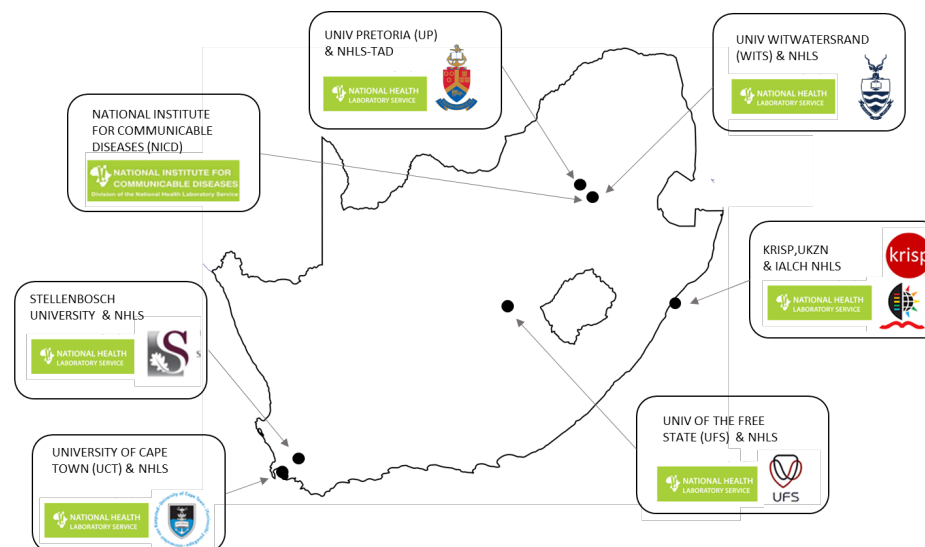


SARS-CoV-2 Sequencing Update 25 November 2021



Supported by the DSI and the SA MRC
Msomi N. Mlisana K. et al. Lancet Microbe 2020

Summary of new variant

- New variant detected in South Africa (lineage **B.1.1.529**) with **high number of mutations**, which are **concerning for predicted immune evasion and transmissibility**
- B.1.1.529 genomes produced from **samples collected 12-20 Nov from Gauteng, SA** (n=77), **Botswana** (n=4) and **Hong Kong** (n=1, traveler from SA)
- **B.1.1.529 can be detected by one particular PCR assay** (before whole genome sequencing) – this will help us to track and understand spread
- **Early signs from diagnostic laboratories** that B.1.1.529 **has rapidly increased in Gauteng** and may already be present in most provinces
- We can **make some predictions about the impact of mutations** in this variant, but **full significance uncertain** and the **vaccines remain the critical tool to protect us against severe disease**

Covid-19: Increased Gauteng cases driven by cluster outbreak among students

news24 Nicole McCain

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News24 – 23 Nov 2021

First signs of fast increase of cases in Gauteng.

Is this a cluster outbreak?

