

Respiratory Viruses in Luxembourg (ReViLux)

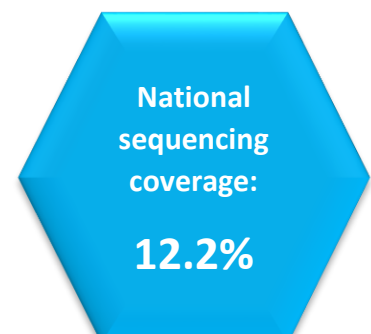
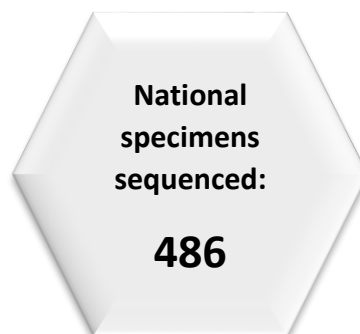
Weekly report (13 – 19 June 2022)

Executive summary

The sentinel network reported 3.2% 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, Human rhinovirus was the most frequently detected virus over the last four weeks (42.4%), followed by SARS-CoV-2 (33.3%) and Parainfluenzavirus (9.1%).

Regarding the SARS-CoV-2 genomic surveillance, LNS sequenced 486 specimens from residents in Luxembourg in week 24 (of 3985 total cases in the Grand Duchy of Luxembourg; 12.2%). This does not reach the ECDC recommendations to detect emerging variants at 2.5% prevalence.

The Omicron variant remains the only one detected in the representative sample. The Omicron BA.5 lineage is the most frequent one (71.6%, confidence interval: 67.2 - 76.0%), followed by Omicron BA.2 (22.7%, confidence interval: 18.6 - 26.8%).



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).

Season 2021/2022 ended by week 20, and we are currently in the interseason period. 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. In the week of study, 3.2% of consultations were reported as ILI, thus exceeding the threshold for baseline circulation during the interseason, according to ECDC (1.14%).

Table 1. Syndromic surveillance over the last 4 weeks

Week	ARI		ILI		Total consultations
	N	%	N	%	
2022/21	25	15.62	5	3.12	160
2022/22	14	7.22	3	1.55	194
2022/23	15	8.88	7	4.14	169
2022/24	55	15.80	11	3.16	348

