Scientific Advisory Panel
COVID-19

# *Scientific Advisory Panel COVID-19 (SciAP)*

*On how to handle COVID-19 and other respiratory viruses in the future* — *23 January 2023*

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# *On how to handle COVID-19 and other respiratory viruses in the future*

## 1 Initial situation

### 1.1 General information on the work of the Scientific Advisory Panel

The Scientific Advisory Panel COVID-19 (SciAP) started its work on 1 November 2022. All 14 members meet weekly for internal consultations on the current state of scientific knowledge and its possible implications for both policy and society. Every second week, an exchange takes place between the institutions providing the mandate (FOPH, GS-FDHA, Conference of Cantonal Health Directors), representatives of the cantonal physicians and the management of the Scientific Advisory Panel. During the exchange, the SciAP proactively contributes scientific information on COVID-19 and answers these institutions' questions from a scientific point of view.

The Scientific Advisory Panel acts as an "honest broker" vis-à-vis policymakers and the public. In other words, it explains the scientific evidence with all its existing uncertainties and presents a

number of options for action on current decision-making issues with their respective opportunities and risks. The political goals of the institutions providing the mandate in dealing with COVID-19 are "to protect the health of the population in Switzerland as far as possible" (see Confederation Link) and "to stop the healthcare system from being overloaded" (see Cantons Link). The SciAP takes an integrative view of COVID-19. In other words, it takes into account other diseases and strains on society that are related to the pandemic and the measures to contain it. In so doing, it directly incorporates the goals of the institutions providing the mandate into its work.

## 1.2 Specific to this document

With the gradual transition to the post-acute phase of the pandemic, a new situation is arising. Society's way of handling COVID-19 is becoming similar to the approach to other respiratory pathogens. In epidemiological terms, the Omicron waves are becoming less intense, while other respiratory pathogens (especially RSV, influenza, *Streptococcus pneumoniae*, *H. influenzae* and Group A streptococcal infections) are once again infecting more people after their circulation had been inhibited by the general containment measures and behavioural adjustments as part of the COVID-19 pandemic in 2020 and 2021. As a result, the healthcare system continues to contend with a heavy burden, although the bottlenecks have shifted and are now more likely to occur in emergency and general wards, as well as in paediatric clinics. During the acute phase of the pandemic, it mainly affected intensive care. In addition, persistent excess deaths, long COVID and the fact that adolescents are increasingly receiving treatment for mental health problems illustrate just how different the current situation is from the (pre-)pandemic situation.

With effect from 1 January 2023, the Swiss Federal Government will no longer cover the costs of COVID-19 testing.[1] As test numbers have plummeted, these tests' function as a health monitoring tool has largely ceased to exist. Consequently, at the monitoring level too, how SARS-CoV-2 is being handled is also becoming aligned with the approach taken towards other infectious diseases. Due to the fact that the healthcare system remains severely strained and there is ongoing uncertainty with regard to the spread of infection, now is the right time to review which methods and tools Switzerland should use to monitor infectious diseases in the future.

[1] People can use inexpensive self-tests to learn if they have COVID-19. If a patient needs to present a positive COVID test for treatment, the costs will continue to be covered (see link); testing in the early stage of infection is important for treatment.

Below, we have outlined the current state of knowledge on the epidemiological situation of SARS-CoV-2 and other respiratory diseases. Building on this, we will discuss a topic that is central to an integrative public health perspective on infectious diseases: evidence-based pathogen surveillance. We then go on to develop different, combinable courses of action for Switzerland to monitor the circulation of both SARS-CoV-2 and other viruses, and briefly explain their respective advantages and disadvantages.

# 2 Current state of scientific knowledge

## 2.1 Epidemiological situation of SARS-CoV-2

### 2.1.1 Acute disease burden

The situation in hospitals is currently far removed from what it was during the acute phase of the pandemic. The number of new COVID-19 hospitalisations has been decreasing since the beginning of December 2022 (see Link). Intensive care units are not experiencing an extraordinary burden of patients with COVID-19-related pneumonia. Less than 5% of available ICU beds are currently occupied by patients infected with SARS-CoV-2 (see Link). However, hospitals are reporting heavy burdens on emergency departments, general wards and paediatric clinics due to high circulation of various respiratory pathogens (SARS-CoV-2, RSV, influenza, *Streptococcus pneumoniae*, *Haemophilus influenzae* and Group A streptococcal infections) and ongoing staff shortages.

