Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 4th of January 2022
(report 2021_62)

Executive summary

76,132 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID; compared to last week's report, 1,576 sequences have been added.

1022 sequences of positive SARS-CoV-2 samples collected between 20/12/2021 and 2/1/2021 have at this stage been analyzed in the context of baseline surveillance. For samples collected during the week of 27/12/2021, Omicron represented 69% of the strains analyzed.

To provide more updated information on the evolution of the Omicron variant, we follow-up on a daily basis the percentage of diagnostic PCRs harboring the S gene target failure (SGTF). On 3/1/2022, SGTF was present among [83% - 90%] of the positive samples, analyzed at one of the 8 federal platforms.

Based on the current trend, the high positivity rate and the recent decisions that will lead to lower effectiveness of the prevention pillars, we expect that the current rise of infections will continue and reach unprecedented levels.
Despite the presumed lower severity of Omicron, this sharp increase will presumably lead to a considerable number of hospital admissions (not specifically ICU admissions), in particular among unvaccinated adults and will thus probably impact the organization of hospitals.

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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

While first identified on the 24th of November 2021 in Belgium, the BA.1 Variant of Concern (Omicon) has become the dominant lineage in Belgium one month after the first case was detected. This viral population replacement has happened at a very rapid pace, which cannot be fully captured by the baseline sequencing-based surveillance due to the initial strategy to specifically target SGTF samples, which were strictly classified as active surveillance, causing a delay in the observation of the rise of Omicron cases in the baseline surveillance approach (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 (SGTF) (Figure 2, data from the eight federal testing platforms). During week 51, 100% of SGTF samples were further confirmed as Omicron infections by a marker PCR or whole-genome sequencing.

As illustrated in Figure 3, Belgium could delay the Omicron surge by approximately 2 weeks compared to the UK and DK despite being the first European country to report an Omicron infection. This delay is probably linked to the effective integration between genomic surveillance and the active case finding. This delay allowed to segregate the peak of Delta from the foreseen peak of Omicron infections and to accelerate the booster vaccination campaign. These important efforts will probably lead to a major impact mitigation during this wave of infections.

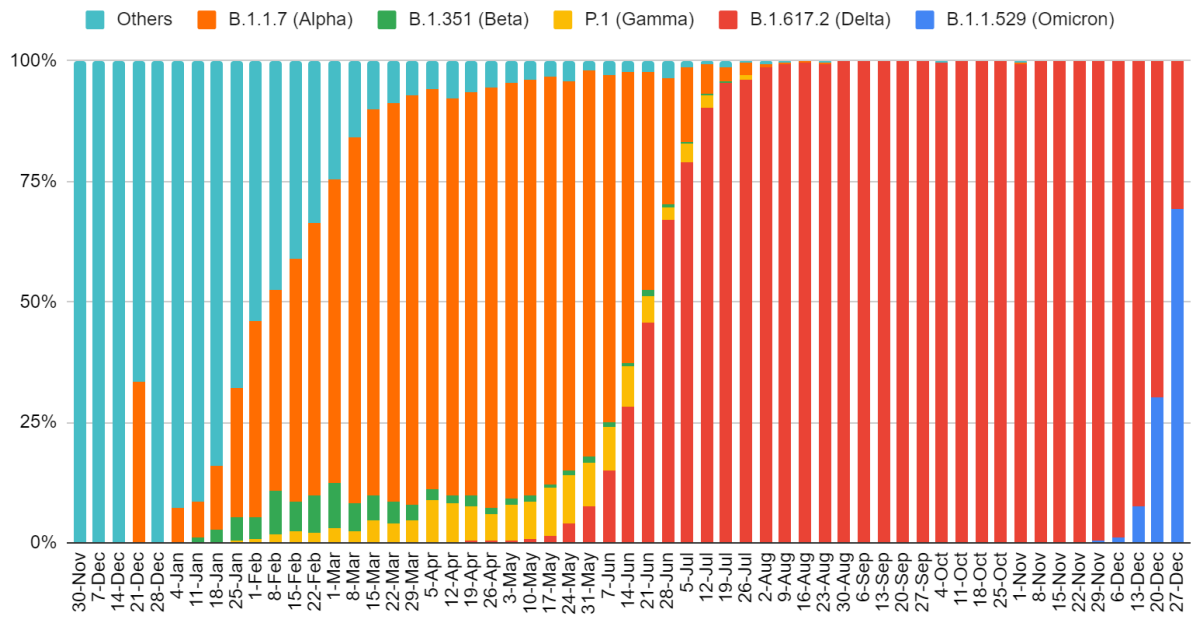

Figure 1: *Weekly evolution of the frequency of variants of concern reported by the baseline surveillance network using a whole genome sequencing (WGS) approach.*

