KU LEUVEN

DEPARTMENT OF MICROBIOLOGY, IMMUNOLOGY AND TRANSPLANTATION

UZ LEUVEN | LABORATORIUMGENEESKUNDE

Genomic surveillance report

Update for Belgium, 03/05/2022

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Content

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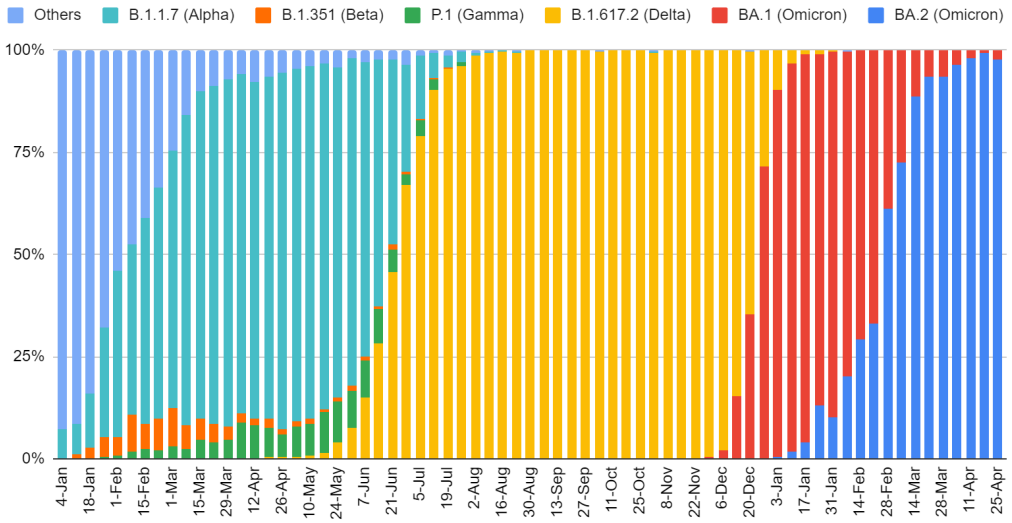
Executive summary

The Omicron BA.2 lineage (including sublineages of BA.2) currently represent 95-98% of new infections diagnosed in Belgium, and this situation is currently associated with a high but declining circulation of the virus (reported incidence during the last 14 days: 654 cases/100.000 habitants).



Worldwide, the number of reported BA.4 (667, including 10 from Belgium), BA.5 (318, including two cases detected in Belgium last week) and BA.2.12.1 (8154, including two cases detected in Belgium) cases continues to increase. Phylogenetic analysis of the early BA.4 genomes in Belgium highlight one single cluster, suggesting local transmission.

At this stage, there is no indication that these emerging variants will lead to more severe disease compared to other Omicron sublineages but, as it has been the case with previous variants, the efficacy of monoclonal antibodies used for the treatment of high risk patients may be affected.

1 Epidemiological context and indicators related to diagnostic activities

Since the Alpha wave, the federal platform laboratories have been used for genomic surveillance purposes in addition to their diagnostic function to monitor real-life viral population replacement dynamics. We therefore used the share of positive samples (Cq <25) presenting or not an S gene target failure (SGTF) to reflect in real time rapidly evolving situations. This approach has been particularly efficient thanks to the very high number of samples referred to these laboratories and to the chronological sequence of the different variants of concern which have emerged in Belgium: Alpha (SGTF), Delta (no SGTF), Omicron BA.1 & BA.1.1 (SGTF), Omicron BA.2 (no SGTG). The upcoming BA.4 and BA.5 present again the deletion 69/70 in the S gene and therefore are characterized by an SGFT.

Samples without SGTF (most likely to be BA.2 infections) currently represent up to 95-98% of positive samples tested in the federal platform laboratories.

