WHO global technical consultation: global standards and tools for influenza surveillance

GENEVA, SWITZERLAND
8–10 MARCH 2011

World Health Organization

WHO global technical consultation: global standards and tools for influenza surveillance

GENEVA, SWITZERLAND
8–10 MARCH 2011

World Health Organization

WHO/HSE/GIP/2011.1

Contents

Executive summary

The influenza pandemic of 2009 highlighted many areas of influenza surveillance that require strengthening, one of the most important being standardized data collection and reporting systems. To this end, WHO organized a global consultation to review influenza surveillance standards and the current data-sharing and reporting tools, with the goal of preparing a manual of global standards and improving the reporting tools. This report summarizes the discussions and recommendations of that consultation with regard to the influenza surveillance manual and the tools for global surveillance.

Global surveillance standards for influenza

The participants focused on topics that had previously been identified by a group of technical advisers and the WHO regional offices:

- objectives of surveillance,
- case definitions of influenza-like illness (ILI) and severe acute respiratory illness (SARI),
- qualitative indicators,
- selection and location of sentinel sites,
- minimum data elements and age breakdown,
- surveillance data collection methods,
- baseline and epidemic threshold and
- monitoring and evaluation.

Main conclusions: The manual to be developed should provide a minimum, standardized framework for sentinel surveillance of seasonal influenza and methods for monitoring future influenza pandemics or other large-scale outbreaks of respiratory disease. It should accommodate regional and national differences in capacity and should include revised, standardized case definitions of ILI and SARI.

Tools for global surveillance

The participants reported that they found the situation updates and data published by WHO useful but made some proposals for improving them, including:

- provision of links to relevant guidance and influenza information products;
- information on severity (mortality, proportions of hospitalizations and hospital deaths) for risk assessment purposes;
- trends broken down by age group, with age-specific data on cases of influenza; and
- data on antiviral resistance.

1. Background

Influenza surveillance draws on information from a range of sources and includes clinical, virological and epidemiological data. The influenza pandemic of 2009 demonstrated the difficulties of monitoring a large-scale event without standardized surveillance data and reporting systems. The lack of standardization results in data for different countries that are not comparable. As a consequence, the data cannot be compiled to create a comprehensive picture that could easily be used to monitor changes as the virus spreads from country to country or to understand the factors that might result in differences in influenza between countries. Countries also cannot interpret their own data in the context of what others are observing. In addition, the lack of an effective mechanism for reporting epidemiological data results in significant delays in reporting, analysing and sharing information.

In the aftermath of the pandemic, it is important to review the existing tools and current and future surveillance requirements and to design methods for monitoring seasonal epidemics and future pandemics at global, regional and country levels. For this purpose, WHO organized a technical consultation with the aim of reviewing the existing influenza surveillance practices, evaluating the tools for reporting, and identifying the priorities for further development.

The specific objectives of the meeting were:

- to reach consensus on the objectives, case definitions, minimal data set and other standards for a global influenza surveillance; and

- to review and recommend improvements to the global influenza data-sharing platforms, FluNet and FluID.

Participants from 27 Member States and the six WHO regional offices and representatives from certain organizations attended the 3-day meeting. (See **Annex 1** for the agenda and list of participants.) The meeting was organized by the epidemiological surveillance team jointly with the virus monitoring and vaccine support unit of the Global Influenza Programme.

Before the consultation, several smaller meetings and discussions were held with technical experts to provide guidance on surveillance issues that should be standardized (**Annex 2**). The consultations included meetings and teleconferences with the WHO Epidemiological Network, which is made up of epidemiologists from nearly 40 countries, representing all six WHO regions, two teleconferences with WHO regional advisers and one meeting of a technical working group, which then prepared the technical briefing notes that were used as a background for the consultation (**Annex 3**). These notes summarize the main points to be discussed, the relevant literature and opinions expressed at the previous consultations. The briefing notes cover:

- case definitions for ILI and SARI,

- selection and location of sentinel sites,

- minimum data elements,

- breakdown of data by age,

- surveillance data collection methods,

■ baselines and epidemic thresholds and

■ monitoring and evaluation.

Once these standards are agreed upon, they will be incorporated into a global surveillance manual for distribution. The manual will, with the new WHO epidemiological surveillance data compilation tool, FluID, and the existing virological surveillance database, FluNet, help WHO Member States to report all their data in an easy, globally standardized way. The objective of the manual is to provide a minimum, standardized framework for sentinel influenza surveillance that can be adapted to match available national public health resources. The manual is not intended to require countries to alter their existing respiratory disease surveillance systems dramatically but to establish standards for inpatient and outpatient respiratory disease surveillance reporting, data collection and analysis. The administrators of systems that do not use international standard case definitions or procedures are encouraged to change to the standards described in this document. The manual is intended to serve as a tool for all public health professionals and institutes involved in influenza surveillance. Where there are regional guidelines, they will be more detailed than this global manual and are the recommended standard to be followed locally and nationally.

2. Outcome of discussions on influenza surveillance standards

Objective of surveillance systems

All disease surveillance systems should be based on clear objectives for the use of the data, which guide what kind of data should be collected and the selection of sites for surveillance that will provide the most appropriate data. The objectives that will be described in the manual will be those considered to be the basic, minimum objectives for both epidemiological and virological surveillance. The needs of different countries may, however, vary, and more comprehensive objectives, implying more data collection, could be added by countries or regions. The participants discussed the objectives proposed by previous consultations and agreed on the lists below.

Epidemiological surveillance objectives

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

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.
- Monitor antiviral sensitivity.
- Understand the relation between virus strain and severity.
- Provide candidate viruses for vaccine production.
- Provide information for vaccine virus selection.

Qualitative indicators

During the 2009 pandemic, WHO asked all Member States to report weekly on four qualitative indicators: subjective estimates of geographical spread, trends in number of cases, the intensity of disease and the impact on the health-care system. These indicators were designed so that all Member States, including those with no formal surveillance system, could contribute data to the global system. The proposal from the previous consultations was that these should be continued in some form as part of global surveillance.

An analysis of the usefulness and accuracy of the qualitative indicators used during the pandemic was presented by Nusrat Homaira, ICDDR,B. Qualitative information reported by Member States was compared with data from FluNet and EURO-Flu data to determine the level of correlation. It was found that nearly all Member States (183/192) reported qualitative indicators, and for 78 Member States, these indicators were the only information on the pandemic situation. When both quantitative and qualitative indicators were available, they generally correlated well. All countries except those in the WHO European Region, which was using similar indicators before the pandemic, discontinued reporting immediately after the pandemic was over.

The participants agreed that qualitative indicators are perhaps most useful in situations in which there is no other influenza surveillance; however, their accuracy for countries with no formal surveillance cannot be evaluated. These indicators provide a useful summary of the situation and are less likely to result in reporting delay. At the global level, these data are useful because they provide an overview of the epidemiological picture of the pandemic. These indicators have a number of limitations; they do not provide a detailed picture of the situation, especially at national level. The indicator of impact is particularly vulnerable to political pressure, as ministries do not wish to be seen as unable to cope with the situation. The indicators are sometimes based on widely different data sources, some of which may be unreliable; and qualitative indicators provide data that may add to existing systems but are not a substitute for formal data collection. Countries should be encouraged to set up formal surveillance.

The consensus was that at least a subset of qualitative indicators might be useful, but, when possible, reporting should be based on quantitative data.

Case definitions of influenza-like illness and severe acute respiratory illness

Currently, several case definitions are used globally for influenza and respiratory disease surveillance. The definitions of ILI and SARI were reviewed and evaluated in the light of data on their sensitivity and specificity, with the goal of establishing standardized, widely accepted definitions.

Influenza-like illness

The WHO definition of ILI has been in use for a number of years but is not used by all Member States. It has proved to be useful for tracking seasonal influenza outbreaks and for obtaining samples for virological characterization and vaccine strain selection; however, a number of studies and the experience of many Member States have called into question certain elements of the definition. The sensitivity of the definition is generally about 60%; the specificity is lower, ranging from about 5% when influenza is not prevalent (that is, 5% of people who meet the case definition do actually have influenza) to 60–70% during the influenza season.[1,2] The usefulness of specific influenza signs and symptoms for detecting influenza have been evaluated in a number of studies. The most important are cough, fever and myalgia or fatigue.[1,2,3,4,5] Notably, sore throat has been found in several studies to be a negative indicator of influenza, meaning that people with a sore throat are more likely to have an illness other than influenza.

A presentation was made on how the European Centre for Disease Prevention and Control reviewed and revised their case definitions, with some of the data on which this was based. Data were presented from two studies conducted by the International Emerging Infections programme of the United States Centers for Disease Control and Prevention to evaluate the performance of the SARI case definition in Guatemala and Kenya. They found that the sensitivity of the definition could be improved by using the term 'history of fever' rather than measured temperature as part of the definition, as described below.

[1] Kasper MR et al. Evaluation of an influenza-like illness case definition in the diagnosis of influenza among patients with acute febrile illness in Cambodia. *BMC Infectious Disease*, 2010, 10:320.

[2] Monto AS et al. Clinical signs and symptoms predicting influenza infection. *Archives of Internal Medicine*, 2000,160:3243–3248.

[3] Boivin G et al. Predicting influenza infections during epidemics with use of a clinical case definition. *Clinical Infectious Diseases*, 2000, 31:1166–1169.

[4] Lambert SB et al. Influenza surveillance in Australia: we need to do more than count. *Medical Journal of Australia*, 2010, 193:43–45.

[5] Call SA et al. Does this patient have influenza? *Journal of the American Medical Association*, 2005, 293:987–997.

The working group on case definitions made a number of general recommendations, to be taken into account in revising the current case definitions:

- Any changes should result in the most accurate case definitions possible, on the basis of the available published and unpublished literature, and should reflect the surveillance objectives outlined above.

- Any increase in sensitivity should also take into consideration the consequences for specimen collection and the burden on laboratories.

- The definitions should be clear and simple and should be easy to use by Member States in a variety of settings.

- They should refer to something that clinicians recognize (e.g. acute respiratory illness)

- They should be comparable with previous definitions.

The current definition of ILI is a sudden onset of fever, a temperature > 38 °C and cough or sore throat in the absence of another diagnosis.

