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

1. Introduction: description of the Swiss national SARS-CoV-2 genomic and variants surveillance program.

Geneva Centre for
Emerging Viral Diseases

Division of Infectious
Diseases

Department of Medicine

Laboratory of virology

Division of Laboratory
Medicine

Diagnostic Department

Currently, 8 diagnostic laboratories have joined the program, including university hospital centres in Switzerland (Geneva, Lausanne, Bern, Basel, Zurich, St-Gall, Ticino), in addition to private laboratories (Viollier, Dianalabs Genève), cantonal-based laboratories (Hôpitaux du Valais) 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). Because of the decrease in the number of cases, additional laboratories have been requested to join the program.

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 was also planned, initially 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 Marc Friedli, Pauline Vetter, Samuel Cordey, Erik Boehm, Richard Neher, Christian Althaus, Martina Reichmuth, Cornelius Römer, Niko Beerenwinkel, Chaoran Chen, Tanja Stadler, 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 May 3 to May 30 (weeks 18, 19, 20, 21).

All data presented in this report are based on the sampling date.

2. Variants of concern, variant of interest and other surveilled variants: brief summary and special focus

Currently, 4 variants are considered variant of concerns (VOCs) by the WHO, B.1.1.7 (first identified in the UK – VOC Alpha, currently dominant in Switzerland), B.1.351 (first identified in South Africa – VOC Beta), P.1 (first identified in Brazil – VOC Gamma), and most recently B.1.617.2 (first identified in India, Delta – with its sublineage AY.1 corresponding to Delta + 417N). Alpha in particular was by far the most dominant strain in Europe and much of the world dominant, but now seems to be being displaced by Delta, calculated to be up to 60% more transmissible than Alpha (<https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---29-june-2021>). The full set of mutations responsible for its particularly increased transmissibility are currently unclear.

Two doses of the mRNA vaccines available in Switzerland have shown to keep a good effectiveness in real life observational studies against both symptomatic and severe disease due to the B.1.1.7 (Alpha) and B.1.617.2 (Delta) variants. One dose already seems to confer a good protection against severe disease, but has only minimal effect in protecting against symptomatic disease. A minimal decrease in protecting against infection has been showed against the B.1.351 (Beta) and B.1.617.2 (Delta) variants. Of note, no data is available regarding protection against the AY.1 variant (Delta + 417N). (<https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---29-june-2021>).

Greater transmissibility and/or immune escape potential may lead to a renewed surge in infections despite the vaccination campaign. While we have identified some mutations that lead to greater transmissibility or reduced vaccine efficacy in vitro, there are many more such mutations or combinations of mutations which have not been identified. Therefore any variants displaying mutations known to be linked with either increased transmissibility and/or immune escape potential should be closely monitored, lest they acquire further enhancing mutations and develop into an even worse variant.

Therefore variants presented below will be particularly surveilled:

- variants classified as VOCs by the WHO

- P.1
- B.1.351
- B.1.617.2 (and its sublineage AY.1)
- B.1.1.7

- new variants (until sufficient monitoring suggests they do not have a replicative advantage) that include E484K + N501Y: higher transmissibility, immune escape risk, resistance to mAbs, such as:

- B.1.621 (N501Y + E484K)
- B.1.1.7 + E484K in particular
- B.1.315

- variants that include E484K but not N501Y: immune escape risk, resistance to mAbs, such as:

- B.1.1.318
- B.1.525 (eta)
- B.1.526: part of the lineage carries E484K, the other S477N (iota)
- B.1.620
- B.1.621
- P.3 (theta)

- variants that include L452R: slightly more transmissible relative to N501, resistance to mAbs, such as:

- C.36
- B.1.427/429 (epsilon)

-variants that include L452R + N501Y, such as A.27 and/or B.1.1.7 + L452R

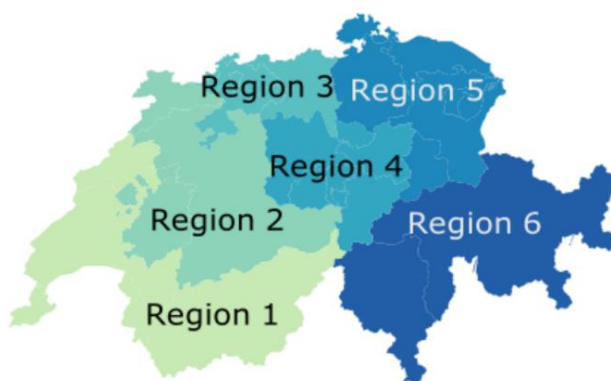
3. Epidemiology in Switzerland and number and origin of sequences produced through the program during the surveilled period