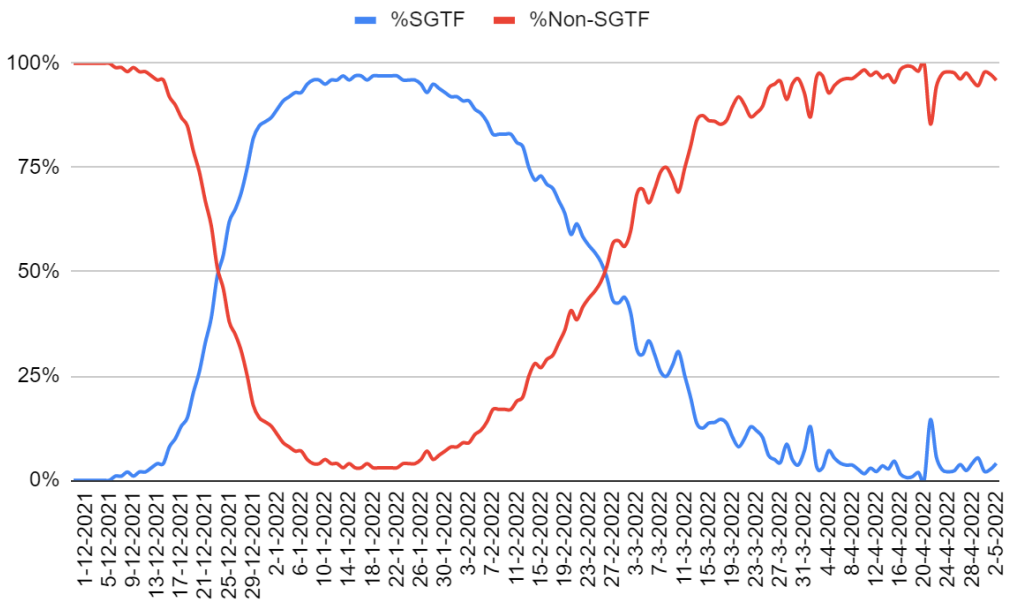


Figure 1: *S gene target failure (SGTF; blue: BA.1 & BA.1.1, and potentially already BA.4 and BA.5) and others (red: currently considered predominantly BA.2) among positive samples reported by the federal platform laboratories.*

Figure 2 highlights the total number of positive cases tested in the federal platform laboratories based on the presence or absence of SGTF for the last four weeks. BA.4 has been identified in Belgium since 29/3/2022 (so far 10 genomes), and BA.5 since 24/4/2022 (the first two cases have been identified), with both lineages presenting an SGTF.

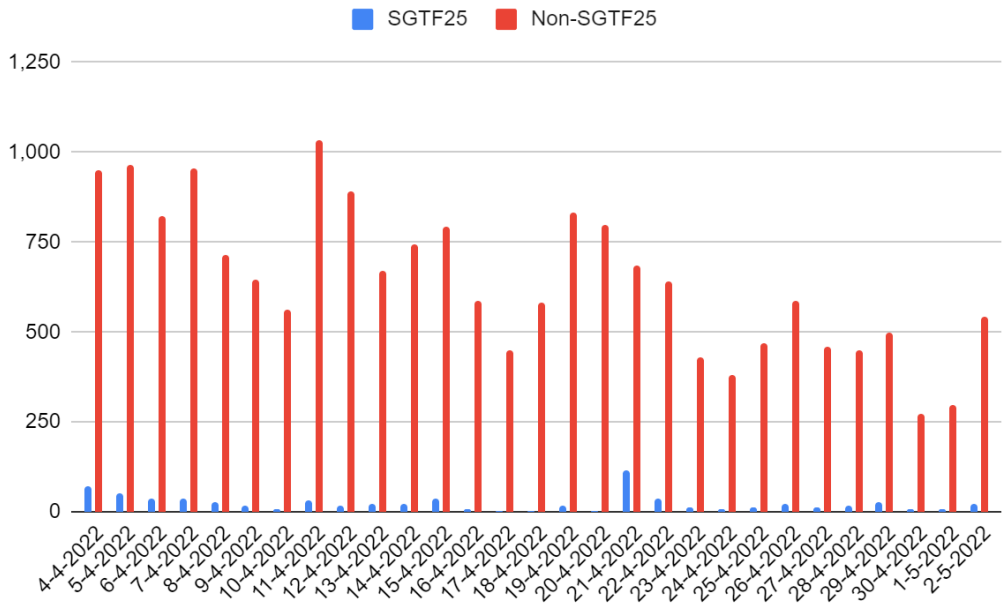


Figure 2: *Number of samples tested positive in the federal platform laboratories with S gene target failure (SGTF; blue, compatible with BA.4 and BA.5) and without SGTF (non-SGTF; red, compatible with BA.2). The absolute numbers are less representative of the actual epidemiology since a couple of weeks, as a result of a change in testing indications and a lower testing intensity. Therefore, only the last four weeks are visualised in the graph.*

2 Monitoring of Variants of Concern in Belgium

During the last two weeks of baseline surveillance - 18/4/2022 and 1/5/2022 - (588 sequences collected at this stage), BA.1 and BA.1.1 jointly represented 1.2% (↘) of the circulating strains, while BA.2 represented 98.8% (↗) of the strains. No Delta sequence was reported for the last six weeks (Figure 3). So far, only 10 BA.4 genomes and 2 BA.5 genomes have been detected in Belgium, a separate graph (Figure 4) visualizes the progress of the cases over time.

