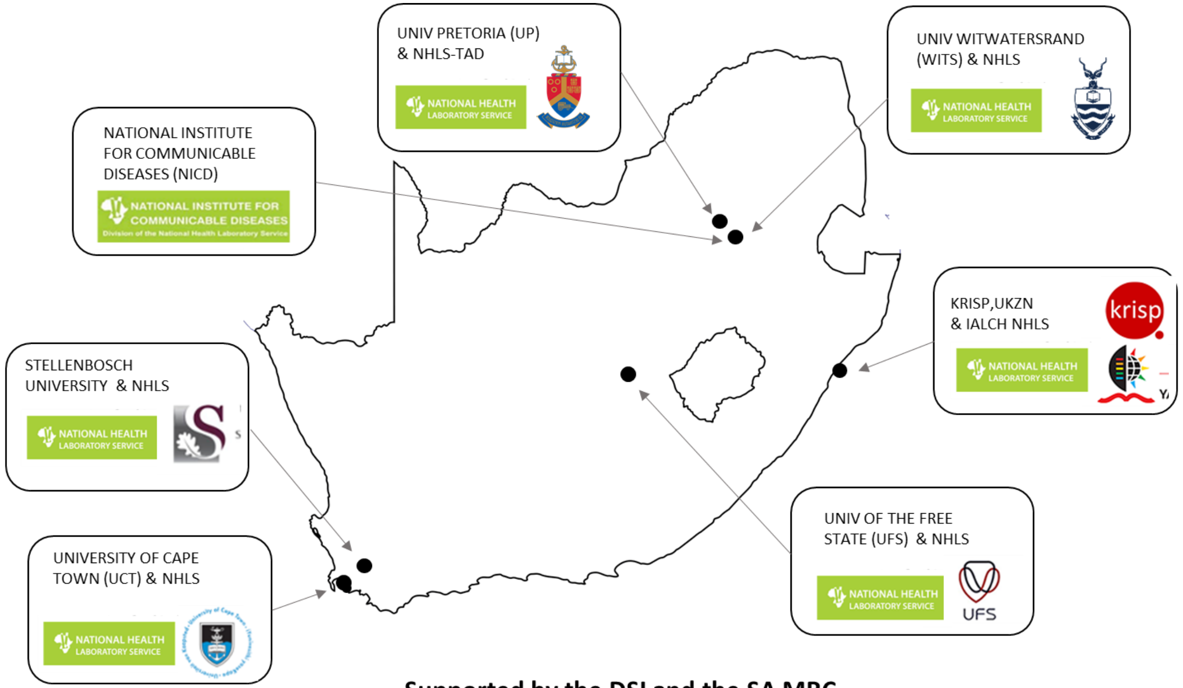
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update

31 March 2023



UNIV PRETORIA (UP) & NHLS-TAD

UNIV WITWATERSRAND (WITS) & NHLS

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES (NICD)

KRISP,UKZN & IALCH NHLS

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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)

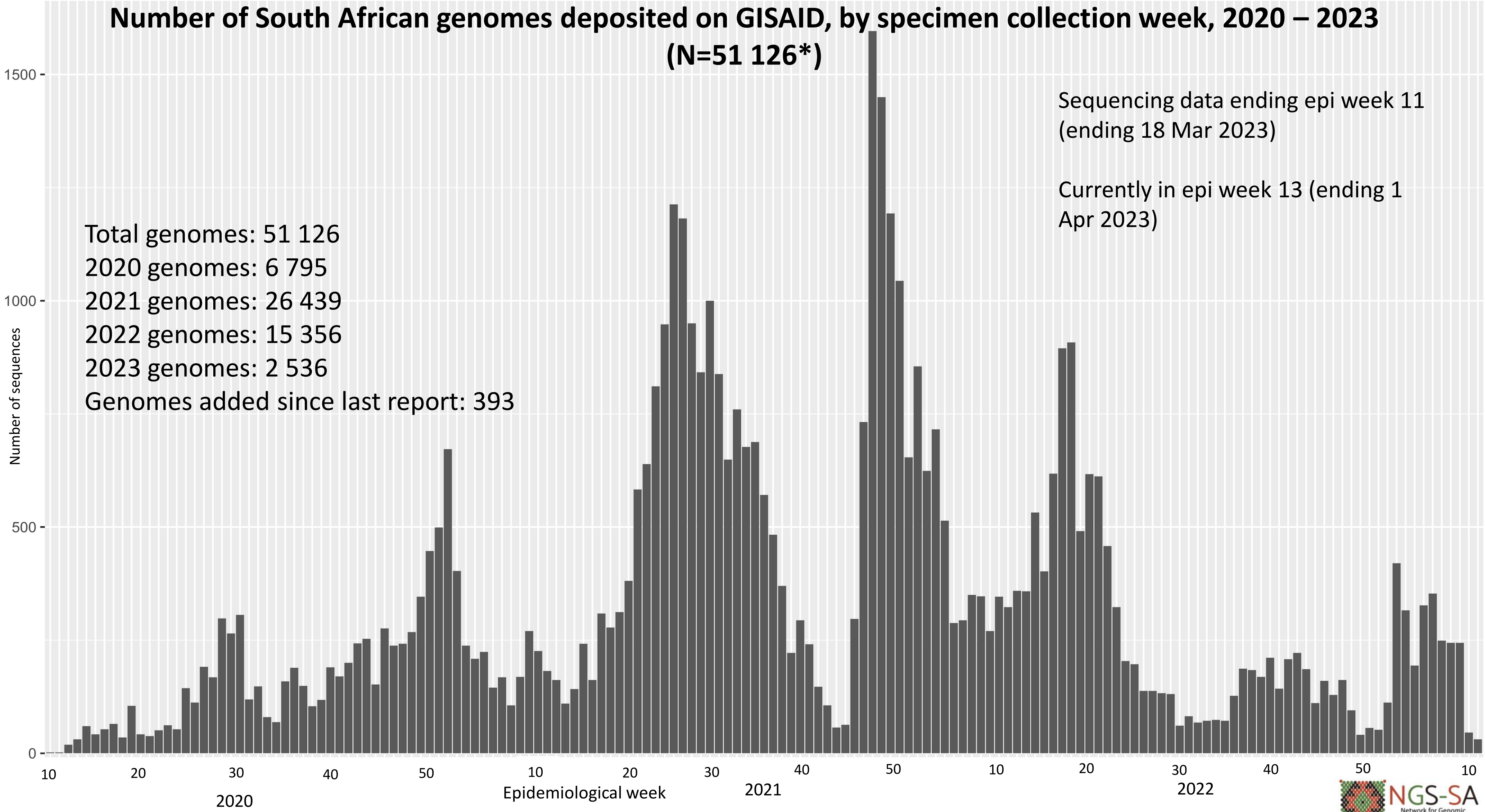
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 31 March 2023 at 08h43

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=51 126*)



Sequencing data ending epi week 11 (ending 18 Mar 2023)

Currently in epi week 13 (ending 1 Apr 2023)

Total genomes: 51 126
2020 genomes: 6 795
2021 genomes: 26 439
2022 genomes: 15 356
2023 genomes: 2 536
Genomes added since last report: 393

