Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 8 of June 2021
(report 2021_31)

Executive summary

25.921 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID.

For baseline surveillance samples collected during the last two weeks (1060 sequences collected between 24 May and 6 June),
- B.1.1.7 (*Alpha*) represented 81.8% (compared to 84,6% in the last report) ↘
- P.1 (*Gamma*) represented 9,0% (compared to 10,5% in the last report) ↘
- B.1.617.2 (*Delta*) represented 3,9% (compared to 1,3% in the last report) ↗
- B.1.351 (*Beta*) represented 1,3% (compared to 0.1% in the last report) ↗

Other points of attention:
- The NRC performed 230 VOC PCRs on unselected positive samples analyzed during the last 7 days. B.1.1.7, P.1 and B.1.617.1/.2 represented respectively 81,3%, 11,3% and 7% (↗) of the results.

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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

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1. Monitoring of VOCs in Belgium

Over the last month, during which a representative and stable genomic surveillance could be ensured, B.1.1.7, P.1 (together with P.1.1) and B.1.617.2 represented respectively 80%, 10% and 4% of the sequences reported to GISAID from Belgium (combining baseline and active surveillance). All other variants together currently represent 5% of the circulating strains. The evolution of B.1.617.2 continues to increase. Considering the current incidence and the consolidated information on higher transmissibility of this variant, it is possible that an important viral population replacement phenomenon will occur during the coming weeks.

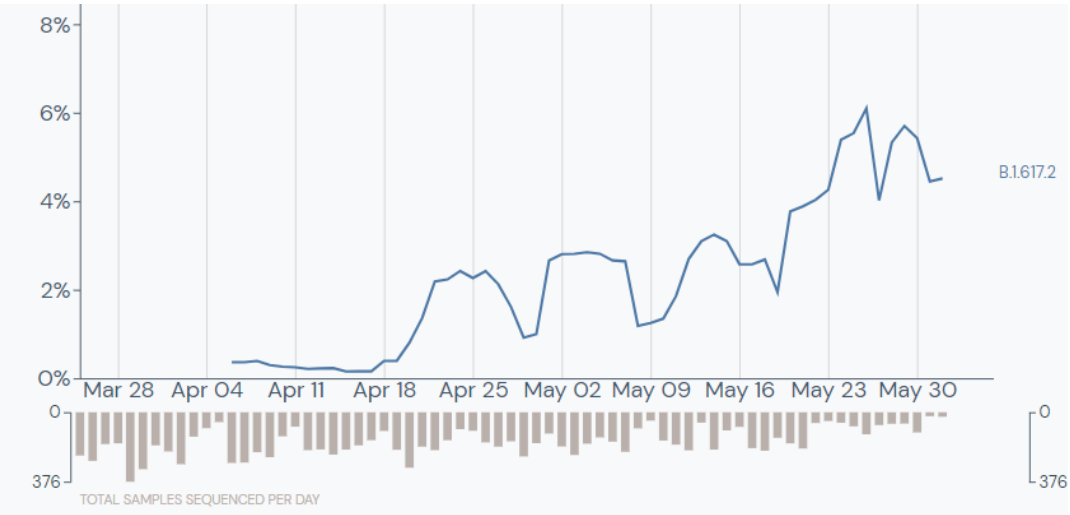

Figure 1: *B.1.617.2 prevalence over time in Belgium (combined active and baseline surveillance). (source: outbreak.info & GISAID).*

Over the last week, the NRC performed 230 VOC PCRs on unselected positive samples. B.1.1.7, P.1 and B.1.617.1/.2 represented respectively 81,3%, 11,3% and 7% of results. These proportions are slightly higher for P.1 and significantly higher for B.1.617.1/.2 compared to the proportions observed through the genomic surveillance system. This increase is in line with the growth advantage of these two VOCs.

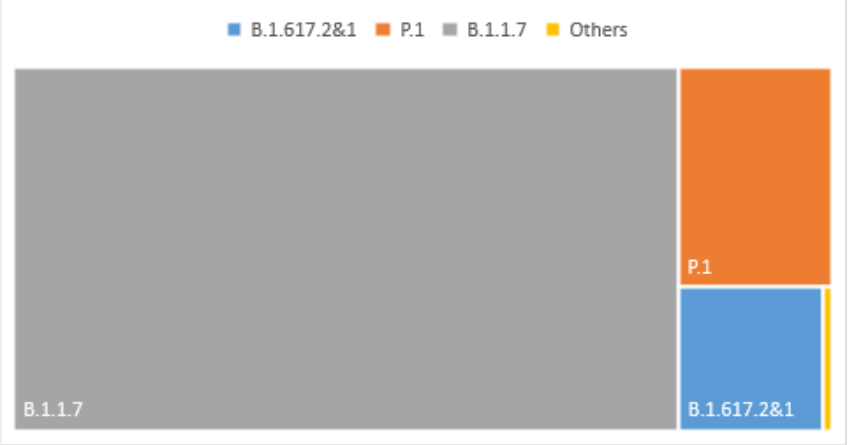

Figure 2: *VOC PCR results for the last week at the UZ Leuven/KU Leuven clinical laboratory. The NRC performed 230 VOC PCRs on unselected positive samples. B.1.1.7, P.1 (together with P.1.1) and B.1.617.1/.2 represented respectively 81,3%, 11,3% and 7% of results.*

Lineage	Number of Belgian cases reported on GISAID	First reported
B.1.1.7 (alpha)	15.512	30/11/2020
B.1.351 (beta)	934	20/12/2020
P.1 (gamma)	1.166	29/1/2021
B.1.617.2 (delta)	182	6/4/2021
B.1.1.7 +S:E484K B.1.1.7 +S:S477R	25 21	31/3/2021 15/3/2021
B.1.214.2	687	3/1/2021
B.1.525 (eta)	54	30/1/2021
B.1.620	64	31/3/2021
B.1.1.318	34	3/3/2021
A.27	19	11/1/2021
B.1.617.1 (kappa)	10	25/3/2021

Table 1: *List of VOCs (red) and VOIs (orange) identified in Belgium to date and cumulative number of sequences available on GISAID (total of 25.921 sequences)*

2. Turn-around-time of WGS in Belgium and demand for faster VOC identification by the Risk Management Group

The Risk Management Group (RMG) has informed the National Reference Laboratory that there was a demand to accelerate the identification of VOCs at the individual level in order to enhance the capacity of outbreak control.

