The Potential of an Institutionalised Early Warning System for Pandemics in Switzerland

An Economic Benefit-Cost Analysis

A Study by the Think Tank Pour Demain in Collaboration with Eraneos and INFRAS

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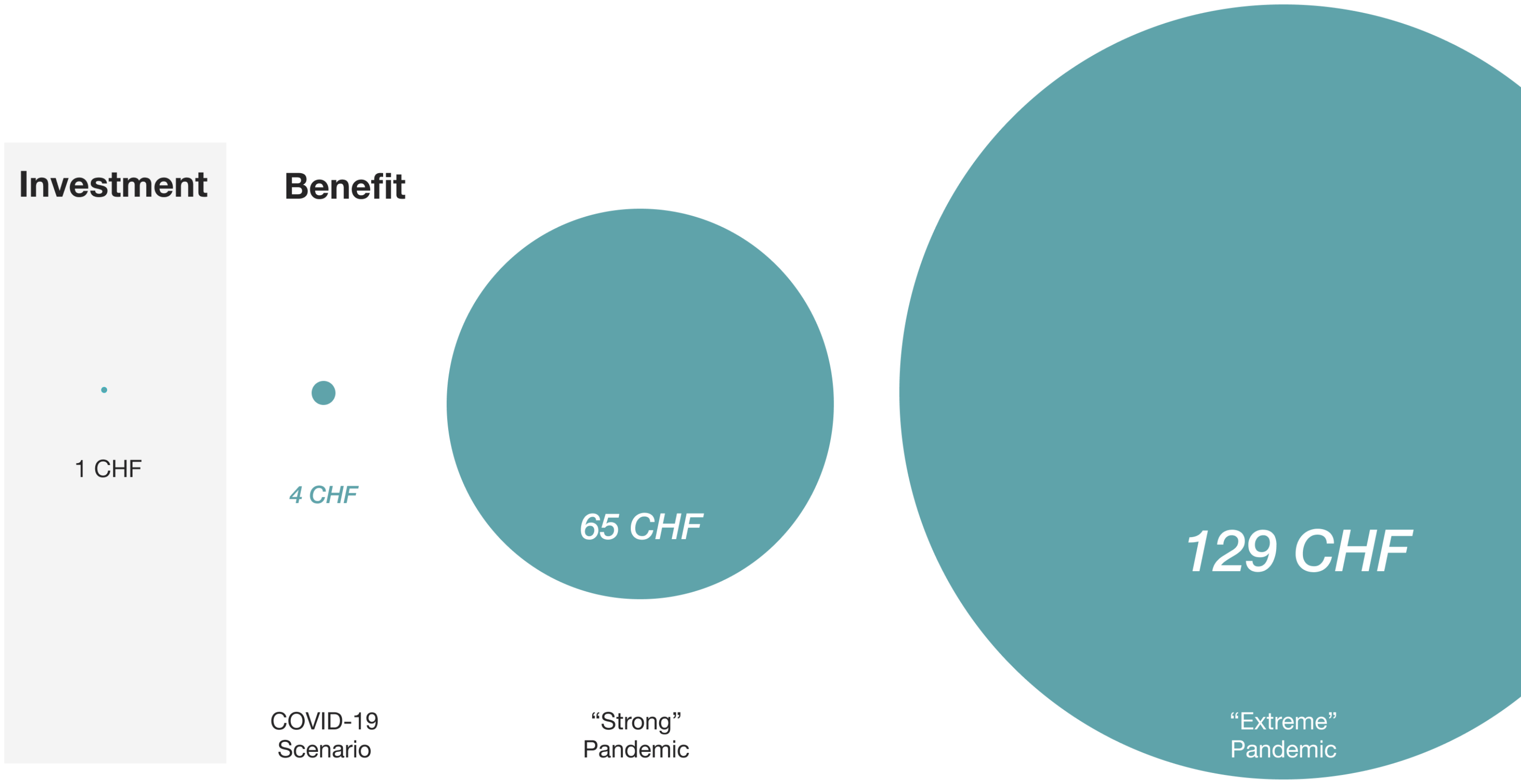
Management Summary

The investment of one Swiss franc in the early detection and monitoring of a pandemic leads on average to a benefit of four to 129 francs for Switzerland. This is the result of the present benefit-cost analysis by the think tank Pour Demain in collaboration with the research offices Eraneos and INFRAS.

The study quantifies only a small part of the actual benefit, namely the human and economic damage avoided in a first pandemic wave. Thus, the actual value of a pandemic early warning system is significantly higher. The next pandemic is only a matter of time. Moreover, an increased surveillance of pathogens also has immediate public health benefits outside of a pandemic (e.g. surveillance of antibiotic resistance).

Switzerland's early warning system must therefore be strengthened and institutionalised as soon as possible, inter alia by an expansion of wastewater monitoring and the regular sequencing of pathogens from hospitals, medical practices, and wastewater.

More than three years after the outbreak of the COVID-19 pandemic, the issue of pandemic preparedness in Switzerland has been somewhat forgotten in the wake of more recent crises. However, the current debates on the debt brake and the partially COVID-19-related budget deficit have brought back to mind the high economic damage associated with a



pandemic and highlight the importance of reducing such damage in the event of a new pandemic outbreak in the future. Furthermore, the full extent of the human loss is only now becoming visible: A study concludes that for Switzerland, COVID-19 is the second largest disaster in terms of mortality after the 1918 influenza pandemic.[1] Furthermore, the official hospital statistics for the first two years of the pandemic, available for the first time since COVID-19, show that a total of 72,605 people had to be hospitalised due to COVID-19 during this period[2] – almost twice as many as originally reported by the Federal Office of Public Health (FOPH).[3]

Switzerland has effective clinical systems for the early detection and surveillance of communicable diseases and, in the course of the pandemic, has established the monitoring of wastewater as well as a programme for sequencing individual cases for genomic surveillance of SARS-CoV-2. The sequencing data could be coordinated, analysed and shared with health authorities such as the FOPH via a common central database – the Swiss Pathogen Surveillance Platform. This allowed (i) the early detection of emerging new variants of concern (VOCs) and an assessment of whether the infection rate is increased and the vaccination protection of the population is at risk. Furthermore, (ii) the number of cases and the dynamics of the pandemic development with regard to the infection rate and the expected case load of the following weeks could be predicted with epidemiological-mathematical models. These important components of early detection and surveillance of infectious diseases, hereinafter referred to as the “early warning system”, are an excellent basis for reducing and, at best, completely avoiding high human and economic loss that could occur on an even larger scale due to a future pandemic. Furthermore, a better data basis also enables more efficient planning for hospitals and laboratories, e.g. to better anticipate and avoid logistical bottlenecks. In order for an early warning system for future pandemics to function and detect dangerous pathogens at an early stage, it must both be in regular operation, i.e. become institutionalised, and be able to detect and continuously monitor other, potentially pandemic pathogens.

This study considers the institutionalisation of a strengthened pandemic early warning system. This includes:

1. Continuous monitoring of five pathogens with the greatest pandemic potential in 50 wastewater treatment plants (WWTPs) throughout Switzerland and short-term scaling to 100 WWTPs in the event of a pandemic.
2. Continuous sequencing of five pathogens from different sources (hospitals, doctors’ practices, wastewater)
3. Data processing, management, analysis & interpretation for ordinance on measures

The benefit-cost analysis shows that the investment in an institutionalised early warning system for pandemics in Switzerland is extremely worthwhile.

1. Under conservative assumptions, the benefits in the event of a pandemic range from one to around 31 billion francs.
2. This means that the benefits are four to a maximum of 129 times higher than the associated costs.
3. In a COVID-19-like pandemic, each franc invested yields a benefit of around four francs, in extreme pandemic scenarios even up to 129 francs.
4. Since the study only visualises a small part of the benefits mathematically, it can be assumed that the actual benefits are many times higher.

SWITZERLAND HAS AN EXCELLENT BASIS FOR INSTITUTIONALISING AN EARLY WARNING SYSTEM FOR PANDEMICS. THE BENEFIT-COST ANALYSIS OF THIS STUDY SHOWS THAT THIS IS WORTHWHILE.

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Pour Demain is a non-profit think tank working towards a safe and positive future for our children, grandchildren and their descendants. Biosecurity and pandemic preparedness are among its focus areas. Pour Demain is committed to effective and science-based policy.
www.pourdemain.ch

INFRAS is a Swiss research and consulting company founded in 1976.
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1. Introduction

Worldwide, the COVID-19 pandemic has claimed over 6.6 million lives.[4] In Switzerland alone, almost 14,000 people have died to date.[5] Added to this are the economic losses, which have caused great hardship for states, companies and private individuals. The pandemic has led to a debt of 30 billion francs at the federal level[6], the debt of the municipalities and cantons has also increased[7]. Even though Switzerland suffered lower GDP losses by international standards when the pandemic broke out in 2020, the GDP fell by a full 2.5%, the biggest slump since the oil price crisis of 1975.[8] The pandemic also increased the global poverty rate[9] and inequality – including in Switzerland – since low-income households in particular suffered greatly from the Corona crisis[10] .

The numerous negative effects of COVID-19 underline the importance of preventing or at least cushioning pandemics[11] as far as possible – on the one hand because of the threat of health-related losses, and on the other because of the economic and – associated with it – the social damage. Further pandemics are very likely due to various factors. For example, 56% of the world's population already lives in cities, and by 2050 it will be two-thirds.[12] Population density and the associated mobility are strong risk factors that favour the rapid transmission of infectious pathogens. Historically, three to four pandemics occur each century, which cause more than one million deaths – in 1889, 1918, 1957, 1968 and 2019[13] – or in other words: In the last 100 years, four influenza pandemics have occurred at intervals of 15 to 30 years.[14] Considering that HIV/AIDS, cholera and tuberculosis are also defined as pandemics that are currently taking place, the probability of new pandemics, especially pandemics with a similar scale of damage as the COVID-19 pandemic, is likely to be much greater than previously assumed.[15] Researchers at *Duke University's Global Health Institute* conclude that the annual probability of the occurrence of a COVID-like pandemic is about 2% and could double in the coming decades.[16] Researchers at the start-up *Metabiota*, which specialises in collecting global data to forecast disease outbreaks, estimate that the probability of a COVID-like pandemic occurring is currently about 2.5-3.3% over the course of one year, or about 50% in the next 25 years.[17] An analysis of historical data on the frequency and geographical distribution of epidemics further suggests that the next pandemic could have even more devastating consequences than COVID-19: The frequency and severity of infectious diseases transmitted directly from wildlife hosts to humans are steadily increasing.[18]

Early detection and surveillance of pathogens can reduce high health and economic damage by providing important epidemiological information earlier and in greater detail, and by enabling earlier and more targeted decisions at government level to contain a pandemic. Researchers at Imperial College London have calculated that the number of deaths prevented by investing in pandemic preparedness averages between about 50 and 125 per 100,000 people. Each US dollar invested would therefore result in a gain of about 2,800 US dollars (health plus economic benefit).[19] Furthermore, a study by the consulting firm *McKinsey & Company* shows that globally, about five US dollars per person would be sufficient to significantly reduce the probability of the next pandemic.[20] Overall, however, few economic studies exist on pandemic preparedness.

Lessons learnt from the pandemic have shifted out of focus worldwide – including in Switzerland – in the wake of the Ukraine war and its global impact and since the "special situation" in the COVID-19 ordinance was lifted. However, thanks to its progress in reacting to COVID-19, Switzerland is ideally placed to anticipate and avoid the damaging pattern of panic and neglect in pandemics[21]. It has already established elements of an early warning system for the surveillance of SARS-CoV-2 and partially institutionalised it for other pathogens:

- **Reporting systems:** Switzerland has established and reliable reporting systems for clinical and laboratory findings of infectious diseases (cf. Chapter 3.1).[22]
- **SARS-CoV-2 wastewater monitoring:** During the pandemic, the FOPH, together with partner organisations, set up an wastewater monitoring system to monitor SARS-CoV-2; its longer-term continuation, however, remains unclear.
- **Genomic surveillance programme for SARS-CoV-2**: Genetic surveillance of SARS-CoV-2 is an essential part of controlling the COVID-19 pandemic.[23] Sequencing of the viral genome allows the information of a pathogen's genetic make-up to be decoded

at the highest resolution, allowing problematic variants (so-called variants of concern, VOCs) to be identified easily and quickly. The longer-term continuation remains unclear.

- **Digital platforms**: With the COVID-19 dashboard and the Swiss Pathogen Surveillance Platform, Switzerland has digital tools for data processing, data management, data analysis and interpretation, and visualisation of pathogens. Furthermore, the FOPH is working to establish a national infectious disease information portal (EPI) that will go beyond data on SARS-CoV-2. The longer-term continuation of the SPSP is unclear.

It makes sense to expand and institutionalise these important elements of an early warning system, which are currently mainly limited to the SARS-CoV-2 pathogen. This will enable Switzerland to contain both waves of COVID-19 infections and other emerging epidemics and pandemics at an early stage in the future. In the context of digital platforms, this requires not only a coordinated and rapid exchange of data within Switzerland, but also the linking with international and European databases.

At the same time, it is important to emphasise that **an early detection system for pandemics is only one of several important instruments** that ensure that Switzerland is better prepared for the next pandemic. The think tank Pour Demain is committed to further effective measures in the impact chain Prevent, Detect, Respond.[24]

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2.

Data Collection

For the study, the authors interviewed experts from the authorities, academia and the health sector orally and/or in writing. The following persons – listed in alphabetical order – were interviewed:

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The responsibility for the development of the cost and benefit models and all statements in this study lies with Pour Demain as well as Eraneos and INFRAS. The above persons provided input in the context of expert discussions but were not involved in the analysis and/or writing of the study.

Furthermore, scientific studies and articles were consulted which in particular served to elaborate the benefit model (cf. bibliography in Chapter 9).

3. Institutionalised Early Warning System for Pandemics

3.1. Definition of Institutionalised Early Warning System

Switzerland has effective systems for the early detection and surveillance of communicable diseases via the reporting system for infectious diseases, the Sentinella reporting system, the hospital-based sentinel surveillance system CH-SUR, laboratory reporting systems and the national survey system for recording rare paediatric clinical pictures (Swiss Paediatric Surveillance Unit; cf. Chapter 1).

The clinical and laboratory reporting systems, together with the wastewater monitoring established in the course of the COVID-19 pandemic, form a suitable basis for a further developed early warning system for monitoring potentially pandemic pathogens. By early warning system, the study understands the mandate for early detection and monitoring according to the Epidemics Act (esp. Art. 2 EpG, Art. 4 para. 1 EpG, Art. 11 EpG and Art. 3 Epidemics Ordinance EpV).

An institutionalised early warning system should be understood as the institutionalisation of the following key components of the current SARS-CoV-2 surveillance programme to four additional pathogens:

- **Wastewater monitoring:** Systematic monitoring of pathogen load and variants in wastewater through pathogen or variant detection in wastewater.
- **Genomic sequencing[25] of positive wastewater and patient samples from hospitals/ doctors' practices (individual cases) via laboratory and reporting systems (reporting system for infectious diseases, Sentinella, CH-SUR)**: Genetic surveillance of pathogens to observe mutations with epidemiological or clinical implications (increased risk of infection, increased pathogenicity) as well as determining of transmission chains.
- **Data processing, management, analysis and interpretation for the ordinance on measures**: Central platform for the data from the sequencing laboratories and additional federal offices for rapid and accurate interpretation of the data for specific Ordinance of Measures and communication on epidemiological events.

On the one hand, institutionalisation is understood as the expansion of the following components to four further, potentially pandemic pathogens. Thus, in the future, wastewater monitoring and sequencing should also be important, mutually complementary instruments for combating other or future epidemics/ pandemics. On the other hand, the two components of monitoring should not only be in operation in existing epidemic/ pandemic contexts, i.e. in special and extraordinary situations, but also in normal situations[26]. In this way, a pathogen circulating in the population can continue to be monitored even after the transition to the normal situation, and the risk of a further wave can thus be minimised. At the same time, it is possible to react promptly to new epidemics/pandemics that could hit Switzerland in the future.