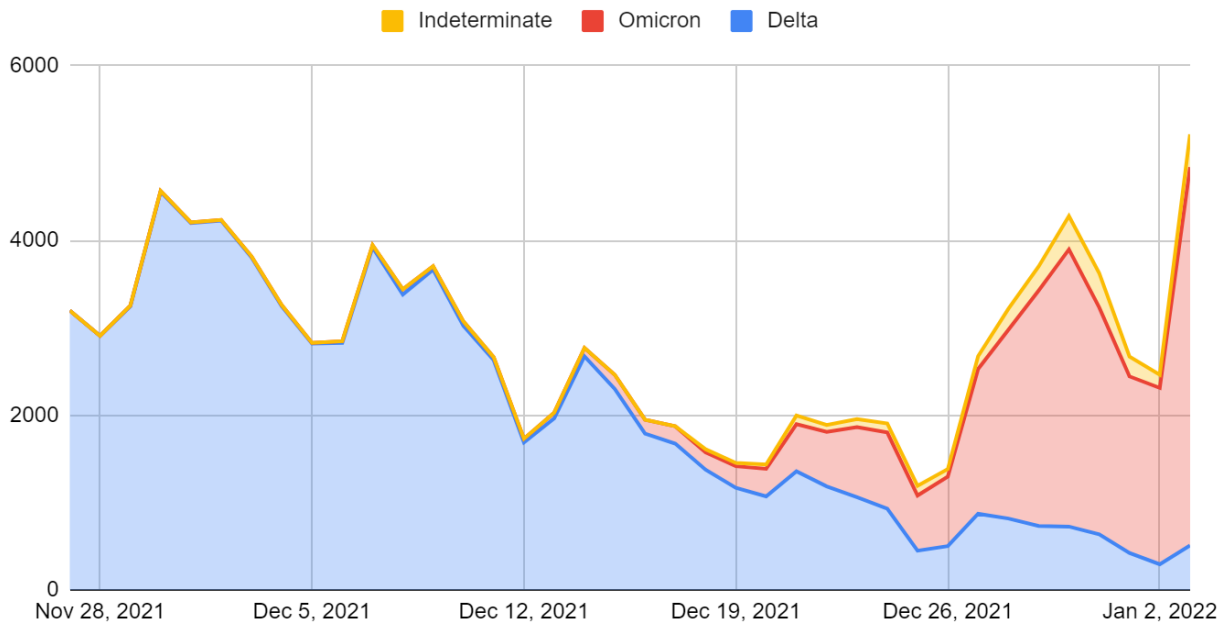

Figure 2: *Evolution of the number of positive PCR results and positive samples harboring SGTF in the federal platform laboratories.*

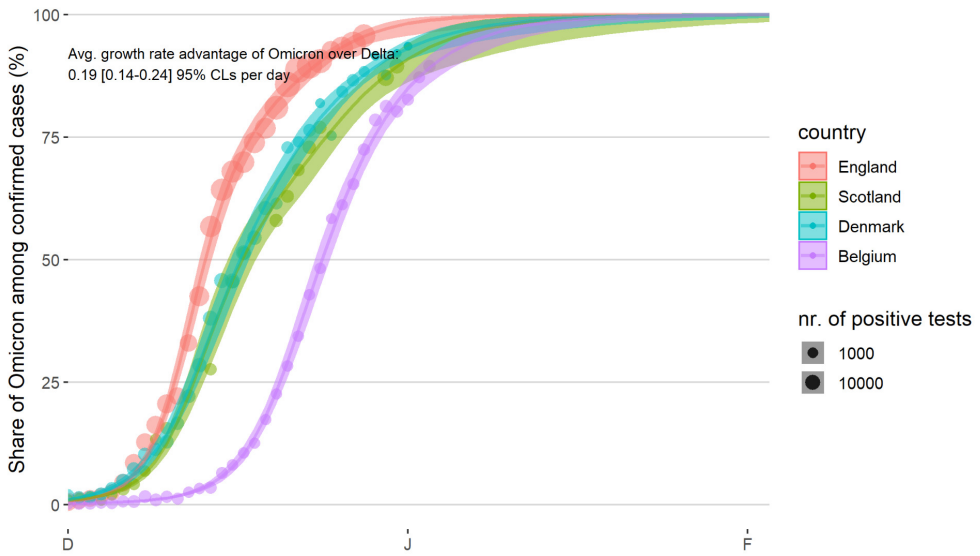

Figure 3: *Spread of Omicron variant interfered from S gene target failure data (UK & BE) and variant PCR data (DK). As illustrated in this figure, Belgium could delay for approximately two weeks the Omicron wave compared to the UK and DK.*

2. Estimating the short-term impact of Omicron in Belgium

Current estimates of the effective reproduction number Re clearly show a growing number of infections (in all provinces) and an early - but significant - growth in hospital admissions (Figure 4) . Although the growth in ICU admissions is still estimated to remain moderate, current evolutions suggest that hospitals should prepare for a significant number of hospital admissions in the coming weeks. The impact on hospitals will be driven mainly by an unprecedented number of infections in the community, staff shortage and unvaccinated populations.

