

Genomic surveillance of SARS-CoV-2 in Belgium

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

**Situation update – 21 of December 2021
(report 2021_60)**

Executive summary

73,069 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID; compared to last week's report, 3,190 sequences have been added.

1,323 sequences of positive SARS-CoV-2 samples collected between 06/12/2021 and 19/12/2021 have at this stage been analyzed in the context of baseline surveillance. The large majority of samples have been typed as Delta, since the follow-up of Omicron cases has been up until now mainly situated within the context of active surveillance (active selection of cases characterized by S gene target failure (SGTF)).

The evolution of the Omicron variant is followed-up on a daily basis through the percentage of diagnostic PCRs harboring the S gene target failure (25% today). During week 50, 96% of the samples presenting SGTF were further confirmed as Omicron. The total number of Omicron infections (estimated around 1,400 cases for Belgium today) increases every day, while the number of Delta infections decreases significantly. Overall, the total number of infections in Belgium will likely start rising again as soon as Omicron will represent 50% of all documented infections. We estimate that this phenomenon could be observed within the coming week...

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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 the 24th of November 2021 in Belgium, the BA.1 Variant of Concern (Omicron) will most likely become the dominant lineage in Belgium in the coming days. This viral population replacement is happening at a very rapid pace, which cannot be fully captured by the baseline sequencing-based surveillance¹ due to relatively long turn-around time (see Figure 1). This phenomenon is better captured by the evolution of the share of positive PCR results which present an S gene target failure (Figure 2). During week 50, 96% of SGTF samples were further confirmed as Omicron infections by a marker PCR or whole-genome sequencing (Figure 3).

Since the threshold of 20% of presumed Omicron cases, identified as the percentage of diagnostic tests harboring SGTF (Figure 2), has been exceeded, and over 95% of the SGTF samples were confirmed to be Omicron infections (Figure 3) it's no longer necessary to confirm all SGTF samples by WGS. We propose to include the sequencing of these samples within the baseline surveillance approach, where they will be fairly represented, providing a clear view on the actual and unbiased circulation of the Omicron variant within the Belgian population. On top, this will also allow us to detect the BA.2 lineage of Omicron, however at the moment only rarely detected (27 genomes across the whole world), since this sublineage is not characterized by SGTF. This communication has been sent out to all sequencing and diagnostic labs by the NRC on Tuesday 21/12/2021.

Overall, the total number of infections in Belgium will likely start rising again as soon as Omicron will represent 50% of all documented infections. We estimate that this phenomenon could be observed within the coming week.

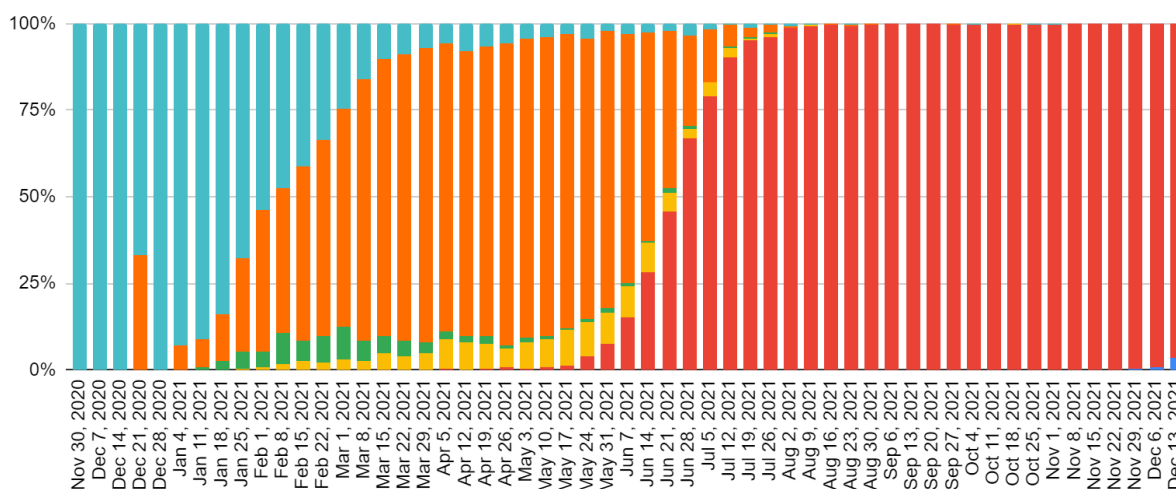


Figure 1: Weekly evolution of the frequency of variants of concern reported by the baseline surveillance network using a whole genome sequencing (WGS) approach.

¹ We have revised the number of Omicron cases reported during the previous weeks, as some of them have been re-classified as part of active surveillance interventions. Figure 1 only reports the sequences of unbiased sampling.

