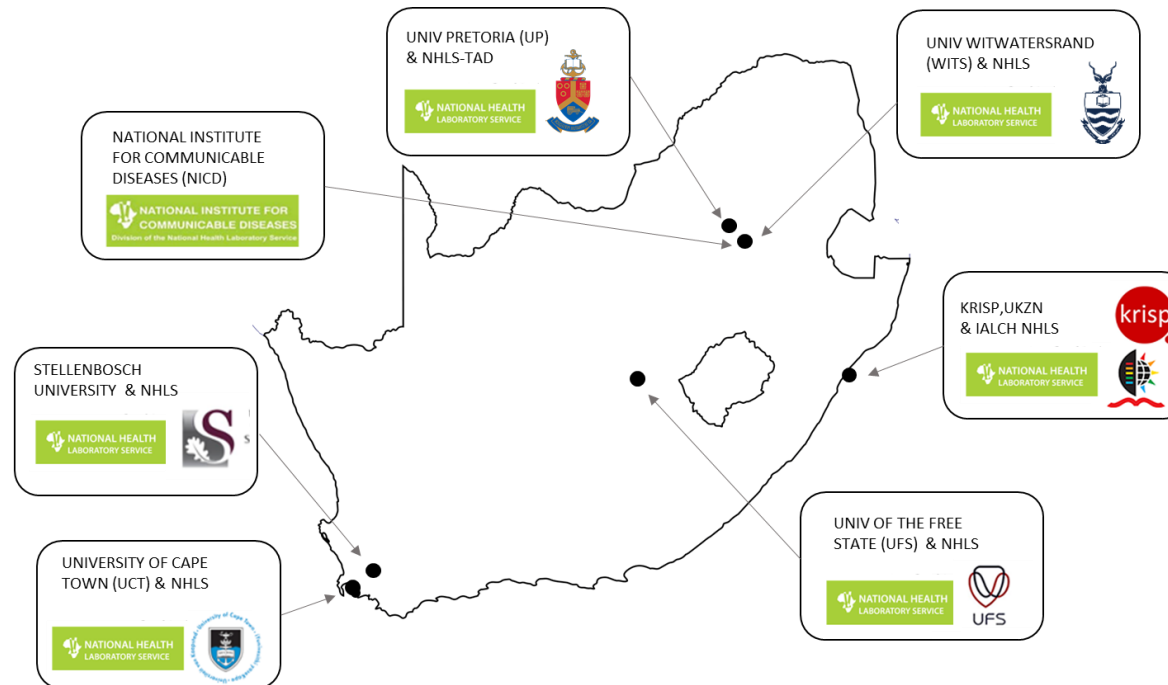


## SARS-CoV-2 Sequencing Update 18 November 2022



Supported by the DSI and the SA MRC

Msomi N, Mlisana K, et al. Lancet Microbe 2020

The genomic data presented here are based on South African SARS-CoV-2 sequence data downloaded from GISAID ([www.gisaid.org](http://www.gisaid.org)) on 18 November 2022 at 10h15

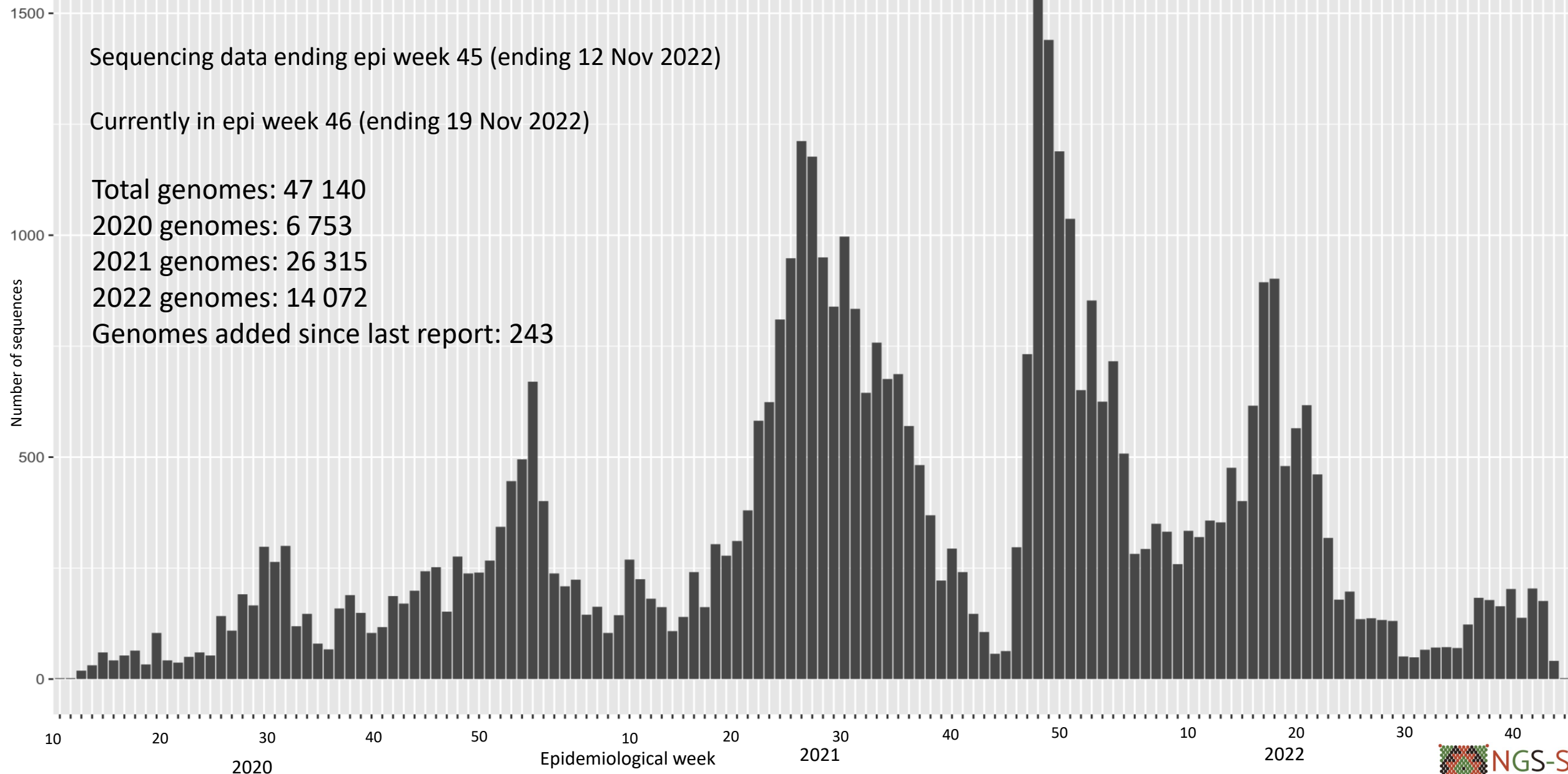


Data license: <https://www.gisaid.org/registration/terms-of-use/>

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

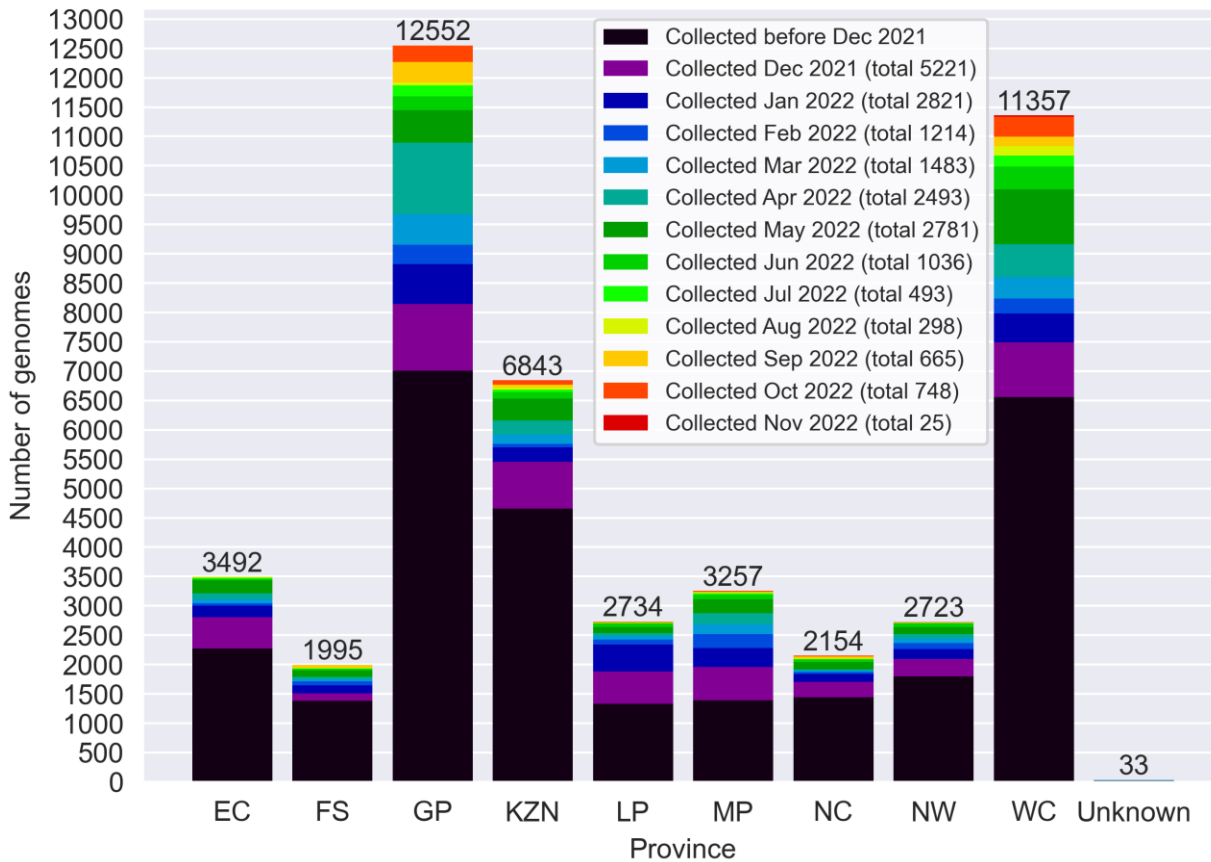
# Number of South African genomes deposited on GISAID, by specimen collection week, 2020 – 2022 (N=47 140\*)



