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Influenza Surveillance in Saudi Arabia

ASSISTANT AGENCY FOR PREVENTIVE MEDICINE
MINISTRY OF HEALTH

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Ministry of Health

Influenza Surveillance
In Saudi Arabia

Influenza is a serious disease that can lead to hospitalization and sometimes death. Every flu season is different, and an influenza infection can affect people differently. Even healthy people can get very sick from the flu and spread it to others.

Contents

Introduction

- Influenza infections cause substantial morbidity and mortality every year around the world.
- Due to high mutation rate of the virus, a particular influenza vaccine usually confers protection for no more than a few years.
- Every year, World Health Organization predicts which strains of the virus are most likely to be circulating in the next year allowing pharmaceutical companies to develop vaccines that will provide the best immunity.

Vision

Provide accurate and reliable data essential to make our health system better prepared against seasonal, zoonotic and pandemic influenza threats to populations and individuals.

Mission

Establish, standardize and share influenza surveillance data collection and analyze the data in local and global context to guide national influenza control strategies.

Objectives of influenza surveillance

The goal of influenza surveillance is to minimize the impact of the disease by providing useful information to public health authorities, which will help in planning appropriate control and intervention measures, allocate health resources, and make case management recommendations.

Epidemiological Surveillance Objectives:

- Establish and monitor baseline trends of influenza – Like Illness (ILI) and Severe Acute Respiratory infections (SARI) to help understand annual changes in severity.
- Signal the start of the influenza season.
- Describe the seasonality of influenza in the country.
- Provide data that can be used to understand disease burden and the impact of influenza in relation to other disease.
- Identify and monitor groups at high risk for severe disease, in order to set priorities for use of resources.
- 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.

Virological Surveillance Objectives:

- Identify locally circulating types and subtypes of influenza viruses and their relations to global and regional patterns.
- Describe the antigenic character and genetic make-up of circulating influenza viruses.
- Detect/identify any novel influenza strain/type or known stain but unexpectedly circulating in Eastern Mediterranean area.
- Monitor antiviral sensitivity.
- Understand the relation between virus strain and severity.
- Provide candidate viruses for vaccine production.
- Provide information for vaccine virus selection.
- Provide a platform for evaluation of effectiveness of vaccine and other interventions.
- Establish a foundation to distinguish between ILI/SARI caused by influenza or by other respiratory viruses.

Objectives of influenza surveillance and its use in decision-making

Principal objective	Use of surveillance in decision-making
Determine when and where influenza activity is occurring, and who is affected	• Alert healthcare 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 no 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 Healthcare	• Improve clinical management and prevention of disease in high risk patients. • Inform national policies such as priority groups for vaccination and treatment.

resources. Describe the Clinical patterns of disease	
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

In order to achieve these objectives, the Generic Protocol recommends conducting two types of influenza surveillance:

• **Sentinel surveillance of:**
  - **ILI** in the outpatient setting
  - **SARI** in hospitals and health facilities that provide inpatient treatment

• **Intensified national surveillance** to detect unusual or unexpected cases of severe acute respiratory infection, which all health facilities should be equipped to detect.

Establishment of national influenza surveillance

To establish an effective national surveillance system, this surveillance should use clear surveillance standards to ensure that data can be understood and interpreted; Performance indicators for supervision and monitoring to identify the weaknesses and corrective actions taken where necessary. A basic needs have to be included as the following functions:

1. Case Definition (Figure 1)

Key messages:

- Influenza Sentinel Surveillance for ILI and SARI is not necessarily intended to capture all cases but to describe trends over time.
- Influenza infection causes a clinical syndrome not easily distinguished from other respiratory infections.
- Using one common case definition globally will allow national authorities to interpret their data in an international context.
- ILI case definition is generally intended for use in outpatient centers and SARI for inpatient hospital settings.

ILI-case definition

An acute respiratory infection with:

• Measured fever of ≥38°C
• And cough
• With onset within the last 10 days

SARI-case definition (for all age groups)

An acute respiratory infection with:

• Measured fever of ≥38°C
• And cough

• With onset within the last 10 days
• And requires hospitalization

2. Surveillance of ILI and SARI using automated electronic data collection

Eastern Mediterranean Flu Network (EMFLU) is a regional platform for sharing of epidemiological and virological data on influenza in the WHO Eastern Mediterranean Region. The platform provides quantitative and qualitative data on trend, spread, intensity and impact of influenza in the Eastern Mediterranean Region. EMFLU connects existing databases at country level in Eastern Mediterranean Region and can also be used to directly enter data at country level using a web based interface. The tool is intended to provide useful information for informed decision making regarding influenza prevention and control strategies.

3. Selection and location of sentinel sites: (Appendix 1)

The sentinel sites has been selected based on the following factors:

a. **Geographical Representation considering diverse climate.**
b. **Population Representativeness:** For ILI sentinel sites, general outpatient clinics are often appropriate choices. For SARI sentinel sites, general or community hospitals are more likely to be representative of general population. 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 sites should be representative of the target age and socioeconomic groups in the population under surveillance.
c. **Reasonable number of patients for sufficient numbers for testing.**
d. **Facility feasibility, acceptability and available resources:** Facility staff and leadership motivated and committed to voluntarily implement and sustain surveillance. Efficient, consistent, and sustainable mechanisms for collection, storage, and transport of clinical specimens. Ability to 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.
e. **Known population catchment size (for disease burden estimation);and availability of reliable numerator and denominator data:** Ability to capture all cases meeting the case definition or to reliably estimate the fraction captured by adequate patient volume and performing a register review to estimate the number of ILI and SARI patients by the facility throughout the year. It is necessary to have population denominators for the catchment area of the sentinel sites. Estimation of denominators will require a review of admission statistics of the facilities and the admissions that are due to influenza-associated SARI or visits to the outpatient department for influenza associated ILI per week or month.
f. **Consider special groups; pilgrims.**