Proposed changes

CHANGE	RATIONALE
Change 'sudden onset of fever' to 'acute respiratory illness'	Encompasses a broad, well-known diagnosis.
	Relates the definition to a clinically recognized condition.
	Simpler
> 38 °C to ≥ 38 °C	Many clinicians and record-keepers round down to 38 °C when the observed value is between 38 °C and 39 °C; therefore, cases of temperature of 38.2 °C, for example, are not counted.
	Already in use in many programmes
Delete 'sore throat'	This symptom is not associated with influenza in cases of respiratory disease.
	Increases specificity
	Impossible to assess in infants

The changes proposed by the working group were discussed in plenary, with general agreement. A recommendation from the floor to change the temperature to ≥ 37.8 °C was not generally accepted because of concern that the increased sensitivity and decreased specificity might overwhelm the surveillance system. The group recommended that the concept of 'recent onset' should also be reflected in the definition, preferably with a specific time frame. For ILI, it was considered that fever should be to a 'measured fever', as 'history of fever' is too broad for a mild outpatient illness.

> **Proposed new definition:** An acute respiratory illness with a measured temperature of ≥ 38 °C and cough, with onset within the past 7 days.

Severe acute respiratory illness

The surveillance case definition for SARI in adults has been in use in parts of the world since it was formulated by the WHO Regional Office for the Americas in 2005. Definitions derived from the PAHO definition were subsequently published by the WHO regional offices for Europe and the Western Pacific. The intent of the SARI definition was to capture the severe end of the spectrum of disease related to influenza. It was intended to include patients who might not have been admitted to hospital for pneumonia, such as those with congestive heart failure or chronic lung disease exacerbated by influenza. These non-pneumonia cases represent the large majority of the burden of severe disease related to influenza in industrialized countries, where it has been studied. The definition of SARI for children under

the age of 5 years adopted by the three regional offices is a modification of the clinical case definition of pneumonia used in the Integrated Management of Childhood Illnesses (IMCI) programme.

The current definitions of SARI are:

■ for patients > 5 years: meets ILI case definition (sudden onset of fever of > 38 °C and cough or sore throat in the absence of another diagnosis) *and* shortness of breath or difficulty in breathing *and* requiring hospital admission;

■ for patients < 5 years: in some areas, the IMCI case definition for pneumonia and severe pneumonia, which is any child aged 2 months to 5 years with cough or difficulty in breathing *and* breathing faster than 40 breaths/min (ages 1–5 years) or breathing faster than 50 breaths/min (ages 2–12 months); *or*

the IMCI case definition for severe pneumonia in any child aged 2 months to 5 years with cough or difficult breathing *and* unable to drink or breastfeed, or vomits everything, or convulsions, or lethargic or unconscious, or chest indrawing or stridor in a calm child.

and requires hospital admission.

Proposed changes

CHANGE	RATIONALE
Add 'acute respiratory illness'	Encompasses a broad, well-known diagnosis.
	Relates definition to a clinically recognized condition
	Simpler
'History of fever' instead of '≥ 38 °C'	Many patients have taken antipyretics.
	The illness may have progressed since presentation with ILI.
	Fever may be absent in older adults, especially those who are chronically ill.
	May need explanatory footnotes
	Data from Guatemala and Kenya indicate an improvement in sensitivity.
	Many sites do not see enough cases to test because of the stringent criterion of measured fever, especially in sub-Saharan Africa, where temperature is unlikely to be measured.
Add 'recent'	New illness superimposed on old must be distinguished.
	May need to clarify meaning in footnotes or use time parameter
Delete 'sore throat'	No association with influenza in cases of respiratory disease
	Impossible to assess in infants
	Improves specificity and helps compensate for increased sensitivity of past fever (above)
Delete 'shortness of breath' and 'difficulty in breathing'	Not specific; does not add to accuracy of definition
	Often misunderstood, e.g. nasal obstruction does not constitute difficulty breathing.
	Deletion will simplify the definition.
	Reasons for admission can be explained in footnotes.

There was general consensus in both the working group and plenary on the proposed changes to the definition of SARI. Nevertheless, several concerns and issues were raised. A strong recommendation was made, with wide support, that there be only one definition of severe illness for all age groups, because the IMCI guidelines are used by first-level care providers in outpatient departments but are generally not known or used by clinicians in hospitals; the definition does not include infants under 2 months; and the definition is complicated for clinical management and might not be useful for surveillance. It was considered preferable to have a simple definition that is easy to remember for surveillance purposes. Explanatory notes would be required to clarify terms like 'acute' and 'severe'.

Some participants expressed concern about deleting 'shortness of breath or difficulty in breathing', which they considered a useful clinical indicator of severity. The group concluded, however, that inclusion of the term did not change the sensitivity or specificity of the definition. Furthermore, there is no indicator of severity that can be applied in every setting; such a definition would be overly complex. The requirement for hospitalization as a marker of severity also reflects the impact of influenza on health resources. Any comparison of data from different countries or even areas within the same country will have to take into account aspects such as differences in policies for admission and in access regardless of the definition used.

Some participants suggested addition of 'constitutional symptoms', but it was generally considered that this would not improve the definition.

Changing the definition to include 'recent history' (e.g. 7 or 10 days) of illness will improve specificity. Changing measured fever to history of fever will make it more sensitive and will not require standardized measurements.

Generally, using 'history of fever' rather than measured temperature > 38 °C would increase the work required to find a positive case by a factor of 4 in the data from Guatemala and Kenya. Removing 'sore throat', however, increases the specificity, so that the final group of signs and symptoms is more specific and more sensitive than the current definition, resulting in a similar work load for the laboratory.

All the ramifications of any change should be considered, including not only the scientific benefits but also the costs associated with training staff. A change could also provide an opportunity for advocacy.

The manual might include variables that would allow use of previous case definitions for comparison with past data. For example, if 'history of fever' is added to the definition, the inclusion of the recording of temperature at the time of hospital admission as part of the minimum data set would allow selection of a subset of cases for comparison with previous data. The manual should include the diagnoses and diagnostic codes corresponding to SARI, so that they can be used as proxies or substitutes for SARI in countries with computerized medical records, which are unlikely to set up new, separate systems for reporting SARI.

> **Proposed new definition (for all age groups):** An acute respiratory illness with a history of fever or measured fever of ≥ 38 °C and cough, with onset within the past 7 (or 10, more data needed before finalization) days, requiring hospitalization

Selection and location of sentinel sites

The selection and location of sentinel sites will depend on a country's information requirements, resources, demographics and geography. Therefore, there is no prescribed method for selecting these sites; however, recommendations were made in the briefing note about the factors to be considered:

- representativeness of the site for the population under surveillance;

- geographical representation, especially for regions with diverse climates;

- a volume of patients that is not too high as to be unmanageable but high enough to give sufficient numbers for testing;

- manageability and feasibility;

- availability of communication and transport;

- acceptability to facility managers and health-care providers;

- ability to determine or estimate population catchment size (for disease burden estimation); and

- ability to collect unbiased data (for describing risk factors for severe disease).

A brief presentation was made on surveillance site selection in Morocco from Ahmed Rguig.

The recommendations of the briefing note were considered generally acceptable. It was proposed that the manual should outline the benefits and uses of measuring ILI and SARI, so that countries can decide on the balance to achieve between the two on the basis of their surveillance objectives. When a choice must be made, priority should be given to SARI surveillance, as it provides information on severe disease; however, ILI surveillance should not be abandoned, especially if the information is already being collected.

The participants considered that site selection should be based on the country's objectives and data requirements. For example, it might depend on whether the primary objective is to collect information on risk factors, disease burden or only virological types. Ideally, sentinel sites should cover a representative sample of the general population. In a small district hospital, it might be possible to define a catchment area and estimate its disease burden, whereas it might be difficult to identify the catchment area of a large referral facility, and the risk factors might not be representative of those prevalent in the general population. A large referral hospital will, however, probably have more patients, allowing rapid collection of viruses for study, and more viruses from severely ill patients.

It is difficult to define the minimum number of cases necessary for an accurate epidemiological picture or the maximum number beyond which no additional useful information is added. The consensus of the meeting was that countries setting up a sentinel system should start with a few sites and evaluate their effectiveness, before expanding the system. A small number of sites are easier to monitor, to apply corrective measures and to improve the quality of the data.

When selecting the location of a sentinel site, the following should be taken into account:

■ geographical representativeness;

■ demographic and socioeconomic attributes of the area, e.g. age, use of public and private hospitals;

■ climatic representativeness and virus activity; and

■ the presence of special groups of interest, such as vulnerable ethnic groups, and multiple catchment populations.

Minimum data elements and age breakdown

The group discussed the minimum set of data that should be collected on cases from which clinical samples are collected. This information should be feasible to collect in countries at any resource level; countries might decide to include more variables if necessary.

A brief presentation of the recommendations in the briefing note was made, with the rationale for each element.

There was general consensus on the variables listed in the briefing note. Currently, different age breakdowns are recommended in different regions and countries, which makes it difficult to compare and pool data from different countries. The age groups proposed as a standard for both ILI and SARI are 0–< 2, 2–< 5, 5–< 15, 15–< 50, 50–< 65 and ≥ 65 years. The participants agreed on these age ranges but noted that the global standard should accommodate the ranges used in existing programmes. Large programmes with a long history of data collection are unlikely to be able to change their data collection and reporting format.

For global surveillance, large categories with agreed break-points are sufficient; however, national governments might decide to use smaller groupings, depending on their demographics, which could be aggregated for global reporting. For example, countries with older populations might find it useful to have additional age groups over the age of 65 years, while countries with younger populations or with a high infant mortality rate might specifically monitor infants.

There was no general consensus on the issue of reporting by sex. Although previous data do not indicate a large difference in influenza by sex, this variable could provide information on factors such as health-seeking behaviour or social networks. It was noted that WHO policy is generally to break data down by sex.

The consensus was that either the total number of medical consultations (or admissions in the case of SARI) or the total population could be used as a denominator for aggregated counts of ILI or SARI cases. Another proposed indicator was the proportion of SARI cases in which influenza virus is found.

Additional recommendations were:

■ The same kind of data should be collected for patients with ILI and SARI.

■ Information should be collected on vaccination status.

■ A distinction should be made between sentinel and other data, to make the date more reliable and to improve consistency, so that it can be used for research purposes. This might require changes in the way FluNet data are reported.

■ The location at which a patient was infected should be included, although this might not be covered in most standard systems.

■ Additional signs and symptoms could be included, such as measured fever and respiratory rate, to ensure that patients meet the case definition. The measured temperature is an important data element in SARI cases to allow comparison with data collected before the changes in case definition.

■ Smoking could be added to the list of risk factors as an option.

■ SARI-related deaths should be reported, although prospective reporting of individual cases is time-consuming, labour-intensive and not feasible in most programmes.

Duration of surveillance

It was recommended that all Member States conduct some form of year-round surveillance. In temperate countries in which influenza seasonality is well defined, routine data collection could be restricted to the influenza season, with additional event based surveillance between seasons to monitor outbreaks or other unusual events. In tropical countries that do not have well-defined influenza seasons and where transmission is sometimes continuous, year-round surveillance with routine data collection is more important.

