Operational Guidelines for Sentinel
Severe Acute Respiratory Infection (SARI) Surveillance

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Contents

Executive Summary

The influenza A(H1N1) pandemic of 2009 highlighted the importance of collecting information about disease severity in a standardized manner and having historical data available for countries to assess current influenza seasons in the context of previous ones. To address these objectives and help promote comparability of surveillance data between countries in the Region of the Americas, PAHO developed the *Operational Guidelines for Intensified National SARI Surveillance* in January 2011. Based on country experiences operationalizing these guidelines, feedback from surveillance and laboratory field personnel, and the development of global influenza surveillance guidance by WHO, the following updates have been made to the PAHO guidelines:

- **The surveillance scope has been changed from intensified, national surveillance to sentinel surveillance**
    - *Justification:* Rather than collecting large quantities of poor quality data, the focus should be on collecting high quality data from a small number of carefully selected sentinel sites

- **The SARI case definition has been updated**
  SARI cases are now defined as patients with an acute respiratory infection who
      - have a history of fever, or measured fever of ≥ 38 C°
      - AND cough
      - AND onset within the last ten days;
      - AND require hospitalization.
    - *Justification:* Based on an analysis of the characteristics of globally used case definitions, WHO recommends the above SARI case definition. In order to reflect advances in thinking about the best case definition and to align the Region with global practices, the recommended case definition has been changed.

- **Sampling methodologies have been described to assist facilities in selecting patients for respiratory sample collection in an unbiased and standardized matter**
    - *Justification:* Although influenza diagnostic testing of all SARI patients in the sentinel sites is ideal, for sites in which this is not feasible, alternate sampling options have been provided.

- **Guidance on calculating baselines and thresholds and constructing endemic channels is provided**
    - *Justification:* Countries must build baselines in order to interpret current season data.

- **Additional laboratory guidance regarding specimen collection, transport and shipping to WHO CC has been included**

- o   *Justification:* Countries should adhere to best practices for collecting, transporting, and shipping samples in order to ensure high-quality information is available for vaccine strain selection.

- **Guidance on how to calculate disease burden estimates is provided**
    - o   *Justification:* Once surveillance data are collected, understanding the burden of disease can be helpful for targeting interventions and resource management.

1. Acronyms

ARI – Acute respiratory infection

CDC – Centers for Disease Control and Prevention, USA

FluID – WHO global platform for epidemiological influenza surveillance

FluNet – WHO global platform for virologic influenza surveillance

GISRS – Global Influenza Surveillance and Response System

ICD – International Classification of Diseases

ICU – Intensive Care Unit

IFA – Immunofluorescence assay

IHR – International Health Regulations

ILI – Influenza-like illness

NIC – WHO-recognized National Influenza Centre

ORV – Other respiratory viruses

PAHO – Pan American Health Organization

PPE – Personal protective equipment

RT-PCR – Reverse transcription polymerase chain reaction

SARI – Severe acute respiratory infection

SARInet – SARI network in the Americas

VTM – Viral transport media

WHO – World Health Organization

WHO CC – WHO Collaborating Centre for Reference and Research on Influenza

2. Introduction

Emerging respiratory infectious diseases pose a substantial risk for humans because of their extremely high potential to spread from person-to-person. Four pandemics involving emerging respiratory infectious diseases have occurred in the last century, with the most recent being the 2009 influenza A(H1N1) pandemic. Some of the lessons learned from the 2009 pandemic included the need to collect data about severe cases, utilize a standard methodology for collecting information, and have historical data to asses the current influenza activity in the context of previous seasons. The purpose of these guidelines is to describe SARI surveillance objectives and to provide recommendations for standardized methods based on global standards. The information in this document should be used by clinical-epidemiologic and laboratory public health professionals and national health authorities involved with influenza surveillance to support the implementation, monitoring, evaluation, and improvement of the national surveillance system. It can be used by countries in the initial stages of surveillance implementation as well as those that are trying to improve and refine their existing systems. Countries should adapt this framework to their own specific needs and try to integrate SARI surveillance into existing public health systems to promote sustainability and to benefit from efficiencies in data collection, sample collection and transport to laboratories, data analysis and reporting.

In addition to providing country-specific influenza data, SARI surveillance should complement national early warning surveillance systems designed to meet the International Health Regulations (IHR) requirements for surveillance and response. The IHR (2005) are a set of binding legal instruments adopted by the Member States of the WHO to contain the spread of disease. The described core competencies include the capacity to detect, assess, notify and report diseases or health events that could constitute public health emergencies of international significance. Under the IHR (2005) Annex II, PAHO/WHO should be notified immediately of all cases of smallpox, poliomyelitis (due to wild poliovirus), SARS, human influenza caused by new virus subtypes, and any event of potential international public health concern (including unusual disease clusters, significant changes in influenza epidemiology, cholera, pneumonic plague, yellow fever, viral hemorrhagic fevers, West Nile fever and other diseases of special national or regional concern).

3. Influenza

a. Types and Subtypes

There are three types of influenza viruses that cause disease in humans: A, B, and C. Human influenza A and B viruses cause seasonal epidemics. Influenza B viruses cause sporadic outbreaks with high mortality in older adults. Influenza type C viruses cause a mild respiratory illness and are not thought to cause epidemics. Only influenza A viruses have caused pandemics.

Influenza A viruses are divided into subtypes based on the hemagglutinin and neuraminidase proteins present on their surface (Figure 1). Eighteen hemagglutinin subtypes and 11 neuraminidase subtypes have been identified. Currently influenza A(H1N1) and A(H3N2) are the circulating subtypes responsible for the seasonal epidemics. The H5, H7, and H9 viruses rarely produce disease in humans. Influenza B viruses are not divided into subtypes, but can be further broken down into different lineages (Victoria and Yamagata).
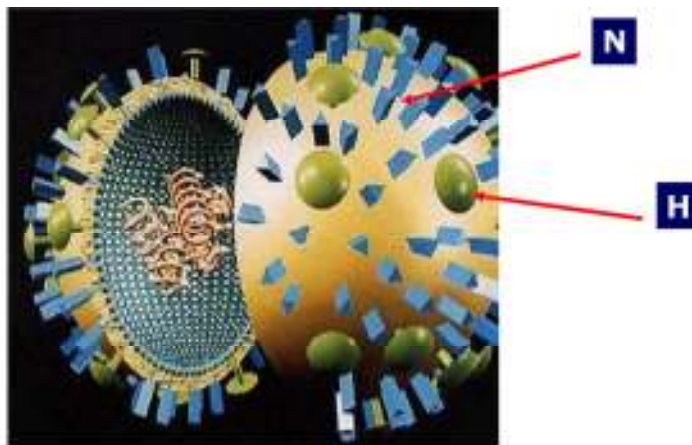
Figure 1: Characteristics of the Influenza A Virus

Influenza A and Pandemics

Two main features of influenza A viruses give them major pandemic potential:

- antigenic variability
- an extensive animal reservoir

The phenomenon of influenza A epidemics and pandemics is due to the frequency with which the genetic composition of influenza A viruses changes. Minor genetic changes are known as "**antigenic drift**" and cause alterations of the antigens on the surface of the influenza virus. Drift is a continuous process that produces new antigenic variants and hence necessitates annual modification of influenza vaccine composition. Major genetic changes are known as "**antigenic shift**" and are more radical, involving the appearance of viruses with new hemagglutinins or new combinations of hemagglutinin and neuraminidase. There are two main mechanisms of antigenic shift: (a) **reassortment**, which involves an exchange of genetic material between an influenza virus of nonhuman origin and one of human origin when both are present in a human being or intermediate host mammal such as a pig, and (b) a more

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gradual process of **adaptive mutation** through replication in successive human infections, which gives the virus an increasing ability to join with human cells and transform itself into a new virus with full capacity to circulate in humans. Influenza A viruses undergo both antigenic shifts and antigenic drifts whereas influenza B viruses change only through antigenic drift.

The influenza A virus is found in numerous animal species. However, its principal reservoir is wild aquatic birds, which can transmit the infection to other birds, both wild and domestic, and to various mammals, including humans, whales, pigs, horses, and domestic and wild felines. The pig has been considered an intermediate reservoir serving as a "mixing vessel" for the exchange of genetic material between different influenza viruses.

b. Transmission

The influenza virus is transmitted:

- from one person to another by **direct contact**, especially through droplets of 5 μm that are generated when an infected individual coughs or sneezes and can travel up to one meter. In special situations during the production of aerosols, droplet nuclei of up to 5 μm can travel over one meter.
- by **indirect contact** with contaminated objects (fomites). Hands play a major role in this type of transmission.

The virus can survive for some time outside a living organism, approximately

- five minutes on the hands
- 8-12 hours on paper, cloth, and other fibers
- 24-48 hours on hard surfaces.

The **contagious period** ranges from one day before the onset of symptoms to 3-7 days after. Infected persons can transmit the virus even if they are asymptomatic. Individuals with immunodeficiencies may carry and shed the virus over longer periods of time. The **incubation period** for the virus ranges from one to four days, and averages two days. The disease's clinical manifestations vary widely. The infection may be asymptomatic, may produce an influenza syndrome, or may develop into an illness serious enough to cause death. The **symptoms** span a broad clinical spectrum and may include fever of ≥38°C, cough, sore throat, nasal congestion, headache, myalgia, prostration, coryza, and gastrointestinal symptoms. The cough is usually intense and persistent, while the other symptoms are shorter-lived, with patients recovering in two to seven days. Clinically, influenza is not always distinguishable from diseases caused by other respiratory viruses. Symptoms vary according to the patient's age, underlying comorbidities, and individual immune response. In children, the clinical presentation might include high fever, cervical lymphadenopathy, bronchiolitis and bronchitis, and gastrointestinal symptoms are also common. Although young children may be unable to describe their symptoms, they will generally show signs of a sore throat, such as difficulty swallowing or crying when eating drooling, vomiting, or changes in voice tone. Older adults almost always present with fever, though not as high as that observed in children, and sometimes they show no other symptoms.

Serious complications and death occur mainly in the elderly, children, institutionalized individuals, and persons with chronic disease or immunosuppression (e.g., heart disease; hemoglobinopathies; metabolic, pulmonary and renal diseases; AIDS; and respiratory diseases, including asthma). Pregnant women have shown a greater tendency to develop severe forms of the disease.

While the influenza virus can cause a primary infection of the upper and/or lower respiratory tract, on rare occasions it can occur in conjunction with another virus or bacteria—a situation known as **co-infection**. Bacterial co-infections are often secondary infections that occur as a result of initial changes caused by the influenza virus in the respiratory tract, which facilitate the invasion of bacteria. Secondary bacterial co-infections are most often due to *Streptococcus pneumoniae, Haemophilus influenzae or Staphylococcus aureus.*

Since influenza viruses do not cause a specific clinical syndrome that differentiates it from other pathogens, it is not possible to identify patients with influenza without a diagnostic test. Moreover, as resources can be limited, it is not feasible to collect specimens from all patients in order to identify the etiologic agent for surveillance purposes. Consequently, a proxy syndrome is used. **Influenza-like illness (ILI)** is used to monitor less severe influenza and other respiratory virus infections in the outpatient setting, and **severe-acute respiratory infection (SARI)** is used to monitor more severe manifestations resulting in hospitalization (Figure 2).
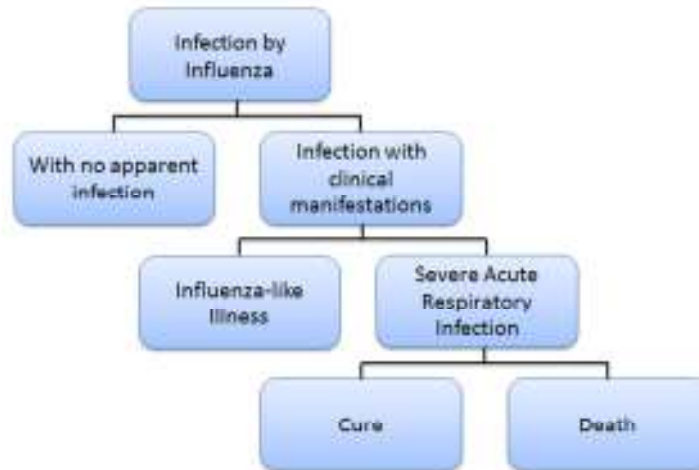

Figure 2: Spectrum of influenza infection manifestations

4. Disease Surveillance

a. Overview

Surveillance is essential for monitoring events that might jeopardize the health of a population so that appropriate prevention and control measures can be implemented in a timely manner. An effective surveillance system includes the following:

- collection, reporting, and consolidation of data
- routine analysis and interpretation of data
- feed-forward of surveillance data to decision makers
- feedback of surveillance data to those providing the data and other interested parties
- detection, evaluation, and response to unusual patterns in the data
- quality assurance

The overarching goal of influenza surveillance is to minimize the impact of the disease by providing useful information to public health authorities so that they may better plan appropriate control and intervention measures, allocate health resources and make case management recommendations.

The specific goal of influenza surveillance is to provide timely and high- quality data and viral isolates in order to perform the following:

- Describe the seasonality of influenza where feasible
- Signal the start and end of the influenza season
- Provide candidate viruses for vaccine production
- Describe the antigenic character and genetic makeup of circulating viruses
- Identify and monitor groups at high-risk of severe disease and complications from infection
- Establish baseline levels of activity for influenza and severe influenza-related disease with which to evaluate the impact and severity of each season and of future pandemic events
- Generate influenza data that can be used during focused studies to estimate influenza burden and help decision-makers prioritize resources and plan public health interventions.
- Identify locally circulating virus types and subtypes and their relationship to global and regional patterns
- Assist in understanding the relationship of virus strains to disease severity
- Monitor antiviral sensitivity
- Detect unusual and unexpected events such as outbreaks of influenza outside the typical season, severe influenza among healthcare workers, or clusters of vaccine failures that may herald novel influenza virus

Additionally, by producing baseline data, surveillance systems may also provide a platform for evaluating the effectiveness of vaccines and other interventions. Not every system will be able to accomplish all of these objectives, so it is important that countries prioritize activities based on their needs and capabilities. Table 1 describes the public health- related decisions that can be informed by meeting some of the different surveillance objectives.

