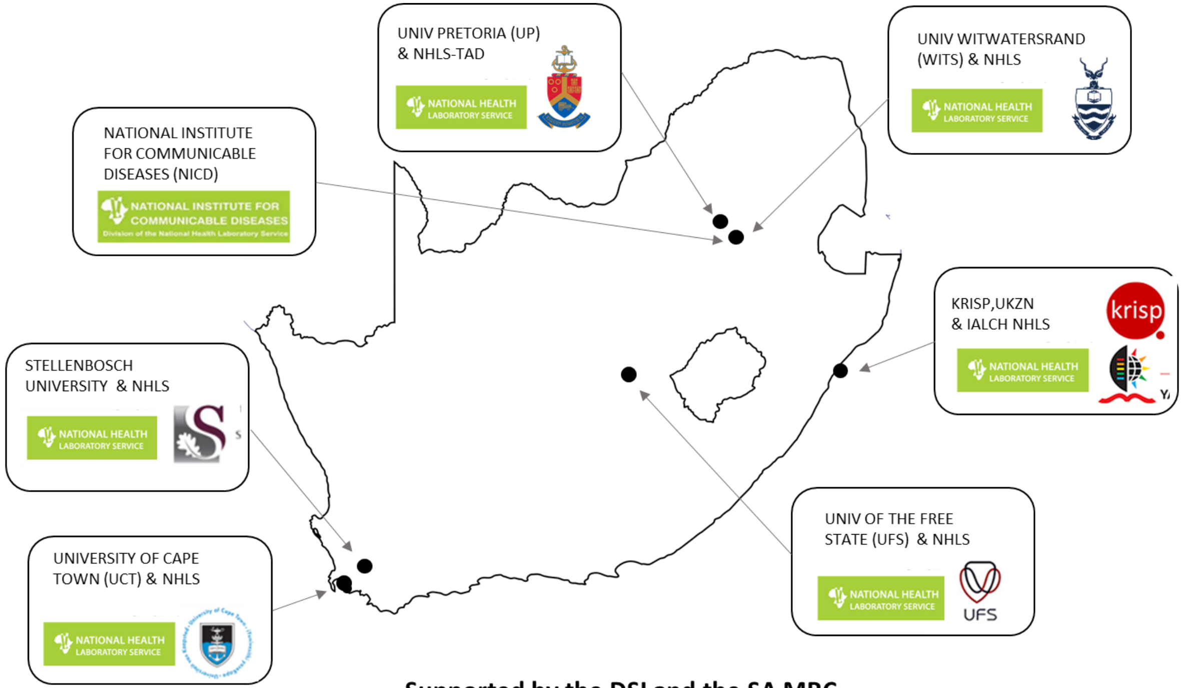
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update
24 February 2023


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)

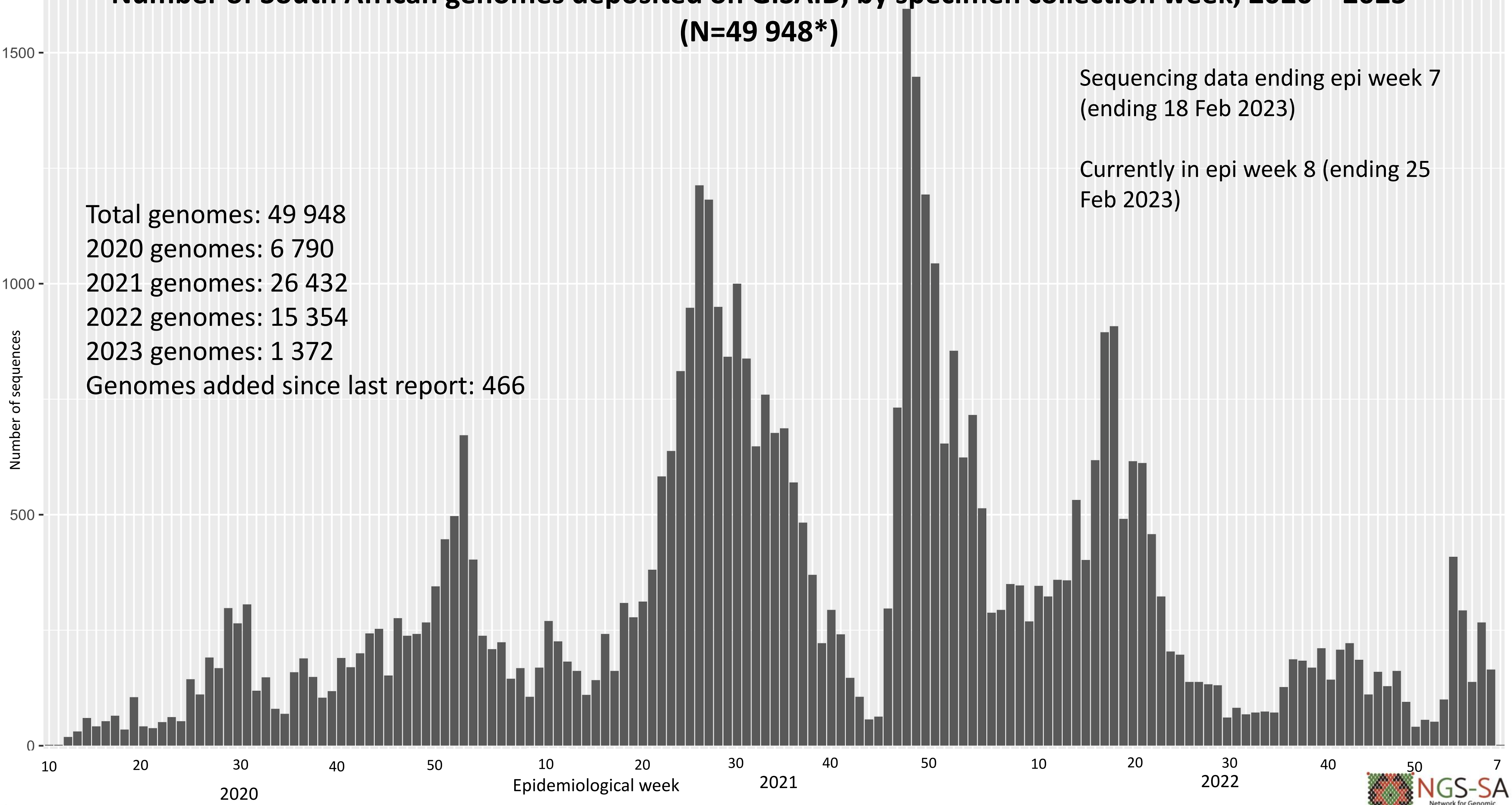
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 24 February 2023 at 11h47

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 – 2023 (N=49 948*)



Total genomes: 49 948
2020 genomes: 6 790
2021 genomes: 26 432
2022 genomes: 15 354
2023 genomes: 1 372
Genomes added since last report: 466

Sequencing data ending epi week 7 (ending 18 Feb 2023)

Currently in epi week 8 (ending 25 Feb 2023)

