alpha				H										
Alpha+E484K				H										

- 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 recombinant sequences are pictured

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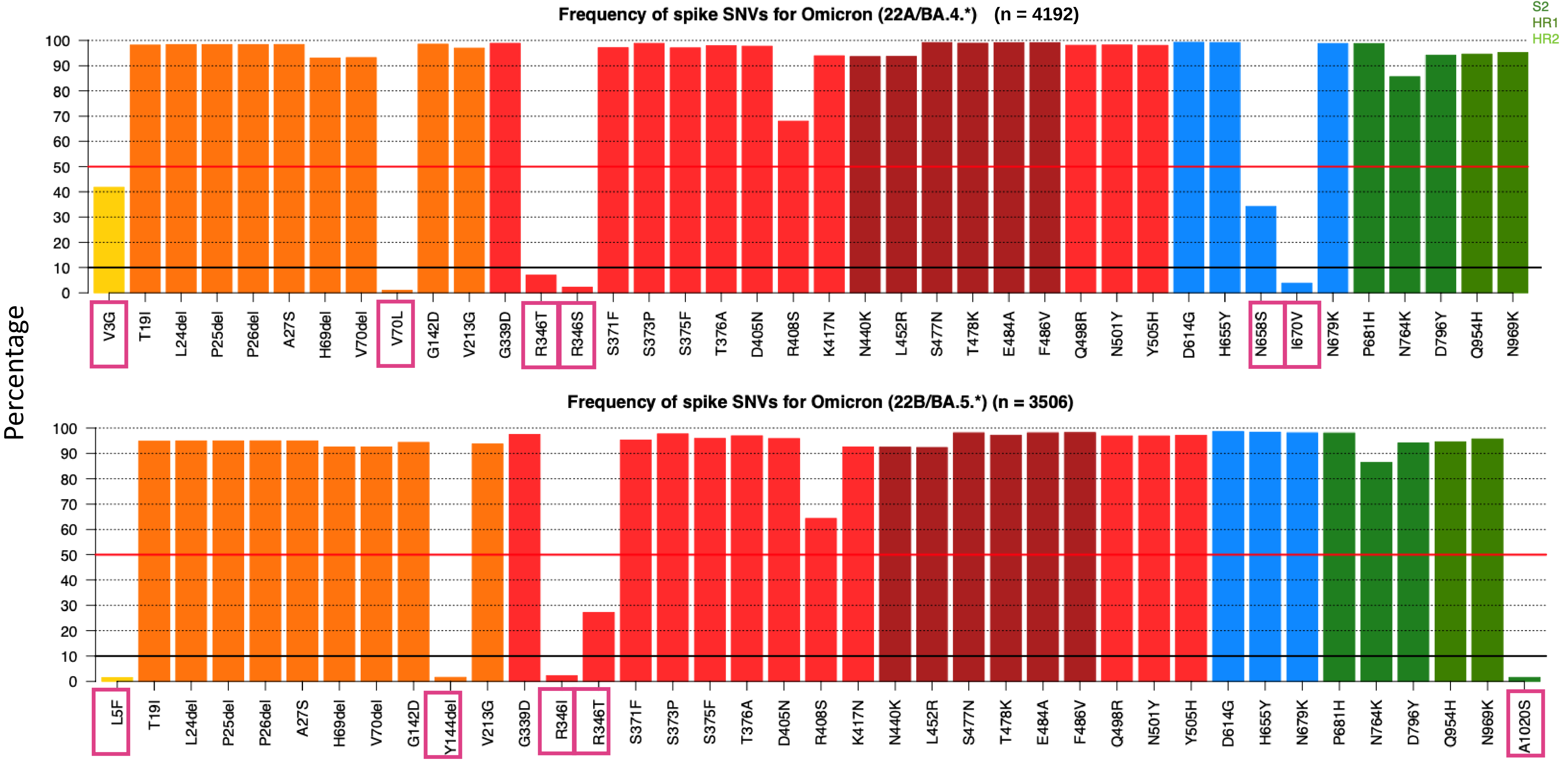
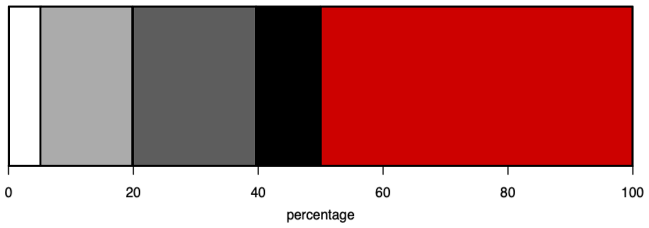
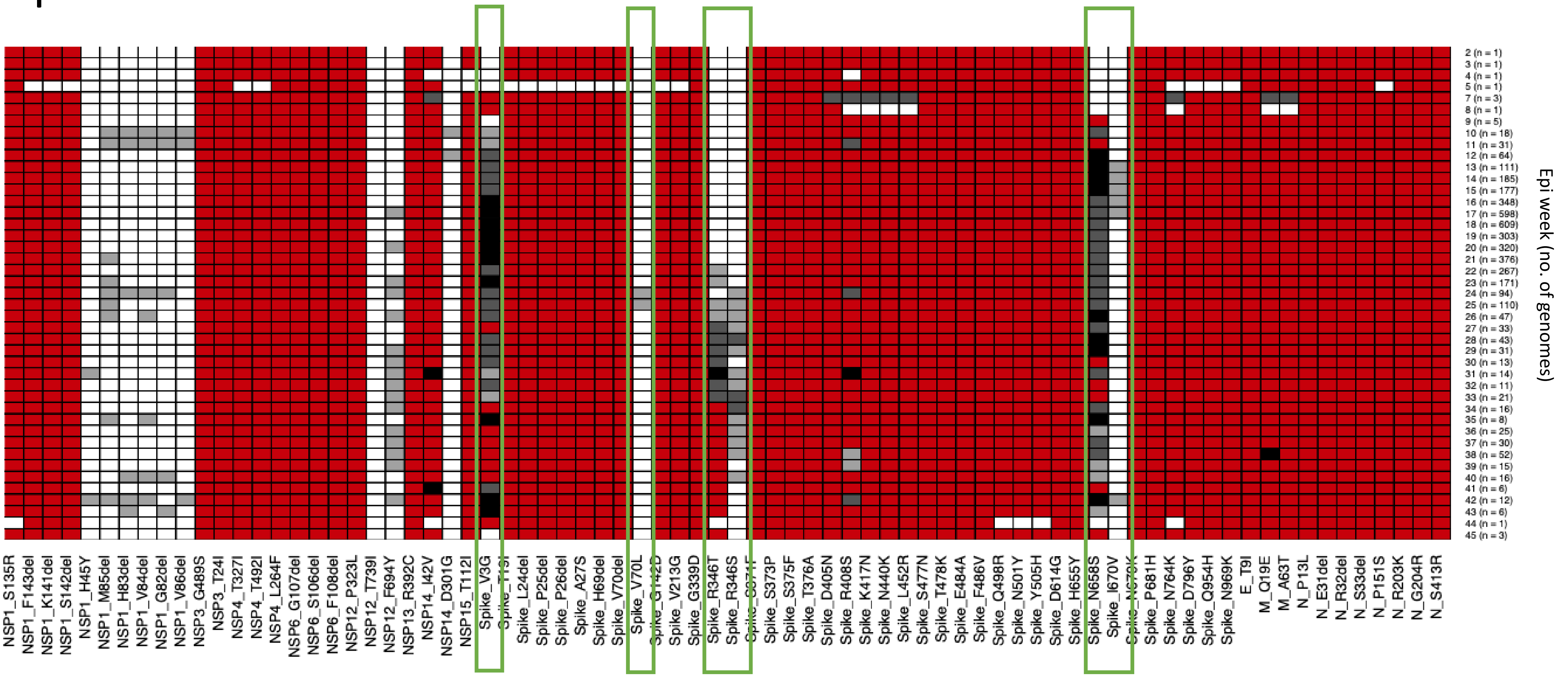
BA.4 and BA.5 spike mutations*



