Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 11th of February 2021
(report 2021_10)

Executive summary

Genomic surveillance in Belgium is based on whole genome sequencing (WGS) of a selection of representative samples, complemented with targeted active surveillance initiatives and targeted molecular markers aiming to early detect and precisely monitor the epidemiological evolution of variants of concern (VOCs). Currently, 5.050 sequences of samples collected in Belgium are available on GISAID in open access. During week 3 of 2021, Belgium achieved a coverage of 3,5% of all positive sequences being sequenced.

During the last 2 weeks (week 5 and 6), 146 samples have been sequenced as part of the baseline surveillance, among which 48 (33%) were 501Y.V1 and 8 (5%) were 501Y.V2.

Since week 52 of 2020, Belgium has experienced multiple introductions of VOCs followed by sustained local transmissions. As a consequence of a higher transmissibility of these variants, we observe a progressive shift in viral populations, with 501Y.V1 expected to represent the majority of circulating strains by early March. Together with the rollout of vaccination, genomic surveillance will monitor the eventual positive selection of VOCs harbouring immune escape mutations such as S:E484K.

During the last 2 weeks, the progressive phenomenon of viral population replacement by more transmissible strains did not alter the overall stability of the epidemic in Belgium. This is probably due to a combination of active public health response and limited number of social interactions in the population. The risk of disruption of this equilibrium remains, as the proportion of more transmissible viruses will continue rising, but this risk can be mitigated by a combination of active outbreak control interventions, maintained efforts to reduce transmission in the population and rapid roll-out of vaccination.

Authors (National Reference Laboratory – UZ Leuven and KU Leuven):
Piet Maes, Lize Cuypers, Guy Baele, Els Keyaerts, Elke Wollants, Marc Van Ranst, Emmanuel André

With the scientific collaboration of *Simon Dellicour (ULB), Niel Hens (U Hasselt, U Antwerpen) and Tom Wenseleers (KU Leuven)*

With the collaboration of the laboratories of UCL, ULB, UMons, UNamur, ULiège, Ugent, UAntwerpen, Jessa ZH, AZ Delta, AZ Klina and UZ Leuven/KU Leuven.

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1. International context

Since the end of the year, 4 variants of concern (VOCs) have arisen independently of one another in the United Kingdom (501Y.V1), South Africa (501Y.V2) and Brazil (501Y.V3 and 20B/S.484K). These variants harbour several mutations and deletions associated with higher infectiousness and immune escape. All variants are spreading internationally, with 501Y.V1 and 501Y.V2 having been detected to date in Belgium.

Together with other mutations of concern, the E484K mutation in the S gene is associated with immune escape mechanisms and causes a possible decrease of efficacy of some vaccines. This mutation is always present in 501Y.V2 and 501Y.V3. It was initially not described in 501Y.V1, but recent reports from the UK highlight independent events of acquisition of this mutation.