The objective of baseline genomic surveillance is to inform public health makers about the emergence of variants and trends in their evolution over time. The inherent delay between the actual spread of variants and the moment when WGS results are made available is related to (1) the incubation phase after infection, (2) the delay between the indication of the test (ex: onset of symptoms) and the actual swabbing, (3) the TAT of the PCR test, (4) the transport of the sample to a sequencing laboratory and (5) the TAT of the whole genome sequencing analysis. Although TAT of WGS can certainly further improve, we do not expect that it will constitute the necessary tool to support targeted contact tracing interventions: the coverage of WGS is too low (less than 10% of the positive cases are currently analyzed by WGS) and the typing result will systematically be available with a delay incompatible with optimal contact tracing.

In order to overcome this challenge, our suggestions are:

- To introduce the VOC PCR currently used at the NRC at a larger scale. The updated design of this test includes the detection of 12 point mutations (4 PCR reactions) located in the Spike protein (501NYT, 484EKQ, 417KTN and 452LR/450K). This test could be available at least for the federal platform laboratories participating in the testing of returning travellers from June 15th on, and would allow detection of all current circulating VOCs and even some VOIs. Of note, there is currently no nomenclature foreseen for this test, and this may constitute an obstacle for scale-up.
- To extend backward contact tracing from (currently) 2 days to 7 days before onset of symptoms (or positive test result in case of absence of symptoms). This strategy has been used in the KU Leuven tracing approach and allowed to identify over ⅓ of the total infected contacts, which would otherwise have been missed. This approach has recently caught the attention of WHO and has been introduced in Ireland since then. This is a VOC-agnostic strategy, but constitutes a cornerstone to break transmission chains and identify super-spreading events.
- To include the vaccination status of both the index case and their high risk contacts in the assessment of transmission risk

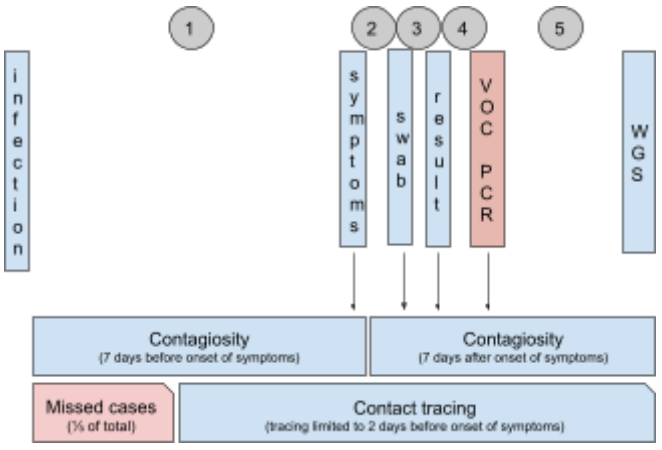

Figure 3: *Role of VOC PCR and extended backward contact tracing in strengthening VOC control.*

3. Monitoring of epidemiologic trends in different continents

The upcoming two months will be associated with intense travels in Europe and beyond, resulting in a significantly increased risk of massive importations of VOCs and VOIs by returning travellers, as it was the case at several occasions in the past (see report 30 for a more detailed discussion).

Hereunder, we highlight some potentially relevant epidemiological situations in different countries, with the aim to guide the testing & quarantine recommendations applied for travellers returning to Belgium.

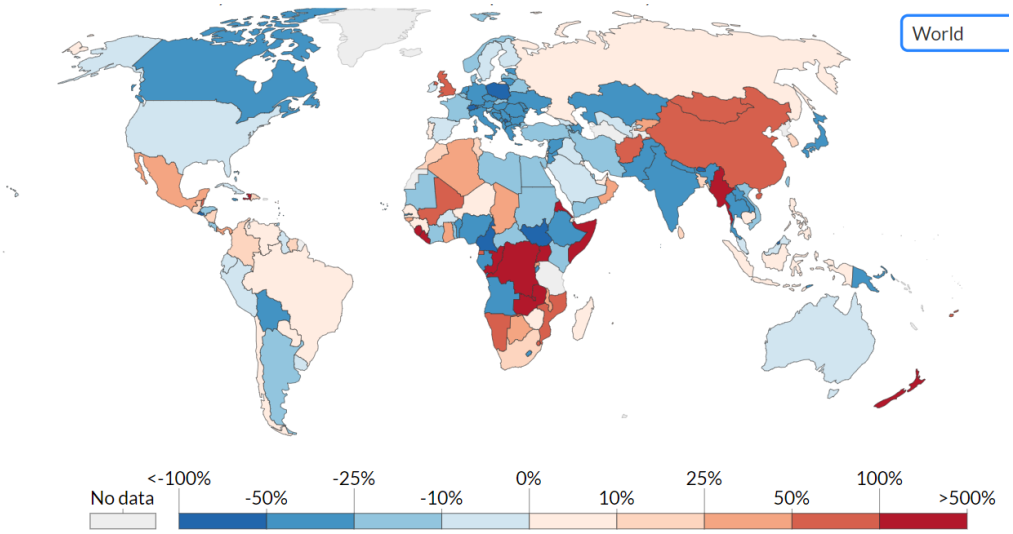

Figure 4: *Week by week change in confirmed COVID-19 cases (source: Our World in Data)*

In the European region, 3 countries (UK, Portugal and Russia) currently show a negative epidemiological trend associated with a rapid rise of the variant B.1.617.2. The United Kingdom has a >40% full vaccination coverage (important share of AZ vaccine), Portugal has a vaccination coverage of 20% (similar to other European countries in terms of vaccines used and vaccination coverage), and Russia has vaccination coverage of 10% (important share of Sputnik vaccine).

Although B.1.617.2 is associated with a certain level of immune escape, the majority of the infections in these countries are probably occurring among unvaccinated and not fully people. This phenomenon has not yet translated into a significant increase of new hospitalizations in the United Kingdom and Portugal (data not available for Russia).

While not showing at this stage any sign with regard to a surge of cases, Greece seems to be undergoing a rapid viral replacement phenomenon, with B.1.1.38 now representing the majority of new infections. This variant is currently not recognized as a variant of concern, but nevertheless harbours a number of mutations in the Spike protein also seen among other VOCs (in particular S:E484K and S:P681H). The situation in this country should therefore be closely monitored during the upcoming weeks.