Objective	Use of Surveillance Data in Decision-Making
Determine when and where influenza activity is occurring, and who is affected.	• Alert health care providers to anticipate influenza disease in clinics and hospitals • Inform and target national prevention and treatment policies such as vaccination timing and the use of pharmaceutical and non-pharmaceutical interventions to control spread
Detect changes in the antigenic and genetic characteristics, and antiviral sensitivity of influenza viruses	• Inform local clinician use of antiviral therapies • Inform choice of vaccine locally and selection of appropriate viruses globally.
Determine and monitor underlying risk conditions that are associated with severe disease and use of health care resources. **Describe the clinical patterns of disease.**	• Improve clinical management and prevention of disease in high risk patients • Inform national policies such as priority groups for vaccination and treatment
Assess and monitor relative severity of annual epidemics or an outbreak of a novel virus	• Assist policy makers in making decisions about public interventions • Inform cost-benefit type decisions related to public interventions
Estimate contribution of influenza to severe respiratory illness or overall disease burden	• Allow appropriate allocation of limited health resources among competing disease-related priorities. • Establish epidemic thresholds for comparison of disease severity between years and localities • Contribute to global knowledge base regarding burden of disease attributable to influenza disease
Detection of unusual events	• Rapid detection to alert the International Health Regulation focal points about potential public health events of international concern
Measure impact of interventions	• Inform choice of intervention strategies

b. Types of Surveillance

There are two main types of surveillance - event-based and indicator-based (Figure 3). Although their functions differ, these systems are both essential components of a national surveillance system and should complement each other.

Figure 3: Types of Surveillance Systems (From: WHO A Guide to Establishing Event-based Surveillance)

Indicator-based surveillance involves the routine collection of standardized information to establish historical trends and baselines to which the current situation can be compared. Data collection and analysis is very structured and specific to the disease or syndrome being monitored. Public health responses are triggered when pre-defined threshold activity levels are surpassed.

Event-based surveillance involves rapidly detecting events that potentially pose a high risk to public health. These systems are designed to detect rare and new events, such as high-impact outbreaks or emerging and unknown diseases, at a very early stage when the event is geographically localized and involves a relatively small number of people, so that rapid assessments and responses can be made to contain or mitigate the situation. In order to accomplish this, event-based systems use broader and more sensitive definitions and flexible reporting structures than indicator-based systems. Although one of the critical functions of sentinel SARI surveillance is to detect novel strains of influenza or other respiratory viruses, the methods used for these systems are not designed for the timely detection and response to outbreaks or other important public health events. **Event-based surveillance should be used for rapid detection of unusual respiratory events** such as emerging novel influenza or other respiratory virus strain (e.g., Middle East coronavirus (MERS-CoV), avian influenza A(H7N9)) or outbreaks of respiratory disease**.** In the context of novel strains of influenza and other respiratory viruses, the objective of early detection is to detect the first evidence of sustained human-to-human transmission of a respiratory virus with pandemic potential when circulation of the virus is limited.

See **Annex 1** for more information on implementation of a pandemic early warning system

c. Sentinel Surveillance

Sentinel surveillance is the most efficient way to collect high-quality data in a timely way. It is typically carried out with indicator-based surveillance and involves systematically collecting data on a routine basis from a limited number of surveillance sites. Ideally, the sites are chosen to be representative of the population so that the information gathered can be applied to the population as a whole.

As mentioned previously, the spectrum of influenza infections varies widely in terms of severity and various indicator-based systems are used to monitor these syndromes. Specifically, **sentinel ILI surveillance** is focused on mild manifestations of influenza in the outpatient setting while **sentinel SARI surveillance** is used to monitor persons with more severe illness who have been admitted to a hospital for their respiratory illness (Figure 4).

Figure 4: The spectrum of influenza infections and the respective surveillance methods based on EURO/WHO's *Guidance for Sentinel Influenza Surveillance in Humans*

d. Selecting Sentinel SARI Surveillance Sites

In order to achieve the objectives of the national surveillance system, sentinel sites should be carefully selected. During this process it is most important to consider how feasible it is for the site to conduct SARI surveillance and how the site represents the population of interest. It is also critical to remember that this is no ideal number of sentinel sites for each country. In general, small amounts of good quality data are more useful than large amounts of poor quality data. Therefore, it is best to start small, with only one or a small number of sites, and expand only if they function well.

Feasibility and Sustainability

The feasibility of a facility to participate in a sentinel system and the sustainability of the surveillance system are important criteria to consider when selecting a sentinel site. These attributes will depend on the facility having:

- Staff and leadership that are motivated and committed to voluntarily implement and sustain surveillance
- Efficient, consistent, and sustainable mechanisms for collection, storage and transport of clinical specimens

- The ability to reliably manage and report surveillance data, including the necessary communications infrastructure
- Stable and long term funding to cover the general cost of the surveillance operations at the site

Laboratory capacity at a site to test specimens may facilitate surveillance, but it is not absolutely necessary if specimens can be tested at a central facility (e.g., National Influenza Center (NIC)). However, it is critical that the sentinel site be able to ensure proper sample storage and timely transport.

Representativeness

Sentinel sites should include patients that will appropriately represent the population. Some issues to consider with regard to representativeness:
- General or community hospitals are more likely to be representative of the general population than specialty or tertiary care referral hospitals.
- Within the hospital facility, the surveillance system should include all wards where SARI patients are expected to be treated.
- Urban versus rural representativeness
- The population served by the sentinel site should be representative of the target age and socioeconomic groups in the population under surveillance.
- When multiple sentinel sites are being selected, consideration should be given to representing additional population centers or climate zones, each of which may have unique demographic and socio-economic characteristics resulting in differences in transmission patterns.

Disease Burden

If there is interest in developing disease burden estimates for influenza and other respiratory viruses, several things must be considered when selecting sites (see Chapter 5, Section D for more information). Population-based incidence (i.e. the number of new cases of a disease per 100,000 people in the population per year), is the classic way to express burden. This requires the ability to either count or reliably estimate the number of cases that occur in a year and the size of population that generally seeks care at the sentinel site facility. Some considerations when selecting sites for surveillance when disease burden estimates are desired:

Availability of reliable numerator data
- Ability to either capture all cases meeting the case definition or to reliably estimate the fraction captured. This may not be feasible, for example, in very large, busy, chaotic tertiary care centers.
- Adequate patient volume. It is just as important that a facility have sufficient patient volume to make the surveillance data meaningful. Accordingly, a register review may therefore be necessary to estimate the numbers of SARI patients seen by the facility throughout the year

Availability of useful denominator data
- Having population denominators for the catchment area of the sentinel site is necessary when estimating disease burden by population incidence. Estimation of denominators may require additional work, such as a health facility utilization survey in the catchment area to determine the

proportion of the population that uses the sentinel site for health care; or a review of admission statistics of other facilities in the area to determine the fraction of the population with respiratory disease that is admitted to the sentinel site.

- When population denominators are not known, the proportion of all admissions to the facility that are due to SARI per week or month will reflect the burden placed on the health care system by SARI. This information will also allow the comparison of severity between one influenza season and the next. Required hospital denominators will include number of admissions for all causes. With additional data, it might be possible to extrapolate estimates from sentinel sites to national health care systems.

- The proportion of related diseases such as pneumonia or other respiratory disease caused by influenza will reflect disease burden. As with the proportion of all admissions, knowing the proportion of pneumonia cases caused by influenza is also a useful parameter for tracking influenza severity from season to season and for estimating the burden placed on the healthcare delivery system by influenza. This proportion will not permit an estimate of the true overall burden of influenza, however, as severe disease caused by influenza very often does not present as pneumonia.

Even if disease burden estimation is not an objective for national health authorities, these data can serve as basic indicators to monitor trends in the severity of respiratory disease over time.

Number of sites and expansion of the system

There is no ideal minimum number of sentinel sites for SARI surveillance. This is because of the high degree of variability in national population sizes, variation in the geographic distribution of populations and ethnic groups, and variation in climate and geography in many countries. All sentinel systems should begin small and expand only as data needs expand and sites have been appropriately evaluated. The more important concerns are that the data represent the population, meet the needs of policy makers and be of good quality.

In general, small amounts of good quality data will be more useful than large amounts of poor quality data. Therefore, when establishing a system it is important to not establish more sites than can be effectively managed, monitored, and sustained (see Chapter 5 for more information on monitoring and evaluating the surveillance system). Annex 2 provides a checklist for selection of sentinel sites.

5. Surveillance Steps

SARI surveillance includes the following five components:

a. Step 1: Case Identification

Among hospitalized patients, identify daily those who meet the following SARI case definition:

SARI Surveillance Case Definition

An acute respiratory infection with:

- history of fever or measured fever of ≥ 38 C°;
- and cough;
- with onset within the last ten days;
- and requires hospitalization.

Medical Codes for SARI Cases

To facilitate the identification of all possible SARI cases or deaths, active case-finding using various sources of hospital data is recommended. The 10th revision of the International Classification of Diseases (ICD-10) can serve as a reference. **Upper respiratory tract infections** (URI) are classified from J00 to J06 and **influenza, pneumonia, and other lower respiratory tract infections** (LRI) from J09 to J18 and from J20 to J22 (**Annex 3**). Care should always be taken to ensure that the SARI case definition is met. For example, it should be confirmed that a hospitalized patient with bronchitis had a history of fever or a measured fever of ≥ 38 C°, and cough.   These ICD-10 codes can also be used to complement the data collected through sentinel surveillance to create a better picture of respiratory infection activity in the country.

If ICD-10 codes are used in hospital discharge records and are not available until after discharge, the codes can be used for quality control of data collected through SARI surveillance by comparing the number of patients captured by ICD-10 codes to those captured using the SARI case definition.

b. Step 2: Data Collection and Data Entry

Complete the individual data collection form(s)

To determine the epidemiological characteristics of SARI cases, data should be collected on all hospitalized cases (see **Annex 4** for the case report form). The essential data to be reported include:

- Sex of patient
- Age of the patient
- Date of onset of fever
- Risk factors and/or co-morbidities
- Presence/absence of a specimen
- Identified etiologic agent.

This information should be reported <u>immediately</u> after a case has been identified. **All hospitalized patients meeting the SARI case definition should be reported, even if a specimen was not collected.** As additional information is collected it should be entered into the form or reporting database as soon

as possible. Once all clinical, epidemiological and laboratory elements have been completed, including the patient's outcome (alive or deceased), mark the case as closed in the information system.

c. Step 3: Respiratory Specimen Collection and Testing Results

Sentinel SARI surveillance is most effective when case patients are laboratory tested for respiratory viruses. When combined with laboratory testing, surveillance of both mild and severe disease syndromes contributes to understanding the complete spectrum of respiratory virus illness, including differences in the epidemiology of various influenza virus types and subtypes, factors that place individuals at increased risk for severe disease, and the impact that SARI is having on health-care delivery systems.

Systematic Sampling of SARI patients

Laboratory testing all SARI patients at a site for respiratory viruses is ideal. If this is not feasible, a sampling strategy should be implemented for selection of patients for testing. It is important that cases be selected in a manner that minimizes bias so that the data collected accurately depict the distribution of risk factors, the impact of SARI on different age groups, the general pattern of disease, and can be extrapolated to the total number presenting for care.

In general, the larger the proportion of SARI cases from which clinical specimens for virologic testing are collected, the less bias will be introduced. However, the total number of patients chosen for virologic testing will depend on the ability of the health-care facility to process, store and ship specimens as well as the capacity of the laboratory to process, store and test the samples.

It is best to use a systematic approach for selecting cases to test rather than requiring health-care providers to choose which patients to test. The approach should cover different times of the day and different days of the week (every week) while providing reasonably representative data. The following systematic sampling methods, in order of increasing potential bias, can be used:

Interval sampling – A straightforward method that would yield data similar to that from a random sampling strategy would be to select every Nth SARI case at the sentinel site. For example, every 5th (or 7th, or 10th) patient that meets the SARI case definition would be selected for testing and data collection. Some previous knowledge of the volume of cases at the site is required so that the appropriate sampling interval can be selected. This type of sampling would likely require a designated person to oversee case selection on a daily basis and it is somewhat complicated.

Alternate day sampling – A second systematic sampling method is to select all patients who meet the SARI case definition presenting to a facility on a certain day or days of the week. This can reduce the logistical challenges of surveillance by confining laboratory specimen collection efforts to a single day. In order to remove the bias introduced by differences in health-seeking behavior associated with particular days of the week, the day on which cases are selected should be systematically alternated from week to week.

Modified convenience sampling – A third approach involves testing the first X number of cases that meet the SARI case definition. If this method is used, the time frame for selection should be systematically rotated to take into account local health-seeking behaviors such as differential use of evening or weekend clinics. For example, a site might select the first 2 cases admitted to the hospital in the morning, afternoon and the evening of each day of the week, including weekends. Care would need to be taken not to introduce systematic biases in the types of cases selected.

Specimen Collection, Storage and Transport

- Prepare materials for specimen collection
- Collect the specimens, with special attention to infection control and biosafety standards (**Annex 5**), using appropriate personal protective equipment (PPE).
- Record the specimen data on the individual report form.
- Prepare the specimens for storage and transportation (**Annex 6**) in accordance with biosafety standards and send them to the hospital laboratory with a copy of the report form.

