Hôpitaux Universitaires Genève

REPUBLIQUE ET CANTON DE GENEVE
Département de la sécurité, de la population et de la santé
Direction générale de la santé
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Geneva Centre for Emerging Viral Diseases

Division of Infectious Diseases

Department of Medicine

Laboratory of virology

Division of Laboratory Medicine

Diagnostic Department

SARS-CoV-2 genomic surveillance in Geneva: weekly update
Focus on Omicron B.1.1.529

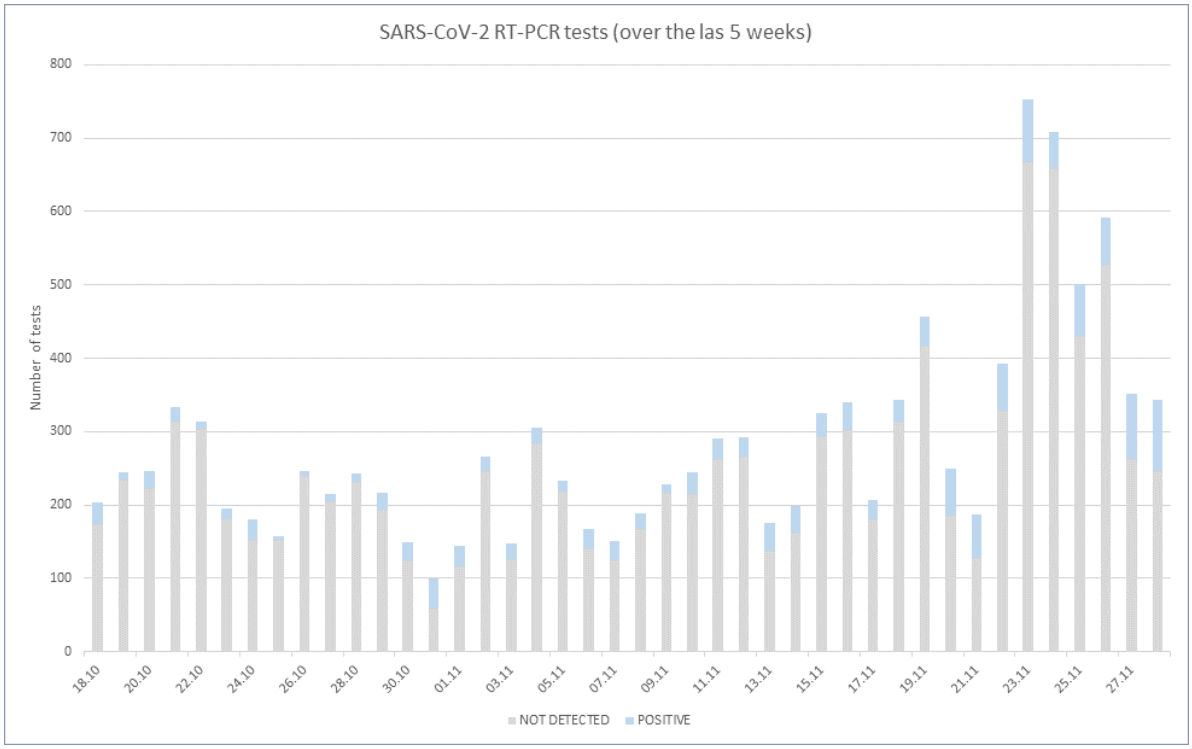
The laboratory of virology of the Geneva University Hospitals as a sentinel site for the Geneva area

The number of tests (PCR and antigen tests) performed at the laboratory of virology of the Geneva University Hospitals represents around 19% of the total number of tests performed in the canton of Geneva during week 47 (4760/24520). Roughly **23% of the positive specimens collected in the Geneva area were processed at HUG** (583/2495) **during week 47**. Tests performed at our outpatient testing center are either PCR-based or antigen-based. Most symptomatic patients are screened by RT-PCR and all positive antigen-based tests are confirmed by PCR, allowing screening for variants.
The number of positive tests in the canton and the total number of tests done during the surveilled week come from the website of the Direction Générale de la Santé in Geneva (available at https://infocovid.smc.unige.ch/), accessed November 30, at 11 am.