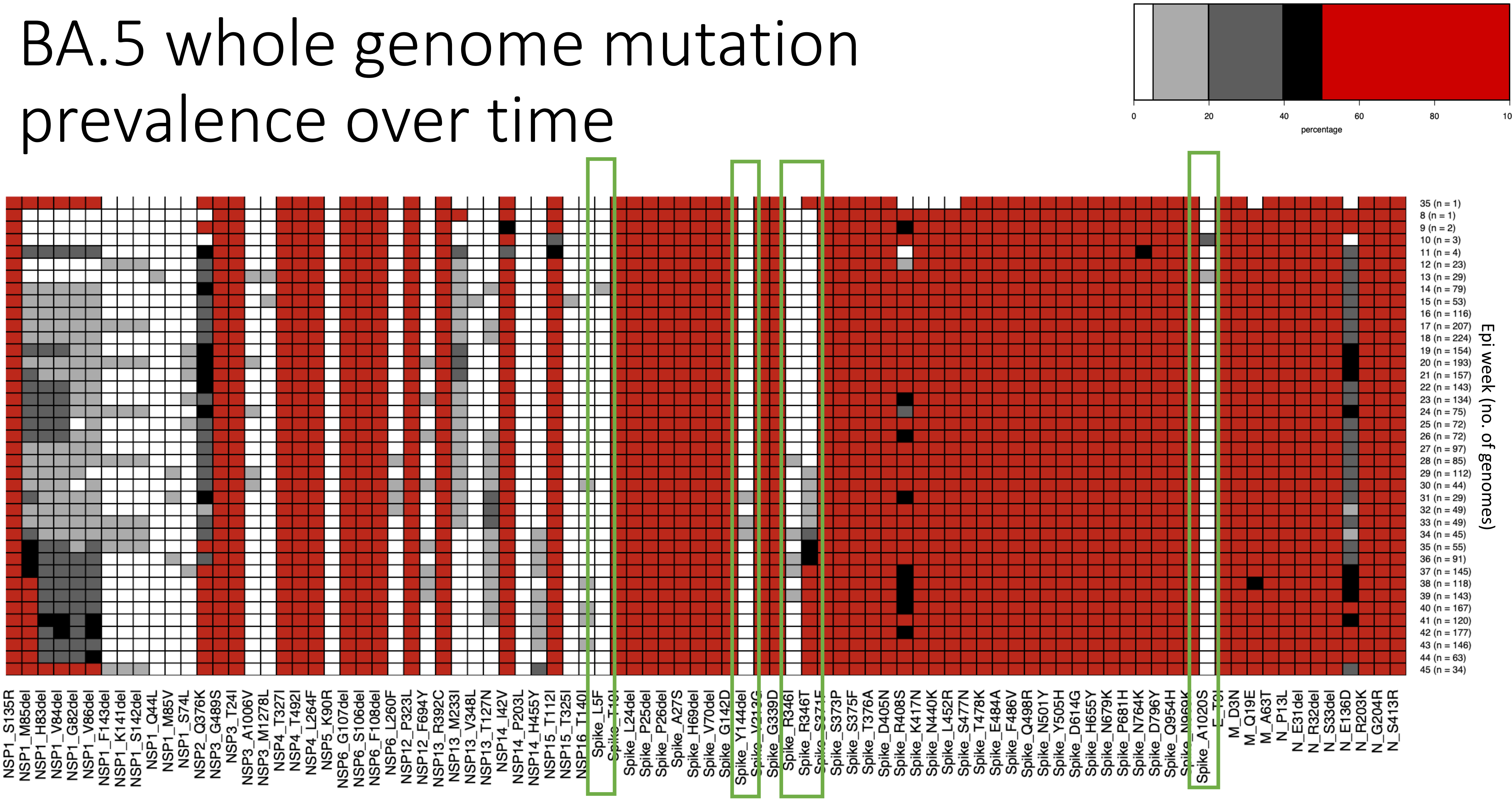
*Only mutations present in ≥1% of sequences are shown

