Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 21 of September 2021
(report 2021_46)

Executive summary

46,004 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID.

699 sequences of positive SARS-CoV-2 samples collected between 06/09/2021 and 19/09/2021 were analysed in the context of baseline surveillance. Among these, B.1.617.2 and its sublineages (*Delta*) represented 100% of the circulating strains.

The genomic diversity of SARS-CoV-2 in Belgium is comparable with the situation described over the last 7 weeks.

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

Table of contents

1. Sequencing coverage
2. Monitoring of VOCs in Belgium
3. Testing of travellers
4. Update on re-infections and variants
5. Update on hospitalisations and variants
6. Update on post-vaccination infections and variants
7. Spatial mixing in Belgian Delta infections

1. Sequencing coverage

1.1. Historical overview

While sequencing of positive samples has been initiated by the National Reference Laboratory at UZ/KU Leuven and a limited number of academic laboratories from March 2020 on, the formal setup of the genomic surveillance program in Belgium has been initiated in December 2020.

As represented in Figure 1, the setup of the sequencing consortium allowed to significantly increase the proportion of sequenced positive samples incorporated in the surveillance system, which has been maintained at over 5% of the positive samples from February 2021, and over 10% of the positive samples since May 2021. The complex process of sample transport, analytical process and upload of sequencing data on GISAID explains the underestimation for the most recent month of September. Moreover, it needs to be considered that a share of the total positive cases (Figure 1, in orange) were classified as 'weakly positive', hence who are not a candidate for sequencing due to a too low viral load (technical limitation of the whole-genome sequencing process).

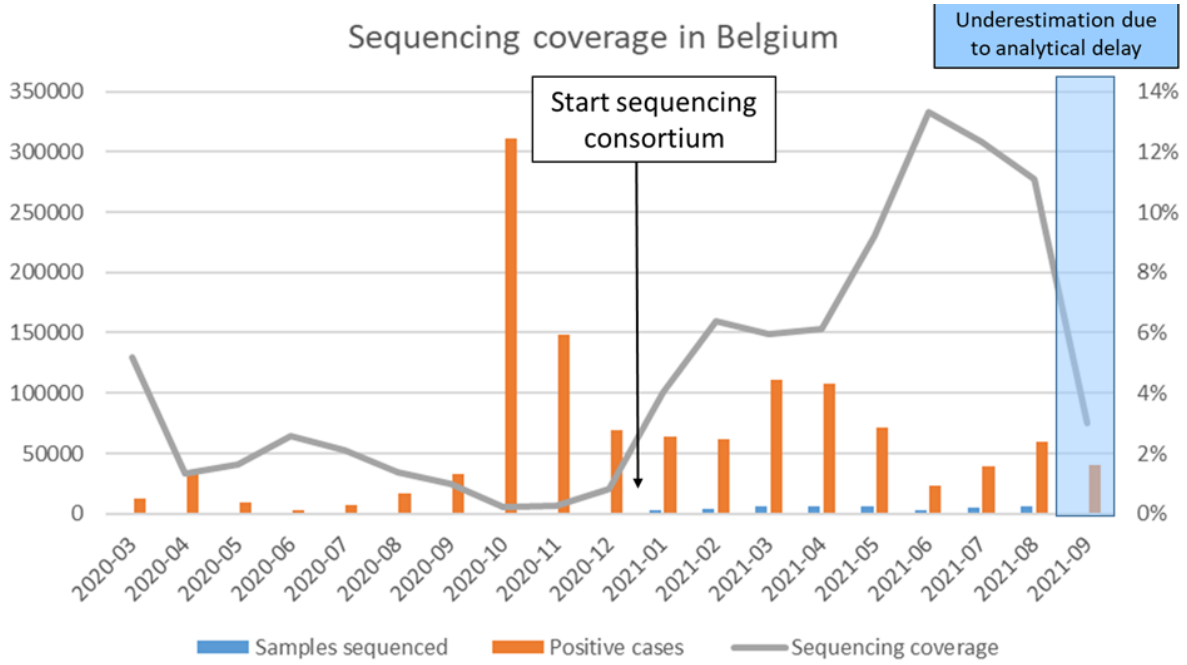

Figure 1: *Sequencing coverage in Belgium (grey line), from the start of the epidemic in March 2020 until September 2021. Both the number of positive cases (in orange) as well as number of samples sequenced (in blue) are plotted over time.*

