MEETING REPORT

Annual meeting of the European Influenza Surveillance Network (EISN)

Stockholm, 2–3 June 2009

Executive summary

The objectives of this meeting were to describe the epidemiological and virological situation of influenza during the 2008/09 season in Europe and prepare the network members to use TESSy as a new IT infrastructure, with new variables and database structure discussed.

The transfer of the coordination of the influenza surveillance network to ECDC was concluded successfully and the operation of the network continued without any problems. In addition to clinical surveillance at the primary care level, countries are now encouraged to establish systems of surveillance of severe acute respiratory infection. The Community Network of Research Laboratories looks forward to develop A(H1N1)v molecular and serological diagnostics and to asses the proficiency of member laboratories. The emergence of the new virus strain posed new challenges and tested the preparedness in the Member States. A meeting on influenza surveillance in a pandemic is planned for the middle of July 2009.

Stockholm, May 2010

1 Background

The European Centre for Disease Prevention and Control (ECDC) is an EU agency[1] with a mandate to operate the EU surveillance networks (former dedicated surveillance networks) and to identify, assess, and communicate current and emerging threats to human health from communicable diseases.

This annual meeting aimed to be a forum to discuss experiences during the first season of operating under ECDC coordination and to prepare for a new season using a new IT infrastructure, The European Surveillance System (TESSy). Training on TESSy was organised at the end of the meeting.

Objectives

The objectives of this meeting were to describe the epidemiological and virological situation of influenza during the 2008/09 season in Europe and prepare the network members to use TESSy as a new IT infrastructure, with new variables and database structure discussed.

Planned outcomes

Participants were updated on the influenza situation in Europe during 2008/09 season and established virological task groups with clear tasks and time frames.

[1] Established by the European Parliament and Council Regulation 851/2004 of 21 April 2004. For more information about the structure and organisation of ECDC please refer to http://www.ecdc.europa.eu

2 Annual flu meeting discussions

2.1 Flash season report 2008/2009

Rod Daniels and Flaviu Plata presented the following aspects of the 2008/09 flu season:

- the 2008/2009 influenza season started in week 49 of 2008 with medium intensity reported in Ireland, UK (Northern Ireland), Malta and Portugal;
- this was earlier than the last two seasons and the rise was steep in the first affected countries;
- most influenza virus detections occurred between weeks 48/2008 and 15/2009 (a 20-week period)
- influenza A predominated, with the H3 subtype dominating;
- an H1N1 variant with pandemic potential [A(H1N1)v] emerged in North America during late April 2009;
- as of week 18/09 (26 April 2009—5 February 2009), countries began reporting A(H1N1)v detections to EISS and consequently WHO moved to Phase 5 of pandemic alert on 29.05.09;
- the functioning of the sentinel surveillance of influenza shall continue beyond week 20/09.

2.2 The integration of the European Influenza Surveillance Scheme (EISS) into ECDC

Andrew Amato presented the current situation and next steps, including the following:

- a call for outsourcing the Coordination of the Community Network of Research Laboratories (CNRL) activities;
- coordination of the former EISS transferred from the Netherlands Institute for Health Services Research (NIVEL) to ECDC;
- contract extension with sub-contractor to use the EISS platform for the influenza surveillance activities during the 2008-09 season;
- appointment of all official epidemiological and virological flu contact points;
- internal analysis on various databases and modules for the bulletin— what needs to be set up in TESSy or in the ECDC web portal;
- The European Centre for Disease Prevention and Control and WHO-Europe agree to expand the joint surveillance framework for all 54 countries in Europe, determining responsibilities, data flow and bulletin production modalities; and
- transfer of ownership of the EISS website; all historical documents and logo to ECDC.

2.3 Joint surveillance situation and roles of National Influenza Centres (NIC)

Caroline Brown presented the following ideas and concepts:

- further spread of the novel virus is expected;
- surveillance of seasonal influenza should continue uninterrupted and should preferably integrate with surveillance for the novel virus;
- gaps in influenza surveillance, like severe illness and mortality, will need to be considered;
- the NIC's were mobilised to meet the needs of the new virus.