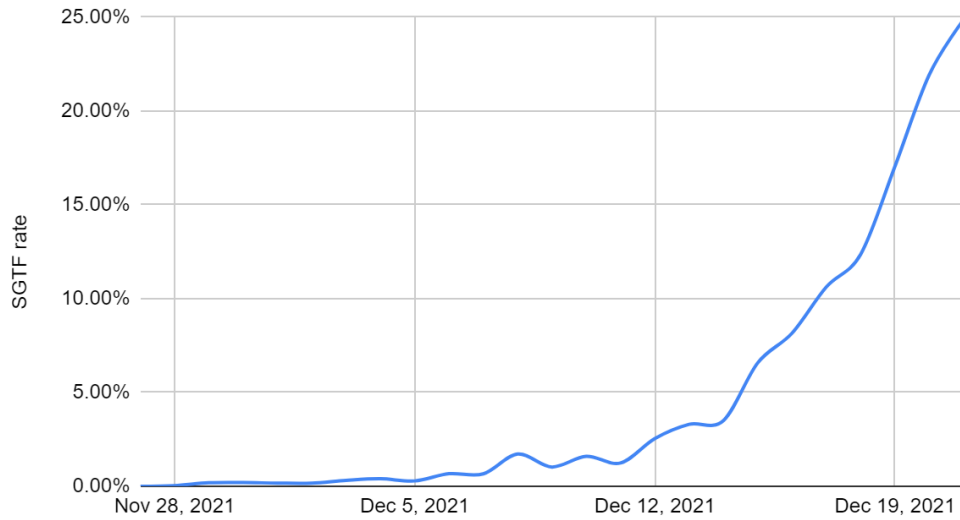


Figure 2: SGTF (S dropout with Cq <25) rate over the past 24 days in Belgium (data from the eight federal platform laboratories).

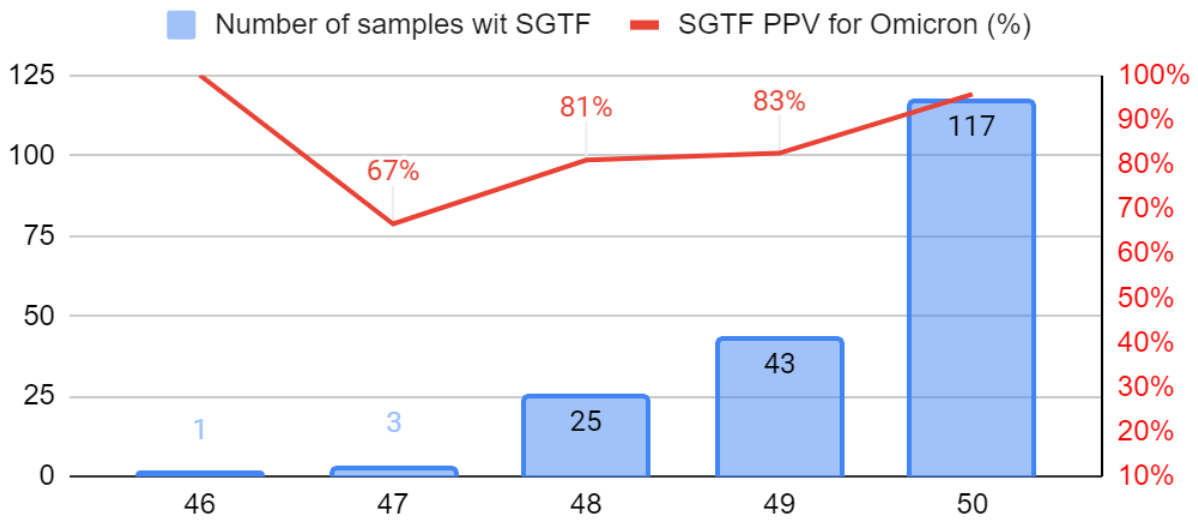


Figure 3: Weekly evolution of the percentage of samples harboring SGTF which are confirmed as Omicron by sequencing. Data from the UZ Leuven/KU Leuven diagnostic laboratories, per epidemiological week.