4. Influenza sentinel surveillance team & roles and responsibilities (Figure 2 & 3)

	Job title	Responsibilities
A. At the sentinel site level		
A.1 Hospital site team	Physician	1. Identify cases meeting the ILI and SARI case definition 2. Select ILI and SARI cases for which specimens are to be collected 3. Collect respiratory specimens (two specimens) utilizing appropriate infection control practices, including PPE. 4. Complete required Forms. 5. Enter and assess data on the selected days for surveillance.
	Assisting nurse	Prepare specimens to be delivered to the laboratory under the appropriate biosafety conditions.

	Laboratory coordinator	Responsible for sample preparation for shipment to the regional laboratory and National Health Laboratory under appropriate biosafety conditions.
	Health inspector	Complete required Forms.
A.2 Primary care center team	Physician	6. Identify cases meeting the ILI and SARI case definition 7. Select ILI and SARI cases for which specimens are to be collected 8. Collect respiratory specimens (two specimens) utilizing appropriate infection control practices, including PPE. 9. Complete required Forms. 10. Enter and assess data on the selected days for surveillance.
	Assisting nurse	Prepare specimens to be delivered to the laboratory under appropriate biosafety conditions.
	Laboratory coordinator	Responsible for sample preparation for shipment to the regional laboratory and National Health laboratory under appropriate biosafety conditions.
	Health inspector	Complete required Forms.
B. At the regional coordinator level		
B.1 Epidemiological assessment coordinator		1. Immediately notify the Ministry of Health of any unusual SARI cases 2. Generate an epidemiological report of the regional site sites on a weekly basis from the on lone data base system. 3. Report any situation outside normal parameters to the Ministry of Health via email **CDCGD-SI@moh.gov.sa** or fax number **0112124056**
B.2 Regional laboratory coordinator		1. Confirm that biosafety standards for handling and transporting specimens are being followed. 2. Process specimens on a timely basis for influenza A and B. 3. Complete approved laboratory Form with the laboratory test results and the test date. 4. Communicate results to the surveillance site and the Ministry of Health.
C. At the national level		
C.1 At Agency assistance for preventive medicine	Epidemiology specialist& information technology specialist	1. Coordinate the surveillance process, including providing the resources needed to sustain the surveillance program. 2. Collaborate with the laboratory to conduct surveillance training and awareness activities. 3. Monitor activities in each hospital to identify and resolve problems.
	Laboratory specialist	Promote integrated work between the laboratory and each hospital.
	Team coordinator	1. Prepare, in collaboration with the local surveillance team and laboratory personnel, the national report on a weekly basis. 2. Disseminate the weekly report to all relevant stakeholders, including WHO. 3. Disseminate public health alerts regarding events of national and/or international importance.
	Quality specialist	Periodically evaluate the quality of the data being obtained.
C.2 At National Health laboratory (NHL)		1. Routinely store specimens at or below -70˚C then send according to the protocol to WHO Collaborating Centers until be processed in the NHL. 2. Send unsubtypeable influenza viruses specimens to the WHO collaborating center, as soon as possible.

		3. Send viral culture and antiviral sensitivity specimens to the WHO collaborating center, as soon as possible. 4. Collaborate in data analysis and process evaluation. 5. Collaborate in the preparation and dissemination of reports. 6. **Communicate results to the Ministry of Health.** 7. Report virologic results to WHO through the systems established for the purpose.

5. Case Selection and Sampling Strategy:

- The number of patients chosen for laboratory testing of specimens and epidemiological data collection will depend on the capacity of the health-care facility to process, store and ship specimens and the capacity of the laboratory to process, store and test samples.
- To minimize bias for selection of patients for testing and data collection **Alternate day sampling method** will be used. This method is to select all patients who meet the case definition presenting to a facility on a certain days of the week. This can reduce the logistical challenges of surveillance by confining laboratory specimen and data collection efforts to a single day.
- Samples from all ILI patients who meet the case definition will be taken on **SUNDAY** and **TUESDAY** only.
- Samples from all SARI patients who meet the case definition will be taken **DAILY,** including weekend days.

6. Laboratory testing:

- The sensitivity and specificity of any test for influenza depends on the type and quality of specimen collected, the transport and storage conditions, the methodological differences in the laboratories performing the test, and the type of test used.
- Reverse transcriptase-polymerase chain reaction (RT-PCR) is the most sensitive method for detecting influenza virus and is the recommended influenza surveillance assay for most laboratories.
- Virus culture is also needed on at least a subset of specimens in order to allow detailed antigenic and genetic characterization of the virus. It can also be used to proliferate and ultimately identify new emerging or novel influenza virus stains.
- Antiviral resistance testing should be considered for high-risk patients if capacity exists in the laboratory in addition to taking a sample from non-high-risk patients.