The sequencing coverage in August 2021 was estimated at 11% of the positive cases diagnosed at a national level. All but one of the 11 provinces had a coverage above 5%. The sequencing lab that generates the majority of the sequences for this province reported technical issues during the summer, which resulted in a coverage of only 4%. Currently, their backlog is being cleared and coverage is expected to increase again soon to >5%, however this effort is accompanied with an extensive increase in turn-around-times. Priority is being granted to samples originating from returning travellers to control the potential influx of new variants or variants other than Delta, as well as baseline surveillance of the most recent weeks since throughout the entire summer it has been already reported that the Delta variant was predominantly circulating.

1.2. Evolution of the age profile of patients for which a sample has been sequenced

While the Alpha variant became dominant (>50% of circulating strains) on week 8 (22 February), the Delta variant took over from week 26 (28 June). Inbetween, a massive vaccination campaign has been rolled-out in the country, reaching >50% full coverage among people aged 55+ mid June.

Interestingly, the age profile of the patients infected seems to have evolved importantly: while the age distribution of patients infected with the Alpha variant (launch of the vaccination campaign) was relatively flat, the proportion of infected people in the older age groups decreased significantly for the variant Delta (consolidation phase of the vaccination campaign). We illustrate hereunder this change in age distribution for the city of Brussels.

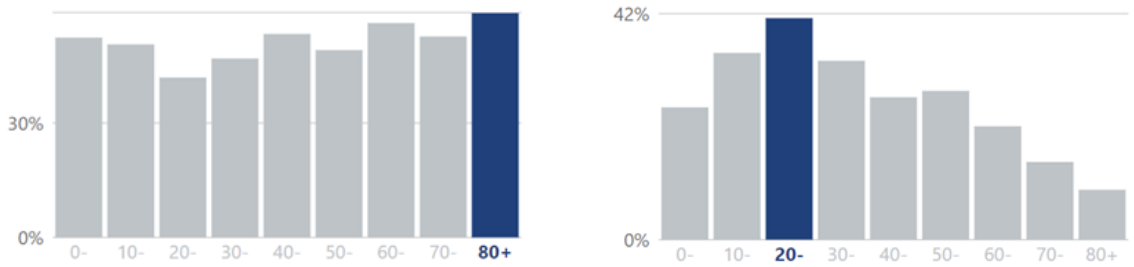

Figure 2: *Age distribution of infected people infected with the Alpha variant (left) versus the Delta variant (right) in the city of Brussels. For the Alpha variant, all age groups were affected similarly, with the age group of 80+ being most at risk; for the Delta variant, older age groups were less affected with people in their 20s being most at risk (source: https://cov-spectrum.ethz.ch/).*

2. 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.

