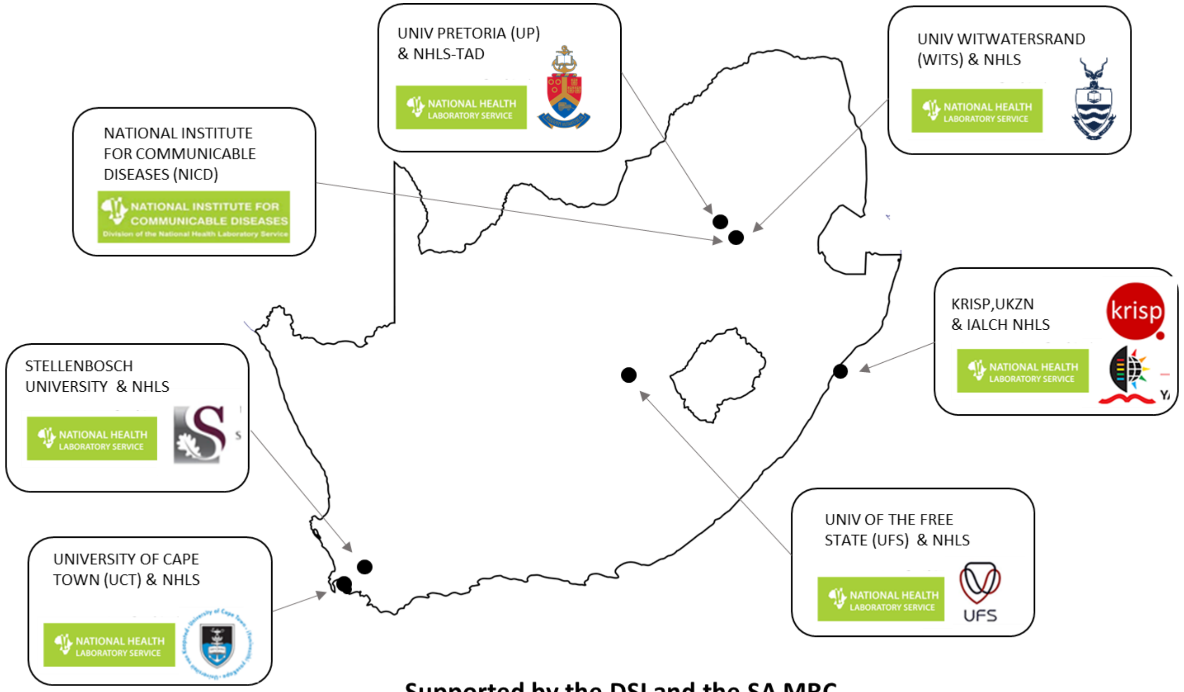
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update

09 September 2024



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

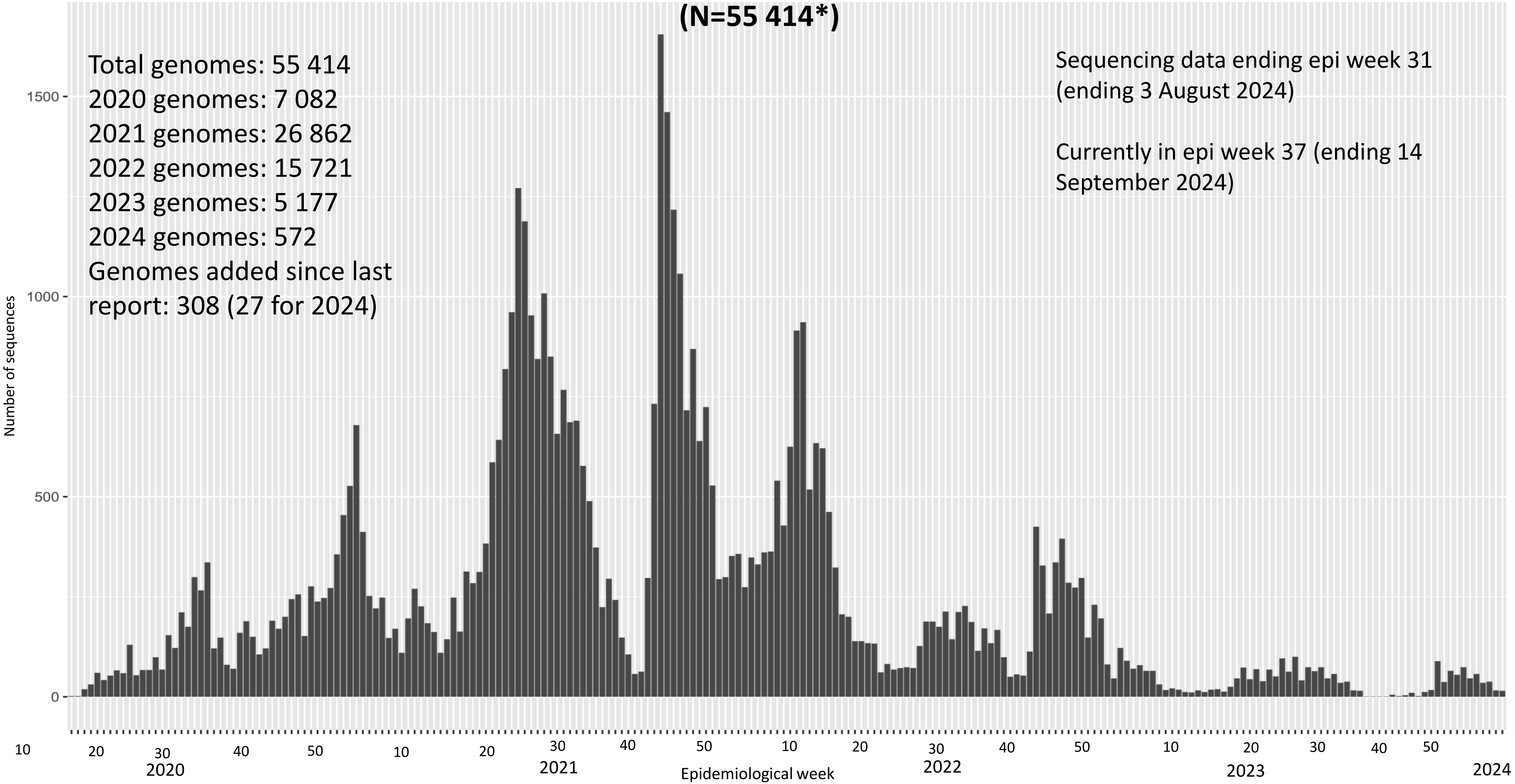
Prepared by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory (NHLS) on behalf of the Network for Genomics Surveillance in South Africa (NGS-SA)

The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 09 September 2024 at 11h30

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 – 2024 (N=55 414*)



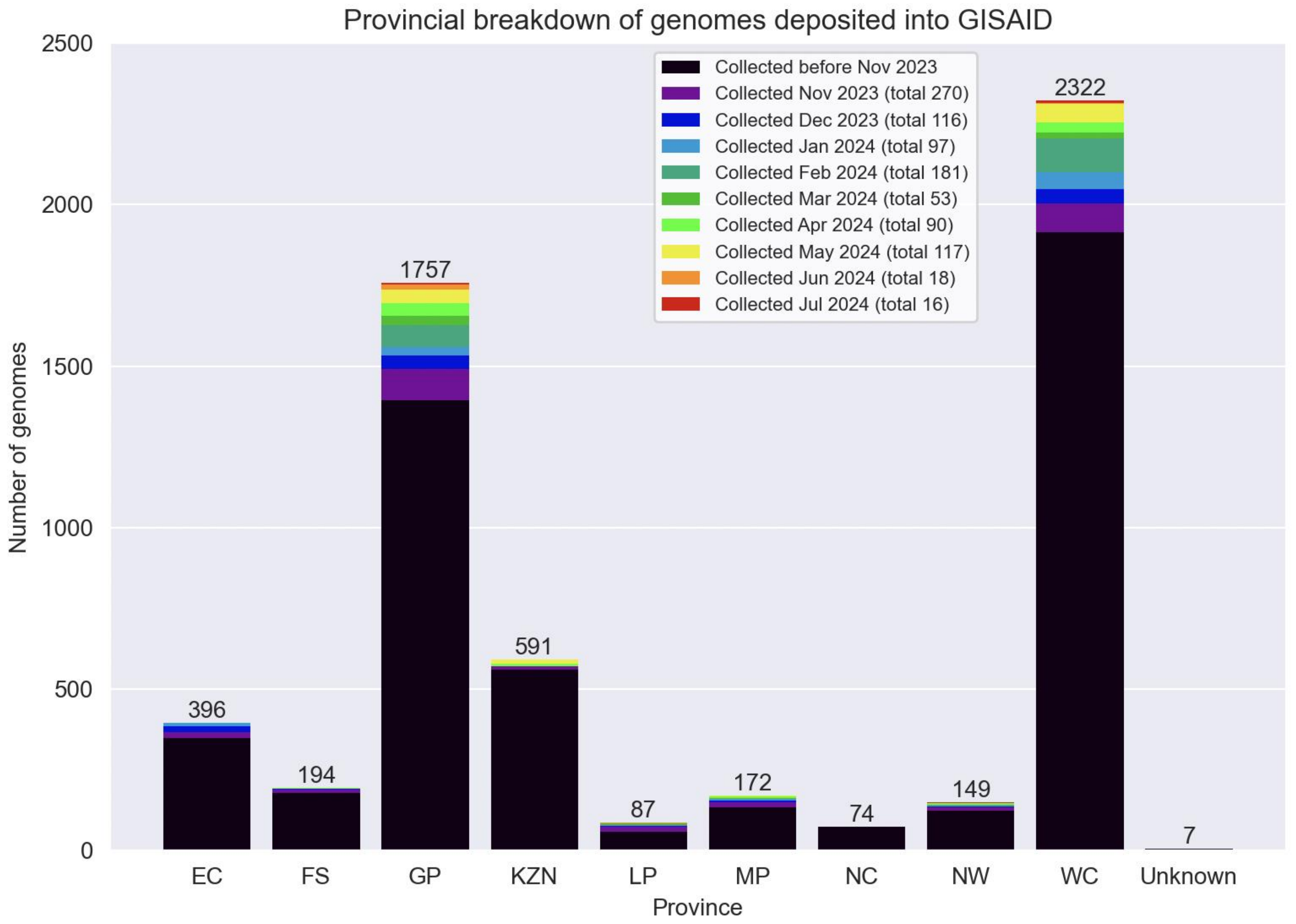
Total genomes: 55 414
2020 genomes: 7 082
2021 genomes: 26 862
2022 genomes: 15 721
2023 genomes: 5 177
2024 genomes: 572
Genomes added since last report: 308 (27 for 2024)

Sequencing data ending epi week 31 (ending 3 August 2024)

Currently in epi week 37 (ending 14 September 2024)

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

Provincial breakdown of genomes deposited on GISAID, 2023 – 2024 (N=5749)