6.1 Specimens for laboratory diagnosis

- Specimens should be obtained for influenza virus testing as soon as possible after illness onset, ideally within 7 days. However, as some persons who are infected with seasonal influenza viruses are known to shed virus for longer periods (e.g., children and immunocompromised persons). Reverse transcription polymerase chain reaction (RT-PCR) still positive beyond one week from symptom onset, but the likelihood of a positive test decreases rapidly after that time. Viral cultures, however, are most likely to be positive only if the sample is taken within three days of symptom onset
- Specimens from nasal and nasopharyngeal specimens have a higher yield of virus detection in **ILI cases** than do oropharyngeal specimens.
- For specimens collected from **SARI cases**, however, the relative sensitivity of nasal versus oropharyngeal swabs is unknown. If patients are intubated, endotracheal aspirates or bronchoalveolar lavages can also be used where clinically indicated and may have a higher yield than upper respiratory specimens in these severe cases.
- WHO guidelines for collecting, preserving and shipping specimens, the use of non-sterile gloves, surgical facemasks and eye protection (modified universal precautions) should be followed.
- Avoid contamination of the sample by glove's powder as this might inhibit PCR and affect the result or give false negative result.

- Respiratory specimens from the upper respiratory tract should be collected and transported in 1-2 ml of virus transport media. (Insert the fiber tip of the swab immediately into the VTM and break off the shaft so that the swab fits completely within the tube. Please tighten the cap securely and place at 4-8°C immediately in an upright position).
- Using the recommended synthetic (non-cotton) swab with plastic (not wooden) shaft.
- Transfer the specimens to the laboratory that is to process them as soon as possible (preferably within 24 hours at most)
- If they cannot be processed within 24-48 hours, they should be kept frozen at or below -70˚C.
- Care should be taken to prevent repeated freeze/thaw cycles that can result in the loss of viral capsid subunits and consequent escape and loss of RNA integrity**.**
- **Collect one nasopharyngeal specimen for all required diagnosing testing, send to regional laboratory, which will send the specimen to Saudi National Health Laboratory (NHL) for other diagnostic testing not done in regional laboratory.**
- Specimens will stored at or below -70˚C in national health laboratory then send to WHO Collaborating Centers until be processed in the NHL.
- ILI specimens will be collected and **shipped by** the transporting company to regional laboratory for processing of specimens on **Monday and Wednesday.**
- SARI specimens will be collected and **shipped by** the transporting company to regional laboratory for processing of specimens on **daily basis including weekend days.**

6.2 Diagnostic testing for influenza

- Molecular assays are more sensitive and specific for detecting influenza viruses than other influenza tests. A proper primers and probes are used by RT-PCR to detect and discriminate between infection with **influenza A and B viruses**.
- For SARI cases MERS Co-V will be tested in addition to Influenza panel.
- Positive specimens subsequently used for further analysis to identify specific influenza subtypes A: H1, H3, H5 and B: Yamagata, Victoria, will be send to the National Health Laboratory.
- The following samples should be collected and stored in the Saudi National Health Laboratory (where cloning and sequencing can be implemented when it will be available) or sent to the to one of the **WHO Collaborating Centers (WHO CCs) for diagnosis and further characterization until processed in NLH**:
  - Viruses that cannot be sub typed locally.
  - Any virus of a new subtype.
  - A representative sample of viruses collected at the beginning, peak, and end of each season.
  - Viruses from particularly severe or unusual cases.
  - A sample of viruses isolated from outbreak investigations.
  - Virus culture.

6.3 Antiviral testing

- Antiviral resistance data will influence the management decisions of clinicians caring for influenza patients. In addition, data shared internationally through Flu Net from countries that experience early influenza activity can aid other countries that have not yet experienced influenza activity or do not have laboratory capacity to perform antiviral resistance testing.
- Antiviral testing from sentinel sites can give useful information about the background rate of resistance in circulating viruses; however, it is also important to specifically monitor resistance in high-risk cases.
  a. **Treatment failures in case patients given antiviral within 48 hours of symptom onset.**
  b. **Patients on long-term treatment with antiviral including patients with severe immunosuppression.**
- Viruses found to have oseltamivir or zanamivir resistance should be sent to a WHO CC for further characterization, along with information regarding the clinical setting in which they were collected.
- If antiviral resistance is detected and confirmed, it is also important to document through careful investigation of cases and contacts whether or not human-to-human transmission has occurred. If sustained human-to-human transmission

of resistant viruses is noted, this event should be reported immediately through the International Health Regulations focal point of the country (NFP).

- This test not available in our laboratories now, specimens will forward to one of the **WHO Collaborating Centers (WHO CCs) for diagnosis and further characterization.**

7. Data Collection and reporting-minimum data set: (Appendix 2 & 3 & 4)

- **Data sheet was created for ILI data collection at the primary care health centers (Appendix 2 & 3).**
- **For individual SARI and ILI patients tested for influenza viruses, the following data are recommended as a minimum for each patient from whom a specimen is collected:**

• Unique identifier (to link laboratory and epidemiological data, and for tracking patient if necessary).
• Sex.
• Age.
• Nationality
• Visitor or not (Hajj, Umrah seasons & other reasons for visiting)
• Smoking history.
• History of fever and body temperature at presentation.
• Date of symptom onset.
• Date of hospitalization (SARI patients only).
• Date of specimen collection.
• Antiviral use for present illness at the time of specimen collection.
• Pregnancy status.
• Patient outcome (death, survival).
• Seasonal influenza vaccination status and date of administration.
• Travel history (within 2 weeks)? Place?
• Presence of chronic pre-existing medical illness(es):
  a. Chronic respiratory disease
  b. Asthma
  c. Diabetes
  d. Chronic cardiac disease
  e. Chronic liver disease
  f. Chronic renal disease
  g. Chronic neurological or neuromuscular disease
  h. Hematological disorders
  i. Immunodeficiency, including HIV infection.

