



REGIONAL OFFICE FOR Europe

MEETING REPORT

Annual influenza meeting 2012

Warsaw, 30 May-1 June 2012

Background

The European Centre for Disease Prevention and Control (ECDC) and the World Health Organization Regional Office for Europe coordinate the surveillance of influenza in the European Region¹. From 30 May to 1 June 2012, the WHO Regional Office for Europe and ECDC held their second joint annual influenza meeting hosted by the Polish authorities in Warsaw. The meeting was attended by more than 125 participants representing national focal points for epidemiological and virological surveillance of influenza in 38 countries of the WHO European Region, including 29 EU/EEA Member States, six candidate or potential candidate EU enlargement countries, Israel, Republic of Moldova and Switzerland.

This report summarises the main content of the meeting's working group sessions and the recommendations and next steps identified. It describes how influenza surveillance in the WHO European Region and EU/EEA Member States will continue, supported by ECDC and the WHO Regional Office and contribute to global surveillance through the WHO Global Influenza Surveillance and Response System (GISRS). Topics around seasonal influenza vaccines were major features of the meeting. In addition, key-note lectures by a leading clinician from the European Respiratory Society and the Coordinator of the Influenza programme at WHO headquarters helped put European surveillance in a wider context. Presentations and full working group reports from this meeting have been posted on the ECDC website², the password-protected EuroFlu library and the ECDC extranet³. For more information about this meeting, please contact influenza@ecdc.europa.eu or influenza@euro.who.int.

The views expressed in this publication do not necessarily reflect the views of the European Centre for Disease Prevention and Control (ECDC).

Stockholm, November 2012

¹ See the WHO European Region EuroFlu bulletin at <u>http://www.euroflu.org/</u> and the ECDC Weekly Influenza Surveillance Overview (WISO) for EU/EEA countries at

http://ecdc.europa.eu/en/healthtopics/seasonal influenza/epidemiological data/pages/weekly influenza surveillance overview.a spx 2

Available at:

http://ecdc.europa.eu/en/press/events/Lists/Events/ECDC_DispForm.aspx?List=43564830%2D6b8a%2D442f%2D84e7%2D2495f a49489b&ID=195&Source=http%3A%2F%2Fstaging%2Eecdcdmz%2Eeuropa%2Eeu%2Fen%2Fpress%2Fevents%2FLists%2FEv ents%2FAllItems%2Easpx%3FSortField%3DModifi

Available at:

https://login.ecdc.europa.eu/adfs/ls/?wa=wsignin1.0&wreply=https%3A%2F%2Fextranet.ecdc.europa.eu%2F&wct=2012%2d10 %2d30T10%3a01%3a12Z&wctx=6bf4bbc0-39c2-4dd9-b49e-0fb2e99284f8

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Objectives of the meeting

The main objectives of the meeting were to:

- provide a situation update on the 2011-2012 influenza season, with respect to epidemiology, virology and vaccination;
- review developments in the surveillance of severe disease caused by influenza as well as in mortality monitoring
- prepare for the upcoming 2012–2013 influenza season, with respect to developments in the European Surveillance System and Euroflu influenza surveillance platforms.

Hence, the topics covered in varying depth this year were:

- reviewing the 2011–2012 influenza season,
- primary care surveillance,
- implementation of epidemic thresholds,
- quantisation of qualitative indicators for seasonal influenza,
- case definitions,
- virological surveillance including molecular epidemiology,
- virus characterisation,
- antiviral susceptibility monitoring,
- molecular diagnosis and sequencing,
- the annual influenza risk assessment,
- laboratory training and quality assurance,
- progress in developing seroepidemiology and protocols,
- influenza immunisation,
 - progress with coverage against the WHO Standard/Council Recommendation,
 - vaccine effectiveness monitoring,
- proposals for future reporting and the data needs of clinicians.

In addition to these formal objectives and topics, the delegates and ECDC and WHO staff worked on protocol development and addressing practical surveillance issues.

Meeting agenda and presentations

1. Introduction and European surveillance 2011–2012, plenary

Annual risk assessment and overview of the season (A. Nicoll)

This described the implementation in Europe of the recommendation of the 2011 World Health Assembly and the Review of the Functioning of the International Health Regulations (2005) in relation to Pandemic (H1N1) 2009⁴, namely to perform a risk assessment in the early phase of each influenza season.

<u>Conclusion and recommendations</u>: The 2011-2012 season brought special challenges, e.g. severe disease reported by different countries and no obvious disease progression, highlighting the importance of conducting annual risk assessments of the epidemics and their impact. A risk assessment in the first affected countries will inform other countries and identify areas for control and management actions (see session 7).