*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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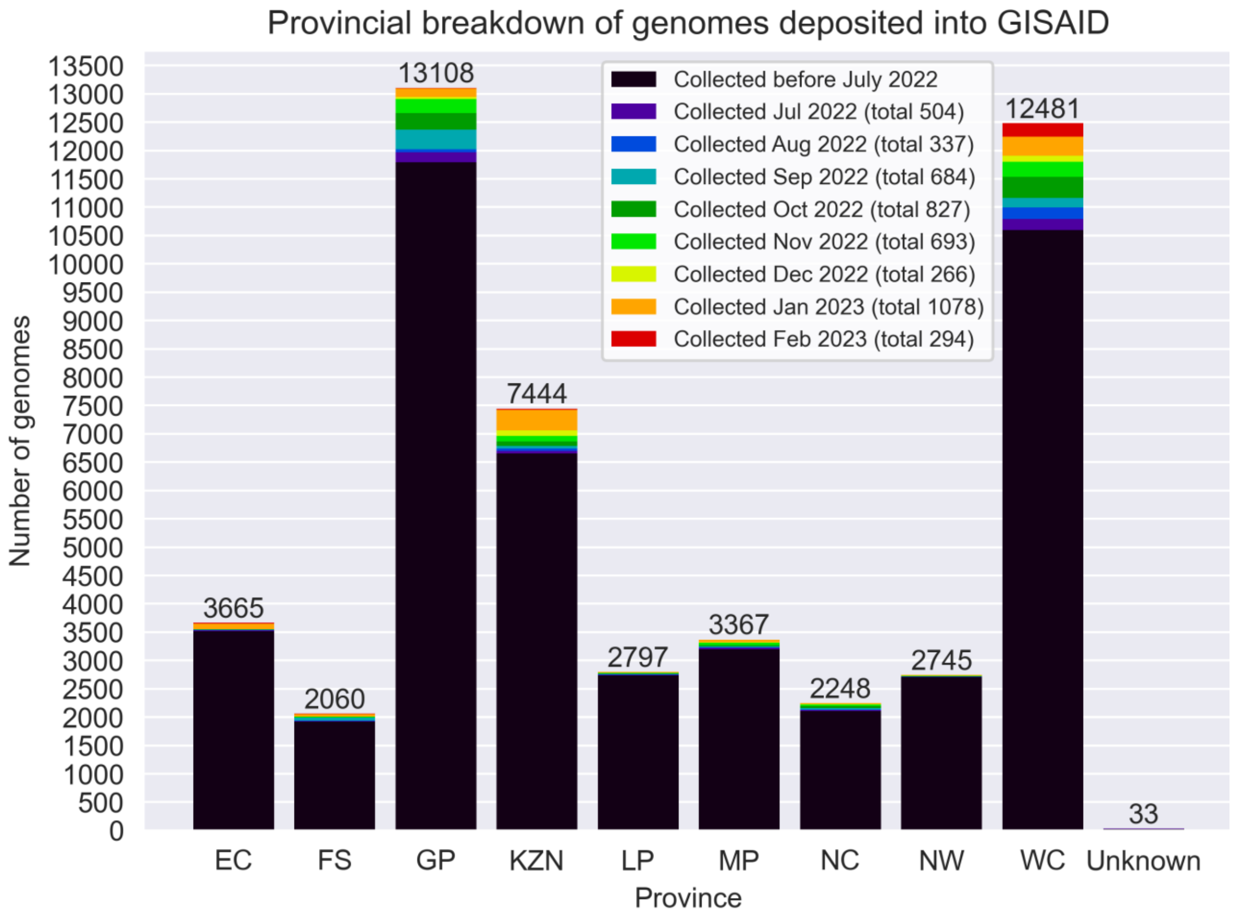
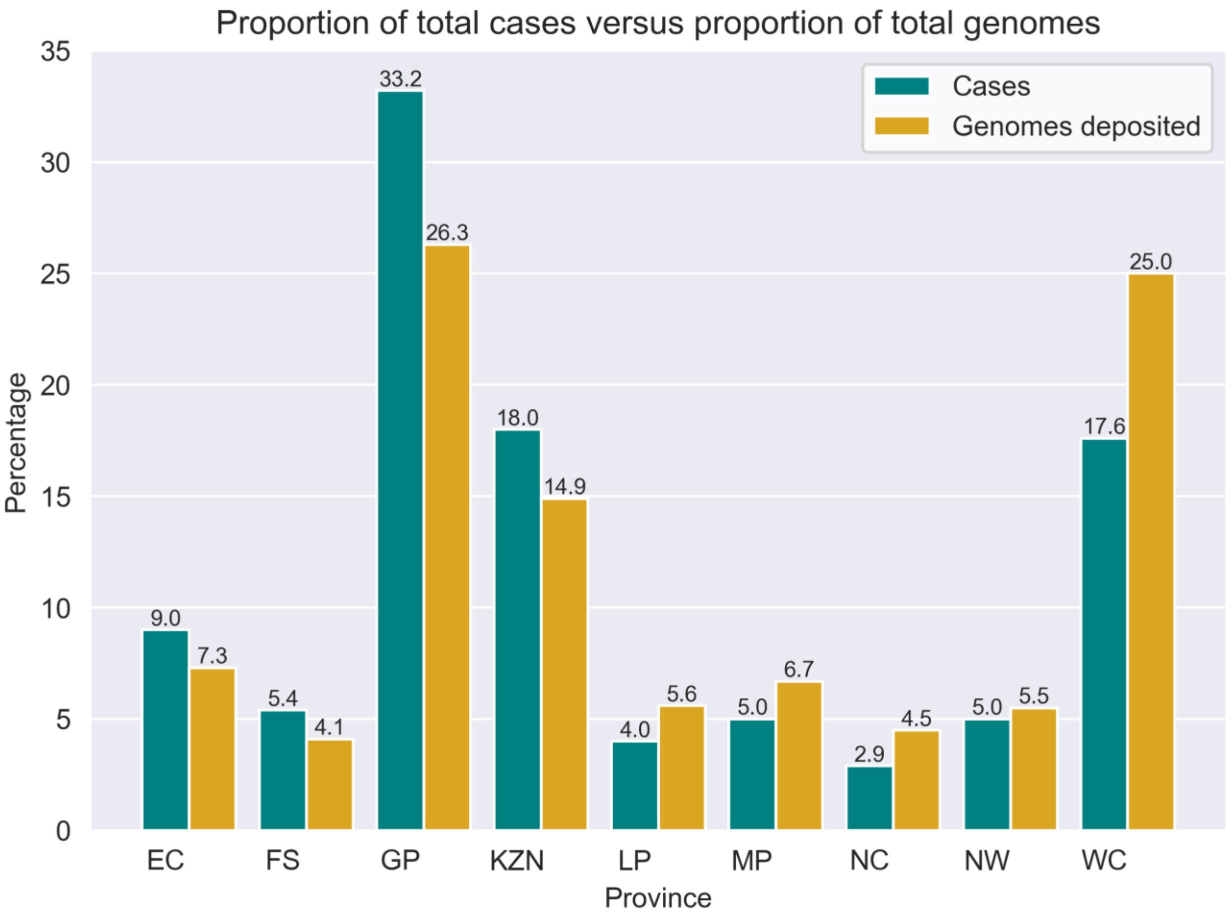
GISAID genomes vs total cases, 2020 – 2023 (N=49 948)





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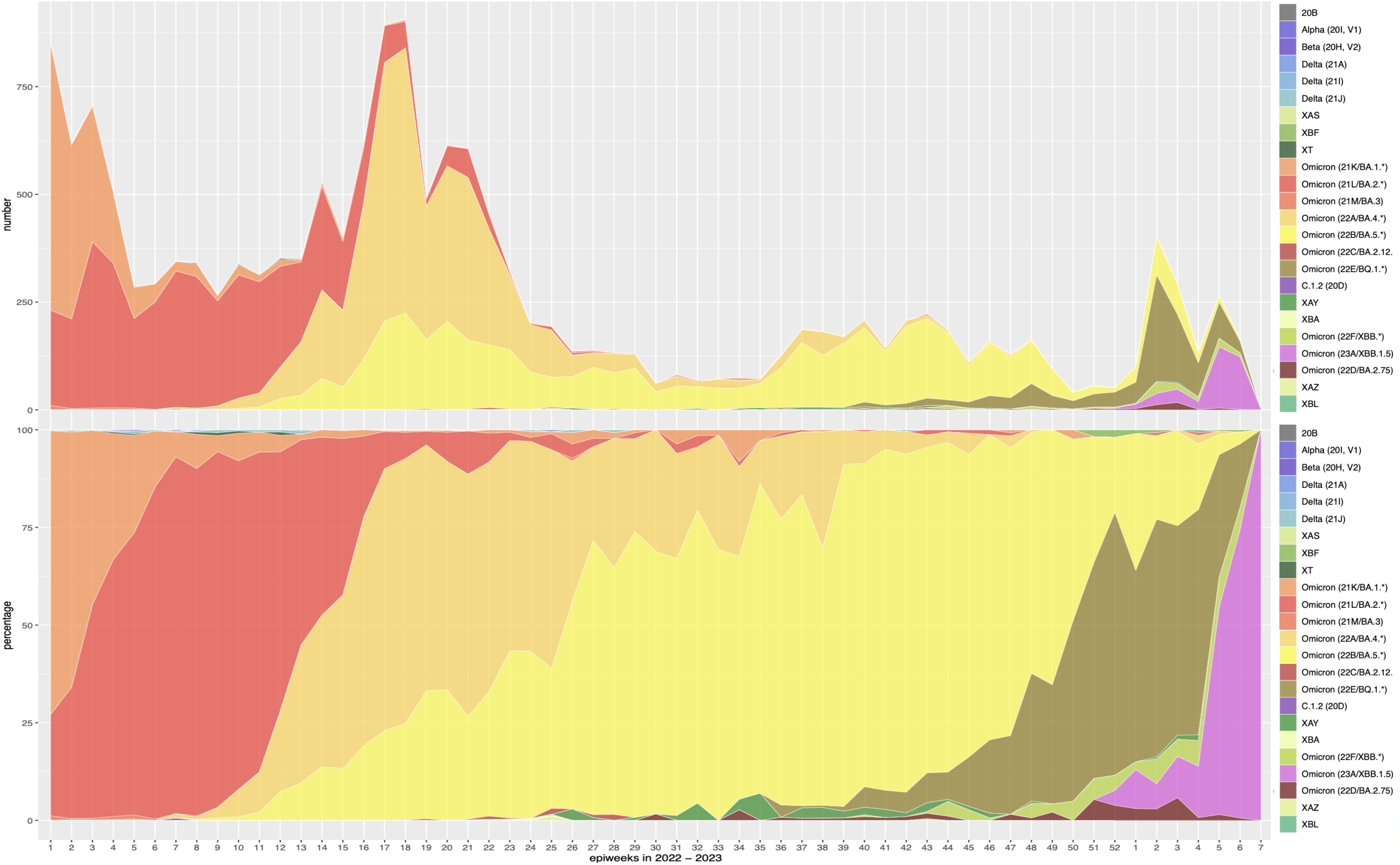
Number and percentage of clades by epiweek in South Africa, 2022-2023 (16 683*)



Sequencing data ending epi week 7 (ending 18 Feb 2023)

Currently in epi week 8 (ending 25 Feb 2023)

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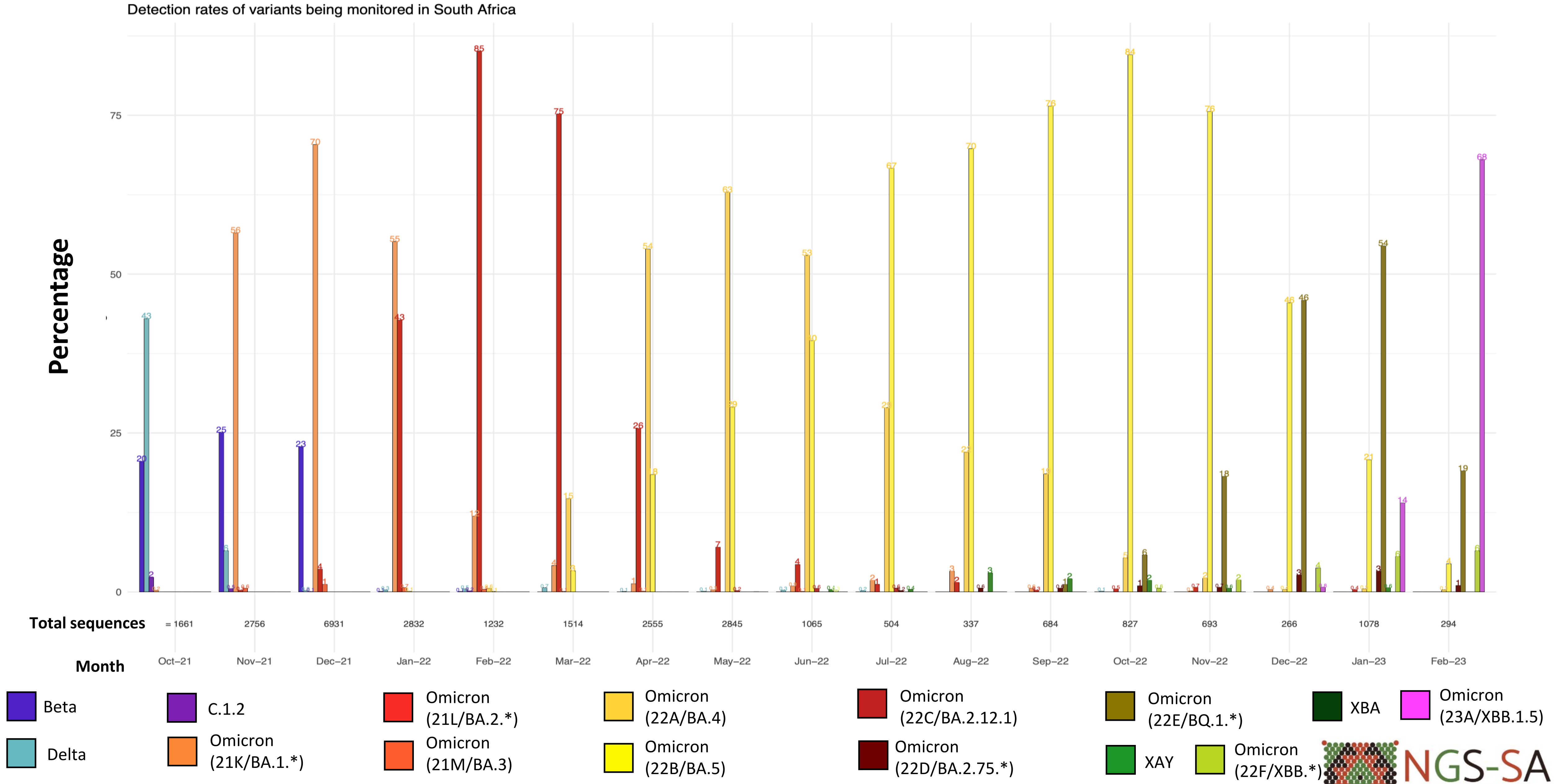
Detection Rates: Beta, Delta, C.1.2, recombinants, and Omicron