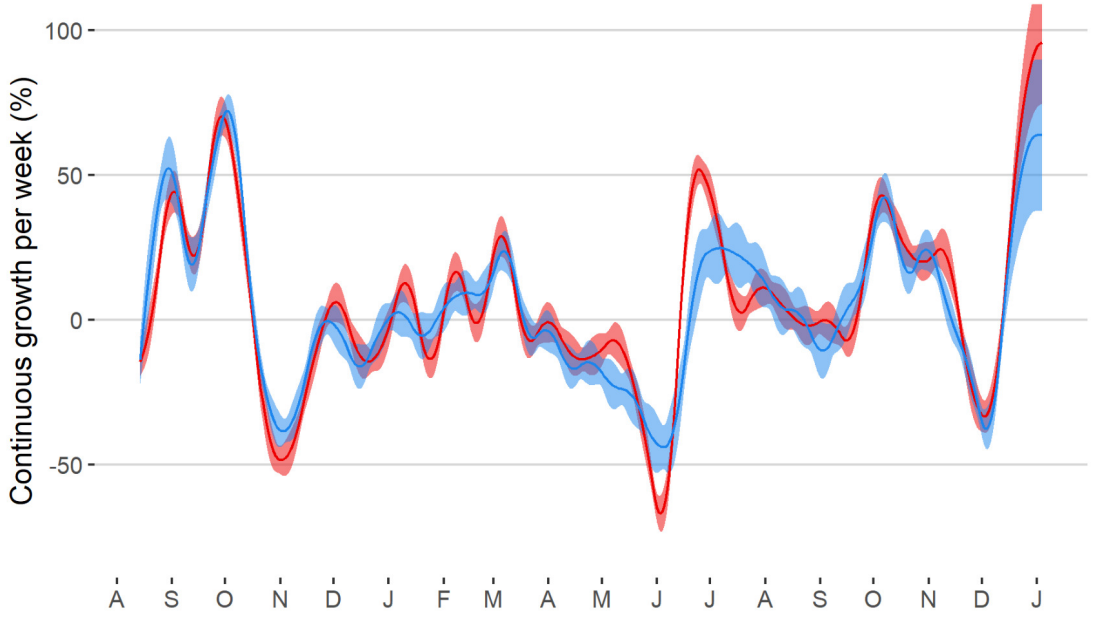

Figure 4: *Growth in new SARS-CoV-2 infections (red) and hospital admissions (blue) per week in Belgium.*

If the generation time of Omicron would be as short as suggested by a recent South Korean study, the growth rate advantage of Omicron could in large part be explained by this shortened generation time, which would result in the initial transmission advantage of Omicron over Delta to be estimated at a factor of 2.2 (ratio of the effective Re values) - much lower than that estimated before if one would assume a constant, fixed generation time for both - and a lower Re of Omicron would then result in the epidemic peaking much faster. Nevertheless, this hypothesis is currently based only on this single South Korean study and will need to be confirmed.

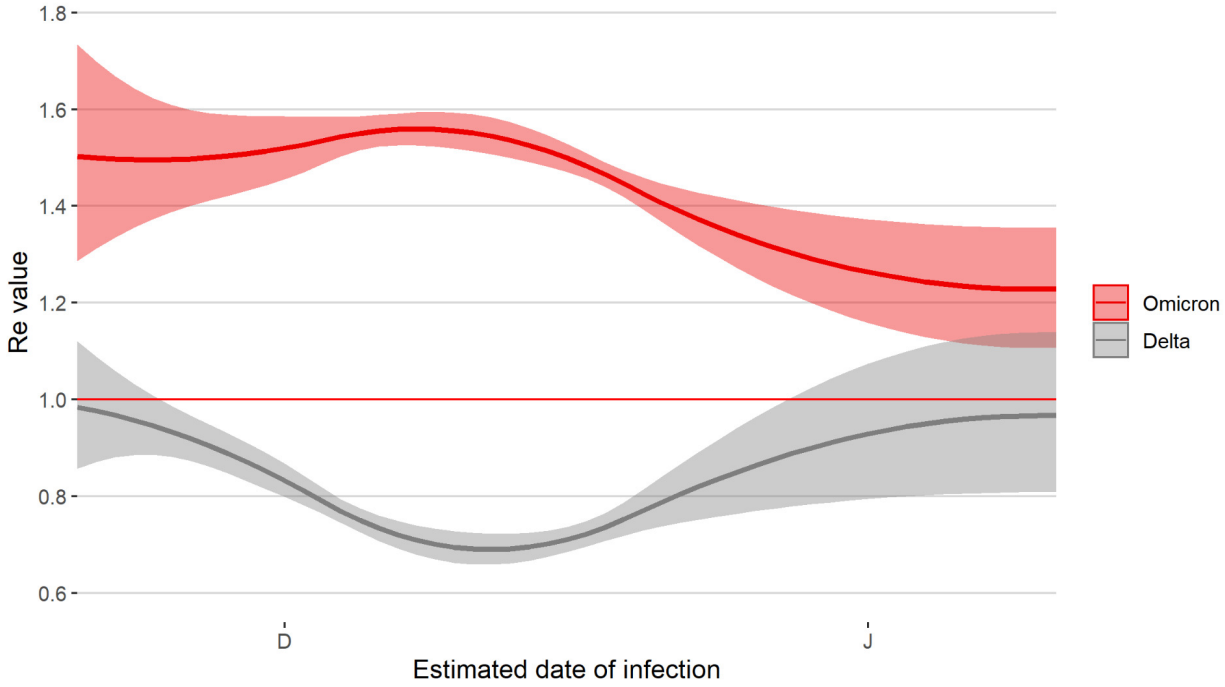

Figure 5: *Evolution of Re values of Omicron and Delta in Belgium using generation time of 2.2 days for Omicron (Kim et al. 2022) and 3.9 days for Delta (Hart et al. 2022).*