*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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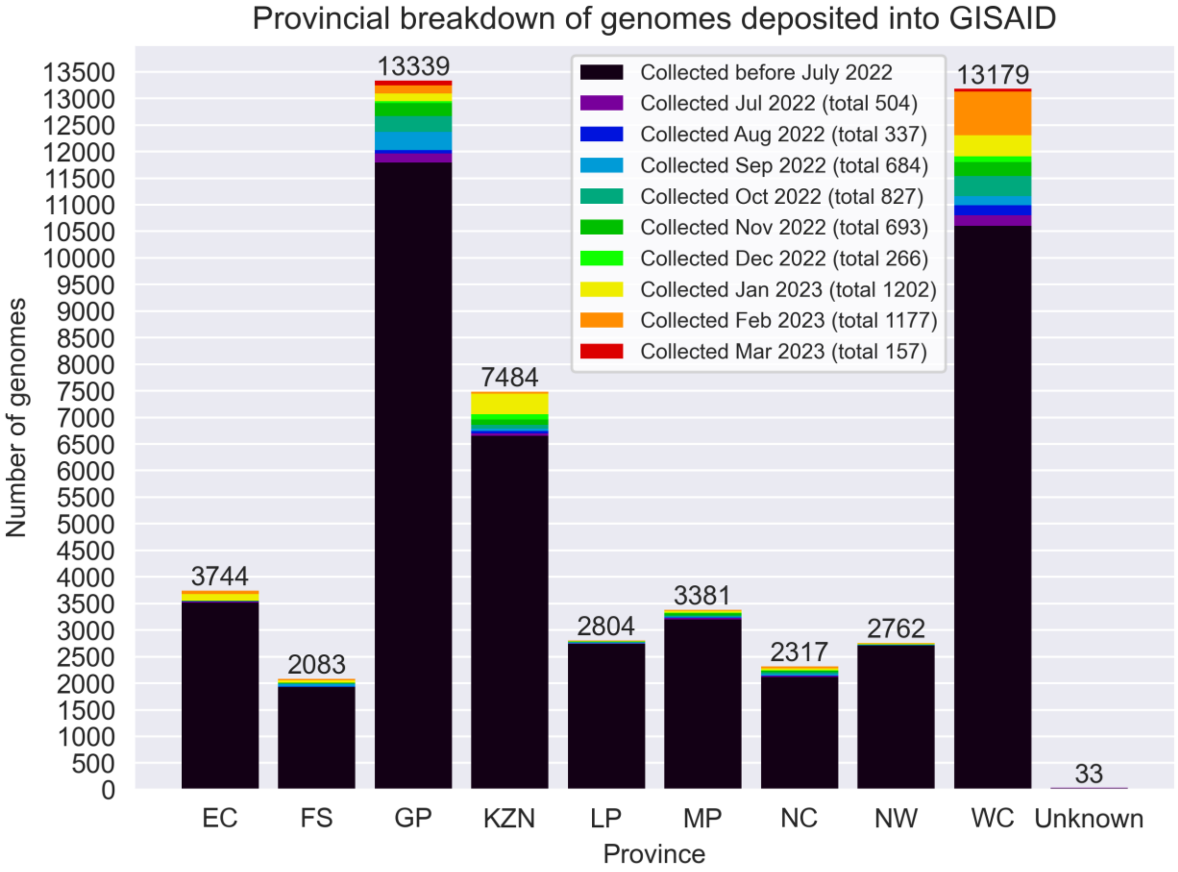
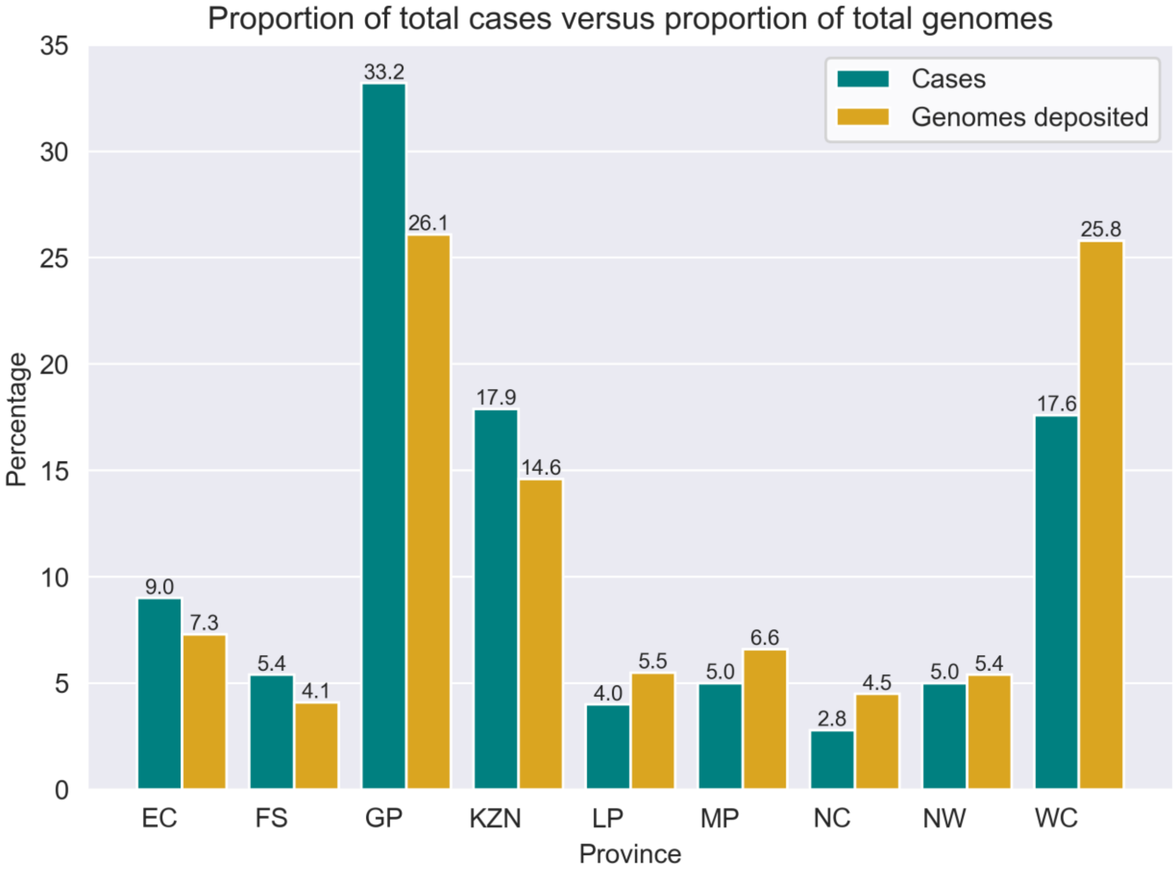
GISAID genomes vs total cases, 2020 – 2023 (N=51 126)





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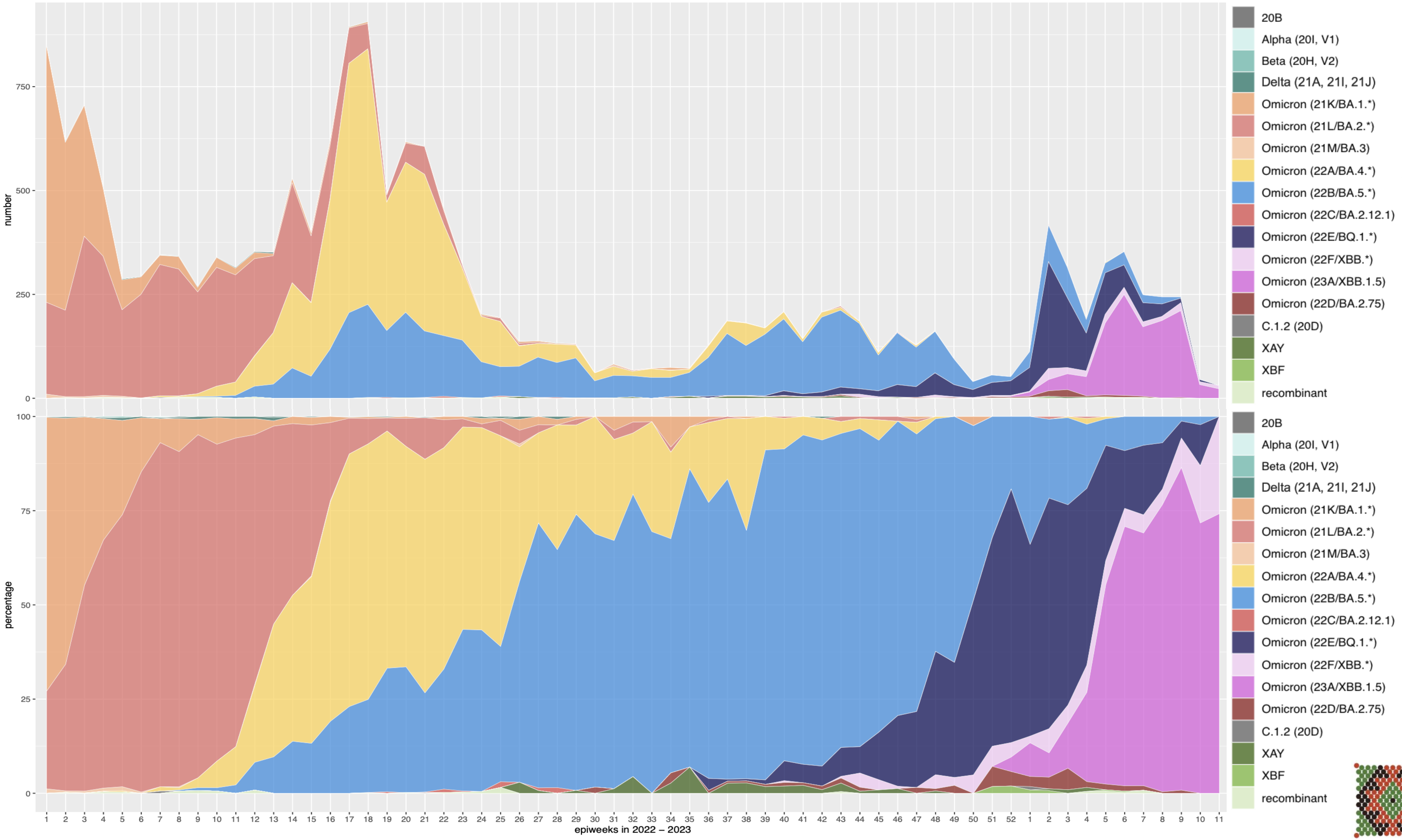
Number and percentage of clades by epiweek in South Africa, 2022-2023 (17 849*)



Sequencing data ending epi week 11 (ending 18 Mar 2023)