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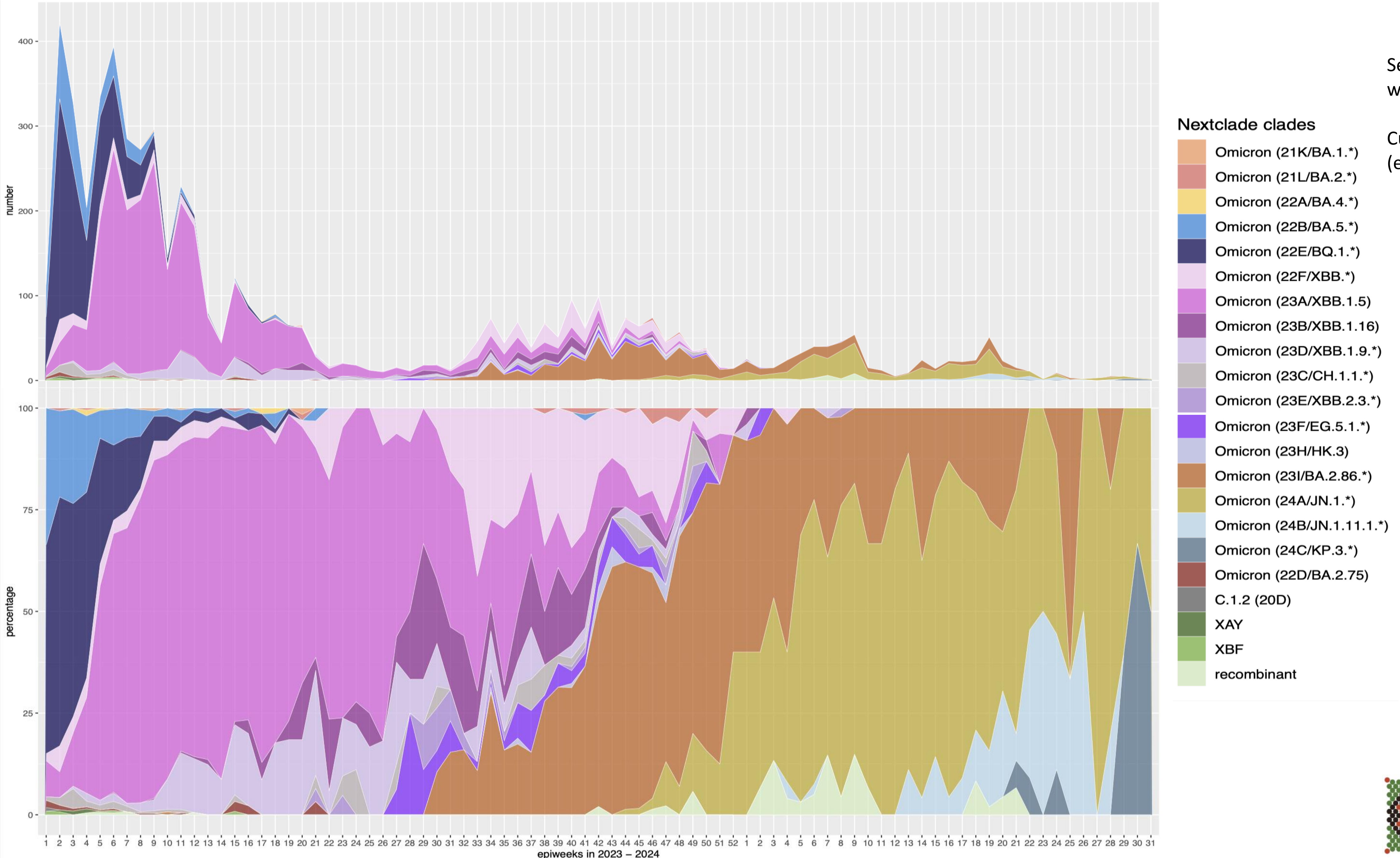
Number and percentage of clades by epiweek in South Africa, 2023-2024 (N=5749)



Sequencing data ending epi week 31 (ending 3 Aug 2024)

Currently in epi week 37 (ending 14 Sep 2024)

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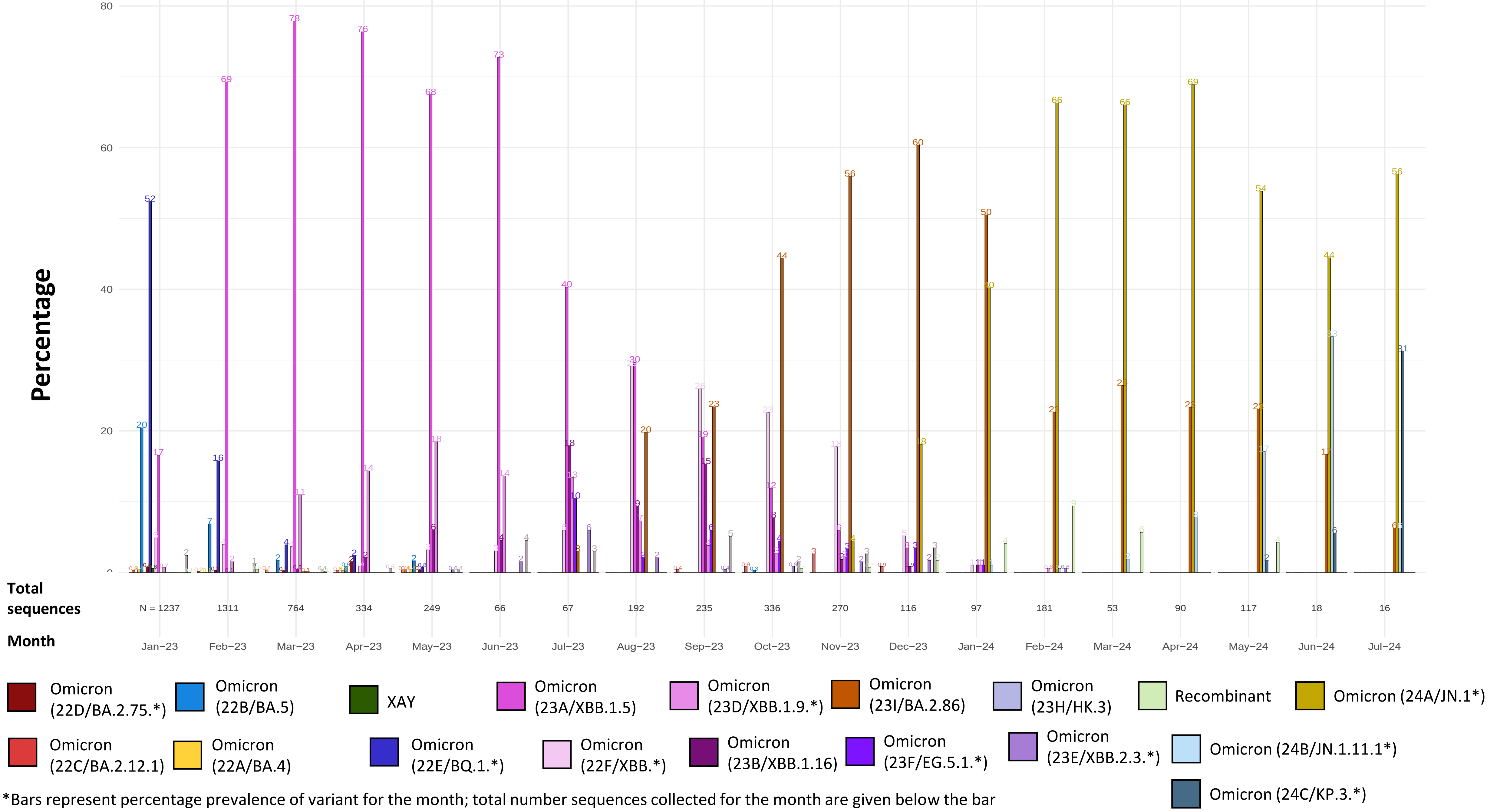
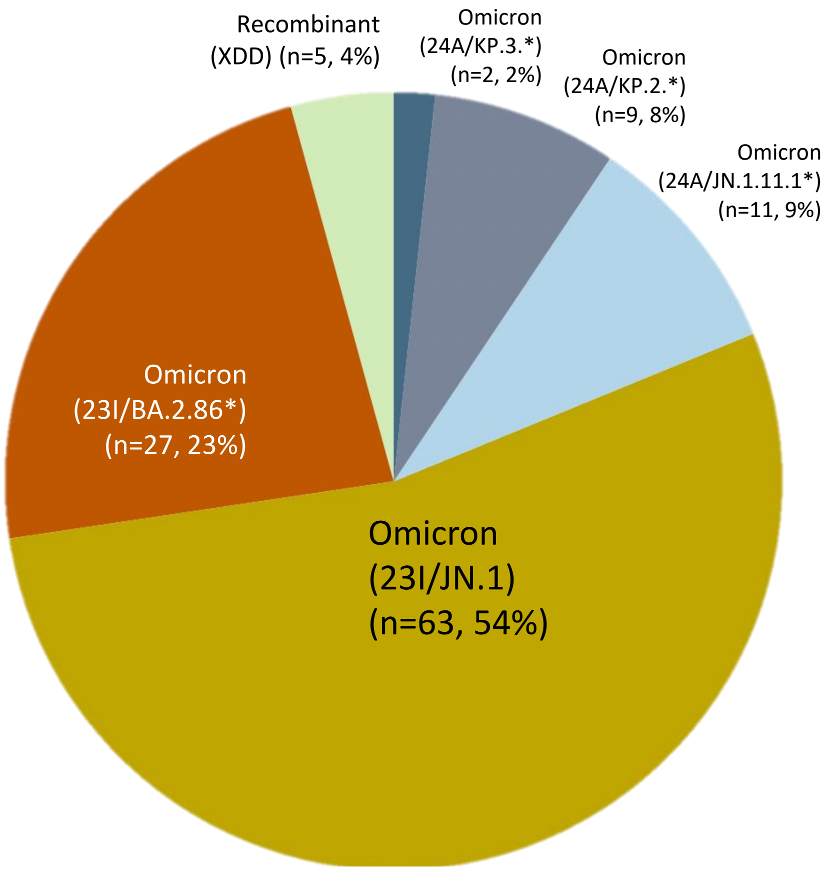
Detection Rates: Omicron and recombinants



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

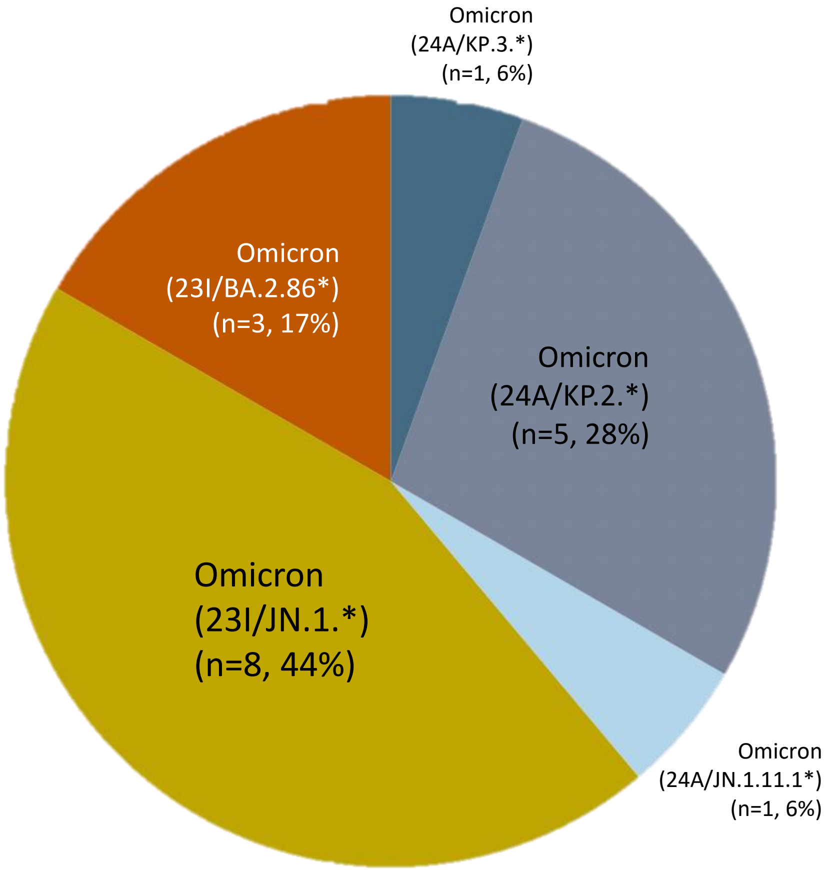
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in MAY – JULY 2024

May (N=117)



