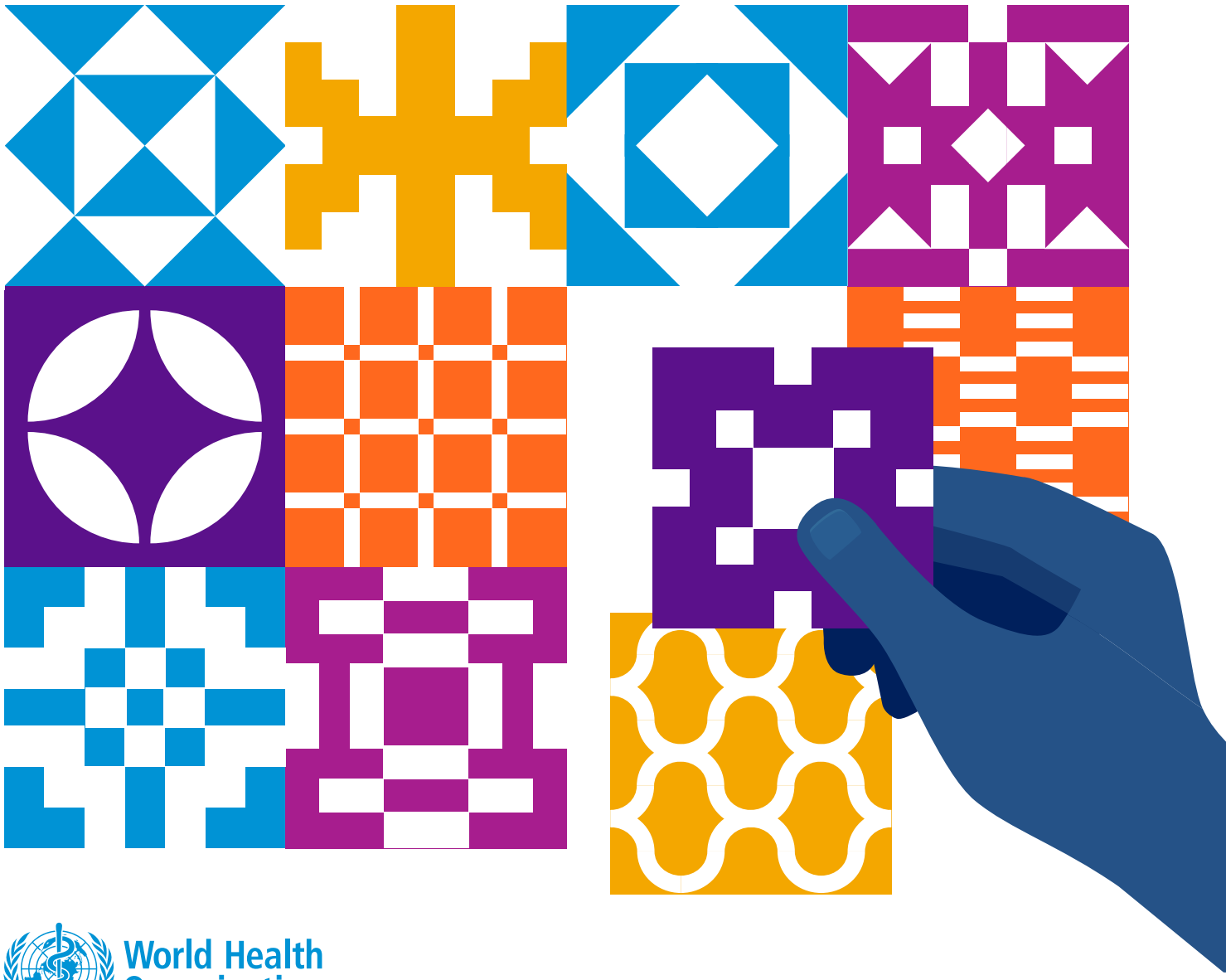
“Crafting the mosaic”

A framework for resilient surveillance for respiratory viruses of epidemic and pandemic potential



World Health Organization

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Preface

It is impossible to address the many complex needs of respiratory virus surveillance with a single surveillance system. Multiple systems, investigations and studies must each be fit-for-purpose to specific priority surveillance objectives, and only together can they provide essential information to policy-makers. In essence, each surveillance approach fit together as "tiles in a mosaic" that provides a complete picture of respiratory viruses and the impact of associated illnesses and interventions at the country level. This mosaic framework demonstrates how surveillance approaches may be implemented as coordinated and collaborative systems, well-matched to specific priority objectives. To do so, this framework presents appropriate uses of surveillance systems and refers to existing global and regional surveillance guidance wherever it exists. *However, it does not supersede any existing global or regional normative surveillance guidance*. While this framework has a specific focus on respiratory viruses of epidemic and pandemic potential, there is also a noted applicability in several sections to other respiratory and non-respiratory pathogens. The framework also addresses the surveillance and investigations to be undertaken in human populations. Although the One Health approach regarding the coordination of surveillance and response with animal and environmental health partners is essential and emphasized, this framework is not meant to fully address the separate surveillance approaches specific to these contexts.

Finally, the focus of this document is primarily on interpandemic surveillance to meet early warning and routine monitoring needs, understanding that adaptations will be made with the emergence of a novel pathogen of pandemic potential. This framework is not pandemic surveillance guidance, but it does include some suggestions for how to leverage interpandemic surveillance in order to provide some of the more robust data that may be required during epidemic and pandemic periods.

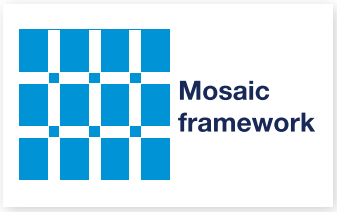
What is new about this framework?

For the first time, this framework:

- demonstrates how surveillance approaches may be implemented as coordinated and collaborative systems, well-matched to specific priority objectives;
- identifies the most important surveillance approaches needed for: 1) early warning; 2) resilient interpandemic monitoring; and 3) informing the use of interventions in both high and lower resourced contexts;
- illustrates how recent innovations from the coronavirus disease 2019 pandemic may support ongoing surveillance initiatives;
- guides how properly focused interpandemic surveillance may support epidemic, pandemic and other emergency monitoring needs; and
- aligns technical and funding partners to focus on highest priority surveillance enhancements.

How to use the mosaic framework

This framework is to be used in electronic format and is divided into two parts.



The **mosaic compass** Click to view → (pages 1-15) provides the key recommendations of the complete mosaic framework, including suggested core and enhanced surveillance approaches to be used within early warning, sustainable monitoring and intervention assessment surveillance domains. These surveillance approaches are presented for quick review by domain within figures.

The **mosaic framework** Click to view → (pages 16-66) may also be read as a stand-alone document. This longer document includes all descriptions and rationale for each surveillance approach, additional topics, and case studies of implementation in context.

Within both the **mosaic compass**, and **mosaic framework** the reader is encouraged to click on each of the surveillance approaches within the mosaic figures to be taken to a more detailed description of the surveillance approach and the rationale for its suggested positioning within the mosaic.

Furthermore the viewer can click on the variety of special topics, global initiatives, innovations in surveillance, case studies and a section on implementation planning to obtain more topic-specific information.

To then return to relevant key sections of the document, the viewer can utilize the navigation bar at the bottom of the page.

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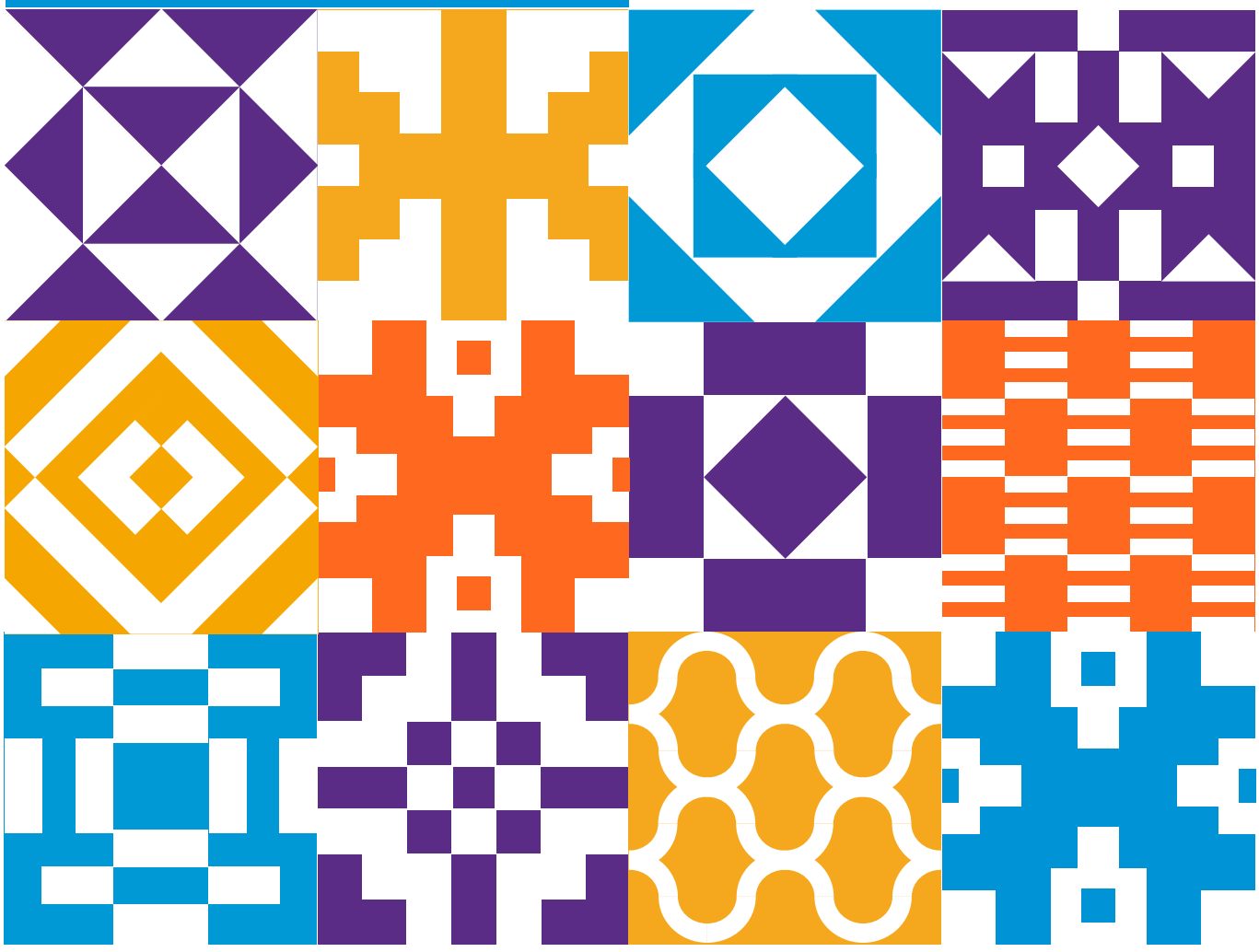
Assessment and management of conflicts of interest

In accordance with WHO policy, experts completed the WHO form for Declaration of Interest before they were invited to the WHO Consultation. The interests declared were reviewed by WHO and determined not to present a conflict with the objective of the WHO Consultation, which led to the development of the guidance.

Abbreviations and acronyms

ARI	acute respiratory infection
CDC	Centers for Disease Control and Prevention
CEBS	community event-based surveillance
CONSISE	Consortium for the Standardization of Influenza Seroepidemiology
COVID-19	coronavirus disease 2019
DHIS	District Health Information Software
DRC	Democratic Republic of the Congo
ECDC	European Centre for Disease Prevention and Control
EHR	Electronic Health Records
EOIS	Epidemic Intelligence from Open Sources
EuroMOMO	European mortality monitoring
EWARN	early warning, alert and response networks
EWARS	early warning, alert and response system
FAO	Food and Agriculture Organization of the United Nations
GISRS	Global Influenza Surveillance and Response System
GOARN	Global Outbreak Alert and Response Network
HIV	human immunodeficiency virus
HL7	health level-7
ICD	International Classification of Diseases
IDSR	Integrated Disease Surveillance and Response (strategy)
IHR (2005)	International Health Regulations (2005)
ILI	influenza-like illness
IOA	integrated outbreak analytics
JEE	joint external evaluation
MERS-CoV	Middle East respiratory syndrome coronavirus
MOH	ministry of health
NNDS	nationally notifiable diseases and conditions surveillance
NGO	non-governmental organization
PHSM	public health and social measures
PISA	Pandemic Influenza Severity Assessment (tool)
RSV	respiratory syncytial virus
SAGE	Strategic Advisory Group of Experts
SARI	severe acute respiratory infection
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SPAR	State Party Self-Assessment Annual Report
TWG	technical working group
WHO	World Health Organization

Mosaic compass



1. Introduction

1.1 Background and rationale

Public health surveillance provides the critical information to inform the response to emerging public health threats and resource allocation. The specific needs to be addressed will determine the shape that a surveillance approach should take. In addition, the design of any new surveillance system should start with a consideration of the purpose for which the data will be used. The needs of public health authorities differ depending on the actions to be taken, the policies to be defined, and even the disease process to be monitored. As a result, it is impossible to meet all needs with a single system. The basic, primary roles for which surveillance systems are generally designed are usually event/outbreak detection or monitoring trends in transmission. However, there are many special situations in which systems will be modified or adapted to provide more detailed information on risk groups, transmission dynamics or the burden of disease, as well as providing data for the production of testing and treatment methods or vaccines, or to dig deeper and answer specific questions about transmission dynamics. This document fits together the many surveillance approaches into a 'mosaic' that might be considered in a single framework to enable policy planners to establish collaborative surveillance systems that are fit for purpose.

This document focuses on respiratory viruses with observed epidemic or pandemic potential in humans as a prototypical example of the way surveillance systems can work together resiliently to provide a comprehensive picture of disease emergence, spread and impact. There are several respiratory viruses that have important commonalities in specimen collection needs and surveillance approaches. However, there are areas where this framework has applicability beyond respiratory viruses, and in some cases beyond respiratory pathogens irrespective of the biological class of a novel pathogen, several attributes are likely to be essential components of any pathogen with pandemic potential. These traits include efficient human-to-human transmissibility, the absence of an effective or widely available medical countermeasure, an immunologically naïve population, virulence factors enabling immune system evasion, and a respiratory mode of spread. Additionally, the ability to transmit during incubation periods and/or the occurrence of mild illnesses would further augment spread. Several features of respiratory viruses make this class of microbial agents the most likely to cause future pandemics *(1)*.

Surveillance approaches are grouped into three general domains based on their general purpose.

Domain I:
detection and assessment of an emerging or re-emerging respiratory virus;

Domain II:
monitor epidemiological characteristics of respiratory viruses in interpandemic periods; and

Domain III:
informing use of human health intervention

Within each domain, multiple surveillance approaches must work together to address multiple objectives, but with the understanding that sources of information from different approaches may each contribute to answer one epidemiological question (for example, multi-source surveillance *(2)*). This framework will help users to quickly identify priority objectives and then consider surveillance approaches that work best according to country contexts and needs. Within this framework, surveillance approaches may then be implemented as coordinated and collaborative systems, well-matched to specific priority objectives (see *Figs. 1 and 2*). In essence, they

form a mosaic of approaches to resiliently support the prevention, detection and control of respiratory viruses of epidemic and pandemic potential over time. Each surveillance approach represents a tile in the mosaic and only when viewed together will they provide the complete and understandable picture of the human health risk and impact associated with respiratory viruses.

The coronavirus disease 2019 (COVID-19) pandemic generated new innovations as surveillance systems were developed or enhanced to monitor mortality trends, disease severity, clinical outcomes, health system capacities, the evolution of viruses, transmissibility, and the effectiveness of interventions *(3)*. Some examples of these include the use of new laboratory methods, expanded environmental surveillance, novel diagnostic techniques, and the implementation of non-traditional surveillance in community settings. To inform longer term surveillance planning, the benefits, limitations and most appropriate applications of these innovations must be considered. Some should now be institutionalized and incorporated into surveillance for future emerging events.

Figure 1 Vision, domains and aims of the mosaic framework

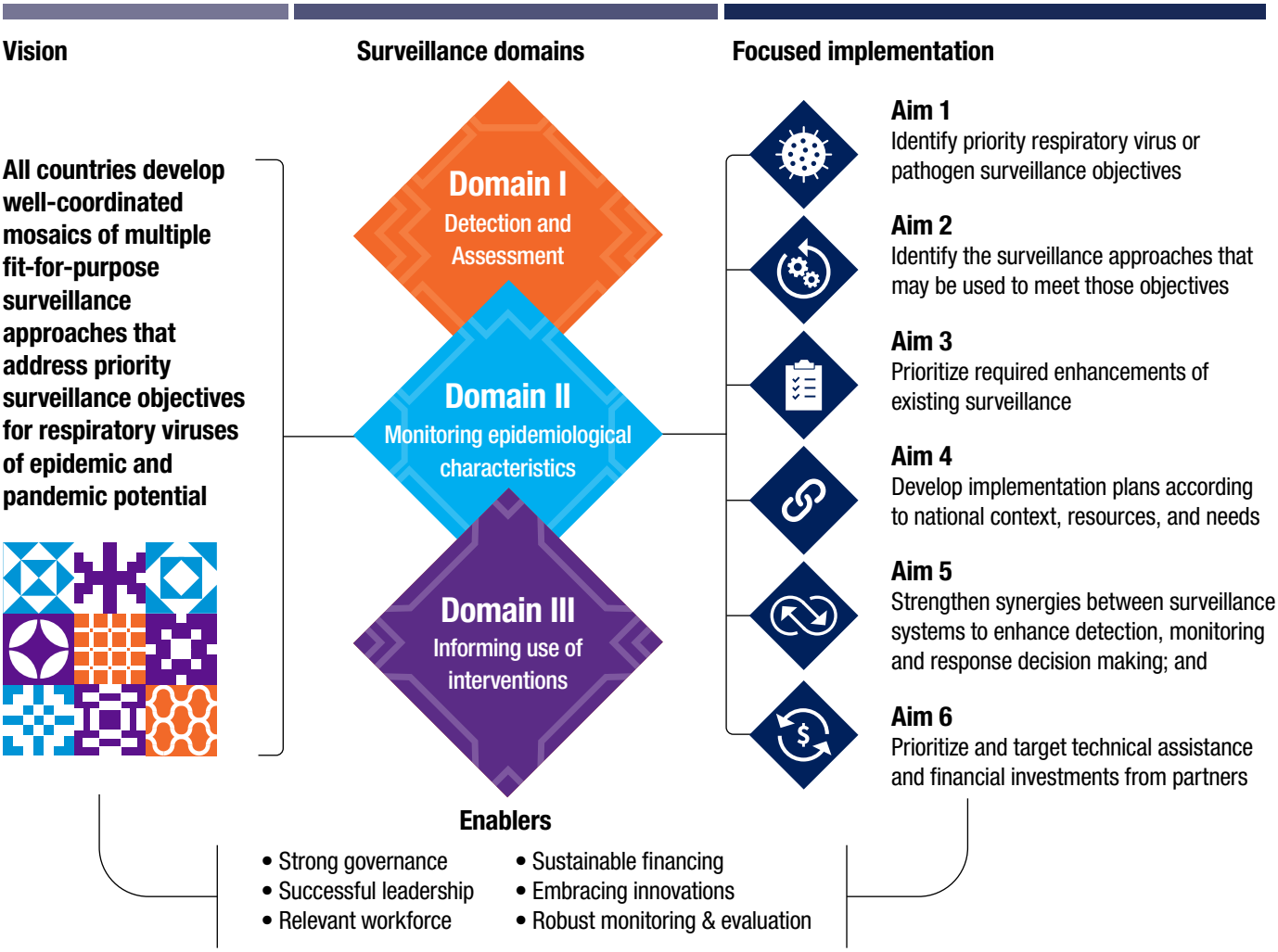


Figure 2 Summary of priority surveillance objectives for each domain

Domain I:
Detection and assessment of an emerging or re-emerging respiratory virus

Surveillance objectives

1. Rapidly detect emerging or re-emerging respiratory virus outbreaks and other events
2. Assess transmissibility, risk factors for transmission, and extent of infection from an emerging or re-emerging respiratory virus
3. Describe clinical presentation and risk factors for severe outcomes associated with an emerging or re-emerging respiratory virus

Domain II:
Monitor epidemiological characteristics of respiratory viruses in interpandemic periods

1. Monitor epidemiologic and clinical characteristics of illness over time
2. Monitor virologic and genetic characteristics of circulating viruses
3. Monitor situation in high-risk settings and vulnerable populations
4. Monitor impact on and coping abilities of health care systems

Domain III:
Informing use of human health interventions

1. Monitor the impact of non-medical interventions in the population
2. Provide candidate vaccine viruses for vaccine composition, production, and risk assessment
3. Monitor vaccine coverage, effectiveness, impact, and cost-effectiveness
4. Monitor the effectiveness of antivirals and other therapeutics
5. Monitor the effectiveness of diagnostic tests
6. Monitor the effectiveness of clinical care pathways, including Infection, Prevention and Control (IPC)
7. Monitor adverse events to vaccines and therapeutics

Resilience has been defined as the “ability to prepare for, manage, recover and learn from a sudden and extreme disturbance” *(4)*. The concept of resilience in public health surveillance is associated with system attributes *(5)* such as flexibility, acceptability, stability, sustainability, and utility *(6)*. Resilience of surveillance may also be improved if surveillance systems are targeted to priority surveillance objectives that they can most efficiently address (that is, they are “fit-for-purpose") and if there is a commitment by public health authorities to sustain these systems. The mosaic framework considers the existing surveillance systems and networks that have been successfully leveraged to resiliently monitor multiple respiratory viruses over time. As a primary example, the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS) *(7)* began to integrate respiratory syncytial virus (RSV) surveillance in selected locations in 2015 *(8)*. At the 150th session of the WHO Executive Board meeting in January 2022 and the Seventy-fifth World Health Assembly in May 2022 *(9)*, Member States supported GISRS sentinel surveillance platforms to be further leveraged to meet key monitoring needs not only for influenza, but also for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other respiratory viruses *(10)*. The majority of GISRS institutions have leveraged the GISRS laboratory, reporting, surveillance and outbreak response network and integrated SARS-CoV-2 monitoring into GISRS sentinel surveillance. This framework builds on this experience and suggests the objectives that may be addressed by GISRS and, importantly, those that require the complementary contributions of different surveillance approaches.

The process leading to the development of this framework systematically considered surveillance experiences before and during the COVID-19 pandemic and organized regional and global conferences and consultations to formulate recommendations. Throughout the process, care was taken to consider what surveillance approaches may be fit-for-purpose in both higher and lower resourced environments. The framework seeks to also highlight recent surveillance innovations, while suggesting important considerations to take into account when evaluating their use in local contexts.

1.2 Vision

All countries develop well-coordinated mosaics of multiple fit-for-purpose surveillance approaches that address priority surveillance objectives for influenza, SARS-CoV-2, and other respiratory viruses of epidemic and pandemic potential according to country context.

A well-crafted mosaic of surveillance approaches should engender ongoing collaboration, as well as trust and investment by authorities who will also seek to scale-up, enhance and/or leverage these systems in an emergency *(11).*

1.3 Aim and scope

This framework is intended to be a practical tool to assist individual countries and regions as they conceptualize and design their own context-appropriate mosaic of surveillance approaches to address their priority respiratory virus surveillance objectives.

To that end, this framework will serve as a tool to help countries (see *Fig. 1*):

- identify priority respiratory virus or pathogen surveillance objectives;
- identify the surveillance approaches that may be used to meet these objectives;
- prioritize required enhancements of existing surveillance;
- develop implementation plans according to the national context, resources and needs;
- strengthen synergies between surveillance systems to enhance detection, monitoring and response decision-making;
- prioritize and target technical assistance and financial investments from partners.

The framework is intended to serve the needs of all countries, regardless of the income or humanitarian context, and draws upon examples of how indicator-based and/or event-based surveillance are addressing priority objectives in each region (see *Fig. 2*). The desired impact is for the national surveillance of respiratory viruses of epidemic and pandemic potential to be strengthened, expanded, consolidated, and modernized in a coordinated and resilient manner *(12)*.

1.4 Alignment with existing initiatives and structures

This framework is a conceptual structure that underpins and supports current initiatives and *does not supersede any existing global or regional normative surveillance guidance*. Rather, it is intended to place the systems represented by existing guidance into a context where they may address the objectives for which they are best intended. The framework presents appropriate uses of existing systems for respiratory virus surveillance and refers to existing global and regional surveillance-specific guidance and operating procedures wherever they exist.

This framework is a tool to support the implementation of the International Health Regulations (IHR) 2005, specifically the core capacity requirements for surveillance and response *(13)* and therefore also National Action Plans for Health Security *(14)* and will be adapted if the ongoing discussion related to the revision of the IHR (2005) requires it. In addition, it is in-line with the collaborative surveillance component of the WHO Global Architecture for Health Emergency Preparedness, Response and Resilience (*12*). This tool will evolve to ensure it meets countries needs and synchronizes with the ongoing discussion for the "pandemic convention accord +". It does so by:

- strengthening and coordinating systems for the detection (early warning) and monitoring of respiratory pathogens;
- supporting the expansion of laboratory capacity for pathogen and genomic surveillance;
- fostering integration of best practices, technologies and innovation.