Laboratory Testing Results

- Laboratory testing results should be entered into the appropriate database/reporting system as soon as possible.

d. Step 4: Data Analysis and Interpretation

Monitoring and Evaluation

Monitoring and evaluating surveillance systems is done to ensure that data collected are of consistent quality, that the system is meeting its stated objectives and that it is performing as expected. It is important to routinely review data prior to analysis in order to ensure that data are timely, complete and consistent.

A thorough periodic review of the surveillance system provides users and stakeholders with a more detailed understanding of how well the system is functioning, whether all sites are functioning in a satisfactory manner, and where the system might benefit from updated employee training, data management and analysis, or other activities.

A comprehensive evaluation of the system should be done regularly, beginning one to two years after initial implementation of the surveillance system. This is especially important if an expansion of the system is being considered. System reviews should evaluate the system at all levels – national, site, and laboratory to ensure that all parts of the system are working together as effectively as possible.

The following performance indicators can be used to monitor the sentinel surveillance process (see **Annex 7** for more information):

Sentinel Surveillance Steps	Associated Monitoring and Evaluation Indicators
Step 1 Identify hospitalized patients	• Percent of week's with timely notification of denominators • Percent of hospitalized SARI cases that are captured by the

that meet the SARI case definition	surveillance system • Median interval in days between hospitalization date and notification date
Step 2 Complete data collection form and data entry	• Percent of cases investigated and closed
Step 3 Respiratory sample collection and testing results	• Percent of SARI cases with collected sample • Percent of quality samples received • Percent of quality samples processed • Median interval from hospitalization date to sampling date • Median interval from sample collection date to receipt of sample in laboratory • Median interval from receipt date to start of processing • Median interval from receipt date to delivery of result • Percent of SARI ICU cases with collected sample • Percent of SARI-associated deaths with collected sample
Step 4 Data analysis and interpretation	• Number of SARI cases reported each month • Number of specimens submitted each month • Percent of submitted specimens that test positive for influenza
Step 5 Data dissemination and outputs	• Percent of weeks that data are sent to the national/regional level • Timeliness of data presented in weekly influenza surveillance report

Data analysis

Consolidate surveillance data weekly in order to calculate and analyze the following (**Annex 8**):
- By all ages and age groups
  - o Proportion of hospitalizations for SARI
  - o Proportion of ICU admissions for SARI
  - o Number and proportion of deaths associated with SARI
- For hospital cases of SARI, ICU cases of SARI, and SARI deaths:
  - o Cumulative number and proportion of patients with comorbidities
  - o Cumulative number and proportion of patients who received the current influenza vaccine
  - o Cumulative number and proportion of patients who received antiviral therapy
- Of all specimens tested, the weekly proportion of specimens positive for influenza
- The weekly distribution of specimens positive for influenza by type and subtype
- Of all specimens tested, the weekly proportion of specimens positive for any respiratory virus
- The weekly distribution of specimens positive for respiratory virus
- Distribution of cumulative specimens positive for respiratory virus by age group
- Distribution of cumulative respiratory virus cases by severity (hospital cases of SARI, ICU cases of SARI, and SARI deaths)

Additionally, the total number of all-cause hospital admissions, ICU admissions, and deaths should be reported weekly on a form designed for this purpose (**Annex 9**). These data will be used as denominators to calculate proportions and should be collected by sex and age group, using the following classification:

< 2 years

2 to <5 years

5 to <15 years

15 to <50 years

50 to <65 years

65 and more years

The rationale for using these age groups is that:

- Vaccine efficacy can be evaluated because many countries vaccinate children under 2 years of age and adults over 60.
- Case distribution can be analyzed according to the most affected groups. Schoolchildren play an important role in transmission, but the most severe cases usually occur in people at the extremes of life (children under 5; adults >60 years). Mortality in pandemics tends to be higher among young adults.

Baselines and Thresholds

Two important uses of the data gathered through influenza surveillance systems are to compare current activity to previous years and to detect periods of increased activity such as the start of an influenza epidemic. These two concepts are expressed by the terms baseline and threshold. The terms are often used interchangeably and used to represent different concepts by different programs. The term **baseline** is also used to mean different things by different researchers. Some use it to mean the lowest level of respiratory disease or influenza activity that occurs between seasons. Others use it to mean the average level of activity that occurs throughout the year. In order to avoid confusion, this document will use the term **average epidemic curve** to mean the usual level of influenza activity, which varies over time during the influenza season and the off-season. **Threshold** is used to mean a level of activity that indicates the occurrence of a specific situation such as the start of a season or an unusually high season. Thresholds are set at values that exceed average epidemic curve values by a previously established amount.

- **Average Epidemic Curve**: The usual level of influenza activity that occurs during a typical year. This is the calculated average of several epidemic years. The average epidemic curve level will vary throughout the year. Sometimes referred to as baseline activity. Note that some also use the term baseline to mean the lowest level of influenza activity which occurs between influenza seasons.
- **Seasonal threshold**: The level of influenza activity that signals the start and end of the annual influenza season(s). When a weekly rate exceeds the seasonal threshold, sustained community transmission is presumed to be occurring and the influenza season started.

- **Alert threshold**: A level above which, varying by time of year, influenza activity is higher than most years. An analogous lower correlate of the alert threshold below the average epidemic curve can also be used to indicate an unusually mild season. This term may also be known as the thresholds for different levels of intensity.
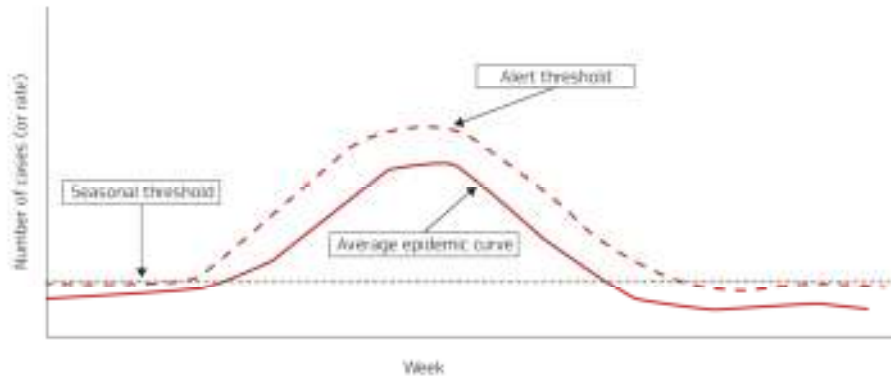

Figure 5: Average epidemic curves and thresholds

Typically, average epidemic curves and thresholds are expressed as:
- the number or rate of SARI cases per week
- the proportion of total hospitalizations
- the number or rate of pneumonia and influenza deaths
- the percentage of specimens testing positive for influenza
- the number or rate of respiratory deaths
- the number or rate of confirmed influenza cases.

Knowing the usual average epidemic curve level of disease and the seasonal pattern as a point of reference aids in determining whether the current season is atypical both in timing and relative severity compared to previous ones. This information can help improve the accuracy of clinical diagnosis, appropriate use of antiviral medication, and the uptake and timeliness of seasonal influenza vaccines.

For each of these parameters the values to be used need to be determined for each country individually based on historical data and may even vary from place to place within a country. While there is no single method that is universally applicable for every country, there are some relatively simple ways of expressing average epidemic curves by creating an average curve centred around the median week of peak transmission for several years and using simple statistical measures of variance to define an **alert threshold** above the average weekly values to detect unusually severe seasons (**Annex 10**). A useful lert threshold is the value 1.645 standard deviations above the mean for each week, which defines the 90% confidence interval of the mean. This would result in 1 out of every 20 seasons significantly exceeding the upper threshold.

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The **seasonal threshold** defines a value above which the country or area is considered to be in an influenza season (seasonal threshold is sometimes referred to as **epidemic threshold**, using epidemic in the sense of recurrent seasonal epidemics). This value indicates an increased likelihood that a respiratory illness seen by a treating clinician in the community is actually related to influenza because influenza is transmitting in a sustained manner. The same parameters that define average epidemic curve values can also be used to define the seasonal threshold; experience in country will determine the most useful parameter(s) to use. In some cases a combination of parameters may be preferable. For example, a seasonal threshold could be defined as the week in which the ILI rate crosses a certain value and the percentage of specimens testing positive reaches a certain point. To be useful, the seasonal threshold needs to be set low enough to signal the start of the season in a timely manner but high enough to avoid false signals. Tropical countries may find it more challenging to define a seasonal threshold as influenza seasons may not be as clearly distinguished from non-seasons; and indeed in some tropical countries it has been observed that sustained low-level community transmission can occur during inter-seasonal periods. The implication of crossing the threshold value may be slightly different than it would be in temperate countries as being below the threshold would not necessarily indicate that community transmission was not occurring.

Endemic channels

Endemic channels provide another option for displaying and interpreting current surveillance data in the context of historical data. Using this approach, the median and four quartiles are calculated to determine various zones of activity. As illustrated in the Figure 6, the lowest quartile corresponds to the "success zone", the next zone below the median is the "security zone", the zone above the median is the "alarm zone", and the highest quartile represents the epidemic zone. For more detailed instructions regarding how to develop an endemic channel using Microsoft Excel, please refer to the following article or contact PAHO (flu@paho.org) for assistance: Bortman, M. Elaboración de corredores o canals endémicos mediante planillas de calculo. *Revista Panamericana de Salud Publica*. 1999; 5(1)
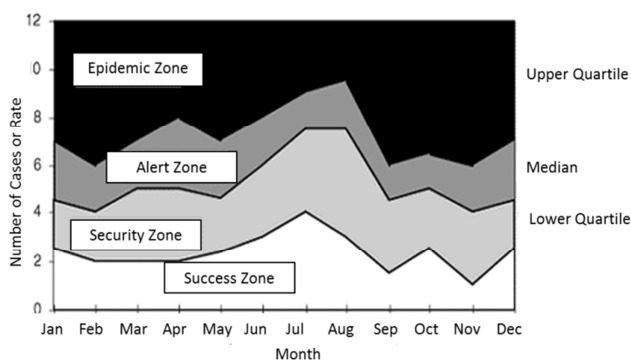

Figure 6: Schematic with the four zones of the endemic channels

Disease Burden

Understanding the burden of influenza and other respiratory viruses is helpful for gaining a better picture of the impact of these illnesses in each country. These national estimates are helpful to Ministries of Health and other organizations for resource allocation and planning public health

interventions. To estimate the disease burden of SARI-associated morbidity and mortality, the following data elements will be needed:

- **By epidemiological week or month, age group and sex**:
    - Total number of new SARI cases admitted to the hospital
    - Total number of SARI cases from whom respiratory samples were taken
    - Viral testing results (e.g., positives, negatives, pathogens, influenza types and subtypes)
    - Number of SARI-associated deaths
    - The number of SARI cases, influenza-positive SARI cases and influenza-positive SARI deaths with the following medical conditions:
        - Pregnancy
        - Chronic obstructive pulmonary disease
        - Asthma
        - Diabetes
        - Chronic cardiac disease
        - Chronic liver disease
        - Chronic renal disease
        - Immunodeficiency, including HIV
        - Severe genetic anemia, including sickle cell disease and thalassemia major
- Mid-year population of the sentinel site's catchment area (by age group and sex)

Although there are multiple ways to express SARI burden, one of the most common methods is to calculate **incidence**. Incidence indicates the number of new events that occur in a population over a specified period of time and is usually expressed per 100,000 population at risk. As the incidence of influenza and other respiratory virus infections varies by age, it is ideal to calculate age-specific incidence. The following formula can be used to calculate annual incidence:

$$\textbf{Annual Incidence} = \frac{\text{Number of SARI influenza-cases in a calendar year}}{\text{Mid-year catchment population for the sentinel site}} \times 100{,}000 \text{ population}$$

In order to calculate incidence for each sentinel site, it is necessary to estimate the catchment population (denominator) for that site. This involves identifying the area where the majority of patients seeking care at the hospital reside. If multiple health care facilities are located in the same area then the proportion of the total population served by the sentinel site must be determined. To do this, Hospital Admission Surveys (HAS) are used and involve determining the proportion of SARI patients from the catchment area who visit the sentinel site for treatment and combining it with stratified age and sex data from the census or municipal records.   An alternate procedure for estimating the catchment population is to carry out a healthcare utilization survey (HUS). This involves conducting a house-to-house survey in a sample of representative households to find out which health care facility the family uses.

Please contact the PAHO Flu Team (flu@paho.org) if you have any questions regarding SARI disease burden estimates.

Data Interpretation

The aforementioned data tables and graphs (including baselines and endemic channels) should be analyzed weekly to assess disease patterns for the current situation as well as how they compare to previous seasons. This process should include:

- Examining trends over time to detect unusual behavior.
- Identifying which risk groups are most affected.
- Assessing severity.
- Evaluating viral patterns to identify possible variations.

e. Step 5: Data Dissemination and Outputs

Reporting data to PAHO/WHO

Member States are strongly encouraged to share data internationally. Routine data sharing will facilitate global tracking and monitoring of influenza progress and impact. This will help inform all Member States of the location and occurrence of seasonal epidemic disease, the types of viruses currently circulating, and the impact of the season. Such information can be of great value to national health authorities for planning and resource allocation purposes.

- **Epidemiologic and virologic data should be reported to PAHO by Monday of each week in order to be included in the PAHO regional weekly report and the WHO's FluNet and FluID international platforms** (see **Annex 11** for examples of laboratory and epidemiological data)

Weekly Influenza Surveillance Report

Routine epidemiological summary reports should be created. The report should contain the tables and figures describe above, as well as an interpretation of them. Any changes in place, time, person, or predominant virus type should be compared with previous weeks or other periods. Recommendations should be included for the treatment, prevention, and control of influenza in the surveillance area, based on the available information. Examples of data distribution in tables and figures are shown in **Annex 8**.