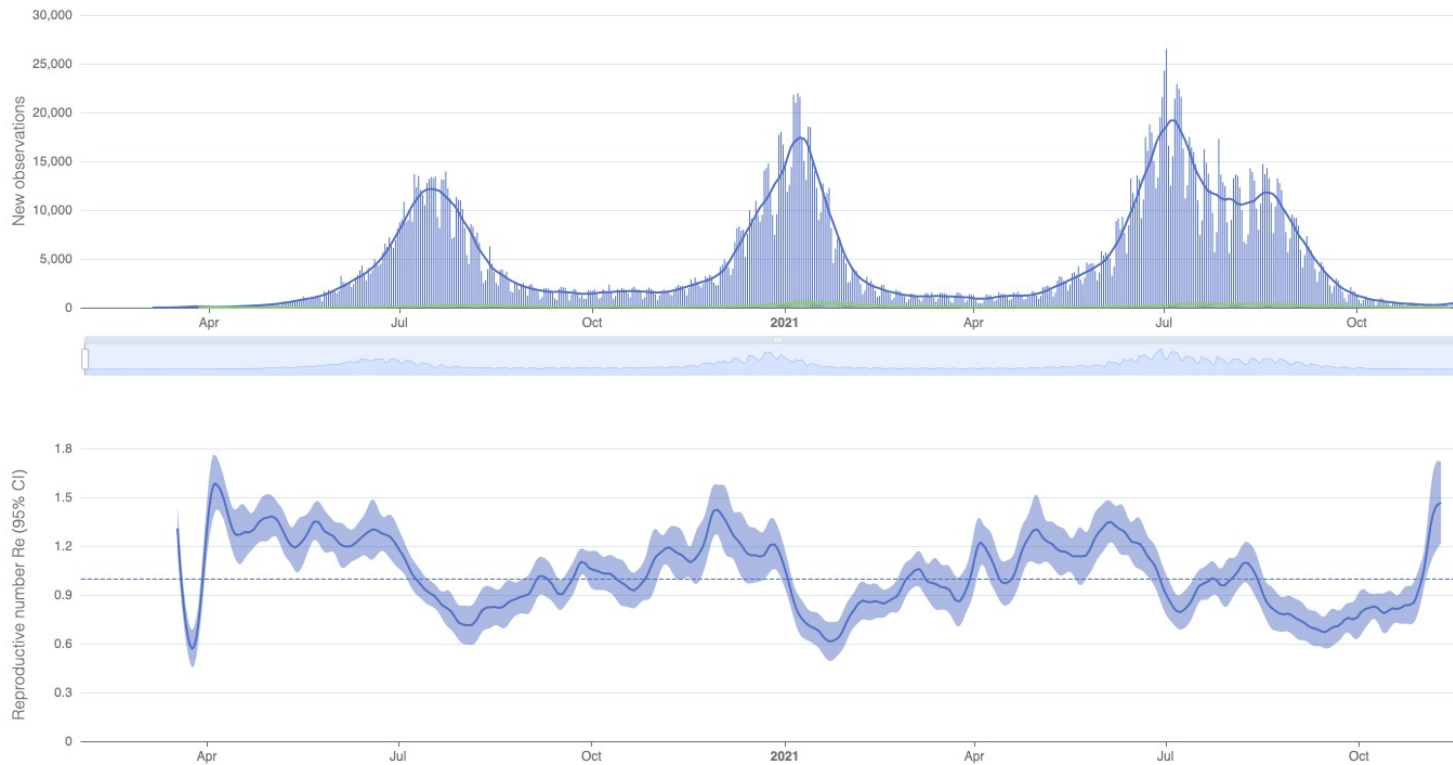
Real resurgence?

Start of 4th wave?

Timeline of discovery of new variant (36h from this media briefing).

- **Tuesday 23 November 2pm** – Discovery of new variant from samples from Lancet by NICD that showed different results in qPCR. Samples from 14 to 16 of November, which is the start of rise in infections in JHB.
- **Tuesday 23 November 3pm** – Urgent meeting of the NGS-SA to discuss results, during the meeting message to NDoH and DSI.
- **Wednesday 24 November** – Detailed analysis of the NHLS data, more genomes produced at KRISP and NICD, support the new variant to be concerning. Informed DSI and NDoH.
- **Wednesday 24 November** – First news reports from similar variant found in Botswana and China (from SA traveler) from sequences in databases on 23 November.
- **Thursday 25 November** – 8 am presentation to ministers of NDoH and DSI, 10:30 to president. 1pm talking to media
- **Friday 26 November** – Requested and approved an urgent sitting of WHO TWG on virus evolution.