### 2.1.2 Immunity

As early as July 2021, over 90% of the population aged 65 and older and about 75% of the population aged between 20 and 65 had antibodies. At that time, however, antibody levels varied widely, ranging from positive but low levels (as a result of mild infection) to medium-to-high levels (after moderate infections) and high levels (after vaccination and/or severe infections). Since the beginning of 2022, more than three million infections have been confirmed (mostly Omicron) (see Link), although the estimated number of unreported cases is likely to be high (see Link). So very many vaccinated and recovered individuals went through at least one infection (again) in 2022. As a result, 98% of the Swiss population currently have antibodies against SARS-CoV-2 (see Link).

Since mid-2022, antibody levels have been high to very high in the majority of the population as a result of vaccination or vaccination plus infection (referred to as "hybrid immunity"). Consequently, protection against severe illness with COVID-19 is likely to have increased significantly once again compared to 2021 – despite the circulation of variants with increasing immune escape. As long as SARS-CoV-2 continues to circulate in the population (which will increase the incidence of long COVID) and no variants fundamentally undermine the existing protection against severe infection, immunity in the population should remain high, so most people will be protected from severe symptoms. Vulnerable individuals will, according to current knowledge, need periodic booster vaccinations to maintain a high level of protection.

### 2.1.3 Variants

Subvariants of BA.2 and BA.5 are currently circulating. Although the virus still appears to be rapidly changing and evading existing immunity in populations that have had complex immunity since early 2022, we have not seen a sudden emergence of highly modified variants with distinctly different transmission and disease patterns (such as Alpha and Delta) since then. The immune escape of the currently circulating variants is leading to increased reinfections and vaccine breakthroughs, yet protection against severe infections remains robust. The oral medication nirmatrelvir/ritonavir (Paxlovid®), which is used in patients at increased risk of a severe COVID-19 infection, is still effective on all known variants provided that it is used early (usually within five days of the onset of symptoms). Patients with severe immunosuppression may develop a prolonged or persistent infection despite treatment with Paxlovid® (see Link). One key treatment option for immunosuppressed individuals is monoclonal antibody therapies. However, virtually all of them have been ineffective against BQ.1.1, which is currently dominant in Switzerland.

In China, there are currently variants spreading that are also appearing throughout the rest of the world (see Link, Link). Thus, according to current knowledge, people entering Switzerland from China are not introducing any viruses into the country that would have a lasting impact on the epidemic here. Although a large number of people entering the country from China may be infected, the continuing high level of virus circulation in Switzerland means that entry restrictions or testing on entry would not have a significant impact on the number of infections in the country. In Switzerland, based on this epidemiological analysis of the situation, travellers entering the country are not required to take tests (see Link). There is a possibility of a variant that proves problematic for Switzerland emerging in China. However, the risk is moderate: the virus in China is circulating in a population with low immunity. So, in China, it does not gain any

advantage if it mutates in such a way that it would escape the defences built up in a society with high immunity, such as Switzerland.

In the United States, where immunity is already high, XBB.1.5 is currently spreading and displacing other Omicron variants (see Link, Link). There is currently no data indicating more severe symptoms for those infected with XXB.1.5 compared to other Omicron variants (see Link, Link).

Overall, there is currently no known variant that would have a lasting impact on the pandemic.

## 2.2 Strong circulation of various respiratory pathogens

Influenza and RSV have been in strong circulation between October 2022 and January 2023. This increased circulation is real and cannot only be attributed to a change in testing behaviour compared to before the pandemic. This conclusion can be drawn using data from Sentinella: there was no influenza wave and little RSV circulation in Switzerland until the COVID-19-related containment measures were lifted (see Link). In November 2022, an exceptionally high increase in RSV circulation was recorded, placing a heavy burden on Swiss children's hospitals (see Link). In December 2022, RSV circulation was already declining, while there was a striking wave of influenza A infections with an increase observed about one month earlier than in the years preceding the COVID-19 pandemic (see Link). Positivity (see Link, Link) and virus traces detected in wastewater (see Link) confirm this observation. Quantification of the virus in wastewater and the epidemiological curves of individuals testing positive indicate that the peak of the influenza A wave has been passed as well (see Link).

Following a high level of influenza activity, December 2022 and January 2023 showed a sharp increase in invasive pneumococcal infections (reportable) in Switzerland and likely other bacterial infections of the respiratory tract such as *Haemophilus influenzae* (reportable if invasive) and Group A streptococcal infections (not reportable) (see Link, Link and Link). An epidemiological and pathogenetic association between pneumococcal infections and preceding influenza activity is known and has been observed in Switzerland for years (see Link, Link and Link).

RSV is also a viral precursor for bacterial pathogens of respiratory infections (see Link); this has not yet been clearly demonstrated for SARS-CoV-2. The epidemiological data from winter 2021/2022 rather argues against SARS-CoV-2 being a contributing factor for

pneumococcal disease, as no corresponding accumulation of invasive pneumococcal infections was observed despite the extremely high circulation of Omicron (see Link).
In the coming weeks, the epidemiology of bacterial respiratory pathogens is expected to follow the epidemiological curves of respiratory viruses, and influenza in particular, with a certain delay.