2.4 The activity report of CNRL for 2008/20009

Rod Daniels presented the tender for co-ordination function of CNRL that was awarded in October 2008 to a consortium comprised of members from the Health Protection Agency (HPA), National Institute for Medical Research (NIMR) and the National Institute for Public Health and the Environment (RIVM). With regards to antiviral resistance testing, 20 countries reported data to the former EISS platform throughout 2008/09. Data validation and analysis were performed for inclusion in the weekly bulletin. Isolates from CNRL laboratories were tested by HPA/Virgil.

The CNRL contributed to the former EISS bulletin drafting and reviewing during the 2008/09 season. The CNRL provided advice on configuring TESSy for influenza surveillance, assessing the severity of season, virological match of circulating and vaccine strains, antiviral resistance, risk assessments of H6 (avian outbreak/no human cases) and A(H1N1)v.

The external quality assurance proficiency panel on detection and culture was sent in Nov 2008 and the report was circulated in March 2009. A questionnaire on recent H3N2 viruses was sent to member laboratories in April 2009. The CNRL Task Group Chair meeting took place in May 2009 and the following key points for action/reflection emerged:

- CNRL to assess diagnostic capability for A(H1N1)v— most likely rapid evolution over recent weeks;
- WHO proficiency panel June 2009;
- CNRL to provide A(H1N1)v protocols, accompanying guidance and control materials to labs;
- CNRL to provide technical support to labs;
- CNRL to assess sequencing capability & capacity; and
- task group meetings and development of work plans for coming year.

The CNRL forward look included the following:

- Implementation of influenza surveillance in TESSy;
- A(H1N1)v diagnostics – molecular and serological;
- A(H1N1)v impact assessment;
- proficiency testing (CNRL future plans);
- task group co-ordination;

2.5 Studies and surveillance in a pandemic rationale

Angus Nicol's presentation focused on how pandemics differ and why they can be difficult. What are the 'known knowns' and the 'known unknowns' of a pandemic and why they need to be recognised. A subset of the 'known unknowns' were considered strategic parameters as they are needed in order to take actions in response to the pandemic. Some of the methods that can be used to determine these strategic parameters include the following:

- laboratory based investigations;
- sentinel surveillance (combined microbiology and epidemiology);
- individual case reporting–paradoxes;
- hospital based surveillance–severe disease;
- outbreak investigations;
- serological investigations;
- mortality monitoring;
- vaccine effectiveness investigations; and
- detecting and investigating adverse reactions.

2.6 Linking antigenic, genetic, and epidemiological data

A method to compare influenza viruses based on the antigenic differences and to allocate geographic patterns based on antigenic properties was presented by Colin Russell. Based on these patterns, different hypotheses of virus behaviour were tested. Questions about whether viruses persist locally between epidemics or are they seeded from outside were asked. The pattern of the A(H3N2) influenza virus over seven years was described and it shows that A(H3N2) is circulating in south-east Asia continuously and seeds epidemics around the world. An antigenic map of the new A(H1N1) virus and a web based tool to build maps based on antigenic characteristics are under development.

3 Epidemiological working group discussions

3.1 The objectives of influenza surveillance

General introductory remarks from Andrew Amato focused on the following:

- the transition of EISS to ECDC makes sense but needs to respect the special characteristics of influenza;
- the EISS was based on individual participants' initiatives, whereas surveillance under ECDC is based on the initiatives and wishes of the Member States (MS).
- the EISS followed a bottom-up approach; ECDC will not try to use a top-down approach to run the network.

The general aim and objectives of influenza surveillance include:

- the mitigation of the burden of influenza; and
- surveillance and control (not just vaccination).

Specific objectives for influenza surveillance include:

- report on seasonal, pandemic, avian influenza; and
- provide information on outbreaks, mortality, and SAR.

3.2 Challenges and issues in influenza surveillance

Philip Zucs introduced some of the challenges and general issues of influenza surveillance including:

- Influenza-like illness (ILI) model—it is not the only approach;
- illness in the wider community (internet initiatives);
- acute respiratory illness (ARI);
- impact measures;
- year round surveillance;
- clinical surveillance needing virology and validity grounding.

The group listed some information that the current case-based reporting system did not capture, including:

- mortality;
- outbreaks;
- hospital surveillance data;
- paediatric surveillance data;
- mild cases that do not see a doctor; and
- how the case was detected.