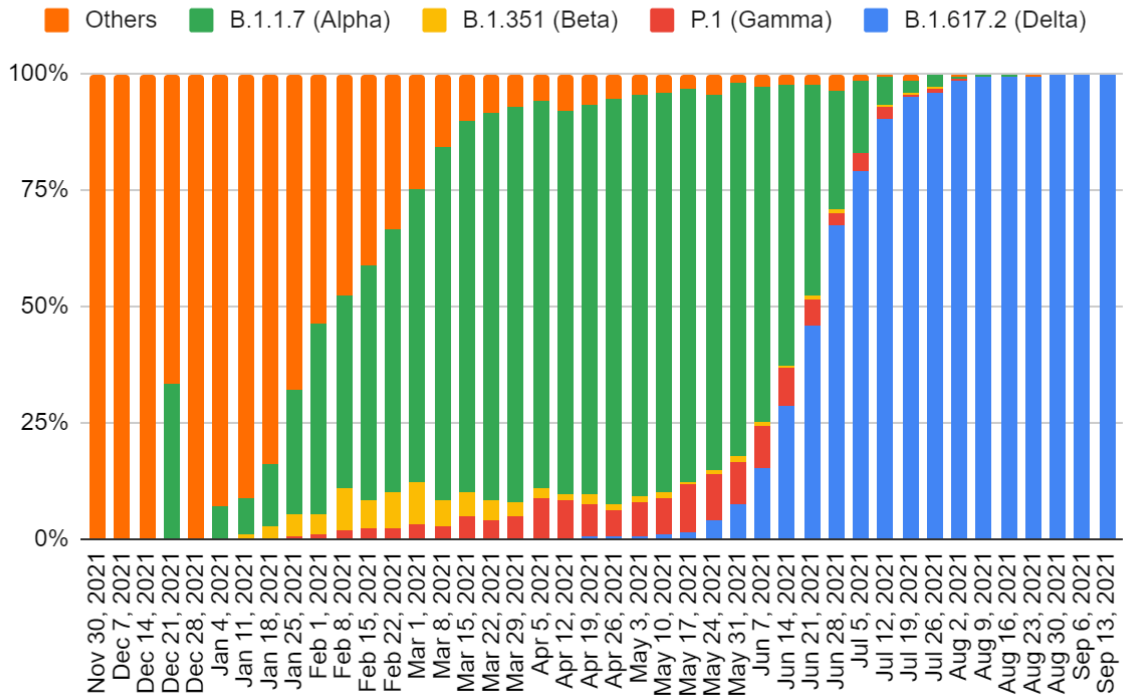

Figure 3: *Weekly evolution of the frequency of variants of concern reported by the baseline surveillance network using a whole genome sequencing (WGS) approach.*

The current worldwide surge of infections caused by the variant Delta has been until now relatively well contained in Belgium, particularly in the older age groups which present the highest vaccination coverage. The impact of the vaccination is visible both in the number of cases diagnosed and the hospitalized patients, particularly when comparing with the previous waves of infection.

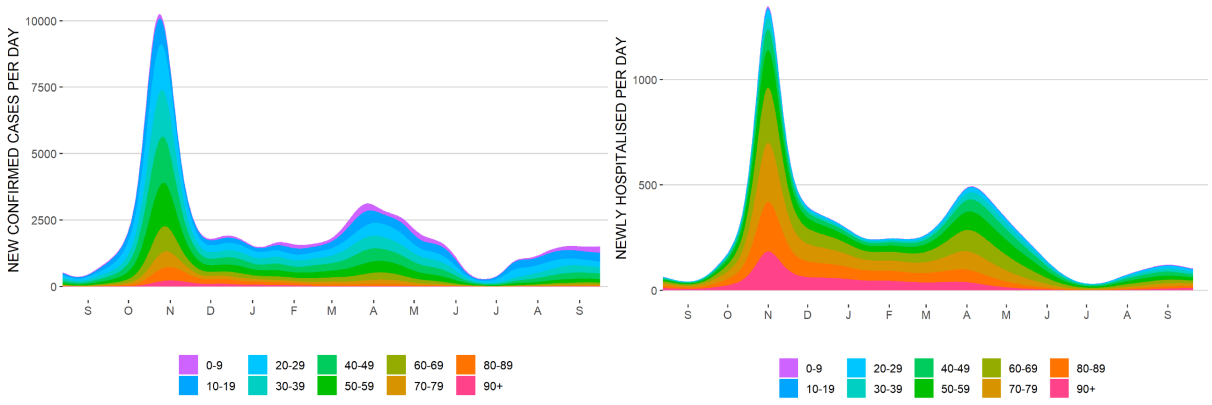

Figure 4: *Evolution of the number of diagnosed COVID-19 infections (left) and related hospitalisations (right) in Belgium per age group.*

