KU LEUVEN
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UZ LEUVEN | LABORATORIUMGENEESKUNDE

Genomic surveillance report

Update for Belgium, 01/02/2022

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Content

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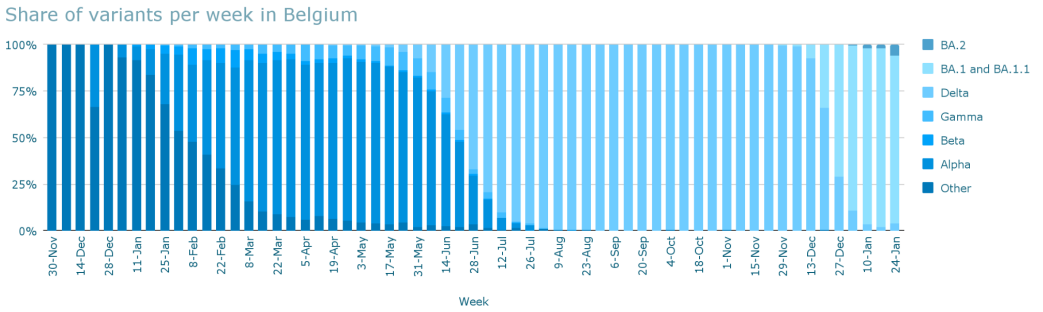
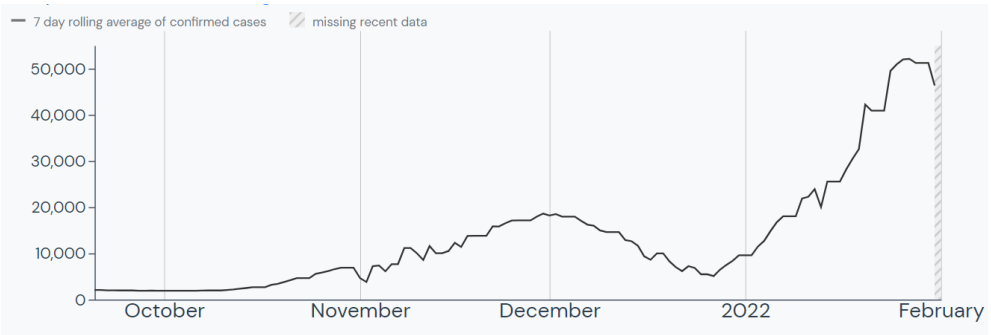
Executive summary

During the last two weeks (17/1/2022 to 30/1/2022, representing 849 sequences at this stage), we observed a significant growth in the share of samples classified as BA.1.1 and BA.2, while BA.1 samples seemed to have peaked around 12/1/2022. During the week of 24/1/2022, BA.1 and BA.1.1 jointly represented 90.1% (↘) of the circulating strains, while BA.2 and Delta represented respectively 5.8% (↗↗) and 4% (↘↘) of the strains sequenced as part of the baseline surveillance.



While a peak seems to have been recently observed in terms of the number of infections in the country, it remains possible that a prolonged high viral circulation will be observed as a consequence of the ongoing viral population replacement. At this stage, we cannot exclude a second peak of infections associated with BA.2, which seems to be associated with a higher transmission rate compared to BA.1. Such evolution would nevertheless be mitigated by expected cross-immunity between the different sublineages of Omicron. At this stage, we have no argument to presume that these lineages would significantly differ from BA.1 in terms of virulence or vaccine efficacy.



1 Epidemiological context and indicators related to diagnostic activities

The current decline in the reported number of samples is associated with a recent decline in the positivity rate among diagnostic PCR tests performed in the Federal Platform Laboratories (Figure 1). This trend is consistent with a non-artificial decline, although the positivity rate remains high (45%), highlighting an inadequate testing capacity or testing strategy. We therefore consider that the peak of infections related to BA.1 infections has been observed.