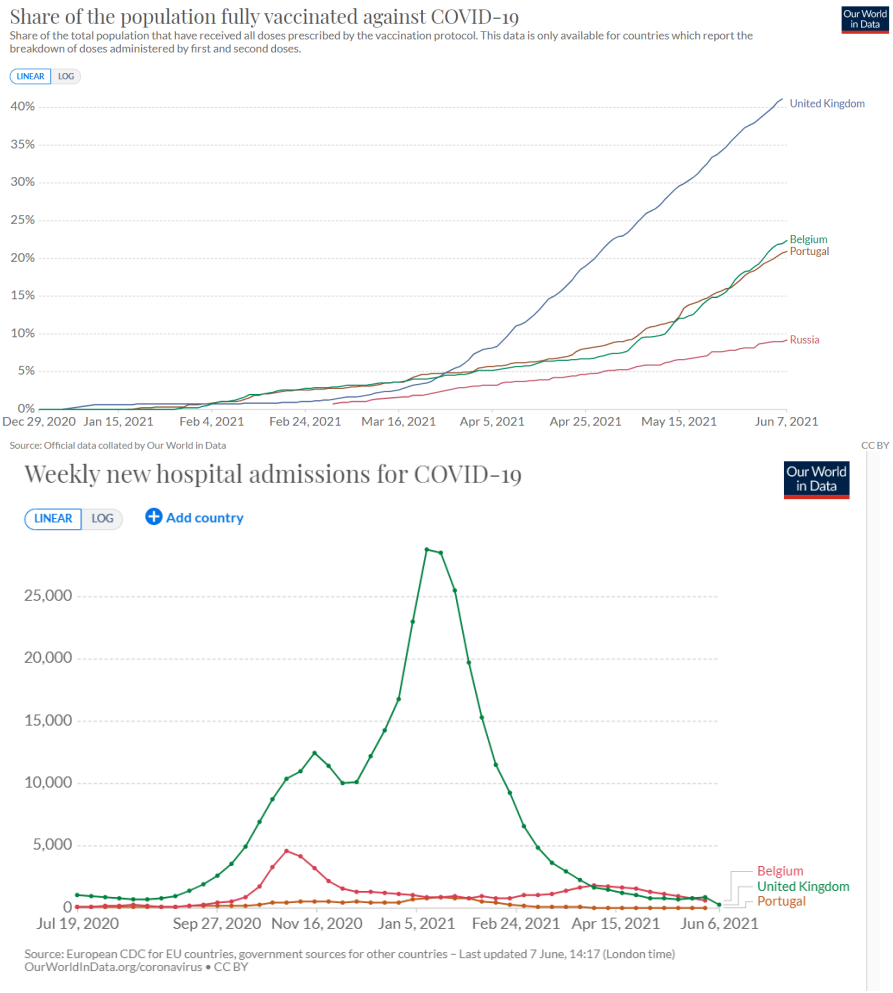

Figure 5: *Share of the population fully vaccinated and weekly new hospital admissions for COVID-19 in the UK, Portugal, Russia and Belgium.*

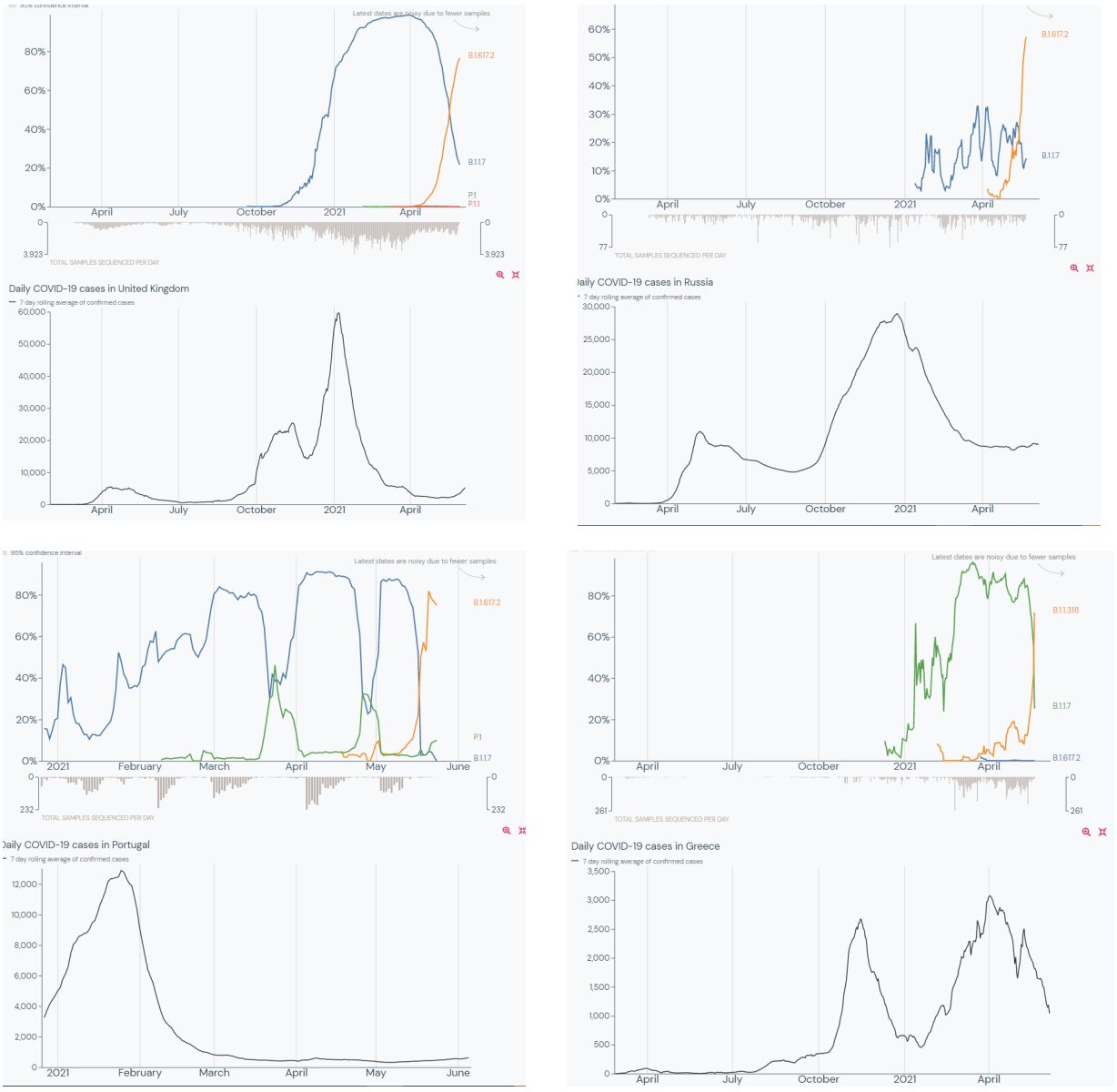

Figure 6: *Evolution of the share of viral populations and epidemiological situation in the United Kingdom, Russia, Portugal and Greece. (source: outbreak.info & GISAID).*