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

# GISAID genomes vs total cases, 2020 – 2022 (N=47 140)

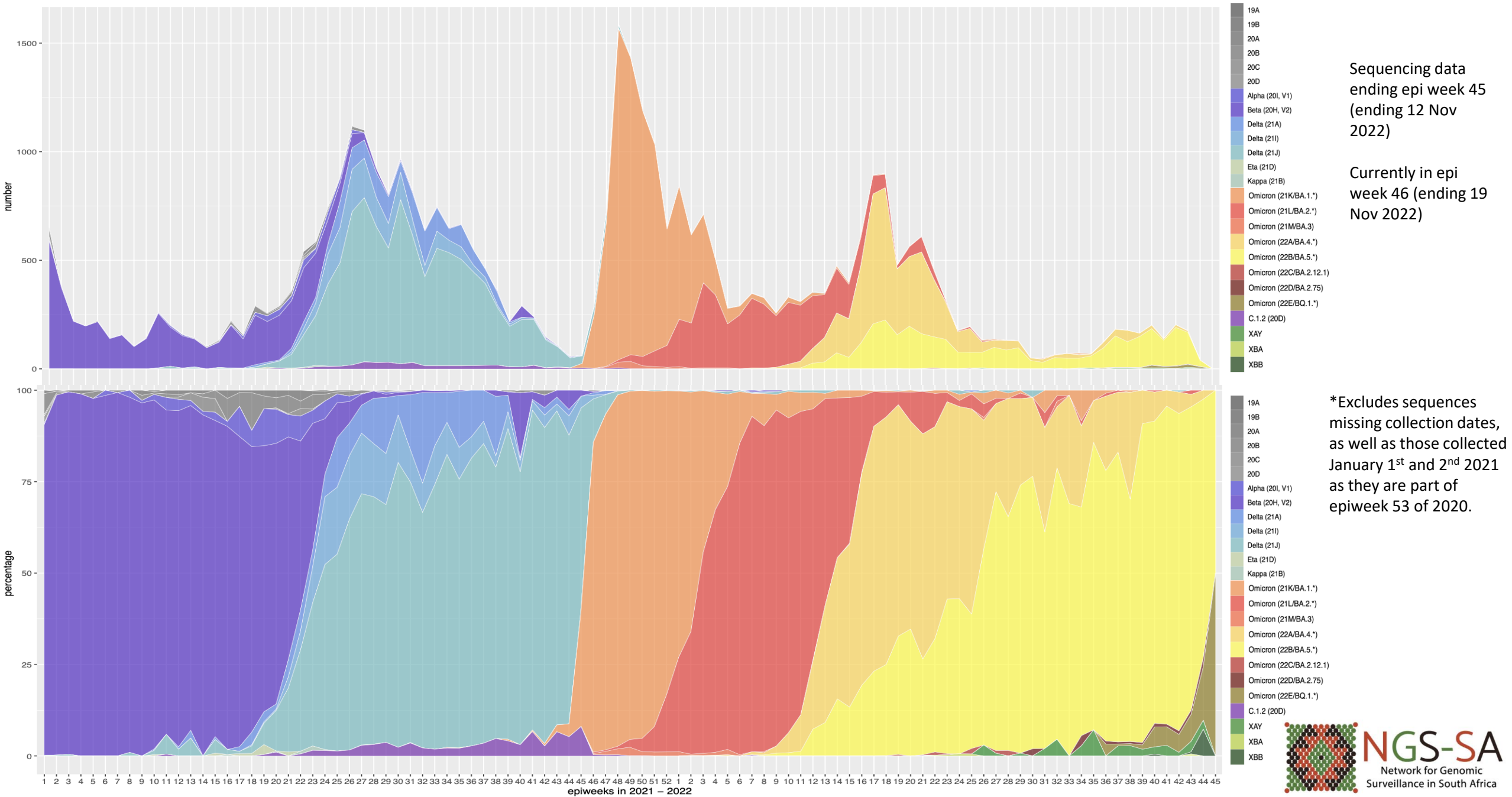
Provincial breakdown of genomes deposited into GISAID



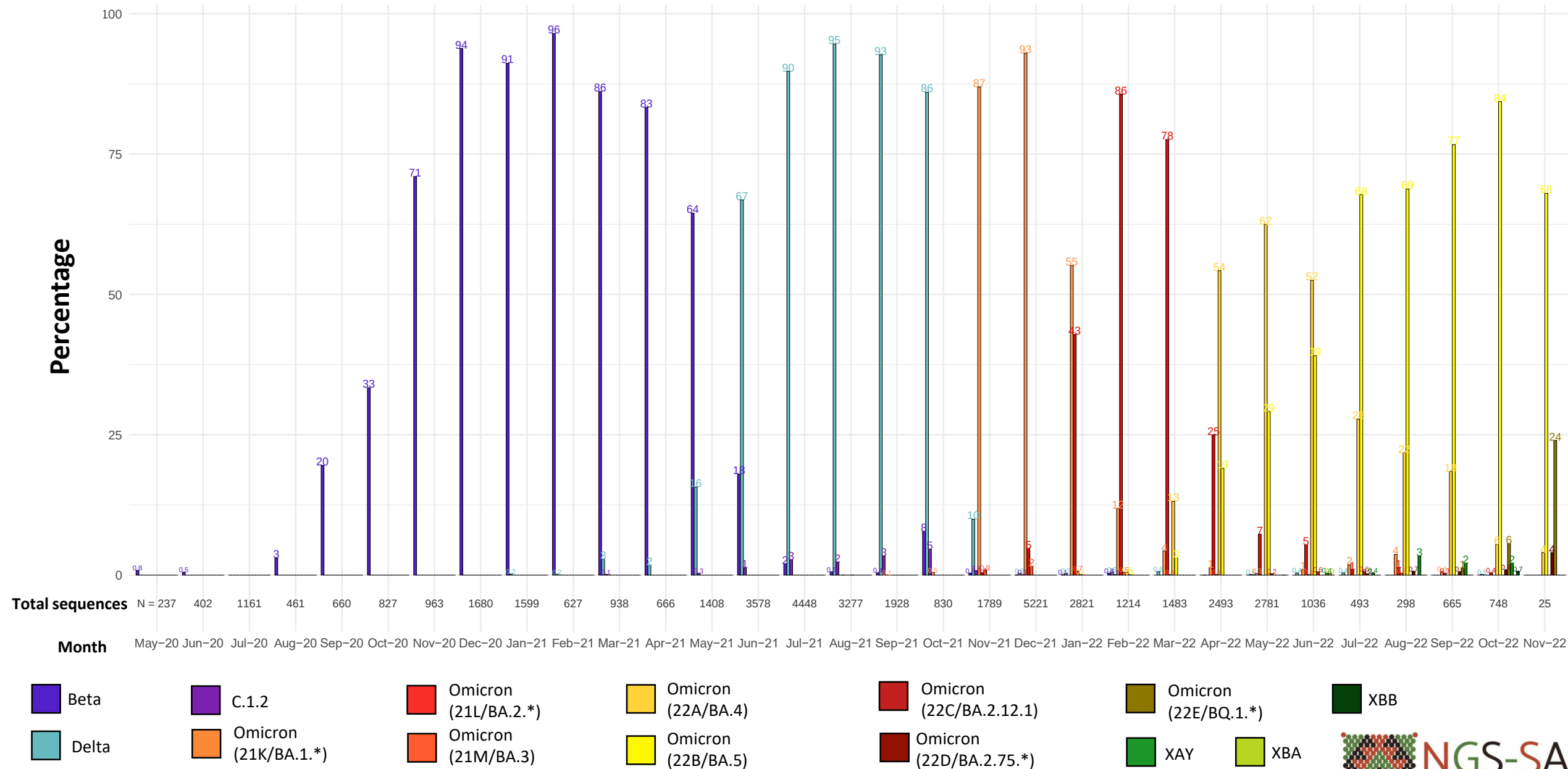
Proportion of total cases versus proportion of total genomes



# Number and percentage of clades by epiweek in South Africa, 2021 – 2022 (40 300\*)



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

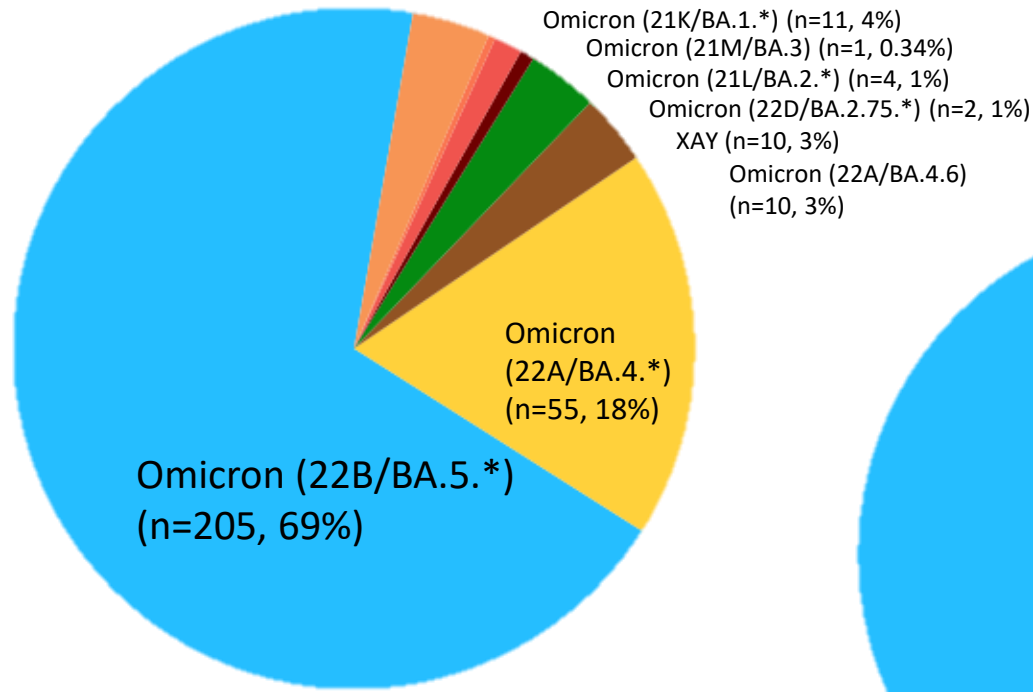


\*Bars represent percentage prevalence of variant for the month; total number sequences collected for the month are given below the bar