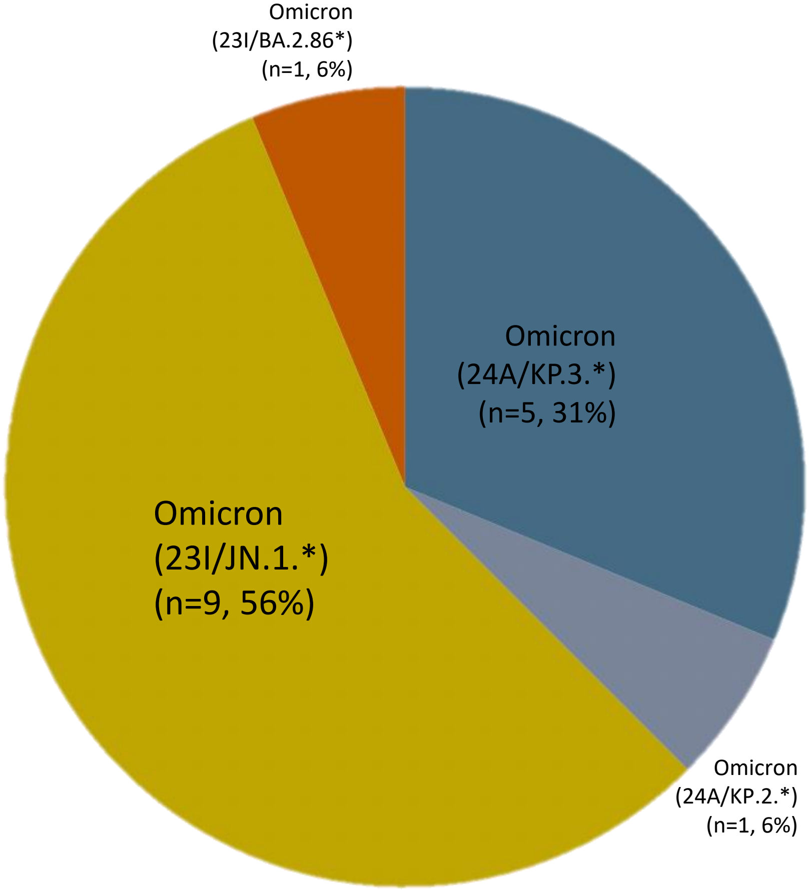
Total Omicron in May: 117 (100%)

June (N=18)



Total Omicron in June: 18 (100%)

July (N=16)

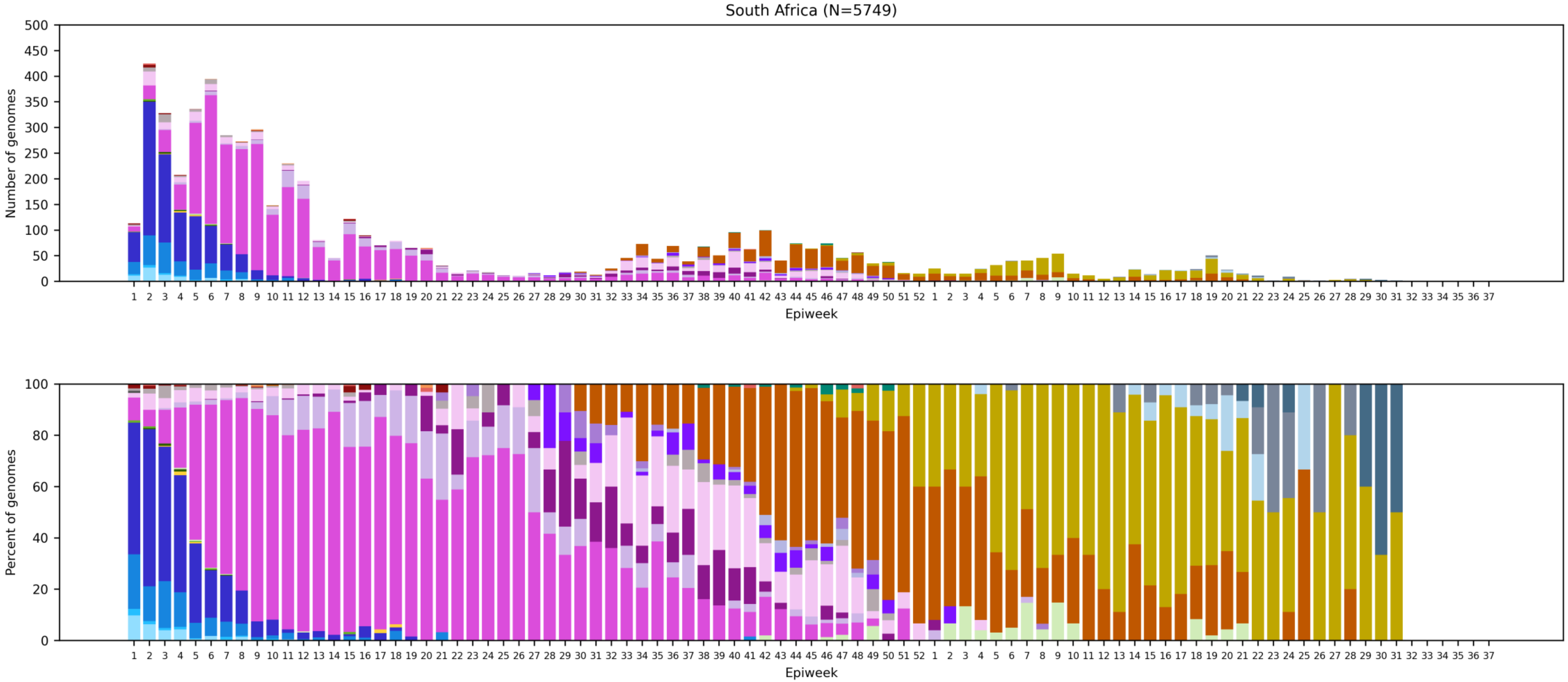


Total Omicron in July: 16 (100%)

Clade key (bar graph)

- ■ XAY
- ■ XBF
- ■ recombinant
- ■ Omicron (23B/XBB.1.16)
- ■ Omicron (23A/XBB.1.5)
- ■ Omicron (23D/XBB.1.9.*)
- ■ Omicron (22F/XBB.*)
- ■ Omicron (21K/BA.1.*)
- ■ Omicron (21L/BA.2.*)
- ■ Omicron (22C/BA.2.12.1)
- ■ Omicron (22D/BA.2.75)
- ■ Omicron (23C/CH.1.1.*)
- ■ Omicron (23F/EG.5.1.*)
- ■ Omicron (23H/HK.3)
- ■ Omicron (23E/XBB.2.3.*)
- ■ Omicron (23I/BA.2.86.*)
- ■ Omicron (24A/JN.1.*)
- ■ Omicron (24B/JN.1.11.1.*)
- ■ Omicron (24B/KP.2.*)
- ■ Omicron (24C/KP.3.*)
- ■ Omicron (21L/BA.2.87.1)
- ■ Omicron (21M/BA.3)
- ■ Omicron (22A/BA.4.*)
- ■ Omicron (22B/BE.7)
- ■ Omicron (22B/BE.8)
- ■ Omicron (22B/BA.5.*)
- ■ Omicron (22E/BQ.1.*)
- ■ Alpha (20I, V1)
- ■ Beta (20H, V2)
- ■ Delta (21A, 21I, 21J)
- ■ C.1.2 (20D)
- ■ 20B
- ■ unassigned

South Africa, 2023-2024, N=5749*



Clade key (bar graph)

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- ■ XBF
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- ■ Omicron (23B/XBB.1.16)
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- ■ Omicron (22A/BA.4.*)
- ■ Omicron (22B/BE.7)
- ■ Omicron (22B/BE.8)
- ■ Omicron (22B/BA.5.*)
- ■ Omicron (22E/BQ.1.*)
- ■ Alpha (20I, V1)
- ■ Beta (20H, V2)
- ■ Delta (21A, 21I, 21J)
- ■ C.1.2 (20D)
- ■ 20B
- ■ unassigned

*Excludes sequences missing collection dates. Lineages of particular interest (mainly WHO Omicron subvariants under monitoring) are separate from the main clade groupings.
#Recombinants include all recombinant lineages (viruses consisting of segments of two different lineages) detected in South Africa at low levels. Currently it consists of XT, XAS, XAZ, XBA, XBF.

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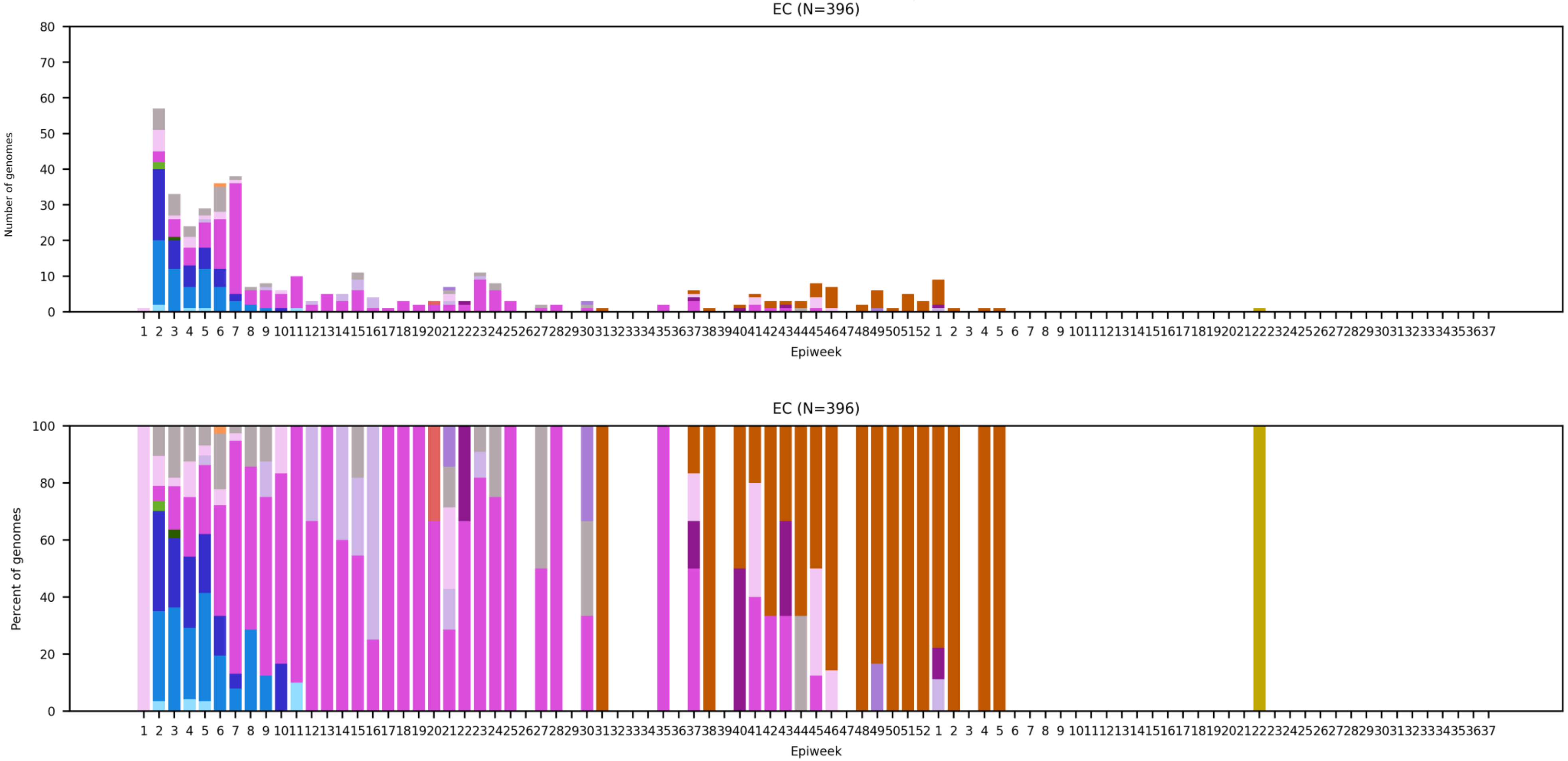
Eastern Cape Province, 2023-2024, N=396

Genomes added since last report: 1



Clade key (bar graph)