In the African region, a significant number of countries (including the Democratic Republic of Congo (DRC), South Africa and Morocco) currently show a negative epidemiological trend, and it is difficult to understand the potential role played by different variants as the genomic surveillance is insufficiently representative in most countries. South Africa observed a recent rise of B.1.617.2 cases. The most alarming situation at the moment seems to be observed in Central African countries, in particular the DRC. But once again, the under-reporting of cases and the absence of reporting of new hospitalizations makes the assessment particularly difficult.

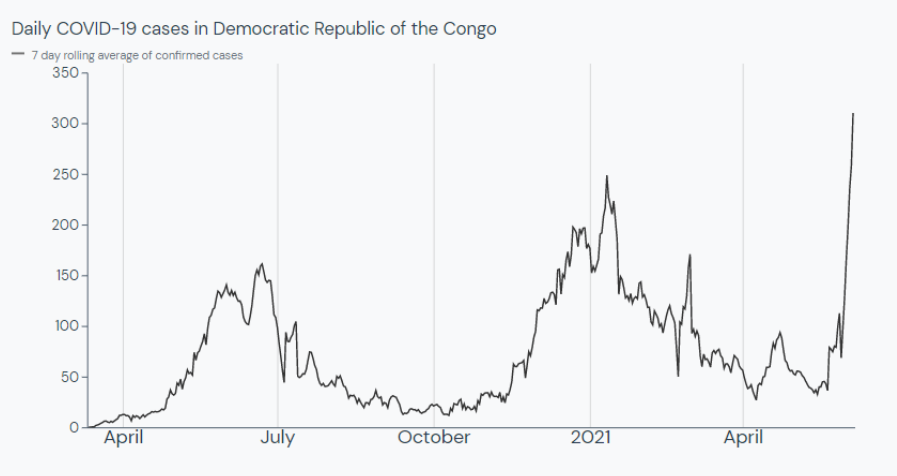

Figure 7: *Important increase of the number of COVID-19 infections in the Democratic Republic of Congo. It should be noted that the absolute numbers are very limited, possibly highlighting a very significant problem of underdiagnosis (scarcity of diagnostic ressources).*

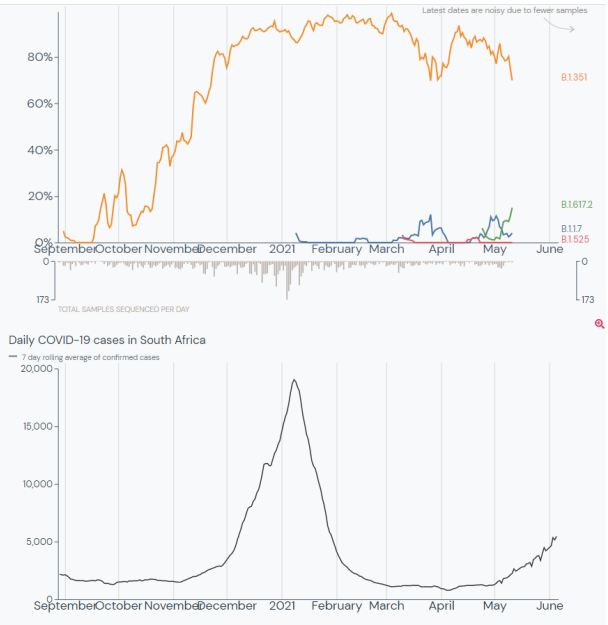

Figure 8: *Surge of COVID-19 infections in South-Africa (now in the winter season), possibly associated with B.1.351 resurgence and/or with a recent rise of B.1.617.2 infections.*

Morocco currently has a vaccination coverage of 15% (mainly Sinopharm and Sinovac vaccines), but other countries across the continent including DRC have a very low (anecdotal) vaccination coverage. An important surge with important sanitary consequences could therefore be ongoing on the African continent.

In the central and South American regions, several countries are now observing a surge of cases. Aside from Brazil, Mexico and Colombia currently show a negative trend. Due to insufficient genomic surveillance in these countries, the role of the different variants is still unclear, and may be multifactorial. As an illustration, P.1, B.1.617.2 and B.1.526 are currently rising in Mexico and are probably playing a synergistic role.

