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

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1. Summary

In February, COVID-19 cases numbers began to steeply decline in Switzerland, largely driven by decreased circulation of the BA.1 Omicron variant. In parallel, circulation of the BA.2 variant increased throughout February, and case numbers were trending upward again by the end of February, following the lifting of some of the prevention measures in the community.

In the midst of this decline in case numbers, approximately 2.6% of the total number of cases identified in Switzerland in February were sequenced by the Surveillance program, yielding over 9,700 sequences.

Delta is now extremely rare in Switzerland, with less than 40 sequences detected in February. Unsurprisingly, the BA.1 and BA.2 Omicron sub-lineages were the most frequent variant detected. BA.1 was dominant at the start of the month, but by the end of February, BA.2 had clearly displaced it. Circulation of all variants other than Omicron and Delta was essentially nonexistent in February. One AY.43 x BA.1.1 recombinant was described in Switzerland at the end of January.

On the clinical level, both BA.1 and BA.2 Omicron are apparently milder than Delta, especially in a population with large immune background. Of note, vaccination is highly effective at preventing hospitalization or death due to BA.1 and BA.2, but it seems to have only moderate efficacy at reducing infection by and transmission of BA.1/2. Importantly, for unvaccinated individuals without previous exposure, infection with Omicron does not prevent reinfection with Delta, and vice versa. Infection of vaccinated or previously exposed individuals with Omicron does, however, result in an increase in neutralizing antibodies against Delta and other variants as well. Infection with BA.1 generally does offer cross-protection against BA.2, and vice versa. Short-time reinfections with BA.2 in patients previously infected by BA.1 are observed at low rates.

The immunosuppressed population, who is less likely to adequately respond to vaccines is however still at risk, and active direct antiviral treatments active against Omicron are still fully necessary. Notably, Sotrovimab is the only available monoclonal antibody (mAb) in Switzerland that is effective against BA.1, but accumulating and disparate in vitro data suggests that it is much less effective at neutralizing BA.2. Whether doubling the treatment dose would be sufficient to compensate for this increased resistance is currently undergoing investigation.
As there is no significant circulation of non-Omicron variants, and as “S-gene dropout” is observed in all Omicron sublineages except BA.2, SARS-CoV-2 positive samples not displaying “S-gene dropout” can be considered to be BA.2. No additional diagnostic or treatment issues were noted in February.

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, Michael Bel, 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 January 31 to February 27, 2022 (weeks 5, 6, 7, 8). 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. Worldwide Omicron is now almost exclusively retrieved in samples collected within the last 30 days (https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---22-march-2022).

Omicron

The Omicron VOC (B.1.1.529) 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 split into 3 sublineages: BA.1-3, with BA.1 giving rise to a further sublineage, BA.1.1.

BA.1 was initially the most common sub-variant, but BA.2 has replaced BA.1 in many parts of the world, and by week 9 (28-February to 6-March 2022) BA.2 was dominant in Switzerland too. BA.2 has a unique set of N-terminal Spike mutations compared to BA.1; but the two sublineages share 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.3 is currently rare worldwide.

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 Omicron within Switzerland, the absence of S-gene target failure is currently a good proxy for BA.2 infection. All Omicron variants contain deletions in the N-gene that results in N-gene dropout when using the PCR test from Huwel Life Sciences, Hyderabad, India. Antigenic tests are still able to detect this variant.

Immune escape

Extensive data now demonstrates that BA.1 and BA.2 are able to evade neutralizing antibodies (nAbs) raised against previous variants or after 2 doses of vaccine. Notably, all Omicron sublineages display complete escape from combination of casirivimab/imdevimab (REGN-CoV2), one of the monoclonal antibody treatments available in Switzerland. Sotrovimab is currently the only antibody available in Switzerland that retains substantial neutralizing activity against BA.1. According to *in vitro* data, BA.2 is significantly more resistant than BA.1 and ancestral variants to Sotrovimab – in vitro studies using live virus show severe reductions to the IC_{90} titer against BA.2. The clinical relevance is still somewhat unclear at the moment, but reduced efficacy is probable. While all Omicron sublineages largely escape humoral immunity, cell mediated immunity remains mostly intact.

A 3rd vaccine dose or a combination of previous infection and 2 vaccine doses has been shown to retain moderate neutralization of Omicron. In the community setting, this moderately effective humoral response after a 3rd dose and the retained cellular response translates to moderate (>50%) vaccine effectiveness against symptomatic infection, high effectiveness against severe outcomes, and very high efficacy at preventing hospitalization and death.

Despite both being considered “Omicron”, BA.1 and BA.2 are differ from each other (in terms of mutation counts) more than the earlier VOCs differed from the original Wu-1 strain, which raises concerns about cross protection from the Omicron sublineages. Studies have found that infection with BA.1 generally does offer cross-protection against BA.2, and vice versa. Despite this, a low rate of reinfection with BA.2 has been noted after a previous BA.1 infection. Similarly, some subjects are known to have failed to develop neutralizing antibodies against BA.2 after BA.1 infection.

Severity

Data on severity is complicated by substantial population level immunity world-wide, and an over representation of reinfections/vaccine breakthroughs in new Omicron cases. To date, no study has properly controlled for pre-existing immunity through serology studies. Nonetheless, a multitude of studies measuring hospitalization/ICU rates, in addition to *in vitro* and animal studies suggest that BA.1 causes intrinsically milder disease. Interestingly animal studies also suggest that BA.2 may be more severe than BA.1, but to date, no clinical difference between BA.1 and BA.2 infections has been noted.

