

Respiratory Viruses in Luxembourg (ReViLux)

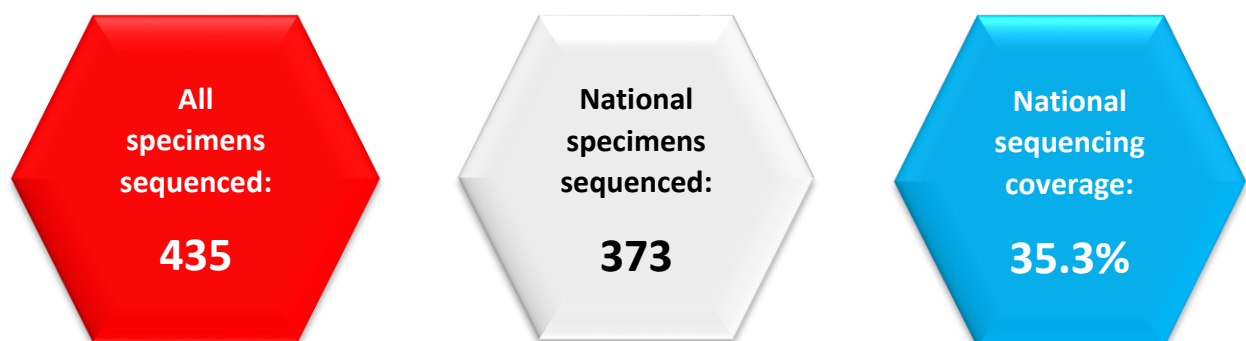
Weekly report (29 November 2022)

Executive summary

The sentinel network reported 2.5% consultations for influenza-like illness, thus exceeding the baseline circulation threshold, according to the European Centre for Disease Prevention and Control (ECDC). Within the specimens collected by the sentinel network, Respiratory syncytial virus was the most frequently detected virus over the last four weeks (32% positivity rate), followed by Human rhinovirus (28%) and Adenovirus (16%).

Regarding the SARS-CoV-2 genomic surveillance, LNS sequenced 373 specimens from residents in Luxembourg in week 46 (of 1058 total cases in the Grand Duchy of Luxembourg). This represents a coverage of 35.3%, which reaches the ECDC recommendations (36.2%) to detect emerging variants at 5% incidence.

The Omicron variant remains the main one detected in the representative sample. The Omicron BQ.1 lineage is the most frequent one (47.7%, confidence interval: 42.7 - 52.8%), followed by Omicron BA.5 (43.4%, confidence interval: 38.4 - 48.5%).



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. There are currently two active projects:

- **The Sentinel Surveillance Network.** It provides a broad picture of respiratory diseases affecting the Luxembourgish population, based on its double monitoring system (syndromic and virological).
- **The National SARS-CoV-2 Genomic Surveillance Program.** It enables detailed observation of SARS-CoV-2 mutations and variants through time and space, and also monitoring specific groups of interest.

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

Sentinel Surveillance Network

The **Sentinel Surveillance Network** aims at monitoring the circulating respiratory viruses, including SARS-CoV-2, and hence underpin public health actions. Following the World Health Organization (WHO) and European Centre for Disease Prevention and Control (ECDC) guidance, it focuses on cases of acute respiratory infection (ARI) and influenza-like illness (ILI).

Syndromic surveillance

The season 2022/2023 started in week 40. 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. Last week, 2.5% of consultations were reported as ILI, thus exceeding the threshold for baseline circulation, according to ECDC (2.19%).