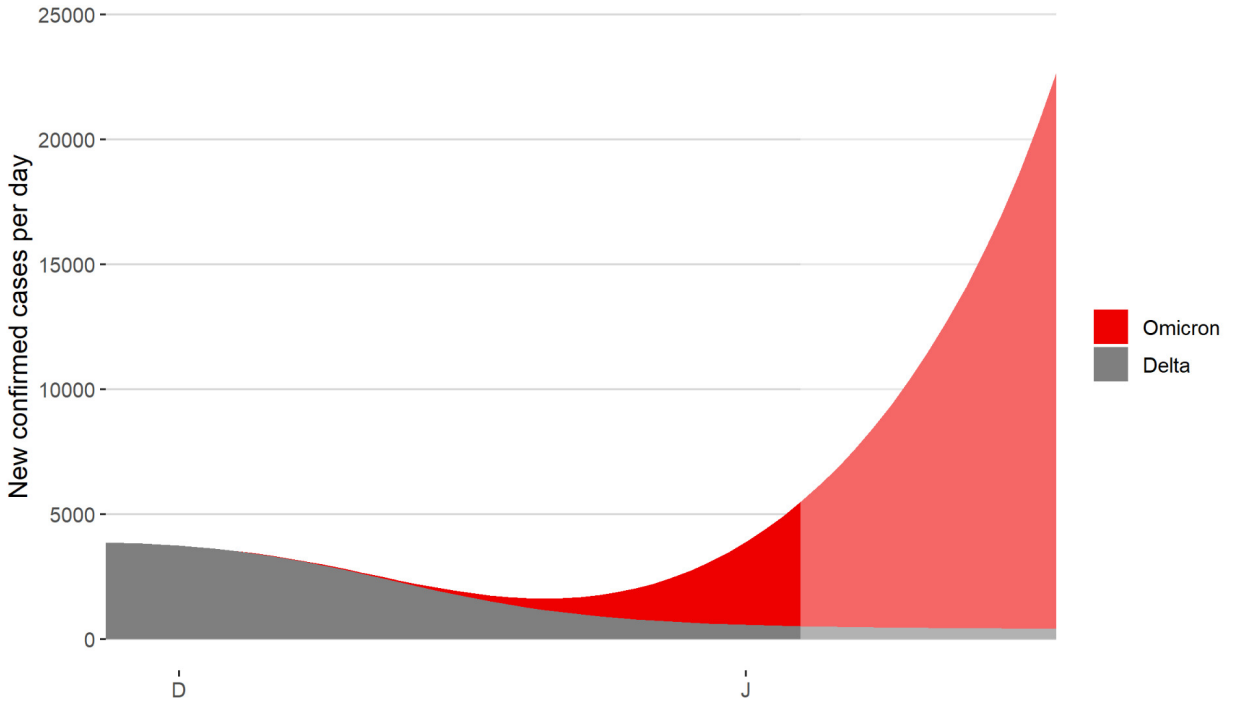

Figure 6: *Foreseen evolution of the number of infections in Belgium based on the data of the Federal Platform laboratories. Projections based on negative binomial GAM fit to S dropout and S positive counts, adjusted for proportions of S dropouts that were Omicron.*

3. Impact of Omicron on the testing-tracing-isolation & quarantine strategy

Beyond the foreseen impact of Omicron on the testing capacity, there has been some anecdotal evidence and a few pre-print manuscripts (source) suggesting that nasopharyngeal swabs lead to a decreased sensitivity of both PCR and rapid antigen tests compared to samples such as breath, saliva or oropharyngeal swabs in the context of Omicron.

Also, considering a possible shorter generation time for Omicron compared to previous variants, the impact of prolonged "time-to-lab result" and "time-to-isolate" indicators, typically observed when the system is getting closer to its maximal capacity, will be more deleterious compared to previous waves. Further, an insufficient testing capacity typically results in an increased positivity rate, which is already observed today in all provinces as described below.