- ■ XAY
- ■ XBF
- ■ recombinant
- ■ Omicron (23B/XBB.1.16)
- ■ Omicron (23A/XBB.1.5)
- ■ Omicron (23D/XBB.1.9.*)
- ■ Omicron (22F/XBB.*)
- ■ Omicron (21K/BA.1.*)
- ■ Omicron (21L/BA.2.*)
- ■ Omicron (22C/BA.2.12.1)
- ■ Omicron (22D/BA.2.75)
- ■ Omicron (23C/CH.1.1.*)
- ■ Omicron (23F/EG.5.1.*)
- ■ Omicron (23H/HK.3)
- ■ Omicron (23E/XBB.2.3.*)
- ■ Omicron (23I/BA.2.86.*)
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- ■ Omicron (24B/JN.1.11.1.*)
- ■ Omicron (24B/KP.2.*)
- ■ Omicron (24C/KP.3.*)
- ■ Omicron (21L/BA.2.87.1)
- ■ Omicron (21M/BA.3)
- ■ Omicron (22A/BA.4.*)
- ■ Omicron (22B/BE.7)
- ■ Omicron (22B/BE.8)
- ■ Omicron (22B/BA.5.*)
- ■ Omicron (22E/BQ.1.*)
- ■ Alpha (20I, V1)
- ■ Beta (20H, V2)
- ■ Delta (21A, 21I, 21J)
- ■ C.1.2 (20D)
- ■ 20B
- ■ unassigned

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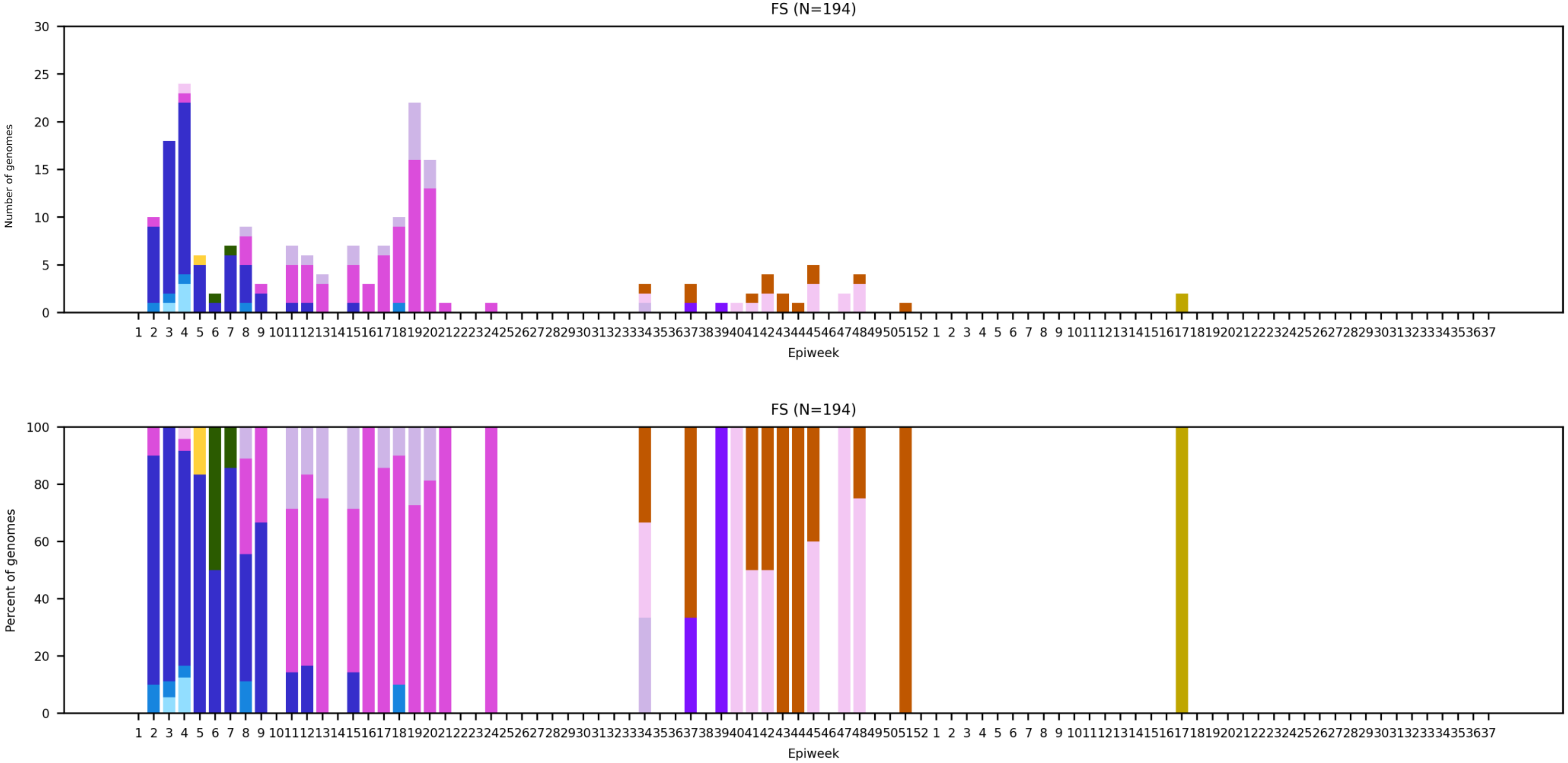
Free State Province, 2023-2024, N=194

Genomes added since last report: 0



Clade key (bar graph)

- XAY
- XBF
- recombinant
- Omicron (23B/XBB.1.16)
- Omicron (23A/XBB.1.5)
- Omicron (23D/XBB.1.9.*)
- Omicron (22F/XBB.*)
- Omicron (21K/BA.1.*)
- Omicron (21L/BA.2.*)
- Omicron (22C/BA.2.12.1)
- Omicron (22D/BA.2.75)
- Omicron (23C/CH.1.1.*)
- Omicron (23F/EG.5.1.*)
- Omicron (23H/HK.3)
- Omicron (23E/XBB.2.3.*)
- Omicron (23I/BA.2.86.*)
- Omicron (24A/JN.1.*)
- Omicron (24B/JN.1.11.1.*)
- Omicron (24B/KP.2.*)
- Omicron (24C/KP.3.*)
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- Omicron (21M/BA.3)
- Omicron (22A/BA.4.*)
- Omicron (22B/BE.7)
- Omicron (22B/BE.8)
- Omicron (22B/BA.5.*)
- Omicron (22E/BQ.1.*)
- Alpha (20I, V1)
- Beta (20H, V2)
- Delta (21A, 21I, 21J)
- C.1.2 (20D)
- 20B
- unassigned

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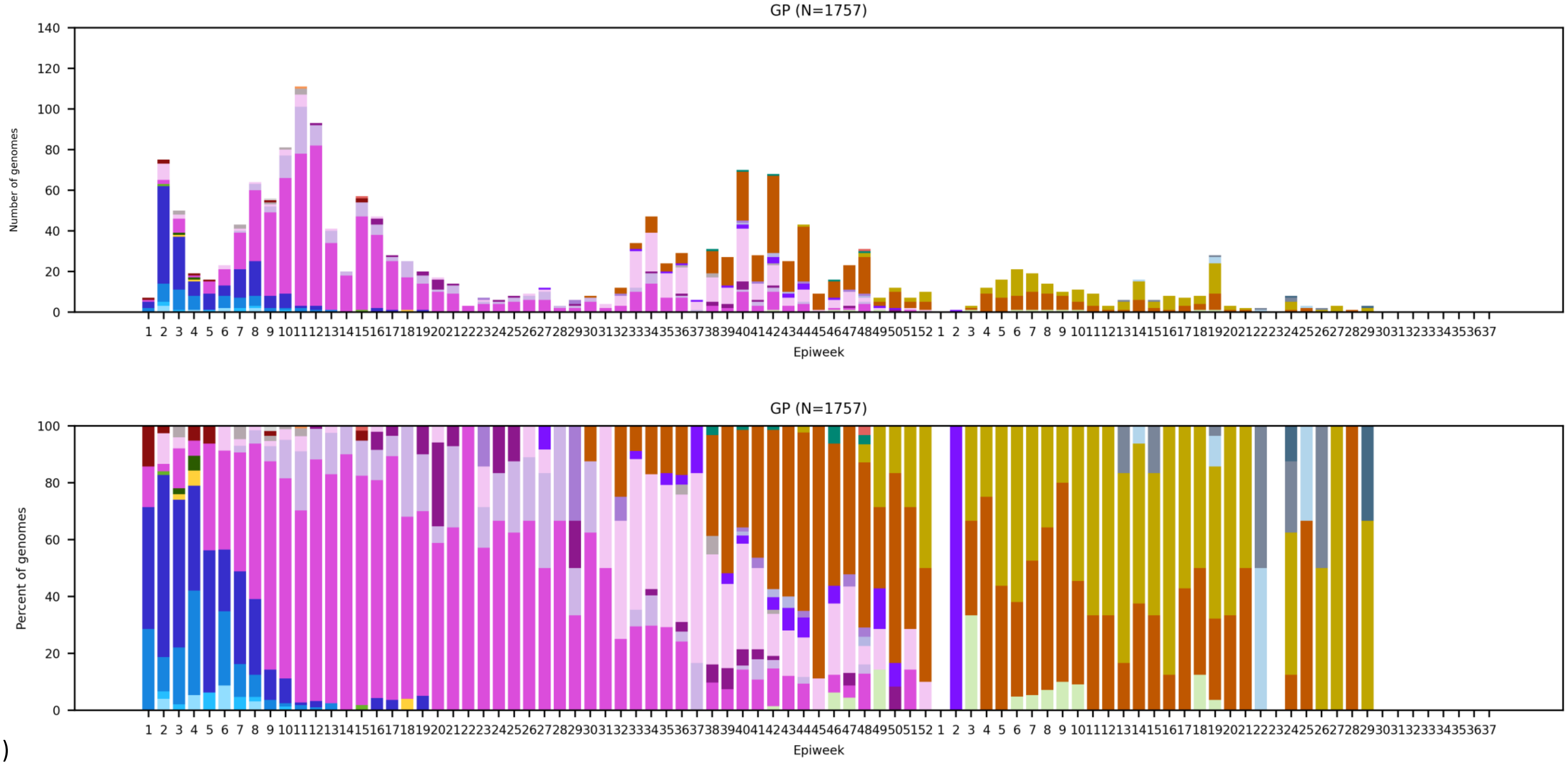
Gauteng Province, 2023-2024, N=1757

Genomes added since last report: 11



Clade key (bar graph)

- XAY
- XBF
- recombinant
- Omicron (23B/XBB.1.16)
- Omicron (23A/XBB.1.5)
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- Beta (20H, V2)
- Delta (21A, 21I, 21J)
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- 20B
- unassigned

