RISK ASSESSMENT

Seasonal influenza in the EU/EEA countries, 2014–2015

January 2015

Executive summary

- The EU/EAA influenza season started in week 1/2015, with 26% of sentinel specimens positive for influenza.
- Subtype A(H3N2) viruses are dominant in almost all reporting European countries, and the majority of genetically characterised A(H3N2) viruses belong to subgroups distinct from the currently recommended vaccine-strain A/Texas/50/2012.
- As a consequence of the mismatch between vaccine and circulating strains, reduced vaccine effectiveness is expected, as suggested by early effectiveness estimates (< 25%) in the USA, where similar circulating drift variants were detected.
- Among laboratory-confirmed influenza cases admitted to ICUs, 95% were related to influenza A viruses, 73% of which were A(H3N2) viruses.
- Post-exposure prophylaxis and early treatment with neuraminidase inhibitors should be offered to high-risk groups and influenza-infected elderly.

Scope and objectives

This risk assessment covers the 2014–2015 influenza season in the European Union and European Economic Area (EU/EEA). The main objectives of this assessment are:

- to provide an early description of the epidemiological pattern of seasonal influenza in the first affected countries;
- to anticipate the progression of influenza activity for the rest of the season;
- to identify particularly affected populations and estimate the possible impact on primary and secondary healthcare services;
- to assess the implications for public health management in terms of influenza vaccine effectiveness and susceptibility to antiviral drugs during this season;
- to suggest scientific and public health advice on measures to be taken to reduce the burden of seasonal influenza in 2015.

Suggested citation: European Centre for Disease Prevention and Control. Seasonal influenza in the EU/EEA countries, 2014–2015. Stockholm: ECDC; 2015.

Methodology

This risk assessment is based on three data sources:

- Clinical, epidemiological and virological data from primary care and hospital surveillance, routinely collected and reported by public health institutes and national influenza centres to ECDC through the European Influenza Surveillance Network (EISN) and the European Reference Laboratory Network for Human Influenza (ERLI-Net).
- A short questionnaire (see Annex 2) on the pattern and interim impact of influenza that was sent by EU/EEA countries to ECDC when one of the following criteria was met:
  - medium intensity or widespread geographic activity reported
  - or ≥ 10 % influenza-positive sentinel specimens reported (with at least 10 specimens)
  - or severe influenza cases reported
  - or any unusual event reported.
- Other information available such as peer-reviewed literature, serological surveys, data gathered through ECDC epidemic intelligence and results from public health projects: European Monitoring of Excess Mortality for Public Health Action (EuroMOMO) and Vaccine European New Integrated Collaboration Effort (VENICE).

Source and type of request

ECDC internal decision; planned risk assessment.

Epidemiology in primary healthcare services

Influenza activity in Europe started in week 50/2014, with the Netherlands, Sweden and England (UK) reporting medium intensity. One week later, influenza-like illness (ILI) rates in the Netherlands were reported to be three times higher than during the same period of the previous season (with medium intensity, medium geographic spread, and 14% sentinel specimens positive for influenza virus).

During week 1/2015, three additional countries (Iceland, Malta and Portugal) reported medium intensity of influenza activity. Overall, 26% of sentinel specimens tested in EU/EAA countries were positive for influenza virus, which indicated that the influenza season had started without a particular geographic pattern.

Overall, since the start of the season, children under 14 years of age – particularly those between 0 and four years of age – have been the most affected age groups in all reporting countries, except in Iceland and Norway where rates were higher in adults and older people. Since week 1/2015, rates in adults (15–65 years) and older people (≥ 65 years) in almost all countries that report ILI or ARI (acute respiratory infections) have been increasing.

According to data collected through the seasonal risk assessment questionnaire in the first two weeks of January from Finland, France, Germany, Greece, Malta, the Netherlands, Slovakia, Spain, Sweden and two UK countries (England and Scotland), almost all surveyed countries reported greater pressure on primary healthcare services during this season compared to the peak activity in the previous season.

Respiratory syncytial viruses (RSV) activity seems to continue to increase at high level in week 3/2015 in all countries that report on a regular basis (France, Germany, Ireland, Latvia, the Netherlands, Slovenia, Spain, Sweden and the UK).

Epidemiology in secondary healthcare services

In the seven countries (Finland, France, Ireland, Romania, Spain, Sweden and the UK) which report weekly hospitalised influenza cases, 1 042 laboratory-confirmed influenza cases have been admitted since the start of reporting on week 40/2014: 877 to intensive care units (ICUs) and 165 admitted to regular wards. Sixty-three per cent of hospitalised cases were reported by the UK alone.