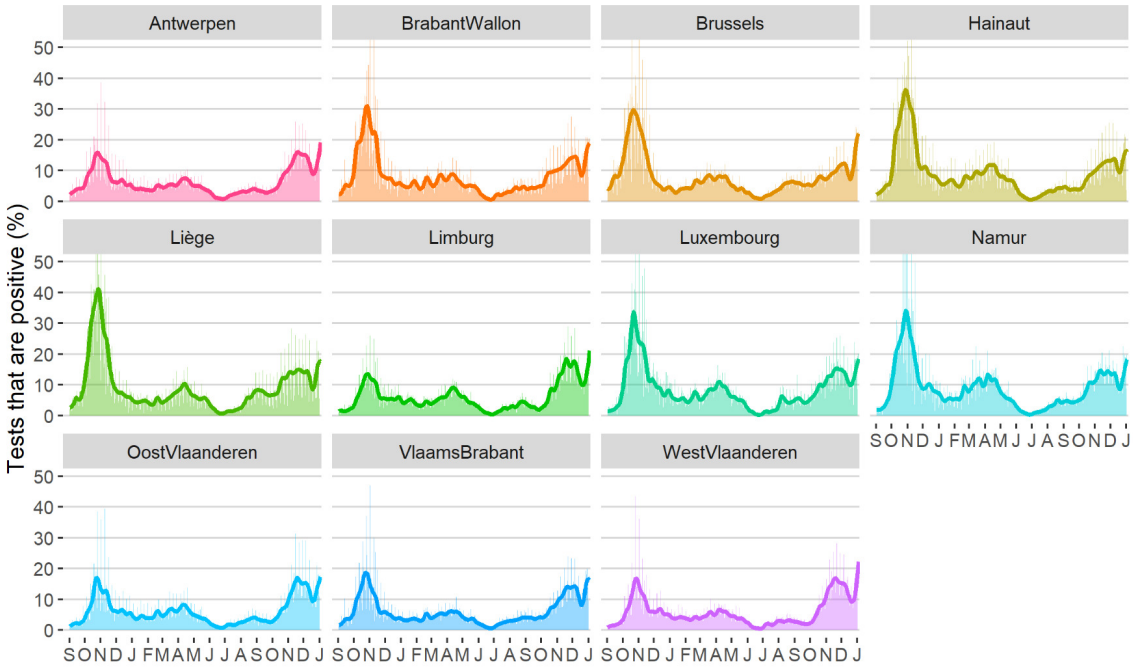

Figure 7: *Positivity ratios by province in Belgium with correction for weekday effect.*

When looking specifically at the Federal Platform laboratory of Leuven for the period 1-4/1/2022, positivity rates have already reached alarming levels and sign **insufficient testing intensity** in the community. Illustratively, the positivity rate reached 19,4% for high risk contacts and 47% for self-referred individuals reporting mild symptoms.

A South Korean preprint recently reported that the mean (± standard deviation) serial interval of Omicron was 2.22 (± 1.62) days, and the basic reproduction number was 1.90 (95% Credible Interval, 1.50–2.43). Compared with the previous finding of a Korean study on the Delta variant (mean serial interval of 3.3 days), these findings suggest that the Omicron variant possesses faster spreading potential in the community. The authors conclude that quarantine, rapid contact tracing, isolation of asymptomatic contacts, strict adherence to public health measures, and COVID-19 vaccination (including booster doses) remain essential to reduce the community transmission of the Omicron variant.

We have recently observed a political tendency to promote rapid antigen self-tests, to reduce the utilization of testing strategies well integrated with the tracing system and to reduce the duration of quarantine. We consider that, while strategies aiming to reduce the pressure on the prevention pillars of the health system and mitigate the socio-economic impact of this pandemic are welcome, **it is at this stage hazardous to head towards a structural dismantling of the preventive pillars of the pandemic response**. Indeed, the centralized system cannot yet be replaced in its function of precise monitoring of the epidemiology and the effective compliance of the patients to testing and tracing indications. Further, **we have no scientific arguments at this stage to support the suppression or the reduction of the duration of quarantine among vaccinated people**. We consider at this stage of our knowledge that such measures may play an accelerating effect on the actual rise of the number of infections if not sufficiently compensated by general measures.

If not precisely accompanied by scientific evidence, this politically-driven tacit shift, which is gambling on the hypothesis that Omicron is the last weapon SARS-CoV-2 is bringing to the fore before becoming a harmless virus, may lead to 'raging endemicity' with consequences that are unmeasurable at this stage. We therefore recommend strengthening all layers of the disease control strategy, and not dismantling the core of the actual disease surveillance & control system being an integrated Testing, Tracing, Isolation & Quarantine system.

Awaiting consolidated evidence, we recommend taking these elements into consideration when revising strategies and prioritizations.

4. Disease severity associated with Omicron infections

Assessing the severity of Omicron remains a challenge due to the very recent surge of infections, the heterogeneity of the vaccination coverage in the different countries affected and the evolving age-distribution of people affected in each country. Nevertheless, we consider that in most settings in Belgium, a lower surge of ICU admissions is expected compared to the Delta wave of infections, although this may be less obvious in larger cities (lower vaccination coverage) or if the total number of infections rises to levels not experienced by other countries.

In London, the Omicron peak of infections seems to have been reached, but the number of patients in ICU and on ventilators has barely budged so far (Figure 8). When compared to pre-COVID winters, ICU occupancy is relatively similar to usual figures at this stage. The situation in hospitals may still evolve, as the number of infections among 65+ is still rising.