Table 1. Syndromic surveillance over the last 4 weeks

Week	ARI		ILI		Total consultations
	N	%	N	%	
2022/44	36	16.51	6	2.75	218
2022/45	80	22.35	12	3.35	358
2022/46	72	15.58	15	3.25	462
2022/47	90	18.75	12	2.50	480

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

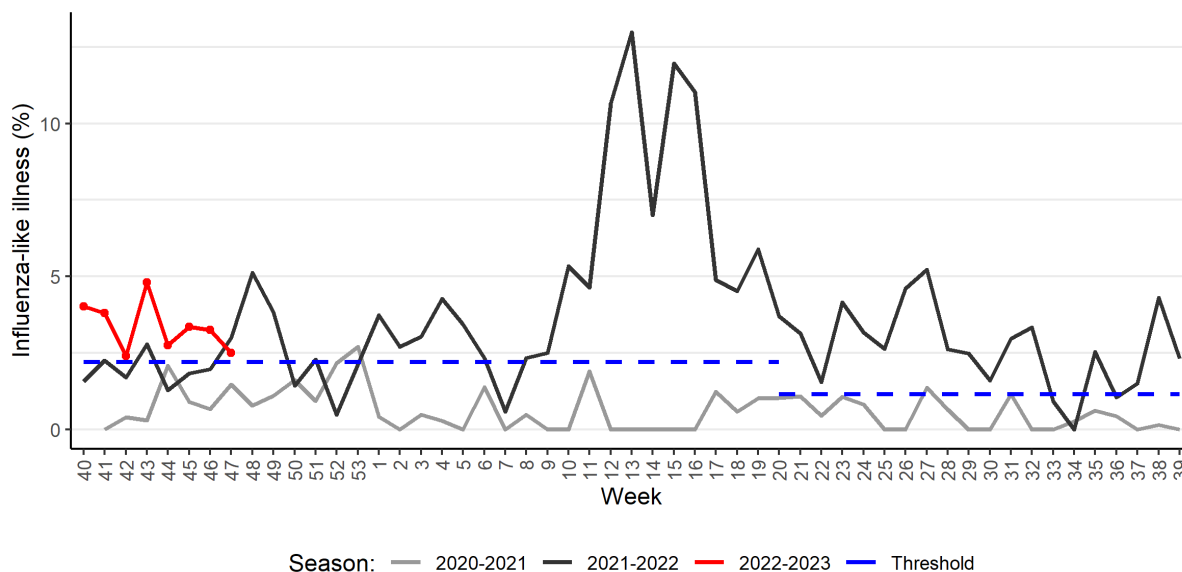


Figure 1. Percentage of patients with influenza-like illness over the last three seasons

Virological surveillance

Additionally, a selection of sentinel cases is further studied in order to monitor the circulation of respiratory viruses in the country, as shown in Figure 2. Over the last 4 weeks, the most frequently detected viruses (and their positivity rates) were Respiratory syncytial virus (32%), Human rhinovirus (28%) and Adenovirus (16%).

