Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 11th of May 2021
(report 2021_26)

Executive summary

18,530 Belgian sequences of SARS-CoV-2 are publicly available on GISAID.

For baseline surveillance samples collected during the last two weeks (1.077 sequences collected between 26 April and 9 May),
- B.1.1.7 (20/501Y.V1) represented 89,5% (compared to 87.3% in the last report).
- P.1 (20J/501Y.V3) represented 4.3% (compared to 5,3% in the last report).
- B.1.351 (20H/501Y.V2) represented 0,9% (compared to 2.3% in the last report)

Other points of attention:
- Twelve sequences of B.1.617.2 were deposited on GISAID between 6 and 29 April. These observations are to be associated with recent reports of travel-related and non-travel-related infections. The NRC is aware of 20 infections of B.1.617.1 and B.1.617.2 on top of 2 clusters (one cluster of travellers from India and one cluster in a nursing home).
- Six sequences of B.1.1.7 with the S:E484K mutation were deposited on GISAID between 31 March and 25 April.

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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

Three variants of concern (VoCs) have been introduced in Belgium around the end of the year 2020. The B.1.1.7 variant which has been introduced through numerous parallel introductions, has since then become the dominant lineage in the country and is considered as responsible for the latest epidemic resurgence ("third wave").

Over the last month, during which a representative and stable genomic surveillance could be ensured, VoCs (B.1.1.7, P.1, and B.1.351) represented respectively 82%, 10% and 2% of the sequences reported to GISAID from Belgium. The evolution of the viral population is thus relatively stable for the moment, and the constant increase of P.1 cases does not seem to accelerate.