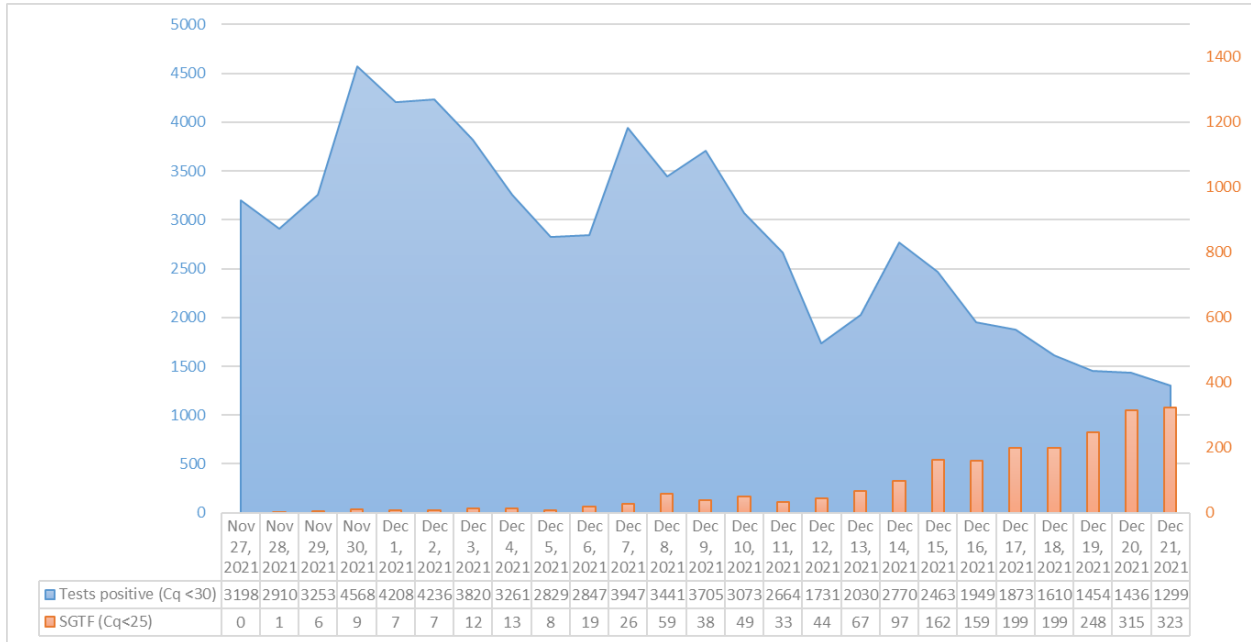


Figure 4: Evolution of the number of positive PCR results and positive samples (Cq<25) harboring SGTF in the federal platform laboratories. While the total number of positive samples (mainly Delta) tends to decrease, we observe an underlying and increasing trend with regard to SGTF samples. The total number of infections is expected to start rising as soon as Omicron infections represent >50% of the infections. Data of the last 24 hours may still be incomplete.

2. Current status with regard to Omicron in the world

As of 21 December 2021, 78 countries shared 19,101 Omicron genome sequences on GISAID. This variant has now spread at an unprecedented speed in all regions of the world.

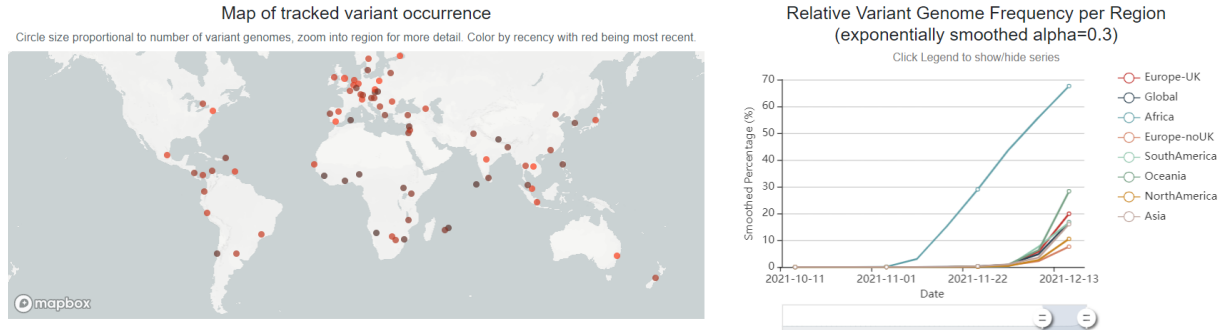


Figure 5: Countries reporting confirmed Omicron infections. Many countries, particularly in the African continent where genomic surveillance capacity is limited, probably currently under-report the real number of infections (source: GISAID)

The pace of viral population replacement is consistently faster for Omicron than what has been observed with previous variants of concern. The average growth rate advantage of Omicron over Delta is currently estimated at 0.29 per day (Figure 6). This replacement has first been observed in South Africa, but is also observed in many other countries. The United Kingdom and Denmark are probably among the most advanced western European countries in this regard, and Belgium has a delay of several days compared to these countries which currently apply a comparable (UK) or lower stringency index (Figure 7).

Another element that we need to look at when assessing Belgian's vulnerability to Omicron is the overall deployment of booster vaccination dosis. On December 20/12/2021, Belgium reported a booster coverage of 29% compared to 35% in DK and 42% in the UK (Figure 8).

