Operational considerations for respiratory virus surveillance in Europe

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Contents

Key messages

- The European Centre for Disease Prevention and Control (ECDC), the World Health Organization (WHO) Regional Office for Europe, and the European surveillance networks for COVID-19 and influenza agree on the urgent need to develop and sustain resilient population-based integrated surveillance systems for influenza, COVID-19, and potentially other respiratory virus infections (such as RSV or new viral diseases of public health concern) in Europe.
- Effective integrated respiratory surveillance systems should provide data sufficient for monitoring the spread and intensity of respiratory viruses to guide control measures and mitigate their impact. These systems will also be important in the event of future pandemics.
- Well-designed, representative sentinel surveillance systems in primary and secondary care should remain the central surveillance method for acute respiratory infections. Sentinel systems provide robust epidemiological data that are routinely collected using common syndromic case definitions with reliable denominators and integral microbiological testing that can be extended to multiple viruses. This makes them ideal as the basis of integrated impact assessment of influenza, COVID-19, and potentially other respiratory virus infections.
- Monitoring systems should provide accurate national and regional level estimates of indicators of severity such as hospitalisations, admissions to ICU, and mortality.
- At the same time, these systems should be sensitive enough to detect virus variants, accurately follow virus-specific disease incidence by level of severity/age/place and to assess vaccine effectiveness.
- Strategic prioritisation and sustained financing are required to further expand and develop sentinel systems to make them fit for purpose. Countries should aim to enhance the number and representativeness of sentinel sites and increase the number of tests performed, informed by the considerations for sizing surveillance systems in this document.
- Countries should plan for a potential upscaling of testing for influenza viruses and SARS-CoV-2 if required in response to the emergence of a new SARS-CoV-2 variant of concern or influenza variant.
- The acute respiratory infection (ARI) case definition can be used for primary care sentinel integrated respiratory surveillance, with the benefit that it is more sensitive than the influenza-like illness (ILI) case definition and will result in a much larger number of cases presenting to the sentinel system. Countries that choose to extend to ARI are strongly encouraged to continue to collect the number of consultations from ILI patients, to allow the use of the more specific ILI syndromic indicator for monitoring influenza activity and calculation of epidemic thresholds with historical data.
- Data on COVID-19-specific hospital and ICU admissions and occupancy reported by many countries during the pandemic should continue to be collected and expanded where possible to influenza.
- It is essential to continue reporting epidemiological information from patients with respiratory symptoms testing positive for influenza viruses, SARS-CoV-2 and other relevant respiratory viruses in non-sentinel primary or secondary care laboratories and registry-based systems, including information on where the specimens were obtained. These data will be used to complement data from sentinel systems, particularly while sustainable sentinel systems are being expanded.
- Specimens from patients with respiratory symptoms should be tested using multiplex PCR assays to simultaneously detect influenza viruses, SARS-CoV-2 and other relevant respiratory viruses where possible.

- Genomic monitoring should be integrated within overall respiratory virus monitoring strategies to ensure reliability and interpretability of findings.
- Where possible, all specimens from primary and secondary care sentinel surveillance testing positive for influenza viruses or SARS-CoV-2 should be sequenced. A carefully selected sample (balanced across age groups, geography, and clinical spectrum, including primary and secondary care settings) of influenza virus- and SARS-CoV-2-positive specimens from non-sentinel and registry-based systems should also be sequenced to increases achieve desired sequencing volumes. The number of sequences required and the relative contribution of sentinel and non-sentinel specimens should be informed by the considerations for sizing surveillance systems presented in this document.
- A subset of specimens from sentinel and non-sentinel sources should be shared for further virus characterisation and antiviral/therapy resistance testing at National Influenza Centres (NIC), SARS-CoV-2 reference laboratories, and/or WHO reference laboratories.
- Specimens testing positive for influenza viruses and SARS-CoV-2 from specific population groups and settings (targeted surveillance) should be sequenced for the purpose of detecting signals of emergence of novel virus variants with potentially changed characteristics, and as a minimum, a subset sent to the NICs, SARS-CoV-2 reference laboratories, and/or WHO reference laboratories for further characterisation.
- Consensus sequences for SARS-CoV-2 and influenza viruses should be deposited in the GISAID database. If available, raw data of SARS-CoV-2 sequences should be deposited in the COVID-19 data portal through the European Nucleotide Archive (ENA).
- Year-round data collection and reporting to The European Surveillance System (TESSy) from sentinel and non-sentinel systems should be maintained in order to be able to identify upsurges and outbreaks during the summer months.
- During the 2022/23 winter season, there will be considerable disparity in the level of implementation of integrated respiratory surveillance among countries in the European region. Data should therefore be interpreted with caution and due consideration of the differences between, and limitations of, the underlying surveillance systems.

Background

Since 2014, influenza surveillance in the European Region has been jointly coordinated by the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) Regional Office for Europe [1,2]. In the European Union (EU), the surveillance of influenza is conducted according to the Commission Implementing Decision (EU) 1082/2013 and (EU) 2018/945 [3-5]. For WHO, the surveillance of influenza is conducted based on the Pandemic Influenza Preparedness [6] framework and terms of reference for National Influenza Centres (NICs) and the Global Influenza Surveillance and Response System (GISRS) [7].

Most countries, territories, and areas (hereafter referred to as countries) in the European Region have established comprehensive surveillance systems based on the reporting of all positive SARS-CoV-2 specimens to monitor the progression and evolution of the COVID-19 pandemic. These systems have provided critical information for public health decision-making. However, considerable variation between countries and over time in the quality and quantity of weekly reported data, testing strategies employed, and the lack of common syndromic case definitions with well-defined populations under surveillance, have all limited the utility of the data for monitoring the intensity and severity of COVID-19 in Europe.

Following a joint ECDC/WHO Regional Office for Europe document in 2020, outlining the need for the integration of SARS-CoV-2 into existing sentinel surveillance systems [8], WHO published global guidance on integrated sentinel surveillance in March 2022 [9], and the European Commission's communication on 27 April 2022 called for countries and EU bodies to establish, as soon as possible, year-round integrated surveillance based on sentinel systems [10]. The results of a recent survey by ECDC and the WHO Regional Office for Europe to members of the European COVID-19 and Influenza surveillance networks [11] confirmed that countries consider integrated respiratory virus surveillance to be a priority, with many reporting having already started the process of setting this up. However, the COVID-19 pandemic has caused lasting disruption, particularly to primary care sentinel systems, and considerable time and investment will be required in many countries before expanded, sustainable systems can be established. At the same time, the ongoing COVID-19 pandemic remains unpredictable, with many countries planning to continue the collection, reporting, and use of non-sentinel COVID-19 data in 2022/23 to inform policy decisions.

Scope and target audience

This document outlines operational considerations to support the continuity of national surveillance systems and public health laboratories for epidemiological and virological surveillance for influenza, SARS-CoV-2, and potentially other respiratory viruses (such as RSV or new viruses of public health concern) in the 2022/2023 winter season and beyond. It builds on previously published documents on COVID-19 and influenza surveillance [8,12]. The intended audience for this document is those with national responsibility for influenza and COVID-19 surveillance in Europe.

Overarching surveillance strategy

Monitoring of COVID-19 during the pandemic has largely been based on trends in counts of positive cases, deaths, and other indicators, the interpretation of which has been made challenging due to a lack of common syndromic case definitions, consistency in testing strategies, and lack of denominators based on well-defined populations under surveillance. Several countries have changed or are in the process of changing testing strategies, aiming at targeting older age groups or individuals with risk factors for severe disease [11]. At the same time, countries have started the process of adapting and further developing the systems previously used for influenza surveillance to other respiratory viruses, in particular SARS-CoV-2. ECDC, the WHO Regional Office for Europe, and the European surveillance networks for COVID-19 and influenza agree on the urgent need to develop and sustain resilient population-based integrated surveillance systems for influenza, COVID-19 and potentially other respiratory virus infections in Europe. These systems will also be important for future pandemic respiratory virus events.

Well-designed, representative sentinel surveillance systems in primary and secondary care should remain the core surveillance method for acute viral respiratory infections, providing data sufficient for monitoring the spread and intensity of respiratory viruses to inform control measures and mitigate their impact. Systems should provide accurate national and regional level estimates of indicators of severity such as hospitalisations, admissions to intensive care units (ICUs), and mortality. At the same time, they should be sensitive enough to monitor changes and characteristics of circulation viruses; accurately follow virus-specific incidence by level of severity, age, and place; and assess vaccine effectiveness. Genomic monitoring should be integrated into overall respiratory virus monitoring strategies. Sentinel syndromic surveillance, virological monitoring, and reporting to The European Surveillance System (TESSy) should be maintained year-round.

The COVID-19 pandemic has had a lasting impact on existing systems designed for influenza. Pre-existing surveillance systems for influenza and those established for SARS-CoV-2 monitoring during the COVID-19 pandemic are not yet fully suitable for integrated respiratory virus surveillance and need to be complemented by other systems during a transition period. Establishing and maintaining systems that are fit for purpose will require considerable political will and priority, sustained financing, and expertise. Until sentinel systems are sufficient in quality and quantity to form the basis of integrated epidemiological and virological monitoring of respiratory infections, data from non-sentinel sources, with improved reporting to aid their interpretation, will be an important complement. During the 2022/23 winter season, there will be considerable disparity in the level of implementation of integrated respiratory surveillance among countries in the European region. Data should therefore be interpreted with caution and due consideration of the differences between, and limitations of, the underlying surveillance systems.

There is an urgent need to establish robust, integrated surveillance systems that are sustainable and resilient should a new pandemic arrive. At the same time, countries should plan for a potential upscaling of testing for influenza viruses and SARS-CoV-2 if required in response to the emergence of a new SARS-CoV-2 variant of concern.

Objectives for integrated surveillance of respiratory viruses in Europe

Overarching surveillance objectives for the integrated surveillance of influenza, COVID-19, and other respiratory virus infections in Europe are as follows:

1. Monitor the intensity, geographical spread and temporal patterns of influenza, COVID-19, and other respiratory virus infections to inform mitigation measures.
2. Monitor severity, risk factors for severe disease, and assess the impact on healthcare systems of influenza, COVID-19, and other respiratory virus infections to inform mitigation measures.
3. Monitor changes and characteristics of circulating and emerging respiratory viruses, particularly virological changes of influenza viruses, SARS-CoV-2, and other respiratory viruses to inform treatment, drug, and vaccine development.
4. Describe the burden of disease associated with influenza, COVID-19, and other respiratory virus infections.
5. Assess vaccine effectiveness against influenza, COVID-19, and other respiratory virus infections where locally feasible.

These objectives may be linked to different aspects of the surveillance system for which TESSy data are currently collected and other data sources that may be used when available (Table 1).