1.5 Audience

The document is intended to be used **at national, regional and global levels to support national respiratory virus surveillance strengthening through the creation of implementation plans.** National governments (often including ministries of health and/or national institutes of public health in close collaboration with ministries of agriculture and the environment for zoonotic diseases) are accountable for implementation of this framework within their own territory and WHO across territories as an organization of Member States who are under IHR obligations, including its associated Joint External Evaluation framework.

Implementation of this mosaic can also help international partners and donor agencies, academia, the private sector, and other partners to focus technical and financial resources on the most essential surveillance needs in a country or region in a meaningful and non-duplicative manner.

1.6 Living guidance and country experience underpinning the framework

This framework exists on-line which will allow for regular updates and is complemented by a virtual repository of guidance Click to view →, tools and case studies Click to view →, which may all be accessed on the WHO website Click to view →. Importantly, it ensures access to the latest versions of any documents that will support countries to define and implement their respective surveillance mosaics.

The mosaic framework was developed using extensive consultations with WHO regional offices and Member States, and external technical partners. For more details on the process and methods of framework development, please click here Click to view →

2. Surveillance approaches

The mosaic figures (*Figs. 3-5*) and associated text below provide a summary of suggested surveillance approaches by surveillance domain. As the basis for a maturity model, “core” surveillance approaches are suggested as those that countries of any resource level might aspire to implement. Surveillance approaches indicated to be “enhanced” may also be valuable to meet objectives in each domain, but may require more resources or capacities at the national level than core approaches. Where appropriate, these figures also indicate surveillance innovations and considerations for implementation that may support mosaic surveillance implementation. As this is a ‘mosaic compass’, the reader may “click” on any surveillance approach to be taken to a description and the rationale for its placement in the mosaic. In some cases, this will also bring the reader to case studies of implementation. Similarly, clicking on specific innovations and global initiatives will bring the reader to more details on those topics. For those who wish to read the entire document with system descriptions, innovations, global initiatives, special topics and case studies placed in context, the longer framework begins on page 16 Click to view →

2.1 Domain I: Detection and assessment of an emerging or re-emerging respiratory virus

An emerging virus may be the result of a newly-introduced virus in the human population, or a known virus that has re-emerged and/or developed novel or unique transmission dynamics or clinical manifestations (including novel phenotypically relevant variants and subtypes). The timely detection of a virus that could emerge, spread and cause illness in humans requires multiple event-based and indicator-based systems to work together. Communication and collaboration across sectors (including with the agricultural and environmental sectors for the investigation and assessment of animal reservoir species) and between national, intermediate and primary public health response levels of authority *(16)* is of the utmost importance for this Domain.

Within Domain I, priority surveillance objectives are to:

1. *rapidly detect emerging or re-emerging respiratory virus outbreaks and other events;*
2. *assess transmissibility, risk factors for transmission, and the extent of infection from an emerging or re-emerging respiratory virus;*
3. *describe the clinical presentation and risk factors for severe outcomes associated with an emerging or re-emerging respiratory virus.*

The early warning, alert and response capability is a critical requirement of the IHR (2005) core capacities and serves to prevent the emergence of, or mitigate the impact of, a future respiratory epidemic or pandemic. This includes the strengthening of coordinated systems in health care and community settings throughout the year and at the animal-human interface (for pathogens with a zoonotic reservoir). Once detected, emerging events will necessitate the modification of surveillance methods, including intensive case-finding and specialized investigations and studies to fully characterize a novel or re-emerging respiratory viral pathogen. However, it is essential to have a pre-existing monitoring system in place to enable a rapid transition to more intensive case detection and provide a platform for further investigations. Table 1 outlines the questions that may be addressed by national authorities in Domain I.

Table 1 Questions that may be addressed by national authorities in Domain I

- Has there been a new respiratory virus or variant detected in my country?
- What are the virological characteristics of the emerging or re-emerging viruses (including novel variants or sub-types)?
- What is the descriptive epidemiology of the disease (time, place, person)?
- How many people are known or likely to have been exposed and does it spread easily in humans?
- How severe is the disease and what are the high risk groups for infection and severe disease?
- What is the risk that this emerging or re-emerging respiratory virus has epidemic or pandemic potential?
- Is it relevant for me to activate a national pandemic response plan or 'state of emergency' and related funding support?
- Is it the right time for the government to communicate to the population that this emerging or re-emerging virus has epidemic or pandemic potential?
- How do I translate the scientific facts into messaging that empowers the community for action?

Core surveillance approaches within Domain I include strong **health facility event-based surveillance** that can be complemented by the mandates of **nationally notifiable diseases and conditions' surveillance**. **Community event-based surveillance** is also important to identify emerging threats in populations with limited access to health care and **at the animal-human interface**. **Established laboratory networks** are essential to identify pathogens responsible for reported illnesses and events and to provide timely phenotypic and genotypic characterizations. Laboratory networks may also support the detection of pathogens that are immediately notifiable, rare pathogens, and unexpected increases in the detection of organisms over a specific time period or from an unusual place. Finally, **investigations and studies** are core in this domain to assess transmissibility and its subsequent risk factors, extent of infection, but also to describe clinical features and risk factors for severe outcomes. These core systems may be enhanced by **media event-based surveillance**, **targeted special population surveillance**, and **syndromic surveillance** that can play a particularly important role in humanitarian settings. In many instances, these surveillance approaches also have applicability to detect events beyond those associated with respiratory pathogens.

Fig. 3 illustrates the priority surveillance objectives and dedicated surveillance approaches for Domain I.

Figure 3 Domain I: Priority objectives and dedicated surveillance approaches to address the detection and assessment of an emerging or re-emerging respiratory virus

(click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)

Detection and Assessment

Priority surveillance objectives	**Core** recommended surveillance approaches and investigations to fulfill objectives	**Enhanced** surveillance approaches and investigations that may help to fulfill objectives
1 Rapidly detect emerging or re-emerging respiratory virus outbreaks and other events	Health facility event-based surveillance; Notifiable disease surveillance; Laboratory networks; Community event-based surveillance	Targeted special population surveillance; Media event-based surveillance; Syndromic surveillance
2 Assess transmissibility, risk factors for transmission, and extent of infection from an emerging or re-emerging respiratory virus	Investigations and studies	Targeted special population surveillance; Laboratory networks; Notifiable disease surveillance
3 Describe clinical presentation and risk factors for severe outcomes associated with an emerging or re-emerging respiratory virus	Investigations and studies	Targeted special population surveillance; Laboratory networks; Notifiable disease surveillance

Innovations and initiatives

- Integrated Disease Surveillance and Response (IDSR)
- Epidemic Intelligence from Open Sources (EIOS)
- Unity Studies initiative
- Integrated Outbreak Analytics (IOA)

Supportive initiatives

Surveillance innovations

- EWARS in a box
- Wastewater surveillance
- Rapid testing
- Participatory surveillance

2.2 Domain II: Monitoring epidemiological characteristics of respiratory viruses in interpandemic periods

Surveillance approaches in Domain II are for monitoring respiratory viruses that are circulating in human populations during interpandemic periods. These may also be leveraged and enhanced during pandemic periods (see leveraging and scaling interpandemic surveillance during emergencies in section 2.5 Click to view →. Therefore, these approaches may have applicability beyond viruses of pandemic potential and may play essential roles in monitoring respiratory pathogens of public health importance or epidemic potential, given similarities in required specimen and data collection needs. Finally, Domain II surveillance approaches also provide support to the early warning objectives of Domain I. From an epidemiological standpoint, established baselines and thresholds or systems in place to monitor changes in clinical or demographic characteristics of cases identified in surveillance may provide signals of potential new events, such as the onset of a seasonal epidemic or the occurrence of an unusually severe season. Similarly, the laboratory components of surveillance may support the detection of changes in circulating viruses (for example, emerging variants or antigenic changes), thus triggering further investigations as applicable.

Within Domain II, priority surveillance objectives are to:

1. *monitor the epidemiological and clinical characteristics of illness over time;*
2. *monitor the virological and genetic characteristics of circulating viruses;*
3. *monitor the situation in high-risk settings and vulnerable populations;*
4. *monitor the impact on and coping abilities of health care systems.*

Table 2 outlines the questions that may be addressed by national authorities in Domain II.

In general, the surveillance approaches in Domain II have applicability to respiratory viruses (and in some case non-viral pathogens) of epidemic and pandemic potential. Core surveillance approaches within Domain II include **sentinel influenza-like illness (ILI)/acute respiratory infection (ARI)/severe acute respiratory infection (SARI) case-based surveillance systems with the integration of laboratory testing**. These systems can collect high quality epidemiological data and respiratory specimens from a representative sample of the population under surveillance. This can support virological and trend monitoring and provide epidemiological and clinical descriptions of illness associated with specific respiratory viruses. Although less well-suited to monitoring common conditions, **nationally notifiable diseases and conditions surveillance systems** provide an important complement to sentinel monitoring by being more comprehensive and therefore reaching more specific priority subgroups of the population that may not be well represented in sentinel surveillance. More detailed monitoring of high-risk subgroups may also be achieved

Table 2 Questions that may be addressed by national authorities in Domain II

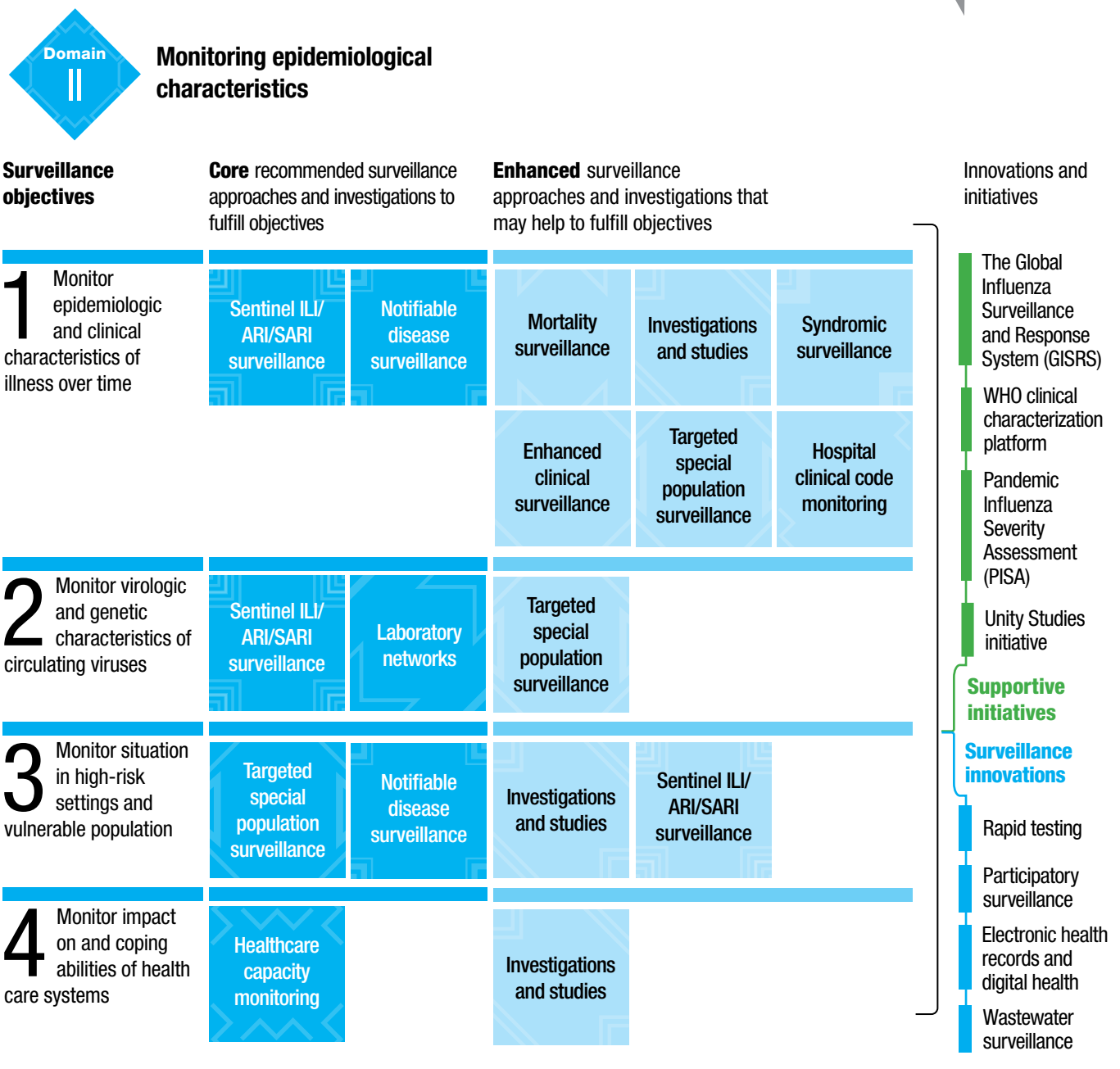
- When is the optimal time of year to use vaccines? Is there seasonal transmission?
- When should clinicians be alerted to the onset of a seasonal epidemic?
- How severe is this season compared to previous ones?
- How close is the match between vaccines in use and the viruses they target?
- How should resources be allocated for different respiratory viral threats?
- Who is at highest risk for severe disease? What is the impact in high-risk settings and vulnerable groups? Which priority groups need additional attention, response measures and funding to reduce the impact of the disease?
- Do interventions need to be modified based on changes in the behaviour of the virus?
- How is the virus moving through the community and country? Are there reservoirs of transmission? Areas of higher/lower transmission?
- What are the characteristics of the virus and epidemiology of the disease (time, place, person) and has this changed? Are there genetic characteristics of the virus that may predict transmission behaviour, virulence, susceptibility to pharmaceuticals, or vaccine effectiveness?
- How is the health care system coping?

through specifically **targeted special population surveillance**.

Strong laboratory networks remain essential in this domain to identify and characterize pathogens associated with illness. Notably, the integration of clinical, academic, and surveillance laboratories can help generate larger sample sizes needed to monitor virological changes in circulating pathogens at a lower prevalence. Sustaining systems for **health care capacity monitoring** also represents a core system for monitoring the impact of seasonal epidemics on the health care infrastructure. Within Domain II, enhanced approaches such as **mortality surveillance, hospital clinical code monitoring systems**, **enhanced clinical surveillance**, and the implementation of **investigations and studies** could help address specific objectives within this domain more robustly.

Fig. 4 demonstrates the priority objectives and dedicated surveillance approaches for Domain II.

Figure 4 Domain II: Priority surveillance objectives and dedicated surveillance approaches to address them (click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)



2.3 Domain III: Informing the use of human health interventions

Within Domain III, priority surveillance objectives are to:

1. *monitor the impact of non-medical interventions in the population: including public health and social measures (PHSM) and Risk Communication and Community Engagement;*
2. *provide candidate vaccine viruses for vaccine composition, production and risk assessment;*
3. *monitor vaccine coverage, effectiveness, impact and cost-effectiveness;*
4. *monitor the effectiveness of antivirals and other therapeutics;*
5. *monitor the effectiveness of diagnostic tests;*
6. *monitor the effectiveness of clinical care pathways, including infection prevention and control;*
7. *monitor adverse events to vaccines and therapeutics.*

The ongoing evaluation of interventions should be integrated into more routine surveillance activities, provided that the needed data collection does not inhibit system resilience or sustainability. In many locations, 'off-the-shelf' protocols for complementary investigations and studies may be the most feasible mechanism to quickly obtain needed information. Table 3 outlines the questions that may be addressed by national authorities in Domain III.

Within Domain III, the detailed data requirements associated with intervention evaluation most often necessitate **studies and investigations**. These should be developed and exercised in interpandemic periods to support routine policy needs and to increase pandemic preparedness. However, **sentinel ILI/ ARI/SARI case-based surveillance systems** have served as core systems for the routine monitoring of vaccine effectiveness using test-negative designs. With the support of strong **laboratory networks,** sentinel systems also provide information on circulating viruses and associated data needed to inform vaccine strain selection. Furthermore, **enhanced clinical surveillance** provides important models to evaluate clinical care during the current COVID-19 pandemic. The implementation of medical interventions in the community also makes the **pharmacovigilance** functions of adverse event monitoring a core component of the Domain III mosaic. **Health care capacity monitoring and hospital clinical code monitoring** are enhanced approaches that may provide an indication of changes in the hospital impact with the implementation of PHSM. Finally, **community and media event-based surveillance** provide support to Domain 1, but may also be leveraged as a mechanism to understand community knowledge, attitudes, and practices related to intervention implementation.

Fig. 5 demonstrates the priority surveillance objectives and dedicated surveillance approaches for Domain III.

Table 3 Questions that may be addressed by national authorities in Domain III

- Which PHSMs will be the most effective to reduce the impact of the virus?
- How should the government respond effectively and cost-effectively to the deteriorating health situation?
- Are the current pharmaceutical interventions (for example, vaccines and antivirals) in use effective in the real-world setting and do they remain effective as the virus evolves? Should they be changed?
- How can I be confident in the real-world effectiveness (that is, outside a very controlled, randomized clinical trial environment) of the vaccine that a vaccine manufacturer is proposing to supply me with?
- Is the vaccine well-matched to viruses in our country and does it remain so as the virus evolves?
- What is the uptake of current interventions and are there any adverse events?
- How can we improve our clinical care?

Figure 5 Domain III: Priority objectives and dedicated surveillance approaches to address them
(click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)

Informing use of interventions

Surveillance objectives	**Core** recommended surveillance approaches and investigations to fulfill objectives	**Enhanced** surveillance approaches and investigations that may help to fulfill objectives
1 Monitor the impact of non-medical interventions in the population	Investigations and studies	Community event-based surveillance; Media event-based surveillance; Healthcare capacity monitoring; Hospital clinical code monitoring
2 Provide candidate vaccine viruses for vaccine composition, production, and risk assessment	Sentinel ILI/ ARI/SARI surveillance	Laboratory networks
3 Monitor vaccine coverage, effectiveness, impact, and cost-effectiveness	Investigations and studies	Sentinel ILI/ ARI/SARI surveillance
4 Monitor the effectiveness of antivirals and other therapeutics	Investigations and studies; Enhanced clinical surveillance	Laboratory networks
5 Monitor the effectiveness of diagnostic tests	Investigations and studies	
6 Monitor the effectiveness of clinical care pathways	Enhanced clinical surveillance; Investigations and studies	
7 Monitor adverse events to vaccines and therapeutics	Pharmaco-vigilance	

Innovations and initiatives

- Regional networks to evaluate vaccine effectiveness
- Unity Studies initiative
- PHSM research agenda

Supportive initiatives

Surveillance innovations

- Rapid testing
- Participatory surveillance
- Electronic health records and digital health

The mosaic framework also highlights several cross-cutting surveillance considerations. These include priorities for low- and middle-income countries, viewing and interpreting surveillance data in the context of other data, the use of regional and global data to address local policy needs, and leveraging interpandemic surveillance during emergencies. The framework also includes sections on developing a local implementation plan, necessary enablers to mosaic surveillance within national governments, and monitoring and evaluation. Please click on any of these topics below for more information.

2.4 Additional topics in surveillance

(click on any topic to read more about the system or subject. To return, use the navigation bar at the bottom of the page)

Contextualizing surveillance data >

Prioritizing surveillance enhancements in low resource settings >

The use of regional and global data for country-level decision making >

Leveraging and scaling inter-pandemic surveillance during emergencies >

Implementation: action plans and roadmaps >

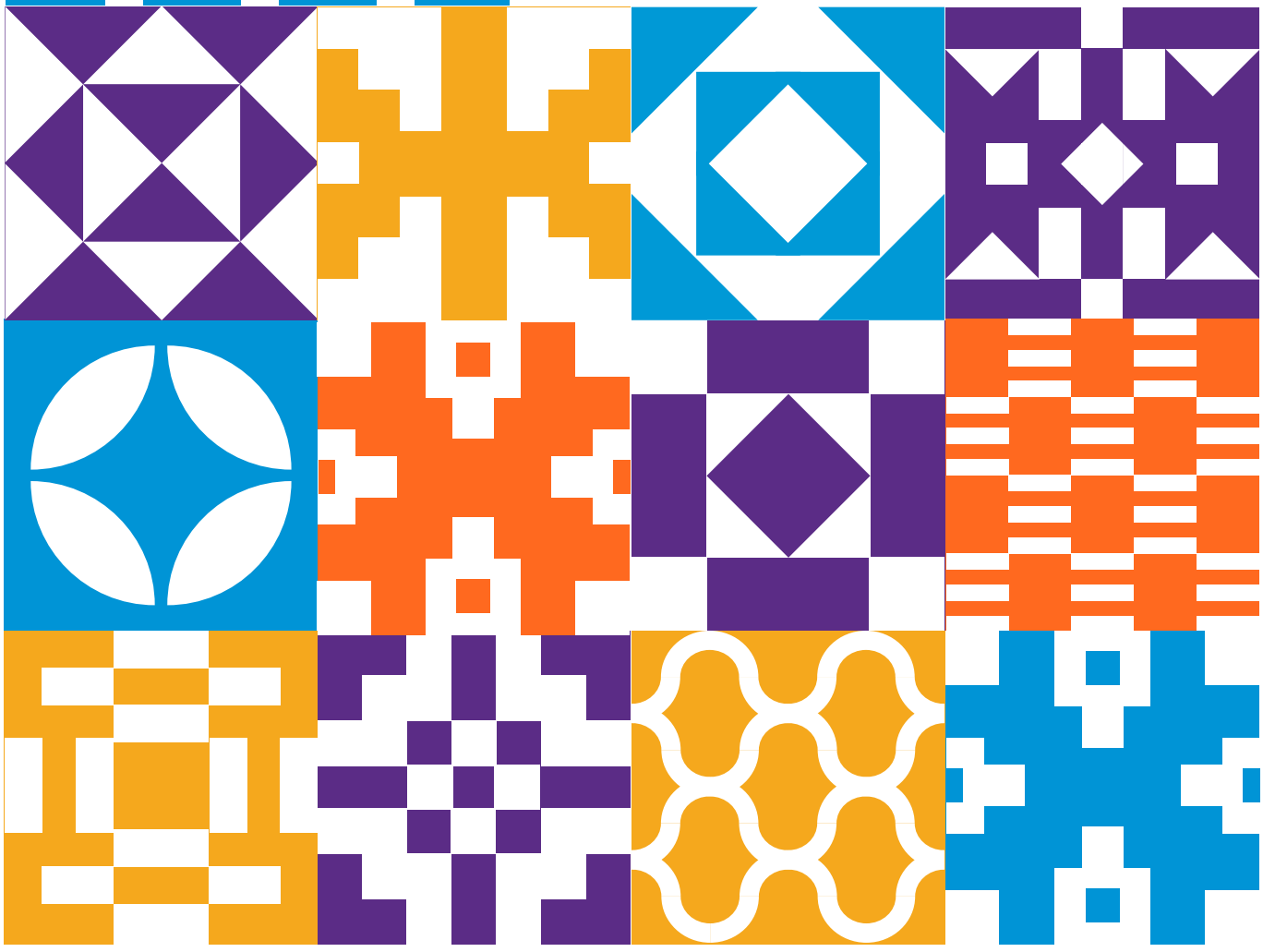
Monitoring and evaluation >

3. Conclusions

No single surveillance system can meet all priority objectives for the surveillance of respiratory viruses of epidemic and pandemic potential. To address objectives related to early warning, sustainable monitoring and intervention evaluation, a mosaic of surveillance systems and complementary investigations is necessary. While this framework suggests core and enhanced systems that may be included in each of the three surveillance domains, this is intended only as a guide and any mosaic must be adapted to country-specific contexts, Countries are encouraged to:

- review all the priority objectives outlined in this framework to determine those most important for local policy decisions;
- identify needed surveillance enhancements required to address each objective using the mosaic as a general guide/example;
- work with WHO and domestic and international partners to develop implementation plans to enhance surveillance and sustainably support the systems needed to resiliently address priority objectives on an ongoing basis.

Mosaic framework



1. Introduction

1.1 Background and rationale

Public health surveillance provides the critical information to inform nearly all decisions about public health policy, the response to emerging public health threats, and decisions about resource allocation. The specific needs to be addressed will determine the shape that a surveillance approach should take and the design of any new surveillance system should start with a consideration of the purpose for which the data will be used. The needs of public health authorities differ depending on the decisions to be made, the actions to be taken, the policies to be defined, and even the disease process to be monitored. As a result, it is impossible to meet all needs with a single system. The primary roles for which surveillance systems are generally designed are usually event/outbreak detection or monitoring trends in transmission. However, there are many special situations in which systems or complementary studies may be needed to provide more detailed information on risk groups, transmission dynamics, the burden of disease, or to dig deeper and answer specific epidemiological or clinical questions. This document fits together the many approaches into a 'mosaic' that might be considered in a single framework to enable policy planners to establish collaborative surveillance systems that are fit-for-purpose.

This document focuses on respiratory viruses with observed epidemic or pandemic potential in humans as a prototypical example of the way surveillance systems can work together resiliently to provide a comprehensive picture of disease emergence, spread and impact. However, irrespective of the biological class of a novel pathogen, several attributes are likely to be important components of any pathogen with pandemic potential. These traits include efficient human- to-human transmissibility, the absence of an effective or widely available medical countermeasure, an immunologically naïve population, virulence factors enabling immune system evasion, and a respiratory mode of spread. Additionally, the ability to transmit during incubation periods and/or the occurrence of mild illnesses would further augment spread. Several features of respiratory viruses make this class of microbial agents the most likely to cause future pandemics *(1)*.