Measures to contain COVID-19 greatly slowed the circulation of respiratory pathogens in 2020 and 2021, resulting in a cohort of young children with reduced or a complete lack of immunity to certain pathogens (documented for RSV; see Link). Due to decreases in immunological memory against respiratory pathogens, there is a slightly increased susceptibility to these pathogens in the population. Increased susceptibility means larger and earlier waves when the corresponding pathogen recirculates after a longer period of time. This is particularly pronounced when transmission is strong in highly susceptible sectors of the population (e.g. RSV in young children).

From the perspective of individuals, with a few exceptions (e.g. Epstein-Barr virus; see Link), there is no advantage to early infection. Preventing infection in very young children is advantageous in the case of many pathogens, which is why childhood vaccinations against various pathogens are given during the first year of life, as soon as maternal passive immunity decreases. In the case of RSV, which there is no vaccine for yet, it has been demonstrated that the risks of severe acute and chronic disease such as asthma are higher the younger a child is when they are infected for the first time (see Link).

## 2.3 Summary

With increased immunity in the population, the public health burden of SARS-CoV-2 has decreased significantly. However, other respiratory pathogens are circulating with greater intensity following on from the contact restrictions phase. Since the various respiratory pathogens SARS-CoV-2, influenza and RSV, followed by *Streptococcus pneumoniae*, *H. influenzae* and Group A streptococcal infections, are circulating, both hospitals and GP and paediatric practices are still struggling with a heavy burden. In view of this situation, we must ask ourselves how the future surveillance of respiratory viruses and other pathogens should be structured. Depending on how this question is answered, the social, medical and political approach to these pathogens may also change accordingly.

## 3 Possible courses of action

During the acute phase of the pandemic, surveillance of viral pathogens was strongly focused on SARS-CoV-2 for obvious reasons. So the data on COVID-19 was much more comprehensive than the data on other viruses. This made it easier for policymakers and the medical community to implement evidence-based measures to manage the pandemic. The cases of monkeypox and hepatitis in 2022 have shown that having an ongoing overview of circulating pathogens is valuable. It is important to find out in a timely manner whether new infections and disease patterns are originating from new characteristics of the virus or from changes in immune defences, the environment or social behaviour. These insights enable prompt, evidence-based responses.

The question now is how to monitor both SARS-CoV-2 and other pathogens in the future so that evidence-based pathogen management is possible. Here, we will take a look at SARS-CoV-2 surveillance and how it can be expanded to other viruses. Bacteria, of course, also require surveillance. The type of surveillance differs, however, due to the different characteristics of viruses and bacteria, and it will not be discussed in detail below.

**Currently, the following surveillance tools are used for respiratory viruses:**

**Determining the circulation of respiratory viruses**

This allows trends in the pattern of infections to be estimated (increase/decrease in infections):

- **Sentinella** surveillance of respiratory viruses. In other words, symptomatic patients in defined GP practices are tested for respiratory viruses (see Link); within the hospital sentinel surveillance system (CH-SUR), some of hospitalised patients are tested (see Link).
- The measurement of SARS-CoV-2 virus levels in **wastewater** at around 50 sites (see Link); RSV and influenza are also measured at six sites (measurements by quantitative or digital PCR).
- For notifiable infectious diseases, the mandatory reporting system also provides information (see link).

**Determining SARS-CoV-2 variants**

This allows us to assess whether emerging mutations and variants could alter the pattern of infection and the burden of the disease in the future (variants of concern):

- **Genome sequencing** of SARS-CoV-2 in wastewater at seven sites and in samples from about 200 hospitalised patients per week, plus some Sentinella patients. The data is presented in Link, Link and Link.

Several courses of action are available for surveillance of viral pathogens in the future. They are not mutually exclusive; rather, they can be combined. These different options are listed below along with their respective advantages and disadvantages:

Option 1: **"Business as usual"**

+ Established system
+ The dynamics of virus circulation can be estimated (increase/decrease) by determining the amount of virus in wastewater and testing patients in the Sentinella system.
+ SARS-CoV-2 sequencing can be used to observe variants and quantify their spread.
+ Clinical samples of SARS-CoV-2 that are sequenced and demonstrate conspicuous mutations can be phenotypically characterised.
- The samples collected are not comprehensively analysed (see option 2 for further possible analyses).

Option 2: **Option 1, plus detailed analysis of the samples currently collected**

Option 2.1: Expansion of **wastewater monitoring** so that **virus levels of other major pathogens** are determined in all samples collected (option 1) (instead of focusing on SARS-CoV-2 as before).

