SURVEILLANCE REPORT

Influenza in Europe

Season 2011–2012

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DISEASE PREVENTION
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Errata
The following corrections were made on 24 October 2012.
Page 12: the original early season estimate of 43 % vaccine effectiveness was changed to between 43% and 55%.
Page 13: a reference was added in relation to the above change.

Contents

Abbreviations

ARI	Acute respiratory infection
CNRL	Community Network of Reference Laboratories for Human Influenza in Europe
ECDC	European Centre for Disease Prevention and Control
EISN	European Influenza Surveillance Network
EISS	European Influenza Surveillance Scheme
EU	European union
EEA	European economic area
EMA	European Medicines Agency
Euromomo	European monitoring of excess mortality for public health action
GP	General practitioner
GISRS	Global Influenza Surveillance and Response System
ILI	Influenza-like illness
ITU	Intensive treatment unit
MEM	Moving epidemic method
RSV	Respiratory syncytial virus
SARI	Severe acute respiratory infection
TESSy	The European Surveillance System
VENICE	Vaccine European New Integrated Collaboration Effort
WHA	World Health Assembly
WHO	World Health Organization

Executive summary

The 2011–12 influenza season started later than usual and did not exhibit any clear pattern of geographic progression. Compared to the previous seasons, the intensity was mild, except in four countries where the ILI/ARI rates were slightly higher than average. Among influenza A viruses detected in sentinel patients and subtyped, A(H3N2) viruses vastly outnumbered A(H1N1)pdm09 viruses (98.5% vs. 1.5%). The proportion of influenza type B viruses increased after week 5/2012 and two different lineages circulated in similar proportions until the end of the epidemic, although at low numbers compared with the A(H3N2) viruses.

In severe influenza cases that were hospitalised, the most frequently isolated virus was A(H3N2) and larger proportions of cases were observed in the youngest and oldest age groups. Mortality from all causes increased in persons ≥ 65 years and peaked in week 7/2012, but other studies are needed to estimate the influenza-related mortality, especially as a period of cold weather occurred concomitantly in most countries reporting to the European mortality monitoring project, Euromomo. No resistance to neuraminidase inhibitors was observed. Antigenic and genetic characterisations of circulating strains showed an imperfect match with the A(H3N2) component of the current influenza vaccine. Observational studies later confirmed a reduced vaccine effectiveness. These findings support the decision of the World Health Organization (WHO) to recommend a change in the seasonal influenza vaccine composition for the 2012–2013 season.

1. Background

The coordination of influenza surveillance in Europe started in 1987 in successive schemes: Eurosentinel, ENS Care and the European Influenza Surveillance Scheme (EISS). Later, the project was funded by the European Commission and influenza surveillance was extended to all EU countries[1] . In 2003, a Community Network of Reference Laboratories for Human Influenza in Europe (CNRL) was established, with participation of the United Kingdom-based World Health Organization (WHO) Collaborating Centre, to standardise virological methods across Europe and regularly assess and improve the quality of laboratory performance (Meijer et al. 2005). Since 2008, the coordination of the influenza surveillance network, now called the European Influenza Surveillance Network (EISN), has been transferred to the European Centre for Disease Prevention and Control (ECDC) by agreement and under legislation. National data are reported to The European Surveillance System (TESSy) of ECDC. All data are also supplied to the WHO Global Influenza Surveillance and Response System (GISRS)[2] through working closely with the WHO Regional Office for Europe and the WHO Collaborating Centre based in Europe.

As recommended by the World Health Assembly (WHA) and done in the 2009 pandemic, ECDC published an annual risk assessment[3] as early as possible in the 2011/12 season (9 March), providing preliminary data analyses from first affected countries to inform the whole of Europe (Nicoll A, 2011, WHO report, 2011). For this purpose, data were collected by questionnaire, pooled with information from epidemic intelligence and reviewed by external experts. As in the risk assessment performed in 2010/11[4], the objectives were to: give an early description of the situation in first affected countries; to estimate the possible pressure on primary and secondary healthcare services (impact); to obtain information from other sources or networks such as Euromomo (mortality, Mazick A. et al. 2012), WHO, Vaccine European New Integrated Collaboration Effort (VENICE) (vaccine coverage and policies, Mereckiene J et al. 2010), I-MOVE (Influenza Monitoring Vaccine Effectiveness in Europe, Kissling E. et al. 2009) and the European Medicines Agency (EMA) (vaccine safety); and to address uncertainties, where possible, and the public health actions indicated.

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[1] Decision 2000/96/EC. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:185:0055:0058:en:PDF

[2] http://www.who.int/influenza/gisrs_laboratory/en/

[3] Available at: http://ecdc.europa.eu/en/publications/Publications/120312-TER-Seasonal-influenza-risk-assessment.pdf

[4] Available at: http://ecdc.europa.eu/en/publications/Publications/110125_RA_Seasonal_Influenza_EU-EEA_2010-2011.pdf

2. Objectives

The main objectives of influenza surveillance are to describe the epidemiology and virological characteristics of influenza in primary healthcare and hospital settings. Weekly results are available on the ECDC website and there is an overall aim of contributing to the Global Influenza Surveillance and Response System of WHO. Specific objectives are:

- to estimate the overall intensity of influenza activity, the geographic spread, impact and trends;
- to also estimate the influenza activity with sentinel virological data, i.e. the percentage of specimens positive for influenza;
- to identify the influenza types and subtypes in circulation and the dominant type from sentinel and non-sentinel sites;
- to check whether circulating strains are susceptible to antiviral treatment;
- to analyse variations in antigenic and genetic characterisations, to assess the match with vaccine strains and to estimate vaccine effectiveness;
- to assess the role of respiratory syncytial virus (RSV) circulation on the burden of influenza-like illness (ILI)/Acute respiratory infection (ARI), especially in young infants;
- to describe epidemiological characteristics of severe (hospitalised) influenza cases and deaths, and to determine influenza (sub)types responsible for them;

During and after the 2009 influenza pandemic and evaluations of the response, ECDC placed particular emphasis on a more risk-based approach. Consequently, the surveillance outputs are linked to a series of specific public health and clinical objectives with related actions (Table 1).

