KU LEUVEN

DEPARTMENT OF MICROBIOLOGY, IMMUNOLOGY AND TRANSPLANTATION

UZ LEUVEN | LABORATORIUMGENEESKUNDE

Genomic surveillance report

Update for Belgium, 15/03/2022

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Content

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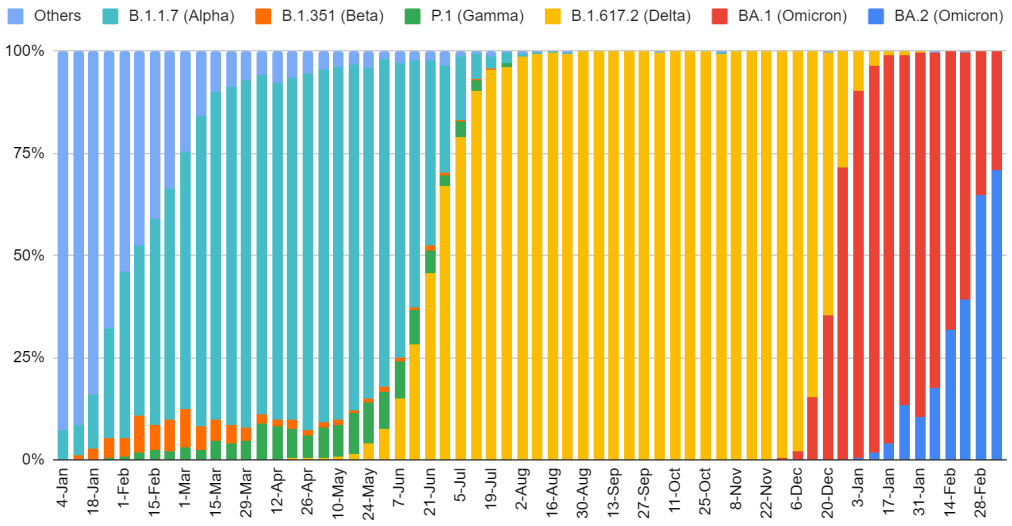
Executive summary

The share of BA.2 has reached 85% of new cases diagnosed during the last few days, as confirmed by the share of SGTF among positive qPCR results (data federal platform labs). This phenomenon starts to be visible through sequencing-based surveillance as well (for the past week at 71.9% for BA.2), although a delay is observed compared to surveillance based on PCR results, due to the turn-around-time of this surveillance system.

Between 28/2/2022 and 13/3/2022 (1,137 sequences collected at this stage), BA.1 and BA.1.1 jointly represented 34.4% (↘) of the circulating strains, while BA.2 represented 65.5% (↗) of the strains sequenced as part of the baseline surveillance. Only one Delta sequence was reported during the last two weeks.



We further report a summary of recently published new observations with regard to the frequency of long-term brain damage following COVID-19 infection, the impact of BA.2 on the efficacy of antiviral treatments, and the international evolution of the pandemic. Based on the latter and the recent epidemiological evolution in Belgium, we expect that there will be an increase in the number of infections during the coming weeks.

1 Epidemiological context and indicators related to diagnostic activities

The share of positive samples (Cq <25) presenting an S gene target failure (SGTF) reflects the share of BA.1 and BA.1.1 samples circulating in the country. Samples which are negative for this marker can be Delta or BA.2, although from genomic baseline surveillance we know that Delta is only sporadically detected for more than one month (three genomes for the last five weeks through the baseline surveillance initiative). Samples without SGTF (most likely to be BA.2 infections) have taken over, now representing 85% of positive samples diagnosed (Figure 1).