*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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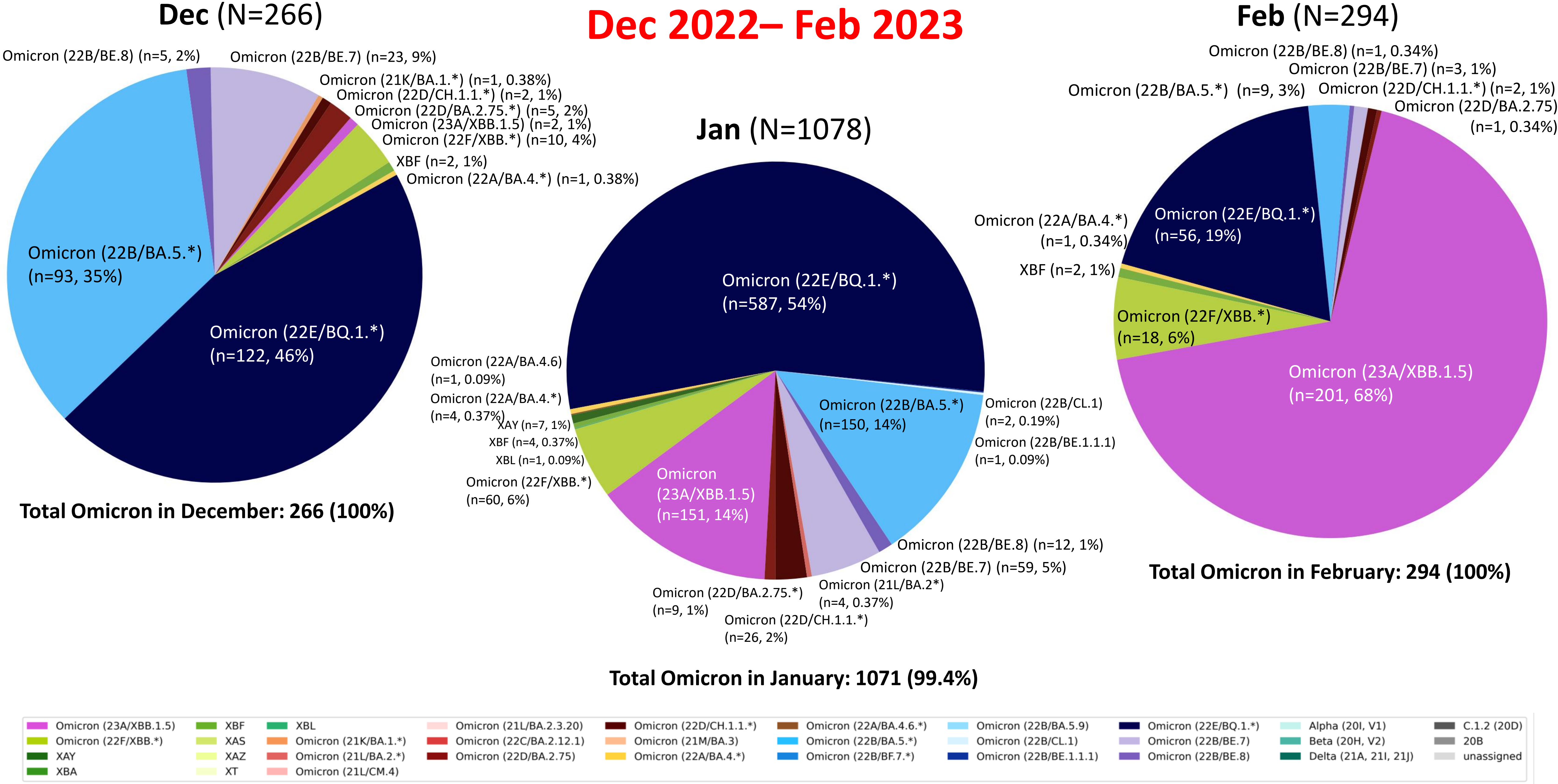
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in Dec 2022– Feb 2023



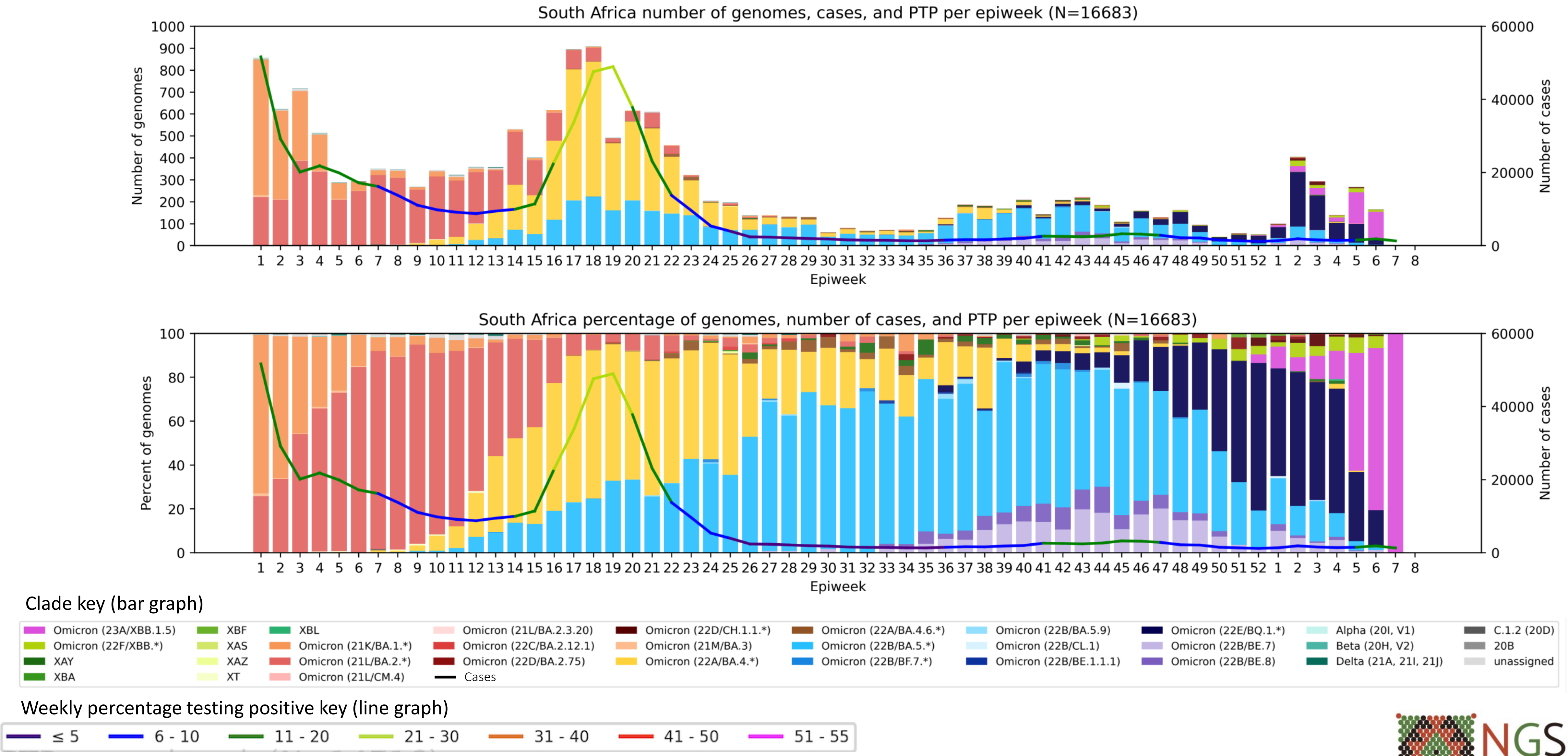
Total Omicron in December: 266 (100%)

Total Omicron in January: 1071 (99.4%)

Total Omicron in February: 294 (100%)

Note: XBF and XBL are Omicron-Omicron recombinants and so are counted in the total number of Omicrons.