Sentinel severe acute respiratory infections (SARI) monitoring in the WHO European region (T. Meerhoff)

Hospitalised SARI cases were reported by eleven countries, mostly in the Eastern part of the region. Most SARI cases occurred in the 0–4 age group. The proportion of specimens positive for influenza was lower in 2011–2012 compared to the previous season. In SARI cases due to influenza, 93.8% were caused by influenza A viruses and 6.2% by influenza B viruses.

<u>Conclusions and recommendations</u>: Sentinel SARI surveillance in hospitals is a recent development and regular evaluation is needed (see also Session 5).

Overview of virological surveillance in 2011–2012. (J. McCauley)

Among influenza viruses, 47% were A(H3N2) viruses, 2% were A(H1N1)pdm09 viruses, 42% influenza A (unsubtyped, but presumed mostly to be A(H3N2)) and 9% were B viruses. The WHO recommendation for the A(H3N2) component of the influenza vaccine for the Northern Hemisphere 2012/2013 was changed from A/Perth/16/2009 to a virus antigenically similar to A/Victoria/361/2011. Particular difficulties have been experienced in interpreting the results of antigenic characterisations this season.

<u>Conclusions and recommendations</u>: The vaccine has been updated, but problems remain in analysing seasonal A(H3N2) viruses and predicting their effectiveness.

The European Surveillance System (TESSy) (S. Sarbu)

The European Surveillance System is the single point for reporting to ECDC and for retrieving surveillance data from 30 countries and over 60 diseases including influenza. Recent developments and features were presented to delegates.

<u>Conclusions and recommendations</u>: individual advice sessions were much appreciated by participants and should continue to be offered in the meeting by an experienced data manager as a valuable supplement to the year-round on-line and telephone assistance.

⁴ Available at: <u>http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf</u>

2. Epidemiology working groups (WG)

Epidemic thresholds. (J. Beauté).

Epidemic thresholds calculated with the Moving Epidemic Method (MEM) is an effective way to indicate the start of the influenza season, helping to determine influenza activity and comparing results across countries. The first assessment of the use of MEM has shown both good specificity and sensitivity (timely and accurate detection of the start of the season). In addition, the MEM was used to good effect by eight countries in the WHO European region. However, it was noted that other indicators, percentage of positive specimens positive for influenza or intensity are still useful. The report was presented to the plenary

<u>Conclusion and recommendations:</u> it was agreed that the use of the MEM should continue and Member States are encouraged to adopt it.

Quantification of qualitative indicators. (T. Vega and T. Meerhoff)

Qualitative indicators have been used since the beginning of influenza surveillance at the EU level. Reporting on these indicators by countries does not always follow the definition for the qualitative indicator in question, and at least for some of the qualitative indicators it may be feasible to quantify them. The aim would be to improve comparability between countries and seasons, reduce inconsistencies and to simplify the automatic online display. An e-mail survey on qualitative indicators was completed by 30 countries. The majority of countries are interested in the quantification of the indicators and eleven countries use some method to quantify intensity. The results of use of statistical methods on historical data from several countries had been presented to a working group of Member States, ECDC and the WHO Regional Office, in May, 2012, as well as at this <u>meeting</u> (available on the extranet). Preliminary results demonstrated the feasibility and usefulness of quantification.

Conclusions and recommendations:

- More discussion is needed on the current definitions of the qualitative indicators to define possible changes;
- Pilot-test different methods to quantify intensity, trend and dominant virus indicators during the 2012–2013 season; select a minimum number of volunteer countries: 4–6 for ILI data, 2–3 for ARI data and 3–6 for virus dominance indicator to be piloted
- Evaluate the 2012–2013 pilot study and present at the 2013 annual meeting

ILI case definition. (A. Larrauri)

An earlier assessment was updated with data from three countries. The results suggest that the EU3 ILI case definition⁵ with fever OR sudden onset of symptoms as compulsory criterion during the epidemic period is the most suitable. But as many clinical manifestations with fever are due to other pathogens, a respiratory criterion is needed. The report was presented to the plenary

<u>Conclusion and recommendations</u>: In countries with well-established influenza surveillance systems, the EU3 ILI case definition will ensure a more timely detection of the epidemic with reasonably good specificity. However, in countries with limited virological resources and not so well established influenza surveillance systems, the simple WHO 2011 ILI case definition is an acceptable alternative.