# Prevalence of Variants of Concern (VOC) and Variants of Interest (VOI) in

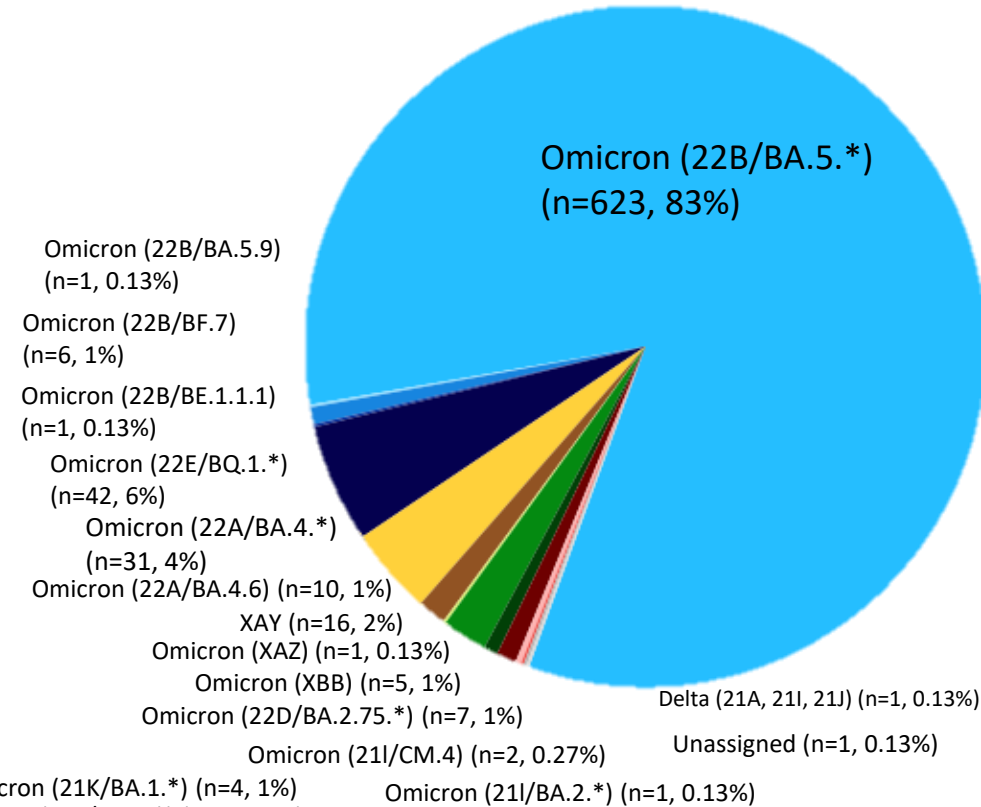
**August – October 2022**

**Aug (N=298)**



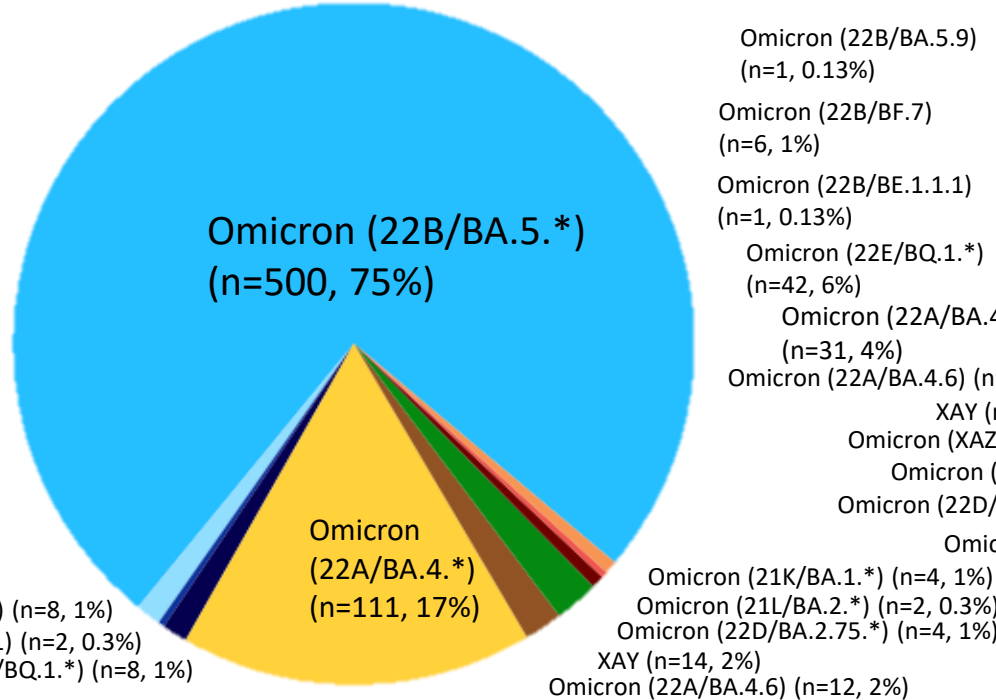
**Total Omicron in August: 288 (96.6%)**

**Oct (N=748)**

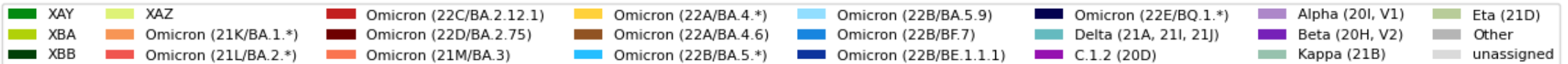


**Total Omicron in October: 744 (99.5%)**

**Sep (N=665)**

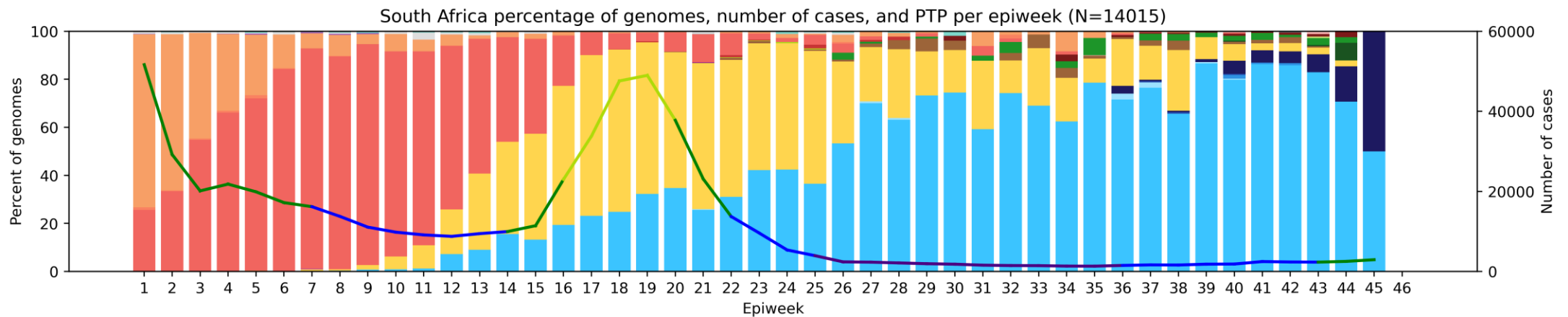
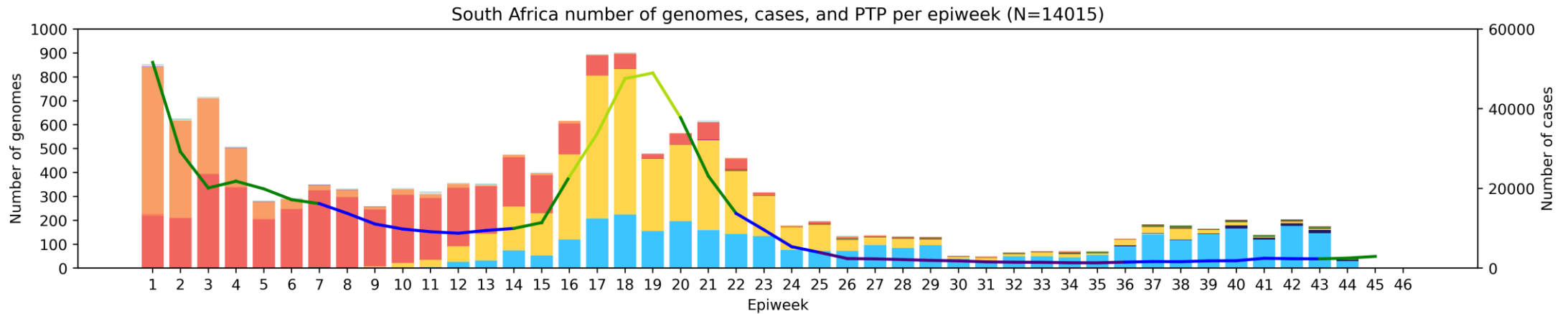


**Total Omicron in September: 651 (97.9%)**

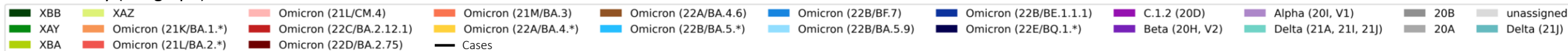




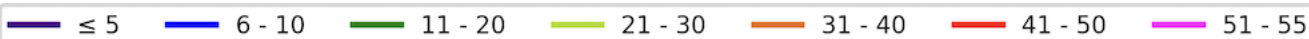
# South Africa, 2022, n = 14 015\*



## Clade key (bar graph)



## Weekly percentage testing positive key (line graph)

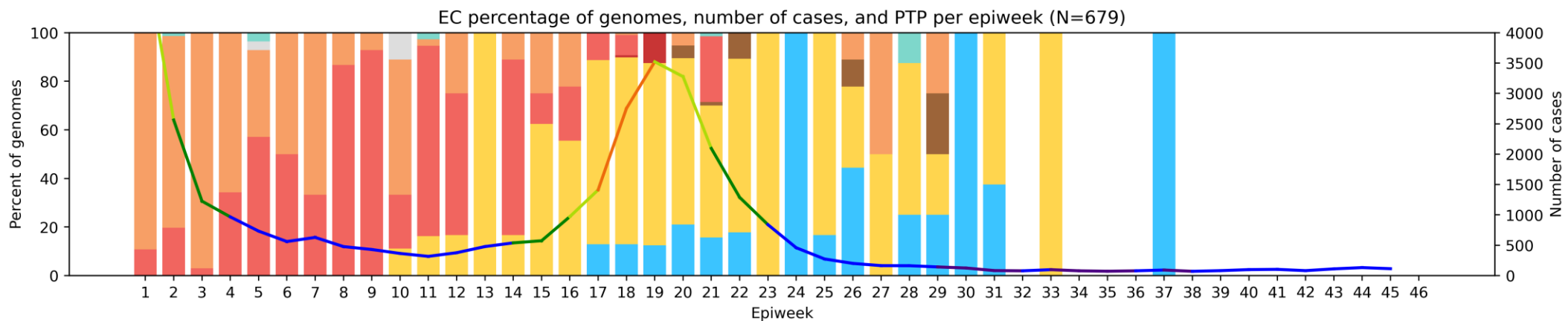
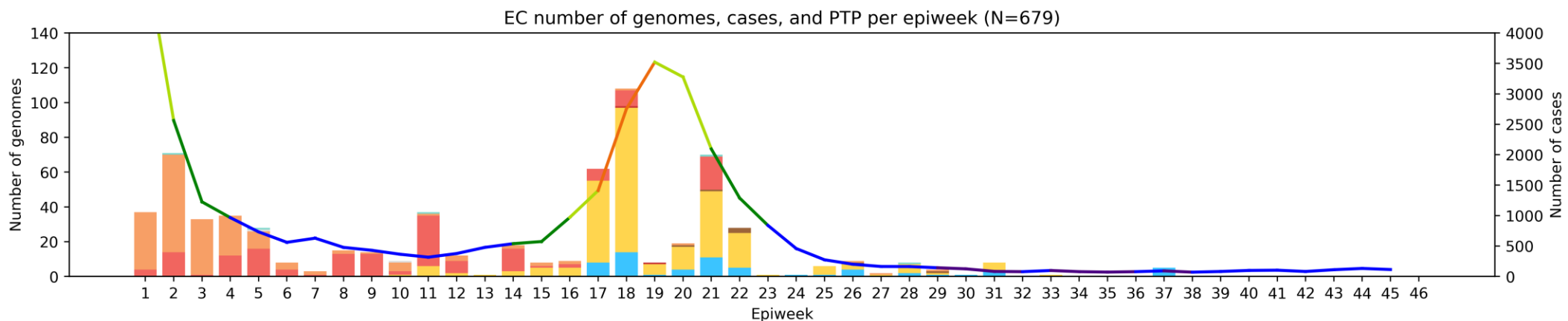


\*Excludes sequences missing collection dates. Lineages of particular interest (currently WHO Omicron subvariants under monitoring) are separate from the main clade groupings.