Currently in epi week 13 (ending 1 Apr 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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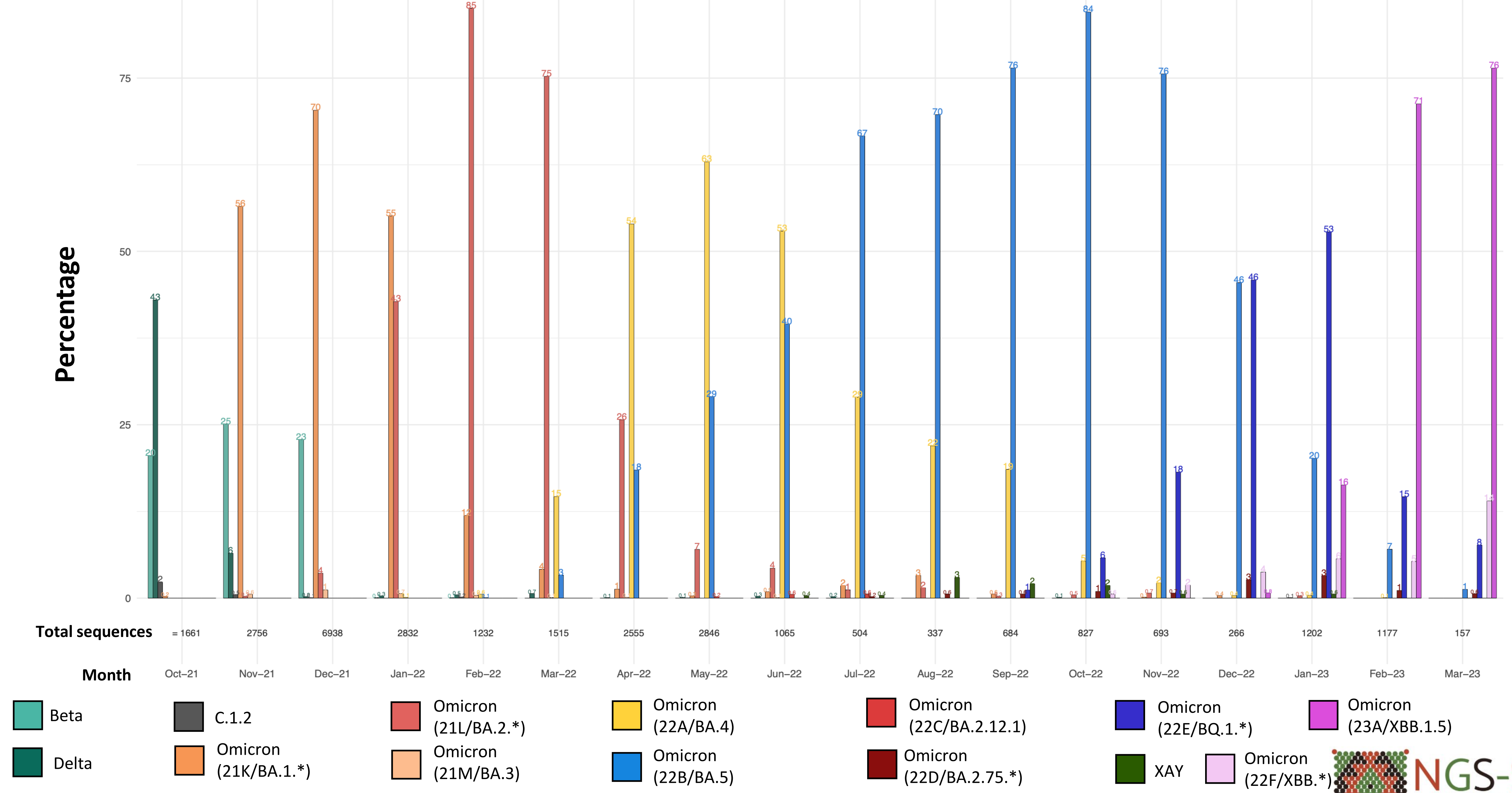
Detection Rates: Beta, Delta, C.1.2, recombinants, and Omicron



*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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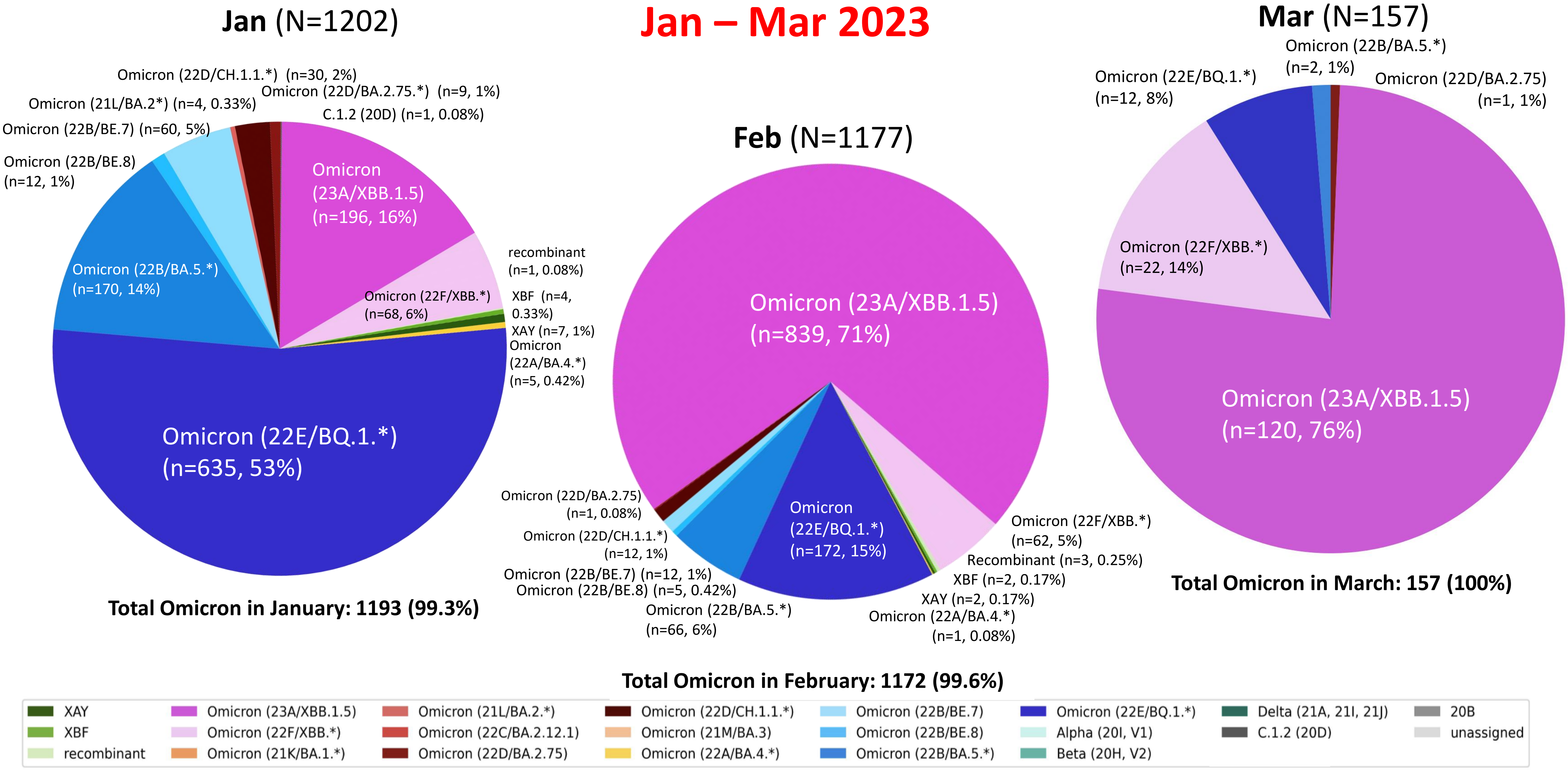
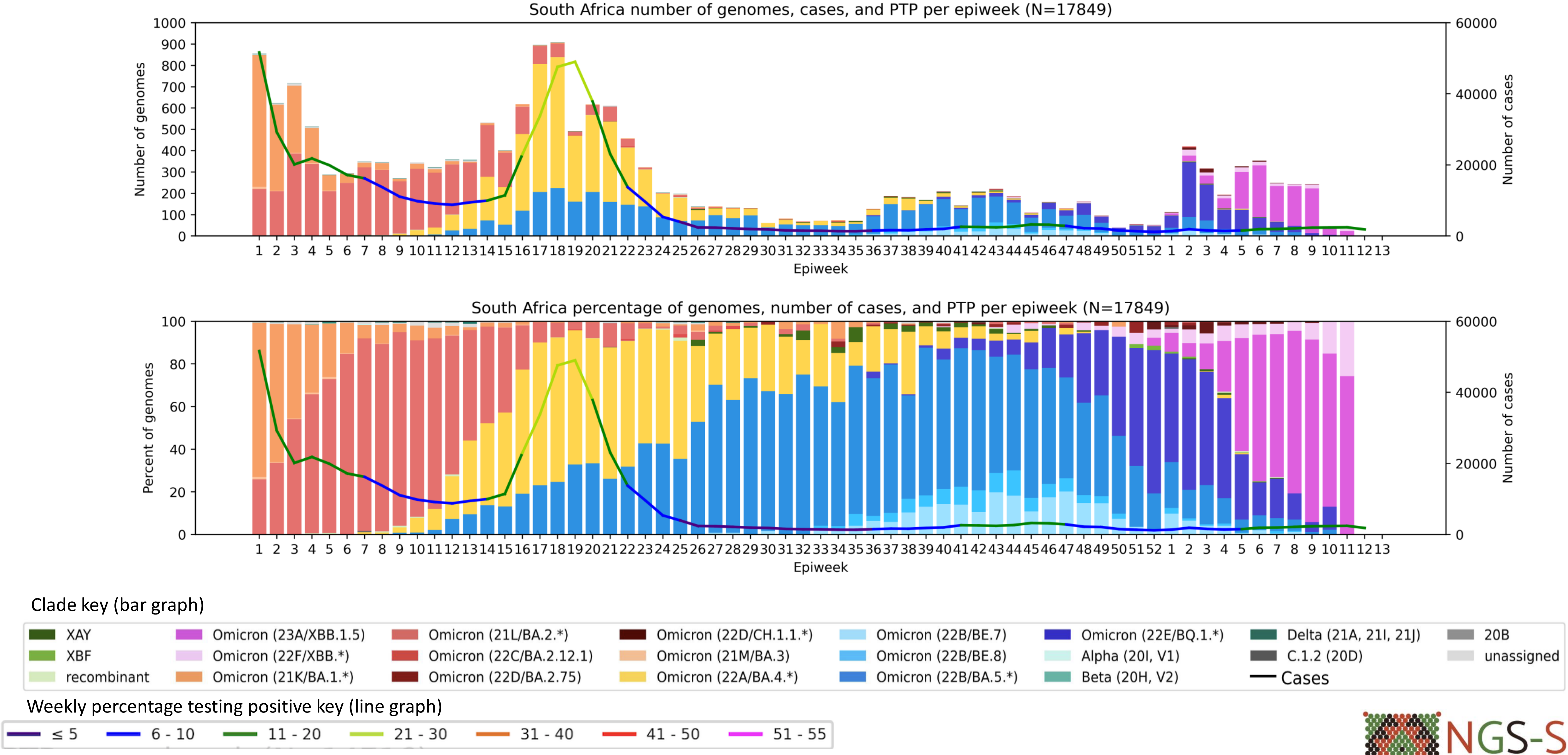
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in Jan – Mar 2023



Note: XBF is an Omicron-Omicron recombinant and so is counted in the total number of Omicrons.