Feedback Reports

Feedback should be given to those who provide data and respiratory specimens including health personnel in hospitals and sentinel sites as well as managers and directors of health facilities. A summary of the monitoring and evaluation indicators should be provided to surveillance and laboratory staff. This information is useful to provide quality control and identify areas of improvement.

6. Facility Roles and Responsibilities

SARI surveillance should be integrated into countries' epidemiological surveillance systems. To that end, each country should determine the system structure that will best utilize the country's resources and account for its realities. Similarly, hospitals should consider how SARI surveillance can be integrated into other hospital surveillance systems, so as to create a sustainable program in the hospital setting. One approach is to create a department of hospital surveillance and epidemiology that deals both with community-acquired infections and with health care-associated infections. The general tasks to be completed at each level are outlined below.

a. Local-level responsibilities

- Identify cases that meet the SARI case definition
- Select SARI cases for which specimens are to be collected.
- Collect respiratory specimens utilizing appropriate infection control practices, including PPE
- Prepare specimens for shipment to the laboratory.
- Arrange for shipment of specimens to the laboratory under the appropriate biosafety conditions.
- Complete the individual report form.
- Immediately notify the Ministry of Health of any unusual case or event
- Within 24 hours of case capture, enter the data from the individual record in the information system designed for this purpose.
- Request information weekly from the appropriate statistics office and other complementary sources on new admissions and deaths.
- Enter these data in the information system no later than Monday of each week.
- Enter laboratory results in the database (if not done by laboratory personnel)
- When clinical, epidemiological, and laboratory investigation is complete, mark the case as closed in the information system.
- Complete data analysis and periodically prepare epidemiological reports.
- Report any situation outside the normal parameters to the Ministry of Health.

b. Laboratory responsibilities

- Train staff on the proper technique for collecting, preparing, and transporting specimens.
- Ensure compliance with biosafety standards for handling and transporting specimens.
- Process specimens on a timely basis.
- Complete the individual form, indicating laboratory results and test date.
- Communicate results to local surveillance authorities and to the Ministry of Health.
- Monitor percentage of positive cases to ascertain whether it is within the expected ranges.
- Identify issues with specimen collection, preparation, and transport that may affect laboratory test results.
- Routinely send influenza viruses, according to the protocol, to a WHO-CC.
- Send unsubtypeable influenza viruses immediately to a WHO CC.
- Collaborate in data analysis.

- Participate in the preparation and dissemination of reports.
- Report virologic results to PAHO/WHO through the systems established for this purpose.

c. National-level responsibilities (Ministry of Health)

- Coordinate the surveillance process, including providing the resources needed to sustain the surveillance program.
- Collaborate with the laboratory to conduct surveillance training and awareness activities.
- Monitor performance indicators from each sentinel hospital to identify and solve problems detected in the process.
- Promote coordinated work between the laboratory and each hospital.
- Periodically evaluate the SARI performance indicators and the quality of the obtained data.
- Prepare, disseminate and publish the national report on a weekly basis, in collaboration with the local surveillance team and laboratory staff.
- Disseminate the weekly report to all relevant stakeholders, including PAHO.
- Disseminate public health alerts involving events of national and/or international concern.

7. Laboratory

Virologic data play a critical role in SARI surveillance and therefore it is important that viable specimens be collected and properly handled, and that the appropriate tests are performed relative to specimen viability and symptom onset (see Figure 7). **For immunofluorescence assays, it is ideal to collect specimens within 5 days of symptom onset.** Specimens from influenza-infected individuals may still test positive using molecular diagnostic methods such as RT-PCR up to 10 days from symptom onset, but the likelihood of a positive test decreases rapidly after day 7.
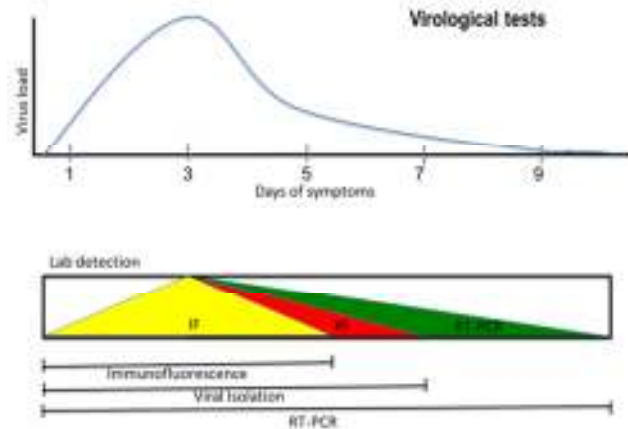
Figure 7: Specimen viability for influenza diagnostic tests by specimen onset date

Specimens for laboratory diagnosis

A variety of specimens are suitable for influenza and other respiratory virus detection and isolation. Nasopharyngeal and oropharyngeal swabs should be collected from adults and children five years and older. For children under five years of age, a nasopharyngeal aspirate is recommended. Note that if a patient is intubated, an endotracheal aspirate or bronchoalveolar lavage can be used if clinically indicated.

Specimen Storage

Respiratory specimens for direct detection of viral antigens by immunofluorescence staining should be aliquoted and refrigerated at 4°C immediately after collection. Ideally all respiratory swabs should be kept and transported refrigerated (without prior freezing) to the laboratory in viral transport media (VTM) and with the collection forms, within 24 to 48 hours of collection. The maximum storage time at 4°C is 48 hours. **If specimens cannot be processed within 48–72 hours, they should be kept frozen (if possible) at or below -70°C**. Care should be taken to prevent repeated freeze/thaw cycles that can result in the loss of virus viability and consequent loss of RNA integrity. Do not store specimens in standard household freezers (-20°C) with a freeze-thaw ("defrost") cycle; it is preferable to keep a sample at 4°C for as long as one week, than to subject it to sudden changes in temperature (e.g. freeze and thaw repeatedly).

Specimen Transport

The United Nations (UN) has developed guidelines for shipment of infectious substances. **Category A** infectious substances are those that if exposure occurs, are capable of causing permanent disability, or life-threatening or fatal disease in otherwise healthy humans or animals. This category includes viral isolates of highly pathogenic (avian) influenza. **Category B** infectious substances include those that do not meet the criteria for inclusion in Category A. In general, influenza and other respiratory virus specimens that are collected for virus detection and are considered Category B and, as such, must be packed and transported in compliance with packaging instructions P650 for UN 3373 Category B infectious substances.

Category B specimens should be packed in three layers of packing:
- A primary watertight, leak-proof container holding the specimen that has enough absorbent material to absorb the fluid in case of breakage
- A secondary, durable watertight and leak-proof container to enclose and protect the primary container. Multiple primary containers may be placed in the secondary packaging, but enough absorbent material should be included to absorb all of the fluid in case of breakage;
- An outer container with sufficient cushioning into which the secondary container is placed. The smallest overall external dimension should be 10x10 cm.

All appropriate forms, labels and shipping documents should accompany this package.

Diagnostic Tests for Influenza

In addition to the sensitivity and specificity inherent to each technique, successful detection also relies on the type and quality of specimen collected, proper transport, and optimal storage conditions. Available tests include viral isolation (cell culture or embryonic eggs), RT-PCR, rapid diagnostic testing (antigen detection), immunofluorescence assays (direct or indirect) and serological tests (hemagglutination inhibition, microneutralization). While each technique has particular uses, advantages and limitations, with all other things being equal, **RT-PCR has the highest sensitivity for detection and therefore is the recommended test for most laboratories**.

RT-PCR and other molecular methods provide a variety of important virologic information:
- differentiate influenza virus types
- determine the subtype of human influenza A viruses and lineage of B viruses
- presumptively identify influenza A(H5, H7) from respiratory specimens
- detect potentially novel or newly evolving influenza A viruses
- detect antiviral resistance

Despite sensitivity limitations, immunofluorescence may be used as a screening test for surveillance in regional laboratories that do not have the capacity to perform molecular assays. However, to increase laboratory surveillance sensitivity, **it is recommended that the following samples tested by IFA be sent to the NIC or reference laboratory**:
- All samples positive for influenza A (for subtyping)

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v11

- All samples positive for influenza B (for lineage characterization, if available)
- 10% of samples that tested negative for influenza (to rule out infection and perform indirect quality control)
- All samples from fatal cases that do not have an obvious etiology (regardless of IFA test result)
- All unusual SARI cases (as described in Annex 1)

The aggregated laboratory results should be shared with PAHO/WHO (flu@paho.org) to be uploaded to the FluNet global platform.

For laboratories that have the resources, combined use of virus isolation and RT-PCR is recommended for virus characterization. Specimens can be tested by RT-PCR to obtain results rapidly at the beginning of an outbreak. Virus isolation can produce sufficient quantities of virus for further antigenic and genetic characterization, and for drug-susceptibility testing if necessary. Depending on the number of positive specimens and availability of epidemiological and clinical information, criteria should be developed for selecting which samples should undergo viral isolation.

Specimen Submission to WHO CC

To better understand the antigenic and genetic properties of the influenza viruses circulating in the region, NICs are highly encouraged to send representative clinical specimens and/or virus isolates to a WHO CC for additional virus characterization. It is important that the following guidelines be followed to ensure that adequate data are available for vaccine strain selection (in February for the Northern Hemisphere and in September for the Southern Hemisphere) and, in accordance with the 2005-IHR, new influenza A subtypes are detected immediately.

Shipment timing

Under normal surveillance conditions, it is recommended that 2-4 shipments of samples (or isolates) be sent to the WHO-CC each year, taking into account the timing of the upcoming WHO meetings for vaccine recommendations and strain selection. Samples received before the third week of January and before the third week of August can be characterized in time to be included for consideration during the meetings held in February and September, respectively. However, **samples from unusual cases or outbreaks, and unsubtypeable viruses should be sent at any time of the year**.

Sample selection

Original samples or viral isolates selected for shipment should **have been collected 4-6 weeks before shipping**. To achieve a good representation of seasonal activity, it is recommended that 5-10 samples be selected from each of the following groups:
- All affected age groups (e.g., children, older adults)
- All affected geographic regions of the country
- All phases of the seasonal epidemic (e.g., beginning, middle, end)

Other samples that should also be selected for characterization include:
- Viruses with lower than expected titers by hemagglutination (according to WHO reference case)

- 5-10 representative samples from unusual outbreaks (e.g., cases identified outside the expected season)
- **All unsubtypeable viruses should be sent to a WHO-CC immediately** (please notify the WHO-CC immediately)

It is important to note that samples taken at the beginning of an epidemic are important for determining if there are new antigenic variations (e.g., emerging viruses). Additionally, during a pandemic or periods of enhanced surveillance shipments can be made more frequently, based on WHO guidelines.

Funding for specimen shipments
NIC's have the responsibility to ship seasonal influenza viruses and novel viruses to a WHO CC. Funding to support the shipment of specimens is available through the WHO Global Shipping Fund Project. This project covers the costs for 1-3 shipments (varies by country) of seasonal influenza viruses per season and shipments of potentially novel influenza viruses as needed. Additional funding for shipments is available through PAHO. For information about these additional funds, please contact PAHO at flu@paho.org.

8. Additional training resources

SARI Surveillance

If you would like more information regarding SARI surveillance and implementing a national surveillance system, PAHO has created online training courses that are accessible through the PAHO Virtual Campus: http://cursos.campusvirtualsp.org/ ("Intensified National SARI Surveillance Training").

Unusual SARI Surveillance

For information regarding unusual SARI surveillance, please contact PAHO (flu@paho.org).

Laboratory Training

Additional training and certification regarding proper transport of infectious substances is available through WHO. Although not all laboratory personnel are required to take this course, it is required that individuals responsible for the transport of Category A specimens receive this training. A reference document is also available via the following link:
http://apps.who.int/iris/bitstream/10665/78075/1/WHO_HSE_GCR_2012.12_eng.pdf

For laboratory personnel interested in learning more about epidemiologic analysis of laboratory data, PAHO has created online training courses accessible through the PAHO Virtual Campus: http://cursos.campusvirtualsp.org/ ("Laboratory Training in the Epidemiology of Influenza").

PAHO has also prepared three instructional videos about:
- Proper use of personal protective equipment (PPE)
- Techniques to collect nasopharyngeal and oropharyngeal swabs
- Respiratory specimen packaging and transport

http://www.paho.org/hq/index.php?option=com_content&view=article&id=7919&Itemid=39738&lang=en

SARInet platform

www.sarinet.org

9. References

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Centers for Disease Control and Prevention. ***Seasonal Influenza***. Available at: http://www.cdc.gov/flu/about/viruses/index.htm (Accessed on February 27, 2014).

Country Data
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Ecuador Ministry of Health (http://www.salud.gob.ec/category/comunicamos/noticias/) Accessed October 2, 2013

Chile Ministry of Health (http://epi.minsal.cl/) Accessed November 18, 2012

10.　Annexes

Annex 1: Implementation of Unusual Respiratory Event Surveillance

An early warning system for outbreaks should have three basic components:
- A defined list of signal events that need to be immediately notified to public health authorities.
- A clear mechanism for reporting signal events.
- A mechanism for investigating, evaluating and responding to signal events.

The primary focus of early detection is to detect events that may signal human-to-human transmission of a new influenza virus with the potential to spread widely in humans. Examples of specific respiratory triggers include the following:
- Abrupt, unexpected changes in the trend of respiratory disease observed in routine surveillance systems (e.g., SARI surveillance).
- Clusters of severe respiratory disease or pneumonia in families, work places, or social networks.
- An unexpected pattern of respiratory disease or pneumonia such as an increase in apparent mortality, a shift in the age group associated with severe influenza, or a change in the pattern of clinical presentation of influenza-associated disease.
- Persistent changes noted in treatment response or outcome of severe lower respiratory illness.
- Severe, unexplained lower respiratory illness occurring in a healthcare worker who provides care for patients with respiratory disease.
- Unusually high levels of sales of pharmaceuticals used for respiratory disease treatment.
- Respiratory disease in humans that is associated with illness in animals.
- Outbreaks of death or illness in fowl (e.g. poultry or ducks) or other animals (e.g. swine, cats).
- Human cases of infection with any influenza virus not currently circulating in human populations.