Among the 385 hospitalised cases reported with information on age, 120 (31%) were between 40 and 64 years old, and 184 (48%) were 65 years old or older. Hospitals reported 34 fatal outcomes, two thirds of which occurred in the elderly (≥ 65 years).

Among the cases reported from ICUs, 95% were related to influenza A viruses and 5% to B viruses. Of 226 subtyped influenza A viruses, 166 (73%) were A(H3N2) and 60 (37%) were A(H1N1)pdm09. Among all hospitalised cases with known subtype, A(H3N2) predominated in all reporting countries, except in France and Romania.

According to national experts responding to the questionnaire, the pressure on ICUs during the first weeks of the season was similar to the 2013–2014 influenza season, but slightly higher in France and the UK (England and Scotland). France reported more cases in risks groups and older people and more outbreaks in healthcare facilities. Germany and the UK reported closed settings outbreaks with some fatal cases, in particular in long-term healthcare facilities. Reported risk factors were similar to the two previous influenza seasons, mainly chronic cardiovascular disease, chronic pulmonary disease and malignancies. Age distributions reported by all responding countries were similar to the previous season.

Virology

Circulating viruses from sentinel sources

From week 40/2014 to week 3/2015, influenza viruses were detected in 2 025 (15%) of 13 376 sentinel specimens: 1 623 (80%) were positive for type A influenza virus and 402 (20 %) for type B. Of the type A viruses, 1 182 (73%) were A(H3N2), 282 (17%) A(H1N1)pdm09, and 159 (10%) remained un-subtyped. A(H3N2) virus was dominant in 19 EU countries and co-dominant in Luxembourg. In Italy and Slovenia, the proportions of A(H1N1)pdm09 were higher.

The lineage of 142 type B viruses was determined: 136 (96%) were B/Yamagata lineage and six (4%) B/Victoria.

Circulating viruses from non-sentinel sources

From week 40/2014 to week 3/2015, 8 962 (7%) of 124 561 specimens from non-sentinel sources have tested positive for influenza virus: 7 421 (83%) were type A and 1 541 (17%) type B. Of the typed A viruses, 3 368 were subtyped: 2 654 (79%) as A(H3N2) and 714 (21%) A(H1N1)pdm09. The lineage of 224 influenza B viruses was determined: 222 (> 99%) were B/Yamagata and two (< 1%) were of the B/Victoria lineage.

Antigenic and genetic characteristics

From week 40/2014 to week 3/2015, antigenically and genetically characterised A(H1N1) viruses were similar to the current vaccine-strain recommended by WHO for 2014–2015 [1].

Of 91 characterised A(H3N2) viruses, 27 (30%) have antigenically drifted compared to the vaccine A/Texas/50/2012 strain and belong to the group containing A/Switzerland/9715293/2013, which was also detected in the USA during this season.

Twelve EU/EEA countries genetically characterised a total of 288 A viruses. The majority (67%) of the 235 characterised A(H3N2) viruses belonged to two genetic subgroups (A/Switzerland/9715293/2013 and A/Hong Kong/5738/2014), which are antigenically distinct from the A(H3N2) component of the current vaccine virus; 78 (33%) clustered in subgroups similar to the current vaccine A(H3N2) reference virus.

The latest data on genetically characterised B viruses indicated that circulating B viruses do not belong to the vaccine-strain subgroup.

Susceptibility to antiviral drugs

Between week 40/2014 and week 2/2015, 93 A(H3N2), 20 A(H1N1)pdm09 and four type B viruses were tested by phenotypic and genotypic methods in eight EU/EEA countries for susceptibility to the neuraminidase inhibitors oseltamivir and zanamivir. None of the tested viruses showed evidence of reduced susceptibility. All 55 A(H3N2) and two A(H1N1)pdm09 viruses tested for adamantane M2-ion channel blocker antiviral drugs were resistant, a usual pattern for current influenza A viruses.

Seroepidemiology

In Norway, the immunity against A(H1N1)pdm09 in sera collected in August 2014 was the highest ever since the pandemic peak and mass vaccination in January 2010. Similarly, overall sero-prevalence against the current A(H3N2) and B vaccine variants was around 40%. Antibodies against the A/Switzerland/9715293/ 2013(H3N2) drift variant were detected in approximately half of the individuals who were seropositive against the current H3N2 vaccine virus, suggesting some cross-reactivity. So far, the drift variant has neither dominated nor has it been increasing in frequency among influenza A(H3N2) viruses in Norway. [O. Hungnes, personal communication].