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. We aim to have a “harmonized” data set in the future with publicly available FOPH data and sequence data from SPSP. The overall goal of the program is to provide epidemiological trends and to highlight meaningful observations. In the current situation of decreasing number of cases detected in the country, the active investigation of specific clusters in some cantons can impact the precision of our observations.

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 Nidwalden), 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 the period covered by the present report, the FOPH reported a total of 33 417 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.

The laboratories participating in this program reported 8435 positive tests during the surveilled program, which represents 25% 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. Of note, antigen-based tests are by definition excluded of the surveillance, which applies only to PCR tests (although in some instance antigen positive cases may be asked to be re-tested by RT-PCR when part of VOC's clusters).

Number of SARS-CoV-2 sequences produced through the surveillance program

A total number of 5'288 SARS-CoV-2 sequences have been submitted to GISAID during this period. This represents 62.7% of the total number of the positive cases processed by the laboratories participating in the surveillance program (see Supplementary Table 2 in Appendix for details).

Table 1 shows the number of sequences successfully submitted to GISAID through the surveillance program during the surveilled period by calendar week.

Week	Date	Number of sequences successfully submitted to GISAID
18	May 3 to 9	1643
19	May 10 to 16	1442
20	May 17 to 23	1326
21	May 24 to 30	877
	Total	5'288

Table 1: number of sequences submitted to GISAID through the surveillance program

The total number of SARS-CoV-2 sequences submitted to GISAID by each laboratory during the month of May 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 progressively decreased during the month of May (reflecting the decrease in cases within Switzerland). The vast majority of the sequences available in GISAID (green curve) and those on which the surveillance is conducted, come from the national surveillance program. Around 16 % of the total number of cases each week are sequenced and submitted to GISAID (blue curve).

Figure 2 displays the fraction of SARS-CoV-2 cases sequenced for each Swiss region. The fraction of sequenced cases is reaching or above 15% for all Swiss regions, except region 4, for which the total number of sequences is also the lower among Switzerland. Despite a sharp decrease in the absolute number of sequences retrieved in regions 1, 3 and 5, the proportion of cases that have been sequenced remains high and above the aim of the program, indicating that this decrease reflects the decrease in incidence in those regions. Similarly, during the month of May, the proportion of sequences produced by regions 2 and 6 sharply increased, whereas the absolute number of available sequences for those regions remained stable.

Figure 3 shows the covering of sequencing among the different Swiss cantons over the last 3 months, presented by fraction of cases sequenced among the total number of reported cases in the canton. It reveals a large disparity of sequencing coverage within the cantons, and will help identify the cantons in which the surveillance is less effective.