As will be explained in detail in the chapter on the benefits of an early warning system (cf. Chapter 6.1), the combination of wastewater monitoring and sequencing not only enables the early detection of pathogens, but also allows for a better understanding of the occurrence, transmission chains, geographical distribution and evolution of pathogens, as well as circulating variants, including those that are of concern (VOC) and therefore of particular interest. The information thus obtained allows the government to make better, evidence-based decisions on the implementation of earlier and more targeted measures, which, depending on the timing of a pandemic, may refer to non-pharmaceutical interventions such as requirements for face masks, lockdowns, entry restrictions, assembly bans, etc., or vaccination campaigns, more intensive group-specific testing, etc. Furthermore, these two components of the early warning system allow the prescribed measures to be tested more thoroughly for their actual effectiveness.

EARLY WARNING SYSTEM FOR MONITORING PATHOGENS

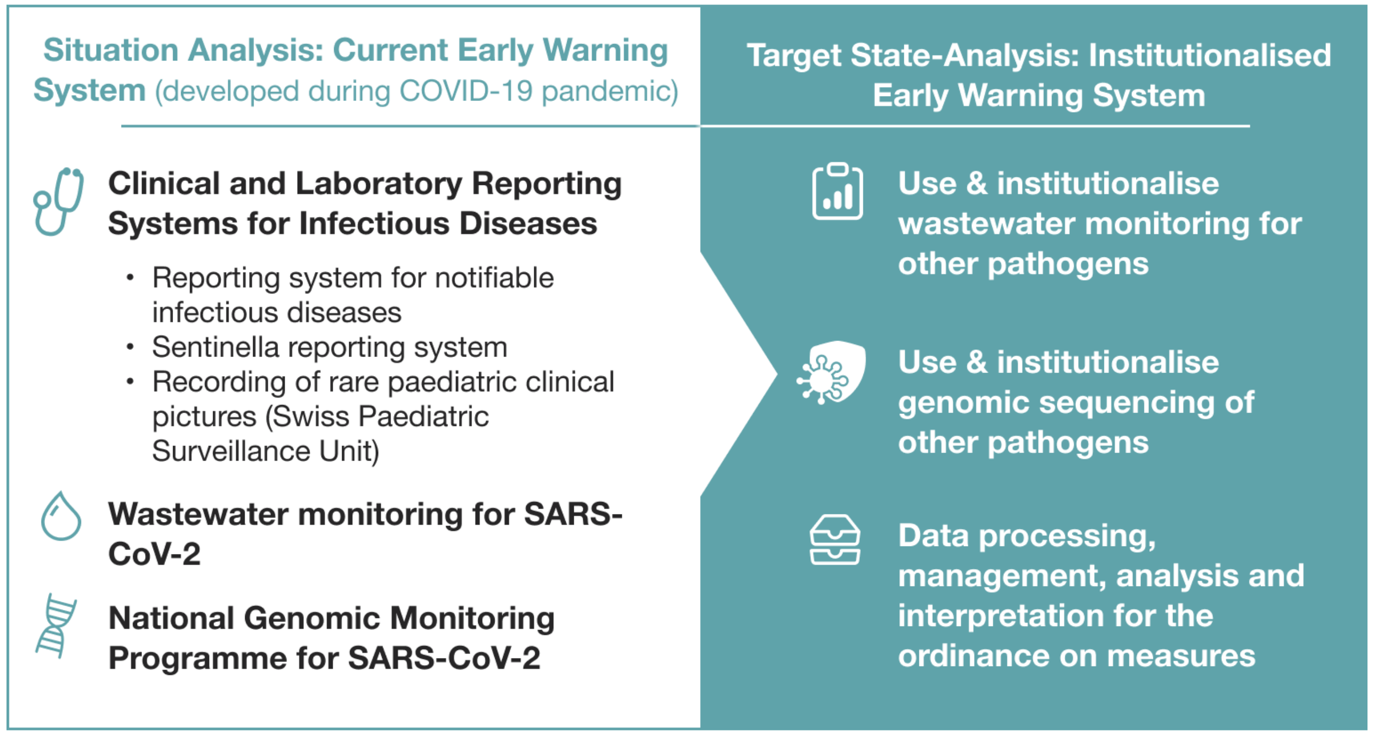

Illustration 1: Institutionalised Early Warning System, Focus of the Study

PROCESSES INSTITUTIONALIZED PANDEMIC EARLY WARNING SYSTEM

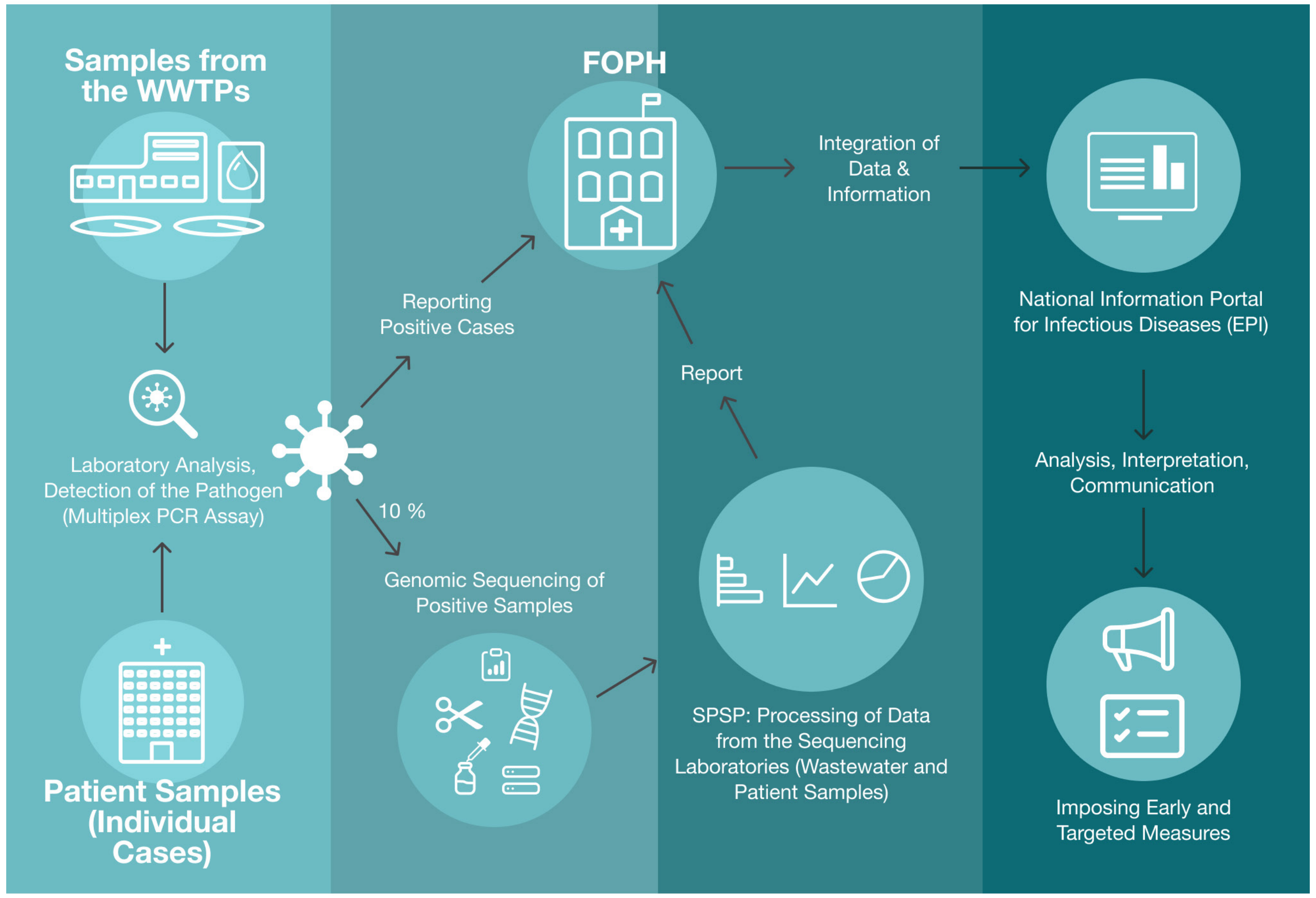

Illustration 2: Processes Institutionalised Early Warning System

In order for measures to be derived quickly and easily from the information obtained in wastewater and through sequencing, there is also a need for a centralised data portal that collects, interprets and visually processes the epidemiological course of infections through data from the sequencing laboratories. The Swiss Pathogen Surveillance Platform was developed as part of the NRP72 programme of the Swiss National Science Foundation as a platform for the molecular-epidemiological surveillance of antibiotic resistance. The database was rebuilt during the pandemic and currently collects all genomic sequencing of individual cases – at peak times from a total of 17 partner institutions. It will therefore occupy a central place in the context of the third component of the early warning system, while the national information portal for infectious diseases (EPI) is not the subject of the benefit-cost analysis, as the FOPH has already launched the planning of the EPI and the digitalisation of reporting processes project. Furthermore, the third component includes federal offices for data analysis and interpretation for targeted and rapid Ordinances of Measures as well as the communication of the same to the appropriate addressees. The diagrams below (cf. Illustrations 1 and 2) offer a schematic representation of the target system, which is the subject of this study, and the individual processes.

For the operation of the early warning system to be as cost-efficient as possible, it is able to adapt/tailor its level of effort to normal or special/extraordinary situations, respectively. Therefore, situations and situation-specific scenarios for the extended early warning system are defined in the following.

3.2. Definition of Normal and Special/Extraordinary Situation

The study models the course of a future pandemic according to the experience with SARS-CoV-2 in order to build on the most recent pandemic event in the Swiss context. **A pandemic course in the time horizon of 37 years** – the period within which it is assumed that a pandemic occurs (cf. Chapter 4.1.) – is therefore defined as follows:

- **Normal situation, pre-pandemic**: A long, pre-pandemic period with few infections – 31 years and eleven months
- **Special/extraordinary situation**: A high number of infections and deaths at the outbreak of the pandemic – two years and one month[27]
- **Normal situation, post-pandemic**: The period immediately after the pandemic in which infections are still to be expected but the numbers are lower and surveillance can be reduced again – three years.

3.2.1.Normal Situation

A normal situation is understood to mean two situations:

- On the one hand, a pre-pandemic situation according to Art. 2 and Art. 8 para. 2 lit. a. EpG, in which the outbreak and spread of communicable diseases must be prevented and controlled[28] by the Confederation and cantons taking preparatory measures "for the detection and surveillance of communicable diseases"[29]. This situation is comparable to the regular surveillance of endemic pathogens and seasonal pandemics such as influenza, which circulate in Switzerland for a limited period of time. It is also comparable to the years leading up to the outbreak of a pandemic in Switzerland, e.g. 2018-2019, when regular surveillance by the early warning system allows a rapid response to a new pathogen that is quickly spreading across the globe.
- On the other hand, the normal situation is to be understood as a post-pandemic situation in which the special situation declared due to a pandemic (Art. 6 EpG[30]) has been lifted, although the pathogen is still circulating in the population and the WHO is speaking of a pandemic[31] (corresponds, for example, to the COVID-19 situation from April 2022). In this situation, it is assumed that the number of unreported cases is relatively high, as the population largely only tests itself at home using rapid antigen tests, which are not recorded by the reporting systems.

3.2.2. Special/Extraordinary Situation

According to Articles 6 and 7, the EpG distinguishes between a special and an extraordinary situation[32], which are combined for the sake of simplicity; the two situation classifications are sometimes fluid and difficult to distinguish, and , according to experts, Switzerland currently lacks a definite and efficient process for situation assessment[33].

3.2.3. Consideration of the Different Situations in the Benefit-Cost Balance

According to experts, the benefit of an early warning system is difficult to calculate within the time horizon of an entire pandemic event. The factors influencing the estimation of the actual benefit are manifold. During a pandemic, rapidly changing dynamics are to be expected, in which, for example, new variants emerge, and the level of immunity within the population changes due to infections, vaccinations and the introduction of various and successive non-pharmaceutical measures.

Since it is therefore difficult to precisely delineate the effective contribution of an early warning system within an entire pandemic event with several waves, the study is limited to **calculating the benefit in a first wave**, i.e. to the lockdown-defined period in a special/extraordinary situation– in the case of COVID-19, this corresponds to the period from 17 March to 26 April 2020[34]. In this way, the benefit of an early warning system can be most accurately captured in a clearly defined period with a clear start and end of the lockdown. Further waves during the peak phase of the pandemic are not considered.

The costs of an early warning system, on the other hand, are calculated not only for the first wave, but over a time horizon of 37 years, during which all situations (pre-pandemic, pandemic, post-pandemic) are passed through (cf. Chapter 4.1). Even if this massively underestimates the **benefit-cost balance**, this calculation considers the fact that an institutionalised early warning system for pandemics not only operates in an extraordinary situation during a pandemic wave, but is continuously in use.

3.3. Responsibilities

Wastewater monitoring and the sequencing of wastewater and patient samples (individual cases) are to be understood as a system for early detection and surveillance in accordance with Art. 11 EpG[35]. The Confederation and the cantons share responsibilities for the detection and monitoring of communicable diseases. To identify the level of government responsible for early detection and surveillance, it is decisive whether outbreaks and epidemics occur locally, regionally or nationally.[36]

In the context of a pandemic, which by definition affects many countries[37], the responsibility would therefore appear to lie with the Confederation. However, an early warning system in a normal situation that does not immediately follow the lifting of a special situation is comparable in its function to regular epidemiological monitoring, for which the cantons are responsible according to Art. 15 EpG, unless there is "a special situation" that requires "measures (...) in the international movement of persons" or it concerns "epidemics that affect more than one canton"[38].

The Conference of Cantonal Ministers of Health (GDK) attaches great importance to the federal surveillance system for COVID-19. Especially with regard to new virus variants of concern, national and international data are important from the point of view of the cantons, as they only have their own systems for local and regional surveillance.[39] Especially in smaller cantons, there is usually not enough sequencing data available to determine the growth rate of a new pathogen variant. Data on a larger scale, i.e. at the national and international level, are therefore urgently needed in order to be able to assess courses of pandemics as accurately as possible.

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31 There are no generally agreed criteria that define when a pandemic is over.

32 Cf. footnote 28, articles 6 and 7.

33 University of Bern, Prüfung des Eskalationsmodells (Art. 6 und 7 EpG) unter besonderer Berücksichtigung der Epidemiologie übertragbarer Krankheiten sowie von Public-Health-Aspekten: **https://www.ispm.unibe.ch/unibe/portal/fak_medizin/ber_vkhum/inst_smp/content/e93993/e95206/e1295336/e1295350/Thesenpapier-Eskalationsmodell_eng.pdf** (12.12.2022).

34 ETH Zürich, Center for Security Studies: **https://css.ethz.ch/content/dam/ethz/special-interest/gess/cis/center-for-securities-studies/pdfs/Bulletin_2020_07_Chronologie.pdf** (12.12.2022).

35 Cf. footnote 28, article 11.

36 Cf. footnote 26.

37 Cf. footnote 11.

38 Ausbruchsuntersuchungen und epidemiologische Abklärungen, BAG: Ausbruchsuntersuchungen, epidemiologische Abklärungen (admin.ch) (12.12.2022).

39 Rebound Papier III, GDK: **https://www.gdk-cds.ch/fileadmin/docs/public/gdk/themen/praevention_gesundheitsfoerderung/ansteckende_krankheiten/NZ_Rebound_III_def_d.pdf**, S.4 (12.12.2022).

4.

Preliminary Assumptions Cost and Benefit Model

The present study is based on a number of assumptions made in order for a quantifiable benefit-cost ratio to be ascertainable. They are explained in the following.

4.1. Time Horizon by Means of the Return Period of a Pandemic

Fortunately, pandemics that trigger an "epidemic emergency" or even a "national threat" do not occur every year. In order to determine the annual benefit-cost ratio of an early warning system, it is therefore necessary to calculate the average return period during which one pandemic occurs on average.