Methods and collaborations

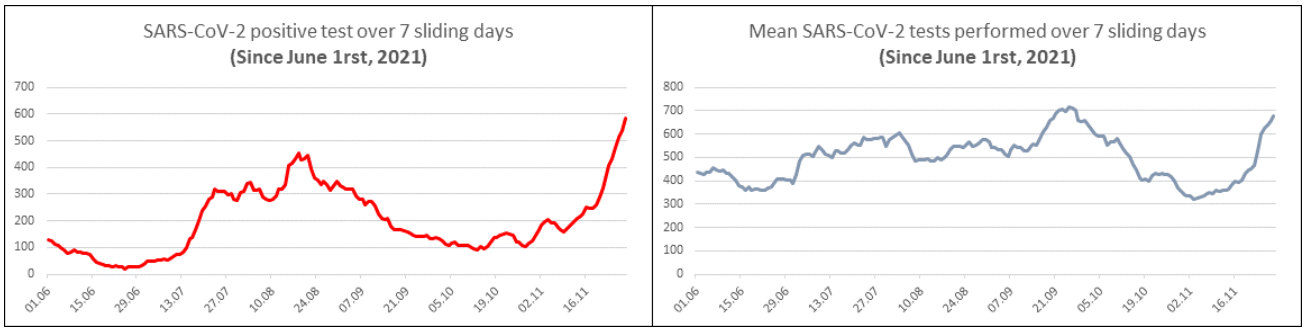
WGS is carried out in close collaboration with the Health 2030 Genome Center in Geneva and Philippe Le Mercier from the Swiss Institute of Bioinformatics. Since March 1, 2021, the sequencing has been done within the Swiss national SARS-CoV-2 genomic and variants surveillance program. All specimens collected at HUG with a Ct value ≤32 are sequenced. In some instances, sequencing can be done on specimens sent by other laboratories in Switzerland within the surveillance program. Phylogenetic analysis data are produced by Nextstrain, in collaboration with Richard Neher's group at the University of Basel.
Geographic distribution, transmission advantage estimates and detailed number of available sequences over time in the canton of Geneva is available via CoVspectrum, maintained by the group of Tanja Stadler at ETH Zurich.

These reports are produced in collaboration with the Geneva Cantonal Physician team, which provides information on epidemiological links and post-vaccination infections (see below).