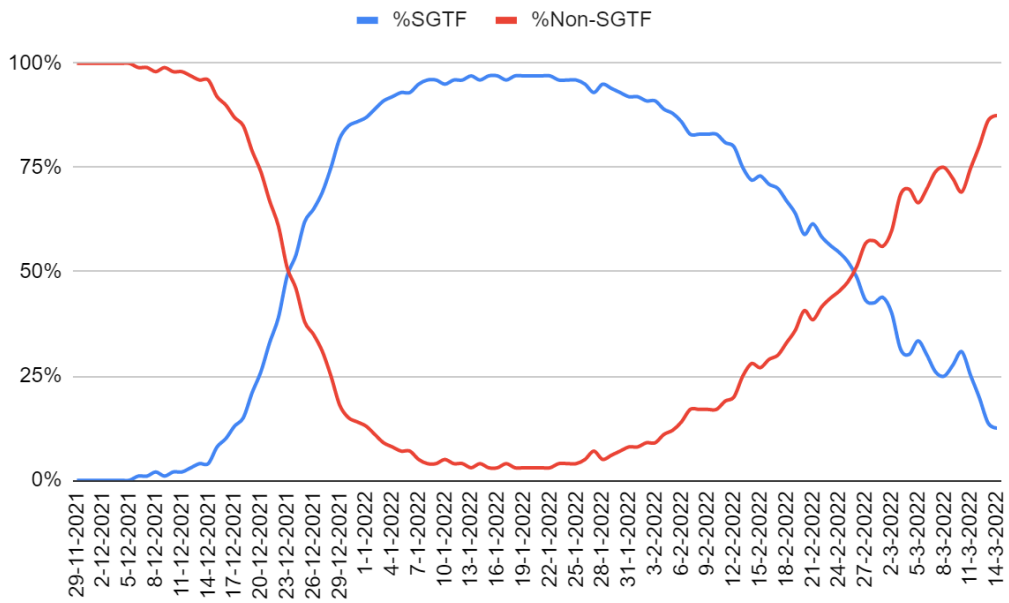


Figure 1: *S gene target failure (SGTF; blue: BA.1 & BA.1.1) and others (red: currently considered predominantly BA.2) among positive samples reported by the federal platform laboratories.*

As shown in Figure 2, the increasing share of non-SGTF positive PCR results was first associated with a steep decrease in SGTF samples (BA.1, BA.1.1 and BA.3). More recently, and despite de-intensification of PCR testing at national level, we observe a rise in the number of non-SGTF infections (BA.2). The recent release of general disease control measures most likely has led and will further lead to an increase of infections in the coming days. These observations are also reflected in the recent discrete increase of infections (R_t = 1.05) and hospitalizations at national level. Nevertheless, accurately monitoring this situation will be difficult, as the general PCR testing indications have been reduced and no equivalent surveillance system has yet been put in place by the health authorities.

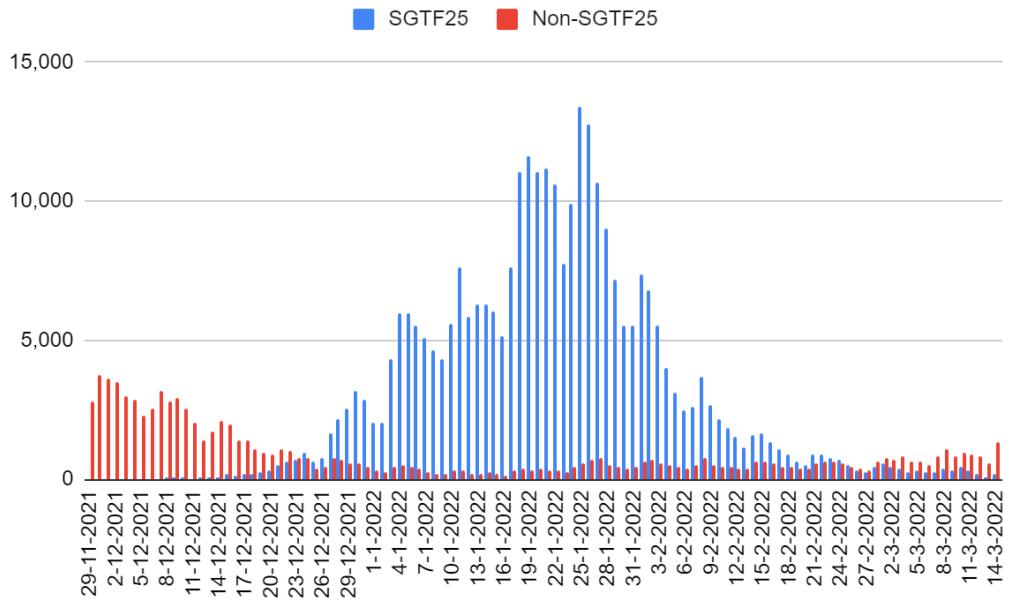


Figure 2: *Number of samples tested positive in the federal platform laboratories with S gene target failure (SGTF; blue) and without SGTF (non-SGTF; red).*

2 Monitoring of Variants of Concern in Belgium

During the last two weeks of baseline surveillance - 28/2/2022 and 13/3/2022 - (1,137 sequences collected at this stage), BA.1 and BA.1.1 jointly represented 34.4% (↘) of the circulating strains, while BA.2 represented 65.5% (↗) of the strains. Only one Delta sequence was reported for the last two weeks (Figure 3).