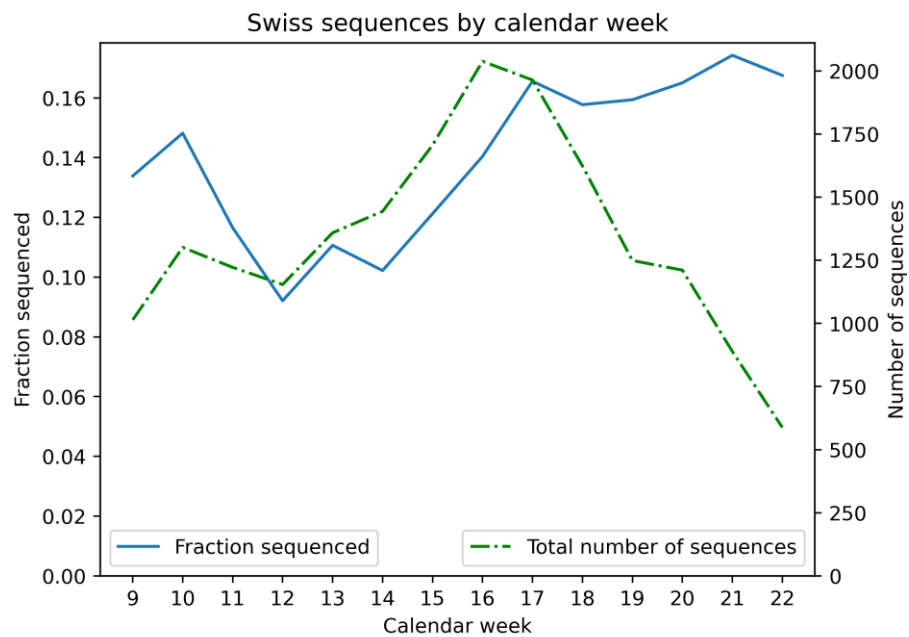


Figure 1: Number of SARS-CoV-2 sequences available for Switzerland (total available Swiss sequences in GISAID in green) and fraction of the total number of positive cases declared to the FOPH that have been sequenced (blue curve).

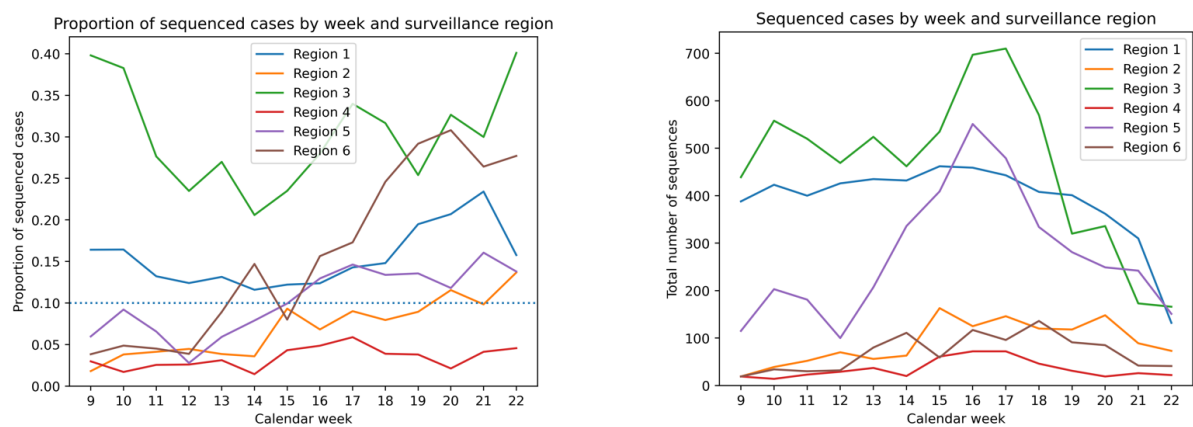


Figure 2: Covering of sequencing among the different Swiss regions per week, presented by fraction of cases sequenced (A) and by number of sequences (B)

Sequencing Intensity by Attribute

Select up to two attributes:

- ☒ Division
- ☐ Age group
- ☐ Sex
- ☐ Hospitalization status
- ☐ Death status

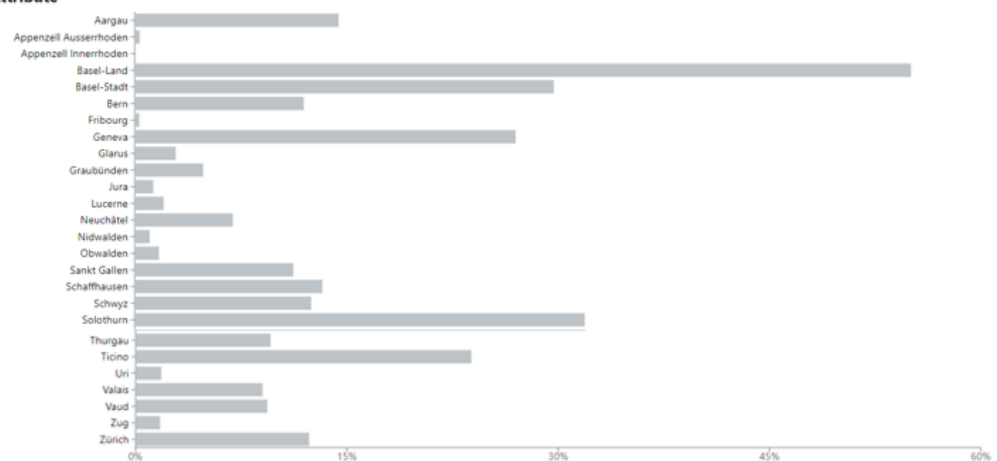


Figure 3: Covering of sequencing among the different Swiss cantons over the last 3 months, presented by fraction of cases sequenced. Screenshot from CoVspectrum website. Online dynamic navigation is available at <https://cov-spectrum.ethz.ch/explore/Switzerland/AllSamples/Past3M/sequencing-coverage>

4. 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).

While B.1.1.7 was still generating most of the new cases in Switzerland during the surveilled period, the proportion of the Delta variant (here shown in green) is progressively increasing during the month of May all over Switzerland. An increase in the number of the Gamma P.1 (light pink) sequences has also been noted, mainly coming from region 5 (see Table 2 below representing the number of the main VOCs/VOIs by region).

An estimate of the total number of VOCs circulating in Switzerland, corrected by taking in account the 12.5 % fraction of sequencing in Switzerland is available through the covSPECTRUM program developed at ETHZ at <https://cov-spectrum.ethz.ch/explore/Switzerland>.

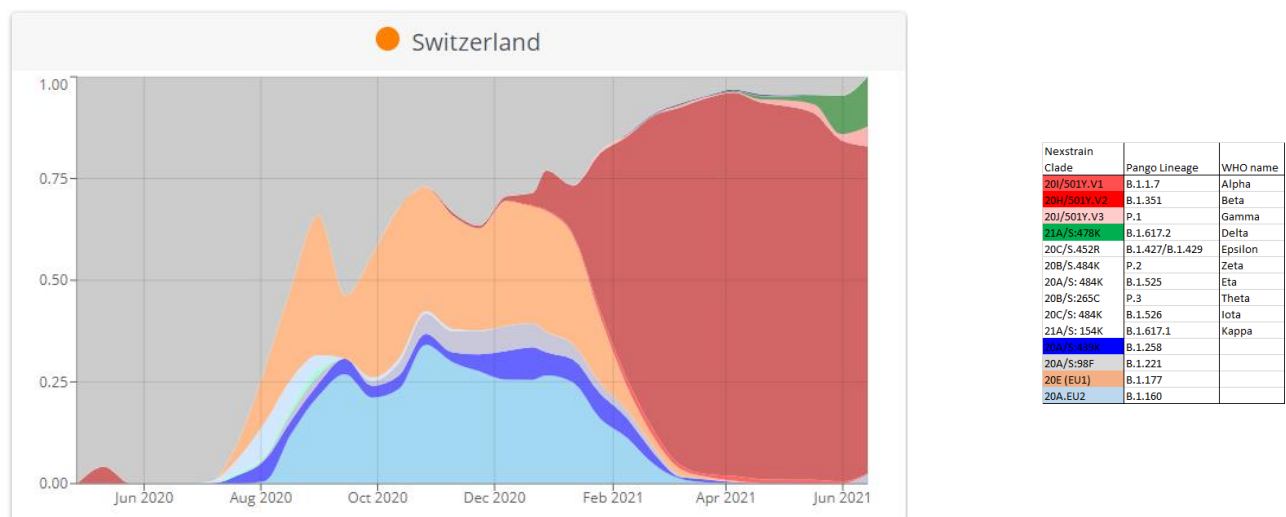


Figure 3: proportion of total number of sequences (not cases), over time, that fall into defined variant groups, for Switzerland. Screenshot from CoVariant website. Dynamic navigation is available at <https://covariants.org/per-country>. Dark red indicates lineage B.1.1.7 (Alpha). Note the rapid increase in prevalence and rise to dominance. Light red indicates B.1.351 (Beta). Green indicates lineage B.1.617.2 (Delta), detected since mid-April in Switzerland.

Because of an issue during sequence attribution in one sequencing center during the month of May, data can't be presented by region this month. The problem has been quickly identified, and all necessary measures taken in order to correct the accuracy of the data. The GISAID platform is currently working on updating corrected data. The proportion of total number of sequences over by variant groups and by region will be available online at <https://covariants.org/per-country>.

