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Summary

After the emergence of the influenza pandemic virus in 2009, a number of European Union/European Economic Area (EU/EEA) countries decided to introduce surveillance of severe disease and deaths due to influenza and this has continued in subsequent influenza seasons.

Conventional sentinel surveillance of Severe Acute Respiratory Infection (SARI) is already carried out in a number of countries across the WHO European Region, mostly in countries to the east of the European Union.

The mechanisms for surveillance and reporting of hospitalised cases of influenza have varied significantly in EU/EEA countries. It has generally been impossible to implement conventional sentinel SARI surveillance without providing external support to countries. However, innovative solutions have been found, such as reporting by intensive care networks.

In 2011, a series of common objectives were developed and agreed among experts and representatives of Member States.

To further explore the options, a questionnaire on surveillance systems in use in 2011 to monitor severe influenza disease was sent to each EU/EEA Member State. Results from this questionnaire confirmed that the monitoring systems are highly diverse. A summary of these results is available at the end of the document.

Background

Prior to the 2009 pandemic, few countries in the WHO European Region had implemented routine hospital surveillance for severe disease due to influenza. During ECDC's fourth meeting entitled 'Surveillance and Studies in a Pandemic' [1], organised shortly after the start of the 2009 pandemic (Stockholm, July 2009), surveillance specialists from the EU/EEA Member States agreed to try and introduce surveillance of severe influenza disease for the pandemic. It was proposed that this should be done using sentinel syndromic SARI (Severe Acute Respiratory Infection) surveillance, along with case-based reporting of severe influenza A(H1N1) 2009[1] cases and related deaths in hospitals. Prior to this, work by WHO's Regional Office for Europe in 2008 had culminated in the publication of the WHO guidance for influenza surveillance in humans [2]. At that time, a number of countries were in the process of establishing sentinel SARI systems.

In 2009, laboratory testing for the new pandemic virus rapidly became available in all countries and from the start numerous countries introduced mandatory notification of laboratory-confirmed cases. Notification included hospital cases and/or intensive care unit (ICU) cases and/or deaths.

Between October 2009 and April 2010, ten EU countries reported 9 476 hospitalised laboratory confirmed cases of influenza A(H1N1) 2009 virus and 571 related fatalities to ECDC [3]. At the same time, sentinel surveillance for SARI was being established in eleven countries of the WHO European Region, in keeping with global recommendations for monitoring severe disease. These countries were mostly in the central or eastern part of the Region. Three EU/EEA countries within this group performed additional SARI surveillance. Reasons for the difference between the surveillance systems may be the variable familiarity of clinicians with syndromic case definitions[2], difficulties in coding hospital records, variation in laboratory capacity[3] and different hospital capacities.

After the pandemic, formal evaluations of the response to the pandemic consistently reported that the lack of severe disease surveillance represented a significant weakness in monitoring the burden and features (risk factors) of the pandemic. It was also recognised to be a weakness for seasonal influenza surveillance [3]. A review of sentinel SARI systems in several countries showed these systems to have made progress [4]. However, in other EU/EEA countries, attempts to establish new severe disease surveillance during the pandemic had been unsuccessful, especially using syndromic SARI surveillance [5]. This was in contrast to primary care and virological surveillance systems which were already in place and generally performed well during the pandemic [4]. It was agreed that severe disease pandemic surveillance should be based on routine surveillance, which was also needed to investigate and monitor seasonal influenza.

Following the pandemic, specialists in influenza surveillance discussed future 'severe end surveillance' at a series of meetings in order to compare experience and agree on objectives.

[1] The virus is now officially named A(H1N1)pdm09 but it is the only A(H1N1) human virus infection circulating in humans.

[2] SARI posed particular difficulties as it brought together conditions not usually combined for diagnosis or reporting (e.g. adult pneumonia and bronchiolitis in children) and required significant human resources.

[3] Many hospitals were increasingly able to diagnose influenza infection and found that reporting influenza cases was easier (and required less resources) than syndromic surveillance based on SARI.