Table 1. Respiratory virus surveillance objectives and corresponding surveillance system data sources

Objectives	Primary care sentinel	Secondary care sentinel	Non-sentinel data	Hospital and ICU capacity	Genomic and antigenic data	Other possible data sources
1. Monitor the intensity, geographical spread, and temporal patterns of influenza, COVID-19, and other respiratory virus infections to inform mitigation measures	X	(X)	(X)			Wastewater, environmental, participatory
2. Monitor severity, risk factors for severe disease, and assess the impact on healthcare systems of influenza, COVID-19, and other respiratory virus infections to inform mitigation measures.	(X)	X	(X)	X		Excess mortality
3. Monitor changes and characteristics of circulating and emerging respiratory viruses, particularly virological changes of influenza viruses, SARS-CoV-2, and other respiratory viruses to inform treatment, drug, and vaccine development.	X	X	X		X	Wastewater, EWRS, IHR, EpiPulse, epidemic intelligence
4. Describe the burden of disease associated with influenza, COVID-19, and other respiratory virus infections.	X	X	(X)	X		Excess mortality
5. Assess vaccine effectiveness against influenza, COVID-19, and other respiratory virus infections where locally feasible.	(X)	(X)				Vaccine effectiveness studies. Vaccine uptake monitoring

For the 2022/2023 season, X: system used, (X): system to be partially used or established during the season

Using results from a survey [11] conducted with the countries to review the main priorities and objectives for respiratory virus surveillance, a list of specific objectives considered as a priority by more than half of responding countries have been mapped to the above overarching surveillance objectives (Annex Table A5).

Sentinel surveillance systems

Well-designed, representative sentinel surveillance systems in primary and secondary care should remain the central surveillance method for acute respiratory infections. Sentinel surveillance systems offer many advantages that make them ideal as the basis of integrated impact assessment of influenza, COVID-19 and other respiratory virus infections. Robust epidemiological data are routinely collected using systematic and standardised approaches based on common syndromic case definitions to allow reliable monitoring and timely detection of changes in trends. Microbiological data based on testing of cases are an integral part of the system, with the possibility to simultaneous test for multiple viruses. Cases come from well-defined, representative populations, providing reliable denominators for the estimation of disease incidence. Reliable analysis can be conducted comparing historical data collected in similar ways. Standardised approaches to sampling and testing are employed in these systems, which should limit the impact of changes in national testing strategies which can affect other COVID-19 surveillance approaches [13].

Sentinel primary care surveillance

Sentinel surveillance of influenza in primary care is conducted by representative national networks of primary care practitioners, typically covering 1-6% of the population [14]. It relies on the use of syndromic case definitions for influenza-like illness (ILI) and/or acute respiratory infection (ARI). Although challenging to set up and maintain new sentinel primary care sites, train staff, and ensure good quality data, countries are encouraged to try to increase the number of participating practitioners in sentinel surveillance, guided by the sample size considerations outlined later in this document. Continual support and motivation of participating practitioners is key to expanding and maintaining a high-quality sentinel system.

Site selection to achieve representativeness

When selecting sentinel primary care sites, countries should consider factors such as the geography, age structure, population density, whether urban or rural, and specific social factors of the respective population. The aim is to achieve a sample that represents the general population at the national or subnational level.

Before increasing the size of the surveillance system, countries should assess the representativeness of their existing systems according to the above-mentioned characteristics to determine where there are discrepancies to be corrected through recruitment of new sites. Documentation of the sampling processes (e.g. systematic, probability, cluster sampling), any known biases present in the sentinel population that arise due to the structure of primary healthcare and patterns of healthcare seeking behaviour is recommended. The level of representativeness achieved should be considered before deciding if it is appropriate to extrapolate findings from the sentinel system to the general population.

Case definitions for syndromic surveillance

Some countries have shifted from the ILI to ARI case definition as the basis of sentinel syndromic surveillance in primary care during the COVID-19 pandemic to better monitor SARS-CoV-2 circulation [2]. As the clinical spectrum for COVID-19, RSV infection, and other respiratory virus infections does not always include high temperature, the ARI case definition is more sensitive than ILI for integrated sentinel surveillance; it does, however, have much lower specificity compared to ILI (Table 2).

Table 2. Sensitivity and specificity of influenza-like illness (ILI), acute respiratory infection (ARI) and severe acute respiratory infection (SARI) case definitions for influenza and COVID-19

	Influenza		COVID-19 (2020 Assessment)		COVID-19 (2021 Assessment)	
	Sensitivity %	Specificity %	Sensitivity %	Specificity %	Sensitivity %	Specificity %
ILI	45-55	85-95	20-51	60-90	20-55	38-90
ARI	94	27	86	23	60-96	10-45
SARI	45-70	45-70	40-55	33-60	33-62	31-77

Source: WHO [9,15], case definitions see Annex

Use of the ARI case definition for the collection of respiratory illness consultation data will also result in substantially higher numbers of consultations and consultation rates (Figure A1, Annex), which will be important for sample size considerations for respiratory swabbing. For example, among EU/EEA countries reporting ILI and ARI data during the 2021/22 winter season, the weekly median (interquartile range) number of ARI cases ranged from 2 438 (612 to 13 701) to 8 350 (1 843 to 32 349) and ILI cases from 70 (20 to 273) to 386 (65 to 1 805).

Countries that choose to extend to ARI as the case definition for the collection of respiratory illness consultation data are strongly encouraged to continue to collect the number of consultations from patients based on existing ILI case definitions. This will allow the use of the more specific ILI syndromic indicator for monitoring influenza activity and calculation of epidemic thresholds with historical ILI data. A substantial number of countries already have monitoring systems based on ARI in place; of 54 countries reporting influenza data in the European Region, 29 report ILI and ARI consultations, 21 report ILI consultations only, two report ARI consultations only and one reports neither ILI nor ARI consultations [2,16].

Data interpretation and Moving Epidemic Method (MEM) thresholds

Moving Epidemic Method (MEM) thresholds have been established to compare weekly ARI and/or ILI consultation rates across countries together with respective viral data to assess the start and end as well as the intensity of respiratory virus activity in the outpatient population [17]. MEM thresholds have been estimated using typically at least five years of historical ILI/ARI consultation data for defining the different intensity levels as well as the start and end of activity. Changes to the underlying sentinel systems affects the ease in which these thresholds can be determined and used. The COVID-19 pandemic altered health seeking behaviour, such as the through the replacement or supplement of physical GP visits with telephone or video consultations. Increasing the number of reporting sentinel physicians or representativeness of the population under surveillance, as proposed in this document, may also affect comparability with historic data.

Setting thresholds at national level is the responsibility of each individual country. MEM thresholds for 2022/23 should be based on historical data prior to the COVID-19 pandemic. As systems are expanded and improved, the performance of MEM thresholds should be continually assessed using data over longer periods.

For the definition of the start of the seasonal influenza activity at the regional level, a 10% threshold of sentinel positivity (the first of two consecutive weeks in at least two countries) has previously been used. Such thresholds to determine the onset of activity have not yet been established for COVID-19.

Thresholds and sample sizes for identifying the start of epidemic activity are discussed under sample size considerations below.

Severe acute respiratory infection (SARI) surveillance

Countries vary in their hospital surveillance approaches, with sentinel SARI surveillance historically implemented mainly in the Eastern part of the European region (some of these were comprehensive systems), while countries in the Western part of the European region have conducted hospital surveillance mainly based on laboratory-confirmed hospitalised and/or ICU-admitted influenza cases. During the COVID-19 pandemic, more countries have implemented sentinel SARI surveillance with laboratory testing of SARI patients for SARS-CoV-2 and influenza viruses. It is important for countries to enhance and maintain SARI surveillance using the existing SARI case definition, including collecting information on whether the cases present with fever, where possible.

All members of the European Union SARI surveillance network (E-SARI-Net) and those elsewhere in the European Region that have not yet commenced reporting to TESSy should do so as soon as possible.

Virological testing

Outside of the influenza season, sentinel ILI and/or ARI surveillance data may be a good proxy for the incidence of COVID-19 when the proportion of positive sentinel specimens that are due to SARS-CoV-2 virus is high. When multiple respiratory viruses are co-circulating, data from sentinel syndromic surveillance can be combined with the results of virological testing to better understand the relative contribution of the viruses among ARI/ILI cases presenting to primary care and SARI cases to secondary care.

Where possible, all specimens taken from primary and secondary care sentinel surveillance should be tested concurrently using multiplex PCR assays to simultaneously detect influenza viruses, SARS-CoV-2, and other relevant respiratory viruses. When this is not possible due to limited testing capacity, a subset of patients representing all age-groups and a range of sentinel sites should be tested for both influenza viruses and SARS-CoV-2.

All sentinel specimens positive for influenza viruses or SARS-CoV-2 should be sequenced, and a subset shared for further virus characterisation and antiviral/therapy resistance testing at National Influenza Centres (NIC), SARS-CoV-2 reference laboratories, and/or WHO reference laboratories. Further details on laboratory considerations and options in resource-limited situations are provided under 'Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants and virus characteristics'. Countries are encouraged to use these NICs to support integrated respiratory surveillance.

Non-sentinel data sources

Data from primary and secondary care laboratory confirmations

In many countries SARS-CoV-2 testing strategies are being shifted from comprehensive towards targeted testing or to only collecting laboratory confirmations, which will limit available information on viral circulation in the population. This also affects testing for influenza viruses, which is often performed together with SARS-CoV-2 in a multiplex PCR. Nevertheless, specimens from patients with respiratory symptoms that are not submitted from sentinel networks, will continue to be tested in primary or secondary care laboratories for influenza viruses, SARS-CoV-2, and other relevant respiratory viruses. Countries should continue to collect these non-sentinel data, focusing on the epidemiological information about positive detections and the number of tests performed (denominator data) in each setting (primary or secondary care). To enhance interpretability, linkage of laboratory data with epidemiological data at a national level can be a powerful tool for integrated surveillance. Data should be collected and reported to the national authorities and TESSy, on a weekly basis year-round, and be used to complement data from sentinel systems.

Monitoring of laboratory-confirmed hospitalised cases

Data on patients in hospitals (ICU or non-ICU wards or both) with laboratory-confirmation of influenza infection were previously collected in a case-based format (INFLSARI). The collection of detailed metadata from patients enabled the analysis of risk factors related to different outcomes such as death, vaccine breakthrough or ICU admission. However, many countries have shifted to SARI surveillance systems in hospital settings and have discontinued this laboratory-based system.

Countries that continue to collect epidemiological information on laboratory-confirmed cases that are hospitalised due to influenza (previously reported to INFLSARI) or COVID-19 (reported to NCOV) are encouraged to instead report these data to RESPISURV (see 'Reporting to TESSy' section), clearly indicating the source system.

Registry-based surveillance

Registry-based systems collect in a systematic and comprehensive way uniform information about individual persons, serving a predetermined purpose which may or not be related to monitoring of specific diseases [18]. Some countries have central systems based on personal identifiers (personal numbers) that enables the identification of when a person has been tested, tested positive, vaccinated and/or hospitalised. The registries can also include international classification of diseases (ICD) codes for diagnosis of respiratory disease. Other countries use comprehensive systems that collect all laboratory data and link these with registry data [19,20]. Several countries across the European region have implemented comprehensive registry-based data collection systems that allow a very timely and detailed monitoring of the performed testing, laboratory-confirmed diagnoses as well as hospitalisations and mortality in the population.