Over the month of May, VOCs Beta, Gamma and Delta and the VOI C.36 represented 5.5% of the sequences retrieved in Switzerland. This proportion progressively increased during the month, mainly because of the increase of Delta (see Figure 4 and 5 and Table 2). B.1.351 (Beta) is circulating at a very low level. A sharp increase both in the proportion and the absolute of the P.1 (Gamma) variant has been noted over 2 consecutive weeks before returning to low level detection. We can't exclude that this effect is due to a sequencing bias of a large geographic cluster.

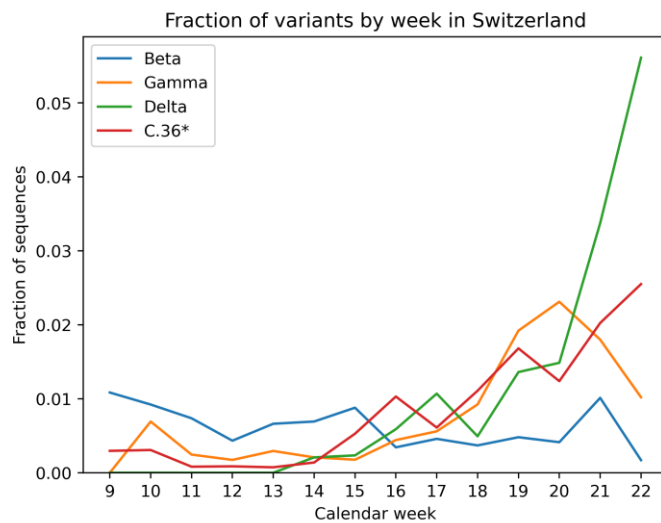


Figure 4: Percentage of circulating VOCs and VOIs in Switzerland by week, excluding B.1.1.7, over the 22 first weeks of 2021 (total number of B.1.351 (Beta), P.1 (Gamma), B.1.617.2 (Delta) and C.36 sequences from Switzerland and successfully submitted to GISAID are counted here).

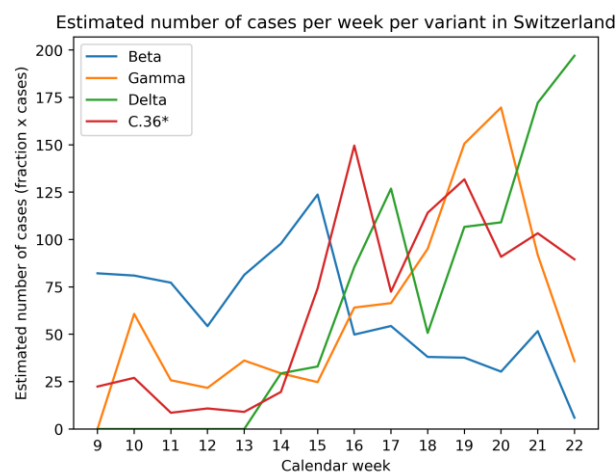


Figure 5: Estimated number of sequences of the main VOCs/VOIs (excluding B.1.1.7) and variants under monitoring retrieved during the surveilled period.

Region	C.36*	beta	delta	gamma	others	sequences	cases	Proportion sequenced
Total	87	27	104	89	5233	5540	34082	0.163
1	37	5	49	5	1500	1596	8724	0.183
2	3	3	8	5	529	548	5549	0.099
3	7	8	30	17	1499	1561	5081	0.307
4	0	1	2	3	138	144	4002	0.036
5	14	8	12	51	1173	1258	9278	0.136
6	24	2	2	8	359	395	1448	0.273

Table 2: Number of variants of concerns (except B.1.1.7) and variant of interest C.36 by region, among the positive cases that have been successfully sequenced and analyzed by CoVspectrum.