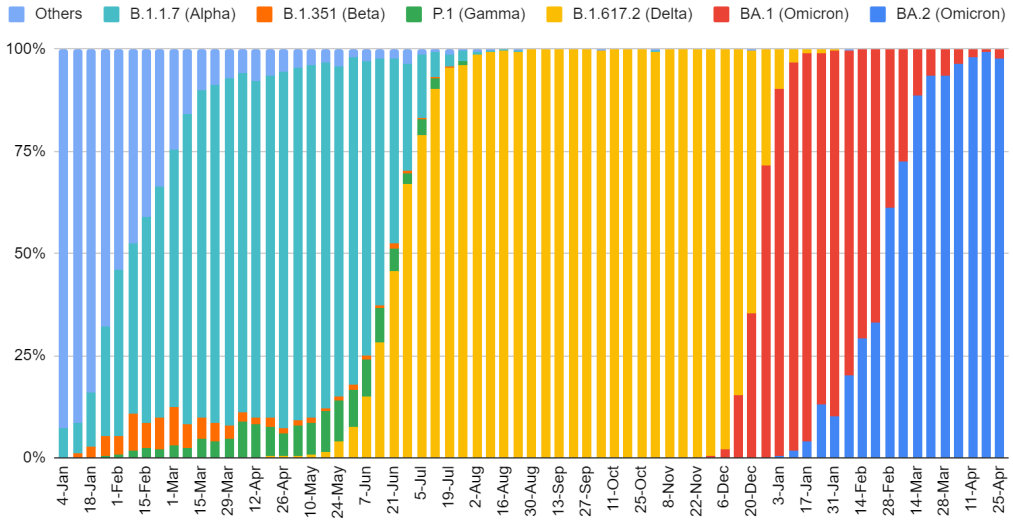


Figure 3: *Share of variants of concern per week in Belgium*

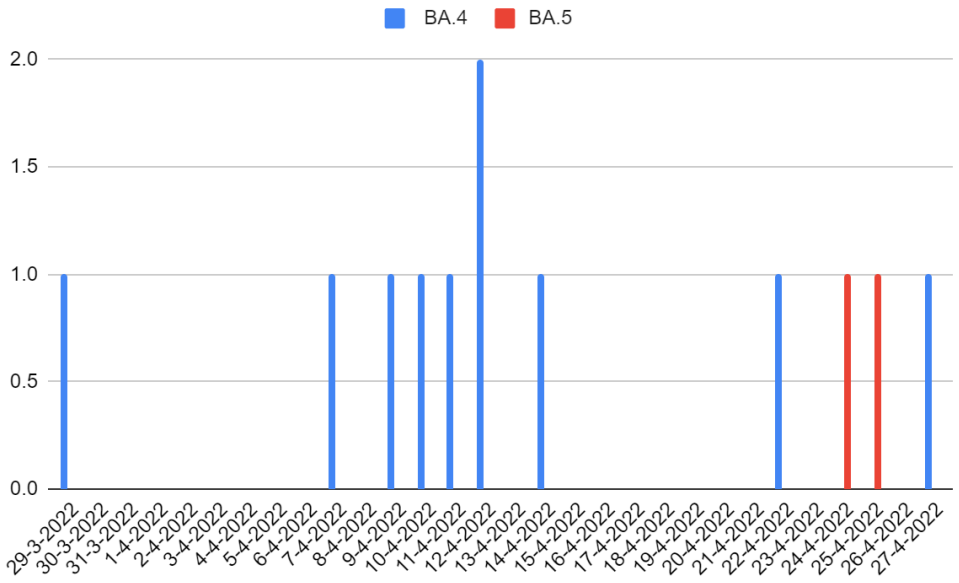


Figure 4: *Number of BA.4 and BA.5 cases reported on GISAID in Belgium over time. The first detection of BA.4 in Belgium dates from 29/3/2022 (in blue), while the first BA.5 case was sequenced on 24/4/2022 (in red).*

3 Relationship between the initial Belgian BA.4 cases

In Belgium, so far, 10 BA.4 genomes and 2 BA.5 genomes have been identified and published on GISAID by our genomic surveillance consortium. Through phylogenetic analysis on the currently available data, we were able to determine that the Belgian BA.4 genomes form a single (monophyletic) cluster. This leads to the current hypothesis - based on the available data - of a single introduction into Belgium followed by local transmission within Belgium. Note that more data are needed to further resolve the relationships between the BA.4 cases, as the origin of the clade (see Figure 6) is currently very unclear.