Countries with a registry-based system should continue to collect data on the number of tests performed, positive detections for influenza viruses and SARS-CoV-2, and to report to TESSy (Table 4).

Aggregate data on hospital and ICU admissions and occupancy

Data on COVID-19-specific hospital and ICU admissions and occupancy reported by many countries during the pandemic should continue to be collected, with age disaggregation added if available. These data should be expanded where possible to include influenza-specific admissions and occupancy. Reporting to RESPIHOSP TESSy should be done a weekly basis year-round.

Long-term care facility surveillance

To date, 17 countries (Austria, Belgium, Croatia, Cyprus, Denmark, France, Germany, Ireland, Italy, Lithuania, Luxembourg, the Netherlands, Norway, Portugal, Slovenia, Spain, and Sweden) have reported aggregate data on COVID-19 in long-term care facilities (LTCFs) to TESSy [21]. At least two thirds of the countries reported have national (>98%) coverage for these reported data. Countries should implement, if not already, and continue to report data on COVID-19 cases and outbreaks from LTCF settings. Additionally, countries are encouraged to expand this reporting to include influenza cases and outbreaks from LTCF settings.

Virological sequencing and characterisation

A carefully selected sample of influenza virus and SARS-CoV-2 positive specimens from non-sentinel and registry-based systems should be sequenced to supplement any shortfall of specimens from sentinel sources [9] and a subset shared for further virus characterisation and antiviral/therapy resistance testing at National Influenza Centres (NIC), SARS-CoV-2 reference laboratories, and/or WHO reference laboratories. For targeted investigation, positive specimens from specific population groups and settings should be prioritised for sequencing, antigenic and resistance characterisation.

Further details are provided under 'Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants and virus characteristics'.

Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants and virus characteristics

Timely genomic, antigenic and antiviral or monoclonal antibody resistance monitoring should be integrated in the overall respiratory virus monitoring strategies [22,23]. Information on the number of detections, the epidemiological characteristics of sequenced cases and the source (sentinel, registry, or non-sentinel) of specimens selected for sequencing is important to aid interpretation. Wastewater surveillance may also be considered for monitoring of genomic trends for SARS-CoV-2, but detailed guidance for this is beyond the scope of this document.

Source of specimens for sequencing for monitoring of SARS-CoV-2 variant circulation

Sequencing of specimens from sentinel sites should be prioritised for the monitoring of SARS-CoV-2 variant circulation. When specimens from sentinel sites are insufficient in quantity (according to sample size calculations below) to form the basis of variant prevalence estimates, additional RT-PCR-positive specimens from non-sentinel and registry-based systems should be used to reach the desired sample size for variant detection. In selecting these non-sentinel specimens, countries are encouraged to aim at achieving a balance across age groups, geography, and clinical spectrum, including primary and secondary care settings.

In the situation of limited resources, WHO recommends that priority for sequencing and virus characterisation should be given to specimens from targeted surveillance and from sentinel surveillance (sequence a minimum of 15 specimens per week [9]).

Targeted surveillance to detect the emergence or introduction of a new strain/lineage/variant

In addition to sequencing for the purpose of monitoring SARS-CoV-2 variant circulation, sequencing should also be undertaken on specimens testing positive from patients from special settings (targeted surveillance), as these may provide important signals of the emergence of novel virus variants with potentially changed characteristics. This can include samples from outbreaks with an unusually high number of secondary cases, from immunocompromised patients or patients with other underlying conditions associated with prolonged viral replication and shedding, cases with severe or unusual clinical presentation or poor response to therapeutics, including antiviral treatments, but also cases suggestive of zoonotic transmission or if there is suspicion of changes in the performance of diagnostics (antibody, antigen, molecular assay) or failure of treatment (antiviral, antibody). In the event of a novel SARS-CoV-2 variant of concern (VOC) or influenza strain/lineage that needs to be detected early to delay introduction, specimens testing positive from patients with recent travel history to an area with a high incidence of this VOC or strain/lineage can be used for targeted sequencing to assess the prevalence in this group. Several countries have implemented testing of returning travellers as a mechanism for early detection of new strains/variants of potential interest. This should be combined with rapid risk assessment of the characteristics of such new strains – in particular, the transmissibility, infection-severity, and immune/vaccine escape.

Further virus characterisation

Further virus characterisation beyond sequencing and strain/lineage/variant identification should be carried out. As outlined above and based on sample calculations, a subset of available and technically suitable specimens testing positive for influenza viruses and/or SARS-CoV-2 from targeted surveillance and sentinel surveillance should be sequenced and genotypic antiviral characterisation should be carried out on these. Based on the genotypic results, further antigenic characterisation and phenotypic testing for antiviral drug or monoclonal antibody resistance should be carried out on a subset of specimens from the targeted surveillance and sentinel surveillance [22,23]. A representative selection of all available specimens should be sent to the NICs, SARS-CoV-2 reference laboratories and/or WHO reference laboratories to confirm the virus characterisation results and to perform additional antigenic characterisation and testing for antiviral drug or monoclonal antibody resistance [22]. In particular, specimens and/or virus isolates of un-subtypeable influenza A viruses and new SARS-CoV-2 variants under monitoring, of interest or of concern [22], should be shared with NICs or SARS-CoV-2 national reference laboratories and be shipped to WHO reference laboratories [24,25] to perform more in-depth virus characterisation analysis and collect specimens for potential future vaccine composition [22]. Storage of clinical specimens at the site of collection and transport to the testing laboratory should follow the WHO manual for laboratory diagnosis for influenza viruses and the WHO guidance for laboratory testing for influenza viruses and SARS-CoV-2 [26,27].

Laboratory considerations

- Frequent and regular sequencing and data-sharing is preferred over batch sequencing in irregular intervals.
- Nasopharyngeal swabs or combined nasopharyngeal and throat (oropharyngeal) swabs are considered appropriate specimens both for influenza virus and SARS-CoV-2 molecular detection; other suitable respiratory specimens are listed in the WHO guidance document [9].
- Specimens collected should be stored in non-inactivating viral transport medium (VTM) or dry swabs if VTM is unavailable to facilitate the sharing of specimens for subsequent virus isolation.
- It is important that NICs and SARS-CoV-2 reference laboratories continue to perform virus culture (BSL2 for SARS-CoV-2 negative, influenza positive specimens and BSL3 for unknown or SARS-CoV-2 positive specimens).
- Where possible, multiplex assays are preferred as there is a reduced use of reagents, needed consumables, and turnaround time. Alternative algorithms for when this is not possible are described in the WHO guidance document [9].
- Whole genome sequencing (WGS) is considered the gold standard, but amplicon sequencing and screening single nucleotide polymorphism (SNP) based NAAT assays can be used to identify and characterise strains/lineages/variants [28].
- Specimens with a cycle threshold (Ct) value of ≤25 are considered appropriate for good quality whole genome sequences. Samples with Ct>30 may not give WGS results but may still be appropriate to determine influenza virus subtypes/lineages and SARS-CoV-2 strains/lineages/variants.

Considerations for sizing surveillance systems

The calculations in this section are intended to support countries to determine the correct size for their surveillance systems to be able to meet the following objectives:

- Estimate virus-specific positivity to determine when epidemic activity has crossed pre-defined thresholds;
- Detect SARS-CoV-2 variants circulating at a target threshold prevalence.

The first objective applies exclusively to sentinel surveillance. In primary care systems, a 10% threshold has traditionally been used to signal the start of epidemic influenza activity. More data and evidence are required to establish thresholds for the start of SARS-CoV-2 epidemic activity. Precise estimates of positivity from primary care systems will aid this. The calculations may also be applied to SARI surveillance where positivity thresholds could be used as triggers for healthcare preparedness and if required other public health and social measures.

For the second objective, it is important to note that existing sentinel systems in the European region are alone unlikely to produce sufficient specimens for sequencing of SARS-CoV-2, especially if the target is to detect SARS-CoV-2 variants circulating at low prevalence. The calculations presented here can be used to understand how viral circulation, the size of the population under surveillance, and the swabbing schemes employed (fraction of cases that are swabbed) within national sentinel systems, will influence the number of sentinel specimens available. The number of carefully selected (as described earlier) non-sentinel specimens that must additionally be sequenced to be able to detect a variant circulating at a target threshold prevalence can then be estimated. If a country's priority is to achieve representative estimates of circulating variants, it is desirable to maximise the proportion of sequences originating from sentinel surveillance and to size sentinel systems appropriately.

Additional sequencing of non-sentinel positive specimens from special settings will also be required for targeted surveillance, which has the purpose of detecting signals of emergence of novel variants with potentially changed characteristics (see 'Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants and virus characteristics').

ECDC and the WHO Regional Office for Europe can provide further tailored advice on sizing and site selection for primary care and SARI sentinel surveillance.

Key variables and concepts

The sample size calculations use the formula published in Annex 1 of ECDC's 'Guidance for representative and targeted genomic SARS-CoV-2 monitoring' [23]. They use as a starting point, and are adjusted for, the number of presenting ARI/ILI or SARI cases (objective 1) or the number of RT-PCR-positive specimens available for sequencing (objective 2). They are not influenced by the population of the country or region and can be applied at the subnational level in countries that have sentinel systems designed to be regionally representative.

The number of weekly ARI/ILI or SARI cases presenting to sentinel primary care practices or hospitals is driven by the level of viral circulation, proportion of infections that result in symptomatic cases, their health-seeking behaviour, and disease severity. Of these factors, it is only possible to control the size of the population under surveillance, which can be increased by recruiting more sentinel sites. The reported weekly distribution of ILI and ARI cases reported in the 2021/22 winter season by EU/EEA countries is shown in Figure A1.

A second variable that can be controlled is the number of tests performed among presenting ARI/ILI or SARI cases. This can be altered by modifying the swabbing scheme to test a higher or lower fraction of cases. Since the number of presenting cases is likely to change according to the epidemic

situation, it may be desirable to alter the swabbing scheme at different times of the year to have greater consistency in the number of swabs that are taken each week. Similarly, positivity will reduce in line with viral circulation, so the swabbing scheme can also be a way to influence the expected number of positive specimens available for sequencing.

The final variables to consider are the target level of positivity and the desired relative precision around the estimate. A 10% positivity target estimated with 10% relative precision means that the 95% confidence interval (CI) around the estimate would span 9-11%. The CI widens to 7.5-12.5% and 5-15% for 25% and 50% relative precision, respectively. A narrower CI requires a larger sample size. Similarly, at a level of given relative precision, the required sample size will be higher for a lower target positivity.