South Africa, 2022-2023, n = 17 849*



*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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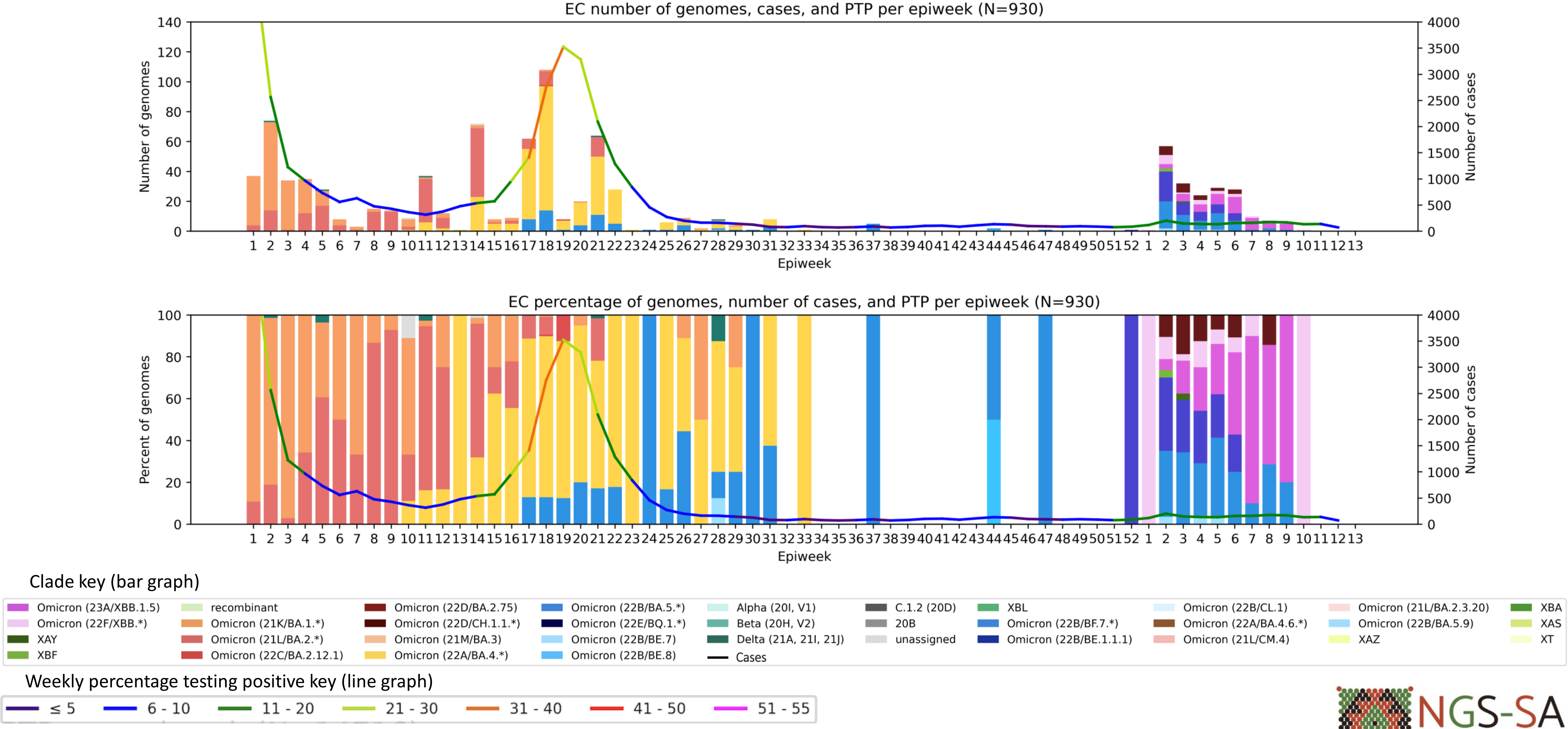
Eastern Cape Province, 2022-2023, n = 930

