Respiratory Viruses in Luxembourg (ReViLux)

Weekly report - 07 March 2023

Executive summary

The sentinel network detected a moderate epidemic activity over the last week (2023/09), based on 7.1% of consultations being associated with influenza-like illness. Among the specimen collected by the sentinel network over the last two weeks, the percentage of positive tests for Influenza type B was 32.3%, followed by Human rhinovirus (30.2%) and Adenovirus (12.8%). Overall, during this season, influenza A (H3) with 90.1% is the most frequent detected strain in submitted specimens, but in recent weeks, increased circulation of Influenza A (H1) pdm and Influenza B have been observed compared to H3.

Concerning SARS-CoV-2 genomic surveillance, the recombinant sub-variant XBB.1.5 has been the most frequent detected variant for the past three weeks with 46.1% (95%CI: 39.8-52.4%), followed by Omicron BQ.1 with 22.6% (95%CI: 17.4-27.9%).

IN THE SPOTLIGHT

SARS-CoV-2: recombinant sub-lineages

XBB is a recombinant of two lineages: BA.2.10.1 and BA.2.75. Early evidence suggests higher infection risk compared to other circulating lineages, due to the mutations it carries in the Receptor-Binding Domain (RBD) of the spike protein. **XBB.1.5** is a subtype with additional spike RBD mutation F486P. The lineage was first detected in October 2022 in the USA and is estimated to have a large growth advantage to other previously circulating lineages. Currently, there are no signals that the infection severity of XBB.1.5 is different from that of other circulating Omicron sub-lineages (ECDC, 2023).

In early 2022 and up to now, a large number of Omicron sub-lineages emerged and continuously monitored in Luxembourg. If proportions of sub-lineages increase, LNS will distinguish and report them separately from its parent lineage.

Introduction

The Laboratoire national de santé, as **National Reference Laboratory for Acute Respiratory Infections** in Luxembourg, performs close surveillance on respiratory viruses, with a special focus on SARS-CoV-2. The main monitoring activities are:

- **The Sentinel Surveillance**. It provides a broad picture of respiratory diseases affecting the Luxembourgish population, based on clinical and laboratory data.
- **The SARS-CoV-2 Genomic Surveillance**. It enables detailed observation of SARS-CoV-2 variants and mutations through time and space, as well as studying specific groups of interest.

The objective of the ReViLux report is to inform public health actions in Luxembourg.

Sentinel Surveillance Network

The Sentinel Surveillance aims at monitoring the circulating respiratory viruses, from traditional ones like Influenza to more recent ones like SARS-CoV-2, and hence underpin public health actions. The Sentinel Network is a group of general practitioners and paediatricians spread over the country. They report the weekly number of patients showing symptoms suggestive of acute respiratory infection (ARI) and influenza-like illness (ILI), and those patients are then sampled and tested for a panel of respiratory viruses. The circulation of respiratory viruses in the north hemisphere is generally monitored by seasons that go from week 40 to week 20. The period between weeks 20 and 40 is usually called interseason.

Clinical results

Last week, 7.1% of consultations were reported as ILI, which represents a moderate epidemic activity for Luxembourg, according to ECDC and the Moving Epidemic Method. The history of ILI consultations is displayed in Figure 1, and a detailed summary of the number of ARI and ILI cases during the last four weeks is included in Table 1.

Laboratory results

Over the last two weeks, the most frequently detected viruses (according to positivity rates) were Influenzavirus B (32.3%), Human rhinovirus (30.2%) and Adenovirus (12.8%). An overview of the viral circulation during the current season is displayed in Figure 2 and Table2.

