

Scientific Briefing - LNS

The rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom

Background

A new SARS-CoV-2 variant referred to as SARS-CoV-2 VUI 202012/01 (Variant Under Investigation, year 2020, month 12, variant 01), has been declared by the British authorities. The variant was detected via genomic sequencing in the United Kingdom (UK). It is defined by multiple spike protein mutations (deletion 69-70, deletion 144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H) present.

The new variant is correlated with a rapid increase in COVID-19 incidence. This increase was reported in South East England. Analysis using viral genome sequence data identified a large proportion (>50%) of cases that belonged to a new single lineage. Overall, around 5 to 10% of all COVID-19 cases are regularly sequenced in the UK. As of 26 December 2020, more than 3000 individuals had been identified with this virus variant in England, with the earliest case identified from 20 September 2020. Several countries had reported sporadic cases caused by the new variant from other EU/EEA countries (Belgium, Denmark, France, Germany, Iceland, Ireland, Italy, the Netherlands, Norway, Portugal, Spain and Sweden) and globally (Australia, Canada, Hong Kong SAR, Israel, Japan, Jordan, Lebanon, South Korea, Switzerland, Singapore).

South Africa reported another SARS-CoV-2 variant of potential concern, designated 501.V2 that was first observed in samples from October and since then evolved to be the dominant circulating variant in South Africa.

In response to the emergence of the new variant several countries had issued a travel ban from the UK raising many concerns on the consequence of the transmission to this variant globally.

Situation analysis of *Circulating variants* in Luxembourg

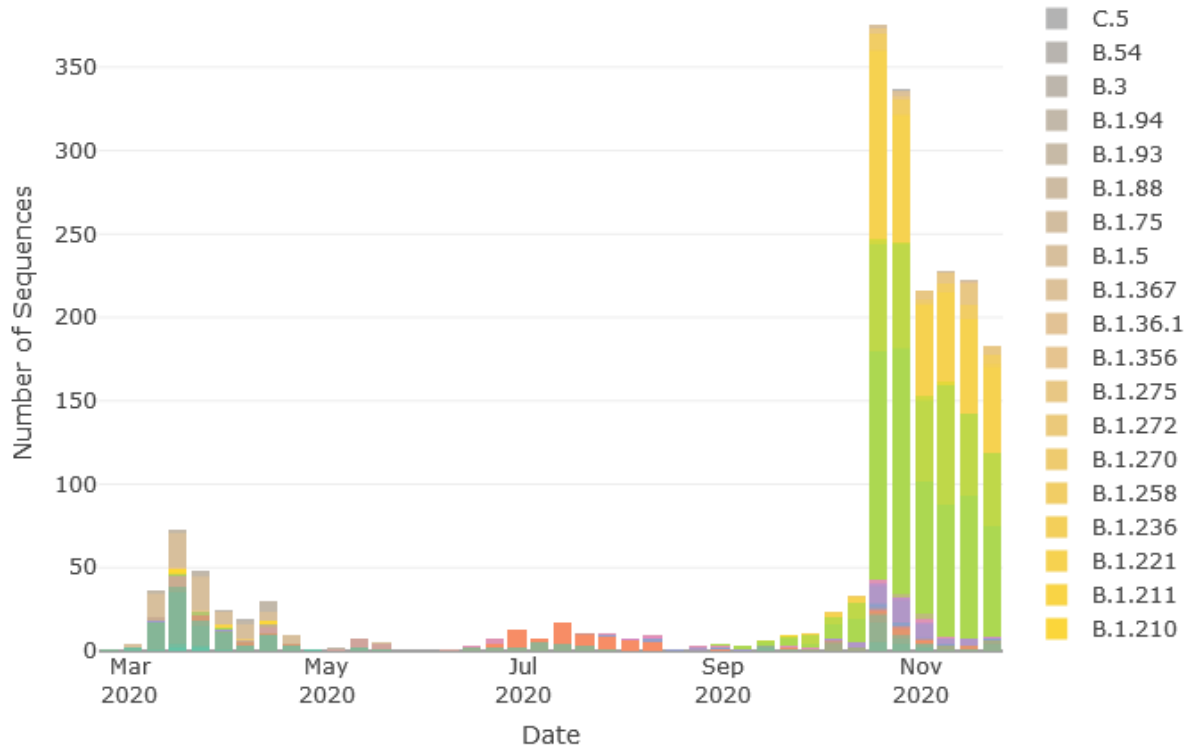
The microbiology department at the Laboratoire national de Santé (LNS) sequenced 3027 SARS-CoV-2 positive samples since 29/02/2020, wherein 2285 have been added to the sequencing pool since 01/10/2020. We currently had increased our sequencing capacity to reach 10% of community circulating variants.