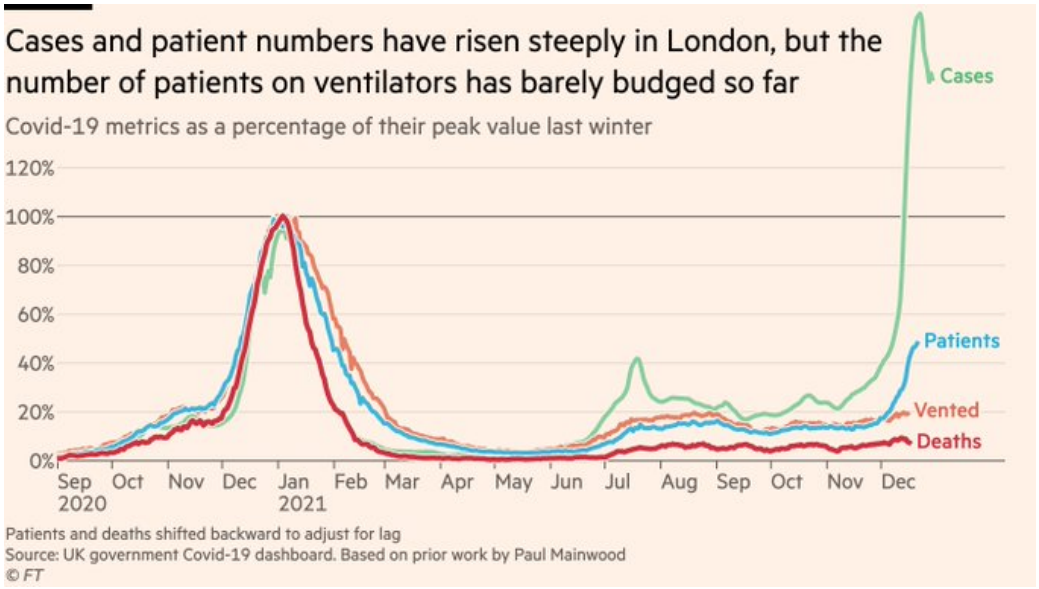

Figure 8: *Evolution of cases, patient numbers, vented patients and deaths in London, UK.*

The situation may be perceived as relatively different in countries where, unlike in the UK or Belgium, the Omicron wave has emerged on top of the Delta winter wave. In such circumstances, even a limited number of severe Omicron infections may severely impact hospital capacities.

Finally, the effective severity of Omicron may be less attenuated in countries with low vaccination rates (Figure 9).

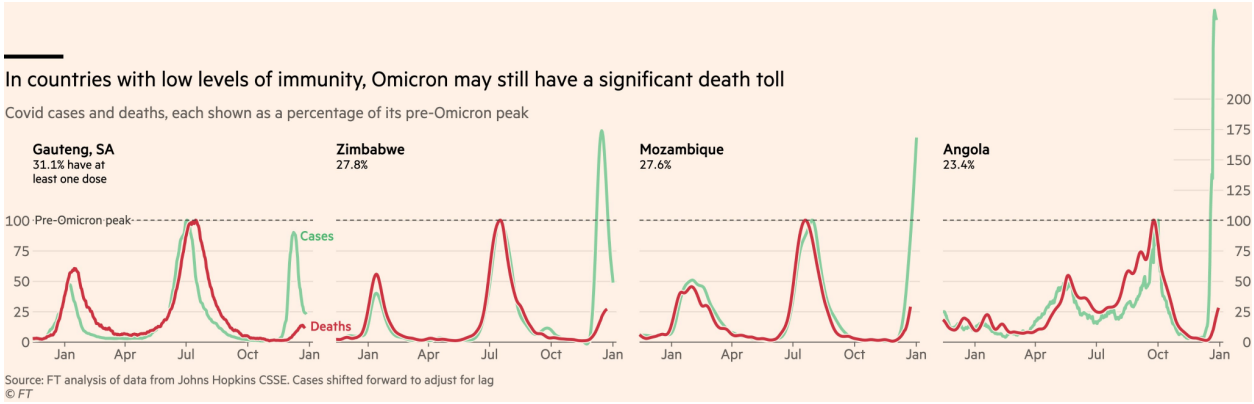

Figure 9: *Omicron waves in countries with a low vaccination coverage*

A recent report from the United Kingdom has looked into the impact of vaccination on Omicron severity. It appears from this report that there has been a recent increase in the percentage of critical care admissions related to non-vaccinated individuals. The percentage of patients admitted to critical care with confirmed COVID-19 that were unvaccinated decreased from 75% in May 2021 to 47% in October 2021, consistent with the decreasing proportion of the general population who were unvaccinated, before increasing again to 61% in December 2021 (Figure 10).

These data align with the preliminary and still incomplete Belgian data which report 6 hospital admissions, all occurring among non-vaccinated patients.