The focus of this framework is primarily on interpandemic surveillance to meet early warning and routine monitoring needs, understanding that adaptations will be made with the emergence of a novel pathogen of pandemic potential. This framework does not serve as pandemic surveillance guidance, but it does include some suggestions for how to scale up inter-pandemic surveillance to provide some of the more robust information that may be required during epidemic and pandemic periods.

Surveillance approaches are grouped into three general domains, based on their general purpose.

Domain I:
detection and assessment of an emerging or re-emerging respiratory virus;

Domain II:
monitor epidemiological characteristics of respiratory viruses in interpandemic periods; and

Domain III:
informing use of human health intervention

Within each domain, multiple surveillance approaches must work together to address multiple objectives (see *Figs. 1 and 2*), but with the understanding that sources of information from different approaches may each contribute to answer one epidemiological question ("multi-source" surveillance (2)). This framework helps users to quickly identify priority objectives and then consider surveillance approaches best matched to their specific contexts and needs. Within this framework,

surveillance approaches may then be implemented as coordinated and collaborative systems, well-matched to specific priority objectives. In essence, they form a mosaic of approaches to resiliently support the prevention, detection and control of respiratory viruses of epidemic and pandemic potential over time. Each surveillance approach represents a tile in the mosaic and only when viewed together will they provide the complete and understandable picture of the human health risk and impact associated with respiratory viruses.

The coronavirus disease 2019 (COVID-19) pandemic generated new innovations as surveillance systems and complementary investigations were developed or enhanced to monitor mortality trends, disease severity, clinical outcomes, health system capacities, the evolution of viruses, transmissibility, and the effectiveness of interventions *(3)*. Some examples of these include the use of new laboratory methods, expanded environmental surveillance, novel diagnostic techniques, and the implementation of non-traditional surveillance in community settings. To inform longer term surveillance planning, the benefits, limitations, and most appropriate applications of these innovations must be considered. Some should now be institutionalized and incorporated into surveillance for future emerging events.

Figure 1 Vision, domains, aims, of the Mosaic surveillance framework

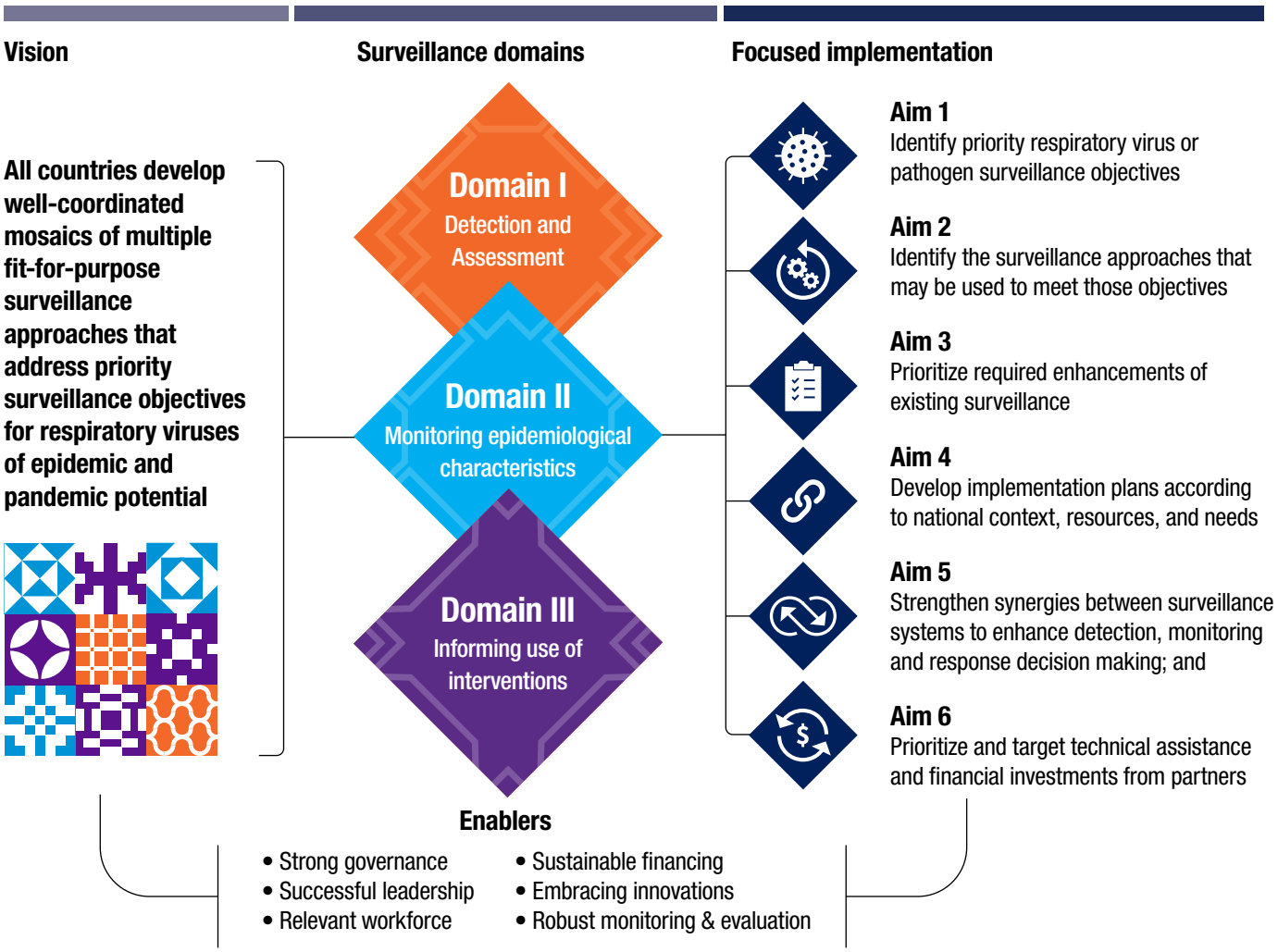


Figure 2 Summary of main surveillance objectives for each surveillance Mosaic domain

Domain I:
Detection and assessment of an emerging or re-emerging respiratory virus

Surveillance objectives

1. Rapidly detect emerging or re-emerging respiratory virus outbreaks and other events
2. Assess transmissibility, risk factors for transmission, and extent of infection from an emerging or re-emerging respiratory virus
3. Describe clinical presentation and risk factors for severe outcomes associated with an emerging or re-emerging respiratory virus

Domain II:
Monitor epidemiological characteristics of respiratory viruses in interpandemic periods

1. Monitor epidemiologic and clinical characteristics of illness over time
2. Monitor virologic and genetic characteristics of circulating viruses
3. Monitor situation in high-risk settings and vulnerable populations
4. Monitor impact on and coping abilities of health care systems

Domain III:
Informing use of human health interventions

1. Monitor the impact of non-medical interventions in the population
2. Provide candidate vaccine viruses for vaccine composition, production, and risk assessment
3. Monitor vaccine coverage, effectiveness, impact, and cost-effectiveness
4. Monitor the effectiveness of antivirals and other therapeutics
5. Monitor the effectiveness of diagnostic tests
6. Monitor the effectiveness of clinical care pathways, including Infection, Prevention and Control (IPC)
7. Monitor adverse events to vaccines and therapeutics

Resilience has been defined as the "ability to prepare for, manage, recover and learn from a sudden and extreme disturbance" *(4)*. The concept of resilience in public health surveillance is associated with system attributes *(5)* such as flexibility, acceptability, stability, sustainability, and utility *(6)*. Resilience of surveillance may also be improved if surveillance systems are targeted to priority objectives that they can most efficiently address (that is, they are fit-for-purpose) and if there is commitment by the public health authorities to sustain these systems. The mosaic framework considers the existing surveillance systems and networks that have been successfully leveraged to resiliently monitor multiple respiratory viruses over time. As a primary example, the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS) *(7)* began to integrate respiratory syncytial virus (RSV) surveillance in selected locations in 2015 *(8)*. At the 150th session of WHO Executive Board meeting in January 2022 and the Seventy-fifth World Health Assembly in May 2022 *(9)*, Member States supported GISRS sentinel surveillance platforms to be further leveraged to meet key monitoring needs not only for influenza, but also for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other respiratory viruses *(10)*. To date, 115 countries have leveraged the GISRS laboratory, reporting, surveillance and outbreak response network and integrated SARS-CoV-2 monitoring into GISRS sentinel surveillance. This framework builds on this experience and suggests the objectives that may be addressed by GISRS and, importantly, those that require the complementary contributions of different surveillance approaches.

The process leading to the development of this framework systematically considered surveillance experiences before and during the COVID-19 pandemic and organized regional and global conferences and consultations to formulate recommendations. Throughout the process, care was taken to consider what surveillance approaches may be fit-for-purpose in both higher and lower resourced environments. The framework seeks to also highlight recent surveillance innovations, while suggesting important considerations to take into account when evaluating their use in local contexts.

1.2 Vision

All countries develop well-coordinated mosaics of multiple fit-for-purpose surveillance approaches that address priority surveillance objectives for influenza, SARS-CoV-2, and other respiratory viruses of epidemic and pandemic potential according to country context.

A well-crafted mosaic of surveillance approaches should engender ongoing collaboration, as well as trust and investment by authorities, who will also seek to scale-up, enhance and/or leverage these systems in an emergency *(11)*.

1.3 Aim and scope

This framework is intended to be a practical tool to assist individual countries and regions as they conceptualize and design their own context-appropriate mosaic of surveillance approaches to address their priority respiratory virus surveillance objectives.

To that end, this framework will serve as a tool to help countries (see *Fig. 1*):

- identify priority respiratory virus or pathogen surveillance objectives;
- identify the surveillance approaches that may be used to meet these objectives;
- prioritize required enhancements of existing surveillance;
- develop implementation plans according to the national context, resources and needs;
- strengthen synergies between surveillance systems to enhance detection, monitoring and response decision-making;
- prioritize and target technical assistance and financial investments from partners.

This framework is intended to serve the needs of all countries, regardless of the income or humanitarian context and draws upon examples of how indicator-based and/or event-based surveillance are addressing priority objectives in each region (see *Fig. 2*). The desired impact is for the national surveillance of respiratory viruses of epidemic and pandemic potential to be strengthened, expanded, consolidated, and modernized in a coordinated and resilient manner *(12)*.

1.4 Alignment with existing initiatives and structures

This framework is a conceptual structure that underpins and supports current initiatives and *does not supersede any existing global or regional normative surveillance guidance*. Rather, it is intended to place the systems and studies represented by existing guidance into a context where they may address the objectives for which they are best intended. The framework presents appropriate uses of existing systems and studies for respiratory virus surveillance and refers to existing global and regional surveillance-specific guidance and operating procedures wherever they exist.

This framework is a tool to support the implementation of the International Health Regulations (IHR) 2005, specifically the core capacity requirements for surveillance and response *(13)*, and therefore also National Action Plans for Health Security *(14)* and will be adapted if the ongoing discussion related to the revision of the IHR (2005) requires it. In addition, it is in-line with the collaborative surveillance component of the WHO Global Architecture for Health Emergency Preparedness, Response and Resilience *(12)*. This tool will evolve to ensure it meets countries needs and synchronizes with the ongoing discussion for the pandemic convention accord + (CA+). It does so by:

- strengthening and coordinating systems for the detection (early warning) and monitoring of respiratory pathogens;
- supporting the expansion of laboratory capacity for pathogen and genomic surveillance;
- fostering integration of best practices, technologies, and innovation.

1.5 Audience

The document is intended to be used **at national, regional and global levels to support national respiratory virus surveillance strengthening through the creation of implementation plans.** National governments (often including ministries of health and/or national institutes of public health in close collaboration with ministries of agriculture and environment for zoonotic diseases) are accountable for implementation of this framework within their own territory, and WHO across territories as an organization of Member States who are under IHR obligations, including its associated Joint External Evaluation (JEE) framework.

Implementation of this mosaic can also help international partners and donor agencies, academia, the private sector, and other partners to focus technical and financial resources on the most essential surveillance needs in a country or region in a meaningful and non-duplicative manner.

1.6 Living guidance and country experience underpinning the framework

This framework exists on-line which will allow for regular updates and is complemented by a virtual living repository of guidance Click to view →, tools and case studies Click to view →, which may be accessed on the WHO website Click to view →. Importantly, it ensures access to the latest versions of any documents that will support countries to define and implement their respective surveillance mosaics.

1.7 Framework development and stakeholder engagement (methods)

The mosaic framework was developed using several approaches, using the following specific steps.

- **Review of current WHO global and regional strategic guidance** for the surveillance of respiratory viruses of pandemic potential, together with more specialized documents (Annex).

- **Establishment of a secretariat** including the senior advisor to the WHO Department of Epidemic and Pandemic Preparedness and Prevention, a lead epidemiologist, a programme specialist, and two consultant epidemiologists who have spent their careers working on global surveillance.
- **Technical working group** (TWG) formation comprising WHO experts, with experts invited from more than 20 teams/departments at WHO headquarters and representing each WHO regional office.
- **Support to WHO regional offices** as they worked with country offices and MOH partners to implement surveys and gather data on priority objectives, surveillance systems currently used to meet those objectives, and priority surveillance enhancements needed.
- **Convening of regional consultations and focused discussions** with countries, informed by surveys to obtain input for the global consultation (Table 4).
- **Hosting of a global consultation** entitled *'Crafting the mosaic': resilient surveillance systems for respiratory viruses of pandemic potential* on 10-11 May 2022. The consultation included 340 in-person and on-line attendees, including those working in surveillance at country level, representatives from WHO country offices, all six regional offices, WHO headquarters, and external partner organizations. The list of external partners involved and their expertise can be found in the acknowledgements section. The consultation was followed by a one-day meeting with TWG experts and external partners on 12 May 2022 to agree on priority messages taken from the consultation.
- **Obtaining feedback from partners** including the TWG (WHO headquarters and regional offices), WHO country offices, external experts, and the COVID-19 incident management team leadership at regional office and headquarter levels through an iterative review of this framework. A minimum of two opportunities were provided for input by all stakeholders.
- **Collection of case studies** by working with WHO regional offices to obtain examples of implementation of different surveillance systems and studies to meet priority objectives. These case studies provide examples of the use of different systems to move the framework from the theoretical to the practical level.

Table 4 Summary of approaches taken by each WHO region to obtain input for the global consultation to support the surveillance framework development

	WHO REGIONS					
	African Region	Eastern Mediterranean Region	European Region	Region of the Americas	South-East Asia Region	Western Pacific Region
Country-level survey	X		X		X	X
Regional office survey	X	X	X	X	X	X
Country focused discussions	X		X			
Country consultations		X	X	X	X	

2. Mosaic surveillance

2.1 Domain I: Detection and assessment of an emerging or re-emerging respiratory virus

An emerging virus may be the result of a newly-introduced virus in the human population, or a known virus that has re-emerged and/or developed novel or unique transmission dynamics or clinical manifestations (including novel phenotypically relevant variants and subtypes). The timely detection of a virus that could emerge, spread and cause illness in humans requires multiple event-based and indicator-based systems to work together. Communication and collaboration across sectors (including with the agricultural and environmental sectors for the investigation and assessment of animal reservoir species) and between national, intermediate and primary public health response levels of authority is of the utmost importance for this Domain *(16).*

Within Domain I, priority surveillance objectives are to:

1. *rapidly detect emerging or re-emerging respiratory pathogen outbreaks and other events;*
2. *assess transmissibility, risk factors for transmission, and the extent of infection from an emerging or re-emerging respiratory virus;*
3. *describe the clinical presentation and risk factors for severe outcomes associated with an emerging or re-emerging respiratory virus.*

The early warning, alert and response capability is a critical requirement of the IHR (2005) core capacities and serves to prevent the emergence of or mitigate the impact of a future respiratory pandemic. This includes the strengthening of coordinated surveillance systems in health care and community settings throughout the year and at the animal-human interface (for pathogens with a zoonotic reservoir). Once detected, emerging events will necessitate the modification of surveillance methods, including intensive case-finding and specialized investigations and studies to fully characterize a novel or re-emerging respiratory viral pathogen. However, it is essential to have a pre-existing monitoring system in place to enable rapid transition to sustained and standardized case detection and to provide a platform for further investigations. Table 1 outlines the questions that may be addressed by national authorities in Domain I.

Table 1 Questions that may be addressed by national authorities in Domain I

- Has there been a new respiratory virus or variant detected in my country?
- What are the virologic characteristics of the emerging or re-emerging viruses (including novel variants or subtypes)?
- What is the descriptive epidemiology of the disease (time, place, person)?
- How many people are known or likely to have been exposed and does it spread easily in humans?
- How severe is the disease and who are the high-risk groups for infection and complications?
- What is the risk that this emerging or re-emerging respiratory virus has epidemic or pandemic potential?
- Do we need to activate a national pandemic response plan or 'state of emergency' and related funding support?
- Is it the right time for the government to communicate to the population that this emerging or re-emerging virus has epidemic or pandemic potential?
- How do I translate scientific facts into messaging that empowers the community for action?

Fig. 3 demonstrates the priority objectives and dedicated surveillance approaches for Domain I.

Figure 3 Domain I: Priority objectives and dedicated surveillance approaches to address the detection and assessment of an emerging or re-emerging respiratory virus

(click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)

Detection and Assessment

Priority surveillance objectives	**Core** recommended surveillance approaches and investigations to fulfill objectives		**Enhanced** surveillance approaches and investigations that may help to fulfill objectives		
1 Rapidly detect emerging or re-emerging respiratory virus outbreaks and other events	Health facility event-based surveillance	Notifiable disease surveillance	Targeted special population surveillance	Media event-based surveillance	Syndromic surveillance
	Laboratory networks	Community event-based surveillance			
2 Assess transmissibility, risk factors for transmission, and extent of infection from an emerging or re-emerging respiratory virus	Investigations and studies		Targeted special population surveillance	Laboratory networks	Notifiable disease surveillance
3 Describe clinical presentation and risk factors for severe outcomes associated with an emerging or re-emerging respiratory virus	Investigations and studies		Targeted special population surveillance	Laboratory networks	Notifiable disease surveillance

Innovations and initiatives

- Integrated Disease Surveillance and Response (IDSR)
- Epidemic Intelligence from Open Sources (EIOS)
- Unity Studies initiative
- Integrated Outbreak Analytics (IOA)

Supportive initiatives

Surveillance innovations

- EWARS in a box
- Wastewater surveillance
- Rapid testing
- Participatory surveillance

Core surveillance and study approaches for Domain I

By design, event-based surveillance strategies are sensitive systems and may overwhelm the public health system if not implemented optimally. This necessitates capacity-building for triage, verification, and risk assessment at the national and sub-national level. These systems should be implemented broadly to detect any significant or unusual outbreak or other event (according to the national context) and may be integrated within indicator-based systems.

Health facility event-based surveillance: sensitized health workers detecting and reporting conditions and other signals, with verification (contributions to objective 1)

Networks of trained and astute health workers in health facilities (including clinicians, nurses, hospital epidemiologists, preventive medicine specialists, etc.) have proven to be essential to event detection in the past. There are multiple examples of their involvement in the detection and reporting of signals associated with early cases and outbreaks of avian influenza A(H5N1) *(17)* or A(H7N9) viruses *(18)*, Middle East respiratory syndrome coronaviruses (MERS-CoV) *(19)* and other viruses, for example, human immunodeficiency virus (HIV) *(20)*. Clinician acuity, an understanding of available reporting methods and sensitization to reportable signals for priority epidemic/pandemic-prone diseases may be maintained through regular training and trust building, often with the support of organized clinical groups or networks coordinated with health authorities. Where possible, private facilities that may not be routinely part of notifiable disease surveillance should be included. Any health facility-detected signal should be reported to the public health authorities and followed up with verification and risk assessment, leading to a proportionate public health response. The role of health workers is further strengthened through their regular connection to local health departments, timely and accurate diagnostic testing from established laboratory networks, and timely feedback of results and actions taken to the reporting health worker. (See case study webpage Click to view → for example: *Clinician early warning of SARS in China, 2002*).

Signal definitions for respiratory events (sometimes called 'event definitions' or 'alerts') for use by health workers have been well-described in global epidemiological surveillance standards for influenza. These criteria are broadly applicable to emerging respiratory pathogens of epidemic and pandemic potential and include (but are not limited to): clusters of severe respiratory disease or pneumonia in families, workplaces, or social networks; a change in the pattern of clinical presentation of respiratory illness; persistent changes noted in the treatment response or outcome of severe lower respiratory illness; a sudden surge in emergency department, hospital or intensive care unit admissions; and severe, unexplained lower respiratory illness occurring in health workers who care for patients with respiratory disease *(21)*. *Health facility event-based surveillance must be flexible to support broad reporting of any signals considered to be unusual by health workers.* Signals may also be integrated within or supported by the mandate of a nationally notifiable disease or condition reporting system (described further below), for example, through the Integrated Disease Surveillance and Response (IDSR) strategy used in some regions of the world *(22)*.

Emerging epidemic or pandemic threats identified by public health authorities elsewhere may also be shared with local clinical networks to sensitize health workers to be alert for events, stimulate reporting of additional cases, and provide resources for investigation, including laboratory testing and standardized data collection requirements. (See case study webpage Click to view → for example: *United States Centers for Disease Prevention and Control [CDC] Health Alert Network to monitor for A(H5N1) in the United States, 2022*). These clinician-based systems are particularly sensitive in the event of a moderate-to-high severity emergent virus or pathogen, coupled with prompt health care seeking in the population.

Community event-based surveillance (CEBS): detection, reporting and verification of signals in the community, including at the animal-human interface (contributions to objective 1)

CEBS is the 'systematic detection and reporting of events of public health significance within a community by community members' *(23)*. 'Community' can be more broadly defined to include high-risk communities

(for example, sex workers, workers in the tourism and transportation industries, ethnic or religious communities) *(24)* or specific settings such as wet markets along the animal-human interface, the food sector industry (for example, large-scale breeding farms, such as poultry, swine, mink or other farms), community organizations (for example, schools and prisons), refugee or displaced persons camps, and the government sector (multi-sectoral), with awareness that there may be multiple communities within one area. Community-level signal detection has some advantages over health care facility-level detection as it occurs in a setting where the reporter recognizes the social connections of the affected members of the community. It can also alert to the early appearance of an event before enough severe cases requiring a health care intervention occur to raise an alarm at the facility level.

CEBS should include enhancing mechanisms for outbreak detection at the human-animal interface. The One Health concept requires multi-sectoral and multidisciplinary coordination by environmental, human and animal health counterparts to detect and respond to the emergence of new viruses from animals at a time that is sufficiently early to support containment efforts. Following the report of a signal, cross-notification of alerts between animal health and human health authorities should take place at every level (local, regional, national), with a coordinated One Health risk assessment and response *(25)*.

For event detection, signals may represent any unusual disease patterns in humans or animals (for example, cluster of illness or deaths or an unusual clinical presentation) or any event that poses a risk to public health that could signify early signs of an outbreak or event and should be based on local health concerns *(26, 27)*. The active identification and reporting of community signals may be facilitated through the recruitment and sensitization of local community health workers, animal health workers (including joint sensitization of animal and human health workers) and/or volunteers. Volunteers need to be well-connected within their respective communities, for example, community health volunteers, religious, union, village or social group leaders, and others with a strong local community network. The use of these key persons to monitor for signals can help avoid overburdening the system that may occur if all members of a community are encouraged to report. Different models exist for CEBS, but reports should ideally be to local public health authorities or facilities for rapid verification, assessment and response *(24)*. CEBS may provide added sensitivity in the event of low/moderate severity of an emergent virus and/or poor health care seeking in the population. A crucial secondary benefit of CEBS is engendering and maintaining trust in the community for a public sector-led response. (See case study webpage Click to view → for example: *Event-based surveillance at community and health care facilities, Viet Nam*).

CEBS may also involve indirect reporting of signals through community organizations (for example, religious organizations, long-term care facilities, schools, detention facilities, public utilities, and non-governmental organizations). Examples of signals from these sources may include (but not be limited to) high levels of absenteeism from schools, increases in the sale of medicines from pharmacies, local deaths in domestic poultry, livestock or wildlife, and clusters of illness within specific closed or social settings *(27)*. (See case study webpage Click to view → for example: *Community-based outbreak surveillance identifies re-emergence of influenza A(H3N2) during the COVID-19 pandemic in Cambodia*).

Beyond early signal detection at the animal-human interface, some countries may also be able to collect and test individual specimens from selected animals (domestic and wildlife) in targeted populations under surveillance. Where feasible, specimen collection from animals (and possibly their environment) will also provide needed viruses for phenotypic and genomic characterization, risk assessment, and pandemic candidate vaccine virus selection, in addition to providing some added support for One Health early warning detection of spillover events in humans. (See case study webpage Click to view → for example: *Rapid cooperative actions between human and animal health networks in response to the first confirmed human infection of Influenza A (H3N8), 2022*) *(28)*.

National notifiable diseases and conditions surveillance (contributions to objectives 1 and 3)

Nationally notifiable diseases and conditions surveillance (NNDS), including those within disease surveillance system frameworks such as the IDSR (see **Box 1**. *Supporting initiative 1: the Integrated*

Disease Surveillance and Response (IDSR) Strategy), involves public health officials working with health care providers, laboratories, hospitals and other partners to monitor, control, and prevent priority diseases and conditions in their communities. Local laws and regulations specify which diseases and conditions (using clinical case definitions; sometimes with laboratory criteria for confirmed cases) must be reported (aggregate or case-based data) and their frequency (for example, immediate for some and weekly for others). Once baselines and thresholds have been established, NNDS may be used to detect unusual increases in notifiable diseases/conditions.