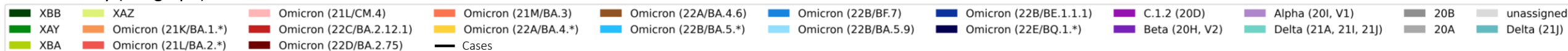


# Eastern Cape Province, 2022, n = 679

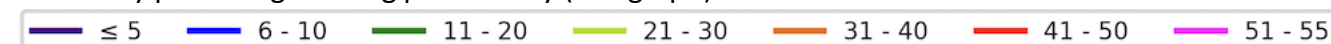
Genomes added since last report: 2\*



## Clade key (bar graph)



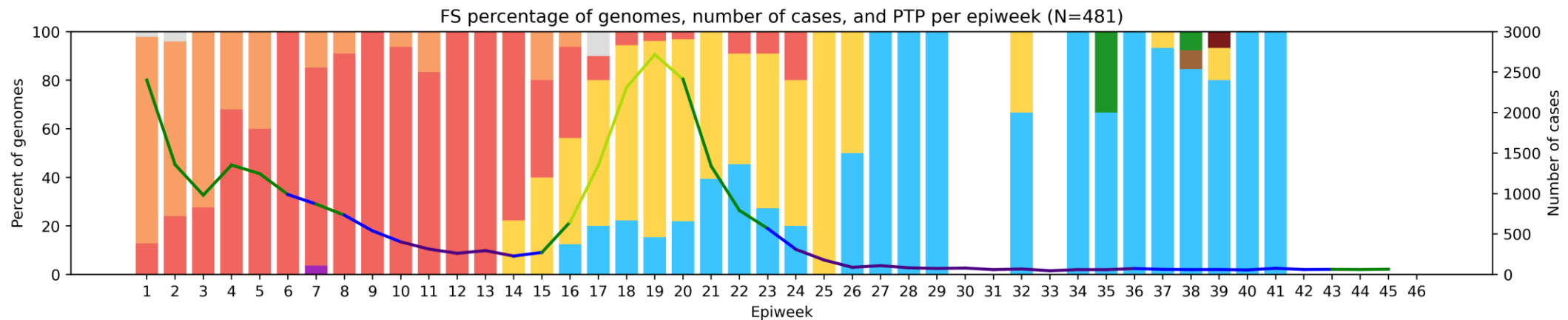
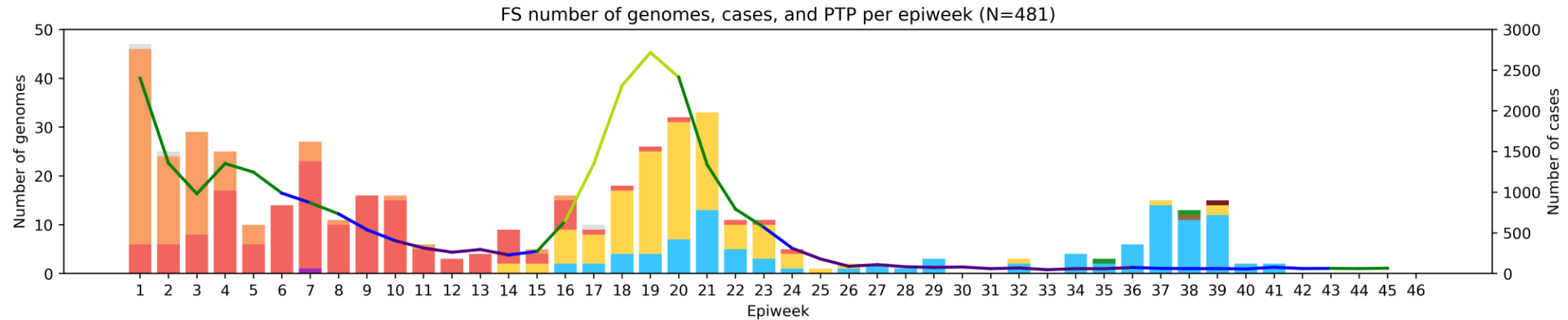
## Weekly percentage testing positive key (line graph)



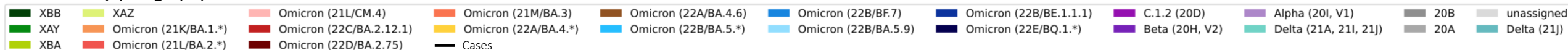
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Free State Province, 2022, n = 481

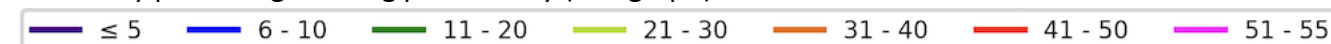
Genomes added since last report: 0\*



## Clade key (bar graph)



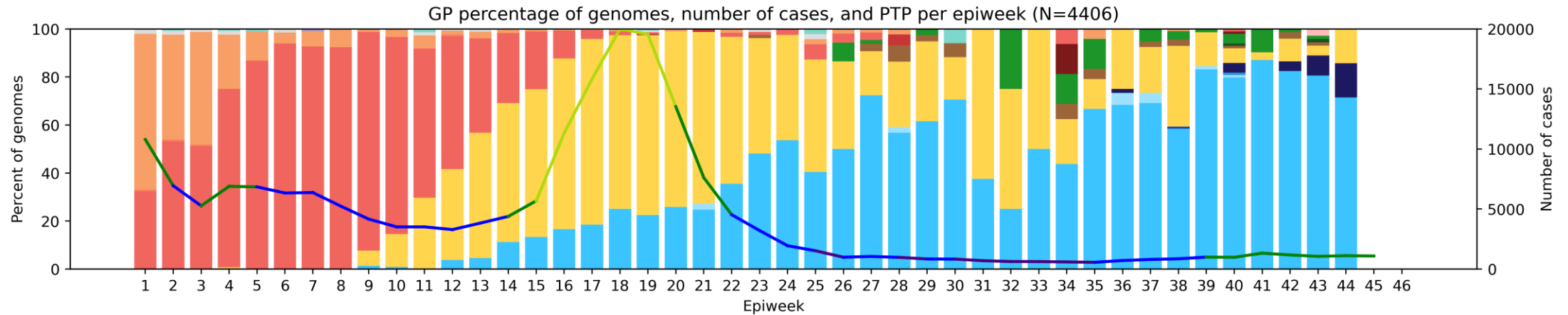
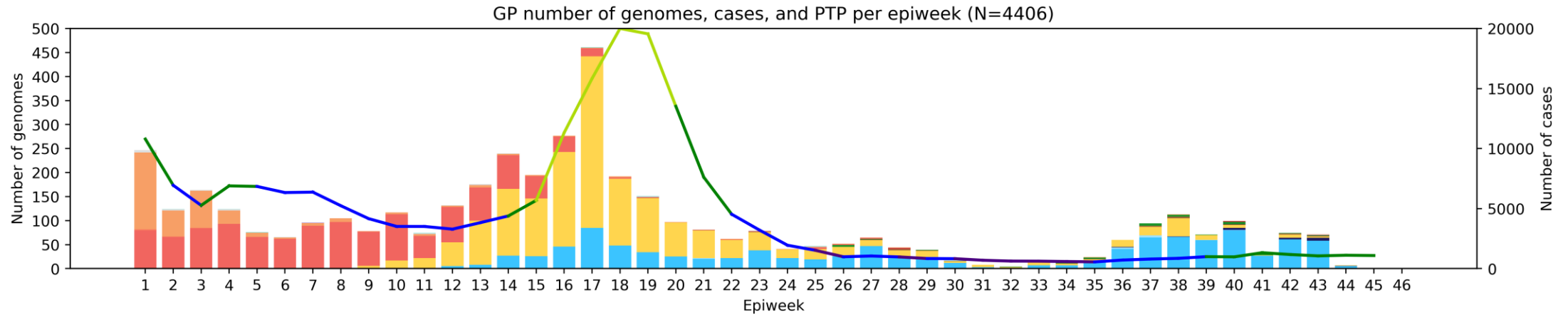
## Weekly percentage testing positive key (line graph)



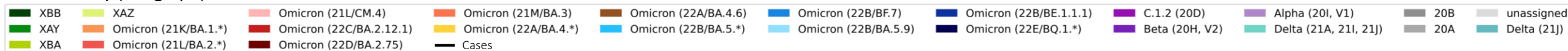
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Gauteng Province, 2022, n = 4406

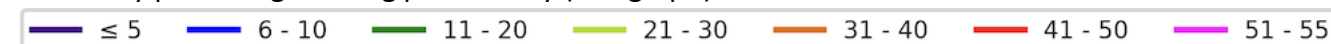
Genomes added since last report: 29\*



## Clade key (bar graph)



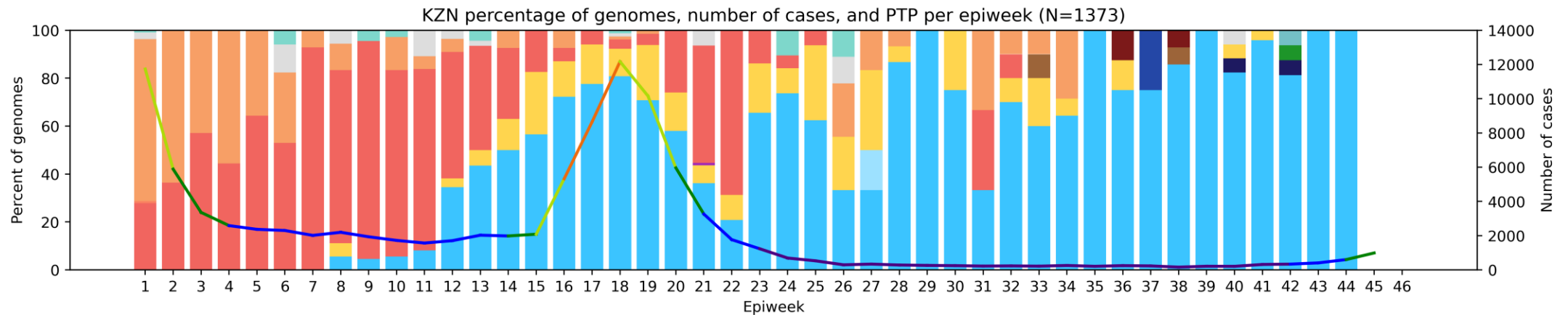
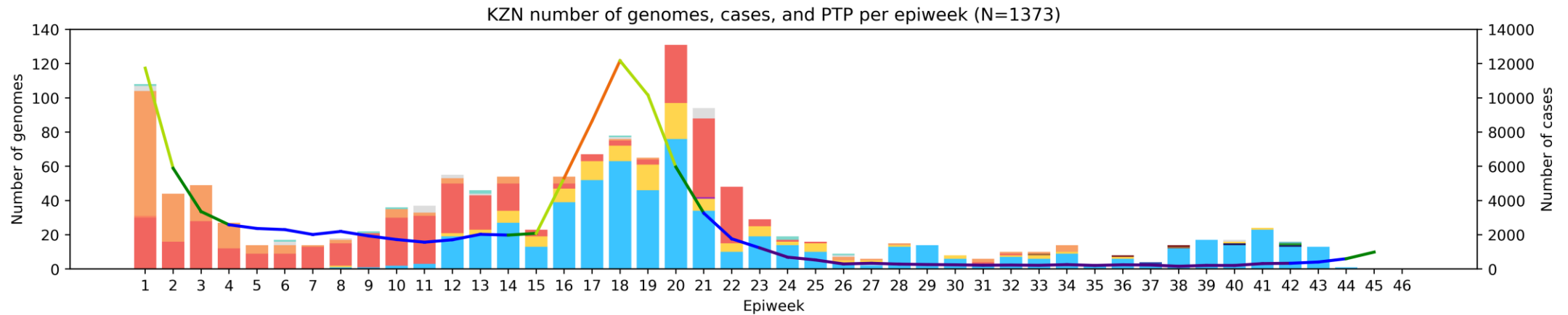
## Weekly percentage testing positive key (line graph)