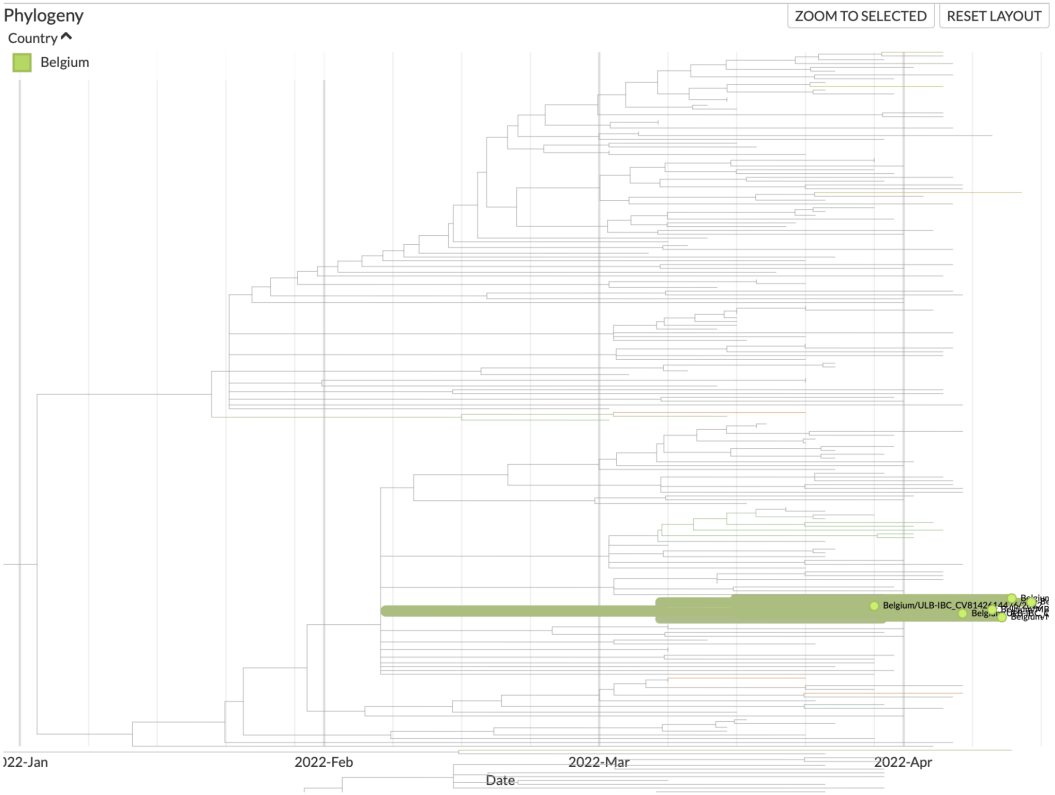


Figure 5: *The initial Belgian BA.4 cases are shown to cluster together (along with an Austrian BA.4 case; see Figure 6).*