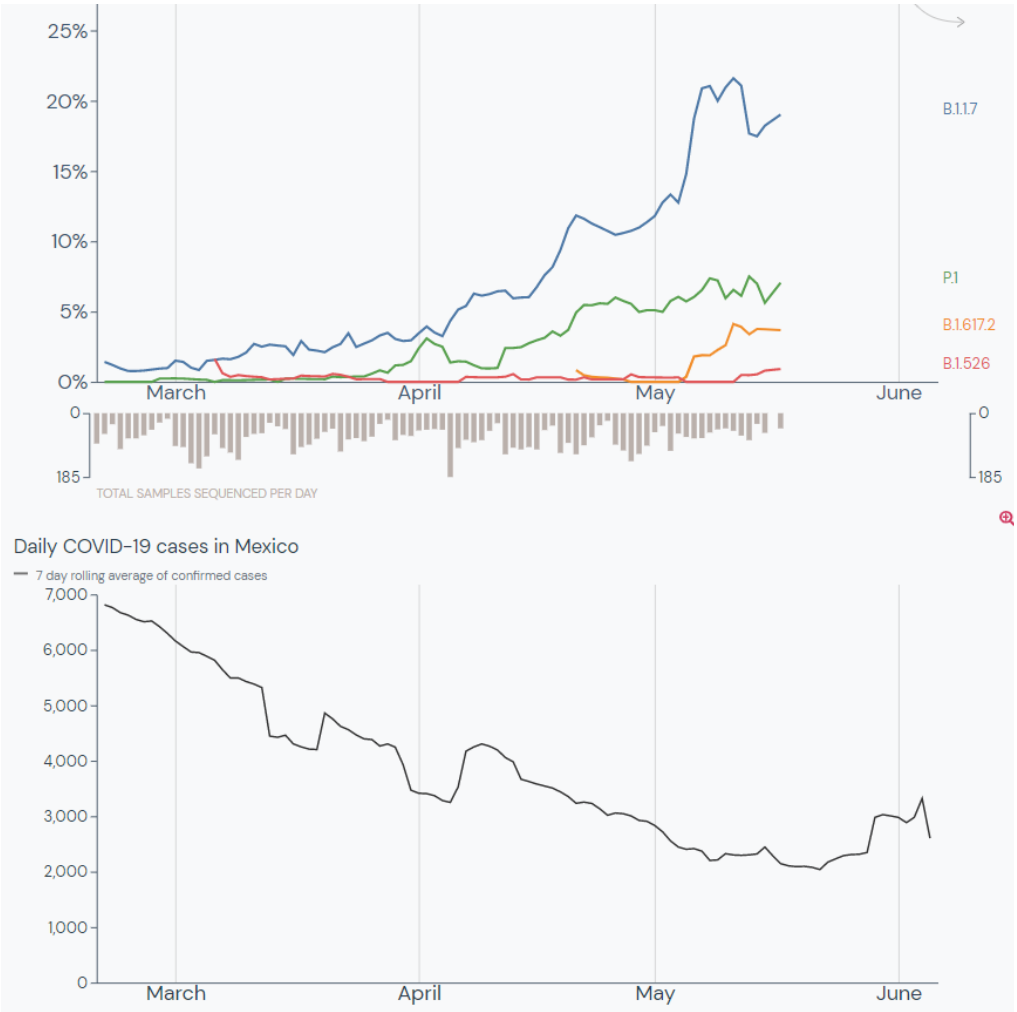

Figure 9: *Recent increase in the number of cases in Mexico in the context of a concomitant rise of B.1.1.7, P.1, B.1.617.2 and B.1.526.*

4. Update on B.1.525 in Belgium

We provide hereunder an overview with regard to the epidemiologic situation of B.1.525, a variant which has been under active surveillance for several weeks following a number of imported cases. This VOI harbours the E484K and F888L mutations (see Figure 10, B.1.525 shown in light green at the top of the phylogeny). In Belgium, only une genome has been shared on GISAID during the last month (a sample from early May).

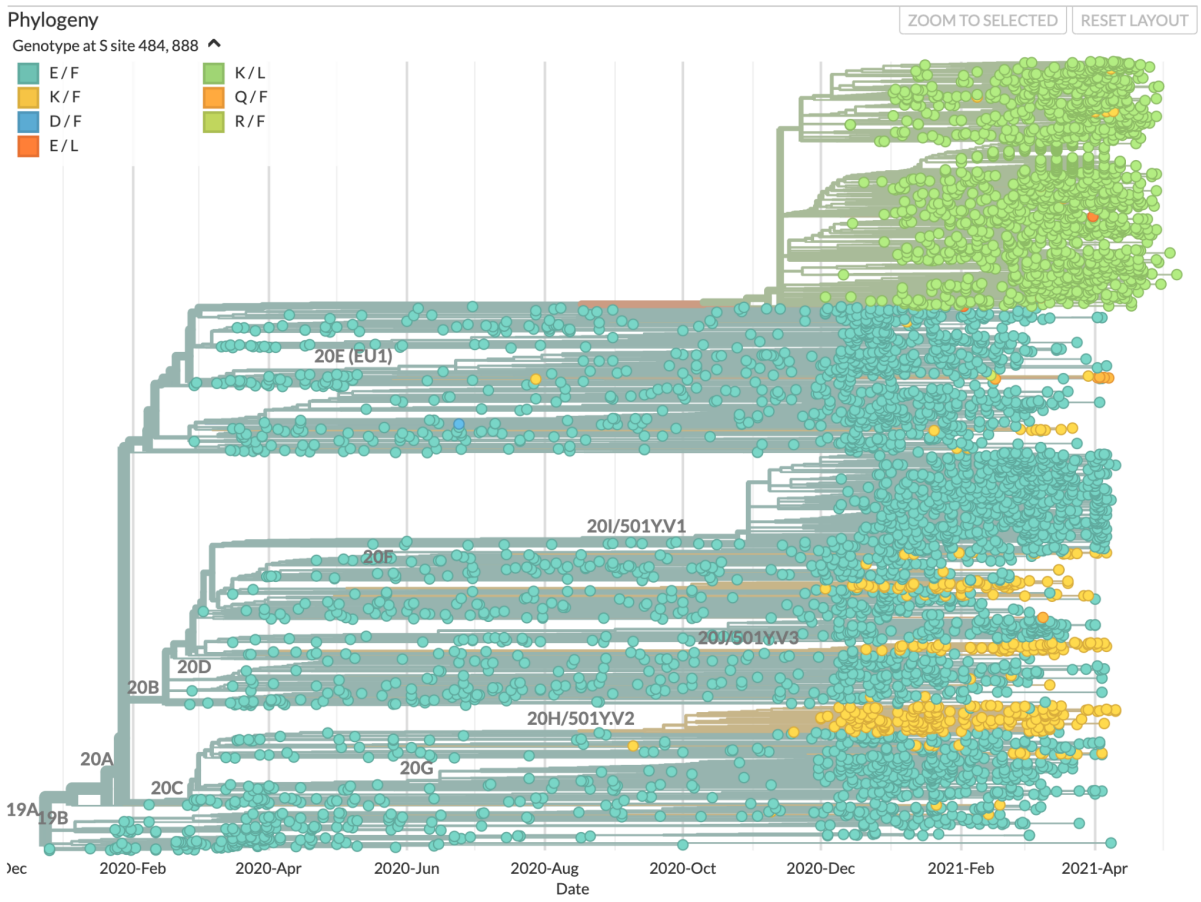

Figure 10: *Overview of the global B.1.525 phylogeny including all currently available Belgian genomes. All Belgian genomes were included while for other countries a representative set is part of the tree.*