• sudden onset of symptoms OR fever AND

⁵ EU3 definition of ILI:

[•] at least one of the following systemic symptoms: malaise, headache or myalgia, AND

[•] at least one of the following three respiratory symptoms: cough, sore throat, shortness of breath, during the epidemic period

Virology plenary

Overview of laboratory network activities and looking forward (C. Brown)

Current activities and capacities of national influenza centres were reviewed. The capacity to perform RT-PCR has increased and many laboratories use kits provided by WHO Collaborating Centres (CDC - Atlanta). Fewer laboratories perform virus isolation than in the past and those that do, perform fewer tests. As an improvement, some laboratories have established antiviral susceptibility (AVS) testing.

<u>Conclusion and recommendations</u>: The reduced capacity and capability to isolate viruses represents a threat to the laboratory work because of their importance in detecting new viruses and informing vaccine strain selection. The WHO Regional Office and the Community Network of Reference Laboratories for Human Influenza (CNRL) should continue to provide training and external quality assessment (EQA) programs to support the performance of virus isolation by laboratories throughout the Region.

CNRL activities (M. Zambon)

The public health functions of laboratories and the network are

- the ability to detect novel virus strains
- mitigating influenza transmission and disease by informing vaccine strain selection, vaccination policy and use
 of antivirals
- monitoring of vaccine effectiveness
- optimising influenza treatment with resistance monitoring
- promoting the application of modern public health tools (surveillance, modelling, risk communication).

Comparative analysis of CNRL `influenza virus rapid detection and virus culture EQA', 2008 and 2010 (C. Thompson)

Results of a comparative analysis of rapid detection and virus culture EQA panels in 2008 and 2010 were summarised. There were more subtyping and strain determination errors in 2010 than in 2008 and less laboratories returning results for virus culture.

External quality assurance project (EQAP) review (D. Pereyaslov)

The latest ten RT-PCR EQA panel results for the Region were reviewed. They show that the RT-PCR performance is at a very high level in European laboratories and that the capacity to perform RT-PCR has increased through the years.

Laboratory capability database (F. Plata)

The latest development and implementation stages of the laboratory capability database (Lab Cap: the former EISS 'who's who') were introduced. The implementation will require volunteers to test the platform during the summer and to finalise the development in the autumn, so that the platform can be used from the beginning of the next season.

The report of the virology working group was presented to the plenary.

Virology discussion sessions

The objectives of the session were to discuss the current status of the network, to address network's needs and to draft a practical working model for the future. Raised questions:

- What does the network see as the main gaps in the network capacities and data generated/provided?
- What is the current capacity for early warning and response?
- What support from ECDC, the WHO Regional Office and CNRL is needed?
- What are the next suggested EQAs and training courses?

Conclusions and recommendations:

- Most laboratories have capability for virus culture
- It is a requirement to maintain capability to culture viruses (NIC and CNRL key task)
- To produce a summary culture report at the end of the season (as well as a characterisation summary including algorithms used; a separate data call for this report)
 - To enhance and maintain communication:
 - Share protocols and methodology
 - Use inventory of laboratory capabilities and activities (LabCap Database)
 - More technical support for problem solving
 - Increase use of extranet; mailing lists; EZCollab

- To maintain EQA panel(s)

 Include more contemporary strains
 Include some novel strains
 Retain culture EQA
- Training •
 - Include basic virological techniques (succession planning)
 Twinning visits
 Support laboratories with more limited capability

3. Serology and protocol development plenary.

The Global Consortium to Standardize Influenza Seroepidemiology (CONSISE) to Inform Public Health Policy, Report from 'INFLUENZA SEROEPIDEMIOLOGY MEETING' held in Stockholm, Sweden, 1–2 December 2011 (J. Wood and M. van Kerkhove)

The overall objective of CONSISE is to build a global seroepidemiology consortium to improve the ability and speed in assessing and evaluating threats from respiratory pathogens. This will enhance pandemic preparedness compared to the pandemic (H1N1) 2009 when the lack of early seroepidemiological data was one of the major limitations. In April 2012, ECDC funded a small working group meeting to review earlier protocols and to come up with consensus protocols that will be posted on the Global Health Network⁶ for general discussion. Both the epidemiology and laboratory working groups are welcoming interested European experts to join them.

<u>Conclusion and recommendation</u>: for this global work to continue in 2012–13 with a regional workshop and to be launched in 2013 at the Options for Control of Influenza conference⁷.