Surveillance data collection methods

At surveillance sites with large patient volumes, it may not be feasible to test and collect data on every ILI or SARI case. In order to avoid bias in selection of cases and to have a representative dataset, a method must be available for choosing patients. This session was devoted to discussing sampling methods for selecting patients with ILI or SARI for further laboratory testing and data collection.

The working group and plenary agreed that countries should determine a sampling method on the basis of their surveillance objectives and capacity. The manual should therefore present the advantages and disadvantages and the limitations of the various sampling methods. The strategies that should be discussed are:

■ Random selection:
— Advantage: provides most representative sample
— Disadvantage: difficult to implement; more suited for research

■ Systematic interval sampling:
— Advantage: provides reasonably unbiased sample when done appropriately
— Disadvantage: easier than random sampling but still complicated, requiring record-keeping and dedicated staff; some methods are easier than others (e.g. collecting all cases on alternate days of the week).

■ Ad hoc:
— Advantage: easy to use
— Disadvantage: Least desirable, as it results in biased sampling because of differences in health-seeking behaviour by groups at different risks.

In order to ensure accurate identification of risk groups, the system must avoid bias in the selection of cases. The manual might include recommendations for sampling groups of special interest, such as vulnerable populations. It was noted that ethical issues might be involved in choosing one group over another.

With regard to the amount and extent of data collection, the manual should include a discussion on the minimum number of samples, even if it does not make a clear recommendation.

The appropriate time frame should also be stated, e.g. for up to 7 or 10 days after onset.

Baseline and epidemic threshold

The baseline influenza activity is the level between seasons. When the baseline is exceeded, a seasonal epidemic of influenza has arrived. The baselines currently in use usually consist of confidence intervals, within which seasonal epidemics occurred in the past; however, a wide variety of methods are used to calculate baselines and epidemic thresholds.

Dr Alexander Burmaa described an example of calculating a baseline and a threshold, by comparing a normal influenza season with one with high influenza rates used in Mongolia.

In general, the meeting participants considered that use of a baseline or threshold is useful in a surveillance system, as baselines can be used to communicate the level of influenza activity to clinicians, media and the public. A simple, clear method for calculating a baseline would be the ideal; however, given the different types of data and different patterns of influenza activity globally, it might be difficult to standardize methods. Establishing seasonal baselines in tropical regions is particularly problematic, as many years of data are required to calculate a reliable baseline and epidemic threshold.

The meeting recommended that the manual include an explanation of the methods that can be used under different circumstances.

Monitoring and evaluation

A surveillance system must be monitored regularly in order to ensure the consistency and quality of the data and to fully understand trends in the data. Monitoring and evaluation of a system ensures that the objectives are being met and allows the administrators to address issues that are identified in system performance, data production, staff training, site performance or any of the many problems that can occur in a surveillance system.

Maria Tereza Costa Oliveira described the sentinel surveillance system for ILI and SARI in Belo Horizonte (Brazil).

The participants stressed the importance of continuous monitoring and evaluation of surveillance systems and generally agreed to the recommendations made in the briefing note. They noted, however, that the intervals for monitoring and evaluation vary from country to country. For example, newer systems might report less frequently, requiring less frequent evaluation. The variables to be measured routinely in a monitoring and evaluation system are timeliness, completeness, validity, sensitivity and consistency of reporting.

An additional aspect of system monitoring is to observe any aberrations in the data, i.e. a pattern that is different from that expected, which might indicate problems in the surveillance system or events that require further investigation.

A detailed evaluation should be conducted before a surveillance system is expanded, in order to ensure that the sentinel sites are functioning and the system is well established. It could include a review of admissions records, an evaluation of the application of case definitions and completeness and a review of the timeliness of transport of laboratory samples.

3. Outcome of discussion on tools for global surveillance

The Global Influenza Programme has two Internet tools for reporting the results of global influenza surveillance: FluNet and FluID. FluNet provides information on circulating influenza viruses, and FluID contains epidemiological data on influenza. FluNet (**www.who.int/flunet**) is the interactive data reporting, query and mapping system of the Global Influenza Surveillance Network, which has been used since 1996. The influenza data entry fields, interface and analysis functions of FluNet are being updated in the light of new techniques and new surveillance requirements, in collaboration with the WHO regional offices and the Global Influenza Surveillance Network.

FluID (**www.extranet.who.int/fluid**) is a platform for collecting epidemiological data on influenza. It is flexible, in that it includes the data that are available at country level, such as qualitative assessments of ILI, acute respiratory infection, SARI, pneumonia or mortality rates. The system is being pilot-tested and further developed.

The Global Influenza Programme asked the participants to recommend ways in which the reporting of information to Member States could be improved, including the main focus of information from WHO and the input of influenza surveillance data globally. The participants said that, in broad terms, countries require regular information on circulating viruses (especially from neighbouring countries) and the spread of different strains; interpretation of global influenza trends, with detailed information on regional situations; and information on severity. The information that countries found most useful were:

■ the bi-weekly situation updates, specifically the executive summaries;

■ lists of circulating viruses, including from neighbouring countries, giving the dominant virus among those tested;

■ maps and pie charts; and

■ the EzCollab network site and email messages with alerts about new web updates, new recommendations and virological findings of interest.

Participants suggested that an integrated virological and epidemiological data collection tool would facilitate data entry and reporting. Nevertheless, contributing data to global surveillance should not prevent the publication of new, relevant data. Furthermore, sharing of sensitive data sometime requires approval from ministries of health.

The main obstacles to data entry are insufficient human resources (trained personnel, use of staff time) and problems of Internet connectivity. It might be possible in the future to use new technology, such as mobile phones and hand-held devices.

It was agreed that qualitative indicators are useful and informative, but more guidance in their use is required. For example, it is difficult to judge impact and intensity from such data, and use of quantitative cutoffs might be considered.

Proposals for improving the information reported back to Member States included:

■ provision of risk assessments, with information on severity (mortality, proportion of hospitalizations, hospital deaths), which would, however, depend on the input to FluID;

■ trends broken down by age group, with age-specific rates of influenza;

■ data on resistance to antiviral agents;

■ data from sentinel and other data for calculating percentage positivity;

■ geographical spread and timing of epidemics;

■ information on mortality;

■ epidemiological information the number of cases of SARI admitted for intensive care and baselines and thresholds;

■ the antigenic characteristics of the viruses before the end of the season; and

■ information on other respiratory viruses.

Suggestions were made for improving the presentation of information. For instance, the bi-weekly updates should include more graphics and less text, and information should be provided in more languages. Dynamic maps would give a global picture with the possibility of focusing on certain areas; they could include regional data in large countries.

The WHO website and web report could include links to regional office websites, sites of ministries of health and other useful summary sites. Any sensitive information could be shared on secure platforms, such as focal points for the International Health Regulations, ministries of health and electronic distribution lists. The WHO website could also include links to relevant guidance and information documents on influenza. It would be useful, for example to have:

■ a summary of how surveillance is working, by country;

■ national vaccine policies;

■ other viral infectious diseases, especially in an outbreak;

■ recommendations for vaccination, side-effects of vaccination and the extent to which the vaccine matches the virus strain implicated in the outbreak;

■ information on risk groups such as indigenous people;

■ a glossary; and

■ information on the data (e.g. number of countries reporting).

Information should be updated a minimum of every 2 weeks. E-mail alerts on unusual events, such as a mutation of clinical importance, should be sent immediately and might include recommendations for action.

The group made the following suggestions for the reporting tools:

■ The reporting should continue to be weekly and from the national level, with the possibility for sub-national data for very large countries like China.

■ As denominators, either population or number of patient visits/admissions should remain possible and consideration be given to reporting of admissions for intensive care management.

■ Countries should be able to send data through institutional software that links country or regional databases with FluNet and FluID.

■ Distinction should be possible between samples collected within a surveillance system and random clinical samples.

■ Information on other viruses such as respiratory viruses, adenoviruses and parainfluenza should be considered for addition to the data collection system.

■ Data on resistance to antiviral agents be included.

■ Links between the epidemiological data and the virological results should be made.

Clearer instructions are needed about how to enter qualitative data into FluID. Reporting mortality due to pneumonia and influenza is complicated in some locations and recommendations should be made on how to use the *International Classification of Diseases Codes* for reporting.

The Global Influenza Programme will finalize the manual and review the electronic reporting tools on the basis of the recommendations of the meeting.

World Health Organization

Global Alert and Response (GAR)

fluID
FLU INFORMED DECISIONS

A global influenza epidemiological data sharing platform

FluID is a global platform for data sharing that will link regional influenza epidemiological data into a single global database.
The platform provides connections between existing databases and can also be used to directly enter data through a web-based interface, if desired.
It complements the existing virological data collection tool FluNet.

The platform will accommodate both qualitative data and quantitative data which will allow the tracking of global trends, spread, intensity, and impact of influenza.
These data are made freely available to health policy makers in order to assist them in making informed decisions regarding the management of influenza.

Currently FluID is in a pilot test phase. The tool links with one regional database and allows countries to enter epidemiological data online directly. These data can be accessed instantly for individual countries. Global summary maps and charts will be made available as more countries and regions come online.

learn more about FluID
pdf, 301kb

How to sign up?

