Genomic surveillance of SARS-CoV-2 in Belgium

Report of the National Reference Laboratory (UZ Leuven & KU Leuven)

Situation update – 31st of August 2021
(report 2021_43)

Executive summary

40,404 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID.

Among these, 934 sequences of positive SARS-CoV-2 samples collected between 16th and 29nd of August were reported in the context of baseline surveillance,
- B.1.617.2 (*Delta*) represented 99.4% (equal to the last report)
Other variants currently represent less than 1% of the circulating strains.

Other points of attention:
- The NRC performed 1075 tests among departing travellers and 1760 tests among returning travellers during the week of August 23. The positivity rate among returning travellers was 4.5 times higher compared to departing travellers (3.8% against 0.8%). This difference **highlights the risk of infection associated with travels** and the potential benefits of extending testing criteria among returning travellers. The current restrictive testing indications and financial barriers for testing could contribute to a continuous importation of undetected infections associated with secondary clusters.

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With the collaboration of the laboratories of UCL, ULB, UMons, UNamur, ULiège, UGent, UZA/UAntwerpen, Jessa ZH, AZ Delta, AZ Klina, IPG, AZ St Lucas Gent, OLVZ Aalst, Briant network, ZNA, AZ St Jan Brugge, UZ Brussel, LHUB-ULB, and UZ Leuven/KU Leuven; and Sciensano HealthData.

Previous reports can be downloaded using the following link:
https://www.uzleuven.be/nl/laboratoriumgeneeskunde/genomic-surveillance-sars-cov-2-belgium

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1. Monitoring of VOCs in Belgium

While first identified on 6 April 2021 in Belgium, the B.1.617.2 Variant of Concern (Delta) is now the dominant lineage in the country.

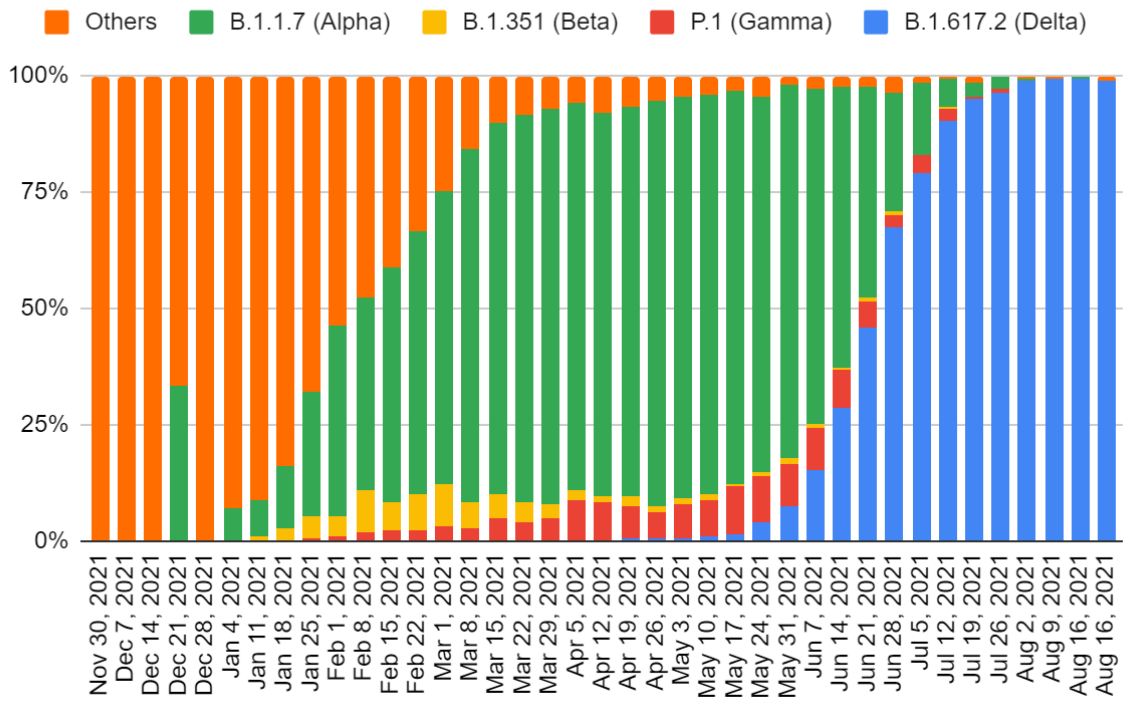

Figure 1: *Weekly evolution of the frequency of variants of concern reported by the baseline surveillance network using a whole genome sequencing (WGS) approach.*