However, if not integrated with laboratory testing, this will require follow-up investigations to determine the etiology of illness and confirm if the signal/alert is a true public health event.

NNDS (and other forms of indicator-based surveillance) are a complement to event-based approaches and they should run in tandem to contribute to the early warning function critical for a prompt and proportioned response *(26)*. Increasingly, signal/alert reporting from event-based surveillance is integrated into NNDS as a part of epidemic intelligence.

Box 1. Supporting initiative 1: The Integrated Disease Surveillance and Response (IDSR) strategy

The IDSR strategy was developed by the WHO Regional Office for Africa in 1998 to improve the infectious disease outbreak response and has facilitated case-based and syndromic surveillance of many conditions, including influenza-like illness (ILI) and severe acute respiratory illness (SARI) *(29)*.

IDSR aims to strengthen national public health surveillance and response systems at the community, health facility, district and national level *(30)* by increasing capacity to ensure the correct use of case definitions, laboratory confirmation, data analysis, interpretation of findings and reporting *(29)*. This strategy facilitates the timely detection of, and response to, communicable disease threats, specifically those viewed as high priorities for national public health programmes such as respiratory illness *(22, 30)*.

IDSR has been implemented in differing ways across countries, resulting in numerous lessons learnt. Several capacities developed to respond to the COVID-19 pandemic have helped strengthen components of IDSR including many Member States' ability to conduct in-country genomic sequencing and the use of automated data management tools like dashboards. Ideas to improve existing systems include: conducting training in data collection, management and reporting; the creation of robust digital tools; increasing access to scientific publications through funding initiatives, which would allow for the timely dissemination of results; the streamlining of data collection (such as the pioneering approach of Sierra Leone who integrated influenza surveillance with IDSR); and the creation of robust accountability frameworks *(29, 30)*.

The implementation of the multi-partner, collaborative initiative *Transforming African Surveillance Systems* flagship project aims to assist in updating countries' surveillance systems to be aligned with the 2019 IDSR guidelines *(31, 32)* and in making the infectious disease outbreak response more effective and efficient. Focus areas of the project include improving laboratory capacity, modernizing data collection and management, workforce management, and assisting with high-level advocacy to ensure financing for surveillance and response efforts.

MERS-CoV can cause severe respiratory illness and remains a pandemic threat. Continued robust MERS-CoV surveillance is pivotal for the early ascertainment of cases and the effective implementation of control measures. (See case study webpage Click to view → for example: *Surveillance and testing for MERS-CoV, Saudi Arabia*).

Laboratory networks: reporting data on specimens tested, with phenotypic and genomic characterization as needed (contributions to objectives 1, 2 and 3)

While not a surveillance system *per se*, high-quality organized laboratory networks are a cornerstone of public health surveillance that cross-cut nearly all surveillance objectives in each Domain. All laboratories, including clinical and academic and in the public and private sectors, should be engaged as part of the surveillance network in reporting notifiable diseases and other signals to public health authorities. There is a need to promote strong linkages between laboratory testing and clinical/epidemiological data. This will support the monitoring of circulating viruses for pathogen confirmation, isolation, sequencing, risk assessment, and medical countermeasure and diagnostic development. (See case study webpage Click to view → for example: *The Canadian Public Health Laboratory Network Best Practices for COVID-19*).

For event detection purposes, strong laboratory networks are essential to the assessment of signals received from health care or community settings as the clinical presentation of many novel/emergent and endemically circulating respiratory pathogens are indistinguishable. Signals reported from laboratories include detection of pathogens that are immediately notifiable, rare pathogens, and unexpected increases in detections of organisms over a specific time period or from an unusual place *(24)*.

For laboratories participating in networks, ongoing molecular, phenotypic and genetic characterization of a sample of viruses from specimens at designated surveillance sites, but also from additional laboratories beyond the surveillance networks, are needed to help alert public health authorities to the presence of a new virus or variant that requires further investigation, and to add sensitivity to the detection of emerging pandemic threats. Laboratory specimens accompanied by comprehensive clinical and epidemiological data (for example, epidemiological and clinical data from outbreak investigations, or the sentinel surveillance, targeted surveillance, or clinical monitoring systems described further in Domain II) should be prioritized. The mechanisms by which genomic surveillance for pathogens with epidemic and pandemic potential may be integrated into surveillance is described further in the WHO global genomic surveillance strategy for pathogens with pandemic and epidemic potential, 2022–2032 *(33)*. Where feasible, the inclusion of laboratories involved in the phenotypic and genetic characterization of relevant samples from animals (known to transmit influenza and SARS-CoV-2 at the animal-human interface) and the environment (see **Box 2** for *Surveillance innovation 1: Surveillance for human respiratory viruses in wastewater*) can provide an early warning and added genetic information on emerging viruses.

Organized laboratory networks may not only help alert national authorities to the detection of emerging viruses, but may also help participating laboratories to access timely surveillance updates and situation reports, training and capacity-strengthening opportunities, external quality assurance programmes, updated reference viruses, protocols for detection and characterization, and other benefits.

Box 2. Surveillance innovation 1: Surveillance for human respiratory viruses in wastewater

A surveillance approach implemented during the COVID-19 pandemic that has previously been used to support polio eradication involves the testing of wastewater. Wastewater monitoring for SARS-CoV-2 can complement additional sources of surveillance data to indicate the presence, absence, or trends in circulating viruses or variants of concern in local populations. This type of surveillance has been most effectively implemented in low-prevalence environments *(34)*. Wastewater surveillance may also be used in screening for increasing or decreasing trends at a targeted site (for example, building, conveyance or facility) to trigger additional case-based surveillance and mitigation measures *(35)*. While this approach may provide early warning of the viruses that may be circulating in populations near the testing sites, considerations for the interpretation of surveillance data include whether the respiratory virus is present in the gastrointestinal or urinary tracts of humans, the ambient temperature of the water, the flow rate of the wastewater, and other factors *(15, 36)*. Wastewater surveillance does not include the additional epidemiological data that are ideally associated with specimens from human surveillance. For the management of the COVID-19 pandemic, the European Commission recommended European countries to monitor SARS-CoV-2 in wastewater using a common approach to allow for comparability of results *(37)*. As SARS-CoV-2 now becomes more prevalent globally, there is a need to better understand the quality of genomic sequences and epidemic intelligence received from this approach. The cost-effectiveness of this approach compared to other surveillance approaches to address the same objectives should also be assessed for endemically circulating respiratory viruses during interpandemic periods.

Investigations and studies, including outbreak investigations (contributions to objectives 2 and 3)

With the detection of a new virus or a new variant of a virus, rapid outbreak investigations (including in closed/institutional and health care settings) are vital to provide important epidemiological parameters to characterize the outbreak (such as transmission parameters, incubation period, attack rates, risk groups, case fatality rates, serial interval, generation time) and enable initial risk assessment *(38)*. Globally, public health workforces trained through Field Epidemiology Training Programs can play a vital role in these investigations.

Outbreak investigations usually involve case investigations, active case-finding, contact tracing, a descriptive epidemiology of the outbreak and generation of hypotheses on risk factors, which can then be tested by further analytic investigations (for example, case-control or cohort studies). There is also an immediate need to protect the community's health and address its concerns *(39)*. Internationally, the WHO Global Outbreak Alert and Response Network (GOARN) *(40)* engages staff and resources from partner institutions to support countries in the control of disease outbreaks or public health emergencies, including the Integrated Outbreak Analytics (IOA) platform (see **Box 3** for *Supporting initiative 2: Integrated Outbreak Analytics*).

Investigations (such as the 'first few X cases and contact', 'household transmission', 'closed setting transmission', 'health workers' transmission and risk factor investigations) and other sero-epidemiological studies *(41, 42)* are essential to be implemented during the early stages of virus emergence. These allow to rapidly estimate key transmission and epidemiological parameters, including secondary attack rates, the basic reproduction number (R_0) and the effective

reproduction number (Rt), severity, seroprevalence, and to determine if human-to-human spread is occurring. They also provide critical initial data about clinical presentations and infection severity (for example, the probability of a severe outcome for a given infection) and risk factors for transmission *(43).* Susceptibility and transmission studies at the animal-human interface are also necessary as the potential for zoonotic and anthroponotic transmission can directly inform One Health coordination and the focus of further surveillance activities *(44)*. These investigations and studies fill the gaps in our understanding about what and when specific measures should be optimally applied in the face of an evolving epidemic *(45)*. As these studies may be resource-intensive and technically demanding, regional pooled data could be used to inform a specific country's action if the population context is similar (see section on use of regional and global data, page 56 Click to view →). Where possible, high-quality investigations and studies should be conducted within a standardized framework such as the WHO SARS-CoV-2 Unity Studies initiative (see **Box 4** for *Supporting initiative 3: The Unity Studies initiative*) *(41, 42, 46)* or the Consortium for the Standardization of Influenza Seroepidemiology (CONSISE) *(47)* so that parameters can be compared across different settings *(43)*. (See case study webpage Click to view → for example: *SARS-CoV-2 household transmission investigation in Madagascar; Burkina Faso implemented timely and high-quality longitudinal SARS-COV-2 sero-survey*)

Box 3.
Supporting initiative 2: Integrated Outbreak Analytics (IOA)

The seeds for IOA were sown during the 2018 Ebola response in the Eastern Democratic Republic of the Congo (DRC), with the aim to collaboratively perform real-time, systematic, operational research to inform an evidence-based response. In 2020, the IOA partnership was formalized to establish a platform for exchange for all partners in the GOARN network. Since then, IOA has operated as a multidisciplinary approach to understanding outbreak dynamics in many different public health emergencies, including plague, cholera, measles, polio and malnutrition, and to inform responses with multiple partners. Today, IOA aims to drive comprehensive, accountable and effective public health and clinical strategies by enabling communities and national and subnational health authorities to use data for operational decision-making. IOA embraces a holistic approach: from the research questions to the data that are collected or accessed to the interpretation of results and recommendations that follow. In addition, IOA promotes the co-development and monitoring of evidence-informed recommendations with MOH.

***Sources*:**

IOA YouTube channel *(48)*

GOARN-IOA and IOA field exchanges *(40)*

Cellule d'Analyse Intégrée (CAI) en DRC *(49)*

Animation videos:

1. What is IOA ? *(48)*

2. How IOA is a multi-actor and multi-discipline approach? *(48)*

3. What is the IOA approach for decision-making in public health emergencies? *(48)*

Box 4.
Supporting initiative 3: The Unity Studies initiative

The WHO Unity Studies are a global initiative *(42)* which aimed at increasing the evidence-based knowledge for action. It provided a standardized and timely international investigation framework during the COVID-19 pandemic. Ten sero-epidemiological protocols using eight study methodologies were developed and implementation was supported by WHO and its partners globally, supporting capacity-building of enhanced surveillance and operational research capacities, particularly in low- and middle-income countries, and thus have been an invaluable tool for operational research equity *(46, 50, 51)*. More than 100 countries had implemented one or more Unity protocols and studies as of December 2021, two years into the COVID-19 pandemic.

These studies serve as important specialized instruments to supplement routine surveillance systems in order to address specific questions that may arise in the early stages of a pandemic, but also over time through a continuous, periodic or alert-driven (for example, emergence of a new variant or lineage) assessment process. They provide a standard preparedness and readiness framework for conducting targeted investigations and studies critical for risk assessment of a re-emerging or novel respiratory pathogen.

Building on lessons learned during the COVID-19 pandemic and for the Unity Studies initiative to be operational during a future pandemic, Unity Studies 2.0 is planned to create a global network of "champion" sites and partners to rapidly implement country-specific, pre-planned and pre-approved standardized protocols (including as "sleeping studies" in interpandemic periods that are scalable for use in future pandemics) by multidisciplinary teams. These will be supported by the development of a relevant architecture and governance, toolkits, and data platform by WHO and partners.

Source: **https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations**

Enhanced surveillance and study approaches for Domain I

Media event-based surveillance: detection and reporting of signals from media and social media (contributions to objective 1)

In most countries, the media and social media are informal sources of information ('signals') that might be public health events that have not yet been reported. As a result, signal detection may be undertaken through the systematic monitoring of traditional media and digital media including specific social media sources, government and official web sites, news sites, blogs and collaborating initiatives. This monitoring may also involve public health authorities engaging and working with the media as partners by sensitizing and training their networks of reporters and journalists to report signals to them. Staff persons employed within the public health system should then review these signals to triage and verify them (often through a network of public health professionals, but also through other means, such as the crowdsourcing EpiCore platform *(52)*, followed by risk assessment, and rapid alert and response as required. The *Epidemic Intelligence from Open Sources* (EIOS) initiative can be used to facilitate and augment media monitoring activities *(53)* (see **Box 5** for *Supporting initiative 4: Epidemic Intelligence from Open Sources).* In support of the systems described above, media event-based surveillance may further help identify events that need to be reported from the local to the national levels and provide national and international authorities with another source of signals that may not be reported in a timely way through official channels.

Box 5.
Supporting initiative 4: Epidemic Intelligence from Open Sources (EIOS)

The EIOS initiative is a unique collaboration between various public health stakeholders around the globe. It brings together new and existing initiatives, networks and systems to create a unified all-hazards approach to identify unreported threats using publicly-available information and then to implement verification, assessment and communication. Creating a community of practice for public health intelligence that includes Member States, international organizations, research institutes and other partners and collaborators is at the heart of the initiative.

The EIOS community of practice is supported by an evolving EIOS system, which not only connects other systems and actors – including ProMED, HealthMap and the Global Public Health Intelligence Network – but also promotes and catalyzes new and innovative collaborative development. The EIOS system builds on a long-standing collaboration between WHO and the Joint Research Centre of the European Commission to develop a system for public health intelligence and responds to the need for a global initiative to bring together public health intelligence efforts. It is aimed at consolidating a wide array of endeavours and platforms to build a strong public health intelligence community supported by robust, harmonized and standardized public health intelligence systems and frameworks across organizations and jurisdictions. In September 2017, WHO accepted leadership of EIOS under the Health Emergencies Programme, with a governance structure involving multiple stakeholders. The EIOS Coordination Group is made up of 12 organizations, networks and government bodies who serve two-year terms.

Source: https://www.who.int/initiatives/eios *(53)*.

Targeted special population surveillance in groups at high risk of infection or severe disease (contributions to objectives 1, 2 and 3)

After an emerging virus has been identified in humans, countries may introduce or enhance surveillance in targeted special populations with greater risk of exposure to the virus to identify additional persons with respiratory illness that may share a common exposure with earliest known cases, for example, health workers, animal health workers (for zoonotic diseases) and/or other groups identified to be at high risk of infection or severe disease. These data are also important to public health officials who will need to take public health action and may inform situation updates to the public and other stakeholders. This targeted surveillance approach can also provide early data on clinical characteristics, possible at-risk exposures, and phenotypic and genotypic characteristics of viruses. However, as all known risk factors may not be well understood, persons identified through early targeted surveillance may not remain representative of all future cases, especially if human-to-human transmission is occurring. It is therefore important that the context of such surveillance be clearly articulated for the appropriate interpretation of surveillance data, linked to risk communication and community engagement to address possible stigma and discrimination, and linked to additional systems that are in place to detect and monitor the possible broader spread of the emerging viruses in the population.

Syndromic surveillance without integrated laboratory testing (contributions to objective 1)

Syndromic surveillance without integrated laboratory testing (referred to here as 'syndromic surveillance') can form part of the routine monitoring of syndromes in a country as described in Domain II (for example, seasonal variations in transmission or risk groups,

etc.) and can also inform early warning. In this type of surveillance, each epidemic-prone disease or other condition of interest is defined and reported using a syndromic case definition (for example, fever ≥ 38 C° and cough). For early warning purposes, a threshold value for 'alert of an outbreak' is set for each of the syndromes and whenever the threshold is passed, the system flags the event for rapid verification and investigation *(54)*. This approach may be implemented in one or more health care facilities and may focus on certain units or departments. (See case study webpage Click to view → for example: *Rapid surveillance using the Public Health Rapid, Emergency, Disease and Syndromic Surveillance system in New South Wales, Australia*). The pathogen(s) associated with the syndrome may then be identified in subsequent investigations. The value of syndromic surveillance is largely dependent on the surveillance case definitions used. System stability may be a challenge in locations that require frequent manual reporting of common respiratory syndromes. Thus, the reporting of commonly occurring case definitions may be most efficiently implemented in locations where the system can leverage existing electronic medical data. Important and less frequently occurring severe syndromes may alternatively also be incorporated into NNDS systems.

There are unique surveillance needs following an acute humanitarian emergency and during a protracted emergency when routine public health surveillance systems of a country may be underperforming, disrupted or non-existent. There may also be an increased risk of transmission of infectious diseases or of emerging infectious diseases in the context of vulnerable populations. In these contexts, special early warning, alert and response systems (EWARS) and tools, such as 'EWARS-in-a-box' (see **Box 6** for *Surveillance innovation 2: 'EWARS-in-a-box'*), are established to serve a specific early warning function or may be an add-on to an existing system during an emergency.

Box 6. Surveillance innovation 2: 'EWARS-in-a-box'

WHO developed 'EWARS-in-a-box' (early warning, alert, and response system) *(55)*, which contains equipment needed to establish syndromic surveillance and response activities in contexts without a reliable internet connection or electricity. EWARS is deployed during an emergency as an adjunct to the national disease surveillance system. WHO works with MOH and health sector partners to train local health workers to use the system. After the emergency, EWARS should re-integrate back into the national system. Through this mechanism, early warning and indicator-based surveillance capacities can be maintained in difficult and remote field settings. Additional guidance for humanitarian operations, camps, and other fragile settings for COVID-19 are available *(56)*.

2.2 Domain II: Monitoring epidemiological characteristics of respiratory viruses in interpandemic periods

Surveillance approaches in Domain II are for monitoring respiratory viruses circulating in human populations during interpandemic periods. These may also be leveraged and enhanced during pandemic periods. Therefore, these approaches may have applicability beyond viruses of pandemic potential and may play essential roles in monitoring respiratory viruses of epidemic potential or public health importance, given similarities in required specimen and data collection needs. Domain II surveillance approaches also provide support to the early warning objectives of Domain I. From an epidemiological standpoint, established baselines and thresholds, or systems in place to monitor changes in clinical or demographic characteristics of cases identified in surveillance, may provide signals of potential new events such as the onset of a seasonal epidemic or the occurrence of an unusually severe season. Similarly, the laboratory components of surveillance may support the detection of changes in circulating viruses (for example, emerging variants or antigenic changes), triggering further Domain I investigations as applicable.

Within Domain II, priority surveillance objectives are to:

1. *monitor epidemiological and clinical characteristics of illness over time;*
2. *monitor virological and genetic characteristics of circulating viruses;*
3. *monitor the situation in high-risk settings and vulnerable populations;*
4. *monitor the impact on, and coping abilities of health care systems.*

Domain II requires surveillance systems and networks that can resiliently and sustainably monitor the trends in disease incidence, clinical parameters and the severity and impact of viruses that are circulating more widely in human populations. Table 2 outlines questions that may be addressed by national authorities in Domain II.

Fig. 4 demonstrates the priority objectives and dedicated surveillance approaches for Domain II.

Table 2 Questions that may be addressed by national authorities in Domain II

- When is the optimal time of year to use vaccines? Is there seasonal transmission?
- When should clinicians be alerted to the onset of a seasonal epidemic?
- How severe is this season compared to previous ones?
- How close is the match between vaccines in use and the viruses they target?
- How should resources be allocated for different respiratory viral threats?
- Who is at highest risk for severe disease? What is the impact in high-risk settings and vulnerable groups? Which are the priority groups that need additional response measures and funding to reduce the impact of the disease?
- Do interventions need to be modified based on changes in behaviour of the virus?
- How is the virus moving through the community and country? Are there reservoirs of transmission? Areas of higher/lower transmission?
- What are the characteristics of the virus and epidemiology of the disease (time, place, person) and has this changed? Are there genetic characteristics of the virus that may predict transmission behaviour, virulence, susceptibility to pharmaceuticals, or vaccine effectiveness?
- How is the health care system coping? Where do we need to allocate resources?

Core surveillance and study approaches for Domain II

Sentinel ILI/ARI/SARI case-based surveillance with integration of laboratory testing (contributions to objectives 1, 2 and 3)

Once respiratory viruses are widely circulating within human populations, high quality and representative sentinel, syndromic, case-based surveillance using standard case definitions (for example, outpatient ARI or ILI, or inpatient SARI) with a virological surveillance component (referred to here as 'sentinel' surveillance) is an efficient method to monitor trends in virus circulation, illness and severe illness, the relative circulation of different viruses under surveillance, and to monitor virological characteristics of circulating viruses *(21, 57)*.

Figure 4 Domain II: Priority surveillance objectives and dedicated surveillance approaches to address them (click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)

All cases (or a representative subset) meeting the surveillance case definition provide respiratory specimens to be tested for one or more respiratory pathogens *(21).*

Sentinel surveillance may be used to monitor the impact and severity of each season or epidemic period relative to historical baselines (for example, the proportion of hospitalizations or intensive care unit admissions associated with a specific pathogen) (see **Box 7** for *Supporting initiative 5: Pandemic influenza severity assessment (PISA) tool*). Sentinel surveillance systems that systematically monitor multiple respiratory pathogens are also uniquely placed to report the relative co-circulation of viruses and rates of co-infections in the form of the relative proportion of cases that are associated with infection by one virus compared to another. They also allow the projection of the relative health care burden of viruses under surveillance. Positive specimens in these case-based, data collection systems should have standardized, associated epidemiological data and be prioritized for virological characterization to inform local and global response planning. (See case study webpage Click to view → for example: *Sentinel ILI and SARI surveillance in Cote d'Ivoire and Kenya*). In many settings, sentinel surveillance systems will typically capture descriptive clinical information of a case on admission to a hospital or other health facility, but may not capture health information at the time of hospital discharge or beyond. Therefore, sentinel surveillance systems may work well in coordination with enhanced clinical surveillance. (See case study webpage Click to view → for example: *Integrating laboratory, epidemiologic and clinical surveillance into the ILI and SARI sentinel system in Costa Rica*) or stand-alone epidemiological investigations to implement more detailed investigations of the severity and sequelae of illness associated with viruses in circulation. Sentinel systems also may provide an added value as a complement to existing event-based surveillance systems that address Domain I objectives. To this end, sentinel surveillance systems have also detected novel viruses circulating undetected in human populations. (See case study webpage Click to view → for example: *ILI sentinel surveillance provides support for the identification of novel human influenza virus infections and a coordinated One Health response, in Lao People's Democratic Republic*).

Additional surveillance systems may also complement sentinel surveillance with larger sample sizes of severe cases and/or vulnerable populations. These include NNDS and/or mortality surveillance and targeted surveillance of high-risk populations and settings beyond patient subgroups represented in sentinel surveillance.

To correctly interpret sentinel surveillance data, information on representativeness, the stability or evolution of the system over time, and the extent to which private and public facilities are included in the

Box 7. Supporting initiative 5: Pandemic influenza severity assessment (PISA) tool

The Pandemic Influenza Severity Assessment (PISA) tool has been developed by WHO to be used by Member States as a methodology to assess the severity of influenza in seasonal epidemics and pandemics when sustained human-to-human transmission occurs. Ongoing work to adapt this methodology to monitor the severity of additional circulating respiratory pathogens is currently being evaluated. To be most effective, the assessment draws on severity parameters coming from multiple surveillance components of the mosaic, including sentinel surveillance, hospital administrative and mortality data, NNDS, hospital capacity monitoring systems, participatory surveillance, and other systems that collect data on respiratory pathogen transmissibility, severity and impact. The current version of PISA is located on the WHO website *(58)* with additional updates to the methodology anticipated soon. For an example of an experience of how these indicators were adapted and used during the COVID-19 pandemic. (See case study webpage Click to view → for example: *Using syndromic surveillance and PISA indicators to monitor COVID-19 pandemic severity in Ireland*).

sentinel surveillance system need to be understood. 'Representativeness' can be understood in terms of climate and geography or in terms of the demographics and perhaps ethnicity of groups where sites are placed. 'Stability' would include an understanding of how the system has changed over time, including changes in case definition, numbers of sites, approach to case selection, etc. Many of these contextual factors changed over time during the COVID-19 pandemic.

Countries should consider reviewing and updating sentinel surveillance systems to assure that the required quality and quantity of data are available for moving forward sustained epidemiological and virological monitoring of respiratory infections (see **Box 8** for *Supporting initiative 6: The Global Influenza Surveillance and Response System (GISRS)*). Pandemic plans should also include strategies to adapt to any future impact of emergency triaging of patients to assure that essential sentinel surveillance operations are maintained. Surveillance preparedness planning may also consider ways that surveillance can be enhanced during an event, making use of rapid point-of-care testing (see **Box 9** for *Surveillance innovation 3: Rapid testing*) and participatory surveillance (see **Box 10** for *Surveillance innovation 4: Participatory surveillance*), and similar strategies that may complement sentinel health care-based surveillance systems during future emergencies. The strengths and limitations of these additional approaches are described further in **Boxes 9 and 10** (*Surveillance Innovations 3 and 4*) below.