Epidemic curve – South Africa

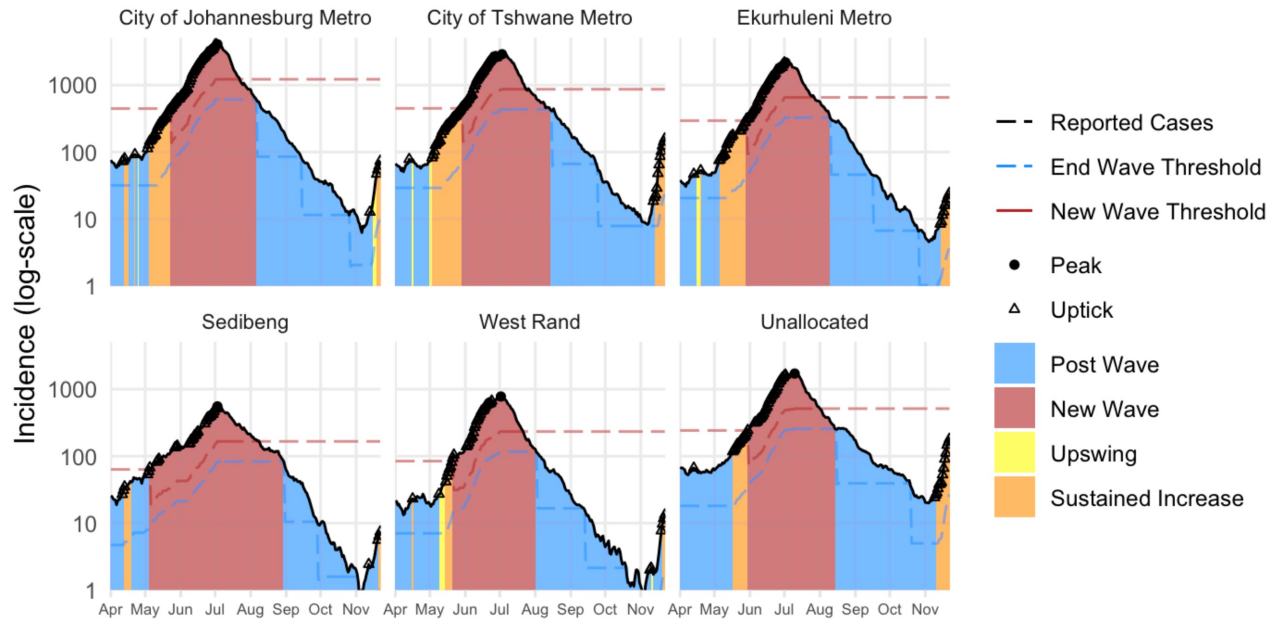


Estimated effective reproduction number $Re = 1.47$ (1.22 - 1.72)

Gauteng $Re = 1.93$ (1.67 - 2.19)

<https://ibz-shiny.ethz.ch/covid-19-re-international/>

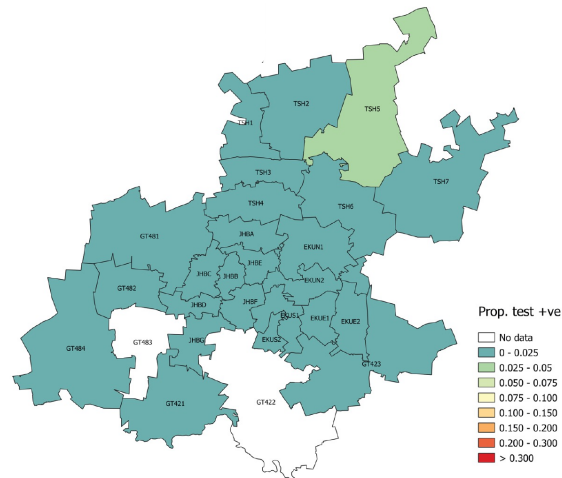
Sustained Increase Monitoring Gauteng - SACMC



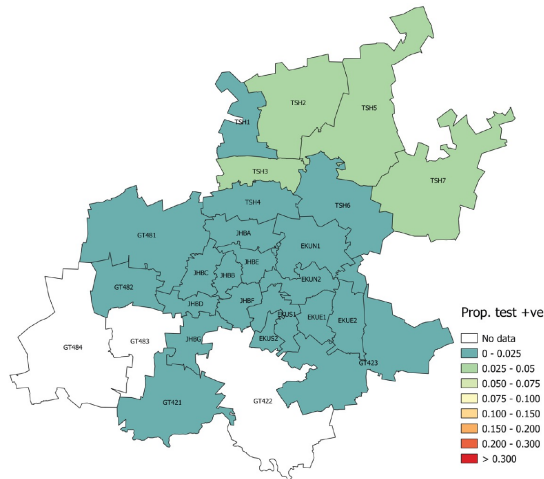
Sustained increase in incidence across all Gauteng municipalities
Estimated effective reproduction number Gauteng = 1.93 (1.67 – 2.19)

<https://www.sacmcepidemicexplorer.co.za/>
<https://ibz-shiny.ethz.ch/covid-19-re-international/>