1. create a user account
2. complete the country set up document
3. send us your completed form as well as your username

(material and contact are provided in the right column)

access FluID

Related links

Latest influenza update

Previous influenza updates

FluNet

FluID material

Create a user account

Country set up document
pdf, 242kb

Quick reference card
pdf, 83kb

Guidance on qualitative indicators

Contact us
Please contact us by e-mail
fluid@who.int

ANNEX 1

Agenda, list of participants and working groups

Agenda

Welcome and opening remarks: Sylvie Briand, Wenqing Zhang and Anthony W. Mounts

Theme: Standards for global surveillance of influenza

- Current status of the manual: way forward: Siri Helene Hauge
- Surveillance strategy: Justin Ortiz
- Sentinel site selection: Ahmed Rguig
- Minimum dataset: Mark Katz
- Qualitative indicators: Evaluation of qualitative data: Nusrat Homaira

Plenary discussion

- Case definition: John McCracken
- Case definition: Changing experience in Europe: Andrew Amato
- Sentinel SARI surveillance in the WHO European Region: Josh Mott
- Baseline/tolerance level: Burmaa Alexander
- Data sharing and data use in the WHO Region of the Americas: Otavio Oliva
- Monitoring and evaluation: Maria Tereza da Costa Oliveira

Group work on the technical briefing notes, including preparation of short presentations for plenary

DAY 2

Theme: Standards for global surveillance of influenza

- Presentations and discussion of group work on case definition
- Presentations and discussion of briefing notes

Theme : Influenza surveillance tools: current status and future directions

- FLuID (Julia Fitzner, WHO Global Influenza Programme)
- FLuNET (Maja Lievre,WHO Global Influenza Programme)
- EuroFlu (Caroline Brown, WHO Regional office for Europe)
- AMRO platform (Otavio Oliva, WHO Regional Office for the Americas)
- Early warning systems (Angela Merianos, WHO Regional Office for the Americas)

Questions and discussion

Theme: Needs for the global surveillance tools: focus on output

- Group work: expectations of a global system

DAY 3

Theme: Tools for global surveillance: focus on data input

- ■ Group work: needs for data input
- ■ Summary of group work
- ■ Summary of data input and data output group work

Plenary discussion

Closing remarks and closure of meeting (Maged Younes and Anthony Mounts)

Participants

Michael Adjabeng, Ghana Health Services, Accra, Ghana

Henry Akpan, Federal Ministry of Health, Abuja, Nigeria

Salah Al Awaidy, Ministry of Health, Muscat, Oman

Said Al Baqlani, Ministry of Health, Muscat, Oman

Ivan Allende, Ministry of Public Health and Social Welfare, Asunción, Paraguay

Burmaa Alyeksandr, National Center of Communicable Diseases, Ulaanbaatar, Mongolia

Andrew Amato, European Centres for Disease Prevention and Control, Stockholm, Sweden

William Kwabena Ampofo, University of Ghana, Accra, Ghana

Barnabas Bakamutumaho, National Influenza Center, Entebbe, Uganda

Amal Barakat, National Institute of Hygiene, Rabat, Morocco

Edgar Gildardo Bautista, National Institute of Respiratory Diseases, Mexico

Eldonna Boisson, Caribbean Epidemiology Centre (CAREC/PAHO/WHO), Port of Spain, Trinidad-and-Tobago

Susana Marta Borroto Gutierrez, MINSAP, Havana, Cuba

Michal Bromberg, Israel Centre for Disease Control, Israel

Silke Buda, Robert Koch Institute, Berlin, Germany

Wallace Bulimo, Kenya Medical Research Institute, Nairobi, Kenya

Maria Tereza da Costa Oliveira, Municipal Health Secretariat, Minas Gerais, Brazil

Malinee Chittaganpitch, Ministry of Public Health, Nonthaburi 11000, Thailand

Sylvia Guerra, Ministry of Public Health, Montevideo, Uruguay

Jean-Michel Heraud, Institut Pasteur, Antananarivo, Madagascar

Nusrat Homaira, Respiratory Viruses Cluster, Dhaka, Bangladesh

Huang Sue Qui, Environmental Science and Research, Upper Hutt, New Zealand

Mark Katz, Kenya Medical Research Institute, Nairobi, Kenya

Shashi Khare, National Center for Disease Control, Delhi, India

Issa Makumbi, Ministry of Health, Kampala, Uganda

Margaret McCarron, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America

John McCracken, Centers for Disease Control and Prevention, Regional Office for Central America and Panama, Guatemala

Alla Mironenko, Academy of Medical Sciences of Ukraine, Kiev, Ukraine

Alain Moren, Epiconcept, Paris, France

Joshua Adam Mott, WHO Regional Office for Europe, Copenhagen, Denmark

Philip M. Muthoka, Ministry of Health, Nairobi, Kenya

Angus Nicol, European Centres for Disease Prevention and Control, Stockholm, Sweden

Sonja Olsen, Ministry of Public Health, Nonthaburi, Thailand

Justin Ortiz, University of Washington Medical Center, Seattle, Washington, United States of America

Paba Palihawadane, Ministry of Health, Colomb, Sri Lanka

Richard Pebody, Health Protection Agency, London, United Kingdom

Helena Rebelo de Andrade, National Institute of Health, Lisbon, Portugal

Ahmed Rguig, Ministry of Health, Rabat, Morocco

Anil Samaranayake, Ministry of Health, Colombo, Sri Lanka

Mukunda Sharma, Ministry of Health and Population, Kathmandu, Nepal

Anand Kumar Shrestha, Ministry of Health and Population, Kathmandu, Nepal

R.S. Shukla, Ministry of Health, New Delhi, India

Elizaveta Smorodintseva, WHO National Influenza Center, Research Institute of Influenza, St. Petersburg, Russian Federation

Christoph Steffen, Agence de Médecine Préventive, Ferney-Voltaire, France

Maha Talaat, Naval Medical Research Unit No. 3, Cairo, Egypt

Olga Tarkhan-Mouravi, National Center for Disease Prevention and Control, Tbilisi, Georgia

Marc-Alain Widdowson, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America

Thitipong Yingyong, Ministry of Public Health, Nonthaburi, Thailand

Khatuna Zakashvili, National Center for Disease Prevention and Control, Tbilisi, Georgia

Laurentiu Zolotusca, Ministry of Health, Bucharest, Romania

WHO Secretariat

WHO Regional Office for Africa: Adama Berthe

WHO Regional Office for the Eastern Mediterranean: Martin Opoka

WHO Regional Office for Europe: Caroline Brown. Josh Mott

WHO Regional office for the Americas: Otavio Oliva

WHO Regional Office for the South-East Asia Region: Zobaidul Haque Khan

WHO Regional Office for the Western Pacific: Jeffrey Partridge

WHO Lyon: Pierre Nabeth

WHO headquarters: Cindy Aiello, Terry Besselaar, Anna Bowman, Sylvie Briand, Patrick Briand, Hien Doan, Sayora Esser, Melodie Fadriquela, Julia Fitzner, Varja Grabovac, Sandra Garnier, Rebecca Harris, Siri Helene Hauge. Siddhivinayak Hirve, Vernon Lee, Maja Lievre, Carsten Mantel, Sara Martins, Claire McMillan. Angela Merianos, Anthony Mounts, Charles Penn, Nikki Shindo, Maged Younes, Kaat Vandemaele, Philippe Velstos, Stephane Vouillamoz, Lara Wolfson, Wenqing Zhang

Working groups

1. Case definitions
   Chair: Richard Peabody
   Facilitator: Siddhi Hirve
   Members: Michael Adjabeng, Henry Akpan, Said Al Baqlani, Sylvie Briand, Caroline Brown, Silke Buda, Shashi Khare, John McCracken, Anthony W. Mounts, Sonja Olsen, Anil Samaranayake, Azzouz Samri, Nikki Shindo, Olgha Tarkhan-Mouravi, Thitipong Yingyong, Wenqing Zhang

2. Selection and location of sentinel sites
   Chair: Eldonna Boisson
   Facilitator: Josh Mott
   Members: Ivan Allende, Barnabas Bakamutumaho, Susana Maria Borroto Gutiérrez, Patrick Briand, Wallace Bulimo, Zobaidul Haque Khan, Issa Makumbi, Carsten Mantel, Paba Palihawadane, Mukunda Sharma, Christof Steffen, Kaat Vandemaele

3. Minimium data elements and breakdown by age
   Chair: Andrew Amato
   Facilitator: Mark Katz
   Members: Burmaa Alexander, Edgar Gildardo Bautista, Malinee Chittaganpitch, Julia Fitzner, Belinda Hall, Maja Lievre, Alla Mironenko, Pierre Nabeth, Paba Palihawadane, Ahmed Rquig, Anand Kumar Shrestha, Maha Talaat, Philippe Velstos, Stephane Vouillamoz, Khatuna Zakshvili

4. Surveillance data collection methods
    Chair: Helena Rebelo de Andrade
    Facilitator: Justin Ortiz
    Members: William Kwabena Ampofo, Amal Barakat, Siri Helene Hauge, Jean-Michel Heraud, Claire McMillan, Angela Merianos, Alain Moren, Otavio Oliva, Martin Opoka, Jeffrey Partridge, Elizaveta Smorodintseva, Laurentiu Zolotusca

5. Baseline and epidemic threshold and monitoring and evaluation
    Chair: Maha Talaat
    Facilitator: Meg McCarron
    Members: Salah Al Awaidy, Adama Berthe, Michal Bromberg, Maria Tereza da Costa Oliveira, Sandra Garnier, Varja Grabovac, Silvia Guerra, Nusrat Homaira, Philip M. Muthoka, Tim Nguyen, Angus Nicoll, R.S. Shukla, Marc-Alain Widdowson, Lara Wolfson

ANNEX 2

Timeline of discussions on the manual

With the influenza epidemiology working group (52 countries in the six WHO regions):

Discussions on the platform (date posted):	
Case definitions	21 July 2010
Age breakdown	13 August 2010
Selection of sentinel sites	13 October 2010
Qualitative indicators	17 November 2010
Sampling methods	19 January 2011
Minimum dataset	19 January 2011
Baseline and epidemic threshold	12 February 2011
Monitoring and evaluation	12 February 2011
Revised case definition	12 February 2011

Teleconference on the briefing notes with the epidemiological working group 1 March 2011

Meeting of ad-hoc advisory group 13–16 December 2010 in Geneva with 9 members from 8 countries and participation at a distance; follow-up by distance communication

ANNEX 3

Technical briefing notes

1. Case definitions for influenza-like illness and severe acute respiratory illness

2. Selection and location of sentinel sites

3. Minimum data elements

4. Breakdown by age

5. Surveillance data collection methods

6. Baseline and epidemic thresholds

7. Monitoring and evaluation

We acknowledge the work of Mark Katz, Justin Ortiz, Meg McCarron, Tamara Meerhoff, Sidddhi Hirve, Josh Mott, Celia Woodfill, Alexander Burmaa and Maria Tereza da Costa Oliveira in preparing these briefing notes.

1. Case definitions for influenza-like illness and severe acute respiratory illness

In order that data from one country can be understood in the global context or be comparable with that from other countries, one case definition should be used. A common case definition allows comparisons of data among regions and countries and over time. A surveillance case definition is not meant to be a complete clinical description of influenza for diagnostic purposes but rather a tool to ensure comparable data over time and across regions.

One of the main challenges in influenza surveillance is the wide clinical spectrum of the disease. The symptoms observed are often nonspecific and are similar to those of not only influenza but also respiratory diseases caused by other microbiological agents. No single symptom or group of symptoms will cover all cases of influenza infection or those seen in influenza patients. This uncertainty poses challenges both for diagnosing influenza and for surveillance and has resulted in a plethora of case definitions.

