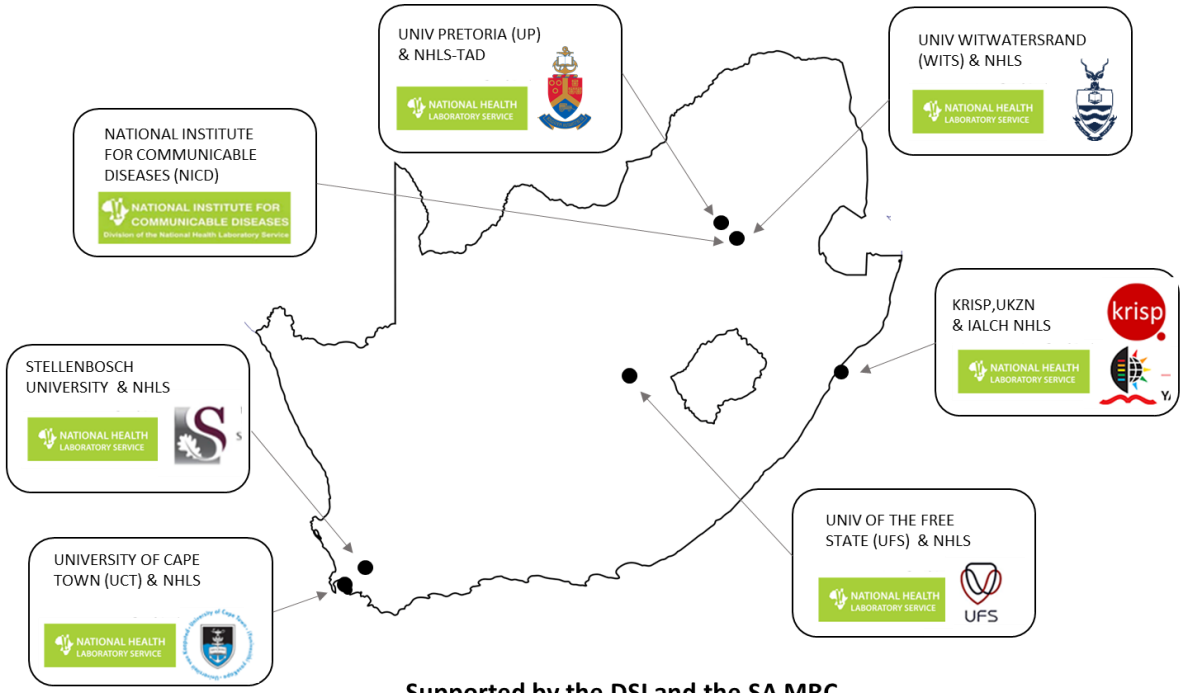
Network for Genomic Surveillance in South Africa (NGS-SA)

SARS-CoV-2 Sequencing Update
15 December 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)

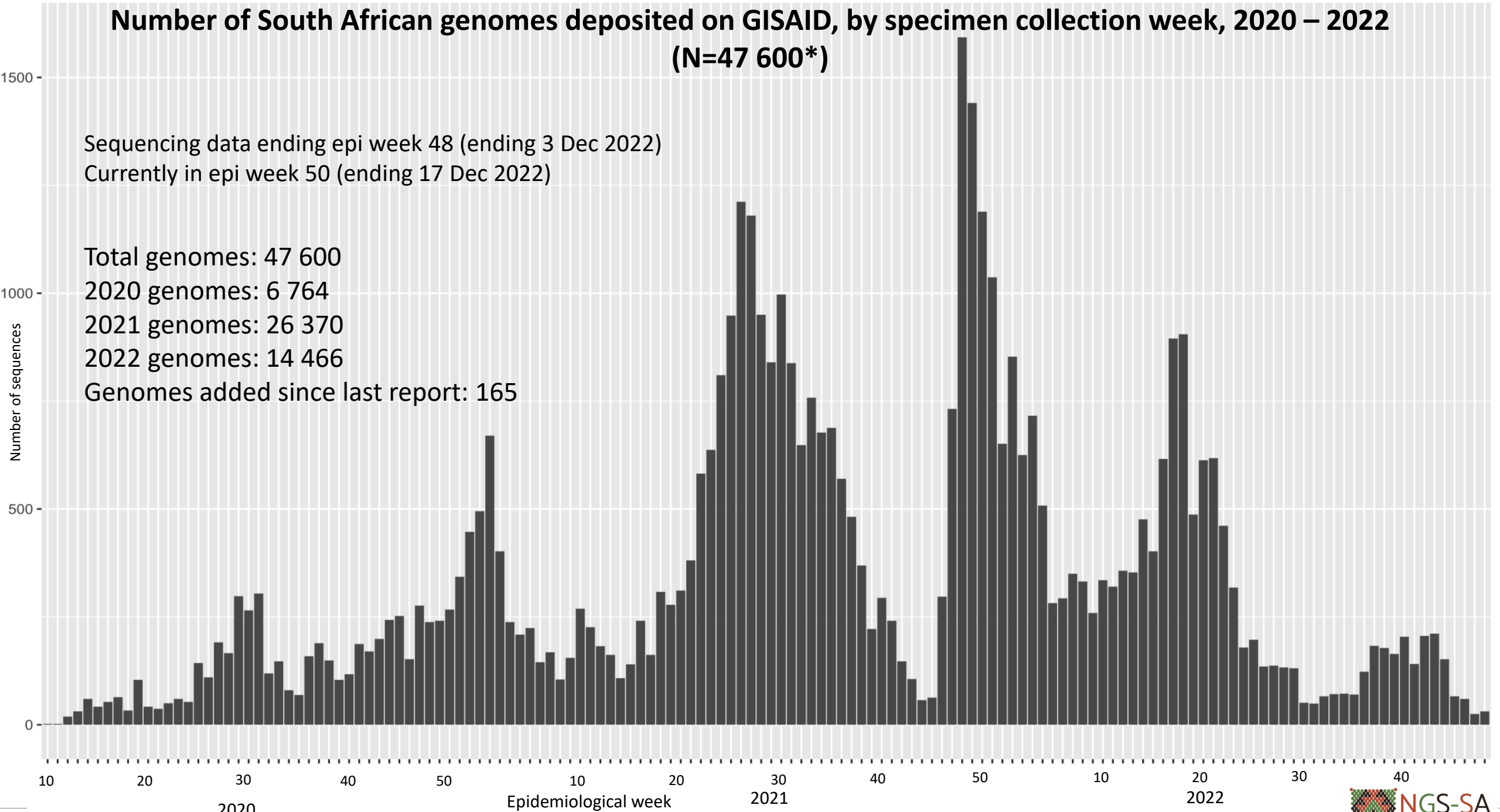
The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID (www.gisaid.org) on 15 Dec 2022 at 07h30

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=47 600*)



*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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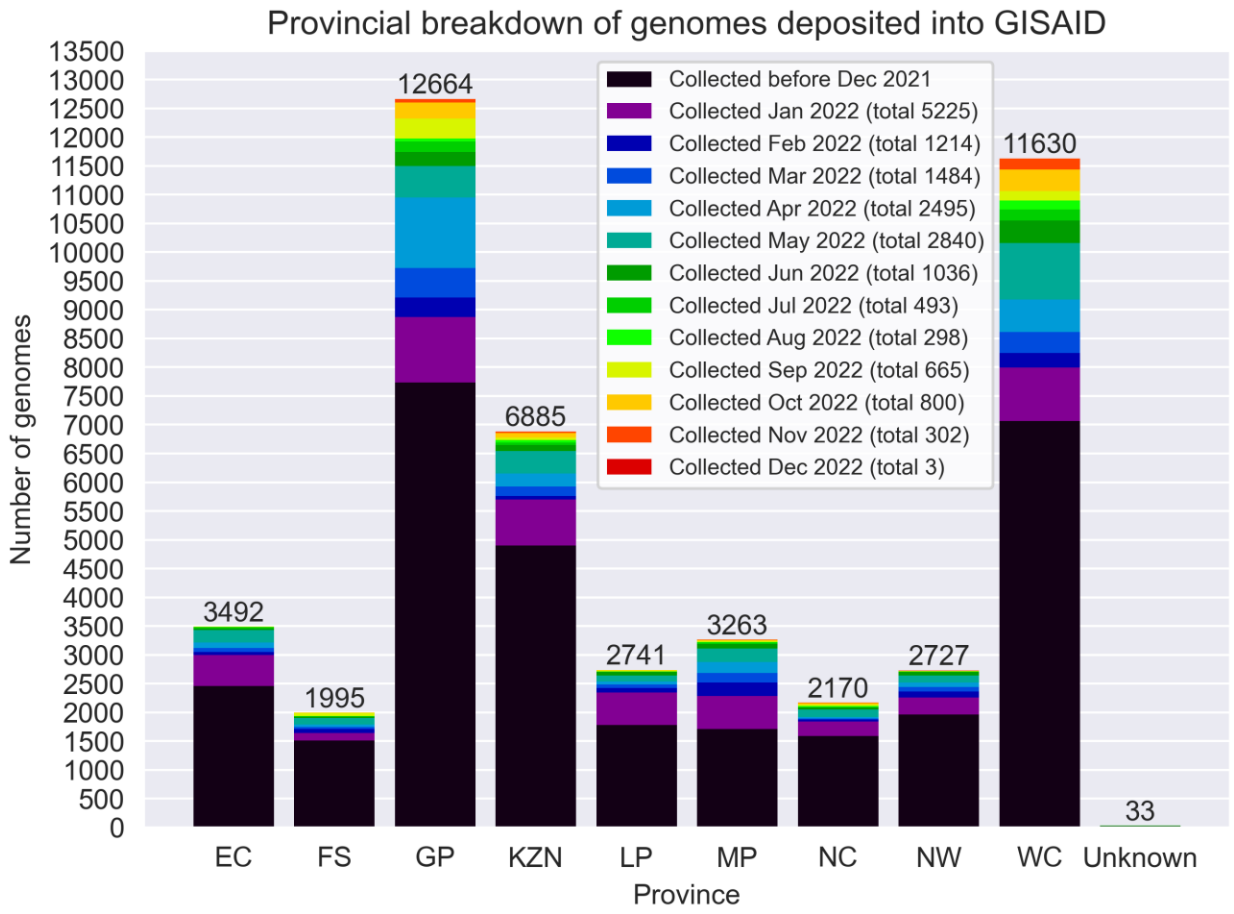
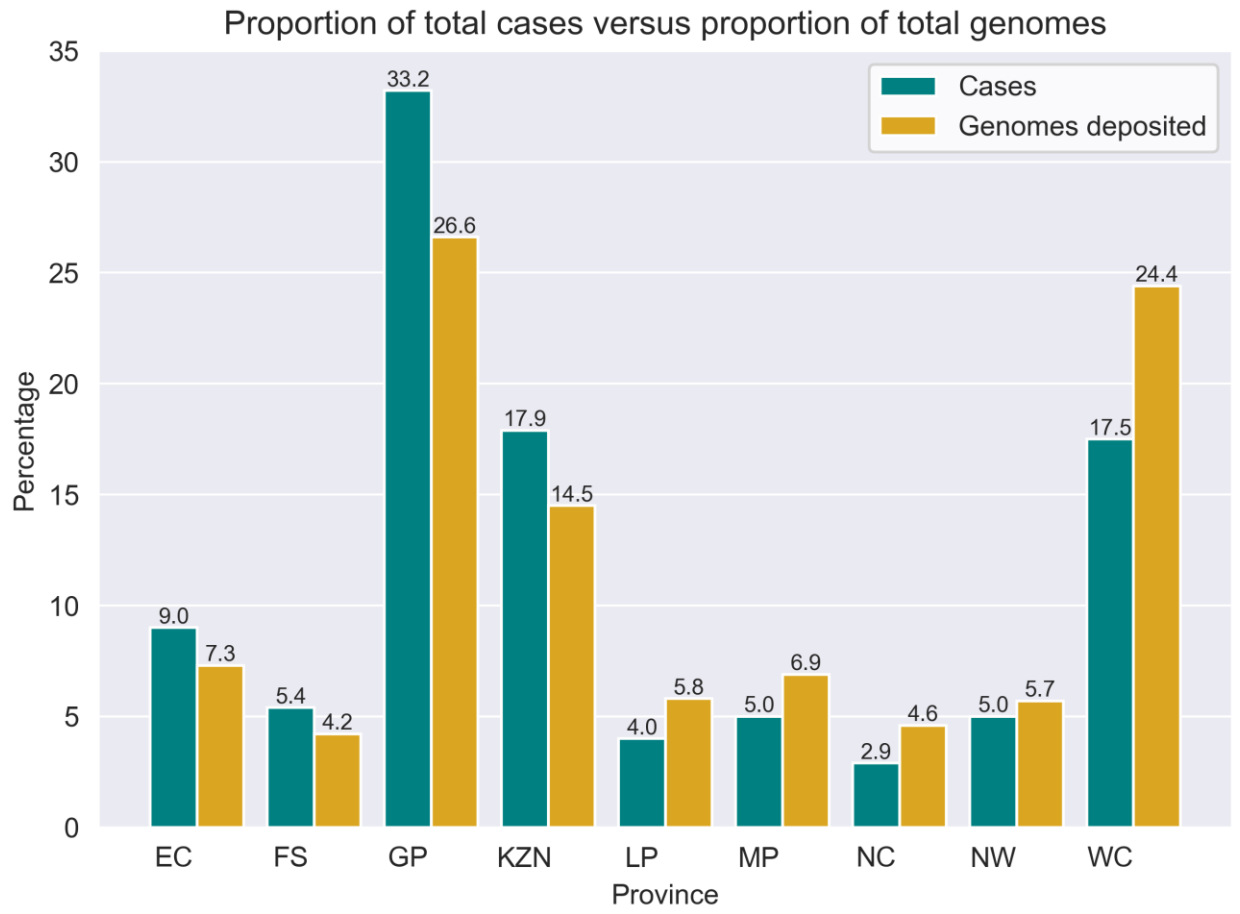
GISAID genomes vs total cases, 2020 – 2022 (N= 47 600)