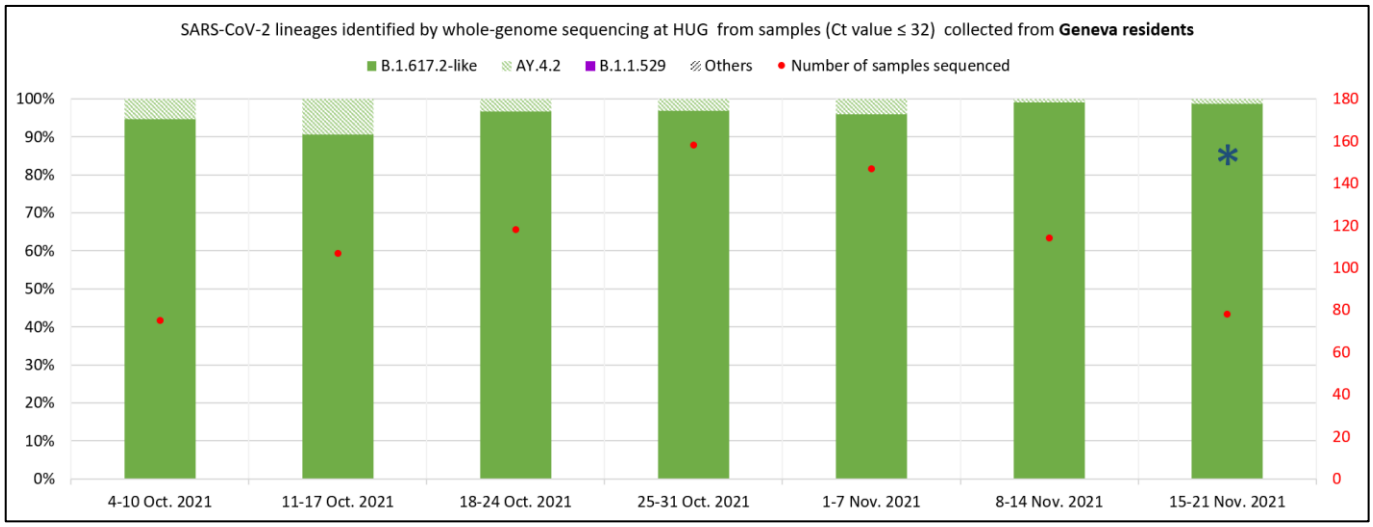


During week 47, the **absolute number of positive SARS-CoV-2 tests sharply increased** (doubled), along with the mean positivity rate over 7 sliding days, which reached more than 14%.

Similarly, at our **outpatient symptomatic testing center**, the **mean positivity rate continued to increase and reached 26% on average**.



SARS-CoV-2 lineages identified by whole-genome sequencing at HUG from samples (Ct value ≤32) collected from Geneva residents



Results of WGS of 797 sequences submitted to GISAID between September 27 and November 14, 2021.

*Partial data for week 46 (November 15 to November 21), as sequencing is still ongoing. Numbers will be updated in the next report.

Delta or one of its sub-lineage has been identified in all the available SARS-CoV-2 sequences collected over the last 2 months. Worldwide, this variant and its sub-lineages are retrieved in more than 99% of available sequences.

AY.4.2 is circulating in the community since the beginning of October. It hasn't been increasing in frequency in the canton of Geneva over the last 6 weeks.

We still observe a large variety of different Delta sub-lineages circulating in the community, without any trend towards any out-competition by a specific variant. As Delta sub-lineage diverge, more sub-lineages are being delineated (not depicted here).

Note that the Omicron variant has been confirmed by Sanger sequencing on a sample collected on November 25 (see below).

Focus on B.1.1.529: the Omicron variant

On 26 November 2021, the lineage B.1.1.529 was designated and the WHO upgraded it to **variant of concern** (VOC) status on 26 November. The earliest known case was detected on 9 November 2021 in South Africa.

This variant is notable for having the **highest number of mutations ever seen** along the whole genome (> 50) and in the gene coding for the Spike protein (> 30), many of which occur at sites linked to increased transmissibility (ie: N501Y, P681H), or immune escape (E484A). In particular it has a large number of mutations (15) in the RBD, as well as a heavily mutated N-terminus (4 mutations, 7 deletions, and 3 insertions). Both the RBD and the N-terminus are major antibody targets. It furthermore carries the R203K and G204R mutations in the nucleocapsid protein that have been linked to greater transmissibility as well.

Preliminary results confirm that despite the set of its mutations, **Omicron can still be detected by common RT-PCR tests used in Switzerland** (COBAS-6800 and Liat, Roche; GeneXpert, Ceipheid; TaqPath), **and by rapid antigenic diagnostic tests** (including SD Biosensor/Roche, Abbott, Flowflex, CTK Biotech, Premier Medical Corporation). Confirmation is pending. Notably, the deletions in the N-terminus of the Spike protein result in S-gene target failure (also called “S drop out”) in some RT-PCR screening, as was observed with the Alpha variant. In the context of world-wide dominance of Delta with the Alpha variant having essentially disappeared, the “S drop out” may thus be used as a proxy for the presence of Omicron.