In addition, severe influenza often presents as an atypical illness, and certain subgroups of patients might not show the classical signs and symptoms of influenza-like illness (ILI). This is especially true in the most vulnerable people, such as those at the extremes of age (infants and the elderly) and those with chronic medical problems. Studies of disease burden in China (Hong Kong Special Administrative Region), the United States of America and other industrialized countries indicate that about three quarters of cases of severe influenza and influenza-related deaths are not recognized as respiratory illness but are classified according to the underlying condition that placed the patient at risk, such as congestive heart failure, chronic lung disease, asthma or diabetes.[1,2]

In surveillance, it is not necessary to identify every case of a disease, as the main purpose is to observe trends, describe patterns of risk and estimate impact. The surveillance definition must, however, cap-

---

[6] Wong CM et al. Influenza-associated hospitalisation. *Hong Kong Medical Journal*, 2009; 15(Suppl 9):35–37.
[7] Barker WH, Mullooly JP. Underestimation of the role of pneumonia and influenza in causing excess mortality. *American Journal of Public Health*, 1981; 71:643–645.

ture a (stable) portion that is representative of the whole. The proportion of the total that is missed by use of a particular surveillance definition can be estimated by extrapolating surveillance data to obtain an estimate of the total number of cases and subtracting the representative portion.

Several factors should to be considered in making or changing a case definition:

- the objectives of the surveillance (for example, timely detection of outbreaks, estimating burden of disease, modelling) and how a new case definition would effect these objectives;

- existing case definitions and their strengths and weaknesses;

- the feasibility and economic implications of changing case definitions, including the flexibility of surveillance systems;

- the sensitivity and specificity of the definition and the relation between the two; and

- the positive and negative predictive value of the case definition.

Sensitivity and specificity

A surveillance case definition will never capture all cases of a disease (the sensitivity will be lower than 100%). A highly sensitive case definition will capture a larger proportion of the total cases but will also pick up many cases due to other microbes. A highly specific case definition will mean that a larger proportion of tested cases will be positive but that a smaller proportion of the actual total number of cases is identified.

A highly sensitive case definition may result in clinical and epidemiological data with a lot of nonspecific 'noise', so that it is difficult to detect patterns due to influenza. The reduced sensitivity of a more specific system, however, may raise the epidemic threshold, signalling a delayed start of the seasonal activity. Therefore, it is important to achieve the right balance with an appropriate case definition.

The implications of increasing the sensitivity therefore are:

- a larger proportion of all cases is captured, including atypical presentations;

- a smaller proportion of tested samples are positive;

- a greater work load for laboratories for same number of positive tests; and

- a higher total number of positive results, as more people are tested.

The implications of increasing the specificity are:

- more accurate data, in that more cases will be due to influenza viruses and fewer to other respiratory agents;

- not enough cases to provide useful information on outbreaks and risk groups;

- a lower workload for laboratories, as there are fewer patients to sample;

- a risk of not identifying atypical influenza presentations and patients with fewer symptoms (e.g. the elderly and immunocompromised patients, who less often have fever); and

- underestimation of the actual number of influenza cases.

Although some countries use the WHO surveillance case definition, other definitions are in use. An overview of case definitions used in western Europe[1] showed that case definitions varied both between and within countries. Some countries do not have a case definition for use in influenza surveillance.

Influenza-like illness: The WHO case definition for ILI has been in use for a number of years but is not used by all Member States. It has proved valuable for tracking the rise and fall of influenza during seasonal outbreaks and for selecting clinical samples for virological testing, which are then used for

---

[1] Aguileira JF et al. Heterogeneous case definitions used for the surveillance of influenza in Europe. *European Journal of Epidemiology*, 2003; 18:751–754.

vaccine strain selection. ILI surveillance systems have not provided epidemiological data or information about severe cases. The sensitivity and specificity of the definition is 60–75%, so that 25–40% of people with influenza who are screened do not meet the criteria for inclusion with this definition. The specificity is low, from about 5% when influenza is not prevalent (that is, 95% of the people who meet the case definition actually have influenza) to 60–70% during the influenza season.[1,2] It has been shown that the most important signs and symptoms for identifying influenza are cough, fever, myalgia and fatigue.[1,2,3,4,5] Importantly, sore throat has been found in some studies to be a negative indicator of influenza, so that people with a sore throat are likely to have an illness other than influenza.

Severe acute respiratory infection: The surveillance case definition for SARI in adults has been in use since it was defined by the Pan American Health Organization in 2005. The intent of the definition was to capture the severe end of the spectrum of influenza, including cases without associated pneumonia. The definition is meant to cover patients with congestive heart failure or chronic lung disease, for example, whose underlying illness is exacerbated by influenza. As noted above, non-pneumonia cases probably represent the large majority of the burden of severe disease related to influenza. For children under the age of 5 years, the clinical case definition for pneumonia used by the Integrated Management of Childhood Illnesses (IMCI) programme, or some version of it, was adopted. This definition is known to be relatively nonspecific for radiographically confirmed pneumonia and was therefore considered to be an acceptable definition, which would capture both pneumonia caused by influenza and other respiratory disease related to influenza (e.g. exacerbation of asthma triggered by influenza and requiring hospitalization).

The sensitivity and specificity of the SARI case definition have been evaluated.,, Overall, hospitalized patients with laboratory-confirmed influenza have the same spectrum of respiratory symptoms as outpatients with ILI, but the ILI case definition is in general less sensitive for hospitalized patients than for outpatients. Fever is reported less frequently in SARI patients than in outpatients. Inclusion of measured fever results in a relatively specific but insensitive case definition, while inclusion of history of fever increases sensitivity but decreases specificity. As noted above, an increase in sensitivity increases the number of cases to be tested and captures a larger proportion of the disease burden due to influenza but decreases the likelihood that a test will be positive. More tests must therefore be done to result in the same number of positive samples.

1 Kasper MR et al. Evaluation of an influenza-like illness case definition in the diagnosis of influenza among patients with acute febrile illness in cambodia. *BMC Infectious Disease*, 2010; 10:320.

2 Monto AS et al. Clinical signs and symptoms predicting influenza infection. *Archives of Internal Medicine*, 2000; 160:3243–3248.

3 Boivin G et al. Predicting influenza infections during epidemics with use of a clinical case definition. *Clinical Infectious Diseases*, 2000; 31:1166–1169.

4 Lambert SB et al. Influenza surveillance in Australia: we need to do mroe than count. *Medical Journal of Australia*, 2010; 193:43-45.

5 Call SA et al. Does this patient have influenza? *Journal of the American Medical Association*, 2005; 293:987–997.

6 Babcock H, Merz LR, Fraser V. Is influenza an influenza-like illness? Clinical presentation of influenza in hospitalized patients. *Infection Control and Hospital Epidemiology*, 2006; 27:266–270.

7 Babcock HM et al. Case–control study of clinical features of influenza in hospitalized patients. *Infection Control and Hospital Epidemiology*, 2008; 29:921–926.

8 Jeung I et al. Mild form of 2009 H1N1 influenza infection detected by active surveillance: implications of infection control. *American Journal of Infection Control*, 2010; 38:482–485.

Suggestions for new case definitions of ILI and SARI

CURRENT CASE DEFINITIONS	PROPOSED CASE DEFINITIONS
ILI:[a,b] sudden onset of fever > 38 ºC and cough or sore throat in the absence of other diagnosis	**ILI:** an acute respiratory illness with fever ≥ 38 ºC and cough in the absence of other diagnosis
SARI:[b]	*Changes:*
Patient > 5 years: meets ILI case definition and shortness of breath or difficulty in breathing and requiring hospital admission	‘sudden’ changed to ‘acute’ ‘respiratory illness’ added > 38 ºC changed to ≥ 38 ºC ‘or sore throat’ deleted
Patient < 5 years: WHO case definition for pneumonia and severe pneumonia from the Integrated Management of ChildhoodIllness (IMCI)[c] programme. Pneumonia: any child aged 2 months– 5 years with cough or difficulty in breathing and breathing faster than 40 breaths/min (age 1–5 years) or breathing faster than 50 breaths/min (age 2–12 months). Severe pneumonia: any child aged 2 months–5 years with cough or difficulty in breathing and any of the general danger signs: unable to drink or breastfeed, or vomits everything, or convulsions, or lethargic, or unconscious, or chest indrawing or stridor in a calm child and requires hospital admission	**SARI:** *Patient > 5 years:* an acute respiratory illness with history of fever and cough *and* requiring hospital admission *Changes:* ‘sudden’ changed to ‘acute’ ‘respiratory illness’ added ‘≥ 38 ºC’ changed to ‘history of fever’ ‘or sore throat’ deleted ‘and shortness of breath or difficulty in breathing’ deleted *Patient < 5 years:* no change

[a] *WHO recommended surveillance standards.* 2nd Ed., Geneva, World Health Organization, 1999. **http://www.who.int/csr/resources/publications/surveillance/WHO_CDS_CSR_ISR_99_2_EN/en/**

[b] *Human infection with pandemic (H1N1) 2009 virus: updated interim WHO guidance on global surveillance.* Geneva, World Health Organization, 2009. **http://www.who.int/csr/resources/publications/swineflu/interim_guidance/en/index.html**

[c] *WHO IMCI chart booklet—standard*, 2008. **http://www.who.int/child_adolescent_health/documents/IMCI_chartbooklet/en/index.html**

Arguments for and against changing the case definition

ARGUMENTS FOR	ARGUMENTS AGAINST
WHO case definition has not been evaluated or changed for many years. New data should be reviewed to check the validity of the case definition.	A new case definition will create extra work and accrue costs for informing and training personnel at sentinel sites in its use.
A more accurate case definition provides more accurate data on influenza.	Influenza surveillance is not intended to identify all infections or to be highly accurate but to give an idea of activity and show trends.
One global case definition will make it easier to compare data across countries and regions.	A change in case definition will make it difficult to compare data collected before and after the change.
A global case definition will help countries with no case definition to undertake surveillance.	Many different case definitions are used, which will probably not change if a new case definition is issued.
The symptom ‘sore throat’ has low positive predictive value for laboratory-confirmed influenza and should be excluded from the case definition.	Exclusion of ‘sore throat’ from the case definition might not increase the positive predictive value enough to justify the work associated with changing the case definition.
The requirement of fever ≥ 38 ºC is too strict and causes loss in sensitivity, which could be resolved by changing ‘fever ≥ 38 ºC’ to ‘feverishness’ or ‘history of fever’. Furthermore, there is a tendency to round down to 38 ºC, resulting in loss of some cases.	Removal of the requirement for documented fever will reduce the specificity, thereby significantly increasing the workload of laboratories to find the same number of cases; it will also increase ‘noise’ in the data, making it harder to distinguish influenza outbreaks from those due to other respiratory pathogens.
As different age groups show different clinical pictures, the case definition should be age-appropriate.	Different case definitions for different age groups will make the collection of data more complicated and time-consuming.