South Africa, 2022-2023, n = 16 683*



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

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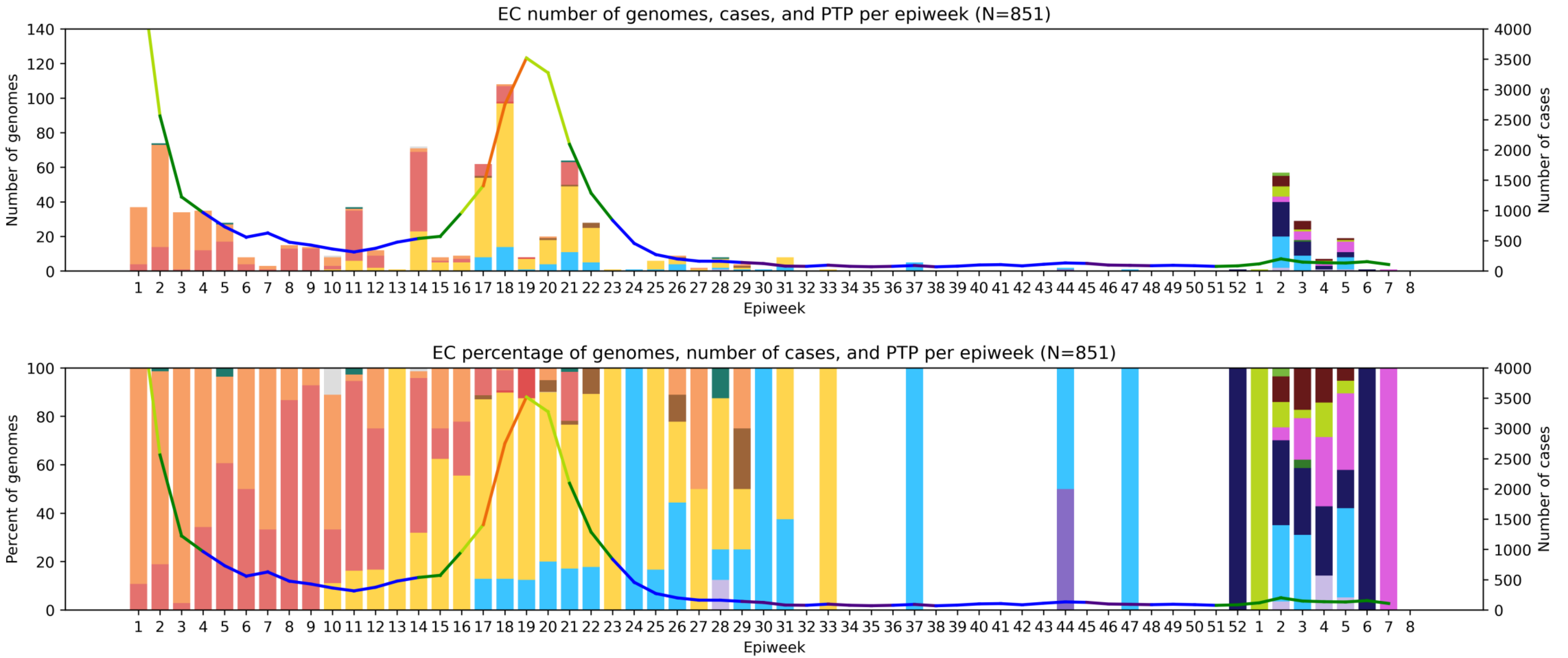
Eastern Cape Province, 2022-2023, n = 851

Genomes added since last report: 34*


EC number of genomes, cases, and PTP per epiweek (N=851)

EC percentage of genomes, number of cases, and PTP per epiweek (N=851)

Clade key (bar graph)

- ■ Omicron (23A/XBB.1.5)
- ■ Omicron (22F/XBB.*)
- ■ XAY
- ■ XBA
- ■ XBF
- ■ XAS
- ■ XAZ
- ■ XT
- ■ XBL
- ■ Omicron (21K/BA.1.*)
- ■ Omicron (21L/BA.2.*)
- ■ Omicron (21L/CM.4)
- ■ Omicron (21L/BA.2.3.20)
- ■ Omicron (22C/BA.2.12.1)
- ■ Omicron (22D/BA.2.75)
- — Cases
- ■ Omicron (22D/CH.1.1.*)
- ■ Omicron (21M/BA.3)
- ■ Omicron (22A/BA.4.*)
- ■ Omicron (22A/BA.4.6.*)
- ■ Omicron (22B/BA.5.*)
- ■ Omicron (22B/BF.7.*)
- ■ Omicron (22B/BA.5.9)
- ■ Omicron (22B/CL.1)
- ■ Omicron (22B/BE.1.1.1)
- ■ Omicron (22E/BQ.1.*)
- ■ Omicron (22B/BE.7)
- ■ Omicron (22B/BE.8)
- ■ Alpha (20I, V1)
- ■ Beta (20H, V2)
- ■ Delta (21A, 21I, 21J)
- ■ C.1.2 (20D)
- ■ 20B
- ■ unassigned

Weekly percentage testing positive key (line graph)

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

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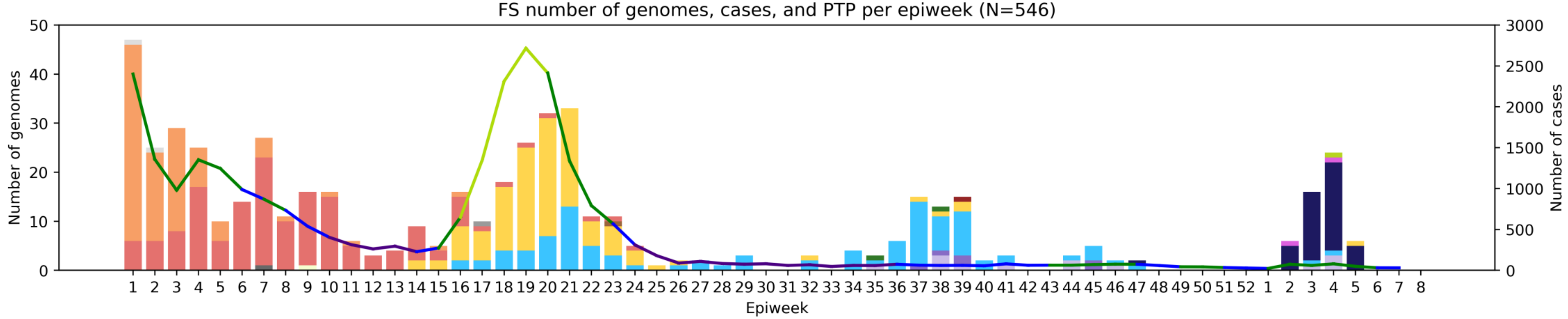
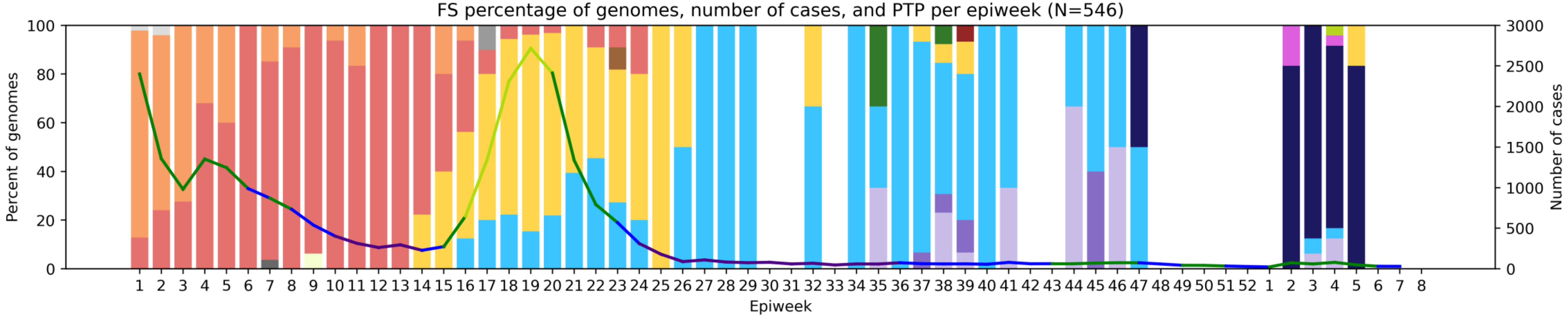
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

Free State Province, 2022-2023, n = 546

Genomes added since last report: 23*


FS number of genomes, cases, and PTP per epiweek (N=546)


FS percentage of genomes, number of cases, and PTP per epiweek (N=546)

Clade key (bar graph)

- ■ Omicron (23A/XBB.1.5)
- ■ Omicron (22F/XBB.*)
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- ■ XAZ
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- ■ Omicron (21L/BA.2.*)
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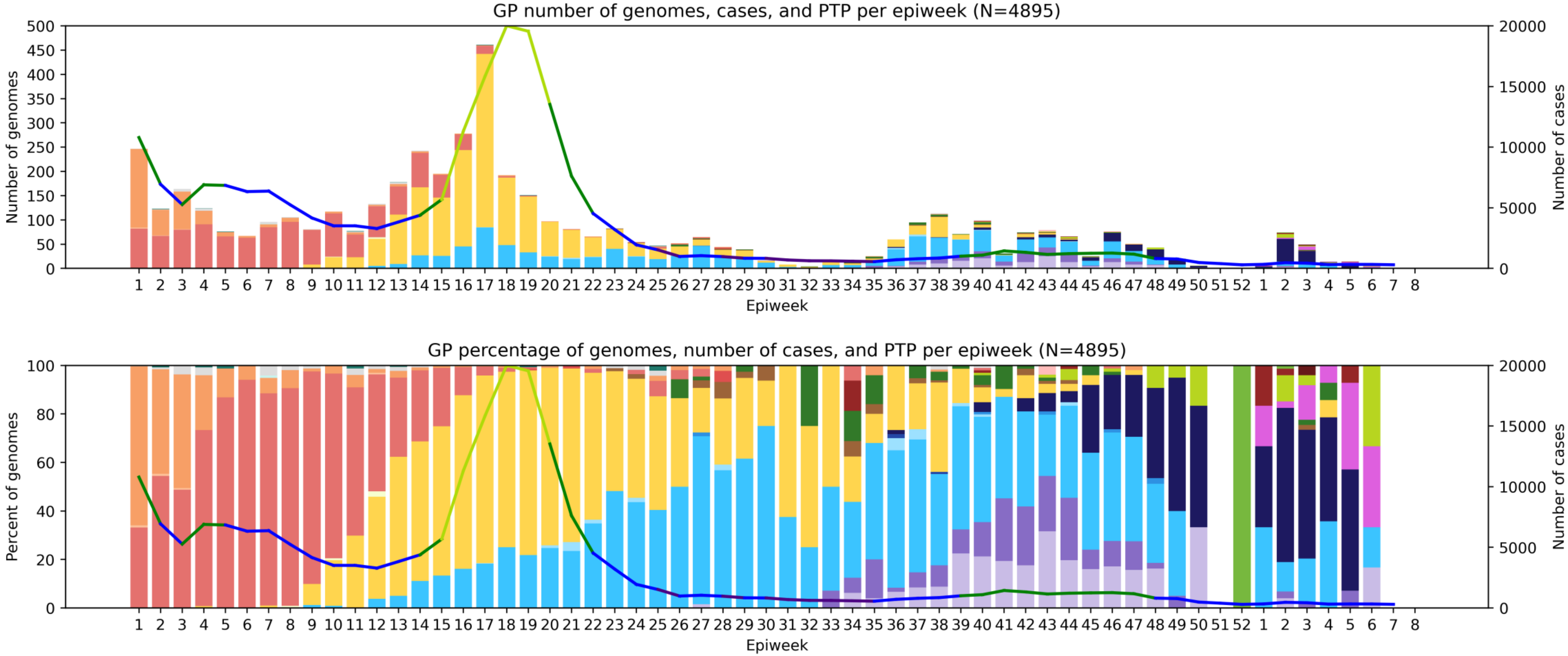
Gauteng Province, 2022-2023, n = 4895