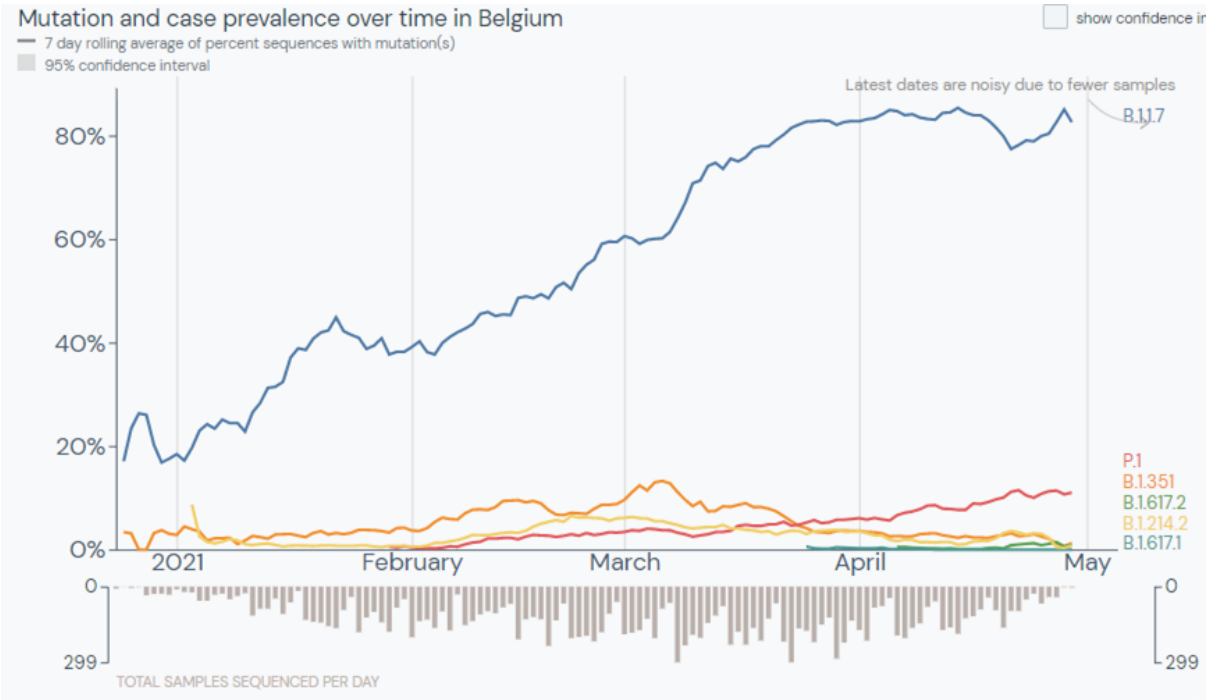

Figure 1: *Lineage prevalence over time in Belgium. B.1.1.7, P.1, B.1.351 and B.1.617.2 are currently classified as VoCs. B.1.617.1 and B.1.214.2 are among the variants actively monitored in the country (source: outbreak.info & GISAID).*

<u>Particular attention to be given to B.1.617.2 (new VoC originally described in India)</u>

Belgium should remain very attentive to the potential risks associated with the B.1.617.2 lineage. Although evidence should be consolidated, recent reports from New Delhi and the UK suggest that this lineage could rapidly replace other viral populations, even though the lineage B.1.1.7 is dominant. This variant has demonstrated a certain level of immune escape (laboratory experiments[1], post-vaccination infections and re-infections already notified in Belgium and elsewhere) while the spike mutation P681R could potentially lead to an increased severity of disease (only studies performed on animal models at this stage[2]). Deploying important efforts to limit the introduction and spread of this variant and contain its spread will allow to gain time used for vaccination rollout.

[1] https://www.biorxiv.org/content/10.1101/2021.05.08.443253v1
[2] https://www.biorxiv.org/content/10.1101/2021.05.05.442760v1

2. Evaluating the transmission advantage of SARS-CoV2 variants of concern in Belgium

To estimate the difference in growth rate (per day) between the variants of concern B.1.351, and P.1 compared to that of B.1.1.7, we fitted a multinomial model to the baseline surveillance sequencing variant counts (aggregated by week) reported in the weekly Sciensano report of the 8th of May 2021 (Figure 2)[3]. We should note here that these estimates do not include the presence of B.1.617.2 in Belgium. The further evolution of the situation will thus importantly depend on the upcoming ability of the country to prevent and control infections associated with this highly transmissible variant.

The resulting estimates are listed in Table 1. Compared to B.1.1.7, B.1.351 is currently decreasing in abundance. By contrast, P.1 has a small but significant growth rate benefit of 1.5% per day ([0.3%,2.6%] 95% CLs) compared to the variant B.1.1.7, which corresponds with a 7% transmission advantage ([1%-13%] 95% CLs). From this multinomial fit, B.1.1.7, B.1.351 and P.1 are estimated to make up 87% [84-90%], 0.6% [0.3-0.9%] and 10% [7-13%] of all lab diagnoses today (on the 10th of May 2021).

Table 1. Estimated growth rate contrasts (differences in growth rate per day) among different pairs of SARS-CoV-2 variants of concern as well as the wild type (here defined as all other lineages) and corresponding transmission advantages, evaluated on 10th of May 2021.

Comparison	Growth rate contrast Dr [95% CLs] (per day)	Transmission advantage (fold difference)	*p* value
B.1.1.7 *versus* wild type	0.033 [0.026,0.40]	X 1.16 [1.13,1.21]	< 0.0001
B.1.351 *versus* B.1.1.7	-0.046 [-0.059,-0.034]	X 0.80 [0.76,0.85]	< 0.0001
P.1 *versus* B.1.1.7	0.015 [0.003,0.026]	X 1.07 [1.01,1.13]	0.006

[3] This model was fit using the *multinom* function in the *nnet* R package and used a 2 degree of freedom natural cubic spline in function of sample collection date. Subsequently, the differences (contrasts) in growth rate (Dr) among the different variants evaluated on the 5th of May 2021, were calculated using the *emtrends* function in the *emmeans* R package, using a Tukey correction for multiple testing (for details on methodology see Davies *et al. Science* 2021). From these growth rate contrasts, the relative transmission advantage was calculated as the exponent of the product of these growth rate differences Dr and the generation time, which we set here at 4.7 days (Nishiura *et al.* 2020) (see Davies *et al. Science* 2021).