ARGUMENTS FOR	ARGUMENTS AGAINST
'Shortness of breath or difficulty in breathing' does not add to sensitivity or specificity and may be misinterpreted by health-care workers; e.g. obstructed nasal passages could be interpreted as 'difficulty in breathing'.	No reason to change, as 'shortness of breath and difficulty in breathing' makes it clear that respiratory disease is being sought.

Summary

The suggestion is to simplify but to keep relatively specific case definitions for ILI and SARI.

Questions to be discussed by the group

1. Do you agree that the IMCI case definition for children < 5 years should be maintained?

2. Should the requirement 'shortness of breath or difficulty in breathing' be maintained in the SARI case definition?

3. What are the advantages and disadvantages of changing the case definitions of ILI and SARI?

4. Should there be different requirements in the case definitions of ILI and SARI?

5. Are there other case definitions that should be used?

2. Selection and location of sentinel sites

This briefing note addresses the following:

- definitions of 'sentinel surveillance systems', 'sentinel sites' and 'population under surveillance';

- criteria to consider in determining whether a facility could be a sentinel site for ILI or SARI surveillance;

- criteria to consider in choosing the location of sentinel sites in a country; and

- considerations for determining the number of sites to establish.

Discussion points

(1) SARI surveillance is not intended to capture all cases of hospitalized influenza. It is, however, intended as a standard for monitoring a large subset of severe influenza and can provide high-quality data on severe cases to policy-makers. It is acknowledged that influenza-associated severe illness is likely to be perceived as a higher public health priority than mild disease, and countries often give greater priority to severe illness when allocating resources for disease control and prevention. Furthermore, factors associated with severe outcomes often have a greater influence on vaccine policy and resource allocation decisions in countries. This indicates the importance of data quality and of ensuring that an adequate number of cases are captured in order to allow meaningful descriptive epidemiology of hospitalized cases. For this reason, when establishing a new system, some priority should be given to setting up sentinel sites for SARI before sites for ILI or acute respiratory infection.

(2) A sentinel site is defined as 'a single facility, a small cluster of facilities or clusters of specific wards or departments within facilities'. This definition is used because in many parts of the world there are hospitals that serve patients of specific ages (e.g. paediatric and adult hospitals) or types (e.g. separate hospitals for infectious and chronic diseases).[1] Thus, a sentinel site might consist of a cluster of small groups of facilities in order to adequately represent the population under surveillance. In some places, the same may also be true for outpatient surveillance.

---

[1] *WHO European Regional guidance for influenza surveillance in humans*. Copenhagen, WHO Regional Office for Europe, 2011:14. **http://www.euro.who.int/__data/assets/pdf_file/0020/90443/E92738.pdf**

Counterpoint: An alternative approach is for a sentinel site to be associated with a specific facility, and several sites might be grouped to form 'sentinel units' to achieve better representativeness. An advantage of this approach is that the site is associated with a single facility; a disadvantage is a requirement for more complicated terminology throughout a document.

(3) The population under surveillance should be determined on the basis of the priorities of national health authorities and their plans for using surveillance data. For example, if one goal of surveillance is to monitor the age distribution of recent cases, patients surveilled at sentinel sites should proportionally represent a range of age groups or the national population. In other situations, the national influenza programme may place more emphasis on surveillance of specific groups. For example, if a programme focuses on childhood or maternal immunization, additional efforts might be made to obtain robust, representative estimates of morbidity in infants and children. Therefore, surveillance might focus on paediatric clinical facilities. If the public health objectives include reducing morbidity and mortality in the elderly, older age groups must be adequately represented.

Before selecting sentinel sites, the objectives and the priority populations under surveillance should be clearly specified, so that sites are representative.

Counterpoint: An alternative approach is to specify that the population under surveillance should represent the national population in terms of demographic and socioeconomic characteristics. An advantage approach is that, over time, if the sentinel sites are well chosen, all the systems will provide data on the age and population groups with the underlying conditions most frequently represented among hospitalized influenza cases. A disadvantage of this approach in many locations is that many years of data might be needed to demonstrate such representativity, and certain populations that are priorities for the national health authorities might not be well represented in short-term surveillance data.

(4) Several Member States would like to have concrete guidance on the appropriate number of sentinel sites. The number and type of sentinel site depends on the goals of the surveillance system. As a general guide, ILI and acute respiratory infection surveillance systems in Europe and North America consist of 1–5% of physicians working in appropriate practices in the country or region. For surveillance of hospitalized cases of SARI, however, there is no ideal number of sentinel sites, nor is there a single algorithm for determining an appropriate initial number of sentinel sites (e.g. number of sites per million population), because of wide variations in national population sizes, the geographical distribution of populations and the resources available for hospital-based sentinel surveillance.

For example, the population of country X, which initiated SARI sentinel surveillance with 10 sentinel sites, is 140 million. Application of the very conservative rule of 'one SARI sentinel site for every 5 million population' would mean that the number should be increased to 28; however, this should not be undertaken until the current sites, data, financing and laboratory systems have been appropriately evaluated. Many countries with populations of 5 million or fewer would interpret this rule to mean that they require only one sentinel site, even though they may have resources and wish to better represent their populations in the sentinel surveillance system. A similar problem might arise by specifying that a certain number of sentinel sites should be at the 'first administrative level' of a country, as the definition of this level varies widely with respect to the number, size and resident population.

In a second example, country Y might have a population of 7 million, with large areas that are sparsely populated and populations living in widely different climatic zones or latitudes. Placing one or two sites in the capital city would meet a standard for an 'optimal' number of sentinel sites, but the sites might not represent all the populations in the different geographical regions of the country.

When establishing a system, it is important not to set up more sites than can be offered effective training and then closely monitored to ensure production of a manageable amount of high-quality, complete data. Once a sentinel system has been established, more sites should not be added until the existing sites have been routinely monitored and evaluated to determine that the data they produce are sufficient for surveillance.

Counterpoint: An alternative would be to state arbitrary minimum numbers of sentinel sites needed. An advantage would be that countries would not expand surveillance too quickly and better assure high

data quality. A disadvantage is that the number will inevitably be too high for some countries and too low for others.

(5) Feasibility is one of the most important criteria in evaluating facilities for their suitability for participating in a sentinel system. Other criteria include patient representativeness, the availability of numerators and denominators and adequate patient volume. Feasibility is defined as the availability of the infrastructure and support necessary to ensure efficient collection and transport of clinical specimens, routine adherence to case definitions, high-quality data collection and management and timely reporting of surveillance results. Human resources and administrative commitment are required to implement and sustain surveillance, and technical resources are required to ensure high-quality specimen and data collection, timely analysis and reporting.

If the initial sentinel site(s) selected to participate are not located in places where local staff and administrators support the site's participation in the system, or if basic adherence to case definitions or collection of data are not maintained, the entire system may fail. Even if the initial sentinel sites selected for participation in the surveillance system are not fully representative of the population being surveilled, motivated staff and suitable infrastructure can result in successful demonstration of the sentinel surveillance concept. Representativeness can be improved over time with the addition of new sentinel sites, but only if the system is shown to work at the initial site(s).

For example, in country Z, the initial SARI sentinel sites were established at large private hospitals in the capital city; however, the hospital administrators were willing to collect data only on 'what is mandated by law'. In addition, lack of access to administrative records, a large volume of cases and the lack of a dedicated surveillance coordinator at the hospital meant that only those few SARI cases that were tested for influenza could be recorded. The system essentially amounted to a virological surveillance system with no meaningful epidemiological component and included no numerators or denominators for monitoring trends. After 4 years of trying to improve surveillance at this hospital, country Z is now considering starting SARI sentinel surveillance at smaller hospitals in other populated areas, which have staff and administrators who are better able to devote time and resources to sentinel surveillance.

(6) Additional criteria for selecting sentinel sites are demographic representativeness and the availability of numerators and denominators. The former is essential for ensuring that the surveillance system provides information about the population under surveillance; the latter is necessary to ensure that the data can be used to monitor trends and the intensity of respiratory disease activity routinely. Data on hospital admissions for any cause in the wards under surveillance (for SARI) or total consultations on the days of surveillance (for ILI) could be used as a minimum standard surveillance denominator.

At many sentinel sites, it may not be possible to estimate a population denominator for calculating incidence rates, although sites should be selected on the basis of the theoretical possibility of determining the denominator in the future. If sites are also selected on the basis of ease of access to medical records, total hospitalizations and consultations for all causes can be used to establish a minimum standard monitoring indicator based on 'proportional morbidity'. If a large referral hospital is being considered as a SARI sentinel site, the catchment population may not be ascertainable. In this case, careful consideration must be given to the feasibility of complete ascertainment of SARI cases and of total hospitalizations for all causes in the wards under surveillance.

Counterpoint: It could be argued that sentinel sites should be selected only if they are in locations where the population catchment area can be estimated and incidence rates calculated (e.g. hospitals located in demographic surveillance sites or outpatient clinics with well-defined patient lists). An advantage of this approach is that a comparison of incidence rates (if accurately estimated) with the percentage of total admissions for SARI (or total consultations for ILI) is a more stable indicator of respiratory disease in a population, because it is not influenced by fluctuations in the number of hospital admissions not attributable to SARI (or consultations not attributable to ILI). This will also result in a more solid estimate of the burden of disease. A disadvantage is that the approach will result in elimination of many hospitals or clinics that the national surveillance authorities consider are priorities for surveillance, while monitoring proportional morbidity can identify both mild and severe cases of influenza over time. The

proportion of hospitalizations due to SARI and SARI confirmed to be influenza is in itself an estimate of burden.

(7) The records of any facility or group of facilities under consideration as a sentinel site should be reviewed to determine that there will be a sufficient number of patients with respiratory disease during the influenza season for meaningful monitoring of trends in respiratory disease in priority populations. The size of a facility or group of facilities that comprise a sentinel site should therefore strike a balance between having enough cases to monitor trends, viruses and epidemiology in priority populations and the feasibility of routinely detecting all cases that meet the surveillance case definition.

In reviewing records to determine whether a possible sentinel site has enough severe cases of influenza to monitor SARI trends in the priority population reliably, it might be assumed that 15% of all cases of SARI (or hospitalized severe respiratory disease) during an influenza season (weeks 40–20) and 30–50% of SARI cases during the peak month of influenza season will test positive for influenza by polymerase chain reaction.[1]

(8) Demographic representativeness and geographical and climatic representativeness should be considered in deciding on the location of sentinel sites. The population served by the sites should be representative of the age and socioeconomic groups in the population under surveillance. As influenza virus activity varies with latitude, longitude and climate,[2] consideration should be given to representing several populations in different parts of the country. In addition, sentinel sites might be chosen in populated areas in different climatic regions of a country, if this is feasible logistically.