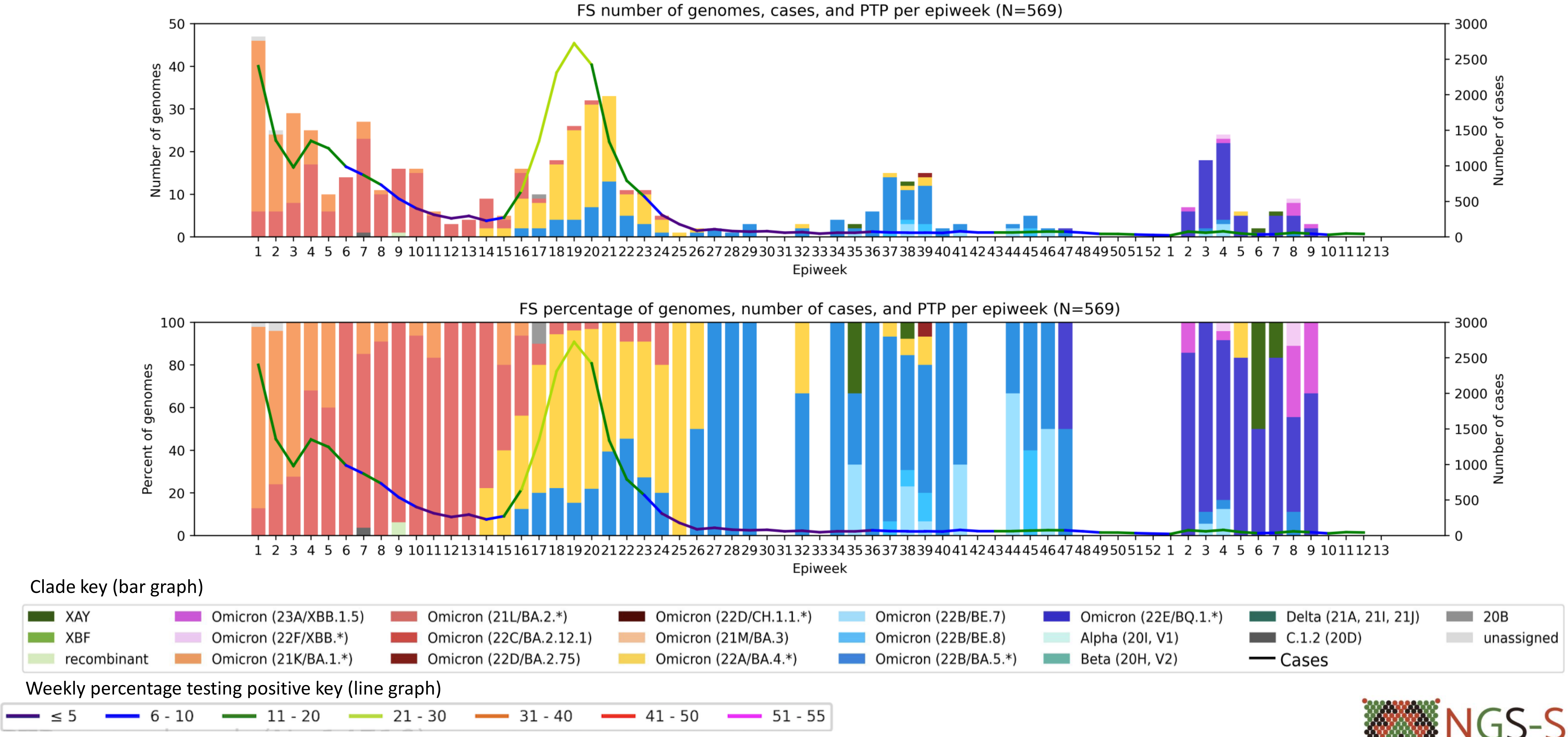
Genomes added since last report: 8*



*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 = 569

Genomes added since last report: 2*



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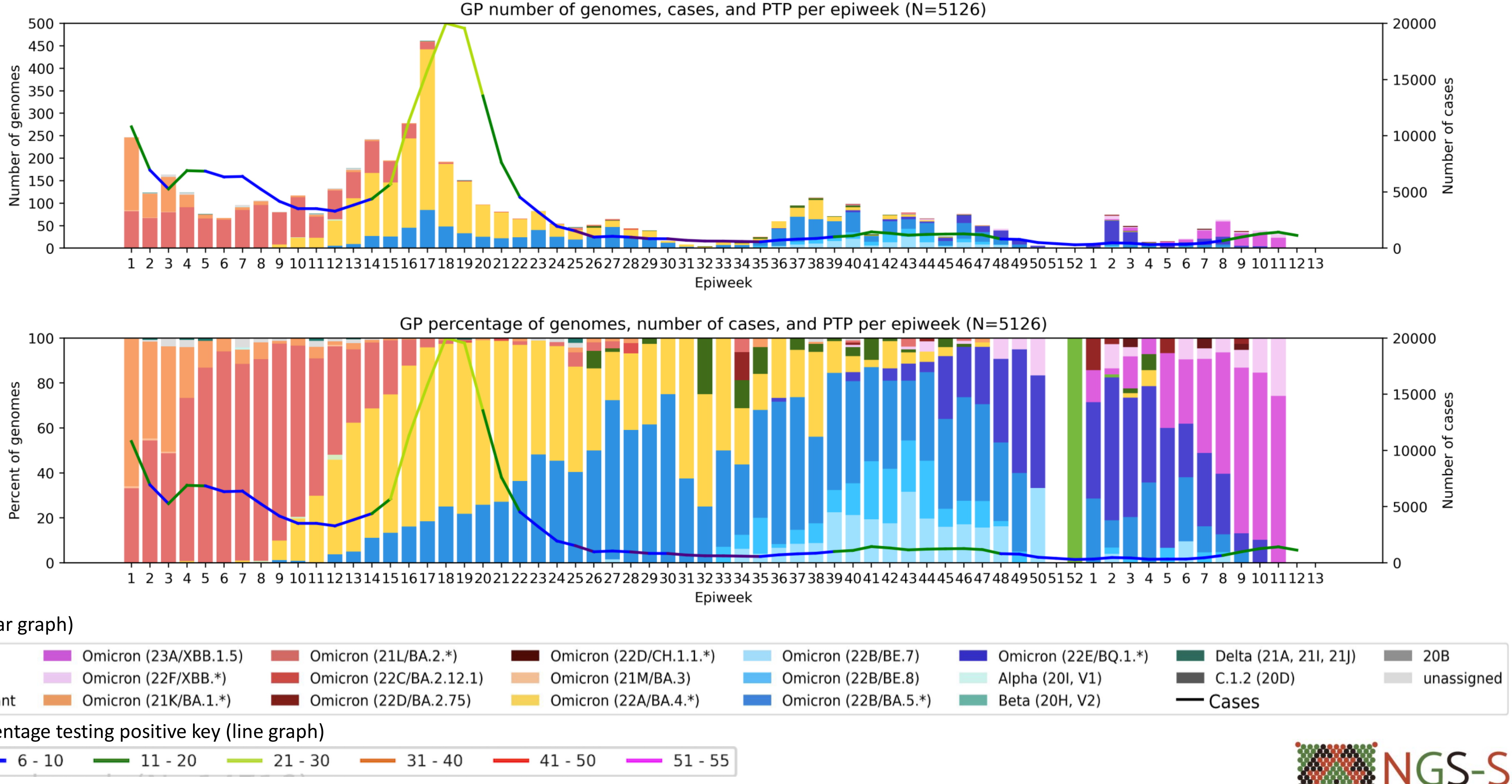
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

Gauteng Province, 2022-2023, n = 5126

Genomes added since last report: 125*



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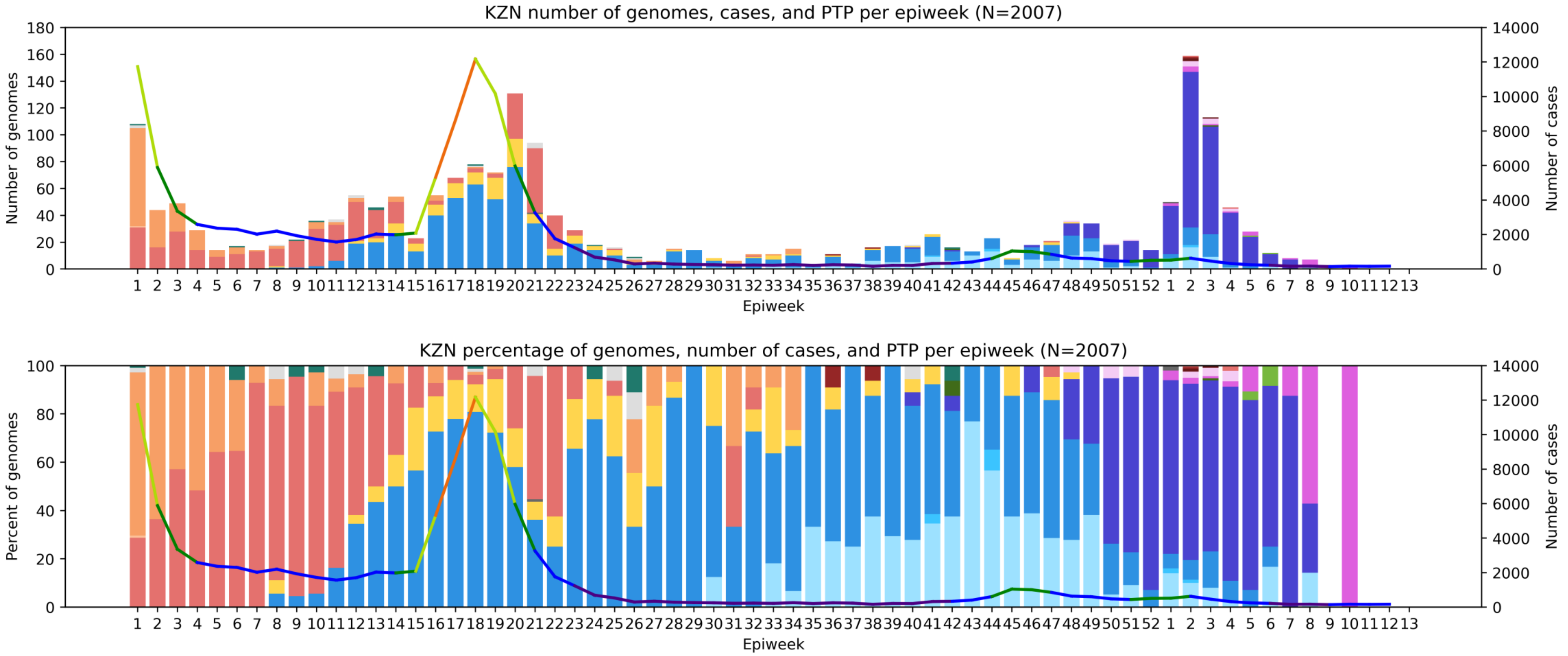
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

KwaZulu-Natal Province, 2022-2023, n = 2007

Genomes added since last report: 11*



Clade key (bar graph)

- ■ XAY
- ■ XBF
- ■ recombinant
- ■ Omicron (23A/XBB.1.5)
- ■ Omicron (22F/XBB.*)
- ■ Omicron (21K/BA.1.*)
- ■ Omicron (21L/BA.2.*)
- ■ Omicron (22C/BA.2.12.1)
- ■ Omicron (22D/BA.2.75)
- ■ Omicron (22D/CH.1.1.*)
- ■ 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)
- — Cases
- ■ 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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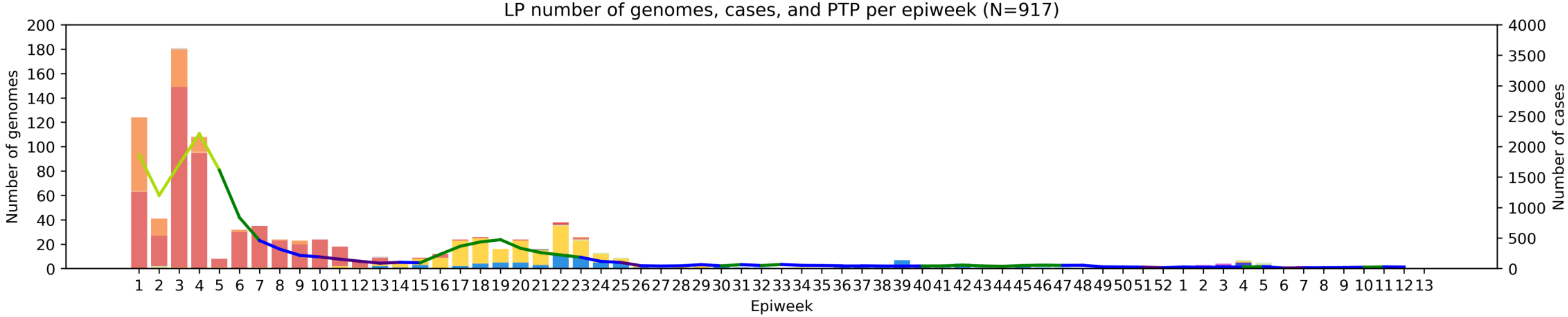
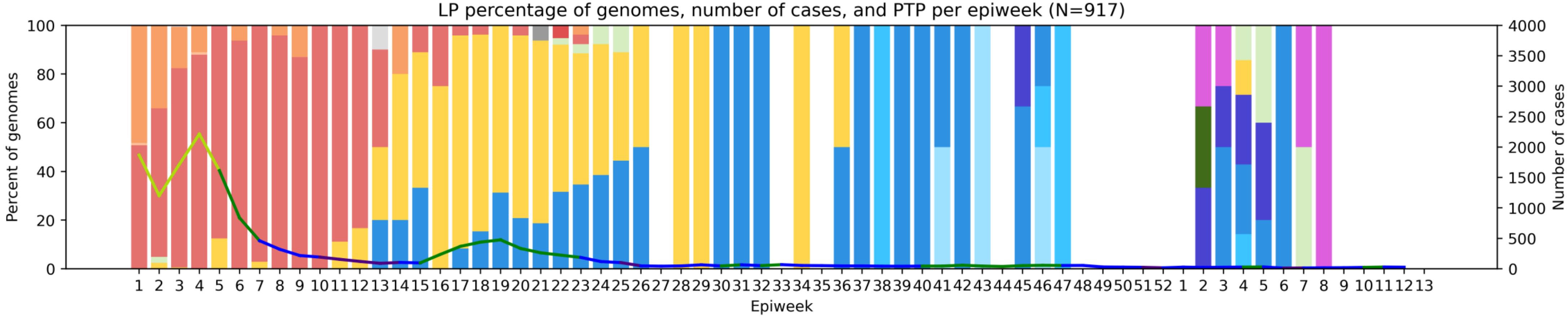
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