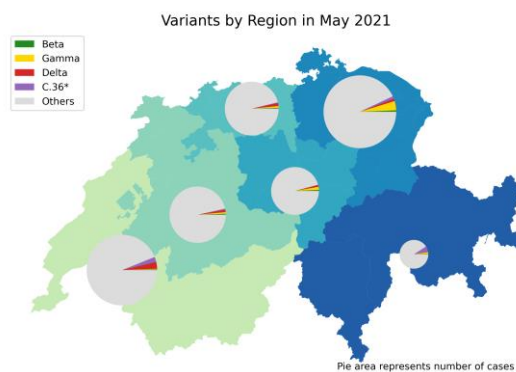


Figure 6: Distribution of variants per region, for May, shown on a map. The total number of sequences in that month, in the region, is shown in parentheses next to each region name. The size of the pie chart corresponds to the total number of sequences. B.1.1.7 (Alpha) represent the large majority of the variants classified in the “others” category, as shown in Figure 3.

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

Those data have been produced using multinomial logistic regression on all GISAID available data by Christian Althaus' group. This analysis suggest that the frequency of Delta is around 30% in Switzerland in mid-June 2021.

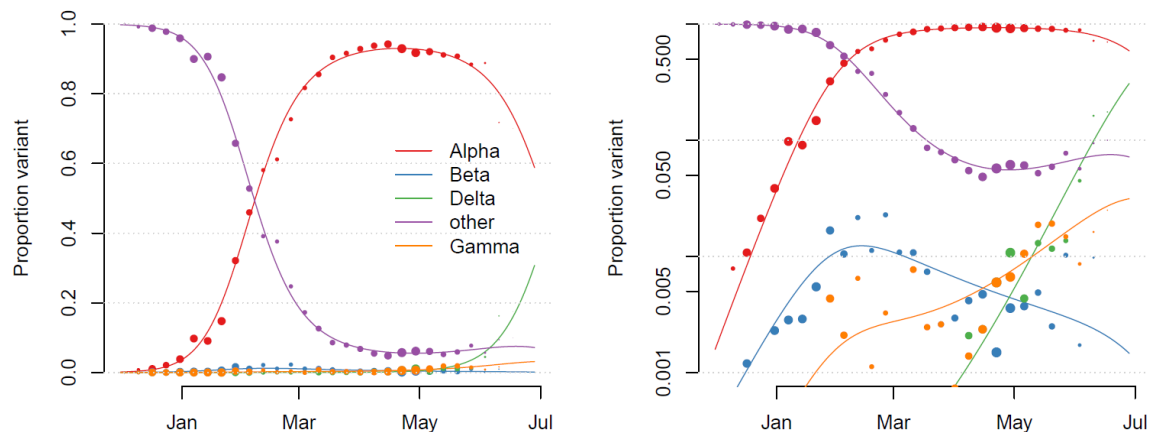


Figure 8: Observed and modeled proportion of SARS-CoV-2 variants over time in Switzerland. The proportion of Alpha and Beta started to grow in Switzerland in December 2020 and January 2021. Beta was subsequently outcompeted by Alpha in February and March 2021. In April and May 2021, Gamma and Delta started to replace Alpha with Delta currently having the highest growth rate. Model fits are based on a multinomial logistic regression with splines. The size of dots corresponds to the weekly sample size.

The estimated proportion of the Delta variant through time calculated based on its estimated transmission advantage is available on CoVspectrum.