Genomes added since last report: 25*


GP number of genomes, cases, and PTP per epiweek (N=4895)

GP percentage of genomes, number of cases, and PTP per epiweek (N=4895)

Clade key (bar graph)

- Omicron (23A/XBB.1.5)
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- Omicron (22A/BA.4.6.*)
- Omicron (22B/BA.5.*)
- Omicron (22B/BF.7.*)
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- Omicron (22B/CL.1)
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- C.1.2 (20D)
- 20B
- unassigned

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

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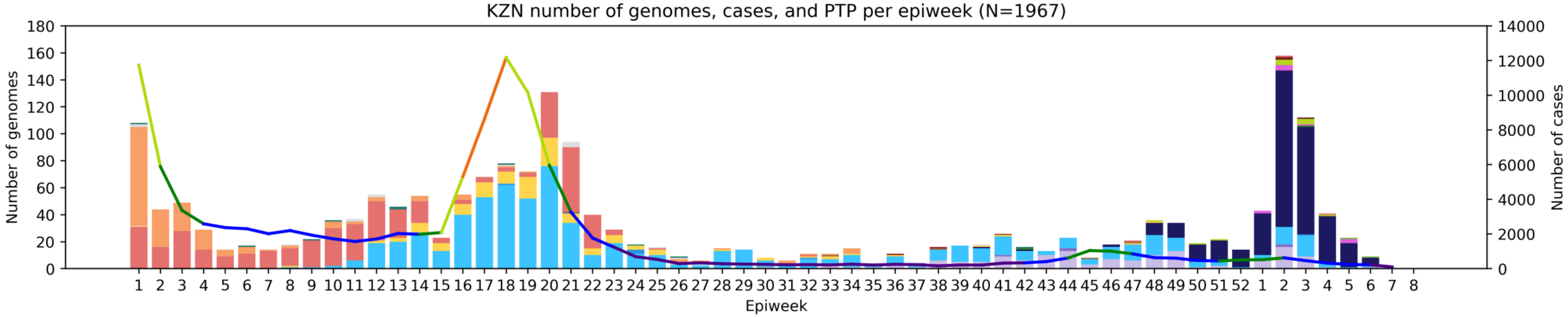
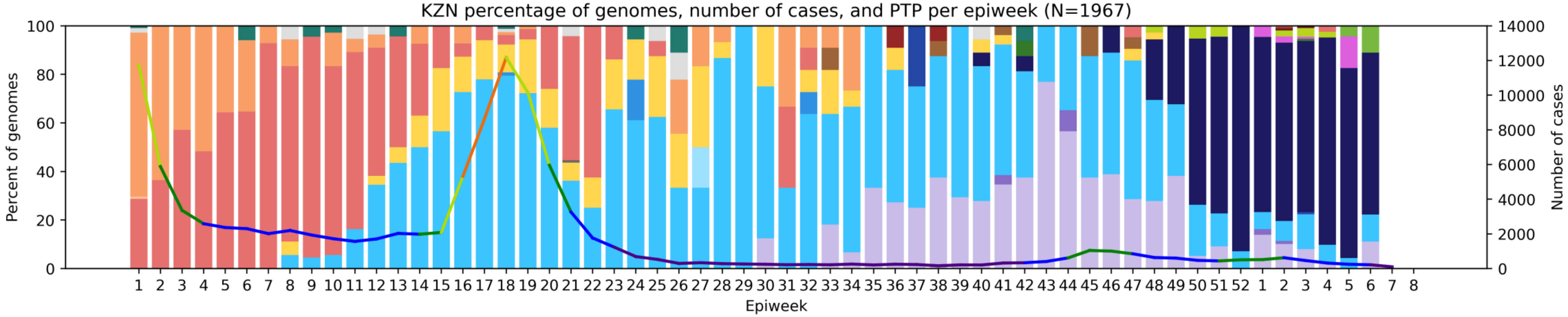
KwaZulu-Natal Province, 2022-2023, n = 1967

Genomes added since last report: 66*





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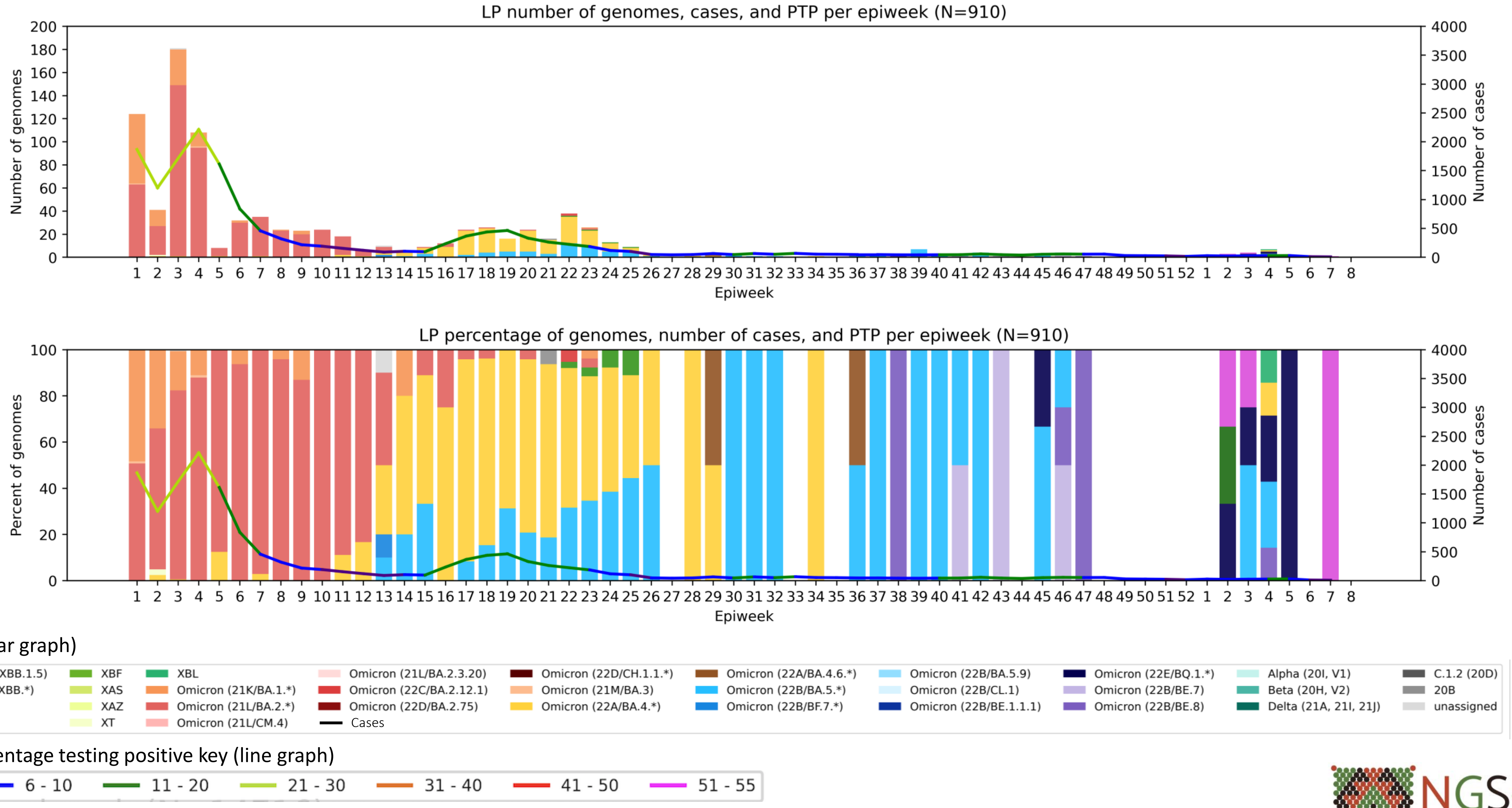
Limpopo Province, 2022-2023, n = 910