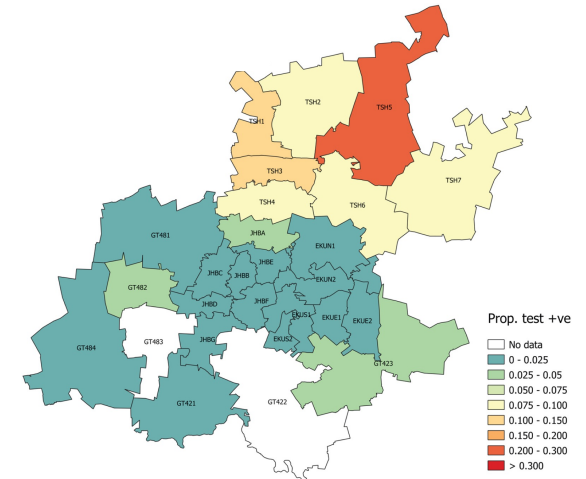
Test positivity rate - Gauteng



Week 44 (31 Oct – 6 Nov)



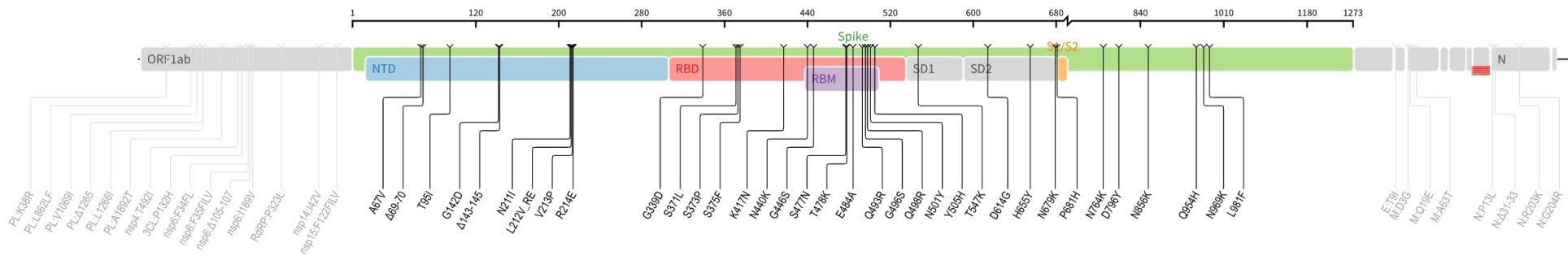
Week 45 (7-13 Nov)



Week 46 (14-20 Nov)

Rapid increase in test positivity in Tshwane in last week

B.1.1.529 – mutation profile

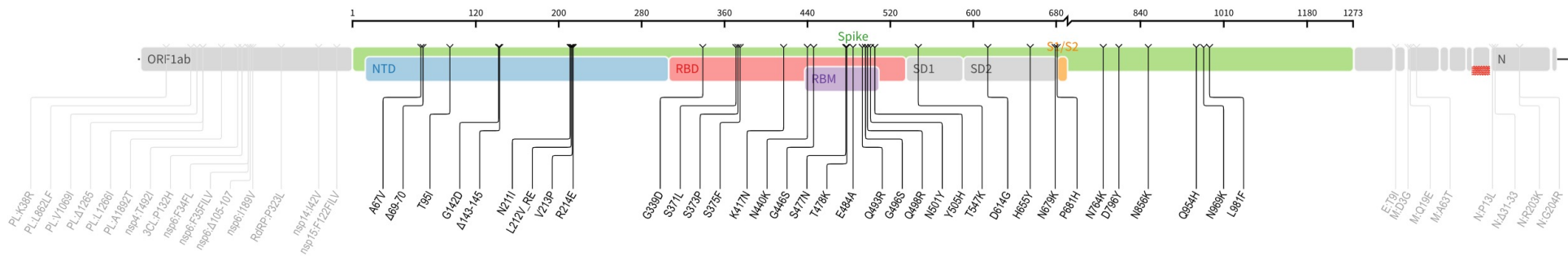


Very unusual constellation of mutations - multiple mutations across the SARS-CoV-2 genome, with >30 mutations in spike protein

