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Swiss national SARS-CoV-2 genomic and variants surveillance program: report of the month of December

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1. Summary

In December, COVID-19 cases numbers continued to dramatically increase in Switzerland, and this increase was largely driven by the B.1.1-529 (Omicron) variant or its sub-lineages, which overtook Delta to become the dominant lineage in Switzerland.

In the midst of this steep increase in case numbers, approximately 3% of the total number of cases identified in Switzerland in December were sequenced by the Surveillance program, yielding over 9,300 sequences. Each week since this surveillance program started, it has contributed almost all of the Swiss SARS-CoV-2 sequences available on GISAID.

This 3% sequencing is a significant decrease from the month before (below the goal of 10%), and reflects a large increase in case numbers. With over 9 thousand sequences generated from all over Switzerland, coverage is deemed to be satisfactory despite falling below the arbitrary 10% threshold. Region 4 and 5 remain the least represented geographical areas.

Notably, Omicron has displaced Delta to the greatest extent in region 6, and to the least extent in region 4. Unsurprisingly, B.1.1.529 (Omicron or its sub-lineages) was also the most frequent variant detected in wastewater during the month of December. Circulation of all variants other than Omicron and Delta was essentially nonexistent in December.

Omicron has already split into 3 sub-lineages: BA.1-3. BA.1 is currently the most common variant. All sub-lineages are still detected by RT-PCR tests, but S-gene target failure in some assays can be used as a proxy for BA.1 and BA.3 prior to sequencing, as previously seen with VOC Alpha. BA.2 has replaced BA.1 in Denmark and India, but it is still only rarely detected in CH, and thus S-gene target failure is still a good proxy for Omicron within Switzerland. No additional diagnostic or treatment issues were noted for any variant other than Omicron in December.

The Omicron infections appear to result in milder infections than Delta. At the population level, signs of milder disease are partially explained by high levels of previous exposure and/or vaccination (which still confer protection from severe disease) in the reporting communities. Lines of evidence from *in vitro* and animal studies do support the idea that the virus is intrinsically milder. Note that milder does not mean mild, and it is still capable of causing severe disease and death.

2. Description of the Swiss national SARS-CoV-2 genomic and variants surveillance program.

The overall goal of the program is to provide epidemiological trends and to highlight meaningful observations.

Because greater transmissibility and/or immune escape potential of the different VOCs and VOIs can result in new surges in COVID-19 numbers despite the vaccination campaign, this program aims to closely monitor each variant displaying mutations known to be linked with either increased transmissibility or immune escape potential.

Currently, 13 diagnostic laboratories are participating in the program, including university hospital centres in Switzerland (Geneva, Lausanne, Bern, Basel, Zurich, St-Gall, Ticino), in addition to private laboratories (Viollier; Medisupport including Dianalabs, Polyanalytic, Dianalabs Valais, Proxilab and Bioanalytica; Labor Team W, Risch), cantonal-based laboratories (Hôpital du Valais – Institut Central), Spital Region Oberaargau (Bern, Solothurn, Aargau, Luzern), and 3 high-throughput sequencing platforms (Health 2030 Genome Centre in Geneva, Functional Genomics Centre Zurich run by ETH Zürich and University of Zürich, Genomics Facility Basel run by ETH Zürich and University of Basel).

Processed sequencing data are shared openly within 14 days from positive PCR result through the GISAID platform (https://www.gisaid.org) and eventually through the Swiss Pathogen Surveillance Platform (SPSP). The centralized analysis of this National Surveillance will be performed by the groups of Pr. Neher, Pr. Stadler and Dr. Althaus, where variants of concern are counted, analyzed and all sequences scanned for new variants with potential changes in antibody-Spike interactions (https://nextstrain.org/groups/swiss, https://covariants.org/per-country, https://cov-spectrum.ethz.ch). This work is done in close collaboration with the Swiss National COVID-19 Science Task Force and the Swiss Institute of Bioinformatics (SIB).

In order to complement the genomic surveillance based on patient samples, sequencing of SARS-CoV-2 in wastewater samples is also performed, initially funded for 6 months. Samples are collected daily in six wastewater treatment plants (WWTP), under the coordination of Eawag. Up to 50 samples per week over the first 26 weeks have been performed. The sequencing and analysis of these samples, including detection of variants, is done under the coordination of Prof Niko Beerenwinkel. It started in December 2020 for Lausanne and Zurich, and in February 2021 for all six WWTP (https://bsse.ethz.ch/cbg/research/computational-virology/sarscov2-variants-wastewater-surveillance.html). The analysis of wastewater samples is envisaged to run until the end of the surveillance program on 31.3.2022.

Immunological characterization of the variants within the surveillance program is coordinated by Professor Trono's team at EPFL.

This report has been produced by Erik Boehm, Pauline Vetter, Marc Friedli, Samuel Cordey, Richard Neher, Christian Althaus, Martina Reichmuth, Cornelius Römer, Niko Beerenwinkel, David Dreifuss, Chaoran Chen, Tanja Stadler, Priscilla Turelli, Didier Trono, Emma Hodcroft, Nadja Wipf, Damir Perisa, and Laurent Kaiser. The list of the participants and collaborators of the program can be found at the end of this report in the appendix.

This report covers the period of December 6, 2021 to January 2, 2022 (weeks 49, 50, 51, 52). All data presented in this report are based on the sampling date.

3. Variants of concern (VOCs), variant of interest (VOI) and other surveilled variants: brief summary and special focus

Five variants and their sub-lineages are considered VOCs by the WHO, B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.617.2 (Delta), and B.1.1.529 (Omicron). While still a VOC for WHO, the European Centre for Disease Prevention and Control de-escalated Alpha as a VOC.

Omicron

A new B.1.1.529 VOC (Omicron), which spread worldwide, was first identified in southern Africa during November 2021. It carries an unprecedented number of mutations on the genome (>50), with most being on the gene coding for the Spike protein (>30) and in particular within the receptor binding domain (15). These mutations are associated with both immune escape and/or increased transmissibility, conferring this variant a growth advantage. It has already split into 3 sublineages: BA.1-3, with BA.1 being, by far, the most common variant. BA.1 has established itself in Switzerland, becoming the dominant lineage in Switzerland by the end of December. In other European countries, a rapid doubling time was also observed. BA.2 lacks many of the N-terminal Spike mutations seen in BA.1, and retains the mutations within the RBD. BA.2 also has mutations that alter the glycosylation (affecting immunogenicity) as well as the furin cleavage site. BA.3 appears to be more closely related to BA.2 than BA.1. BA.2 amd BA.3 are currently only rarely found in CH, but there is some signal that BA.2 can outcompete BA.1 in some locations (Denmark, India), although the specific reasons for this are currently unclear.