3. Testing of travellers

According to data provided by Sciensano, at the Belgian level and during the last 8 weeks, 97.6% of the travellers who tested positive upon return were infected with the Delta variant. During this same period, 17.0% 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	36,4% (20/55)	2,2% (20/913)
Beta	0% (0/1)	0,0% (0/913)
Gamma	20% (2/10)	0,2% (2/913)
Delta	17,0% (891/5227)	97,6% (891/913)

Table 1: *(*) Ratio of the number of returning travelers tested positive for a given VOC and the total number of persons tested positive for that VOC; (**) Ratio of 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 30-37).*

4. 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 are provided by Sciensano. For the last two months, no variant information is available for re-infection cases. To facilitate the identification of re-infections, a similar alert message has recently been set up by HealthData notifying the lab that a particular sample meets the criteria of a re-infection case. Such samples can be transferred to the NRC.

5. 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.

For the last two months, of the 180 COVID-19 patients that were hospitalised and for which variant data is available, the large majority (76.7%) was reported to be infected with the Delta variant. Of note, for about 22% (40/180), no details were specified with respect to the Pangolin lineage that was identified. Both for the Beta and Gamma variant, no cases were identified, while for Alpha only one.

The low number of hospitalized patients for which variant data is available can be explained by the fact that disease severity was until recently 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. According to a recent RAG advice (revision date 30/8/2021), a more representative and systematic sample of infections in hospitalized patients should be targeted.

6. 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 receive an automatic message from HealthData notifying them that a particular sample meets the criteria of a post-vaccination breakthrough case. According to a recent RAG advice (revision date 30/8/2021), there is no longer a need to systematically sequence all breakthrough cases. It was agreed that only samples of infections of fully vaccinated persons with a severe disease course (hospitalisation) should be systematically sequenced, as well as samples of fully vaccinated residents of nursing homes.

According to data provided by Sciensano, the weekly evolution of the frequency of variants of concern for the post-vaccination breakthrough infections largely overlaps the trends that are observed according to the baseline surveillance of the last two months (see Figure 3).

7. Spatial mixing in Belgian Delta infections

As mentioned in one of the previous reports, a few predominantly Belgian clusters can be determined in the overall Delta phylogeny (see Figure 5). This is not uncommon and has been observed for the Delta genomes from the United Kingdom as well.