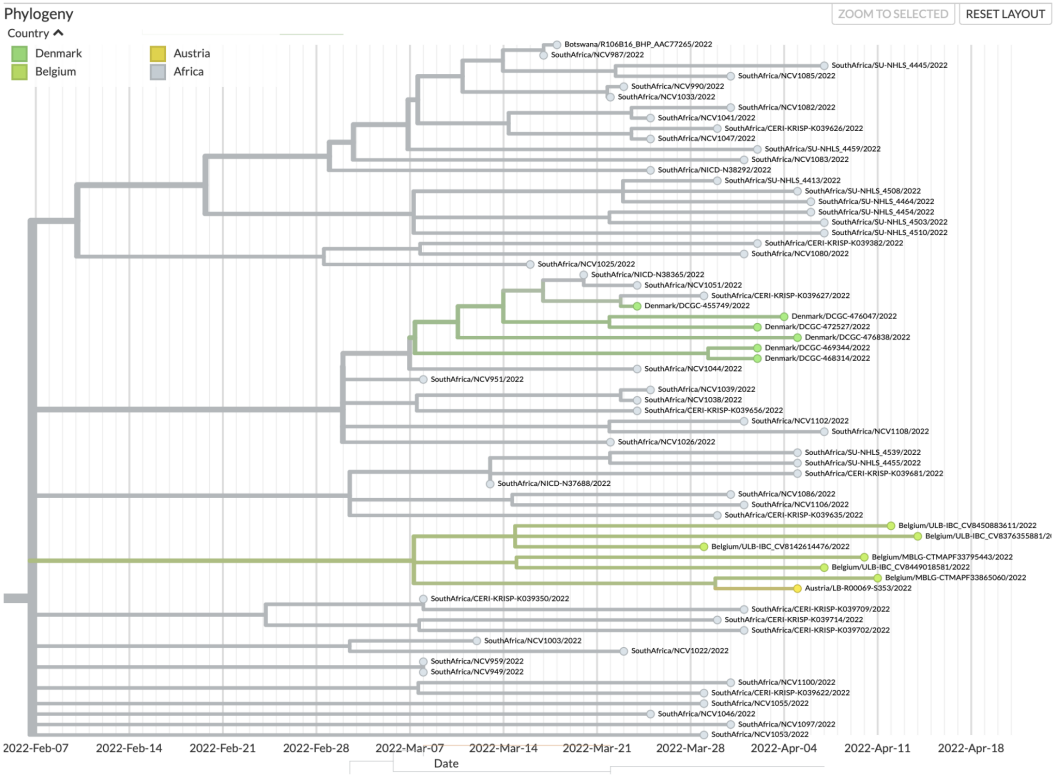


Figure 6: *The initial Belgian BA.4 cases are shown to cluster together with an Austrian BA.4 case. Currently, the majority of BA.4 cases in the larger cluster are from South Africa, and hence any estimation of origin for the Belgian BA.4 cases would (perhaps incorrectly) determine that South Africa is the likely origin of the Belgian BA.4 cases. More data - from a wide range of countries - are needed to resolve the origin of the clade shown here.*

Of the 10 Belgian BA.4 cases currently on GISAID, 6 appeared in the Brussels Capital Region (2 from Vorst /Forest, 3 from Brussels and 1 from Schaerbeek), 2 from Limburg, 1 from Hainaut and 1 from Brabant Wallon. There are currently 2 Belgian BA.5 cases: 1 from Schaerbeek (probably infected with three other relatives during a trip in Austria) and 1 from Hainaut. Our follow-up phylogenetic analysis will (hopefully) shed more light on where these BA.4 and also the BA.5 infections originated and how they are related to one another.

4 Preliminary investigations of BA.4 and BA.5 lineages in South Africa

Tegally and colleagues have recently posted a preprint presenting preliminary investigations of Omicron lineages BA.4 and BA.5 that were first identified in South Africa (https://www.medrxiv.org/content/10.1101/2022.05.01.22274406v1.full.pdf). Here is a short summary of their key findings:

- "The spike proteins of BA.4 and BA.5 are identical, and comparable to BA.2 except for the addition of 69-70del, L452R, F486V and the wild type amino acid at Q493. The 69-70 deletion in spike allows these lineages to be identified by the proxy marker of S-gene target failure" [see section 1 of the present report].