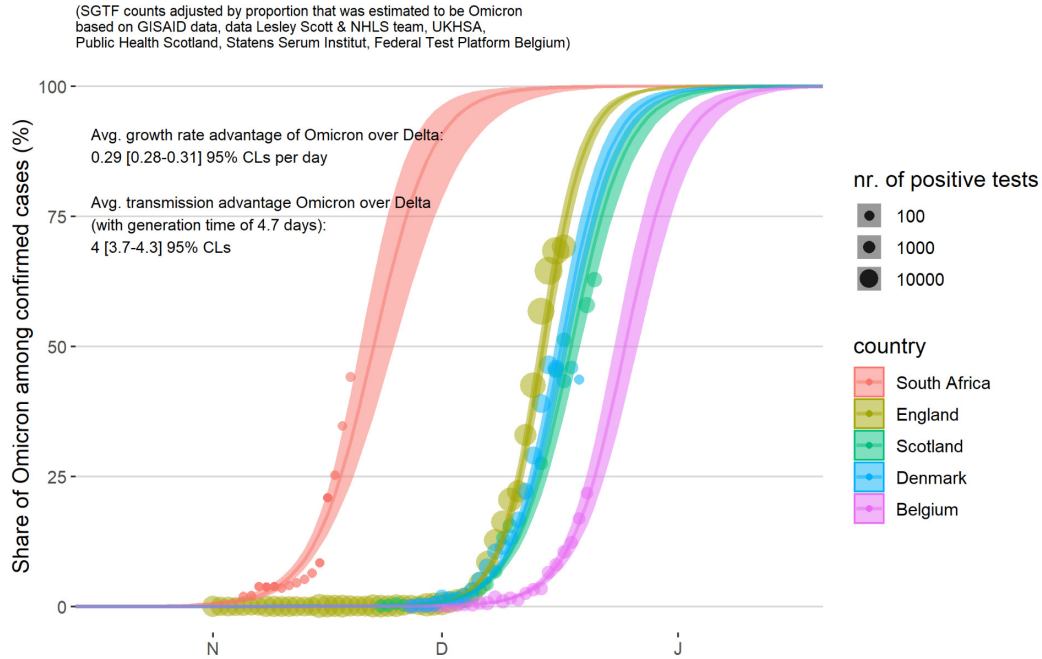


Figure 6: Logistic regression model shows the rapid rise in the share of Omicron infections among newly diagnosed infections inferred from variant-specific PCR data (for Denmark) or S dropout (SGTF) PCR test data (other countries shown). The model used allows for overdispersion via the inclusion of an observation-level random effect.

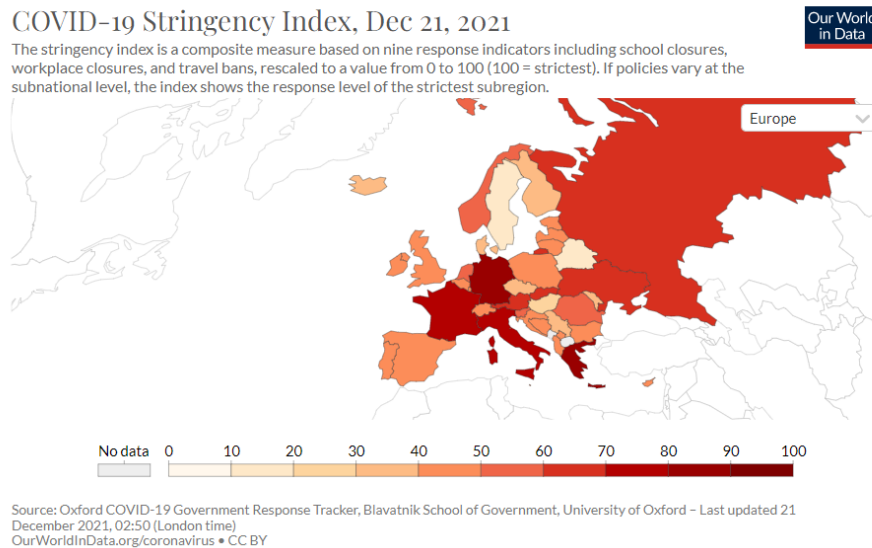


Figure 7: Current stringency index for European countries. The current stringency index for Belgium is comparable to the UK and higher compared to Denmark. These two countries, which are also at a more advanced stage in terms of Omicron spread, can therefore be considered by Belgium as reliable indicators of the upcoming epidemiological evolution in Belgium. ([source](#))

COVID-19 vaccine booster doses administered per 100 people

Total number of vaccine booster doses administered, divided by the total population of the country. Booster doses are doses administered beyond those prescribed by the original vaccination protocol.