The Delta VOC

Delta was still detected sporadically in Switzerland during February, but in very low and continuously decreasing numbers. Vaccination, particularly after a booster, is highly effective at preventing infection by and transmission of the Delta VOC. As Omicron is antigenically distinct from prior variants, including Delta, an Omicron infection in unvaccinated and previously unexposed people generally does not result in significant neutralizing activity against Delta – however, infection with Omicron in vaccinated people or people who were exposed to a non-Omicron variant does boost neutralizing titers against Delta.

Notably, Delta's decreasing numbers mean fewer chances for recombinant "Deltacron" variants to form from Delta and Omicron.

Recombinants

Natural formation of recombinant viruses formation requires coinfection by 2 different strains within the same host. After some dubious initial reports, numerous verified recombinants between Delta and Omicron BA.1 have been detected, as well as between Omicron BA.1 and BA.2. Some of those recombinants have already been given the Pango lineage designations: YD, YE and XF. Currently, there is no indication that any of these variants are more competitive nor more severe than the main Omicron lineages. A synthetic recombinant has been made between Omicron and an earlier SARS-CoV-2 variant that resulted in a virus that replicated to higher titers in animal models, but this synthetic recombinant does not closely correspond to any of the recombinants known to be circulating.

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, Omicron BA.1 escapes all mAbs approved for use in Switzerland except Sotrovimab, while BA.2 substantially escapes neutralization by Sotrovimab. As Sotrovimab is still being used mutations causing escape from it will thus be closely followed (Table 1, and section 7).

AA position	World	Europe	Switzerland	Mutations
337	55	25	2	R/L/H/T
340	175	112	17	K/A/G
356	74	41	2	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, February 2022

In addition to mAbs, there are a number of other antiviral treatments under development, such as 3CL like protease inhibitors 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. In contrast, serial passage of virus in the presence of Molnupiravir led to resistance to Molnupiravir at the cost of significantly reduced overall viral fitness. As such mutations are detrimental when Molnupiravir is not present, limited use is unlikely to lead to resistant strains. 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 7), but no substantial increase in their prevalence has been noted.

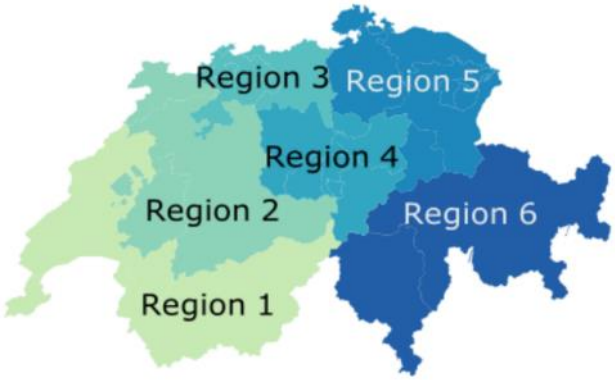
4. Epidemiology in Switzerland and number and origin of sequences produced through the program during the surveilled period

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 February, the FOPH reported a total of 380,590 confirmed SARS-CoV-2 cases in Switzerland, representing a substantial decline from January. 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 214,245 positive tests during the surveilled program, which represents over 56% (a significant increase from the previous month) of the total number of cases reported in Switzerland (including both PCR and antigen-based tests). 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 9,734 SARS-CoV-2 sequences have been declared to have been submitted to GISAID during this period. There are 10,352 sequences are available for this period on GISAID as of 23 Mar 2022, and the difference may be explained by reporting delays.

This represents around 2.6% 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
5	Jan 31 to Feb 6	2 306
6	Feb 7 to Feb 13	2 586
7	Feb 14 to Feb 20	2 499
8	Feb 21 to Feb 27	2 343
	Total	9 734

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 February 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 declined through February (weeks 5-7), while the fraction sequenced increased, reflecting the decrease 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.

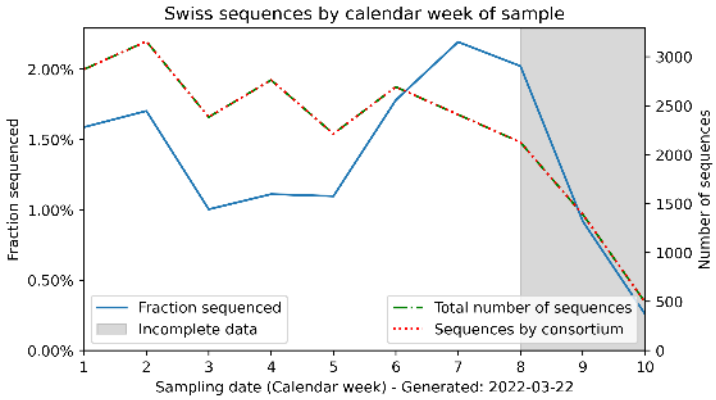


Figure 1: Number of SARS-CoV-2 sequences available for Switzerland (total available Swiss sequences in GISAID in green, Swiss sequences submitted through the program in dotted orange) and fraction of the total number of positive cases declared to the FOPH that have been sequenced (blue curve).

During the surveilled period, the absolute number of sequences generated remained high, but due to high circulation of the virus, the total proportion of positive sequenced cases remained well below the 10% aim of the program due to high case numbers. These sequences include those from sites with hospitalized patients, 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 Region 4 continued to have the lowest fraction of cases sequenced.