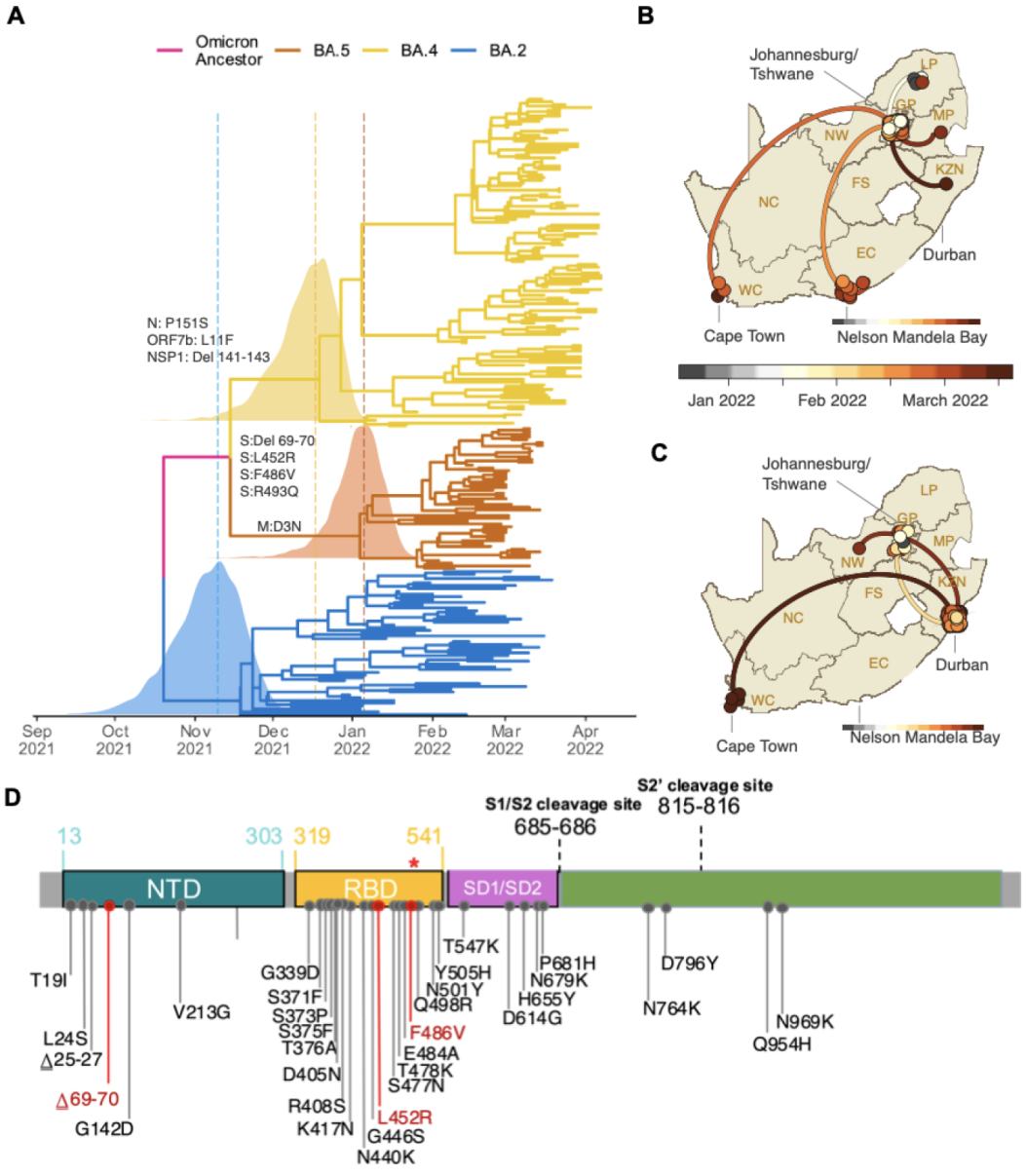
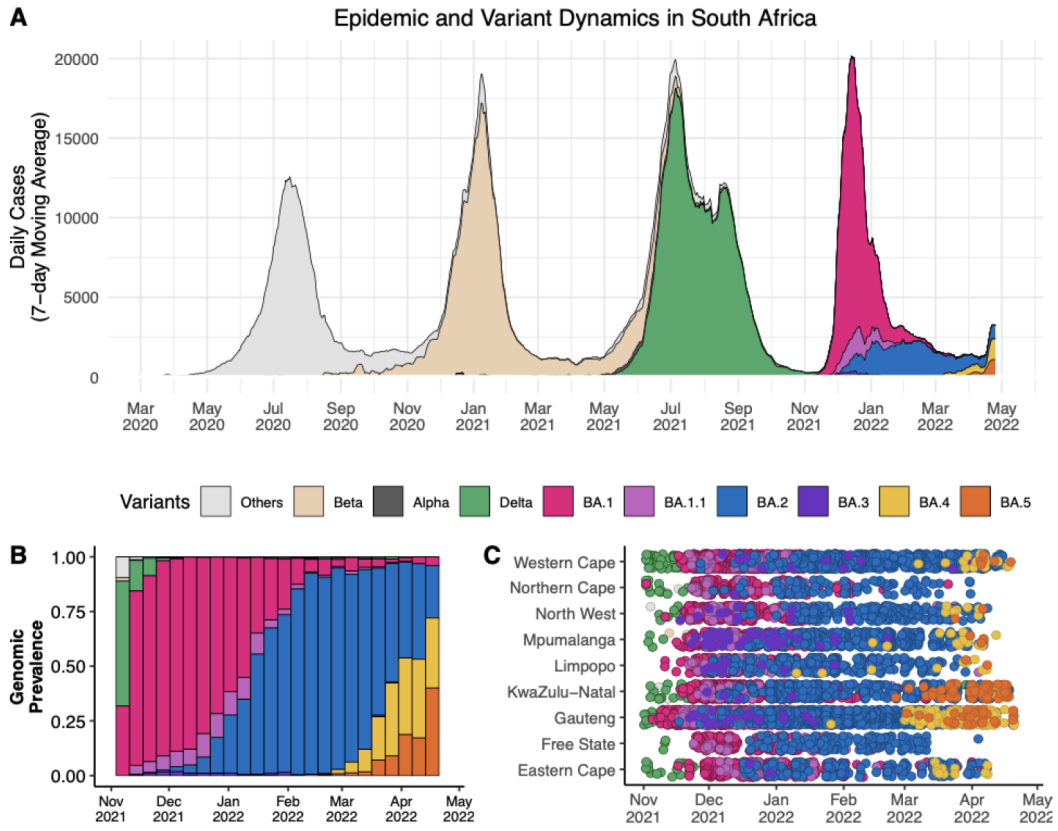