Although not visualized in Figure 3, recently a rise in the detection of Omicron BA.3 has been observed for Belgium, with currently 30 genomes detected (until the end of February). Nevertheless, overall the number of reported BA.3 cases worldwide remains low compared to the other Omicron sublineages, in total 604 genomes being reported on GISAID. Both for the UK and Denmark, characterized by a high level genomic surveillance, numbers remain low, respectively 34 and 14 genomes. We will however closely follow the share and circulation of BA.3 within the Belgian SARS-CoV-2 epidemic by sequencing as this variant is characterized by SGTF (presence of the deletion 69-70 in the spike protein) when performing a TaqPath COVID-19 PCR, which has currently served as a marker for BA.1 and BA.1.1.

Finally, partners of the national sequencing consortium have reported potential “recombinant” sequences. These results still need to be confirmed before a complete assessment can be communicated.

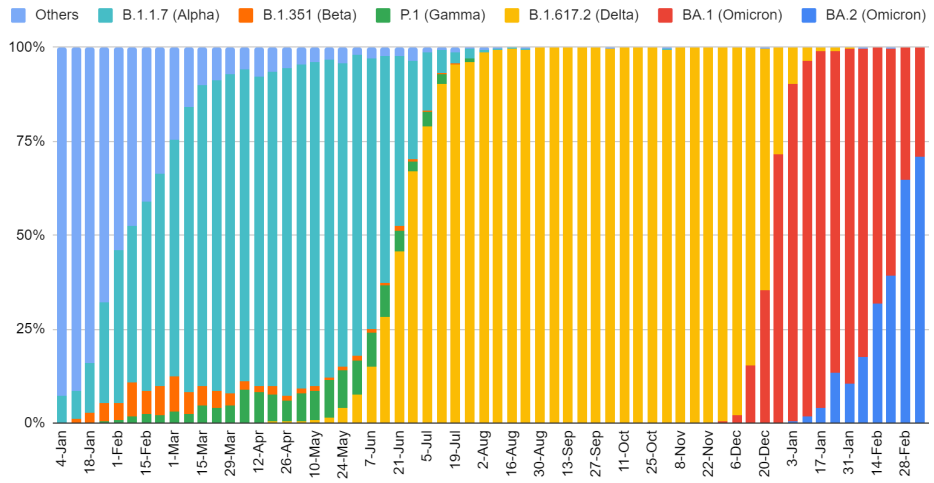


Figure 3: *Share of variants of concern per week in Belgium*

3 Brain changes after COVID infection

A large number of neuropsychiatric symptoms have been attributed to infection with the SARS-CoV-2 virus, from a lost sense of smell and taste to headaches, fatigue, exhaustion after limited physical exercise, memory problems and more. There is also strong evidence for brain-related abnormalities for COVID-19. Large-scale brain-imaging studies can provide quantitative measures of subtle changes in the brain as a result of COVID, and may be able to detect the impact of SARS-CoV-2 infection in milder cases, and whether this can reveal possible mechanisms contributing to brain pathology. However, such brain-imaging studies are very complex. Recently, a study that used imaging before and after infection by the SARS-CoV-2 virus has now revealed substantial changes in the brain after infection.

In a recent Nature publication, Douaud and colleagues describe brain scans that mark the first step in tackling this challenge, by investigating brain changes in 785 UK Biobank participants. The UK Biobank is a large-scale biomedical database and research resource that gathers and shares genetic and health-related information for about half a million people (www.ukbiobank.ac.uk). In 2020, the biobank launched a COVID-19 repeat-imaging study in which participants who had completed their medical-imaging session before the start of the pandemic returned for an identical, second scan session. The Biobank has released the data from 785 sets of these 'before and after' scans, from people between the ages of 51 and 81; 401 of the participants had tested positive for COVID-19 between the two sessions (the case group, with 141 days on average separating their diagnosis and second scan), and 384 had not (the control group). The variant that infected each person was unknown, but the scans were conducted before the emergence of the Omicron variant.