According to the FOPH, a look at recurrent, novel epidemics or pandemics in the past century shows that "infectious diseases still represent a serious health risk".[40]

Based on the explanations in Chapter 1, the study assumes that the **probability of a pandemic of the magnitude of COVID-19 occurring in the next 25 years is about 50%**.[41] Based on the FOCP hazard file on influenza pandemics[42] and as is usual in hazard/risk analyses, the study calculates the return period x as follows:

$$\left(1 - \frac{1}{x}\right)^{25} = \frac{1}{2}$$

$$x = \frac{1}{\left(1 - \sqrt[25]{\frac{1}{2}}\right)} = 36.57$$

The costs of an institutionalised early warning system are therefore considered for a time horizon of 37 years– the period in which a pandemic is statistically to be expected – and compared with the benefits in the period of the first wave (cf. Chapter 3.2.3). With 37 years, a more conservative value is assumed than in the report of the "Pandemic insurance" project carried out by representatives of the insurance industry and the federal administration (SIF, SECO, Federal Office of Justice), which reckons with a return period of 33 years.[43] This figure compares with the 55 years estimated by the FOCP for influenza pandemics.[44] However, many more pathogens with pandemic potential than just influenza are possible. The calculation of the return period with COVID-19 as a reference should also be classified as conservative, since smaller, more frequently occurring events are not taken into account.

4.2. Damage Scenarios

The intensity of a future pandemic is divided into the damage scenarios "**severe**" and "**extreme**" in accordance with the FOCP's risk file for influenza pandemics[45]. The damage scenarios serve to anticipate the possible effects of a pandemic (number of infections, hospitalisations, etc.) depending on their intensity. The **COVID-19 scenario is considered the baseline scenario** and reference value. The damage scenario "considerable", which would be less severe than COVID-19 according to the FOCP numbers, is not taken into account in this study, as only pathogens with the highest pandemic potential are screened with the early warning system analysed here.

The study **follows the FOCP** and characterises the damage of a pandemic on the basis of the following criteria: **number of infections, hospitalisations, deaths and hospitalisations in intensive care**. However, the values are not defined with regard to an entire pandemic, but only to the first wave.

4.2.1. Damage Values COVID-19

In Switzerland, the first lockdown, understood as the "closure of publicly accessible facilities with the exception of essential businesses", took place between 17 March and 26 April 2020.[46] To quantify the benefit, the infections avoided by the early warning system during this period are considered. Since the consequences of an infection occur with a delay, hospitalisations during the lockdown and one week after its termination are considered for stays at intensive care units up to ten days longer and for deaths up to two weeks beyond its lift.[47]

THE STUDY IS BASED ON THE CONSERVATIVE ASSUMPTION THAT A PANDEMIC WILL OCCUR IN THE NEXT 37 YEARS.

Table 1 summarises the key data for COVID-19 during the first lockdown. These represent the basic scenario for the study:

Consequences of the First COVID-19 Wave, Spring 2020[48]					
	Infections (= tested positive)	Hospitalisations	Hospitalisations in intensive care unit	Deaths	Long COVID cases49
Period under review	17.3.2020-26.4.2020	17.3.2020-3.5.2020	17.3.2020-6.5.2020	17.3.2020-10.5.2020	No time period, percentage of infections
Cases	29'313	3'991	1'099[50]	1'689	2'931
Share	0.34% of population	13.6% of those tested positive/ infected	27.5% of hospitalised	5.76% of those tested positive/ infected	10% of those tested positive/ infected

Table 1: Consequences of the First COVID-19 Wave, Spring 2020

Based on the COVID-19 values for hospitalisations (in intensive care), deaths and long COVID Covid cases, i.e.long-term health problems, the corresponding damage values are estimated for the pandemic scenarios "severe" and "extreme", which are more critical than COVID-19. The infections are simulated using the Renewal Equation formula, whose input values, in turn, are based on the COVID-19 scenario.

4.2.2. Estimation of Potential Infections of a Future Pandemic Wave with the Renewal Equation Formula

The number of new infections or total infections of a wave are simulated using the so-called "discrete renewal process", a stochastic model that predicts the distribution of expected values over continuous time. For this purpose, the following formula[51] is used, which has been applied several times in scientific studies to assess the effect of non-pharmaceutical measures in the pandemic context[52]. The formula calculates the number of infections *c* at time *t* in country *m* iteratively on the basis of the past infection figures relative to the population size *N*. To do this, it uses the reproduction number *R* at time *t*, i.e. the average number of people an infected person infects, as well as the generation time *g*, i.e. the time interval between a person's infection and the secondary infections that originate from that person.

The generation time *g* is calculated assuming a gamma distribution with constant mean and coefficient of variation. The decisive factor that varies over time is the reproduction number *R*. Since the formula is based on past infection numbers,

$$C_{t,m} = \left(1 - \frac{\sum_{i=1}^{t-1} C_{i,m}}{N_m}\right) R_{t,m} \sum_{\tau=0}^{t-1} C_{\tau,m}\, g_{t-\tau},$$

the model must be recalculated for each day, starting from time t_0. The baseline reproduction number R_0 corresponds to the initial value at the beginning of a pandemic and changes over its course depending on the immunity levels and behaviour of the population (effective reproduction number R_e). In this study, R_e, which is impacted by a lockdown, is simulated (cf. also Chapter 6.3.3, Step 1). The effectiveness of this measure is expressed in terms of the time until the R value falls below one and the exponential spread of infections is thus brought under control. For COVID-19, the study assumes an R_e value of 1.75 at the time the lockdown was introduced in Switzerland.[53]

To simplify matters, the study also assumes that the R-value falls to 0.9 within seven or 14 days after the introduction of measures and remains constant at this level, although in reality it may well fall even further. Furthermore, the development of infections is only considered over a period of 41 days, assuming that a lockdown for future pandemic scenarios lasts for as long as was the case for COVID-19 during the first wave.

In the COVID 19 pandemic scenario, the development of the infection figures is known up to and also after the introduction of the measure. In the "severe" and "extreme" pandemic scenarios, the course of the pandemic before and after the introduction of the measure is not known and must be simulated. In line with Flaxman et al.54, the infection figures are generated for the first six days before time t_0, i.e. before the start of a pandemic wave, using a Poisson process with exponential intervals in-between infections with mean value 1/τ (τ=0.03).

Table 2 summarises the corresponding values for COVID-19 during the first wave in Switzerland, based on which the values for the "severe" and "extreme" pandemic are estimated.

In the event of a more severe pandemic, it can be assumed that the Swiss government would react more quickly than in spring 2020, even without an early warning system. For the simulation of the scenarios "severe" and "extreme", the introduction of measures was therefore defined as occurring on day eleven, t_{11}, since at this point the daily infections are already above 3,500 and it can be assumed that the government would act in such a case even without an early warning system.

COVID-19 Pandemic, First Wave	
Reproduction number R_e on 17/03/2020	1,75[55]
Generation time assuming a gamma distribution g	Mean value = 6,5 Tage[56] Coefficient of variation = 0,62 Gamma (2,6; 2,5)[57]
Time span until R_e <1	7 days[58]

Table 2: COVID-19 Pandemic, Values First Wave

For pandemics that are more damaging than COVID-19, the study further assumes that the causative pathogen is more contagious, i.e. that the baseline reproduction number R0 is slightly higher than for COVID-19 (2.78[59]) and the time span between infections is shorter (i.e. the generation time is shorter than 6.5 days on average). Furthermore, it is assumed that the spread of the pathogen can be controlled similarly well by introducing a lockdown as with COVID-19, but that the time span until Re falls from the higher initial value to a value below one is somewhat longer (14 instead of seven days).

Accordingly, the following values are assumed for the pandemic scenarios that are more severe than COVID-19:

Pandemics “Severe” and “Extreme”, First Wave	
Reproduction number R_0	4
Generation time assuming a gamma distribution g	Mean value = 4.5 days Coefficient of variation = 0,62 Gamma (2,6; 1.73)
Time span until R_e <1	14 days

Table 3: Pandemic “Strong” and “Extreme”, First Wave

Based on the values presented in Table 3, 204,321 people become infected within the lockdown period of 41 days, i.e. 2.3% of the Swiss population.

4.2.3. Damage Values “Severe” Pandemic

Damage Values First Wave, “Strong” Pandemic					
	Infections first wave	Hospitalisations[60]	Hospitalisations in intensive care unit	Deaths	Long-term health effects (comparable with Long Covid)
Cases	204’321	40’864	4’086	20’432	20’432
Share	2,3 % of population	20% of infected[61]	10% of hospitalised	10% of infected	10 % of infected

Table 4: Damage Values First Wave, “Strong” Pandemic

From the infection numbers, the following damage values are estimated for the first wave of a “strong” pandemic:

4.2.4. Damage Values “Extreme” Pandemic

While no additional infections are assumed in the first wave for an “extreme” pandemic compared to the “severe” one, a pathogen with higher virulence, and correspondingly, a higher number of hospitalisations and deaths are assumed for an “extreme” pandemic according to Table 5. The damage values are thus calculated as follows:

Damage Values First Wave, “Extreme” Pandemic					
	Infections first wave	Hospitalisations	Hospitalisations in intensive care unit	Deaths	Long-term health effects (comparable with Long Covid)
Cases	204’321	61’296	12’259	40’864	20’432
Share	2,3 % of population	30 % of infected	20 % of hospitalised	20 % of infected[62]	10 % of infected

Table 5: Damage Values First Wave, “Extreme” Pandemic

4.3. Expansion of the Early Warning System & Baseline

The present study examines the benefit-cost balance of an early warning system that monitors four additional pathogens. **With SARS-CoV-2, a total of five pathogens would be integrated into the early warning system**. It is assumed that the existing infrastructure for monitoring SARS-CoV-2 can be extended to similar pathogens without additional investment costs and used over the next few years.

The study is currently limited to four additional pathogens, as all experts interviewed internally by Pour Demain prominently named the following four pathogens: **Influenza viruses, corona viruses outside SARS-19, smallpox and measles**. However, the exact composition could be determined in a structured process outside of this study, and an expansion to more than five monitored pathogens would also be conceivable.

The selected pathogens are assumed to behave similarly to SARS-CoV-2 in various ways: They are also detectable in wastewater, have the same detection limit in wastewater and comparable test parameters (incubation period, diagnostic window, correlation of the extent of pathogens detected in wastewater with the extent of the burden of disease caused by the pathogens), and precautions can be taken that prove to be similarly effective as the governmental packages of measures in spring 2020.

4.4. Probability of Detection of a Pandemic

The study makes the following assumptions in terms of a narrow definition of benefits: The early warning system

- regularly monitors a total of five different, already known pathogens
- can be quickly adapted to new globally emerging pathogens
- detects the pathogens earlier than without an early warning system with a probability of 80%

The probability of detection of a pandemic by an early warning system depends on the pathogens to be monitored and their probability of being pandemic. It is therefore crucial to monitor the pathogens that experts consider to be the most dangerous. From a historical perspective, a small number of human pathogens, which are similar in many respects, seem to be responsible for a large number of pandemics (e.g. corona viruses: COVID-19, MERS, SARS; influenza: swine flu, Spanish flu[63]).

The study's narrow understanding of benefits (cf. Chapter 6.2) does not capture the benefits that an institutionalised early warning system would have if new, as yet unknown pathogens were detected in Switzerland for the first time. Instead, it is assumed that a new pandemic would not emerge in Switzerland, but would first be detected abroad – which also fits with historical experience. **An institutionalised early warning system could be adapted to detect new pathogens that occur in a global context. According to experts, an already existing wastewater monitoring system for influenza in Switzerland would have enabled an immediate and uncomplicated switch to SARS-CoV-2**.

Various factors, such as unfavourable weather conditions with heavy precipitation, which impede the detection of pathogens in wastewater, mean that a pathogen cannot be detected or recognized early in 100% of cases. An **predicted 80% probability of earlier detection** therefore ensures that the benefit of an early warning system is not overestimated. If only a single pathogen is observed in the early warning system, the probability of detecting the pathogen in question is correspondingly lower than if several pathogens were observed.

4.5. Parameter Situation-Specific Scenarios

For both wastewater monitoring and sequencing, the question arises of how often samples should be taken, analysed and sequenced, and how many wastewater treatment plants (WWTPs) are needed for effective wastewater monitoring. Pour Demain's internal expert discussions provided no conclusive answer, as this question is and will remain the subject of research, can be examined from different perspectives, and is also dependent on the pathogens and the courses of the pandemics to be investigated.

However, researchers as well as public health officials agree that the **smallest necessary number of WWTPs and of samples that are still sufficiently representative and meaningful should be aimed for.**[64] At the same time, based on experience from the national wastewater monitoring programme, practical and cost-effective approaches are currently being discussed, for example the combining and pooling of samples to obtain information from wastewater more frequently in relation to the number of samples.

Number of WWTPs

For the number of WWTPs included in wastewater monitoring, this means that (1) all cantons must be covered in a balanced manner, (2) the plants with the largest number of connected persons are selected, (3) urban areas are covered for the most part, but also a selection of rural areas, and (4) those plants are of particular interest that are located in so-called strategic places (tourism region, border region, proximity to airports, urban areas, etc.). For example, according to the

Guidelines on Environmental Surveillance for Detection of Polioviruses of the Global Polio Eradication Initiative (GPEI), preference should be given to WWTPs with a catchment area of 100,000 to 300,000 inhabitants.[65]

The 10 largest WWTPs in Switzerland, which are located in the cantons of Bern, Basel-Stadt, Geneva, Lucerne, Ticino, Vaud, Zug and Zurich, have a catchment area of around 120,000 to a maximum of 450,000 inhabitants.[66] They alone already cover 25% of the population. If, for example, the largest plants in almost every canton were selected, 50 WWTPs would cover 50% of the population. These 50 WWTPs could provide a balanced picture of the situation with regard to the distribution across cantons and urban areas in the most populous cities or cantons, and occasionally also represent smaller catchment areas (less than 50,000) in more rural regions, so that even for pathogens with a lower detection limit an already small number of infections can trigger a signal.

The study therefore assumes that 50 WWTPs are involved for wastewater monitoring in a normal situation, both pre- and post-pandemic. This assumption is congruent with the planning of the FOPH, which will reduce the number of facilities to 50 in 2023, since this would still cover a large part of the population and trends could be adequately assessed.[67]

For a special/extraordinary situation, as was the case for SARS-CoV-2 in the corresponding situation, the study assumes 100 WWTPs, covering approximately 70% of the population,[68] since, according to the experts interviewed by Pour Demain, it is worthwhile in a pandemic situation to ramp up wastewater monitoring to as many plants as possible.

Detection Limit WWTPs

The detection limit[69] in wastewater samples depends on the pathogen in question and, according to the experts interviewed, is, **in the case of SARS-CoV-2, between one and ten infections per 100,000 persons**. As mentioned, the study assumes that the same detection limit applies to other pathogens. The 100 largest WWTPs in Switzerland have an average catchment area of about 60,000 inhabitants, which means that on average a signal could already be detected in the wastewater with as few as six infected persons. Only ten WWTPs have a catchment area of more than 100,000 inhabitants (as of 2017). Since none is larger than 500,000, a maximum of 50 people would have to be infected at this detection limit for the signal of a new pandemic to be detected in the wastewater.

Number of Sequencings and Samples per Week

The necessary frequency of sequencing depends strongly on the characteristics of a circulating pathogen: how quickly does it spread, how often does it mutate, etc. The frequency of sequencing should be determined by the number of positive clinical samples. Based on the information provided by the experts interviewed, it is assumed that **five to 10% of the positive clinical samples** should be sequenced in order to be able to draw an accurate picture of the course of the pandemic. This is also in line with **WHO recommendations** for genomic surveillance of SARS-CoV-2 variants.[70]

For the present study, the sequencing frequency is calculated based on the number of weekly COVID-19 infections in the first year since the outbreak. The study also assumes the higher sequencing frequency of 10%.

Sequencing Frequency in a Special/Extraordinary Situation		
Layers	Sequencing frequency of weekly infections, basis COVID-19	
Special/extraordinary situation	Weekly infections on average in the first COVID-19 pandemic year	10'640
	Sequencing frequency 10%	1'064[71]

Table 6: Sequencing Frequency, Basis COVID-19

For the “severe” and “extreme” pandemics scenarios, which cause higher infection numbers in the first wave, the weekly frequency of sequencing in the first pandemic year would in principle have to be higher than in the COVID-19 scenario. However, since it can be assumed that a higher infection rate also results in broader immunity and the simulation of infections for fictitious scenarios over a period longer than one wave could be very inaccurate, the study assumes the same sequencing frequency for the two more severe scenarios as well. The frequency of sequencing has implications for the cost calculation. A potential underestimation of costs due to the possible need for a higher frequency of sequencing in “severe” and “extreme pandemic” scenarios is compensated insofar as the benefit-cost balance compares the costs in a period of 37 years with the benefits in the period of only one wave.