Limpopo Province, 2022-2023, n = 917

Genomes added since last report: 1*





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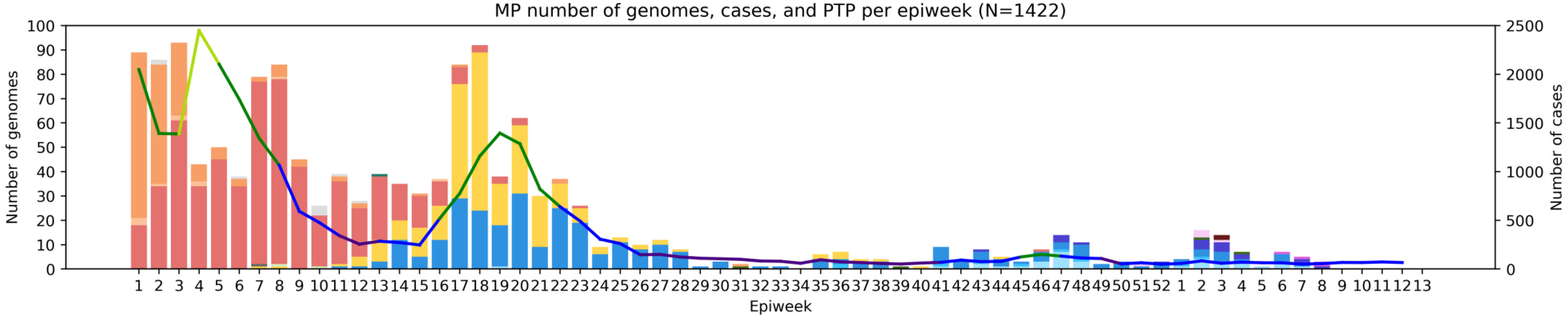
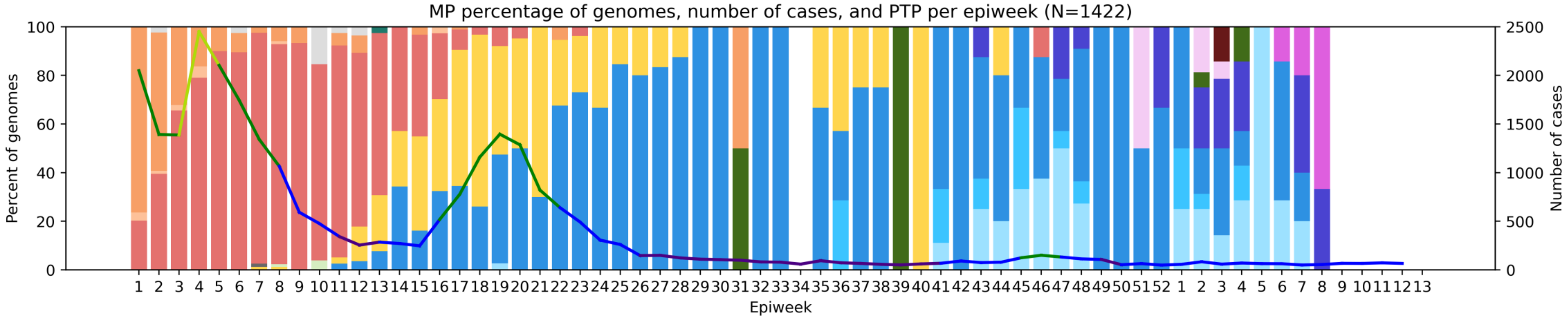
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

Mpumalanga Province, 2022-2023, n = 1422

Genomes added since last report: 5*





Clade key (bar graph)

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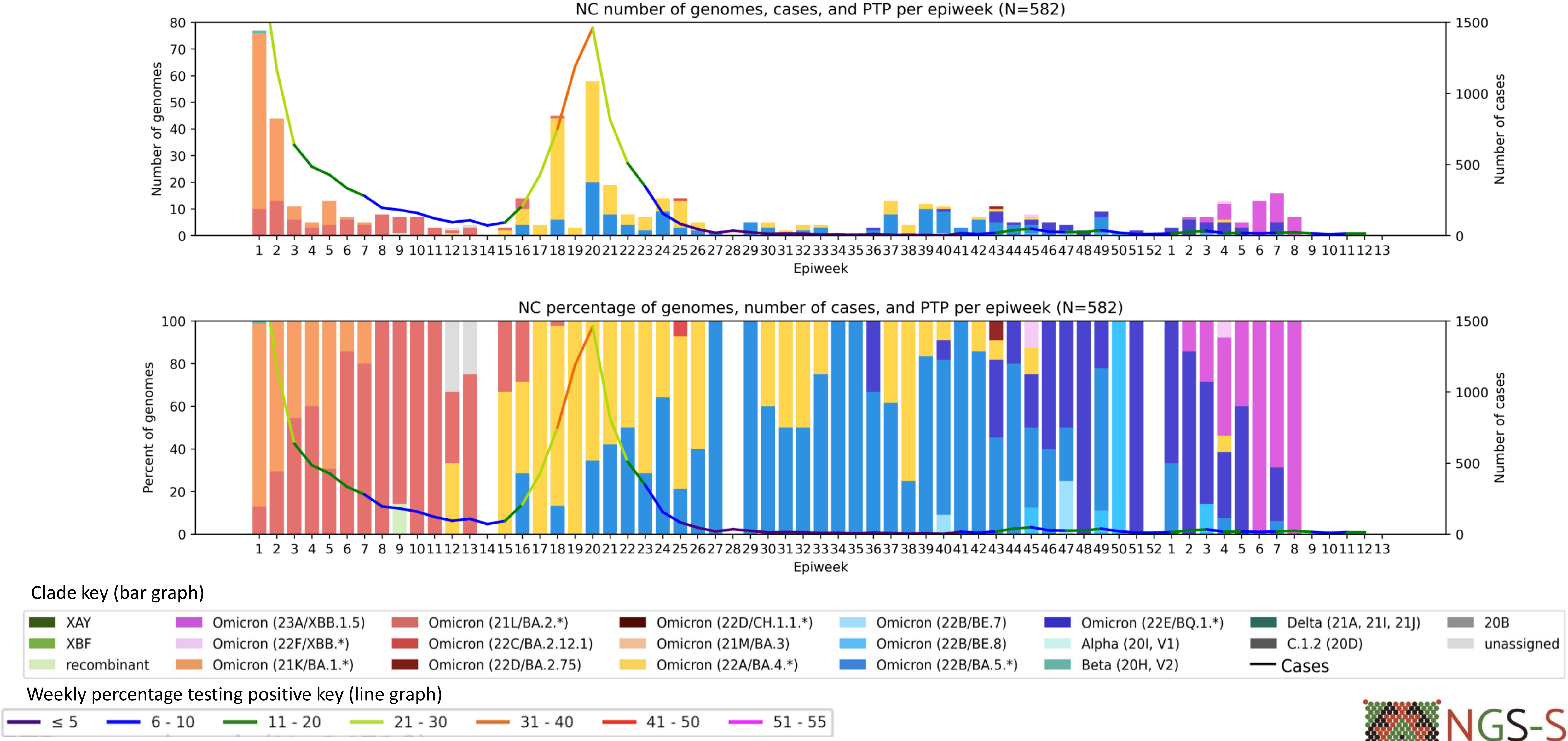
Northern Cape Province, 2022-2023, n = 582

Genomes added since last report: 18*


NC number of genomes, cases, and PTP per epiweek (N=582)

NC percentage of genomes, number of cases, and PTP per epiweek (N=582)

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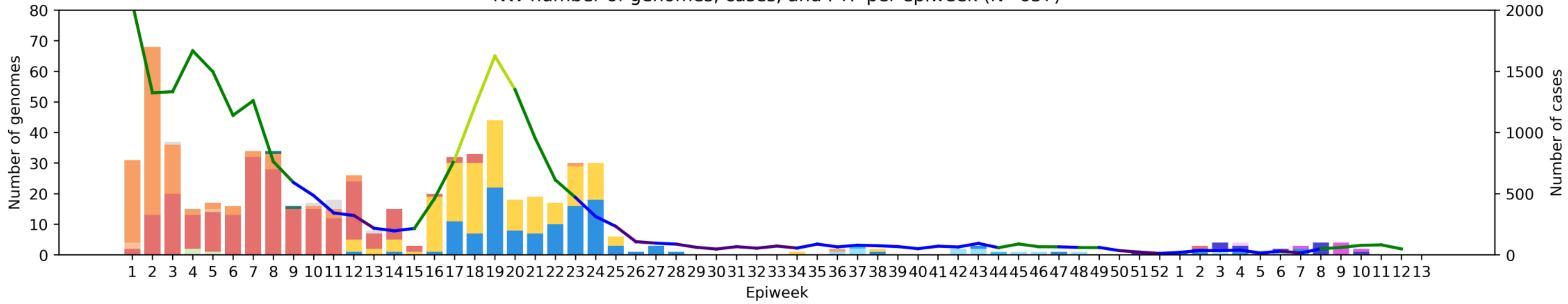
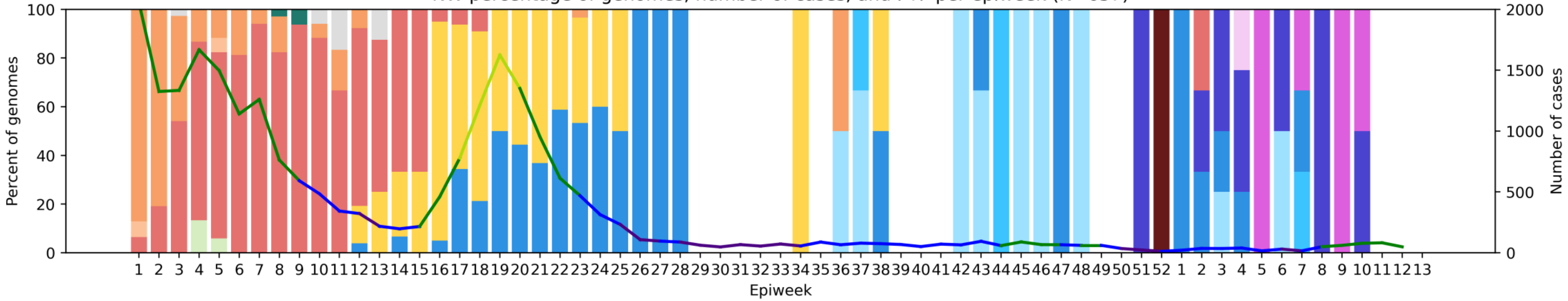
North West Province, 2022-2023, n = 657