Douaud and colleagues revealed significant differences between the people who had tested positive for SARS-CoV-2 (the case group) and those who had not (the control group), including: (i) greater reduction in grey matter thickness and tissue-contrast in the orbitofrontal cortex and parahippocampal gyrus, (ii) greater changes in markers of tissue damage in regions functionally-connected to the primary olfactory cortex, and (iii) greater reduction in global brain size. The infected participants also showed on average larger cognitive decline between the two timepoints. Importantly, these imaging and cognitive longitudinal effects were still seen after excluding the 15 cases who had been hospitalised.

Douaud and colleagues performed confounder analyses using the extensive, non-imaging characterization data available in the UK Biobank — indices of neuropsychiatric disease, for instance — to show that, both individually and using a clustered approach, no differences between the case group and the control group, in terms of pre-existing characteristics, could account for the reported brain changes. The authors also carefully showed that no differences between IDPs in the baseline imaging session could account for their findings. However, there is no way to exclude the possibility that the reported differences are due to some other, unconsidered differences between the groups.

The authors mention that these mainly limbic brain imaging results may be the *in vivo* hallmarks of a degenerative spread of the disease via olfactory pathways, of neuroinflammatory events, or of the loss of sensory input due to anosmia. Whether this deleterious impact can be partially reversed, or whether these effects will persist in the long term, remains to be investigated with additional follow up.

Douaud *et al*. (2022) SARS-CoV-2 is associated with changes in brain structure in UK Biobank. Nature. https://www.nature.com/articles/s41586-022-04569-5

Gollub (2022) Brain changes after COVID revealed by imaging. doi: https://doi.org/10.1038/d41586-022-00503-x

4 Impact of BA.2 on the efficacy of monoclonal antibodies and novel antiviral therapies

Recent studies by the National Reference Laboratory and others have highlighted the impact of BA.2 on the expected clinical efficacy of monoclonal antibodies and novel antiviral therapies.

The findings highlight an important impact of BA.2 on the efficacy of several monoclonal antibodies, in particular Sotrovimab and Adintrevimab which still had a residual activity for BA.1 (Figure 4). These observations have been published in a preprint involving the Institut Pasteur Paris, the Belgian NRC and the Rega Institute (KU Leuven) and in a letter to the editor by scientists from Japan. At this stage, no resistance to novel antivirals have been observed with this emerging subvariant of Omicron.