Table 1.**Objectives of human influenza surveillance in Europe**

Objectives: Determining	Public health purpose
Circulating influenza viruses	Supplying information on start and circulation of influenza in and between countries
Duration, shape, number and tempo of the waves of infection across Europe	Informing countries yet to be affected, especially about the intensity and impact so that preparations can be made
Antigenic and genetic characterisations	Supplying information and isolates to the Global Influenza Surveillance and Response System (GISRS) of WHO to collectively review and update the annual seasonal vaccine. Early detection of new variants (untypable and unsubtypable strains)-potential emergence of pandemic strain, animal-to-human transmissions
Susceptibility/resistance to antiviral drugs	Detecting the emergence of resistant viruses indicating a need to amend recommendations for the use of antiviral drugs
Age and clinical groups most infected and affected	Reviewing and optimising recommendations on the groups to be targeted for immunisation and antivirals (risk and other target groups)
Susceptibility in the population-age groups with most transmission (seroepidemiology)	idem
Clinical presentation of severe disease and impact, complicating other infections and underlying disease (including cerebrovascular and cardiovascular)	Informing testing and case-detection policies Alerting clinicians to new clinical presentations.
Unusual features of clinical presentations	Informing testing and case-detection policies Alerting clinicians to new clinical presentations
Complicating conditions (superinfections etc.)	Informing testing and case-detection policies Alerting clinicians to new clinical presentations and complications
Pathogenicity (case/infection fatality rates)	Estimating impact and burden of disease and helping inform policy on interventions, including vaccination
Excess premature mortality by age group	Estimating burden of disease and helping inform policy on interventions, including vaccination
'Impact and severity' of an influenza epidemic (or pandemic) (a complex variable best seen as a matrix)	Information about the possible pressure on health care services including primary care, emergency rooms, secondary care, intensive treatment units (ITU) and so alerting clinicians and managers on whether to implement contingency plans
Effectiveness and safety of interventions and counter-measures including influenza vaccines and antiviral pharmaceuticals-detecting treatment and preventive failure, monitoring and evaluating vaccination programmes	Informing decisions on vaccines and antivirals for regulatory agencies, clinicians, the public, researchers and industry.

3. Methods

3.1. Period and countries under surveillance

The influenza surveillance season in Europe lasts from week 40 (beginning of October) of any given year to week 20 (mid-May) of the following year. Between seasons, more limited information is gathered on the virological characteristics of circulating viruses, quantitative clinical data and severe acute respiratory infections. ECDC also maintains a year-round epidemic intelligence function to detect unusual events including those possibly related to influenza transmission. This report describes data and analyses from week 40/2011 to week 20/2012. Data were received from all EU Member States, Iceland and Norway, but not all participating countries contributed to each component of the surveillance system every week.

3.2. Primary care surveillance

3.2.1. Clinical surveillance

Influenza-like illness /acute respiratory infection surveillance is carried out by nationally organised sentinel networks of physicians, mostly general practitioners (GPs), covering at least 1% and up to 5% of the population in their countries (Lobet MP et al., 1987).

Recommended clinical case definitions of both ILI and ARI are the following EU definitions[5]:

For ILI:

- sudden onset of symptoms;
- AND at least one of the following four systemic symptoms: fever or feverishness, malaise, headache, myalgia;
- AND at least one of the following three respiratory symptoms: cough, sore throat, shortness of breath.

For ARI:

- sudden onset of symptoms;
- AND at least one of the following four respiratory symptoms: cough, sore throat, shortness of breath, coryza;
- AND a clinician's judgement that the illness is due to an infection.

Both indicators are adequate in estimating influenza activity (Paget et al. 2007). As a denominator, most countries use population covered by GPs which allows the calculation of rates per 100 000 inhabitants, while some use the total number of consultations by 100 GPs.

Sentinel physicians report the weekly number of patients seen with ILI, ARI or both (broken down by age groups), and the denominator, to a nominated national focal point who then reports the data to ECDC. Numerators and denominators by country, and definitions of epidemiological indicators are available in annex 1.

During the 2011–12 season, a pilot model, the moving epidemic method (MEM), was used by eight countries to define a baseline of influenza activity and to calculate a pre- and post-epidemic threshold. These thresholds were calculated with data from previous years (Vega et al. 2012). One additional country used its own baseline and thresholds. This method generates:

- an average curve based on historical data (five years or more);
- a pre-epidemic threshold (horizontal line at the beginning of the season): when exceeded by the ILI/ARI curve, the week is considered the start of the epidemic period with 95% confidence (virological confirmation is needed);
- a post-epidemic threshold (horizontal line at the end of the season): when crossed by the decreasing curve of the current season, the epidemic can be declared over with 95% confidence (here again, no or few isolates should be detected); the number of weeks between the end of the pre-epidemic and the beginning of the post-epidemic period is the duration of the epidemic;
- a 90% confidence interval: when the current curve is peaking above this threshold, it means that the current epidemic is above 90% of historical peak values.

The epidemic thresholds are displayed on the ECDC website for countries that have agreed to it (link here, select season table by week, select specific epidemiological graph).