BA.4 whole genome mutation prevalence over time





BA.5 whole genome mutation prevalence over time



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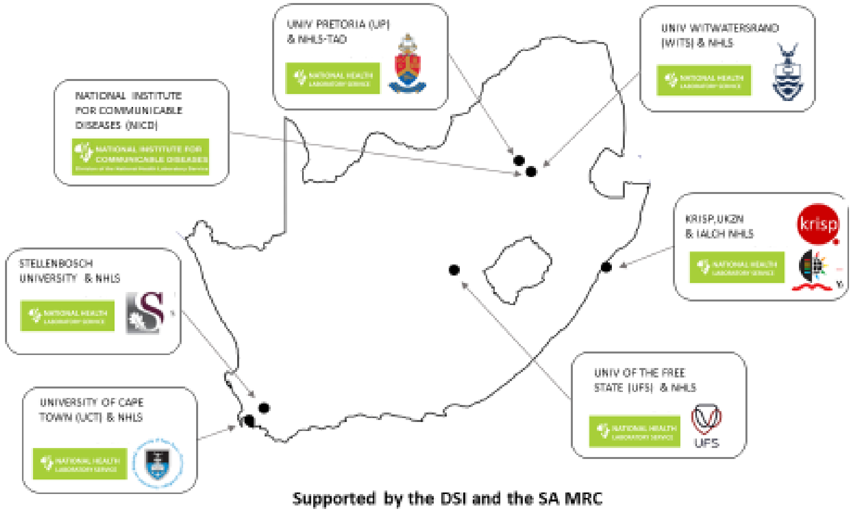

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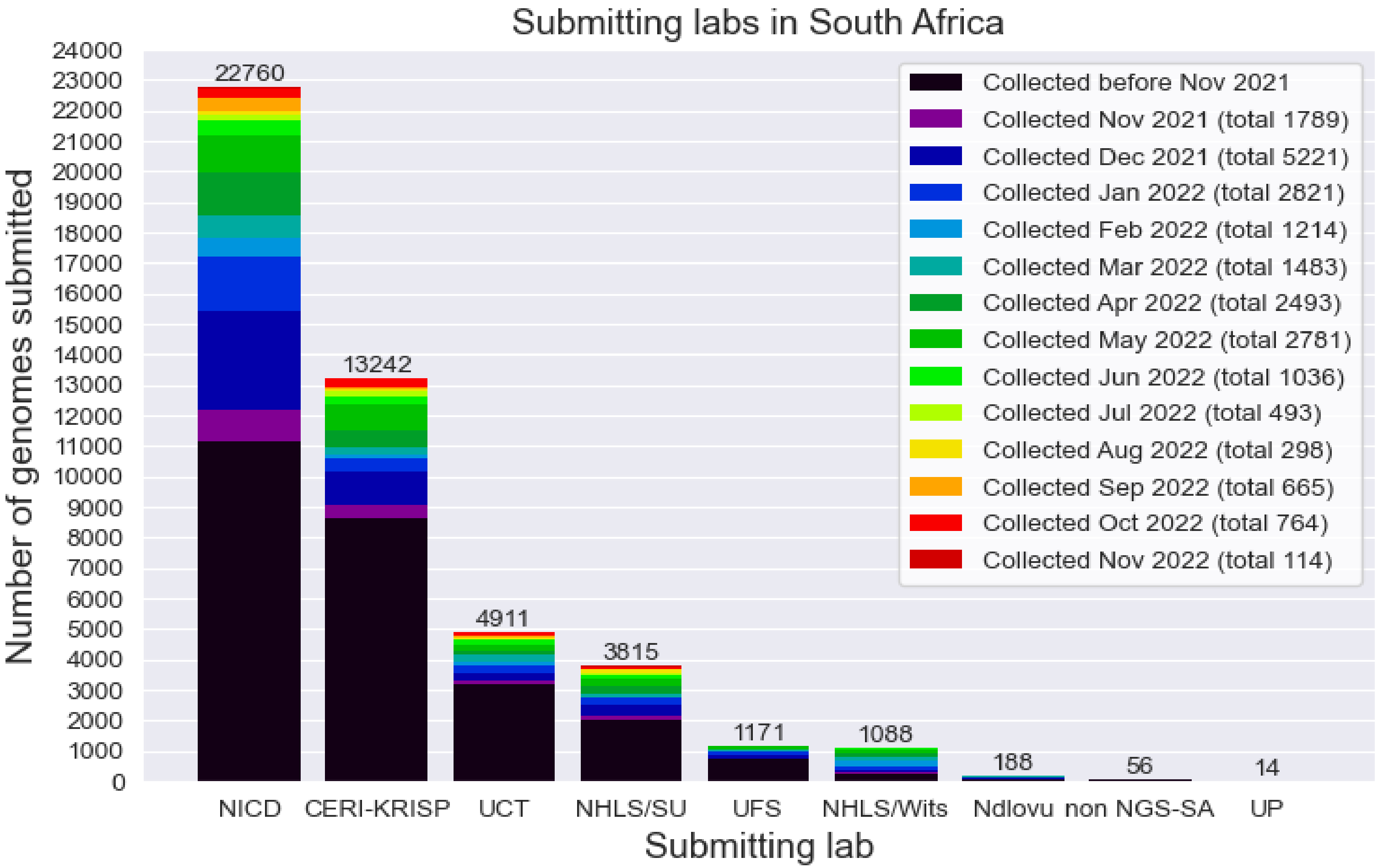
South African genomes submitted per submitting lab, 2020 - 2022 (N=47 245)