3.3 Need for epidemiology task groups

The group agreed that past EISS epidemiological task groups had failed due to lack of adequate funding and that they only made sense if ECDC funded them. Based on previous experience, and given that the European monitoring of excess mortality for public health action (EuroMOMO) already covers mortality monitoring and EpiConcept covers influenza vaccine effectiveness, the group concluded that should an epidemiological group within the European influenza surveillance network be set up it could function as follows:

- serve as a think tank for ECDC, advising it on funding opportunities;
- link with existing external projects rather than trying to duplicate their work;
- form subgroups to tackle surveillance issues; and
- outsource bigger projects.

One group member suggested that a task group explore web-based population surveillance.

3.4 Geocoding at sub-national level

Some group members expressed scepticism as to whether geocoding of sentinel surveillance data might demonstrate the weakness of the system rather than disease spread. The group agreed that regional geocoding made more sense than coding for the exact location of each sentinel practice. One suggestion was that detailed geocoding may be useful if applied to web-based population surveillance data.

3.5 The calculation of an ILI/ARI baseline

The EISS epidemiology group worked on ways to standardise the calculation of an ILI/ARI baseline and had favoured a method developed in Spain that was based on surveillance data from the previous five years.

3.6 The surveillance of severe acute respiratory infections (SARI)

Some of the countries represented in the group (Romania, United States) had already set up a hospital surveillance system or were planning to do so (Spain). Other participants voiced criticism in that SARI was aetiologically unspecific, had no clearly defined denominator and would be more useful in countries without any well-established influenza surveillance system. Nevertheless the MS were encouraged to set up SARI surveillance, if possible.

3.7 Early estimation of ILI incidence

Jose Marinho Falcao's presentation showed that in Portugal, ILI incidence estimation earlier in the week was based on less sentinel data and resulted in lower numbers. The main conclusion was that a higher proportion of electronic reporting might lead to an improved validity of early estimates.

Virological working group

3.6 The Netherlands' experience: preparing Outbreak Assistance Laboratory (OAL) network for A(H1N1)swl

A laboratory network was created based on these minimal requirements:

Availability 24 hours, 7 days a week; minimum capacity of 100 samples a day over 2–3 months; ability to work under Biosafety Level 3 conditions; routine molecular diagnostics, with internal control; eight hour turnaround time; willingness to participate in quality control programs and to share results; and a willingness to work under aegis of NIC for control purposes.

In conclusion, the OAL network is prepared for detection of A(H1N1)v, although some sensitivity and specificity issues need to be resolved. For the most sensitive and specific performance of assay, use protocols, primers and probes as provided. Matrix gene-based assays should be used for general influenza A virus detection. Next steps include the following: validation of the in-house developed H1v and N1v assays and preparation of kits for OAL network; more challenging panel for OAL network and other labs that want to check the performance of their assays; and distribution of positive control to other regional/hospital labs.

3.7 The Spanish experience

Up until 28 May 2009, 407 samples were tested and 181 confirmed. The first sample was diagnosed by sequencing after it was classified A unsubtypable by using the seasonal sera.

Screening is done regionally; only "influenza A" positive samples are sent to the reference laboratory.

Later in the season it is planned to send a QCA panel to regional labs. The protocols will be updated and the controls used by the reference lab will be sent to the regional labs.

The Center for Disease Control and Prevention (Atlanta) kit was sent to regional labs, so most have the capacity to confirm the A(H1N1)v strain.

Short presentations explaining their experiences in dealing with the rapidly evolving pandemic where given by representatives from the following 14 countries: Belgium, Bulgaria, Denmark, Finland, France, Germany, Greece, Malta, Poland, Portugal, Romania, Slovenia, Spain, and Turkey.

3.8 Influenza virus protein micro-array

Presented by Andrew Meijer, this is an ongoing study with the aim to develop a multiplex protein array to detect simultaneously antibodies to different influenza virus types and subtypes. The micro-array technique has a series of advantages including the following: no limitation in number of plexes, in theory until 400; no coupling, proteins are trapped (membrane viruses); flexible system—proteins (viruses) can be quickly put on the slide; it is quantitative—non-contact spotter; low amounts of antigen needed; and it is sensitive.

In conclusion, the newly developed protein array can discriminate between different HA subtypes, and there is no cross-reaction with the haemagglutination inhibiting antigens of different haemagglutinin subtypes (H1, H3 etc) with specific anti-sera. Additionally, specific blocking of the signals in human sera is possible for H1 and H3. Also, validation of the assay for the avian (H5, H7 and H9) and the A(H1N1)v influenza viruses is difficult because serum from well-defined human cases are rare.