Detection

All sub-lineages are still detected by RT-PCR tests, but BA.1 and BA.3 (but not BA.2) exhibit S-gene target failure with some assays that can be used as a proxy prior to sequencing, as seen with VOC Alpha (and due to the same deletion as found in Alpha). Due to the dominance of BA.1 within Switzerland, S-gen target failure is currently a good proxy for Omicron infection, but this may change in time. Antigenic tests are still able to detect this variant.

The Health 2030 Genome Center highlighted an issue with the ARTICv4 primers that are routinely used for sequencing COVID samples. This primer set, which fixes the issue of the amplification dropout in the region of the Spike for the Delta lineage, has a problem amplifying the ~22780-22920 region in the Omicron lineage, corresponding to position 405-452 of the Spike protein, thus this region is not covered by our sequencing most of the time. Coverage is still sufficient for determining the variant. Attempts are currently being made to solve this issue through with two approaches: (1) a longer read (2) a new version of kit, namely COVIDSeq V4. Note: this issue does not affect primary RT-PCR detection.

Immune escape

Preliminary in vitro and epidemiological data suggests that Omicron has a significant growth advantage relative to Delta. Early in vitro data demonstrates that it is able to evade neutralizing antibodies raised against previous variants or after 2 doses of vaccine. Notably, this includes the combination of casirivimab/imdevimab (REGN-CoV2), one of the most used monoclonal antibody treatments in Switzerland, losing their ability to neutralize Omicron. Sotrovimab is currently the only antibody available in Switzerland that retains substantial neutralizing activity.

While Omicron largely escape humoral immunity/neutralizing antibodies, cell mediated immunity appears to remain largely intact. Administering a 3rd vaccine dose or a combination of previous infection and 2 vaccine doses has been shown to be retained substantial neutralization in vitro. In the community setting, this moderately effective humoral response and retained cellular response translates to moderate (>5060%) vaccine effectiveness against symptomatic infection, high effectiveness against severe outcomes, and very high efficacy at preventing death.

Severity

Data on severity is suggests that it causes intrinsically milder disease. This assessment is complicated by substantial population level immunity world-wide, having continually grown since the start of the pandemic through vaccination or exposure. Reinfections/vaccine breakthrough infections are over-

represented in new Omicron cases. To date, no study assessing hospitalization and ICU admission rates has properly controlled for pre-existing immunity through serology studies.

The Delta VOC

Delta is still circulating at significant levels in Switzerland and much of the world, although we observed a progressive replacement by Omicron in CH during the month of December, with Omicron becoming dominant by the end of December.

Therapeutic intervention effectiveness

Numerous mutations have been reported to substantially reduce the therapeutic effectiveness of mAbs currently used to treat COVID-19, as well as those under development (Table 1). Notably, the Delta variant retains susceptibility to all mAbs approved for use in Switzerland, while Omicron escapes all except Sotrovimab. As some point mutations may annihilate the *in vitro* neutralizing effect of the Sotrovimab, mutations known to do this will be closely followed (Table 1, and section 7).

AA position	World	Europe	Switzerland	Mutations
337	24	7	0	R/L/H/T
340	28	11	0	K/A/G/V
356	23	11	0	T

Table 1: Positions where mutations are known to result in escape from sotrovimab, and their prevalence, and the specific amino acid mutations known to result in escape

In addition to mAbs, there are a number of other antiviral treatments under development, such as protease inhibitors (either targeting host cell proteases such as TMPRSS2, or virally encoded ones such as 3CL like proteases) like Paxlovid® (PF-07321332) or RNA nucleotide analogues (which interfere with replication of the viral genome such as Molnupiravir). No data is available regarding mutations enabling escape from these proteases (and there are unlikely to be any for treatments targeting host cell proteases). In contrast, serial passage of virus in the presence of Molnupiravir lead to the accumulation of mutations that increased viral resistance to Molnupiravir. Despite this, the mutations conferring resistance to Molnupiravir significantly reduced overall viral fitness, and were thus detrimental to the virus when Molnupiravir was not present. Preliminary data confirms that Molnupiravir, Paxlovid, and Remdesivir all retain full *in vitro* efficacy again Omicron.

The circulation of specific mutations leading to decreased effectiveness of known therapeutics available for clinical use in Switzerland will be surveilled (see Section 6 below).

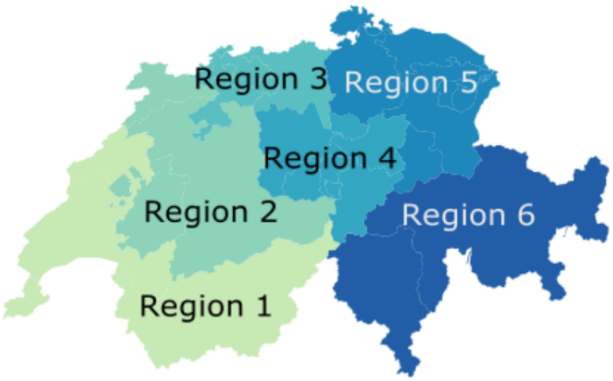
4. Epidemiology in Switzerland and number and origin of sequences produced through the program during the surveilled period

Data in this report comes from 3 sources: 1) The publicly available data on COVID-19 as reported by the FOPH (https://www.covid19.admin.ch), including data that is declared to the FOPH by the different laboratories in Switzerland; 2) data originating from laboratories participating in the surveillance program; and 3) sequences submitted to GISAID, for which the corresponding infected person was in Switzerland (resident or recent travel history to Switzerland).

General caveat: the numbers and denominators are fluid and variable over time; and are subject to change depending notably on the different databases used, and variable declaration delays. All data generated by this program is also submitted to SPSP.

The number and origin of sequences submitted to GISAID by each laboratory during January and February, 2021, prior to the start of the surveillance program can be found in the first report covering the months of March and April 2021.

Data will be presented here by regions, using the same region definitions that are used for the influenza sentinel surveillance system in Switzerland. Data are presented according to residency post-code.



Region 1 includes the cantons of Geneva, Neuchatel, Vaud and Wallis

Region 2 includes the cantons of Bern, Fribourg and Jura

Region 3 includes the cantons of Aargau, Basel (Basel-Stadt and Basel-Land) and Solothurn

Region 4 includes the cantons of Luzern, Unterwalden (Obwalden and Niedwalden), Schwitz, Uri and Zug

Region 5 includes the cantons of Appenzell (Appenzell Ausserrhoden and Appenzell Innerrhoden), Glarus, Sankt Gallen, Schaffhausen, Thurgau and Zurich.

Region 6 includes the cantons of Graubünden and Ticino.

Divisions of the different regions, from https://covariants.org/per-country

Number of cases processed by the laboratories participating in the surveillance program

During December, the FOPH reported a total of 304,974 confirmed SARS-CoV-2 cases in Switzerland. Supplementary Table 1 provides an overview of the number and incidence of confirmed cases, the effective reproduction number R_e, the number and incidence of tests, test positivity, the number and proportion of sequenced samples, and the number and proportion of VOCs by canton, region and for Switzerland overall.