4. Immunisation plenary

Seasonal influenza vaccination in Europe: vaccination policy and coverage. Summary of VENICE surveys (D. O'Flanagan)

The main objective of the Vaccine European New Integrated Collaboration Effort (VENICE)⁸ work for ECDC is to monitor vaccine coverage, policies and practices and so promote and share best practices in vaccination among EU countries. The most recent results indicate little progress since the pandemic and, if anything, a little decline in coverage in countries that previously were doing well in Western Europe. Also, many countries do not collect the data needed for the whole group of surveys

<u>Conclusions and Recommendations</u>: These surveys are essential for evaluation of influenza vaccination, though the results are disappointing. Countries need to establish more routine monitoring of coverage and ECDC should continue to support these surveys.

SAGE recommendations (C. Brown).

The SAGE working group performed a systematic literature review on the burden of disease, vaccine performance, feasibility of vaccination programmes and cost-effectiveness. Main changes in 2012 over the 2005 recommendations: First priority: pregnant women, followed (without any order of priority) by health care workers, children from 6 to 59 months, older people and those with high-risk conditions. These recommendations were held up against the Regional survey of seasonal influenza vaccine policies and strategies conducted by the WHO Regional Office in collaboration with ECDC and VENICE: most countries monitor vaccine uptake only in the elderly. In addition, only a handful of countries reported monitoring of adverse events following immunisation (AEFI) to be implemented. These systems need to be in place when considering vaccination of new risk groups. Also, data on the burden of seasonal influenza in pregnant women, other than the pandemic H1N1 virus, is largely lacking in European countries. The SAGE recommendations are shortly to be published as a WHO position paper.

<u>Conclusion and recommendations</u>: It will be necessary to determine how to apply these recommendations in a European setting. Countries considering revising their national seasonal influenza vaccine campaigns to be in line with the new SAGE recommendations will need to measure disease burden and the ability to monitor uptake and detect and investigate AEFIs in new target groups. This work will be supported by ECDC, EC and the WHO Regional Office at the country and inter-country level.

Effectiveness monitoring 2011–2012, report from I-Move meeting and further work to be done (E. Kissling).

Early estimates of vaccine effectiveness (VE) in 2011–2012 were presented for a number of countries, target groups and over time. The initial adjusted VE was low (ca. 40% compared with 54% in previous season) and declined further later in the season. The reasons for this were unknown

<u>Conclusion and recommendations</u>: Yearly studies measuring effectiveness are needed and should be conducted with larger samples and ECDC support. Estimates of VE for specific vaccine type and brand are needed.

⁶ http://tghn.org/

⁷ http://optionsviii.controlinfluenza.com/

⁸ http://venice.cineca.org/

5. Epidemiology working group on severe disease

Severe disease – the ECDC proposal (J. Beauté).

The session demonstrated the usefulness of severe disease surveillance, to note the advantages and disadvantages of the different methods available (sentinel SARI, laboratory-confirmed influenza in hospitalised or ITU patients), to support countries that are undertaking or developing such surveillance, and to agree on ways to improve the reporting of severe influenza cases.

Severe disease – experience from Spain: (A. Larrauri).

The objectives of the monitoring in Spain are the detection of severe laboratory-confirmed influenza cases, to describe their epidemiology and virology and to assess the burden of disease. The analysis during the 2011–2012 season showed that youngest and eldest age groups were the most affected. Severity increased with age, as expected with A(H3N2) being the dominant circulating virus. There was no unusual pressure on primary and secondary health care.

Severe disease – experience from the UK (N. Boddington). (see presentation 5a3)

In 2011–2012, the objectives of the surveillance were to estimate the impact of influenza, to describe the epidemiology of severe influenza, to timely detect novel influenza viruses and to inform policy and response at regional and national levels. Results in 2011–2012 showed important numbers of cases in the younger age group. The proportions of hospitalised cases with influenza A(H1N1)pdm09 and A(H3N2) were comparable. After some adjustments, the surveillance will continue as it provided useful results.

Severe surveillance – experience from Romania (O. Nicolae)

Romania performs sentinel SARI surveillance. Its objectives are the estimation of SARI incidence in the area under surveillance, the description of the aetiology of SARI cases and the evaluation of underlying conditions. Romania is planning to continue this model.

The report of the severe disease surveillance working group was presented to the plenary.

<u>Conclusion and recommendations</u>: severe influenza surveillance (hospitalised infections and deaths) is important and should continue to be supported by ECDC and WHO/Europe with the objectives agreed at the 2011 annual meeting, even if the methods vary. The WHO Regional Office and ECDC will strive to collate and interpret these data for publication in the EuroFlu and WISO bulletins.