2. Testing of travellers

Departing travellers

During the last 9 full weeks (June 28 to August 29), the National Reference Center in Leuven has tested 49,213 departing travellers, among which 320 were tested positive (0.65%). The positivity rate increased from 0.28% during the first week to 0.90% during the week of August 2, while it decreased to 0.46% in the week of August 16, to increase again to 0.84% last week. The Delta variant represented 89.1% of all positive samples.

Returning travellers

For the last 9 full weeks (June 28 to August 29),

- Among the travellers returning from abroad to the region of Leuven, 8299 people were tested, among which 246 were tested positive (3.0%). The Delta variant represented 93.3% of the positive samples tested during the last week.
- Currently, incomplete data are available to calculate the positivity rate and associated distribution of SARS-CoV-2 variants, according to the countries from which travellers return to Belgium. Sciensano HealthData is looking into the possibility to perform such an analysis.

According to data provided by Sciensano, at the Belgian level and during the last 8 weeks, 94.5% of the travellers who tested positive upon return were infected with the Delta variant. During this same period, 13.2% of the people tested positive for the variant Delta were returning travellers (Table 1).

	% of returning travelers among persons positive for the considered VOC*	**% of persons positive for the considered VOC among all positive returning travelers****
Alpha	12,1% (50/414)	5,1% (50/988)
Beta	11,1% (1/9)	0,1% (1/988)
Gamma	2,8% (3/106)	0,3% (3/988)
Delta	13,2% (934/7071)	94,5% (934/988)

Table 1: *(*) Ratio between the number of returning travelers tested positive for a given VOC and the total number of persons tested positive for that VOC; (**) Ratio between the number of returning travelers tested positive for a given VOC and the total number of returning travelers tested positive for one of the four VOCs. N.B.: We only considered positive persons for which the travel history status is known (estimated for the last 8 weeks, i.e. weeks 27-34).*

3. Update on re-infections: which variants do we observe?

A re-infection is defined as a distinct clinical episode of SARS-CoV-2 infection after a first positive SARS-CoV-2 test. Data is provided by Sciensano.

Table 2 highlights for the last two months the number of re-infection cases (with one of the four listed VOCs) documented. Of the 6.140 infections reported (only considering cases for which pre-infection status is known), 114 re-infections were observed (1.9% of total).

	% of re-infections among persons positive for the considered VOC*
Alpha	1,5% (5/335)
Beta	0,0% (0/8)
Gamma	1,4% (1/71)
Delta	1,9% (108/5726)

Table 2: *Percentage of re-infections among persons tested positive for each VOC (only considering positive persons for which the pre-infection status is known) during the last 8 weeks (W27-34).*

4. Update on hospitalisations: which variants do we observe?

For the hospitalised cases, the reported numbers are purely descriptive as the data were derived from COVID-19 patients who were hospitalized and registered by the hospitals in the Clinical Hospital Survey (CHS) coordinated by Sciensano. The CHS is not exhaustive and covers approximately 60% of all hospitalized COVID-19 patients in Belgium. As a consequence, absence of a link between variant data and registration in the CHS does not automatically imply that this patient did not require hospitalization. Approximately 40% of hospitalized COVID-19 patients are not registered in the CHS.

Table 3 highlights for the last two months the number of hospital admissions documented. Of the 114 COVID-19 patients that were hospitalised and for which variant data is available, the large majority (79.8%) was reported to be infected with the Delta variant. The low number of hospitalized patients for which variant data is available can be explained by the fact that disease severity is currently not considered as a prioritized indication to perform SARS-CoV-2 WGS, complemented by the limitation of the viral load that needs to be sufficiently high to be able to perform detailed typing.