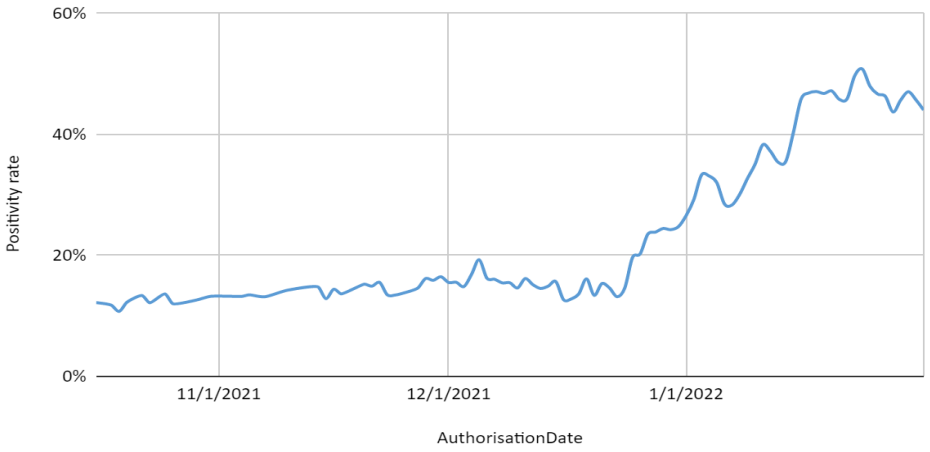


Figure 1: *Positivity rate among the Federal Platform Laboratories.*

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. Samples presenting SGTF currently represent 93% of positive samples diagnosed (Figure 2).

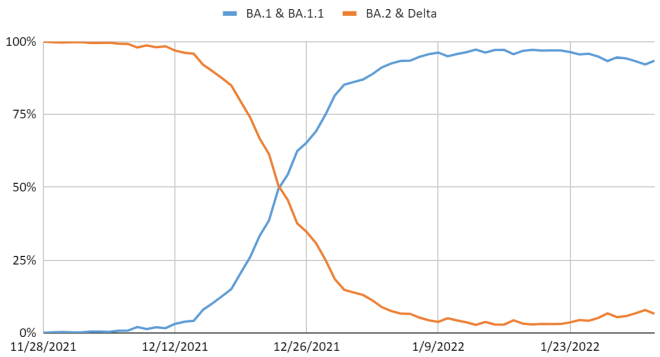


Figure 2: *S Gene Target failure among positive samples reported by the Federal Platform laboratories*

2 Sequencing activity

83,106 Belgian sequences of SARS-CoV-2 are now publicly available on GISAID; compared to last week's report, 1,739 sequences have been added. For the last two weeks (17/1/2022 to 30/1/2022) 849 sequences were available at the time of writing the present report (Figure 3).

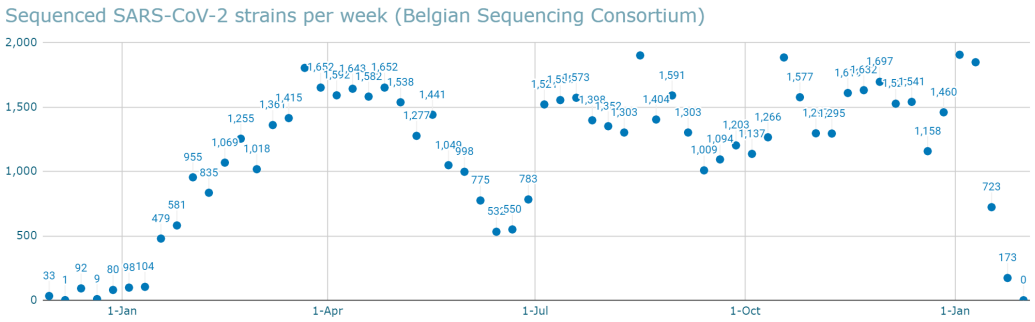


Figure 3: *Number of positive samples sequenced per week by the sequencing consortium laboratories. Due to technical delays, the data for the last two weeks is incomplete.*

3 Monitoring of Variants of Concern in Belgium

3.1 Sequencing surveillance (Belgian Sequencing Consortium)

During the week of 24/1/2022, BA.1 and BA.1.1 jointly represented 90.1% (↘) of the circulating strains, while BA.2 and Delta represented respectively 5.8% (↗↗) and 4% (↘↘) of the strains sequenced as part of the baseline surveillance. Despite still representing a minority of the circulating strains, the share of BA.2 has doubled over one week. This evolution will have as a consequence that BA.2 will become dominant within the next month, possibly provoking a new rise of infections within the same timeframe.