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[5] Available at: http://ecdc.europa.eu/en/activities/surveillance/EISN/surveillance/Pages/influenza_case_definitions.aspx

3.2.2. Virological surveillance

The sentinel physicians take nasal and/or pharyngeal swabs from a subset of their ILI/ARI patients according to nationally defined sampling strategies. The specimens are sent to the national CNRL laboratory for influenza virus detection, typing and subtyping. Further analyses, for instance antigenic and genetic characterisation and antiviral susceptibility testing, are performed by some national reference centres or CNRL consortium laboratories (WHO Collaborating Centre for Reference and Research on Influenza at the Medical Research Centre in London). Influenza viruses detected in samples that were not collected in sentinel healthcare settings are also reported. Some laboratories also test these specimens for the presence of RSV and other respiratory viruses (the latter are not reported to TESSy). Laboratory results, including those obtained for non-sentinel specimens, are reported to ECDC by nominated national focal points every week.

3.3. Hospital surveillance

Seven countries reported hospital surveillance data in 2011/12. Four countries (France, Ireland, Spain and the United Kingdom) reported only hospitalised cases due to confirmed influenza infection while three countries (Belgium, Romania and Slovakia) reported severe acute respiratory infection (SARI) cases caused by influenza or any other pathogen (Beauté J et al. 2012).

A clinical SARI case was defined as:

- sudden onset of fever over 38°C, and
- cough or sore throat in the absence of any other diagnosis, and
- shortness of breath or difficulty breathing, and
- requiring hospital admission.

Data were reported to ECDC on a weekly basis.

Collected variables were demographic data (age, gender), clinical data (underlying conditions, clinical presentation, oxygen support, complications, fatal outcome), virological data (influenza type, subtype, other respiratory pathogen), level of hospital care (intensive treatment unit, regular care), antiviral treatment (including prophylaxis) and vaccination status. Cases were reported by the so-called 'date used for statistics' which is a date applied by the reporting country for the publication of data at national level. This date could be the date of onset, notification, hospitalisation or any other date.

4. Results

4.1. Primary care

4.1.1. Clinical surveillance

The 2011–12 influenza season in Europe, the second season after the 2009 pandemic, started late, in week 3/2012, when five countries reported medium intensity of influenza activity (Bulgaria, Iceland, Italy, Malta and Spain) and nine countries reported local or regional geographic spread. There was no clear geographic progression. ILI/ARI rates peaked during weeks eight and nine (range: 5–11) when 18 countries reported medium intensity. In week eight, 19 countries reported regional or widespread activity (see figure 1).The intensity of ILI/ARI primary care consultations as compared with the 2010/11 season was notably mixed across countries. In Iceland, Malta, Portugal and Sweden, it was comparable or slightly higher. In the Czech Republic, Denmark, Lithuania, Romania, Slovakia and the United Kingdom, intensity was considerably lower than in the previous season. In almost all reporting countries, the most affected age group was 0–4 years.

Figure 1. Geographic spread for week 8/2012

Geographic spread
- No Report
- No Activity
- Sporadic
- Local
- Regional
- Widespread

Liechtenstein
Luxembourg
Malta

(C) ECDC/Dundas/TESSy
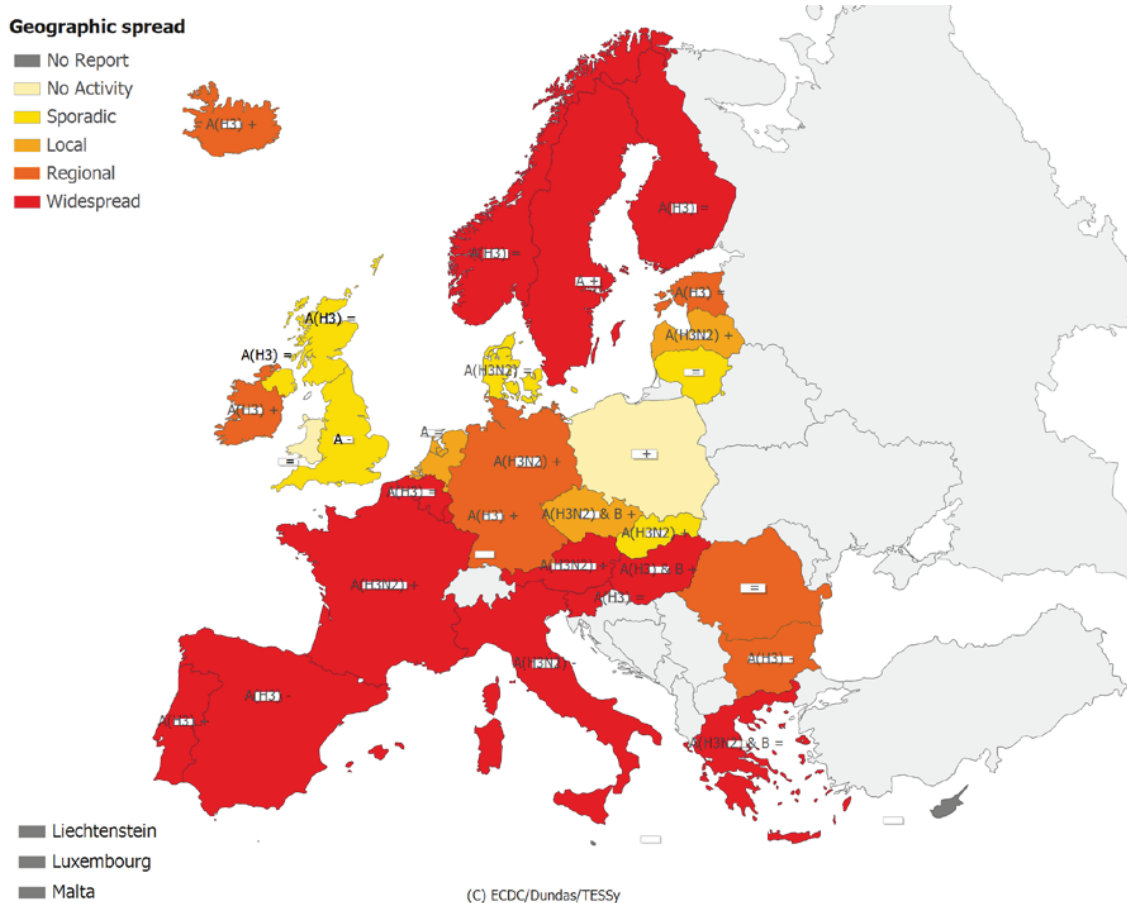
* A type/subtype is reported as dominant when at least ten samples have been detected as influenza positive in the country and of those > 40 % are positive for the type/subtype.