	Share (%) of VOCs represented in hospital admissions*
Alpha	2,6% (3/114)
Beta	0,0% (0/114)
Gamma	1,8% (2/114)
Delta	79,8% (91/114)

Table 3: *Share of VOCs among hospital admissions (only considering approximately 60% of all hospitalised COVID-19 patients in Belgium) during the last 8 weeks (W27-34).*

5. Update on post-vaccination infections: which variants do we observe?

A breakthrough infection is defined as a positive SARS-CoV-2 test at least 7 days after the full completion of a vaccination scheme. To facilitate the transfer of samples that meet the definition to a sequencing lab, laboratories that submit RT-PCR test results to HealthData will receive an automatic message from HealthData notifying them that a particular sample meets the criteria of a post-vaccination breakthrough case. Following prior communication, such samples can be transferred to any of the sequencing laboratories, preferentially geographically the closest or for which logistic flows already are in place.

According to data provided by Sciensano, the weekly evolution of the frequency of variants of concern is summarized in Figure 2 for the post-vaccination breakthrough infections. Details on age category, gender and vaccine brand are available, however, these are not yet included in this week's report as they are highly influenced by the design and roll out of the vaccination campaign in Belgium, which in priority targeted elderly persons and healthcare workers and hence resulted in an overrepresentation of the female gender and the BioNTech/Pfizer (Comirnaty) vaccine. To avoid misinterpretation, the data will be evaluated in more detail before sharing it in this report.

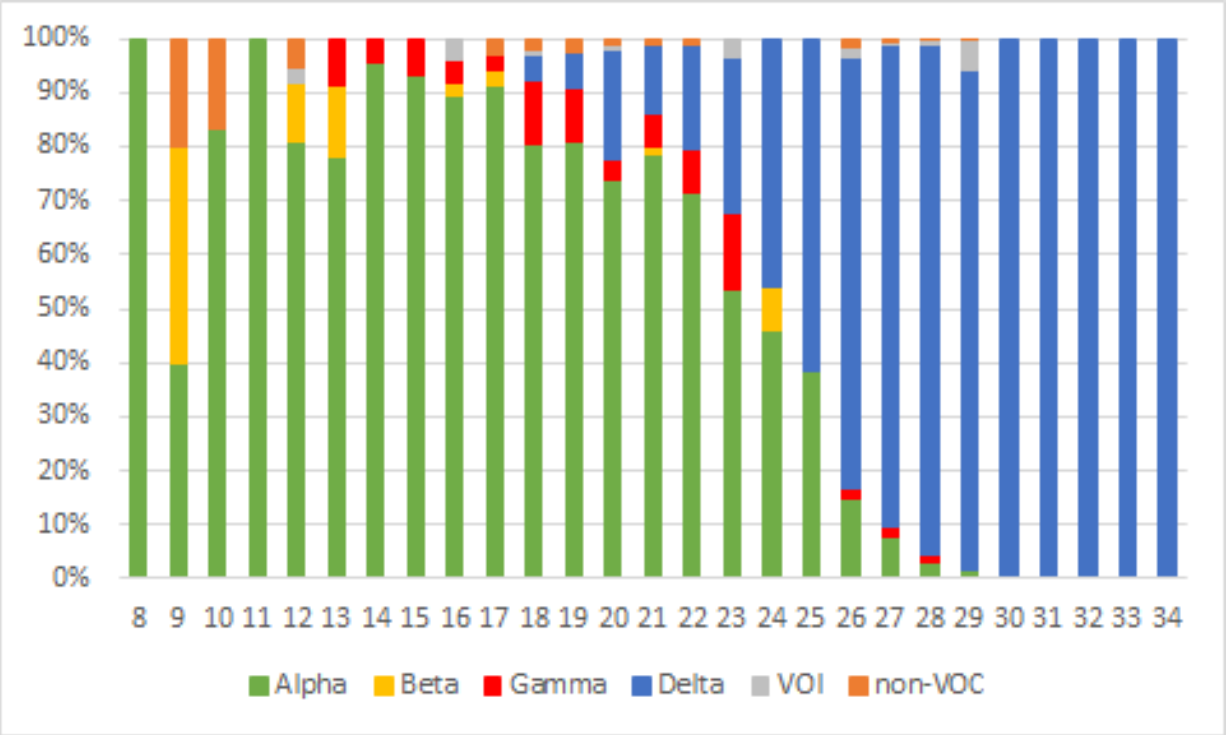

Figure 2: *Weekly evolution of the frequency of variants of concern reported for post-vaccination infections using a WGS approach (source: HealthData).*