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

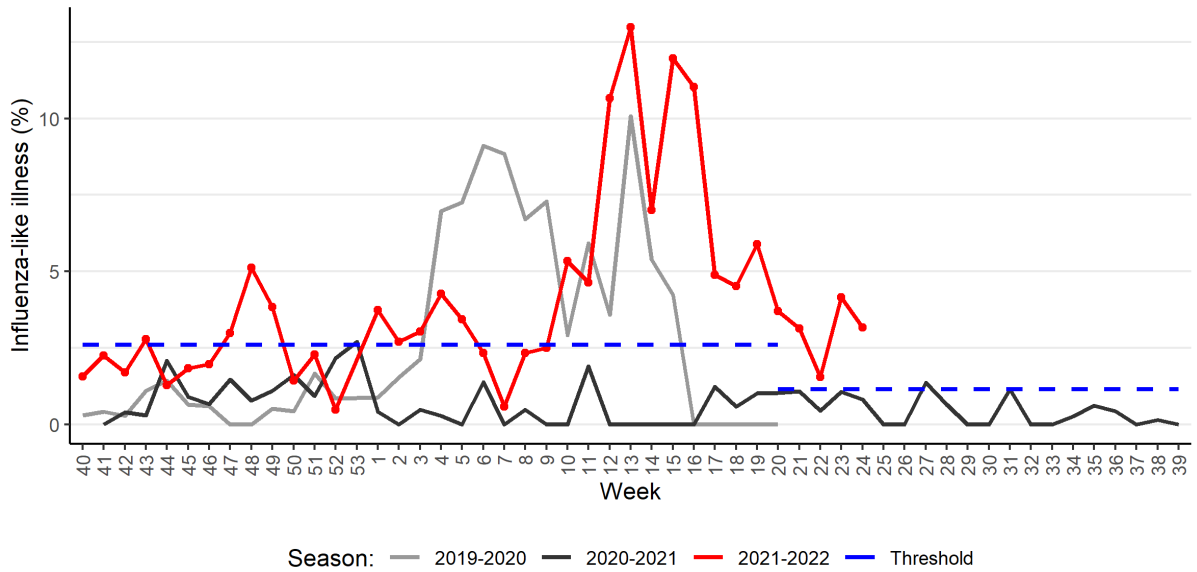


Figure 1. Percentage of patients with influenza-like illness over the last three seasons

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 positivity rate was at 61%, and the most frequently detected viruses were Human rhinovirus (42.4%), SARS-CoV-2 (33.3%) and Parainfluenzavirus (9.1%). Co-infections were detected in 3 specimens, all involving SARS -CoV-2. These results are displayed more in detail in Table 2.

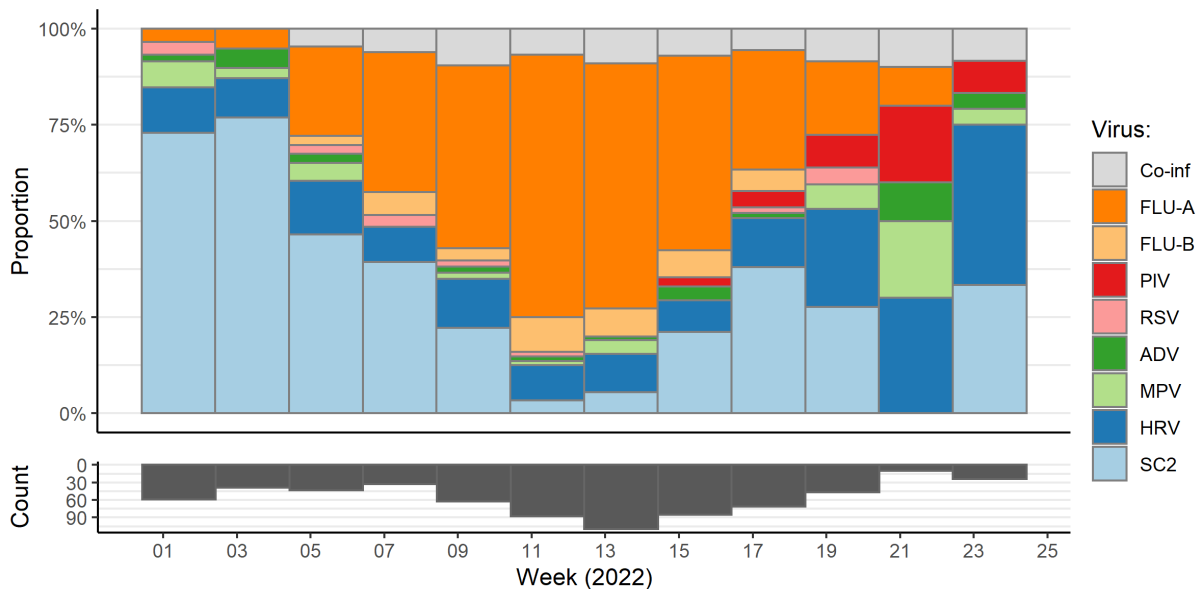


Figure 2. Distribution of respiratory viruses detected within the Sentinel Network, by two-week periods. Results from last weeks are not yet consolidated.

Co-inf: co-infection; FLU-A: influenza A; FLU-B: influenza B; PIV: parainfluenzavirus; 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 and during the current season.

Virus	Last 4 weeks		Current season	
	N*	%	N*	%
SARS-CoV-2	11	33.3	342	35.0
Influenzavirus A	0	0.0	289	29.6
Human rhinovirus	14	42.4	191	19.5
Metapneumovirus	2	6.1	35	3.6
Influenzavirus B	0	0.0	34	3.5
Parainfluenzavirus	3	9.1	34	3.5
Adenovirus	2	6.1	27	2.8
Respiratory syncytial virus	1	3.0	25	2.6
Total	33	100.0	977	100.0

Co-infection cases counted once for each virus detected.