Legend:

No report	Activity level was not reported	+	Increasing clinical activity
No activity	No evidence of influenza virus activity (clinical activity remains at baseline levels)	-	Decreasing clinical activity
Sporadic	Isolated cases of laboratory confirmed influenza infection	=	Stable clinical activity
		A	Type A
Local outbreak	Increased influenza activity in local areas (e.g. a city) within a region, or outbreaks in two or more institutions (e.g. schools) within a region (laboratory confirmed)	**A(H3)**	Type A, Subtype H3
		A(H3) & B	Type B and Type A, Subtype H3
		A(H3N2)	Type A, Subtype H3N2
Regional activity	Influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population (laboratory confirmed)	**A(H3N2) & B**	Type B and Type A, Subtype H3N2
Widespread	Influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population (laboratory confirmed)		

4.1.2. Virological surveillance

In the 2011–2012 surveillance period, 9 472 respiratory specimens from sentinel patients tested positive for influenza: 8 462 (89.3%) for influenza A viruses and 1 011 (10.7%) for influenza B viruses (table 2). The latter became dominant at the end of the epidemic even though the absolute number of detected viruses was decreasing (figure 2).

Of 7 799 sentinel influenza A viruses subtyped, 7 682 (98.5%) were A(H3) viruses and 117 (1.5%) were A(H1)pdm09 viruses. No A(H1N1) virus circulating before 2009 was detected. The lineage of 187 influenza B viruses was determined: 113 (60.4%) were B-Victoria and 74 (39.6%) were B-Yamagata lineage (table 2).

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Table 2. **Number of influenza virus detections by type, subtype and lineage from week 40/2011 to week 20/2012 in 29 EU/EEA countries.**

Virus type/subtype	Season sentinel
Influenza A	8462
A(H1)pdm09	117
A(H3)	7682
A(sub-type unknown)	663
Influenza B	1011
B(Vic) lineage	113
B(Yam) lineage	74
Unknown lineage	824
Total influenza	9473

Figure 2. **Number of sentinel specimens testing positive for influenza A and B from week 40/2011 to week 20/2012 in 29 EU/EEA countries.**
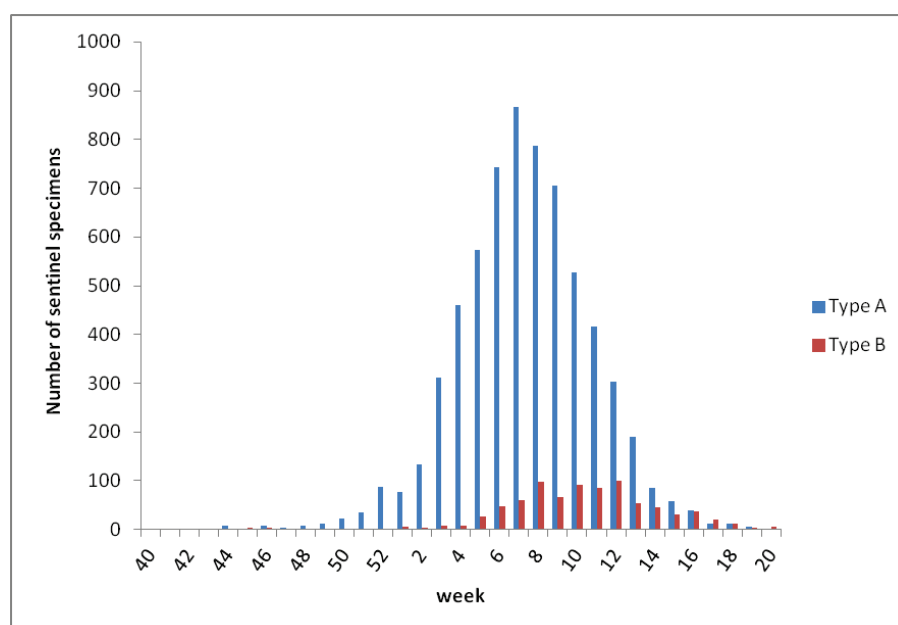
The weekly percentage of sentinel specimens positive for influenza peaked in week 8/2012 (figure 3).