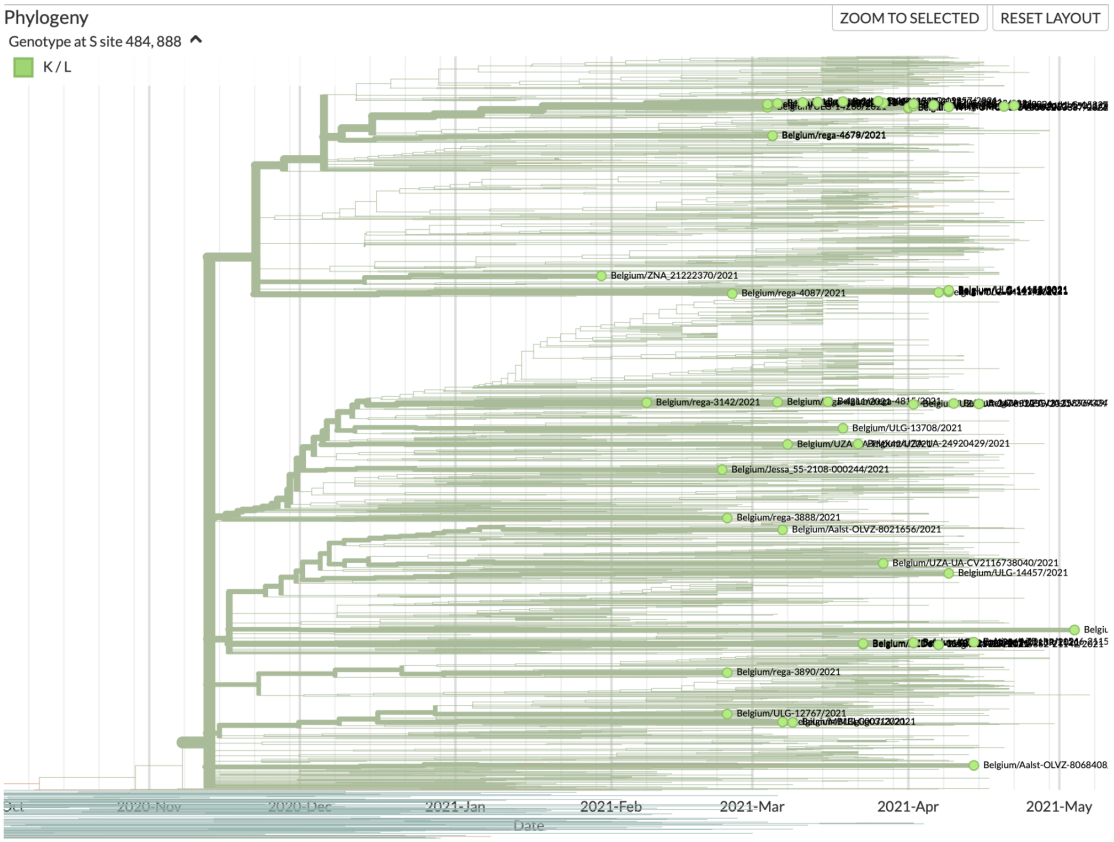

Figure 11: *The B.1.525 infections in Belgium were imported by mostly independent introductions from abroad. Some of these introductions have led to small localized clusters of infections (Figure 12).*

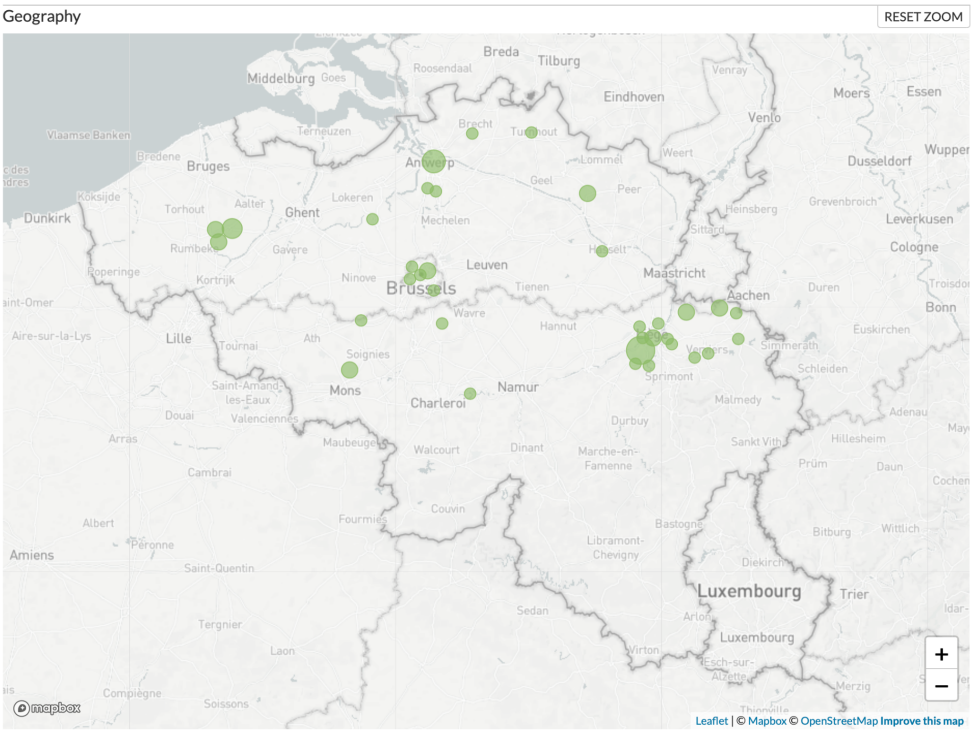

Figure 12. *Small local B.1.525 outbreaks have been observed in Liège, Brussels, Antwerp and West Flanders (region surrounding Tielt).*

5. Update on B.1.617.2 (delta) and B.1.617.1 (kappa) in Belgium

Our custom B.1.617 Nextstrain build that focuses on the situation in Belgium clearly shows the two major variants (B.1.617.1 and 2) that were first identified in India in Figure 13. Both variants are characterized by the occurrence of the amino acid Arginine (R) on position 452 in the S-gene or the so-called mutation L452R. While variant B.1.617.2 did not harbour an amino acid change on position 484, variant B.1.617.1 is characterized by the presence of mutation E484Q.