In the normal, post-pandemic situation, a weekly sequencing frequency of 191 is assumed. This is the result of 10% of the mean of the seven-day average of new COVID-19 infections of 2068 and 1748 between 12/12. and 19/12/2022[72] – a reference week in a post-pandemic, normal situation. **Ten sequencings per week are assumed for the pre-pandemic phase**, as the study expects about 100 infections per week, of which 10% are sequenced. The assumption is based on the relatively low number of infections of many diseases requiring notification such as tuberculosis or measles. In principle, the sequencing of only ten samples per week for five different pathogens in the normal, pre-pandemic situation is very low. However, in view of the fact that the study can only calculate the benefits for a first wave, but considers the costs over a time horizon of 37 years (cf. Chapter 3.2.3), the low sequencing frequency is justified.

Even in a pandemic and post-pandemic situation, in which surveillance is primarily focused on the pathogen causing the pandemic, 10 samples per week are sequenced in parallel for ongoing surveillance of other, non-pandemic pathogens. In a pandemic situation, a total of 1,074 samples are thus sequenced, in a post-pandemic situation 201 samples.

For PCR detection of those pathgens from the wastewater samples, the study assumes a similar frequency of sampling as is currently done for SARS-CoV-2 wastewater monitoring[73], namely six samples per week in a special/extraordinary situation and three samples per week in a normal situation (pre-pandemic and post-pandemic). The same frequency is assumed for the sequencing of the wastewater samples.

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41 Cf. footnote 17.

42 Gefährdungsdossier Influenza-Pandemie, BABS: **https://www.babs.admin.ch/content/babs-internet/de/aufgabenbabs/gefaehrdrisiken/natgefaehrdanalyse/gefaehrddossier/_jcr_content/contentPar/accordion/accordionItems/gesellschaftsbedingt/accordionPar/downloadlist/downloadItems/157_1604483556672.download/30-Influenza-Pandemie-GD-de.pdf** (12.12.2022).

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45 Ibid.

46 Cf. footnote 34.

47 According to Marschner 2021, approximately 18 days elapse between COVID diagnosis and time of death. We conservatively assume 14 days.

48 The figures refer to the values in the indicated observation period according to the FOPH's COVID 19 dashboard, cf. footnote 5.

49 Many studies assume a frequency of around 20%, but other results show a lower percentage of around 4% of all COVID-infected persons, cf. e.g. Hanson et al. 2022. Since the new values are subject to great uncertainty, we assume an approximate mean value of 10%.

50 According to the source in footnote 5, between 03/30 and 05/06/2020 between 122 and 482 people were in intensive care every day. Assuming that a person spends an average of 2 weeks in intensive care, this results in 444 to 1,755 cases for the period of 51 days (03/17/2020-05/06/2020), i.e. an average of 1,099 cases.

51 Flaxman et al. 2020.

52 In addition to Flaxman, e.g. also Fraser 2007, Nouvellet et al. 2018, to a certain extent also Huisman et al. 2020.

53 Scire et al. 2020 conclude that the R e -value in the first third of March 2020 was between 1.5 and 2. The study therefore assumes a mean value of 1.75.

54 Cf. footnote 51.

55 Cf. footnote 53.

56 As in the simulation by Flaxman et al. 2020.

57 Gamma distribution with parameters shape k und scale θ, where mean = $k^* \theta = 6.5$ and coefficient of variation = $k^{-1/2} = 1/\sqrt{k} = 0.62$
$k = (1/0.62)^2 = 2.6$, $\theta = 6.5/2.6 = 2.5$.

58 According to Rugizzi/Gashi 2021, R_e fell below 1 on 23.03.2020, according to Lemaitre et al. 2020 even already on 03/19/.2020.

59 According to Althaus 2020, Lemaitre et al. 2020 arrive at a similar figure of 2.8.

60 Once a certain number of infected persons have to be hospitalised, the hospital capacities are reached, but theoretically these persons would need hospitalisation.

61 This is a hospitalisation rate that is about two times higher than in the first COVID 19 wave.

62 20% is a conservative assumption, considering that the mortality rate for MERS-CoV infection, for example, is around 35%, cf. Centers for Disease Control and Prevention: **https://www.cdc.gov/coronavirus/mers/clinical-features.html** (12.12.2022) or for Ebola event at 50%, cf. WHO, Ebola virus disease: **https://www.who.int/news-room/fact-sheets/detail/ebola-virus-disease** (12.12.2022).

63 Piret/Boivin 2021.

64 According to Pour Demain's interviews with experts.

65 Global Polio Eradication Initiative: **https://polioeradication.org/wp-content/uploads/2016/07/GPLN_GuidelinesES_April2015.pdf** (12.12.2022).

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67 Newspaper Article (Tages-Anzeiger), 27.12.2022: **https://www.tagesanzeiger.ch/die-zeit-der-extremen-omikron-wellen-scheint-vorbei-414839150203**.

68 Press release 28.05.2021, BAG: **https://www.admin.ch/gov/de/start/dokumentation/medienmitteilungen.msg-id-88615.html** (12.12.2022). The EU is expected to propose the value of 70 % in the revised Wastewater Treatment Directive, cf. European Commission, Proposal for a directive of the European parliament and of the council concerning urban wastewater treatment (recast): **https://environment.ec.europa.eu/system/files/2022-10/Proposal%20for%20a%20Directive%20concerning%20urban%20wastewater%20treatment%20%28recast%29.pdf** (12.12.2022).

69 Definition: The smallest detectable amount of the pathogen in a sample.

70 WHO, Guidance for surveillance of SARS-CoV-2 variants: **https://apps.who.int/iris/rest/bitstreams/1361901/retrieve** (12.12.2022).

71 In May 2021, around 2,000 positive COVID-19 samples were sequenced in Switzerland, cf. Newspaper Article (SRF), 19/05/2021: **https://www.srf.ch/news/schweiz/erbgut-des-virus-erforschen-schweiz-sequenziert-weniger-corona-proben-als-andere-laender** (12.12.2022). Über einen Zeitraum eines ganzen Jahres, in der Wellen abflachen und wieder ansteigen, sind die knapp über 1'000 Sequenzierungen pro Woche nicht unterschätzt.

72 Cf. footnote 5.

73 According to the FOPH's media release on the expansion of wastewater monitoring to over 100 wastewater treatment plants, samples are taken two to six times a week, cf. footnote 68.

5.

Costs of the Institutionalised Early Warning System

5.1 Cost Structure

The costs of an institutionalised early warning system consist of the three components (1) wastewater monitoring, (2) sequencing, (3) data processing, management, analysis and interpretation for an ordinance on measures (cf. Chapter 3). For components 1 and 2, the costs are generally based on the operating costs of genomic and wastewater monitoring of SARS-CoV-2, but are calculated somewhat higher to be on the safe side.

For example, 30-50% of additional, indirect costs were integrated into the calculation of the costs for sequencing, and costs for sample collection by the WWTPs were also considered in the calculation, although these could be coordinated with other routine analyses. Transport costs were also included conservatively, even though at certain WWTPs the operating staff can bring the samples directly to the analysis laboratory themselves, in which case no external costs would arise.

Personnel costs for data analysis and interpretation for the targeted and early ordering of measures are factored in, thus including additional expenses that do not yet exist within the framework of the current COVID-19 monitoring or could be increased.

Since the individual costs are based on several cost estimates from different experts, a range with the lowest and highest value as well as an average value was determined.

5.1.1. Costs Wastewater Monitoring

The wastewater monitoring cost item can be divided into the following four cost centres for the ongoing operating costs:

Cost centre	Costs in CHF	Description
Sampling of wastewater treatment plant (WWTP)*.	0-50; average 25	Effort for sampling (taking sample at the WWTP)
Transport*	20	Packaging and refrigerated transport from WWTP to laboratory
Laboratory (basic rate)*	185-200; average 192,50	Basic rate for laboratory analysis: sample preparation, extraction/concentration etc. incl. bottles for sampling
Laboratory (pathogen detection)**	5-10; average 7,5	Test for the detection of pathogen with multiplex PRC assay

** Depending on the number of samples per week and WWTPs*

*** Depending on the number of pathogens, number of samples per week and WWTPs. These costs only refer to the primers and probes of the multiplex PCR assay per new pathogen, as the costs for sample preparation with extraction/concentration are included in the basic laboratory tariff costs.*

The study also assumes that no further investment costs are necessary to extend wastewater monitoring to other pathogens, since an adequate infrastructure was built during the COVID-19 pandemic that is sufficient for the operation of wastewater monitoring as a complementary, but not exclusive, element of the pandemic early warning system.

5.1.2. Costs Sequencing

The cost item for sequencing includes the following cost centres for wastewater and patient samples from the reporting systems:

Cost centre	Costs in CHF	Description
Sequencing per sample (incl. bioinformatic analysis and overhead costs of up to 50%)*	Wastewater samples: 200-300; average 250	In addition to the costs for sequencing, costs for a bioinformatic standard analysis as well as overhead costs of 20-50% are also included, if these are not already accounted for in the basic rate for sequencing.
Sequencing per sample (incl. bioinformatic analysis and overhead costs of up to 30%)**	Patient samples: 100-350; average 225	In addition to the costs for gene sequencing, costs for a bioinformatics standard analysis and overhead costs of 20-30% will be included, unless these are already accounted for in the basic rate for gene sequencing.
Transport***	20	Costs for refrigerated transport from the laboratory to the three competence centres for Next Generation Sequencing.

** Depending on the number of samples per week and WWTPs. Overhead costs are determined as higher for wastewater samples than for patient samples, as sequencing wastewater samples is more time-consuming.*

*** Depending on the number of samples per week.*

**** Depends on the number of samples per week. If a laboratory does its own sequencing, these costs would be omitted.*

In general, the costs refer to the sequencing of viruses and not, for example, bacteria, as antibiotic resistance, for example, is not integrated in the narrowly defined benefit model (cf. Chapter 6.2).

The study assumes that prices will remain stable over the next 37 years, even though they are likely to fall in the future. Nor does it take into account the economies of scale that can be achieved with the automation of sequencing machines in increments of 96 samples. These assumptions are made in accordance with a conservative cost calculation, so as not to underestimate the actual costs of the early warning system.

5.1.3. Data Processing, Management, Analysis & Interpretation for Ordinances on Measures

The following costs are incurred for the operation of the SPSP data platform and its expansion to integrate four additional pathogens as well as wastewater data:

Cost centre	Cost in CHF	Description
Operation SPSP (annual)	183,500-300,000; average 241,750	Costs for coordination of partners, quality control of data, communication with international databases, IT infrastructure, minor adjustments (bioinformatics tools etc.)
Expansion SPSP*	71,000-150,000; average 110,500	Costs for integration of new pathogens as well as wastewater data, corresponding IT adjustments, connection to new databases, etc.

** These costs do not incur every year, but once.*

Furthermore, approximately three to four federal positions in salary grades 18-24 are needed. On the one hand, two people with expertise in epidemiology and bioinformatics are needed who can interpret data from the early warning system quickly and accurately; on the other hand, one or two communication specialists are needed who can communicate the relevant information in a timely manner and in a way that is appropriate for the target group.

Cost centre	Cost in CHF	Description
Personnel expenses (annual)	450'0000*	Time spent on data analysis, interpretation and communication on the specific measure prescription

** This is a rough cost estimate.*

5.2. Total Cost Estimate Early Warning System

The annual costs of an institutionalised early warning system differ depending on the situation.

- The costs in the period of a **special/extraordinary situation** amount to around 31 million francs per year on average.[74]
- Since fewer cases need to be detected and sequenced in the period immediately after the pandemic, the costs are lower at around **seven million francs** after the special situation is lifted.
- Even **in the normal, pre-pandemic situation**, the **total costs of the early warning system** are lower than during a pandemic, averaging around **five million francs**.
- Over a **time horizon of 37 years, the annual costs for the entire early warning system** in operation in all three situations amount to an average of slightly more than **six million francs**, since the lowest costs are located in a situation that lasts the longest (according to the study assumption 31 years and 11 months), while the higher costs are incurred in the special/extraordinary situation over the comparably short period of only two years and one month. **In a normal year, the costs of the early warning system amount to about five million francs**.

The highest costs are incurred for the sequencing of wastewater and patient samples. In a special/extraordinary situation with a high infection rate, the weekly frequency of sequencing increases, which is why the costs for sequencing wastewater and patient samples account for almost 70% of the total costs. The cost for wastewater monitoring are lower at around 28% of the total cost. The costs for data processing, management, analysis & interpretation for potential ordinances of measures represent a less substantial cost component with – depending on the situation – a two to 18% share of the total costs of the early warning system. The exact calculation of the annual costs with the various parameters for the different situations can be found in Appendix A.2.

Average Annual Costs Early Warning System				
Situation	Wastewater monitoring	Sequencing	Data analysis & interpretation	Overall early warning system
Normal prepandemic	CHF 2’145’000	CHF 2’145’000	CHF 922’250[75]	CHF 5’147’770
Special/Extraordinary	CHF 8’580’000	CHF 21’488’633	CHF 691’750	CHF 30’760’383
Normal postpandemic	CHF 2’145’000	CHF 4’513’860	CHF 691’750	CHF 7’350’610

Table 7: Average annual costs for an Early Warning System by situation

References

74 The average costs were determined as the mean value of the minimum and maximum costs.

75 The costs in this situation are higher than in the other situations because the one-off costs for the expansion of the SPSP were offset here.

6.

Economic Benefit of the Institutionalised Early Warning System

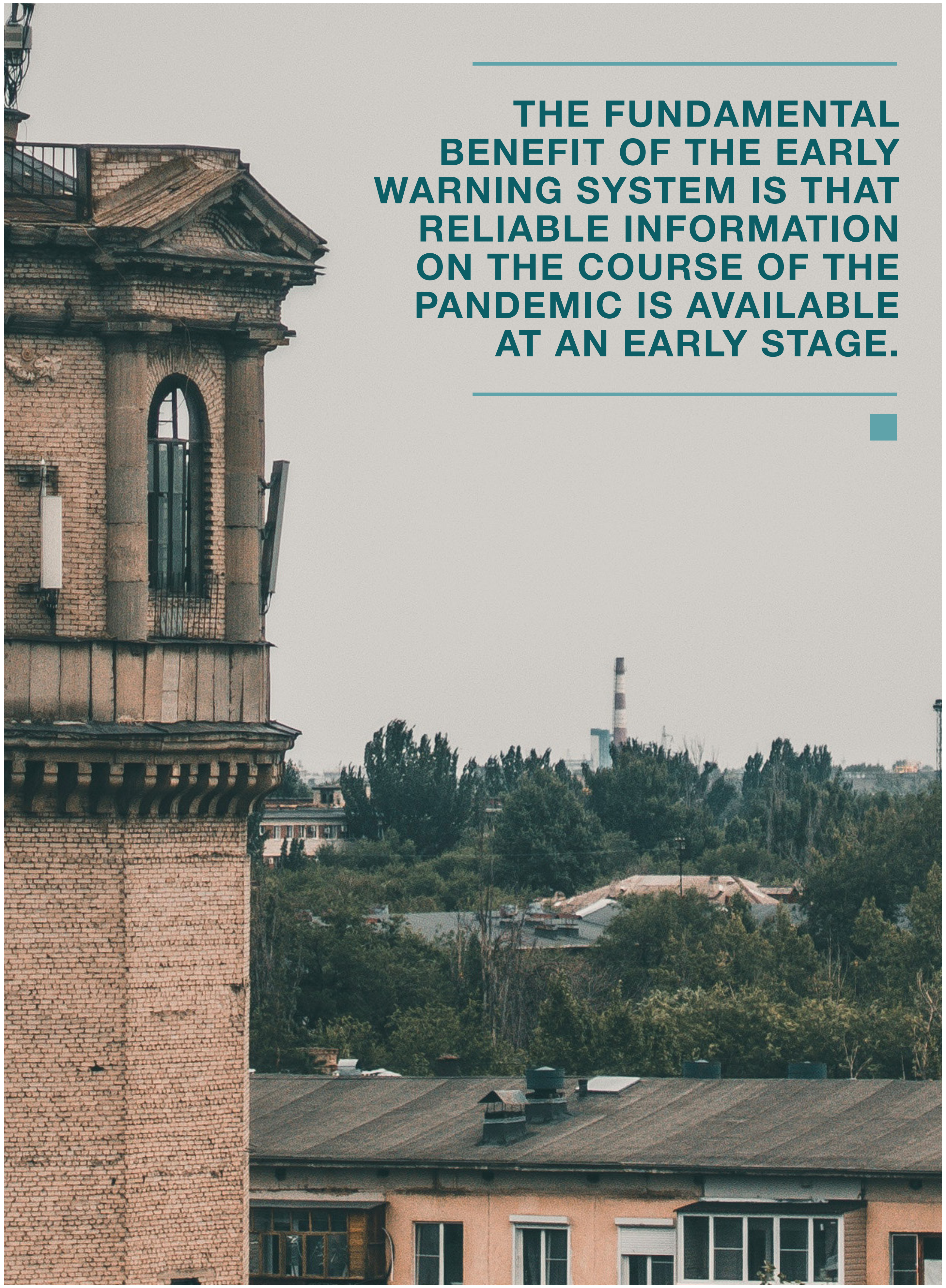
6.1. Impact Model Benefit

The fundamental benefit of the early warning system is that reliable information on the course of the pandemic is available at an early stage, which can be used to contain the exponential spread of infectious diseases. Specialists and government officials are thus more precisely informed about the epidemiological situation, which serves as a basis for decision-making both for pathogens already present in Switzerland and for those that could soon appear in Switzerland due to an epidemic/pandemic. In this way, sensible measures tailored to the situation (non-pharmaceutical interventions, vaccine provision) can be passed at an early stage. Epidemiological developments can also be processed and visualised in a comprehensible way via publicly accessible information platforms, from which the population can derive voluntary measures.