Figure 3. **Number of sentinel specimens and proportion of specimens positive for influenza virus from week 40/2011 to week 20/2012 in 29 EU/EEA countries.**
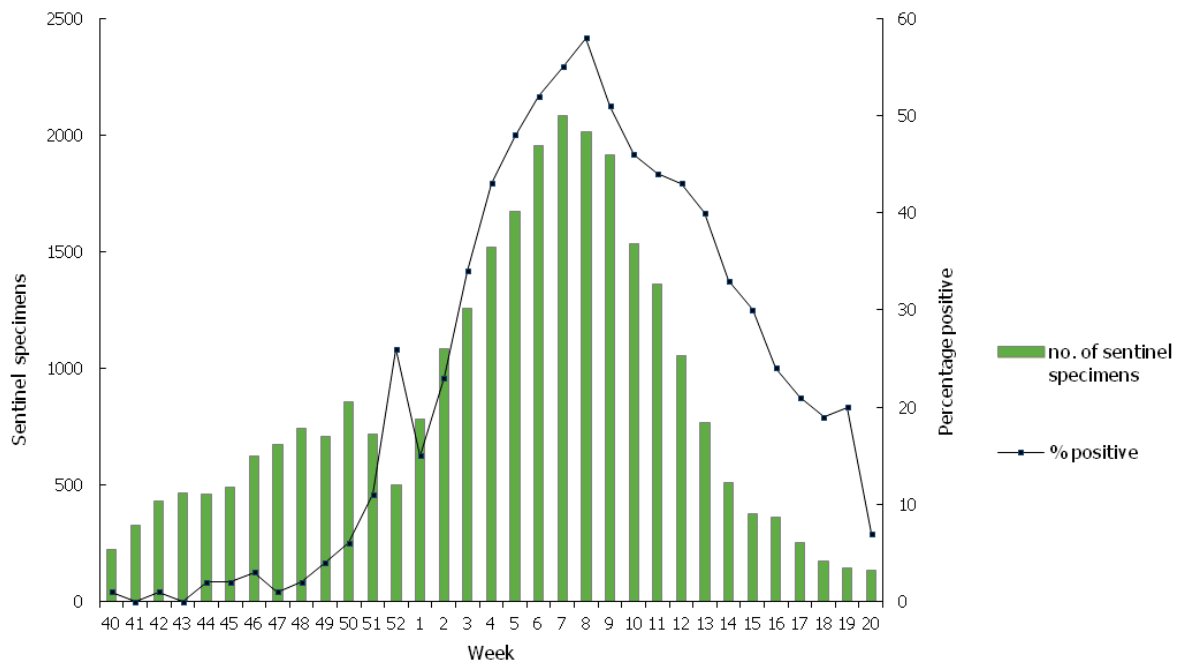
Antigenic and genetic characterisation of circulating viruses

From week 40/2011 to week 20/2012, 1 796 antigenic characterisations of viruses were reported, of which 1 335 (74.3%) were A/Perth/16/2009 (H3N2)-like. Sixty-eight viruses were reported without category: 40 A(H3), 19 B(Yamagata-lineage) and 9 B(Victoria-lineage) viruses, reflecting changes in the reference viruses towards the end of the season.

From week 40/2011 to week 20/2012, 1 385 genetic characterisations of viruses were reported, 1 177 (85.0%) of which were A(H3) viruses. Of the latter, 684 (58.1%) fell within the A/Victoria/208/2009 clade, genetic group 3 represented by A/Stockholm/18/2011. Viruses falling within this genetic group are antigenically diverse, causing an imperfect match with the current vaccine virus, A/Perth/16/2009.

The antigenic distance between wild and vaccine virus was also suggested by results from the CNRL showing that recently circulating A(H3N2) viruses yielded low titres with post-infection ferret antisera raised against A/Perth/16/2009 (CNRL, 2012).

Antiviral resistance

From week 40/2011 to week 20/2012, influenza viruses were tested for antiviral susceptibility by ten countries. None of the A(H1)pdm09, A(H3) and B viruses tested against neuraminidase inhibitors showed resistance or reduced susceptibility. All A(H1)pdm09 and A(H3) viruses assessed for M2 blocker susceptibility were resistant (table 3).

Table 3. **Antiviral resistance by influenza virus type and subtype in ten EU/EEA countries, weeks 40/2011 to 20/2012**

| Virus type and subtype	Resistance to neuraminidase inhibitors						Resistance to M2 inhibitors		
	Oseltamivir			Zanamivir					
	Isolates tested	Resistant	%	Isolates tested	Resistant	%	Isolates tested	Resistant	%
A(H3)	778	0	0	765	0	0	179	179	100
A(H1)pdm09	54	0	0	54	0	0	11	11	100
B	68	0	0	63	0	0	NA	NA	NA

NA = not applicable, as M2 inhibitors do not act against influenza B viruses.

Data are from single location (e.g. H275Y only) or multiple location mutation analysis (full sequencing) and/or phenotypic characterisation (IC50 determination; a cut-off of 100nM oseltamivir/zanamivir/M2 blockers for subtypes H1and H3 and 200 nM oseltamivir/zanamivir for B viruses has been applied for inclusion). Therefore, data should be interpreted in this context.

Respiratory syncytial virus

Compared to the previous year, the time series of weekly detections of RSV in 15 EU countries was similar, but peaking one week earlier figure 4).

Figure 4. **Sentinel and non-sentinel respiratory syncytial virus (RSV) detections during seasons 2010-2011 and 2011-2012 in 15 EU countries**
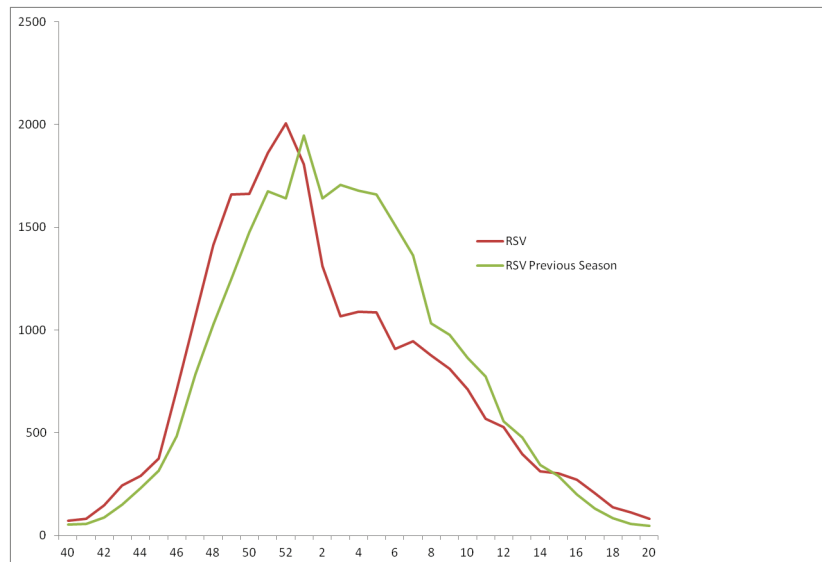
4.2. Hospitalisations due to influenza

From week 40/2011 to week 20/2012, four countries reported 1 164 hospitalised laboratory-confirmed influenza cases (19 cases reported by France were excluded because the laboratory information was missing) while three countries reported 646 SARI cases, of which 152 (23.5%) had laboratory-confirmed influenza infections. The proportion of SARI cases aged below five years was significantly higher in non-confirmed cases (50 % vs 30 %; p < 0.01). The number of SARI cases reported peaked during week eight of 2012 (figure 5) shortly after the peak of hospitalised laboratory-confirmed influenza cases in week seven (figure 6).