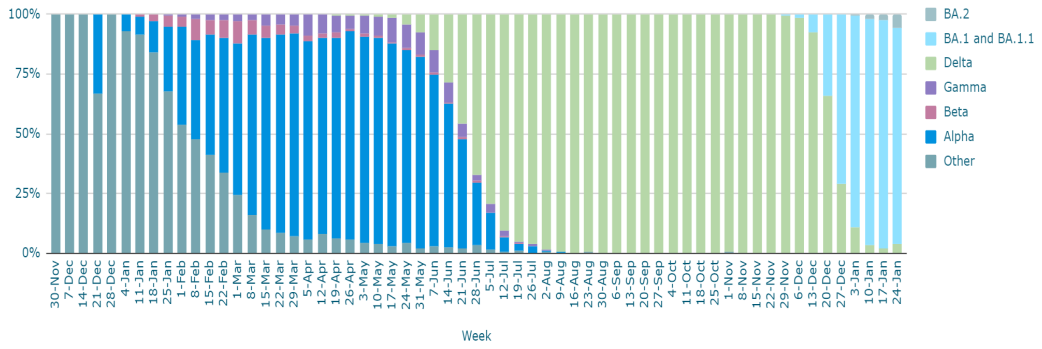


Figure 4: *Share of variants of concern per week in Belgium*

Omicron lineage currently consists of 4 main sublineages (BA.1, BA.1.1, BA.2 and BA.3) which present different evolutions. While BA.1 infections currently decline and BA.3 remains anecdotal, two sublineages currently present a rising evolution: BA.1.1 and BA.2 and BA.1.1 (Figure 5).

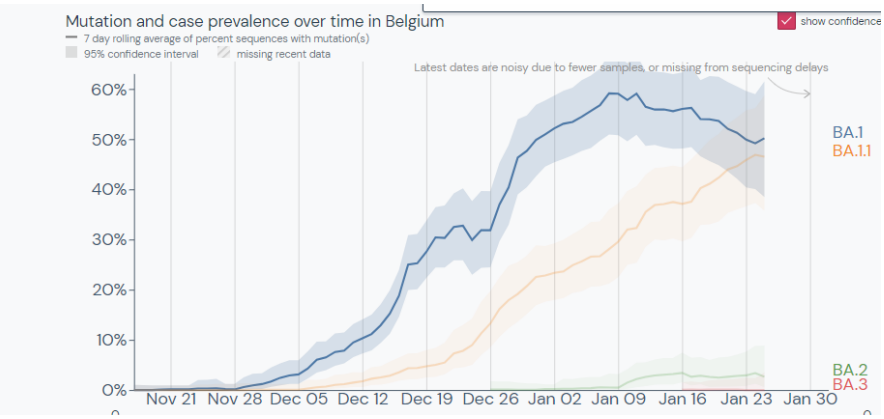


Figure 5: *Share of Omicron sublineages in Belgium (source)*

The level of antigenic diversity between the different variants of concern is a major driver of breakthrough infections, as these subtle changes facilitate immune escape. In the figure below (Figure 6), we highlight that the changes have been relatively important between the different variants which have provoked major waves of infections in Belgium (wildtype -> Alpha -> Delta -> Omicron). The same figure also highlights the antigenic diversity among sublineages of Omicron. The very limited difference between BA.1 and BA.1.1 (one mutation in the S gene) suggests that BA.1.1 will probably not provoke a major change with regard to the general epidemiology when this variant will become dominant. For BA.2, we observe marked differences in several genes of the virus, what suggest that the immunity built after an infection with BA.1 (and certainly after infection with other previous variants) will not be totally efficient in preventing breakthrough infections with BA.2