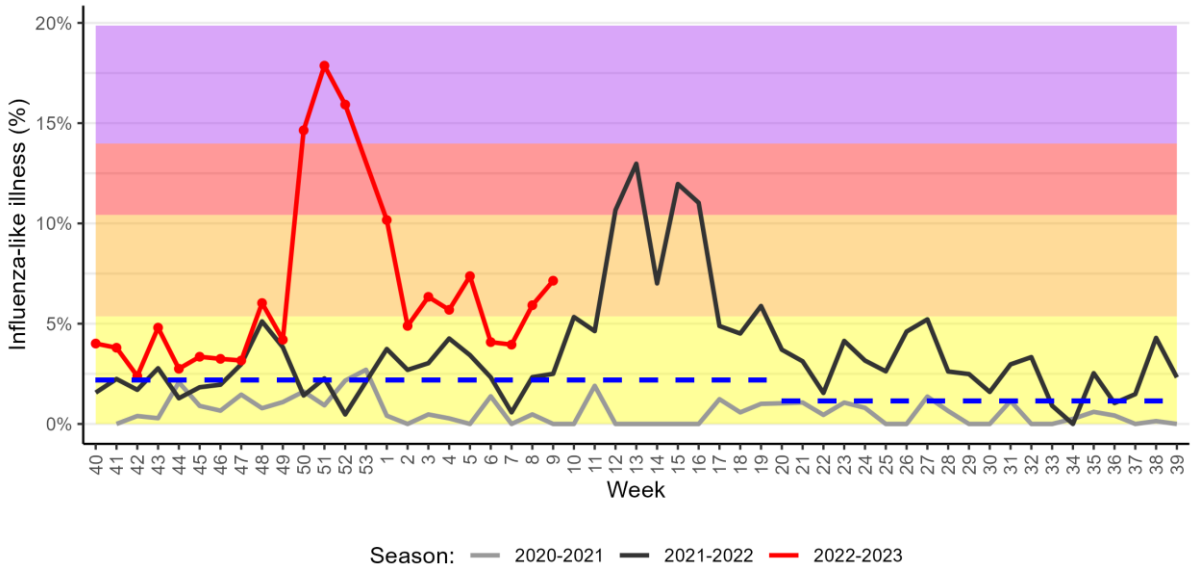

Figure 1. Percentage of patients with influenza-like illness over the last three seasons
Background colours according to intensity of circulation: low, medium, high, very high.

Table 1. Syndromic surveillance over the last 4 weeks

Week	ARI		ILI		Total consultations
	N	%	N	%	
2023/6	61	15.56	16	4.08	392
2023/7	36	20.34	7	3.95	177
2023/8	58	19.08	18	5.92	304
2023/9	66	22.45	21	7.14	294

ARI: Acute Respiratory Infections; ILI: Influenza-Like Illness.

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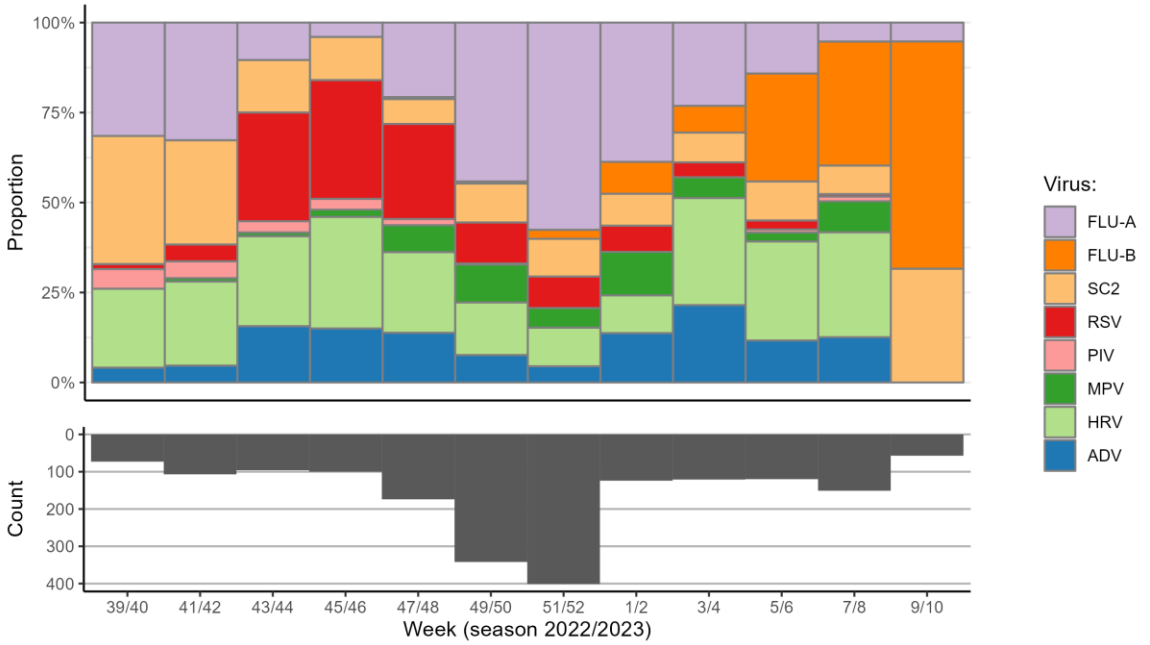