Figure 5. Sari cases and proportion due to influenza infection by week of reporting in Belgium, Romania and Slovakia, weeks 40/2011–20/2012
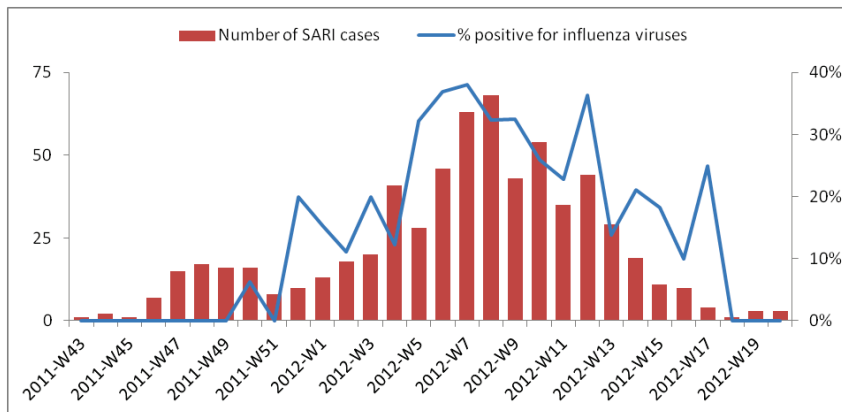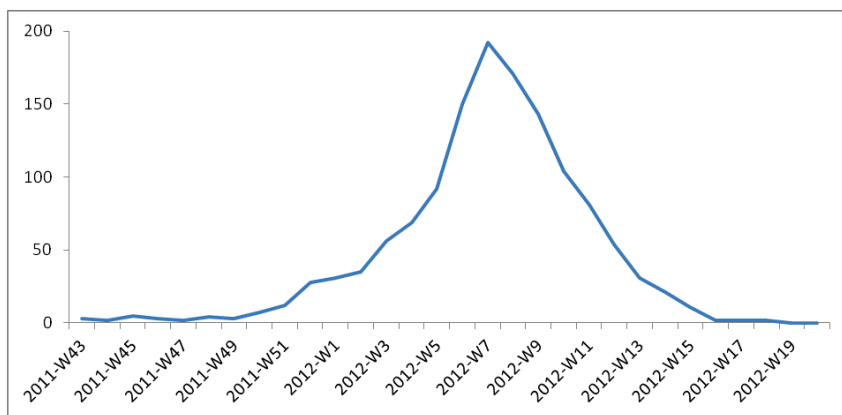

Figure 6. Number of hospitalised laboratory-confirmed influenza cases in seven EU countries by week of reporting, weeks 40/2011–20/2012.

Overall, an influenza virus infection was laboratory-confirmed in 1 316 cases, of which 1 269 (96.4%) were type A and 47 (3.6%) were type B. Of the 1 269 influenza A viruses, 774 (61.0%) were A(H3), 47 (3.7%) were A(H1)pdm2009 and 448 (35.3%) were not subtyped. The male to female ratio was 1.2:1. The distribution of cases by age group was driven by the most frequently isolated virus subtype A(H3) and showed the largest proportion of cases in the youngest and oldest age groups (Figure 7). Of the 845 hospitalised influenza laboratory-confirmed cases with known outcome, 98 (11.6%) died. The median age of the 98 fatal cases was 75 years.

Of 560 hospitalised influenza laboratory-confirmed cases with information on underlying conditions, 452 (80.7%) had at least one recognised risk factor for severe disease, most commonly chronic respiratory disease (131), cardiac disease (90) and diabetes (82).Of the 723 hospitalised influenza laboratory-confirmed cases with known vaccination status, 489 (67.6%) were not vaccinated.

Figure 7. Number of hospitalised laboratory-confirmed influenza cases in Belgium, France, Ireland Romania, Slovakia and Spain, by type, subtype and by age group, weeks 40/2011 to 20/2012.
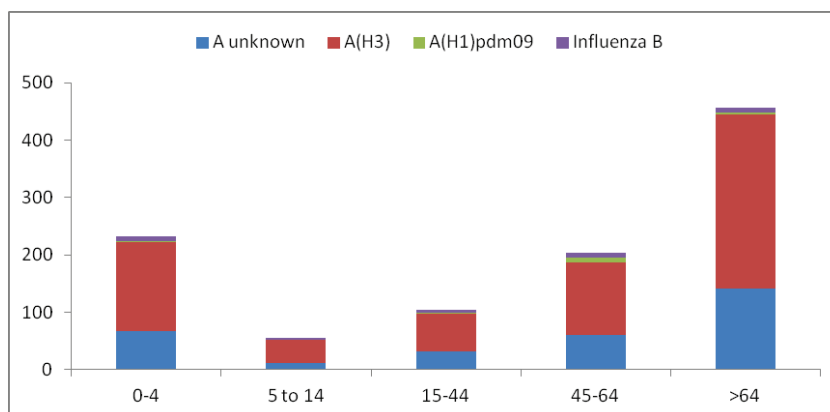
5. Discussion

Results from routine surveillance during the 2010–2012 season were in accordance with the results of the abovementioned risk assessment performed in early 2012, in addition to other observational studies.

This late and mild influenza season did not exhibit a west-east progression as observed during previous seasons (1999-2007) (Paget J. et al., 2007).