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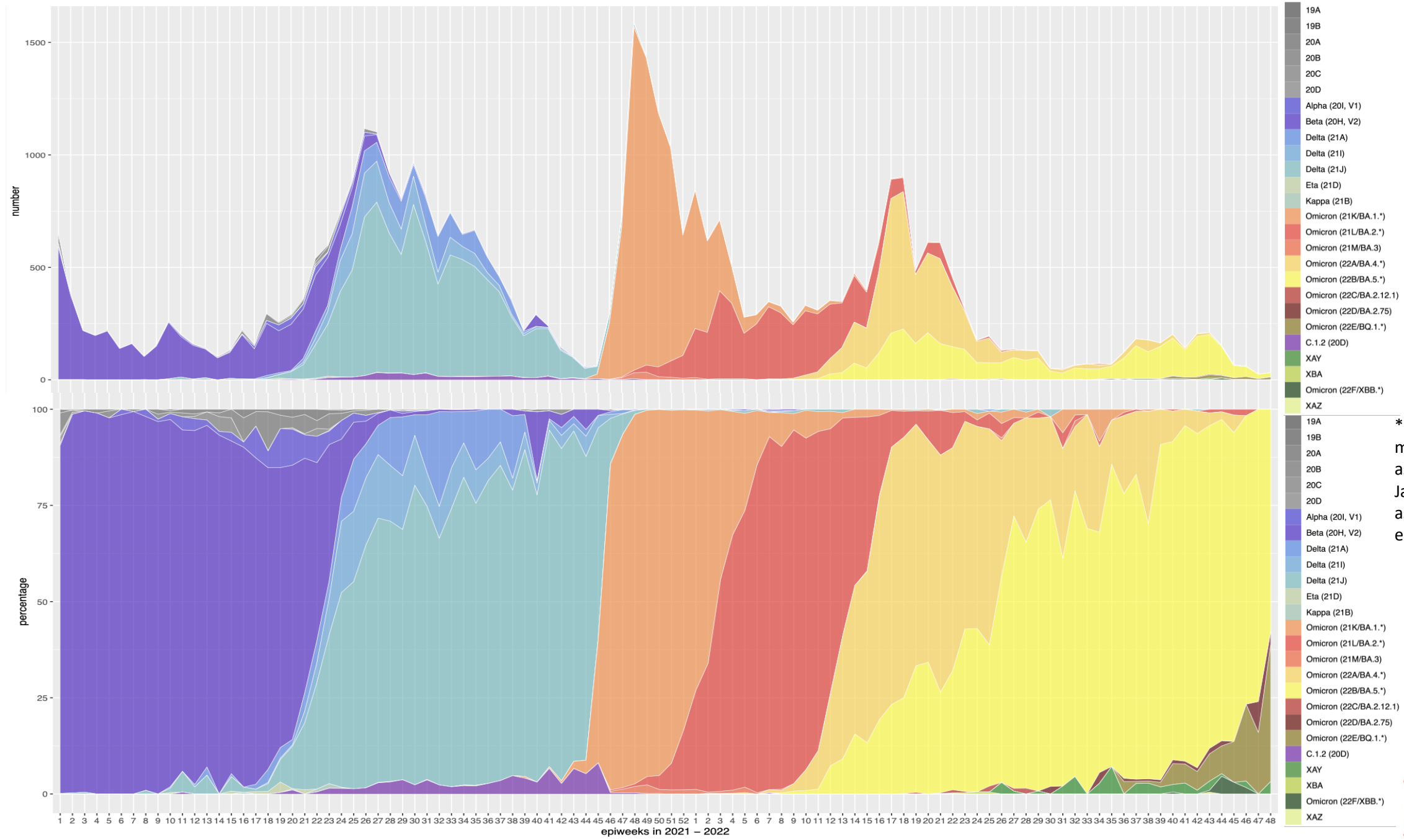
Number and percentage of clades by epiweek in South Africa, 2021 – 2022 (40 764*)



Sequencing data ending epi week 48 (ending 3 Dec 2022)

Currently in epi week 50 (ending 17 Dec 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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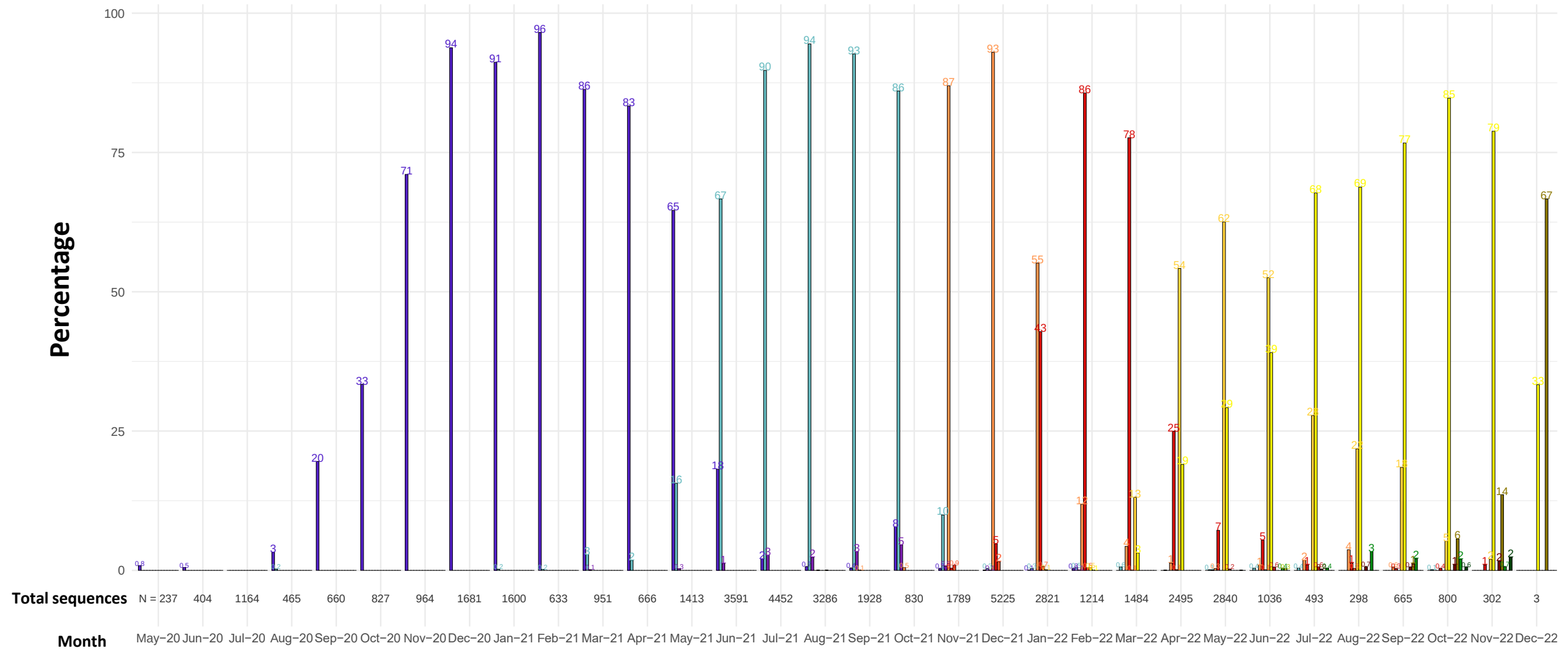
Detection Rates: Beta, Delta, C.1.2, recombinants, and Omicron