In Scotland (UK), 2000 samples from residual sera collected from June to September 2014 were tested and showed that while immunity to A(H3N2) had increased, A(H1N1)pdm09 antibody prevalence had unexpectedly halved. Vaccination status in children in Scotland was examined but while sero-positivity was marginally higher in those vaccinated, it was not statistically significant [J. McMenamin, personal communication].

Influenza vaccine

Vaccine coverage

Vaccination coverage in EU/EEA Member States appears likely to remain at suboptimal levels. According to the seasonal risk assessment questionnaire, the vaccine uptake in Sweden in 2014 was higher compared to previous seasons, while it remained at the same level in France and the UK (England and Scotland) and was lower in Malta.

Provisional data from the joint ECDC/VENICE III project suggest that during the 2012–2013 season, vaccination coverage met the target of 75% in the older population only in the Netherlands and the UK (Northern Ireland and Scotland). Compared with 2012–2013, the proportion of vaccinated persons was slightly higher in six EU countries. In people with underlying conditions, the vaccination coverage was much lower than in the elderly, and only Northern Ireland (UK) met the target of 75% vaccinated persons in this risk group [2].

Vaccine effectiveness

In the USA, the early estimates of overall adjusted vaccine effectiveness against laboratory-confirmed influenza in 2014–2015 cases was 23% (95% confidence interval: 8–36%) and the adjusted effectiveness for persons 50 years of age or older was 14% (95% CI: -31–33%). These low estimates may reflect the high proportion (two thirds) of antigenically characterised A(H3N2) viruses which have drifted away from the vaccine strain. Another factor influencing influenza vaccine effectiveness is the age and health of the person being vaccinated. In general, the flu vaccine works best in young, healthy people and is less effective in people 65 years of age and older [3]. In the seasonal risk assessment questionnaire, France reported that 43% of influenza patients admitted to ICUs were 65 years and older and vaccinated.

Mortality

During week 3/2015, based on pooled data of mortality monitoring from 15 EU countries [4], excess all-cause mortality was observed among the elderly (≥ 65 years) in seven countries: England, France, Portugal, the Netherlands, Scotland, Spain and Wales. Excess all-cause mortality cannot be attributed with certainty to specific causes, but may be associated with influenza, increase in acute respiratory illness and extreme cold snaps.

Situation in the temperate countries of the northern hemisphere

In Canada, seven of 13 provinces reported widespread influenza activity, which may have peaked as the proportion of specimens positive for influenza has decreased since week 1/2015. However, this decrease could be connected to underreporting during the Christmas and New Year's holidays. The vast majority of circulating influenza viruses was type A (98%), and almost all (> 99%) were subtype A(H3N2). Of 55 antigenically characterised A(H3N2) viruses, 49 were antigenically similar to A/Switzerland/9715293/2013 and thus drifted away from the current vaccine strains [5].

In the USA, for week 1/2015, the proportion of visits for ILI in all 10 US Department of Health & Human Services Surveillance Regions was at, or above, the region-specific baseline. The proportion of specimens positive for influenza virus was 30% and declined to 20% for week 2/2015. The vast majority of positive specimens were type A (96%), more than 99% of which were subtype A(AH3N2). For week 1/2015, two thirds of circulating A(H3N2) viruses were antigenically and genetically distinguishable from A/Texas/50/2012 (an A/Texas/50/2012 (H3N2)-like virus was recommended for the 2014–2015 vaccine) and were antigenically similar to A/Switzerland/9715293/2013, which has been recommended by WHO for the composition of the 2015 influenza vaccine in the southern hemisphere. This variant A(H3N2) virus was already detected in March 2014 and has been reported increasingly since then [6].

In northern China and Japan, influenza activity is still increasing, with A(H3N2) dominating [7].

Situation in the temperate countries of the southern hemisphere

Compared with the 2013 season, ILI rates in 2014 were similar or lower in all countries, except in Paraguay and Australia. Circulation and dominance of influenza viruses varied widely throughout the southern hemisphere. Influenza A(H3N2) virus was predominant in South America (56%) and southern Africa (74%), A(H1N1)pdm09 in Australia and New Zealand (46%), and B virus in Central America (74%). Of B viruses ascribed to a lineage, 79% were B Yamagata and 21% were B Victoria, except in Central America where all circulating B viruses were B Yamagata [8, 9].

An antigenic drift of the majority of circulating A(H3N2) viruses was observed and in September 2014. Consequently, WHO recommended the replacement of the A/Texas/50/2012 vaccine virus by A/Switzerland/9715293/2013 which better matches the circulating A(H3N2) viruses [10].