The sample sizes for monitoring variant circulation all assume a 50% relative precision, which is in line with the 'Guidance for representative and targeted genomic SARS-CoV-2 monitoring' published in May 2021 [23]. However, the perspective applied to the calculations presented here is different than it was in May 2021. Then, the starting point was the large numbers of RT-PCR-positive SARS-CoV-2 specimens obtained from comprehensive population testing that were assumed to represent all cases in the country. The question was how many of these needed to be sequenced to be able to detect a SARS-CoV-2 variant circulating at 2.5% prevalence or lower. Now, the starting point is a limited number of representative sentinel specimens. The level of variant detection possible with these specimens can then be assessed. If this fails to meet national objectives for variant detection, the calculations can support planning for a scaling up of sentinel systems and/or topping-up with carefully selected non-sentinel specimens.

An additional assumption now is that there is a technical maximum of 60% of all RT-PCR-positive specimens that can be sequenced due to variations in cycle-threshold (Ct) values, which may differ among non-vaccinated and vaccinated, or previously infected individuals [29]. For example, to achieve 100 sequences, approximately 167 positive specimens must be available.

The national surveillance system structure and available resources, including laboratory capacity and future sequencing budgets are also important factors to consider alongside the calculations to understand what is practically achievable within the current system as it is improved and expanded.

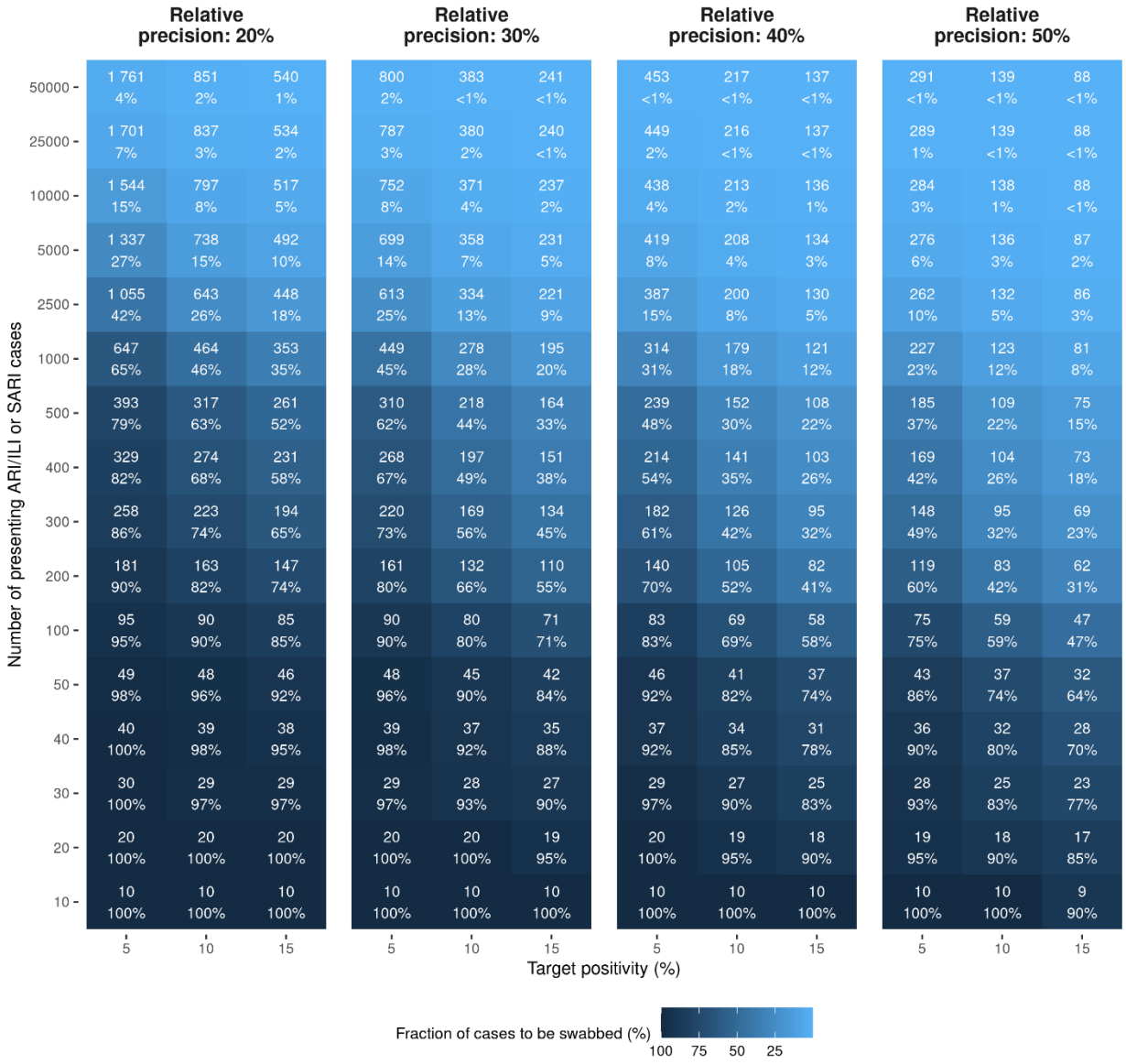
Estimate virus-specific positivity to determine when epidemic activity has crossed pre-defined thresholds

The relative precision in an estimate of positivity is determined by the number of presenting ARI/ILI cases and the fraction of these cases that are tested. For example, to detect the start of epidemic influenza activity in primary care, among 1 000 weekly presenting ARI/ILI cases it would be necessary to test at least 647 (65%), 334 (13%), 179 (18%) and 123 (12%) to estimate 10% positivity with relative precision of 20% (95% CI: 8-12%), 30% (95% CI: 7-13%), 40% (95% CI: 6-14%) and 50% (95% CI: 5-15%), respectively (Figure 1a). For a given number of weekly consultations, targeting a lower positivity or lower relative precision requires a higher number and proportion of cases must be swabbed (Figure 1a, b).

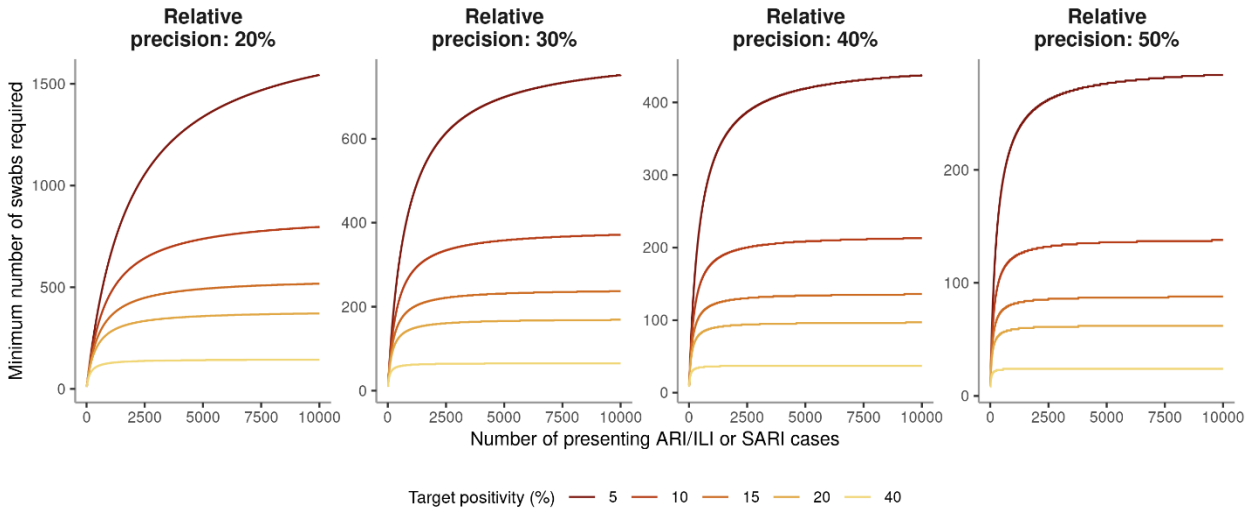
If detection of 10% positivity is the sole objective of a country's primary care sentinel system, or resources are limited, and a relative precision of 30% or higher is acceptable, it is worth noting that once 2 500 weekly presenting ARI/ILI cases are achieved, the minimum number of swabs to be taken starts to plateau at around 370 (relative precision 30%), 210 (relative precision 40%) and 135 (relative precision 50%) (Figure 1b). Recruiting more sentinel sites would have very little impact on the total number of tests to be undertaken nationally, but the fraction of presenting cases to be swabbed by each sentinel practitioner would decrease.

Figure 1. Relationship between numbers of presenting ARI/ILI or SARI cases and the minimum number of swabs to be taken to estimate different target positivity at relative precision of 20%, 30%, 40% or 50%

a) Numbers and fraction of cases to be tested (%) for discrete numbers of cases



b) Continuous relationship between number of presenting cases and swabs required



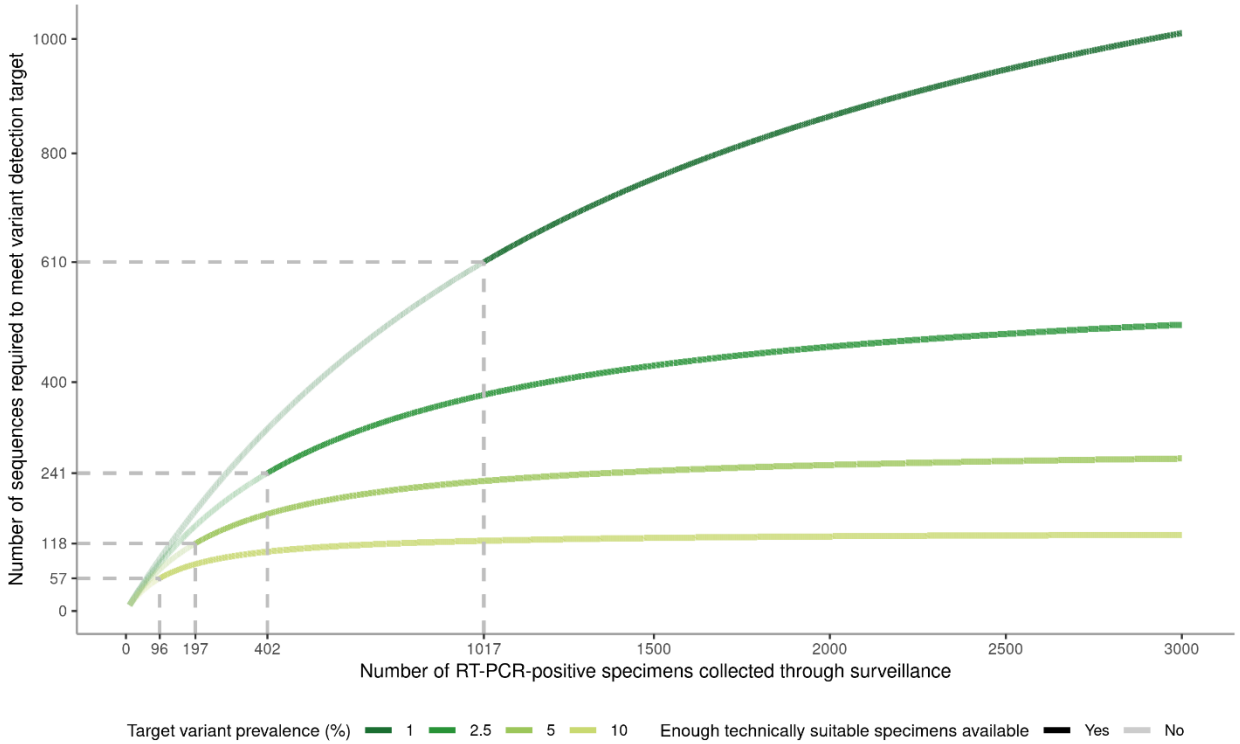
Detect SARS-CoV-2 variants circulating at a target threshold prevalence

Assuming a maximum of 60% of all RT-PCR-positive specimens are technically suitable for sequencing, weekly collection within the surveillance system of 1 017, 402, 197 or 96 RT-PCR-positive specimens is the minimum number that would provide a sufficient sequencing volume to detect a SARS-CoV-2 variant circulating at a prevalence of 1% (95% CI: 0.5-1.5%), 2.5% (95% CI: 1.25-3.75%), 5% (95% CI: 2.5-7.5%) and 10% (95% CI: 5-15%), respectively (Figure 2).