As of the writing of this report, the laboratories participating in this program reported 115,242 positive tests during the surveilled program, which represents over 37% of the total number of cases reported in Switzerland (including both PCR and antigen-based tests). Because of reporting delays, this number may be underestimated. Detailed data regarding the total number of tests performed each week by the laboratories participating in the surveillance program (including negative and positive tests numbers, and the number of the positive tests that have been sequenced) are available in appendix Table 3.

Number of declared SARS-CoV-2 sequences produced through the surveillance program (presented by submission date, further declarations are still ongoing)

A total of over 9,300 SARS-CoV-2 sequences have been declared to have been submitted to GISAID during this period. There are 9,630 sequences are available for this period on GISAID as of 21 Jan 20222, and the difference may be explained by reporting delays.

This represents around 3.1% of all cases detected in Switzerland during the surveilled period (see Supplementary Table 2 and 3 in the Appendix for details). Of note, this number includes sequences from samples received from other laboratories at the request of the Cantonal physician teams.

Table 2 shows the number of sequences successfully submitted to GISAID through the surveillance program during the surveilled period by calendar week (data is incomplete).

Week	Date	Number of sequences declared and successfully submitted to GISAID during the surveilled period, by all laboratories in the program
49	Dec 6 to Dec 12	2724
50	Dec 13 to Dec 19	2641
51	Dec 20 to Dec 26	2616
52	Dec 27 to Jan 2	1355
	Total	9336

Table 2: number of sequences submitted to GISAID through the surveillance program. Note these data are not by sampling date but rather by submission to GISAID date. Data are incomplete due to late reporting by one laboratory

The total number of SARS-CoV-2 sequences declared and submitted to GISAID by each laboratory during the month of November is available in Supplementary Table 3 in the appendix.

Covering of sequencing in Switzerland and contribution of the national SARS-CoV-2 surveillance sequencing program

As shown in Figure 1, the total number of SARS-CoV-2 sequences submitted per week generally remained stable through November and December (weeks 44 to 52), while the fraction sequenced dropped, reflecting the increase in cases within Switzerland in this period. Since the beginning of this program, almost all of the sequences available in GISAID (green curve) and those on which the surveillance is conducted, come from the national surveillance program.

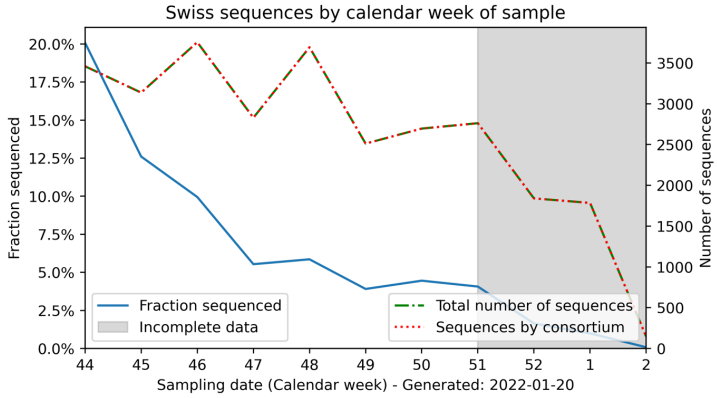


Figure 1: Number of SARS-CoV-2 sequences available for Switzerland (total available Swiss sequences in GISAID in green, Swiss sequences submitted through the program in dotted orange) and fraction of the total number of positive cases declared to the FOPH that have been sequenced (blue curve).

During the surveilled period, the total proportion of positive sequenced cases dropped below the 10% aim of the program due to a rapid rise in case numbers, despite relatively constant sequencing volume. The absolute number of sequences generated remains high, and thus should be adequate for surveillance.

Figure 2 displays the number and fraction of SARS-CoV-2 cases sequenced for each Swiss region. Regions 4 and 6 continued to have the lowest total number of sequences, while regions 4 and 5 continued to have the lowest fraction of cases sequenced.

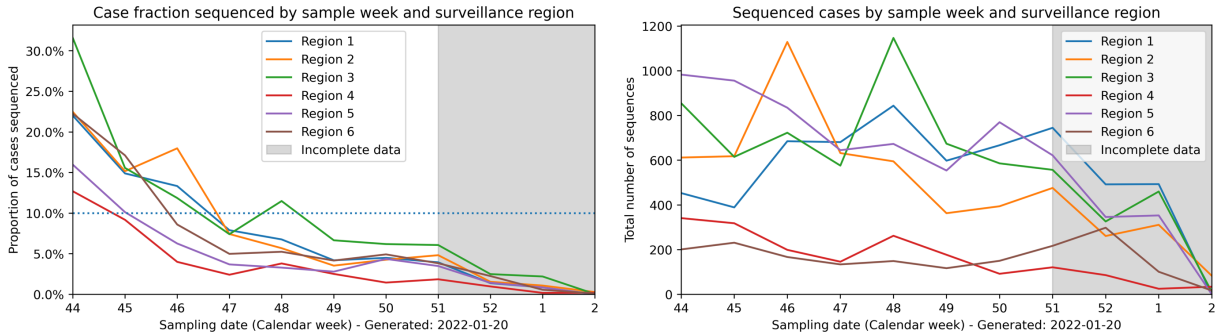


Figure 2: Sequencing coverage among the different Swiss regions per week, presented by fraction of cases sequenced (left) and by number of sequences (right).

5. Variants circulating in Switzerland since January 2021, with a focus on the surveilled period

Determination of the proportion of total number of sequences over time falling into defined variant groups is done by Emma Hodcroft's team and displayed on the CoVariant website (https://covariants.org/per-country). Those results are based on the total number of sequences submitted to GISAID over the time period for Switzerland. Those data mainly, but not exclusively, come from the national genomic surveillance program since its beginning (see Figure 1).

The B.1.617.2 Delta variant (in green in Figure 4) and its sub-lineages were the most commonly retrieved lineages early in December, but was overtaken by Omicron by the end of the month all over Switzerland (Table 3, also Figures 5 and 6). Only 3 sequences were identified that were neither Omicron nor Delta.

Region	Delta	None	Omicron	Others	sequences	cases	% sequenced
All	5763	27	2859	3	8652	304974	2.8%
1	1551	5	723	1	2280	83744	2.7%
2	947	1	438	0	1386	46246	3.0%
3	1360	14	477	1	1852	41842	4.4%
4	317	1	100	0	418	28726	1.5%
5	1282	5	720	1	2008	79672	2.5%
6	228	1	370	0	599	24744	2.4%

Table 3: number of sequences corresponding to selected variants in each region of Switzerland from 6 December 2021 to 2 January 2022, according to data received by January 21, 2022. None indicates no lineage could be assigned, due to poor sequencing coverage.