Figure 7 (from Tegally *et al.*): (***A***) *Time-resolved maximum clade credibility phylogeny of the BA.2, BA.4 and BA.5 lineages (n = 221, sampled between 29 December 2021 and 7 April 2022). Mutations that characterize the lineages are indicated on the branch at which each first emerged. The posterior distribution of the time of the most recent common ancestor (TMRCA) is also shown for BA.2, BA.4 and BA.5. (**B**) Spatiotemporal reconstruction of the spread of the BA.4 lineage in South Africa. (**C**) Spatiotemporal reconstruction of the spread of the BA.5 lineage in South Africa. In B and C, circles represent nodes of the maximum clade credibility phylogeny, coloured according to their inferred time of occurrence (scale shown). Solid curved lines denote the links between nodes and the directionality of movement (anti-clockwise along the curve). (**D**) Amino acid mutations in the spike gene of the BA.4 and BA.5 lineages. Mutations that differ from BA.2 are denoted in red, including the wild-type amino acid at position Q493 (denoted by the red *).*

- "BA.4 and BA.5 have rapidly replaced BA.2, reaching more than 50% of sequenced cases in South Africa from the first week of April 2022 onwards. Using a multinomial logistic regression model, we estimate growth advantages for BA.4 and BA.5 of 0.08 (95% CI: 0.07 - 0.09) and 0.12 (95% CI: 0.09 - 0.15) per day respectively over BA.2 in South Africa."



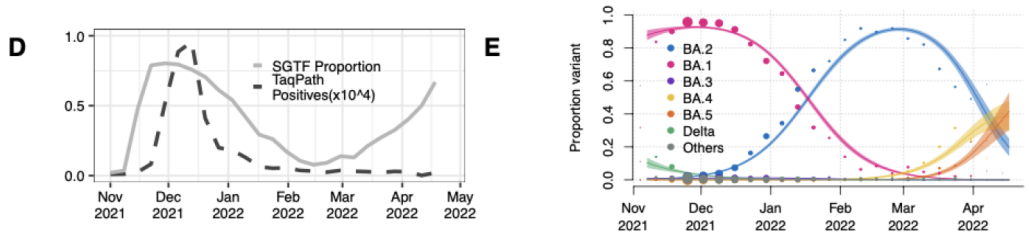


Figure 8 (from Tegally *et al.*): (***A***) *The progression of the 7-day rolling average of daily reported case numbers in South Africa over two years of the epidemic (April 2020 – April 2022). Daily cases are coloured by the inferred proportion of SARS-CoV-2 variants prevalent at a particular period in the epidemic. (**B**) Changes in the genomic prevalence of Omicron lineages in South Africa from November 2021 (when BA.1 dominated) to April 2022 (when BA.4 and BA.5 were increasing in frequency). (**C**) The count of Omicron lineage genomes per province of South Africa over November 2021 – April 2022. BA.4 and BA.5 have been detected in seven of the nine provinces. (**D**) Changes in the proportion of positive TaqPath qPCR tests exhibiting SGTF from November 2021 to April 2022. The number of TaqPath positives are to the order of 10^4 to the scale shown. (**E**) Modelled linear proportions of the Omicron lineages in South Africa. BA.1 rapidly outcompeted Delta in November 2021 and was then superseded by BA.2 in early 2022. BA.4 and BA.5 appear to be swiftly replacing BA.2 in South Africa. Model fits are based on a multinomial logistic regression and dot size represents the weekly sample size.*

5 Situation in the United Kingdom

The situation in the UK regarding the variants BA.4, BA.5 and BA.2.12.1 is relatively similar to the situation observed in Belgium: these variants still represent a very low proportion of all sequences.