6. Mutations within the overall Delta phylogeny

Currently, 4.416 B.1.617.2 (Delta) genomes from Belgium are available on GISAID. We have added a randomly sampled proportion (>40%) of these genomes to a global phylogeny (Figure 3). While this creates an artificial bias in the geographical representation, it does allow to visually assess large-scale clustering patterns. However, Figure 3 does not reveal any immediately apparent clustering of Belgian genomes with those from other countries, with the Belgian genomes being well represented in each part of the global Delta phylogeny. What can be seen however, is that a few predominantly Belgian clusters can be determined in the phylogeny. This is not uncommon and has been observed for the Delta genomes from the United Kingdom as well. However, given the clear sampling bias in the phylogeny, a dedicated study on this clustering pattern would have to be performed.

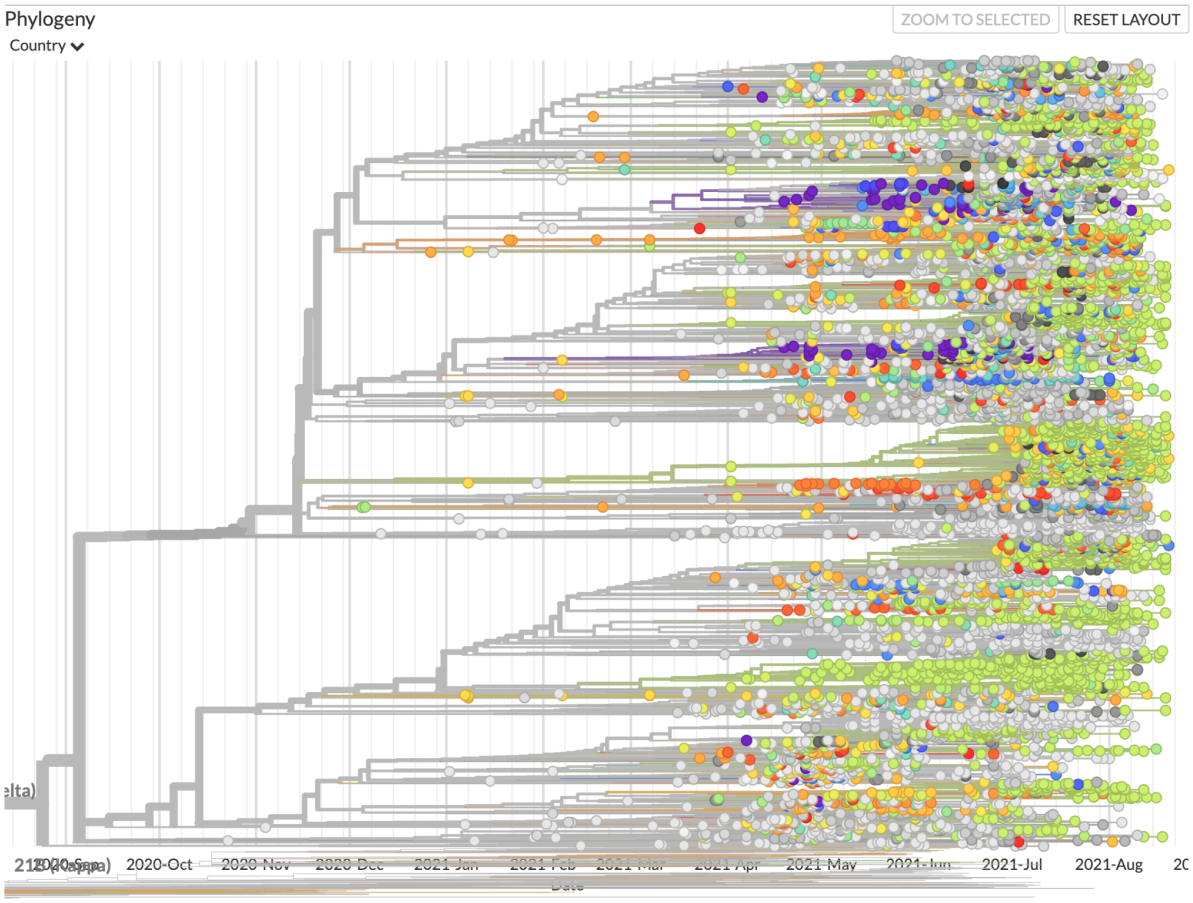

Figure 3: Delta phylogeny of nearly 7.000 genomes including almost 2.000 Belgian genomes (green dots) reveals geographic mixing as well as specific clusters mostly *composed* of Belgian genomes.

In Figure 4, we show the same phylogeny as in Figure 3 but coloured by mutations and focusing on the Belgian genomes. Despite the random sample of Belgian genomes, we are able to distinguish 2 Belgian genomes containing the L452Q mutation (both from the province of West Flanders) which is most notable associated with the **Lambda variant**. We also see 4 Belgian genomes (all from the province of Antwerp) with the E484Q mutation, known for occurring in the **Kappa variant**. For future reports, we will make the decision to include all available Belgian genomes carrying these mutations. For the latter (B.1.617.2 + E484Q), currently seven genomes are available on GISAID.