Many Delta sequences are assigned to AY* lineages, which are Delta sub-lineages. AY.43 remains the most common Delta sub-lineage in Switzerland. With the rapid increase in Omicron cases following its first detection, and its estimated transmission advantage over over 100% relative to Delta (Figure 3), it is possible that Delta will disappear completely.

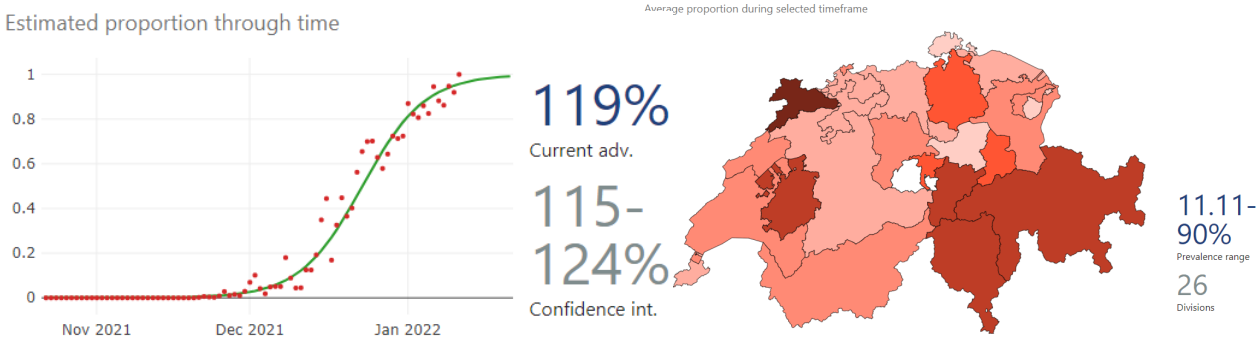


Figure 3: B.1.1.529 (Omicron) estimated transmission advantage over time compared to co-circulating strains (left) and geographic distribution across Switzerland and average proportion during the surveilled period (right). Dynamic navigation available at https://cov-spectrum.ethz.ch/explore/Switzerland.

Notably, Omicron has displaced Delta to the greatest extent in region 6, and to the least extent in region 4 (Figure 6). Among other sequences identified in Switzerland during the surveilled period, only 3 samples with identifiable non-Delta and non-Omicron lineages were detected.

An estimate of the total number of VOCs circulating in Switzerland, corrected by taking in account the fraction of sequencing in Switzerland is available through the covSPECTRUM program, developed at ETHZ, at https://cov-spectrum.ethz.ch/explore/Switzerland.

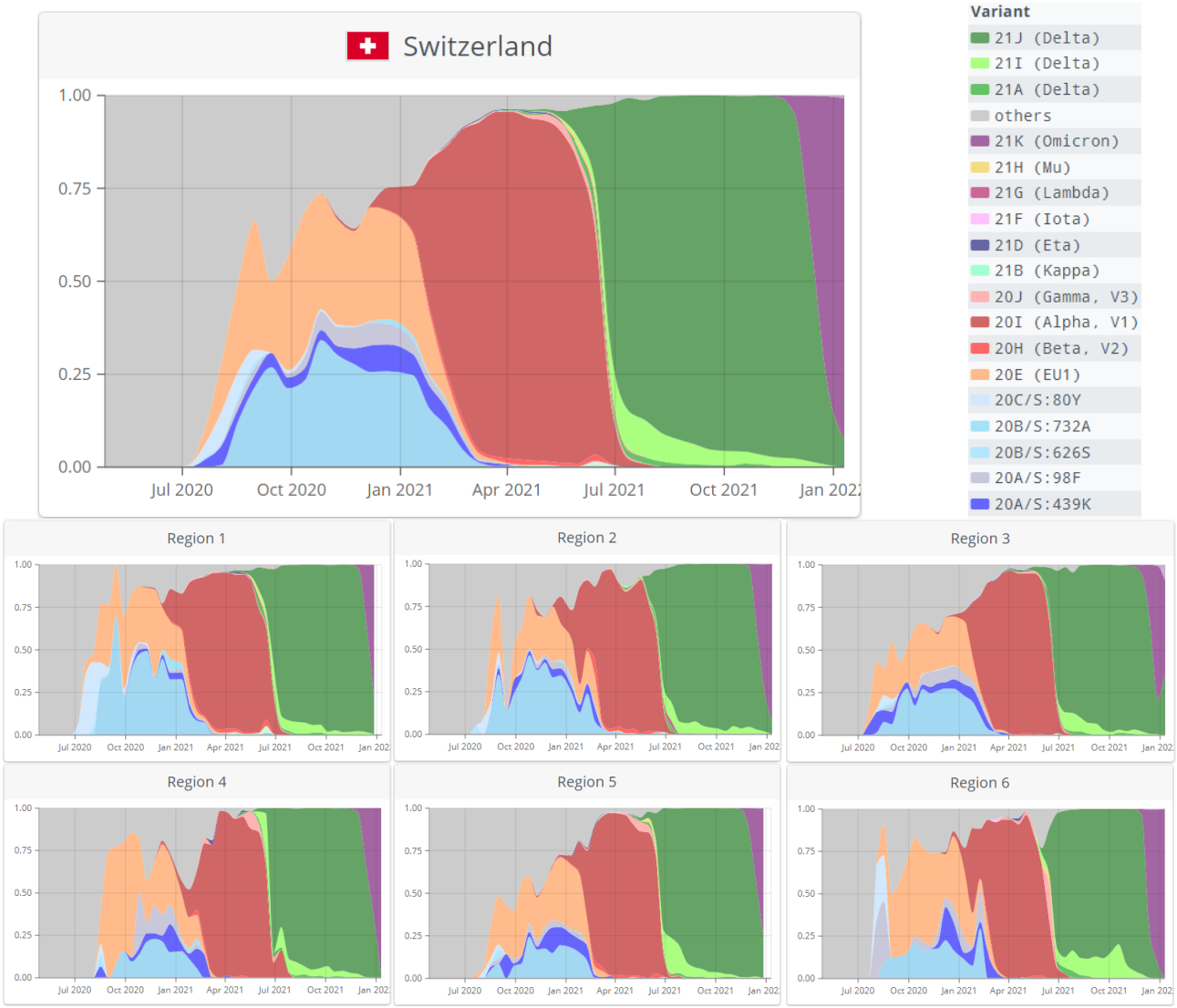


Figure 4: proportion of the total number of sequences (not cases), over time, that fall into defined variant groups, for Switzerland. Screenshot from CoVariant website. Dynamic navigation is available at https://covariants.org/per-country. Dark green indicates the currently dominant B.1.617.2 (Delta) lineage or its sub-lineages. Dark Red indicates B.1.1.7 (Alpha), the previously dominant lineage in Switzerland. Purple indicates.1.1.529 (Omicron), Light purpl3 indicates Omicron sublineage BA.2, with 9 sequences detected in CH in before 10 January 2021.