Risk assessment for the remaining season (as of week 3/2015)

- Based on the situation in the countries which were affected first and other countries in the northern hemisphere, medium or high rates of ILI/ARI (intensity) are likely to be observed in the vast majority of EU/EAA countries.
- A(H3N2) drift variants, i.e. strains different from the vaccine strains, appear likely to predominate.
- Influenza A(H3N2) tends to cause more severe illness than A(H1N1)pdm09 among the elderly and medical risk groups. The reduced effectiveness of the seasonal influenza vaccine, already estimated at below 25% in the USA, may increase the severity of the season, i.e. the number of severe cases and fatal outcomes in older persons and risk groups is estimated to rise.
- A(H1N1)pdm09 circulated in lower proportions in 10 EU countries and only predominated in Italy and Slovenia. An increased natural or vaccine-induced immunity against this virus, as observed in Norway, is likely to prevent extensive late circulation of this subtype in some EU countries. However, strong population immunity may cause increasing immune selection pressure and therefore close attention should be paid to the possible emergence of A(H1N1)pdm09 drift variants.
- As often observed during previous seasons, the emergence of B viruses after the peak of type A viruses cannot be excluded.

ECDC's scientific and public health advice

Simple protective measures

Evidence of the effectiveness of self-isolation, hand-washing and good respiratory hygiene/cough etiquette supports the continued recommendation of these simple measures.

Vaccination

Circulating A(H1N1)pdm09 viruses, even if circulating less widely, match the vaccine strain. Even if a lower overall vaccine effectiveness due to the circulation of drift A(H3N2) viruses is likely, the vaccine may still reduce complications and severe outcomes associated with this subtype.

Antivirals

Treatment and post-exposure prophylaxis with antivirals protects the elderly and people in risk groups against serious influenza illness. The circulating viruses analysed so far show susceptibility to the antiviral drugs oseltamivir and zanamivir. As advised during previous seasons, and especially in a potentially severe season dominated by A(H3N2) virus, physicians should always consider early treatment (i.e. within 48 hours of symptom onset) or post-exposure prophylaxis with antivirals when treating influenza-infected patients and exposed individuals who belong to risk groups.

Surveillance

Surveillance of hospitalised cases, in particular in high-risk groups, should be enhanced or implemented in countries where such monitoring does not exist. This would facilitate early public health risk assessment as well as management and treatment of severe cases.

Conclusions

- Influenza activity started to increase in week 1/2015 in almost all EU countries.
- Subtype A(H3N2) is dominant in almost all EU/EEA countries and, as observed on other continents, antigenic drift variants of A(H3N2) have been reported, mainly from genetic groups represented by reference viruses A/Switzerland/9715293/2013 and A/Hong Kong/5738/2014.
- As observed in the US, where such variants were also reported, a low vaccine effectiveness (< 25%) is to be expected. As a consequence, higher rates of complications and severe cases may occur in EU/EEA countries.
- Early antiviral treatment should be offered to patients with influenza, and post-exposure prophylaxis should be considered for high-risk groups.
- In February, WHO will most probably recommend a change in the A(H3N2) component of the seasonal influenza vaccine for the next winter season (2015–2016) and include a strain similar to the variants currently circulating, as previously recommended for the southern hemisphere for the forthcoming 2015 season.

References

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[10] World Health Organization. Recommended composition of influenza virus vaccines for use in the 2015 southern hemisphere influenza season. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/2015_south/en/

Annex 1. Consulted experts

ECDC: C. Adlhoch, J. Beauté, M. Catchpole, D. Coulombier, E. Broberg, P. Penttinen, R. Snacken, P. Zucs

External experts: I. Bonmarin, SH. Hauge, O. Hungnes, A. Larrauri, B. Lina, J. McMenamin, A.Meijer, R. Pebody, S. Tsiodras and W. van der Hoek. Declarations of interest have been received from every expert involved. They have been reviewed by ECDC and none are considered to represent a conflict of interest.

Respondents to the questionnaire: I. Bonmarin, M. Brytting, H. Englund, N. Ikonen, O. Lyytikäinen, J. McMenamin A.Meijer, T. Melillo, J. Mikas, S. Murtopuro, R. Pebody, A. Reuß, S. Tsiodras and W. van der Hoek

ECDC is very grateful for the expert input from the persons above. They were consulted as individuals on the basis of their expert knowledge and experience rather than as representatives of their institutions or countries. It should also be noted that responsibility for the content of this risk assessment rests with ECDC rather than with these individuals.