4 Web-based queries

4.1 Google Flu Trends

Google Flu Trends is an additional tool in the influenza surveillance toolkit, and complements traditional surveillance methods. Google Flu Trends estimates levels of flu activity using aggregated Google search queries and provides these estimates online for free in near real-time. Google Flu Trends estimates are published 1–2 weeks ahead of traditional surveillance systems in the USA. This finding and the methodology described during the ECDC meeting were published in the *Nature* article 'Detecting influenza epidemics using search engine query data'[2] available on the Google Flu Trends website.

Corrie Conrad's presentation on Google Flu Trends also served as a springboard to announce Australia and New Zealand's inclusion into the product, as both countries were added to Google Flu Trends during the talk. In addition, preliminary findings for a number of European countries were shared in June 2009. As of October 2009, estimates for 14 European countries will be available through Google Flu Trends. These include Austria, Belgium, Bulgaria, France, Germany, Hungary, the Netherlands, Norway, Poland, Russia, Spain, Sweden, Switzerland, Ukraine. Google Flu Trends is a project of Google.org.

4.2 Influenzanet

Influenzanet is a population based project using the internet to collect data about ILI in population and was presented by Sander van Noort. The project is running in the Netherlands, Belgium, Italy and Portugal. Symptom-based case definitions are proposed based on the following criteria: a temperature of at least 38º degrees; acute onset of fever; cough and/or sore throat and/or chest pain; and muscle pain. Influenza-like illness onset is determined by day of fever onset, and exact case definitions used in different states are locally adapted. Users have to submit a questionnaire at the moment of enlisting. A weekly newsletter is sent to registered users and the results are published online. The advantages of this system are as follows:

- uniform data collection worldwide;
- a channel for influenza-related information;
- its extreme flexibility; and
- it is a valuable tool for monitoring pandemic spread across countries.

4.3 Swedish web queries

Two models, presented by Anette Hulth, were developed for estimating the timing of the peak and intensity of the yearly influenza outbreaks in Sweden as approximated by the laboratory and the sentinel surveillance, respectively. The developed models are based on queries related to influenza and submitted to a medical web site[3]. Web queries give unique access to ill individuals who are not yet seeking care, and are a cheap and labour efficient source. This research demonstrates that web queries can indeed complement current influenza surveillance.

4.4 The European monitoring of excess mortality for public health action (EuroMOMO) project

The project aims at monitoring excess mortality attributed to influenza and other public health threats. The project has European Commission funding until January 2011. It includes 21 European countries and is coordinated by the Serum Statens Institut in Denmark.

4.5 EuroMOMO methods

- simple cyclical Poisson regression model fitted on weekly, all-cause mortality in spring and autumn;
- reference period lasts 3–5 years (until May 2009);
- correction for reporting delay;
- Model available in STATA;
- Weekly bulletin and map of Z scores (based on standard deviation around baseline).

[2] Ginsberg J, Mohebbi MH, Patel RS, Brammer L, Smolinski MS, Brilliant L. Detecting influenza epidemics using search engine query data. Nature. 2009 Feb 19;457(7232):1012-4.

[3] http://www.vardguiden.se/

4.6 Next steps

- Introduce age-specific mortality monitoring;
- define indicators;
- translate at least into R; and
- expand to more countries.

5 Conclusion

Transferring the coordination of the influenza surveillance network to ECDC was concluded successfully and the operation of the network continued without any problems.

In addition to clinical surveillance at the primary care level, countries are now encouraged to establish systems of surveillance of SARI.

The coordination of CNRL was awarded to a consortium comprised of members from the HPA, NIMR, and RIVM. The CNRL looks forward to develop A(H1N1)v molecular and serological diagnostics and to asses the proficiency of member laboratories.

The emergence of the new virus strain posed new challenges and tested the preparedness in the MS. A meeting on influenza surveillance in a pandemic is planned for the middle of July 2009.