To detect signal events early enough to permit effective investigation and possible intervention, a very sensitive system with wide participation is needed. The early detection activities that individual Member States carry out will vary greatly according to available resources, but may include any of the following:
- Education of health care providers about signal events that should be immediately reported.
- Monitoring and analysis of the routinely reported data from existing surveillance networks.
- Monitoring media sources for reports of unusual clusters or patterns of respiratory disease.
- Involving the national education authorities in reporting school outbreaks or unusually high levels of absenteeism.
- Monitoring rates of absenteeism in the workplace.
- Monitoring sales of "flu medicines" and other pharmaceuticals used for treatment of respiratory symptoms.
- Monitoring for outbreaks of respiratory disease in animals.

Reporting can happen in a number of ways from toll-free numbers to web-based reporting. Reported events should always be followed up. An investigation of an event reported by a member of the public could consist of a phone call to gather enough detail to determine if the report is worthy of an actual field investigation. More serious reports require more aggressive responses. Failure to respond not only risks missing a significant event that could have been effectively managed while small, but also discourages further reporting.

See also: *A Guide to Establishing Event-based Surveillance*, available at: http://www.wpro.who.int/entity/emerging_diseases/documents/eventbasedsurv/en/index.html)

Annex 2: Checklist for selecting sentinel sites for SARI Surveillance

This checklist may be used to assess a health facility for its appropriateness as an influenza sentinel surveillance site. It examines certain key aspects:

- Human infrastructure and communication capacities.
- Sufficient and appropriate patient population.
- Geographic representativeness.
- Infrastructure.

Site Description	
Is hospital management agreeable to implementing influenza surveillance?	☐ Yes ☐ No
Is the staff willing to work with influenza surveillance?	☐ Yes ☐ No
Does the site offer outpatient services?	☐ Yes ☐ No
Does the site offer inpatient services?	☐ Yes ☐ No
Are patients attending the clinic are from all age groups?	☐ Yes ☐ No
Are patients attending the clinic from all socioeconomic strata and ethnic groups?	☐ Yes ☐ No
What is the 3-month average number of outpatient consultations?	
What is the 3-month average number of in-patient medical admissions?	
Can the catchment population of the site be estimated?	☐ Yes ☐ No
Human Resource Capacity	
Does the site have permanent clinical staff that could be trained in the identification of ILI and SARI and in respiratory sample collection?	☐ Yes ☐ No
Does the site have at least one permanent lab worker that can be trained in the collection, storage, testing and transportation of respiratory sample specimens?	☐ Yes ☐ No
Infrastructure	
Does the site have a laboratory?	☐ Yes ☐ No
Does the surveillance staff have access to computers?	☐ Yes ☐ No
Does the surveillance staff have access to the Internet?	☐ Yes ☐ No
Does the site have a reliable power supply and fridge where the sample specimens can be kept?	☐ Yes ☐ No

Annex 3: International Classification of Diseases (ICD) Codes for Acute Respiratory Illness

Table 1—ICD 10, Upper ARI

ICD-10, upper ARI	Description
J00	Acute nasopharyngitis [common cold]
J01	Acute sinusitis
J02	Acute pharyngitis
J03	Acute tonsillitis
J04	Acute laryngitis and tracheitis
J05	Acute obstructive laryngitis [croup] and epiglottitis
J06	Upper respiratory infections of multiple and unspecified sites

Table 2—ICD 10, Influenza, pneumonia, and other lower ARI

ICD-10, influenza, pneumonia, and other lower ARI	Description
J09	Influenza due to identified avian influenza virus
J10	Influenza due to other identified virus
J10.0	Influenza with pneumonia, other influenza virus identified
J10.1	Influenza with other respiratory manifestations, other influenza virus identified
J10.8	Influenza with other manifestations, other influenza virus identified
J11	Influenza, virus not identified
J11.0	Influenza with pneumonia, virus not identified
J11.1	Influenza with other respiratory manifestations, virus not identified
J11.8	Influenza with other manifestations, virus not identified
J12	Viral pneumonia not elsewhere classified
J12.0	Adenoviral pneumonia
J12.1	Respiratory syncytial virus pneumonia
J12.2	Parainfluenza virus pneumonia
J12.8	Other viral pneumonia
J12.9	Viral pneumonia, unspecified
J13	Pneumonia due to *Streptococcus pneumoniae*
J14	Pneumonia due to *Haemophilus influenzae*
J15	Bacterial pneumonia, not elsewhere classified
J16	Pneumonia due to other infectious agent, not elsewhere classified
J17	Pneumonia in diseases classified elsewhere (see specific diseases in ICD-10)
J18	Pneumonia, organism unspecified
J20	Acute bronchitis (see specific causes in ICD-10)
J21	Acute bronchiolitis
J21.0	Acute bronchiolitis due to RSV
J21.8	Acute bronchiolitis due to other specified organisms
J21.9	Acute bronchiolitis, unspecified
J22	Unspecified acute lower respiratory infection

Source: World Health Organization. International Classification of Diseases and Related Health Problems 10th Revision (ICD-10), 2008 version. Geneva: World Health Organization; 2008.

Annex 4: Case Report Form

Clinical, Epidemiological and Laboratory Investigation Form for Sentinel SARI Surveillance

> **Case Definition**: An acute respiratory infection with history of fever or measured fever of ≥ 38 C°, and cough, with onset within the last ten days, and requires hospitalization

1. CAPTURE

1. Today's Date: / / Day /mon/year	**2. Case Code:**	**3. Establishment Name:**

4. Clinical History Number: **5. Capture Date:** ___/____/____ (day/mon/year)

6. Patient Name:

First Last Name	Second Last Name	First Name	Second Name

7. ID #:	**8. Birth Date:** __ /__ /__ Day /mon/year	**9. Age:** _____ _____ _____ Years Months Days

10. Age Group: ☐ <2y ☐ 2-4y ☐ 5-19y ☐ 20-39y ☐ 40-59y ☐ 60+ y | **11. Sex:** ☐ Male ☐ Female

2. CONTACT INFORMATION

12. Telephone Number:

13. Place of Residence:

Department/Province/State	Municipality/City	Neighborhood

Address

3. CLINICAL HISTORY/RISK FACTORS

14. Did patient receive influenza vaccine during current season: ☐ Yes ☐ No ☐ Unknown

If yes, date of vaccination: ___/___/___ (Day /mon/year)

If child, < *9 years:* Specify number of doses and dates received**:** ☐ 1/1: ___/___/___ (Day /mon/year)

☐1/2: ___/___/___ (Day/mon/year) ☐2/2: ___/___/___ (Day/mon/year)

If child, < *6 months*: Did mother receive influenza vaccine? ☐ Yes ☐No ☐Unknown

If yes, date of vaccination: ___/___/___ (Day /mon/year)

Did mother breastfeed child? ☐Yes ☐No

15.Risk Factors: ☐ Yes ☐ No

Other Factors[1]

☐ Pregnant (☐1T ☐2T ☐3T)
☐ Postpartum

Comorbidities

☐ Asthma
☐ Chronic heart disease
☐ Chronic liver disease
☐ Chronic kidney disease
☐ Hematological disorders
☐ Obesity

☐ Other chronic pulmonary disease
☐ Diabetes
☐ Neurological or neuromuscular disorder
☐ Immunodeficiency (due to illness or treatment)
☐ Other:

4. HOSPITALIZATION

16. Fever onset date: / / EW _____
 Day /mon/year | **17. Hospitalization Date:** / / EW _____
 Day /mon/year

18. Antiviral Use: ☐ Not used ☐ Oseltamivir ☐ Zanamivir ☐ Other **Antiviral Start Date:** ___/ ___ /___ Day/mon/year

19. ICU Admission: ☐ Yes ☐ No **ICU Admission:** / / EW ___ **ICU Discharge:** / / EW ___
 Day/mon/year

20. Sample Collection: ☐ Yes ☐ No   Day/mon/year

1° ☐ **Type:** ☐ Swab ☐ Aspirate ☐ Bronchial wash ☐ Tissue ☐ Serum ☐ Other **☐ Collection date** __ /__ /__

2° ☐ **Type:** ☐ Swab ☐ Aspirate ☐ Bronchial wash ☐ Tissue ☐ Serum ☐ Other **☐ Collection date** __ /__ /__

5. LABORATORY DATA

21. Processing:	**Receipt Date** Day/mon/year	**Processed**	**Processing Start Date** Day/mon/year
1° Sample:	/ /	☐ Yes (☐PCR ☐IFA) ☐ No, reason:	/ /
2° Sample:	/ /	☐ Yes (☐PCR ☐IFA) ☐ No, reason:	/ /

22. Results[2]**:** ☐ Positive ☐ Negative **Delivery Date:** (Day/mon/year)**:** __ /__ /__

☐ A, not subtyped ☐ A(H1N1)pdm09 ☐ A/H1N1 ☐ A/H3N2

☐ Influenza B ☐ B(Victoria) ☐ Influenza B(Yamagata)

☐ RSV ☐ Adenovirus ☐ Parainfluenza I ☐ Parainfluenza II ☐ Parainfluenza III ☐ Other

6. DISCHARGE

23. Discharge Date: __ /__ /__ (Day/mon/year) EW ___ | **24. Outcome:** ☐ Discharged ☐ Deceased ☐ Transferred

25. Date Case Closed: __ /__ /__ (Day/mon/year) | **Responsible Signature:**

[1] You may include other factor based on your specific circumstances, for example: ethnicity, HIV/AIDS, tuberculosis, obesity, alcoholism, smoking

[2] You may include other viruses depending on your laboratory capacity, for example, adenovirus, bocavirus, coronavirus, metapneumovirus, rhinovirus, etc.

Conditions associated with increased risk of severe influenza disease or death	
Risk Condition	**Examples/Definitions**
Chronic respiratory condition	Chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema, bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis, and bronchopulmonary dysplasia (BPD). Asthma is not included in this group and should be reported separately.
Asthma	For example, significant asthma would be that which requires continuous or repeated use of bronchodilators, inhaled or systemic corticosteroids, or that with previous exacerbation requiring hospital admission.
Diabetes	Type 1 diabetes Type 2 diabetes requiring insulin or oral hypoglycemic drugs
Chronic cardiac disease	Conditions that require regular medications or follow-up, including Congenital heart disease Cardiomyopathy as the result of prolonged hypertension (hypertension alone in the absence of associated heart disease is not considered a risk factor for severe outcome) Chronic heart failure Ischemic heart disease
Chronic renal disease	Chronic renal failure Nephrotic syndrome Renal transplantation
Chronic liver disease	Cirrhosis Biliary atresia Chronic hepatitis
Chronic neurological disease	Stroke with persistent neurological deficit Neuromuscular diseases associated with impaired respiratory function or risk of aspiration, such as cerebral palsy or myasthenia gravis Severe developmental disorder in children
Chronic hematological disorder Immune compromise (as a result of disease or treatment)	Sickle cell disease, Thalessemia major Aplastic anemia Immunodeficiencies related to use of immunosuppressive drugs (e.g. chemotherapy or drugs used to suppress transplant rejection) or systemic steroids Asplenia or splenic dysfunction (e.g. with sickle cell anemia) Human Immunodeficiency Virus infection or Acquired Immune Deficiency Syndrome (HIV/AIDS)
Obesity parameter, Body Mass Index (BMI)	BMI is calculated as body weight in kilograms divided by the square of the height in meters (kg/m^2). WHO defines obesity as a BMI of > 30 kg/m^2. A commonly used definition for extreme or morbid obesity is a BMI > 40 kg/m^2
Tuberculosis	History of or current symptomatic tuberculosis requiring treatment.

The conditions have been organized in a standard format to facilitate reporting and comparisons between countries. Individual countries may choose to expand some categories or add additional conditions to the list according to their own surveillance objectives.

Additional data to consider in specific circumstances, depending on the needs of the program, include:

- signs and symptoms of illness;
- smoking history;
- infection with (HIV) or Acquired Immune Deficiency Syndrome (AIDS) as a category separate from immunodeficiency;
- infection with tuberculosis and status of infection (i.e. latent or active);
- height and weight (to determine body mass index);
- specific hematological disorders such as sickle cell disease or thalassemia major;
- ethnicity or belonging to a disadvantaged minority group.

Annex 5: Infection Control

Principles of Infection Control

The concept of the chain of infection, with its' links stretching from the infectious agent to the susceptible host through a transmission mechanism, helps to explain how infection occurs and facilitates understanding of infection control mechanisms, which operate by breaking a link in the chain.

Pathogen

Susceptible Host

Reservoir

Portal of Entry

Portal of Exit

Mode of Transmission
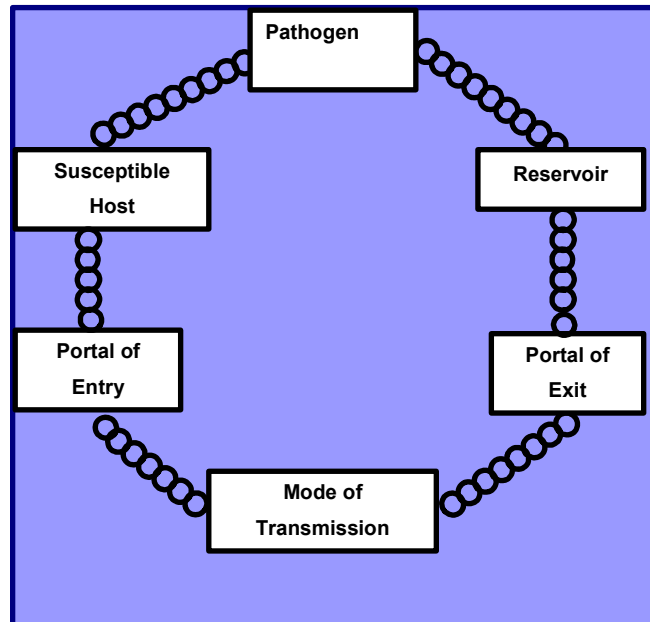
Types of transmission

The mode of transmission varies from one microorganism to another and some can be transmitted by more than one route. The three most important modes of transmission are: contact, droplet, or airborne.