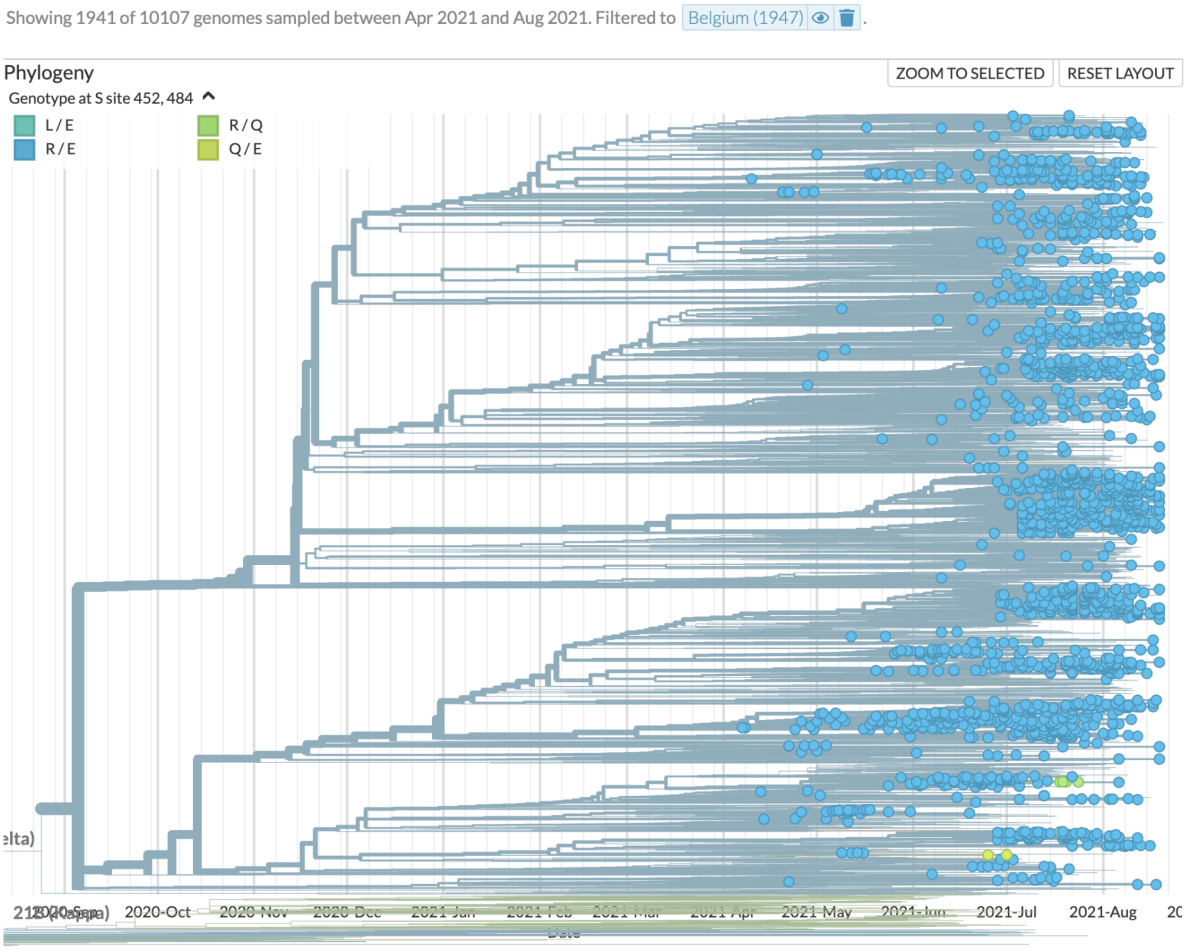

Figure 4: Global Delta phylogeny with Belgian Delta genomes (1.947) highlighted in blue. Specific mutations within Belgian genomes are shown in green and yellow.

Figure 5 focuses on a part of the global Delta phylogeny that contains the Belgian genomes with the L452Q and E484Q mutations. The 4 selected Belgian genomes (shown in green) with the E484Q mutation from the province of Antwerp cluster together, which is also the case for the 2 selected Belgian genomes (shown in yellow) with the L452Q mutation.