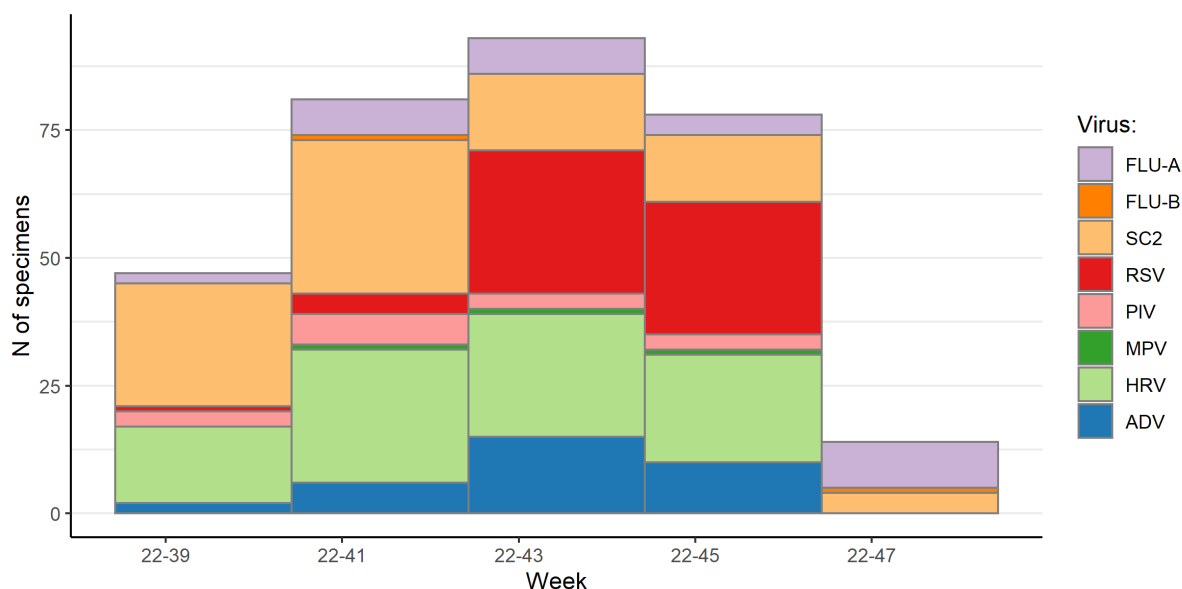


Figure 2. Distribution of respiratory viruses detected within the Sentinel Network, by two-week periods. Results from last weeks are not yet consolidated.

FLU-A: influenza A; FLU-B: influenza B; PIV: parainfluenza virus; 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 4 weeks compared to the interseason period.

Virus	Last 4 weeks		Season 2022/2023	
	N*	Positivity rate (%)	N*	Positivity rate (%)
Human rhinovirus	28	28.0	78	28.1
SARS-CoV-2	20	8.5	78	16.3
Respiratory syncytial virus	32	32.0	58	20.9
Adenovirus	16	16.0	32	11.5
Influenzavirus A	15	6.3	26	5.4
Parainfluenzavirus	4	4.0	14	5.0
Metapneumovirus	2	2.0	3	1.1
Influenzavirus B	1	0.4	2	0.4
Total	118	-	291	-

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

Influenza circulation

To date, the most frequently detected flu virus within the sentinel surveillance during the current season is Influenzavirus A. In order to assess the circulation of different viral strains, genotyping was performed on a selection of positive specimens. The most frequent subtype detected was H3 (88.2%), followed by H1-pdm (11.8%).

SARS-CoV-2 Genomic Surveillance

The current sequencing strategy

The National Reference Laboratory for Acute Respiratory Infections at LNS receives SARS-CoV-2 positive samples (nasopharyngeal or oropharyngeal swabs analysed by RT-PCR) from the national network of laboratories and proceeds as follows:

1. Sequencing a representative sample of specimens.
2. Sequencing specimens from target groups (i.e. hospital cases and post-vaccination cases).
3. Sequencing specimens from clusters with high transmission.

The representative sample of specimens is a systematic selection from all SARS-CoV-2 positive cases registered in Luxembourg to detect emerging variants and early increases in their incidence and transmission within the community in Luxembourg. This sample is selected according to the ECDC guidelines.

A screening by targeted PCR tests is also carried out when a new variant emerges in order to enable earlier evaluation of its spread in the population.

SARS-CoV-2 lineages have been assigned based on Rambaut et al. using the Phylogenetic Assignment of Named Global Outbreak LINEages (pangolin) software (4.1.3, pango-data 1.16, mode UShER). In addition to that, WHO and Nextstrain categorisations are also used to enable easier visualization of links between any evolving variants and their ancestor.

Sequencing activity



Figure 3. Flowchart of specimens collected during week 46/2022

In week 46, 1058 new cases were registered in Luxembourg; hence, the minimum sample size required to detect emerging variants at a 2.5% incidence is estimated to be 383 specimens (36.2%) and 281 specimens (26.6%) at 5% incidence.