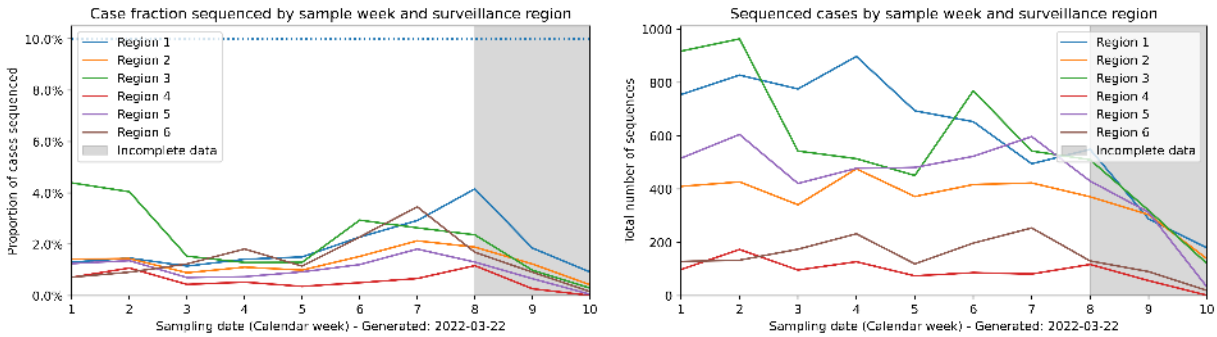


Figure 2: Sequencing coverage among the different Swiss regions per week, presented by fraction of cases sequenced (left) and by number of sequences (right).

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).

Omicron sublineage BA.1 was the most commonly retrieved lineages early in February, followed by BA.2 (Figures 3-5, Table 3).

Region	Alpha	Delta	Omicron (BA.1)	Omicron (BA.2)	sequences	cases	% sequenced
All	0	19	5437	2294	7752	380590	2.0%
1	0	10	1461	432	1904	61536	3.1%
2	0	4	912	394	1311	69559	1.9%
3	0	2	1350	555	1907	71023	2.7%
4	0	0	163	129	292	40973	0.7%
5	0	3	1060	590	1653	113169	1.5%
6	0	0	416	182	598	24330	2.5%

Table 3: number of sequences corresponding to selected variants in each region of Switzerland from 31 January 2022 to 27 February 2022, according to data received by March 23, 2022. Sequences with poor coverage where lineages could not be assigned are excluded.

BA.2 had nearly overtaken BA.1 by the end of February as the most common variant in Switzerland (Figures 4-6). No BA.3 was found during the surveilled period.

Since the last report, only one AY.43 x BA.1.1 recombinant has been found in Switzerland. It was collected on January 26.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.