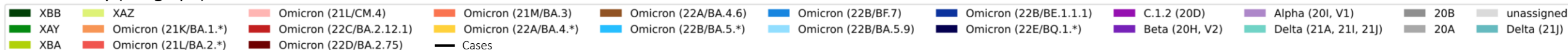
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# KwaZulu-Natal Province, 2022, n = 1373

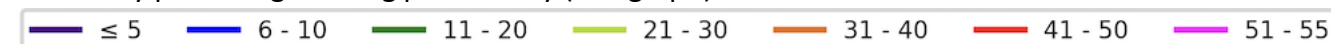
Genomes added since last report: 21\*



## Clade key (bar graph)



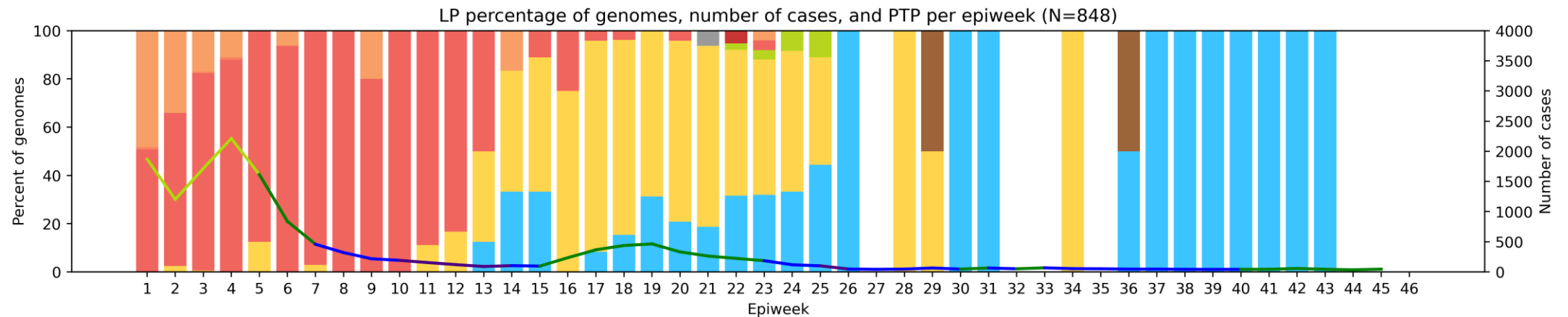
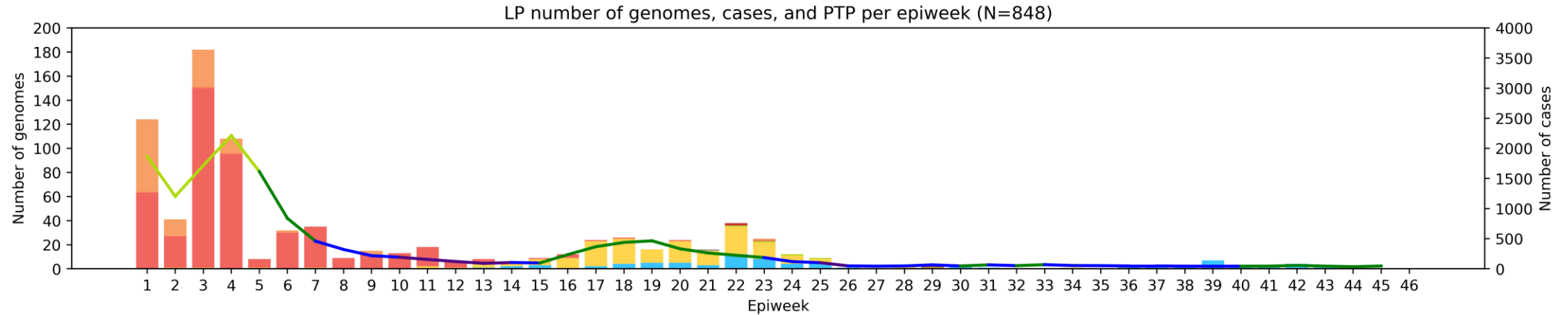
## Weekly percentage testing positive key (line graph)



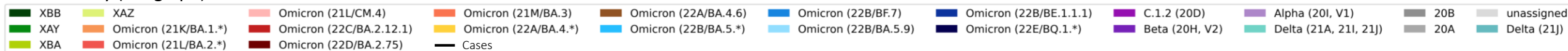
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Limpopo Province, 2022, n = 848

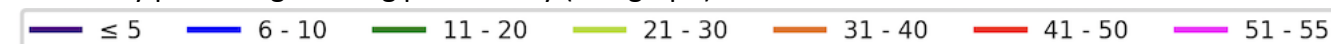
Genomes added since last report: 0\*



## Clade key (bar graph)



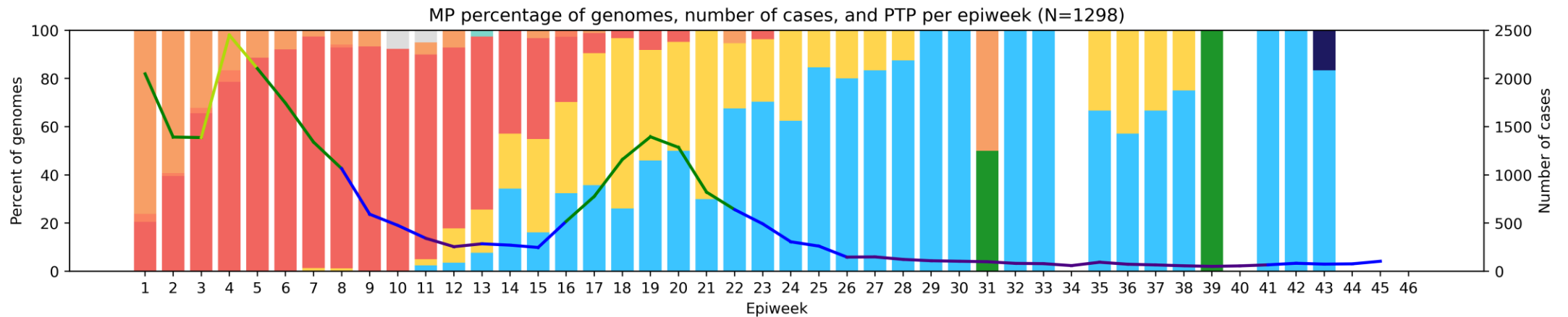
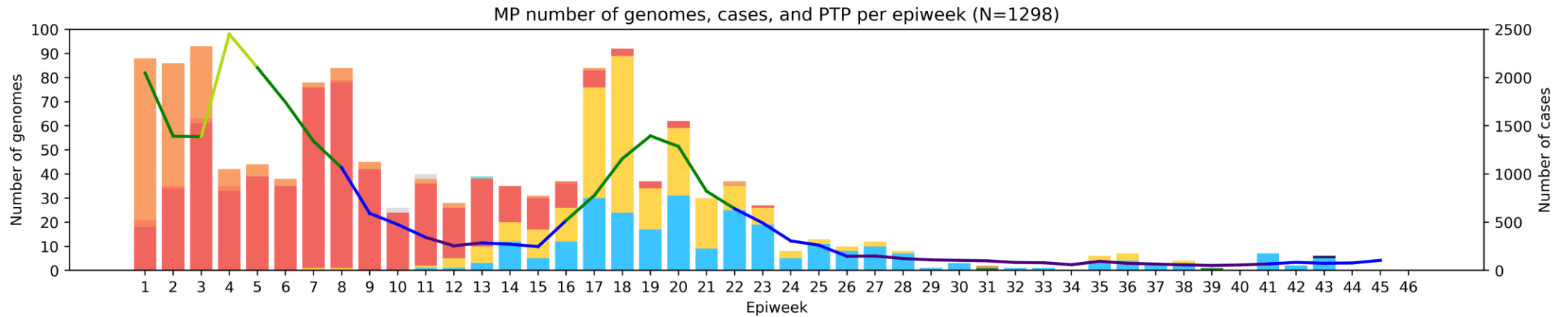
## Weekly percentage testing positive key (line graph)



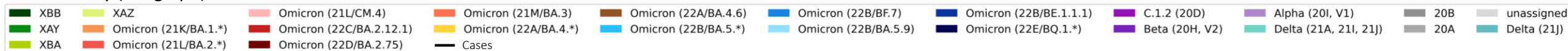
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Mpumalanga Province, 2022, n = 1298

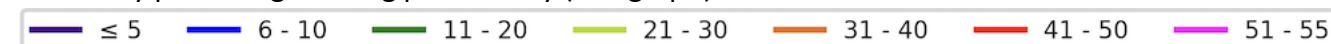
Genomes added since last report: 3\*



## Clade key (bar graph)



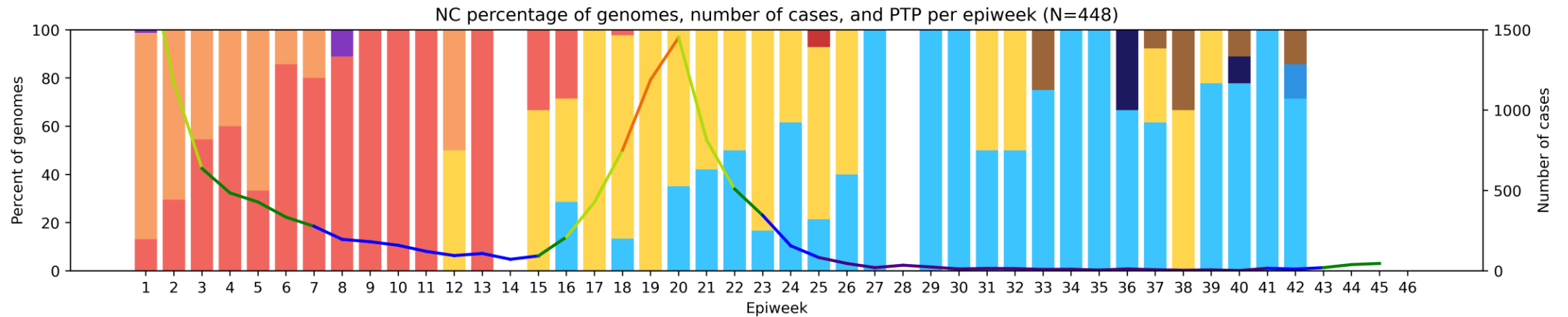
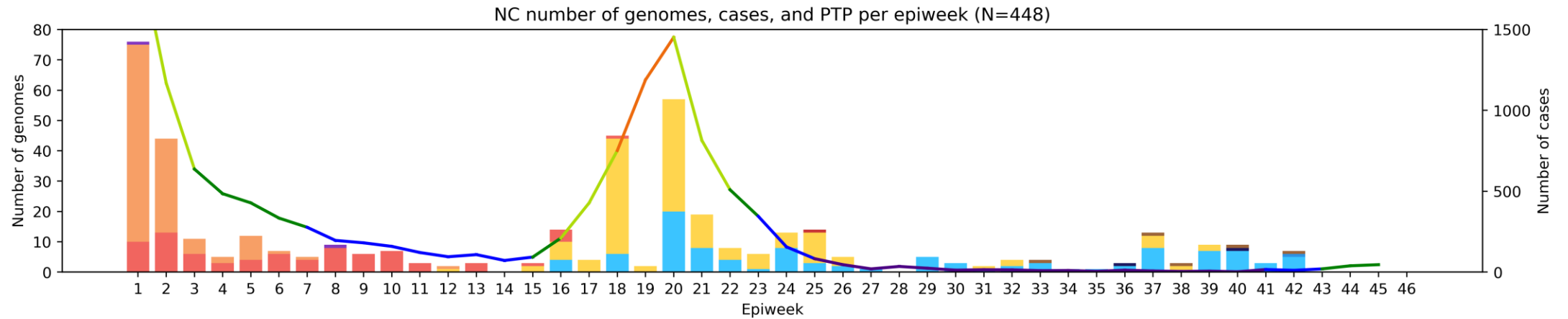
## Weekly percentage testing positive key (line graph)