Genomes added since last report: 9*

NW number of genomes, cases, and PTP per epiweek (N=657)



NW percentage of genomes, number of cases, and PTP per epiweek (N=657)



Clade key (bar graph)

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Weekly percentage testing positive key (line graph)

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

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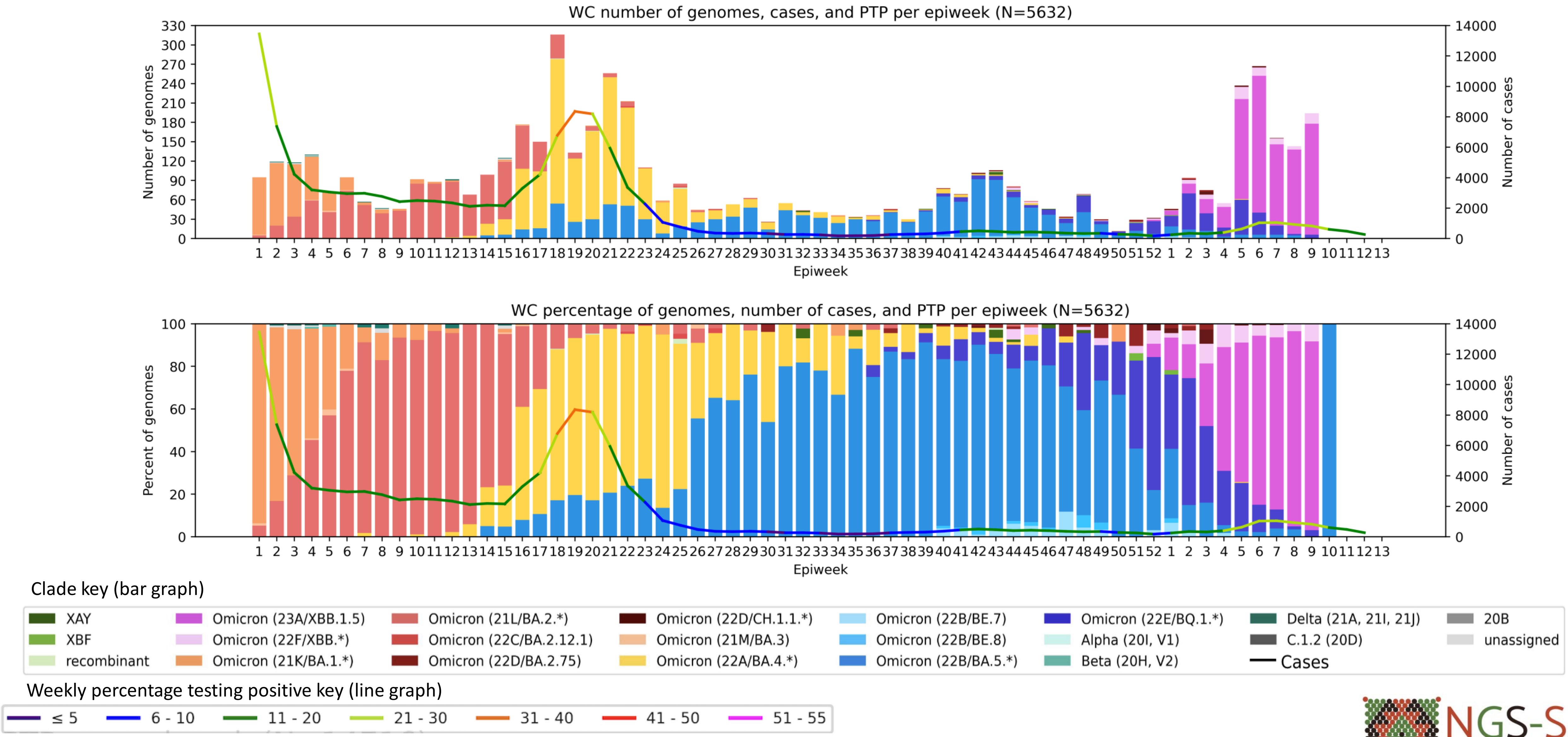
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

Western Cape Province, 2022-2023, n = 5632

Genomes added since last report: 214*


WC number of genomes, cases, and PTP per epiweek (N=5632)

WC percentage of genomes, number of cases, and PTP per epiweek (N=5632)

Clade key (bar graph)

Weekly percentage testing positive key (line graph)

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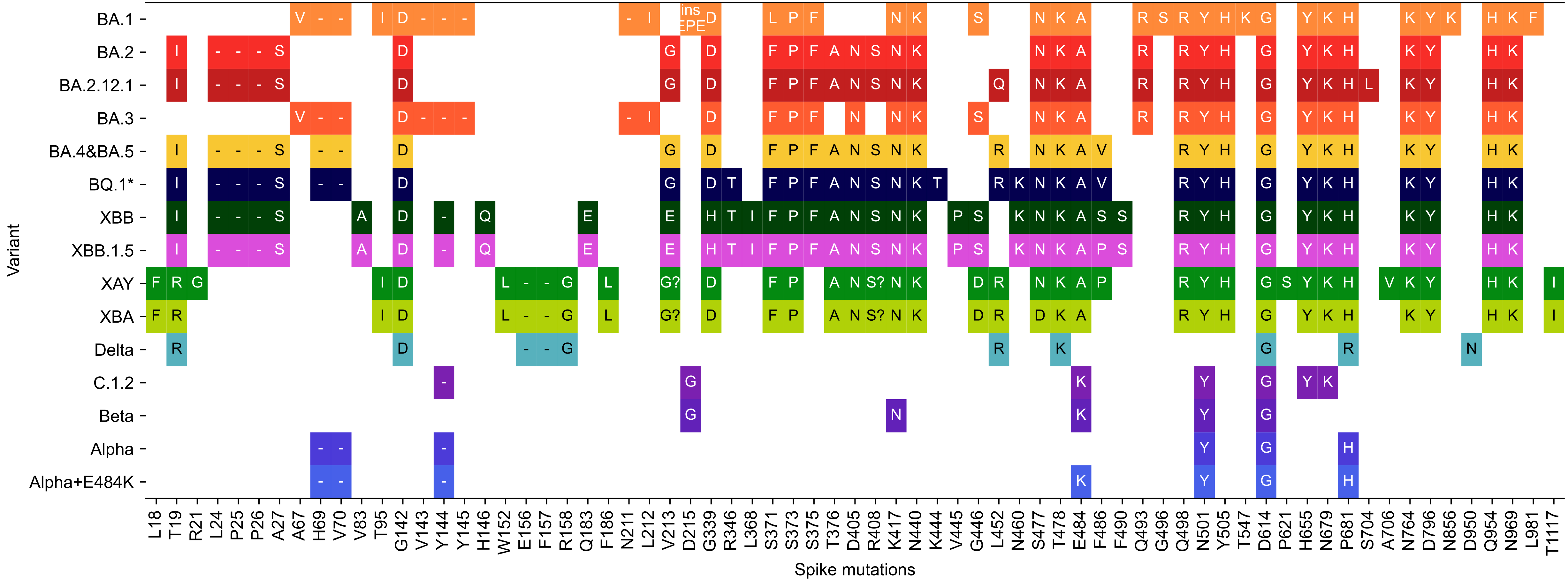
*May include genomes from 2020 and 2021 which are not pictured here and are not included in the slide total.

Summary

- **Sequencing update**
  - All provinces have sequences for January and February 2023. March sequences are from the Eastern Cape, Free State, Gauteng, KwaZulu-Natal, the North West, and the Western Cape.

- **Variant of Concern Omicron in South Africa**
  - Omicron continued to dominate in January (99%), February (100%) and makes up 100% of March sequences
  - BQ.1 and sub-lineages were the dominant Omicron lineage in December (46%) and January (53%)
  - XBB.1.5 was detected in December 2022 (0.8%) and January 2023 (16%), and is the dominant lineage in February (71%) and March (76%)
  - BA.2.75.* continued to be detected at a low prevalence in January through March (≤1%)