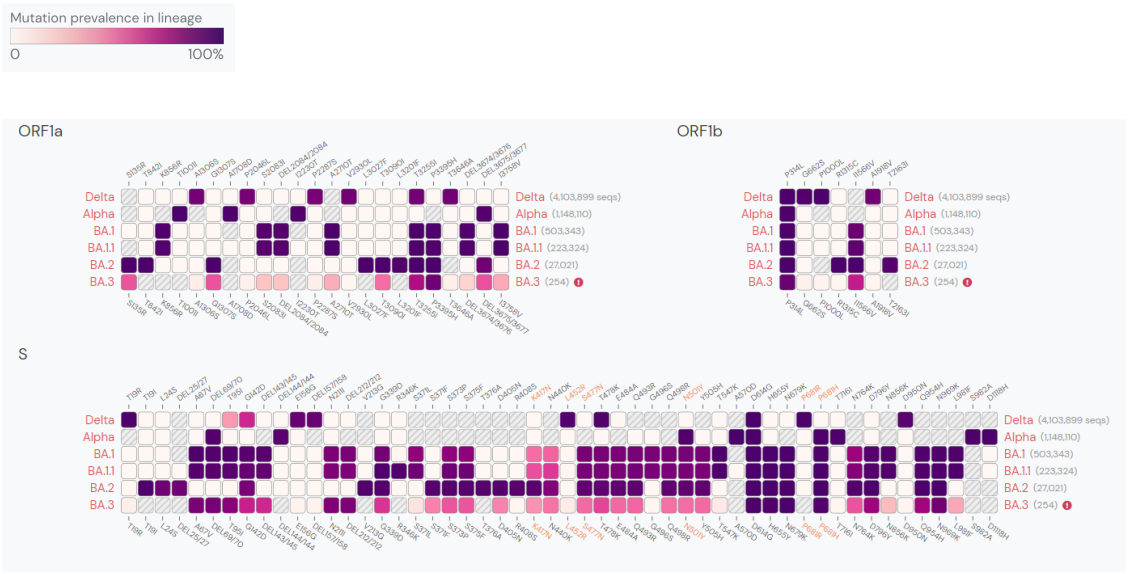


Figure 6: *Orf1a, Orf1b and S mutation prevalence across Omicron sublineages and previous variants of concern which have resulted in a very large number of infections in Belgium (source)*

4 Monitoring of disease severity among hospitalized patients

To monitor the impact of high viral circulation in the community on hospitals, we monitor on a weekly basis the number of patients admitted to UZ Leuven University Hospitals with a diagnosis of COVID-19 infection. Since 13/12/2021, we assessed the severity of symptoms according to WHO classification and performed genotyping among samples presenting sufficiently high viral load.

In total, 308 patients have been evaluated at this stage over a period of 7 weeks. The main observations are:

- The number of patients presenting an asymptomatic or mild COVID-19 infection is important and reflects the high viral circulation in the community. These patients are typically admitted for other reasons than their COVID infection.
- The number of severe and critical infections remain low and relatively stable over the last 3 weeks. Omicron currently represents the large majority of new severe infections.
- The number of severe pediatric infections (MIS-C) remains low and stable.

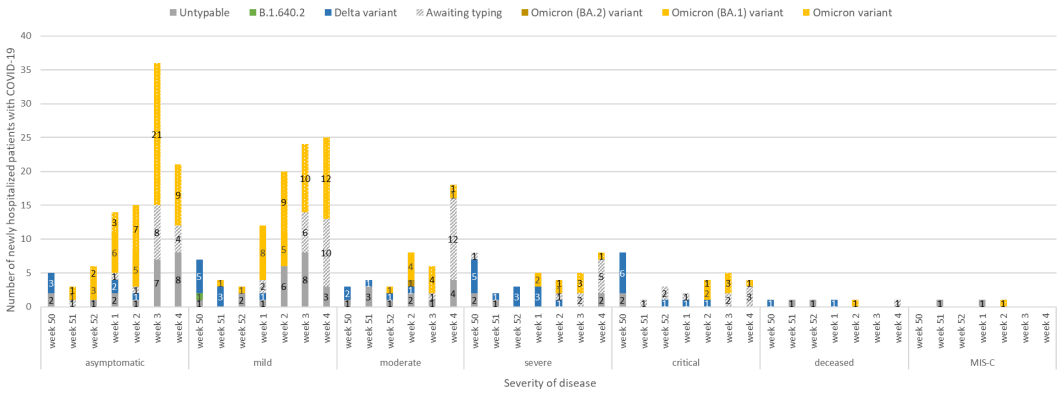


Figure 6: *Severity of COVID-19 disease among patients admitted to UZ Leuven University Hospital with a diagnosis of SARS-CoV-2 infection*

5 Updated overlook on BA.2

5.1 Transmissibility

In a recent preprint, Lyngse *et al*. analyzed >8,500 Danish household cases to estimate and compare the secondary attack rate (SAR), the susceptibility of infection, as well as the transmission between lineages BA.1 and BA.2. Their results can be summarized as follows:

(i) SAR: 29% for BA.1 and 39% for BA.2, resulting in an increase of ~30%, which is higher than the increase of ~13% estimated and reported in a recent UKSHA report;

(ii) susceptibility: odds ratio (OR) vs BA.1 = 2.2 (unvaccinated), 2.5 (vaccinated), and 3 (boosted);

(iii) transmission: OR vs BA.1 = 2.6 (unvaccinated) and <1 (vaccinated).