Figure 2. Distribution of respiratory viruses detected within the Sentinel Network, by two-week periods. Results from last weeks are not yet consolidated.
FLU-A: influenzavirus A; FLU-B: influenzavirus B; PIV: parapneumovirus; RSV: respiratory syncytial virus; ADV: adenovirus; MPV: metapneumovirus; HRV: human rhinovirus; SC2: SARS-CoV-2.

Table 2. Distribution of respiratory viruses detected within the Sentinel Network over the last 2 weeks compared to the whole current season.

Virus	Last 2 weeks		Season 2022/2023	
	N*	Positivity rate (%)	N*	Positivity rate (%)
Influenzavirus B	75	32.3	157	8.1
Human rhinovirus	26	30.2	346	20.2
Adenovirus	11	12.8	181	10.6
SARS-CoV-2	27	11.6	230	25.2
Metapneumovirus	6	7.0	113	6.6
Influenzavirus A	6	2.6	383	19.9
Respiratory syncytial virus	0	0.0	205	12.0
Parainfluenzavirus	0	0.0	21	1.2
Total	**151**		**1636**	

**Co-infection cases counted once for each virus detected.*

Genotyping analyses

In order to assess the circulation of viral strains, genotyping analyses were also performed for Influenzavirus A and Respiratory syncytial virus (RSV) (Figure 3). During the current season, the most frequently detected strain for Influenzavirus A was H3 (90.1%), and for RSV it was type B (74.3%).

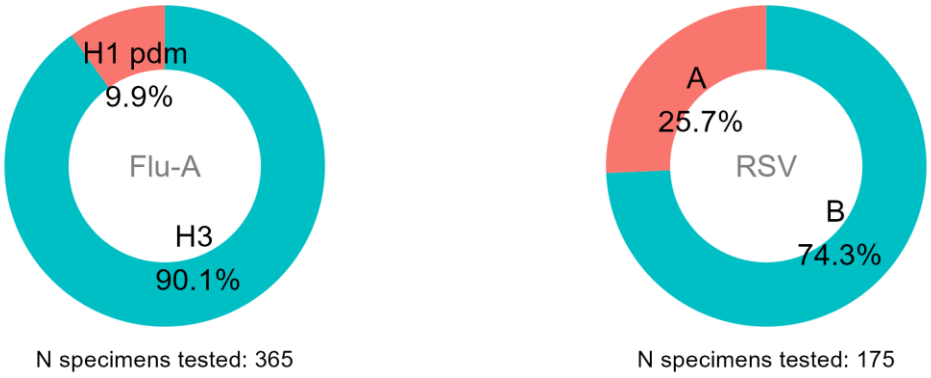

Figure 3. Detection of influenzavirus-A (Flu-A) and Respiratory syncytial virus (RSV) strains in sentinel samples during the current season.