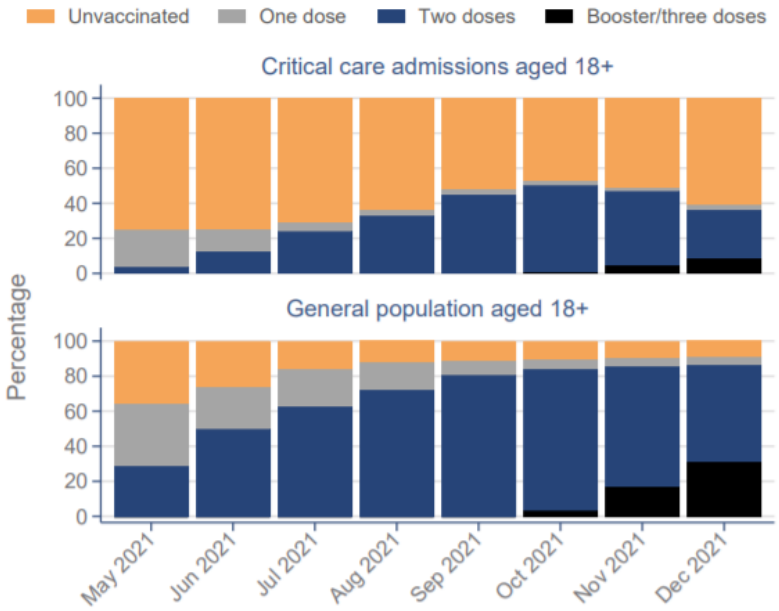

Figure 10: *Percentage of admissions to critical care with confirmed COVID-19 by vaccination status, assessed at 14 days prior to the positive COVID-19 test, for patients admitted 1 May 2021 to 15 December 2021 compared with the general population aged 18 years or older by vaccination status.*

5. Assessment of a potential new SARS-CoV-2 variant detected in Southern France

A recent pre-print publication (not yet peer-reviewed) reported twelve SARS-CoV-2 infected patients living in the same geographical area of Southeastern France, for which the viral genome included 46 mutations and 37 deletions resulting in 30 amino acid substitutions and 12 deletions. Fourteen amino acid substitutions, including N501Y and E484K, and 9 deletions are located in the spike protein. This genotype pattern led to the creation of a new Pangolin lineage named B.1.640.2, which is a phylogenetic sister group to the old B.1.640 lineage which has been renamed B.1.640.1 (see Figure 11). Both lineages differ by 25 nucleotide substitutions and 33 deletions, and at the moment no genomes reside within the B.1.640 lineage definition.

The index case, vaccinated against SARS-CoV-2, returned from a trip in Cameroon three days earlier, and was an adult first diagnosed as infected with SARS-CoV-2 by qPCR performed in a private medical biology laboratory on a nasopharyngeal sample collected mid-November 2021. This person developed mild respiratory symptoms the day before diagnosis. He lives in a small town in Southeastern France. Subsequent detection by qPCR of three mutations in the spike gene to screen for variants, as systematically performed in France in case of SARS-CoV-2 positivity, revealed an atypical combination with L452R-negativity, E484K-positivity, and E484Q-negativity (Pentaplex assay, ID Solution, France) that did not correspond to the pattern of the Delta variant involved in almost all infections at that time.