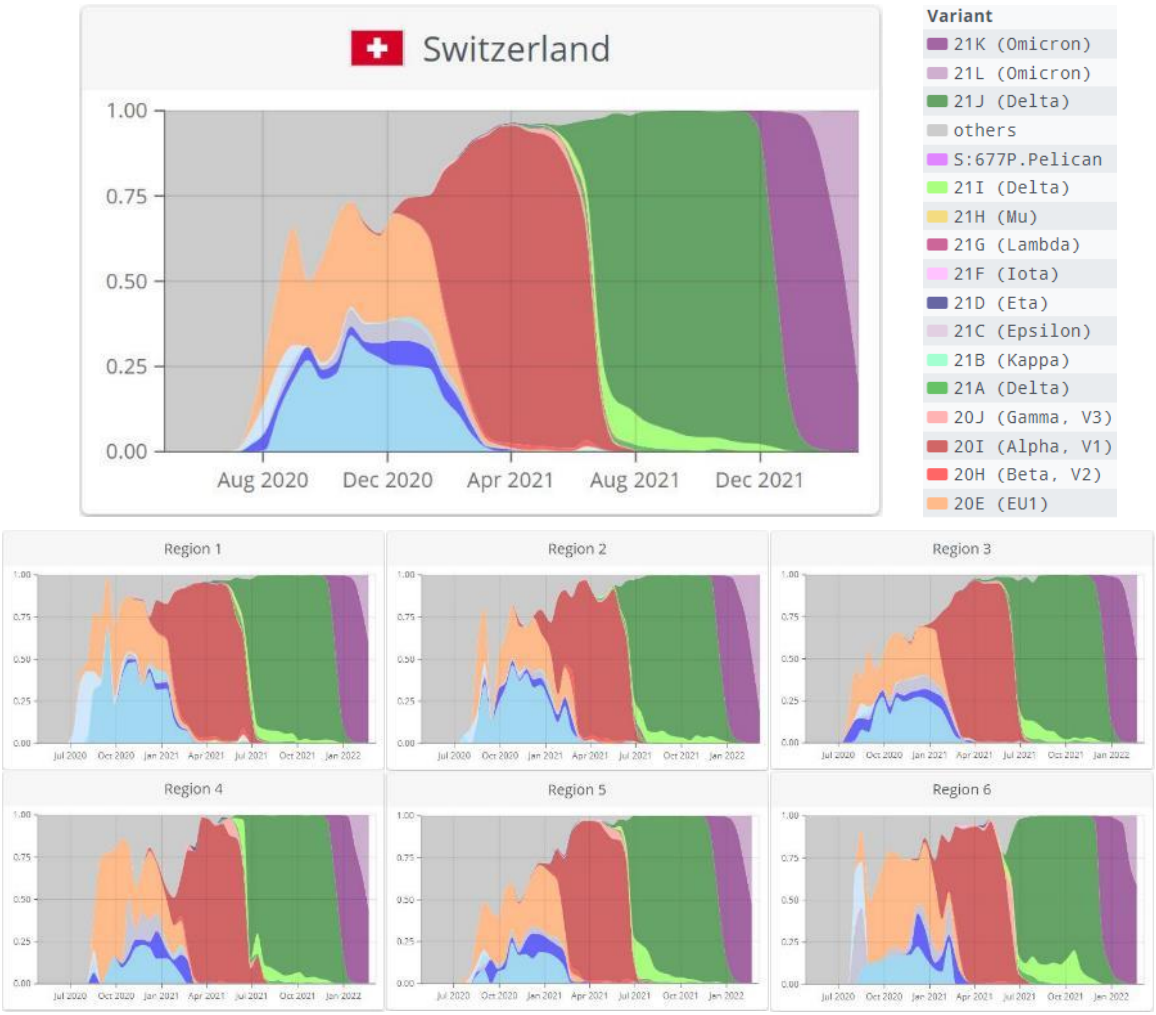


Figure 4: proportion of the total number of sequences (not cases), over time, that fall into defined variant groups, for Switzerland. Screenshot from CoVariants website. Dynamic navigation is available at https://covariants.org/per-country. Dark green indicates the currently dominant B.1.617.2 (Delta) 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 purple indicates Omicron sublineage BA.2, with 478 sequences detected in CH in week 9 (28-February to 6-March 2022), amounting to 60.1% of all cases.

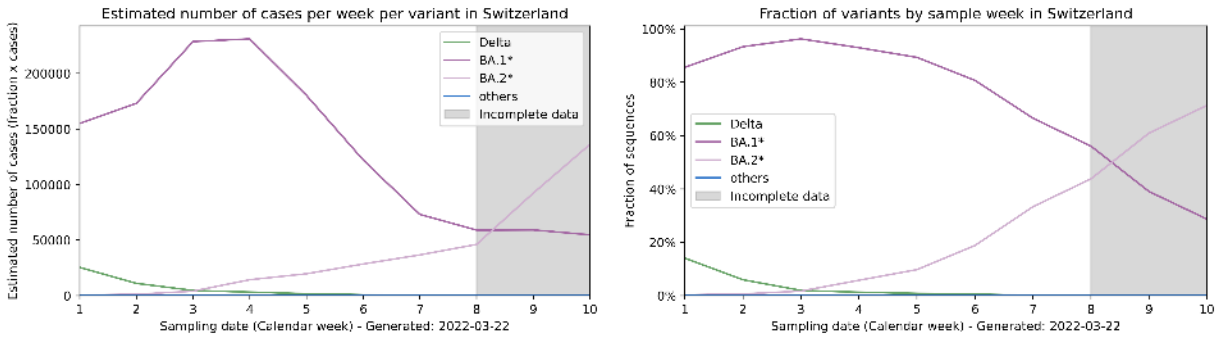


Figure 5: (Left): Percentage of circulating VOCs and VOIs in Switzerland by week, up to the 6 first weeks of 2022 (total number of B.1.617.2 (Delta), BA.1 and BA.2 sequences from Switzerland and successfully submitted to GISAID are shown here). Note the grey shaded area indicates a period of incomplete data.
(Right): Estimated number of sequences of Delta, BA.1, BA.2, and others retrieved during the surveilled period.

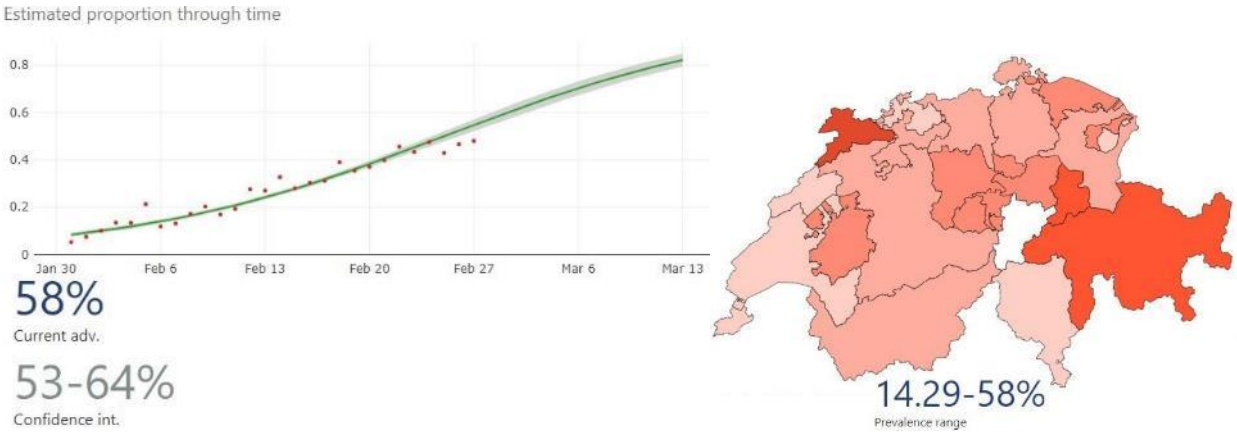


Figure 6: BA.2 estimated transmission advantage over time compared to co-circulating strains (left) and geographic distribution across Switzerland and average proportion during the surveilled period (right). Dynamic navigation available at https://cov-spectrum.ethz.ch/explore/Switzerland