The antigenic diversity in characterisations of A(H3N2) viruses and low titres observed with post-infection ferret antisera raised against A/Perth/16/2009 caused an imperfect match with the vaccine strain. This is consistent with the results of studies showing low vaccine effectiveness (Kissling E. et al., 2012, Bonmarin I. et al., 2012). Early season estimates of vaccine effectiveness varied from 43% and 55%, considerably lower than in 2010–2011 and 2009–2010 (Jiménez-Jorge S. et al., 2012, Kissling E. et al. 2012). In addition, it is known that the percentage continued to decline as the season progressed (Kissling E. et al., 2012. Jiménez-Jorge S. et al., 2012). This is consistent with outbreaks in well vaccinated populations (Castilla J et al., 2012) and the WHO's decision to recommend a change to an A/Victoria/361/2011-like (H3N2) virus in the trivalent influenza vaccines for the northern hemisphere 2012–13 influenza season (WER 2012).

The dominance of A(H3N2) was predicted by annual serological studies performed by Norway and Poland. In Norway, the prevalence of protective antibodies to A(H3N2) in people aged 25–49 was very low (4 %) and therefore they were supposed to be more prone to infection by this subtype. However, the prevalence of antibodies against A(H3N2) in school-aged children was high (31 %). In the Norwegian risk assessment, it was stated that the season would be dominated by A(H3N2), which was the case (Norwegian institute of Public Health report, 2012). In Poland, protective antibody titres against A(H3N2) influenza viruses were highest in the age group 15 to 25 (40.5%) and 8- to 14-year olds (33.8%). (L.Brydak, personal communication).These results suggest that there are country-specific variations in the presence of pre-existing antibodies and different age groups might be affected in different countries.

With the dominance of A(H3N2), a shift to older ages, especially in cases with underlying conditions, was observed in severe influenza cases reported by four EU countries.

In the risk assessment performed during the first months of 2012, an excess mortality from all causes had already been observed in February in three countries — Belgium, the Netherlands and Portugal — in persons ≥ 65 years. As these countries experienced very low temperatures when the influenza activity was increasing, differentiating the cause of premature deaths is difficult (Nicoll A et al., 2012). During the 2011–12 season, a moderate excess mortality was observed in 12 EU countries between week five and week 11/2012, with a peak in week seven/2012 in persons ages ≥ 65 years, possibly related to influenza with added effects of a cold snap (Mazick A. et al. 2012).

6. Conclusions

The influenza season 2011/12 started late and there was no particular pattern in its geographical progression

The intensity of ILI/ARI activity was mild or unusually low in the majority of countries, although in four countries it was slightly higher than the previous season. Infants aged 0–4 years were the most affected outpatients and were the second largest age group after the elderly in hospitalised influenza cases reported by four EU countries. With the return of A(H3N2) virus, a shift to older ages in severe influenza cases was observed. An enhanced reporting of hospitalised influenza cases and influenza-related deaths at EU level would help to better estimate the severity of the disease.

Even if A(H1N1)pdm09 viruses continued to circulate, they were largely exceeded by A(H3N2) and by B viruses, with the latter being especially important late in the season. The dominance of A(H3N2) viruses was hardly surprising, given the fact that there had not been an A(H3N2)-dominated season since 2006/07 which is in accordance with sero-epidemiological studies showing a low prevalence of protective antibodies, especially in young age-groups. Additional data on sero-epidemiology would be useful even if they are difficult to interpret because of the lack of standardisation of serological tests.

Genetic characterisations of A(H3N2) viruses have shown important antigenic diversity resulting in an imperfect match with the vaccine strain. This was also reflected in the relatively low vaccine effectiveness observed and led to the WHO decision to recommend changing composition of the next influenza vaccine.

7. Bibliography

Beauté J, Broberg E, Plata F, Bonmarin I, O'Donnell J, Delgado C, et al., 'Overrepresentation of influenza A(H1N1)pdm09 virus among severe influenza cases in the 2011/12 season in four European countries', Eurosurveill 2012; 17(9). Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20105.

Bonmarin I, Belchior E, Le Strat Y, Lévy-Bruhl D. First estimates of influenza vaccine effectiveness among severe influenza cases, France, 2011/12. Eurosurveill 2012;17(18):pii=20163. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20163

Castilla J, Cía F, Zubicoa J, Reina G, Martínez-Artola V, Ezpeleta C. Influenza outbreaks in nursing homes with high vaccination coverage in Navarre, Spain, 2011/12. Eurosurveill 2012;17(14):pii=20141. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20141

CNRL report on Influenza virus characterisation, ECDC June 2012. Available online: http://www.ecdc.europa.eu/en/publications/Publications/Influenza-visus-characterisation-June-2012.pdf

S Jiménez-Jorge et al. Early estimates of the effectiveness of the 2011/12 influenza vaccine in the population targeted for vaccination in Spain, 25 December 2011 to 19 February 2012. Eurosurveill 2012;17 (12): pii=20129. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20129

Kissling E, Valenciano M, Falcão JM, Larrauri A, Widgren K, Pitigoi D et al. "I-MOVE" towards monitoring seasonal and pandemic influenza vaccine effectiveness: lessons learnt from a pilot multi-centric case-control study in Europe, 2008–9. Eurosurveill 2009; Vol 14 (44): 1–8. Available on line: http://www.eurosurveillance.org/images/dynamic/EE/V14N44/art19388.pdf

Kissling, E, Valenciano M, I-MOVE case–control studies team . 'Early estimates of seasonal influenza vaccine effectiveness in Europe among target groups for vaccination: results from the I-MOVE multicentre case-control study, 2011/12', Eurosurveill 2012; 17(15), 1–7. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20146

Lobet, MP, Stroobant A, Mertens R, Van Casteren V, Walckiers D, Masuy-Stroobant G et al., Tool for validation of the network of sentinel general practitioners in the Belgian health care system. Intern J Epidemiol 16(4), 1987, pp. 612–8.