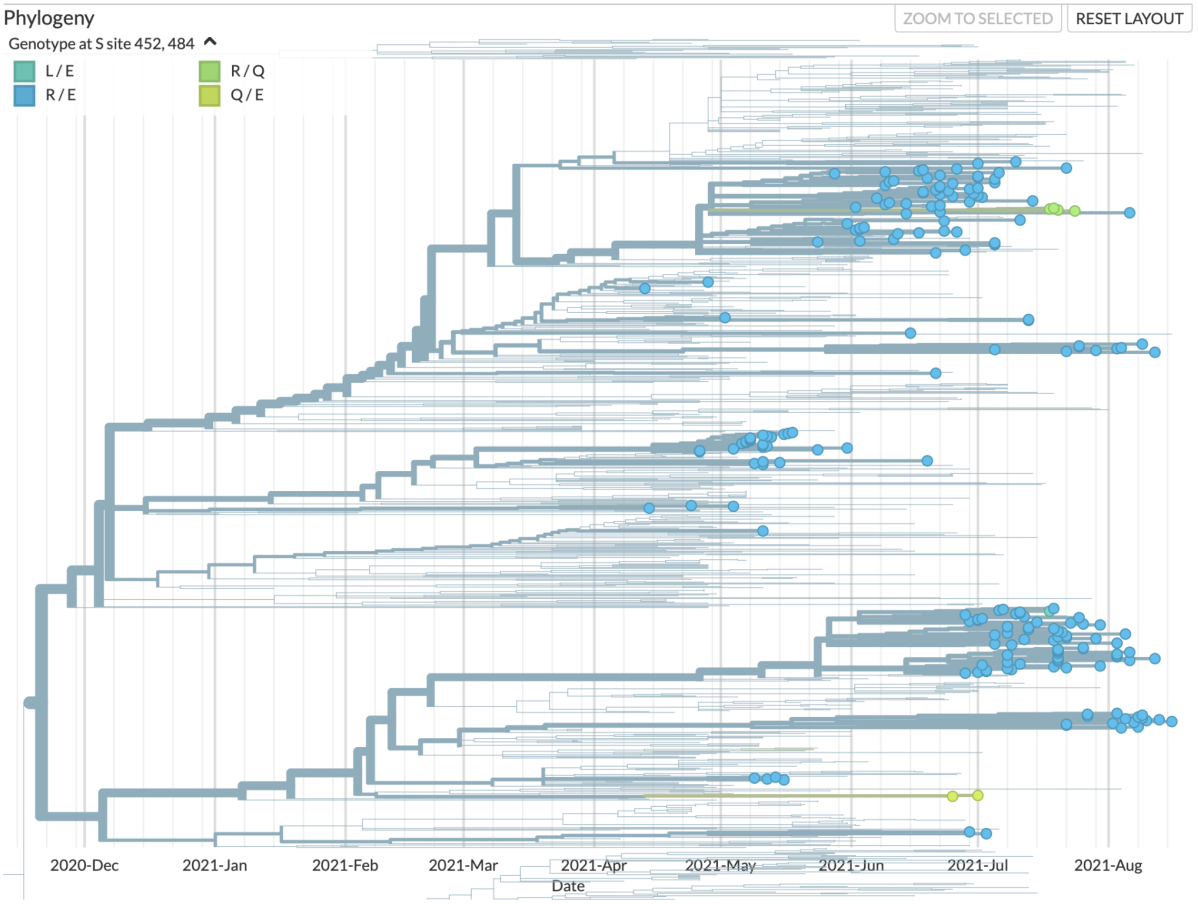

Figure 5: *Selected cluster within the global Delta phylogeny focusing on the Belgian Delta genomes with specific mutations (shown in green and yellow).*

7. Update of the epidemiological risk associated with C.1.2 (South Africa) and B.1.621 (Colombia)

Recently, reports highlighted the potential epidemiological risk associated with the emergence of variants in South Africa (C.1.2) and Colombia (B.1.621). The latter (also associated with the K417N mutation, not present in Colombia) has been involved in a post-vaccination outbreak in Belgium resulting in a significant proportion of fatalities, and has therefore been actively followed-up by the National Reference Laboratory during the last weeks.

To assess the risk of these variants becoming dominant around the world and in Belgium, we assessed the growth advantage of these variants relative to the Delta variant using the data reported by South Africa (Figure 6) and Colombia (Figure 7). These analyses based on the currently available data tend to show that these variants will not be able to compete with the current dominant variant and are therefore not to be considered as an immediate public health threat for Belgium. It should nevertheless be noted that these variants are actively circulating in numerous countries, and that they can therefore be responsible for upcoming imported cases and secondary local clusters, as it has already been the case for B.1.621.