SARS-CoV-2 Genomic Surveillance

SARS-CoV-2 has posed a serious threat to the world population since 2020, and it is still a challenge for health systems. For this reason, the National Reference Laboratory for Acute Respiratory Infections at LNS continues to monitor the genomic characteristics of the SARS-CoV-2 virus detected in Luxembourg.

LNS receives positive specimens (nasopharyngeal or oropharyngeal swabs analysed by RT-PCR) from the national network of laboratories. All hospital specimens are sequenced, as well as a representative selection of community specimens. Illumina and Nanopore devices are used respectively. When needed, an additional screening by targeted PCR is also performed to enable earlier evaluation of the spread of newly emerging variants.

Bioinformatic analyses are based on a standardised pipeline, and lineage assignment is performed through the PANGOLin software (4.2, pango-data 1.18, mode UShER). In order to allow easier visualisation, WHO and Nextstrain categorisations are also used.

Sequencing activity

In week 2023/08, 1427 new cases were registered in Luxembourg; hence, the minimum sample size required to detect emerging variants at a 5% incidence is estimated to be 243 specimens (17%). The microbial genomics unit at LNS sequenced 275 specimens from the week of study, including 250 national ones (sequencing coverage: 17.5%; see Figure 4). This reaches the recommended sample size.

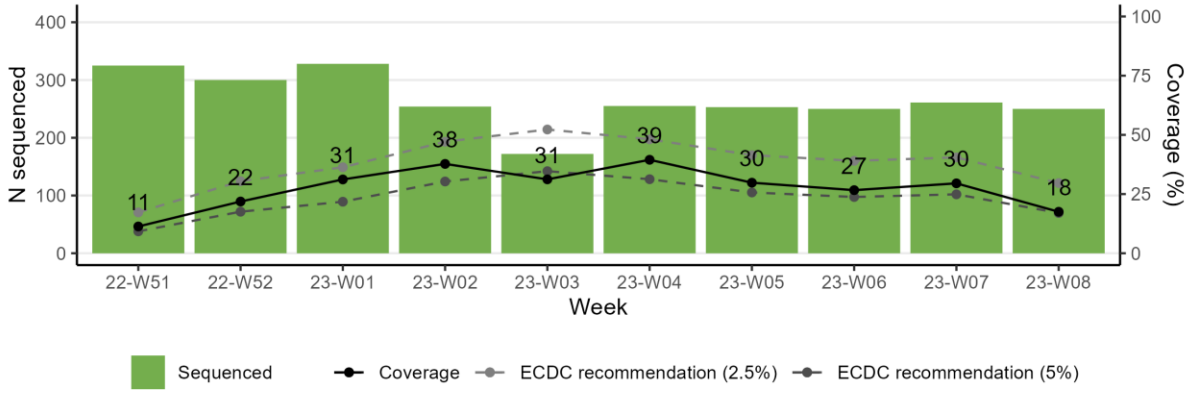

Figure 4. Number of specimens sequenced and national coverage based on weekly number of positive cases in Luxembourg. The coverage from the last two weeks is not consolidated yet.

Variant circulation

The Recombinant variant XBB.1.5 with 46.1% (95%CI: 39.8-52.4%) remains the most frequent detected variant within the representative sample, followed by Omicron BQ.1 (22.6%, 95%CI: 17.4-27.9%). The proportion of Omicron BA.2.75 (including sub-lineages CH1.1 and BN.1) decreased from 16.8 to 11.7% in week 2023/08.

An overview of the variants and lineages circulating over the last weeks is displayed in Figure 5, and further details are shown in Table 3. The history of the circulation of each variant since January 2021 is displayed in Figure 6.