Box 8. Supporting initiative 6: The Global Influenza Surveillance and Response System (GISRS)

The GISRS is a global platform for influenza virus surveillance, preparedness and response that has been in operation for 70 years. Its scope includes laboratory networks, epidemiological surveillance operating procedures, global vaccine strain selection and virus risk assessment, outbreak response for seasonal, avian and pandemic influenza, and preparedness activities. The presence of standard operating procedures within GISRS has enhanced the value of sentinel surveillance data through the systematic use of standard case definitions, standardized data collection, data linkage to laboratory-specimen collection, and genomic diagnostic testing for virus confirmation *(21)*. The roles and responsibilities of national influenza centres that form the laboratory network within GISRS also represent an important framework for the surveillance of additional respiratory viruses. These laboratories serve as a reference laboratory for influenza in their country and as a technical resource on influenza-related matters for their national authorities. The national influenza centres also form a standard point of contact to WHO on issues related to influenza and share influenza virus isolates/sequences and/or influenza virus-positive samples with international laboratories for risk assessment and vaccine development. Additionally, this laboratory network adheres to and implements standards for biosafety and biosecurity and the safe shipping of specimens and participates in external quality assessment programmes provided by WHO.

GISRS Plus (GISRS+) is a current initiative that seeks to build upon the GISRS infrastructure to monitor SARS-CoV-2 and other respiratory viruses of epidemic and pandemic potential. In 2015, selected countries integrated the monitoring of respiratory syncytial virus (RSV) into the GISRS platform and, beginning in March 2020, many countries also began to monitor SARS-CoV-2 with their GISRS-linked sentinel systems *(10)*. External quality assessment programmes of national influenza centres have now been adapted to address the detection of both influenza and SARS-CoV-2 viruses and GISRS+ is one mechanism that may support the sustainable monitoring of influenza, SARS-CoV-2, and other respiratory pathogens in the future.

Box 9. Surveillance innovation 3: Rapid testing

One innovation that has the potential to impact on current approaches to surveillance for influenza, SARS-CoV-2 and other respiratory viruses is the improved sensitivity and growing availability of molecular (for example, polymerase chain reaction) and antigen-based tests *(59)*. These tests provide results within 90 minutes or less and may be used at the patient point of care or by self-testing in some cases by persons that may not have a laboratory background. There are important opportunities to be considered with these technologies. These include diagnostic support for the management of acutely ill persons, reducing the risk of transmission of detected respiratory pathogens to others by reducing the number of patient contacts, increasing the timeliness of appropriate antiviral use, and increasing the number of people enrolled in surveillance. From a public health standpoint, the targeted use of these tests have the potential to increase the sample sizes of specific groups under surveillance and to increase the flexibility of surveillance systems to monitor illness in the context of changing health care-seeking behaviours. However, there are important challenges to the use of these rapid tests in surveillance that should be addressed prior to integrating them into existing systems.

- If these tests are incorporated into health care-based surveillance, the use of standard case definitions should be adhered to if an objective of the surveillance is stable trend/intensity/severity monitoring over time. It should also be documented if persons outside of standard case definitions are being tested to assess how surveillance data may be biased and change over time. The use of case definitions may be less feasible for at-home testing. However, unstructured data points gathered over time that rise and fall with virus transmission may provide additional data to supplement, but not replace, standardized indicator-based surveillance data.
- Ideally, mechanisms should be in place to ensure that all positive and negative test results and associated epidemiological data, and the type of rapid test used, will be received into central surveillance databases. This will allow the proportion of specimens testing positive for a specific pathogen over time to be monitored after taking into consideration any changes in the sensitivity associated with the use of the rapid test.
- Care should be taken to ensure the continued availability of sufficient clinical specimens or virus isolates for virological characterization (which may not be produced by available point-of-care diagnostics). This will help to avoid reductions in specimens available for genetic and phenotypic testing for analysis of strain/variant distribution, treatment effectiveness, and vaccine effectiveness analyses.

In summary, while health care-based, sentinel syndromic surveillance with integrated laboratory components remains a core system to address many priority monitoring objectives, it is important that current surveillance managers continue to evaluate ways to take advantage of new diagnostic technologies and other innovations to increase the reach and flexibility of ongoing surveillance. However, safeguards must be in place to preserve the use of surveillance data for its most important public health actions.

Box 10. Surveillance innovation 4: Participatory surveillance

Participatory surveillance systems, also called 'crowdsourcing', can be used to monitor the health of communities and the impact of medical and non-medical interventions in communities by actively seeking volunteers to regularly report signs/symptoms and other information through digital reporting systems, such as web-based systems or smart phones. These approaches may complement more traditional surveillance approaches with possible advantages in that they may capture information from people who may not seek health care for their illness, extend monitoring to subnational levels and to groups beyond the reach of traditional sentinel surveillance, and identify peaks in activity as early or earlier than sentinel surveillance *(60)*. Participatory surveillance may also provide information on health care seeking and testing behaviours that may be essential to the interpretation of trends in other surveillance systems. Furthermore, this type of surveillance may be used to monitor vaccine uptake and vaccine hesitancy and has the potential to increase sample sizes of test-negative vaccine effectiveness monitoring systems (see Domain III). The main limitation is that they are not representative of the general population as people self-select into the surveillance system and participation tends to decrease over time. This can make participatory surveillance difficult to sustain in a stable manner for the interpretation of findings over time. Examples of participatory surveillance systems for influenza and COVID-19 may be found here (See case study webpage Click to view for example: *Participatory surveillance tracks community illness through self-reporting,examples from Australia and Europe*).

National notifiable diseases and conditions surveillance (NNDS) (contributions to objectives 1 and 3)

NNDS systems, including those within IDSR frameworks and tools (for example, IDSR and District Health Information Software 2 (61)) can support the monitoring of trends in severe respiratory illnesses and deaths. However, since reporting is passive, disease-specific trend interpretation is only feasible if networks of clinicians remain trained, motivated and well-sensitized to currently mandated reportable conditions. These systems may be strengthened by any systematic approaches taken to integrated laboratory testing for respiratory pathogens. In locations where reporting from these systems is reliable over time, established baselines and thresholds allow for more sophisticated trend monitoring by place and time. Due to their comprehensiveness of coverage, NNDS systems have an added value of including higher risk settings and subpopulations that may not be represented in sentinel surveillance systems. Of note, comprehensive reporting may be difficult to sustain in a stable manner over time for very common conditions or syndromes and these systems work best for relatively rare, but well-defined conditions in the population. (See case study webpage Click to view for example: *Influenza-associated pediatric mortality as a nationally reportable condition in the United States of America*). The reporting of respiratory illness deaths or those associated with specific respiratory infections can provide an important indicator of the severity of a current season or epidemic (see **Box 7** for *Supporting initiative 5: Pandemic influenza severity assessment tool*) and serve as a complement to sentinel surveillance approaches that may more effectively monitor more common illness caused by viruses widely in circulation in the population. Before adding a common presentation of a widely circulating respiratory pathogen to a NNDS system, consideration should be given as to whether alternative surveillance approaches, such as sentinel surveillance, could meet the same objectives in a more standardized, sustainable and less resource-intensive manner in order to provide high-quality data that are consistent and interpretable over time.

Laboratory networks (contributions to objectives 2)

As described in Domain I, strong national laboratory networks are of cross-cutting importance to the quality of nearly all surveillance systems and therefore form a critical area of focus for countries. Data associated with specimens collected at designated surveillance sites (with standardized procedures) allow for the interpretation of virological results associated with known clinical presentations, treatments received, epidemiological parameters, or disease outcomes. By definition, sentinel surveillance will not include comprehensive testing of a population. In addition, sites may be vulnerable to changes in health seeking behaviour during an epidemic or pandemic. Thus the reporting of phenotypic and genomic characterization of viruses undertaken in other locations (for example, additional clinical and academic laboratories) or for other purposes (for example, clinical management, non-sentinel surveillance) may help enhance the sensitivity of any national system to detect and monitor changes in circulating viruses, such as a change in the behavior of a virus or the emergence of a new antigenic variant. Indeed, the global selection of influenza vaccine strains has depended heavily on laboratory data derived from both sentinel and non-sentinel surveillance sources. These integrated networks of reporting laboratories are not only a core component of early warning networks, but are also essential to the routine monitoring of viruses currently known to be in human circulation and the associated development and targeting of interventions. This makes it a priority to enhance mechanisms to transmit clinical and epidemiological data linked with virological and sequence data, regardless of their source (See case study webpage Click to view → for example: *The Canadian Public Health Laboratory Network Best Practices for COVID-19).*

Targeted special population surveillance in high-risk settings and vulnerable populations groups (contributions to objectives 1, 2 and 3)

It is important to monitor morbidity and mortality of circulating respiratory viruses in specific high-risk settings or in groups at risk of severe disease that are not well-represented within existing surveillance networks. Targeted surveillance has been used to monitor subpopulations including (but not limited to) the following categories: vulnerable persons in long-term care facilities; health workers to inform infection prevention and control; facilities treating HIV- positive persons; persons with cardiovascular diseases; children with disabilities; pregnant women; disadvantaged and marginalized groups; and displaced persons and/or those in refugee camps. Depending on available resources, this targeted surveillance can be done using standard syndromic case definitions (for example, ILI/ARI) or event-based reporting definitions (for example, clusters of severe respiratory illness or deaths). The rapid reporting, testing, and confirmation of positive cases in these settings can then initiate a timely outbreak response to prevent spread to additional vulnerable persons. Positive specimens linked to associated epidemiological and clinical information from these settings should also be prioritized for genetic and phenotypic characterization to potentially identify any changes in circulating viruses or potentially emerging variants within these populations (also supporting Domain I). (See case study webpage Click to view → for example: *Surveillance of COVID-19 in long-term care facilities in the European Union/European Economic Area; Enhancing respiratory disease surveillance to detect COVID-19 in shelters for displaced persons, Thailand-Myanmar border*).

Health care capacity monitoring (contribution to objective 4)

The routine and systematic monitoring of health care capacity and utilization, either through comprehensive reporting or sentinel-based systems, is important to inform operational decision-making on service delivery and patient referrals and can supplement other data to give a more detailed picture of virus transmission. Health care capacity and utilization data may also be used to inform outbreak response strategies and community intervention evaluations. WHO has outlined 11 core indicators for health care capacity monitoring during the COVID-19 pandemic and these may be adapted to be more applicable to other circulating respiratory pathogens *(62)*. These indicators can provide regular data into the 'dashboards' of policy-makers and in many locations these systems are now one of the most important surveillance innovations from the pandemic to sustain over time *(57, 63).* (See case study webpage Click to view → for example: *Hospital capacity monitoring undertaken by Public Health Scotland*).

Enhanced surveillance and study approaches for Domain II

Mortality and excess mortality surveillance (contribution to objective 1)

Respiratory disease mortality monitoring systems using data reported from existing vital statistics reporting systems may also be used to monitor the overall number of deaths associated with cause-of-death categories for specific respiratory diseases, although often only retrospectively. Excess mortality may also be calculated if data are available and refers to the number of deaths during a specific period (for example, an influenza season or respiratory epidemic) above what would have been expected under baseline conditions. This helps to assess the impact on the population of particularly severe epidemics or seasonal circulation periods. Mortality data are best used with virological surveillance data to adjust models for the viruses that are most prominently in circulation during an epidemic period *(64).* (See case study webpage Click to view → for example: *European mortality monitoring (EuroMOMO): excess mortality monitoring*). After trends in mortality data have been determined to be stable and valid over time, mortality monitoring can provide added evidence of an epidemic impact on the population beyond the limited number of fatal cases typically identified in hospital-based sentinel surveillance systems.

In settings where many deaths occur at home and where civil registration systems do not function, deaths occurring outside health facilities may not be recorded and the cause of death certified. In these settings, verbal autopsies have been used to ascertain the cause of a death based on an interview with next of kin or other caregivers using a standardized questionnaire that elicits information on signs, symptoms, medical history and circumstances preceding death. The use of simplified verbal autopsy tools may help support the monitoring of national mortality trends and meet a need for population-level, cause-specific mortality data to be used in prioritizing and evaluating public health interventions *(65)*.

Investigations and studies (contributions to objectives 1, 3 and 4)

Analytical epidemiological studies can make use of standardized and high-quality sentinel surveillance data to identify the epidemiologic and sociodemographic characteristics of cases and to identify populations at higher risk of severe complications. Case-control studies have commonly been used to assess risk factors for severe outcome ILI/ARI/SARI sentinel surveillance data. Examples include evaluating risk factors for hospitalization by comparing influenza-associated SARI cases to influenza-associated ILI cases. (See case study webpage Click to view → for example: *South Africa used SARI and ILI sentinel surveillance to assess risk factors for influenza associated hospitalization*) and comparing fatal cases to non-fatal cases (See case study webpage Click to view → for example: *Assessing risk factors associated with fatal influenza using sentinel surveillance data in Romania*).

Population-based seroprevalence studies can be undertaken to provide a reliable estimate of infection or exposure from a virus in the general population. They can also inform the cumulative incidence of infection (including asymptomatic and mild disease), risk factors for infection and case fatality ratios. Seroprevalence studies can highlight population differences (for example, age, sex, geography, race, etc.) and high-risk and vulnerable populations (for example, those with comorbidities, refugee populations) and identify susceptible subpopulations and monitor them over time to inform priorities for vaccination coverage and other prevention and control measures *(50, 66)*.

In high-risk settings including hospitals and closed settings (prison, military wards, schools, long-term care facilities) and vulnerable populations (including pregnant women, those with co-morbidities such as HIV, tuberculosis and diabetes), focused cohort or case-control study studies can assess transmission dynamics and clinical presentation. Such operational analytical studies can be effectively implemented in high-risk settings, or with a comprehensiveness of data collection in the general population, which may not always be feasible through routinely operating surveillance systems.

Population-based surveillance and studies involve identifying all new cases of the disease under surveillance in a well-defined population, thus allowing the estimation of disease incidence rates. These estimates are valuable for communicating the health and economic burden of diseases under surveillance to policy-makers and to evaluate the impact of interventions to reduce the burden of disease in the same population over time. Most of the surveillance approaches described within this document may produce incidence rates of illnesses or outbreaks in the community if the denominator of the population under surveillance is well characterized. The most straightforward, but also the most labour-intensive and expensive method of population-based surveillance, is the systematic active surveillance of households or health facilities in a well-circumscribed location *(67, 68)*. (See case study webpage Click to view → for example: *Estimating the incidence of pneumonia in rural Thailand using population-based surveillance*). In other circumstances, techniques may be implemented to estimate the population catchment areas surrounding health facilities using surveys or medical record reviews *(69-71)*. (See case study webpage Click to view → for example: *ILI and SARI sentinel surveillance to inform the influenza burden of disease in Lao PDR, Mongolia and Morocco*). Incidence rates have also been monitored from hospital laboratory *(72-76)* and/or vital statistics data *(77)*. The selection of a population-based, surveillance approach should depend on local priorities and available resources.

Syndromic surveillance (contribution to objective 1)

Once baselines and thresholds have been established, syndromic surveillance without integrated laboratory testing (referred to here as 'syndromic' surveillance) may be used to monitor trends in mild or severe respiratory syndromes, but it requires follow-up investigations to determine the etiology of these syndromes. With stable reporting, syndromic surveillance of this type may be useful to broadly monitor increases in respiratory illness in the population or to provide some reassurance that increases have not occurred. An advantage of these systems is that they rely on information collected during routine patient care and they can be timelier than surveillance that requires laboratory-confirmed diagnoses. However, the absence of integrated laboratory testing and detailed disease-specific data collection make these systems less well-suited to address additional objectives within this domain as respiratory syndrome case definitions may encompass many different diseases and therefore require follow-up investigation. (See case study webpage Click to view → for example: *Rapid surveillance using the Public Health Rapid, Emergency, Disease and Syndromic Surveillance system in New South Wales, Australia*).

Enhanced clinical surveillance linked to existing systems (contributions to objective 1)

The COVID-19 pandemic demonstrated that well-constructed and standardized clinical data reporting systems under the direction of established clinical networks can provide an added level of clinical detail necessary for policy decisions. However, case-based reporting with sufficient data to comprehensively assess the quality of clinical care or to evaluate clinical outcomes and sequelae is resource-intensive. Thus, in most locations, it cannot be sustained indefinitely in the context of prospective data collection associated with routinely operating surveillance systems. Alternatively, enhanced clinical surveillance in a well-selected sample of patients using standardized clinical characterization case report forms can monitor changes in the natural history of illness, the relative severity of disease, risk factors for severe disease and poor outcomes, as well as treatment interventions and outcomes.

Linkages between existing surveillance systems, including with ILI/ARI/SARI sentinel surveillance, and the collection of more detailed clinical data guided by clinical networks can enable a longitudinal follow-up, even if only for a defined period during an acute event. (See case study webpage Click to view → for example: *ILI sentinel surveillance provides support for the identification of novel human influenza virus infections and a coordinated One Health response, in Lao People's Democratic Republic*). Clinical data capture may also be more representative and not prone to reporting biases if specific clinical data collection is also mandated through national registries or NNDS systems (and associated reporting from IDSR and similar networks). Such systems can also be optimized and expanded when clinical data are registered and reported electronically, such as through electronic health records (EHR) (see **Box 11** for *Surveillance*

innovation 5: Electronic health records and digital health). It is envisaged that not all countries may operate 'stand-alone' clinical reporting platforms at the national level, but may benefit from pooled clinical data at the regional or global levels for their own policy decisions as has been the case for those contributing to the WHO Global Clinical Platform for COVID-19 (see **Box 12** for *Supporting initiative 7: Global Clinical Platform for COVID-19 for the clinical characterization and management of patients with suspected or confirmed COVID-19*) *(78).*

Box 11. Surveillance innovation 5: Electronic health records (EHR) and digital health

EHR are an excellent source of data for disease symptoms, laboratory results and medical treatments. They may also improve the completeness of notifiable disease case reporting and enable the longitudinal collection of disease data *(79, 80)*. Over time, the growing number of systems will present important opportunities to advance sustainable global public health surveillance. EHR also provide a unique opportunity to expand the role and vision of current surveillance efforts and to help bridge the gap between public health practice and clinical medicine. The development of strong national EHR systems in several countries has been facilitated by national legislation mandating the use of standardized data exchange systems (for example, Health Level 7, a set of international standards for the transfer of clinical and administrative data between software applications) by healthcare providers and a focus on the interoperability of EHR with existing systems and digital infrastructures. EHR systems have also contributed to influenza incidence and vaccine effectiveness monitoring *(81)*. However, barriers to overcome include fragmented systems, challenges with data linkage, lack of data quality standards, and concerns over patient privacy *(82).* Ideally, the needs of surveillance data analyses would also be considered in the structure of EHR data systems, thus simplifying the routine monitoring of data.

WHO has also undertaken a review of the evidence on emerging digital health interventions that are contributing to health system improvements *(83)* and has published additional guidelines for the accelerated implementation and uptake of digital health technologies *(84)*. Digital health systems are likely to improve the interoperability timeliness and quality of ongoing respiratory pathogen surveillance in the coming years. However, digital health supports, but does not replace the need for targeted respiratory pathogen surveillance systems that incorporate standard, high quality surveillance processes.

Box 12.
Supporting initiative 7: Global Clinical Platform for COVID-19 for the clinical characterization and management of patients with suspected or confirmed COVID-19

WHO has launched a Global COVID-19 Clinical Platform, which provides Member States with a standardized approach and platform to collect clinical data to better characterize the natural history of the disease, identify risk factors for severe disease and describe treatment interventions to gather this information, WHO has devised data collection tools and a global COVID-19 clinical platform to enable harmonized data collection system submissions. In this way Member States implement a standard analytical plan to generate statistics at global, regional and national levels (including among subpopulations) on the different clinical characteristics associated with COVID-19 and risk factors associated with poor clinical outcomes. The reports generated and published from these proposed analyses have helped clinicians and national programmes prepare appropriate management and response strategies.

Source: See **https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform** *(78).*

(See case study webpage Click to view → for example: *WHO Clinical platform for COVID-19 informs treatment practices, characterizes co-infection with HIV, and the impact of omicron variant on disease severity; and Use of clinical networks to monitor "long covid")*

Hospital clinical code monitoring (contribution to objective 1)

Clinical coding data, such as the International Classification of Diseases (ICD) codes from outpatient and inpatient medical facilities, are another complementary data source used by some countries for routine trend monitoring and other surveillance objectives (for example. estimating the burden of disease, assessing disease severity). When these data are registered electronically, such as within EHR (see **Box 11** for *Surveillance innovation 5: Electronic health records and digital health*), and linked to routine diagnostic testing for influenza, SARS-CoV-2 or other viral pathogens, it may be possible to attribute admission or discharge clinical codes to respiratory disease case definitions in medical records and associated laboratory results. Following validation, this surveillance may provide an additional indication of specific respiratory disease trends over time and a useful supplement to hospitalization trend monitoring performed at more limited numbers of ILI/ARI/SARI sentinel sites. (See case study webpage Click to view → for example: *Establishing an ICD-10 code based SARI-surveillance in Germany*). However, as diagnostic tests used to assign specific clinical codes may be less sensitive than 'gold standard' polymerase chain reaction testing, this has the potential to reduce the sensitivity of trends in clinical codes in the surveillance system relative to actual trends in illness in the community, possibly leading to an underestimation of hospitalization incidence. As a result, the validity of clinical coding for influenza, SARS-CoV-2 or any other pathogen under surveillance needs to be initially established in any given location and specific combinations of codes may need to be adjusted, depending on the intended objectives of the system.

2.3 Domain III: Informing the use of human health interventions

Within Domain III, priority surveillance objectives are to:

1. *monitor the impact of non-medical interventions in the population: including public health social measures (PHSM) and Risk Communication and Community Engagement (RCCE);*
2. *provide candidate vaccine viruses for vaccine composition, production, and risk assessment;*
3. *monitor vaccine coverage, effectiveness, impact and cost-effectiveness;*
4. *monitor the effectiveness of antivirals and other therapeutics;*
5. *monitor the effectiveness of diagnostic tests;*
6. *monitor the effectiveness of clinical care pathways, including infection, prevention and control;*
7. *monitor adverse events to vaccines and therapeutics.*

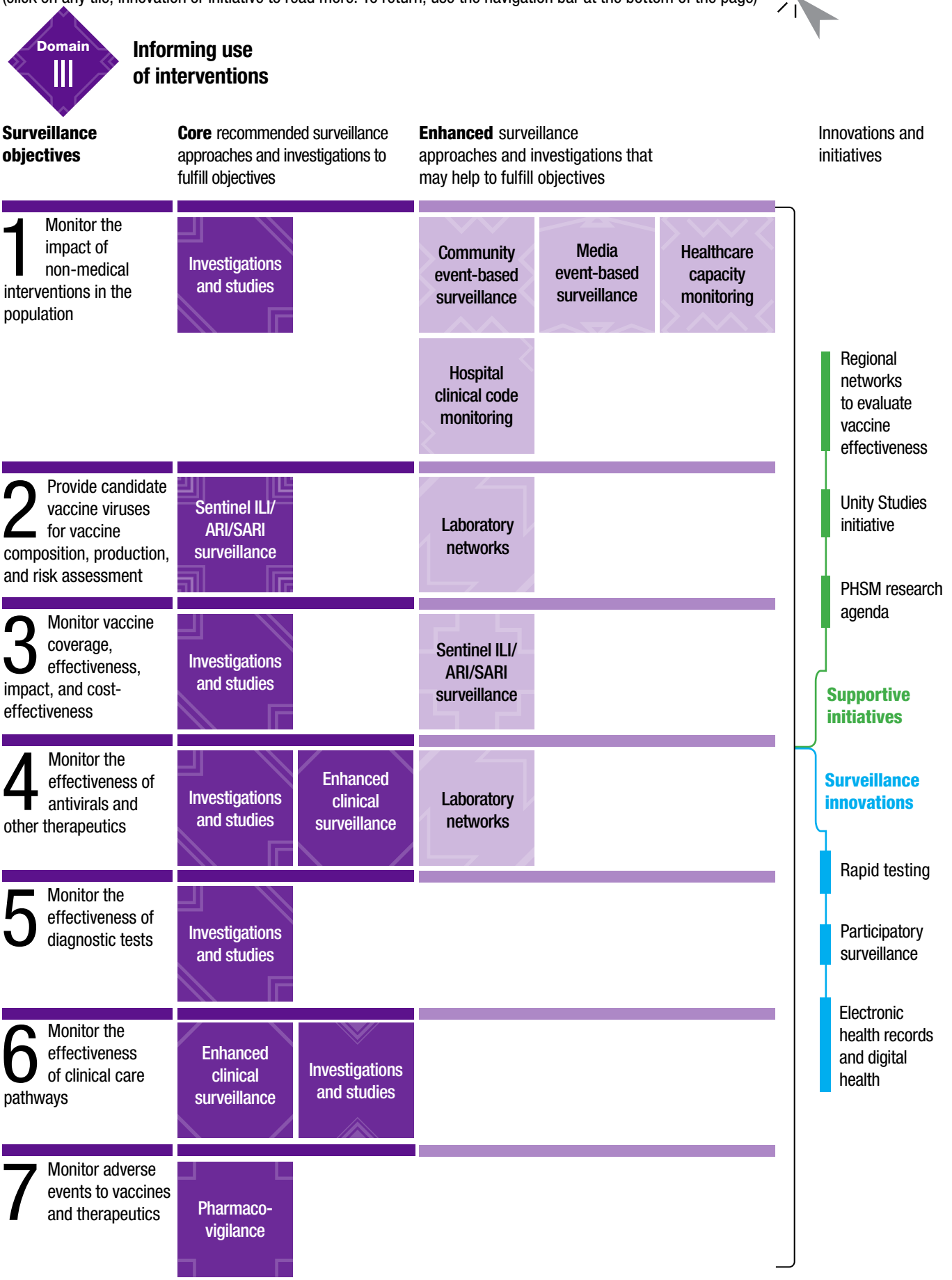
The ongoing evaluation of interventions may be integrated into more routine surveillance activities, provided that the needed data collection does not inhibit system resilience or sustainability. In many locations, 'off-the-shelf' protocols for complementary investigations and studies may be the most feasible mechanism to quickly obtain needed information. Table 3 outlines questions that may be addressed by national authorities in Domain III.