Our World
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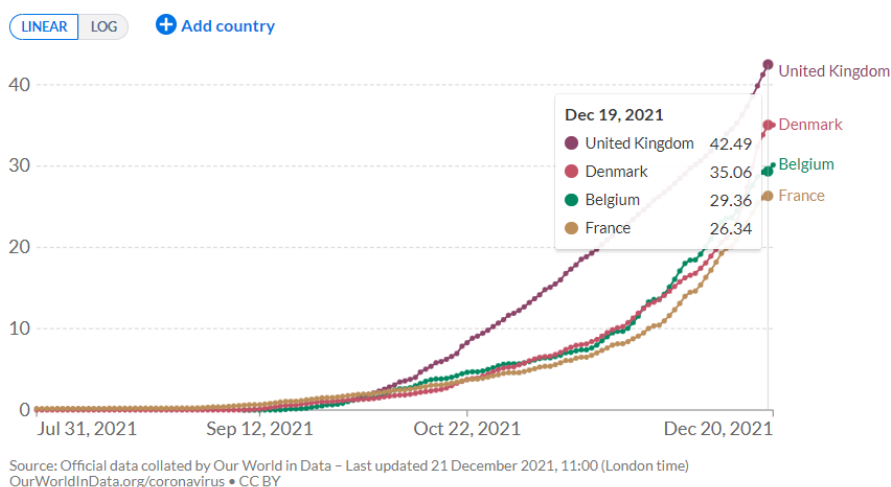


Figure 8: Booster doses administered per 100 people in Belgium, France, the United Kingdom and Denmark ([source](#))

The situation in Denmark has been described in a report published today ([source](#)). Currently, 46% of documented infections are due to Omicron.

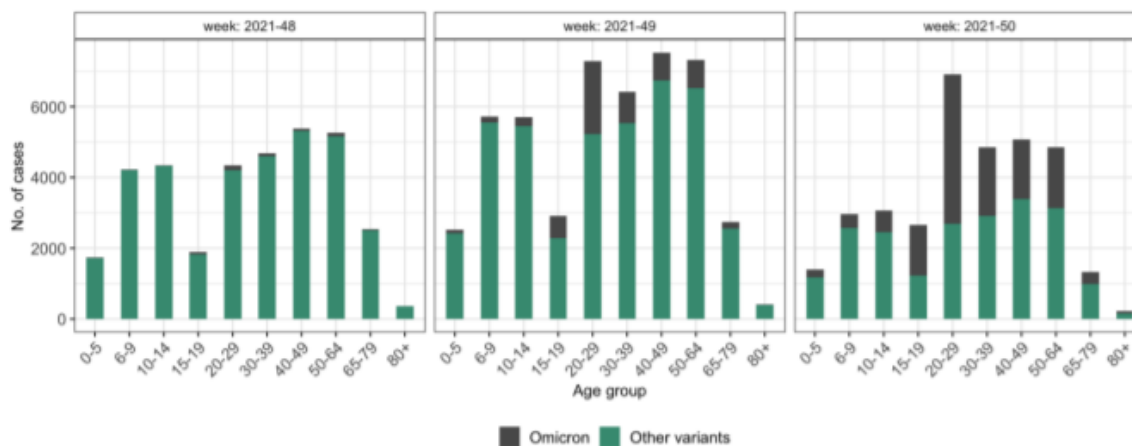


Figure 9: Number of cases with other SARS-CoV-2 variants and Omicron by age group and week, from 22/11/2021 to 15/12/2021 in Denmark.

In Denmark, 79% of the documented Omicron infections have occurred among 2x vaccinated people, while this group represents 78% of the total population. At this early stage, vaccination (2 dosis) does not seem to offer a visible effect against infection. For the other groups, the numbers are, at this stage, still too limited to make any conclusion.

Denmark reports 47 patients currently hospitalized and <5 patients currently in ICU. During the period of 22 November to 15 December 2021, Denmark reported 1,817 admissions associated with other variants,

and 96 admissions associated with an Omicron infection. Overall, Omicron was responsible for 5%² of the recent hospital admissions. These numbers should be interpreted with caution as, as illustrated in Figure 9, Omicron only represented 13%³ of the documented recent infections. If these observations were to be consolidated in the coming weeks (and when the older age groups will become infected), this could signify a lower severity of this more transmissible variant.

² According to the Table 6 of the Danish report, 1,913 SARS-CoV-2 associated hospital admissions (patients who tested positive prior or within 48 hrs after admission) were documented between 22/11/2021 and 15/12/2021, among which 96 (5%) were due to the Omicron variant.

³ According to the Table 2 of the Danish report, 145.934 SARS-CoV-2 infections were documented between 22/11/2021 and 15/12/2021, among which 19.064 (13%) were Omicron (<https://files.ssi.dk/covid19/omikron/statusrapport/rapport-omikronvarianten-21122021-14tk>)

3. Current status with regard to Omicron in Belgium

Currently, the National Reference Laboratory has sequenced or been informed of **184 Omicron cases confirmed by sequencing in Belgium**. The actual number is probably higher, as several probable Omicron infections are currently being confirmed and several clusters of local transmission could not be fully circumscribed. Of note, the baseline surveillance accuracy may currently be impacted by the very high number of Delta infections reported (lower proportion of samples sequenced) and by the interference of active case finding strategies focusing on Omicron/BA.1 (harboring SGTF) outbreaks. At this stage, no BA.2 infections have been documented through baseline surveillance.