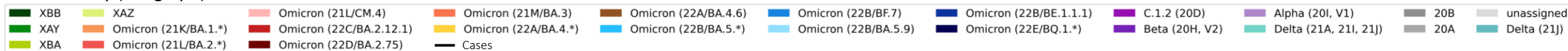
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Northern Cape Province, 2022, n = 448

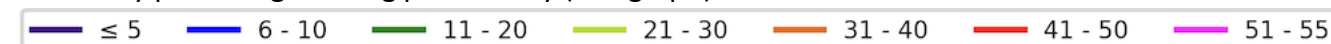
Genomes added since last report: 32\*



## Clade key (bar graph)



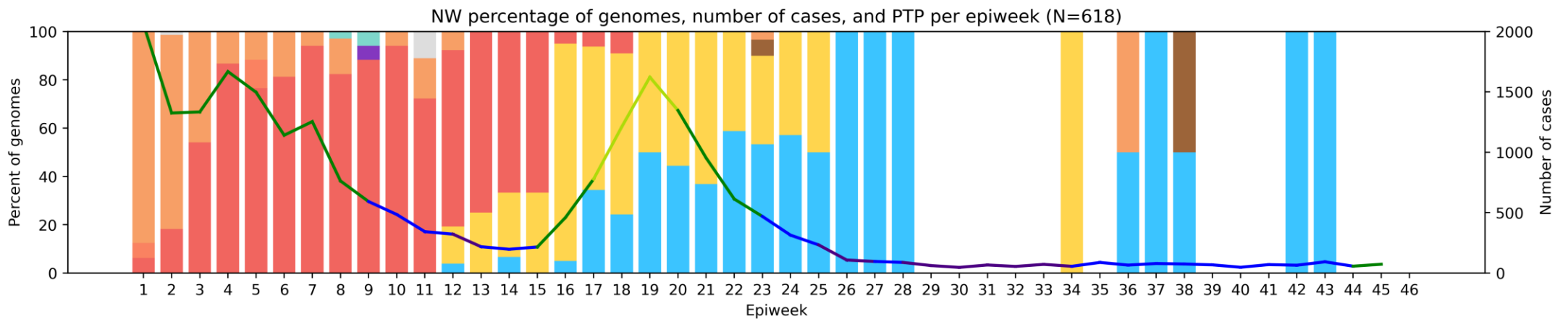
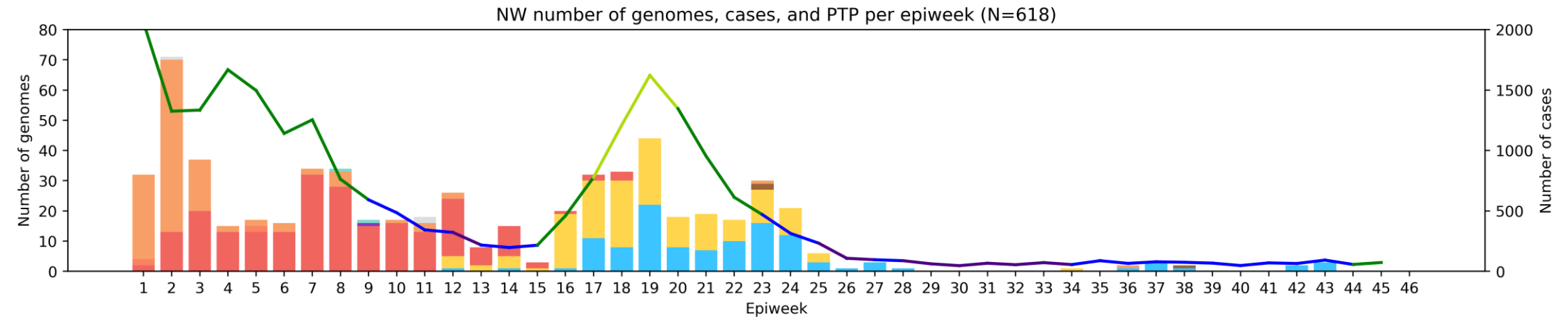
## Weekly percentage testing positive key (line graph)



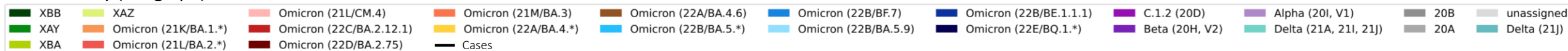


# North West Province, 2022, n = 618

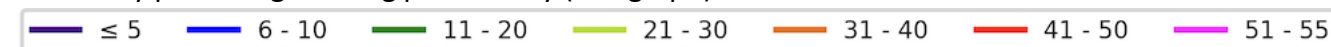
Genomes added since last report: 1\*



## Clade key (bar graph)



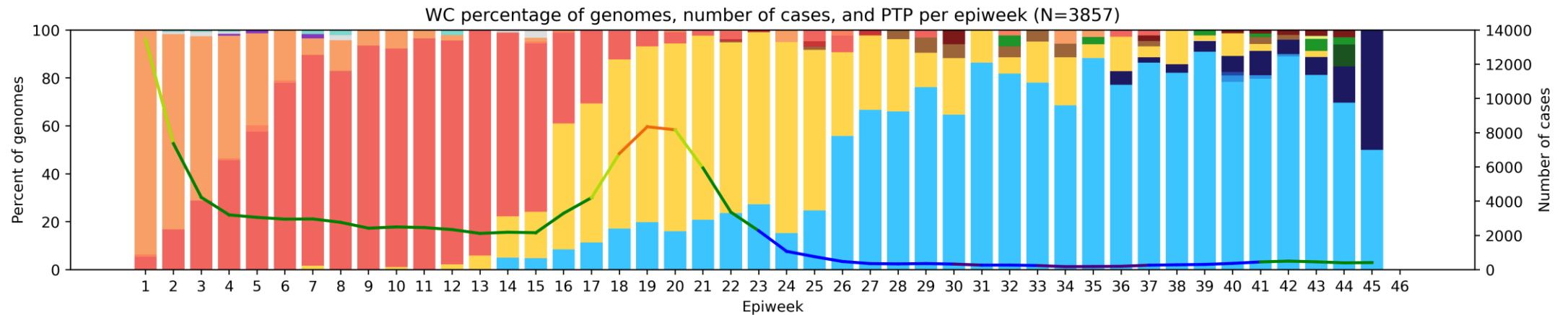
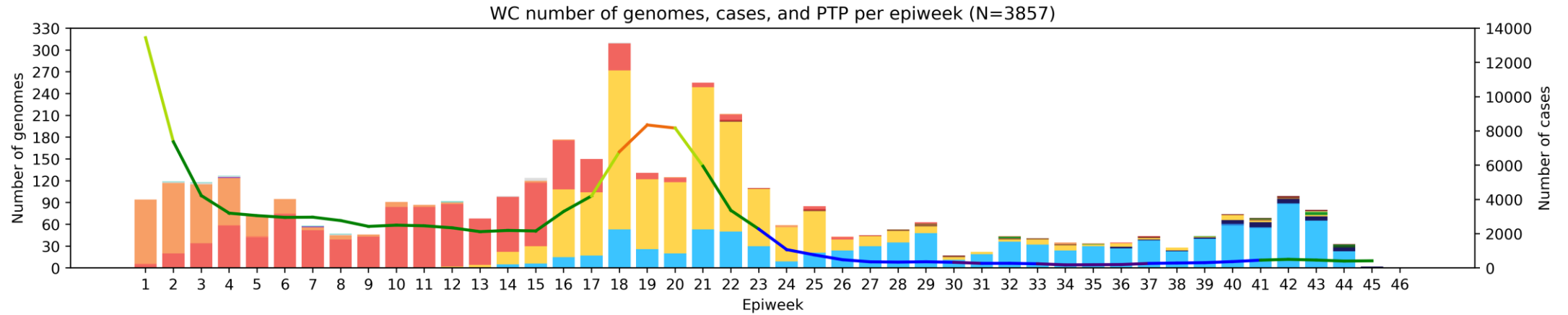
## Weekly percentage testing positive key (line graph)



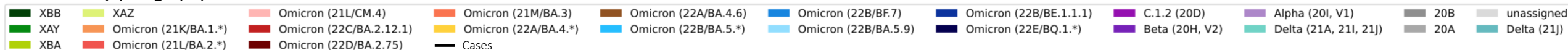
\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Western Cape Province, 2022, n = 3857