Mutation profile clearly very different from other circulating VOCs/VOIs

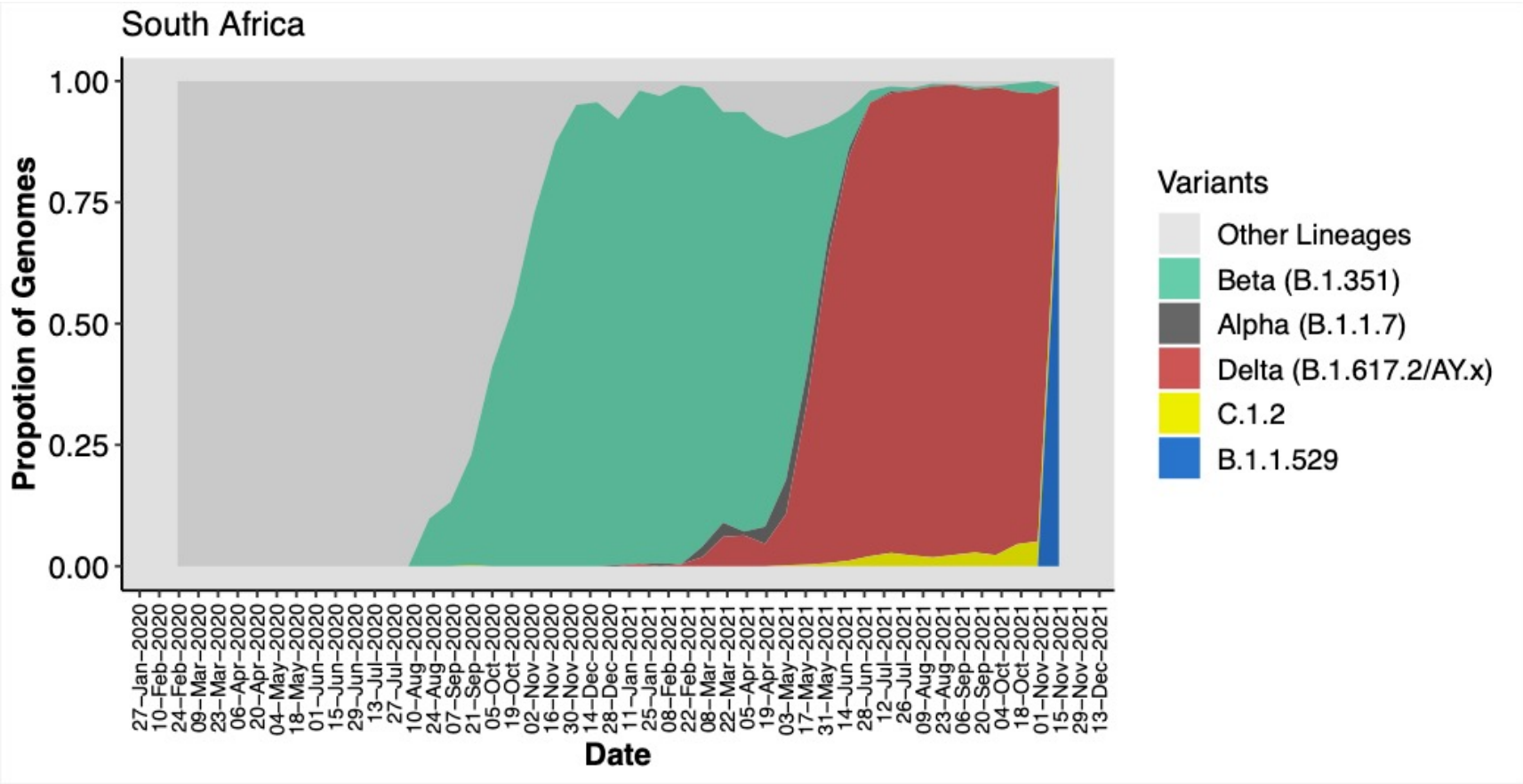
Some mutations well characterized with known phenotypic impact (affecting transmissibility, immune evasion), but many others rarely observed until now and not well characterized – so full significance uncertain