- For individual SARI patient tested for influenza viruses, the following detailed data are recommended for each patient from whom a specimen is collected (**Appendix 5**)

Standard age groupings

To facilitate analysis and reporting Data on ILI and SARI age groups will be aggregated; major age groupings for reporting are:
• 0 to < 2 years.
• 2 to < 5 years.
• 5 to <15 years.
• 15 to < 50 years.
• 50 to < 65 years.
• ≥ 65 years.

8. Laboratory data collection (Appendix 2 & 4):

1. Results from the **regional laboratory** should be registered in the (EMFLU) network case by case.
2. Results from the **regional laboratory** should be collected weekly by the **National Health Authority at MOH**. The following data should be collected:
   - The number of samples tested for influenza during the week.
   - The proportion of samples that were positive for influenza for ILI and SARI (reported separately).
3. Laboratory tests to be done by **National health laboratory** :
   • Subtypes of viruses detected during the week (if applicable).
   • Results from antiviral resistance testing (if applicable).

9. Aggregated data to be collected and reported from each sentinel site

ILI- Surveillance Data (Appendix 6)

The following ILI surveillance data should be sent weekly from the sentinel sites to the national health authority:

- The number of new ILI cases during the week being reported.
- The number of new ILI cases sampled during the week being reported.
- The total number of new visits to the outpatient clinics in which ILI surveillance is being conducted or the catchment population to the sentinel site, by age.

Data should be reported in aggregated form, stratified by age and sex if possible (age groups: 0-<2, 2-<5, 5-<15, 15-<50, 50-<65 and ≥65 years).

SARI- Surveillance Data (Appendix 7)

The following SARI surveillance data should be sent weekly from the sentinel sites to the national health authority:

- The number of new SARI cases during the week being reported.
- The number of new SARI cases in which specimens were collected during the week being reported
- The total number of new hospital admissions to wards in which SARI surveillance is being conducted.

Data should be reported in aggregated form, stratified by sex and age groups (age groups: 1-<2, 2-<5, 5-<15, 15-<50, 50-<65 and ≥65 years).

Time frame of data collection:

Epidemiological and virological data collected from the sentinel sites should be collected and reported regularly to the national health authorities on a weekly basis throughout the year.

10. Reporting of summary analyses

- Regular reporting of the analysis and interpretation of surveillance data to both policy makers and clinicians who collect the data is an important part of maintaining a system and ensuring maximum benefit.
- Weekly surveillance reports should be produced and made accessible to relevant partners.
- A yearly surveillance report with surveillance and risk factor data should be produced.
- Data should be aggregated and reported to the international data sharing platforms according to global standards and protocols.

10.1 Regular surveillance reports

- Regular summary analysis and reporting will help to ensure that the information is available to policy makers, healthcare providers, and the general public, and will also improve the consistency of reporting from sentinel sites.
- Reports should provide timely information on influenza activity and types of influenza viruses circulating. Whenever feasible, such reports should be available to the public on the national surveillance website.
- Minimal information that should be presented in the weekly report includes:

- Graphical presentation of the proportion of SARI cases by catchment population and/or total hospitalizations by week, together with data from previous seasons for comparison, if available.
- Graphical presentation of the proportion of ILI cases by catchment population and/or outpatients visits by week, together with data from previous seasons for comparison, if available.
- Number of SARI/ILI patients from whom samples were laboratory tested and the proportion of positive cases, by influenza type and subtype.
- Number of sentinel sites reporting.

- The data should be presented by age group where available.

10.2 Annual surveillance reports

- **Following each influenza season**, additional analyses should be undertaken with a summary review of influenza activity during that season. These analyses can help inform the future timing of vaccination and identify high risk groups for targeted interventions.
- Ideally the following analyses can be presented in an annual report:
  - Description of laboratory confirmed influenza-associated SARI and ILI cases within each month or week of the year for each age group.
  - Summary data on the proportions of influenza-positive cases with underlying medical conditions.
  - Types and subtypes of circulating influenza viruses during the season and how these matched with the seasonal influenza vaccine.
  - Proportion of samples testing positive for influenza by week or month of the year.
    - Comparison of data from the most recent influenza season to previous seasons. Notable or unusual features of the season when compared to previous seasons should be highlighted.
  - Seasonal vaccine coverage in risk groups (these data could be acquired through surveys or means other than collection of case-specific data from the surveillance system if vaccination status is not part of the data collection scheme).
  - Number of samples collected from ILI and SARI patient which were tested negative for influenza but positive for other respiratory pathogens.
  - Data from the monitoring of the system:
    - Proportion of sentinel sites reporting weekly to the national level.
    - If feasible, the proportion of sentinel sites regularly submitting specimens for laboratory testing.
    - Number of specimens sent from the sentinel sites.
    - Proportion of weeks with reporting to Flu Net and FluID and/or other reporting systems.

10.3 Reporting data to WHO

National aggregated epidemiological data for each age group to be reported to WHO, via FluID, include:

- The number of new influenza-positive ILI and SARI cases during the week being reported.
- The number of total new outpatient visits in outpatient clinics where ILI surveillance is being conducted and/or the catchment population to the sentinel site during the week being reported.
- The number of total new hospital admissions on wards where SARI surveillance is being conducted during the week being reported.
- The number of ILI or SARI cases sampled during the week being reported.
- The proportion of ILI and SARI specimens testing positive during the week being reported.
- Total number of inpatient respiratory deaths during the week being reported.