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 arises 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 (4.0.6, designation v1.9). The Pango nomenclature is used in addition to the WHO nomenclature to enable easier visualization of links between any evolving variants and their ancestor.

Sequencing activity



Figure 3. Flowchart of specimens collected during week 24/2022

In week 24, 3985 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 521 specimens (13.1%).

As shown in Figure 3, the microbial genomics unit at the LNS sequenced 534 specimens from the week of study, including 486 national ones. The weekly sequencing coverage remains at 12.2% (out of 3985 cases registered in Luxembourg; see coverage trend in Figure 4), which does not reach the recommended sample size.

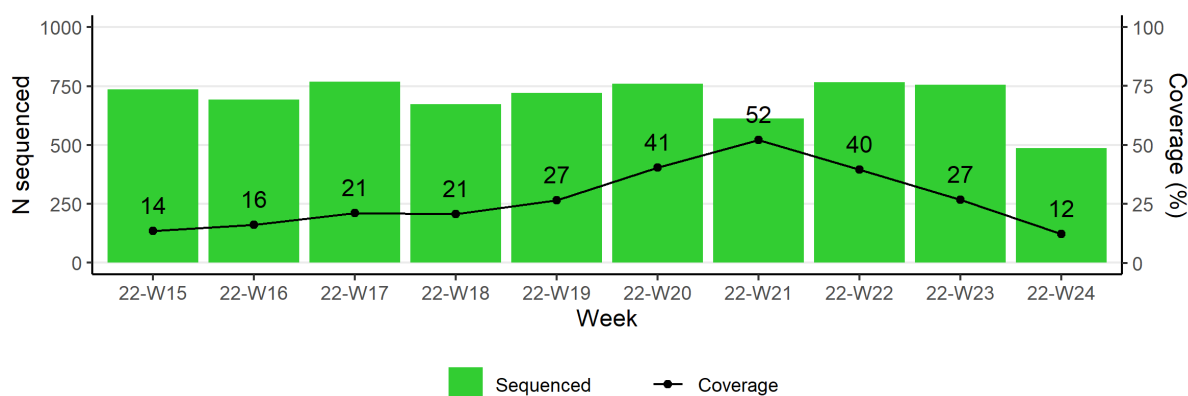


Figure 4. Number of specimens sequenced and national coverage based on weekly number of positive cases in Luxembourg. The coverage from the last two weeks is not consolidated yet.

Screening results

The targeted PCR screening is most useful when a new variant or lineage emerges, in order to monitor its potential introduction and early spread. Given that the Omicron BA.5 is already the dominant lineage in Luxembourg, there is little value on continuing the screening. It will be resumed if a newly emergent variant requires it.

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 dominant one within the representative sample, the most frequent lineage being Omicron BA.5 (71.6%), followed by Omicron BA.2 (22.7%).

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	Previous week			Current week		
	N	%	CI %	N	%	CI %
Omicron BA.5	299	60.4	56.1 - 64.7	290	71.6	67.2 - 76.0
Omicron BA.2	168	33.9	29.8 - 38.1	92	22.7	18.6 - 26.8
Omicron BA.4	28	5.7	3.6 - 7.7	23	5.7	3.4 - 7.9
Total	495	100.0	-	405	100.0	-

CI: Confidence Interval at 95%.