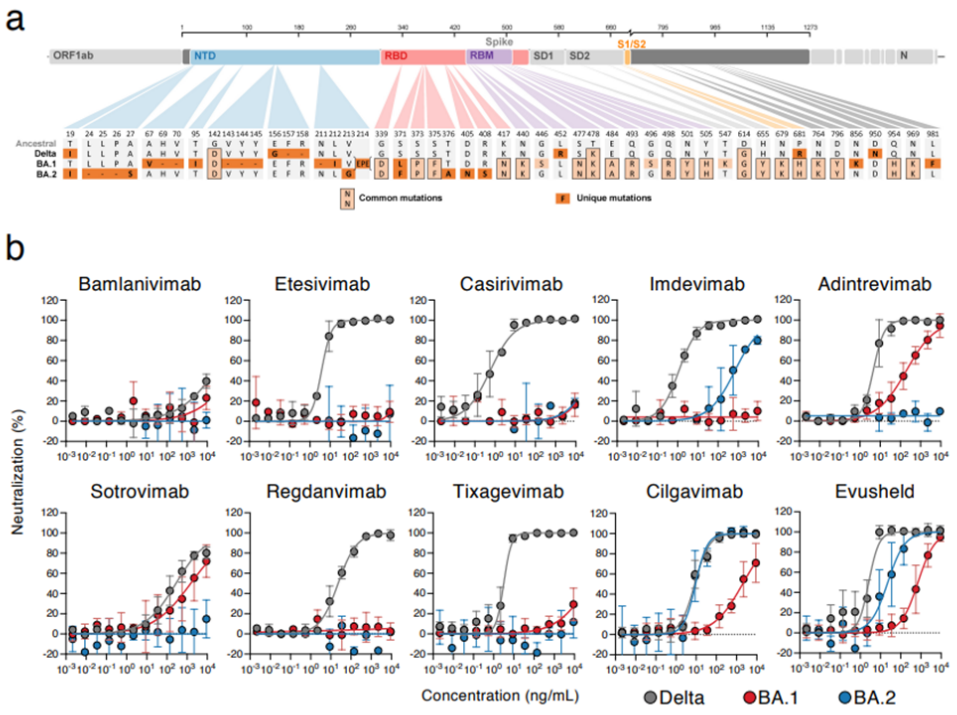


Figure 4: *Sensitivity of Omicron BA.2 to monoclonal antibodies*

5 International situation

Several European countries have recently observed a recent rise of infections which, in terms of timing, follows national releases of disease-control measures and is concomitant with the dominance of BA.2. This phenomenon is for now still modest in Belgium, but a rise of infections is to be expected in the coming weeks (Figure 5).

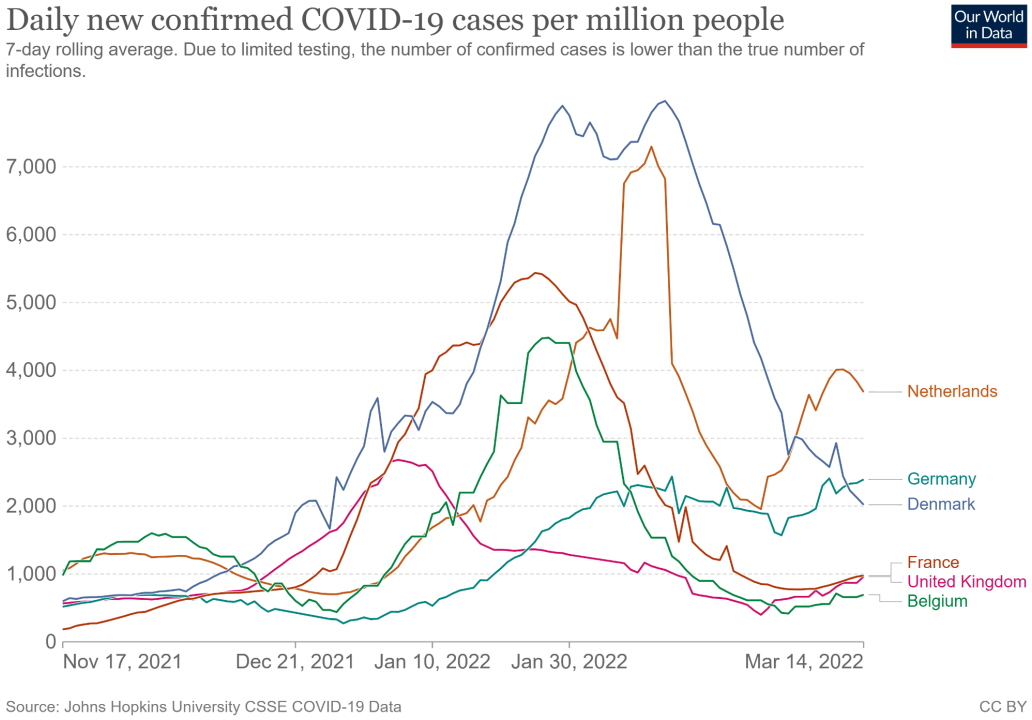


Figure 5: *Evolution of the daily number of confirmed cases over the last few months in several European countries.*

The situation in Hong Kong has recently generated a lot of attention, as the number of infections have recently increased markedly, together with an alarming increase in mortality (Figure 6). The mortality numbers are to be analyzed in the context of a low vaccination rate, in particular for the older part of the population (Figure 7). Indeed, more than 2/3 of people >80 years were unvaccinated when the Omicron wave started in Hong Kong. A comparison can for instance be made with New Zealand, another country recently hit by an Omicron epidemic wave of a similar amplitude in terms of number of confirmed positive cases. In Belgium today, 91% and 81% of the 85+ population have respectively received two and three vaccine doses.