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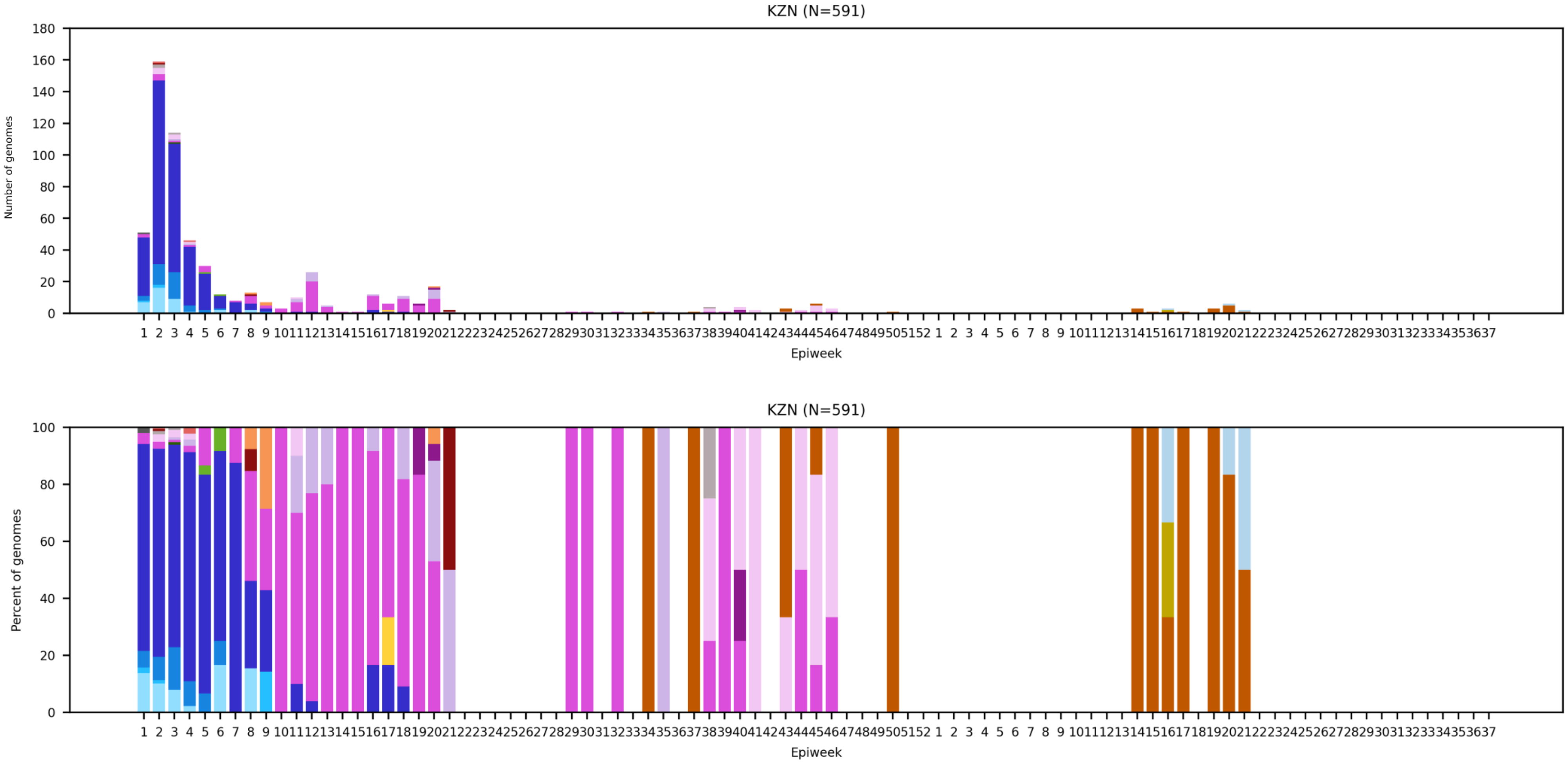
KwaZulu-Natal Province, 2023-2024, N=591

Genomes added since last report: 0



Clade key (bar graph)

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- ■ XBF
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- ■ 20B
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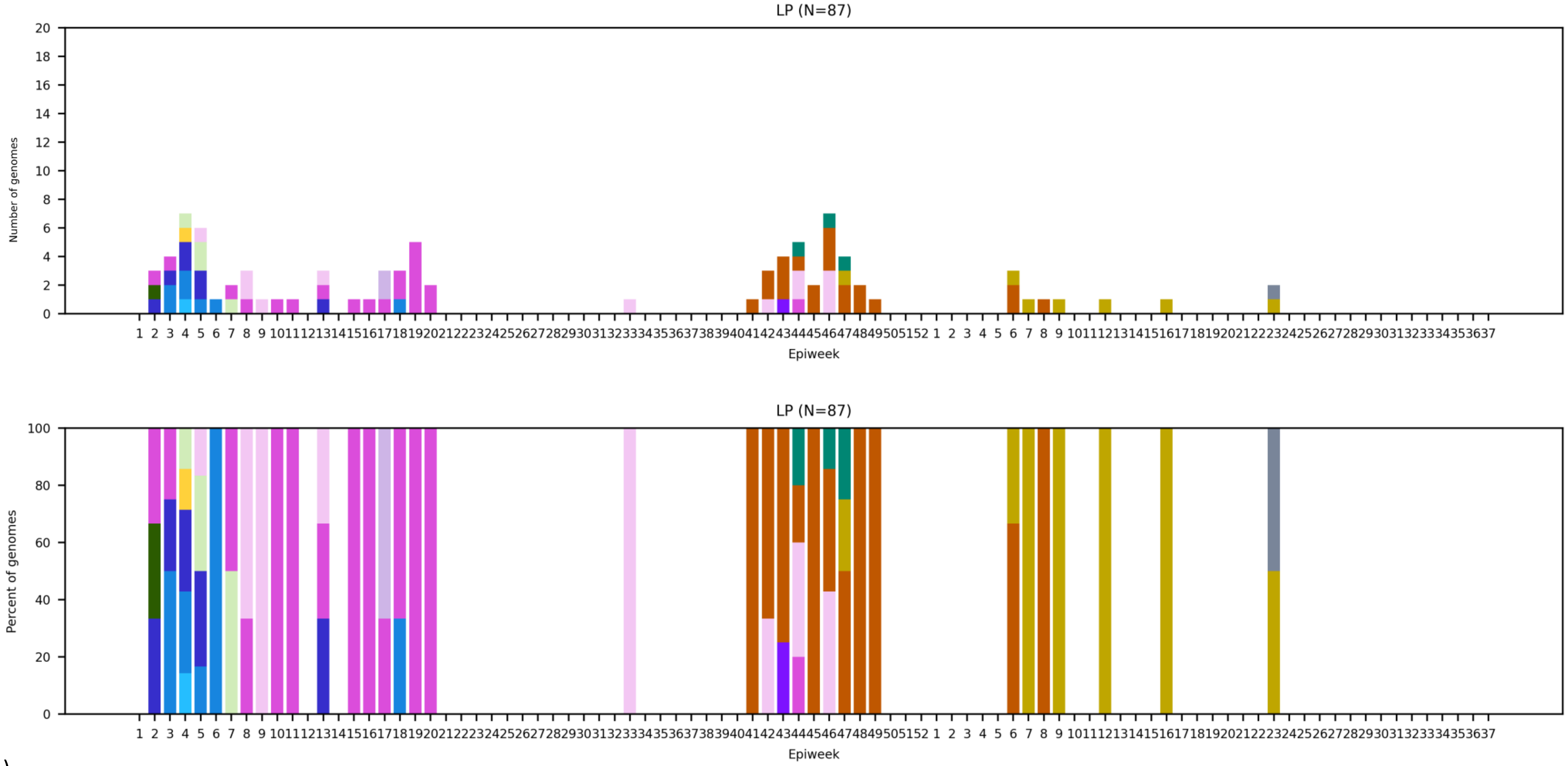
Limpopo Province, 2023-2024, N=87

Genomes added since last report: 0



Clade key (bar graph)

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- ■ 20B
- ■ unassigned

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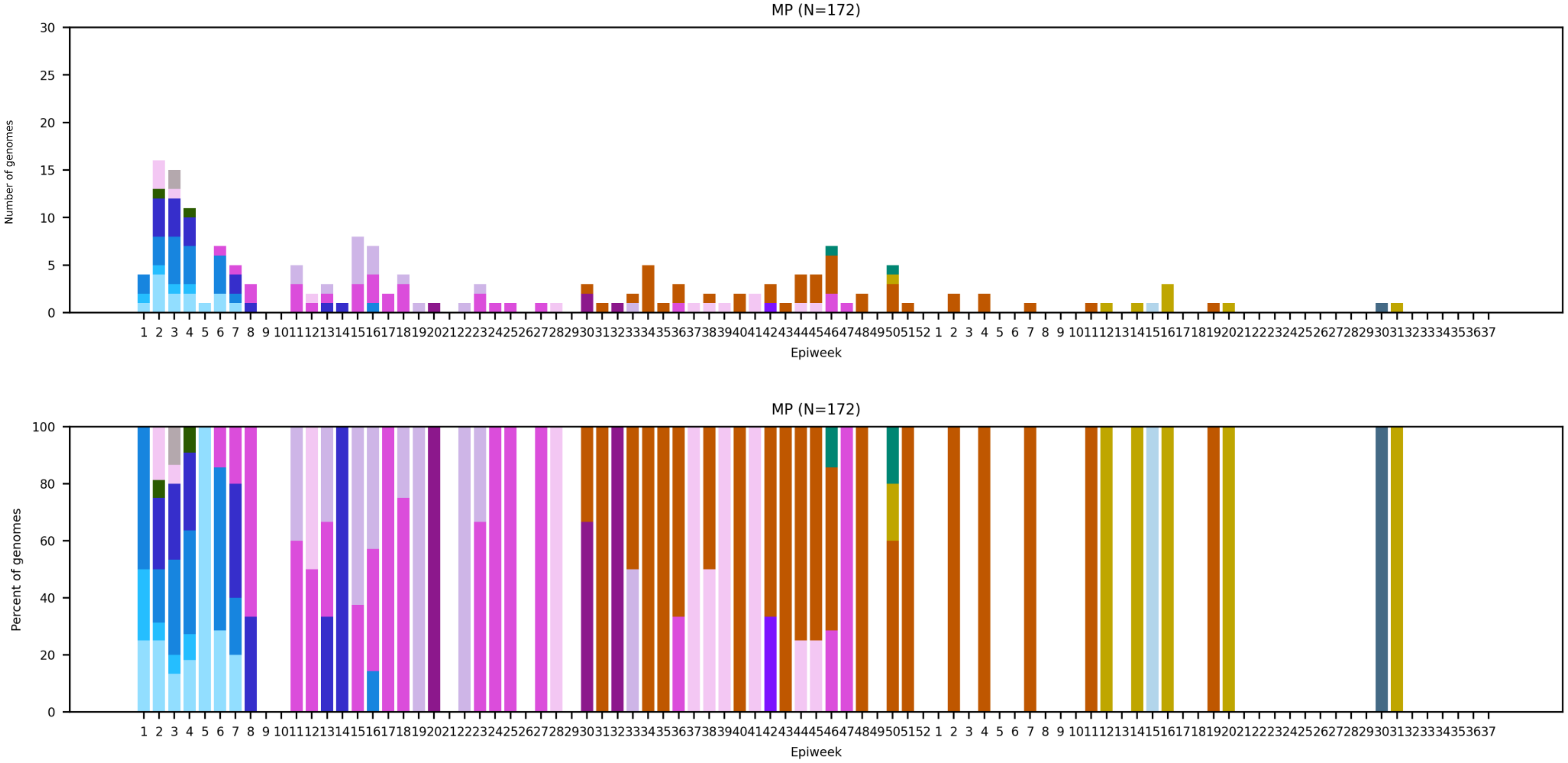
Mpumalanga Province, 2023-2024, N=172

Genomes added since last report: 2



Clade key (bar graph)