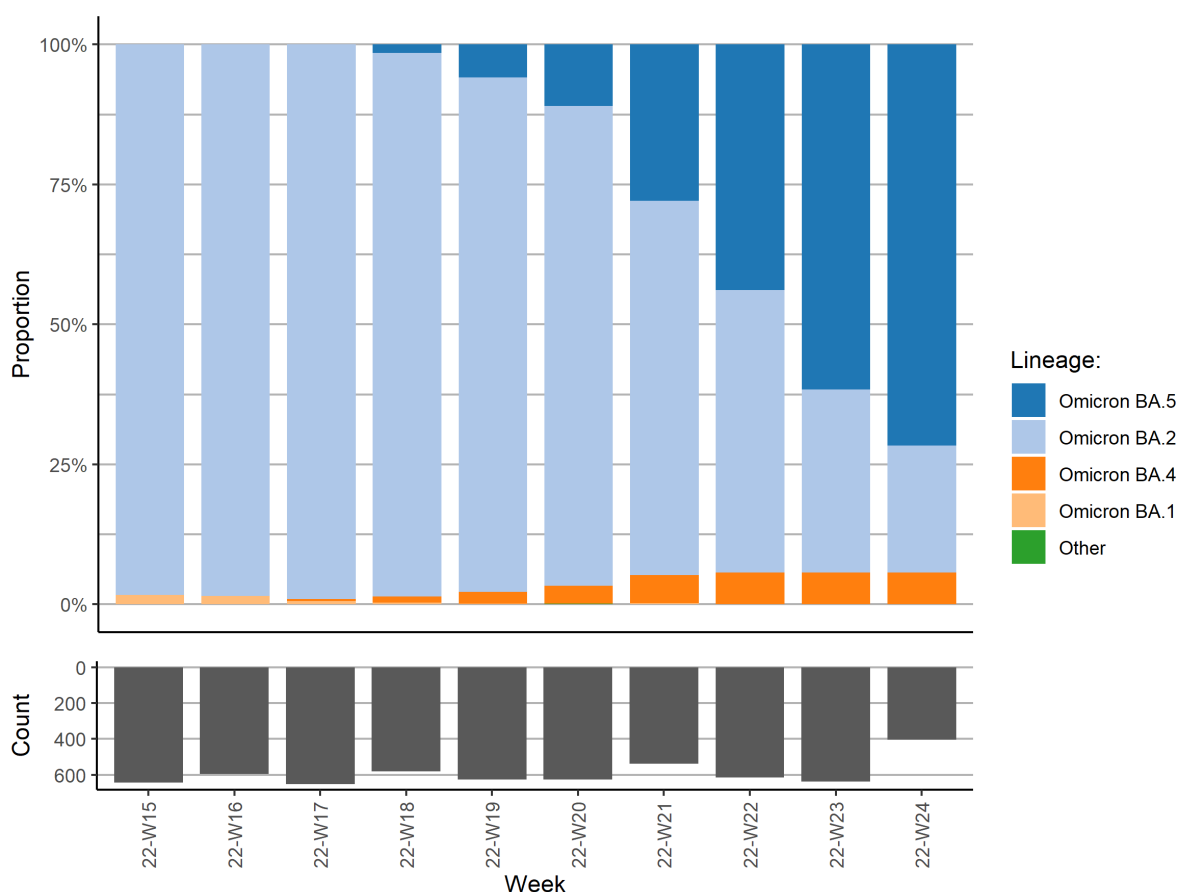


Figure 6. Distribution of lineages within the representative sample during the last 10 weeks.

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	Previous week		Current week		Cumulative count
	N	%	N	%	
Omicron	691	100	436	100	18 239
BA.2.9	26	3.8	16	3.7	1 028
BA.5	156	22.6	110	25.2	353
BA.4	38	5.5	24	5.5	178
BA.2.12.1	30	4.3	18	4.1	160
BA.2.13	1	0.1	3	0.7	44
BA.2.11	-	-	-	-	2
Delta	0	0	0	0	13 678
Others	0	0	0	0	15 006
Total	691	100	436	100	46 923

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).