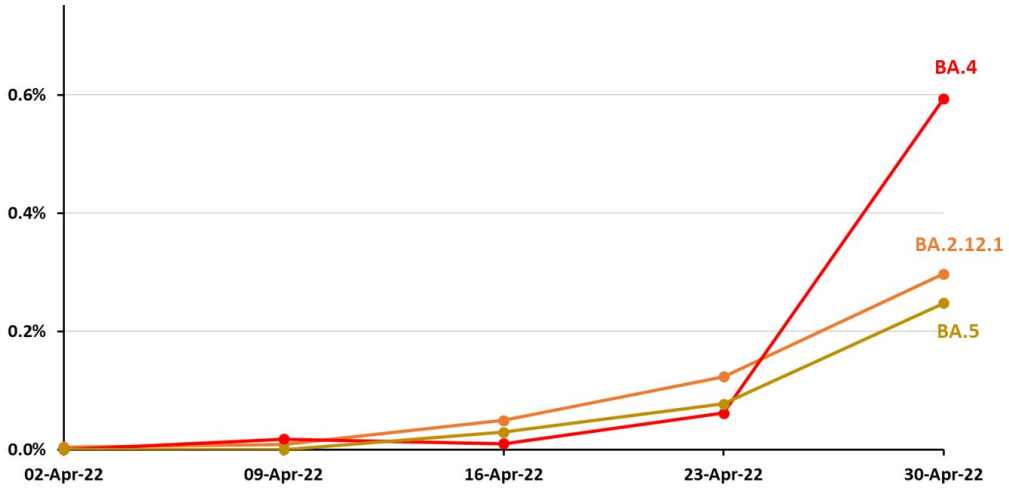


Figure 9 (from Prof. Christina Pagel): *Proportion of sequenced cases in England that are Omicron BA.4, Omicron BA.5 and Omicron BA.2.12.1 from 1 April 2022 to 30 April 2022.*

6 Situation in New York (USA)

New York currently observes a significant proportion of BA.2.12.1, in parallel with a rise of BA.2 infections. This variant has raised some concerns due to the presence of some mutations. Nevertheless, at this stage, this variant does not seem to generate a significant rise in terms of reported infections.

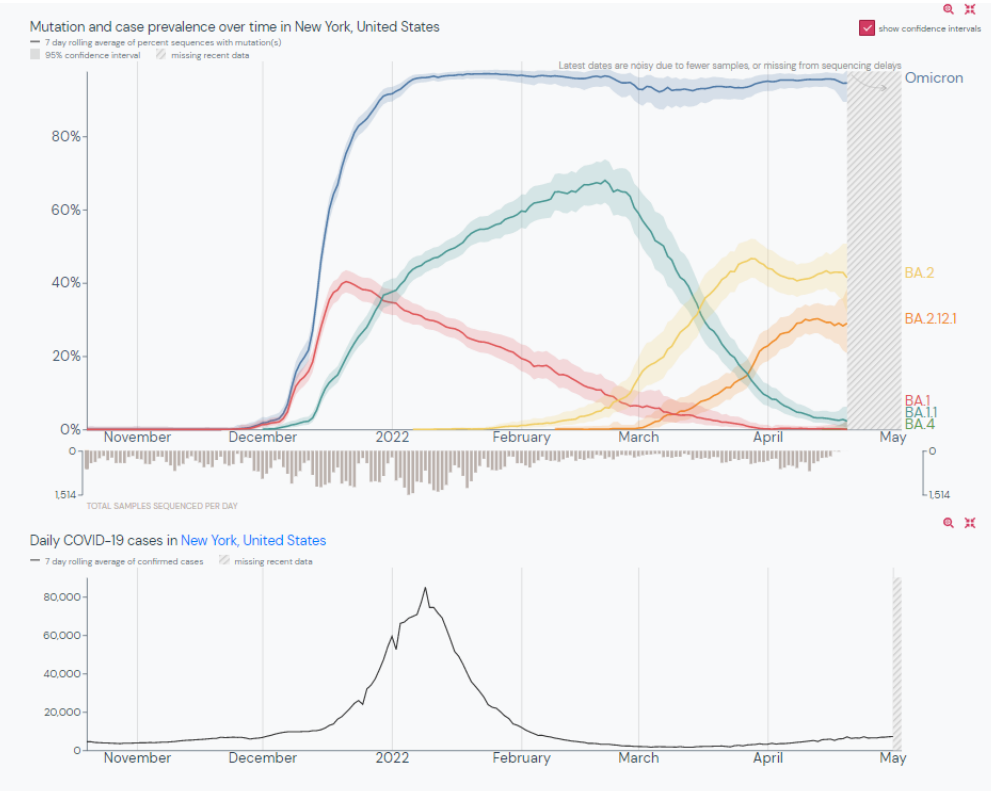


Figure 10 (from outbreak.info): *Share of different Omicron variants in New York, USA (above) and reported number of COVID-19 infections during the same period (below)*