As shown in Figure 3, the microbial genomics unit at the LNS sequenced 435 specimens from the week of study, including 373 national ones. The weekly sequencing coverage remains at 35.3% (out of 1058 cases registered in Luxembourg; see coverage trend in Figure 4), which reaches the recommended sample size for detection of viruses at 5% incidence.

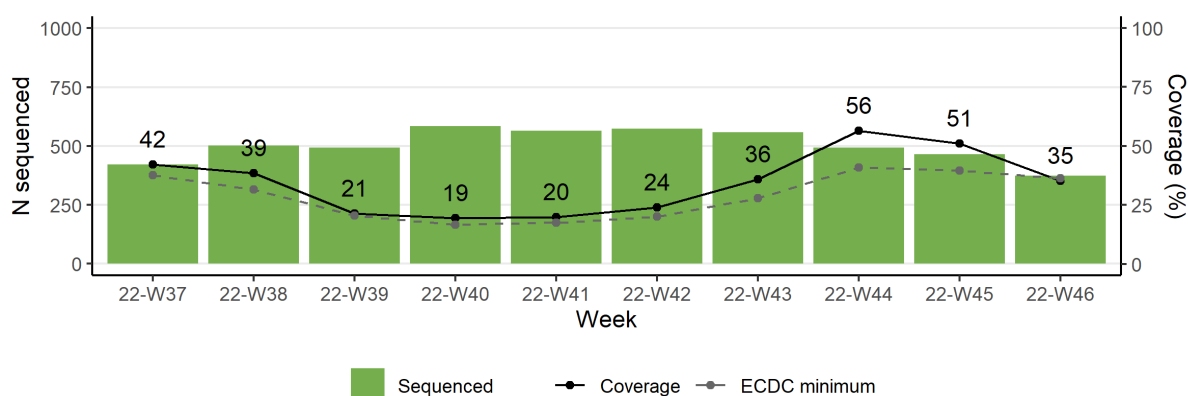


Figure 4. Number of specimens sequenced and national coverage based on weekly number of positive cases in Luxembourg. The coverage from the last two weeks is not consolidated yet.

Circulating lineages detection

The distribution of successfully assigned lineages within the national selection is shown in Figure 6, and it is further detailed in Table 4 (last two weeks). A summary of the VOCs assigned among all specimens sequenced (including non-residents) during the last two weeks and since the beginning of the sequencing activity is shown in Table 5.

The Omicron variant remains the main one detected within the representative sample, the most frequent subvariant being Omicron BQ.1 (47.7%), followed by Omicron BA.5 (43.4%). The lineages at higher circulation are BQ.1.1, BF.7 and BA.5.2. Other variants detected were recombinant lineages (XBB).

Table 4. 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 45		Week 46	
	%	CI %	%	CI %
Omicron BQ.1	51.9	46.8 - 57.1	47.7	42.7 - 52.8
Omicron BA.5	41.2	36.1 - 46.2	43.4	38.4 - 48.5
Others	1.1	0.0 - 2.2	3.8	1.8 - 5.7
Omicron BA.4	2.2	0.7 - 3.7	3.5	1.6 - 5.3
Omicron BA.2.75	3.0	1.3 - 4.8	1.6	0.3 - 2.9
Omicron BA.2	0.6	0.0 - 1.3	0.0	-

CI: Confidence Interval at 95%. *Sub-lineages BA.2.75 and BQ.1 are not included in the count of their parental lineages (BA.2 and BA.5, respectively).