Annex 1: Meeting programme

Tuesday 2 June 2009

12:00–14:00	Registration
14:00–16:00	Plenary session *Chair Andrea Ammon*
	Welcome and opening *Andrea Ammon*
	2008/09 Season report *Flaviu Plata & Rod Daniels*
	First year transition from EISS to ECDC *Andrew Amato*
	Joint surveillance with WHO–Roles of NICs *Caroline Brown*
	CNRL report on activities 2008/09 *Rod Daniels & Adam Meijer*
16:00–16:20	**Break**
16:20–17:40	Plenary session *Chair Caroline Brown*
	Studies in surveillance *Angus Nicoll*
	Surveillance of new influenza virus in US *Joshua Mott*
	Antigenic cartography *Colin Russell*
	Discussion

Wednesday 3 June 2009

Epidemiology group

09:00–10:30	Objectives of influenza surveillance *Chair John Watson*
	Challenges and issues in influenza data collection
	Need for epidemiology task groups

Virology group

09:00–10:30	Preparing regional lab network for A(H1N1)v - experiences from the UK *Rod Daniels*
	Preparing regional lab network for A(H1N1)v - experiences from the Netherlands, results of proficiency testing with CDC protocol and in-house assays *Adam Meijer*
	Short presentations on H1N1v experience with laboratory preparedness, difficulties and solutions.
10:30–11:00	**Break**

Epidemiology group

11:00–13:00	Geocoding, supra- and subnational regions in Europe *Chair Maja Socan*
	Calculation of an ILI/ARI baseline
	Surveillance of severe ARI *Angus Nicoll*
	Early estimation of ILI incidence *José Marinho Falcão*

Virology group

11:00–13:00	Short presentations on H1N1v experience with laboratory preparedness, difficulties and solutions. *Chair Rod Daniels*
	Serology: Advances with microarray based serology *Adam Meijer*
13:00–14:00	**Break**
14:00–15:00	Plenary session *Chair Adam Meijer*
	Reports from the working groups.
	Discussion
15:00–15:30	**Break**
15:30–17:00	Plenary session *Angus Nicoll*
	Web based queries:
	Google flutrans *Corrie Conrad*
	Influenzanet *Sander van Noort*
	Swedish web queries *Anette Hulth*.
	Euromomo progress report *Anne Mazick*
	Discussion
17:00–17:15	Closing remarks *Andrea Ammon*

Annex 2: Meeting participants

Country	Name
Austria	Robert Muchl
Belgium	Francoise Wuillaume
	Isabelle Thomas
Bulgaria	Anna Kurchatova
	Slava Pavlova Ilieva
Czech Republic	Jan Kyncl
Denmark	Martina Havlickova
	Karoline Bragstad
	Anne Mazick
Estonia	Olga Sadikova
	Jelena Hololejenko
Finland	Thedor Ziegler
France	Bruno Lina
Germany	Silka Buda
	Brunhilde Schweiger
Greece	Georgia Spala
	Andreas Mentis
	Athanasios Kossyvakis
Hungary	Zsuzsanna Molnar
	Monika Rozsa
Ireland	Joan O'Donnell
	Joanne Moran
Iceland	Gudrun Sigmundsdottir
Italy	Sandro Bonfigli
Lithuania	Algirdas Griskevicius
Luxembourg	Joel Mossong
	Matthias Opp
Latvia	Raina Nikiforova
	Natalija Zamjatina
Malta	Christopher Barbara
The Netherlands	Jan de Jong
	Gee Donker
	Carl Koppeschaar
	Frederika Dijkstra
	Adam Meijer
	Sander van Noort
Norway	Susanne Dudman
	Siri Hauge
	Olav Hungnes
	Anette Kilander
Poland	Iwona Paradowska-Stankiewicz
	Magdalena Romanowska
	Jose Marinho Falcao
	Gabriela Gomes
	Raquel Moreira Guiomar
Romania	Rodica Manuela Popescu
	Emilia Lupulescu
Spain	Amparo Larrauri Camara
	Casas Inmaculada
	Pilar Perez Brena
Sweden	Anette Hulth
	Annika Linde
	Mia Brytting
Slovenia	Maja Socan
	Katarina Prosenc Trilar
Slovakia	Margareta Slacikova
	Jaroslava Adamcakova
Turkey	Mustafa Bahadir Sucakli
	Basak Altas
United Kingdom	Rodney Daniels
	Colin Russell
	John Watson
	Corrie Conrad

Organisation	Name
CDC	Joshua Mott
ECDC	Andrea Ammon
	Andrew Amato Gauci
	Angus Nicoll
	Flaviu Plata
	Edward Van Straten
	Todd Weber
	Phillip Zucs
WHO EURO	Caroline Brown
	John Paget