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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

Omicron subvariants under monitoring

Pango lineage[#] (+ mutation)	GISAID clade	Nextstrain **clade**	**Relationship to circulating VOC lineages**	Spike genetic features	Earliest documented **samples**
BA.5** (+R346X or +K444X or +V445X or +N450D or +N460X)	GRA	22B	BA.5 sublineages (e.g. BF.7, BF.14, BQ.1)	BA.5 + one or more of these mutations: S:R346X, S:K444X, S:V445X , S:N450D or S:N460X	07-02-2022
BA.2.75***	GRA	22D	BA.2 sublineage	BA.2.75: BA.2 + S:K147E, S:W152R, S:F157L, S:I210V, S:G257S, S:D339H, S:G446S, S:N460K, S:Q493R reversion BA.2.75.2: BA.2.75 + S:R346T, S:F486S, S:D1199N	31-12-2021
BJ.1****	GRA	21L	BA.2 sublineage (B.1.1.529.2.10.1.1)	BA.2+S:V83A, S:Y144-, S:H146Q, S:Q183E, S:V213E, S:G339H, S:R346T, S:L368I, S:V445P, S:G446S, S:V483A, S:F490V, S:G798D, S:S1003I	06-09-2021
BA.4.6	GRA	22A	BA.4 sublineage	BA.4+S:R346T, S:N658S	20-07-2020
XBB[$]		recombinant	Recombinant of BA.2.10.1 and BA.2.75 sublineages, i.e. BJ1 and BM.1.1.1, with a breakpoint in S1	BA.2+ S:V83A, S:Y144-, S:H146Q, S:Q183E, S:V213E, S:G252V, S:G339H, S:R346T, S:L368I, S:V445P, S:G446S, S:N460K, S:F486S, S:F490S	13-08-2022
BA.2.3.20[§]	GRA	21L	BA.2 sublineage	BA.2+ S:M153T, S:N164K, S:H245N, S:G257D, S:K444R, S:N450D, S:L452M, S:N460K, S:E484R	15-08-2022

* these subvariants are tracked under Omicron unless/until sufficient evidence arises that the virus characteristics are substantially different from what is known about the VOC they belong to. If this evidence arises, WHO will decide, in consultation with the TAG-VE, if designation of the emerging variant warrants a separate WHO label.

[#] includes descendent lineages

** additional mutations outside of the spike protein: N:G30-, N:S33F, N:E136D, ORF1a:Q556K, ORF1a:L3829F, ORF1b:Y264H, ORF1b:M1156I, ORF9b:P10F, ORF9b:D16G, ORF9b:M26-, ORF9b:A29I, ORF9b:V30L.

*** additional mutation outside the spike protein: ORF1a:S1221L, ORF1a:P1640S, ORF1a:N4060S; ORF1b:G662S; E:T11A

**** additional mutations outside of the spike protein: Mutations: M:D3Y, N:T282I, ORF1a:K47R, ORF1b:G662S, ORF1b:S959P, ORF7a:I110T

[$] additional mutations outside of the spike protein: E:T11A, ORF1a:K47R, ORF1b:G662S, ORF1b:S959P, ORF8:G8*

[§] additional mutations outside of the spike protein: ORF1a:T727I, ORF1a:I1714T, ORF1a:M2169V, ORF1a:T2174I, ORF1a:T2648I, ORF1a:A2909V, ORF1a:Q3922R, ORF1b:T1404M, ORF3a:L140F, ORF9b:D89E

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 14 October 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.)