Another similarity between Hong Kong and New Zealand is that both locations have implemented a “zero-COVID” policy since the beginning of the pandemic, implying that there is a very low level of post-infection immunity in these countries. The current situation in New Zealand tends to show (at this stage) that vaccination alone can be sufficient to prevent high levels of mortality in a population. As illustrated below, the case fatality rate associated with the Omicron wave in both locations is not comparable (Figure 6), a difference that most probably lies in the much lower vaccination rate in Hong Kong, and in particular for its older population (Figure 7).

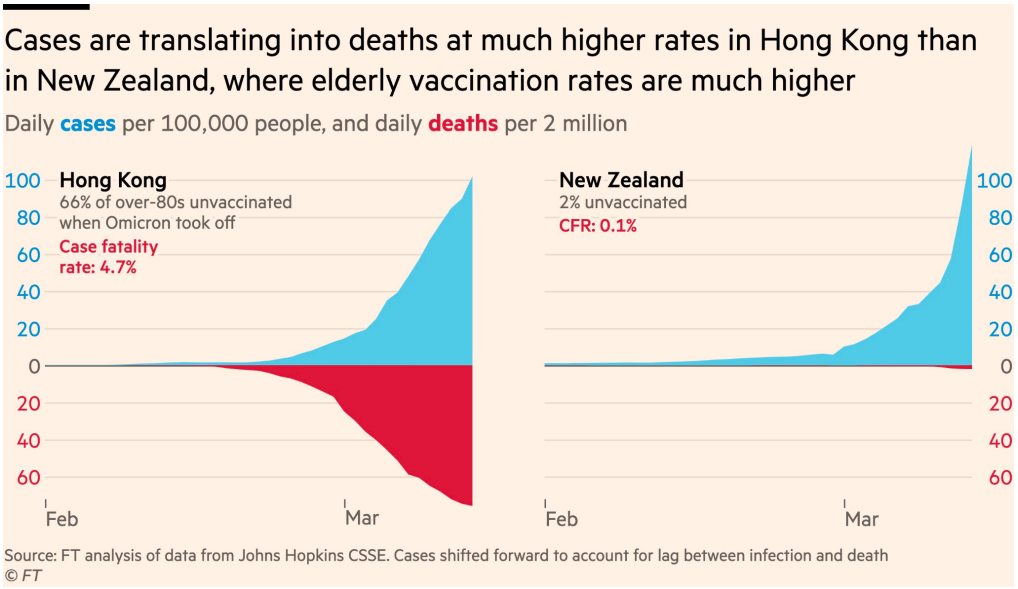


Figure 6: *Comparison of the co-evolution of confirmed cases (in blue) and deaths (in red) between Hong Kong and New Zealand.*

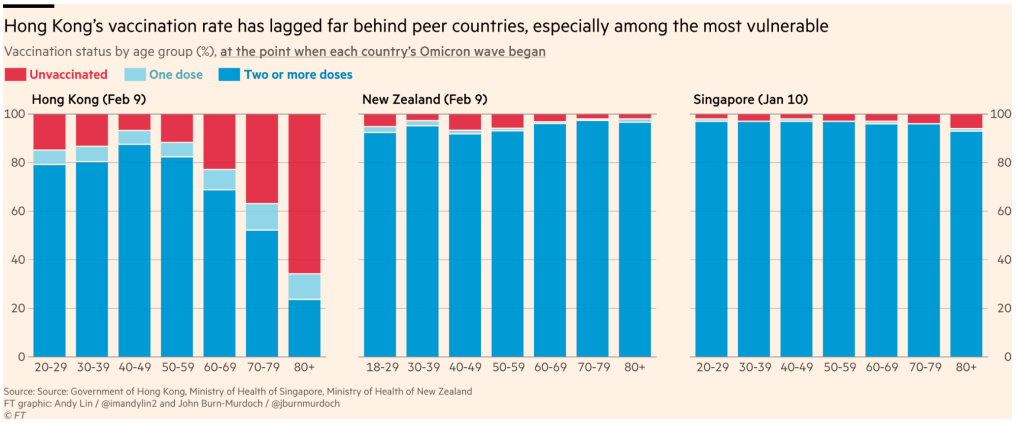


Figure 7: *Comparison of the vaccination rate between Hong Kong and New Zealand (as well as Singapore in the figure). The bar plots display the vaccination rate by age category when the Omicron wave began in each location.*