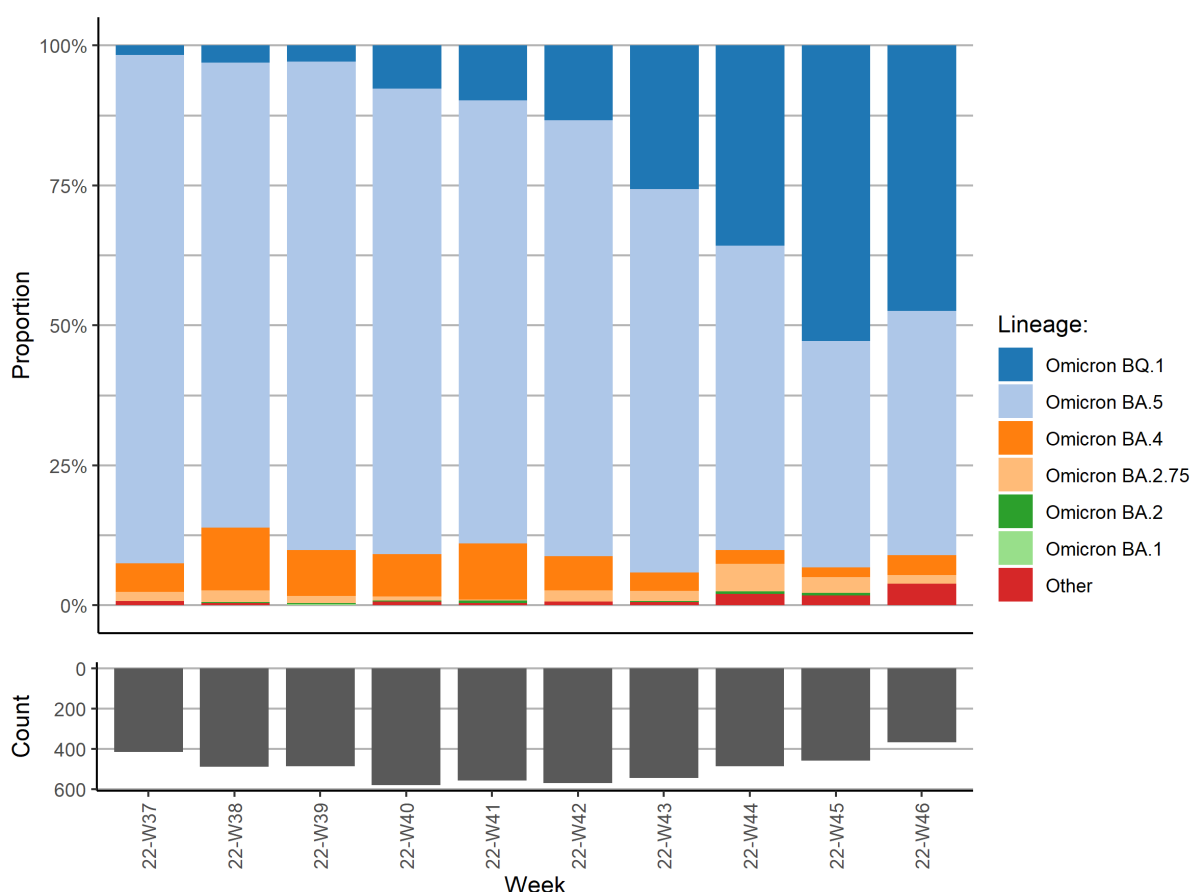


Figure 6. Distribution of lineages within the representative sample during the last 10 weeks.

Table 5. Distribution SARS-CoV-2 variants of concern and lineages under monitoring detected within all samples sequenced since the beginning of the pandemic.

Variant	Week 45		Week 46		Cumulative count
	N	%	N	%	
Omicron	524	98.5	414	96.7	33 289
BA.5	216	40.4	180	42.1	13 018
BA.2	3	0.6	1	0.2	10 165
BA.1	0	0.0	0	0.0	7 666
BQ.1	278	52.1	209	48.8	1 090
BA.4	12	2.2	16	3.7	992
BA.2.12.1	0	0.0	0	0.0	231
BA.2.75	15	2.8	8	1.9	124
Others	8	1.5	14	3.3	15 136
Total	532	100.0	428	100.0	48 425

CI: Confidence Interval at 95%. *Sub-lineages BA.2.75 and BQ.1 are not included in the count of their parental lineages (BA.2 and BA.5, respectively).