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										

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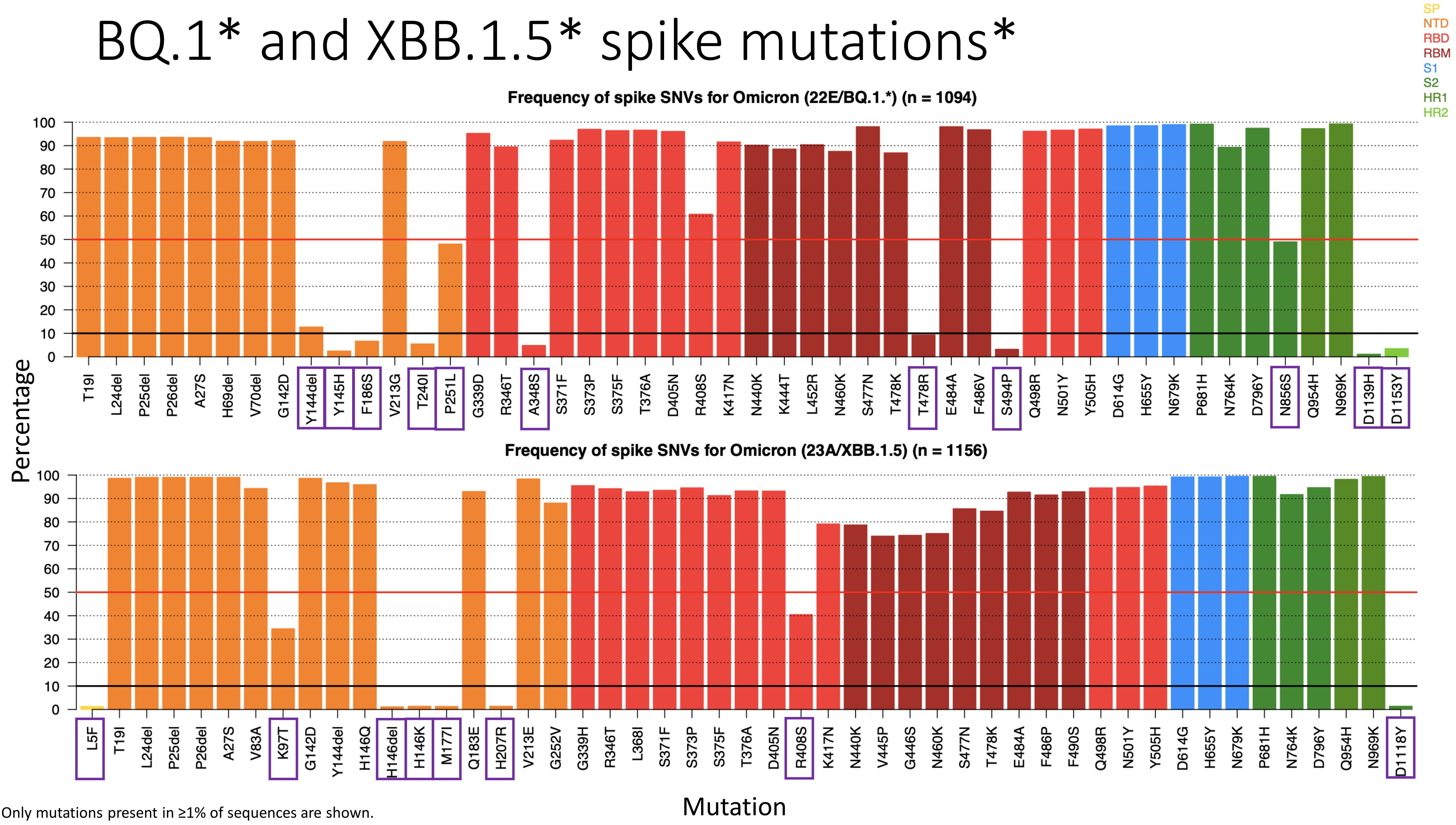
BQ.1* and XBB.1.5* spike mutations*



Frequency of spike SNVs for Omicron (22E/BQ.1.*) (n = 1094)

Frequency of spike SNVs for Omicron (23A/XBB.1.5) (n = 1156)

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

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Karabo Phadu
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UKZN-Inkosi Albert Luthuli Central Hospital

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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

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Richard Lessels
Houriiyah Tegally
Eduan Wilkinson
Jennifer Giandhari
Sureshnee Pillay
Emmanuel James San

AHRI
Alex Sigal
Sandile Cele
Willem Hanekom

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WCG-UCT
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Masudah Paleker
Theuns Jacobs
Erna Morden

NHLS Greenpoint
Annabel Enoch

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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

Zoonotic arbo and respiratory virus program Centre for Viral Zoonoses Department Medical Virology/ NHLS Tshwane Academic division University of Pretoria

ZARV research program/UP
Marietjie Venter (Head: ZARV)
Adriano Mendes (Postdoc)
Amy Strydom (Postdoc)
Michaela Davis (MSc, intern medical scientist)
Carien van Niekerk

NHLS Tshwane
Prof Simnikiwe Mayaphi (HOD)

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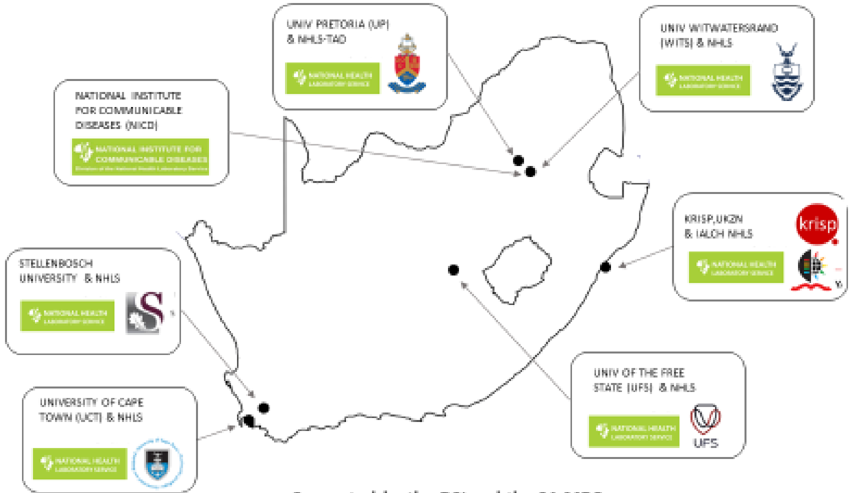

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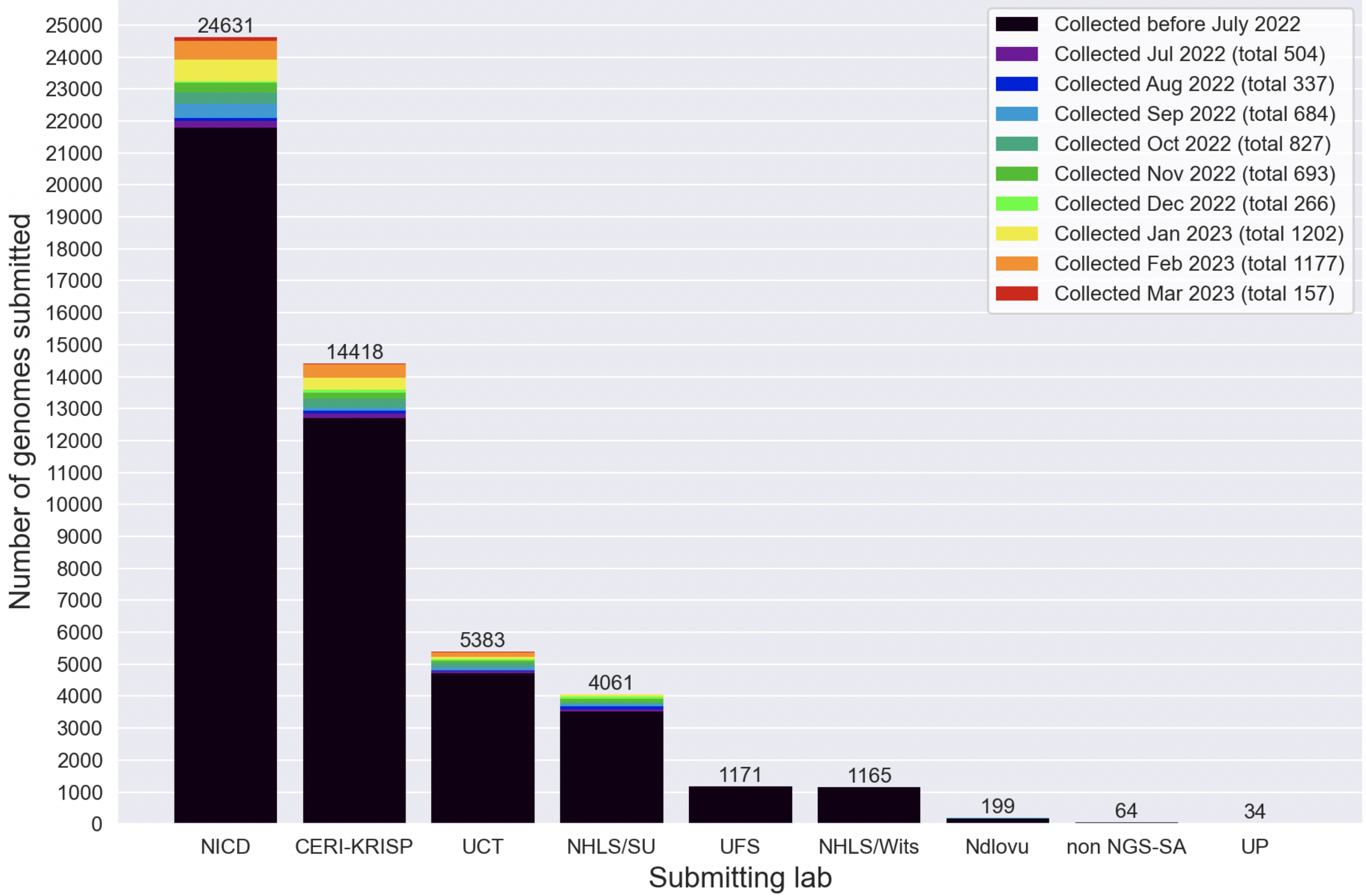
South African genomes submitted per submitting lab, 2020 - 2022 (N=51 126)



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.

NGS-SA
Network for Genomic Surveillance in South Africa

Currently circulating Variants of Interest (VOI) as of 15 March 2023

Pango lineage•	Nextstrain clade	Genetic features	Earliest documented samples	Date of designation
XBB.1.5	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	05-01-2022	11-Jan-2023

https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/ accessed 17 March 2023

Omicron subvariants under monitoring

Pango lineage[#] (+ mutation)	GISAID clade	Nextstrain clade	Relationship to circulating VOC lineages	Spike genetic features	Earliest documented samples
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
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 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 17 March 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.)