Virology working groups⁹

Virus characterisation (TG1)

Performance of virus isolation during 2011–2012. Susceptibility of red blood cells (M Havlickova): haemagglutination inhibition (HI) is still the gold standard for characterising influenza viruses. This season, culture and HI of A(H3N2) viruses proved difficult. Virus isolation efficacy (T Ziegler) is strongly dependent on viral load and therefore of the RT-PCR cycle threshold (Ct) value. The national influenza centre perspective (B Schweiger) and the WHO-CC perspective (J McCauley) were presented. In the influenza serology discussion, comparison of microneutralization protocols – detection of antibodies against A(H1N1)pdm09 (S van der Werf) and Anti-A(H3N2)-antibodies analysed by HI and MN during 2011–2012 (Martina Havlickova) were presented.

The report of TG 1 was presented to the plenary

Conclusion and recommendations: Future activities of this continuous task group include:

- A publication of performance of red blood cells
- Continued monitoring of isolation efficacy
- Continued work on antigenic characterisation: guidelines for characterisation and reporting as well as improvement of comparability
- Comparisons of different HI and microneutralisation (MN) protocols and data between laboratories.

⁹ these working groups were combined with meetings of the CNRL Task Groups (TG)

Molecular diagnosis and sequencing (TG2)

The first discussion topic covered tools & strategies for discovering unusual influenza viruses, e.g. H3N2v.

<u>Conclusion and recommendations</u>: The testing strategy must include a robust influenza A test. Subtyping should signal a problem with an unusual virus. Laboratories should refer any problematic viruses to WHO CC.TG2 will work on a guidance.

The second topic was prospects for multiplexing (K Bragstad).

<u>Conclusion and recommendations</u>: There were concerns about the sensitivity of the assay. General experiences with duplex/multiplex reactions have been good. Multiplex reactions are economical, time-efficient and can diminish the risk of contamination considerably. TG2 will work further on this.

Thirdly, the working group discussed molecular standards and controls including H5N1(I Casas). The influenza A standard is available. TG2 will work further on how an influenza B standard can be provided. Laboratories have several sources of A(H5N1) controls which are acceptable. However, it is uncertain that all the H5N1 viruses/different lineages are covered by these EQA source controls. TG2 will review WHO EQAP 11 materials and discuss the availability of A(H5N1) detection controls further at the WHO GISRS PCR working group meeting on 26-27 June 2012.

<u>Conclusion and recommendations</u>: Up-to-date reference H5 sequences are available, covering the increasing diversity.

The working group also briefly discussed the status of European influenza sequence sharing and reference sequence sharing outside GISAID (Olav Hungnes /M Brytting). A good increasing trend in numbers of shared European sequences from national laboratories and WHO CCs has been observed. Based on the discussions in the working group, there is probably no need to make alternative reference sets available outside GISAID¹⁰ other than in the European Surveillance System. In discussions, the relevance of sharing with Genbank was also raised.

<u>Conclusion and recommendations:</u> There is no need to make alternative reference sets available outside GISAID other than in the European Surveillance System within the EU/EEA context. ECDC will review the technical solutions with GISAID.

The report of TG2 was presented to the plenary.

Antiviral susceptibility (TG3)

Antiviral susceptibility reporting in 2011–2012 influenza season.(A Meijer); no neuraminidase inhibitor resistance was observed, but as expected, all A(H3N2) and A(H1N1) viruses tested resistant against M2 blockers. It was agreed to implement a new variable "immunocompromised" on The European Surveillance System and EuroFlu as well as three interpretation variables with coded standardized interpretation texts for oseltamivir, zanamivir and M2 blockers.

Antiviral Susceptibility Testing Guidance for clinical and public health laboratories: a dissemination plan (F Pozo).

<u>Conclusion and recommendations</u>: Publish the guidance as a peer-reviewed paper in a scientific journal. After publication, an alert and link will be published on the ECDC web portal. This guidance has also been sent to the ECDC Advisory Forum for consultation, and comments are expected by mid June.

Proposal for additional metadata variables for antiviral data reporting (A Meijer).

A WHO antiviral resistance expert group is working on global guidelines for standardized data interpretation. They will meet end of June 2012.

Antiviral resistance analysis tools in The European Surveillance System: Progress, use, and further development (D Faensen).

<u>Conclusion and recommendations</u>: The tools will be available for wider use by beginning of season 2012–13. Volunteers from TG3 will test them beforehand and provide comments.