1. **Transmission by contact**

Microorganisms can be transmitted through direct or indirect contact with the patient or his/her contaminated body fluids. **Direct transmission** occurs when microorganisms are transferred from person to person without an intermediate contaminated object. **Indirect transmission** occurs when an infectious agent is transferred through an intermediate contaminated object. Contact precautions should be observed with various pathogens, which include Varicella and Clostridium difficile. With certain pathogens, contact precautions will be employed in addition to another precaution (e.g. airborne or droplet).

2. **Droplet Transmission**

Droplet transmission involves contact between droplets with particles containing microorganisms from a person who is clinically ill or is a carrier of a microorganism, and the nasal or oral conjunctiva or mucous membranes of a susceptible person. Droplets are most often generated when an infected person coughs, sneezes, or converses. Transmission by droplet requires close contact between source and host, because the droplets do not remain suspended for long and thus usually only travel short distances

through the air (~one meter). The respiratory pathogens transmitted through droplets include adenovirus, human influenza virus, SARS and avian influenza A (H5N1).

Droplet transmission is the most important transmission route for the influenza virus

3. **Airborne Transmission**

Pathogens transmitted via this route are also transmitted via mucosal membrane contact with aerosolized droplets of an infectious person. The difference from droplet precautions is that the aerosolized particles are smaller, can travel larger distances, and remain in the air longer. The management of this type of transmission depends on special air management and ventilation systems (e.g. rooms with negative pressure). Examples of pathogens transmitted via this route are M. tuberculosis and the measles virus

Routine Precautions for Infection Control

1. **Standard Precautions**

Health-care facility recommendations for standard precautions

KEY ELEMENTS AT A GLANCE

1. **Hand hygiene[1]**

   Summary technique:
   - Hand washing (40–60 sec): wet hands and apply soap; rub all surfaces; rinse hands and dry thoroughly with a single use towel; use towel to turn off faucet.
   - Hand rubbing (20–30 sec): apply enough product to cover all areas of the hands; rub hands until dry.

   Summary indications:
   - Before and after any direct patient contact and between patients, whether or not gloves are worn.
   - Immediately after gloves are removed.
   - Before handling an invasive device.
   - After touching blood, body fluids, secretions, excretions, non-intact skin, and contaminated items, even if gloves are worn.
   - During patient care, when moving from a contaminated to a clean body site of the patient.
   - After contact with inanimate objects in the immediate vicinity of the patient.

2. **Gloves**
   - Wear when touching blood, body fluids, secretions, excretions, mucous membranes, nonintact skin.
   - Change between tasks and procedures on the same patient after contact with potentially infectious material.
   - Remove after use, before touching non-contaminated items and surfaces, and before going to another patient. Perform hand hygiene immediately after removal.

3. **Facial protection (eyes, nose, and mouth)**
   - Wear (1) a surgical or procedure mask and eye protection (eye visor, goggles) or (2) a face shield to protect mucous membranes of the eyes, nose, and mouth during activities that are likely to generate splashes or sprays of blood, body fluids, secretions, and excretions.

4. **Gown**
   - Wear to protect skin and prevent soiling of clothing during activities that are likely to generate splashes or sprays of blood, body fluids, secretions, or excretions.
   - Remove soiled gown as soon as possible, and perform hand hygiene.

5. **Prevention of needle stick and injuries from other sharp instruments[2]**

   Use care when:
   - Handling needles, scalpels, and other sharp instruments or devices.
   - Cleaning used instruments.
   - Disposing of used needles and other sharp instruments.

6. **Respiratory hygiene and cough etiquette**

   Persons with respiratory symptoms should apply source control measures:
   - Cover their nose and mouth when coughing/sneezing with tissue or mask, dispose of used tissues and masks, and perform hand hygiene after contact with respiratory secretions.

   Health-care facilities should:
   - Place acute febrile respiratory symptomatic patients at least 1 metre (3 feet) away from others in common waiting areas, if possible.
   - Post visual alerts at the entrance to health-care facilities instructing persons with respiratory symptoms to practise respiratory hygiene/cough etiquette.
   - Consider making hand hygiene resources, tissues and masks available in common areas and areas used for the evaluation of patients with respiratory illnesses.

7. **Environmental cleaning**
   - Use adequate procedures for the routine cleaning and disinfection of environmental and other frequently touched surfaces.

8. **Linens**

   Handle, transport, and process used linen in a manner which:
   - Prevents skin and mucous membrane exposures and contamination of clothing.
   - Avoids transfer of pathogens to other patients and or the environment.

9. **Waste disposal**
   - Ensure safe waste management.
   - Treat waste contaminated with blood, body fluids, secretions and excretions as clinical waste, in accordance with local regulations.
   - Human tissues and laboratory waste that is directly associated with specimen processing should also be treated as clinical waste.
   - Discard single use items properly.

10. **Patient care equipment**
    - Handle equipment soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of pathogens to other patients or the environment.
    - Clean, disinfect, and reprocess reusable equipment appropriately before use with another patient.
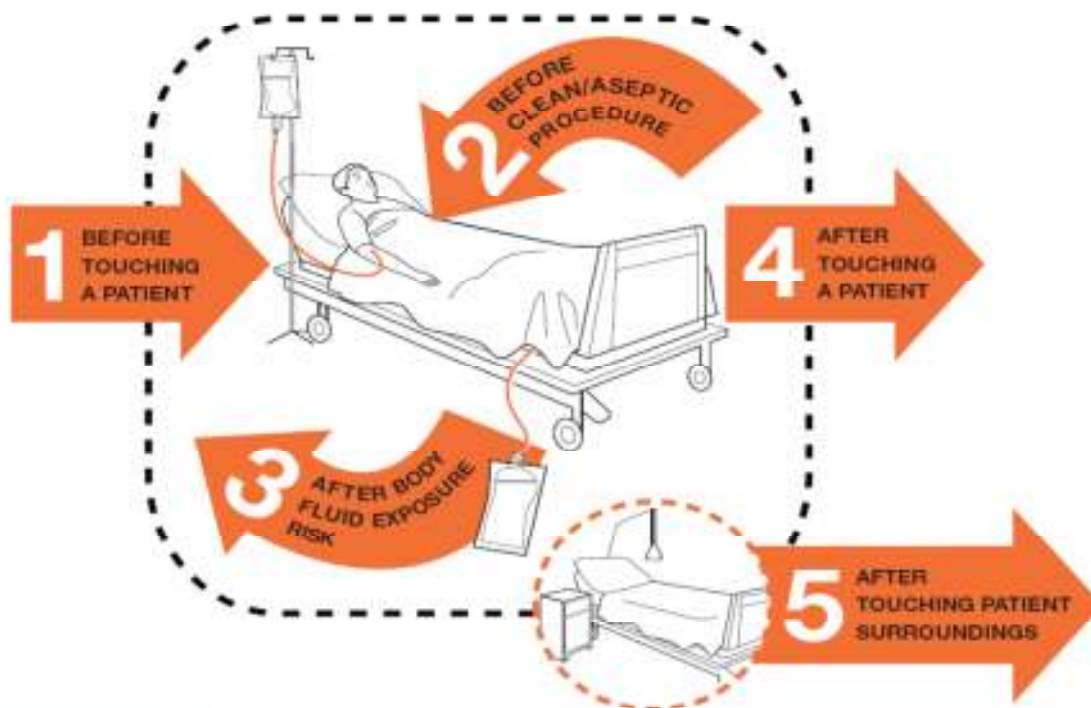
[1] For more details, see: WHO Guidelines on Hand Hygiene in Health Care (Advanced draft), at: http://www.who.int/patientsafety/information_centre/ghhad_download/en/index.html
[2] The SIGN Alliance at: http://www.who.int/injection_safety/sign/en/

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Hand Hygiene

Hand hygiene is one of the most important ways of preventing and controlling the spread of disease in health care facilities and is a principal component of standard precautions. Below, is a diagram depicting the five opportunities for hand hygiene during a clinical encounter in the hospital setting and followed by illustrations of the appropriate techniques for hand-washing with soap and water and hand-rubbing with alcohol.

Your 5 Moments
for Hand Hygiene

1 BEFORE TOUCHING A PATIENT

2 BEFORE CLEAN/ASEPTIC PROCEDURE

3 AFTER BODY FLUID EXPOSURE RISK

4 AFTER TOUCHING A PATIENT

5 AFTER TOUCHING PATIENT SURROUNDINGS

1	**BEFORE TOUCHING A PATIENT**	WHEN?	Clean your hands before touching a patient when approaching him/her.
		WHY?	To protect the patient against harmful germs carried on your hands.
2	**BEFORE CLEAN/ ASEPTIC PROCEDURE**	WHEN?	Clean your hands immediately before performing a clean/aseptic procedure.
		WHY?	To protect the patient against harmful germs, including the patient's own, from entering his/her body.
3	**AFTER BODY FLUID EXPOSURE RISK**	WHEN?	Clean your hands immediately after an exposure risk to body fluids (and after glove removal).
		WHY?	To protect yourself and the health-care environment from harmful patient germs.
4	**AFTER TOUCHING A PATIENT**	WHEN?	Clean your hands after touching a patient and her/his immediate surroundings, when leaving the patient's side.
		WHY?	To protect yourself and the health-care environment from harmful patient germs.
5	**AFTER TOUCHING PATIENT SURROUNDINGS**	WHEN?	Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving – even if the patient has not been touched.
		WHY?	To protect yourself and the health-care environment from harmful patient germs.

World Health Organization

Patient Safety
A World Alliance for Safer Health Care

SAVE LIVES
Clean **Your** Hands

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Figure II.2
How to handwash

Hand Hygiene Technique with Soap and Water

⬤ Duration of the entire procedure: 40-60 seconds

0 Wet hands with water;	**1** Apply enough soap to cover all hand surfaces;	**2** Rub hands palm to palm;
3 Right palm over left dorsum with interlaced fingers and vice versa;	**4** Palm to palm with fingers interlaced;	**5** Backs of fingers to opposing palms with fingers interlocked;
6 Rotational rubbing of left thumb clasped in right palm and vice versa;	**7** Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;	**8** Rinse hands with water;
9 Dry hands thoroughly with a single use towel;	**10** Use towel to turn off faucet;	**11** Your hands are now safe.

Figure II.1
How to handrub

Hand Hygiene Technique with Alcohol-Based Formulation

Duration of the entire procedure: 20-30 seconds

1a **1b** **2**

Apply a palmful of the product in a cupped hand, covering all surfaces;

Rub hands palm to palm;

3 **4** **5**

Right palm over left dorsum with interlaced fingers and vice versa;

Palm to palm with fingers interlaced;

Backs of fingers to opposing palms with fingers interlocked;

6 **7** **8**

Rotational rubbing of left thumb clasped in right palm and vice versa;

Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;

Once dry, your hands are safe.

Annex 6: Collecting, Storing and Transporting Specimens of Respiratory Secretions for Vial Identification

1. **Types of Specimens**
   a. In cases of ILI or SARI, nasopharyngeal and oropharyngeal swabs are collected from adults and children five years of age and older
   b. For children under five years of age, a nasopharyngeal aspirate is recommended.
   c. An aspirate is also recommended when it is not possible to collect a swab
2. **Techniques for Collecting Specimens**
   a. **Nasopharyngeal Swab**
      i. Rayon or polyester fiber swabs should be used; do not use calcium alginate or cotton swabs with wooden stems
      ii. Insert a dry swab in the nostril and move it inward to the nasopharynx
      iii. Hold it there for a few seconds
      iv. Slowly remove the swab while rotating gently.
      v. Put the swab in the tube containing the transport media

Collecting a Nasal Swab

   b. **Oropharyngeal Swab**
      i. Ask the patient to open his or her mouth
      ii. Lower the tongue with the depressor
      iii. Use the swab to take a specimen from the posterior pharynx
      iv. Avoid contact with the tonsils
      v. Place the swab in the transport media
   c. **Nasopharyngeal Aspirate** *(to be done by medical doctor or trained professional)*
      i. Review the expiration date of the transport media, aspiration tube, and vacuum pump
      ii. Break open the envelope with the aspiration kit and connect the smaller-diameter end of the tube to a sterile probe

iii. Use the probe to measure the distance from the nose to the base of the ear; half of this distance equals the distance between the patient's nose and oropharynx

iv. Connect the larger-diameter end of the tube to the vacuum pump

v. Insert the probe in the patient's nostril

vi. Withdraw the probe, rotating gently

vii. Repeat the procedure in the other nostril

viii. Draw a volume of approximately 8-10 ml of cold tampon solution (pH 7.2) through the probe to remove all the secretion

ix. Change the cover of the collector tube

Source: Johns Hopkins Hospital Epidemiology and Infectious Control and Nursing Education Department

NOTE: For all specimens, according to the algorithm, send specimens to the laboratory immediately, along with the form designed to accompany specimens; specimens should be refrigerated until arrival in the laboratory and should never be frozen