For example, if there are 500 PCR-positive specimens collected in a week, at least 377, 273 or 185 specimens would need to be sequenced to reach precision estimates of 1%, 2.5% or 5% respectively (Figure 2, Sample size tables in the annex). Since only 300 (60%) of the 500 specimens are technically suitable for sequencing, detection at only the 2.5% and 5% prevalence thresholds could be achieved.

As the number of available specimens increases so does the number of sequences required for detection at a certain variant prevalence, although the proportion of available specimens that must be sequenced becomes smaller.

Figure 2. Number of sequences required for detection of variants circulating at prevalence of 1 to 10% at 50% relative precision



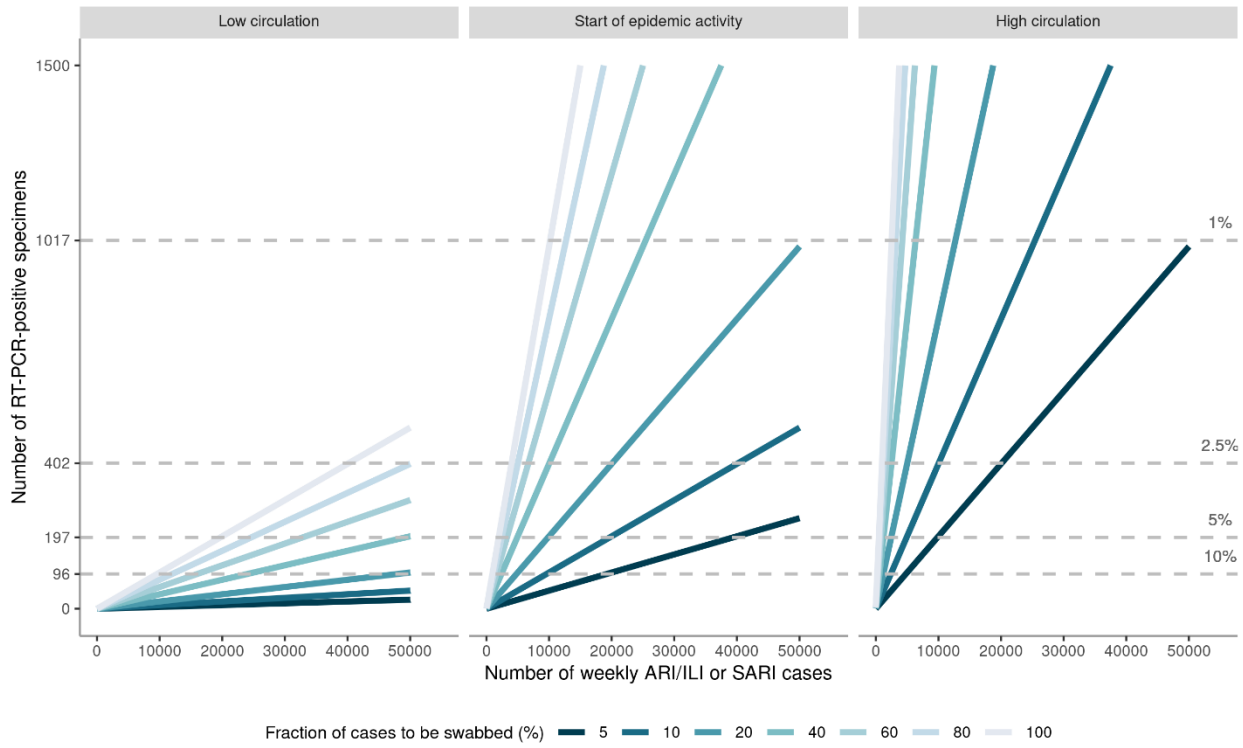
Swabbing schemes, epidemic context and sources of specimens

The sample sizes required to detect SARS-CoV-2 variants circulating at a target threshold prevalence are much more demanding than those needed to estimate virus-specific positivity to determine when epidemic activity has crossed pre-defined thresholds. For example, at the level of swabbing shown in Figure 1a, the expected number of RT-PCR-positive specimens (swabs multiplied by positivity) expected from the swabs taken at the start of epidemic activity (10% positivity) would range from 1 (bottom row of Figure 1a; 10 swabs taken from 10 cases) to 85 (top row of Figure 1a; 851 swabs from 50 000 cases). Even at the upper end of this range, 85 positive specimens, of which 51 would be technically suitable for sequencing, would be insufficient to detect a variant circulating at 10% prevalence with a 95% CI that spanned 5-15%.

Countries seeking to maximise the contribution of sentinel specimens to genomic surveillance can expand their schemes by increasing the population under surveillance and/or by considering optimal swabbing schemes depending on the epidemic context.

Figure 3 illustrates the importance of different, and potentially flexible, swabbing schemes in sentinel surveillance. At the start of epidemic activity (middle panel Figure 3, test positivity 10%), with 20 000 weekly ARI/ILI cases and if 20% of cases were swabbed, it would be possible to obtain around 402 RT-PCR-positive specimens (sufficient to sequence at least 241 of these and detect a variant at 2.5% prevalence in that sample, Figure 2). Only 5% of the cases would need to be swabbed during periods of high viral circulation (right panel Figure 3, test positivity 20%) to achieve the same number of positive specimens. In period of low viral circulation (left panel Figure 3, test positivity 1%), even if all 20 000 of these cases could be swabbed this would produce sufficient positive specimens to detect a variant at 5% prevalence.

Figure 3. Expected number of RT-PCR-positive specimens to be detected with different swabbing schemes depending on numbers of ARI/ILI cases and level of circulation



Note: Levels of circulation indicated based on 1% (low), 10% and 40% (high) test positivity. The number of positive specimens marked on the y-axis are those required for variant detection at the prevalence shown by the labels on the dotted line with 50% relative precision.

Depending on the epidemic context it may therefore be necessary to alter the level of ambition for variant detection, the swabbing scheme, and/or the relative contribution of specimens for sequencing from sentinel and non-sentinel sources. For example, 402 RT-PCR-positive specimens (obtained from swabbing 20% of 20 000 sentinel ARI/ILI cases at the start of epidemic activity), sufficient for detecting a variant at 2.5% prevalence could be supplemented with an additional 615 non-sentinel RT-PCR-positive specimens to have sufficient to detect a variant circulating at 1% prevalence. Considerations for selecting these non-sentinel specimens are outlined under 'Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants and virus characteristics'.

Detailed examples showing the number of expected positive specimens that could be expected from sentinel systems under a range of different scenarios, with implications for the number of additional non-sentinel specimens that would be required to detect variants circulating a different target threshold prevalence are presented in the Annex (Tables A6 and A7).

Population coverage of primary care sentinel systems

It is not possible to recommend a single minimum proportion of the national population to be covered by a primary care sentinel system (Table 3) and in some settings the population under consideration is not known. Countries with large populations may wish to establishing sentinel systems at a more granular level, e.g. at subnational level. If this is the case, all considerations around representativeness and sample sizes need to be applied at the subnational level.

Table 3. Population under surveillance required to achieve target weekly numbers of ARI/ILI cases under different consultation rate scenarios, as a percentage of the total national/ subnational population

Weekly target of ARI/ILI cases	Consultation rate (%)	Population under surveillance required	Population under surveillance as a percentage of different total national/subnational populations (%)			
			500 000	10 million	40 million	80 million
5 000	0.01	500 000	100	5	1.25	0.625
	0.5	10 000	2	0.1	0.025	0.0125
	1	5 000	1	0.05	0.0125	0.00625
	2	2 500	0.5	0.025	0.00625	0.003125
10 000	0.01	1 000 000	200	10	2.5	1.25
	0.5	20 000	4	0.2	0.05	0.025
	1	10 000	2	0.1	0.025	0.0125
	2	5 000	1	0.05	0.0125	0.00625
25 000	0.01	2 500 000	500	25	6.25	3.125
	0.5	50 000	10	0.5	0.125	0.0625
	1	25 000	5	0.25	0.0625	0.03125
	2	12 500	2.5	0.125	0.03125	0.015625
50 000	0.01	5 000 000	1000	50	12.5	6.25
	0.5	100 000	20	1	0.25	0.125
	1	50 000	10	0.5	0.125	0.0625
	2	25 000	5	0.25	0.0625	0.03125

Event-based surveillance

EWRS and IHR

Events such as zoonotic influenza cases or other unexpected events related to respiratory viruses need to be reported to Early Warning and Response System (EWRS) and International Health Regulations (IHR) (2005) according to the respective regulations [30-32].

EpiPulse

EpiPulse [33] is ECDC's online portal for European public health authorities and global partners to collect, analyse, share, and discuss infectious disease data for threat detection, monitoring, risk assessment, and outbreak response. Use of EpiPulse is voluntary and shared information is considered confidential. ECDC strongly encourages using this platform to efficiently interact with the network and share information. Within EpiPulse, workspaces are organised in disease domains reflecting different areas of disease groups. The domain for Influenza and other Respiratory Viruses (IRV) is the one relevant for this network. Access to the IRV domain in EpiPulse can be granted by the respective national coordinator in the country. This system can be used independently of EWRS/IHR criteria and is a way to share and discuss information to the wider network early. A One Health approach can also be applied to events in EpiPulse when applicable to initiate conversation with other stakeholders, such as those from the animal, medicine, or food safety sectors (e.g. the European Food Safety Authority, the European Medicines Agency).

The EpiPulse IRV domain can, for example, be used to post an event on new SARS-CoV-2 variants and thus be used to share microbiological and epidemiological findings early. Routine epidemic intelligence activities are also shared on the platform, such as the long-term monitoring of zoonotic influenza. Find out more about EpiPulse on ECDC's website [33].