Mazick A, Gergonne B, Nielsen J, Wuillaume F, Virtanen MJ, Fouillet A, et al. Excess mortality among the elderly in 12 European countries, February and March 2012. Eurosurveill. 2012;17(14):pii=20138. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20138

Meijer A, Valette M, Manuguerra JC, Pérez-Breña P, Paget J, Brown C. et al., Implementation of the community network of reference laboratories for human influenza in Europe. J Clin Virol 34(2), 2005, pp. 87–96.

Mereckiene J, Cotter S, D'Ancona F, Giambi C, Nicoll A, Lévy-Bruhl D et al, on behalf of the VENICE project gatekeepers group. Differences in national influenza vaccination policies across the European Union, Norway and Iceland 2008–2009. Eurosurveill. 2010;15(44):pii=19700. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19700

Nicoll A. Planning for uncertainty: a European approach to informing responses to the severity of influenza epidemics and pandemics Bulletin of the World Health Organization 2011;89:542–544. doi: 10.2471/BLT.11.089508. Available on line: http://www.who.int/bulletin/volumes/89/7/11-089508/en/index.html

Nicoll A, Ciancio BC, Lopez Chavarrias V, Mølbak K, Pebody R, Pedzinski B et al. Influenza-related deaths - available methods for estimating numbers and detecting patterns for seasonal and pandemic influenza in Europe . Euro Surveill. 2012;17(18):pii=20162 Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20162

Norwegian Institute of Public Health Report, 2012. Folkehelse instituttet. Rapport om scenarioer for influensaepidemi i 2012, 23. January 2012. Available online: http://www.fhi.no/dav/042f3a2a9d.pdf

Paget J, Marquet R, Meijer A, van der Velden K et al., Influenza activity in Europe during eight seasons (1999–2007): an evaluation of the indicators used to measure activity and an assessment of the timing, length and course of peak activity (spread) across Europe. BMC Infect Dis 7, 2007, p. 41 (doi:10.1186/1471-2334-7-141).

Vega T, Lozano JE, Meerhoff T, Snacken R, Mott J, Ortiz de Lejarazu R et al., Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method. Influenza and Other Respiratory Viruses, August 2012.DOI: 10.1111/j.1750–2659.2012.00422.x

Weekly Epidemiological Record 2012; 10 (87): 85–91. Available at: http://www.who.int/wer/2012/wer8710.pdf

WHO Report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza A (H1N1) 2009 (Fineberg Report) Final submitted to the World Health Assembly 2011. Available online: http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf

Annex 1. Clinical influenza surveillance numerator and denominator by country

Country	Numerator	Denominator
Austria	ARI, ILI	Population
Belgium	ILI, ARI	Population
Bulgaria	ARI	Population
Cyprus	ILI	Encounters
Czech Republic	ILI, ARI	Population
Denmark	ILI, ARI	Population
Estonia	ILI, ARI	Population
Finland	–	–
France	ARI	Population
Germany	ARI	Population
Greece	ILI	Population
Hungary	ILI	Population
Iceland	ILI	Population
Ireland	ILI	Population
Italy	ILI	Population
Latvia	ILI, ARI	Population
Lithuania	ILI, ARI	Population
Luxembourg	ILI, ARI	Encounters
Malta	ILI	Encounters
Netherlands	ILI	Population
Norway	ILI	Population
Poland	ILI	Population
Portugal	ILI	Population
Romania	ILI, ARI	Population
Slovakia	ILI, ARI	Population
Slovenia	ILI, ARI	Population
Spain	ILI	Population
Sweden	ILI	Population
United Kingdom — England	ILI, ARI	Population
United Kingdom — Northern Ireland	ILI, ARI	Population
United Kingdom — Scotland	ILI, ARI	Population
United Kingdom — Wales	ILI	Population

In addition to ILI/ARI rates, semi-quantitative and only partly standardised indicators of intensity, geographic spread and trends of influenza activity are reported.

Each country assesses the intensity of clinical activity based on the historical data at its disposal.

- **Low:** no influenza activity or influenza activity is at baseline level. Usually, there will be a 6–12 week period in winter when the level of clinical influenza activity rises above the baseline threshold, but in the very occasional winter (perhaps 1 in 10), activity never gets above the baseline level.
- **Medium:** level of influenza activity usually seen when influenza virus is circulating in the country based on historical data.
- **High:** higher than usual influenza activity compared to historical data.
- **Very high:** influenza activity is particularly severe compared to historical data.

The **geographic spread** can range from no activity, sporadic, local or regional to widespread activity:

- **No activity:** reports indicate no evidence of influenza virus activity. Cases of ILI/ARI may be reported in the country but the overall level of clinical activity remains at baseline levels and influenza virus infections are not being laboratory-confirmed. Cases occurring in people recently returned from other countries are excluded.
- **Sporadic:** isolated cases of laboratory-confirmed influenza infection in a region, or an outbreak in a single institution (such as a school, nursing home or other institutional setting), with clinical activity remaining at or below baseline levels. Cases occurring in people recently returned from other countries are excluded.
- **Local outbreak:** increased ILI/ARI activity in local areas (such as a city, county or district) within a region, or outbreaks in two or more institutions within a region, with laboratory-confirmed cases of influenza infection. Levels of activity in remainder of region, and other regions of the country, remain at or below baseline levels.
- **Regional activity:** ILI/ARI activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population, with laboratory-confirmed influenza infections in the affected region(s). Levels of activity in other regions of the country remain at or below baseline levels. Regional activity generally does not apply to countries with a population of less than 5 million, unless the country is large with geographically distinct regions.
- **Widespread activity:** ILI/ARI activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population, with laboratory-confirmed influenza infections.

The **trend** is assessed by comparing current influenza activity with that in previous weeks and can be increasing, decreasing or stable.