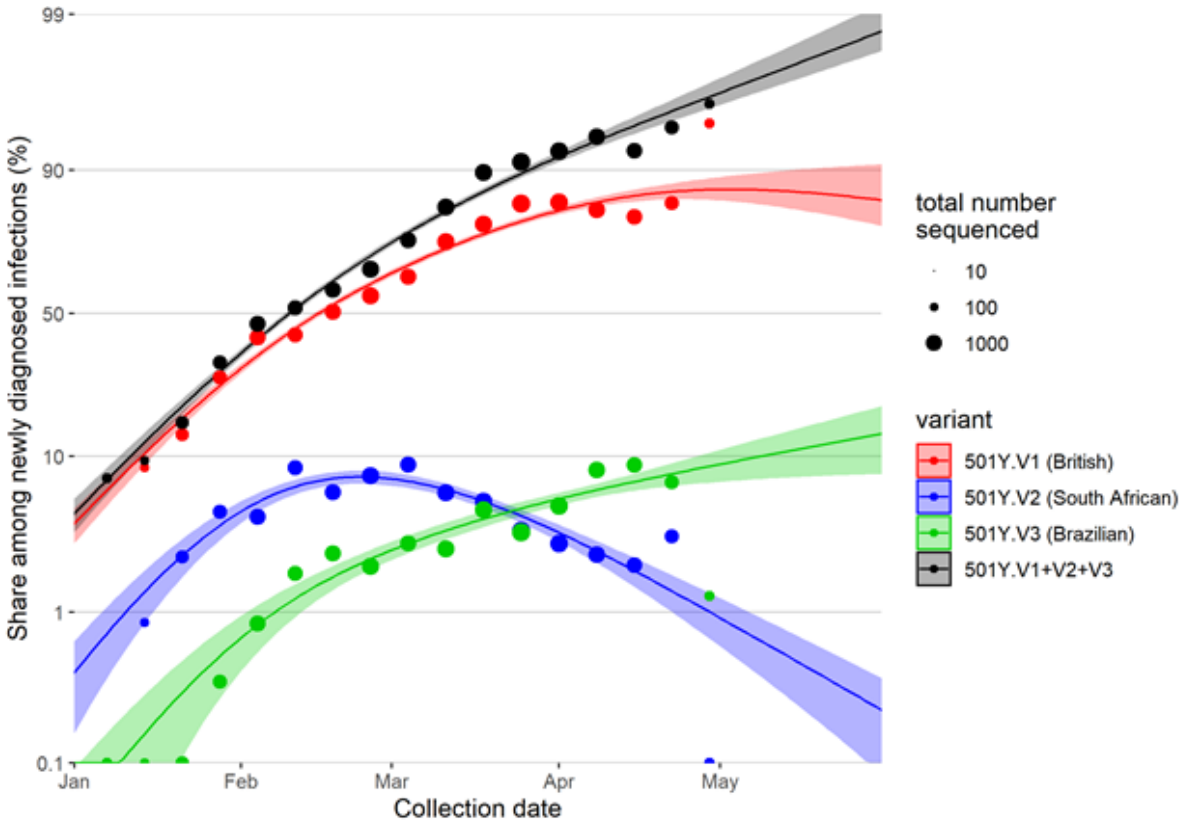

Figure 2. Multinomial fit (using a model with a 2 degree of freedom natural cubic spline in function of collection date) to the share of the 3 VOCs B.1.1.7 (red), B.1.351 (blue) and P.1 (green) shown on a logit Y scale (shaded bands are 95% confidence intervals).

3. Evolution of variants of concern in India and the United Kingdom

India

The current epidemiological situation in India is alarming and appears to be related to the simultaneous increase of three variants of concern: B.1.617.2 (mainly), B.1.1.7 and B.1.617.1. Recently, B.1.617.2 has been categorised as a VoC by the United Kingdom.