Why and how the information available is better and accessible at an earlier stage through an early warning system is specifically explained below for the main components of the early warning system.

6.1.1. Benefits Through Wastewater Monitoring

- **More efficient**: With just a few samples from the wastewater, a representative picture of up to approx. 450,000 inhabitants can be collected. This makes it easier to estimate the viral load in the population, i.e. the total amount of viruses released by the entire population into the catchment area or the sum of all individual viral loads of infected persons as well as the sum of the known viral variants. Since the viral load from the wastewater, according to experts, correlates well with clinically reported cases, the data from the wastewater can be used as a proxy for clinically reported cases. In this way, the wastewater can be used to test potentially large geographical regions and resources for clinical



PCR testing and sequencing can be targeted to where particularly high numbers of infections are detected. Other geographically limited or regional measures, too, such as targeted testing campaigns, partial lockdowns in certain regions, etc. can be better derived in this way.

- **Less bias**: Calculations of epidemiological metrics such as incidence or reproduction number based solely on clinical diagnoses are typically distorted because not all individuals are tested at the same rate. Samples from wastewater monitoring are not distorted by differences in clinical testing behaviour. On the one hand, symptomless cases can also excrete genetic material of the pathogen into the wastewater and thus be detected[76] , and on the other hand, infections of persons who do not get tested in the health care system despite symptoms are also recorded. This effect comes into play especially when no or only few clinical tests are available or when willingness to test in the population is low (e.g. when tests are associated with high costs or stigmatisation, commercial self-tests are widespread or with pathogens that lead to mild, unspecific or asymptomatic courses of disease). This makes it possible to better estimate a possible number of unreported cases, but also to check whether the incidence of disease is overestimated, if, for example, a testing infrastructure is rapidly expanded and many people get tested who were already infected in the preceding weeks.

- **Faster**: Studies from various countries show a time lead of five to 14 days for wastewater monitoring compared to the reporting of clinical cases. This time-related advantage is particularly large when the number of clinically conducted tests is low, e.g. in a pre-pandemic or post-pandemic phase.[77] For many pathogens, wastewater thus provides a more rapidly available assessment basis for the spread within the population.

Important: Despite its advantages, **wastewater monitoring** should be classified as **a complementary indicator and not as a substitute for clinical testing**. Versatile and complementary tools are needed to prevent and control epidemics and pandemics.

6.1.2. Benefits From Sequencing Wastewater and Patient Samples

- **Detection of variants of concern**: The sequencing of wastewater and patient samples can help with the detection of new variants of concern circulating in the population. Wastewater monitoring can infer the growth trajectory of pathogen variants in the entire population with just a few samples.[78]

- **Information on transmission pathways/dynamics through sequenced patient samples**: In addition to determining the pathogen (e.g. the viral variant), the sequencing of clinical samples can analyse transmission pathways/dynamics and clustering (local, regional), as a test result of a specific person can be placed in the larger socio-demographic context. For example, it can be traced whether an accumulation of infections in a hospital or a school is due to the fact that the persons have been infected by each other or outside. Depending on the situation, individual isolation/ closures can be more effective than collective lockdowns/closures; measures can for example be initiated locally for just one school or hospital. Sequencing thus offers a helpful tool for tracing transmission routes, especially if this is not possible via traditional contact tracing – for example, because a person has been in contact with several infected persons on average in the period between infection and development of the first symptoms, or in the case of a high number of unreported cases due to asymptomatic courses of the disease.

- **Tracking the severity of diseases**: By sequencing patient samples, it is possible to track whether infected individuals become more severely ill with new variants of a pathogen (e.g. viral mutations).

- **Monitoring the effectiveness of measures**: Information from the sequencing of patient samples can be used to better evaluate the effectiveness of prescribed measures: Is the correct vaccine being vaccinated? Are the traced transmission pathways effectively interrupted by the measures or not? By sequencing wastewater samples, measures can be tested for their effectiveness and it becomes comprehensible for a wide geographical area what influence the adoption and easing of measures have on the circulation of a virus variant.

- **Efficacy of vaccines against variants**: By sequencing a vaccinated but infected person, it is possible to determine which new variants the immune defence may not respond to.

6.1.3. Data Processing, Management, Analysis & Interpretation for Ordinance on Measures

- Ability to act through data processing: Even if important data from wastewater and patient samples are available, they only become useful to a government through rapid processing. The evaluation and analysis of the data provided by the early warning system is crucial so that they are not purely informative in nature, but can suggest concrete possibilities for action at the government level and, ideally, also voluntary changes in the behaviour of the population: In addition to official measures, contacts with at-risk persons could, for example, be voluntarily reduced in the event of the wide spread of a pathogen (cf. Chapter 6.1).

- Strengthening the trust between the population and the government: A data portal that is accessible to all and that shows the current epidemiological situation in a way that is easy to understand even for laypersons makes it easier to understand ordinances on measures by a government. In this way, the trust of the population in the government can be strengthened.

6.2. Narrow Definition of Benefits for Quantifiable Statements

The total benefit resulting from the different components of the early warning system according to Chapter 6.1 is difficult to quantify due to the different advantages and would go beyond the scope of this study. As already mentioned, the narrow benefit definition **only calculates the benefit of the early warning system in a first wave**. For quantifiable conclusions on the benefit of such a system, only one aspect of the benefit of wastewater monitoring is mapped for simplification, namely that a government can prescribe measures earlier due to the earlier detection of epidemiological trends of known pathogens in wastewater. This means that the first pandemic wave can be broken and flattened earlier. On this basis, the benefits of the less clearly quantifiable benefit aspects of the early warning system (especially sequencing), too, are estimated.

According to current studies on SARS-CoV-2, it is generally assumed that wastewater monitoring has an information advantage of five to 14 days over clinical tests.[79] According to the experts interviewed by Pour Demain, the maximum value of two weeks would be too high an estimation in a situation where many PCR tests have already been carried out and the tests can also be evaluated quickly. However, the study is based exclusively on the scenario of a first pandemic wave, in which 14 days is appropriate as the maximum time lead: At this point, people do not get tested as often (e.g. because tests are not yet available, the government has not yet introduced comprehensive testing campaigns and/or the tests cannot yet be evaluated as quickly as at a later point in the pandemic[80]). The lead in time and information depends on the individual pathogen. For example, researchers estimated a time lead of 17 days for influenza viruses in wastewater in Ottawa.[81] Based on this information, the present study assumes that pathogens can be detected in wastewater a maximum of 14 days earlier.

However, in discussions with Pour Demain, FOPH experts did not consider it realistic that measures could be implemented two weeks earlier on the basis of a single indicator. Other factors also influence the implementation of measures: e.g. the political will to introduce restrictive measures and the actual compliance of the population with the measures. The study therefore takes into account that time elapses before a package of measures is defined and passed, and assumes a realistic time **lead of five to 10 days for an earlier ordinance on measures**.

Instead of a lockdown, various other non-pharmaceutical measures could also be adopted, because in particular thanks to wastewater monitoring, it will be easier to decide on regionally specific measures as a targeted alternative to national lockdowns in a special/extraordinary situation (cf. Chapter 6.1.1). Also for reasons of simplification and in order to be able to determine the effect of the earlier introduction of measures as cleanly and clearly limited in time as possible, **only the lockdown imposed in spring 2020 is considered and no other measure**. In principle, it can be assumed that with an institutionalised early warning system that continuously monitors the epidemiological situation, i.e. also in a normal situation, restrictive measures such as lockdowns are less likely because the infection curve can be flattened at the beginning of a wave through the earlier introduction of less drastic strategies such as a mask requirement and geographically specific measures.

This narrow definition of benefits **ignores** a number of other benefits that are undoubtedly central to a pandemic early warning system but are difficult to quantify **in the context of this study**:

- Discovery of globally novel, potentially pandemic pathogens for the first time in Switzerland (discovery of local outbreaks in the normal situation)
- Detection of direct transmission in local outbreaks (schools, hospitals, etc.)
- Monitoring of the severity of disease progressions with new pathogen variants
- Public health benefits of an epidemiological surveillance system in the normal situation, for example for monitoring antibiotic resistance, drugs (addiction monitoring)[82] or pharmaceuticals in wastewater[83]
- Benefit of an entire pandemic consisting of several waves
- Benefits for vaccine production, adaptation and the purchase of vaccines[84]
- Voluntary implementation of measures through a publicly accessible information platform that is comprehensible to laypersons and continuously documents the epidemiological

situation.
- More targeted ordinance, earlier lifting or even avoidance of restrictive measures through location- and/or group-specific, close to real-time information on the course of the pandemic. This reduces the economic damage caused by official measures.[85]
- Reduction in deaths and illnesses due to fewer necessary medical treatments such as operations being postponed

6.3. Estimation of the Benefit

A quantity and value structure serves as the basis for estimating the benefits in the first wave (cf. also Appendix A.1). For the calculation of the benefit, the study makes conservative assumptions in each case, i.e. in the case of different data or estimates, the more conservative assumption is used. Furthermore, only the benefit of a first wave is depicted. The **benefit of the early warning system is calculated as avoided damage in francs**.

Three aspects are calculated:

1. Avoided production costs as a result of avoided work absences due to lower infection rates
2. Avoided health care costs due to fewer hospitalisations, fewer IPS patients and fewer long COVID-like cases or long-term health problems.
3. Avoided intangible costs due to fewer deaths

6.3.1. Time Factor

In principle, the right time is decisive in combating a pandemic outbreak. If the exponential increase in infections can be stopped early on, instead of reacting only when the number of cases is high or hospitals are overcrowded, serious economic and social consequences of the pandemic can be avoided. Thus the earlier a government knows about an outbreak, the better.

Since time elapses between an infection and the appearance of the first symptoms (incubation period) and the detection in the health care system, the automatic detection of infections in wastewater is more suitable for the early detection of pathogens, especially when tests are performed only rarely and there are delays in clinical reporting (cf. Chapters 6.1.1 and 6.2). As mentioned in Chapter 6.1.1, the present study assumes a time lead of five to 10 days.

6.3.2. Decision on Measures and Implementation

Reliable and early information on the course of the pandemic can support decision-makers in the health sector, the economy and politics, scientists and private individuals. However, this study only calculates the benefits for the economy and society that can be achieved by the authorities through earlier or more targeted measures. In reality, part of the population would also – thanks to the information on infection events on the publicly accessible data platform – voluntarily implement precautionary measures earlier and/or otherwise contribute positively to the containment of the pandemic (cf. Chapters 6.1 and 6.2).

6.3.3. Benefit Calculation in Six Steps

The calculation of benefits in the first wave is done in six steps for the three scenarios COVID-19, "severe" and "extreme" pandemic.

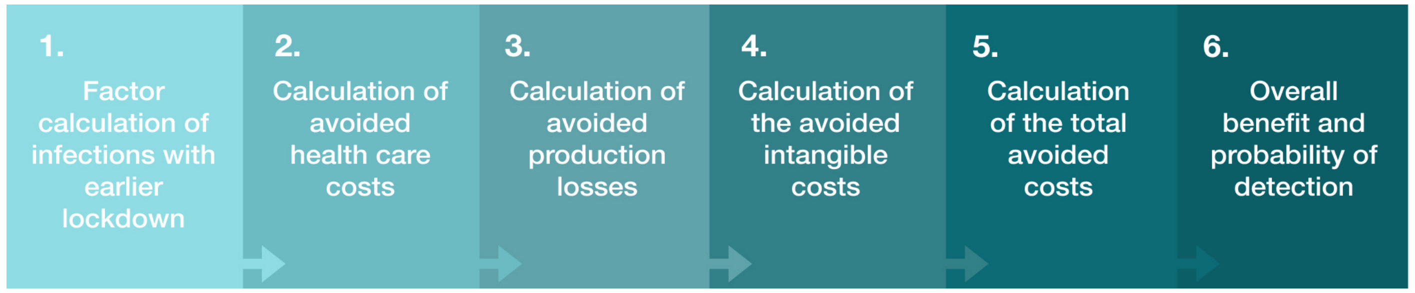


Figure 3: The Six Steps of Benefit Calculation

Step 1: Factor Calculation of Infections With Earlier Lockdown

In the first step of the benefit calculation, it is determined how many infections can be avoided in a first pandemic wave if the lockdown is not introduced on day 23 (corresponds to 17 March 2020 in the COVID-19 scenario), but earlier. For this purpose, the study simulates the cumulative number of infections using the Renewal Equation formula (cf. Chapter 4.2.2) for variants a) without earlier lockdown, b) with lockdown starting five days earlier, c) with lockdown ten days earlier. The comparison of variants a) and b) and a) and c), respectively, results in a factor that describes how many fewer people would be infected. A factor of two, for example, would mean that two times fewer people would be infected due to an earlier lockdown. Accordingly, with an earlier lockdown, half of the infections could be avoided. The simulation is calculated over a period of 70 days. This period is rounded up from the time between the outbreak of the COVID-19 pandemic in Switzerland (on 24 February 2020) to the end of the lockdown (26 April 2020). Furthermore, this also ensures that the simulation only stops when R is stably below one for several weeks and the period of exponential infections is thus over.

For the three scenarios COVID-19, "severe" and "extreme" pandemic, the reproduction number R, generation time, the time until R falls to 0.9, and the definitions of the simulations are taken from Chapter 4.2.2.