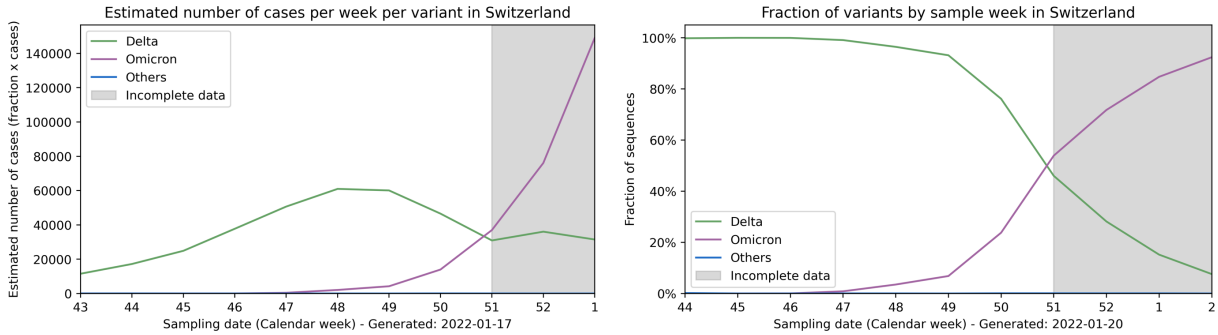


Figure 5: (Left): Percentage of circulating VOCs and VOIs in Switzerland by week, over the 49 first weeks of 2021 (total number of B.1.617.2 (Delta), and B.1.1529 (Omicron) sequences from Switzerland and successfully submitted to GISAID are shown here).
(Right): Estimated number of sequences of Delta, Omicron, and others retrieved during the surveilled period.

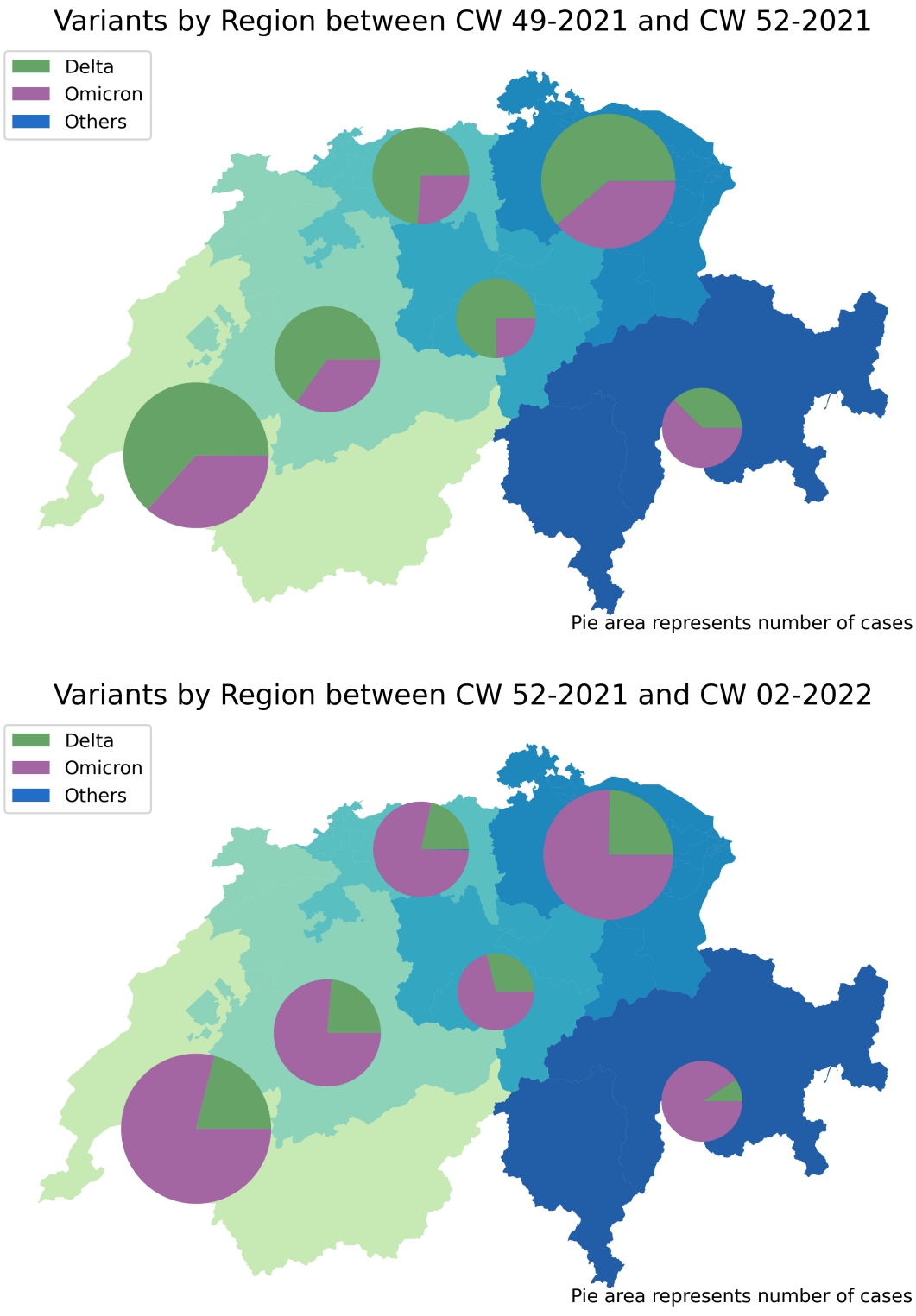


Figure 6: Distribution of variants per region, for December 2021(Top) and since the end of December (bottom), shown on a map. The size of the pie chart corresponds to the total number of sequences. Note the overall dominance of Delta or one of its sub-lineages in all regions except 6 during December. This mainly reflects the dominance of Delta in early December, as Omicron surpassed Delta in late December. Note Omicron dominates in all regions as of the time of this report (bottom).