Using the available Omicron genomic sequences on GISAID on Saturday December 18th, we performed a detailed phylogenetic analysis to investigate how these Belgian cases are linked. This analysis currently - **based on available data and subject to change if more data become available** - reveals the presence of an increasing number of Belgian transmission clusters (Figure 10), some of which we discuss below.

Showing 128 of 7728 genomes sampled between Nov 2021 and Dec 2021. Filtered to [Belgium \(136\)](#)  .

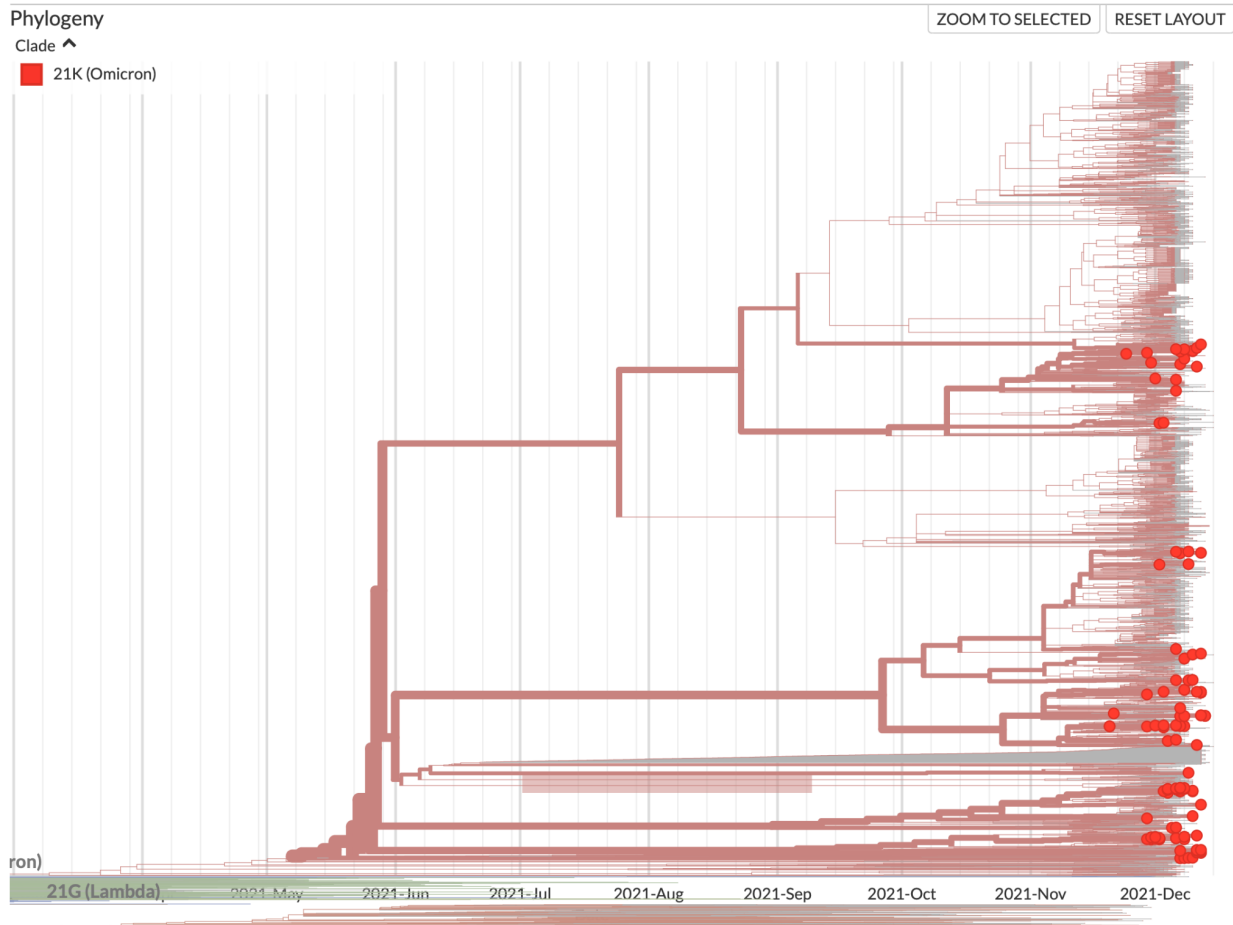


Figure 10. Visualization of the relationship between 128 current Belgian Omicron infections, showing an increasing number of distinct local transmission clusters, along with single introduction events.