¹⁰ http://platform.gisaid.org/epi3/frontend

Use of reference virus panel (A. Lackenby)

ISIRV- AVG – A reference virus panel is available at HPA (10 panels) which contains five pairs of wild type and resistant virus prepared at the WHO CC, Melbourne, Australia. ISIRV-AVG and CNRL TG3 need to monitor performance with those standards for improving harmonisation of data generation and interpretation and will therefore ask the laboratories to share their results with them.

<u>Conclusion and recommendations</u>: The antiviral susceptibility reference virus panels are ready for distribution from HPA. Each Member State will pay for their own shipment.

Antiviral resistance EQA requirements: Next panel composition (T. Kossivakis)

A dedicated panel is proposed specifically for the antiviral EQA:

Smaller panel (six to seven specimens), one or two susceptible viruses and four resistant viruses. Possibility to include at least one highly challenging specimen (mixes and /or dual resistance and/or mixed influenza A and B virus infections).

The report of TG 3 was presented to the plenary.

<u>Conclusion and recommendations</u>: The antiviral EQA panel composition needs further discussion and will be included on the agenda of the CNRL task group meeting in October 2012.

Quality and training (TG5)

Certificate of participation in EQA organised by the CNRL (C Thompson) for laboratories.

This EQA certificate is important to demonstrate EQA participation. Laboratories participating in the WHO EQAP already receive certificates. An open discussion to develop long-term EQA and training plan and coordinated capacity building needs concluded the session.

The report of TG5 was presented to the plenary.

<u>Conclusion and recommendations</u>: to produce a certificate of EQA participation for laboratories in two parts: one for public use and a supplementary page including the individual score and advisory actions to address errors for laboratory use only. ECDC/CNRL cannot provide laboratory accreditation.

6. Epidemiology working group on mortality estimation

Influenza-related mortality in Croatia, 1999–2010 (L. Nielsen).

The main objectives were to estimate influenza-related mortality and determine the burden of influenza over the past ten years. A multivariate regression model (Poisson) was used, accounting for season, trend and size of the population. Data were analysed by cause of death: all causes, cardiovascular, respiratory and pneumonia and influenza deaths. Results and limitations were discussed.

<u>Conclusion and recommendations</u>: In the future, an EU standard method or recommended set of methods is needed.

Influenza-related mortality in Portugal (B. Nunes).

The main objective was to estimate the excess mortality associated with specific events (influenza, heat waves, natural disasters, etc.). Taking into account seasonality and secular trend, the method is based on the observed mortality exceeding the upper 95% confidence limit of the baseline for at least two consecutive weeks. Results, limitations, advantages and disadvantages were discussed.

<u>Conclusion and recommendations</u>: If applied at EU level, information on monitoring of other relevant factors such as temperature changes may be useful.

The Global pandemic mortality burden project (GLaMOR) (J. Paget).

The objective of this project involving some 20 countries is to estimate the global mortality burden of the 2009 influenza pandemic. The model is based on actual mortality data and requires up-to-date weekly mortality and virology data.

Conclusion and recommendations: The model may also be useful for data from 2010 and later.

Estimating influenza-related mortality: optimal approaches (R. Pebody).

The objective of the session was to review the different options for estimating influenza-related mortality and to recommend next steps. Five objectives of mortality surveillance were identified:

- To describe clinical presentation and course of fatal flu cases;
- To ascertain virological characteristics of fatal flu cases;
- To determine risk factors for severe infection (by age, underlying risk factor etc.);
- To measure population impact of influenza-related mortality;
- To estimate premature mortality (PYLL).

There are different approaches to meet these objectives: individual mortality, excess mortality and regression modelling. No single approach meets all objectives. The report of the mortality estimation working group was presented to the plenary.

<u>Conclusion and Recommendation</u>: There will be collaboration between ECDC and WHO/Europe on mortality monitoring.

Virology working group

2012–2013 metadata changes to the European Surveillance System and EuroFlu

Characterisation reporting (O. Hungnes)

This session concentrated on virology metadata changes proposed for the next influenza season. The reporting of antigenic (AG) and genetic (GEN) characterisations by week of sampling (non-cumulatively, but aggregated) was presented. There will be no effect of these changes to the automatic data transfer from the European Surveillance System to EuroFlu.

Conclusion and Recommendation: There was full agreement with the proposed changes.

Antiviral reporting changes (A. Meijer)

Another set of metadata changes are related to antiviral susceptibility reporting. Compromised immune status is already part of the metadata, only the values have been readjusted. Additionally, variables for the interpretation of the susceptibility level will be added to improve comparability.

Conclusion and Recommendation: There was full agreement with the proposed changes.