B.1.1.529 – potential impact of mutations

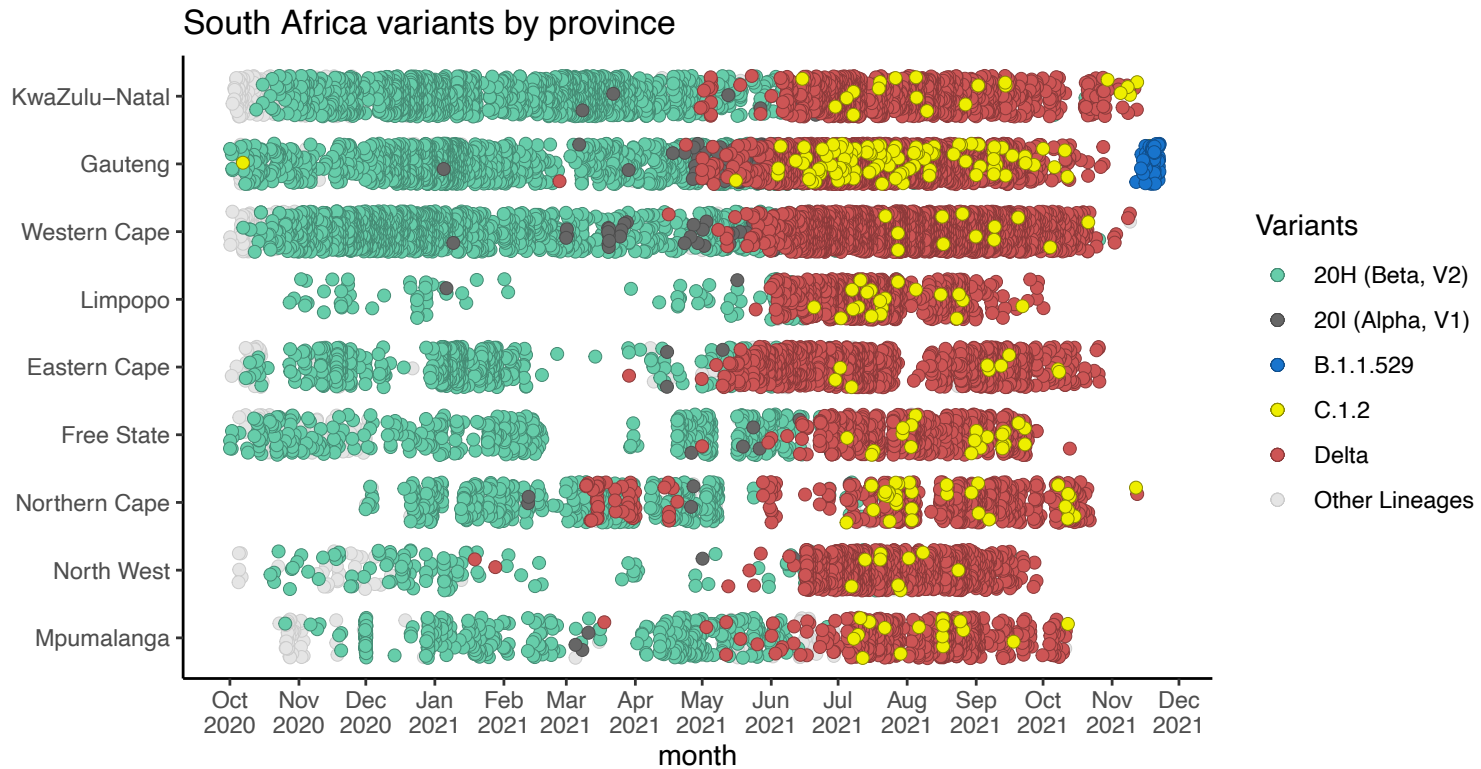


- Multiple RBD and NTD mutations associated **with resistance to neutralizing antibodies** (and therapeutic monoclonal antibodies)
- Cluster of mutations (H655Y + N679K + P681H) adjacent to S1/S2 furin cleavage site – **associated with more efficient cell entry → enhanced transmissibility**
- nsp6 deletion (Δ105-107) – similar to deletion to Alpha, Beta, Gamma, Lambda – may be associated with **evasion of innate immunity (interferon antagonism) → could also enhance transmissibility**
- R203K+G204R mutations in nucleocapsid - seen in Alpha, Gamma, Lambda – associated with **increased infectivity**

B.1.1.529 becoming dominant



B.1.1.529 genomes detected in GP



Sequences from KZN due today or tomorrow. PCR proxy for variant in most other provinces.