11. Defining baselines and thresholds

Using surveillance data for monitoring influenza activity over time.
Key messages
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.

Principal objective	Use of surveillance in decision-making
Average epidemic curve (Baseline)	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.
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.

- For each of these parameters the values to be used need to determine the average epidemic curves by creating an average curve centered 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.
- A useful alert threshold is the value 1.645 standard deviations above the mean for each week, which defines the 90% confidence interval of the mean.

12. Using a routine sentinel surveillance system in an outbreak or pandemic

Key Message

- Routine sentinel surveillance can provide baseline data against which to judge the severity and specific epidemiological features of an epidemic or pandemic of a novel influenza virus.
- An established surveillance system will provide the means with which to monitor the progress of an epidemic.

The program will need to make enhancements in the event of a novel influenza virus with sustained community transmission to provide additional critical information. These might include:

- Expanded data collection to include additional risk factors, additional clinical data on signs and symptoms, course of illness, complications, and outcome.
- Admission and discharge diagnoses from severe cases.
- Additional monitoring of high-risk populations such as minority and other disadvantaged groups.
- Specific monitoring of intensive care units (ICUs) and cases requiring mechanical ventilation.
- Collection of mortality data including cause of death.
  - Cause-specific mortality rates, or similar population-based rates of intensive care admission or mechanical ventilation in comparison to previous years may be useful to estimate overall relative severity.

Useful indicators may include the following:

- The proportion of pneumonias detected as influenza positive from sentinel surveillance using a representative sampling system.
- Ratio of respiratory illness-related hospital admissions and deaths to total admissions at the sentinel site.
- Proportion of respiratory illness hospital admissions that required ICU admission, mechanical ventilation or that died.
- Proportion of influenza hospital admissions, influenza intensive care admissions, and influenza deaths with pre-existing medical conditions.

13. Indicators for monitoring an Outbreak

Key questions to ask at the beginning of an outbreak (and periodically throughout):	Implications, related decisions, Implications, or recommendations:
1. How different is this virus from previous ones?	**Information will aid in projection of how severe**

a. Is it a new subtype? How is it different antigenically from previously circulating viruses? **b.** Is there pre-existing immunity (i.e. cross-reactive antibodies) in the population? How much and in whom? **c.** Is it sensitive to antivirals? **d.** Which virus could be used as a vaccine?	**the event may be and which age groups might have some protection:** • Antiviral sensitivity critical for management recommendations • Inform vaccine production, procurement, and distribution decision.
2. Is community transmission sustained? If so, how fast is it spreading? **a.** From person to person? (i.e. R0,generation time, attack rate) **b.** Geographic spread from community to community; country to country? **c.** c. How is it spreading? (e.g. are schools playing a key role? Other routes?)	**Will inform decisions about feasibility of pharmaceutical and non-pharmaceutical interventions such as school and border closures:** • Allow projections of the period of time over which the event is likely to occur, i.e. the height and breadth of the epidemic curve.
3. What proportion of cases are severe or what number of severe cases are occurring in the population? **a.** What is the mortality rate? **b.** What is the hospitalization rate? **c.** What is the proportion of cases that die? **d.** Proportion that are hospitalized? Proportion that require mechanical ventilation? **e.** How are these figures affected by the local environment (e.g. healthcare access, climate, social factors, prevalence of chronic conditions in the population, or other issues of vulnerability)? **f.** e. How does this event compare to previous ones at this location?	**Projection of impact of the epidemic over a specific period in terms of numbers of severe cases, beds needed, healthcare workers needed, etc.**
4. Who is most vulnerable? **a.** Age group with highest rate/number of severe cases? **b.** b. What are the risk factors for severe outcomes (e.g. pregnancy and obesity)?	**Will inform decisions about feasibility of pharmaceutical and non-pharmaceutical interventions such as school and border closures:** • Formulation of management plans • Inform decisions regarding whom to prioritize for vaccination, treatment, etc.
5. What are the clinical features of the disease? **a.** How does it present? What is the clinical course? **b.** What proportion of cases is asymptomatic? **c.** What kinds of complications are being observed (e.g. secondary bacterial infections, Acute Respiratory Distress Syndrome (ARDS), and renal failure?)	**Clinical management planning: quantities of antibiotics to order; dialysis machines; ventilators; and ECMO machines** • Guide clinical management guidance • Creation of case definitions

In-depth system evaluations

After one year, full system evaluations should be conducted. At the least, an in-depth system evaluation should be conducted before the system is extended beyond its existing sentinel sites.

A full evaluation is required

- To ensure that the system is meeting its stated object
- To ensure that the system is of the right size for the specimen requirements.
- To measure the sensitivity and specificity of the system.
- To evaluate the efficiency of the system in meeting its objective.
- To evaluate the acceptability of the system to the staff, institutions and clinicians participating in data collection.
- To evaluate the usefulness of the data to the health-care providers, policy-makers and others using the data.

- To evaluate the regularity of reporting by national authorities.
- To review records at sites to ensure that cases are identified, enrolled and sampled.
- To ensure adherence to the criteria for collecting specimens.
- To make recommendations for improving quality, efficiency and usefulness.
- To recommend expansion of the system if it is functioning well; and
- To evaluate sentinel sites serving other functions.

Performance indicators to measure quality of influenza sentinel surveillance

To evaluate the efficiency and success of the system, a number of process indicators and outcome indicators have been established.