Post pandemic events

- Annual meeting of the European Influenza Surveillance Network in Sofia, Bulgaria, June 2010
- WHO European Regional Influenza Surveillance Meeting in Brasov, Romania, September 2010
- WHO Regional Office for Europe – publication of the updated WHO European guidance for sentinel influenza surveillance in humans, May 2011
- ECDC expert meeting 'Patterns of Influenza Infection and Disease in Europe 2010–2011 and Future Severe End Influenza Surveillance in Europe' Stockholm, Sweden 3–4 May 2011
- Joint ECDC/WHO influenza surveillance meeting in Ljubljana, Slovenia, 7–9 June 2011
- WHO Regional Office for Europe 'Overview of sentinel systems for hospitalized severe acute respiratory infections (SARI)' presented in the weekly EuroFlu surveillance bulletin http://www.euroflu.org/documents/Overview_of_SARI_Surveillance_Systems_25-03-2011.pdf

These meetings and events offered a forum for discussion of the benefits versus the drawbacks of different approaches, the resources needed and possible extensions to the surveillance of severe respiratory disease caused by other pathogens.

The purpose of this document is to outline the agreed objectives, identify the arguments and propose possible options for continuing the surveillance of severe influenza cases in EU/EEA/WHO European Region countries**.** An earlier draft of the document was discussed at the joint ECDC/Regional Office for Europe Meeting in Ljubljana, Slovenia (7–9 June, 2011) and has been developed by ECDC in consultation with Member States and WHO's Regional Office for Europe.

Objectives of severe influenza surveillance

The following five public health objectives of the surveillance were developed during the ECDC expert meeting in Stockholm during May 2011. They were then modified and endorsed at the joint WHO/ECDC influenza surveillance meeting in Ljubljana in June [3]. They are presented with justifications, i.e. the public health or clinical actions that follow from them:

- To provide timely data on the severity and burden of more severe influenza, enabling comparisons with previous seasons.
  Justification: allows early triggering of alert systems for more severe seasons. Contributes to policy decisions, (e.g. whether to undertake immunisation or offer antivirals) and puts influenza in the context of other infections and diseases.
- To monitor different influenza viruses, and possibly other respiratory pathogens, associated with severe clinical presentations.
  Justification: informs the strain and vaccine selection process.
- To identify underlying risk conditions associated with severe influenza.
  Justification: targets preventive or mitigating interventions (immunisation, antivirals)
- To detect what factors and interventions seem to have a protective effect against severe disease.
  Justification: estimating the possible effectiveness of interventions, such as vaccination and antivirals, will support risk communication.
- To contribute to the detection of emerging respiratory pathogens and events – epidemic intelligence.
  Justification: rapidly detecting new phenomena and triggering immediate investigation and countermeasures to support core capacities as specified in the International Health Regulations.

Other objectives were noted, particularly in relation to the production of routine statistics and research, however these five were agreed to be the most important for determining public health action and they were prioritised.

A number of additional conclusions were agreed at the expert meetings and afterwards:

- Influenza posed particular difficulties because of its heterogeneous distribution, meaning that there could be genuine 'hot spots' that would be missed by sentinel surveillance.
- There could be different surveillance mechanisms that could meet the same objective(s) and it would be unlikely that a single mechanism could be established across Europe. Mechanisms would have to fit into country settings and be cost effective.
- As for primary care and virological influenza surveillance, the main focus for severe influenza disease surveillance should be at national level. A particular role for international bodies such as ECDC and WHO should be working with Member States to agree on types of international analysis, for example based on the 'known unknowns' concept.

- There is a strong case for preferring the collection and forwarding of disaggregate case-reporting to the national level and beyond because this increases the possibility to combine data and undertake varied analyses.
- Not all countries are able to establish comparable systems to address the above objectives and provided that information is shared rapidly it might not be necessary for every country to have sentinel surveillance systems in place for severe disease caused by influenza.
- At the same time, it is important that some form of severe disease surveillance is in place in every country; notably epidemic intelligence for the reporting of unusual phenomena and mortality.
- Linked epidemiological, clinical and microbiological surveillance is essential and although this would require some new investment it might be worthwhile.
- New hospital information systems gave considerable scope for achieving the objectives and mechanisms described below and should therefore be included in the specifications for new and established systems.
- Comparisons of disease burden between countries and even between hospitals within the same country could be difficult and often was not fruitful, except where such comparisons were carried out as special studies, e.g. using modelling techniques. Sentinel reporting was more useful for monitoring trends and detecting change patterns in consistently reporting hospitals and systems.
- Work with networks of intensive care units during and after the pandemic offered particular advantages as these networks could cover very large populations, were used to working together and could be used for other clinical issues. As the 'general practitioners of severe disease' they were particularly suited to an epidemic intelligence function, if linked to national and international surveillance authorities.