Other data sources

Qualitative indicators

Qualitative indicators to assess the level of geographic spread and intensity are established for influenza. The implementation of the Pandemic Influenza Severity Assessment (PISA) indicators might help to assess the epidemiologic situation in a simplified way, but indicators have yet to be established for COVID-19 [34]. Countries are encouraged to submit the influenza-specific PISA indicators to INFLCLIN in TESSy starting in the 2022/2023 autumn/winter season.

Vaccine uptake monitoring

Countries should continue to monitor COVID-19 vaccine uptake, taking potential future booster dose rollouts into particular consideration. Reporting should continue to NCOVVACC in TESSy. Monitoring of influenza uptake in priority **RTPSPX**groups is also important.

Zoonotic influenza and SARS-CoV-2

Countries are strongly encouraged to monitor for zoonotic influenza and SARS-CoV-2 transmission to humans in all available regular surveillance systems in addition to epidemic intelligence and other complementary activities. Systematic data collection of the number of tested and positive detections plus detailed case information of zoonotic influenza cases is established in TESSy in a case-based mode (INFLZOO) (see TESSy reporting section). The reporting of zoonotic transmission of SARS-CoV-2 is not yet fully established and should be done through EpiPulse and EWRS/IHR (2005).

Contact tracing monitoring

Data from contact tracing data platforms such as population-based apps or linked to healthcare follow-ups can also be used to collect information and support studies on transmission and infectiousness in the event a new virus or variant virus emerges. Reporting of aggregated data has been established in TESSy for COVID-19, and countries are encouraged to report these data.

Excess mortality monitoring

Data from national mortality statistics are used to calculate the overall mortality as well as the level of all-cause excess mortality through different networks and organisations, such as EuroMoMo [35] or EuroStat [36]. National and regional all-cause excess mortality monitoring are useful tools to assess the impact on the population, e.g. during hot and cold snaps, severe influenza seasons, and the COVID-19 pandemic.

Wastewater and other environmental surveillance

Wastewater monitoring for SARS-CoV-2 is being used by some countries and has been shown to be a timely source of information to indicate an early increase of viruses likely associated with increasing incidence among the population in the source area of the sewage plant. A European approach for wastewater monitoring is coordinated by the Joint Research Centre (JRC). So far, no data collection in TESSy has been developed. Countries are encouraged to implement, exchange best practices, and report data from wastewater monitoring systems on SARS-CoV-2 to the dedicated central JRC database.

Participatory surveillance

Data from sources collecting information on ILI, ARI, or COVID-19-like illness (CLI) symptoms from population-based studies where members of the public report their symptoms or self-testing results routinely to a central platform could be used to monitor trends of respiratory infections over time. These data are collected from the general population via e.g. applications, telephone surveys, hotline services or other platforms. Participatory surveillance can be used to complement traditional sentinel systems, particularly when physical access to primary healthcare is restricted, or when the primary goal of surveillance is to rapidly detect upsurges of cases. Thresholds and algorithms to evaluate the data need to be established and denominator data need to be collected similar to those established for primary sentinel surveillance. To increase the robustness of the collected data, these systems could be combined with PCR testing for influenza viruses and SARS-CoV-2 (e.g. sampling of a representative number of individuals reporting ILI/ARI/CLI). Self-swabbing and sharing of specimens with dedicated laboratories are already integrated in some countries.

Some countries have set up national reporting platforms and have integrated their data into supranational initiative such as Influenzanet [37]. To date, no data collection in TESSy has been developed.

Sero-epidemiological surveys and other special studies

Some countries will have the resources and capacity to carry out more detailed studies and surveillance activities.

Nationally representative, age-stratified sero-epidemiological studies provide a basis for estimating the proportion of the population with SARS-CoV-2-specific antibodies. Such studies are particularly informative when they apply functional (neutralising titres) or quantitative assays to determine the level of both natural and vaccine-induced antibodies in participating individuals to estimate the contribution of natural, vaccine-derived and hybrid immunity in the population. Given that serum antibodies wane over time, countries are encouraged to establish longitudinal or repeated studies with common sampling strategies and testing methodologies. Such studies are essential for understanding temporal trends.

Countries may also wish to establish time-limited studies that can be activated in the event of a new and emerging respiratory variant or pathogen to answer specific questions not possible from standard surveillance data collection. Examples include first-few X (FFX)/household studies, risk factor studies for severe disease/outcome; serial cross-sectional and longitudinal surveys monitoring, including groups such as immune-compromised for long-term follow-up; and modelling/forecasting/economic evaluation.

Reporting to TESSy

Integrating the collection of data across acute respiratory pathogens can simplify reporting and has the added benefit of being easily expandable to any additional (emerging) pathogens in the future. As many countries are in the process of implementing integrated surveillance at national level, integrated data collection at European level will be implemented in a stepwise manner in close consultation with the European COVID-19 Surveillance Network (ECOVID-Net), the European Influenza Surveillance Network (EISN), and the European Union SARI surveillance network (E-SARI-Net). The changes proposed in TESSy will initiate the process of integrated data collection for the 2022/2023 winter season (implementation anticipated in September 2022). Three new integrated record types will facilitate reporting: a record type to report case-based data (RESPISURV); a record type to report aggregate age-disaggregated hospital/ICU admissions and occupancy (RESPIHOSP); and a record type for long-term care facility surveillance (RESPILTCFAGGR). Focal point access will be adjusted in accordance with the proposal to allow continued reporting.

Except for NCOV and NCOVLTCFAGGR, all COVID-19 record types will continue to be used during the 2022/23 season. All countries should report aggregate COVID-19 into the existing NCOVAGGR. Where possible, a subset of case-based data should continue to be reported into RESPISURV, to capture information on: (a) cases from all settings with known variant (SARS-CoV-2) or subtype (influenza viruses); (b) severe cases (hospital, ICU or fatal, even if variant/subtype is unknown); and (c) case-based data from primary care sentinel systems, if available. RESPILTCFAGGR, a simplified integrated version of NCOVLTCFAGGR, will be used for reporting data on influenza and COVID-19 in LTCF.

The new integrated record types (RESPISURV, RESPILTCFAGGR, RESPIHOSP) should be used for reporting of influenza data where possible. In addition, reporting to INFLVIRWAGGR has been modified; while virological detections should continue to be reported to INFLVIRAGGR, characterisation data should be reported as disaggregated and individual records in INFLANTIVIR.

SARI datasets SARISURVDENOM, SARISURV, and INFLSARIAGGR, will continue to be used for reporting of SARI data, although INFLSARIDENOM will be discontinued.

More details on the changes to the proposed record types for the 2022/23 autumn/winter season in Table 4. The record types will continue to be reviewed beyond the 2022/2023 autumn/winter season.

Table 4. Summary of changes to TESSy data collection to be implemented prior to the 2022/23 autumn/winter season

For the full list of record types for 2022/2023 season, please refer to Tables A3 – A6 in annexes.

Virus or syndrome	Record type	Status	Description
Integrated viruses (case-based)	RESPISURV	New	Case-based dataset to capture information on: a) cases from all settings with known variant (SARS-CoV-2) or subtype (influenza viruses); and/or b) severe cases (hospital, ICU or fatal). c) case-based data from primary care sentinel, if available. The dataset will include a subset of variables from NCOV to ensure continuity of COVID-19 data. Variables will be consistent with SARISURV.
SARS-CoV-2 (case-based)	NCOV	Discontinued	Report data on sequenced and/or severe (hospitalised, ICU, or fatal) to RESPISURV instead.
SARS-CoV-2 (aggregate)	NCOVAGGR	Reporting modified	All countries should report aggregate age-disaggregated data on comprehensive COVID-19 cases and deaths into NCOVAGGR. Where possible, case-based data for a select case with known variant/subtype or severe outcomes or from primary care sentinel) should be reported into RESPISURV. Hospital and ICU indicators should be reported into RESPIHOSP.
Influenza (aggregate)	INFLVIRWAGGR	Reporting modified	Continue to report virological detections from primary care sentinel to INFLVIRAGGR. Aggregate characterisation data to be disaggregated and reported as individual records in INFLANTIVIR. Dominant type should no longer be reported to TESSy.
Integrated viruses (hospital indicators)	RESPIHOSP	New	Report aggregate age-disaggregated data on hospital/ICU admissions and occupancy. If possible, countries are encouraged to report these indicators for COVID-19 and influenza. Age UNK and Pathogen UNK can be used if disaggregation is not possible.
Integrated viruses (SARI denominator)	INFLSARIDENOM	Discontinued	Reporting all SARI denominators to SARISURVDENOM
Hospital-based laboratory-confirmed cases (case-based)	INFLSARI	Discontinued	Report ICU and non-ICU influenza-confirmed hospitalised cases in RESPISURV (with new variable to indicate system) instead.
Integrated viruses long-term care facility surveillance (aggregate)	RESPILTCFAGGR	New	Variables to be mapped to a subset of those in NCOVLTCFAGGR with the ability to report a different row per country-week specific for each virus (SARS-CoV-2 and influenza viruses).
SARS-CoV-2 long-term care facility surveillance (aggregate)	NCOVLTCFAGGR	Discontinued	Report data to RESPILTCFAGGR instead.
Consultations, denominators, indicators	INFLCLIN	Reporting modified	Modifications will be made to include PISA indicators for influenza. Indicators for integrated or SARS-CoV-2 will need to be developed after 2022/23.

Plans for updating

ECDC and WHO Regional Office for Europe continue to monitor the situation closely for any changes that may affect these operational considerations. Should any factors change, ECDC and WHO Regional Office for Europe will issue a further update.

Contributors and methods

The original version of this document was developed by a group of COVID-19 and influenza technical experts, listed below in alphabetical order, from ECDC and the WHO Regional Office for Europe in consultation with the nominated national focal points from the European COVID-19 Surveillance Network (ECOVID-Net) and the European Influenza Surveillance Network (EISN).

ECDC experts: Cornelia Adlhoch, Eeva Broberg, Nick Bundle, Eleonora Chinchio, Theresa Enkirch, Joana Gomes Dias, Luisa Hallmaier-Wacker, Angeliki Melidou, Maximilian Riess.

WHO Regional Office for Europe experts: Margaux Meslé, Piers Mook, Richard Pebody, Mary Sinnathamby.

In the light of the evolving COVID-19 pandemic and the co-circulation of influenza and RSV, the WHO/ECDC expert group reviewed the available surveillance guidance and assessed the regional surveillance needs. The latter was undertaken through a rapid country survey, with the results directly informing this considerations document.

The sample size calculations presented in the 'Considerations for sizing surveillance systems' section and in the Annex (Figure A2, Tables A6 and A7) are based on the formula published in Annex 1 of ECDC's Guidance for representative and targeted genomic SARS-CoV-2 monitoring [23].

The draft document was shared with all countries in the WHO European Region for their input and was discussed in a number of different fora.

Declaration of interests

There are no conflicts of interest to declare from WHO and ECDC.