1. Timeliness

Several time intervals are appropriate for routine measurement as quality indicators:

- Target date for data reporting from the sentinel site to the next administrative level until the actual reporting date.
- Target date for data reporting from the next administrative level to the national level until the actual reporting date.
- Date of specimen collection at facility until shipment to laboratory.
- Date of result availability in laboratory until date of report to referring institution and physician.
- Date of receipt of specimen in the laboratory until result availability.

Two metrics can be used to reflect timeliness indicators:

- Percentage of times that a site achieves its target for timeliness.
- Average number of days for each interval over time for each site.

2. Completeness

- Proportion of reports received with complete data from each site.
- Proportion of weeks when reports are received.
- Proportion of reported cases that have specimens collected.

3. Audit

Regular field evaluations and audits at facility level of a subset of medical records to ensure the following:

- Cases are being counted appropriately and not being underreported.
- Reported cases fit the case definition.
- Epidemiologic data are correctly and accurately abstracted.
- Respiratory samples are being taken, stored, processed, tested, and shipped properly and in a timely fashion from all those who meet sampling criteria.
- Sampling procedures are being done uniformly without evidence of bias.

4. Data to be followed and observed for aberrations over time

- Number of cases reported by month for each site.
- Number of specimens submitted by month for each site.
- Proportion of specimens that are positive for influenza.
- Proportion of specimens that were negative for influenza but positive for other respiratory pathogens.
- Number and proportion of ILI and SARI cases tested.

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3) Advisory Committee on Immunization Practices. *Prevention and control of influenza with vaccine. Recommendations of the Advisory Committee on Immunization Practice*, 2010. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr59e0729a1.htm?s_cid=rr59e0729a1_w

Appendices

Appendix 1: Checklist for selecting sentinel sites for influenza surveillance (adopted from WHO Epidemiological Influenza Surveillance Standards[2])

This checklist may be used to assess a healthcare 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 representation.
- 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 from all age groups attending the clinic?	yes ❑ no ❑
Are patients from all socioeconomic strata and ethnic groups attending the clinic?	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 at least permanent clinical staff who can 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 who 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 ❑

Appendix 2: ILI Data Collection set

Case definition	
ILI case Definition: beginning at the last 10 days, did the patient experience: □ History of sudden onset fever or current fever (≥38˚C) □ Cough	Does the patient meet ILI case definition? □ Yes □ No IF "No", DO NOT CONTINUE
Other suspected disease: _____	
ID number:	Date of First Interview:
Demographic Information	
Primary Health Care: Patient's name: (family name), (given name(s))	Gender: □ Male □ Female
Nationality :	Visitor : □ Hajj □ Umrah □ Other reason
Date of birth (Gregorian)	or age: Years_____ Months (1-12)_____ (Gregorian)
Address: (Village/District/Governorate)	Contact Telephone Number:
Clinical History	
Date of symptom onset Temperature at first review: ___˚C *Chronic medical conditions:* □ Heart disease □ Asthma □ Chronic lung disease □ Chronic liver disease □ Diabetes □ Neuromuscular dysfunction □ Chronic kidney disease □ Chronic hematological disorder □ Immune compromised □ Other _____ □ Unknown	
Pregnancy: □ Yes □ No	
Did the patient receive influenza antiviral within the last 14 days?	
Vaccination for influenza in the last 6 months:	
Specimen Collection	
Nasopharyngeal swab collected?	Throat swab collected? / Date of specimen collection:
Specimen Laboratory Form	
ID number:	Hospital: Date specimen collected: _ _ / _ _ / _ _ _ _ Date of shipment: _ _ / _ _ / _ _ _ _ Ward/Department:
Date Lab received specimen: _ _ / _ _ / _ _ _ _	
Type of specimen - Oropharyngeal Specimen: □ Yes □ No - Nasopharyngeal Specimen: □ Yes □ No	- Blood Specimen: □ Yes □ No Other (specify): _____

Flu A: seasonal H1N1	□	Pos (+)	□	Neg (-)	Adenovirus	□	Pos (+)	□	Neg (-)
Flu A: seasonal H3N2	□	Pos (+)	□	Neg (-)	hPIV 1	□	Pos (+)	□	Neg (-)
Flu A: A(H1N1)pdm09	□	Pos (+)	□	Neg (-)	hPIV 2	□	Pos (+)	□	Neg (-)
Flu A: H5N1	□	Pos (+)	□	Neg (-)	hPIV 3	□	Pos (+)	□	Neg (-)
Flu A: Unsubtypeable/Novel	□	Pos (+)	□	Neg (-)	hMPV	□	Pos (+)	□	Neg (-)
Flu B	□	Pos (+)	□	Neg (-)	MERS-CoV	□	Pos (+)	□	Neg (-)
RSV	□	Pos (+)	□	Neg (-)	Others:	□	Pos (+)	□	Neg (-)

Date results reported: _ _ / _ _ / _ _ _ _
Comments:

Appendix 3: ILI Line List Data Collection set

حالات مشتبهة الأنفلونزا (**ILI**) المسجلة بالمركز

اسم المركز: **التاريخ:** **رقم الأسبوع:**

رقم NO	الاسم Name	رقم الهوية ID Number	العمر Age						الجنس Gender		حرارة Temp 38°	كحة Cough
			2<0	5<2	15<5	50<15	65<50	65+	ذكر M	انثى F		

المراقب الصحي:

المركز: **التاريخ:** **رقم الأسبوع:**

Appendix 4: SARI Data Collection set

Case definition	
SARI case Definition: beginning at the last 10 days, did the patient experience: □ History of sudden onset fever or current fever (≥38˚C) □ Cough	Does the patient meet SARI case definition? □ Yes □ No IF "No", DO NOT CONTINUE
Other suspected disease: _____	
ID number:	Date of First Interview:
Demographic Information	
Hospital: Patient's name: (family name), (given name(s))	Gender: □ Male □ Female
Nationality :	Visitor : □ Hajj □ Umrah □ Other reason
Date of birth (Gregorian)	or age: Years_____ Months (1-12)_____ (Gregorian)
Address: (Village/District/Governorate)	Contact Telephone Number:
Admission information	
Ward of admission:	Date of Admission
Clinical History	
Date of symptom onset Temperature at admission: ___˚C *Chronic medical conditions:* □ Heart disease □ Asthma □ Chronic lung disease □ Chronic liver disease □ Diabetes □ Neuromuscular dysfunction □ Chronic kidney disease □ Chronic hematological disorder □ Immune compromised □ Other _____ □ Unknown	
Pregnancy: □ Yes □ No	
Did the patient receive influenza antiviral within the last 14 days?	
Vaccination for influenza in the last 6 months:	
Specimen Collection	
Nasopharyngeal swab collected?	Throat swab collected? / Date of specimen collection:
Clinical course and Outcome	
ICU admission: □ Yes □ No	Ventilation: □ Yes □ No
Outcome Date:	Outcome: □ Discharge □ Death □ Unknown
Specimen Laboratory Form	
ID number:	Hospital: Date specimen collected: _ _ / _ _ / _ _ _ _ Date of shipment: _ _ / _ _ / _ _ _ _ Ward/Department:
Date Lab received specimen: _ _ / _ _ / _ _ _ _	
Type of specimen - Oropharyngeal Specimen: □ Yes □ No - Nasopharyngeal Specimen: □ Yes □ No	- Blood Specimen: □ Yes □ No Other (specify): _____

Flu A: seasonal H1N1	□	Pos (+)	□	Neg (-)	Adenovirus	□	Pos (+)	□	Neg (-)
Flu A: seasonal H3N2	□	Pos (+)	□	Neg (-)	hPIV 1	□	Pos (+)	□	Neg (-)
Flu A: A(H1N1)pdm09	□	Pos (+)	□	Neg (-)	hPIV 2	□	Pos (+)	□	Neg (-)
Flu A: H5N1	□	Pos (+)	□	Neg (-)	hPIV 3	□	Pos (+)	□	Neg (-)
Flu A: Unsubtypeable/Novel	□	Pos (+)	□	Neg (-)	hMPV	□	Pos (+)	□	Neg (-)
Flu B	□	Pos (+)	□	Neg (-)	MERS-CoV	□	Pos (+)	□	Neg (-)
RSV	□	Pos (+)	□	Neg (-)	Others:	□	Pos (+)	□	Neg (-)

Date results reported: _ _ / _ _ / _ _ _ _
Comments:

Appendix 5: Hospital Data Collection Form (Detailed form)

HBIS ID												Hospital name:	
Comp	Year	Month	Hospital ID		Patient ID		**Department** (Medicine=1; Pediatrics=2)		**Date**				
							Unit (Inpatient=1; Outpatient=2)		**Time** (use 24 hr. time format)				

Name		**Age** (YY-MM)	
Household head		**Sex** (Male=1; Female=2)	
Village / Para / Mahalla		**Health care worker** (Yes=1; No=2)	
Union / Ward		**Poultry worker** (Yes=1; No=2)	
Upazila / Thana		**Poultry raising** (Yes=1; No=2)	
District		**Local Travel within 7 days** (Yes=1; No=2)	
Phone number		**Where?**	
International travel within 30 days (Yes=1; No=2)		**Where?**	

Date of admission (DD-MM-YY)		**Date of discharge** (DD-MM-YY)	
Provisional diagnosis			
Outcome	Fully recovered=1; Partially recovered=2; Remains hospitalized=3; Transferred=4; Death=5; Unknown=9		

Symptoms (Yes=1; No=2, Unknown=9)		**Date of onset**	**Was fever subjective or measured?** (Subjective=1, Measured=2)			
			If measured, record in (in °F):			
			Other symptoms (Yes=1; No=2)			**Date of onset**
Fever			Others 1			
Cough			Others 2			
Difficulty breathing			Others 3			
Sore throat			**Symptoms for <5 yrs.** (Yes=1; No=2)			**Date of onset**
Running nose			Chest indrawing			
Headache			Stridor in a calm child			
Diarrhea			Being unable to drink			
Chills			Lethargy or unconsciousness			
Body ache			Vomits everything			
Hemoptysis			History of convulsions			
Pleuritic chest pain						

Medical History		Has any doctor told you have lung disease? (Yes=1; No=2)	
Do you smoke? (Regularly=1; Sometimes=2; In past=3; Never=4)		Are you pregnant? (Women only) (Yes=1; No=2)	
Has any doctor told you have heart disease? (Yes=1; No=2)		Visited OPD with current illness? (IPD only) (Yes=1; No=2)	
History of underlying or chronic illness (Check all that apply): □ Asthma □ Malaria □ HIV/AIDS □ Diabetes □ COPD(Chronic bronchitis/emphysema) □ Hypertension □ Cancer □ other underlying or chronic illness (Specify)			
History of pneumonia in the prior 30 days: 1=Yes; 2=No; 9=Unknown			