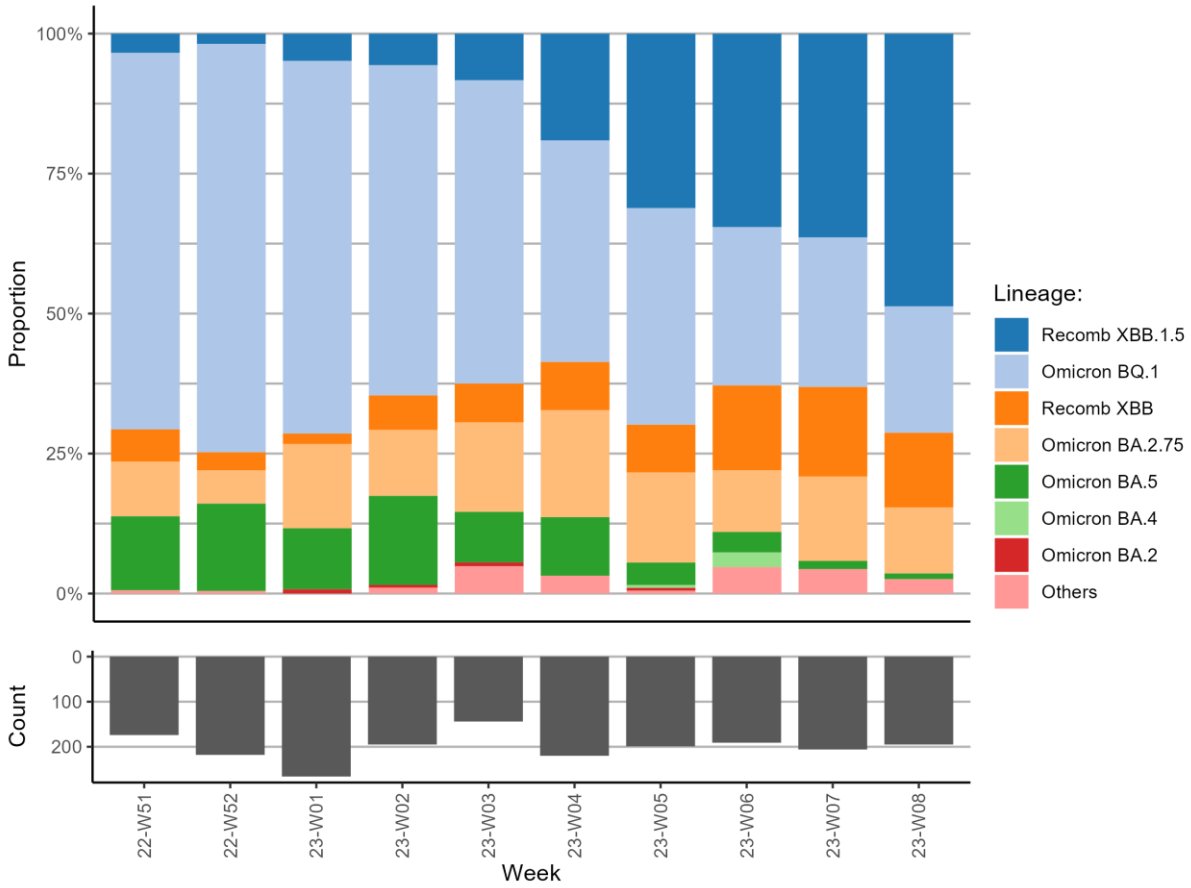

Figure 5. Distribution of lineages within the representative sample during the last 10 weeks.

Table 3. Distribution of SARS-CoV-2 lineages detected within the representative sample during the last two weeks. Previously reported cases might be updated by retrospective analysis.