PCR-based proxy for new variant

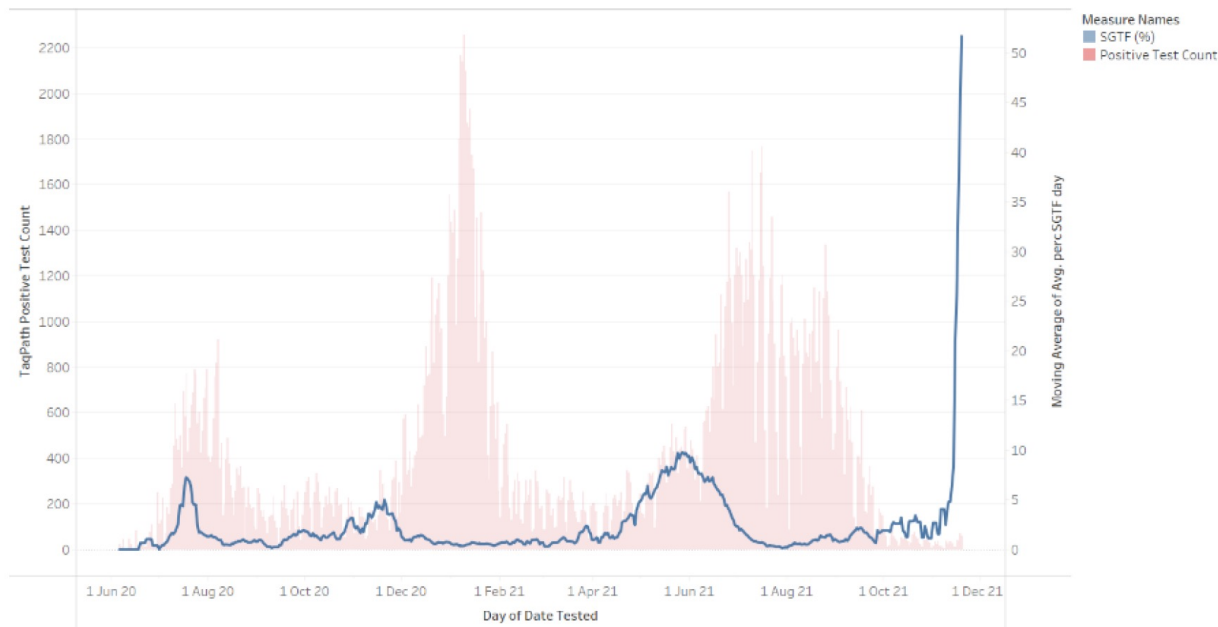
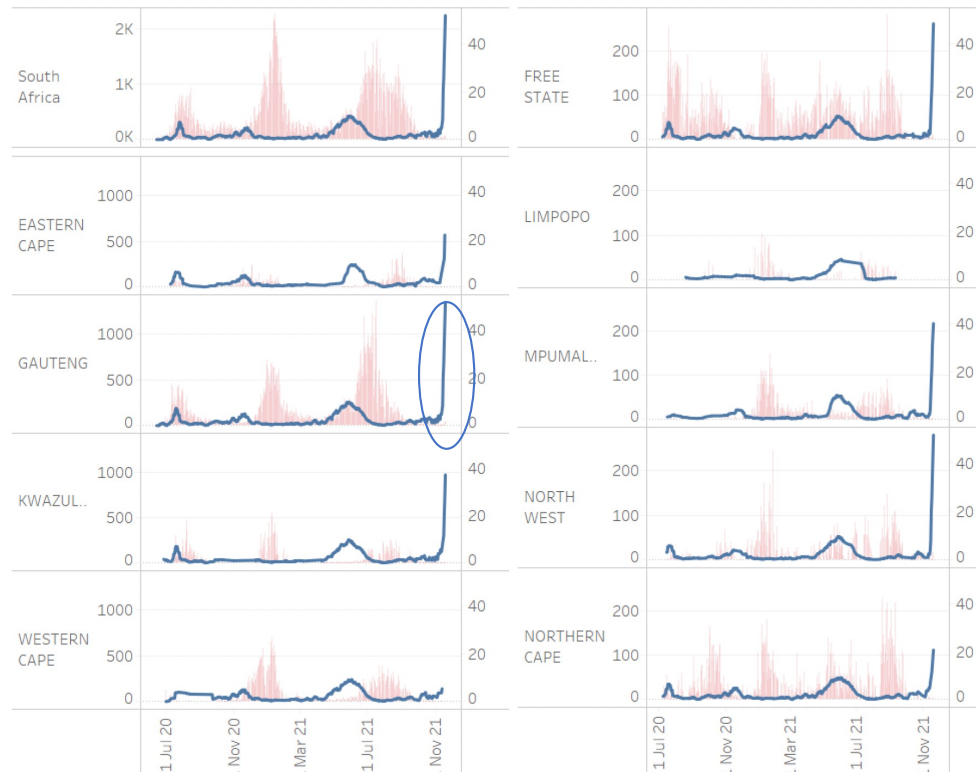