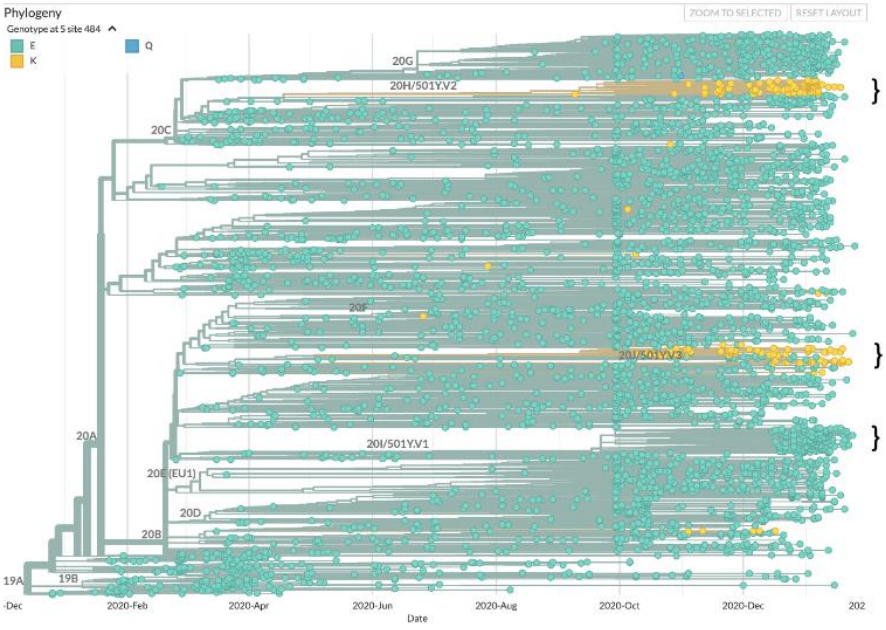

Figure 1: Global view of the S:E484K mutation responsible for partial immune escape, including diminished activity of some vaccines. This mutation is systematically present in variant 501Y.V2 (yellow cluster on the top) and variant 501Y.V3 (yellow cluster in the middle), and has recently emerged among a limited number of 501Y.V1 (third cluster) variants circulating in the UK.

2. Belgian genomic surveillance

The National Reference Centre has put in place genomic surveillance at the national level since the first introduction of the virus in February 2020. Along the way, other laboratories have contributed to this surveillance effort, and the federal government has since 29/12/2020 supported a scale-up of this network, built initially upon the federal platform laboratories. At the date of this report, 18 partners[1] have joined the SARS-CoV-2 WGS consortium and many of them already contributed sequencing data, strengthening this genomic surveillance initiative.
With the recent introduction of VOCs, genomic surveillance is to be composed in the future by 3 layers:

- Baseline surveillance (5% of positive samples from 24 sentinel laboratories) will be based on whole genome sequencing
- Monitoring of VOCs (reflex test to be performed on all positive samples from a restricted number of sentinel laboratories) will be based on a set of PCRs identifying mutations and deletions of concern including but not limited to: S:del69- ; S:E484K ; S:N501Y). Different technical solutions are currently under evaluation.
- Active surveillance: combination of systematic test indications aiming to identify the presence of VOCs in specific groups (returning travellers, chronic infection, re-infection and infection after vaccination)

Over the recent weeks, the ratio of activity between baseline surveillance and active surveillance (mostly focusing on returning travellers and S dropouts) has evolved. The ratio between baseline surveillance and active surveillance is 1,4 for week 5 of 2021.

The objective for the coming weeks is to:

- Achieve a ratio of 1,8 for baseline surveillance for all provinces in order to ensure in all times that uploaded sequences provide a correct representation of the actual genomic diversity
- Achieve a uniform an increased (2-5%) coverage of all provinces of the country. During this evolution, the quality of the sampling will be determined. The NRC therefore invests a lot of efforts to increase sequencing coverage in under-covered provinces, while avoiding over-representation (>5%) of restricted geographical areas (at least as long as the financial envelope allocated to the genomic surveillance remains limited to specific indications). We have to date no valid medical argument to promote genotyping on all samples as there is no direct impact expected for individual patients.

Since support was offered by the federal government on 29/12/2020, both the temporal coverage (number of sequences performed per week) and geographical coverage (number of collection sites) have improved. To date, 5.050 sequences originating from Belgian laboratories were uploaded on GISAID and are available in open access. For week 3 of 2021, the sequencing consortium achieved a coverage of 3,5% of all positive samples.

[1] Federal testing platforms and their associated clinical labs (Antwerp, Ghent, Leuven, Liège, Mons, Namur, ULB and UCL), Jessa Hasselt, AZ Delta Roeselare, AZ Klina, ZNA, AZ Monica, Imelda, ITG, AZ St Lucas Gent, IPG and OLZV Aalst.

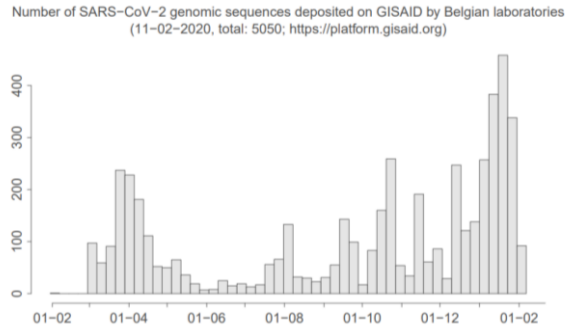

Figure 2: Number of Belgian sequences deposited on GISAID per week since the first case was diagnosed in the country. Federal support for scale-up started on 29/12/2020.