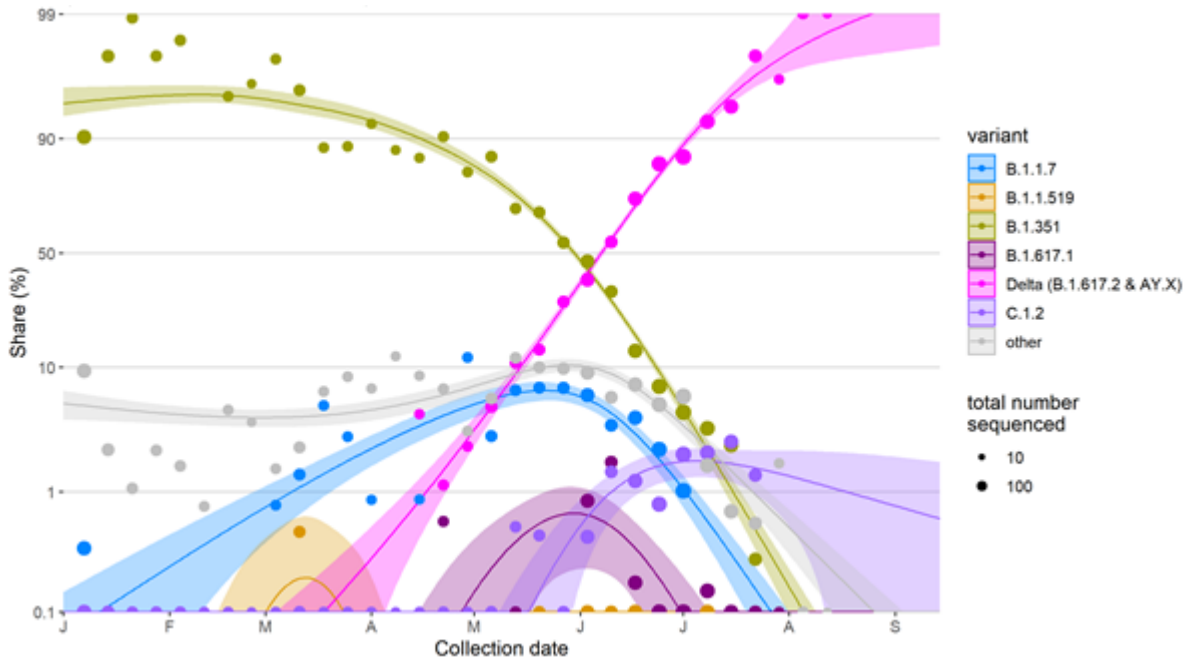

Figure 6: *Multinomial 2 df spline fits to GISAID Pangolin SARS-CoV2 lineage frequencies in South Africa. Based on this fit, lineage C.1.2 currently does not have a significant growth rate advantage relative to Delta, and in fact has a slight disadvantage (growth rate difference with Delta=-1.9% per day, -5.0 - -1.3% 95% CLs).*