Genomes added since last report: 9*



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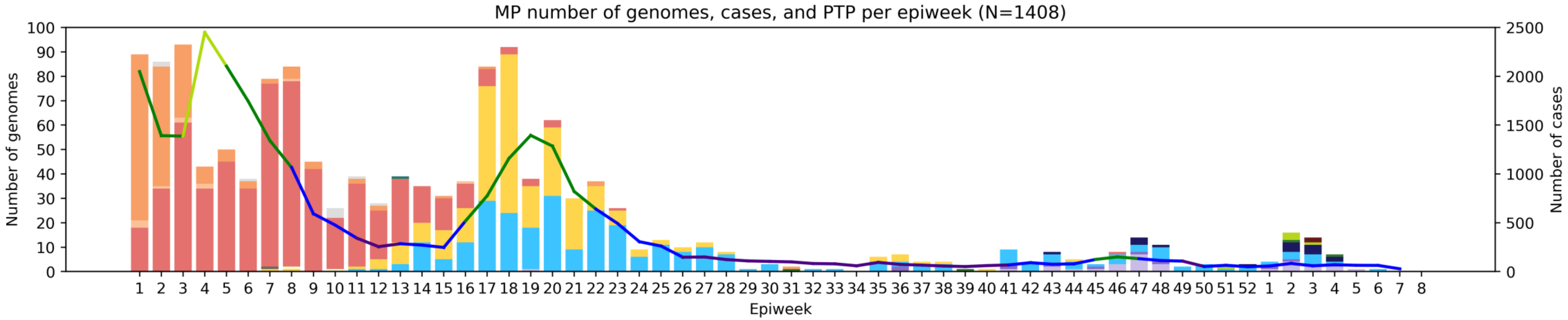
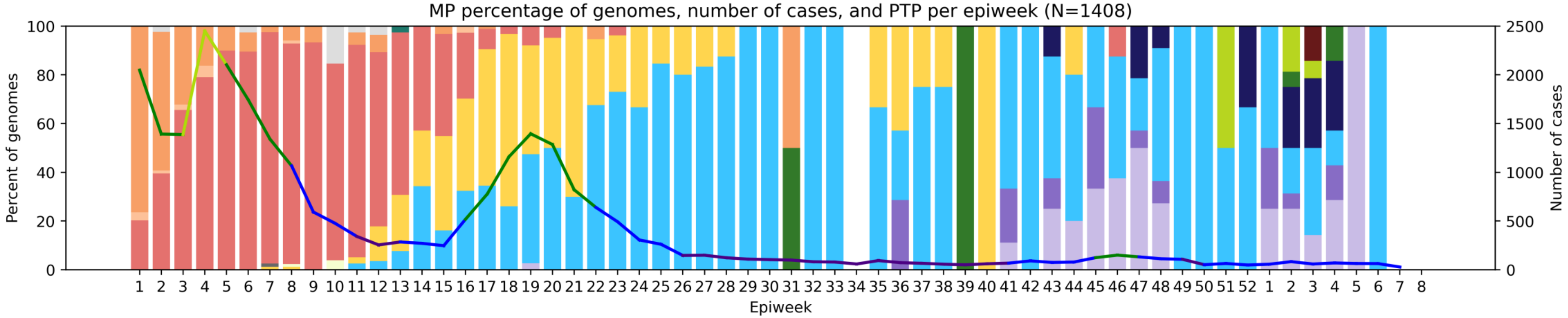
Mpumalanga Province, 2022-2023, n = 1408

Genomes added since last report: 9*





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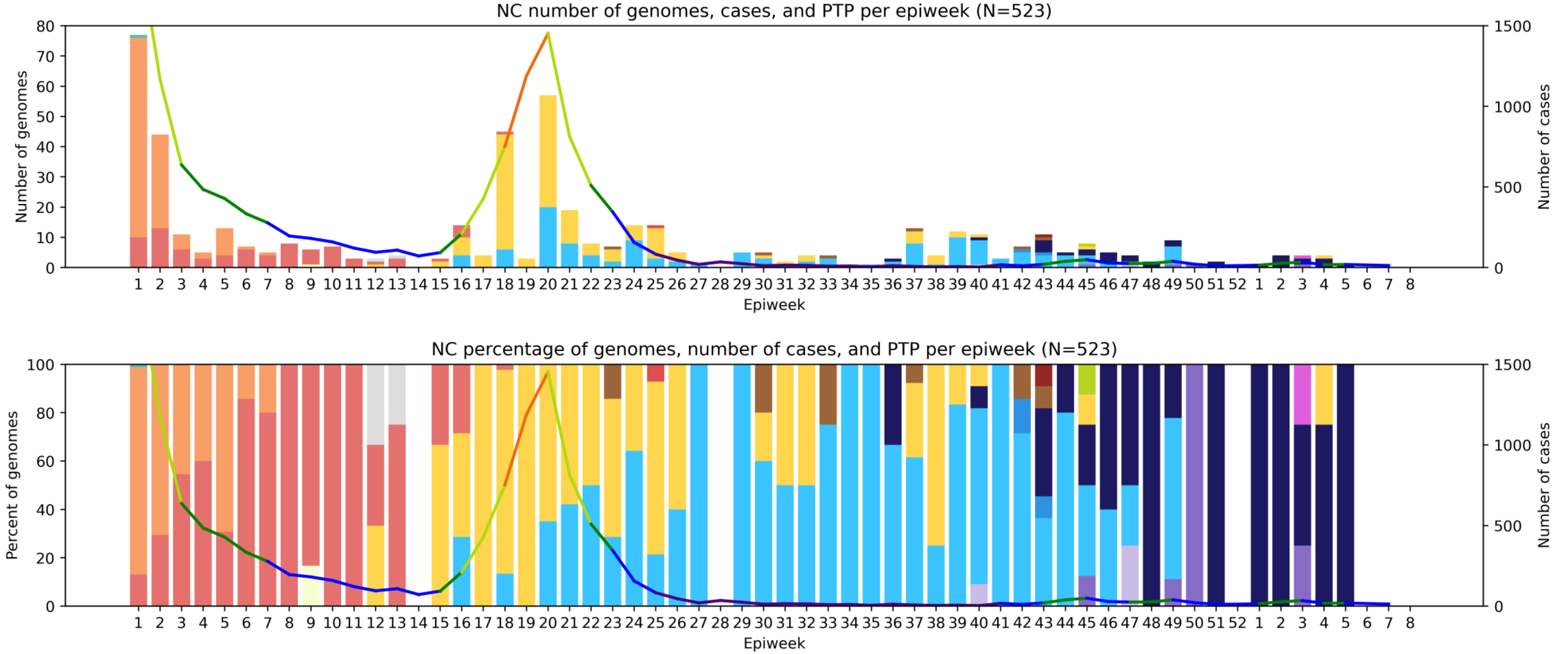
Northern Cape Province, 2022-2023, n = 523

Genomes added since last report: 5*



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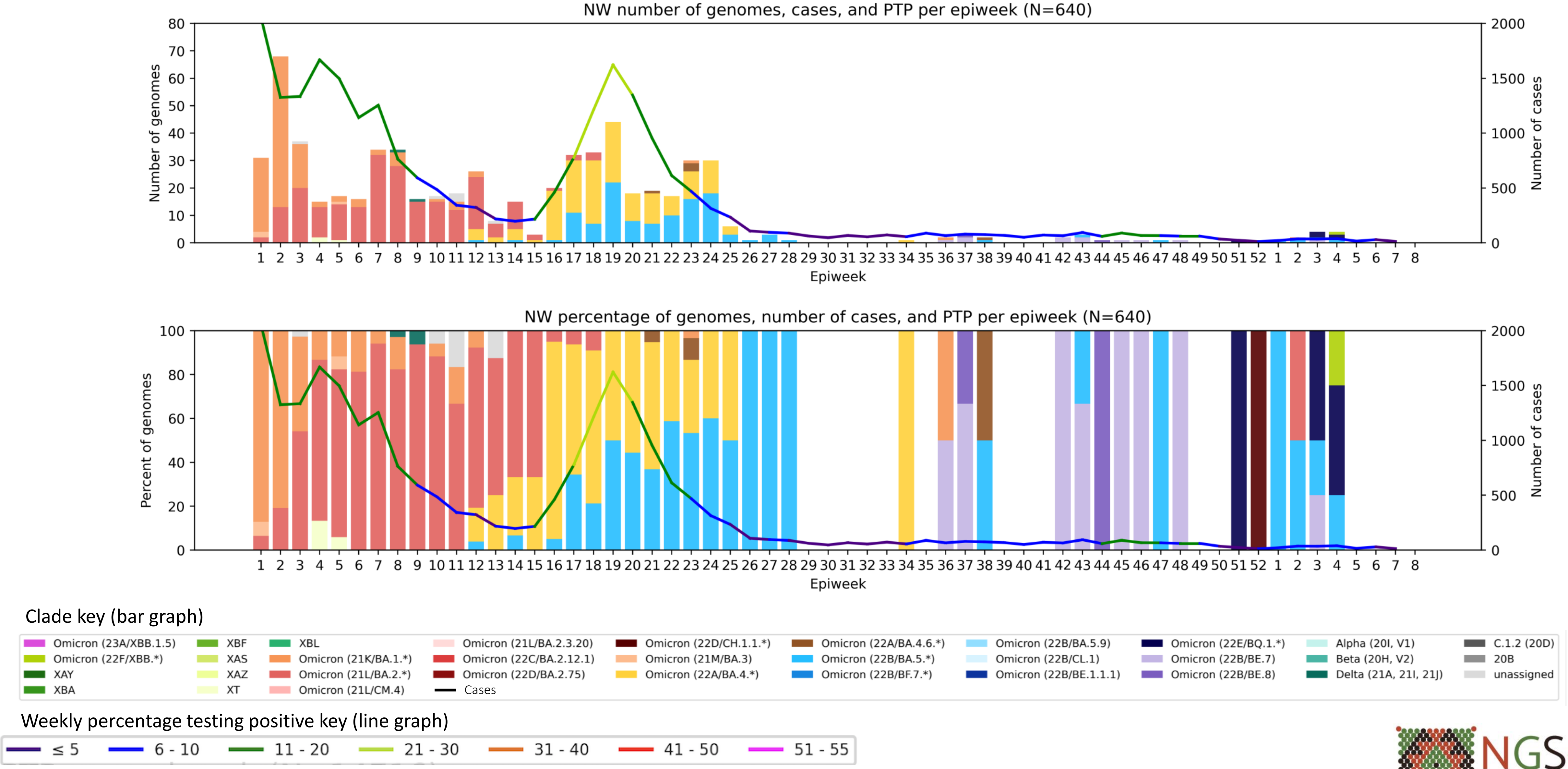
North West Province, 2022-2023, n = 640