Table 2: Effect of Vaccination

	Susceptibility		Transmissibility	
	Omicron BA.2 households	**Omicron BA.1 households**	**Omicron BA.2 households**	**Omicron BA.1 households**
Unvaccinated	1.10	1.23	1.21	0.93
	(0.92-1.32)	(1.09-1.40)	(0.97-1.50)	(0.80-1.08)
Fully vaccinated	ref	ref	ref	ref
	(.)	(.)	(.)	(.)
Booster vaccinated	0.80	0.65	0.79	0.77
	(0.67-0.94)	(0.58-0.73)	(0.64-0.98)	(0.70-0.88)
Number of observations	17,945	17,945	17,945	17,945
Number of households	8,541	8,541	8,541	8,541

Notes: This table shows odds ratio estimates for susceptibility and transmissibility by vaccination status. Column 1 shows the susceptibility based on the vaccination status of the potential secondary case, conditional on being in a household infected with BA.2. Column 2 shows the susceptibility based on the vaccination status of the potential secondary case, conditional on being in a household infected with BA.1. Column 3 shows the transmissibility based on the vaccination status of the primary case, conditional on being in a household infected with BA.2. Column 4 shows the transmissibility based on the vaccination status of the primary case, conditional on being in a household infected with BA.1. Note that all estimates are from the same model, but with a different reference category across column 1-4. The estimates are adjusted for age and sex of the primary case, age and sex of the potential secondary case, size of the household, and primary case sample date. The estimates are furthermore adjusted for vaccination status of the potential secondary case and primary case interacted with the household subvariant. 95% confidence intervals are shown in parentheses. Standard errors are clustered on the household level. The odds ratio estimates for the full model are presented in the appendix Table 12, column I.

Table 3: Relative effect of Omicron VOC BA.2 vs. BA.1

	Susceptibility			Transmissibility		
	Unvaccinated	Fully vaccinated	Booster vaccinated	Unvaccinated	Fully vaccinated	Booster vaccinated
Omicron BA.2 households	2.19	2.45	2.99	2.62	0.60	0.62
	(1.58-3.04)	(1.77-3.40)	(2.11-4.24)	(1.96-3.52)	(0.42-0.85)	(0.42-0.91)
Omicron BA.1 households	ref	ref	ref	ref	ref	ref
	(.)	(.)	(.)	(.)	(.)	(.)
Number of observations	17,945	17,945	17,945	17,945	17,945	17,945
Number of households	8,541	8,541	8,541	8,541	8,541	8,541

Notes: This table shows odds ratio estimates for the effect of living in a household infected with BA.2 relative to BA.1. Column 1 and 4 shows the relative transmission of BA.2, conditional on being unvaccinated. Column 2 and 5 shows the relative transmission of BA.2, conditional on being fully vaccinated. Column 3 and 6 shows the relative transmission of BA.2, conditional on being booster vaccinated. Note, all estimates are from the same model, but with a different reference category across column 1-6. The estimates are adjusted for age and sex of the primary case, age and sex of the potential secondary case, size of the household, and primary case sample date. The estimates are furthermore adjusted for vaccination status of the potential secondary case and primary case interacted with the household subvariant. 95% confidence intervals are shown in parentheses. Standard errors are clustered on the household level. The odds ratio estimates for the full model are presented in Appendix Table 12, column I.

5.2 Virulence

More data to come will soon likely be able to highlight any potential difference between BA.1 and BA.2 in terms of symptoms' severity, but according to an official document of the World Health Organization "*the emerging BA.2 form of the Omicron coronavirus variant does not seem to be any more severe than the original BA.1*" (source: Reuters, see below).

5.3 Immune escape

As for the question of the virulence associated with BA.2, data and therefore conclusions on vaccine effectiveness are at this stage very preliminary. Here is a first assessment reported in the last UKSHA Technical Briefing (#35, 28 January 2022): "*A preliminary assessment did not find evidence of a difference in vaccine effectiveness against symptomatic disease for BA.2 compared to BA.1. However, numbers included in this study are relatively small and it will be iterated. The University of Oxford has reported preliminary unpublished pseudovirus neutralization data. In this study, BA.1 and BA.2 pseudoviruses did not differ substantially in neutralization by sera from vaccinated individuals.*"

Sources:

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