Beta
C.1.2
Omicron (21L/BA.2.*)
Omicron (22A/BA.4)
Omicron (22C/BA.2.12.1)
Omicron (22E/BQ.1.*)
Omicron (22F/XBB.*)
Delta
Omicron (21K/BA.1.*)
Omicron (21M/BA.3)
Omicron (22B/BA.5)
Omicron (22D/BA.2.75.*)
XAY
XBA

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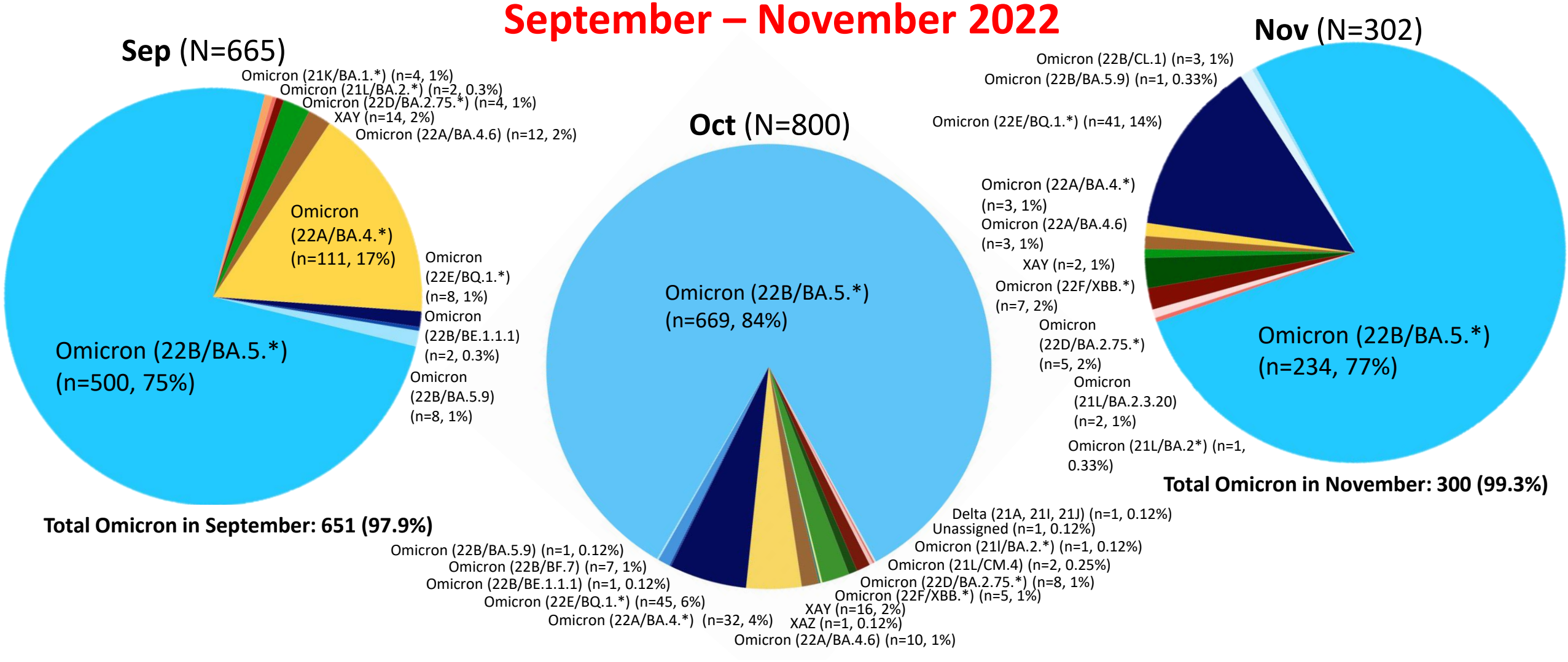
Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in September – November 2022



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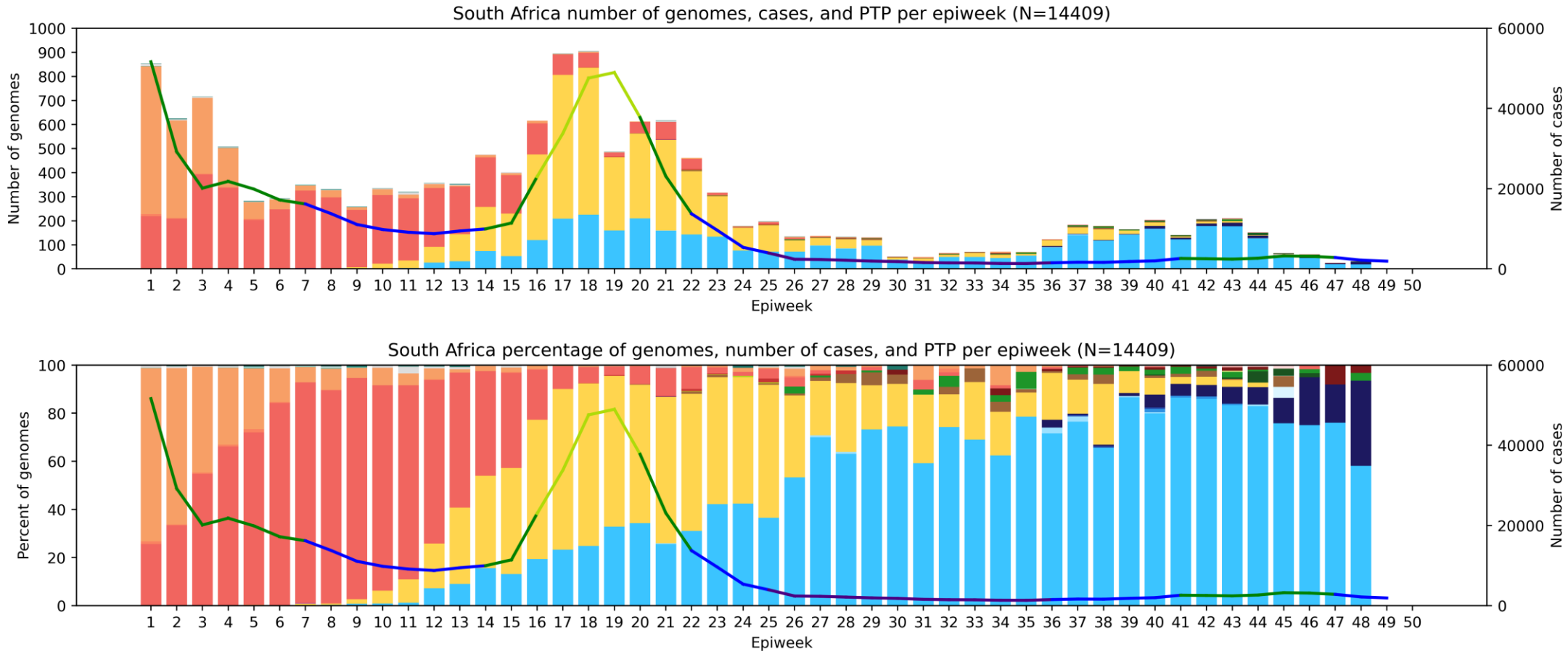
South Africa, 2022, n = 14 409*



Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
XBA | Omicron (21L/CM.4) | Omicron (22D/BA.2.75) | Omicron (22A/BA.4.6) | Omicron (22B/BA.5.9) | Omicron (22E/BQ.1.*) | Alpha (20I, V1) | 20A | Delta (21I) | Eta (21D) | 19B
XAZ | Cases

Weekly percentage testing positive key (line graph)

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

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

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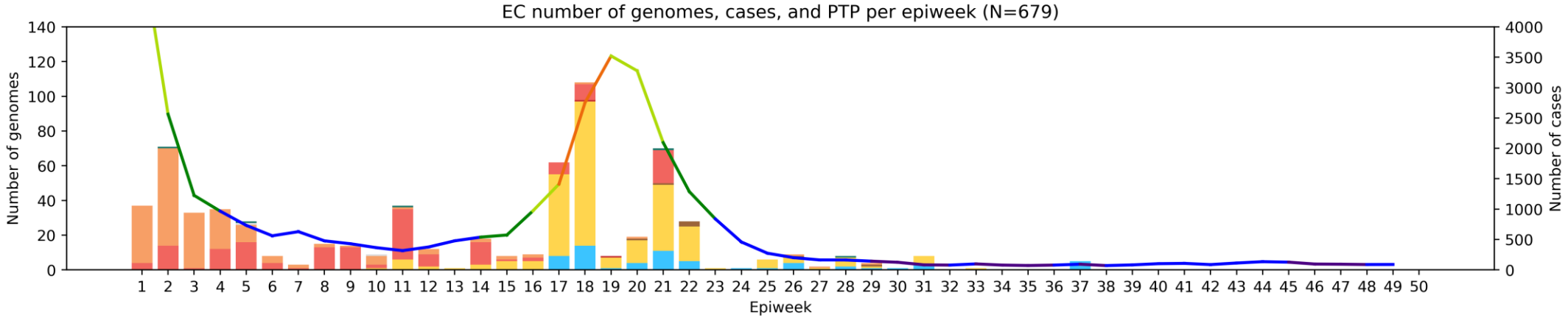
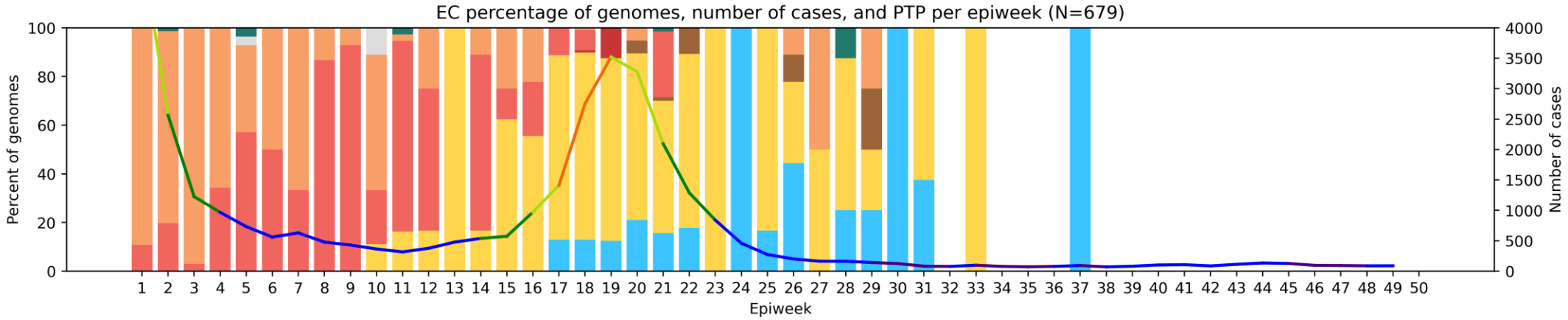
Eastern Cape Province, 2022, n = 679