Fig. 5 demonstrates the priority objectives and dedicated surveillance approaches for Domain III.

Table 3 Questions that may be addressed by national authorities in Domain III

- Which PHSMs will be the most effective to reduce the impact of the virus?
- How should the government respond effectively and cost-effectively to the deteriorating health situation?
- Are the current pharmaceutical interventions (for example, vaccines and anti-virals) in use effective in the real-world setting, and do they remain effective as the virus evolves? Should they be changed?
- How can I be confident in the real-world effectiveness (that is, outside a very controlled, randomized clinical trial environment) of the vaccine that a vaccine manufacturer is proposing to supply me with?
- Is the vaccine well-matched to viruses in our country; does it remain so as the virus evolves?
- What is the uptake of current interventions and are there adverse events?
- How can we improve our clinical care?

Figure 5 Domain III: Priority objectives and dedicated surveillance approaches to address them
(click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)



Core surveillance and study approaches for Domain III

Investigations and studies (contributions to objectives 1, 3, 4, 5 and 6)

Within this domain, investigations and studies are the primary method to assess the impact of non-pharmaceutical PHSM, risk communication messaging, the effectiveness of diagnostics and therapeutics, and to comprehensively assess vaccine coverage, effectiveness, impact and cost-effectiveness. However, ongoing surveillance systems for routine monitoring can support an evaluation of the intervention impact and, in some cases, evaluate the effectiveness of interventions at the individual level.

The COVID-19 pandemic has suggested that much remains to be learned about the effectiveness, cost-effectiveness, and social acceptability of non-pharmaceutical PHSM for targeted implementation in future epidemics and pandemics and, importantly, to maintain trust and transparency with communities and civil societies (see **Box 13** for *Supporting initiative 8: Public health and social measures initiative: generating a global evidence base and research methodologies*). Interventions to be evaluated may be measured at the community level *(85)* (for example, the impact of school closures on illness incidence in that area) or at the individual level (for example, the impact of individual mask or personal protective equipment use on the subsequent risk of illness) *(86)*. The comprehensiveness of data needed to effectively monitor the type and duration of the intervention and participation often requires stand-alone studies and may be aided by the use of open access joint datasets *(87)*. Possible data needs include population mobility data to assess efforts to limit population movement and individual-level data on the start and end dates of participation in specific interventions and on compliance. Existing surveillance systems may be used to refer persons into case-control studies to assess individual participation in interventions. Global-level participatory disease surveillance and crowdsourcing have also yielded new initiatives to generate international data on the effectiveness of interventions during the COVID-19 pandemic and these efforts have the potential to also inform local seasonal policy decisions over time *(88)*.

Surveillance systems capturing health care usage as described in Domain II can also support evaluations of how interventions (for example, monitoring ICD-10 coded admissions in hospital, pharmacy usage, emergency department visits, ambulance calls, etc.) may be related in space and time to areas known to be implementing non-pharmaceutical interventions. Domain I systems, such as media or CEBS, may also provide an important complement to specific investigations and studies to assess population acceptance and understanding of public health measures so as to allow an improvement to risk and health communication messaging. CEBS systems also provide important community access and engagement mechanisms that may be used to promote the value of interventions.

Investigations and studies may also be required to obtain robust estimates of vaccine effectiveness in specific target groups that are not well-represented in sentinel surveillance (see details on leveraging sentinel surveillance for vaccine effectiveness studies below), to collect detailed data on the cost-effectiveness of vaccine implementation, or to implement serial measures needed to understand immunogenicity over time. To monitor specific populations or geographic locations, vaccine coverage and uptake studies may be conducted through specialized surveys or by reviewing immunization programme registries or records of the distribution and sale of vaccines from pharmacies or manufacturers. In some locations, the integration of clinical, epidemiological, molecular, genomic and vaccine registries have taken place to provide robust information to evaluate vaccine effectiveness. (See case study webpage Click to view → for example: *South Africa uses multiple data sources to assess the effectiveness of the Ad26.COV2.S (Johnson & Johnson) vaccine among health care workers; Case-control study to estimate the odds of death within 28 days of a positive test for SARS-CoV-2 prior to vaccination for residents of long-term care facilities in England, 2020–2021*).

In high-risk settings, including hospitals and closed settings (long-term care facilities, prisons, military wards, schools) and vulnerable populations (for example, pregnant women, those with co-morbidities including HIV, tuberculosis, diabetes, or those at high risk of exposure such as health care providers), focused cohort or case-control studies may form the basis for risk factor studies to evaluate the effectiveness of infection prevention and control measures. (See case study webpage Click to view → for example: *Case-control study evaluating risk factors for SARS-CoV-2 outbreak amongst health care personnel at a tertiary care centre*).

Box 13. Supporting initiative 8: Public health and social measures (PHSM) initiative: generating a global evidence base and research methodologies

During the COVID-19 pandemic, non-pharmaceutical PHSM have proven to be an indispensable strategy alongside vaccines and therapeutics. PHSM have been demonstrated to lower hospitalizations and deaths, which in turn contributes to reducing the pressure on the health care system and continuing essential health services and livelihoods. However, the duration of PHSM implementation also resulted in health and socioeconomic impacts on individuals, communities and societies.

Member States requested WHO to advance an understanding of the effectiveness and broader health and socioeconomic impacts of PHSM. In response, WHO launched a multi-year initiative in 2021 to strengthen the global evidence base and research methodologies for PHSM, as well as to support evidence-informed, equitable and balanced public health decisions on PHSM. One of the key deliverables is to strengthen the generation of context-specific, yet comparable and timely data on the effectiveness, uptake and adherence to PHSM in order to allow for evidence-informed decisions on introducing, adjusting and lifting PHSM. WHO (headquarters and European Region) and the European Centre for Disease Prevention and Control (ECDC) are jointly developing a global guidance (to be available in 2023) on monitoring PHSM for multiple hazards to address the need for a harmonized and systematic approach in collecting and tracking PHSM policies. The guidance will include priority domains and indicators for tracking PHSM policies, implementation, and behavioural responses and will be accompanied by a customizable online tool for setting up a tracking system. Guidance will be built on global and regional good practice during the COVID-19 pandemic and will support countries in making agile, balanced and evidence-informed decisions on PHSM implementation in future health emergencies.

Source: **https://www.who.int/activities/measuring-the-effectiveness-and-impact-of-public-health-and-social-measures** *(89).*

Sentinel ILI/ARI and SARI case-based surveillance systems with end-to-end integration of laboratory testing (contributions to objectives 2 and 3)

Sentinel ILI/ARI and SARI surveillance systems are the core system to provide candidate vaccine viruses for vaccine composition, production and risk assessment. Sentinel surveillance systems also serve as a source of specimens to monitor antiviral resistance. There is added value in viruses collected from sentinel systems that also collect clinical data on treatment and underlying health conditions as these data may inform any pressure-driven changes to circulating viruses. For example, algorithms have been established to indicate which samples should be systematically forwarded for analysis at a WHO Collaborating Centre (for example, patients treated with a certain antiviral, with recurrent infection after treatment, immunocompromised individuals, or a genetic mutation emergence).

Sentinel surveillance systems (particularly SARI surveillance systems) have also been leveraged to provide platforms and data to monitor vaccine effectiveness on an ongoing basis for COVID-19 and influenza using test-negative designs. (See case study webpage Click to view → for example: *Leveraging SARI surveillance to monitor vaccine effectiveness in Kyrgyzstan and Ghana).* However, for sentinel surveillance to be used for this purpose, there must be adequate vaccine uptake in the population. Of note, in countries where vaccination uptake is focused only on specific target groups

(for example, according to WHO Strategic Advisory Group of Experts (SAGE) recommendations), sentinel surveillance systems may not provide a large enough sample size of specific target groups to estimate vaccine effectiveness. Thus, networks of countries may be required for data pooling to reach robust sample sizes (see **Box 14** for *Supporting initiative 9:* Regional networks to evaluate vaccine effectiveness) for vaccine effectiveness estimations. Alternatively, other appropriate data sources may be utilized. (See case study webpage Click to view → for example: *Influenza and SARS-Cov-2 incidence and vaccine effectiveness of COVID-19 vaccines in Chile*). In addition, the growing use of home testing has the potential to bias care toward those testing positive at home. Home test use and their results should therefore be measured in the data collected at sentinel sites implementing test negative designs.

Sentinel surveillance systems have also provided a platform for the evaluation of new diagnostic techniques in multiple locations *(90, 91).* These are often specialized studies that leverage molecular diagnostics regularly used in sentinel surveillance as a 'gold standard' by which to assess rapid tests, new point-of-care diagnostics or other testing systems.

Box 14.
Supporting initiative 9: Regional networks to evaluate vaccine effectiveness

REVELAC-i network

In 2012, to generate systematic evidence on vaccine effectiveness to guide interventions and evaluate the impact of existing vaccination programs, the Pan American Health Organization (PAHO), the Influenza Division of the US Centers for Disease Control and Prevention (CDC), and several national Ministry of Health partners began evaluating the effectiveness of the influenza vaccine in a regional, multicenter project based on the existing SARI surveillance platform (92). To date, 15 countries have joined the REVELAC-i network for which the following objectives have been established to:

- generate mechanisms to share experiences, lessons learned and common methods between countries and research centers on the effectiveness of the influenza vaccine, as well as to know the impact of vaccination on morbidity and mortality due to influenza, and to,
- continue the integration of data from epidemiological and virological surveillance and immunization programs to generate evidence for the prevention and control of influenza.

Over time it has been recommended that this evaluation be integrated as another objective of the National SARI surveillance systems, as secondary data analysis of surveillance. The results of the effectiveness analysis may contribute to complementary analyses necessary for vaccination programs, such as measuring their impact, or the costs avoided by vaccination. This platform produces regular updates on influenza vaccine effectiveness and from 2020-2022 six countries additionally leveraged the platform to evaluate COVID-29 vaccine effectiveness.

European Severe Acute Respiratory Infection Vaccine Effectiveness (Euro-SAVE)

Countries in the WHO European region have deployed a variety of COVID-19 and influenza vaccines with evolving schedules to reduce morbidity and mortality in key target groups. Understanding the effectiveness of COVID-19 and influenza vaccine interventions in preventing severe disease is critical to inform optimal guidance about national, regional and global vaccine use.

Box 14.
(cont.)

The European Severe Acute Respiratory Infection Vaccine Effectiveness (Euro-SAVE) is a network of countries that monitor COVID-19 and influenza vaccine effectiveness against hospitalized severe acute respiratory infection (SARI). Countries leverage existing integrated SARI sentinel surveillance platforms to obtain vaccine effectiveness (VE) estimates and follow a standard WHO-defined methodology (93). In each country, some or all of existing SARI sites are included. All studies use the WHO SARI case definition, collect similar core data on enrolled patients, conduct testing by RT-PCR, and conduct genomic sequencing for influenza and SARS-CoV-2 in-country or at regional COVID-19 reference laboratories. In addition to country-level VE analyses, network-wide pooled analyses allows for more precise VE estimates by vaccine type; number of doses; variants of concern; time since vaccination; age group; and underlying comorbidities. For pooled analysis, VE is calculated as 1 – Odds Ratio using a one-stage analysis of pooled individuals.

To date, six countries and areas, including Albania, Georgia, Kyrgyzstan, North Macedonia and Serbia, as well as Kosovo, participate in the network. Patient recruitment began in November 2021. The pooling approach allows for multiple VE subgroup analyses. This network could be expanded to include additional countries that are part of the WHO European region and are undertaking comparable SARI VE monitoring.

AFRO MoVE

The African Region Monitoring Vaccine Effectiveness (AFRO-MoVE) network (94) was launched by WHO and key partners in March 2021 to facilitate VE studies in the region, encourage the use and standardisation of study designs, and build a sustainable network to evaluate pandemic and seasonal respiratory pathogen vaccines. Facilitated by WHO's Unity Studies initiative, AFRO-MoVE proposed to standardise studies to allow comparability and strengthen quality, using two generic protocols to measure COVID-19 VE: a prospective cohort study among health workers (HW) and a test-negative design nested in existing SARI surveillance. As of July 2022, three AFRO countries have adapted the HW protocol, and five the SARI protocol. AFRO-MoVE includes partners from 17 countries and 30 organisations. Twenty-two COVID-19 VE studies have been mapped across 13 countries, and four have published estimates.

A centralised data hub was established to support study sites and enable pooling data. AFRO-MoVE hosts regular technical workshops to discuss methods. Network webinars are organised during which investigators can present their work, discuss study challenges encountered, and share early results. This platform builds awareness for VE studies to build collaborations and enable strategic positioning of research. Countries and investigators of the region are encouraged to share their work and can access peer-review and support. AFRO-MoVE provides a platform for scientific knowledge, quality research, enable comparability of results, and could allow pooling of data to reach adequate sample size for better estimates. Experience from COVID-19 will serve to strengthen VE capacities also for other pathogens in preparedness and response to future pandemics.

Enhanced clinical surveillance linked to existing systems (contributions to objective 4 and 6)

Clinical networks are well-positioned to provide technical guidance on the nuanced and detailed treatment and outcome data required to identify the optimal care process and timing of interventions by doctors, nurses and other health care professionals to best manage illness associated with respiratory viruses. Operating at the national or international level, they can also form a conduit to gather needed data to assess priority risk factors for infection or severe outcomes, or to understand the impact of changing viral characteristics on clinical presentation. In many locations, the amount of data needed to meet this objective is often too burdensome to be sustained in a surveillance system developed for routine disease monitoring, especially if not based on electronic medical records. Therefore, time-limited, enhanced surveillance of clinical characteristics and management is often necessary (see Domain II). Those operating routine surveillance systems that collect limited clinical data may benefit from a collaboration with clinical networks to identify and refer consenting participants for enrolment into specialized studies and investigations that gather more detailed data.

The pooling of clinical data across multiple countries has proven effective to achieve sample sizes for rapid results during prior pandemics. Existing clinical networks can enable the conduct of multicentre, hospital-based clinical or epidemiological studies on the effectiveness of antivirals and other therapeutics. (See case study webpage Click to view → for example: *WHO clinical platform for COVID-19 informs treatment practices, characterizes co-infection with HIV and the impact of omicron variant on disease severity*).

Adverse events and safety reporting systems/ pharmacovigilance (contributions to objective 7)

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem *(95)*. The monitoring of adverse events following immunization is an essential strategy for ensuring the safety of vaccines *(96)* and adverse events to vaccines and therapeutics related to respiratory viruses are ideally addressed through integration into existing safety reporting systems.

Enhanced surveillance approaches for Domain III

Laboratory networks: reporting data centrally, with genomic characterization (contributions to objectives 2 and 4)

Viruses collected from sentinel surveillance networks have the added value of standardized selection and associated host, severity and treatment information. However, the robust sample sizes of viruses from larger laboratory networks (including non-sentinel samples) currently provide important additional sample sizes of virological information (including phenotypic and genomic characterization) for vaccine composition, production, and risk assessment for global vaccine decision-making *(97).* These laboratory networks also provide antiviral resistance monitoring data and larger representative networks can detect known antiviral resistance markers or new variant strains at a lower prevalence of circulation in the population *(57)*. Detection of reduced susceptibility and antiviral resistance involves several laboratory tests, including phenotypic assays (testing in the presence of an antiviral) and molecular techniques (sequencing and pyrosequencing) to look for genomic changes that have been associated with reduced antiviral susceptibility *(98).* (See case study webpage Click to view → for example: *Integration of surveillance for antiviral resistance in health interventions in the United States of America*).

Health care capacity monitoring and hospital clinical code monitoring (see Domain II) are enhanced approaches that may provide an indication of changes in the hospital impact with the implementation of PHSM. Finally, **community and media event-based surveillance** provide support to Domain 1, but may also be leveraged as a mechanism to understand community knowledge, attitudes, and practices related to intervention implementation.

2.4 Cross-cutting surveillance considerations

Contextualizing surveillance data

Domains I, II and III surveillance systems each have their own focus in terms of priority public health objectives. Therefore, reviewing the complementary information from the entire mosaic of surveillance systems together allows national authorities to quickly triangulate information from multiple systems to see the mosaic of respiratory illness and impact in their countries. This can be valuable:

1. *to assess multiple surveillance systems for any evidence of respiratory illness increases (or to determine the absence of increases to allay public fears) surrounding reported signals of potential events;*
2. *when using information from multiple sources during an outbreak or epidemic period to provide hazard, exposure and contextual information (for example, on risk factors, groups affected, geographical areas affected, severity of illness and impact on the health care system) for risk assessment;*
3. *to support the timely detection of changes in transmission, spread, severity and health impact using multi-sourced information (2).*

Thus, a fundamental concept underlying any surveillance mosaic is that data from included systems be viewed in the context of each other and not as independent siloed systems. (See case study webpage Click to view → for example: *Integrated Outbreak Analytics for contextualizing surveillance data).* Countries should therefore consider the development and piloting of regular electronic surveillance dashboards and bulletins, including the adoption of data management systems and standards that allow for simultaneous and coordinated interpretation of all mosaic surveillance data.

Associated contextual data such are also valuable for the interpretation of surveillance data (for example, socio/demographic, scientific, environmental, policy, and political, etc.) *(99, 100)*. See below for some examples.

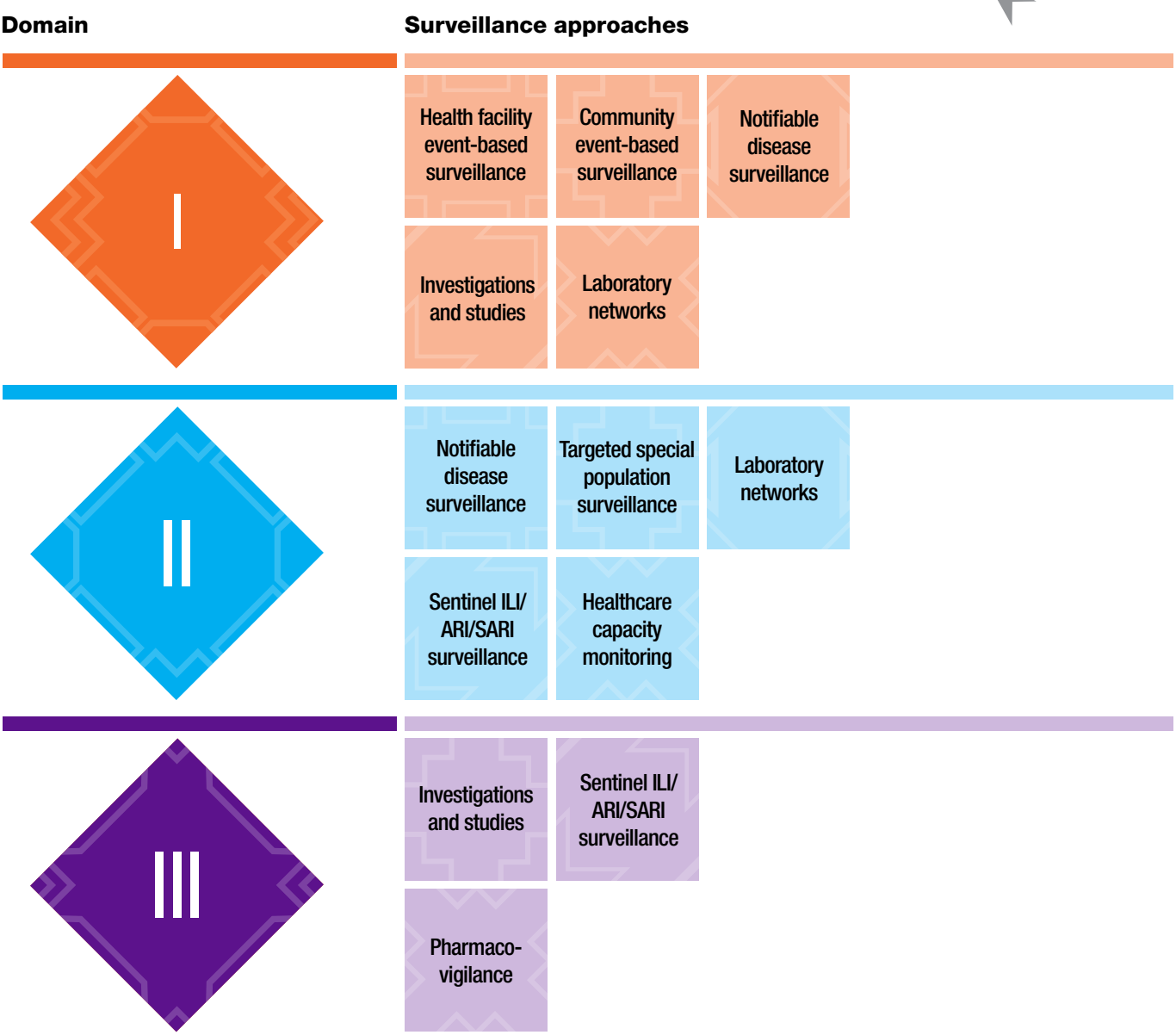
- Contextual data on poultry value chains have helped to identify priority locations for surveillance as they relate to the local risk for avian influenza spread and possible zoonotic transmission *(101)*.
- During the COVID-19 pandemic, early work to target response resources to likely outbreak locations focused on understanding flight connectivity and the volume of travellers between locations *(102)*.
- Monitoring changes in trends in health care-seeking behaviour and the local implementation of and adherence to interventions is also critical to understand any changes in observed trends in existing health care-based surveillance. Participatory surveillance methods using personal devices and the internet to gather information may be particularly useful sources of this contextual data on health care-seeking behaviours *(60)*.
- Local demographic data, such as the proportion of the population that are very old, very young, or have known risk factors or underlying conditions, may influence the implementation of a public health response when surveillance data identifies respiratory virus circulation in that location.
- Surveillance data may be evaluated in the context of climactic, social disruption and human behavioral and intervention data (for example, school closures, etc.). This may allow for focused early warning or monitoring surveillance in vulnerable populations or where conditions favour respiratory virus transmission and add to the evidence base of the potential effectiveness of interventions.

Prioritizing surveillance enhancements in low-resource settings

The text below focuses on the most pertinent surveillance approaches to be considered within each domain in low-resource contexts (see *Fig. 6*). In these contexts, including humanitarian settings, the focus should be on strengthening one or more of the core surveillance systems listed under each domain to meet a country's surveillance objectives. As discussed further in the section on **monitoring and evaluation**, system enhancements should include a review of gaps that prevent the surveillance from meeting IHR core capacities, and associated indicators for surveillance within the JEE tool for early warning. These evaluations

may involve reviewing outbreaks to understand how they were detected, sources of delays in detection and in the reporting and transmission of data. Limited resources should then be focused on building and strengthening the most effective and comprehensive surveillance mechanisms that address multiple objectives. It is important to identify where synergy and exchange between systems is possible and to leverage opportunities for the coordination or integration of activities (including similar methods, terminology, reporting forms and schedules) to enable a coordinated analysis and use of information by each level of the health service for decision-making. Wherever feasible, data from similar countries or pooled regional or global data should be used to inform local policy decisions.

Figure 6 Mosaic framework of surveillance approaches for low-resource settings: pertinent primary surveillance systems and investigations. (click on any tile, innovation or initiative to read more. To return, use the navigation bar at the bottom of the page)



Domain I

Implementing and sustaining event detection does not necessarily require new resources. Rather, it relies on a country's ability to review existing surveillance and information structures, adapt, and connect some of these structures, and to raise awareness of the need to detect and report among critical persons *(24)*. Limited resources should be focused on building a coordinated system with multiple sources of epidemic intelligence, encompassing the detection and reporting of signals from health facilities, communities (including outbreak detection at the animal-human interface) and laboratories. These should include the following elements.

- **Strengthening of existing laboratory capacities and networks** as timely confirmation of respiratory pathogens is required to meet nearly every priority objective in Domains I, II and III.
- **Training of networks of health workers** to maintain understanding of reportable criteria (for example, notifiable diseases and also signals/suspected events), available reporting methods, health worker connections to local health departments, and their access to timely and accurate diagnostic testing from laboratory networks. In these contexts, well-established NNDS systems (for example, as implemented through the IDSR system *(22)*) may play an important contributing role as clinicians may be more likely to report signals if their training is integrated into mandated reporting systems.
- **Strengthening community-based event/ outbreak reporting and response**, assuring that humanitarian settings (for example displaced persons camps), high-risk settings and populations (for example, long-term care facilities) are included, as well as reporting from the human-animal-environment interface.
- **Media event-based surveillance** may be achievable to implement and may provide important support to keep national authorities aware of possible events that have not been, but should be reported.
- **Outbreak investigation capacity** is vital to all countries and should be extendable to measure clinical data, transmissibility, and outcomes (for example, through Field Epidemiology Training Programmes). The scale and approach of outbreak investigations and studies are likely to differ by country and it is recommended that guidelines both for standardized outbreak investigation and other investigations and studies are followed and toolkits used to promote the quality and comparability of key parameters *(41, 42)*. When more resource-intensive investigations and studies are required to generate more sophisticated parameters, the use of regional or national networks can be considered (see the section below on the use of regional and global data for country-level decisions).