Figure 9: S-gene dropout (%) of cases with high VL (Ct value < 30 for ORF or N gene). The red bars are the number of tests reporting the presence of SARS-CoV-2 (daily) on the TaqPath assay. The solid blue line is the moving median of S-gene dropout (%).

*Current (end of Nov '21) dramatically increasing trend in the proportion of SGTF (Ct value < 30 for ORF or N gene)

- Variant can be detected with one particular PCR assay (before whole genome sequencing)
- New increase in S-gene dropout noted by NHLS and private labs very recently - from mid-November
- Now rapidly increasing in most provinces

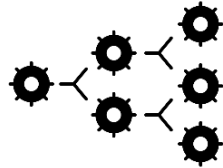
S gene target failure by province



- Rapid increase in proportion with SGTF noted across multiple provinces (caution low number of tests in most provinces)
- 77 samples with SGTF sequenced from Gauteng (samples collected 12-20 Nov) – 77/77 (100%) were B.1.1.529
- Hundreds of recently collected samples being sequenced currently by NGS-SA labs – results available by end of week (today we received 70 samples from Gauteng 67/70 were SGTF and sequencing tonight, in KZN approximately 20%).

Courtesy of Lesley Scott and NHLS team

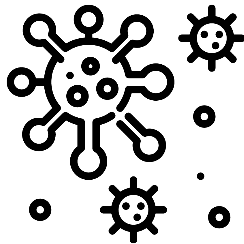
Work needed to understand phenotypic impact



Transmissibility



Vaccines



Risk of reinfection



Disease severity



Diagnostics

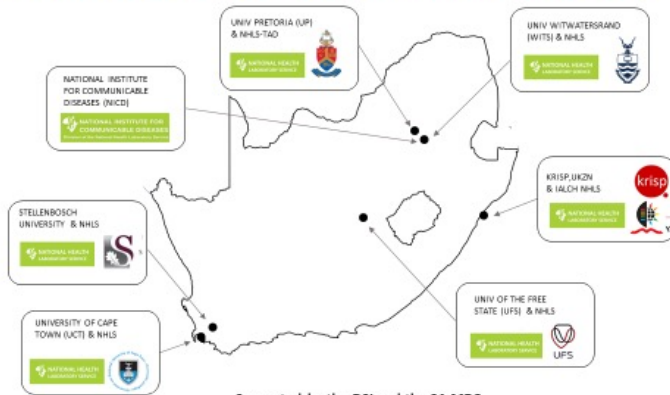
Summary

- Epidemiological data suggest sustained increase in COVID-19 incidence across Gauteng, possibly fueled by cluster outbreaks
- New variant (B.1.1.529) detected in multiple samples from across Gauteng
- Public and private testing labs in Gauteng have noticed a significant and rapid increase in detection of variant (based on PCR proxy), and now increasing in other provinces
- Mutation profile predicted to give significant immune evasion and enhanced transmissibility – urgent work already started to understand full significance
- We can **make some predictions about the impact of mutations** in this variant, but **full significance uncertain and the vaccines remain the critical**



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PATHOLOGISTS
LANCET
LABORATORIES
Key to Diagnostic Excellence



AMPATH
LABORATORIES



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