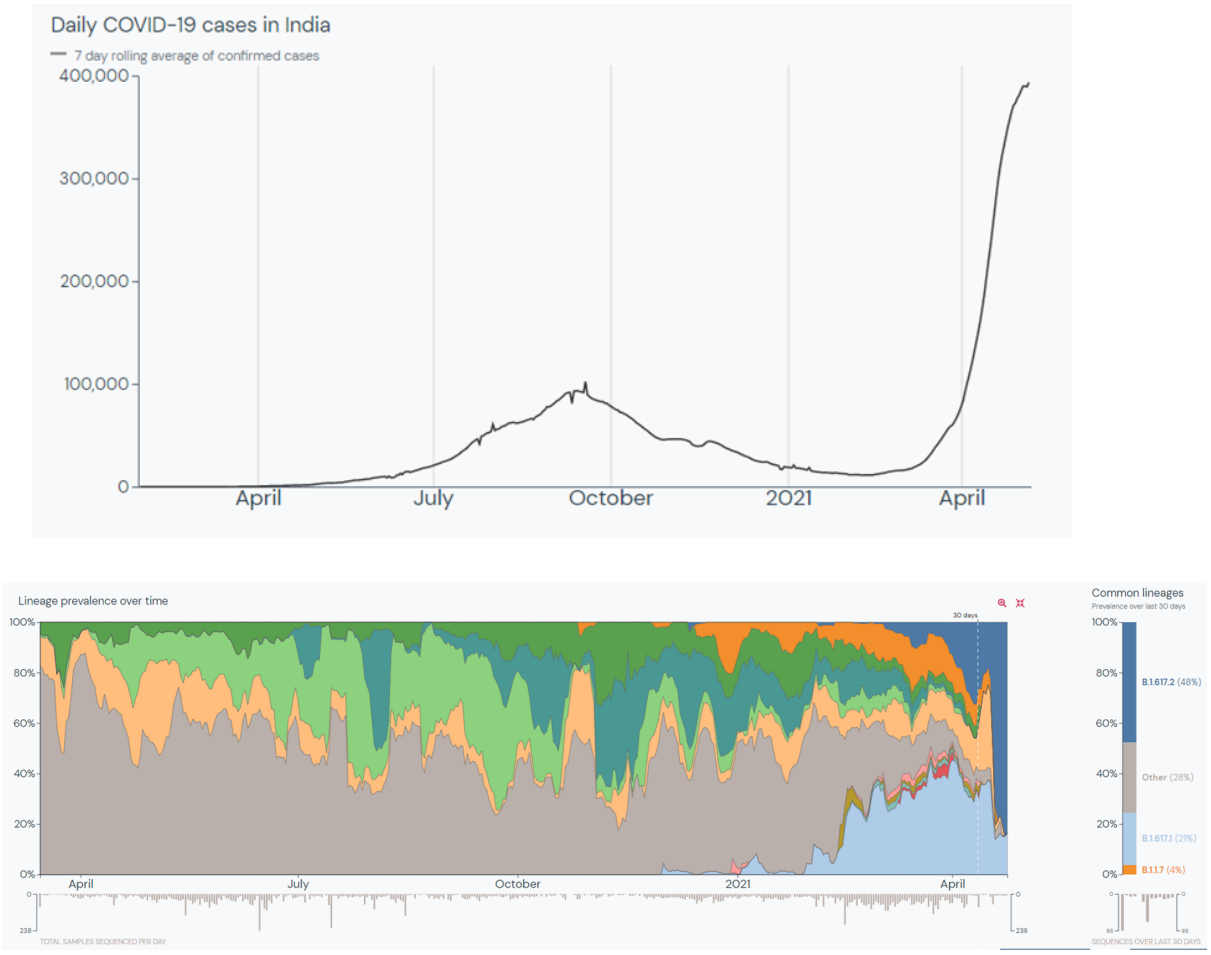

Figure 3: Epidemiological evolution and share of viral populations in India

The United Kingdom

The situation in the United Kingdom is closely monitored as this country has the largest genomic surveillance program, has a more advanced vaccination coverage compared to Belgium and also has B.1.1.7 as the dominant lineage, so observations from the UK are relevant for the belgian context.