3. **Preserving and Transporting Specimens**
   a. If using a commercial media, place the swab in the transport tube and press the bottom of the tube or press the pad at the bottom to release the media; if the media is prepared in the laboratory, cut the stem of the swab so that only the part adhering to the swab remains and close the tube with the cap
   b. Swabs must always be kept moist while being transported
   c. The tube with the media and the swab should be kept refrigerated at 4-8°C in a thermos for holding specimens
   d. Transfer the specimens to the laboratory that is to process them as soon as possible (preferably within 24 hours, but within 48 hours at most)
   e. Follow the recommendations of the United Nations Committee of Experts on the Transportation of Dangerous Goods
   f. Mail the completed case form together with the samples

Annex 7: Surveillance system performance indicators

Sentinel Surveillance Steps	Associated Monitoring and Evaluation Indicators	Indicator	Structure or Calculation	Goal
Step 1 Identify hospitalized patients that meet the SARI case definition	Percent of week's with timely notification of denominators	Timely reporting of denominators	(Number of EWs with timely reporting of denominators / total EWs reported) x 100	80%
	Percent of hospitalized SARI cases that are captured by the surveillance system	Underreporting	(Reported cases of SARI in the period / cases identified in the period by active case-finding) x 100	80%
	Median interval in days between hospitalization date and notification date	Timely case reporting	Median of the interval (number of days) between hospitalization date and reporting date	1 day
Step 2 Complete data collection form and data entry	Percent of cases investigated and closed	Case investigation coverage	(Total SARI cases completely investigated and closed / Total cases reported and discharged) x 100 *** Completely investigated and closed means when test results are included (when available) for etiological diagnosis of the reported and discharged case, as well as complete clinical/epidemiological data**	90%
Step 3 Respiratory sample collection and testing results	Percent of SARI cases with collected sample	Coverage of sampled SARI cases	(Number of SARI cases with collected specimen / Number of SARI cases with valid criteria for sampling) x 100 **Sampling must be within 10 days of symptom onset*	90%
	Percent of quality samples received	Specimen quality	(Number of good quality specimens received / Total specimens received) x 100 *** Good quality means specimens properly taken, preserved, and transported until arrival at the laboratory**	90%
	Percent of processed quality samples received	Processing coverage	(Number of processed specimens / Total specimens correctly received) x 100	90%
	Median interval from hospitalization date to sampling date	Timely sampling	Median of the interval (number of days) between hospitalization date and sampling date	2 days
	Median interval from sample date to receipt of sample	Timely receipt of specimen	Median of the interval (number of days) between sampling date and receipt date *** If the date of receipt is not available, use shipment date for this indicator**	I day
	Median interval from receipt date to start of processing	Timely processing	Median of the interval between date of receipt of the specimen and processing date	3 days
	Median interval from receipt date to delivery of result	Timely delivery of result	Median of the interval between date of receipt of the specimen and date of delivery of the result	3 days
	Percent of SARI ICU cases with collected sample	Coverage of sampled SARI cases in ICU	(Number of SARI cases in ICUs with collected specimen / Number of SARI cases in ICUs) x 100	100%
	Percent of SARI-associated deaths with collected sample	Coverage of sampled cases of SARI deaths	(Number of cases of SARI deaths with collected specimen / Number of cases of SARI deaths) x 100	100%
Step 4 Data analysis and interpretation	Number of cases reported each week			
	Number of specimens submitted each week			
	Percent of submitted specimens that test positive for influenza			
Step 5 Data dissemination and outputs	Percent of weeks that data are sent to the national/regional level	Timely reporting		80%
	Timeliness of data presented in weekly influenza surveillance report	Timely reporting	How many weeks are there between the current epidemiological week and the week for which data are reported	<2 weeks

The following template can be used to tabulate data needed for some of the monitoring and evaluation indicators included in the table above.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X
1	WHO/PAHO Regional Influenza Program																							
2	**Severe Acute Repiratory Infections (SARI)** by age group, sex and geographic distribution.																							
3	Country																							
4	Year																							
5					ALL AGES																			
6					Hospitalizations				ICU						Numerator						Denominator			
7	Country (Reporting Site)	Year	Epidemiological Week	Number of SARI	SARI positive for influenza	SARI positive for Other Respiratory Virus	Total Hospitalizations (Denominator)	SARI in ICU	Total ICU Admission		SARI 0-<2yr	SARI 2-4yrs	SARI 5-19yrs	SARI 20-39yrs	SARI 40-59yrs	SARI 60+yrs	SARI age unknown	Total hospitalizations 0-<2yr	Total Hospitalizations 2-4yrs	Total Hospitalizations 5-19yrs	Total Hospitalizations 20-39yrs	Total Hospitalizations 40-59yrs	Total Hospitalizations 60+yrs	Total Hospitalizations age unknown
8			1			0																		
9			2			0																		
10			3			0																		
11			4			0																		
12			5			0																		
13			6			0																		
14			7			0																		
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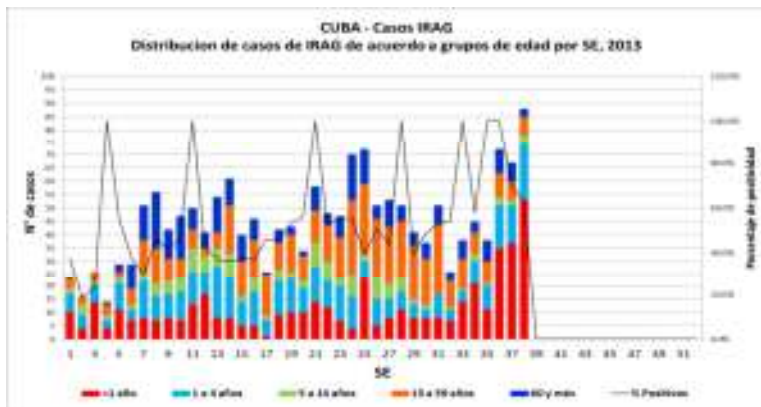## Annex 8: Data presentation in graphics and tables

1. A line graph showing the proportion of hospitalizations, ICU admissions, and deaths associated with SARI overall and by age group.
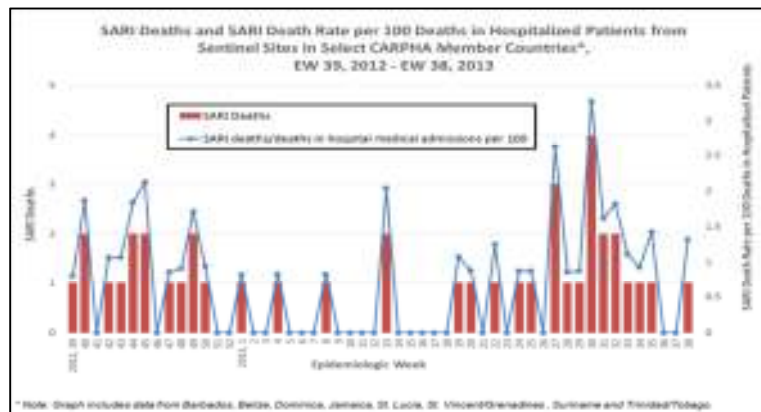
SARI-associated Hospitalizations:
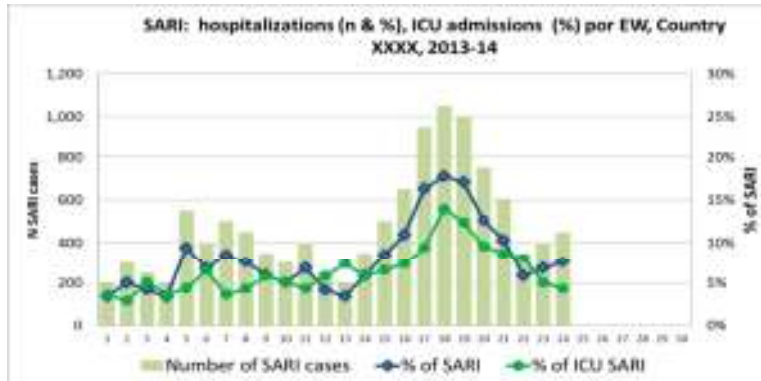
The data shown are fictitious

SARI-Associated Hospitalizations by Age Group:

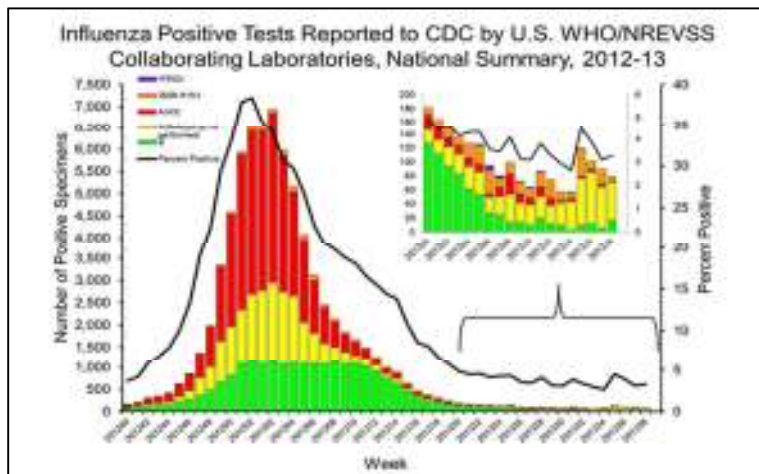Source: Institute Pedro Kourí (Cuba)

SARI-Associated Deaths

Source: Caribbean Public Health Agency (CARPHA)

2. A table showing the proportion of cases in each severity category with underlying medical conditions, history of vaccination, and history of antiviral therapy. The data shown are fictitious.

	SARI hospitalizations (n=100) n (%)	SARI cases admitted to ICU (n=100) n (%)	SARI-associated Deaths (n=100) n (%)
Co-morbidity	50 (50)	75 (75)	75 (75)
Asthma	5 (10)	10 (13.3)	10 (13.3)
Chronic respiratory disease	5 (10)	10 (13.3)	10 (13.3)
Neurological disease	5 (10)	10 (13.3)	10 (13.3)
Immunosuppression	5 (10)	10 (13.3)	10 (13.3)
Chronic kidney disease	5 (10)	10 (13.3)	10 (13.3)
Heart Disease	5 (10)	10 (13.3)	10 (13.3)
Diabetes	5 (10)	10 (13.3)	10 (13.3)
Obesity	5 (10)	5 (6.7)	5 (6.7)
Chronic Liver Disease	10 (20)	0	0
Pregnancy	10 (20)	5 (6.7)	5 (6.7)
Others	10 (20)	0	0
Tobacco Use	10 (10)	0	0
Alcoholism	10 (10)	0	0
Current Influenza Vaccine	10 (10)	10 (10)	20 (20)
Oseltamivir Therapy	10 (10)	10 (10)	10 (10)

Source: Country Ministry of Health

3. A combined line graph and bar chart showing the distribution of <u>influenza cases</u> by type and subtype with the percent positive for influenza.

Influenza Positive Tests Reported to CDC by U.S. WHO/NREVSS Collaborating Laboratories, National Summary, 2012-13

Source: US Centers for Disease Control and Prevention

4. A combined line graph and bar chart showing the distribution of <u>all respiratory viruses</u> with the percent positivity for any respiratory virus. These are data reported to PAHO by Chile.
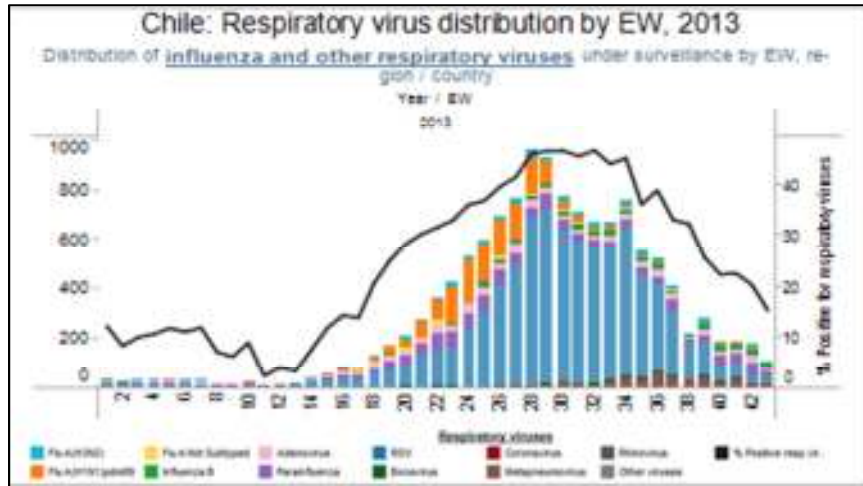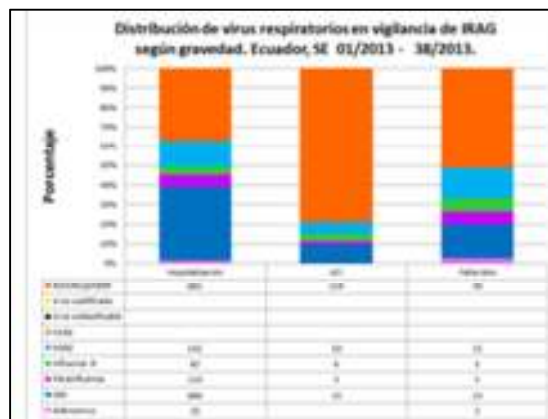
Source: Chile Ministry of Health

5. A bar graph showing the distribution of respiratory viruses by age group. The same age groups should be used as those for the SARI graph.
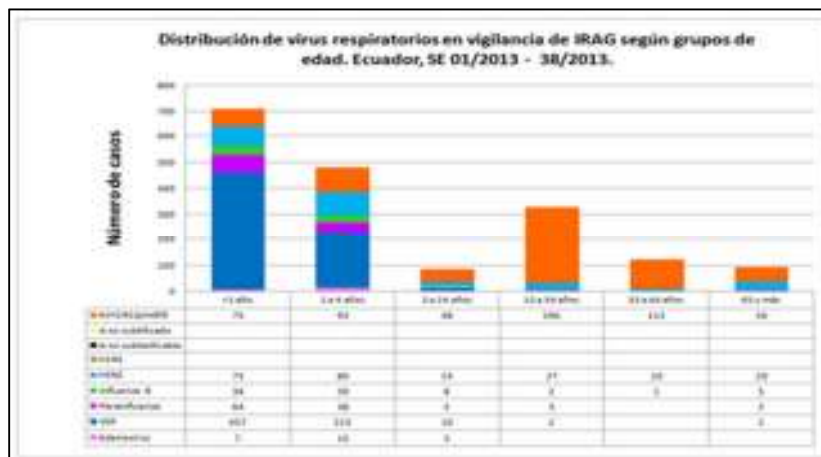
Source: Ecuador Ministry of Health

6. A bar graph showing the distribution of respiratory viruses in each severity category.

Source: Ecuador Ministry of Health

Annex 9: Hospital data table for denominators

Form for Hospitalizations, ICU Admissions and Deaths, From all Causes

1. Health Care Facility:	
2. Municipality:	
3. Epidemiological Week:	Year:
4. Date reported or entered into system: ___/___/___	

Age Groups	Hospitalizations (All units)		Hospitalizations (ICU)		Deaths	
	All Causes		All Causes		All Causes	
	Males	Females	Males	Females	Males	Females
0 to 23 months						
2 to <5 years						
5 to <15 years						
15 to <50 years						
50 to <65 years						
65 years and older						
Total						

Instructions:

This form should be completed weekly.