Lineage*	Week 7		Week 8	
	%	CI %	%	CI %
Recomb XBB.1.5	35.5	29.1 - 41.8	46.1	39.8 - 52.4
Omicron BQ.1	26.4	20.5 - 32.2	22.6	17.4 - 27.9
Recomb XBB	15.5	10.7 - 20.2	14.4	10.0 - 18.8
Omicron BA.2.75	16.8	11.9 - 21.8	11.9	7.9 - 16.0
Others	4.5	1.8 - 7.3	3.7	1.3 - 6.1
Omicron BA.5	1.4	0.0 - 2.9	1.2	0.0 - 2.6

**Sub-lineages are not included in the count of their parental lineages (e.g. BQ.1 not included in BA.5).*
CI: confidence interval at 95%.

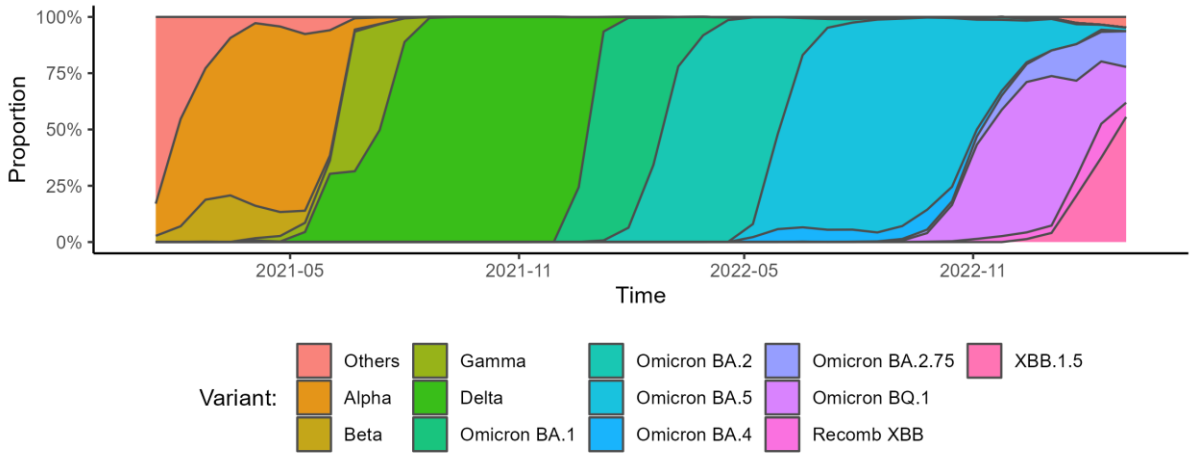

Figure 6. Proportion of each variant circulating in Luxembourg since January 2021.

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Clinical and epidemiological factors

In this section, the lineage distribution of all specimens sequenced over the last month is assessed by demographics (sex and age group, Figure 7) and sampling setting (community vs. hospital, Table 4).