3. Introduction and early local transmission of 501Y.V1

At least 70 (95% credible interval = [65-75]) independent introduction events have been documented by whole genome sequencing from week 53 of 2020 until week 4 of 2021. This analysis was done using the global phylogenetic analysis of 176 B.1.1.7 genomes sampled in Belgium on the 02/02/2021.

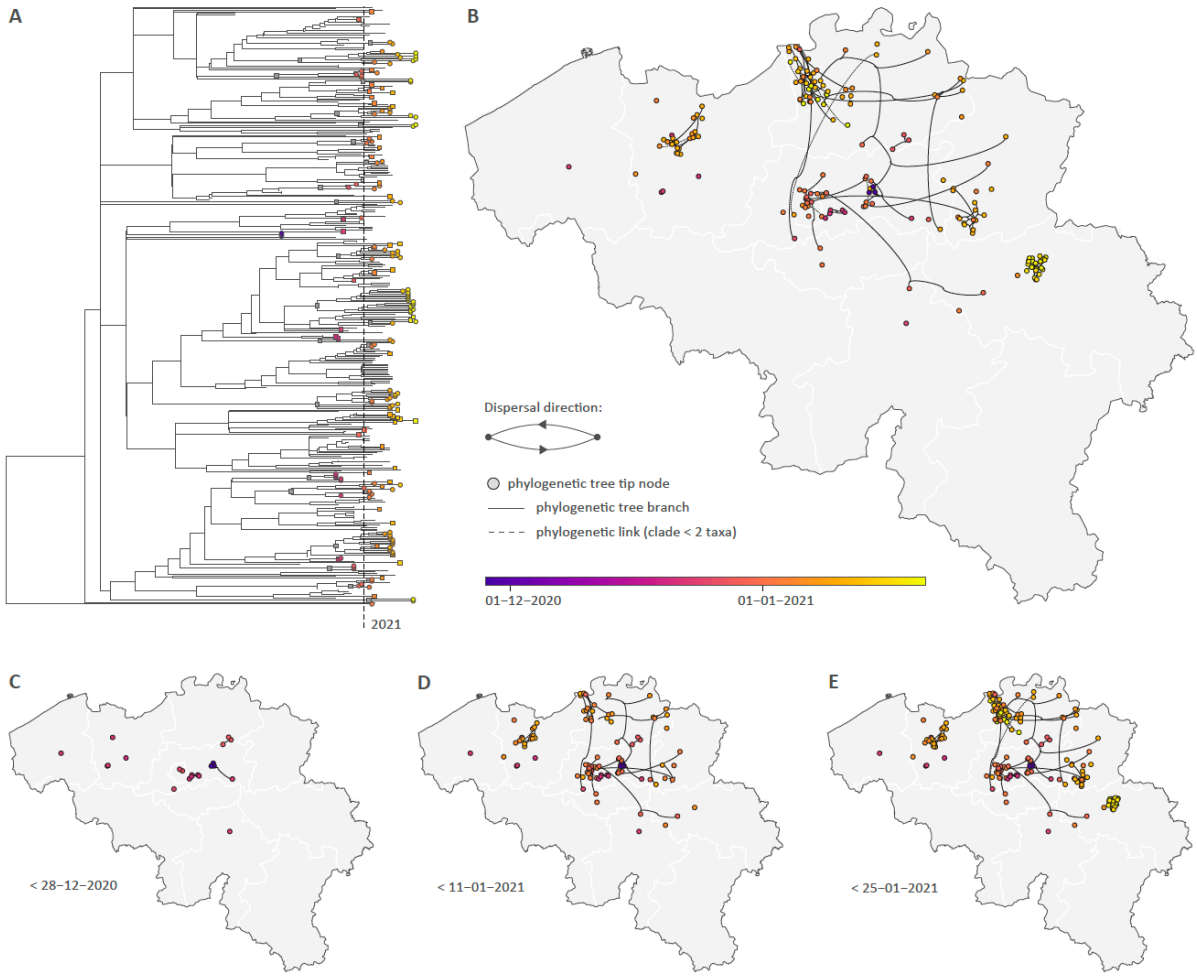

Figure 3: Dispersal history of B.1.1.7 (N501Y.V1) lineages sampled and sequenced in Belgium until 02/02/2021. **A.** Time-scaled phylogenetic tree of B.1.1.7 lineages obtained from the Belgian Nextstrain build (https://nextstrain.org/community/GuyBaele/sars-cov-2-belgium/voc). B.1.1.7 genomes sampled in Belgium are coloured according to their time of occurrence. Sampled genomes are displayed as coloured squares if corresponding to distinct introduction events, and as coloured circles if belonging to a Belgian clade gathering more than two B.1.1.7 samples. Estimated most recent common ancestors (MRCA) of each Belgian clade are displayed as grey squares. **B.** Mapping of the Belgian clades of B.1.1.7 lineages. **C-E.** Snapshots of the evolution of Belgian clades through time. Belgian clades delimitation and subsequent mapping were performed following the analytical pipeline of Dellicour *et al*. (2020, doi: 10.1093/molbev/msaa284).

For 44/70 (63%) of 501Y.V1 introductions, no subsequent signs of local transmission was (yet) identified. These were typically returning travellers with a positive test result which were asked to remain in quarantine.

For 26/70 (37%) of 501Y.V1 introduction events, further local transmission was observed. It must nevertheless be noted that the largest cluster identified to date seems to be secondary to an introduction event which was not documented (patient not tested or sample not referred for sequencing).