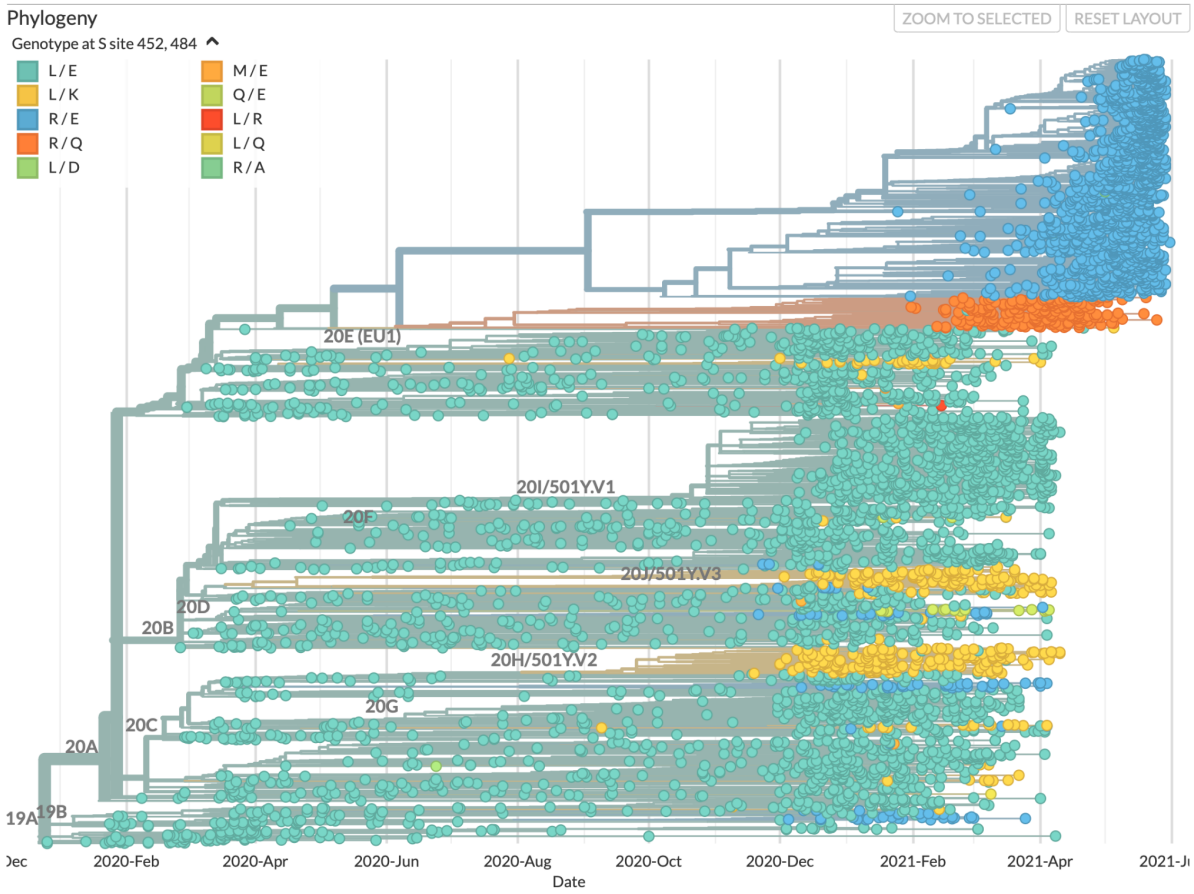

Figure 13. *A large clade of B.1.617.2 genomes (coloured in light blue) and a smaller clade of B.1.617.1 (coloured in dark orange) are shown on the top of the global SARS-CoV-2 phylogeny and shown in more detail in Figure 14.*

Figures 14 and 15 show that the B.1.617.2 infections within Belgium stem from a range of independent introductions into the country, which led to small and larger local transmission clusters.

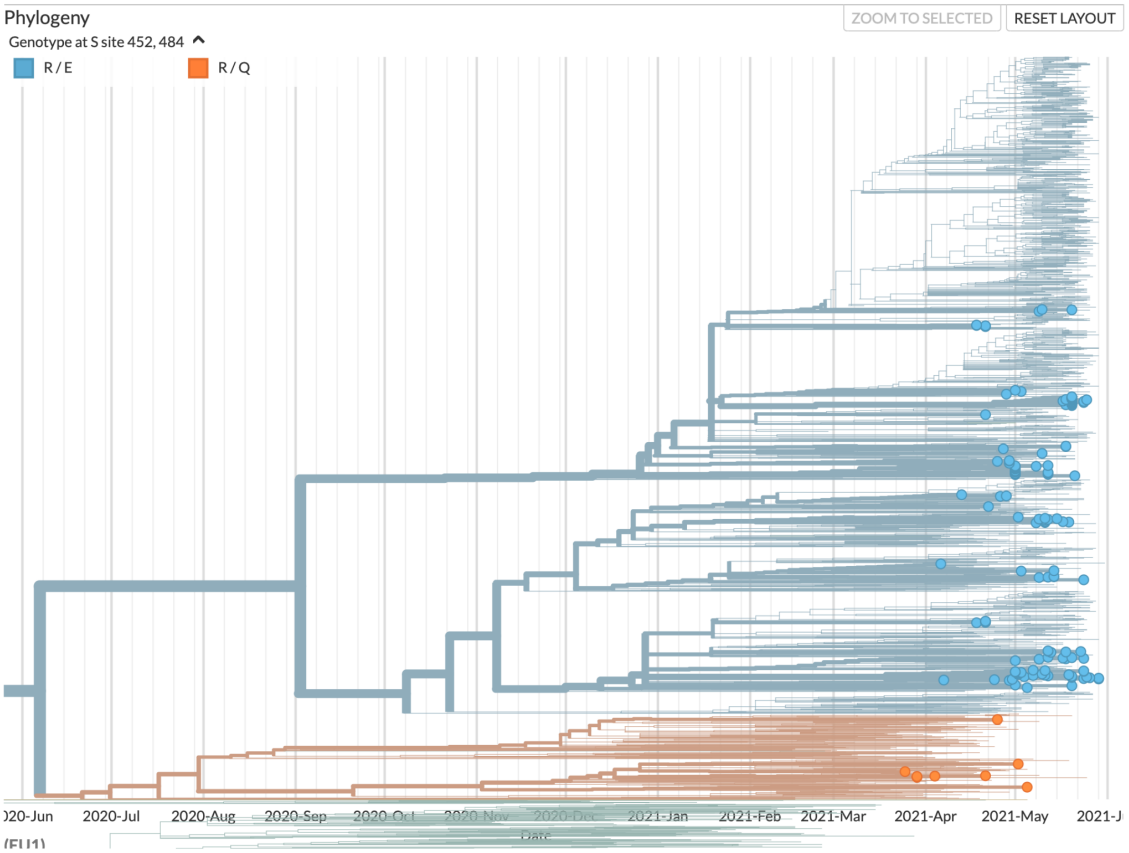

Figure 14: *The currently available Belgian B.1.617.1 (orange) and B.1.617.2 (blue) genomes on GISAID are highlighted in the tree, showing many introductions into Belgium (Belgian genomes indicated as dots in the tree) and are not the result of a single source of origin. This illustrates the importance of screening incoming travelers and performing contact tracing.*