Data are not clear enough regarding its emergence, its transmissibility, its severity or its immune escape properties, and more information will follow in the next reports. However, this variant carries mutations that are known to independently favor immune escape and to decrease neutralization of convalescent and/or vaccinees sera. Of note, the effectiveness of monoclonal antibodies used in clinical practice may be affected.

While it is **too early to say if Omicron can outcompete Delta**, it is clear that it has a sustained transmission chain in southern Africa. Epidemiological data are awaited within the next days/weeks.

As of November 30, 2021, community transmission was announced in the UK, Germany, and in the Netherlands. Given the high proportion of Omicron detection among SARS-CoV-2-positive returning travelers from southern Africa, this variant is likely widespread in this part of the world.

On November 28, a sample tested at Geneva University Hospitals collected in Geneva from a **non-vaccinated returning traveler from South Africa** on November 23 was the **first in Switzerland to be confirmed with a “S drop out” and suggestive of Omicron**. Sequencing failed due to low viral loads.

On November 30, **a second sample** collected on November 25 **in an unvaccinated patient** who had close contact with the first probable case tested positive for the “S drop out” and **confirmed to be Omicron by Sanger sequencing**.

Both of these patients were returning travelers from South Africa who traveled together. Date of arrival in Switzerland was November 21. The confirmed case, who is a Geneva resident, is therefore an imported case who was infected in South Africa. **None were vaccinated.** They did not report any close contacts with other people since their arrival in Switzerland.

The **systematic screening for the “S drop out” was implemented at HUG** on SARS-CoV-2 positive specimens with Ct value < 32 tested for primary diagnostic in our laboratory since November 27. Results will be displayed in the next report.

Post-vaccination infections in the canton of Geneva

Post-vaccination infection is defined here as a positive SARS-CoV-2 test occurring more than 14 days after the second vaccine dose. This surveillance is done in collaboration with the Direction Générale de la Santé (DGS) of Geneva. Data are collected by the DGS of Geneva during contact tracing calls after having obtained informed consent from SARS-CoV-2 positive patients. The list of patients with post-vaccination infections is sent weekly to HUG virology laboratory, which makes an effort to retrieve initial diagnostic samples in order to ensure sequencing, as recommended by FOPH.

Among the 2495 new COVID-19 cases reported by the Direction Générale de la Santé in Geneva over week 47, 709 (28%) have been identified as post-vaccination infections.

Although absolute numbers are still low, there is an increasing trend in the proportion of fully vaccinated hospitalized patients over time, mostly in the elderly > 75 years-old. 40% of them are hospitalized because of a comorbidity, with acute COVID (not because of COVID).

Please refer to the report of the Geneva Center for Emerging Viral Diseases regarding progression of COVID-19 hospitalizations at Geneva University Hospitals distributed on November 30, 2021, which includes data from mid-July to November 28, 2021.

Conclusions

- The **absolute number of positive tests doubled** over week 47, and the **mean positivity rate over 7 sliding days reached 26% in our symptomatic outpatient testing center**.

- Delta or its sub-lineage were the only variants identified by whole genome sequencing in the canton of Geneva since mid-September, in specimen collected until November 21. The Delta sub-lineage AY.4.2 is circulating in the community at a low level.

- **On November 28**, a sample tested at Geneva University Hospitals collected in Geneva on November 23 was the **first in Switzerland to be confirmed with a "S drop out" suggestive of Omicron**. Sequencing failed due to very low viral load.
On November 30, a **second sample** collected on November 25 was **confirmed by Sanger sequencing to be Omicron**. Both of these patients were returning travelers from South Africa who traveled together. None were vaccinated.

- The **systematic screening for the "S drop out" was implemented at HUG on SARS-CoV-2 positive specimens** with Ct value < 32 tested for primary diagnostic in our laboratory since November 27.

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