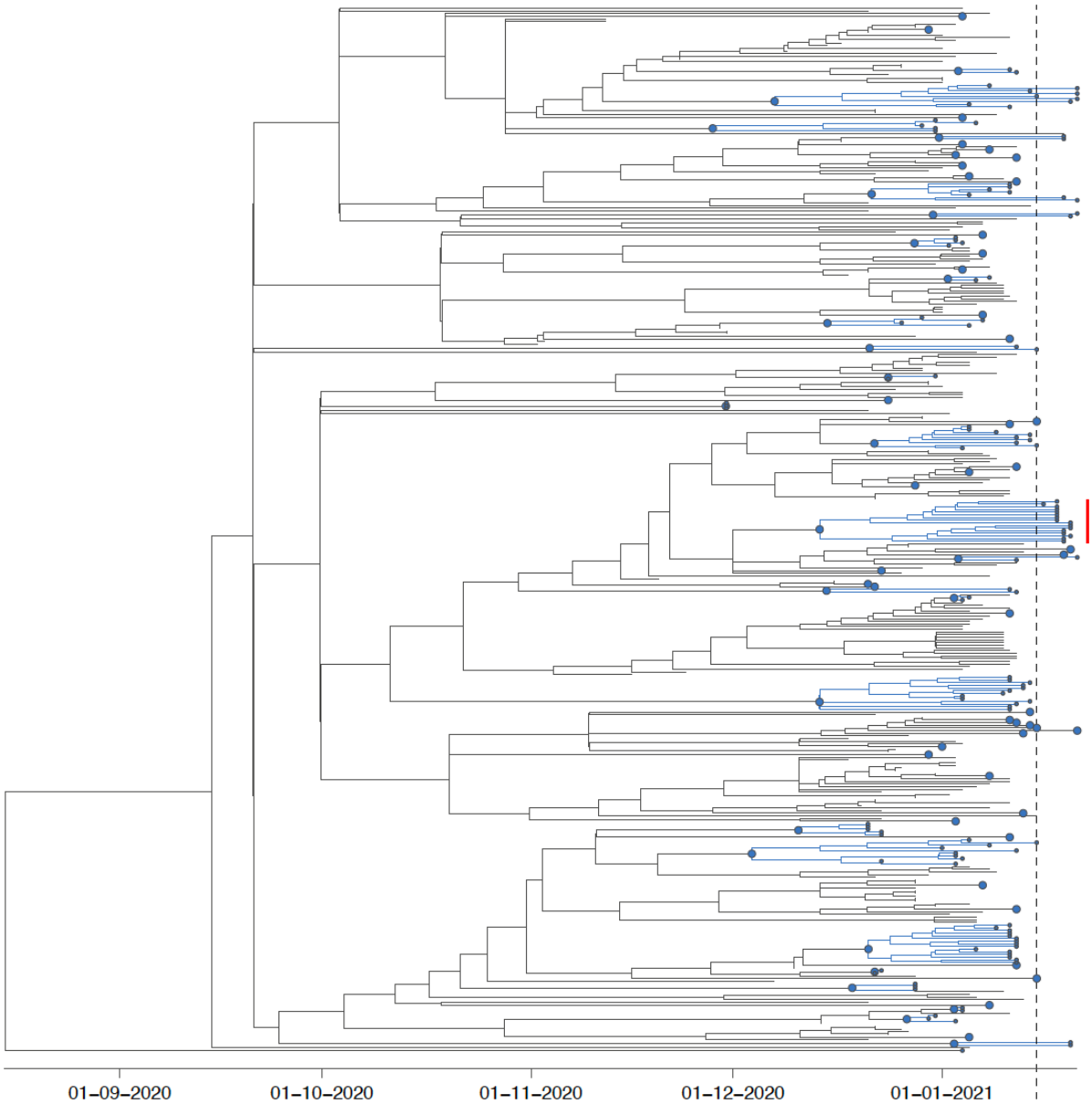

Figure 3: Time-scaled phylogenetic tree in which we identified 501Y.V1 Belgian clusters. A cluster is here defined as a phylogenetic clade likely corresponding to a distinct 501Y.V1 introduction into the Belgian territory. We delineated these clusters by performing a discrete phylogeographic reconstruction along the time-scaled phylogenetic tree used in the Nextstrain build for Belgium. We identified a minimum number of 70 B.1.1.7 (501Y.V1) lineage introduction events (95% credible interval = [65-75]) for 176 501Y.V1 samples sequenced in Belgium on February 2, 2021. On the tree,

lineages circulating in Belgium are highlighted in blue, small blue nodes correspond to sequenced 501Y.V1 samples, and large blue nodes correspond to the