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 6).

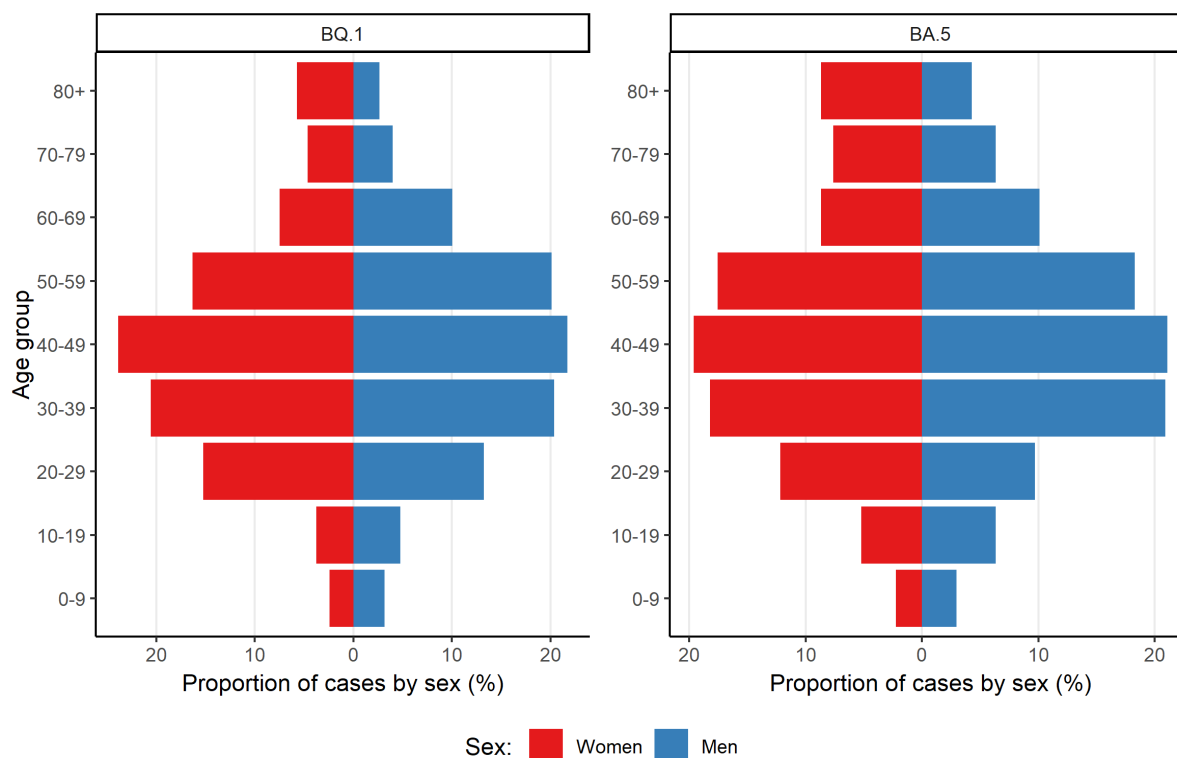


Figure 7. Age group and sex distribution of specimens sequenced over the last 4 weeks, by lineage.

Table 6. Comparison of lineage distribution by sampling setting.

Lineage	Community			Hospital		
	Women	Men	Total	Women	Men	Total
Omicron BA.5	54.8%	58.5%	56.6%	61.6%	59.2%	60.6%
Omicron BQ.1	45.2%	41.5%	43.4%	38.4%	40.8%	39.4%
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 7. Mutations detected at a higher proportion in Luxembourg

Lineage	Mutation	Gene	% in LU	% in EU	Ratio
BA.5	R346T	S	57.18	46.8	1.22
BQ.1	R346T	S	79.31	67.6	1.17
BQ.1	G184D	S	7.28	<5.00	-

LU: Luxembourg; EU: Europe.

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