Questions to be discussed by the group

1. What are the criteria for selecting facilities to act as sentinel sites?

2. What are the criteria for the location of sentinel sites?

3. How many sentinel sites are needed, and when should the system be expanded?

3. Minimum data elements

This briefing note suggests the minimum dataset to be collected and reported in the surveillance system at a local level. A country may choose to extend data collection with more variables. Each country will usually report a smaller dataset, with fewer variables, to WHO. The data to be reported are discussed in a later section.

ILI surveillance data

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; and

■ 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.

---

[1] EuroFlu. Weekly surveillance bulletins, 2010–2011 influenza season (**www.euroflu.org**).

[2] Viboud C, Alonso WJ, Simonsen L. Influenza in tropical regions. *PLoS Medicine*, 2006; 3:e89. doi:10.1371/journal. pmed.0030089.

SARI surveillance data

The minimum SARI surveillance data to be sent weekly from the sentinel sites to the national health authorities are:

- 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 and

- 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 age group and sex.

These are the minimum data required for determining syndromic trends in health-care facilities. The total number of cases sampled allows hospital to follow trends in influenza-associated hospitalization once the results of testing are available. Total hospital admissions allow sites to determine the relative contribution of SARI to all hospitalizations.

Sites need not follow SARI patients prospectively but simply tally and report the total number of SARI-related deaths every week. This can be done daily or weekly from the available hospital data. Records of SARI-related deaths allow identification of outbreaks of respiratory diseases with high mortality.

Tracking trends in the proportion of hospitalizations due to SARI helps policy-makers to understand the severity of an influenza season in relation to previous seasons and gives an indication of the contributions of influenza and other respiratory pathogens to the burden on hospitals.

Data on SARI patients are used to understand the epidemiology of influenza-associated SARI and to identify risk groups. The data to be collected on ILI and SARI patients from whom clinical specimens are collected for laboratory testing are:

- unique identifier

- gender

- age

- temperature

- date of onset

- date of specimen collection

- seasonal influenza vaccine status

- antiviral use

- comorbidity

- other comorbid conditions in accordance with national priorities

- pregnancy status

- travel history (optional)

For comorbidity, the WHO standardized list of comorbid conditions is used, based on data on seasonal and pandemic influenza comprising both known and suspected risk factors for severe influenza infection. The conditions are: chronic respiratory disease, asthma, diabetes, chronic cardiac disease, chronic liver disease, chronic renal disease, chronic neurological or neuromuscular disease, and immunodeficiency, including HIV infection.

Optional additional risk factors

Strongly suspected but as yet unproven risk factors: As new data emerge, other conditions, such as obesity, have been proposed as risk factors for severe disease. Members of some indigenous popula-

tions and other socially defined groups have been found to have higher rates of hospitalization and death than the rest of the population. These factors have not yet been shown definitively to increase the risk for severe outcomes independently of accepted risk factors, such as chronic medical illnesses. Therefore, obesity and other suspected but unconfirmed risk factors should be reported separately.

Other health factors of concern: Certain medical conditions that are highly prevalent in some parts of the world, such as tuberculosis, malnutrition and malaria, may increase the risk for ILI and SARI, but few studies have been conducted to support this suspicion. If there is interest in other potential comorbid conditions, data could be collected on body mass index, tuberculosis and malnutrition.

Health conditions not known to increase risk: Reporting of data on risk factors is sometimes complicated by the inclusion of other common chronic medical conditions that have not been associated with severe disease, such as hypertension in the absence of associated heart disease, smoking in the absence of associated lung disease and hyperlipidaemia in the absence of associated cardiovascular disease. As inclusion of these conditions complicates interpretation of data on risk factors, they should not be reported routinely with influenza data, although they could be collected for special studies and reported separately.

Frequency and seasonality of data collection

Epidemiological and virological data collected from sentinel sites should be reported to the national health authorities every week. In temperate climate zones where influenza seasonality is well established, data should be collected and reported during the known influenza season and for periods around the season. For example, in temperate climates in the northern hemisphere with clear seasonality, surveillance could be performed during epidemiological weeks 40–20. Year-round surveillance in countries with well-defined influenza seasons adds to knowledge on out-of-season influenza activity but results in additional costs and workload. The cost–benefit of this activity should be decided by each country.

In tropical and subtropical countries, unless clear seasonal patterns have been defined, data should be reported throughout the year.

Questions to be discussed by the group

1. What data should be collected from ILI patients and SARI patients, respectively? Is it feasible to collect data on sex?

2. Is it feasible to collect the suggested in resource-poor settings?

3. Should any data be added to or deleted from the list?

4. Is the list of comorbid conditions complete and relevant?

5. Should WHO recommend year-round surveillance?

4. Breakdown by age

Data on ILI and SARI should be reported by age group. Establishing uniform age groups for global reporting will facilitate comparisons and pooling of data from different countries, and age groups should be chosen to provide the best information on age-specific risk for severe disease and the impact of disease in that age group. Various age breakdowns are recommended in different regions and countries. Sentinel surveillance systems are encouraged to use the following age categories for reporting: 0 to < 2 years, 2 to < 5 years, 5 to < 15 years, 15 to < 50 years, 50 to < 65 years, ≥ 65 years.

Additional age groupings can be used within these groups in order to define narrower age patterns of influenza infection; however, they should be standardized for international data reporting.

■ Children < 5 years have a relatively high rate of hospitalization and more complications from influenza than older children and young adults.[1,2] Among children < 5 years, the incidence has been shown to be higher in children < 2 years.[3]

■ The rationale for the cut-off at 15 years is less clear; some programmes use 18 years as the cut-off. Most countries, however, use 15 years, an age at which many children leave school.

■ People aged 15–< 51 years were among the worst affected by the pandemic, in contrast to seasonal influenza seasons, in which this group is largely spared from severe disease.

■ People aged 50–64 years are at slightly higher risk for severe disease, even in developed countries, where they are more likely to have comorbid conditions that put them at risk.[4,5]

■ People aged ≥ 65 years are at high risk for morbidity and mortality from influenza.[4,6]

■ FluID accepts all data broken down into all age categories for data entry.

Examples of age breakdowns in use

WHO Regional Office for Europe: 0–4, 5–14, 15–64 and ≥ 65 years. For SARI surveillance, the groups 15–29 and 30–64 years are added.

WHO Regional Office for the Western Pacific: 0–2, 3–4, 5–17, 18–49,50–64 and ≥ 65

WHO Regional Office for the South-East Asia Region: 0–11 months, 1–4, 5–14, 15–49 and ≥ 50 years

Questions to be discussed by the group

1. Are the suggested age breakdowns appropriate?

2. Would you prefer narrower breakdowns or wider groups?

5. Surveillance data collection methods

Background

The 2009 influenza A (H1N1) pandemic raised questions about the generalizability of surveillance data across geographical areas and about interpretation of gaps in data collection. On the basis of these lessons, WHO drew up influenza surveillance objectives as a basis for the revision of its surveillance guidelines. A combination of inpatient and outpatient sentinel surveillance with integrated virological testing of specimens collected in systematically chosen cases is recommended as the most efficient method for achieving surveillance objectives.

Rationale for ILI surveillance procedures

In many countries, sampling in ILI surveillance tends to be less rigorous than in SARI. The virological data from ILI surveillance are adequate for determining the timing and geographical spread of influenza

---

[1] Neuzil KM et al. The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. *New England Journal of Medicine*, 2000; 342:225–231.

[2] Simmerman JM et al. Incidence, seasonality and mortality associated with influenza pneumonia in Thailand: 2005–2008. *PlosOne*, 2009; 11:e7776.

[3] Kasper MR et al. Evaluation of an influenza-like illness case definition in the diagnosis of influenza among patients with acute febrile illness in Cambodia. *BMC Infectious Disease*, 2010, 10:320.

[4] Monto AS et al. Clinical signs and symptoms predicting influenza infection. *Archives of Internal Medicine*, 2000,160:3243–3248.

[5] 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**

[6] Boivin G et al. Predicting influenza infections during epidemics with use of a clinical case definition. *Clinical Infectious Diseases*, 2000, 31:1166–1169.

activity in a country and for collecting isolates for virological analysis. Use only of clinical judgment to select ILI cases for specimen collection is discouraged. Despite its limitations as a surveillance definition, the incidence of ILI has been shown to correlate with influenza virological surveillance in temperate regions. To gather unbiased demographic and risk factor data on ILI cases, a sampling method such as that described above for SARI should be adopted. This would allow comparisons between data collected on mild disease managed in outpatient departments and data on more severe disease requiring admission to hospital. Some countries might choose to incorporate epidemiological and clinical data on ILI cases captured by this system to allow calculation of risk factors for influenza in outpatients.

Rationale for SARI surveillance procedures

In many low- and middle-income countries, severe influenza-associated illness is a higher public health priority than disease managed in ambulatory services, and factors associated with severe outcomes have a strong influence on vaccine policy and resource allocation. As countries often set higher priority on severe illness when allocating resources for disease control and prevention, high-quality data are needed, with adequate numbers of cases, for meaningful descriptive epidemiology of hospitalized cases of respiratory disease. Data collection and case selection methods are therefore more rigorous in SARI surveillance than in ILI surveillance. SARI surveillance does not capture all cases of hospitalized influenza; however, broadening the definition to capture more cases would result in more specimens to be tested, potentially overwhelming laboratory services in resource-constrained settings. The ideal definition and strategy would result in a sufficient number of positive cases to adequately describe the epidemiology of severe influenza, without placing a disproportionate demand on resources. While many questions relevant to health policy-makers are addressed in routine surveillance, WHO encourages centres with more resources to conduct additional scientific investigations to determine the risk factors for severe influenza virus infection, to assess the utility of alternative case definitions, to study clinical outcomes of respiratory infections and to better ascertain the burden of influenza and diseases due to other respiratory pathogens among patients seeking care. The details of studies of influenza epidemiology are beyond the scope of this document.

Selecting patients for specimen collection

Clinical specimens and epidemiological data should be collected in a manner that minimizes bias, as might be introduced by an ad hoc approach to specimen collection. Selection of the first two cases of the day or reliance on clinical judgment for case selection can result in data that are not representative of all severe cases of influenza. A specimen collection scheme that is representative, including characteristics such as age and severity of disease, and strict adherence to specimen collection criteria are preferable.