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- ■ 20B
- ■ unassigned

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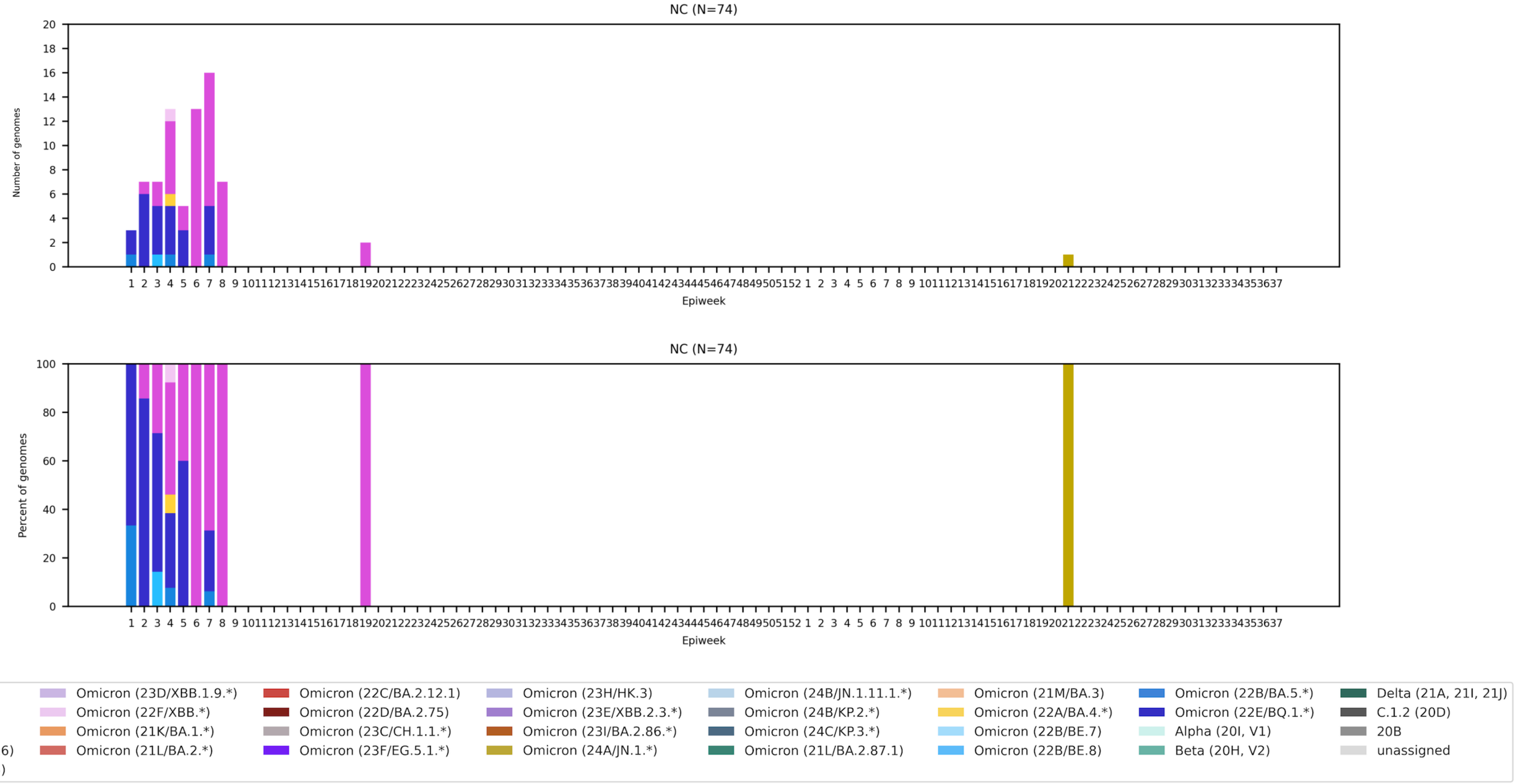
Northern Cape Province, 2023-2024, N=74

Genomes added since last report: 0



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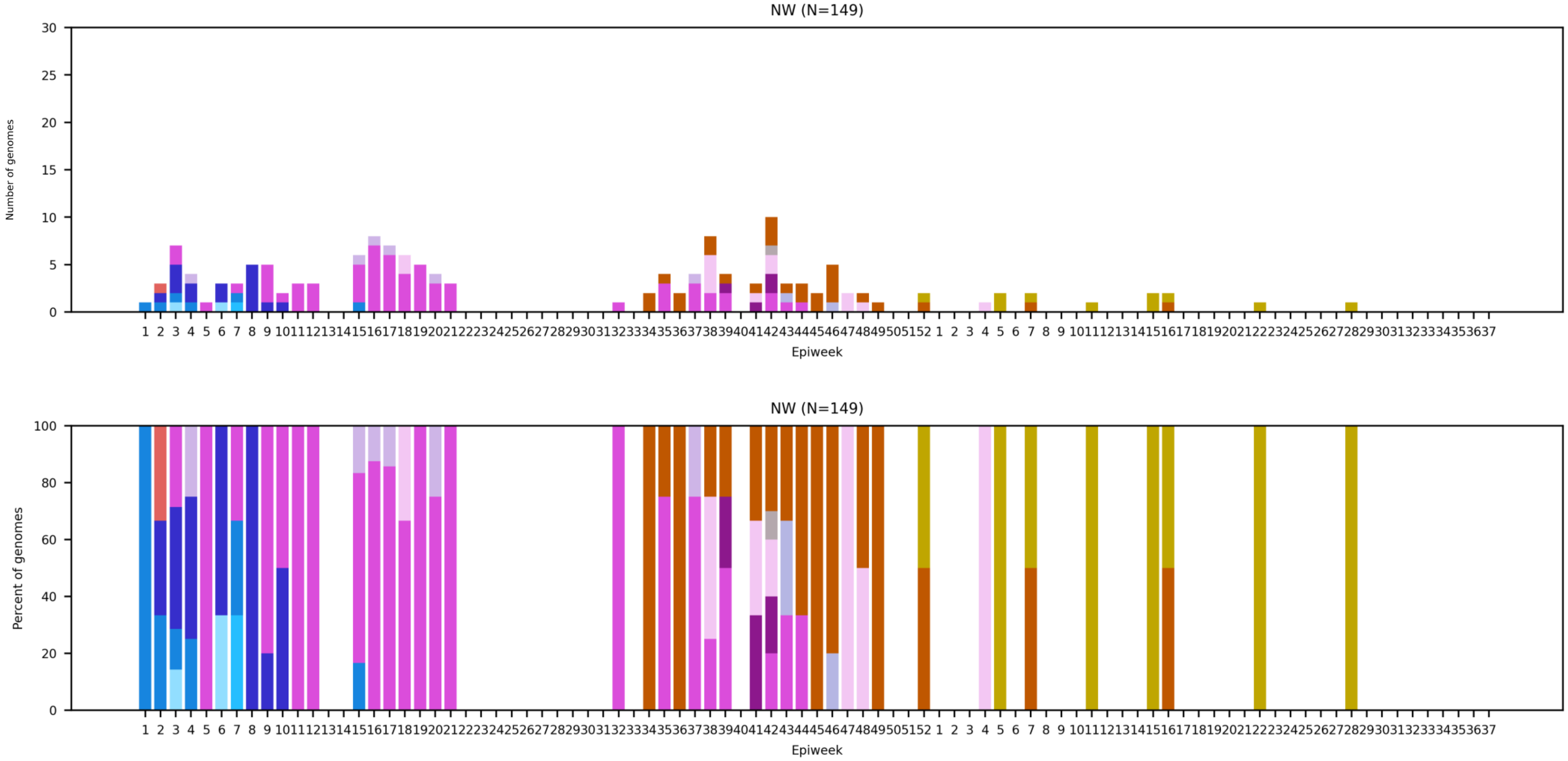
North West Province, 2023-2024, N=149

Genomes added since last report: 1



Clade key (bar graph)

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- ■ 20B
- ■ unassigned

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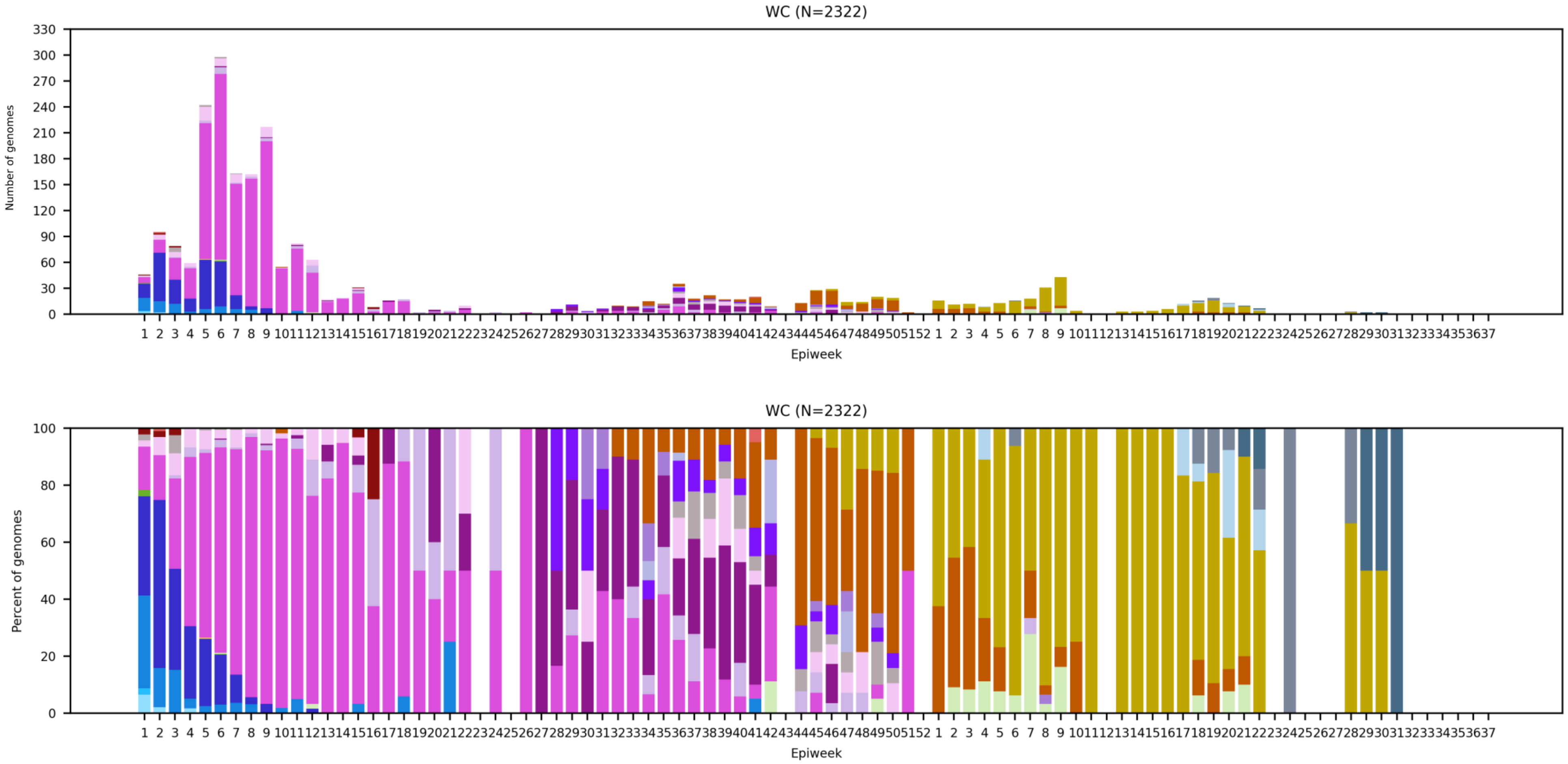
Western Cape Province, 2023-2024, N=2322

Genomes added since last report: 12



Clade key (bar graph)

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- Delta (21A, 21I, 21J)
- C.1.2 (20D)
- 20B
- unassigned

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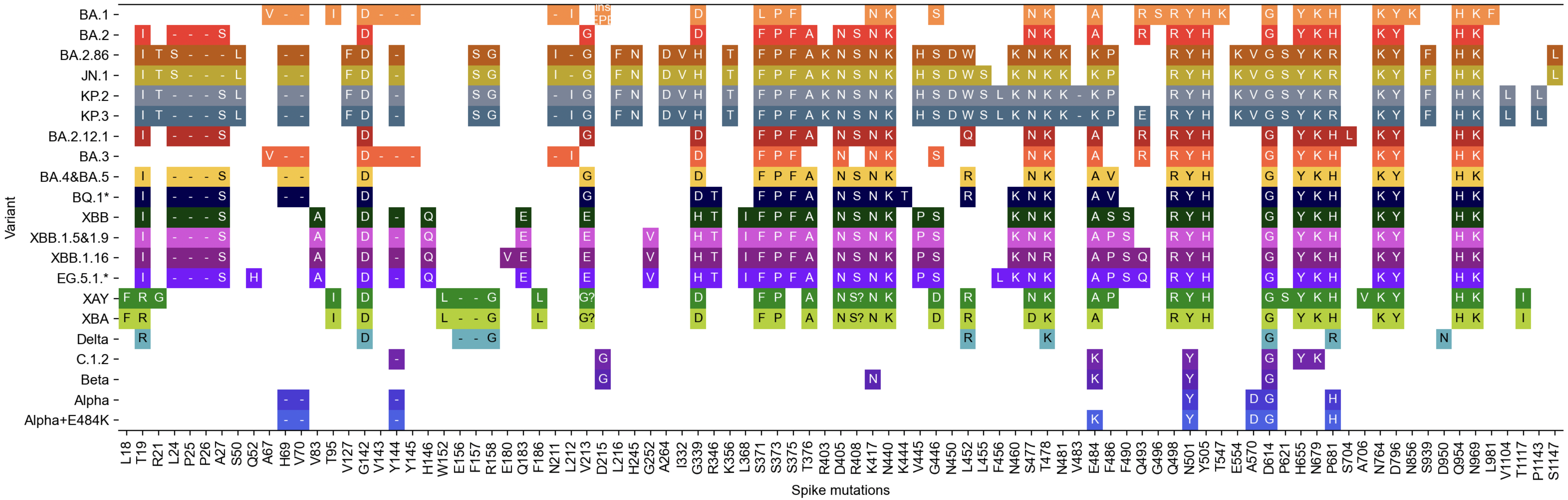
Summary

- **Sequencing update**
  - Testing for SARS-CoV-2 throughout the whole country is very low, and as a result few specimens are being submitted for sequencing
  - SARS-CoV-2 detections remain stable from systematic testing in sentinel syndromic surveillance (**WEEKLY RESPIRATORY PATHOGENS SURVEILLANCE REPORT**)
- **Variant of Concern Omicron in South Africa**
  - The JN.1 lineage is the dominant lineage, accounting for 54% of sequences in May, 44% in June and 56% in July. BA.2.86 lineages (parent lineage of JN.1) continue to be detected, but have declined in prevalence
  - Variants under monitoring (VUM) KP.2 (n=18) and KP.3 (n=8), have been detected in Gauteng, Limpopo, Mpumalanga and the Western Cape between February and July. Both VUMs have increased in prevalence in the recent months
  - Recombinant XDD.1.1 (EG.5.1.1 and JN.1.1) has been detected in Gauteng (n=6) and the Western Cape (n=22). It has a cumulative prevalence of <0.5% worldwide.