6. Assessment of the competition between the different variants in Switzerland

The competition between different SARS-CoV-2 variants can be modelled using multinomial logistic regression. The analysis by Dr. Althaus' group is based on sequences retrieved from CovSPECTRUM. The results correctly predicted that Omicron would be the dominant SARS-CoV-2 variant in Switzerland. These predictive models suggest that Omicron will continue to increase in prevalence and will further displace Delta in Switzerland. This rapid rise is most readily visible when a log scale is used (figure 7)

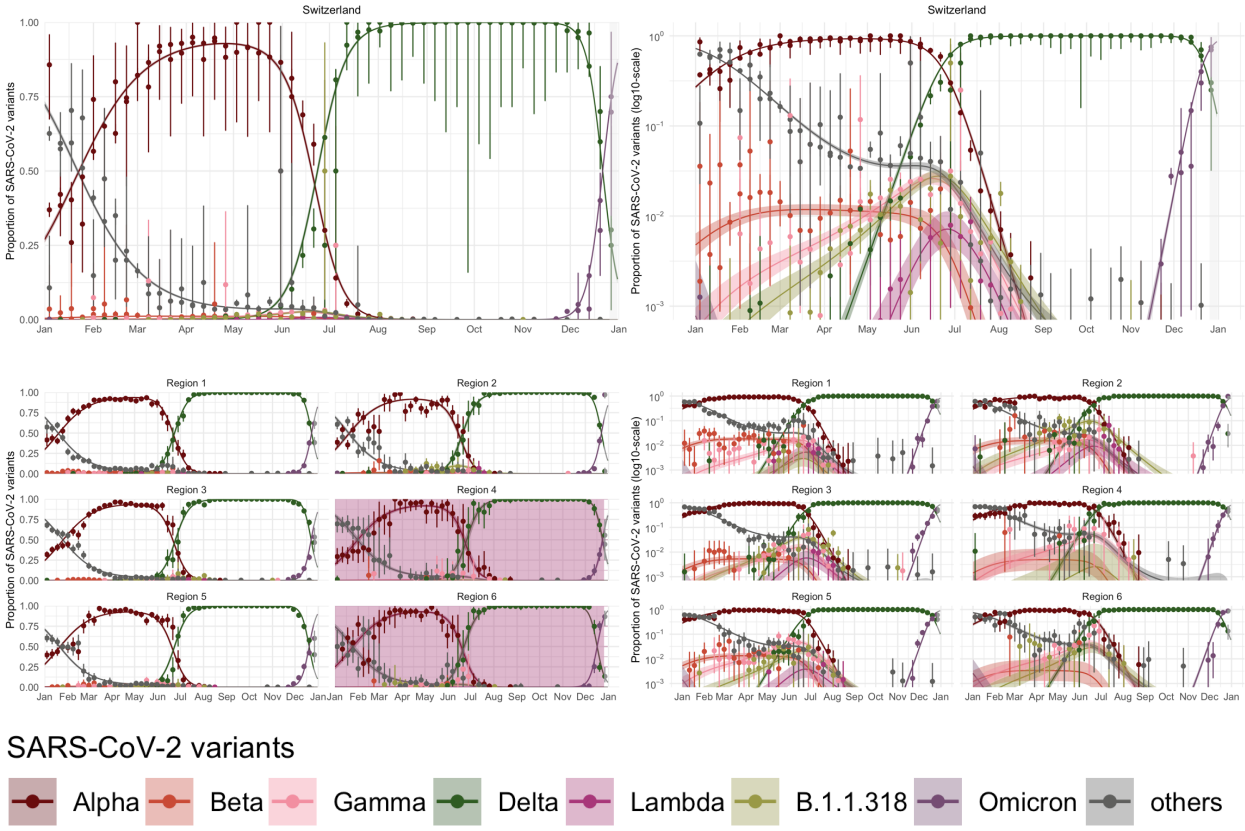


Figure 7: Observed and modeled proportion of SARS-CoV-2 variants over time in Switzerland. In April and May 2021, Gamma and Delta started to replace Alpha, with Delta outcompeting all other variants. At the end of October, more than 99.9% of the retrieved sequences in Switzerland were due to Delta or one of its sub-lineages. In late November, Omicron arrived in Switzerland and began to rapidly displace Delta. Omicron achieved dominance by the end of December, and will likely continue to increase in proportion. Model fits are based on a multinomial logistic regression with splines.

7. Surveillance of mutations associated with reduced mAb treatment efficacy

A number of mutations have been reported to result in significantly reduced *in vitro* effectiveness of the sotrovimab and casirivimab/imdevimab association monoclonal antibodies used to treat patients in Switzerland. Notably, Omicron is completely resistant to neutralization by casirivimab/imdevimab, and sotrovimab remains the only mAb used in Switzerland that retains effectiveness against Delta and Omicron. The prevalences of mutations reported to escape neutralization by sotrovimab are thus being followed (Table 4).

	337H		337L		337R		337T	
date	Global	Switzerland	Global	Switzerland	Global	Switzerland	Global	Switzerland
06.12.2021	2	0	6	0	0	0	4	0
13.12.2021	4	0	2	0	2	1	2	0
20.12.2021	3	0	3	0	0	0	1	0
27.12.2021	0	0	3	0	0	0	1	0

	340A		340K		340G		356T	
date	Global	Switzerland	Global	Switzerland	Global	Switzerland	Global	Switzerland
06.12.2021	3	0	23	2	23	0	0	0
13.12.2021	3	0	7	0	3	0	1	0
20.12.2021	3	0	13	1	2	0	1	0
27.12.2021	2	0	5	0	0	0	1	0

Table 4: Global and Swiss counts of sequences bearing escape mutations from therapeutic mAbs used in Switzerland

Known mutations enabling escape from sotrovimab have been detected in Switzerland, but remain very rare.

8. Wastewater surveillance program

Since August, the B.1.617.2 (Delta) variant had accounted for the vast majority of the sequences identified in all of the six wastewater treatment plants (WWTPs) that are tested on a daily basis. Signatures of the B.1.1.529 (Omicron) variant have been first detected at the earliest in sequenced sewage samples of the Basel-Stadt cantonal wastewater surveillance project, dating from November 21 onwards. Since then, Omicron has been detected in all other surveyed WWTPs, and quickly grew in relative prevalence during the month of December to become the major variant in wastewater samples from Geneva and Zürich. In the other surveyed stations, the growth of Omicron follows a similar path, but is lagging some days behind. The logistic growth rate of the relative prevalence of Omicron can be estimated based on wastewater sequencing data, and the estimates range from 0.18 to 0.27 per day, depending on the location.

Quantification of Omicron in sewage seems to exhibit some peculiar challenges that are also observed in other wastewater analysis projects around the World: there are some indications that this variant is less shed in faeces compared to Delta, although this is currently unclear. This could be due either to Omicron infecting a larger proportion of vaccinated people, and/or to a change in the virus tropism. Differential shedding could lead to an underestimation of the prevalence of Omicron when using wastewater sequencing data. This should however not impact estimates of the logistic growth rate, but lead to an apparent delay (of one to a few days) of the midpoint of the logistic growth.