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Annex

Case definitions for sentinel surveillance

Table A1. EU (2008 and 2012) case definitions for ILI and ARI

Clinical characteristics	
Influenza-like illness (ILI) • Sudden onset of symptoms AND at least one of the following four systemic symptoms: • Fever or feverishness, malaise, headache, myalgia AND at least one of the following three respiratory symptoms: • Cough, sore throat, shortness of breath	*Acute respiratory infection (ARI)* • Sudden onset of symptoms AND at least one of the following four respiratory symptoms: • Cough, sore throat, shortness of breath, coryza AND • A clinician's judgement that the illness is due to an infection
EU laboratory criteria	
At least one the following four: • Isolation of influenza virus from a clinical specimen • Detection of influenza virus nucleic acid in a clinical specimen • Identification of influenza virus antigen by DFA test in a clinical specimen • Influenza specific antibody response Subtyping of the influenza isolate should be performed, if possible	
Epidemiological criteria	
An epidemiological link by human-to-human transmission	
Case classification	
A. Possible case Any person meeting the clinical criteria (ILI or ARI) B. Probable case Any person meeting the clinical criteria (ILI or ARI) with an epidemiological link C. Confirmed case Any person meeting the clinical (ILI or ARI) and the laboratory criteria	

Table A2. WHO (2011) case definitions for ILI

WHO surveillance case definitions for ILI, 2014
An acute respiratory infection with: • measured fever of ≥ 38 C° • and cough • with onset within the last 10 days

The WHO ILI case definition is more specific and has a higher positive predictive value for influenza compared with the EU ILI definition.

Table A3. WHO case definitions for SARI (2014)

WHO SARI case definition
An acute respiratory infection with: • of fever or measured fever of ≥ 38 C° • and cough • with onset within the last 10 days • and requires hospitalisation

Table A4. SARI case definitions used by E-SARI-Net countries [38]

The recommended clinical SARI case definition for questionnaire-based SARI surveillance is the SARI WHO case definition (2014), which was maintained to facilitate historical comparison in countries with existing systems. Some countries that have opted for a broader, more sensitive case definition are recommended to describe the case definition used and to collect data on the symptoms, including fever, required to allow further analysis. 'Proxy SARI', based on admission or discharge codes indicative of the SARI clinical presentation, is used by countries implementing register-based SARI surveillance, since these systems rarely provide access to information on patient symptoms at admission

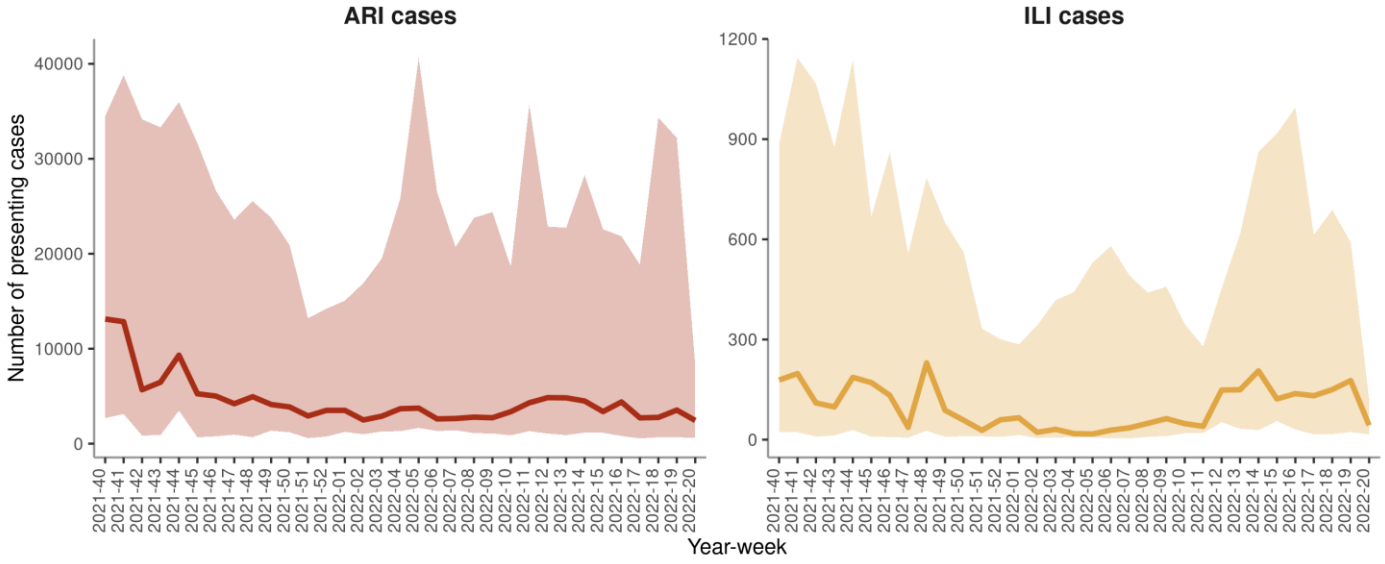
Surveillance objectives and corresponding specific objectives

Table A5. Surveillance objectives and corresponding specific objectives identified from a survey of countries

Surveillance objective	Specific objectives
1. Monitor the intensity, geographical spread and temporal patterns of influenza, COVID-19, and other respiratory virus infections to inform mitigation measures.	• Signal onset and offset of influenza, SARS-CoV-2 and other relevant respiratory virus community activity at defined thresholds; • Describe seasonality of SARS-CoV-2, influenza and other relevant respiratory viruses; • Monitor country-level circulating influenza and SARS-CoV-2 types/subtypes or lineages/sub-lineages.
2. Monitor severity, risk factors for severe disease and assess the impact on healthcare systems of influenza, COVID-19, and other respiratory virus infections to inform mitigation measures.	• Identify and monitor groups at high risk of severe respiratory disease and mortality.
3. Monitor changes and characteristics of circulating and emerging respiratory viruses, particularly virological changes of influenza viruses, SARS-CoV-2, and other respiratory viruses to inform treatment, drug, and vaccine development.	• Rapidly detect, report and investigate unusual and unexpected events of public health importance such as respiratory outbreaks or epidemiologic clusters including zoonotic events; • Describe genetic characteristics of circulating influenza, SARS-CoV-2 and other relevant respiratory viruses where relevant including their relationship to global and regional patterns; • Describe antigenic characteristics of circulating influenza, SARS-CoV-2 and other relevant respiratory viruses where feasible and relevant; • Monitor influenza and SARS-CoV-2 viruses for susceptibility to antiviral drugs; • Provide candidate viruses for influenza and SARS-CoV-2 vaccine composition, production and risk assessment activities; • Assist in developing an understanding of the relationship of respiratory virus strains/genetic composition to disease severity.
4. Describe the burden of disease associated with influenza, COVID-19, and other respiratory virus infections.	• Establish historic levels of activity for illness and severe disease with which to evaluate the intensity, seriousness, and impact of each season/epidemic period and of future pandemic events; • Assess in a timely manner burden of respiratory disease to rapidly understand and prepare for potential increased impact on healthcare.
5. Assess vaccine effectiveness against influenza, COVID-19, and other respiratory virus infections where locally feasible.	• Provide a platform to evaluate vaccine effectiveness and other interventions for influenza, SARS-CoV-2, and other respiratory viruses.

ILI and ARI cases reported in the 2021/22 winter season

Figure A1. Weekly distribution (median and interquartile range) of ILI and ARI cases reported to TESSy from primary care sentinel surveillance in EU/EEA countries, 2021/22 season



Reference tables and examples for sizing surveillance systems

Figure A2. Number and fraction at different levels of precision of a) swabs required from presenting ARI/ILI or SARI cases to estimate target positivity, b) sequences to perform among available RT-PCR-positive specimens to detect variants circulating at target prevalence

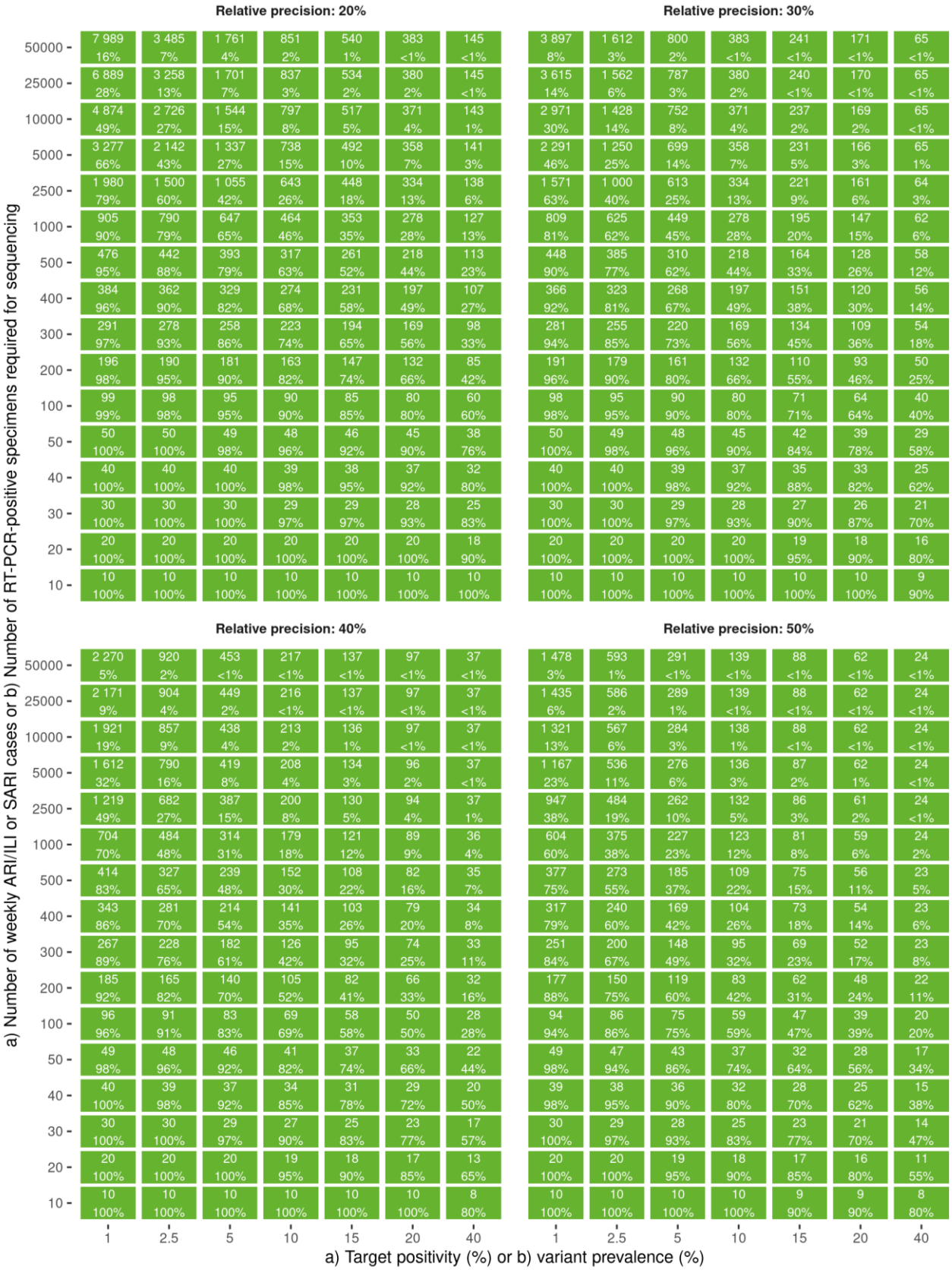


Table A6. Examples of minimum numbers and fraction of sentinel cases needed to swab to estimate positivity thresholds of 5%, 10% and 15% with relative precision of 20%, 30% and 40%, together with the expected resulting number of positive sentinel specimens and the amount of carefully selected top-up non-sentinel specimens needed to have sufficient for sequencing to detect a variant circulating at target threshold prevalence of 1%, 2.5%, 5% or 10%

Additional sequencing of non-sentinel positive specimens from special settings will also be required for targeted surveillance, which has the purpose of detecting signals of emergence of novel variants with potentially changed characteristics (see 'Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants, and virus characteristics').