Genomes added since last report: 0*





Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
XBA | Omicron (21L/CM.4) | Omicron (22D/BA.2.75) | Omicron (22A/BA.4.6) | Omicron (22B/BA.5.9) | Omicron (22E/BQ.1.*) | Alpha (20I, V1) | 20A | Delta (21I) | Eta (21D) | 19B
XAZ | Cases

Weekly percentage testing positive key (line graph)

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

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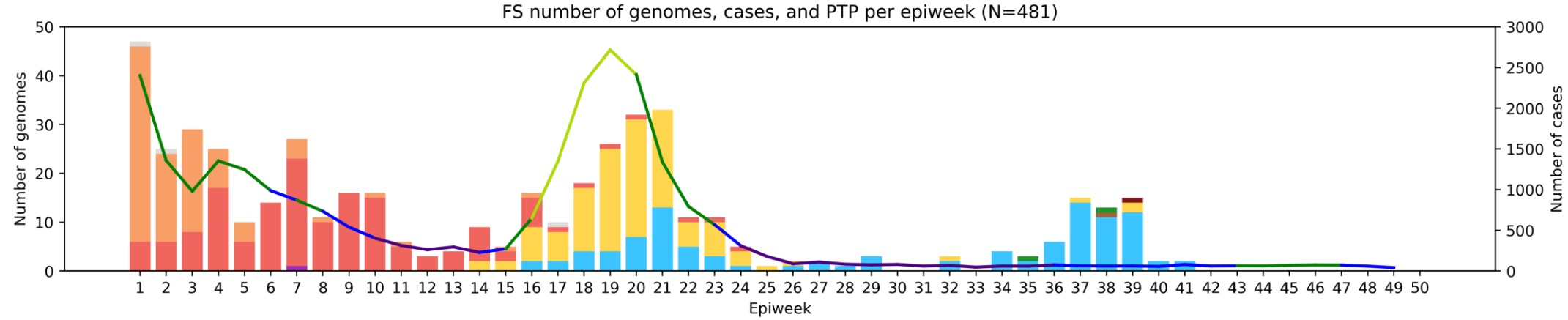
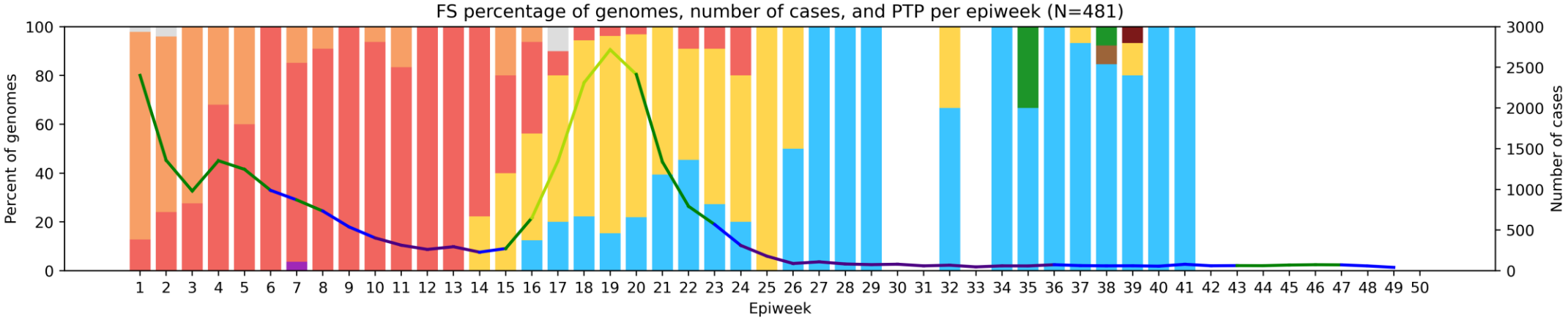
Free State Province, 2022, n = 481

Genomes added since last report: 0*





Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
XBA | Omicron (21L/CM.4) | Omicron (22D/BA.2.75) | Omicron (22A/BA.4.6) | Omicron (22B/BA.5.9) | Omicron (22E/BQ.1.*) | Alpha (20I, V1) | 20A | Delta (21I) | Eta (21D) | 19B
XAZ | Cases

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 and 2021 which are not pictured here and are not included in the slide total.

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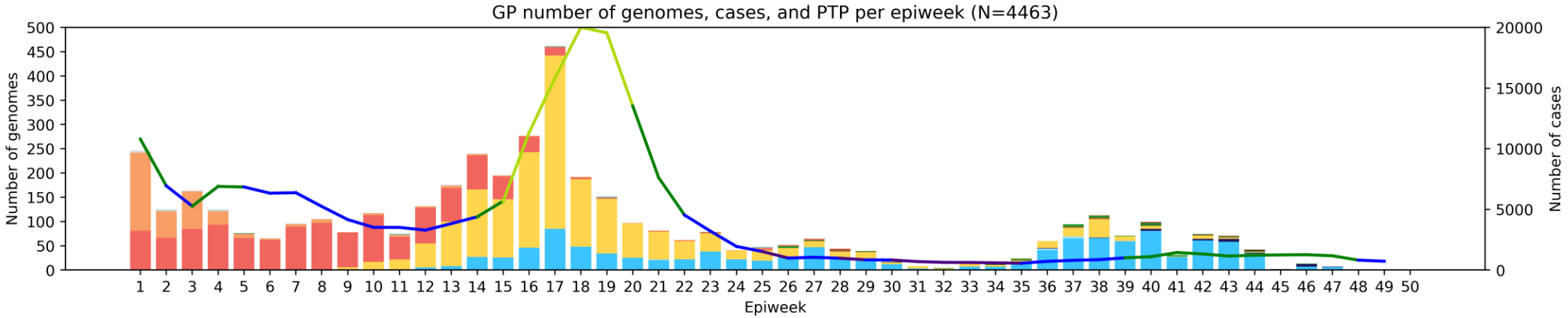
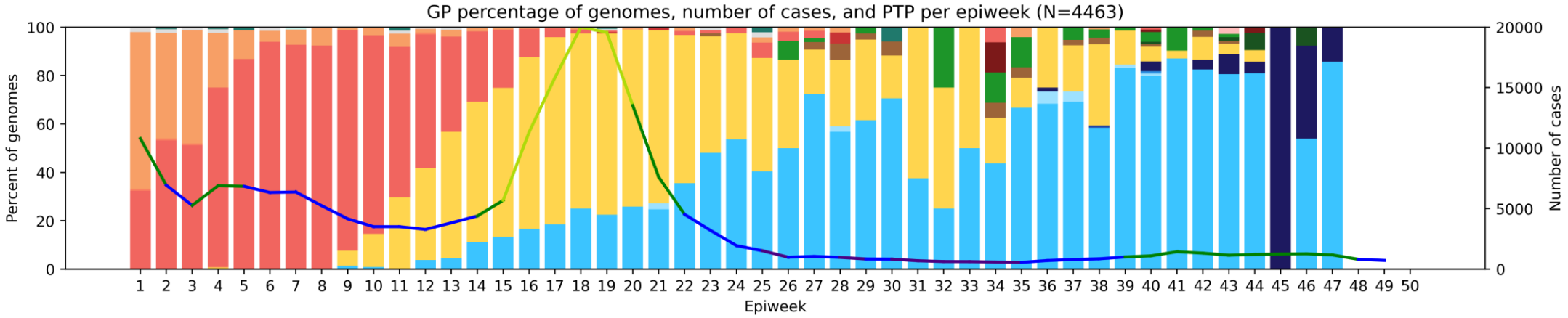
Gauteng Province, 2022, n = 4463

Genomes added since last report: 66*





Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
XBA | Omicron (21L/CM.4) | Omicron (22D/BA.2.75) | Omicron (22A/BA.4.6) | Omicron (22B/BA.5.9) | Omicron (22E/BQ.1.*) | Alpha (20I, V1) | 20A | Delta (21I) | Eta (21D) | 19B
XAZ | Cases

Weekly percentage testing positive key (line graph)