most ancestral common ancestor (MRCA) of each Belgian cluster. The largest cluster documented to date (highlighted by a red line) emerged two weeks after the official end of the holidays (indicated by the vertical dashed line), while no index case was identified by the genomic surveillance. This may be due to a patient not tested upon arrival, a sample not referred for sequencing as recommended, or a technical failure.

4. Evolution of VOCs in Belgium

Since the 1st week of 2021 (week 1), 1.733 501Y.V1 and 116 501Y.V2 VOCs have been confirmed by WGS or PCR-based presumptive genotyping (reflex PCRs or sanger sequencing detecting 501Y and 484K mutations).

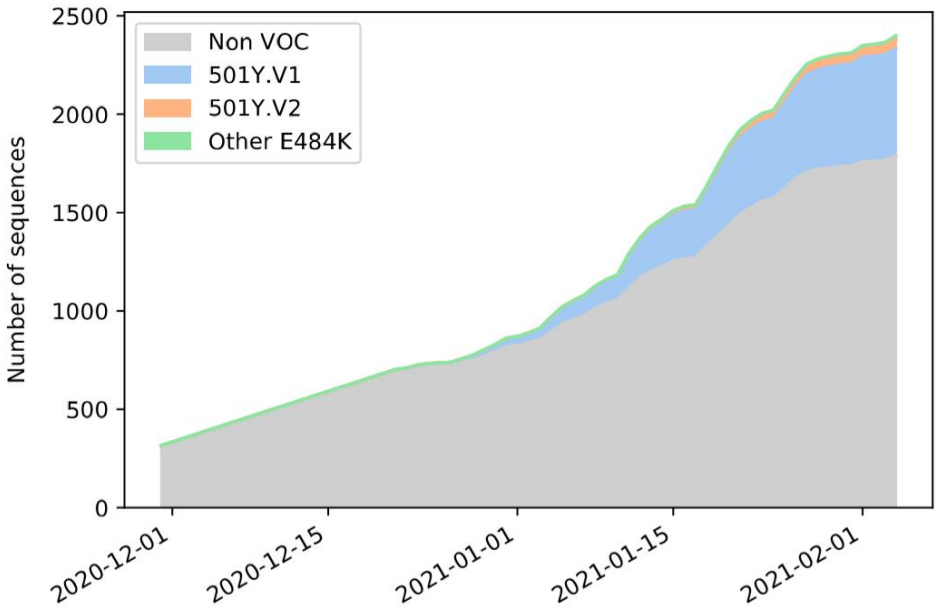

Figure 4: Absolute presence of viral populations in sequences from Belgium.