Analysis plan for weekly influenza surveillance overview bulletin and required changes for online reports (K. Prosenc)

A proposal for data display in online and weekly reports was presented.

- Reporting of characterisation data per week:
 - Agreement on reporting antigenic and genetic characterisation data by week of specimen collection and aggregated by week from season 2012–2013 onward
- Changes in the online reports /weekly influenza surveillance overview for AG and GEN characterisations:
 - Sentinel and non-sentinel detections are presented as one pie chart followed by four separate subtype/lineage-specific pie charts for antigenic and genetic characterisations at European and country level as an online report.
 - In the weekly influenza surveillance overview, these data will be presented in a table or pie charts as currently done.

<u>Conclusion and Recommendation</u>: There was full agreement with the proposed changes to the weekly influenza surveillance overview.

The report of the metadata changes working group was presented to the plenary.

<u>Conclusion and Recommendation</u>: The European Surveillance System will: provide a template file for data upload which can be adapted to its own needs; provide an instruction manual on how data can be uploaded; add instructions to the antiviral data upload document; to implement 1+4+4 pie charts for online reports for each country and for Europe; provide tables for the weekly influenza surveillance overview; share information within the network on how data are exported from each country; use the discussion forum on the EISN extranet.

7. Epidemiology working group on annual risk assessment and seasons overview

The objectives, the procedure, the components, the questionnaire and the virological risk assessment were presented and discussed. The <u>early assessment</u> performed in February 2012, and the early analysis were quite consistent with the end of season findings, though the poor vaccine effectiveness was not anticipated.

<u>Conclusion and recommendations</u>: An ECDC-led influenza risk assessment should be made with WHO and the Member States annually and published every year, not only if something unusual happens.

Virology working groups - proposals for future reporting changes

Quantification of the qualitative indicator dominantvirus (T. Vega)

Two options for quantification of the indicator for dominant virus (sub)types were presented: relative frequencies with and without statistical testing of differences.

The report on quantification of dominant viruses was presented to the plenary.

<u>Conclusion and recommendations</u>: Dominance of 60% was seen as sufficient, but sample size for determination of dominance was not decided.

Age group-based reporting (O. Hungnes)

A proposal to collect and report detection data by age groups was presented. Age distribution can be relevant for assessment of vaccine adequacy and for detection of vulnerable groups. Where data is available, detections would be reported in ILI/ARI age groups. If later on detection data will also be reported case-based, age-group reporting is no longer needed.

The report on age group-based reporting was presented to the plenary.

Conclusion and recommendations:

The public health relevance of the age-group based reporting was demonstrated to be valuable as shown by the Norwegian data example. However, age-group reporting seems challenging since the number of reporting variables will increase sufficiently. It will be harder to enter data manually without an automated solution. In a pre-meeting questionnaire, 18 of 22 European Region (15 of 19 EU/EEA) countries responding supported reporting of age-based detection data. An inventory and revision of virus sample forms was suggested.

Strain-based reporting of characterisation data (E. Broberg)

A proposal to report strain-based influenza virus characterisation data rather than aggregated data was presented. The proposal came from a network expert group. This would provide more options for data analysis and linkage with clinical case-based data. Implementation will start in the laboratories where laboratory management systems are available for reporting of strain-based data. The current ILI/ARI swab forms include very little data and we would need to obtain an overview of the case-data currently being collected on the swab forms by the countries.

The report on strain-based reporting of characterisation data was presented to the plenary.

Conclusion and recommendations:

In a pre-meeting survey, 17 out of 22 European Region (14 out of 19 EU/EEA) countries that responded supported all suggested reporting revisions.

The discussion on the strain-based reporting will continue in the CNRL Task Group meeting in October 2012 with the possible decision on the 2013-2014 metadata structure. The inventory and revision of virus sample forms was suggested as for the previous presentation.

Metadata structure for strain-based reporting (A. Meijer)

A logical choice would be to investigate linking virus-based characterisation data to the INFLANTIVIR record type. Suggestions for characterisation variables were presented.

The report on metadata structure for strain-based reporting was presented to the plenary.

<u>Conclusion and recommendations</u>: Network members to submit proposed metadata for strain-based reporting of AG and GEN characterisations to the European Surveillance System latest by end of November 2012.