+ The circulation of various viruses can be determined independently of the population's testing behaviour.
+ This can be implemented directly with the PCR multiplexing method.
+ It makes use of the synergies of existing wastewater monitoring (samples are being collected and prepared for SARS-CoV-2 anyway).
- Multiplexing is slightly more costly than testing for SARS-CoV-2 alone.

Option 2.2: Expansion of **sequencing to include other major viral pathogens** (instead of SARS-CoV-2 only as before). Sequencing is carried out for **all clinical samples and for all wastewater samples** (instead of, as before, merely a portion of the samples).

+ This surveillance provides timely information on whether conspicuous mutations and variants of the various viruses under investigation are circulating.

+ There are commercial products that make such sequencing directly feasible for clinical samples; for wastewater, the development of primers for sequencing should be feasible without any major technical hurdles.
- Costs increase when a panel of viruses is sequenced instead of just SARS-CoV-2. However, for clinical samples, the step of testing for viruses (option 1) could be omitted, as sequencing directly indicates whether a virus is present.

Option 3: When a virus variant that needs to be monitored in detail due to its characteristics emerges (such as a SARS-CoV-2 variant of concern): performance of **variant-specific PCR testing and sequencing of a single gene** (e.g. sequencing of the S gene if the virus under surveillance is SARS-CoV-2).

+ This allows the variant to be tracked in a timely manner (compared to whole-genome sequencing, which takes about two weeks to collect samples with current logistics) (see Link).
+ Switzerland is not dependent on individual laboratories that carry out analyses voluntarily and at their own expense.
- These analyses incur additional costs.

Option 4: **Weekly testing of a cohort** (such as the COVID-19 Infection Survey conducted by the Office for National Statistics (ONS); see Link and Link; 8,000 – 10,000 tests per week in London; London has a population that is roughly the same as Switzerland).

+ The absolute incidence of various pathogens can be estimated; with representative coverage of the population, the proportion of severe infections can also be determined.
- Very complex and expensive; no existing system at all
- Trend changes (Is the number of infections rising or falling? See option 2) are often sufficient for a reliable picture, and the absolute incidence (How many infections occur in one day?) is not necessary.

Option 5: **Testing and sequencing a portion of travellers entering the country** (on a voluntary basis following the US model; see Link).

+ This gives insight into the global circulation of different viruses and emerging mutations.
+ In the samples, the intact virus can be isolated, a full genome collected and, if necessary, it can be phenotypically characterised in virology laboratories.
+ Technically feasible (identical to Sentinella sample processing)
- Logistics and funding need to be worked out.

Option 6: Expansion of **wastewater monitoring (amount of virus and sequencing) to include airports and aircraft**.

+ This enables the surveillance of globally circulating variants.
+ The wastewater samples from the airport, which are sent to a treatment plant, can be analysed using the same technology as other wastewater samples (options 1 and 2).
- The airport wastewater samples contain a mix of inbound travellers from different flights, outbound travellers and airport employees that cannot be broken down by origin. So, if a particular variant is found, no indication as to where it might have come from is given.
- It is unclear how high the data quality is for samples originating from individual flights; a pilot study would be needed.
- Only virus fragments can be recovered from wastewater, not complete viruses; so, a new variant's full genome cannot be determined, and variants cannot be phenotypically characterised.

In summary, options 1 to 4 allow for the surveillance of virus circulation within Switzerland. Option 2 is based on samples that are currently already being collected and were also proposed in the Science Task Force report entitled "*Aspekte zum Umgang mit SARS-CoV-2 in den kommenden 12 Monaten*" ("Aspects of the management of SARS-CoV-2 in the coming 12 months) published on 15 February 2022 (see link). This option generates added value based on efforts already being made, with only a moderate level of additional effort. Option 3 was proposed in the same report (see link) and ensured surveillance specific to SARS-CoV-2 in the event of the emergence of variants of concern (see link); it can in principle also be used for other viruses with variants requiring special surveillance. Option 4 additionally allows the absolute incidence to be estimated, but it would have to be set up from scratch and would be very costly, especially when pathogens have a low level of circulation (many tests would be needed to detect a sufficient number of infections). The additional information provided compared to option 2 would be the absolute rather than the relative incidence. This information is valuable because it helps us to understand circulation. However, it is often not decisive for public health policy measures.

Options 5 and 6 enable the collection of global circulation data. By collecting such data from passengers travelling from China to Singapore, Japan and South Korea, for example, we know that the variants currently circulating in China are similar to those in the rest of the world.

These options therefore enable monitoring of variants from countries that themselves collect or provide only a little amount of data. Option 5 can be implemented straight away from a technical perspective. Some aspects of option 6 (monitoring individual aircraft) would require a pilot test.