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

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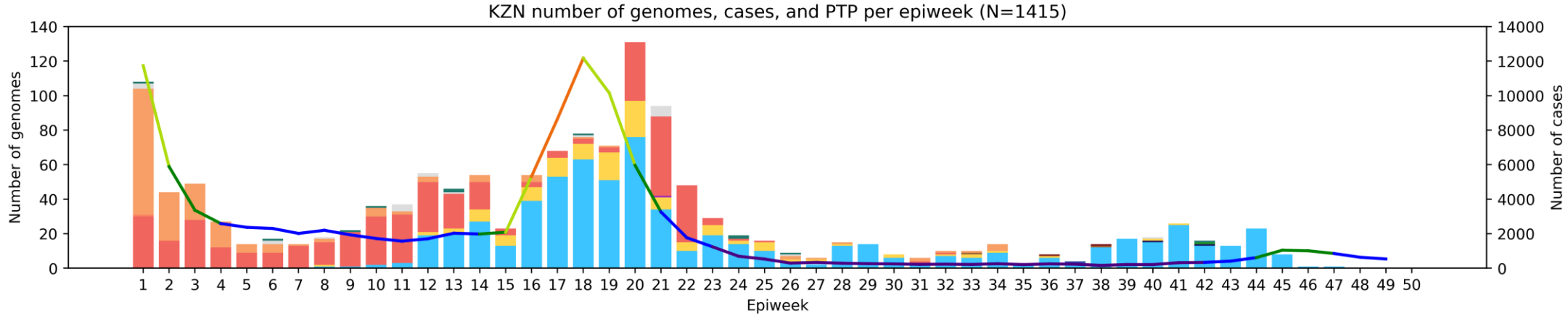
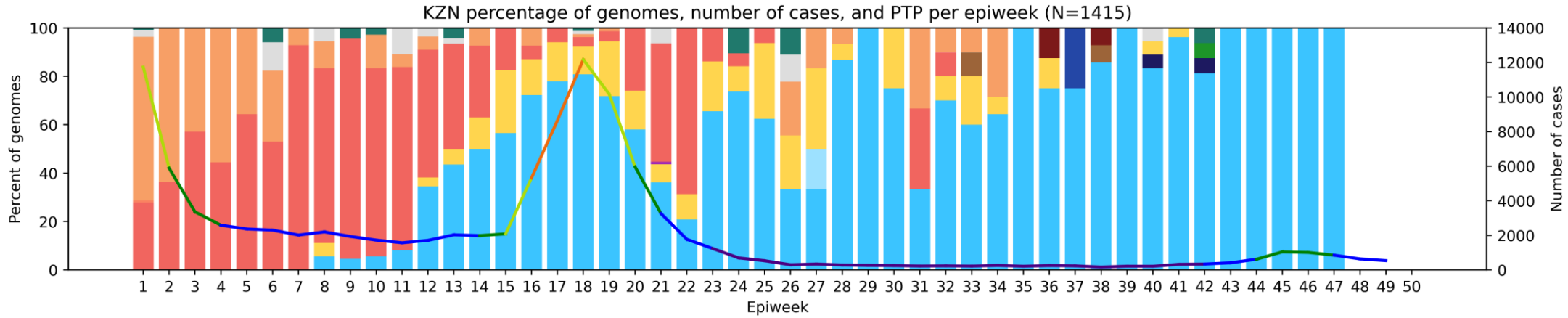
KwaZulu-Natal Province, 2022, n = 1415

Genomes added since last report: 28*





Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
XBA | Omicron (21L/CM.4) | Omicron (22D/BA.2.75) | Omicron (22A/BA.4.6) | Omicron (22B/BA.5.9) | Omicron (22E/BQ.1.*) | Alpha (20I, V1) | 20A | Delta (21I) | Eta (21D) | 19B
XAZ | Cases

Weekly percentage testing positive key (line graph)

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

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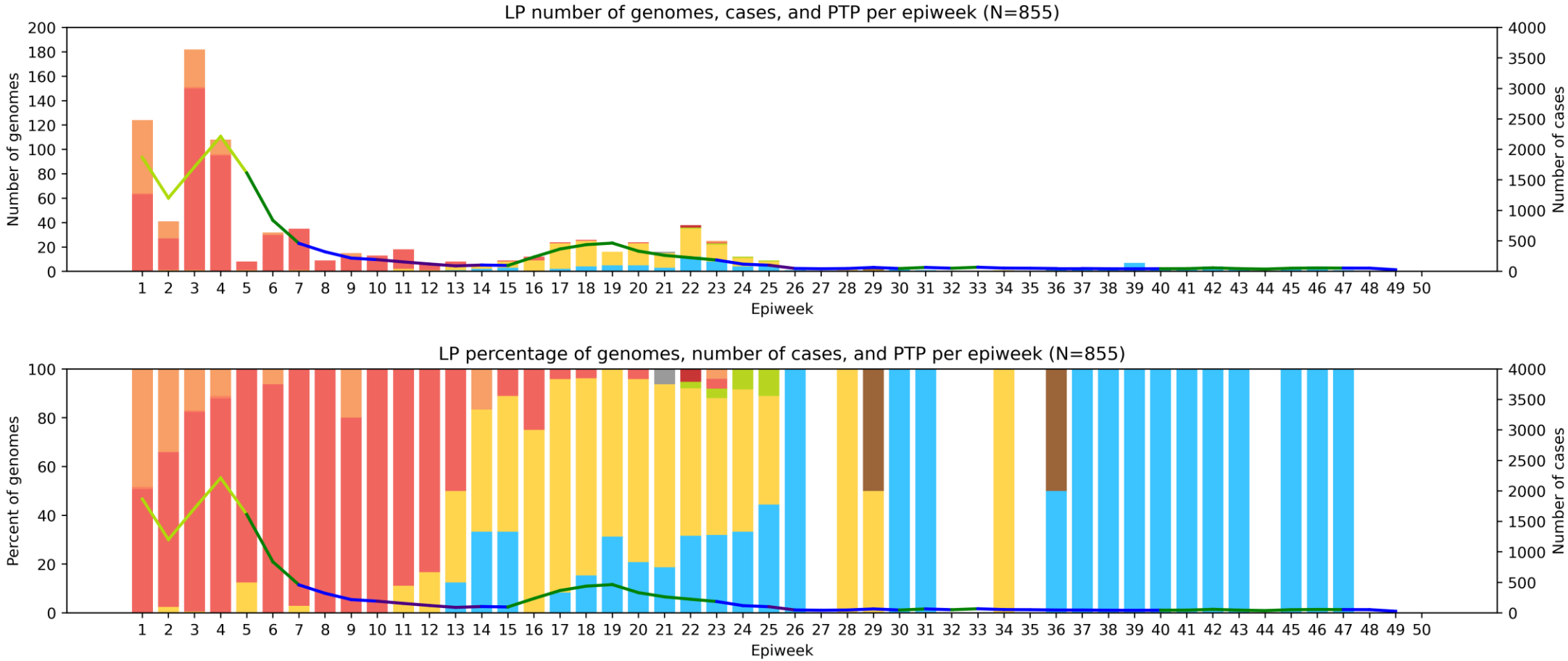
Limpopo Province, 2022, n = 855

Genomes added since last report: 0*



Clade key (bar graph)

Omicron (22F/XBB.*)
XAY
XBA
XAZ
Omicron (21K/BA.1.*)
Omicron (21L/BA.2.*)
Omicron (21L/CM.4)
Cases
Omicron (21L/BA.2.3.20)
Omicron (22C/BA.2.12.1)
Omicron (22D/BA.2.75)
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.*)
C.1.2 (20D)
Beta (20H, V2)
Alpha (20I, V1)
Delta (21A, 21I, 21J)
20B
20A
unassigned
Delta (21J)
Delta (21I)
Kappa (21B)
20D
Eta (21D)
19A
20C
19B

Weekly percentage testing positive key (line graph)

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

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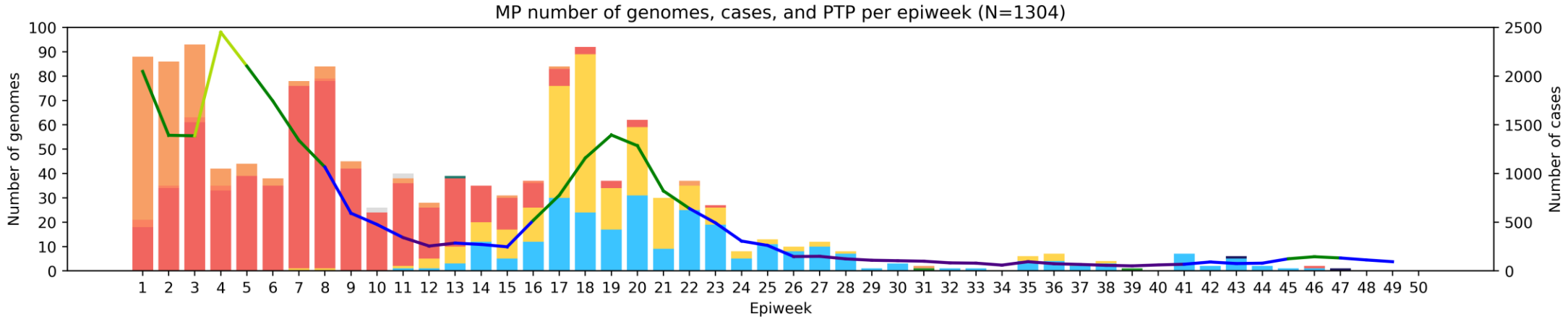
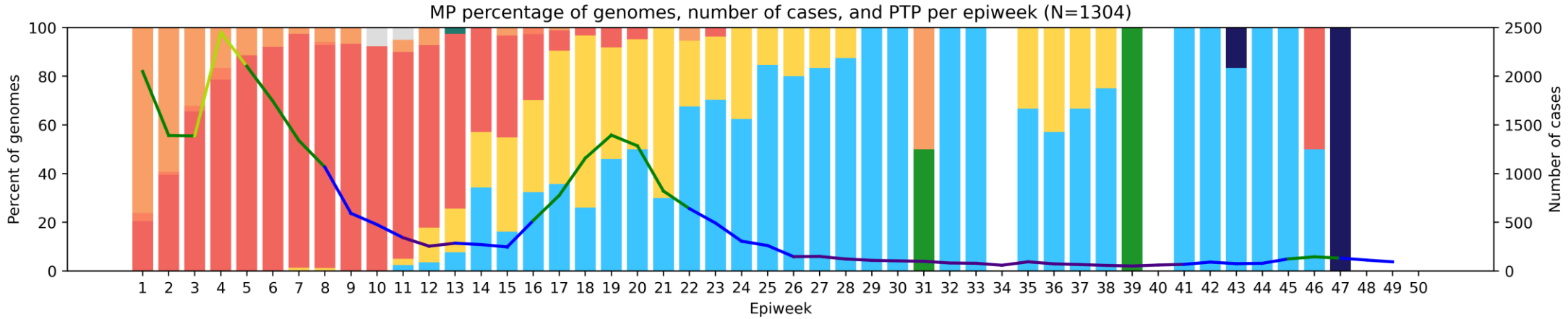
Mpumalanga Province, 2022, n = 1304

Genomes added since last report: 4*





Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
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XBA | Omicron (21L/CM.4) | Omicron (22D/BA.2.75) | Omicron (22A/BA.4.6) | Omicron (22B/BA.5.9) | Omicron (22E/BQ.1.*) | Alpha (20I, V1) | 20A | Delta (21I) | Eta (21D) | 19B
XAZ | Cases

Weekly percentage testing positive key (line graph)