COVID-19-PANDEMIC COURSE FIRST WAVE, EARLIER INTRODUCTION OF MEASURES

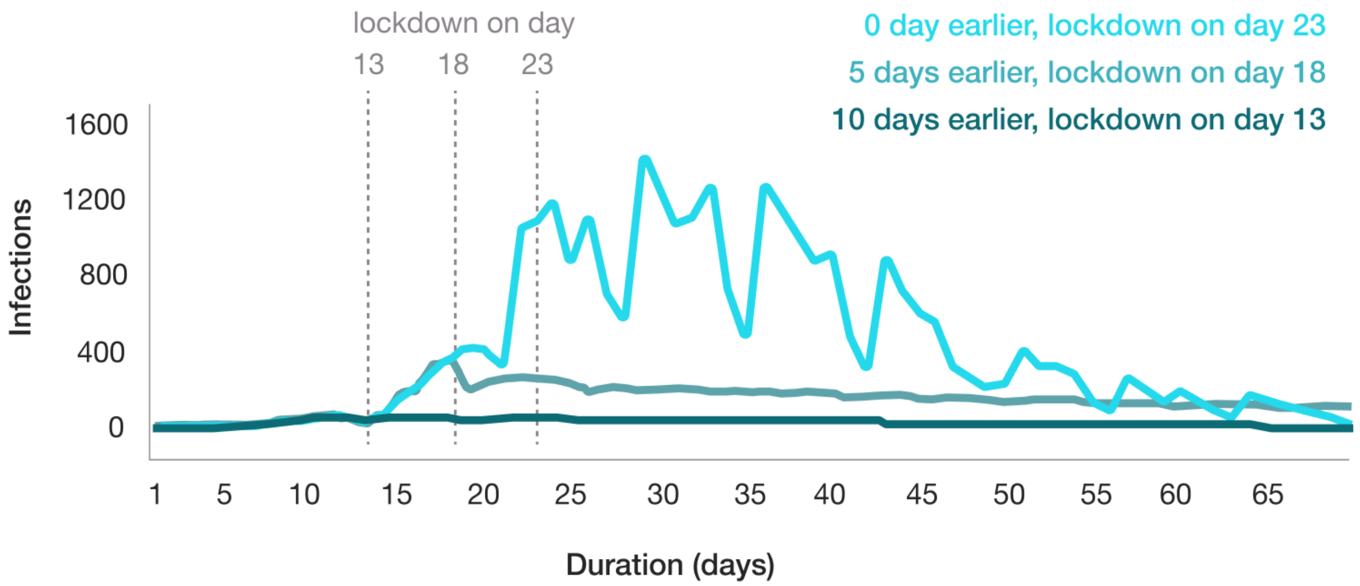


Figure 4: COVID-19 Pandemic Progression of the First Wave, Earlier Introduction of Measures

For the **COVID-19 scenario**, the real infection figures of the first 23 days until the introduction of the lockdown are used, and in the "0 days earlier" scenario all data up to day 70 according to the FOPH COVID-19 dashboard86.

For the other **pandemic scenarios ("severe", "extreme")**, the infection numbers are simulated on the basis of six consecutive days with a predefined rate of increase (cf. Chapter 4.2.2).

Factor COVID-19 Scenario

As Figures 4 and 5 show, the infection curve can be flattened if a lockdown is introduced five or 10 days earlier. The infections within the 70 days considered (defined period of the first wave, cf. Chapter 4.2.2) decrease by a **factor of 2.8** with an introduction five days earlier, and even by a factor of **11.2** if the lockdown is introduced ten days earlier.

Expressed as a percentage, a lockdown five or ten days earlier leads to a reduction in the number of infections by 65% and 91%, respectively. For comparison: Althaus et al. 2020 calculate a factor of 1.25 per day of earlier introduction[87], which, calculated over five or ten days, results in a factor of 3.1 (1.25^5) or 9.3 (1.25^10). Another study in England by Arnold et al.88 comes to a similar conclusion with a reduction of 74% and 93%, respectively, of COVID-19 infections with a one-week and two-week earlier lockdown .

The early warning system has an additional benefit, particularly through sequencing, which cannot be quantified precisely. The study assumes that this factor, which results solely from a benefit aspect of the wastewater monitoring, increases again by a conservatively calculated 10%. For the early warning system with wastewater monitoring and sequencing, this results in a factor of **3.1** for five days and **12.3** for 10 days.

AVOIDED INFECTIONS, EARLIER LOCKDOWN, FIRST WAVE, COVID-19

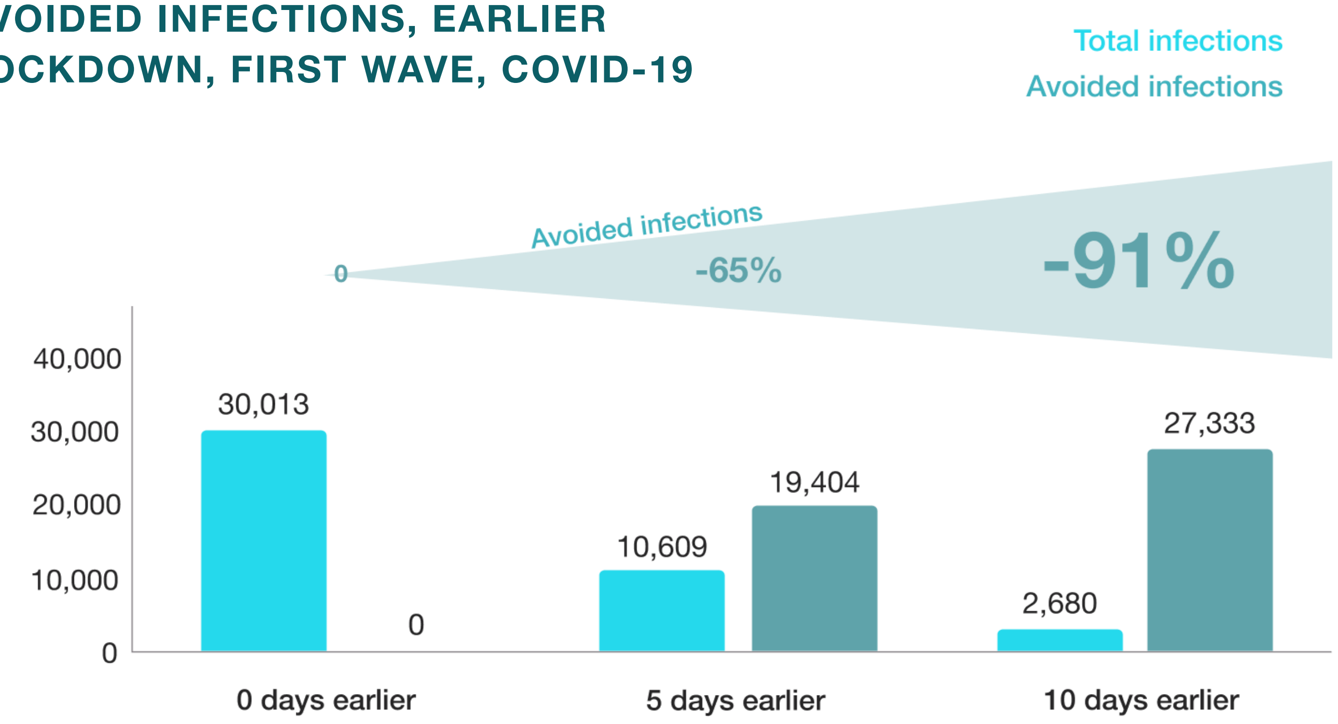


Figure 5: Infections Avoided in the Period of the First Wave, COVID-19

For the pandemic scenarios "severe" and "extreme", which are more serious than COVID-19, a higher R-value and a shorter generation time are assumed (see Chapter 4.2.2). Furthermore, it is assumed that the R-value can also be brought below one in these scenarios as with COVID-19, i.e. the exponential spread of infections can be controlled by introducing measures.

COURSE OF "STRONG" AND "EXTREME' PANDEMICS, EARLIER INTRODUCTION OF MEASURES

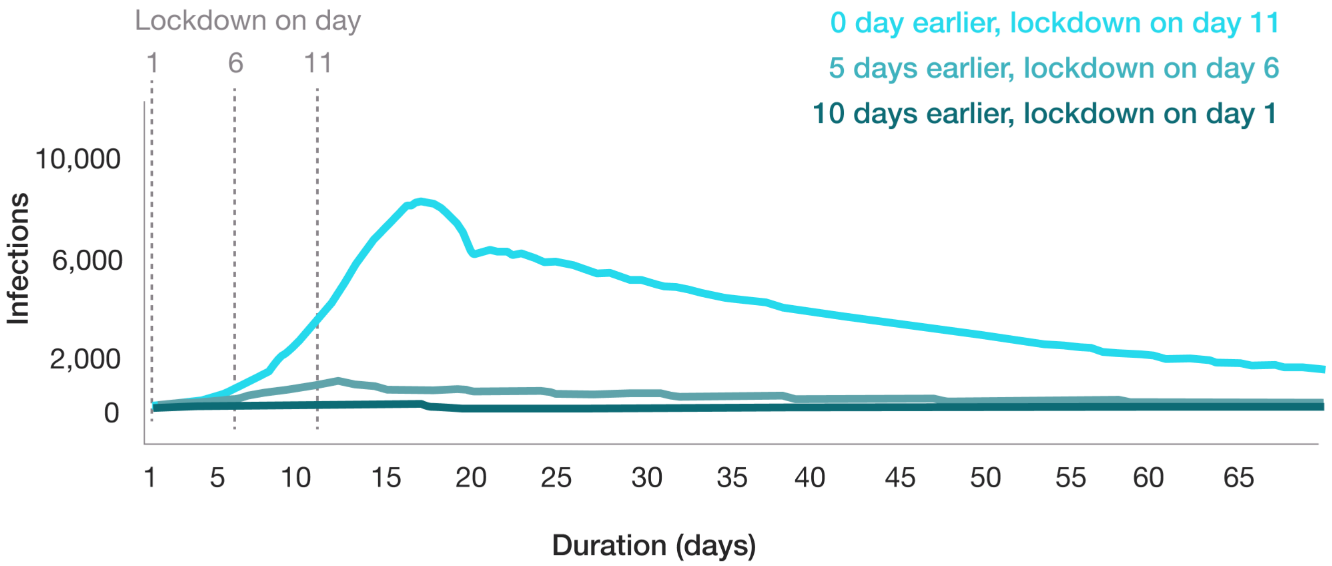


Figure 6: Course of "Strong" and "Extreme" Pandemics in the First Wave, Earlier Inctrduction of Measures

Factor Scenario "Strong" and "Extreme" Pandemics

As Figures 6 and 7 show, the discrepancy between the number of infections when measures are introduced earlier is even greater than in the COVID-19 scenario, as the infection curve rises faster. Accordingly, a higher **factor of seven and 41.5, respectively, is the result if a lockdown were introduced five and 10 days[89] earlier, respectively**. Including the additional benefit of 10 % through sequencing, the factors are 7.7 and 45.7 .

INFECTIONS AVOIDED, EARLIER LOCKDOWN, FIRST WAVE, "STRONG" AND "EXTREME" PANDEMICS

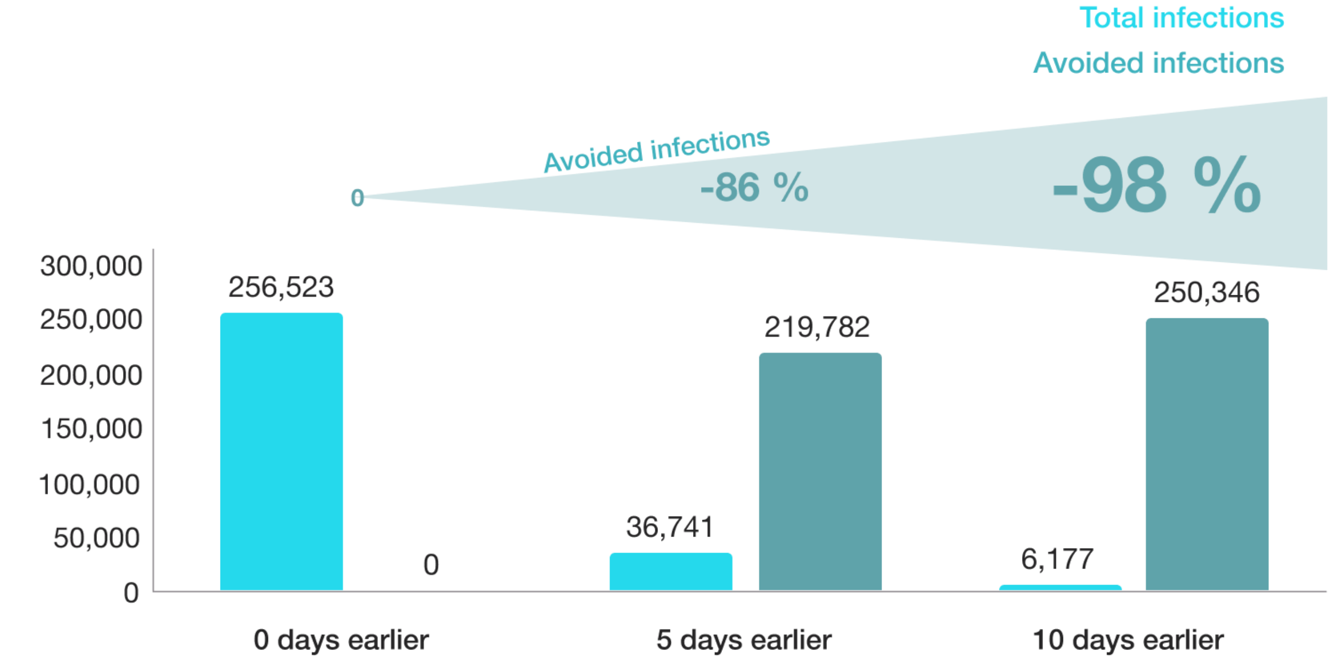


Figure 7: Total Number of Infections, First Wave, "Strong" and "Extreme" Pandemics

Step 2: Calculation of Avoided Health Care Costs

With regard to health care costs, the study considers the costs incurred for hospitalisation, hospitalisation in an intensive care unit and the health care costs per long Covid case or for any long-term consequences. For the costs per hospitalisation and in intensive care units, 7,000 and 100,000 francs, respectively, are assumed according to information from Santésuisse.[90] For the health care costs associated with long COVID or long-term illnesses, a conservative value of 8,500 francs is assumed.[91]

The avoided health care costs result from the sum of the different aspects in the following quantity and value structure:

Aspects of healthcare costs	Values	Costs	Quantities
Costs per hospitalisation	Avoided hospitalisations	CHF 7'000	Number of avoided hospitalisations: • Share of hospitalised persons • Avoided infections
Costs per patient in intensive care units	Avoided stays in intensive care units	CHF 100'000	Number of avoided stays in intensive care units (IPS): • Proportion of IPS patients in hospitalised patients • Hospitalisations avoided
Cost per long COVID case	Avoided long COVID cases or long-term illnesses	CHF 8'500	Number of long COVID cases avoided: • Proportion of long COVID in infected persons • Avoided infections

Step 3: Calculation of Avoided Production Losses

Production losses are calculated using the average **cost of a lost working day** and the **duration of work loss per infection**. For the calculation, the **assumption of an average of five days of lost work is made**[92] . In the case of an influenza infection, the average number of lost working days across all infected persons is 3.2.[93] Furthermore, the costs per lost working day are estimated at 360francs.[94]

The avoided production losses are calculated from the following quantity and value structure:

Values	Costs	Quantities
Costs per lost working day	CHF 360	Number of lost working days: • Avoided infections • Number of working days lost per infected person

Step 4: Calculation of the Avoided Intangible Costs

Intangible costs are calculated exclusively on the basis of the **number of years of life lost**. Other intangible costs, such as avoided economic costs, are not taken into account. For the calculation, it is assumed that the value of a lost life year is constant, i.e. independent of the contribution the life year of a deceased person would have made to society and the economy. Furthermore, based on the COVID-19 scenario, the same number of life years lost is assumed for "severe" and "extreme" pandemics, although this number would probably to be higher. Based on the National Covid Science Task Force[95], the study assumes **six years of life lost for** deceased persons and a monetary value of 175,000 francs for one year of life[96].

The avoided intangible costs are calculated from the following quantity and value structure:

Values	Costs	Quantities
Value of a lost year of life	CHF 175'000	Number of years of life lost that are avoided: • Avoided deaths • Years of life lost per death

Step 5: Calculation of the Total Avoided Costs

Adding up the avoided health costs, production losses and intangible costs.

Step 6: Overall Benefit and Probability of Detection

The total avoided costs calculated in step 5 correspond to the benefit of the early warning system, provided it is actually effective for the pathogen concerned. This is the probability of detection (cf. Chapter 4.4).

The total benefit is equal to the total avoided costs multiplied by the probability of detection.