How to complete the form:

- Enter the name or code assigned to this facility.
- Hospitalizations (all units): enter the TOTAL number of hospitalizations (new admissions) in the epidemiological week for all causes and all units, by sex and age group.
- Hospitalizations (ICU): enter the TOTAL number of ICU admissions (new admissions) in the epidemiological week for all causes and all units, by sex and age group.
- Deaths: enter TOTAL number of deaths (new deaths) in the epidemiological week for all causes and all units, by sex and age group.

Annex 10: Defining average epidemic curves and alert thresholds

Determining average epidemic curves

Even in temperate regions, peak transmission can vary widely from year to year. Simple averaging of weekly data over several years will result in a wide summary curve that is less useful for defining what a typical, hypothetical season will look like. Aligning the curves around their peaks will allow for the description of the average amplitude of a peak, rather than the average amplitude of a given calendar week. To accomplish this, follow these simple steps:

1. Identify the median week of peak occurrence for the years for which data are available. For example, if five years of data are available and the five seasons have peaked during Week 1 in January, Week 2 in December, Week 1 in March, and Week 2 in January, then the median week will be the first week of January – hence, half of the previous years for which there are data will have occurred earlier than the median and half will have occurred later.
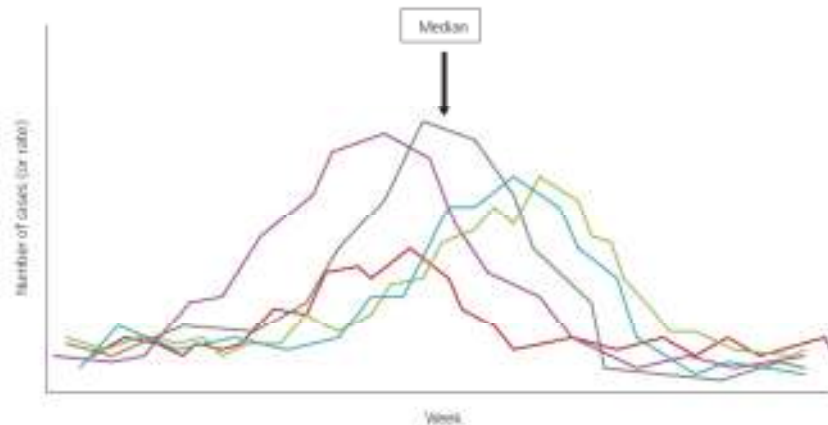
2. Align the data of the previous years' data with their respective peaks aligning on the median week identified in Step 1. This is illustrated graphically below but is most easily done using a spreadsheet, pasting each year's data in a column alongside the previous year's data, with their peaks falling in the same row.

v11
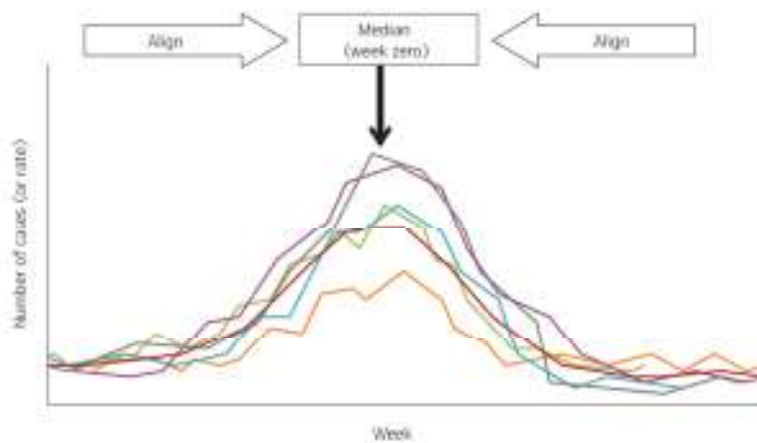
3. Calculate an average for each week. If you have used the spread sheet as described above, this would be the average of each row of data. A four-week running average can be used to smooth the curve.
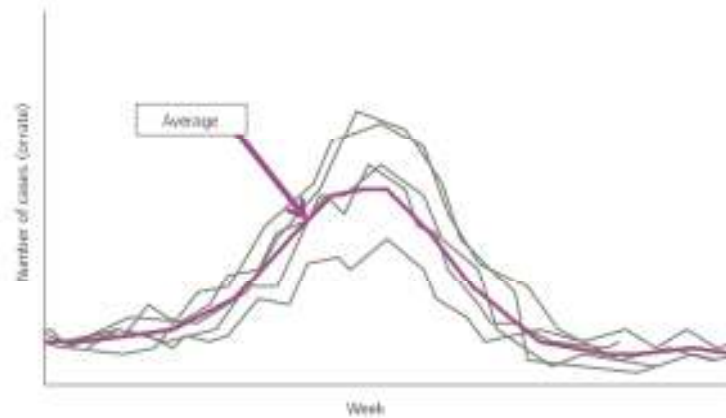
Defining the alert threshold

1. To put a current season into a historical context, it is not enough to describe an average: there should also be limits defined for extreme values, at least for the upper extreme. This will help those looking at the data to understand if the current season is out of range in comparison to a range of previous seasons. The simplest way to do this is to display the highest and lowest seasons, or range, excluding any exceptional events such as a pandemic.
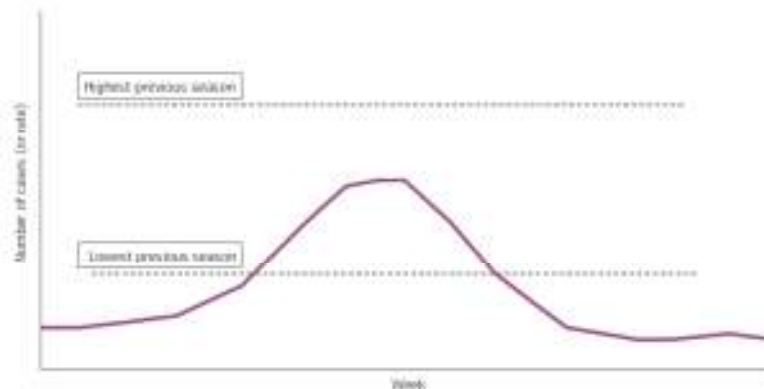
2. Another way to define extreme values is to calculate the standard deviation of the mean for each week and then create a curve for those values. A curve based on 1.65 standard deviations above and below the mean would encompass 90% of all seasons. This would mean that 5% of seasons, 1 out of every 20, would be above the upper limit for the season and 5% would be below. The higher value is used as an alert threshold for severe seasons. For example, countries which track the number of laboratory confirmed, influenza-positive samples could estimate the 90% using a few simple equations.

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a. First, calculate the variance of the values for each week:

$$variance = \frac{\Sigma(x - \bar{x})^2}{n - 1}$$

Where x is the value for that week, x-bar is the average of all the years' data for that week, and n is the number of years for which the data are available.
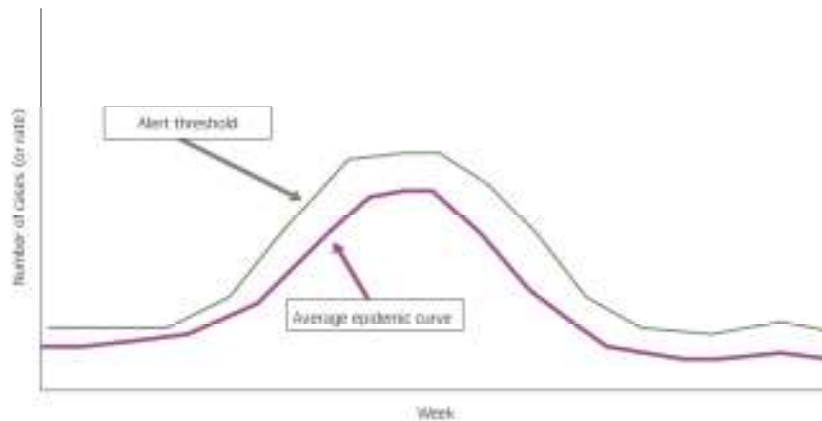
b. Next, calculate the standard deviation (σ) for each week using the square root of the variance:

$$\sigma = \sqrt{variance}$$

c. The upper and lower 90% confidence intervals around the mean for each week will be:

$$\bar{x} \pm 1.645 \times \sigma$$

The upper 90% confidence interval will define the alert threshold.

3. Plot current year data on curve (the example below displays a year which is relatively mild but earlier than usual in comparison to the previous years on average). If the alert threshold is set at the upper 90% confidence interval, only 1 in 20 seasons should exceed this threshold over the course of the entire season.

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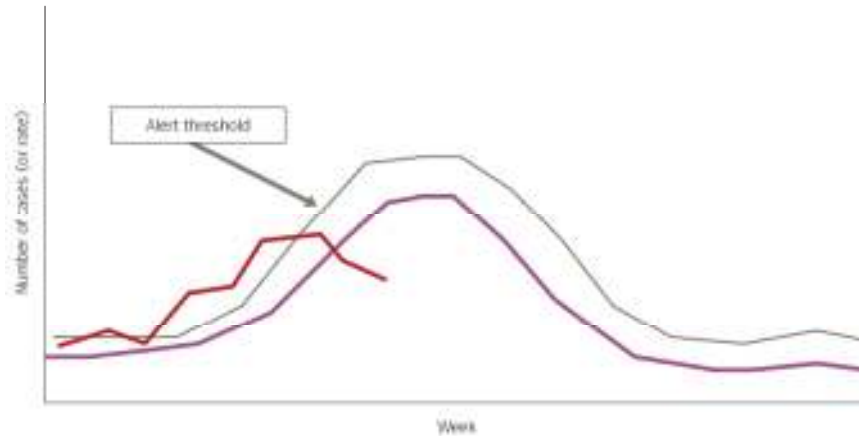
Seasonal threshold

Many methods have been described to determine a threshold that defines the start of a season as described earlier in the text. The simplest method involves a visual inspection of several years of data to determine the point or threshold that would consistently be higher than normal random variation in the off-season baseline, while being low enough to signal the start of an influenza season early enough in the season to be useful.

A simple method that results in a numeric value is to calculate the annual median amplitude for the data being plotted. To use this method, it is important that an entire year's worth of data be available for each of the years used in the calculation. For example, countries that track the weekly proportion of samples that test positive for influenza can use the annual median proportion positivity for the average epidemic curve of the proportion positivity as a threshold for seasonal epidemics. When influenza activity occurs consistently (e.g. two to three weeks) above the annual median proportion positivity, countries may consider influenza transmission as epidemic
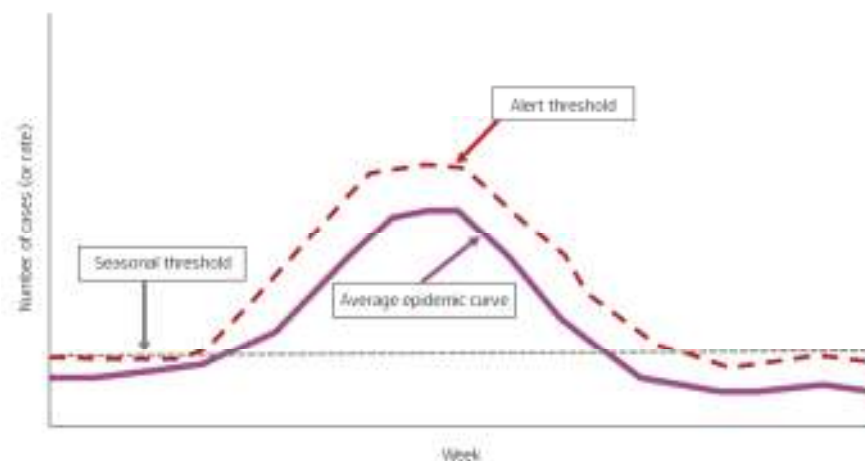
Annex 11: Data Reporting Template and Links

Laboratory data should be collected and provided to PAHO/WHO (flu@paho.org) using the format below. Template Excel files will be sent to each country to facilitate data sharing.

Additionally, data can be shared through WHO's FluID, which can be accessed using the following link: http://www.who.int/influenza/surveillance_monitoring/fluid/en/