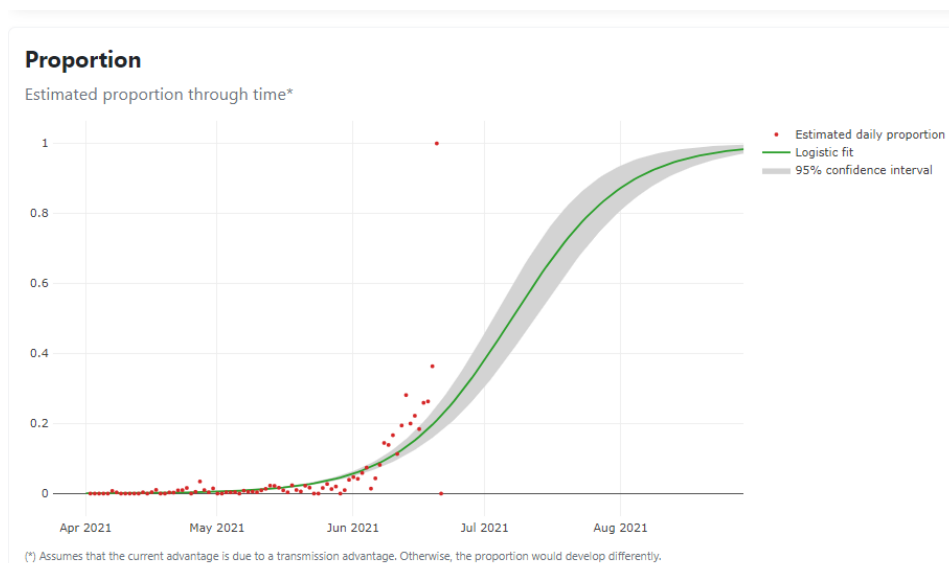


Figure 9: Estimated proportion of the Delta variant through time. The model assumes that the increase or decrease of the proportion of a variant follows a logistic function. It fits a logistic model to the data by optimizing the maximum likelihood to obtain the logistic growth rate a . From that, an estimate of the transmission advantage under a continuous (f_c) and discrete (f_d) model is derived. Dynamic navigation available at <https://cov-spectrum.ethz.ch/>

6. Wastewater surveillance program

Since February, an increased prevalence of the B.1.1.7 (Alpha) variant has been observed over time in all WWTPs tested. The B.1.617.2 (Delta) variant started to appear in wastewater samples around the beginning of June in all WWTPs. By mid-June it had reached the highest levels in Zurich (34%) and Laupen/Berne (47%).

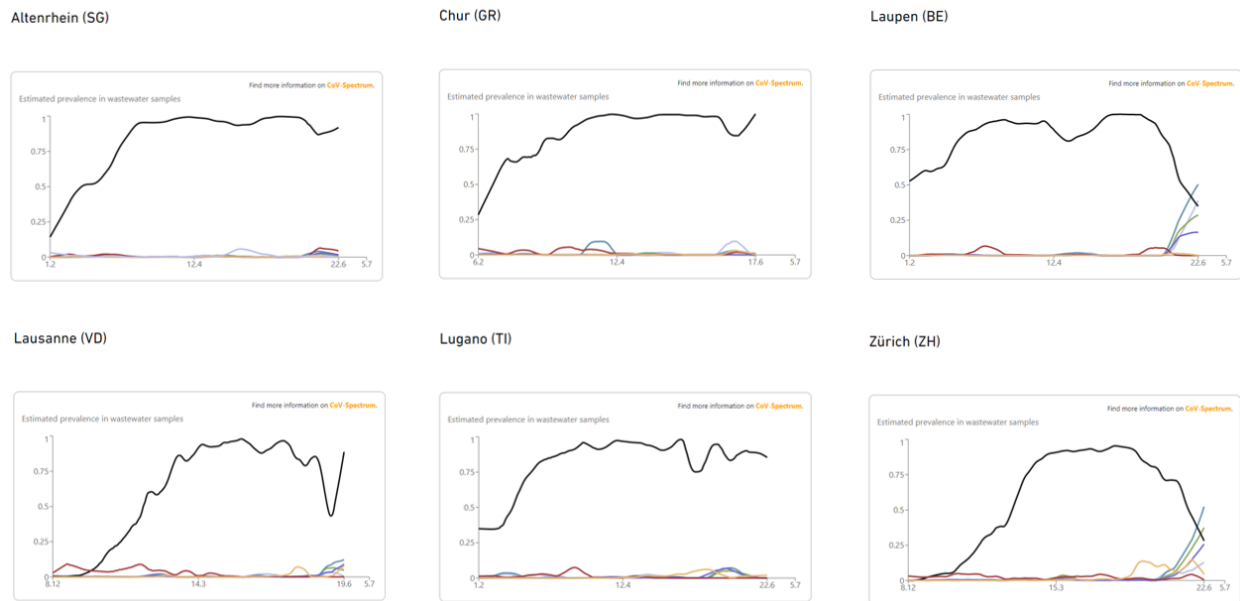


Figure 10 : Prevalence of different genomic variants of SARS-CoV-2 obtained from wastewater samples in different Swiss cantons. Samples are collected daily at six Swiss wastewater treatment plants. C.36.3 is represented in light blue, B.1.617.1 in green, B.1.617.2 (Delta) in dark blue, B.1.617.3 in purple, B.1.1.7 (Alpha) in black, B.1.351 (Beta) in red, P.1 (Gamma) in orange. Screenshot from the website of ETH Zürich. Online dynamic navigation available at <https://bsse.ethz.ch/cbg/research/computational-virology/sarscov2-variants-wastewater-surveillance.html>.