In the context of a stable and low-level circulation of the virus, the UK observes a rapidly increasing number of B.1.617.2 infections. As the proportion of this new VoC is still limited compared to B.1.1.7, it is not yet possible to estimate the foreseen epidemiological impact of this phenomenon on the number of (severe) cases that will be associated with this variant in the coming weeks.

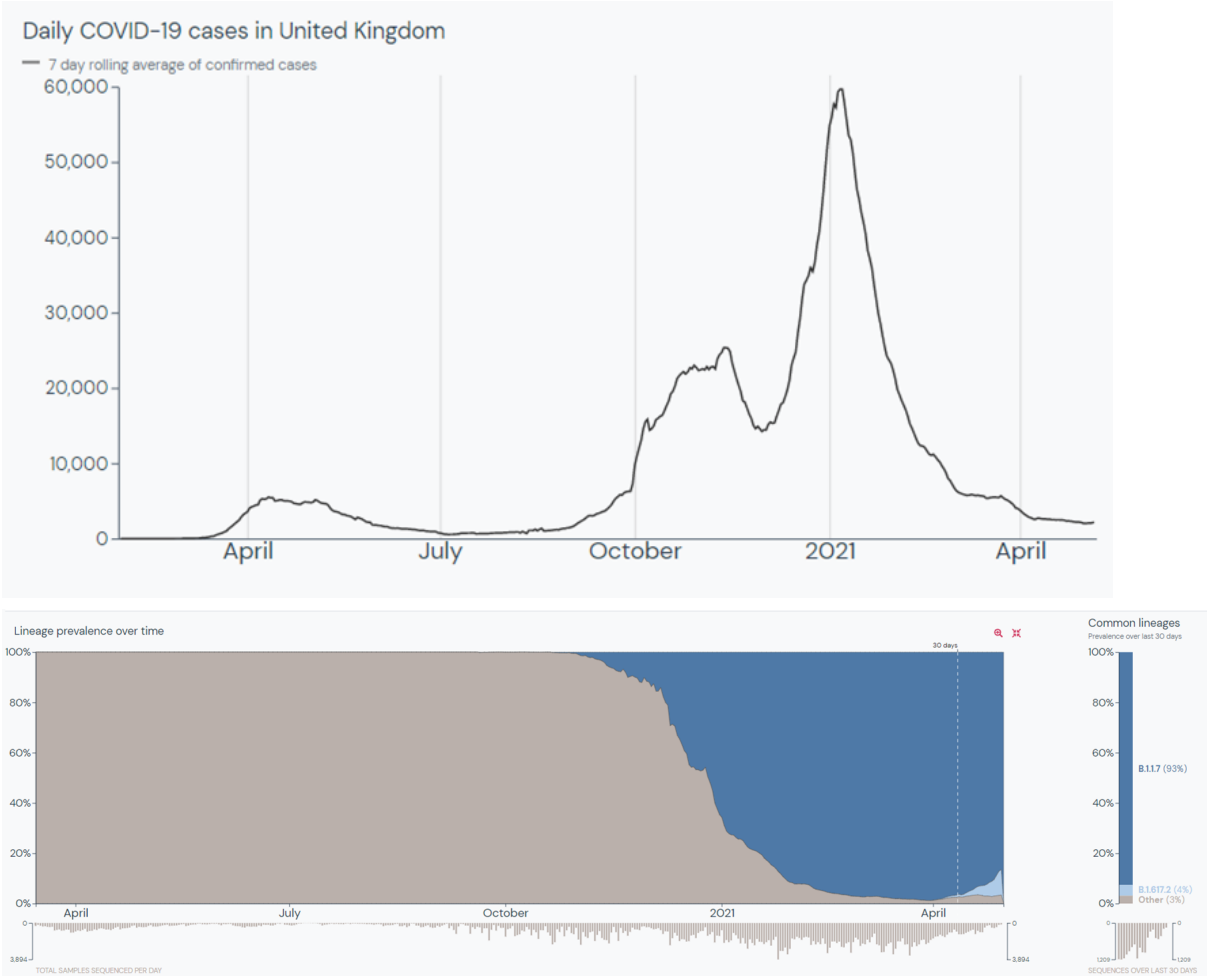

Figure 4: Epidemiological evolution and share of viral populations in the United Kingdom