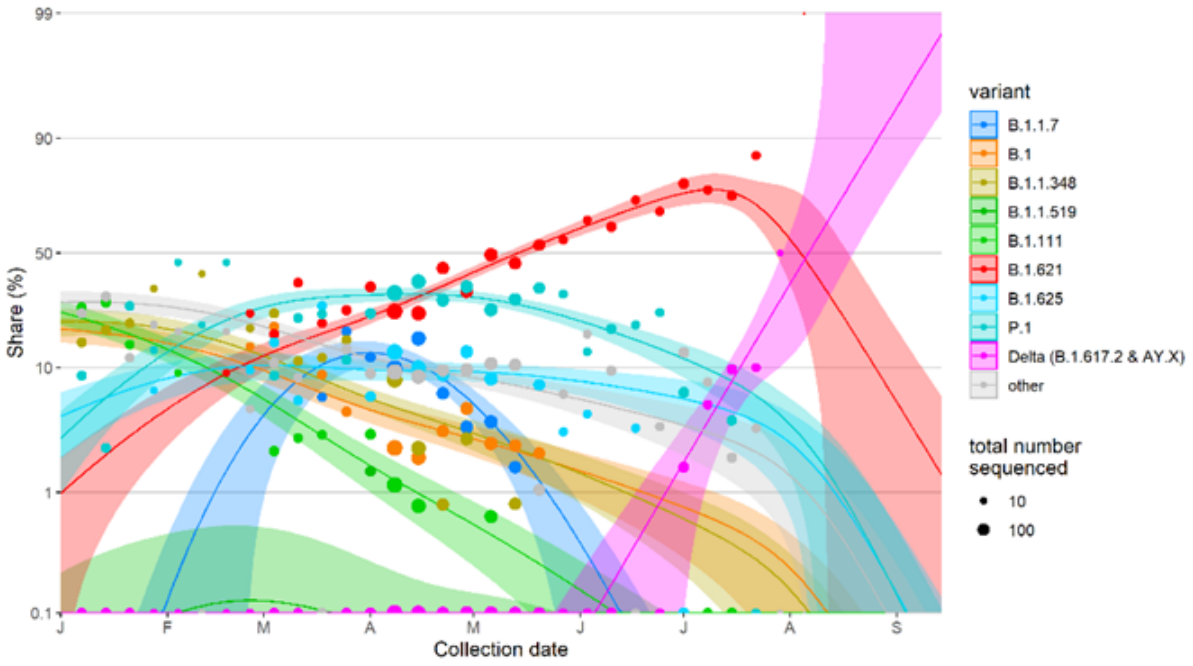

Figure 7: *Multinomial 2 df spline fits to GISAID Pangolin SARS-CoV2 lineage frequencies in Colombia. Based on this fit, lineage B.1.621 currently does not have a growth rate advantage relative to Delta, and in fact has a significant disadvantage (growth rate difference with Delta=-10.7% per day, -17.9 - -6.8% 95% CLs).*