- Going forward this SARS-CoV-2 NGS-SA report will no longer be generated, however circulating SARS-CoV-2 lineages will continue to be monitored and will be reported in the Weekly Respiratory Pathogens Surveillance Report (https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-respiratory-pathogens-surveillance-report-week/)

Spike protein mutation* profile of Variants of Interest and Concern



Variant	L18	T19	R21	L24	P25	P26	A27	S50	Q52	A67	H69	V70	V83	T95	V127	G142	V143	Y144	Y145	H146	W152	E156	F157	R158	E180	Q183	F186	N211	L212	V213
BA.1										V	-	-		I		D	-	-	-									-	I	
BA.2		I		-	-	-	S									D														G
BA.2.86		I	T	S	-	-	-	L			-	-			F	D		-					S	G				I	-	G
JN.1		I	T	S	-	-	-	L			-	-			F	D		-					S	G				I	-	G
KP.2		I	T	-	-	-	S	L			-	-			F	D		-					S	G				-	I	G
KP.3		I	T	-	-	-	S	L			-	-			F	D		-					S	G				-	I	G
BA.2.12.1		I		-	-	-	S									D														G
BA.3										V	-	-				D	-	-	-									-	I	
BA.4&BA.5		I		-	-	-	S				-	-				D														G
BQ.1*		I		-	-	-	S				-	-				D														G
XBB		I		-	-	-	S						A			D		-		Q						E				E
XBB.1.5&1.9		I		-	-	-	S						A			D		-		Q						E				E
XBB.1.16		I		-	-	-	S						A			D		-		Q					V	E				E
EG.5.1.*		I		-	-	-	S		H				A			D		-		Q						E				E
XAY	F	R	G											I		D					L	-	-	G			L			G?
XBA	F	R												I		D					L	-	-	G			L			G?
Delta		R														D						-	-	G						
C.1.2																		-												
Beta																														
Alpha											-	-						-												
Alpha+E484K											-	-						-												

Variant	D215	L216	H245	G252	A264	I332	G339	R346	K356	L368	S371	S373	S375	T376	R403	D405	R408	K417	N440	K444	V445	G446	N450	L452	L455	F456	N460	S477	T478	N481
BA.1	ins EPE						D				L	P	F					N	K			S						N	K	
BA.2							D				F	P	F	A		N	S	N	K									N	K	
BA.2.86		F	N		D	V	H		T		F	P	F	A	K	N	S	N	K		H	S	D	W			K	N	K	K
JN.1		F	N		D	V	H		T		F	P	F	A	K	N	S	N	K		H	S	D	W	S		K	N	K	K
KP.2		F	N		D	V	H		T		F	P	F	A	K	N	S	N	K		H	S	D	W	S	L	K	N	K	K
KP.3		F	N		D	V	H		T		F	P	F	A	K	N	S	N	K		H	S	D	W	S	L	K	N	K	K
BA.2.12.1							D				F	P	F	A		N	S	N	K					Q				N	K	
BA.3							D				F	P	F			N		N	K			S						N	K	
BA.4&BA.5							D				F	P	F	A		N	S	N	K					R				N	K	
BQ.1*							D	T			F	P	F	A		N	S	N	K	T				R			K	N	K	
XBB							H	T		I	F	P	F	A		N	S	N	K		P	S					K	N	K	
XBB.1.5&1.9				V			H	T		I	F	P	F	A		N	S	N	K		P	S					K	N	K	
XBB.1.16				V			H	T		I	F	P	F	A		N	S	N	K		P	S					K	N	R	
EG.5.1.*				V			H	T		I	F	P	F	A		N	S	N	K		P	S				L	K	N	K	
XAY							D				F	P		A		N	S?	N	K			D		R				N	K	
XBA							D				F	P		A		N	S?	N	K			D		R				D	K	
Delta																								R					K	
C.1.2	G																													
Beta	G																	N												
Alpha																														
Alpha+E484K																														

Variant	V483	E484	F486	F490	Q493	G496	Q498	N501	Y505	T547	E554	A570	D614	P621	H655	N679	P681	S704	A706	N764	D796	N856	S939	D950	Q954	N969	L981	V1104	T1117	P1143	S1147
BA.1		A			R	S	R	Y	H	K			G		Y	K	H			K	Y	K			H	K	F				
BA.2		A			R		R	Y	H				G		Y	K	H			K	Y				H	K					
BA.2.86		K	P				R	Y	H		K	V	G	S	Y	K	R			K	Y		F		H	K					L
JN.1		K	P				R	Y	H		K	V	G	S	Y	K	R			K	Y		F		H	K					L
KP.2	-	K	P				R	Y	H		K	V	G	S	Y	K	R			K	Y		F		H	K		L		L	
KP.3	-	K	P		E		R	Y	H		K	V	G	S	Y	K	R			K	Y		F		H	K		L		L	
BA.2.12.1		A			R		R	Y	H				G		Y	K	H	L		K	Y				H	K					
BA.3		A			R		R	Y	H				G		Y	K	H			K	Y				H	K					
BA.4&BA.5		A	V				R	Y	H				G		Y	K	H			K	Y				H	K					
BQ.1*		A	V				R	Y	H				G		Y	K	H			K	Y				H	K					
XBB		A	S	S			R	Y	H				G		Y	K	H			K	Y				H	K					
XBB.1.5&1.9		A	P	S			R	Y	H				G		Y	K	H			K	Y				H	K					
XBB.1.16		A	P	S	Q		R	Y	H				G		Y	K	H			K	Y				H	K					
EG.5.1.*		A	P	S	Q		R	Y	H				G		Y	K	H			K	Y				H	K					
XAY		A	P				R	Y	H				G	S	Y	K	H		V	K	Y				H	K			I		
XBA		A					R	Y	H				G		Y	K	H			K	Y				H	K			I		
Delta													G				R							N							
C.1.2		K						Y					G		Y	K															
Beta		K						Y					G																		
Alpha								Y				D	G				H														
Alpha+E484K		K						Y				D	G				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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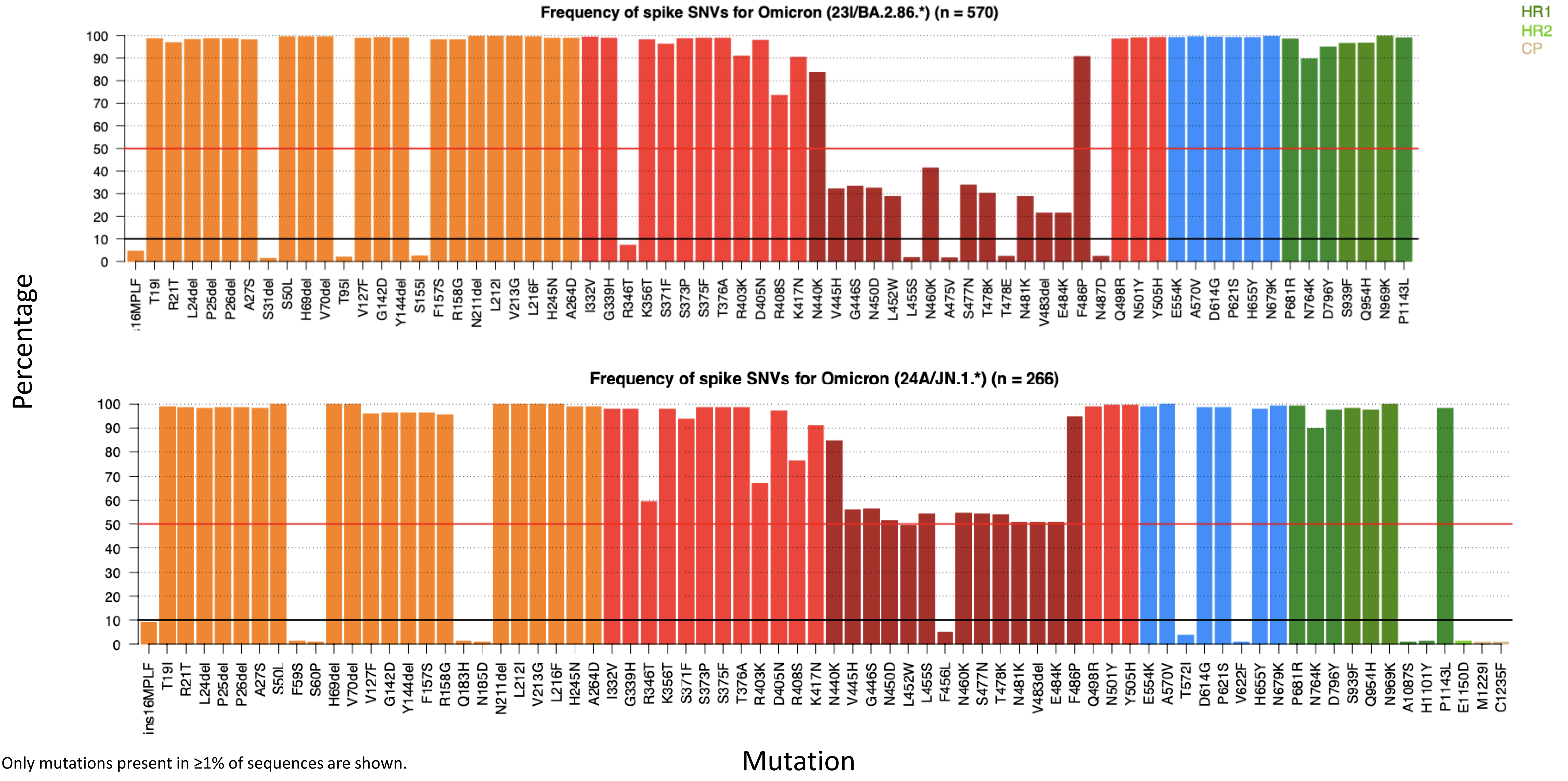
BA.2.86.* and JN.1.* spike mutations*

NTD
RBD
RBM
S1
S2
HR1
HR2
CP


Frequency of spike SNVs for Omicron (23I/BA.2.86.*) (n = 570)

Frequency of spike SNVs for Omicron (24A/JN.1.*) (n = 266)

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

University of Stellenbosch & NHLS Tygerberg Virology

Wolfgang Engelbrecht
Gert van Zyl
Tongai Maponga
Tania Stander
Mathilda Classen
Diagnostic laboratory staff

Tulio de Oliveira
Eduan Wilkinson
Houriiyah Tegally
Monika Moir
Lucious Chabuka
Derek Tshiabuila
Yeshnee Naidoo