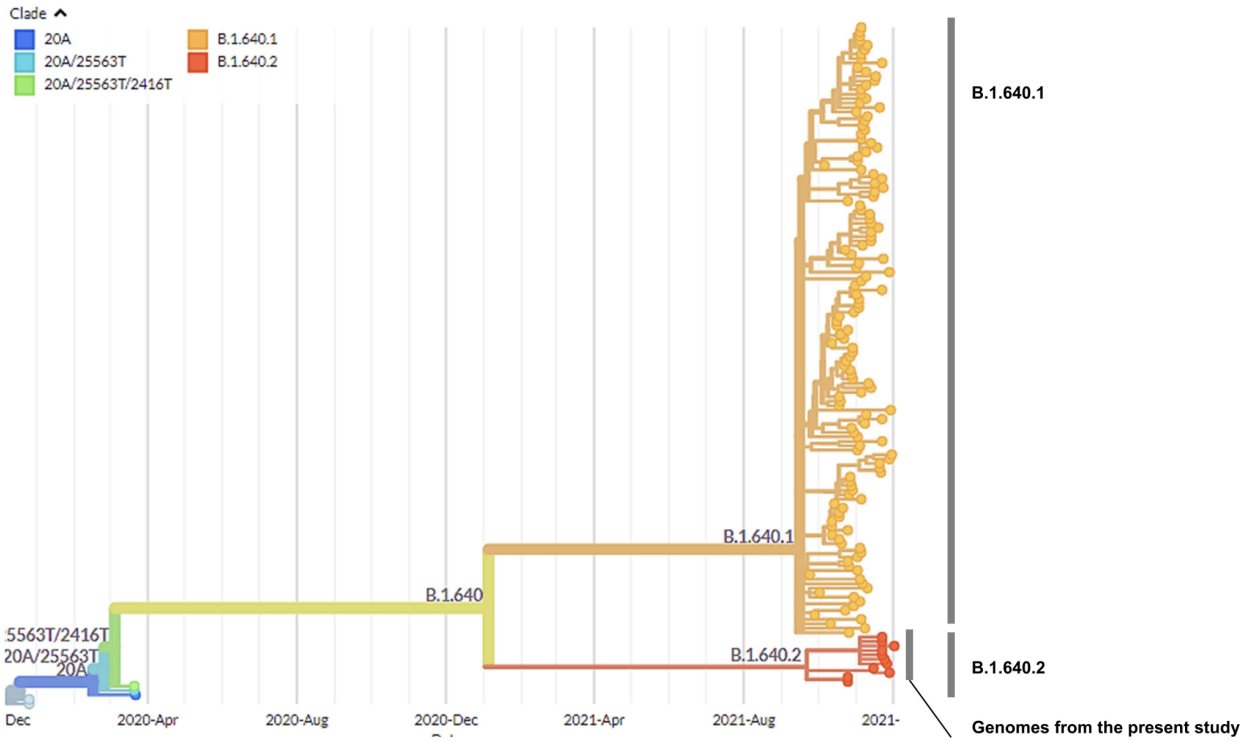

Figure 11: *This new variant detected in southern France is separated from other existing lineages by a long branch, indicating a large number of mutations specific to this variant.*

Apart from the residents in Southeastern France (EPI_ISL_8057576, EPI_ISL_7601710, EPI_ISL_7381031, EPI_ISL_7314514, EPI_ISL_7314417, EPI_ISL_7156959, EPI_ISL_7156955, EPI_ISL_7314302, EPI_ISL_7314471, EPI_ISL_7381062, EPI_ISL_7552465, EPI_ISL_7552470, EPI_ISL_7552483), this new variant definition encompasses three other genomes comprising a sister group including the one recovered late October 2021 in **France** (Ile-de-France) (EPI_ISL_5926666, EPI_ISL_6315910) and more recently (EPI_ISL_7463934), and additional genomes obtained from samples collected late November in **England** (EPI_ISL_7181977, EPI_ISL_7392573), **Wales** (EPI_ISL_7402094), **Germany** (EPI_ISL_7425654) and the **United States** (Texas; EPI_ISL_7412265, EPI_ISL_7412262). So far, three cases of this new variant have been found in **Belgium** (EPI_ISL_7603432, 2nd and 3rd genomes not yet on GISAID). One of these infections concerns a woman who returned from a trip abroad in a red zone (specific country not known at the time of this report). This brings the total known cases to at least 25 worldwide, at the time of writing.

Take note that the novel Pangolin classification has not yet been integrated into the GISAID database, and custom queries were performed to find some of these B.1.640.2 cases.

While the number of mutations associated with this variant can be potentially worrying, we currently don't observe a rapidly increasing number of infections with this variant (Figure 12).

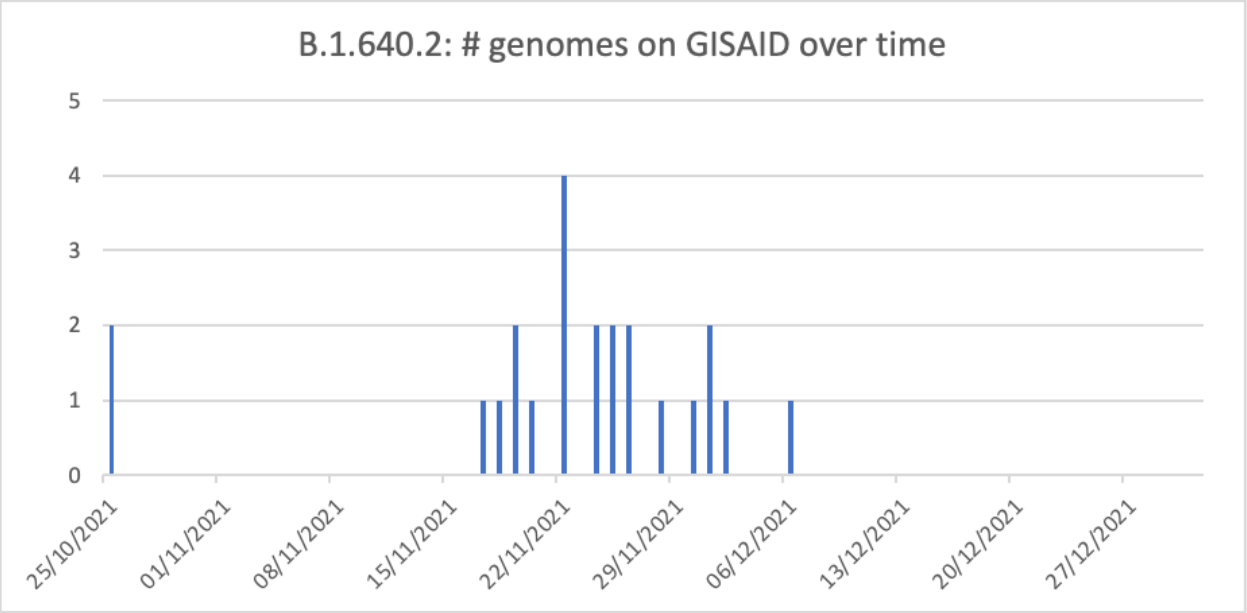

Figure 12: *Currently available number of B.1.640.2 genomes on GISAID over time, based on a custom query (GISAID does not yet distinguish between lineages B.1.640.1 and B.1.640.2).*