Hospital-based influenza surveillance during the 2010–2011 season

In the 2010–2011 season, ten EU/EEA countries reported disaggregate, case-based, hospitalised severe influenza or SARI cases using a sentinel or other methodology [6]. The pattern of reporting was as follows:

- Sentinel severe laboratory-confirmed influenza seen in hospitals in three countries (Austria[4], Portugal and Spain);
- Severe laboratory-confirmed influenza from all strains in cases admitted to ICUs in three countries (Ireland, Finland, France); ICU/ITU-based surveillance was of particular value for monitoring which viruses were associated with severe disease, and risk factors for influenza complications in several countries. In addition, at least six other countries Czech Republic, Denmark, Germany, Greece, the Netherlands, Norway and the United Kingdom (England) reported data from aggregated cases in ICUs. Information from these countries appeared in the European Influenza Surveillance Network weekly report[5] (WISO). A number of countries also established national or sub-national networks of intensive care units which contributed to some of the above objectives, both for severe respiratory disease and other conditions.
- Severe confirmed/probable influenza and SARI cases that were negative for influenza in four countries (Belgium, Romania, Slovakia, Malta).
- Rapid reporting of all-cause mortality within broad age-bands through the EURO MoMo system. This involved 20 EU/EEA countries and regularly produced outputs for around seven countries (July 2011)[6].
- In the WHO European Region another eight countries (Albania, Armenia, Georgia, Kazakhstan, Kyrgyzstan, the Republic of Moldova, the Russian Federation and Ukraine) also report SARI cases from sentinel hospitals, regularly collect administrative data on hospital admissions for respiratory diseases and estimate their correlation with virologically-confirmed influenza from sentinel sites.

In general, specialists working on severe disease surveillance noted at the meetings that there was a lack of clarity as to what surveillance data are available and what surveillance options are possible in WHO European Region countries (and also within EU/EEA countries).

Moreover, the diversity of health care systems within the Region made it very unlikely that a single 'one size fits all' system could be adopted and the most pragmatic solution would be a system of options in order to achieve the five objectives.

4 For Austria they only reported hospitalised cases with A(H1N1)2009 – not other influenza A sub-types or influenza B.

5 The Weekly Influenza Surveillance Overview (WISO)

6 http://www.euromomo.eu/results/pooled.html

Options for Member States

In light of the above, the following options are available for EU/EEA Member States which are not intended to be mutually exclusive at regional or national level:

- Continue/develop sentinel surveillance of laboratory-confirmed severe influenza for in-patients, including those in ICUs at the relevant hospitals
- Continue/develop national surveillance of laboratory-confirmed influenza cases admitted to intensive care units via ICU networks based on individual cases (preferred) or aggregate reports
- Continue or develop sentinel SARI surveillance
- Maintain or introduce all-cause mortality surveillance by EURO MOMO and develop this to include cause specific data.
- Maintain routine death reporting (death certificates).
- Maintain an event detection or epidemic intelligence function for unusual events such as an outbreak of severe respiratory infection in patients or staff
- Allow a mixed economy specifying a limited number of methodology options that could produce data meeting the above objectives and use the data for event detection and trend analysis.
- Discontinue or not establish the surveillance of severe influenza disease.

Table 1: Advantages, disadvantages and technical needs associated with the options