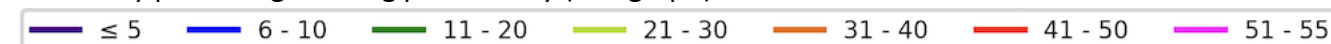
Genomes added since last report: 155\*



## Clade key (bar graph)



## Weekly percentage testing positive key (line graph)

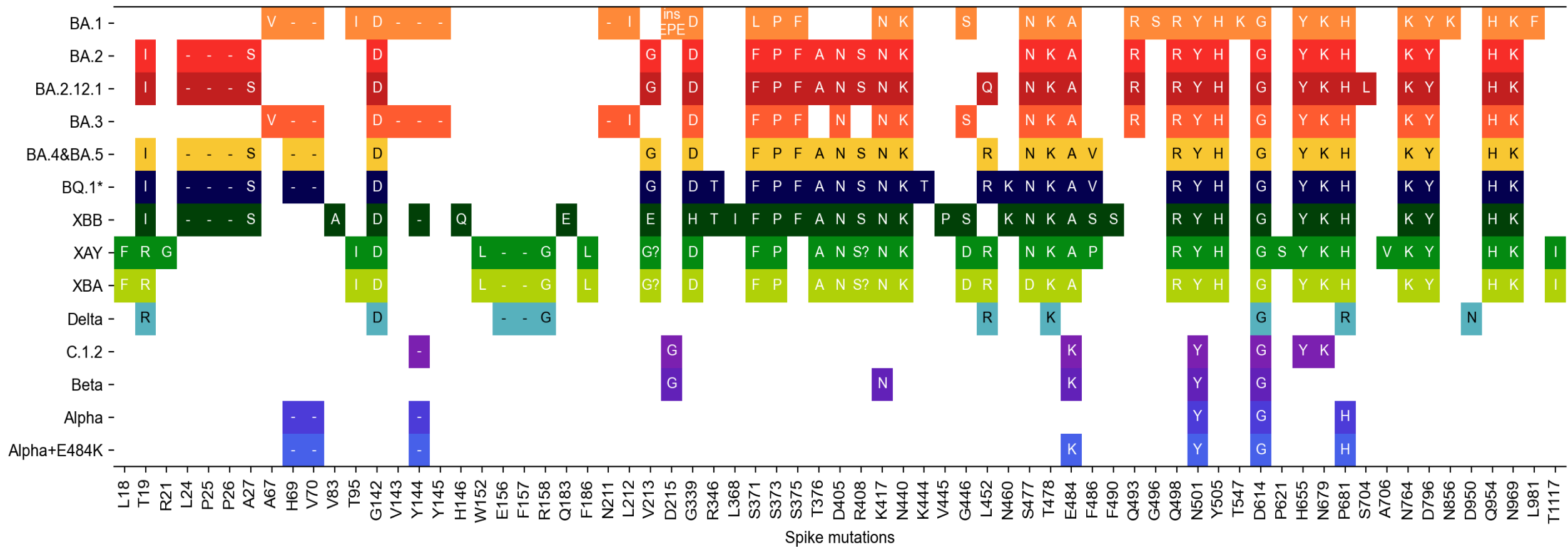


\*May include genomes from 2020 which are not pictured here and are not included in the slide total.

# Summary

- **Sequencing update**
  - All provinces have sequences for August and September.
  - All provinces except the Eastern Cape have sequences for October.
  - Gauteng and the Western Cape have sequences for November.
- **Variant of Concern Omicron in South Africa**
  - Omicron continued to dominate in August (97%), September (98%) October (99%), and currently makes up 100% of November sequences.
  - Omicron BA.5 and sub-lineages were dominant in August (69%), September (78%) and currently make up 90% of October data.
  - BA.2.75.\* has been detected in July through November at a low prevalence ( $\leq 4\%$ ).
  - XAY continues to be detected at a low prevalence ( $\leq 3\%$ )
    - XAY has also been detected in Denmark (n=30), Israel (n=2), the USA (n=2), England (n=1), Italy (n=1), and Sweden (n=1)
  - BQ.1 and sub-lineages have been detected in September, October and November
    - September (1%) – BQ.1\*: n=1 in the Northern Cape, n=6 in the Western Cape, n=1 in Gauteng
    - October (6%) – BQ.1\*: n=2 in KwaZulu-Natal, n=14 in Gauteng, n=24 in the Western Cape, n=1 in the Northern Cape, n=1 in the Mpumalanga
    - November (24%) – BQ.1\*: n=6 in the Western Cape
  - XBB has been detected in South Africa in October (n=2 in Gauteng, n=3 in the Western Cape)
- Delta detected at low frequency until July, and once in October.

# Spike protein mutation\* profile of Variants of Interest and Concern

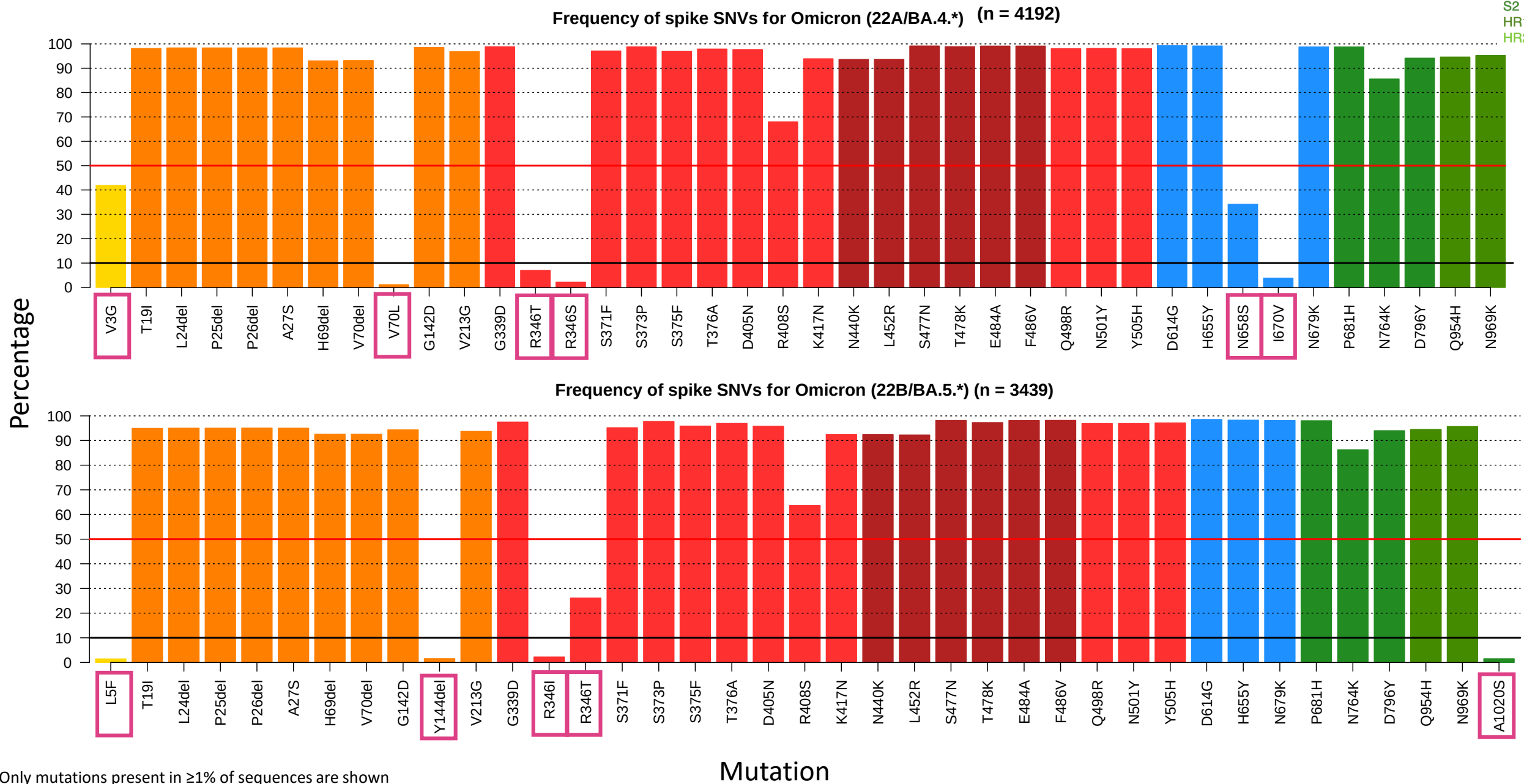


- Multiple changes within the two immunogenic regions in S1 (NTD and RBD)
  - Including a three amino acid insertion
- Accumulation of mutations surrounding the furin cleavage site
  - Including combination of N679K and P681H
- Effect of most spike S2 subunit changes have not been defined, but may be linked to immune escape

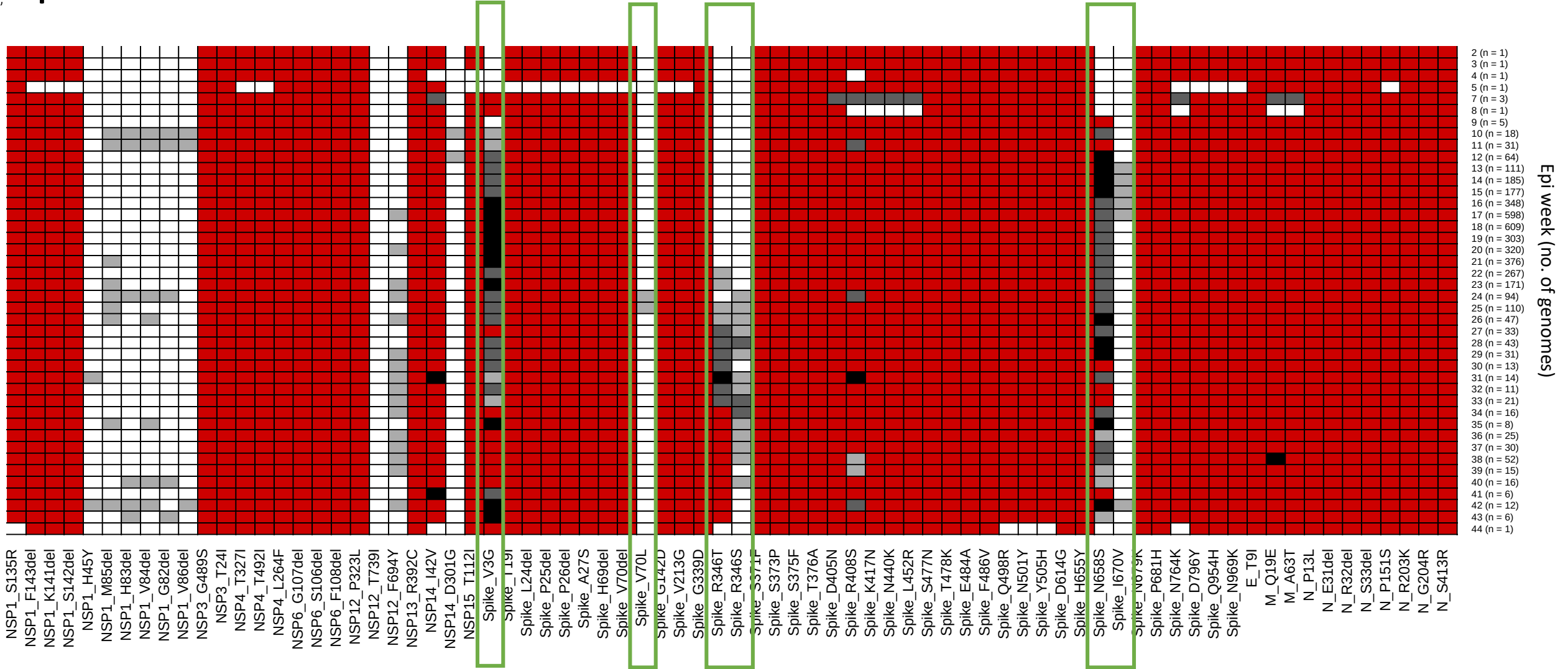
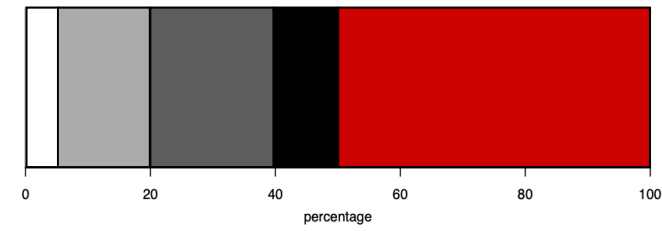
\*Only mutations present in Omicron, Delta, or recombinant sequences are pictured