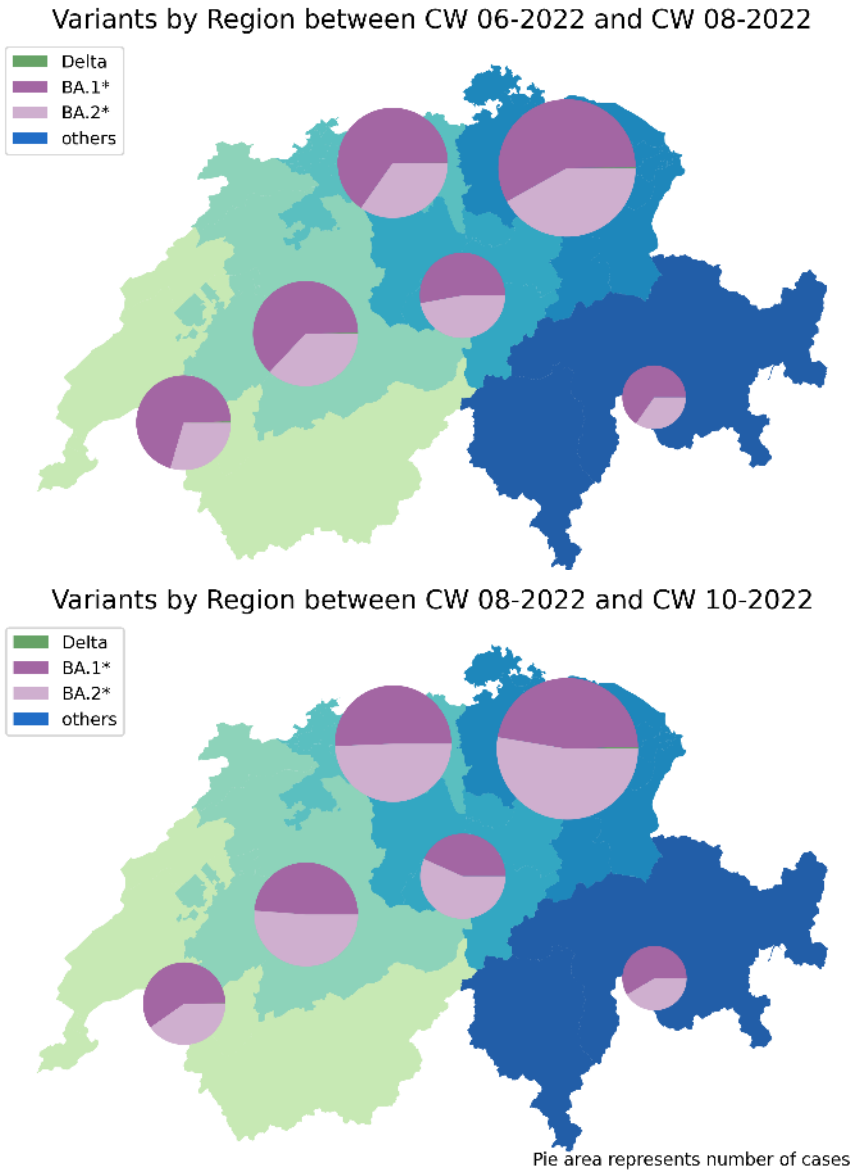


Figure 7: Distribution of variants per region, for early February (top) and the end of February 2022 (bottom), shown on a map. The size of the pie chart corresponds to the total number of sequences. Note Omicron's extreme dominance, and the large share of the BA.2 sublineage, in all regions as of the time of this report.

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 models also correctly predicted that the BA.1 sub-lineage would be replaced by the BA.2 sublineage (figure 8).