Annex 2. Questionnaire

Questions for influenza season 2014–2015 (to date)

Q1: Are current pressures on primary care due to respiratory illness different from the corresponding time after onset of the season in:

(Please highlight the most appropriate answer/s.)

2013–2014?	The same	More than in 2013–2014	Less than in 2013–2014
2012–2013?	The same	More than in 2012–2013	Less than in 2012–2013

No information

Any further comments? . . .

Q2: Are the current pressures on secondary care (hospital admissions, intensive care units, deaths) due to respiratory illness different from the corresponding time after onset of the season in:

(Please highlight the most appropriate answer/s.)

2013–2014?	The same	More than in 2013–2014	Less than in 2013–2014
2012–2013?	The same	More than in 2012–2013	Less than in 2012–2013

No information

Any further comments? . . .

Q3: In relation to questions 1 and 2, are you aware of any more marked geographic heterogeneity (more pressures in some part(s) of the country) than usual?

(Please highlight the most appropriate answer/s.)

Yes

No

If yes, could you further specify? . . .

Q4: Are people in risk groups (including the elderly) for severe disease due to influenza currently affected at rates any different from the corresponding time after onset of the season in:

(Please highlight the most appropriate answer/s.)

2013–2014?	The same	More than in 2013–2014	Less than in 2013–2014
2012–2013?	The same	More than in 2012–2013	Less than in 2012–2013

No information

Which is the more prevalent risk group? . . .

If there are differences, what are they? . . .

Q5: What are the age groups experiencing severe influenza disease compared to:

(Please highlight the most appropriate answer/s.)

2013–2014?	The same	More than in 2013–2014	Less than in 2013–2014
2012–2013?	The same	More than in 2012–2013	Less than in 2012–2013

No information

If there are differences, could they be explained by changes in strain mix in 2013–2014?

If there are differences, what are they? . . .

Q6: At this moment, how does the number of healthy people with severe influenza compare to the corresponding time after onset of the season in:

(Please highlight the most appropriate answer/s.)

2013–2014?	The same	More than in 2013–2014	Less than in 2013–2014
2012–2013?	The same	More than in 2012–2013	Less than in 2012–2013

No information

Q7: Are there any specific issues noticeable this season related to complications of influenza (acute respiratory distress syndrome or secondary bacterial infections/co-infections)?

(Please highlight the most appropriate answer/s.)

Yes

No

If yes, please provide more details. . . .

Q8: Are there any other features that you think deserve attention (e.g. reduced antiviral susceptibility, any subtype causing severe disease, vaccine failure, vaccine shortage, …)?

(Please highlight the most appropriate answer/s)

Yes

No

If yes, please provide more details. . . .

Q9: Do you have any information on immunisation coverage for influenza in 2014–2015 yet?

(Please highlight the most appropriate answer/s.)

Yes

If yes, is it higher or lower (compared to previous season): . . .

No

Q10: Has any variant strain been detected based on antigenic characterisation (with 8-fold or greater drops in HI titre in comparison to the vaccine strain) or based on genetic characterisation? If yes, in what proportion of that subtype?

(Please highlight the most appropriate answer/s)

Yes, based on antigenic characterisation; please indicate the variant strain and the category of reporting.

Yes, based on genetic characterisation; please indicate the variant strain and the category of reporting.

No

% for each variant out of total of detections of corresponding subtype: . . .

Q11: How many (%) of ICU admissions/deaths associated with influenza were vaccinated?

%: . . .

I do not know.

Q12: If influenza outbreaks/clusters are monitored.

(Please highlight the most appropriate answer/s)

a) The number of influenza outbreaks (or clusters) is
the same more than in 2013–2014 less than in 2013–2014.

b) The number of influenza outbreaks (or clusters) in schools
the same more than in 2013–2014 less than in 2013–2014.

c) The number of influenza outbreaks (or clusters) in long-term care facilities is
the same more than in 2013–2014 less than in 2013–2014.

Please provide details on the specific groups affected (e.g. age group of school children, those with intellectual disabilities, the elderly, etc.). . .

Q13: Is it too early to answer all or any of the questions.

(Please highlight the most appropriate answer/s)

Yes

No

If yes, I will send an updated questionnaire later.

Q14: Was there recently any change in the surveillance system?

Yes

No

If yes, which kind of change? . . .

Further comments? . . .

Many thanks for completing this questionnaire.
Please let us know:

Would you be willing to review the draft risk assessment?

Yes No

Would you be willing to have your name or institution listed as contributing to the risk assessment?

Yes No

On any of the questions above (e.g. the clinical picture and impact), are there other persons that you feel we should contact/forward this questionnaire to? If so, how should we best contact them? . . .