The European Surveillance System and external sequence databases (D. Faensen)

By EU law, Member States are obliged to report surveillance data to the European Surveillance System (2119/98/EC) and only the 'competent bodies' nominated by Member States can do so. Efforts to collaborate with an external sequence database are underway with a joint session between ECDC and the external system developers in September. A stepwise process is proposed: Before the 2013/2014 season, upload virus sequences to either the European Surveillance System or an external database (file upload). After that the sequence data can be submitted to an external database if the primary upload is in the European Surveillance System based on an export file or with an export file of an external database to the European Surveillance System. Upload to the respective other platform would be manual. In the next step, from the 2013/2014 season onward, ECDC and the external database will strive to fully automate the sequence data upload between the systems, so that each Member State can still choose its primary sequence data destination, and, if reporting to the European Surveillance System, control what to share with any external database.

Conclusion and recommendations: ECDC will seek further advice from the MS on the future submission of sequence data to ECDC.

GISAID's model of data router (R. Daniels)

GISAID proposes a similar data router model as ECDC. It would reduce the reporting workload through a one-step submission and an automated secure channelling of data to GISAID and ECDC's the European Surveillance System database via a neutral facility hosted by Germany's Federal Office for Agriculture and Food (BLE). Analysis tools would be available in GISAID's database.

8. Plenary

Analysis of regional antiviral and clinical data (C. Brown)

An analysis of influenza antiviral resistance data from 24 European region countries in season 2010/11 was presented. The analysis showed that the European Region provides significant data on antiviral susceptibility but that there were a number of gaps, with relatively few countries reporting, in the timeliness of reporting and the completeness of data. Lack of completeness was due to lack of resources to enter case-based data and lack of availability of data, particularly whether a patient had been hospitalised or not and whether there had been exposure to antivirals prior to illness. All of these are critical if public health action is to be linked to the surveillance.

<u>Conclusion and recommendations</u>: The data analysis will be completed and will include the 2011/2012 season. This will allow fulfilment of the main public health function of detecting emerging resistance which is spreading. The countries should be encouraged to improve completeness and timeliness of data.

Characterisation reporting, link with clinical data (E. Broberg)

The group proposed to introduce optional reporting of virus detections by ILI/ARI age group from season 2013/14 onwards. The main benefit would be a better understanding of age-specific subtype distribution in circulating viruses, informing risk assessment, vaccination policy and possibly vaccine composition. The group's second proposal was to move from cumulative aggregate to weekly virus-based reporting of antigenic and genetic characterisation data from season 2013/14 onwards. This would enable linkage between laboratory and epidemiological data and greatly enhance surveillance data analysis. In a pre-meeting survey, 17 of 22 European Region Member States (14 of 19 responding EU/EEA MS) had supported all these changes.

In the discussion, several participants welcomed the proposed changes emphasising their added value from an epidemiologic point of view. One participant asked to have detections also reported by gender; others said they would like to see some of the wide age groups subdivided. There were a number of comments that agreed with the changes in principle, but cautioned against introducing too many new strata, given the added workload for data providers. One suggestion to solve the dilemma was to keep reporting the number of sentinel samples tested in aggregate format while moving to virus-based reporting for the ones testing positive.

9. What data and analyses do health care workers need?

This was a presentation from a senior representative (G. Dimopulos) of the European Respiratory Society (ERS) emphasising the importance of surveillance data and analyses for clinicians, especially about the properties of the circulating influenza strain(s), severity, and the likelihood of viral pneumonia. Conversely, epidemiologists, virologists and other public health specialists need access to clinical data and information. Knowledge of influenza activity and other surveillance data at national and European level as well as in the southern hemisphere will reinforce appropriate management of cases, infection control and preventive measures, like hand hygiene. It was noted that ECDC has a formal relationship with the ERS and will present at the ERS conference in September in Vienna.

10. The influenza year in review

Sylvie Briand, coordinator Influenza, Hepatitis and PIP Framework at WHO headquarters, reviewed the key-events of 2011 and the 2011–2012 influenza season: human infections with SOIVtrH3N2 [A(H3N2)v]; research on A(H5N1) virus; neuraminidase inhibitor use in children and pregnant women; equal footing of sharing of influenza viruses and sharing of benefits (vaccines, antivirals, diagnostics, publications). The main elements of the Pandemic Influenza Preparedness Framework are available at http://www.who.int/influenza/pip/en.

Evaluation

Of the 110 external guests attending the meeting, 75 returned their evaluation sheets for a response rate of 68%. Ratings were excellent, with 84% of the respondents rating the overall quality of the meeting and the technical content as 4 or 5 on a 1 to 5 scale. The addition of vaccine issues was endorsed. A majority of respondents (73%) found the two and a half day format was 'about right' in terms of length. The full evaluation is available on the <u>extranet</u> and in the EuroFlu library.

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