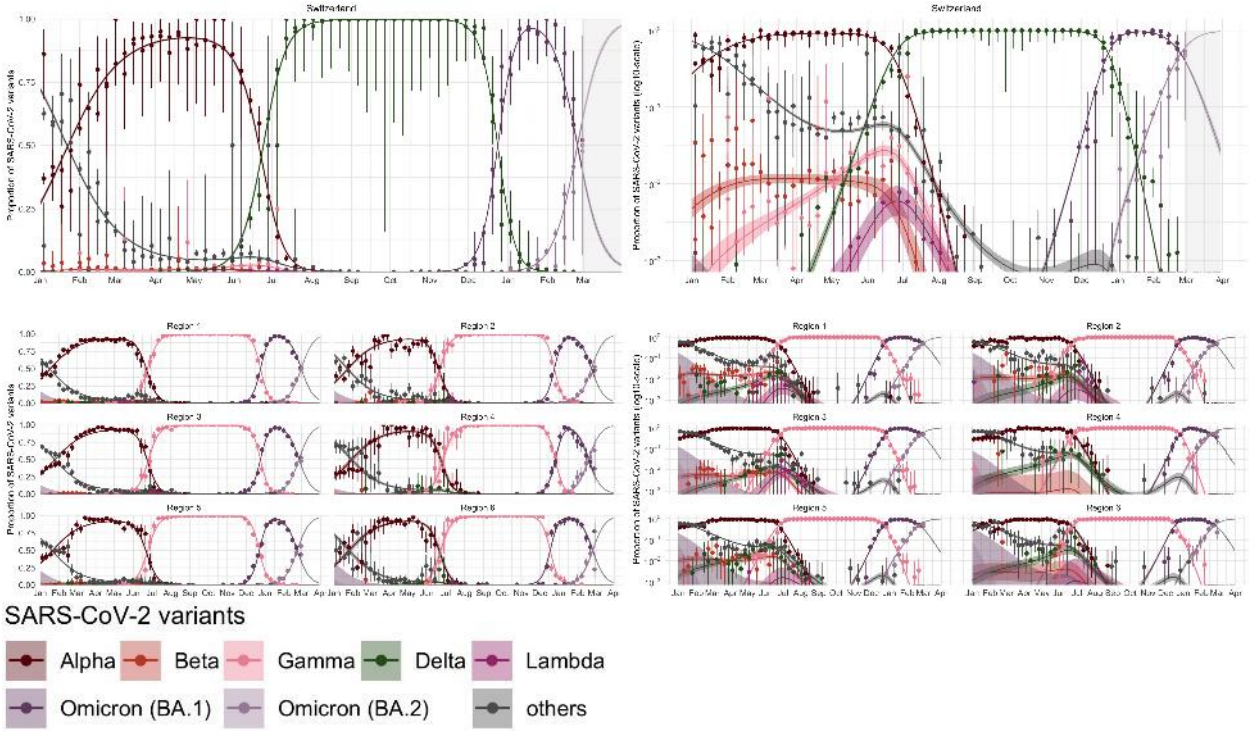


Figure 8: Observed and modeled proportion of SARS-CoV-2 variants over time in Switzerland. In April and May 2021, Gamma and Delta started to replace Alpha, with Delta outcompeting all other variants. At the end of October, more than 99.9% of the retrieved sequences in Switzerland were due to Delta or one of its sub-lineages. In late November, Omicron arrived in Switzerland and began to rapidly displace Delta. Omicron BA.1 achieved dominance by the end of December, but was then replaced by Omicron BA.2. 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 Omicron BA.1. Unfortunately, this effectiveness is expected to be significantly decreased for the BA.2 sublineage (which has replaced BA.1), on the basis of various disparate experiments reporting 8.5 to 340 fold reductions of *in vitro* neutralizing titers. The disparity may be explainable by the use of psuedovirus assays or live virus, and quantifying thresholds for 50% (IC_{50}) or 90%(IC_{90}) neutralization, as well as the comparator virus (*e.g.* the original Wu-1 strain, or Delta). Indeed, a study using live virus found an 8.5 fold reduction in IC_{50} relative to WT, but a 15 fold reduction relative to Delta. When IC_{90} was compared, an 82 fold reduction was found relative to WT, but a 258 fold reduction was found relative to Delta. Despite this disparity, it is clear that the escape is not complete, and Sotrovimab retains significant activity against BA.2 at higher titers – thus the frequencies of mutations reported to escape neutralization by Sotrovimab are still being followed (Table 4).

	337H		337L		337R		337T	
Week	Global	Switzerland	Global	Switzerland	Global	Switzerland	Global	Switzerland
31.01.2022	2	0	3	0	3	0	6	0
07.02.2022	2	0	4	0	4	0	2	0
14.02.2022	2	1	2	0	12	1	3	0
21.02.2022	2	0	4	0	4	0	0	0

	340A		340K		340G		356T	
Week	Global	Switzerland	Global	Switzerland	Global	Switzerland	Global	Switzerland
31.01.2022	12	1	22	2	0	0	14	0
07.02.2022	11	1	33	3	0	0	21	1
14.02.2022	16	0	20	3	1	0	18	1
21.02.2022	22	2	37	5	1	0	21	0

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

As seen in table 4, known mutations enabling escape from Sotrovimab have been detected in Switzerland, but remain rare.

8. Wastewater surveillance program

Sequences are obtained from six wastewater treatment plants (WWTPs) that are tested on a daily basis. Signatures of the BA.1 (Omicron) variant were 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 in most of the surveyed locations by the end of the year, and in all surveyed locations by the beginning of January. Since the end of January, BA.2 has been steadily increasing in all wastewater treatment plants of the program. By the end of the month of February, the BA.2 variant was dominating in all surveyed areas.

Quantification of Omicron in sewage has exhibited some peculiar challenges (in Switzerland and in other countries): some data indicates that this variant is less shed in faeces compared to Delta. The differential shedding could lead to an underestimation of the prevalence of Omicron relative to Delta when using wastewater sequencing data. This bias is not expected at the moment to impact quantification of BA.2 relative to BA.1. Other challenges in the quantification of variants from wastewater sequencing data stem from shared mutations between lineages, which can under some conditions lead to spurious low frequency prevalence estimates of some variants, under noise levels.

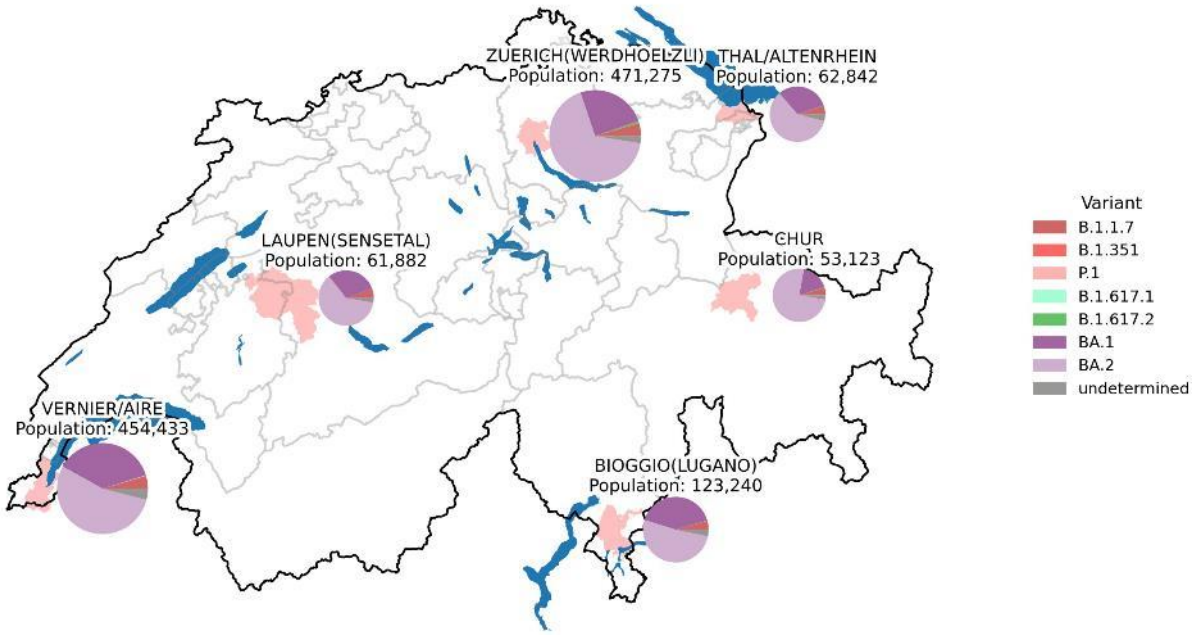


Figure 9:
Overview of the prevalence of variants of SARS-CoV-2 at the end of February 2022, estimated from wastewater samples collected daily during the month in WWTPs located in 6 different Swiss locations. Pie chart areas are proportional to population connected to the wastewater treatment plants. 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, BA.1 (Omicron) in dark purple, and BA.2 (Omicron) in light purple.