6.4. Benefits of Wastewater Monitoring vs. Benefits of Sequencing/Other Aspects of the Early Warning System

The study assumes that with the early warning system, measures can be implemented earlier and in a more targeted manner. The benefits of wastewater monitoring and sequencing as well as other non-quantifiable aspects of the early warning system are considered in isolation. The benefit of sequencing/other aspects of the early warning system excluding wastewater monitoring was not simulated separately. It corresponds to the difference between the total benefit and the separate benefit of wastewater monitoring.

6.5. Overall Benefit Early Warning System

The first wave of a pandemic serves as the basis for calculating the benefit of an early warning system. The calculation is based on the proportion of the population that is infected within the lockdown period.

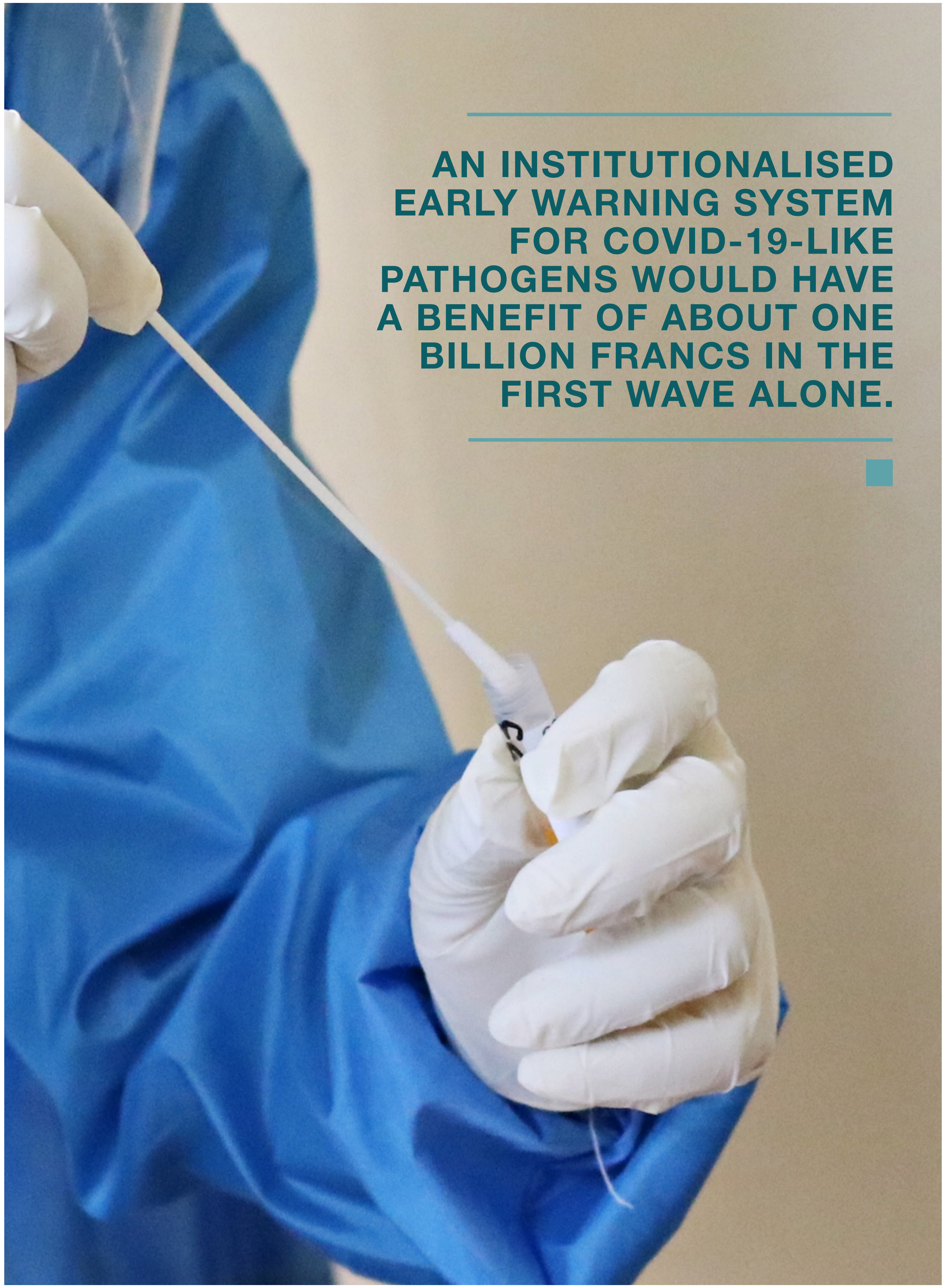
As explained in Chapter 4.4, the study assumes an early warning system that has a probability of detection of 80%. For an early warning system that would cover more than five pathogens, the benefit would be correspondingly greater.

6.5.1. Benefit With Ordinance on Measures Five Days Earlier

The table below presents the results for the COVID scenario as benefits from wastewater monitoring and benefits from sequencing, with the underlying assumption that measures are prescribed five days earlier based on the information gained from wastewater monitoring and sequencing.

- Overall, an institutionalised early warning system for pathogens **with COVID-19-like pandemic severity would have a benefit of approximately one billion francs in the first wave alone**.

Benefit (Five Days Earlier): COVID Scenario, First Wave	
First wave	Benefits of an institutionalised early warning system
Benefit	CHF 1'074'000'000



AN INSTITUTIONALISED EARLY WARNING SYSTEM FOR COVID-19-LIKE PATHOGENS WOULD HAVE A BENEFIT OF ABOUT ONE BILLION FRANCS IN THE FIRST WAVE ALONE.

- In the **"extreme" scenario, an early warning system has a benefit of around 31 billion francs**, which is almost 31 times higher than in the COVID-19 scenario. Since it cannot be assumed that the next pandemic will be exactly like COVID-19, but could also affect younger people – in addition to more senior citizens – more severely[97], an even higher benefit can be expected for the next pandemic, comparable to the "severe" and "extreme" scenarios.

Benefit (Five Days Earlier): Different Scenarios According to Severity, First Wave		
First wave	Severe	Extreme
Benefit	CHF 15'794'000'00	CHF 31'397'000'000

- The avoided **intangible costs** (years of life lost) represent the greatest benefit at – depending on the scenario – **958 million to around 30 billion francs**.

Benefits (Five Days Earlier): According to Avoided Costs and Different Scenarios by Severity, First Wave			
Scenario	Health costs	Production losses	Intangible costs
COVID-19 pandemic	CHF 88'000'000	CHF 28'000'000	CHF 958'000'000
"severe" pandemic	CHF 604'000'000	CHF 256'000'000	CHF 14'934'000'000
"extreme" pandemic	CHF 1'273'000'000	CHF 256'000'000	CHF 29'868'000'000

6.5.2. Benefit With Ordinance on Measures 10 Days Earlier

If measures were introduced ten days earlier, the benefit would increase even more.

- In a **COVID-19-like pandemic context**, this would amount to more than **1.4 billion francs** in the first wave.
- For the **"severe" and "extreme" scenarios, the benefits are around 18 billion francs and 35 billion francs, respectively**.
- The avoided intangible costs (years of life lost) represent the greatest benefit with – depending on the scenario – **1.3 to 33.5 billion francs**.

Benefit (10 Days Earlier): COVID-19 Scenario, First Wave	
First wave	Benefits of an institutionalised early warning system
Benefit	CHF 1’462’000’000

Benefit (10 Days Earlier): Various Scenarios, First Wave		
First wave	severe	extreme
Benefit	CHF 17’754’000’000	CHF 35’293’000’000

Benefits (10 Days Earlier) by Avoided Costs and Different Scenarios by Severity, First Wave			
Scenario	Health costs	Production losses	Intangible costs
COVID-19 pandemic	CHF 119’000’000	CHF 39’000’000	CHF 1’304’000’000
“severe” pandemic	CHF 679’000’000	CHF 288’000’000	CHF 16’787’000’000
“extreme” pandemic	CHF 1’431’000’000	CHF 288’000’000	CHF 33’574’000’000

6.6. Significance of Quantification

The results of the quantification are to be understood as approximations. Both the calculation logic and the underlying data are subject to uncertainties and are partly based on assumptions (cf. Chapter 4 and tables in Appendix A.1.).

In order to evaluate the benefits, they are compared with the costs in the following chapter.

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76 Fernandez-Cassi et al. 2021.

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85 The prevented economic damage is calculated in the benefit model only on the basis of work absences due to illness (cf. 6.3) and therefore does not include absences due to deaths or Long-COVID-like illnesses.

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7.

Synthesis and Assessment of the Benefit-Cost Balance Synthesis and Assessment of the Benefit-Cost Balance

For the benefit-cost balance the total costs for the time horizon of 37 years are compared to the total benefits (= avoided costs) within the first wave. This underestimates the balance; however, this calculation takes into account the fact that an institutionalised early warning system should not only be in operation during a pandemic wave or in a special/extraordinary situation, but in all situations and therefore incurs annual costs.

BENEFIT-COST BALANCE, COVID-19 SCENARIO

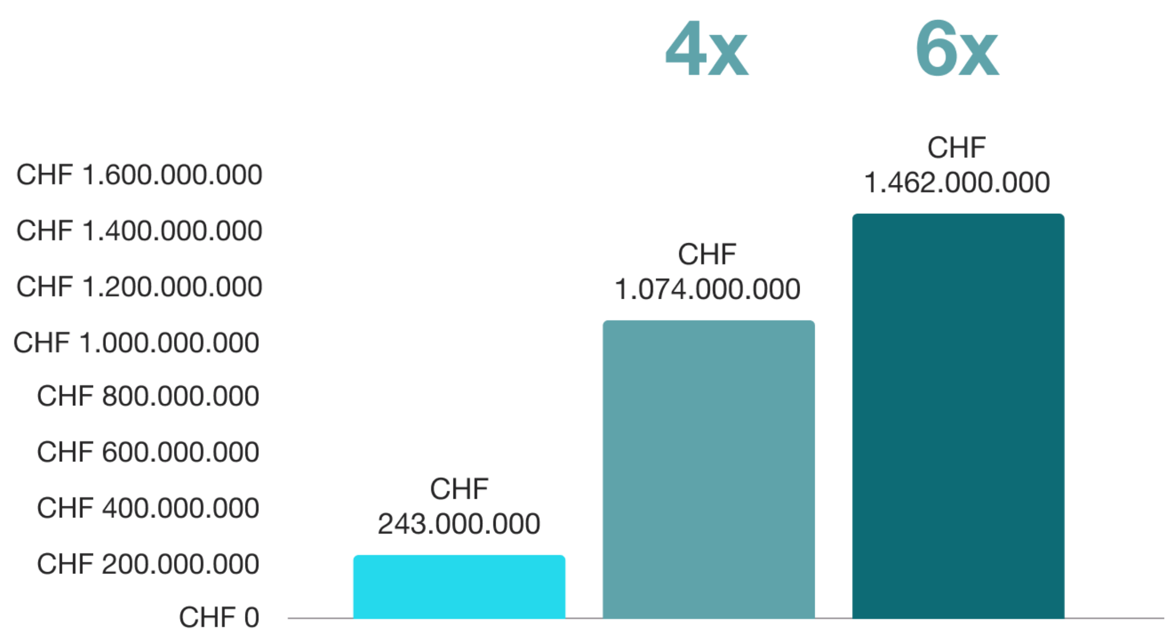

Figure 8: Benefit-Cost Balance, COVID-19 Scenario

BENEFIT-COST RATIO, 5 DAYS EARLIER

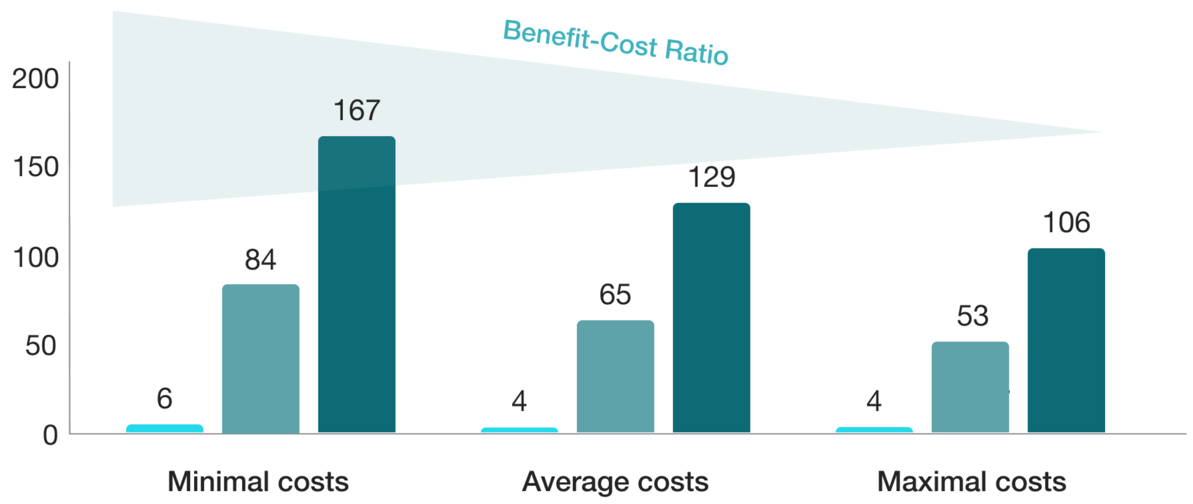

Figure 9: Benefit-Cost Ratio, Different Scenarios, With Five Days Earlier Lockdown

- The graphs below (Figures 9 and 10) show that **the benefits in a COVID-19 scenario are on average four and six times higher, respectively, than the costs of** operating an early warning system **if measures are introduced five and ten days** earlier, respectively.

Depending on the severity of the pandemic, whether measures are prescribed five or ten days earlier and whether the minimum, average or maximum costs are assumed, different factors result for the benefit-cost ratio .

- Even in the case that the costs for the institutionalised early warning system are at a maximum and a lockdown can only be imposed five days earlier, a **factor of 4** results for the **COVID-19 scenario (cf. Figure 9). The factor is significantly higher in a “severe” and “extreme” pandemic scenario at 53 and 106, respectively. At medium costs, the benefit is four times higher in a COVID-19-like pandemic, 65 times higher in a “severe” pandemic and even 129 times higher in an “extreme” pandemic**.

BENEFIT-COST RATIO, 10 DAYS EARLIER

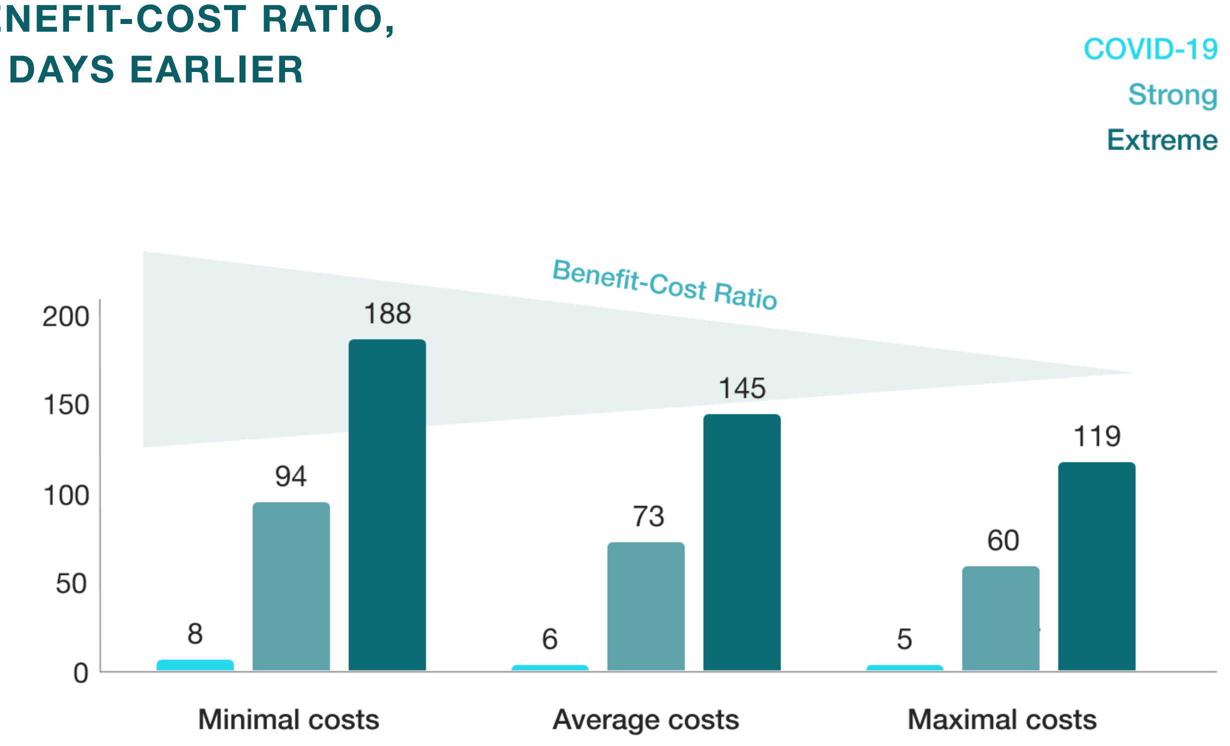

Figure 10: Benefit-Cost Ratio, Different Scenarios, With Lockdown 10 Days Earlier

- The benefit-cost balance **increases with the introduction of** a lockdown 10 days earlier and lies at **8 in the** best case, i.e. with minimal costs. In an extreme pandemic, the **factor is 188** (cf. Figure 10).