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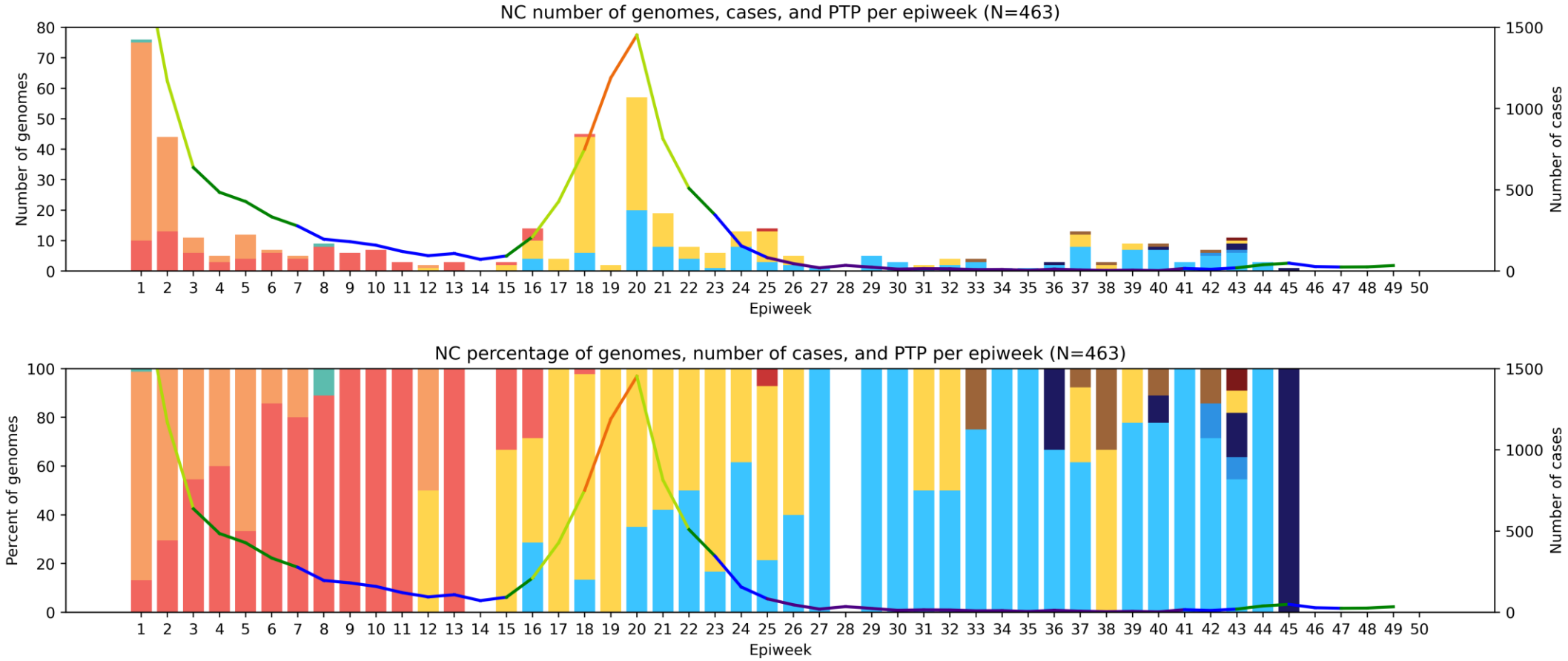
Northern Cape Province, 2022, n = 463

Genomes added since last report: 0*



Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
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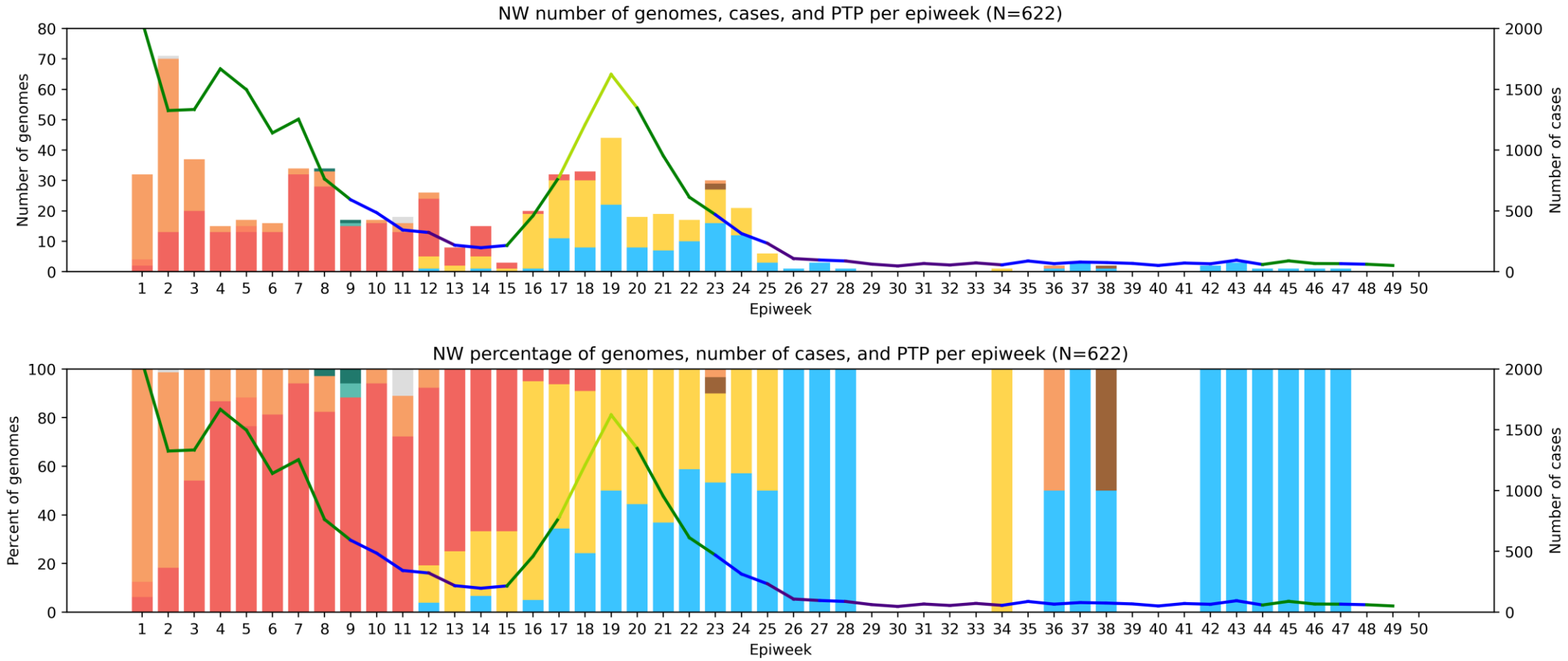
North West Province, 2022, n = 622

Genomes added since last report: 2*



Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
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Weekly percentage testing positive key (line graph)

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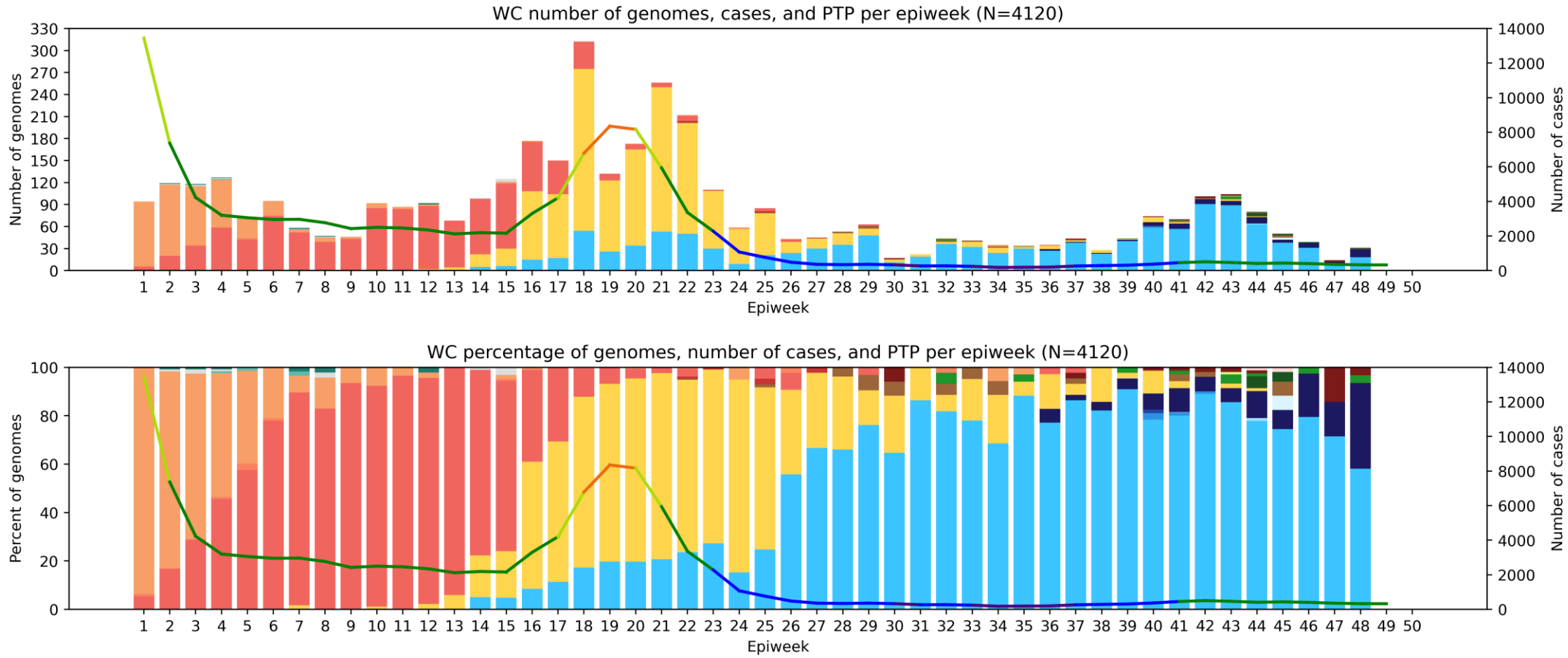
Western Cape Province, 2022, n = 4120

Genomes added since last report: 65*



Clade key (bar graph)

Omicron (22F/XBB.*) | Omicron (21K/BA.1.*) | Omicron (21L/BA.2.3.20) | Omicron (21M/BA.3) | Omicron (22B/BA.5.*) | Omicron (22B/CL.1) | C.1.2 (20D) | Delta (21A, 21I, 21J) | unassigned | Kappa (21B) | 19A
XAY | Omicron (21L/BA.2.*) | Omicron (22C/BA.2.12.1) | Omicron (22A/BA.4.*) | Omicron (22B/BF.7) | Omicron (22B/BE.1.1.1) | Beta (20H, V2) | 20B | Delta (21J) | 20D | 20C
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Summary