Domain II

In low-resource settings, the quality of data is more important than the quantity and a focus should be placed on systems that support the resilient monitoring of widely circulating respiratory viruses.

- **Sentinel SARI case-based surveillance systems with access to laboratory testing** are important to address many Domain II surveillance objectives. The most important criteria for the inclusion of a sentinel site in the system is the feasibility for that site to collect high quality data and laboratory specimens in a sustainable manner. It is also desirable that sentinel surveillance sites are representative of the geographic and demographic diversity of the population within a country. Sentinel SARI surveillance is suggested to be prioritized over ILI or ARI surveillance (if both outpatient and inpatient surveillance are not feasible) as it provides added monitoring of severe illness and provides viruses suitable for further risk assessment or characterization.
- **Strong NNDS** with well-sensitized clinicians reporting into the system is important for many conditions beyond respiratory diseases and provides a comprehensiveness of coverage, which also represents higher risk settings and subpopulations that may not be represented in sentinel surveillance systems. These systems work best for relatively rare, but well-defined, conditions in the population such as very severe respiratory illness presentations or deaths that provide an important indicator of the severity of a current season or epidemic. In this way, they may complement sentinel surveillance approaches that

more effectively monitor less severe illness caused by viruses widely in circulation.

- **Targeted special population surveillance** should cover specific priority vulnerable populations or those at high risk, and may include displaced or refugee populations, or priority populations and high risk groups in closed settings that may not be captured by routine surveillance.
- **The strengthening of existing laboratory capacities and networks** is required to meet many priority objectives within this domain and to identify the relative contribution of pathogens to respiratory illnesses over time. Networks of reporting laboratories will also increase the sensitivity of a system to monitor virological changes in circulating respiratory pathogens in a timely manner.
- **Health care capacity monitoring** is also required for national priority setting and immediate resource allocation, including in humanitarian settings. For example, any monitoring of health system capacity that was successfully implemented during the COVID-19 pandemic should be incorporated into sustainable monitoring systems.

Domain III

In low-resource settings, intervention evaluation should focus on collecting only those data essential for national decision-making that may not be obtained from additional countries or pooled regional or global data. This may be necessary if policy-makers determine that local idiosyncrasies in population behaviour (for example, local acceptance of interventions) or unique local demographics (for example, vaccine effectiveness in a population with a high prevalence of unmanaged HIV) require a context-specific evaluation.

There may also be opportunities to combine the implementation of feasible local investigations with the benefits of pooled regional or global data. For example, there may be local sociocultural or geographical determinants that influence individual participation in non-pharmaceutical PHSM or acceptance of vaccines. These factors may be country-specific and may be explored through locally-implemented evaluations and studies of behavioural and social drivers of intervention uptake, such as ‘knowledge, attitudes and practice’ surveys. These data can help market, target and implement local interventions more effectively. They may also be combined with regional or global data on vaccine effectiveness or mechanistic studies of specific interventions (for example, the effectiveness of mask use) that can be obtained from regional or global data and which may complement local survey data effectively.

- **Investigations and studies** are often the core mechanism to monitor the effectiveness of human health interventions in low-resource settings and protocols for their implementation should be developed as a part of preparedness planning. Sentinel surveillance systems may be leveraged to collect added data for intervention evaluation (for example, vaccine effectiveness monitoring) if the populations they serve have an adequate uptake of the intervention, sufficient numbers of the target group are represented in the surveillance system, and their longer-term sustainability will not be impacted by added data collection.
- **Sentinel surveillance** is a core system for Domain II in low-resource settings and has the added value of assuring that viruses and data from these contexts are considered in global risk assessments and vaccine strain selection. Even small sentinel surveillance systems can contribute to the monitoring of genomic changes in circulating viruses over time.
- **Pharmacovigilance** is needed as for any medical interventions deployed, and routine monitoring systems should be leveraged to assess adverse events.

Use of regional and global data for country-level decision-making

When a respiratory virus is circulating in more than one country, national stakeholders, particularly those in resource-limited settings, should determine when national data are required to meet their priority surveillance objectives and when data from another country or countries would be sufficient to inform national and local evidence-based decision-making.

The use of regional or global data may be appropriate to inform national decision-making in the following circumstances.

- The collection of needed data is not expedient or feasible based on local resource priorities and country capacity (for example, parameters that can only be derived from resource-intensive investigations and studies such as infection severity, transmissibility, population susceptibility/immunity, burden of disease, impact of PHSM, vaccine effectiveness) *(41, 42)*.
- A larger sample size than may be obtained nationally is required for robust estimates (for example, to monitor for new genomic changes at a lower prevalence of detection, to monitor vaccine effectiveness in particular subgroups or for specific vaccine formulations, or for enhanced clinical surveillance to monitor severity, risk factors and outcomes that may be difficult to monitor with sufficient sample sizes nationally) *(43, 78, 92, 103, 104)*.
- Existing networks that are already collecting the data can be used to avoid duplication of efforts (for example, laboratory networks, antiviral resistance networks, vaccine effectiveness networks, clinical monitoring networks, etc.).

If using findings from other countries, these countries should ideally have cultural and sociodemographic similarities so that results are applicable to the national context. Depending on the question being evaluated, there may also be a need to assure that data from other countries reflect a similar epidemic phase, local incidence and, possibly, implementation of public health measures.

Pooled, standardized data from multiple countries in regional or global networks may provide a more robust assessment of the representativeness of data and findings and may also inform sociological and climatological factors that influence transmission, which may not be evident in national data. It is important that countries with a capacity to deliver quality data share timely results (possibly before publication in peer-reviewed journals) into international reporting platforms and engage in regional and global 'pooling' for decision-making. There are many examples of the value of pooling data across countries for national and global decision-making. (See case study webpage Click to view → for example: *Estimating the effective reproductive number for SARS-CoV-2 variants using globally pooled sequence data; Use of clinical networks to monitor 'long covid'; National and international data pooling to enable the identification of risk factors for severe disease in the influenza A(H1N1) pdm09 and COVID-19 pandemics*). An important component of emergency and pandemic planning involves determining which data will be collected locally and which partnerships are needed to inform local decision-making with pooled data resources.

While the use of pooled data from additional countries may be useful for these purposes, **national and sub-national data remain important for:**

- **detection of respiratory outbreaks**, including zoonotic events involving new respiratory viruses, to provide sufficient information for a timely risk assessment and early response;
- **epidemiological investigations and intervention evaluations** in populations specific to a country and whom may not be well represented in other countries;
- **establishing local baseline levels of virus activity** as health care seeking, the decision to hospitalize, and other parameters that often affect trend interpretation may be country-specific;
- **obtaining a local understanding of the relative circulation of viruses** (including lineages and sub-lineages) in the population and for monitoring the relative contribution of different viruses to respiratory illnesses over time;
- **health care capacity monitoring** as local data are often required for internal preparedness planning, to support day-to-day logistics, and to inform targeted interventions;

- **providing the virological data needed to support global risk assessments** and vaccine strain selection as it is important that all countries establish mechanisms to contribute surveillance specimens for genetic sequencing and/or phenotypic characterization;
- **adverse event monitoring and vaccine uptake monitoring** to support prevention and control programmes.

2.5 Leveraging and scaling interpandemic surveillance during emergencies

Bridging from the current COVID-19 surveillance recommendations

Updated recommendations for COVID-19 pandemic surveillance were released by the WHO Incident Management Structure on 22 July 2022 *(3)*. In these recommendations, priority surveillance objectives for COVID-19 and SARS-CoV-2 monitoring included:

- early warning for changes in epidemiological patterns;
- monitoring trends in morbidity and mortality;
- burden/occupancy on health care capacity (health worker, hospitalization, intensive care unit);
- genomic surveillance: variants of concern in circulation, circulation in animal reservoirs;
- describe and monitor vulnerable groups at highest risk of exposure or severe disease;
- severity, particularly new variants;
- post-COVID-19 condition and role of immune status and capacity and risk factors;
- impact on vaccine composition and antiviral resistance.

These objectives as they apply to surveillance in humans are included within Domains I, II and III above. Thus this mosaic framework provides countries with a mechanism to consider how they may choose to address these COVID-19 objectives in a sustainable and resilient manner when moving forward.

Surveillance and investigation evolution and scaling-up during an epidemic or pandemic

Although surveillance and investigation needs will intensify and change as an epidemic emerges and evolves, the existence of established surveillance systems and pre-developed investigation protocols provides the platform upon which new systems can be built. Established surveillance systems will provide the baseline data within which data derived during an outbreak investigation can be put into context. Existing laboratory capacity and data management systems can be repurposed or expanded to accommodate needs that arise as the epidemic expands and develops. As such, strategies to enhance or scale-up these approaches during a pandemic when capacities are stretched and health-seeking behaviour may change need to be developed as part of pandemic preparedness planning.

Once an ‘event’ is detected, the goal of the immediate response will be to determine if it is indeed something unusual, such as an outbreak, if it is due to a known pathogen or a novel microorganism, the extent of spread, the source, and other features critical to containment efforts. However, if an outbreak persists and expands, surveillance needs will change throughout the event. If the outbreak is due to a novel pathogen, there are specialized needs aimed at understanding the organism’s behaviour. Should it become established in a population, surveillance priorities will shift from case-finding and contract tracing to monitoring transmission and ultimately understanding its endemic transmission dynamics.

The following describes some of the potential surveillance needs that occur at various stages in the evolution of an epidemic or pandemic.

1. Emergence/introduction - initial event.	The primary goal will be to verify and understand the scope of the outbreak and then to contain it. In the initial stages of the investigation, it will be important to first verify that the detected event is indeed an outbreak, starting with comparing observed cases to existing surveillance data. Decisions about containment will be informed by understanding how long the event has been going on, how far it has spread geographically, the clinical features of the disease, and its basic transmission pattern including some estimate of transmissibility and speed of spread. Specific surveillance and investigation measures will include the following elements. **a. Active case-finding in the community using a working case definition.** This may include a search of recent hospital records, interviews with local health care providers, and working with local community surveillance focal persons. Contact tracing is also key to finding other cases and understanding transmission. Careful examination of data from existing surveillance systems can provide context regarding usual patterns of occurrence. **b. Virological characterization.** Genetic sequence data can greatly facilitate understanding transmission by demonstrating the relatedness of isolates collected from different hosts. If the outbreak event is due to a novel pathogen or even a known pathogen that is now behaving differently, for example causing a sizable outbreak in populations thought to be previously immune, it is also important to understand key virological characteristics. These will include its cellular binding sites and affinities, its antigenicity and cross-reactivity with other organisms, and its ability to infect hosts other than humans. For known pathogens, the existence of genetic sequence and antigenic data gathered during routine surveillance can again provide context for these investigations. **c. Community and facility-based event surveillance.** Even after an outbreak is confirmed, event-based surveillance is important for detecting the early appearance of the pathogen in new locations and to document sustained community transmission. **d. Environmental surveillance including wastewater surveillance.** Wastewater surveillance can be a useful adjunct to more traditional disease surveillance to detect the appearance in as yet unaffected locations in some settings. The usefulness of wastewater surveillance will depend on the wastewater management infrastructure, climate, and the character of the virus (see **Box 2** for *Surveillance innovation 1: Surveillance for human respiratory viruses in wastewater*). The interpretation of wastewater surveillance data will require knowledge of flow rates, distribution of the service area of the sewer system, local water temperatures and viral shedding characteristics of the specific pathogen, all of which can significantly impact on the sensitivity of this method. **e. Investigations and studies to describe the specific characteristics of the pathogen's epidemiology.** These investigations may require close monitoring of cases and their contacts, detailed investigations of cases to understand the source of exposure, and additional clinical data collection.

Investigations and studies will be especially important in the context of a novel pathogen to determine:

i. sustained community transmission, especially the appearance of cases with no known exposures to suspected putative sources, human or animal;
ii. source of virus, especially if suspected to be zoonotic;
iii. mode of transmission;
iv. incubation period;
v. clinical spectrum of disease;
vi. risk factors including comorbid conditions, age, ethnicity, etc.;
vii. population transmission dynamics (for example. $R_{0,}$ secondary attack rate, serial interval, and period of infectiousness);
viii. virulence and severity (for example, case fatality ratio, proportion of severe disease, etc. Note: these are exceptionally difficult to estimate in the early stages of an outbreak, but should be tracked nonetheless).

Generic protocols that may be adapted to implement these investigations and studies are available on the WHO *(41, 42)* and CONSISE *(47)* webpages.

2. Sustained community transmission.

At the point at which a novel or re-emerging respiratory virus is clearly established and cannot realistically be contained, the goals of surveillance shift and the emphasis becomes more related to the population level control and mitigation, which requires monitoring of the rise and fall of cases and the geographical movement of the virus. There is still a need to monitor changes in virus behaviour that might represent a genetic change. Important surveillance enhancements in this phase include the following elements.

a. Event-based surveillance in the community and health care facilities to monitor for 'hot spots' of transmission and unexpected clusters of cases among populations that have already experienced waves of transmission. The latter could represent changes in the behaviour or transmissibility of the virus as it mutates.

b. Sentinel surveillance to monitor transmission trends, collect clinical, risk factor, and demographic data, and to provide clinical specimens for pathogen characterization.

i. Pandemic planning should include strategies to make health care-based sentinel surveillance more resilient to any changes in pandemic-associated triage patterns or health care seeking behaviors for respiratory illnesses. This may include developing plans to incorporate sentinel surveillance monitoring needs into any new patient flow and triage practices established for a pandemic; and assuring collection of weekly denominators of total respiratory illnesses at sentinel surveillance facilities so the percentage of respiratory illnesses associated with pathogens under surveillance may be interpreted in the context of overall increases or decreases in respiratory visits to the sentinel sites.
ii. Pandemic plans may also include incorporating increased sentinel surveillance, but also de-centralized laboratory testing results (non-sentinel site laboratory testing) to increase sample sizes so as to monitor for emerging variants in virological surveillance, as well as with data from participatory surveillance to monitor trends in illnesses not captured at health care facilities.

c. Serological surveys to characterize population attack rates and the spectrum of disease.
d. Timely and comprehensive monitoring of hospital capacity.
e. Continued investigations and studies to:
   i. further characterize the clinical spectrum and outcomes;
   ii. define virulence and severity more accurately, with improved estimates for the proportion of cases that are severe or fatal;
   iii. determine the impact of interventions, including non-pharmaceutical measures, treatment and vaccines.

3. Disseminated community transmission.

Surveillance needs will continue to be heightened for some time after a novel or re-emerging pathogen takes on an endemic transmission pattern. Evolving surveillance needs will include:

a. sentinel surveillance to understand seasonal trends, define expected levels of transmission at peak circulation, monitor changes in risk groups as the underlying population becomes highly exposed or vaccinated, and to provide specimens for continued pathogen characterization to monitor genetic and antigenic changes over time;
b. continued investigations and studies to monitor vaccine and management effectiveness in the context of an evolving pathogen;
c. event-based surveillance to identify events in the community that might represent a change in the behaviour of the virus related to genetic evolution and changes in population immunity;
d. population-level mortality and hospitalization data monitoring, including modelled estimates of mortality rates.

More is not necessarily better! There is often the assumption that 'more is better' both in terms of the breadth and depth of data collected in an emergency. The approach taken by this mosaic framework to keep surveillance systems fit-for-purpose to priority objectives is drawn from an understanding that data comes at a resource and opportunity cost and the utility of data should always be considered. At times, routine surveillance data collection forms may be long and time-consuming to fill out. While detailed information is necessary in the early stages of disease emergence, these forms may best be placed in time-limited field investigations rather than surveillance systems that need to be sustained over time and shortened as the disease is better understood. An understanding of the current context of an outbreak or pandemic can be acquired by sampling only a proportion of overall cases. Finally, the COVID-19 pandemic has demonstrated the widespread utility of routinely sequencing viral isolates and has led to the explosion of massive volumes of sequence data. In some instances, this represents substantially more information than needed for monitoring the emergence and spread of viral variants *(57, 97).*

3. Implementation approach

3.1 Implementation: action plans and roadmaps

In line with the vision that all countries develop well-coordinated mosaics of multiple fit-for-purpose surveillance systems and studies that address priority surveillance objectives for respiratory viruses of epidemic and pandemic potential, the **desired impact of the mosaic framework** is for the surveillance of respiratory pathogens of epidemic and pandemic potential to be strengthened in a resilient manner. This will allow existing systems to flexibly respond to epidemics and pandemics. This framework serves as a practical tool:

- to inform implementation plans or roadmaps at country and regional levels;
- to create meaningful, non-duplicative workplans among funding partners;
- to strengthen national-level strategies for context-appropriate sets of resilient surveillance systems.

More granular implementation action plans or roadmaps should be developed at the country, regional and global levels. Implementation plans constructed around each of the three surveillance domains are needed and should be guided by comprehensive and regular evaluations of surveillance systems to meet priority objectives *(105-108)*, with country-led prioritization of systems and strengthening efforts. When new surveillance systems are being added into a country-level strategy, piloting and validation of new system performance should be included in implementation plans. This is particularly the case when new technologies or innovations are implemented. Plans at all levels should be linked and made coherent with country-level contexts, while also recognizing and enabling global surveillance needs.

Implementation of this framework will require a **collaborative approach** across governments, networks, programmes and partners for a maximal impact and contribution to public health. It will also need to reflect on the three dimensions of collaborative surveillance according to the WHO Global Architecture for Health Emergency Preparedness, Response and Resilience *(12)*. Additional strategies, frameworks, tools, technical guidance (such as those listed in the Annex) and initiatives may be necessary to articulate and define the implementation of specific systems. WHO encourages adaptation and adoption so that maximal coherence and harmonization are maintained locally to globally.

This framework sets a ten-year horizon for implementation. However an update may be undertaken to the framework during the next five years, if deemed necessary.

3.2 Enablers

There are several enabling factors for the implementation of resilient and sustainable surveillance that should be present in all countries. These include:

- strong governance and leadership;
- sustainable financing and workforce;
- locally-defined objectives and priorities;
- integration of data standards and appropriate innovations.

Strong governance and leadership

Governance will determine the success or failure of implementation of the mosaic framework and additionally influences all other enabling factors for surveillance. Despite differences in the size and complexity of a surveillance mosaic between countries, the government must take accountability for governance of this mosaic within each country.

Effective governance will ensure success by implementing the following steps.

- **Empowering through law and policy** the national and sub-national bodies in charge of surveillance.
- **Ensuring leadership** through identification of an ambitious long-term goal, while also developing a clear, targeted short-term action plan.
- **Ensuring partner engagement and coordination** by acknowledging that there are many different surveillance actors that need to be involved, motivated, accountable and well-coordinated.
- **Developing a harmonized respiratory surveillance operational plan/roadmap** at the country level and at sub-national levels as needed. This may include bringing into collaboration the operators of individual surveillance systems that have not traditionally worked together.
- **Synergizing data and information management infrastructures** and ensuring a collaborative and coordinated assessment of data from the mosaic surveillance systems both within and outside of national borders, thus promoting greater public health intelligence. This may be undertaken under the auspices of a national public health Institute or similar coordinating body.
- **Providing sustainable financial and human resources support** to national stakeholders responsible for surveillance systems and studies within the mosaic.
- **Striving towards accountability through evaluation** of surveillance systems within the mosaic.
- **Fulfilling IHR (2005) reporting and verification requirements.**

National authorities should establish a coordinating body to implement the mosaic by bringing together the operators of different surveillance systems, investigations and studies. This coordinating body can help to define priority surveillance objectives, country-level assessments, and the prioritization of surveillance systems so as to create the relevant national surveillance mosaic. The coordinating body will also ensure surveillance sustainability, development needs, and undertake periodic evaluations of whether the surveillance systems and studies selected continue to meet their objectives. Over time, this coordinating body would use this evidence base to adapt the mosaic accordingly. This coordinating body will also assess workforce competencies to identify gaps and ensure that there are adequate staff that are trained and empowered to deliver on the surveillance objectives.

Sustainable financing and workforce

Medium- to long-term resources needed to support mosaic surveillance development plans at the country, regional and global level should be identified and adequately resourced across all surveillance domains and selected systems. Funding streams supporting a mosaic approach to surveillance should be coordinated to reduce administrative tendencies toward fragmentation. Donors should also seek to coordinate with each other and avoid siloed funding that impedes a mosaic approach to surveillance, recognizing that strengthening the mosaic of surveillance domains and systems benefits all surveillance programmes.

Where feasible, national authorities should provide sustainable funding for the ongoing routine operations of the surveillance systems that are most important for meeting local objectives, with donors and external partners providing funding for one-time or shorter-term general system enhancements to improve the long-term functioning of government-funded systems. This will help ensure that long-term sustainability and resiliency of surveillance is not subject to external partner funding decisions. It has been suggested that countries should expect to spend about US$ 1–4 per capita annually on disease surveillance infrastructure and personnel *(109)*. For low- and middle-income countries, initial one-time investments needed to strengthen laboratory capacities, data systems and human resource capacity may also be supported by coordination among donors. As a way forward, it is important for countries to incrementally increase domestic financing contributions and develop holistic investment cases, which can be used to achieve this goal in a health sector and multisectoral fashion.

Human expertise remains critical to recognizing potential cases of disease, diagnosing disease, reporting diseases or conditions, analyzing and interpreting data, and communicating results. The continued training of health professionals from all disciplines therefore remains vital to sustaining and enhancing public health surveillance capacity.

The expertise/skill sets most needed to run strong surveillance systems have evolved recently and in the coming years the following technical workforce is strongly recommended: health and other front-line workers; surveillance officers (and similar); (field) epidemiologists; laboratory specialists; data scientists (data managers, analysts, modellers, geographic information specialists); IT specialists (systems, software and hardware engineers); leadership, management and administration; social scientists; animal health specialists; and risk communication and community engagement specialists.

National authorities should also help ensure that the public health system can attract, recruit and retain the persons needed to operate essential surveillance systems and to respond to health threats. This must include assuring the availability of programmes to maintain skills among workers commensurate with changes in technology, the establishment and enhancement of systems and data in order to assess and monitor workforce needs. National authorities should also seek to reduce hiring barriers that exist at national and local levels. Field epidemiology training programmes should be supported and graduates should have access to competitive career options in the public health system.

Locally-defined objectives and priorities

A national surveillance mosaic should be comprised of systems that are well-adapted to the local context and local policy needs. The process of reviewing systems and establishing a national respiratory surveillance mosaic must begin with reviewing surveillance objectives and prioritizing those most salient to local policy and public health response needs. This will help to assure the continued interest and support of national authorities to sustain needed surveillance systems and the interest of local surveillance operators to participate in surveillance. The mosaic framework details core and enhanced systems within each domain of surveillance objectives. These are only to be used as a guide when assessing potential gaps in priority surveillance objectives and to help develop sets of collaborative fit-for-purpose components of a resilient surveillance mosaic. One mosaic of systems should address any included domain and consideration should also be given to whether certain objectives may be met with pooled regional or global data. It is also important to acknowledge that certain objectives may not be met by any of the mosaic surveillance parts implemented in a country. That is, national authorities may need to be conscious that some questions just cannot be answered with the data generated (rather than trying to speculate based on data that are not fit-for-purpose).

If targeted to priority surveillance objectives, the country surveillance mosaic may ensure that good quality, meaningful, equitable and accountable public health actions are taken based on data-driven decision-making. The collection, management, analysis and interpretation of a holistic set of data is central to informing efficient public health actions and monitoring their direct and indirect impact. A centralized dashboard and a regular bulletin summarizing surveillance mosaic data should communicate findings in a format friendly to decision-makers and local participants in the surveillance system (for example, assuring feedback loops). Translation science should be implemented to assure that timely and understandable information is available to all contributors of surveillance data and key stakeholders in order to ensure their buy-in and support and to inform timely risk assessment and policy-relevant decisions.

Integration of data standards and appropriate innovations

Technology and innovation play a key role in realizing a resilient country surveillance mosaic. Where appropriate, country implementation plans should include the evaluation of novel surveillance strategies highlighted within this framework and carefully consider their value to support implementation in the local context. National governance should consider adopting incentives and legislation to also bring private health providers and laboratories into national surveillance systems, where needed.

Ensuring electronic data capture at the local level will support timeliness of surveillance reporting, analysis response and feedback mechanisms. Simultaneous support for the digitalization of healthcare data (for example, using the Health Level-7 International (HL7) interface (110) and laboratory data (for example, laboratory information management systems) will

help to standardize data exchange systems, support movement towards EHR and integrated laboratory surveillance platforms, enable secure exchange of information, and allow for easier aggregation and integration of data at national and international levels. Over time, these technologies may enhance the amount of high-quality clinical and laboratory information that is sustainably available in routine surveillance systems.