Admission in hospital in the past 14 days: 1=Yes; 2=No; 9=Unknown	
For this illness episode, any medicine taken in the 24 hours before admission to the study hospital? 1=Yes; 2=No; 9=Unknown If yes, name of the medicine: Is the medicine an antibiotic? (Yes=1, No=2, Unknown=9)	

General signs		Sputum Production (Yes=1; No=2; Unknown=9)	
Respiratory rates (rates per minute)		Does the patient have abnormal breath sounds? (Yes=1; No=2; Unknown=9) if yes, check all the below that apply:	
Pulse (rates per minute)		Decreased breath sounds (Yes=1; No=2)	
Measured temperature (in °F)	.	Rhales (Yes=1; No=2)	
When was temperature measured? (On admission=1, On enrollment=2)		Rhonchi (Yes=1; No=2)	
How was temperature measured? Oral=1, Tympanic/ear-based=2, Axillary=3, Unknown=9		Crepitation (Yes=1; No=2)	
Systolic blood pressure		Stridor (Yes=1; No=2)	
Diastolic blood pressure		Cyanosis (Yes=1; No=2)	

Mental status: Well alert=1; Irritable / restless=2; Lethargic=3; Unconscious=4			
Laboratory findings (if available from existing records)		**Chest radiograph findings:** **X-ray obtained?** 1=Yes; 2=No; 9=Unknown	
Blood Specimen collected? (Yes=1; No=2, 9=Unknown) if yes, Date: Time:		Is finding consistent with pneumonia? (Yes=1; No=2; Others=8; Unknown=9), if others please specify.	
WBC count		Platelet count	
Neutrophils		Hemoglobin (gm/dl)	.
Lymphocytes		ESR	

Treatment received:

Did the patient receive oxygen? (Yes=1; No=2; Unknown=9)	
Was patient admitted to intensive care unit? (0=No; 1=Yes; 9=Unknown)	
During this hospitalization, has patient taken antibiotics prior to swab collection? (Yes=1, No=2, Unknown=9) **If yes, antibiotics received**(Check all that apply)**:** □ Aminoglycoside □ Amoxicillin □ Ampicillin □ Augmentin □ Penicillin □ Cefuroxime □ Ciprofloxacin □ Chloramphenicol □ Clindamycin □ Cloxacillin □ Ceftriaxone □ Cotrimoxazole □ Doxycycline □ Ganciclovir □ Erythromycin □ Oseltamivir □ Paracetamol □ Vancomycin □ Others □ Unknown	
Date of administration: Time of administration:	

Comments	**Signature of Surveillance Physician and Field Assistant**	

Appendix 6: Weekly aggregated data form for ILI

Sentinel site_____
Reporting week no: _____ from (date) _____ to (date) _____

	0 to < 2 years	2 to < 5 years	5 to <15 years	15 to <50 years	50 to <65 years	≥ 65 years
New ILI cases						
Sampled ILI cases						
Proportion of sampled cases positive for influenza						
Outpatient visits						
Catchment population						

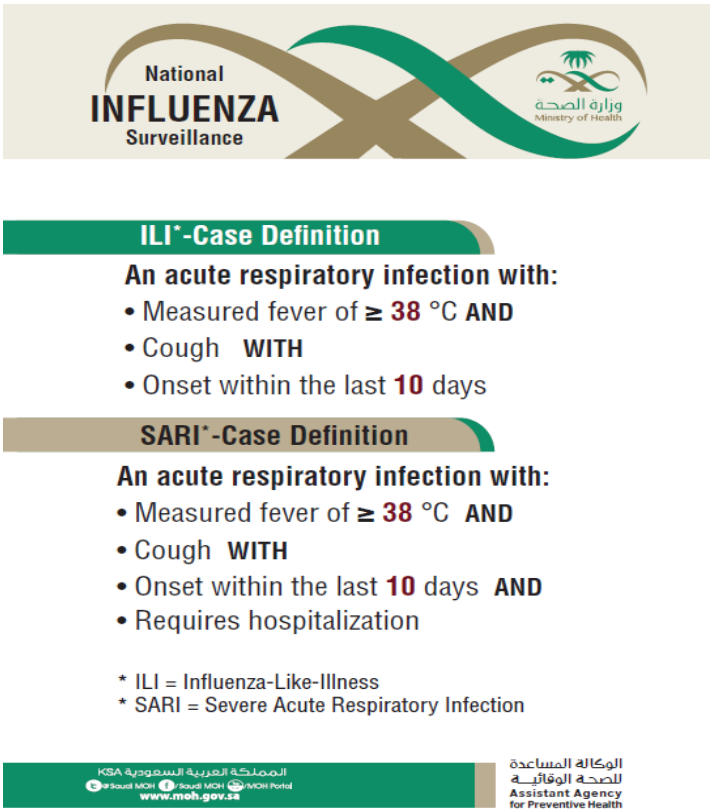
Appendix 7: Weekly aggregated data form for SARI

Sentinel site_____
Reporting week no: _____ from (date) _____ to (date) _____

	0 to < 2 years	2 to < 5 years	5 to <15 years	15 to <50 years	50 to <65 years	≥ 65 years
New SARI cases						
Sampled SARI cases						
Proportion of sampled cases positive for influenza						
New hospital admissions*						
SARI deaths						

*Excluding labour and delivery and elective surgery.

Appendix 8: Case Definitions Poster (In English and Arabic Language)



Appendix 9: Influenza Surveillance Protocol Algorithm Poster (In Arabic Language)

Appendix 10: Influenza Surveillance Protocol Algorithm Poster (In English Language)