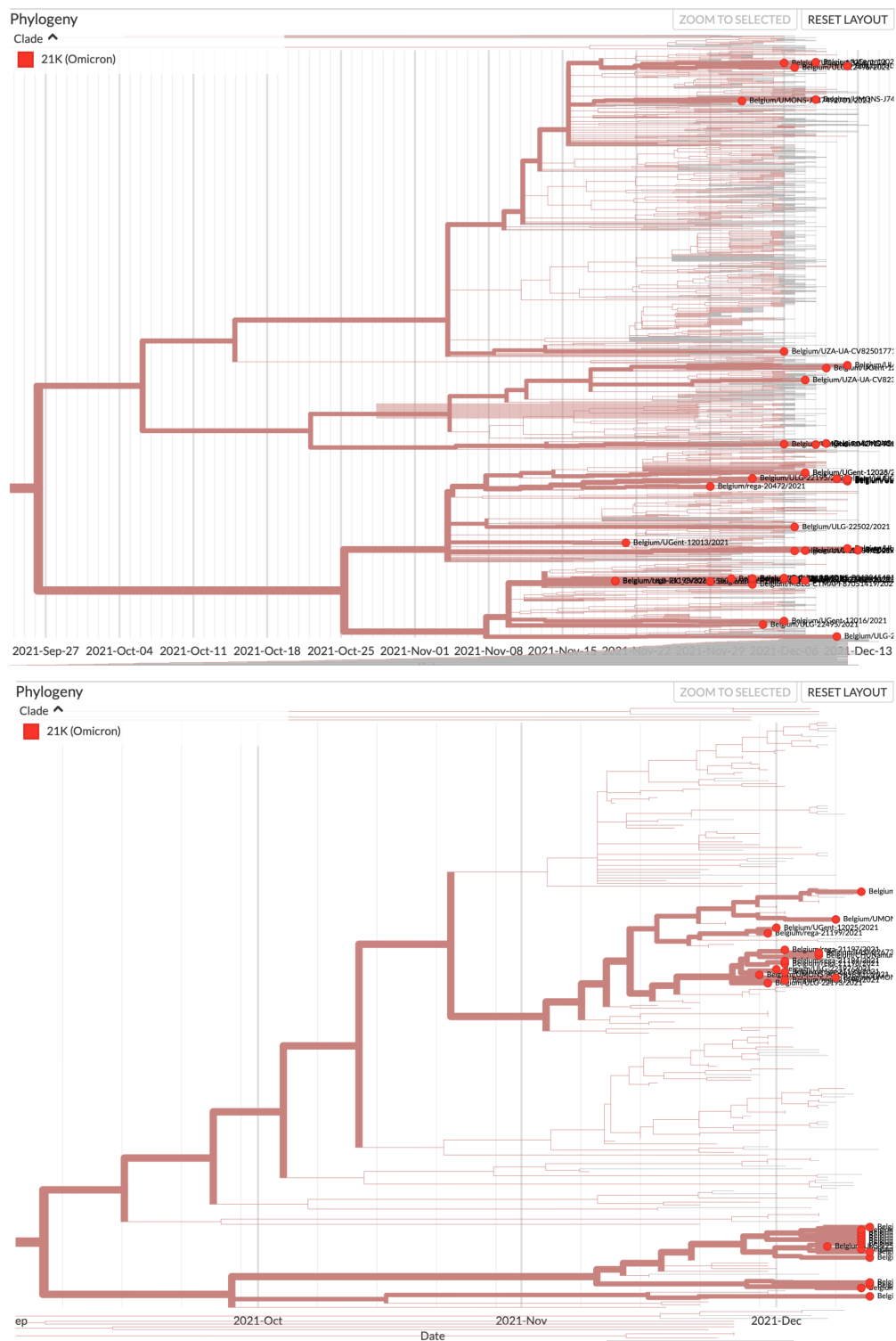


Figure 11. We observe a mixture of single introduction events of Omicron, small transmission clusters (top figure) but also larger transmission clusters (bottom figure), a phenomenon also observed with the previous variants of concern when the number of cases started increasing rapidly.