Genomes added since last report: 8*



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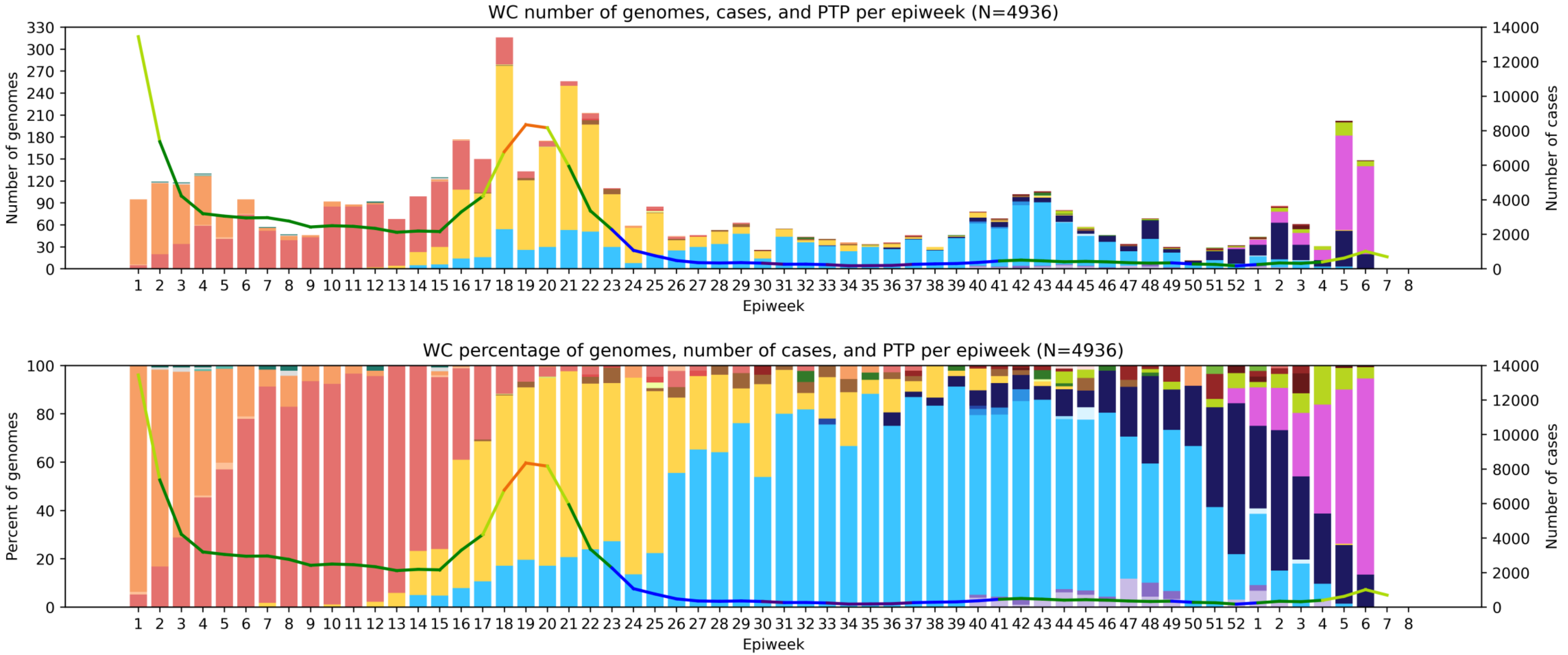
Western Cape Province, 2022-2023, n = 4936

Genomes added since last report: 287*



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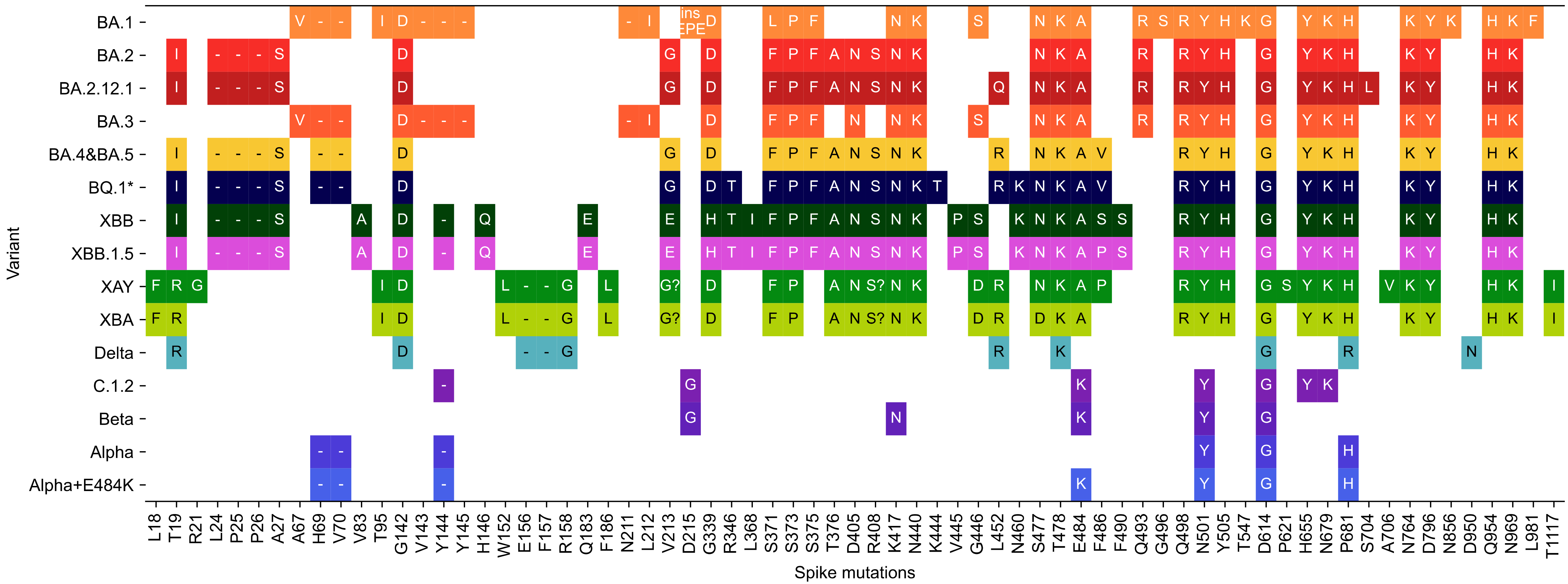
Summary

- **Sequencing update**
  - Eastern Cape, Gauteng, KwaZulu-Natal, Mpumalanga, the Northern Cape, the North West and the Western Cape have sequences for December 2022. All provinces have sequences for January 2023. All provinces, except the North West, have sequences for February 2023

- **Variant of Concern Omicron in South Africa**
  - Omicron continued to dominate in December (100%), January (99%) and makes up 100% of February sequences
  - BQ.1 and sub-lineages were the dominant Omicron lineage in December (46%) and January (54%)
  - XBB.1.5 was detected in December 2022 (n=2, 1%) and January 2023 (n=151, 14%), and is the dominant lineage in February 2023 (n=201, 68%)
  - BA.2.75.* continued to be detected at a low prevalence in December, January and February (≤3%)

Spike protein mutation* profile of Variants of Interest and Concern



Variant	L18	T19	R21	L24	P25	P26	A27	A67	H69	V70	V83	T95	G142	V143	Y144	Y145	H146	W152	E156	F157	R158	Q183	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										
BQ.1*		I		-	-	-	S		-	-			D										
XBB		I		-	-	-	S				A		D		-		Q					E	
XBB.1.5		I		-	-	-	S				A		D		-		Q					E	
XAY	F	R	G									I	D					L	-	-	G		L
XBA	F	R										I	D					L	-	-	G		L
Delta		R											D						-	-	G		
C.1.2															-								
Beta																							
Alpha									-	-					-								
Alpha+E484K									-	-					-								

Variant	N211	L212	V213	D215	G339	R346	L368	S371	S373	S375	T376	D405	R408	K417	N440	K444	V445	G446	L452	N460	S477	T478	E484
BA.1	-	I		ins EPE	D			L	P	F				N	K			S			N	K	A
BA.2			G		D			F	P	F	A	N	S	N	K						N	K	A
BA.2.12.1			G		D			F	P	F	A	N	S	N	K				Q		N	K	A
BA.3	-	I			D			F	P	F		N		N	K			S			N	K	A
BA.4&BA.5			G		D			F	P	F	A	N	S	N	K				R		N	K	A
BQ.1*			G		D	T		F	P	F	A	N	S	N	K	T			R	K	N	K	A
XBB			E		H	T	I	F	P	F	A	N	S	N	K		P	S		K	N	K	A
XBB.1.5			E		H	T	I	F	P	F	A	N	S	N	K		P	S		K	N	K	A
XAY			G?		D			F	P		A	N	S?	N	K			D	R		N	K	A
XBA			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

Variant	F486	F490	Q493	G496	Q498	N501	Y505	T547	D614	P621	H655	N679	P681	S704	A706	N764	D796	N856	D950	Q954	N969	L981	T1117
BA.1			R	S	R	Y	H	K	G		Y	K	H			K	Y	K		H	K	F	
BA.2			R		R	Y	H		G		Y	K	H			K	Y			H	K		
BA.2.12.1			R		R	Y	H		G		Y	K	H	L		K	Y			H	K		
BA.3			R		R	Y	H		G		Y	K	H			K	Y			H	K		
BA.4&BA.5	V				R	Y	H		G		Y	K	H			K	Y			H	K		
BQ.1*	V				R	Y	H		G		Y	K	H			K	Y			H	K		
XBB	S	S			R	Y	H		G		Y	K	H			K	Y			H	K		
XBB.1.5	P	S			R	Y	H		G		Y	K	H			K	Y			H	K		
XAY	P				R	Y	H		G	S	Y	K	H		V	K	Y			H	K		I
XBA					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										

Spike mutations

- 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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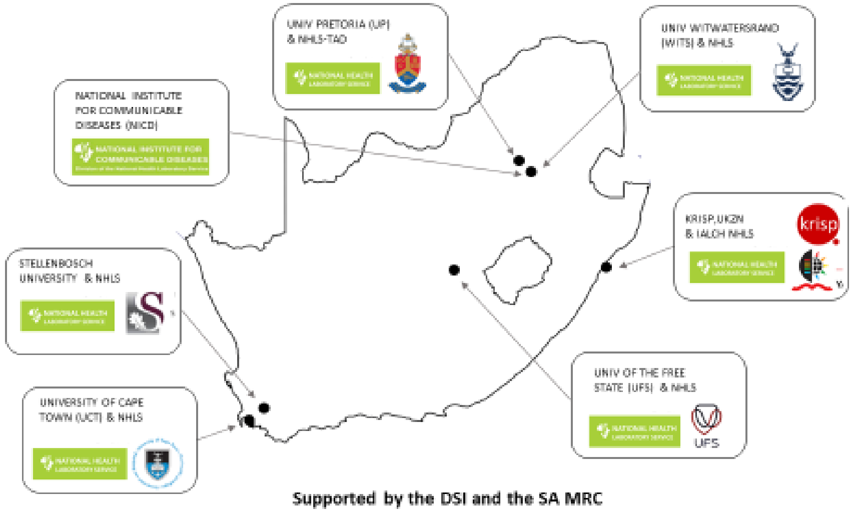