Conclusion

In May, over 5000 sequences have been obtained through this surveillance program. Each week since this surveillance program started, it has contributed 80 % or more of the Swiss SARS-CoV-2 sequences available on GISAID. In May, over 15% of the cases reported in Switzerland were sequenced each week. Region 4 is the least represented geographical area. Additional laboratories have been asked to join the program to ensure a substantial coverage, especially while the total number of new cases are declining, to achieve representative sequencing across the country. The FOPH may have to require participation of additional hospital-based and/or private laboratories in order to reach at least a 10% of sequence coverage in every region of Switzerland.

The B.1.1.7 (Alpha) variant was still the causing more than 90% of the cases in Switzerland during the month of May, with a homogenous representation over the different Swiss regions.

An increase of the P.1 (Gamma) variant has been observed during the month of May, with most cases originating from region 5. Its proportion among the sequenced cases was however still low (between 1 to 2%), and the absolute number of sequences remains also low (<100 over the month for the whole week).

B.1.351 (Beta) continues to circulate at low levels throughout the whole surveilled period, without increasing trends.

B.1.617.2 (Delta) has been detected at a very low level in almost all regions, and is progressively increasing in proportion since its first detection in April, with a sharp and progressive increase at the end of May, when it represented around 3% of the sequences, and similarly in wastewater samples. Both B.1.617.2 (Delta) and its relative sub-lineage AY.1 (Delta + 417N) have been detected and are circulating in Switzerland. Delta is currently the variant having the highest growth rate in Switzerland as of mid-June, 2021.

C.36 was mainly observed in Region 1, and slightly increasing trend in proportion over time. This variant however was still circulating at a very low level at the end of May.

No important geographical breakdown of a particular variant has been noticed.

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>.

As the number of cases of SARS-CoV-2 decline, an effort will be made to add more laboratories to the program in order to keep a representative sequencing over the country.

Acknowledgements:

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

Marc Friedli, Pauline Vetter, Samuel Cordey, Erik Boehm, Richard Neher, Christian Althaus, Emma Hodcroft, Tanja Stadler, Philippe Lemercier, Ioannis Xenarios, Lorenzo Cerutti, Nadja Wipf, Damir Perisa, Laurent Kaiser, for the Swiss national SARS-CoV-2 genomic and variants surveillance program.

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.



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report_May.xlsx

***Supplementary Table 1:** Epidemiological data for Switzerland, its regions and cantons in May 2021: 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
18	May 3 to 9	30 248	2569	1643	8.49%	63.95%
19	May 10 to 16	33 105	2394	1442	7.23%	60.23%
20	May 17 to 23	32 398	2056	1326	6.35%	64.49%
21	May 24 to 30	26 638	1416	877	5.32%	61.94%
	Total	122 389	8435	5'288	6.89%	62.69%

***Supplementary Table 2:** Total number of tests performed by the laboratories participating in the surveillance program from May 3 to May 30, 2021.*

Week	Date	Basic Surveillance		Augmented Surveillance						Sentinella Laboratories		All
		EOC	St-Gallen	UBS	IFIK	Dianalabs Genève	CHUV*	UZH*	ICH-VS	HUG	ETH/Viollier	
18	May 3 to 9	93	46	98	56	0	103	204	0	262	781	1643
19	May 10 to 16	70	46	65	68	94	58	195	93	255	498	1442
20	May 17 to 23	78	47	75	65	78	73	110	94	179	527	1326
21	May 24 to 30	27	0	54	67	54	63	89	94	106	323	877
	Total	268	139	292	256	226	297	598	281	802	2129	5'288

***Supplementary Table 3:** number of sequences submitted to GISAID by each laboratory during the surveilled period (May 3-30, 2021). These sequences are expected to appear later on GISAID, *including sequencing sent to high-throughput platforms*

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