Data interpretation is facilitated if specimens are collected from all SARI cases admitted at a sentinel site, thus resulting in the least bias in case selection; however, this might not be feasible unless sites are carefully selected. Nevertheless, it is recommended that clinical specimens be collected for virological testing and epidemiological data be collected in a large proportion of SARI cases, in order to minimize selection bias. In addition to systematic selection of all SARI patients for specimen collection, some countries may choose to collect specimens from subsets (e.g. all deaths or all admissions to intensive care) if these data are a priority.

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. A register review might be necessary when selecting a site, in order to estimate the numbers of SARI and ILI patients seen throughout the year. Limited surveillance with small numbers of samples tested is unlikely to provide sufficient data for detailed risk factor analyses after one season. Over time, however, there will be an adequate sample size for more rigorous retrospective analyses of risk factors of severe disease and recognition of seasonal trends.

Methods for choosing a representative subset of SARI patients for specimen collection

As data cannot be collected for every SARI case admitted at a sentinel site, methods should be used to reduce sampling bias. The ideal system is random selection of cases; however, achieving true randomness is unlikely to be practical in a non-research setting. Nearly as good would be a systematic sampling method. The systematic method with least inherent bias is testing every 'nth' number of SARI cases, n being equal to the number of cases seen weekly at the facility divided by the maximum number of specimens that the laboratory could process weekly. For example, if a hospital admits 80 SARI patients weekly during the peak influenza season, and if the maximum weekly number of specimens that the laboratory can process is 20, a suitable systematic sampling method during the peak influenza season would be every fourth SARI case. This method might not be feasible in most settings but is ideal for minimizing bias.

A second method is to test and collect data from all patients seen on specific days of the week, such as every SARI case admitted on Tuesday or Thursday. This method has some potential bias, depending on the referral patterns and health-seeking behaviour in the community; for instance, different health-care seeking behaviour might be seen on weekends or on the first day of the working week. Nevertheless, specimen collection in every SARI case on a particular day of the week is preferable to a less structured approach, such as choosing the first few cases of the day. In order to minimize the potential for differential data collection, collection of specimens from all patients on every eighth day has been proposed.

Choosing the first few cases of the day is the most likely method for introducing bias into sampling procedures. Health-seeking behaviour may differ with age; for example, working adults are less likely to go to hospital during the early part of the day. Bias in sampling will mean that the surveillance data do not accurately represent the age distribution, risk profile, disease burden and other important epidemiological characteristics of influenza in the area under surveillance. The data are, however, still useful for monitoring seasonal trends.

When to test

Viral culture is most likely to be accurate if specimens are collected and tested within the first 3 days after onset of illness. Use of reverse transcriptase-polymerase chain reaction maintains the rates of positivity for up to 7 days after onset. For the purposes of surveillance, cases should be included for testing and data collection up to 7 days after onset; however, a programme with limited resources might consider performing culture only on cases seen within the first 3 days of onset. Reverse transcriptase-polymerase chain reaction gives laboratory results sooner than viral culture; however, viral culture is essential for antigen characterization and vaccine strain selection. Ideally, viruses are cultured from a subset of clinical specimens or specimens are transported to a reference laboratory for additional analyses.

Questions to be discussed by the group

1. When setting up a first surveillance system for influenza, would you agree that SARI should be surveilled before ILI surveillance is begun?

2. Will be it feasible to test all SARI cases in your country?

3. If it will not be possible to test all SARI cases, is the suggested sampling method appropriate?

6. Baseline and epidemic threshold

Background

Many different thresholds have been used to define the onset of an influenza epidemic, each method being based on different socioeconomic and epidemic situations. In order to harmonize the presentation of data at regional or global level, it would be useful to have a similar method for calculating a standard epidemic threshold.

The 'influenza baseline' has been defined as the level of influenza activity that is typically seen during the influenza season but outside the epidemic period. The 'epidemic threshold' is the value or percentage over that considered normal for that period and indicates the onset of the influenza season. This alert can trigger public health action, such as initiation of precautionary measures for vulnerable populations, and can stimulate case detection, clinical diagnosis and treatment with antiviral medication. Communicating the start of an epidemic to the general public can increase their awareness of influenza and severe disease caused by influenza.

Methods for defining an epidemic threshold

Methods for establishing an epidemic threshold in influenza surveillance vary from simple methods, such as drawing a line on the basis of past observations, to calculating the 5-year average date of the event with the 95% confidence interval, to more sophisticated mathematical models such as Serfling regression models. Another method, based on short-term data, time series and cumulative sum models, can generate sensitive, specific, timely alerts in both temperate and subtropical regions and is a useful alternative to Serfling-like methods, which require long-term information on past thresholds.[1]

Most of the models mentioned above are based in time series, with virus isolation or other criteria to establish a baseline non-epidemic period. A method known as the 'moving epidemic method' was designed to calculate a baseline and an epidemic threshold for countries in Europe; it is based on clinical data and the rates of ILI or acute respiratory infection for ≥ 5 years previously. The calculations can be automated, and the method can be applied to different countries, irrespective of their reporting weeks or whether they report ILI or acute respiratory infection. The method can be used to calculate a threshold for the entire season, on the basis of pre-epidemic rates and therefore results in a straight line. The program was made available in November 2010.[2]

Discussion points

With different types of data, patterns of influenza activity, surveillance systems and facilities, it may be difficult to determine a standard epidemic threshold. In general, countries are encouraged to report their epidemic threshold and how it was calculated.

Questions to be discussed by the group

1. Does your country use a baseline and threshold? If it does, do you find them useful? If it does not, could they be created?

2. To allow interpretation of data at a global level, should we limit the number of methods that can be used to define the epidemic threshold?

3. Should the manual on global surveillance of influenza recommend use of a baseline or threshold?

---

[1] Cowling BJ et al, Methods for monitoring influenza surveillance data. *Int. J. Epidemiol.* (October 2006) 35(5): 1314–1321
[2] Moving Epidemics Method R Package, by Jose E. Lozano Alonso, 2010-11-26 (**http://cran.r-project.org/web/packages/mem/mem.pdf**)

7. Monitoring and evaluation

Regular, continuous monitoring of a surveillance system is necessary in order to maximize the consistency and quality of the data being produced and to provide the best understanding of trends in the data. Monitoring and evaluation of a system ensure that its objectives are being met and allow the system administrators to address any issues in system performance, data production, staff training, site performance or any of the many problems that can occur in a surveillance system.

The functionality, efficiency and quality of surveillance systems should be evaluated before the number of sites is increased. Problems in the system should be addressed before expansion, to ensure that the existing sites are efficient and functional.

Continuous monitoring

The quality of surveillance should be monitored continuously with the use of a number of indicators and observations. Continuous monitoring can be used to evaluate:

■ the intervals in the collection and transfer of data, the timeliness of collection, transfer and testing of clinical samples and the reporting of results and summary analyses;

■ the completeness of data reporting as a reflection of data quality; and

■ aberrations in data, such as sudden, unexpected increases or decreases in the number of reported cases by monitoring unusual patterns in reported data and investigating their causes.

Continuous monitoring of a surveillance system is an added burden on the staff conducting surveillance and managing the system, both at the site and at national or central level. Continuous monitoring might appear to increase the cost of maintaining the system, because of the extra staff time it seems to take up. Nevertheless, incorporation of this activity into routine data gathering, entry, aggregation and analysis will prevent problems of incomplete data, missed outbreak indicators, irregularly functioning sites and other potential problems. Monitoring also makes staff aware of additional training needs, technical assistance or additional support.

Continuous monitoring of the completeness and timeliness of the data collected will simplify the interpretation of aberrations in the data, making outbreak indicators more obvious and providing a solid signal for when to investigate unusual results. Continuous monitoring of data quality provides good signals for changes in activities at the surveillance site and a possible indicator of a decline in the functionality of the site.

Continuous monitoring will help in:

■ identifying delays in reporting,

■ identifying training needs,

■ identifying weaknesses in data collection,

■ adherence to case definitions,

■ identifying the proportion of sentinel sites that report regularly,

■ evaluating standardized reporting of data,

■ monitoring the numerator and denominator used and

■ adherence to use of standard forms.

Influenza surveillance evaluation and recommended quality indicators were summarized by Ortiz et al.[1] as follows:

1. Timeliness

    a. Several time intervals are appropriate for routine measurement as quality indicators. These include the duration of time from
        i.   Target date for data reporting from the sentinel site to the next administrative level until the actual reporting date
        ii. Target date for data reporting from the next administrative level to the national level until the actual reporting date
        iii. Date of specimen collection at facility until shipment to laboratory
        iv. Date of result availability in laboratory until date of report to referring institution and physician
        v.   Date of receipt of specimen in the laboratory until result availability
    b. Metrics. Two metrics can be used to reflect timeliness indicators:
        i.   Percentage of time that a site achieves target for timeliness
        ii. Average number of days for each interval over time for each site

2. Completeness

    a. Percentage of reports received from each site with complete data
    b. Percentage of data reports that are received
    c. Percentage 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

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

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

    a. Number of cases reported by month for each site
    b. Number of specimens submitted by month for each site
    c. Percentage of specimens that are positive for influenza
    d. Number and percent of ILI and SARI cases tested

The following data should be checked as part of continuous monitoring:

■ proportion of sites that regularly submit data to national level, measured over a fixed period;

■ proportion of sentinel sites that regularly submit specimens for laboratory testing;

■ proportion of data collection forms filled out completely, evaluated by reviewing the national database for missing data from a random selection of forms or by assessing forms over a fixed period;

■ number of specimens sent from the sentinel sites;

■ timeliness of reporting from sentinel sites (or delay between data collection and reporting);

■ timeliness of reporting of results from laboratories to national level and to clinical level;

■ timeliness of data published in the weekly report;

■ proportion of weeks with reporting to FluNet and FluID or other reporting systems; and

■ aberrations in observed trends or data.

---

[1] Ortiz JR et al. Strategy to enhance influenza surveillance worldwide. *Emerging Infectious Diseases*, 2009; 15:1271–1278.

In-depth system evaluations

Even in a well-functioning system with frequent, continuous monitoring, full system evaluations should be conducted at longer intervals. 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 objectives;

- to measure change;

- to ensure that the system is of the right size after review of all sites;

- 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 objectives;

- 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.

Short-term concern about the cost of monitoring and evaluation is countered by the benefit of identifying problems before they become embedded and of having reliable, high-quality data.

Questions to be discussed by the group

1. Which variables are the most important for continuous checking to ensure data quality and completeness?

2. Is it appropriate to evaluate how existing sentinel sites function before extending the surveillance system with new sentinel sites?

World Health Organization

For more information, please contact:

Global Influenza Programme
World Health Organization
20 Avenue Appia
1211 Geneva 27
Switzerland
Email: whoinfluenza@who.int
Web site: www.who.int