Supported by the DSI and the SA MRC

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EDCTP

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

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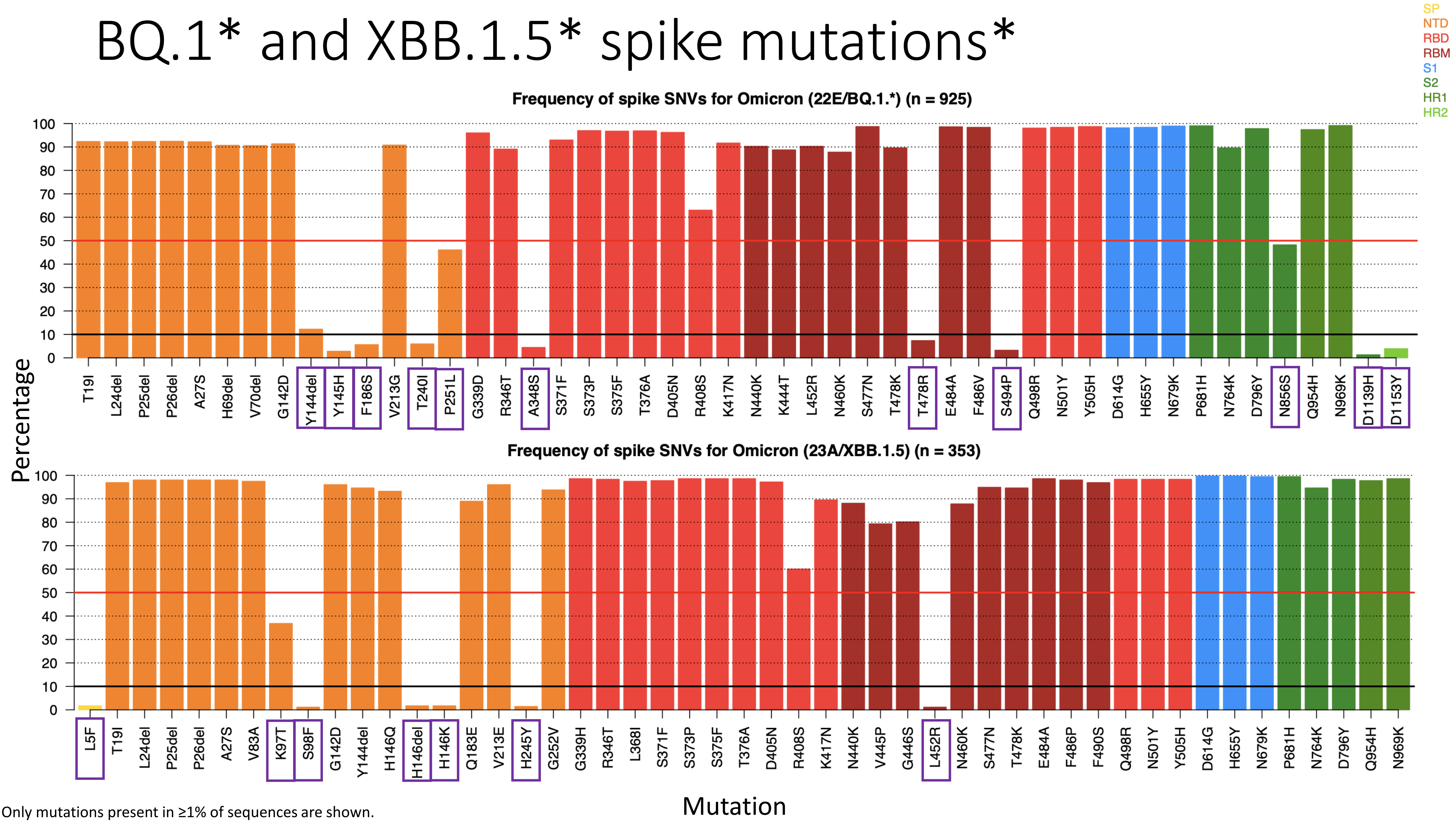
BQ.1* and XBB.1.5* spike mutations*



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

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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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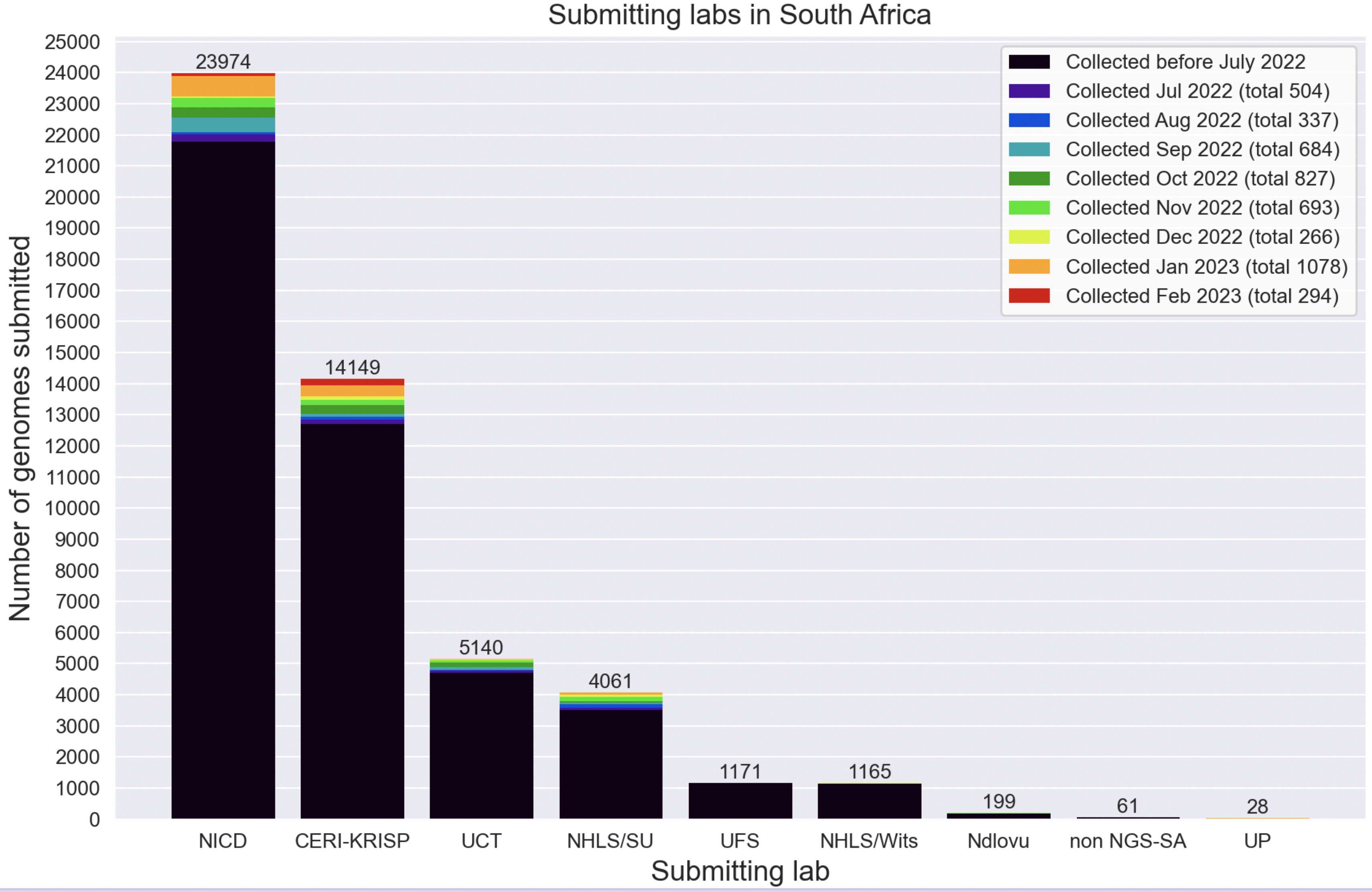
South African genomes submitted per submitting lab, 2020 - 2023 (N=49 948)



Submitting labs in South Africa

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 24 February 2023

Omicron subvariants under monitoring

Pango lineage[#] (+ mutation)	GISAID clade	Nextstrain clade	Relationship to circulating VOC lineages	Spike genetic features	Earliest documented samples
BF.7*	GRA	22B	BA.5 sublineage	BA.5 + S:R346T	24-01-2022
BQ.1[$]	GRA	22E	BA.5 sublineage	BQ.1 and BQ.1.1: BA.5 + S:R346T, S:K444T, S:N460K	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	31-12-2021
CH.1.1[§]	GRA	22D	BA.2 sublineage	BA.2.75 + S:L452R, S:F486S	27-07-2022
XBB[µ]	GRA	22F	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
XBB.1.5	GRA	23A	Recombinant of BA.2.10.1 and BA.2.75 sublineages, i.e. BJ1 and BM.1.1.1, with a breakpoint in S1	XBB + S:F486P (see rapid risk assessment)	05-01-2022
XBF	GRA		Recombinant of BA.5.2.3 and CJ.1 (BA.2.75.3 sublineage)	BA.5 + S:K147E, S:W152R, S:F157L, S:I210V, S:G257S, S:G339H, S:R346T, S:G446S, S:N460K, S:F486P, S:F490S	27-07-2022

includes descendent lineages
* additional mutations outside of the spike protein: N: G30-, S33F, ORF9b: M26-, A29I, V30L
$ additional mutation outside the spike protein: ORF1a: Q556K, L3829F, ORF1b: Y264H, M1156I, N1191S, N: E136D, ORF9b: P10F
§ additional mutations outside of the spike protein: ORF1a: S1221L, P1640S, N4060S, ORF1b: G662S, E: T11A
µ additional mutations outside of the spike protein: ORF1a: K47R, ORF1b: G662S, S959P, E: T11A, ORF8: G8*

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 24 February 2023

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 24 February 2023

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.)