4. Recent publications involving the National Reference Center (not yet peer-reviewed)

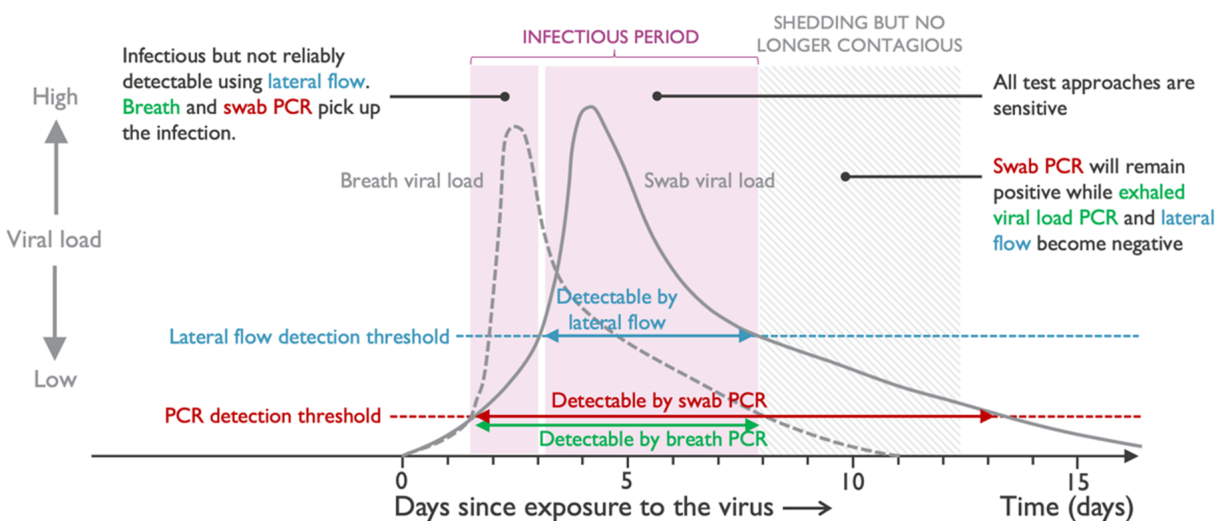
Molecular Detection of SARS-CoV-2 in Exhaled Breath Using a Portable Sampler

Pre-print: <https://www.researchsquare.com/article/rs-1104361/v1>

In this study, we demonstrate that sampling subjects using a one-minute breathing protocol yields sufficient viral RNA to detect infections with a sensitivity comparable to standard NP sampling methods.

A longitudinal study revealed clear differences in the temporal dynamics of viral load for nasopharyngeal swabs, saliva, breath, and antigen tests.

- In the early stage of an infection, PCR-based tests become positive before rapid antigen tests. During the 2 days prior to onset of symptoms, rapid antigen tests performed by trained professionals only detected half of the positive patients.
- During the symptomatic phase of the infection, all tests performed equally.
- During the later stage of an infection, the breath-based test is the first to consistently report a negative result, putatively signaling the end of contagiousness.



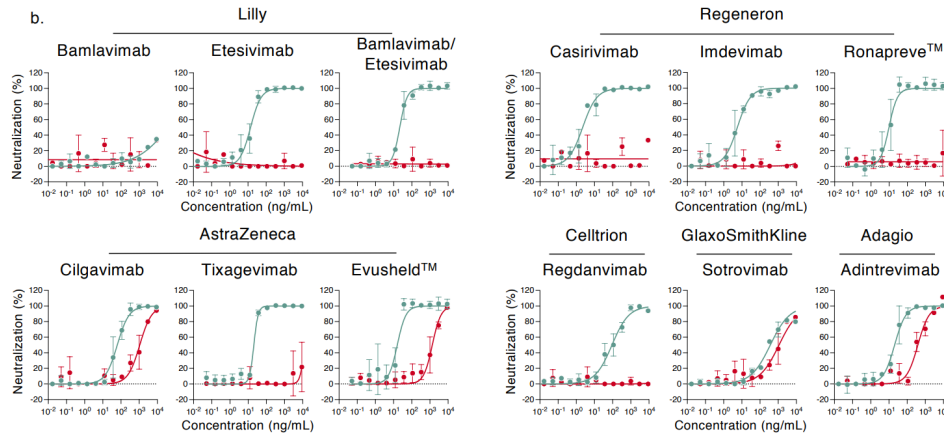
Source: Adapted from FT and Michael Mina et al., "Rethinking Covid-19 test Sensitivity – A Strategy for Containment", N Engl J Med 2020; 383:e120
 Note: lateral flow test = rapid antigen test

Considerable escape of SARS-CoV-2 variant Omicron to antibody neutralization

Pre-print: <https://www.biorxiv.org/content/10.1101/2021.12.14.472630v1>

We examined the sensitivity of Omicron to 9 monoclonal antibodies (mAbs) clinically approved or in development, and to antibodies present in 90 sera from COVID-19 vaccine recipients or convalescent individuals.

- Omicron was totally or partially resistant to neutralization by all mAbs tested.



- Sera from Pfizer or AstraZeneca vaccine recipients, sampled 5 months after complete vaccination, barely inhibited Omicron. Sera from COVID-19 convalescent patients collected 6 or 12 months post symptoms displayed low or no neutralizing activity against Omicron.
- Administration of a booster Pfizer dose as well as vaccination of previously infected individuals generated an anti-Omicron neutralizing response, with titers 5 to 31 fold lower against Omicron than against Delta.