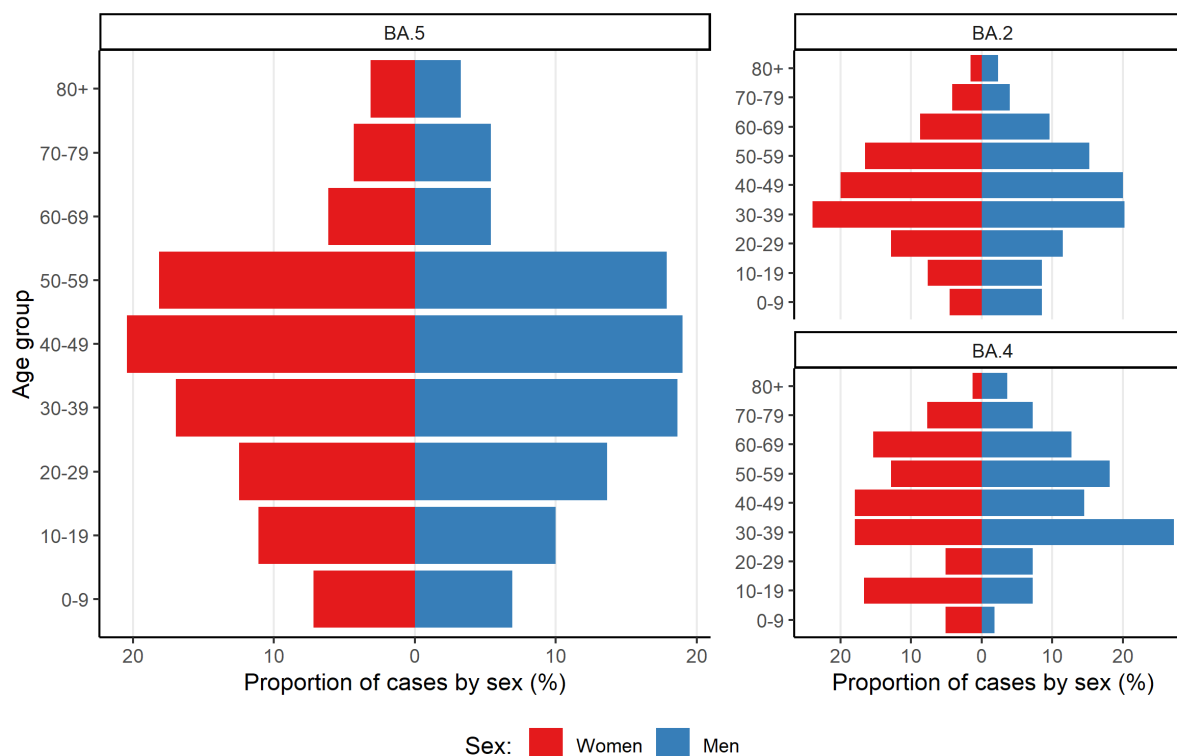


Figure 7. Age group and sex distribution of specimens sequenced over the last 4 weeks, by lineage.

Table 6. Comparison of lineage distribution by sampling setting.

Lineage	Community			Hospital		
	Women	Men	Total	Women	Men	Total
Omicron BA.2	54.1%	60.6%	57.0%	42.9%	49.0%	45.8%
Omicron BA.5	33.4%	27.7%	30.8%	39.3%	45.1%	42.1%
Omicron BA.4	12.5%	11.7%	12.1%	17.9%	5.9%	12.1%
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 reported to have a clinical and epidemiological relevance. Newly acquired mutations may occur and their early detection might be key to expect changes in the epidemic evolution. Following ECDC guidance, the LNS is currently monitoring a selection of mutations to the spike protein frequently associated to VOCs. As each VOC is characterised by a set of defining mutations, which are expected to be highly present, it is interesting to analyse the non-defining ones. Among the specimens collected over the last four weeks, the following mutations were detected:

- L452Q in at least 11.8% BA.2 specimens (increasing trend), higher than the rest of Europe (7.1%, also on an increasing trend, according to GISAID). These sequences are labelled as Variant of Interest by ECDC.
- 69/70del in at least 5.6% specimens (increasing trend), slightly lower than the rest of Europe (6.5%, on a higher increasing trend, according to GISAID).

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