UKZN-Inkosi Albert Luthuli Central Hospital

Dr Khanyi Msomi
Dr Kerusha Govender
Dr Pravi Moodley
Dr Aabida Khan
Dr Lili Gounder
Dr Kerri Francois
Dr Cherise Naicker
Dr Joedene Chetty

Dr Neli Ngcaba
Dr Tshepiso Mosito
Mr Malcolm Ellapen
Mr Kubendran Reddy
The COVID-19 Bench team

University of KwaZulu-Natal & Africa Health Research Institute

KRISP at UKZN:
Tulio de Oliveira
Richard Lessels
Houriiyah Tegally
Eduan Wilkinson
Jennifer Giandhari
Sureshnee Pillay

AHRI
Alex Sigal
Sandile Cele
Willem Hanekom

University of Cape Town, NHLS & Western Cape Government

NHLS-UCT
Carolyn Williamson
Nei-yuan Hsiao
Diana Hardie
Kruger Marais
Stephen Korsman
Ziyaad Valley-Omar

WCG-UCT
Mary-Anne Davies
Andrew Boulle
Theuns Jacobs
Erna Morden

NHLS Greenpoint
Annabel Enoch

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UCT, IDM and CIDRI-Africa
Deelan Doolabh
Arash Iranzadeh
Lynn Tyers
Innocent Mudau
Nokuzola Mbhele
Fezokuhle Khumalo
Thabang Serakge
Bruna Galvão
Arghavan Alisoltani (U. California)

Robert Wilkinson
Darren Martin
Nicola Mulder
Wendy Burgers
Ntobeko Ntusi
Rageema Joseph
Sean Wasserman
Linda Boloko

Emerging Viral Threats & One Health (EVITOH) division, Infectious Disease and Oncology Research Institute (IDORI), University of the Witwatersrand; Centre for Emerging and Reemerging Arbo & Respiratory virus research (CEARV), Department Medical Virology, University of Pretoria

Maritjie Venter
Caitlin MacIntyre
Gadean Brecht

NHLS Tshwane
Prof Simnikiwe Mayaphi (HOD)

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National Institute for Communicable Diseases

Centre for Respiratory Diseases & Meningitis
Anne von Gottberg
Thabo Mohale
Daniel Amoako
Josie Everatt
Boitshoko Mahlangu
Noxolo Ntuli
Anele Mnguni
Amelia Buys
Cardia Fourie
Noluthando Duma
Linda de Gouveia
Jackie Kleynhans
Nicole Wolter
Sibongile Walaza
Mignon du Plessis
Stefano Tempia
Mvuyo Makhasi
Cheryl Cohen
Dikeledi Kekana
Buhle Ntozini

Centre for HIV and STIs
Jinal Bhiman
Cathrine Scheepers
Constantinos Kurt Wibmer
Thandeka Moyo
Tandile Hermanus
Frances Ayres
Zanele Molaudzi
Bronwen Lambson
Tandile Hermanus
Mashudu Madzivhandila
Prudence Kgagudi
Brent Oosthuysen
Penny Moore
Lynn Morris

NICD Groups
NICD COVID-19 response team
NICD SARS-CoV-2 Sequencing Group

Sequencing Core Facility
Zamantungwa Khumalo
Annie Chan
Morne du Plessis
Stanford Kwenda
Phillip Senzo Mtshali
Mushal Allam
Florah Mnyameni
Arshad Ismail

University of the Free State

UFS
Dominique Goedhals
Armand Bester
Martin Myaga
Peter Mwangi
Emmanuel Ogunbayo
Milton Mogotsi
Makgotso Maotoana
Lutfiyya Mohamed

NHLS Division of Virology
Sabeehah Vawda
Felicity Burt
Thokozani Mkhize
Diagnostic laboratory staff

Additional support and collaborators

NHLS
Koleka Mlisana
Zinhle Makatini
Eugene Elliot
Florette K. Treurnicht
Kathleen Subramoney
Oluwakemi Laguda-Akingba
Shareef Abrahams
Greta Hoyland
Gloria Selabe
Elias Bereda
Jeannette Wadula

Hyrax Biosciences
Simon Travers

Cape Town HVTN Laboratory
Erica Anderson-Nissen
Anneta Naidoo

Ndlovu Research
Hugo Tempelman
CJ Umunnakwe

Lancet
Allison J. Glass
Raquel Viana

Ampath
Terry Marshall
Cindy van Deventer
Eddie Silberbauer

Pathcare Vermaak
Andries Dreyer
Howard Newman
Riaan Writes
Marianne Wolfaardt
Warren Lowman

Bridge-the-Gap
Raymond Rott

Cytespace Africa Laboratories
Christa Viljoen

ARC-OVI
Lia Rotherham

CAPRISA
Salim Abdool Karim
Nigel Garret

UKZN - Big Data
Francesco Pettruccione
Ilya Sinayskiy

University of Oxford
José Lourenço

FioCruz, Brazil
Vagner Fonseca
Marta Giovanetti
Luiz Carlos Junior Alcantara

Africa CDC and Africa PGI
John Nkengasong
Sofonias Tessema

Netcare
Richard Friedland
Craig Murphy
Caroline Maslo
Liza Sitharam

DSI
Glaudina Loots

SA MRC
Glenda Gray

Pathcare N1 City
Jean Maritz
Nadine Cronje
Petra Raimond
Kim Hoek

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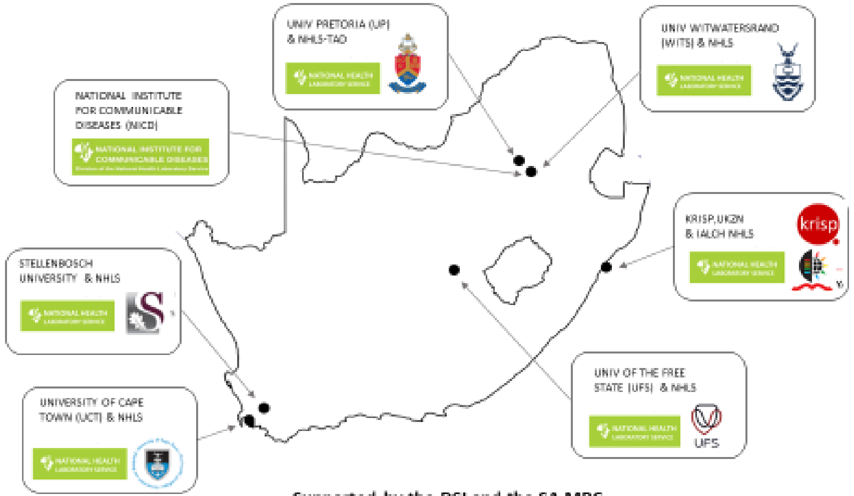

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Department:
Science and Innovation
REPUBLIC OF SOUTH AFRICA

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Division of the National Health Laboratory Service

EDCTP

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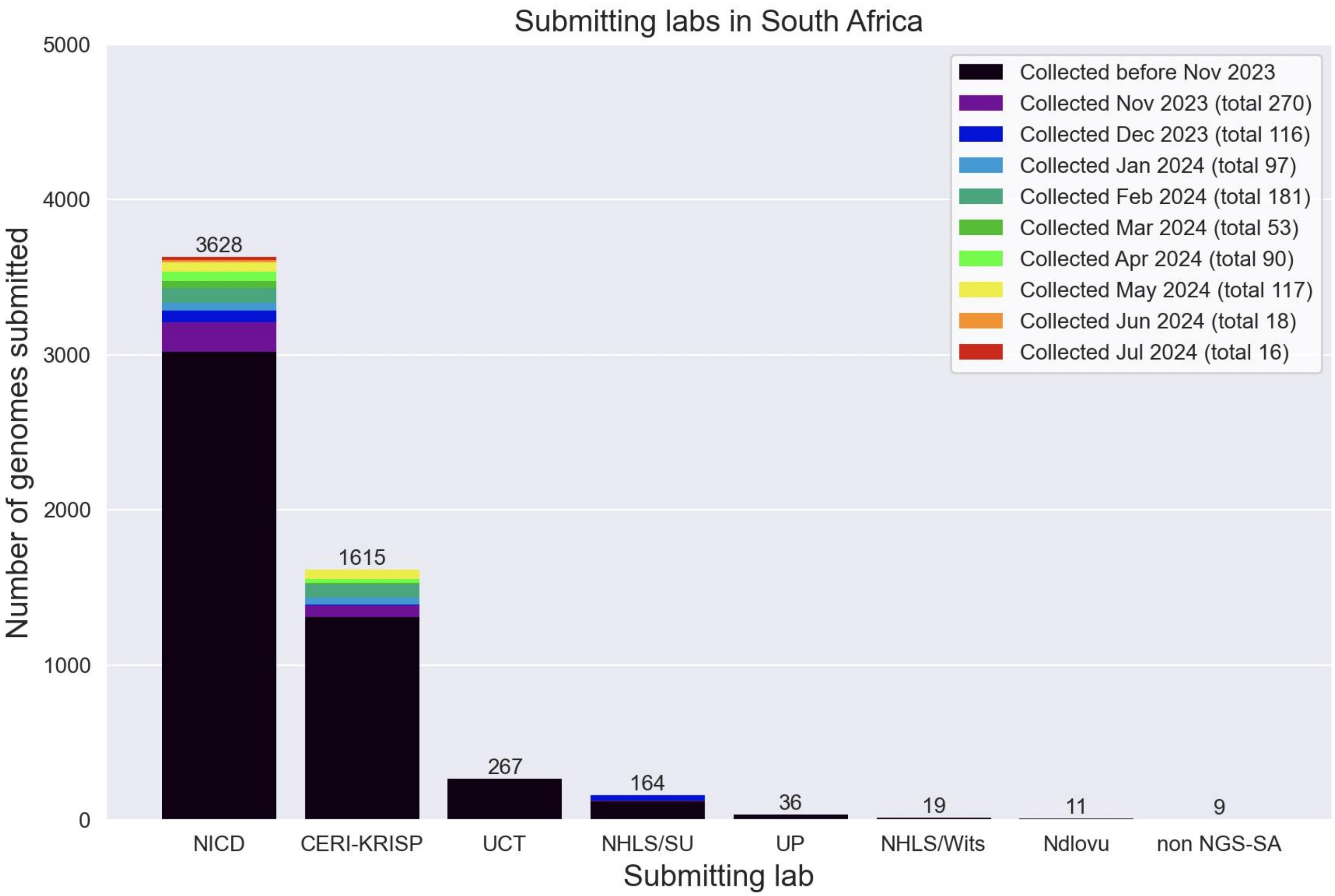
NATIONAL HEALTH LABORATORY SERVICE

South African genomes submitted per submitting lab, 2023 - 2024 (N=5749)



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 interest (VOIs) (as of 28 June 2024)

Pango lineage	Next strain clade	Genetic features	Earliest documented samples	Date of designation and risk assessments
BA.2.86[$]	23I	Mutations relative to BA.2	24-07-2023	21-11-2023 BA.2.86 Initial Risk Evaluation, 21 November 2023
JN.1[#]	24A	BA.2.86 + S:L455S	25-08-2023	18-12-2023 JN.1 Initial Risk Evaluation 18 December 2023 JN.1 Updated Risk Evaluation 9 February 2024 JN.1 Updated Risk Evaluation 15 April 2024

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

Currently circulating variants under monitoring (VUMs) (as of 19 July 2024)

Pango lineage	Next strain clade	Genetic features	Earliest documented samples	Date of designation
JN.1.7	Not assigned	JN.1 + S:T572I, S:E1150D	25-09-2023	03-05-2024
KP.2	24B	JN.1 + S:R346T, S:F456L, S:V1104L	02-01-2024	03-05-2024
KP.3	24C	JN.1 + S:F456L, S:Q493E, S:V1104L	11-02-2024	03-05-2024
KP.3.1.1	24C	KP.3 + S:S31-	27-03-2024	19-07-2024
JN.1.18	Not assigned	JN.1 + S:R346T	02-11-2023	03-05-2024
LB.1	Not Assigned	JN.1 + S:S31-, S:Q183H, S:R346T, S:F456L	26-02-2024	28-06-2024

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

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.)