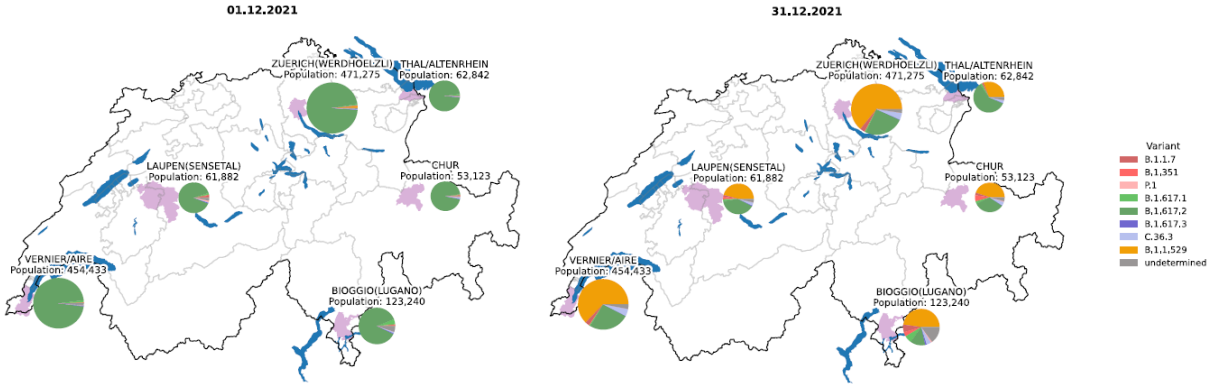


Figure 8: Overview of the prevalence of variants of SARS-CoV-2 at the beginning and end of December 2021, estimated from wastewater samples collected daily during the month in WWTPs located in 6 different Swiss locations. Pie chart areas are proportional to population connected to the wastewater treatment plants. Pink shaded areas represent catchment areas (boundaries from 2017). Population connected to Vernier (GE) wastewater treatment plant also includes ~44,000 inhabitants from neighbouring French communities. B.1.617.2 (Delta) is represented in in dark green, B.1.617.1 in light green (Kappa), B.1.617.3 in purple, B.1.1.7 (Alpha) in dark red, B.1.351 (Beta) in light red, P.1 (Gamma) in pink, B.1.1.529 (Omicron) in orange.

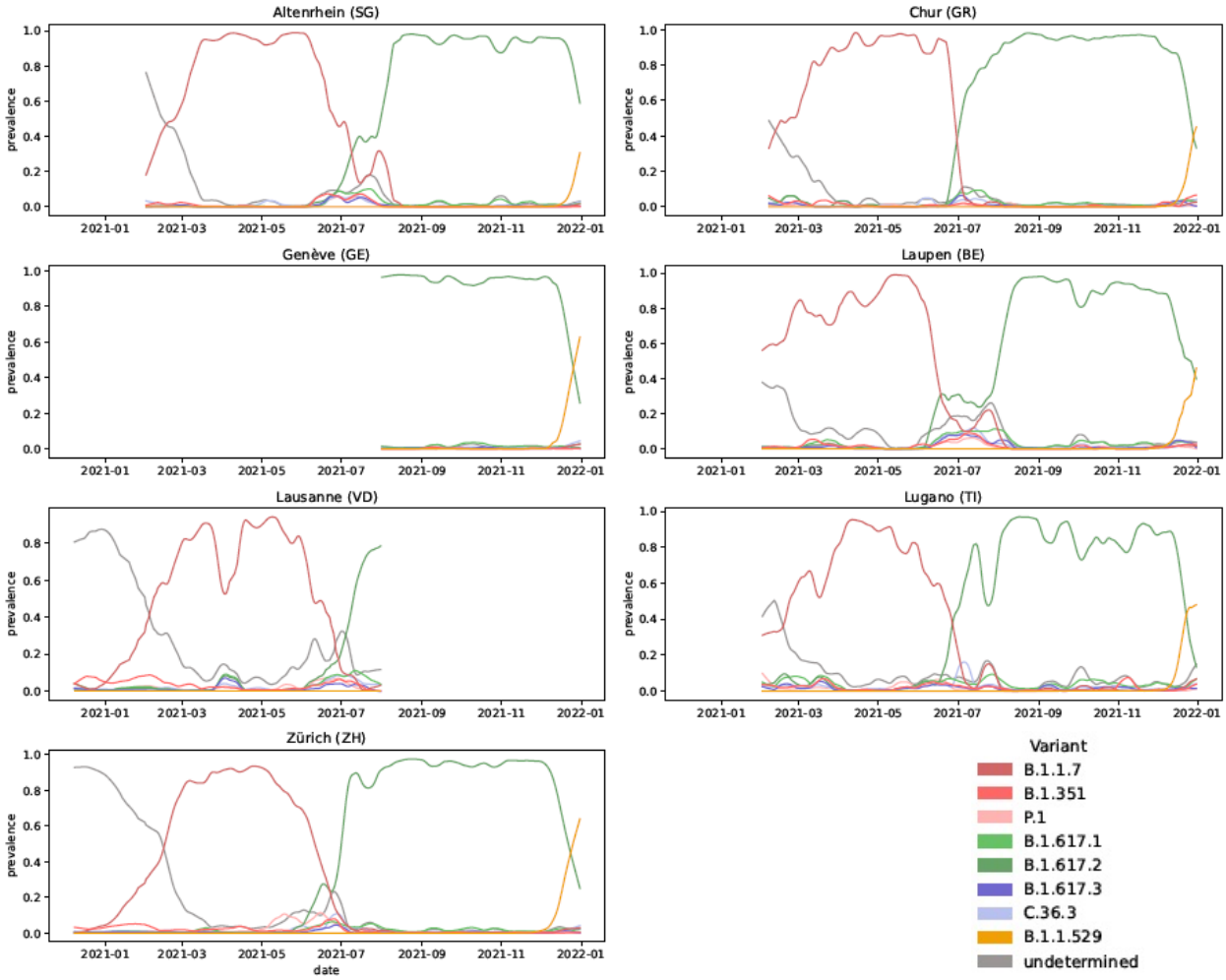


Figure 9: Prevalence of variants of SARS- CoV-2 estimated from wastewater samples collected daily until December 31 (except Lausanne: July 31) in WWTPs located in 7 different Swiss cantons. B.1.617.2 (Delta) is represented in dark green, B.1.617.1 (Kappa), in light green, B.1.617.3 in purple, B.1.1.7 (Alpha) in dark red, B.1.351 (Beta) in light red, P.1 (Gamma) in pink, B.1.1.529 (Omicron) in orange. An online dynamic navigation is available at https://bsse.ethz.ch/cbg/research/computational-virology/sarscov2-variants-wastewater-surveillance.html .

Location	Parameter	Estimate	Lower Bound	Upper Bound
Lugano (TI)	growth rate	0.23	0.17	0.29
Lugano (TI)	midpoint	24.12.21	23.12.21	26.12.21
Zürich (ZH)	growth rate	0.18	0.14	0.21
Zürich (ZH)	midpoint	24.12.21	22.12.21	26.12.21
Genève (GE)	growth rate	0.24	0.18	0.3
Genève (GE)	midpoint	25.12.21	24.12.21	27.12.21
Chur (GR)	growth rate	0.27	0.18	0.35
Chur (GR)	midpoint	29.12.21	27.12.21	31.12.21
Altenrhein (SG)	growth rate	0.24	0.16	0.33
Altenrhein (SG)	midpoint	02.01.22	31.12.21	05.01.22
Laupen (BE)	growth rate	0.18	0.13	0.23
Laupen (BE)	midpoint	28.12.21	26.12.21	31.12.21

Table 5: Logistic growth of the relative prevalence of Omicron. The table shows estimates of the growth rate and midpoints of logistic curves fitted using wastewater sequencing data for the six surveyed WWTPs, along with 95% confidence intervals. The growth rate is per day, and the midpoints correspond to the days where Omicron is predicted to pass 50% of cases in the locations..