# BA.4 and BA.5 spike mutations\*

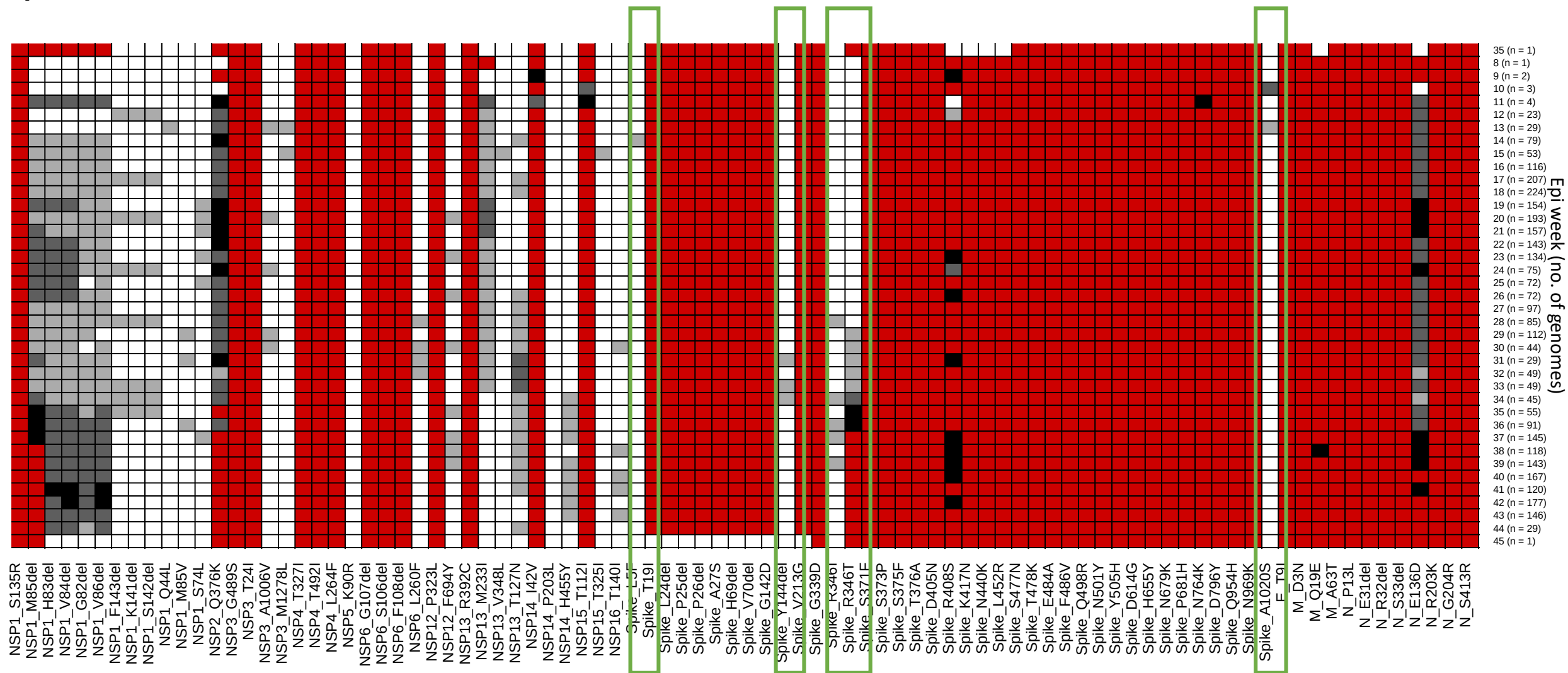
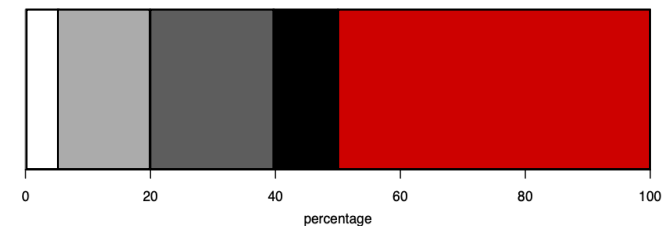
SP  
NTD  
RBD  
RBM  
S1  
S2  
HR1  
HR2



# BA.4 whole genome mutation prevalence over time



# BA.5 whole genome mutation prevalence over time







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KWAZULU-NATAL  
INYUVESI  
YAKWAZULU-NATALI



EDCTP

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## University of Stellenbosch & NHLS Tygerberg Virology



Susan Engelbrecht  
Wolfgang Preiser  
Gert van Zyl  
Tongai Maponga  
Bronwyn Kleinhans  
Shannon Wilson  
Karabo Phadu  
Tania Stander  
Kamela Mahlakwane  
Mathilda Claassen  
Diagnostic laboratory staff

## 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  
Emmanuel James San



**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  
Hannah Hussey  
Andrew Boule  
Masudah Paleker  
Theuns Jacobs  
Erna Morden

**NHLS Greenpoint**  
Annabel Enoch



**UCT, IDM and CIDRI-Africa**

Deelan Doolabh  
Arash Iranzadeh  
Lynn Tyers  
Innocent Mudau  
Nokuzola Mbhele  
Fezokuhle Khumalo  
Thabang Serake  
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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## 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

**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

Koeleka 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

John Nkengasong  
Sofonias Tessema

## Netcare:

Richard Friedland  
Craig Murphy  
Caroline Maslo  
Liza Sitharam

## DSI

Glaudina Loots

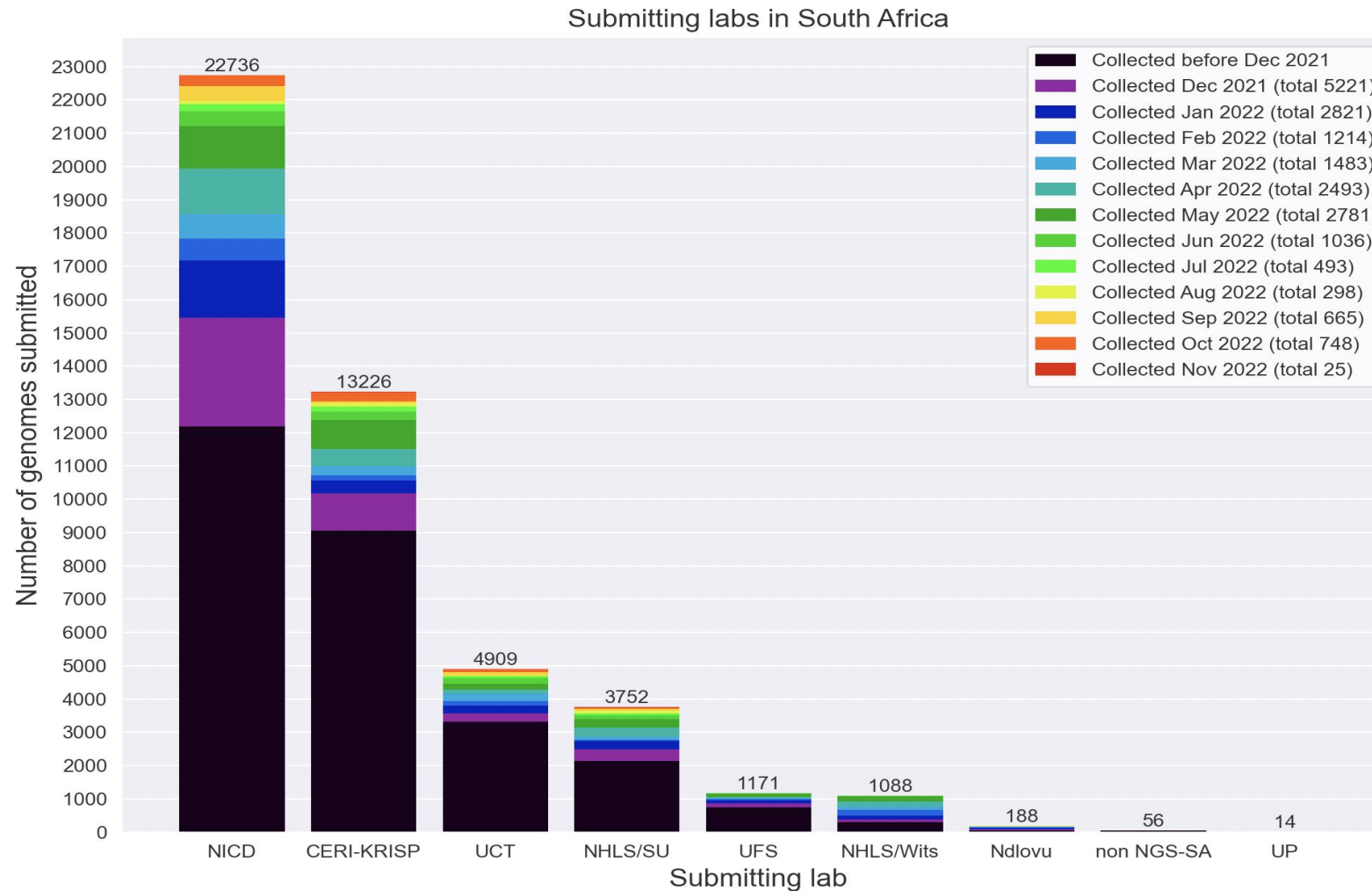
## SA MRC

Glenda Gray





# South African genomes submitted per submitting lab, 2020 - 2022 (N=47 140)



## 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.

# Currently circulating Variants of Concern (VOC)

| WHO label | Pango lineage <sup>•</sup> | GISAID clade | Nextstrain clade                  | Additional amino acid changes monitored <sup>°</sup> | Earliest documented samples  | Date of designation                  |
|-----------|----------------------------|--------------|-----------------------------------|------------------------------------------------------|------------------------------|--------------------------------------|
| Omicron*  | B.1.1.529                  | GR/484A      | 21K, 21L, 21M, 22A, 22B, 22C, 22D | +S:R346K<br>+S:L452X<br>+S:F486V                     | Multiple countries, Nov-2021 | VUM: 24-Nov-2021<br>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.

<sup>•</sup> Only found in a subset of sequences

# Omicron subvariants under monitoring

| Pango lineage <sup>#</sup> (+ 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<br>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 <sup>§</sup>                                        |              | 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 <sup>§</sup>                                  | 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

# 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<br>Previous VOC: 09-Mar-2022                   |
| Beta      | B.1.351        | GH/501Y.V2   | 20H (V2)         | South Africa, May-2020      | VOC: 18-Dec-2020<br>Previous VOC: 09-Mar-2022                   |
| Gamma     | P.1            | GR/501Y.V3   | 20J (V3)         | Brazil, Nov-2020            | VOC: 11-Jan-2021<br>Previous VOC: 09-Mar-2022                   |
| Delta     | B.1.617.2      | G/478K.V1    | 21A, 21I, 21J    | India, Oct-2020             | VOI: 4-Apr-2021<br>VOC: 11-May-2021<br>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 ( $\geq 14$  days after vaccine), especially if hospitalised and clinically severe
- Suspected re-infection ( $\geq 90$  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.)