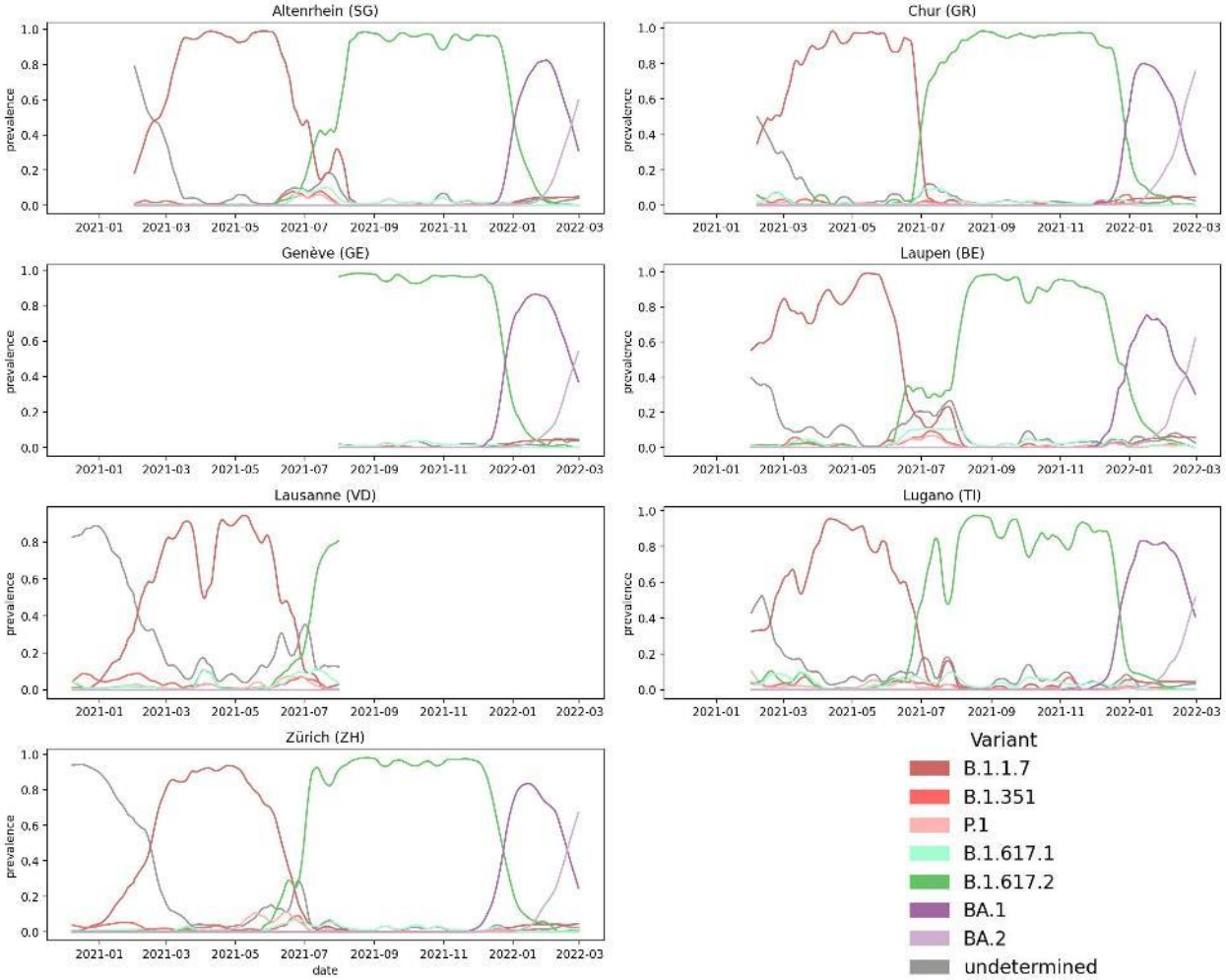


Figure 10: Prevalence of variants of SARS- CoV-2 estimated from wastewater samples collected daily until December 31 (except Lausanne: July 31) in WWTPs located in 7 different Swiss cantons. B.1.617.2 (Delta) is represented in dark green, B.1.617.1 (Kappa), in light green, B.1.617.3 in purple, B.1.1.7 (Alpha) in dark red, B.1.351 (Beta) in light red, P.1 (Gamma) in pink, BA.1 (Omicron) in orange, and BA.2 (Omicron) in light blue. An online dynamic navigation is available at https://bsse.ethz.ch/cbg/research/computational-virology/sarscov2-variants-wastewater-surveillance.html.

9. Immunological characterization of the variants

Assessment of neutralization by plasma from convalescent individuals infected with early-pandemic, Alpha, Beta, Gamma and Delta previously showed that the highest neutralization was obtained against homologous variants with infection by a non-Omicron variant providing only low protection against Omicron.