9. Immunological characterization of the variants

The omicron B.1.529 variant has been shown to be drastically resistant to monoclonal antibodies andto have a >10x reduction in sensitivity to sera from Pfizer or Moderna vaccine recipients.

Approximately 10% of the Omicron variants found in GISAID have an additional R346K mutation previously identified in Mu B.1.621 variant. Therefore the effect of this mutation on neutralization resistance to sera from people who were infected, vaccinated (2 doses), or infected then vaccinated (1 dose) was tested. Figure 10 shows that this mutation does not result in additional immune escape. These results suggest that there should be no change in vaccine effectiveness against the B.1.1.529 + R346K Omicron variants compared to the original Omicron strain.

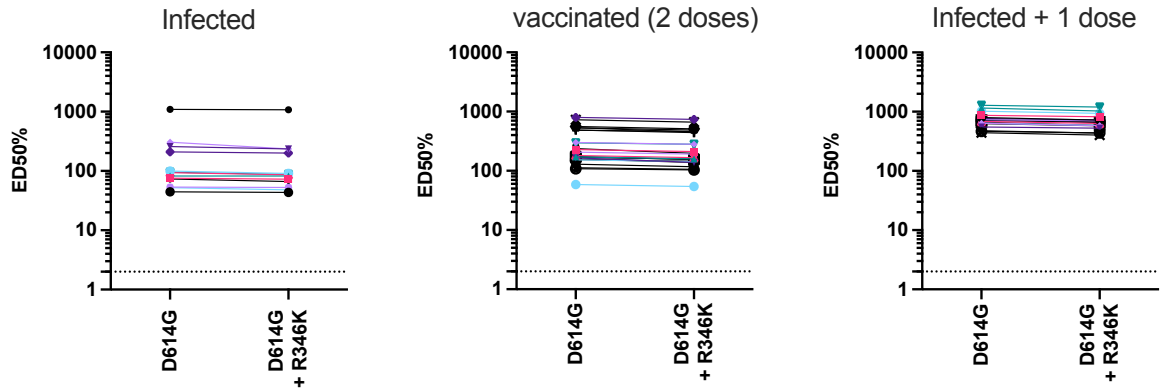


Figure 10: the R346K mutation does not result in additional immune escape
Neutralizing activities of sera from 13 infected, 24 fully vaccinated or 18 infected then vaccinated (1 dose) patients were assessed for their ability to neutralize D614G ancestral- or D614G + R346K- Spike variants in the S^3-ACE2 assay. The mean serum dilution needed to achieve 50% of neutralization inhibition (ED50%) is indicated in the table for each variant.

Conclusion

In December, over 9,300 sequences were obtained for Switzerland through this surveillance program, in the midst of a steep increase in case numbers. Each week since this surveillance program started, it has contributed almost all of the Swiss SARS-CoV-2 sequences available on GISAID. Around 3% of the cases reported in Switzerland were sequenced, reflecting a large increase in case numbers, which is below the goal of 10%. With over 9 thousand sequences generated from all over Switzerland, coverage is deemed to be satisfactory despite falling below the arbitrary 10% threshold. Region 4 and 5 remain the least represented geographical areas.

Notably, Omicron has displaced Delta to the greatest extent in region 6, and to the least extent in region 4. All other variants were only rarely detected, both in clinical samples and in the wastewater surveillance part of the program.

S-gene target failure cannot be used as a proxy for Omicron sub-lineage BA.2, but this sub-lineage is currently very rare in Switzerland. No additional diagnostic or treatment issues were noted for any variant other than Omicron in December.

An estimate of the total number of VOCs circulating in Switzerland, corrected by taking in account the fraction of sequencing in Switzerland is available at https://cov-spectrum.ethz.ch/explore/Switzerland.

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https://bsse.ethz.ch/cevo/research/sars-cov-2/swiss-sars-cov-2-sequencing-consortium.html

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Appendix:

SARS-CoV-2 epidemiology in Switzerland:

We used publicly available data on COVID-19 as reported by FOPH (https://www.covid19.admin.ch) and sequence data submitted to GISAID to provide a summary of the SARS-CoV-2 epidemiology in Switzerland. Data presented here cover the period from 6 December 2021 to 2 January 2022.

sup_table_overview_Dec_2021.xlsx

Supplementary Table 1: Epidemiological data for Switzerland, its regions and cantons from 6 December 2021 to 2 January 2022: population, number and incidence of confirmed cases, effective reproduction number R_e, number and incidence of tests, test positivity, number and proportion of sequenced samples, and number and proportion of VOCs. R_e by region is represented as the median and range of the daily R_e values for all cantons within a region.

week	date	Total PCR tests	Positive tests	Sequenced	% positives	% positives sequenced
49	Dec 6 to Dec 12	168 793	28 590	2 724	16.94%	9.53%
50	Dec 13 to Dec 19	165 717	24 808	2 641	14.97%	10.65%
51	Dec 20 to Dec 26	145 110	26 637	2 616	18.36%	9.82%
52	Dec 27 to Jan 2	99 667	35 207	1 355	35.32%	3.85%
	Total	579 287	115 242	9 336	19.89%	8.10%

Supplementary Table 2: Total number of tests performed by the laboratories participating in the surveillance program from 6 December 2021 to 2 January 2022.

Week	Date	Basic Surveillance						Augmented Surveillance						Sentinella Laboratories		All
		EOC	St-Gallen	Labor Team W *	Risch	SRO	Synlab	USB	IFIK	Diana labs	CHUV	UZH	ICH-VS*	HUG	ETH/ Viollier	
44	Dec 6 to Dec 12	89	47	177	330	72	0	43	143	86	56	207	92	303	1256	2724
45	Dec 13 to Dec 19	96	48		219	57	0	111	145	78	25	177	84	295	1129	2641
46	Dec 20 to Dec 26	99	95	179	230	31	0	248	153	92	41	193	179	435	820	2616
47	Dec 27 to Jan 2	94	48		0	78	0	159	158	0	43	42			554	1355
	Total	378	238	356	779	238	0	561	599	256	165	619	355	1033	3759	9336

*Supplementary Table 3: number of sequences submitted to GISAID by each laboratory during the surveilled period (6 December 2021 to 2 January 2022). *including sequencing sent to high-throughput platforms. ND = No data*

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