- **Sequencing update**
  - All provinces have sequences for September, and all provinces except the Eastern Cape have sequences for October
  - All provinces except the Eastern Cape and the Free State have sequences for November
- **Variant of Concern Omicron in South Africa**
  - Omicron continued to dominate in September (98%), October (98%) and November (99%)
  - Omicron BA.5 and sub-lineages were dominant in September (78%), October (90%) and currently make up 92% of November data
  - BA.2.75.* was detected at a low prevalence (≤2%) in September, October and November
  - XAY was detected in September, October and November at a low prevalence (≤2%)
  - 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 (6%) – BQ.1*: n=2 in KwaZulu-Natal, n=14 in Gauteng, n=25 in the Western Cape, n=3 in the Northern Cape, n=1 in Mpumalanga
    - November (14%) – BQ.1*: n=30 in the Western Cape, n=9 in Gauteng, n=1 in the Northern Cape, n=1 in Mpumalanga
  - XBB has been detected in October (1%) and November (2%)
- Delta detected at low frequency until July, and once in October

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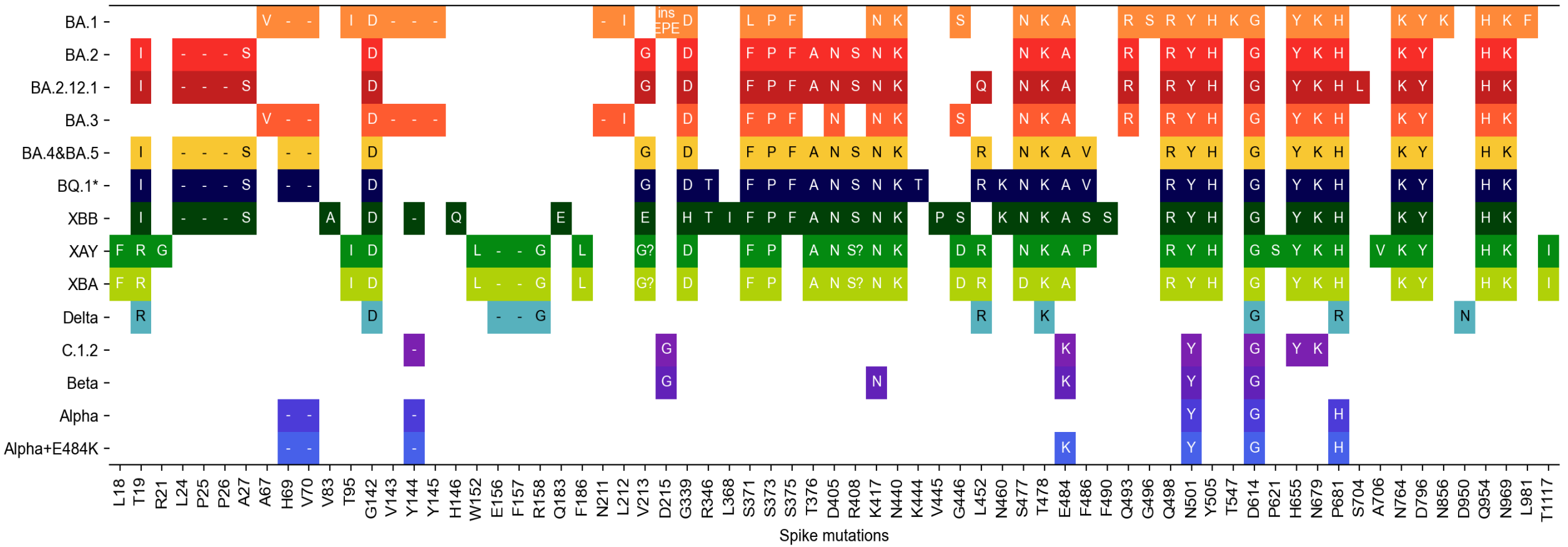
Spike protein mutation* profile of Variants of Interest and Concern



- 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

*As of 09 Dec 2022. Only mutations present in Omicron, Delta, or recombinant sequences are pictured

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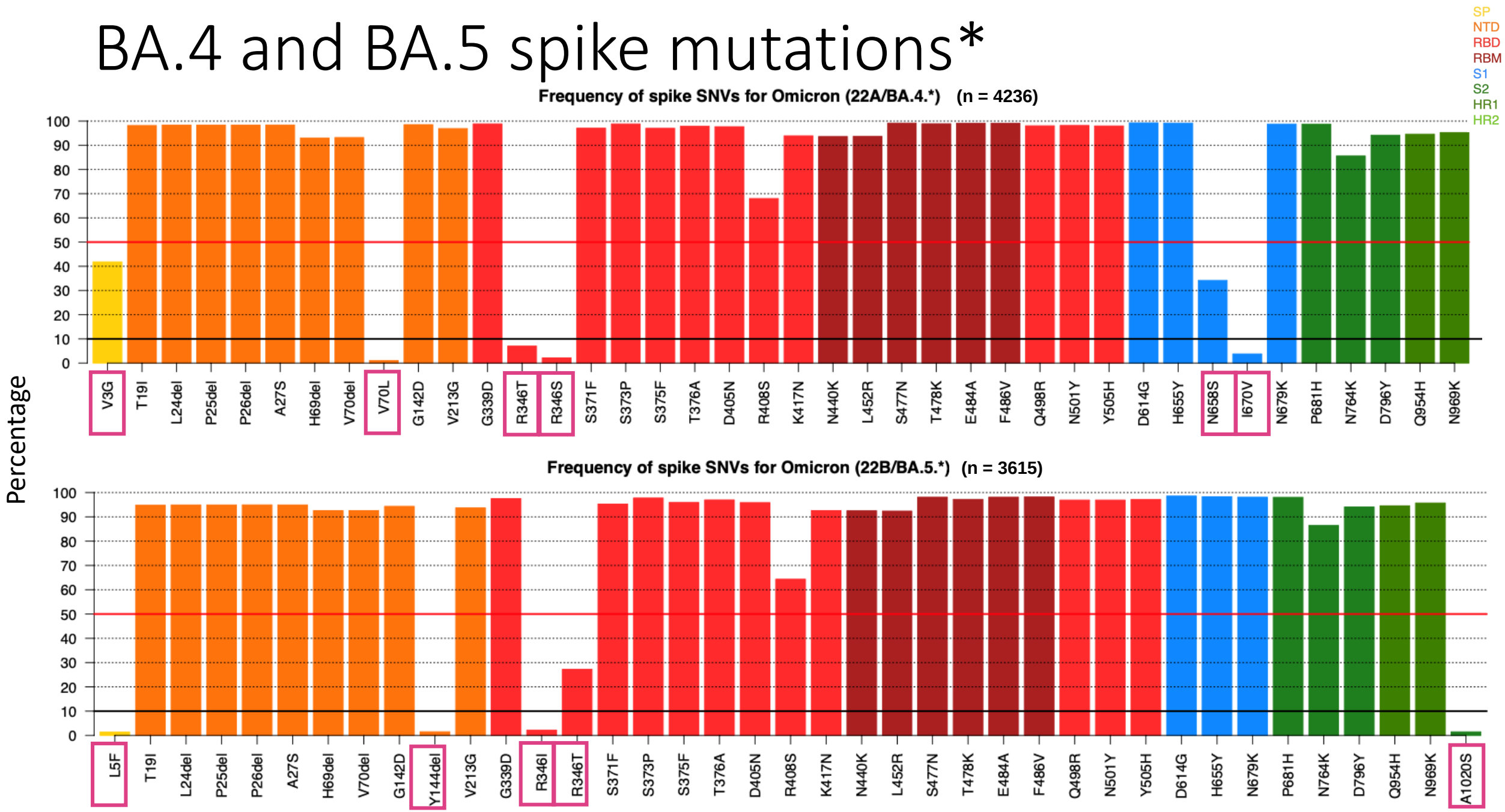
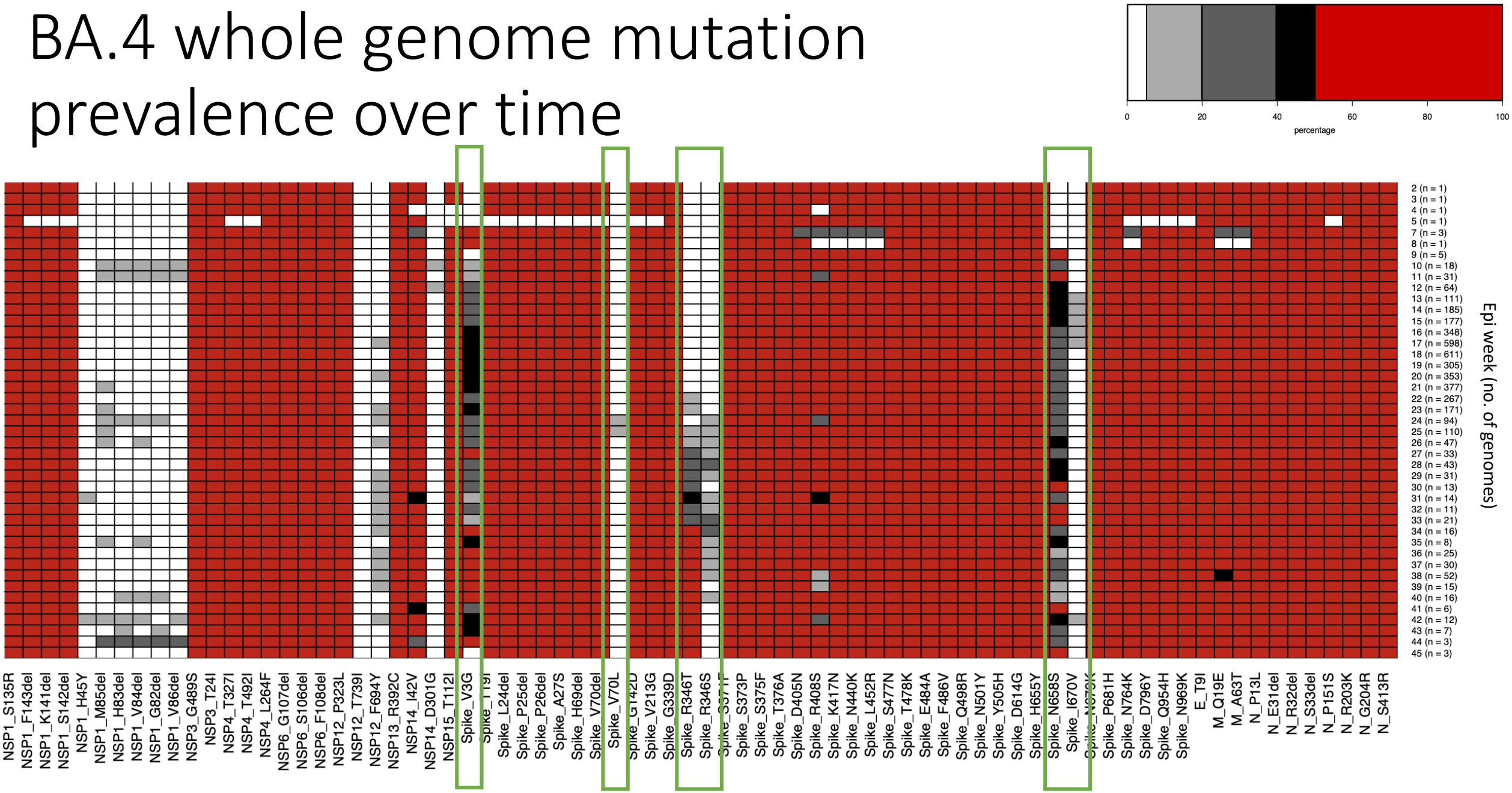
BA.4 and BA.5 spike mutations*