3.3 Monitoring and evaluation

Monitoring and evaluation is important to understanding progress towards achieving framework objectives. Working with Member States and partners, WHO has developed and updated several resources within the IHR (2005) Monitoring and Evaluation Framework that can be used to assess national core capacities for public health emergencies encompassing the surveillance area of work for respiratory pathogen pandemics preparedness. The IHR Monitoring and Evaluation Framework consists of four complementary components: one mandatory, the State Party Self-Assessment Annual Report (SPAR), and three voluntary: JEE, After Action Reviews, and simulation exercises. Among the electronic quantitative components *(16, 111)*, the yearly periodicity and consistency of SPAR reporting make it the most relevant monitoring and evaluation tool for mosaic framework purposes. Key indicators from SPAR for respiratory viruses surveillance are:

- C4.1 Specimen referral and transport system and C4.4 Laboratory testing;
- C5.1 Early warning surveillance function and C5.2 Event management;
- C12.1 One Health collaborative efforts across sectors on activities to address zoonoses.

The framework's key measure of success is that:

By 2033 (ten-year horizon), over 90% of WHO Member States will have implemented their own context-appropriate mosaics of complementary surveillance systems for respiratory viruses with epidemic and pandemic potential that can meet their defined national surveillance objectives.

Monitoring and evaluation will focus on periodic, regular (every two years) **evaluation of surveillance systems' capacities** by countries, leveraging work already undertaken in this regard, and applying these findings in a cycle of systems' strengthening. Too often, evaluation is an afterthought of systems and does not form an integral part of operations or is left up to non-decision-makers to run. It is essential that evaluations inform course corrections or the removal of systems that do not deliver on objectives. Periodic case studies will be used to understand the qualitative aspects of implementation and help refine and shape collective progress. In its convening role, WHO will facilitate the global monitoring of strategy implementation, and work with countries and partners to conduct necessary reviews and course corrections.

A **monitoring and evaluation plan** will be prepared in partnership with WHO regional and country offices to monitor progress of local surveillance mosaic development. Monitoring and evaluation will focus on regional, biennial, updated landscape analyses of progress by countries. Periodic case studies will be used to understand the qualitative aspects of implementation and help refine and shape collective progress. In its convening role, WHO will facilitate the global monitoring of strategy implementation, and work with countries and partners to conduct necessary reviews and course corrections.

Table 5 outlines the **country-level indicators** that may be used to assess implementation of the framework.

Table 5 Framework of monitoring and evaluation indicators

Number	Indicators	Reporting source
0	• Specimen referral and transport system (SPAR C4.1) • Laboratory testing (SPAR C4.4). • Early warning surveillance function (SPAR C5.1) • Event management (SPAR C5.2) • One Health collaborative efforts across sectors on activities to address zoonoses (SPAR C12.1)	Existing, collected yearly (IHR State Party Self-Assessment Annual Report [SPAR]).
1	Proportion (%) of Member States who have designed their mosaic of surveillance systems based on needs assessment and evaluation of existing systems and shared them with WHO.	Not yet existing (indicator to start in 2023).
2	Proportion (%) of Member States who have developed a roadmap or action plan for implementation of their mosaic of surveillance systems in line with priority surveillance objectives as part of updated pandemic preparedness plans.	Partially existing (*Pandemic Influenza Preparedness Framework Partnership Contribution* indicator with disaggregation for surveillance systems).
3	Proportion (%) of Member States who have developed a national coordinating body for their mosaic of surveillance systems.	Not yet existing (indicator to start in 2023).
4	Proportion (%) of Member States that conducted an evaluation of the functional capacities of their mosaic of surveillance systems.	Partially existing (*Pandemic Influenza Preparedness Framework Partnership Contribution* indicator with disaggregation of the exercise to surveillance systems' level).
5	Proportion (%) of Member States who produce a regular (at least quarterly) electronic mosaic surveillance bulletin **or** have an accessible mosaic surveillance dashboard for regular stakeholder interpretation of mosaic surveillance data.	Partially existing in some regions such as the European Region (indicator to start in 2023).
6	Proportion (%) of Member States participating in one or more global or at least regional surveillance, risk assessment and response systems.	Not yet existing (indicator to start in 2023).

3.4 WHO's role in implementation

The role of the WHO secretariat will be to facilitate and advance the framework's purposes. Overall, in its global leadership role, WHO will be the convener of the framework. WHO will advocate for engagement, governance, resourcing, alignment with countries' strategies, as well as the harmonization of partners to develop and implement plans and to monitor progress. Partnerships are critical for achieving the objectives outlined in this framework. Through the regional and country offices, WHO will ensure that global implementation and advancement of the strategy centers around local needs and priorities.

4. Conclusions

No single surveillance system can meet all priority public health objectives for the surveillance of respiratory viruses of epidemic and pandemic potential. To address objectives related to early warning, sustainable monitoring, and intervention evaluation, a mosaic of surveillance systems and complementary investigations is necessary. While this framework suggests core and enhanced systems that may be included in each of the three surveillance domains, this is intended only as a guide and any mosaic must be adapted to country-specific contexts, Countries are encouraged to:

- review all the priority surveillance objectives outlined in this framework to determine those most important for local policy decisions;
- identify needed surveillance enhancements required to address each objective using the mosaic as a general guide/example;
- work with WHO and domestic and international partners to develop implementation plans to enhance surveillance and sustainably support the systems needed to resiliently address priority surveillance objectives on an ongoing basis.

Glossary of key terms and definitions

Clinical care pathway: A tool to support health workers identify and prioritize the current clinical and therapeutic recommendations to be considered in the care plan for patients *(112).*

Collaborative surveillance: is a new concept describing the collection, linkage, and analysis of data and insights from cases, pathogens, and context, which includes intentional collaboration across diseases, sectors, geographies, and event lifecycles, for timely decision making to mitigate public health threats. It links systems and data users. It aims to strengthen capacity and collaboration at all levels to detect an emerging outbreak, communicate information quickly, and rapidly initiate an appropriate response. The objectives of collaborative surveillance include strengthening integrated disease, threat, and vulnerability surveillance; increasing diagnostics and laboratory capacity for pathogen and genomic surveillance; and collaborative approaches to risk assessment, event detection, and response monitoring. *(12)*.

Community event-based surveillance: Detection, reporting and verification of signals in the community, and in specific sub-populations and risk groups within the community, including at the animal-human interface *(24, 113)*.

Event-based surveillance: The organized collection, monitoring, assessment and interpretation of mainly unstructured, ad hoc information regarding health events or risks, which may represent an acute risk to human health *(26)*.

Enhanced clinical surveillance: Clinical surveillance in a well-selected sample of patients using standardized clinical characterization case report forms to monitor changes in the natural history of illness, the relative severity of disease, risk factors for severe disease and poor outcomes, and treatment interventions and outcomes, with or without linkages to existing systems.

Healthcare capacity monitoring: The routine and systematic monitoring of health care capacity and utilization, either through comprehensive reporting or sentinel-based systems, to inform preparedness and response.

Health facility event-based surveillance: Sensitized health workers detecting and reporting conditions and other signals, with verification.

Hospital clinical code monitoring: Attributing clinical coding data (such as International Classification of Diseases [ICD] codes) from outpatient and inpatient medical facilities to respiratory disease case definitions and associated laboratory results to monitor respiratory disease trends, impact, and severity over time.

Indicator-based surveillance: The systematic (regular) collection, monitoring, analysis and interpretation of structured data, that is, of indicators produced by a number of well-identified, mostly health facility-based, formal sources. Includes for example, notifiable disease surveillance systems, sentinel surveillance and laboratory-based surveillance *(26)*.

Investigations and studies: Investigations (outbreak investigations or others) and studies focus on specific objectives not efficiently met by other existing surveillance systems. Their goal is to act as specialized instruments to supplement ongoing surveillance by filling the gaps in our understanding about the descriptive and analytic epidemiology of a circulating pathogen, and the specific measures that may be optimally applied to reduce associated illness or impact *(41, 42)*.

Laboratory networks: Organized networks of laboratories reporting data on specimens tested centrally, with phenotypic and genomic characterization as needed.

Media event-based surveillance: Detection, reporting and verification of signals from the media and social media .

Mortality surveillance: All-cause or respiratory disease mortality monitoring systems using data reported from existing vital statistics or health facilities' reporting systems.

National notifiable diseases/conditions surveillance: Mandated reporting of notifiable diseases or conditions to public health authorities in a specified and timely manner for effective disease monitoring, control and management.

One Health: an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants and the wider environment including ecosystems are linked *(114)*.

One Health surveillance: Where collaboration between surveillance systems of multiple sectors (human, animal, plant, food safety, and environment) allows the integration of surveillance processes to share data, analyze, generate and disseminate relevant information with the view of improving One Health (human, animal, plan or environment) *(25)*.

Participatory surveillance: The collection of data for public health action by directly involving volunteer citizens in the population at risk in submitting relevant data (for example, on symptoms and other pertinent information on public health threats), often through a variety of digital survey tools *(60).*

Pharmacovigilance: The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem *(115).*

Public health surveillance: The ongoing, systematic collection, analysis and interpretation of health-related data essential to planning, implementation and the evaluation of public health practice *(116)*.

Public health and social measures: Non-pharmaceutical interventions implemented by individuals, communities and governments at all levels to reduce the spread of infectious diseases with epidemic or pandemic potential by reducing transmission-relevant contacts and/or making them safer. Public health and social measures play a continuous role across various points of a health emergency, especially when medical countermeasures are not available, particularly in the early stage of a health emergency, and when vaccine availability, vaccination coverage and effectiveness are limited *(89)*.

Sentinel influenza-like illness/acute respiratory infection/severe acute respiratory infection surveillance: Sentinel syndromic influenza-like illness, acute respiratory infection and/or severe acute respiratory infection surveillance with the integration of laboratory testing *(21)*.

Sentinel surveillance: Involves a limited number of recruited participants, such as health care providers or hospitals, who report specified health events that may be generalizable to the whole population *(117)*.

Syndromic surveillance: Syndromic surveillance is the near real-time collection, analysis, interpretation and dissemination of health-related data in order to enable the early identification of the impact (or absence of impact) of potential health threats that may require public health action *(118).*

Targeted special population surveillance: Newly introduced or enhanced surveillance in targeted special populations with a greater risk of exposure to the virus and/or other groups identified to be at high risk of infection or severe disease in order to detect and describe early cases and monitor morbidity and mortality of circulating respiratory viruses.

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Annex: Existing global and regional surveillance guidance

Current WHO global and regional strategic guidance for respiratory viruses of pandemic potential were reviewed together with other more specialized documents as part of the mosaic framework development and are listed below. A virtual repository of guidance can be found here Click to view → and ensures access to the latest versions of any documents that will support countries to define and implement their respective surveillance mosaics.

Global

- Public health surveillance for COVID-19: WHO interim guidance. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/WHO-2019-nCoV-SurveillanceGuidance-2022.2, accessed 21 January 2023).
- Strategic preparedness, readiness and response plan to end the global COVID-19 emergency in 2022. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/WHO-WHE-SPP-2022.1, accessed 21 January 2023).
- Surveillance for human infection with Middle East respiratory syndrome coronavirus (MERS-CoV): interim guidance. Geneva: World Health Organization; 2018 (https://apps.who.int/iris/handle/10665/177869, accessed 23 January 2023).
- Global influenza strategy, 2019-2030. Prevent. Control. Prepare. Geneva: World Health Organization; WHO; 2019 (https://apps.who.int/iris/handle/10665/311184, accessed 21 January 2022).
- WHO guidance for surveillance during an influenza pandemic. Geneva: World Health Organization; WHO; 2017 (https://apps.who.int/iris/handle/10665/259886, accessed 21 January 2023).
- Global epidemiological surveillance standards for influenza. Geneva: World Health Organization; 2013 (https://www.who.int/publications/i/item/9789241506601, accessed 21 January 2023).
- Global genomic surveillance strategy for pathogens with pandemic and epidemic potential, 2022–2032. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/9789240046979, accessed 21 January 2023).
- Global strategy for comprehensive vaccine-preventable disease surveillance. Geneva: World Health Organization; 2018 (https://www.who.int/publications/m/item/global-strategy-for-comprehensive-vaccine-preventable-disease-(vpd)-surveillance, accessed 21 January 2023).
- Ethics in public health surveillance. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/bitstream/handle/10665/255721/9789241512657-eng.pdf, accessed 21 January 2023).
- Global strategy for integrated surveillance for public health emergencies. Geneva: World Health Organization (*in development*).
- Global polio surveillance action plan 2022-2024. Geneva: World Health Organization; WHO, 2022 (https://polioeradication.org/wp-content/uploads/2022/05/GPSAP-2022-2024-EN.pdf, accessed 21 January 2023).accessed 21 January 2023).

Regional

- Operational considerations for respiratory virus surveillance in Europe. Copenhagen: WHO Regional Office for Europe and Stockholm: European Centre for Disease Prevention and Control; 2022 (https://apps.who.int/iris/handle/10665/360349 **or** https://www.ecdc.europa.eu/en/publications-data/operational-considerations-respiratory-virus-surveillance-europe, accessed 21 January 2023).
- COVID-19 surveillance guidance. Transition from COVID-19 emergency surveillance to routine surveillance of respiratory pathogens. Stockholm European Centre for Disease Prevention and Control; 2021 (https://www.ecdc.europa.eu/en/publications-data/covid-19-surveillance-guidance, accessed 21 January 2023).
- Technical Guidelines for Integrated Disease Surveillance and Response in the African Region: Third edition. Brazzaville: WHO Regional Office for Africa; 2019 (https://www.afro.who.int/publications/technical-guidelines-integrated-disease-surveillance-and-response-african-region-third, accessed 21 January 2023).
- Final report. Ad hoc expert consultation in the Region of the Americas: Challenges, gaps and next steps in COVID 19 surveillance and its integration in to influenza and other respiratory viruses surveillance. Pan American Health Organization; 2022 (https://www.paho.org/en/documents/final-report-ad-hoc-expert-consultation-region-americas-challenges-gaps-and-next-steps, accessed 21 January 2023).
- Epidemic analysis for response decision-making: systematic organization of multi-source information to inform response decisions. Manila: World Health Organization Regional Office for the Western Pacific; 2020 (https://apps.who.int/iris/bitstream/handle/10665/333046/9789290619161-eng.pdf?sequence=1&isAllowed=y, accessed 21 January 2023).
- Regional operational guidelines for the integrated surveillance of respiratory viruses. Pan American Health Organization (*in development*).
- Integrated Surveillance for Influenza and Other Respiratory Viruses with Epidemic and Pandemic Potential in the Eastern Mediterranean Region – An Operational Framework. Cairo: World Health Organization Regional Office for the Eastern Mediterranean (*in development*).

Specific systems

- **Sentinel surveillance**
  - o End-to-end integration of SARS-CoV-2 and influenza sentinel surveillance: revised interim guidance. Geneva: World Health Organization; 2022 (https://www.who.int/publications/i/item/WHO-2019-nCoV-Integrated_sentinel_surveillance-2022.1, accessed 21 January 2023).
  - o Operational considerations for influenza surveillance in the WHO European Region during COVID-19: interim guidance. Stockholm: European Centre for Disease Prevention and Control; 2020 (https://www.ecdc.europa.eu/en/publications-data/operational-considerations-influenza-surveillance-european-region-during-covid-19, accessed 21 January 2023).

Specific systems (cont.)

- o Protocol for enhanced severe acute respiratory illness and influenza-like illness surveillance for COVID-19 in Africa. Addis Ababa: Africa Centers for Disease Control and Prevention; 2020. (https://africacdc.org/download/protocol-for-enhanced-severe-acute-respiratory-illness-and-influenza-like-illness-surveillance-for-covid-19-in-africa/, accessed 21 January 2023).
- o Strategy for global respiratory syncytial virus (RSV) surveillance project based on the influenza platform. Geneva: World Health Organization; 2019 (https://cdn.who.int/media/docs/default-source/influenza/rsv-surveillance/who-rsv-surveillance-strategy-phase-26mar2021.-final.pdf?sfvrsn=d8b1c36a_9, accessed 21 January 2023).
  - Sampling strategy for RSV testing. Geneva: World Health Organization; 2019 (https://www.who.int/teams/global-influenza-programme/global-respiratory-syncytial-virus-surveillance/sampling-strategy-for-rsv-testing , accessed 21 January 2023).
  - WHO Global clinical platform for COVID-19. Geneva: World Health Organization; 2023 (https://www.who.int/teams/health-care-readiness/covid-19/data-platform, accessed 21 January 2023).
  - International severe acute respiratory and emerging infection consortium (ISARIC). 2023 (https://isaric.org/, accessed 21 January 2023).

- **Event-based surveillance**

  - o A guide to establishing event-based surveillance. Manila: World Health Organization Regional Office for the Western Pacific; 2008. (https://apps.who.int/iris/handle/10665/207737, accessed 21 January 2023).
  - o Epidemic Intelligence from Open Sources (EIOS). World Health Organization (video: https://www.youtube.com/watch?v=Nklf3l0CTx0&t=3s&ab_channel=WorldHealthOrganization%28WHO%29, accessed 23 January 2023)
  - o EIOS Initiative. World Health Organization (https://www.who.int/initiatives/eios accessed 21 January 2023).
  - o EIOS System. World Health Organization (https://www.who.int/initiatives/eios/eios-technology, accessed 21 January 2023).

- **Investigations and studies**

  - o Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases. Geneva: World Health Organization; 2018 (https://www.who.int/publications/i/item/WHO-WHE-IHM-GIP-2018.2, accessed 21 January 2023).
  - o Protocol for COVID-19 (10 protocols) early investigations and studies, for country use and adaptation. Geneva: World Health Organization; 2020-2022 **(**https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigation**s,** accessed 21 January 2023).
  - o Protocols for Pandemic Influenza Special Investigations & Studies (iPSS). Geneva: World Health Organization (*in development*) (https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/pandemic-influenza-special-investigations-studies-pss#:~:text=The%20Pandemic%20Influenza%20Special%20Investigations,by%20a%20novel%20influenza%20virus, accessed 21 January 2023).

Specific systems (cont.)

- o Pandemic influenza severity assessment (PISA): a WHO guide to assess the severity of influenza in seasonal epidemics and pandemics. Geneva: World Health Organization; 2017 (https://www.who.int/publications/i/item/pandemic-influenza-severity-assessment-(-pisa)-a-who-guide-to-assess-the-severity-of-influenza-in-seasonal-epidemics-and-pandemics, accessed 21 January 2023).
- o A manual for estimating disease burden associated with seasonal influenza. Geneva: World Health Organization (https://apps.who.int/iris/bitstream/handle/10665/178801/9789241549301_eng.pdf?sequence=1&isAllowed=y, accessed 21 January 2023).
- o Seasonal influenza disease burden estimator (Pyramid Webtool) (www.flutool.org, accessed 21 January 2023).
- o WHO Manual for estimating the economic burden of seasonal influenza. WHO. 2016. Cost burden. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/rest/bitstreams/1060971/retrieve, accessed 21 January 2023).
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- o Pebody R, Moyes J, Hirve S, Campbell H, Jackson S, Moen A, et al. Approaches to use the WHO respiratory syncytial virus surveillance platform to estimate disease burden. Influenza Other Respi Viruses. 2020;14:615–621 (https://onlinelibrary.wiley.com/doi/full/10.1111/irv.12667, accessed 21 January 2023).
- o Consortium for the Standardization of Influenza Seroepidemiology (CONSISE) (https://consise.tghn.org/protocols/, accessed 21 January 2023).
- o Middle East respiratory syndrome coronavirus (MERS-CoV)/Technical guidance/Outbreak Toolbox. Geneva: World Health Organization; 2022 (https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/mers-outbreak-toolbox, accessed 21 January 2023).

- **Animal-human interface surveillance**

  - o Taking a multisectoral, one health approach: a tripartite guide to addressing zoonotic diseases in countries. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/325620, accessed 21 January 2023)
    - The Multisectoral Coordination Mechanism Operational Tool (MCM OT) (https://www.who.int/initiatives/tripartite-zoonosis-guide/multisectoral-coordination-mechanism-operational-tool, accessed 21 January 2023).
    - The Surveillance and Information Sharing Operational Tool (SISOT) (https://www.who.int/initiatives/tripartite-zoonosis-guide/surveillance-and-information-sharing-operational-tool, accessed 21 January 2023)
    - The Joint Risk Assessment Operational Tool (JRA OT) (https://www.who.int/initiatives/tripartite-zoonosis-guide/joint-risk-assessment-operational-tool, accessed 21 January 2023)
    - An *online training platform* is available to help countries navigate and implement the Tripartite Zoonosis Guidance.
  - o Zoonotic influena outbreak toolbox. Geneva: World Health Organization (https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/zoonotic-influenza-outbreak-toolbox, accessed 21 January 2023).

Specific systems (cont.)

- o Summary of Key Information Practical to Countries Experiencing Outbreaks of A(H5N1) and Other Subtypes of Avian Influenza. Geneva: World Health Organization; 2016 (https://www.who.int/publications/i/item/WHO-OHE-PED-GIP-EPI-2016.1, accessed 21 January 2023; *revision in development*).

- **Environmental surveillance**

  - o Environmental surveillance for SARS-COV-2 to complement public health surveillance – Interim Guidance. Geneva: World Health Organization; 2022. (https://www.who.int/publications/i/item/WHO-HEP-ECH-WSH-2022.1, accessed 21 January 2023).

- **Participatory surveillance**

  - o Best practices for the design, implementation, analysis and reporting of participatory surveillance for influenza-like illness. Geneva: World Health Organization *(in development*).

- **Surveillance in specific population**

  - o Prevention and Control of COVID-19 in long-term care facilities. Stockholm: European Centre for Disease Prevention and Control; 2022. (https://www.ecdc.europa.eu/en/all-topics-z/coronavirus/threats-and-outbreaks/covid-19/prevention-and-control/LTCF, accessed 21 January 2023).
  - o Considerations for COVID-19 surveillance for vulnerable populations. Manila: World Health Organization Regional Office for the Western Pacific; 2021 (https://apps.who.int/iris/handle/10665/345250, accessed 21 January 2023).
  - o Surveillance protocol for SARS-CoV-2 infection among health workers. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/WHO-2019-nCoV-HCW_Surveillance_Protocol-2020.1, accessed 21 January 2023).

- **Evaluation of surveillance systems**

  - o Overview of evaluation surveillance systems. Atlanta, GA: Centers for Disease Control and Prevention; 2013 (https://www.cdc.gov/globalhealth/healthprotection/fetp/training_modules/12/eval-surv-sys_fieldg_final_09262013.pdf, accessed 21 January 2023).
  - o Centers for Disease Control and Prevention. Guidelines for evaluating surveillance systems. Prepared by Douglas N. Klaucke, James W. Buehler, Stephen B. Thacker, R. Gibson Parrish, Frederick L. Trowbridge, Ruth L. Berkelman, and the Surveillance Coordination Group. MMWR Morb Mortal Wkly Rep 1988; 37(S-5);1-18. (https://www.cdc.gov/mmwr/preview/mmwrhtml/00001769.htm, accessed 21 January 2023).
  - o Data quality monitoring and surveillance system evaluation: A handbook of methods and applications. Stockholm: European Centre for Disease Control and Prevention; 2014 (https://www.ecdc.europa.eu/en/publications-data/data-quality-monitoring-and-surveillance-system-evaluation-handbook-methods-and, accessed 21 January 2023).

Specific systems (cont.)

Overarching

- How global research can end this pandemic and tackle future pandemics. Building a resilient research architecture and capability to protect us all. R&D blueprint. Geneva: World Health Organization; 2022 **(**https://cdn.who.int/media/docs/default-source/blue-print/final-report-of-the-global-research-and-innovation-forum-2022.pdf?sfvrsn=4a59021f_5&download=true, accessed 21 January 2023).

Others

- Tool for Influenza Pandemic Risk Assessment (TIPRA). Geneva: World Health Organization; 2016 (https://apps.who.int/iris/handle/10665/250130, accessed 21 January 2023).
- **IOA partnership**
  - IOA terms of reference: https://drive.google.com/file/d/1FRnw7jfWSkT2frt5J9JKDuxHKl3VGr3F/view, accessed 21 January 2023.
  - Google Drive resources (case studies developed mostly in the Democratic Repubic of the Congo): https://drive.google.com/drive/u/0/folders/1p8ERJxmbGwFfm_bXgGhWbxJnxSxGT2WQ, accessed 21 January 2023.
  - YouTube Channel: https://www.youtube.com/channel/UCORuiEZmQI71nrv-C27cNnQ, accessed 21 January 2023.
  - Global Outbreak and Response Network (GOARN) webpage: https://goarn.who.int/, accessed 21 January 2023.
- **EWARN/EWARS**
  - EWARS in emergencies and EWARS in a box (https://www.who.int/emergencies/surveillance/early-warning-alert-and-response-system-ewars, accessed 21 January 2023).
  - World Health Organization. Early warning alert and response in emergencies: an operational guide. World Health Organization. 2022. (https://apps.who.int/iris/handle/10665/365730, accessed 15 Feb 2023).
- **Preparedness for a high-impact respiratory pathogen pandemic**. Baltimore, MD: Johns Hopkins Center for Health Security report commissioned for the Global Preparedness Monitoring Board. 2019 (https://www.gpmb.org/annual-reports/overview/item/preparedness-for-a-high-impact-respiratory-pathogen-pandemic, accessed 21 January 2023).

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