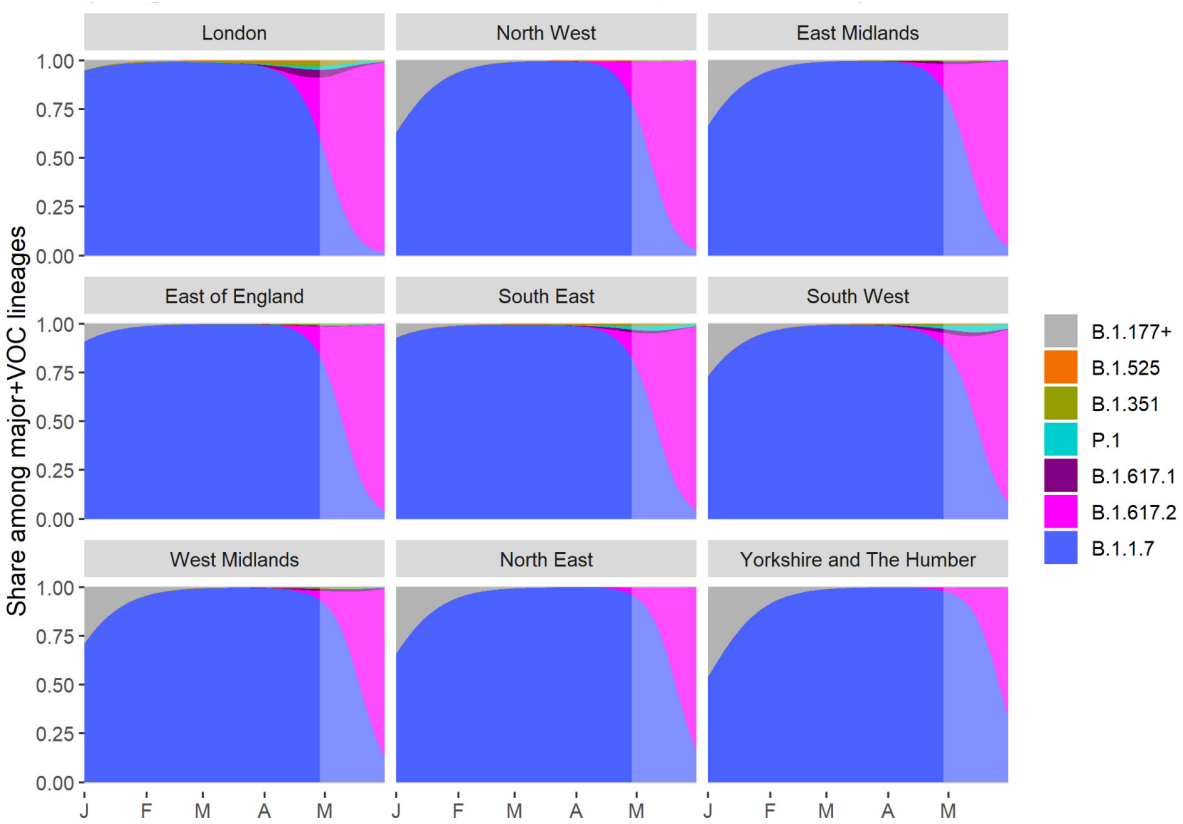

Figure 5: Spread of SARS-CoV-2 variants in different regions of the United Kingdom. A rapid replacement of the current viral population (majority of B.1.1.7) in favour of B.1.617.2 is to be expected (source: Sanger Institute surveillance data, multinomial fit).