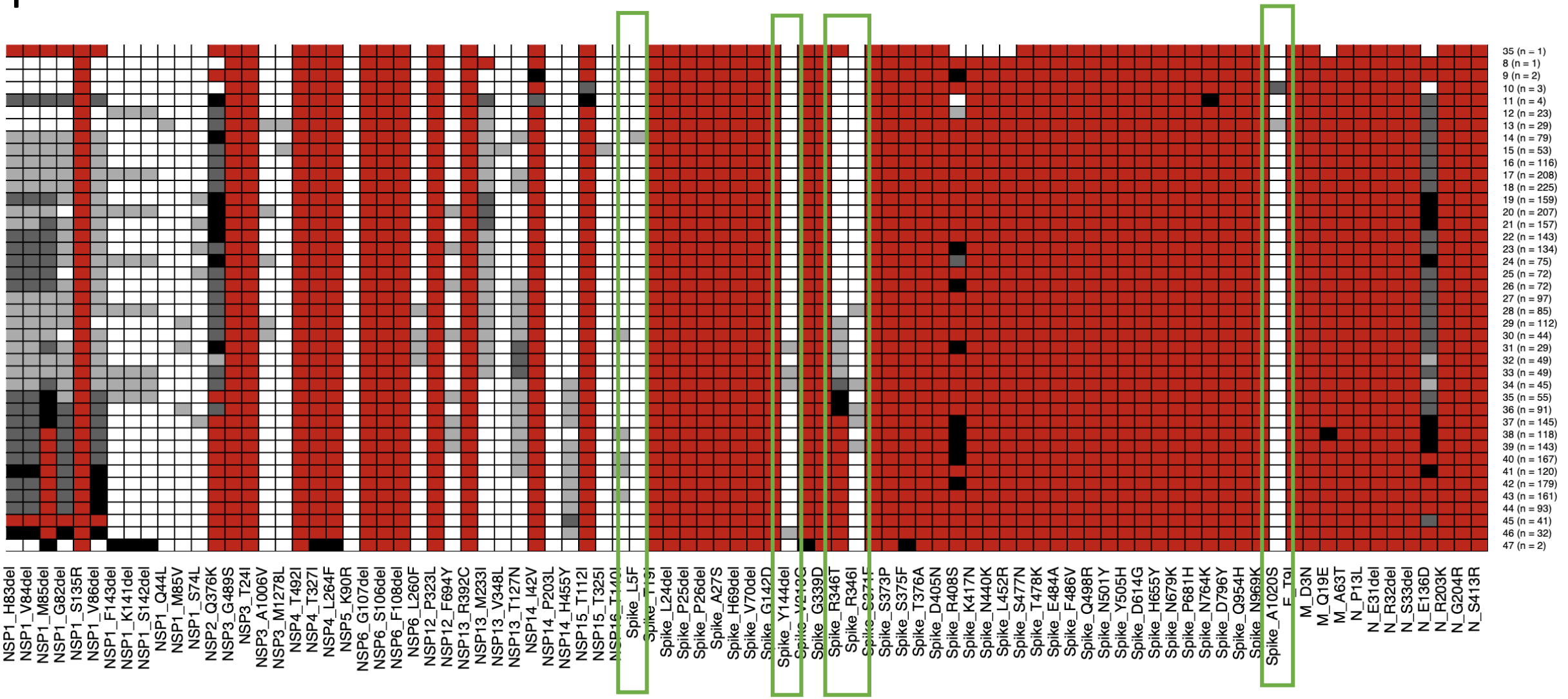
* As of 09 Dec 2022. Only mutations present in ≥1% of sequences are shown

BA.4 whole genome mutation prevalence over time



*As of 09 Dec 2022

BA.5 whole genome mutation prevalence over time



*As of 09 Dec 2022

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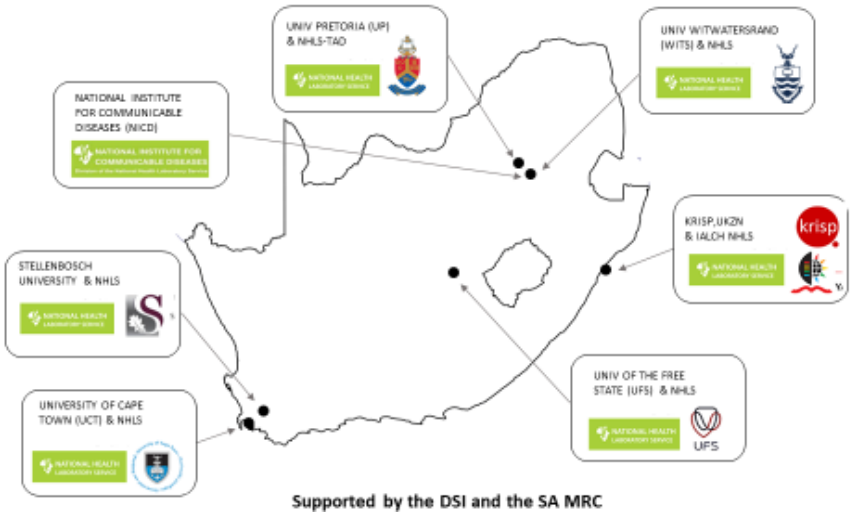

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EDCTP

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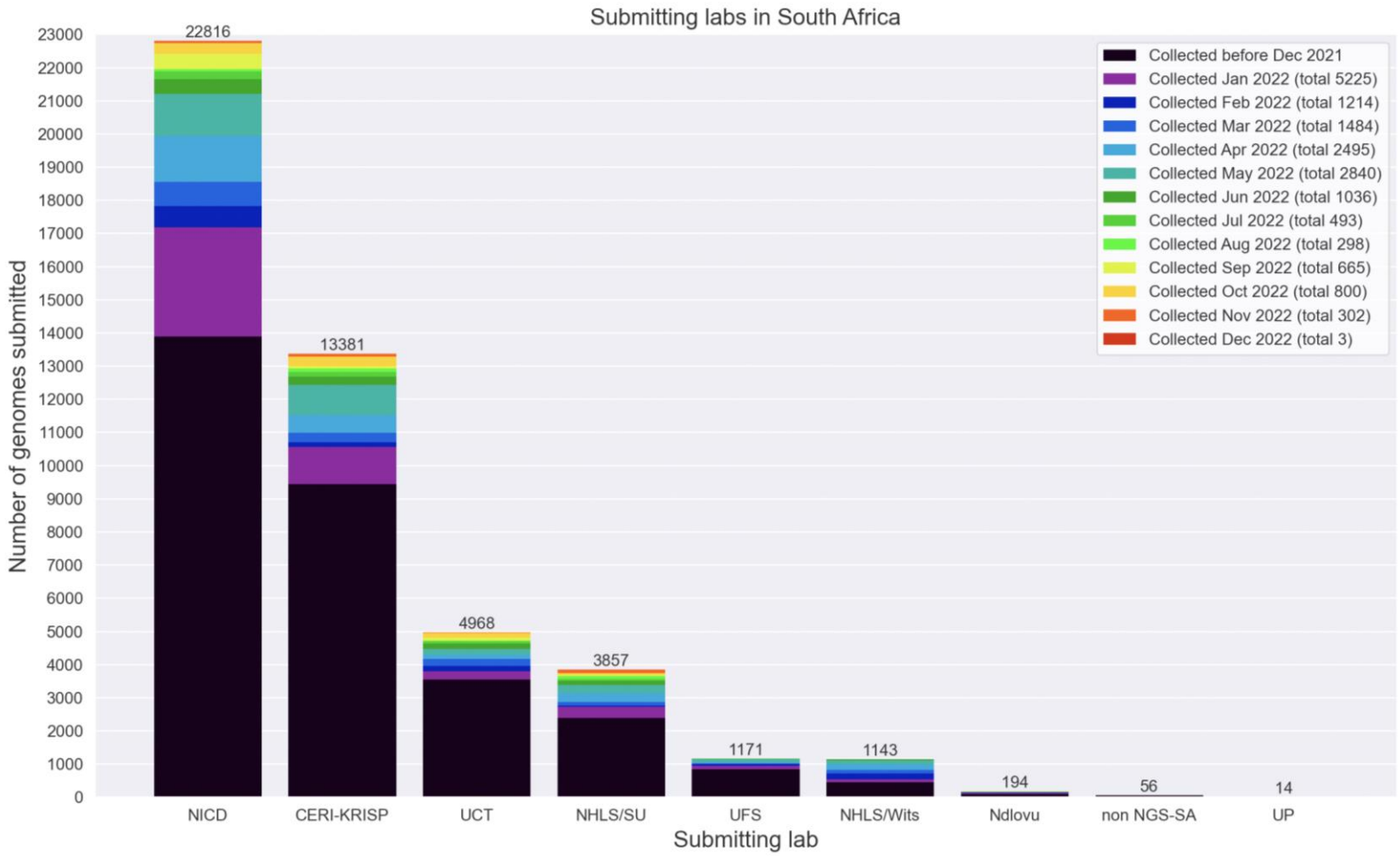
South African genomes submitted per submitting lab, 2020 - 2022 (N=47 600)



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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Network for Genomic Surveillance in South Africa

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.)