Across the 8 laboratories composing the federal testing platform, the proportion of “S dropouts” among positive SARS-CoV-2 PCR continues to increase.

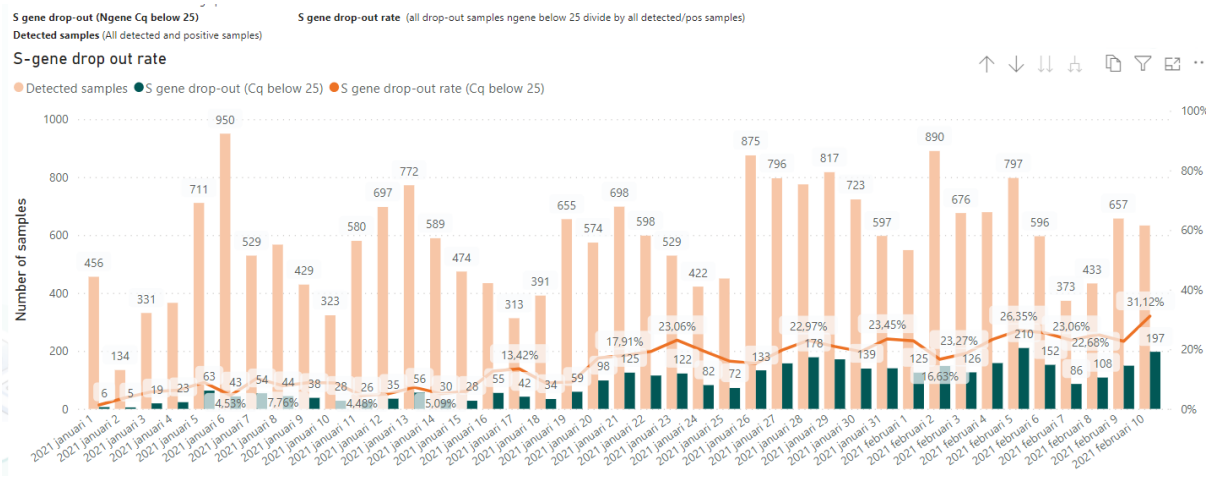

Figure 5: Evolution of the share of S dropout (orange line) in the federal platform laboratories.