Weekly sentinel ILI, ARI or SARI cases	Target positivity threshold (95% CI)	Number (%) to swab	Expected positive sentinel specimens	Additional non-sentinel specimens needed to have sufficient for sequencing to detect target threshold prevalence			
				10%	5%	2.5%	1%
100	5% (4-6%)	95 (95%)	5	91	192	397	1 012
500		393 (79%)	20	76	177	382	997
1 000		647 (65%)	32	64	165	370	985
5 000		1 337 (27%)	67	29	130	335	950
25 000		1 701 (7%)	85	11	112	317	932
100	5% (3.5-6.5%)	90 (90%)	4	92	193	398	1 013
500		310 (62%)	16	80	181	386	1 001
1 000		449 (45%)	22	74	175	380	995
5 000		699 (14%)	35	61	162	367	982
25 000		787 (3%)	39	57	158	363	978
100	5% (3-7%)	83 (83%)	4	92	193	398	1 013
500		239 (48%)	12	84	185	390	1 005
1 000		314 (31%)	16	80	181	386	1 001
5 000		419 (8%)	21	75	176	381	996
25 000		449 (2%)	22	74	175	380	995
100	10% (8-12%)	90 (90%)	9	87	188	393	1 008
500		317 (63%)	32	64	165	370	985
1 000		464 (46%)	46	50	151	356	971
5 000		738 (15%)	74	22	123	328	943
25 000		837 (3%)	84	12	113	318	933
100	10% (7-13%)	80 (80%)	8	88	189	394	1 009
500		218 (44%)	22	74	175	380	995
1 000		278 (28%)	28	68	169	374	989
5 000		358 (7%)	36	60	161	366	981
25 000		380 (2%)	38	58	159	364	979
100	10% (6-14%)	69 (69%)	7	89	190	395	1 010
500		152 (30%)	15	81	182	387	1 002
1 000		179 (18%)	18	78	179	384	999
5 000		208 (4%)	21	75	176	381	996

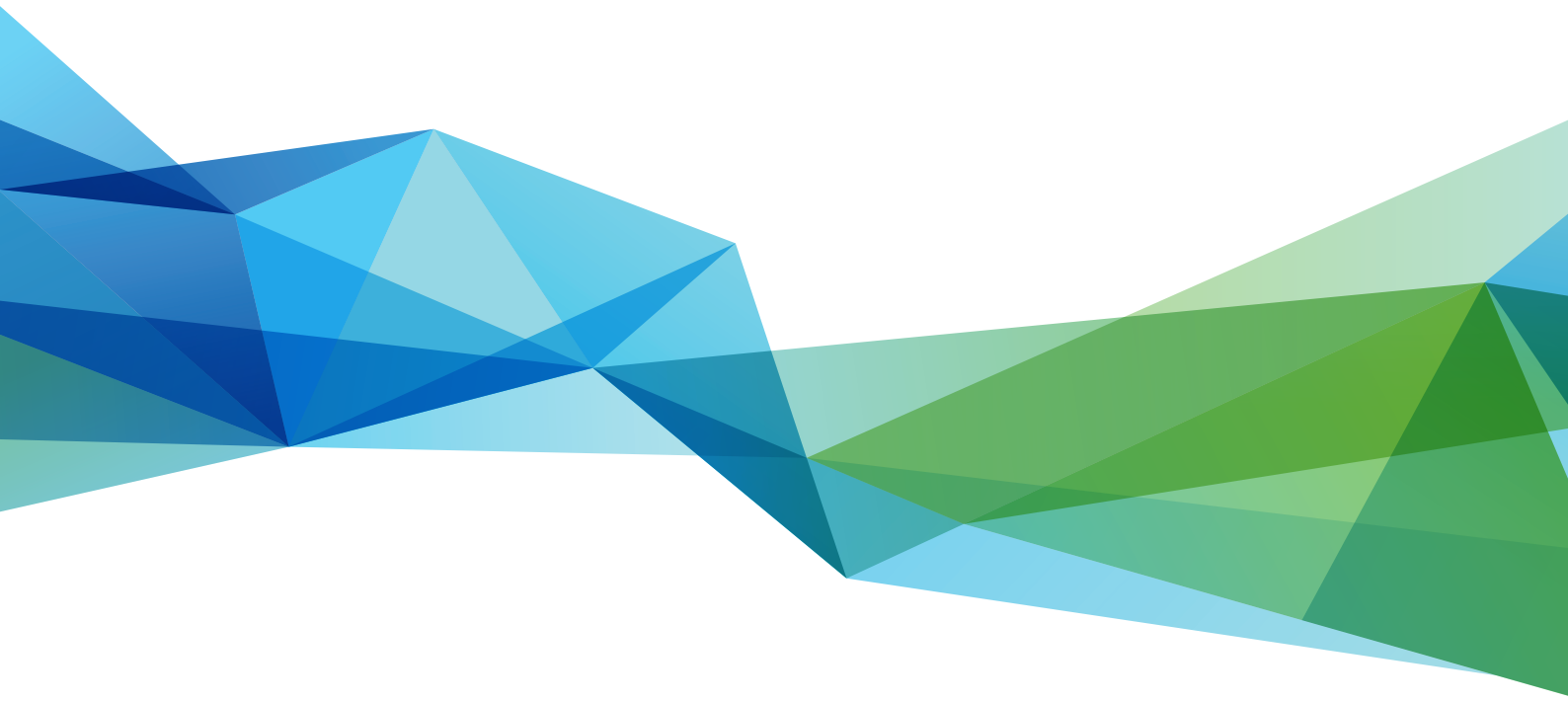
Weekly sentinel ILI, ARI or SARI cases	Target positivity threshold (95% CI)	Number (%) to swab	Expected positive sentinel specimens	Additional non-sentinel specimens needed to have sufficient for sequencing to detect target threshold prevalence			
				10%	5%	2.5%	1%
25 000		216 (1%)	22	74	175	380	995
100	15% (12-18%)	85 (85%)	13	83	184	389	1 004
500		261 (52%)	39	57	158	363	978
1 000		353 (35%)	53	43	144	349	964
5 000		492 (10%)	74	22	123	328	943
25 000		534 (2%)	80	16	117	322	937
100	15% (10.5-19.5%)	71 (71%)	11	85	186	391	1 006
500		164 (33%)	25	71	172	377	992
1 000		195 (20%)	29	67	168	373	988
5 000		231 (5%)	35	61	162	367	982
25 000		240 (1%)	36	60	161	366	981
100	15% (9-21%)	58 (58%)	9	87	188	393	1 008
500		108 (22%)	16	80	181	386	1 001
1 000		121 (12%)	18	78	179	384	999
5 000		134 (3%)	20	76	177	382	997
25 000		137 (1%)	21	75	176	381	996

Table A7. Examples for weekly sentinel case numbers of 100, 500, 1 000, 5 000 or 25 000, showing the impact of different swabbing schemes (10-50% of cases swabbed) and the level of viral circulation (low, started of epidemic activity, high) on the expected number of positive sentinel specimens and the amount of carefully selected top-up non-sentinel specimens needed to have sufficient specimens for sequencing to detect a variant circulating at target threshold prevalence of 1%, 2.5%, 5% or 10%

The table is limited to rows in with an expected positive sentinel specimens of at least 25 (sufficient to be able to sequence the minimum 15 per week recommended for low resource settings, assuming only no more than 60% of specimens are technically suitable for sequencing) and no more than 1 017 (sufficient to detect a variant circulating at a 1% target threshold prevalence). Additional sequencing of non-sentinel positive specimens from special settings will also be required for targeted surveillance, which has the purpose of detecting signals of emergence of novel variants with potentially changed characteristics (see 'Monitoring of influenza virus strains/lineages, SARS-CoV-2 variants and virus characteristics').

Viral circulation	Weekly sentinel ILI, ARI or SARI cases	Fraction swabbed, % (number)	Expected positive sentinel specimens	Additional non-sentinel specimens needed to have sufficient for sequencing to detect target threshold prevalence			
				10%	5%	2.5%	1%
Low (1% positivity)	5 000	50 (2 500)	25	71	172	377	992
	25 000	10 (2 500)	25	71	172	377	992
		20 (5 000)	50	46	147	352	967
		40 (10 000)	100	0	97	302	917
		50 (12 500)	125	0	72	277	892
Start of epidemic activity (10% positivity)	500	50 (250)	25	71	172	377	992
	1 000	40 (400)	40	56	157	362	977
		50 (500)	50	46	147	352	967
	5 000	5 (250)	25	71	172	377	992

Viral circulation	Weekly sentinel ILI, ARI or SARI cases	Fraction swabbed, % (number)	Expected positive sentinel specimens	Additional non-sentinel specimens needed to have sufficient for sequencing to detect target threshold prevalence			
				10%	5%	2.5%	1%
		10 (500)	50	46	147	352	967
		20 (1 000)	100	0	97	302	917
		40 (2 000)	200	0	0	202	817
		50 (2 500)	250	0	0	152	767
	25 000	5 (1 250)	125	0	72	277	892
		10 (2 500)	250	0	0	152	767
		20 (5 000)	500	0	0	0	517
		40 (10 000)	1 000	0	0	0	17
High (40% positivity)	500	20 (100)	40	56	157	362	977
		40 (200)	80	16	117	322	937
		50 (250)	100	0	97	302	917
	1 000	10 (100)	40	56	157	362	977
		20 (200)	80	16	117	322	937
		40 (400)	160	0	37	242	857
		50 (500)	200	0	0	202	817
	5 000	5 (250)	100	0	97	302	917
		10 (500)	200	0	0	202	817
		20 (1 000)	400	0	0	2	617
		40 (2 000)	800	0	0	0	217
		50 (2 500)	1 000	0	0	0	17
	25 000	5 (1 250)	500	0	0	0	517



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