Mechanisms	Advantages	Drawbacks	Technical considerations
Influenza surveillance in hospitals (including ICUs)	Estimates of the burden of pressure on hospitals. Severity should be monitored on the basis of both epidemiological and virological data. Can build on pre-existing systems of clinical, laboratory or hospital reporting as influenza diagnoses are more common in hospitals.	If the surveillance system is not based on an appropriate sentinel approach, some objectives cannot be achieved, notably burden. Similarly, possible effectiveness of public health measures can be estimated using both a sentinel approach and specific studies, the latter probably being less expensive.	Sentinel approach needs at least to be representative of the population, to have selection criteria for inclusion, numerator and denominator.
Influenza surveillance in ICUs	Estimates of the burden of the pressure on ICUs. Regarding severity, see previous option. Routinely operating hospital-based surveillance systems can support timely investigation, if necessary, and could make it possible to meet additional routine influenza monitoring objectives. If persons at risk can be identified rapidly, surveillance can take a specific studies or routine sentinel approach. The latter is preferable in the event of change in severity of the virus which could affect the risk of complication in individuals. Can also provide a simple epidemic intelligence approach which can be used for other severe illnesses. May be based on pre-existing intensive care networks.	May miss severe disease and mortality in units other than ICUs.	As for the option above.
SARI surveillance	In addition to some of the advantages of the preceding two options, this helps to assess the contribution of influenza among other respiratory pathogens when estimating the burden of respiratory infections. Can theoretically be applied in all hospitals, irrespective of laboratory resources, as in its simplest form it does not require microbiological confirmation.	Clinicians in many European hospitals do not usually use the concept of SARI as it combines diverse diagnoses. The extension of the surveillance to other respiratory pathogens with different clinical and microbiological characteristics could be effective for known co-circulating pathogens [7] but this extension will need additional laboratory facilities, human resources and quality assurance. May require external resources to establish and maintain.	May need laboratory capacity to detect respiratory pathogens, apart from influenza.
Mortality surveillance: deaths from all causes (Euro MoMo) and cause-specific surveillance	Pragmatic and facilitates a rapid estimate of the severity of annual epidemics and pandemics. If repeated it allows for comparison year on year. Euro MoMo system relevant for other causes of excess deaths, such as extreme weather and temperature effects. Based on pre-existing systems of mortality reporting.	May not be specific enough to determine if an apparent rise in mortality at international/national level is due to influenza or other causes (e.g. RSV infection and extreme cold). Subject to 'noise' and reporting artefacts, requiring complex interpretation. Has some difficulties with pandemics because these can occur outside the normal influenza season which can make it difficult to know which baseline to apply.	Needs timely – preferably daily – reporting counts of overall deaths (e.g. number of death certificates) at least by age group.
Event reporting (epidemic intelligence)	Allows the detection of novel severe disease.	Clinicians and hospitals sometimes unsure who to report to locally or nationally.	Required for timely IHR reporting and in accordance with EU legislation.
Discontinue surveillance	Would free up some resources.	Would be ignoring expert recommendations and not supporting countries that have severe respiratory disease surveillance underway.	Another view is that data can always be determined in a crisis through special studies. However, that was quite simply not the case during the 2009 pandemic.

The first three options for severe disease surveillance (severe influenza in inpatients, severe influenza in patients admitted to ICU and sentinel SARI surveillance) could be considered for the future. The limitations for the implementation/continuation of sentinel surveillance in hospitals are well-known, e.g. cost, workload, human resource implications, laboratory capacity, data quality and differences in denominators.

It would seem best to formally adopt the fourth option (mortality monitoring), which specifies a limited number of possible methodologies that could produce data meeting the above objectives, and to use such data for event detection and trend analysis.

To obtain a more comprehensive understanding of the range of possible options and their feasibility at European level, a short survey of countries in the EU/EEA was carried out in October 2011. This identified how the above surveillance objectives are being addressed in EU/EEA countries and the options being considered for the future. Of 30 questionnaires sent to EU/EEA countries, 23 countries and two regions from the UK replied.

- Sixteen networks would monitor influenza laboratory-confirmed cases in hospital, of which eight in ICUs.
- Seven networks would monitor SARI and six countries do not intend to monitor severe influenza or SARI. In 2010–2011, seven countries reported influenza confirmed cases and three notified SARI cases, two of which were with laboratory confirmation. Three countries notified only those influenza cases admitted to ICU.
- Nineteen countries would collect case-based data and eight countries would provide aggregate data. In 2010–2011, ten countries sent case-based data.
- All national hospitals were selected in 12 countries, three were selected on a voluntary basis and the of representativeness of nine networks was based on a variety of criteria.
- A denominator was calculated for 50% of the networks and almost all countries reported on a weekly basis.
- Reporting of demographic variables, influenza confirmation, date, risk factors and outcome differs significantly from country to country. New indicators for the coming season were mentioned, e.g. use of ECMO, severity index or cause of death.

Additional projects, for example using aggregate data or monitoring in children, were mentioned by two countries.

The high response rate (>76%) of this questionnaire provides useful data on surveillance of severe influenza. Nevertheless, there was significant diversity, for instance in the selection of sentinel hospitals. An encouraging feature was the number of countries who stated they planned to collect data from national or regional networks of ICUs.

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