4. Current situation of P.1 in Belgium

Belgium is currently among the Western European countries reporting the highest proportion of P.1, and this increasing trend is observed since February 2021. During the last two weeks, 4,3% of the unbiased samples (baseline surveillance) are associated with P.1. The difference observed between the baseline surveillance estimates and the estimates computed hereinabove can be partly associated with the current active case finding efforts (which lead to an over-representation of P.1 sequences on GISAID, but not reported in the baseline surveillance program) and the delay between the date of sample collection of baseline surveillance (this delay inevitably leads to an underestimation in the presence of an increasing trend).

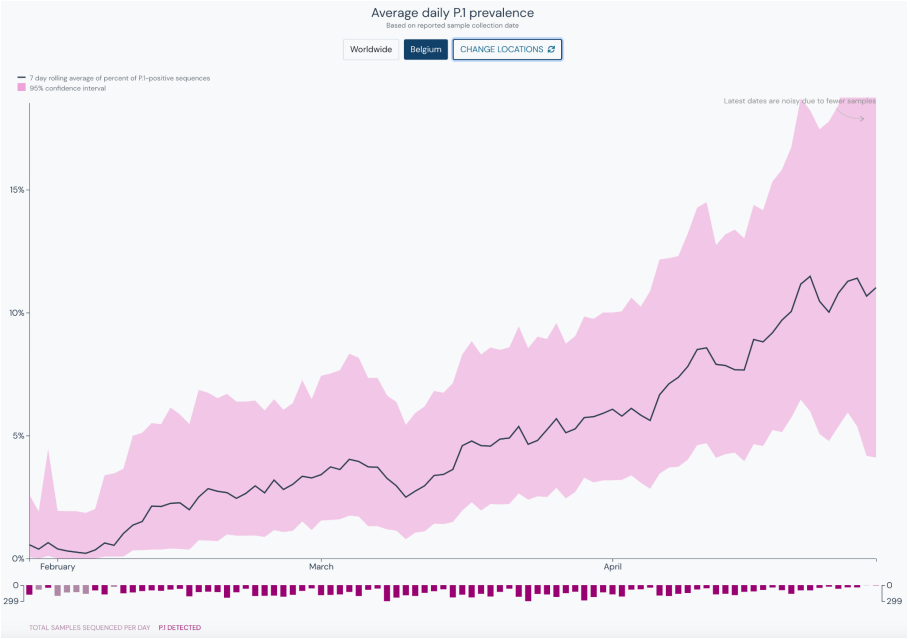

Figure 6: Evolution of P.1 sequences from Belgium deposited on GISAID since February 2021.

Based on a preliminary analysis performed in Belgium, it seems that there are among P.1 infections a significantly higher proportion of re-infections compared to what is observed for B.1.1.7 and B.1.351. These observations can be associated with immune escape properties of this variant and will be discussed in detail in a further report.

The P.1 circulation in Belgium is currently associated with 3 active clusters which are to be linked to returning travellers around the month of January 2020 (see Figure 7 which shows 552 Belgian P.1 genomes). As such, nearly all recent P.1 infections detected in Belgium are part of these 3 clusters.