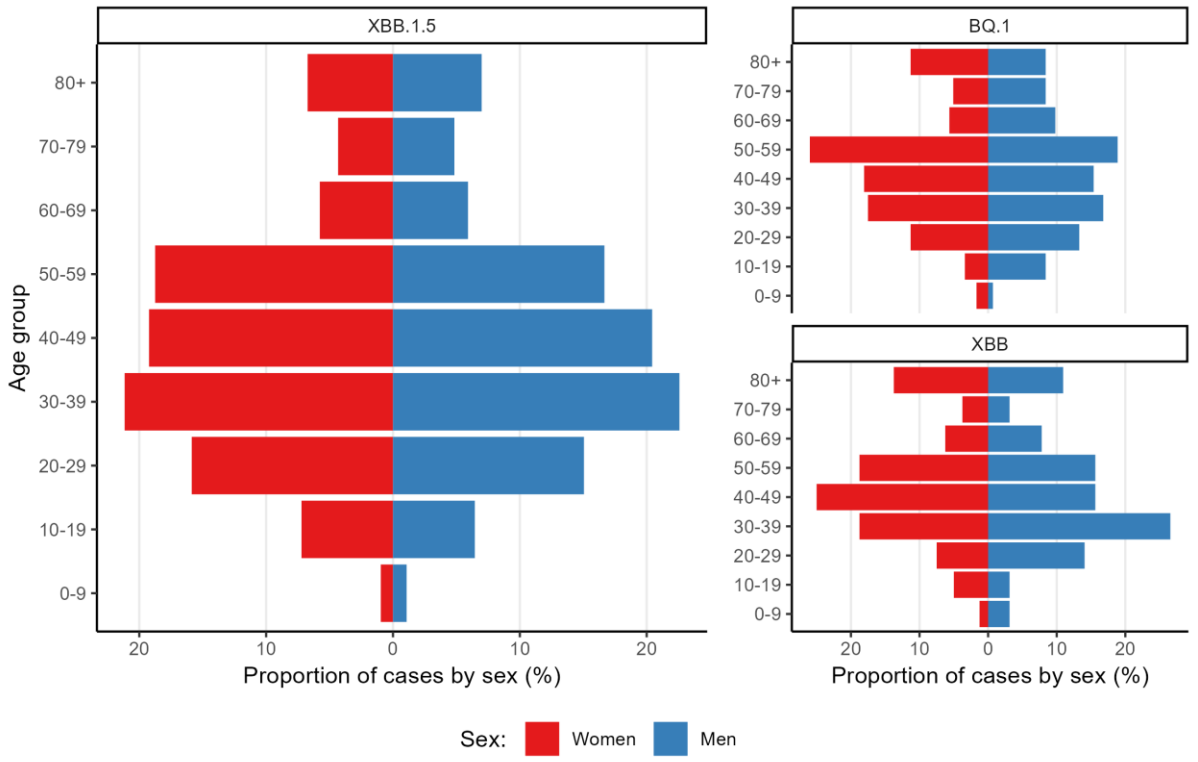

Figure 7. Age group and sex distribution of specimens sequenced over the last 4 weeks, by lineage.

Table 4. Comparison of lineage distribution by sampling setting.

Lineage	Community			Hospital		
	Women	Men	**Total**	Women	Men	**Total**
Recomb XBB.1.5	46.9%	48.7%	**47.7%**	35.9%	42.4%	**39.0%**
Omicron BQ.1	36.2%	35.4%	**35.8%**	45.7%	40.0%	**42.9%**
Recomb XBB	16.9%	15.9%	**16.4%**	18.5%	17.6%	**18.1%**
Total	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**	**100.0%**

Mutation surveillance

In addition to the surveillance of SARS-CoV-2 variants, the LNS monitors the occurrence of SARS-CoV-2 mutations, as their early detection might be key to foresee changes in the epidemic evolution. The LNS is currently monitoring mutations to the spike protein, following ECDC guidance, and comparing their prevalence to that observed in Europe (according to GISAID).

Among the specimens collected over the last four weeks, we detected a higher circulation of the following mutations in Luxembourg (compared to Europe):

Table 5. Mutations detected at a higher proportion in Luxembourg

Lineage	Mutation	Gene	% in LU	% in EU	Ratio
BA.5	R346T	S	73.33	51.0	1.44
BQ.1	F157L	S	8.96	7.4	1.21
BA.5	K444T	S	21.43	18.3	1.17
XBB	Q954H	S	100.00	87.1	1.15
XBB	N969K	S	100.00	87.6	1.14
BA.5	Q954H	S	100.00	87.9	1.14
BA.5	N969K	S	100.00	88.8	1.13
BA.2.75	Q954H	S	100.00	89.2	1.12
BA.2.75	N969K	S	100.00	89.8	1.11
BA.5	P85Q	S	12.50	<5.00	-
BA.5	K182E	S	31.25	<5.00	-
BA.2.75	N211V	S	21.54	<5.00	-
BA.2.75	L212I	S	21.54	<5.00	-
XBB	F486S	S	11.67	<5.00	-
BA.5	F486A	S	20.00	<5.00	-
BA.5	P621S	S	12.50	<5.00	-

LU: Luxembourg; EU: Europe

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