The benefit-cost balance shows that the investment in an institutionalised early warning system is worthwhile, even if the information advantage gained through it about the epidemiological situation is reflected in an ordinance on measures issued only five days earlier.

Assuming medium costs, the benefit is a minimum of four to a maximum of 129 times higher than the associated costs. In a COVID-19-like pandemic, each franc invested achieves a benefit of around four francs, and in extreme pandemic scenarios even up to 129 francs.

Regardless of the costs, **the balance with a benefit comparison that does not only refer to the first wave but depicts an entire pandemic is likely to be many times higher**. In addition, there are other factors that increase the expected benefit but cannot be quantified precisely and were therefore excluded from the calculations in this study (e.g. non-pandemic public health benefits through the monitoring of antibiotic resistance, benefits in the normal situation outside of pandemic peak phases, etc., cf. chapter 6.2).

8.

Conclusions and Recommendations[98]

Early detection and monitoring of dangerous pathogens and variants in wastewater and via reporting systems from hospitals/doctors' practices will continue to be essential for the protection of the Swiss population in the future.

The present study shows that investments in regular wastewater monitoring and ongoing decoding of pathogens with a COVID-19-like extent of damage are worthwhile four to eight times over in the long term. In the case of a higher extent of damage in a **"severe" or "extreme" pandemic, the investments are even more worthwhile: for every franc invested, 53 to 94 or 106 to 188 francs are saved, respectively** (cf. Chapter 7). Thanks to the early warning system, potential damage can be greatly reduced in the special and extraordinary situation during a pandemic. Since the study only calculates a small part of the benefits, it can be assumed that the actual benefits are much higher.

In a normal, pre-pandemic situation, regular surveillance of pathogens generates potential benefits that could not be quantified further within the scope of the study. Regular surveillance can detect the spread of pandemic pathogens at an early stage and thus significantly reduce the risk of disease outbreaks in Switzerland. Although international warnings that a pandemic is also heading towards Switzerland allow certain precautions to be taken, without an early warning system already in operation there is no head start in assessing the actual situation in the country.

INVESTMENTS IN AN INSTITUTIONALISED EARLY WARNING SYSTEM FOR PATHOGENS WITH A COVID-19-LIKE DAMAGE SEVERITY PAY OFF FOUR TO EIGHT TIMES OVER IN THE LONG TERM.

The following recommendations can be derived from the results of the study:

- **Institutionalising wastewater monitoring:** The early detection and monitoring of communicable diseases with the help of wastewater should be extended to other pathogens and implemented in the long term.
- **Institutionalising the sequencing of pathogens:** Pathogens with pandemic potential should be sequenced regularly.

Faster Measures With the Help of the Early Warning System

The study shows that ordering targeted measures as quickly as possible can drastically reduce human and economic damage. This in turn requires rapid decision-making processes on the part of cantonal and national government officials. Accordingly, the following recommendations are made:

IMPROVE DATA FLOW BETWEEN LABORATORIES AND DATABASES

In future, cantonal, national and international data exchange between databases and laboratories must be guaranteed and, if possible, be enabled in real time (sequence databases, genome databases, etc.). The **roles and the expected information gain from the existing data platforms** (e.g. SPSP, Nextstrain, CovSpec) as well as integration of patient and wastewater data for the central information platform EPI must be clearly defined, taking data protection into account.

FURTHER DEVELOP DECISION-MAKING BASES FOR THE EXECUTIVE BRANCH

The capacities within the FOPH to interpret data from the early warning system should be further developed for the timely formulation of appropriate bases of decision-making.

MAKE THE MOST IMPORTANT DATA ACCESSIBLE TO ALL

Epidemiological data should be presented in a user-friendly manner and be easy to read for the general public, so that Swiss citizens can implement their own measures voluntarily and at an early stage, depending on the situation, before official measures are taken or even without official requirements.

STRENGTHEN LABORATORIES

Sequencing should be made more cost-effective and and the turn-around time of sequencing machines needs to be shortened.

Qualitative Recommendations Going Beyond the Scope of the Study

Furthermore, the following qualitative recommendations for an institutionalised early warning system have emerged that go beyond the narrow benefit-cost balance of the study:

- **Monitor antibiotic resistance in wastewater:** Wastewater monitoring can contribute to the containment of antibiotic resistances as "silent pandemics" in that resistances in wastewater are continuously monitored and targeted measures are prescribed on this basis. According to experts, wastewater samples could be tested for antibiotic resistance without major adjustments to the existing procedure. This would not only make it possible to monitor more efficiently which currently harmless but potentially dangerous resistances are already present in the population, but also to derive targeted measures. For example, an adaptation of the national prescription guidelines could be considered, in which it would, for instance, be defined which other alternative antibiotics can be used. Furthermore, the antibiotic concentration in the water can be recorded at the same time in order to check how efficiently wastewater treatment plants break down antibiotics, which in turn has an influence on the development of resistance. Since highly resistant strains are often imported from abroad, especially if people have been hospitalised there[99], it is particularly advisable to detect these strains in wastewater treatment plants in tourist regions and near airports, and possibly also in the wastewater of specific facilities (airports, hotels, asylum centres, etc.). In line with the federal government's Strategy on Antibiotic Resistance[100] , specific monitoring of wastewater in animal production facilities is also recommended. Today, about 300 people die in Switzerland every year because of antibiotic-resistant bacteria – for comparison: According to the Federal Statistical Office, 200 people die in traffic every year[101]. The trend is worrying; between 2010 and 2019, deaths caused by antibiotic resistance increased by 64%[102] The WHO considers antibiotic resistance a global threat for which better data is urgently needed.[103] The surveillance of antibiotic resistance would promise benefits both nationally and internationally.

- **Generate benefit-cost-efficient data:** Defining the necessary number of WWTPs and samples to be collected and sequenced weekly for a rapid and accurate assessment of the epidemiological situation is a scientific issue that needs to be addressed as soon as possible. For this, a maximally accurate and at the same time cost-effective method of data collection, processing and interpretation should be applied in the future, for which national standards will be defined. International best practices should also be taken into account ie Definition der notwendigen Anzahl von ARA und Proben, die wöchentlich für eine schnelle und akkurate Einschätzung der epidemiologischen Lage entnommen und sequenziert werden müssen, ist eine wissenschaftliche Frage, die möglichst schnell angegangen werden muss. Hierfür sollte künftig eine maximal präzise und gleichzeitig kosteneffiziente Methode der Datenerhebung, -verarbeitung und -interpretation zur Anwendung kommen, wofür nationale Standards definiert werden. Dabei sind auch internationale Best Practices zu berücksichtigen.

- **Promote Sentinella reporting system:** Only with the help of different surveillance elements can Switzerland establish a differentiated early warning system. The syndromic surveillance of pathogens via hospitals and doctors' practices should be developed further (including via a doubling and representative distribution of doctors' practices and a rapid adaptation of the reporting form for new pathogens).

- **Include animal disease control:** In view of the increasing importance of the One Health approach for pandemic preparedness[104] , outbreaks of animal diseases should also be monitored more closely, e.g. metagenomically. The corresponding findings should flow into a central data platform such as SPSP.

- **Invest in pathogen-agnostic technologies:** Metagenomic, pathogen-agnostic sequencing methods for the early detection of entire pathogen families and thus potentially worrying, as yet unknown pathogens should be promoted. It is important to define pathogens from individual cases with timely sequencing and a central database where the data can be processed and analysed (e.g. SPSP).

- **Strengthen the use of pandemic tools:** Modelling in favour of predictive scenarios should be used as a standard tool for regular scenario exercises and benefit-cost assessments of measures or for decision-making processes (e.g. modelling by Daedelus, Imperial College[105]).

- **Institutionalise genomic data platform:** In the long term, Switzerland should be able to have a genomic data platform (e.g. Swiss Pathogen Surveillance Platform).

- **Support international surveillance and response:** Switzerland's early warning system depends on international data on pathogens. Even in the normal situation, access to epidemiological data from neighbouring countries and bases for productive cooperation in crisis situations should be guaranteed.

- **Exchange best practices on pandemic early detection internationally:** With the proposed institutionalisation of an early detection system, Switzerland would become one of the world's leading countries in this field. Swiss federal authorities and researchers could bring the relevant findings to international bodies so that other countries can benefit from Switzerland's wealth of experience.

- **Promote rapid political decision-making processes and inclusion of science in crisis management:** The benefits of early detection and surveillance of diseases depend heavily on how quickly measures are taken. Accordingly, timely analyses, interpretations and decision-making processes on the part of the government regarding the most appropriate measures for the specific situation are crucial.[106] The potential of science can be better exploited in the fight against a pandemic in the future by creating "foundations for a culture of trusting cooperation between science, administration and politics"[107] . Examples of this could be adapted legal provisions, but also joint training and exercises of scientists and crisis management experts[108] or the transformation of the scientific advisory board for the COVID-19 pandemic into a permanent body[109].

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A. Appendix

A.1 Basic Data Benefit Calculation

COVID-19 Scenario, Five Days Earlier[110]

Basic Data	Reference value	Value (scenario COVID-19)	Unit	Comment and sources for COVID-19 figures
Benefits of wastewater monitoring				
Trends detectable earlier		Up to 2	Weeks	e.g. Kumar et al. 2022
Decision by authorities on measures possible earlier		5	Days	Acceptance
Infected, hospitalised, deaths				
Population		8,738,800	People	
Proportion infected	Population	0.34 %		Covid statistics BAG, special situation
Number infected		29,313		Covid statistics BAG, special situation
Proportion of infected persons with hospital treatment	Infected	13.6 %		Covid statistics BAG, special situation
Proportion of hospitalised persons with treatment in intensive care	Hospitalised	27.5 %		Covid statistics BAG, special situation
Number of hospitalised		3,991		Covid statistics BAG, special situation
Number of deaths		1,689		Covid statistics BAG, special situation
Proportion of deaths	Infected	5.76 %		Covid statistics BAG, special situation
Proportion of Covid-infected people with long COVID	Infected	10 %		National Covid Science Task Force 2022
Number of people with long COVID		2,931	People	Estimate based on Hanson et al. 2022.
Infections, hospitalisations, deaths if lockdown 2 days earlier	1-factor x less of each variable	2.8	for variable	Factor for wastewater monitoring, which was calculated with Python according to the formula of Flaxman et al. 2020.

110 - For the other scenarios, the values for "infected, hospitalised, deaths" change according to the damage values listed in Chapter 4.2 as well as the factors according to the Python simulations in Chapter 6.3.3, Step 1.

Health costs				
Costs hospitalisation mild cases	per patient	7,000	CHF	Conservative assumption based on the following data: Santésuisse is quoted by Medinside (2020) as stating CHF 7,000 to 25,000; 20 Minuten (2021) states CHF 25,000 to 30,000.
Costs of stay in intensive care	per patient	100,000	CHF	Conservative assumption based on the following data: Santésuisse is quoted by Medinside (2020) as CHF 120,000; 20 Minuten (2021) quotes well over CHF 100,000; Universitätsspital Basel is quoted in the Tagesanzeiger (2021) as stating over CHF 100,000.
Health Costs Long COVID	per person with long COVID	8,500	CHF	Conservative assumption based on the following data: Culter 2022 quotes USD 9,000; Businesswire quotes a study by Nomi Health (US healthcare company) at USD 9,500.
Production losses				
Loss of working hours	per infected person	5	Days	Assumption: more than influenza; Tomonoga et al. 2021 give 3.2 days for influenza.
Costs loss of working hours	per working day	360	CHF	Calculation from Tomonoga et al. 2021. Assumption is independent of whether costs are disease- or mortality-related.
Intangible costs				
Years of life lost of deceased persons		6	Years	Conservative assumption based on National Covid Science Task Force 2021 (5.4-6.8 years) and related to the second wave. SwissRe 2020 assumes 12-14 years for the UK.
Monetary value of a year of life		175,000	CHF	“Reasonable” medical costs per year of life gained according to 2010 Federal Court ruling, cited by National Covid Science Task Force 2021. Conservative assumption based on National Covid Science Task Force 2021 calculating another scenario with costs of CHF 250,000.
Benefit sequencing				
Faster targeted measures Implementation	1-factor x less of each variable	3.1		10% increase in the factor for wastewater monitoring, which was calculated with Python according to the formula of Flaxman et al. 2020.

A.2 Basic Data Cost Calculation (Annual Costs)

Wastewater monitoring (sampling, laboratory costs for pathogen detection, transport)						
	Number of pathogens	**# per week**	**Number WWTPs**	**Total costs / average per year**	**Minimum costs per year**	**Costs Maximum per year**
Scenario normal prepandemic	5	3	50	CHF 2’145’000.00	CHF 1’794’000.00	CHF 2’496’000.00
Scenario normal post-pandemic	5	3	50	CHF 2’145’000.00	CHF 1’794’000.00	CHF 2’496’000.00
Scenario extraordinary	5	6	100	CHF 8’580’000.00	CHF 7’176’000.00	CHF 9’984’000.00

Gene sequencing from wastewater monitoring						
	Pathogen	**# pro Woche**	**Number WWTPs**	**Total costs / average per year**	**Minimum costs per year**	**Costs Maximum per year**
Scenario normal prepandemic	5	3	50	CHF 1’953’120.00	CHF 1’563’120.00	CHF 2’343’120.00
Scenario normal post-pandemic	5	3	50	CHF 1’953’120.00	CHF 1’563’120.00	CHF 2’343’120.00
Scenario extraordinary	5	6	100	CHF 7’806’240.00	CHF 6’246’240.00	CHF 9’366’240.00

Gene sequencing from reporting system						
	Pathogen	**# pro Woche**	**Number WWTPs**	**Total costs / average per year**	**Minimum costs per year**	**Costs Maximum per year**
Scenario normal prepandemic	5	10	N/A	CHF 127’400.00	CHF 62’400.00	CHF 186’160.00
Scenario normal post-pandemic	5	201	N/A	CHF 2’560’740.00	CHF 1’254’240.00	CHF 3’741’816.00
Scenario extraordinary	5	1’074	N/A	CHF 13’682’393.00	CHF 6’701’580.00	CHF 19’993’047.00

Data Analysis & Interpretation for Measures Ordinance						
	Erreger	**# pro Woche**	**Number WWTPs**	**Total costs / average per year**	**Minimum costs per year**	**Costs Maximum per year**
Scenario normal pre-pandemic, post-pandemic and exceptional	N/A	N/A	N/A	CHF 450’000.00	CHF 450’000.00	CHF 450’000.00
Scenario expansion (extraordinary)	N/A	N/A	N/A	CHF 450’000.00	CHF 450’000.00	CHF 450’000.00
SPSP (operating costs)	N/A	N/A	N/A	CHF 241’750.00	CHF 183’500.00	CHF 300’000.00
SPSP (one-off removal costs)	N/A	N/A	N/A	CHF 230’500.00	CHF 161’000.00	CHF 300’000.00

B. Directories

B.1. List of Figures

B.2. List of Tables

A study by the think tank Pour Demain with the participation of Eraneos and INFRAS

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