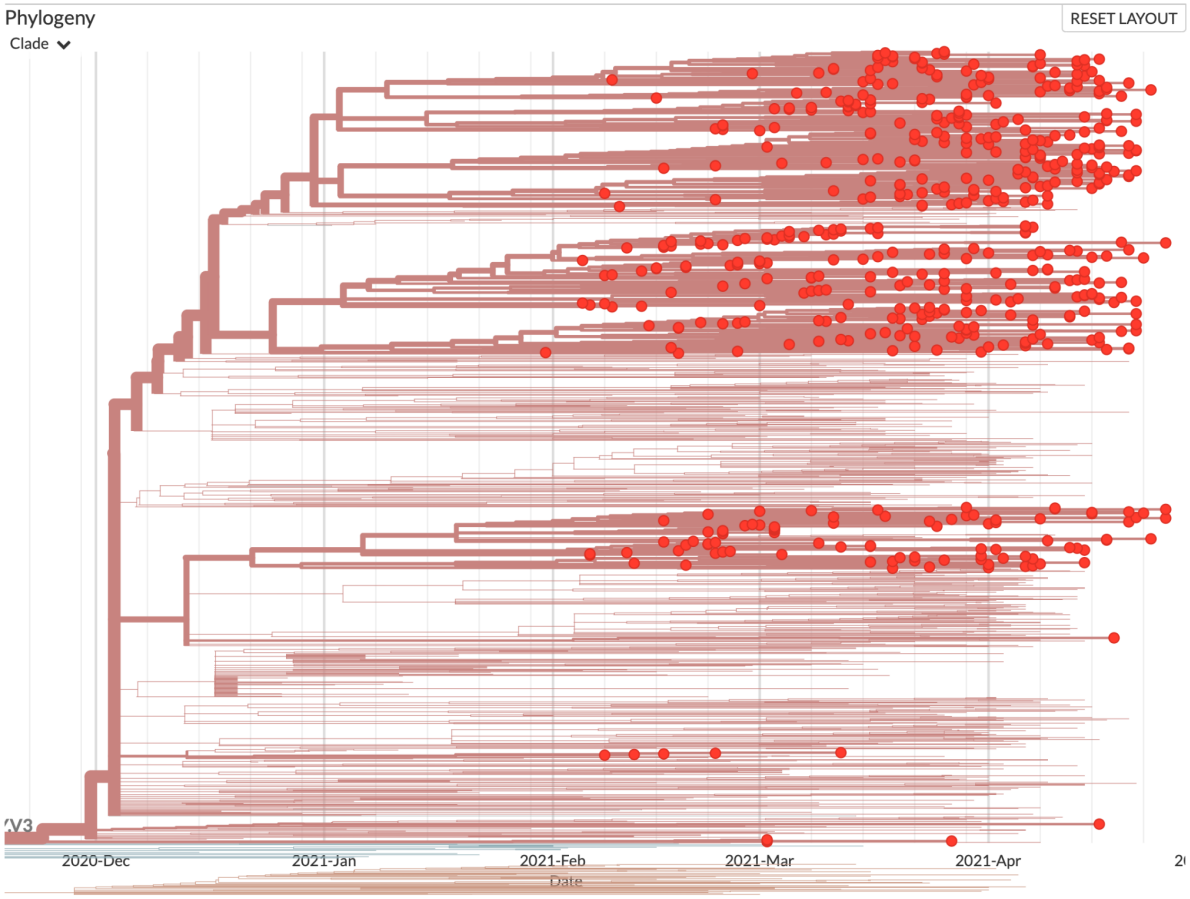

Figure 7: Phylogenetic analysis of P.1 sequences from Belgium. P.1 circulation in Belgium is currently associated with 3 active clusters which are to be linked to returning travellers around the month of January 2020 (see Figure 7, 552 Belgian P.1 genomes shown).

A number of smaller clusters (or what seem to be single introductions) reflect different situations:

- Two isolated sequences reported in April and one sequence reported in March have quality issues (incorrect or excess number of private mutations, or long stretches of missing data that obscure key mutations). They therefore do not correspond to actual foreign introductions into Belgium, but rather to artefacts.
- One sequence reported in March does not show any immediate problem in terms of sequence quality. As such, this could correspond to an additional introduction that did not start an observed transmission chain, possibly as a result of proper quarantining (which would have to be checked through contact tracing).
- One small cluster of five P.1 infections span over 1 month in sampling dates (February 8th until March 12th) and all have different sampling locations: Ranst, Merchtem, Antwerp, Berchem, Sint-Katelijne-Waver. The nature of this cluster will be further investigated.

In conclusion, we see no evidence for recent P.1 introductions from abroad into Belgium, but continued transmission chains which are spawning increasing numbers of infections within the country.