Most recent sequencing data referring to week 50 and 51 confirm observations made since the beginning of September of three main circulating strains. It is to note that annotation data have been updated, so that lineages have been added, might have been regrouped, or renamed. This mainly applies to the high-prevalent Dutch lineage B.1.78, which disappeared, but has been replaced by lineage B.1.221 (22%; Netherlands/Belgium). Accordingly, the geographical source stays consistent. The other two main circulating strains remain as observed in previous weeks; lineages B.1.160 (32%), B.1.177 (38%).

Lineage B.1.160 represents an EU/EEA and UK multi-country cluster which involves Belgium, France, Germany, and the United Kingdom. It is characterized by a spike protein mutation S: S477N, occurring in combination with N: M234I, A376T, ORF1a: M3087I, ORF1b: A176S, and most also with ORF1b: V767L K1141R, E1184D.

Lineage B.1.177 appeared in early summer 2020 and has its origin presumably in Spain. It spread to multiple European countries and its frequency rose to 40-70% in Switzerland, Ireland, and the United Kingdom in September. It is as well prevalent in other Luxembourg neighboring countries like Netherlands and France. It has the mutations A222V in the spike protein and A220V in the nucleoprotein.

The new UK variants attribute lineage B1.1.7 was not detected in our last analysis on samples collected until 18/12/2020. We are currently sequencing further samples from week 50 and 51 to investigate the appearance of the variant in Luxembourg.



Potential global impact of the emergence of the new variant

Since the emergence of the new variant and the declaration of the increased transmissibility (up to 70%), various implications for human health have been considered:

- 1) **The probability of a wider spread of the new virus variant across the European Union (EU) and European Economic Area (EEA);** as initial reports from the UK suggest that the variant had higher transmissibility with an estimated increase in reproductive number (R) by 0.4 or greater with estimated increased transmissibility of up to 70%. These figures need to be confirmed by further epidemiological and virological investigations. Although our sequencing coverage in Luxembourg is close to that of UK (around 10%) we cannot exclude low-level circulation of the variant and further updates from the weekly surveillance would be communicated via <https://lns.lu/en/departement/departement-of-microbiology/revilux/>.

2) The potential impact on SARS-CoV-2 diagnostics;

The diagnostic Rt-PCR tests implemented in Luxembourg are multiplex tests that target more than one gene, the gene in question (S gene) is integrated into various kits but this will not have any implications on the diagnostic capacity in the country.

3) The potential impact on the severity of disease in a population or group

There are no clinical reports on the virulence of the new variants. In the previous investigation of the D614G variant identified to provide a selective advantage, through increased cellular infectivity, there was no identifiable effect on infection severity or outcome in Luxembourg where 99% of the circulating variants carry this mutation, thus the new variant needs to be monitored for its virulence.

4) The potential impact on the occurrence of variant viruses to increase the frequency of reinfections

We have sporadic potential cases of reinfection reported in Luxembourg that are currently under investigation. There is limited evidence on the natural immunity conferred due to SARS-CoV-2. However, the occurrence of variant viruses can potentially increase the frequency of reinfections. In particular, the VUI 202012/01 variant harbor mutations that are related to the receptor-binding site and other surface structures, which may alter the antigenic properties of the virus

5) The potential impact on vaccine match and effectiveness.

As we are starting our national vaccination program for SARS-CoV-2 in the coming days, it is essential to note that there is no phenotypic data available for the new variant, then it is not possible to predict the effect of the planned vaccine on this variant as further studies on the antigenic characteristics is needed.

In Luxembourg, the Laboratoire national de Santé (LNS) will work closely with key stakeholders to implement the ECDC recently published recommendations as follows:

- 1) LNS will continue its national genomic surveillance program promptly to identify cases of the new variant and will notify through the Early Warning and Response System of the European Union.
- 2) Positive cases with an epidemiological link to cases with the new variant or travel history to the UK will be identified immediately to evaluate the virulence and transmission networks in Luxembourg.
- 3) LNS will review the PCR performance and drop-out of the S-gene with partner laboratories. PCR results could be used as an indicator for cases with the new variant for further sequencing and investigation.
- 4) All potential COVID-19 reinfection, LNS will perform sequencing of respective virus isolates if retrieved from the diagnostic laboratories. Similarly, cases with treatment failures using convalescent plasma or monoclonal antibodies should be further studied.

- 5) LNS will implement a vaccination failure follow-up study to identify possible vaccination failure and breakthrough infections. Virus isolates from these cases will be sequenced.

It is essential to reiterate the importance of strict adherence to the sanitary measures implemented in Luxembourg during the festive periods in particular guidance on the avoidance of non-essential travel and social activities.