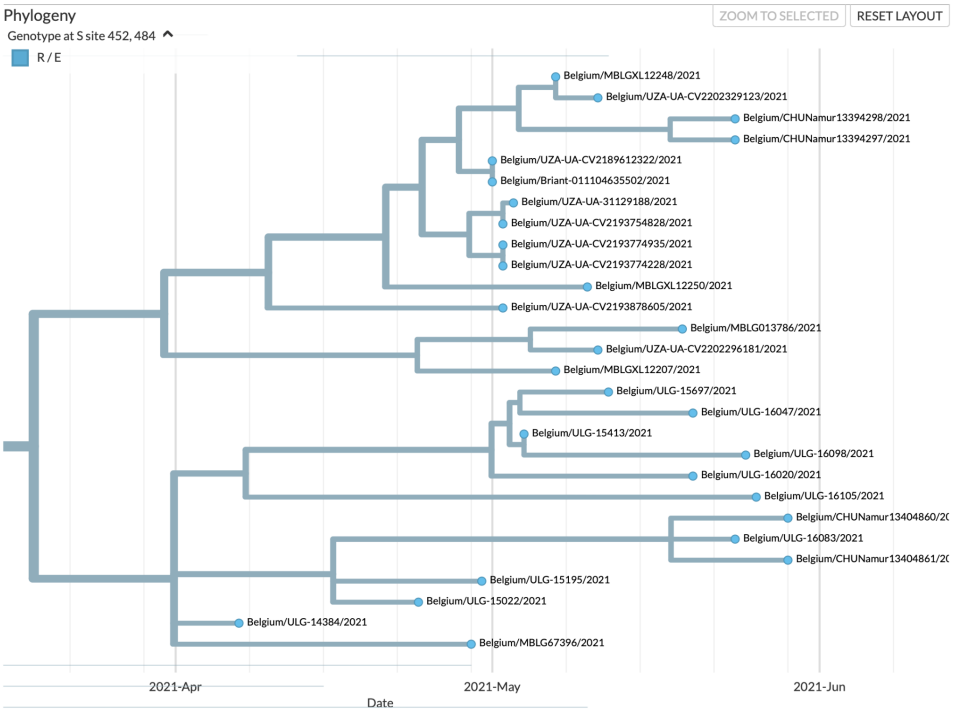

Figure 15. *Example of a large local B.1.617.2 transmission cluster within Belgium.*

Figure 16 shows the geographic spread of both B.1.617.1 and B.1.617.2 lineages, with for each province already documented cases but most infections being situated around the Brussels Capital Region and the city of Antwerp.

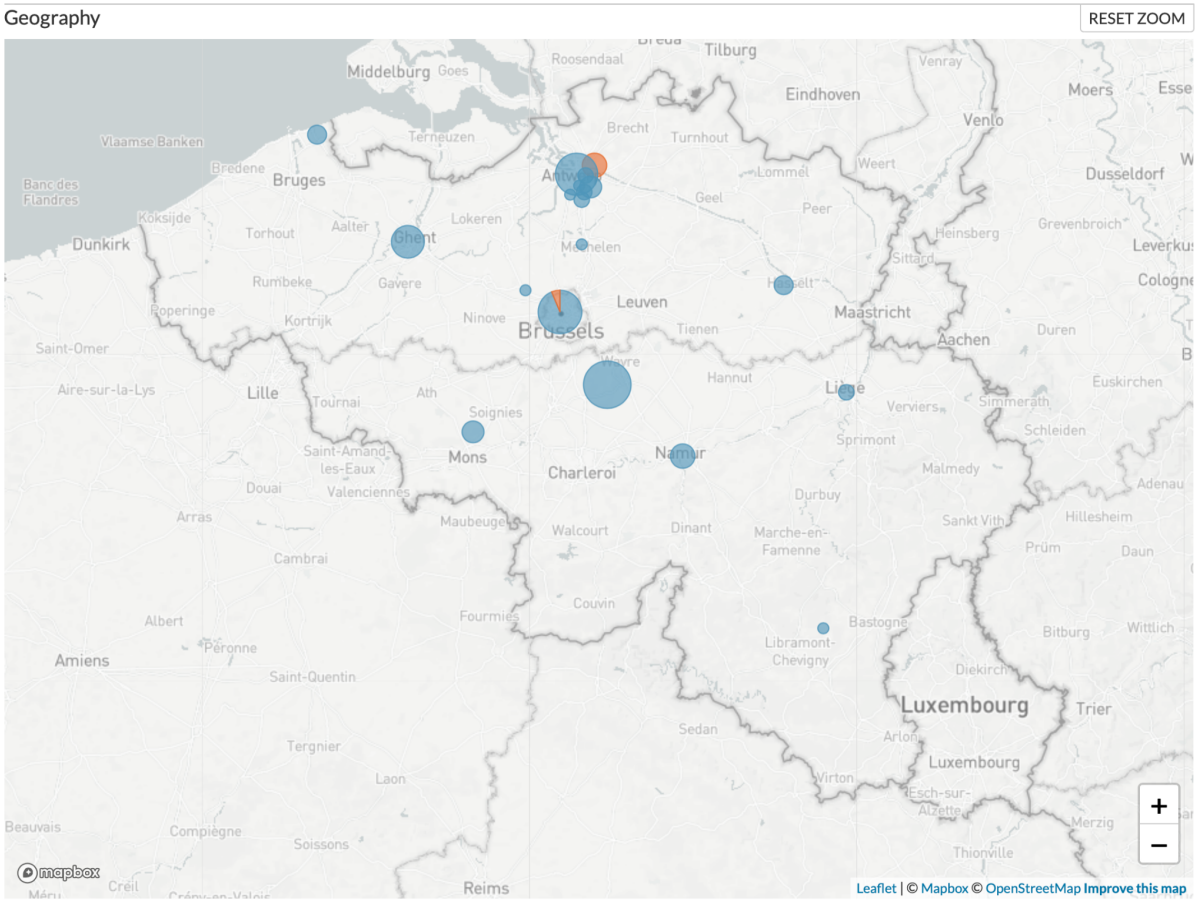

Figure 16. *Geographic spread in Belgium of B.1.617.1 (orange) and B.1.617.2 (blue) genomes.*