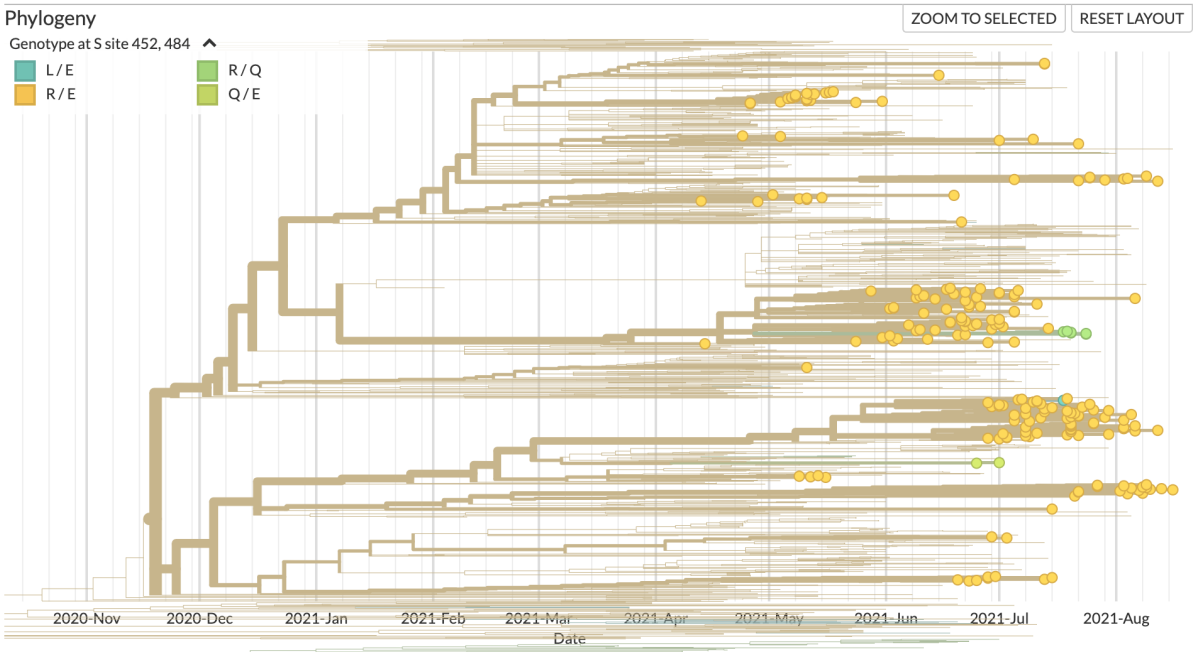

Figure 5: *Updated Delta nextstrain build with focus on Belgium (shown by the highlighted tips), showing specific L452R and E484Q mutations on top of Delta. Additionally, several clades mostly consisting of Belgian Delta genomes can be identified.*

In Figure 6, we focus on one of these predominantly Belgian clades and colour the genomes according to the province of collection. No clear patterns of spatial clustering (per province) can be discerned in such clusters. Some smaller clusters of genomes from West Flanders can be observed, but these may be the result of targeted sampling, for example as a result of studying a local outbreak (as they have similar sampling dates).

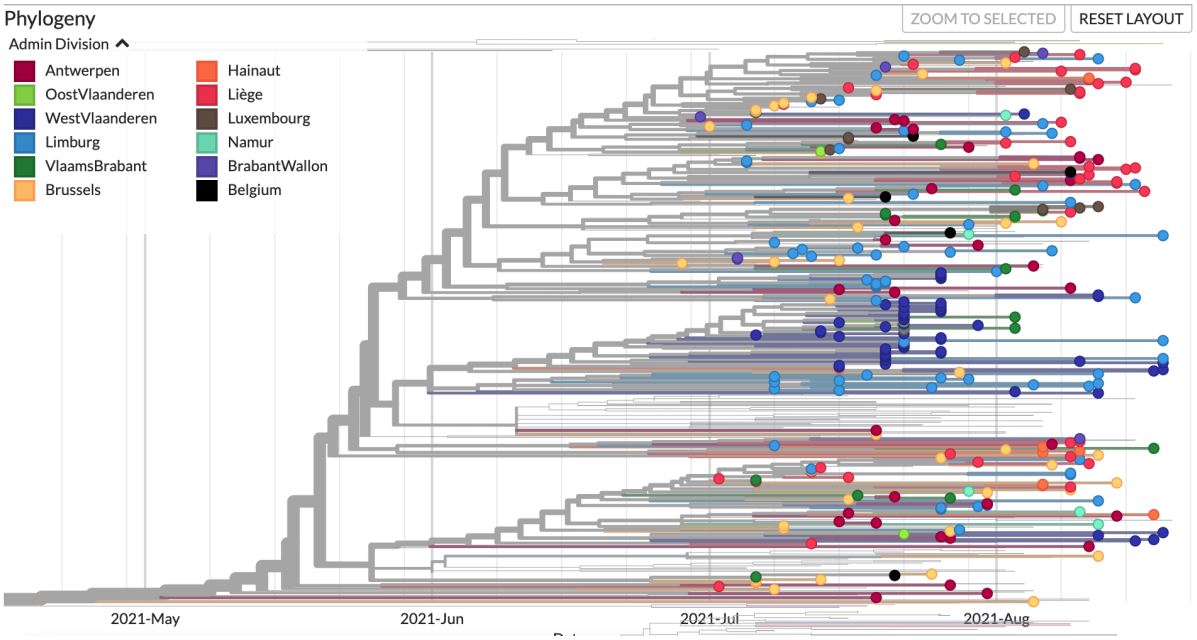

Figure 6: *Focus on one of the larger mostly-Belgian Delta clades shows no obvious clustering at the local (in this case province) level (genomes labeled in black indicate imprecise metadata).*