These results were confirmed here with a cell-free based assay where we measured levels of variant-specific neutralizing antibodies in the serum of a group of otherwise healthy adults infected only by Alpha (n=10) or Delta (n=12) viruses (Figure 11). Of note, all individuals have tested positive for total anti-RBD IgGs (Elecsys® Anti-SARS-CoV-2 S, Roche).

We also used here serum from 16 people recently infected with Omicron without prior exposure to or vaccination against SARS-CoV-2. Each serum was tested on many different Spike variants including the two found in the currently circulating Omicron lineages BA.1 and BA.2. The results show that Omicron infection, on its own, generally induces only low levels of neutralizing antibodies in immunocompetent individuals, and that these antibodies are largely inactive against other SARS-CoV-2 variants.

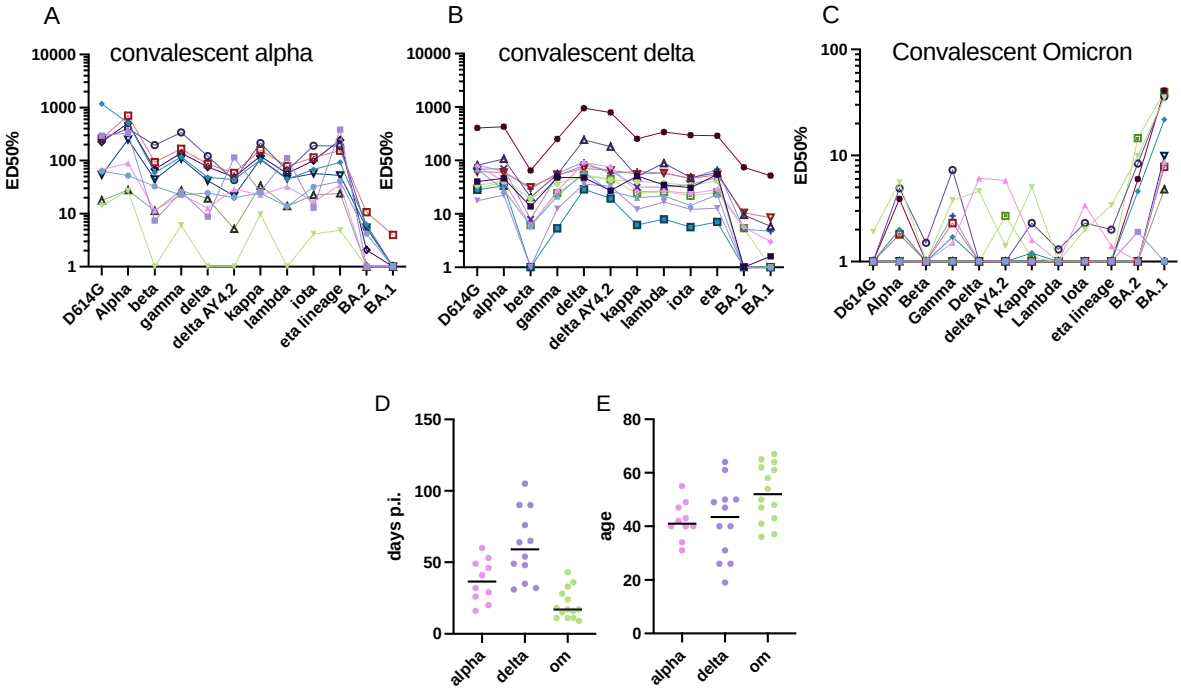


Figure 11. Neutralizing activities of sera from convalescent people infected either with alpha (A), delta (B) or omicron(C) variants were assessed for their ability to neutralize D614G-ancestral or indicated Spike variants in the multiplex S3-ACE2 assay. The mean serum dilution needed to achieve 50% neutralization inhibition (ED50%) is indicated for each variant. The time post infection (D) and age (E) distributions of the 3 different groups is indicated.

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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 31 January 2022 to 27 February 2022.

sup_table_overview_Feb.xlsx

Supplementary Table 1: Epidemiological data for Switzerland, its regions and cantons for January: 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
1	Jan 31 to Feb 6	141 894	74 407	2 306	52.44%	3.10%
2	Feb 7 to Feb 13	112 561	55 901	2 586	49.66%	4.63%
3	Feb 14 to Feb 20	88 543	42 598	2 499	48.11%	5.87%
4	Feb 21 to Feb 27	80 518	41 339	2 343	51.34%	5.67%
	Total	423 516	214 245	9 734	50.59%	4.54%

Supplementary Table 2: Total number of tests performed by the laboratories participating in the surveillance program from 31 January 2022 to 27 February 2022.

Week	Date	Basic Surveillance						Augmented Surveillance						Sentinella Laboratories		
		EOC	St-Gallen	Labor Team W	Risch	SRO	Synlab	USB	IFIK	Diana labs	CHUV	UZH	ICH-VS*	HUG	ETH/ Viollier	All
1	Jan 31 to Feb 6	96	96	0	204	86	ND	145	178	84	81	216	89	322	709	2306
2	Feb 7 to Feb 13	101	96	181	47	88	ND	211	181	82	95	218	90	309	887	2586
3	Feb 14 to Feb 20	95	95	181	59	88	ND	119	168	89	75	220	86	253	971	2499
4	Feb 21 to Feb 27	94	93	0	239	89	ND	212	136	86	73	253	82	268	718	2343
	Total	386	380	362	549	351	ND	687	663	341	324	907	347	1152	3285	9734

*Supplementary Table 3: number of sequences submitted to GISAID by each laboratory during the surveilled period (31 January 2022 to 27 February 2022). *including sequencing sent to high-throughput platforms. ND = No data*

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