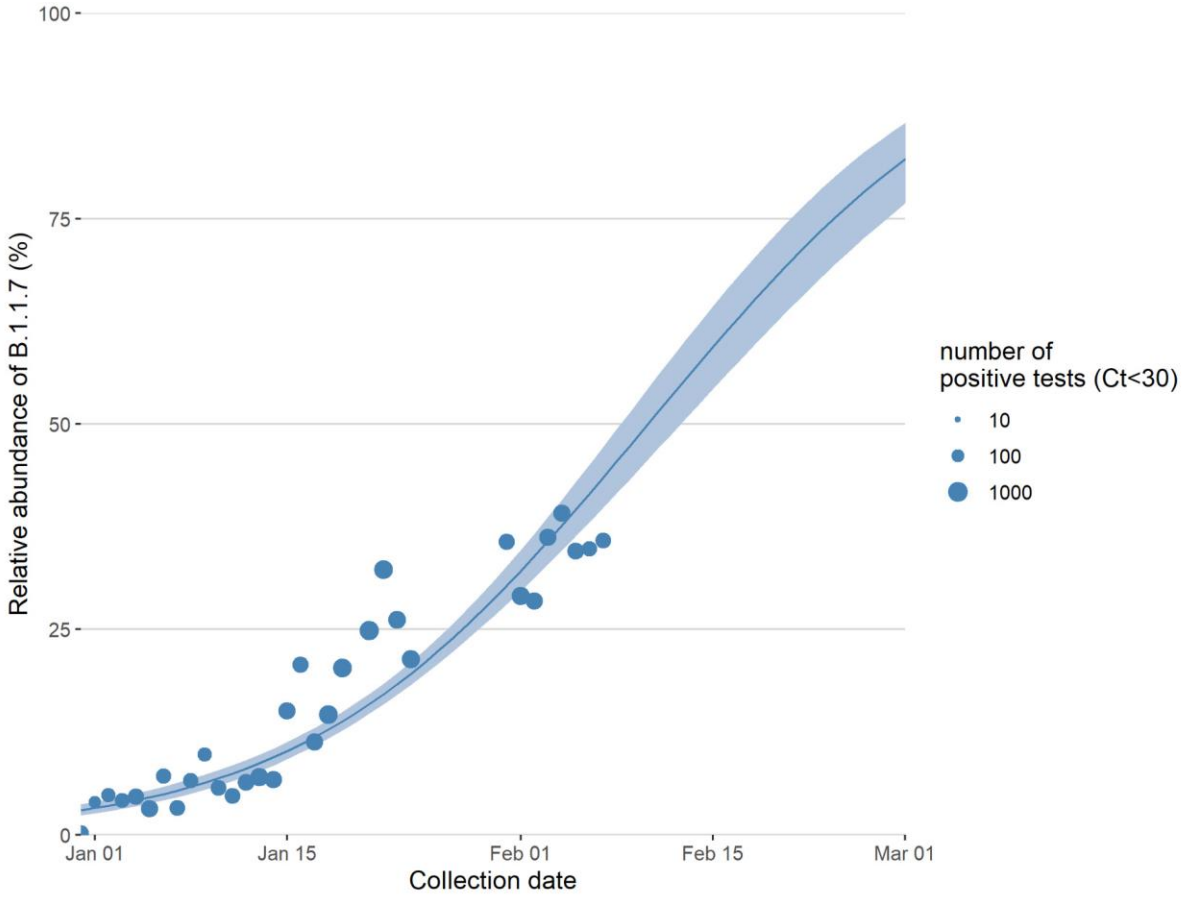

Figure 6: Expected evolution of the viral population shift in the coming 5 weeks. Although the evolution is slightly slower than initially projected, 501Y.V1 is expected to represent the vast majority of circulating strains by early March 2021.

The current positivity rate among tests performed in the 8 federal platform laboratories remained relatively stable (slight increase observed to date) over the last weeks despite the current circulation of VOCs in the country.

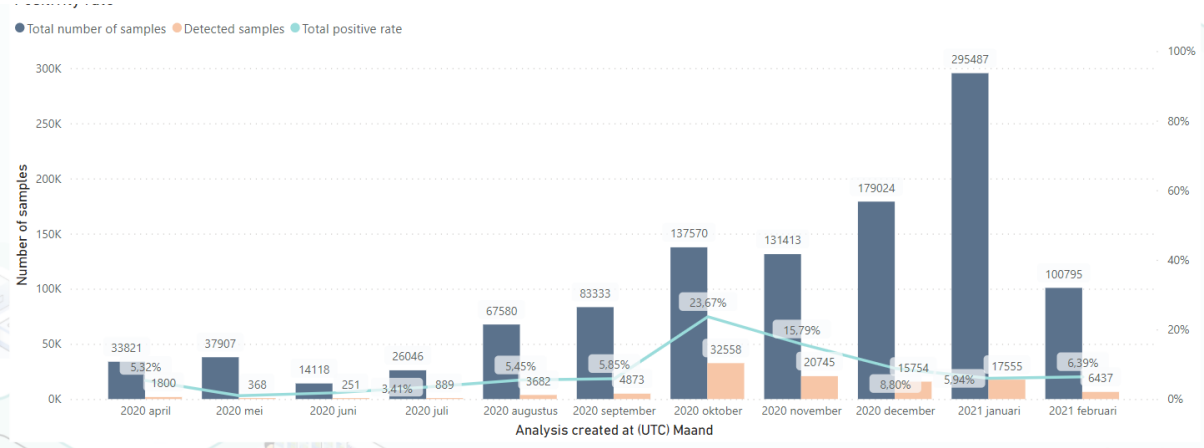

Figure 7: Positivity rate in the federal platform laboratories