RAPID RISK ASSESSMENT

Risk assessment of seasonal influenza, EU/EEA, 2016/2017

24 December 2016

Main conclusions and options for response

This season, influenza viruses, mainly A(H3N2), began circulating early in the EU/EEA. It is too early to anticipate the intensity in primary care and severity in secondary care, but if A(H3N2) continues to predominate, there is a risk that people over 65 years of age will be the most severely affected, possibly putting some healthcare systems under pressure. Influenza A(H1N1)pdm09 may dominate in a few countries where A(H3N2) was dominant last season (Slovenia and Italy).

Although just over half of the A(H3N2) viruses characterised at this early stage of the season belong to a new genetic clade, they all are antigenically less than four-fold different from the vaccine strain in the haemagglutination inhibition test. Preliminary vaccine effectiveness (VE) estimates from Scandinavia suggest levels of effectiveness towards the upper range of those seen during the period 2011—2015. Given the early epidemiological and VE data, vaccination of the elderly and other high-risk individuals remains a priority, in line with the national recommendations of the EU/EEA Member States, to prevent more severe cases. Given the partial effectiveness of influenza vaccines, rapid use of neuraminidase inhibitors for laboratory-confirmed or probable cases of influenza should be considered for vaccinated and non-vaccinated at-risk patients.

Source and date of request

ECDC internal decision, 23 December 2016.

Public health issue

Early rapid risk assessment on seasonal influenza

Consulted experts

(In alphabetical order) ECDC: C Adlhoch, E Broberg, A Melidou, P Penttinen, R Snacken

Disease background information

Since the 2009 influenza pandemic, ECDC has produced early-season risk assessments for EU/EEA countries every season, to inform national public health authorities of the key attributes of the ongoing influenza season. The risk assessments are used to guide local public health measures, such as reinforcing vaccination programmes, guiding antiviral policies and reallocating healthcare resources.

The main objectives of the risk assessment in the early season 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 and the possible impact on susceptible and at-risk populations for the rest of the season;
- to assess the risk of reduced vaccine effectiveness (VE) and susceptibility to neuraminidase inhibitors (NAIs).

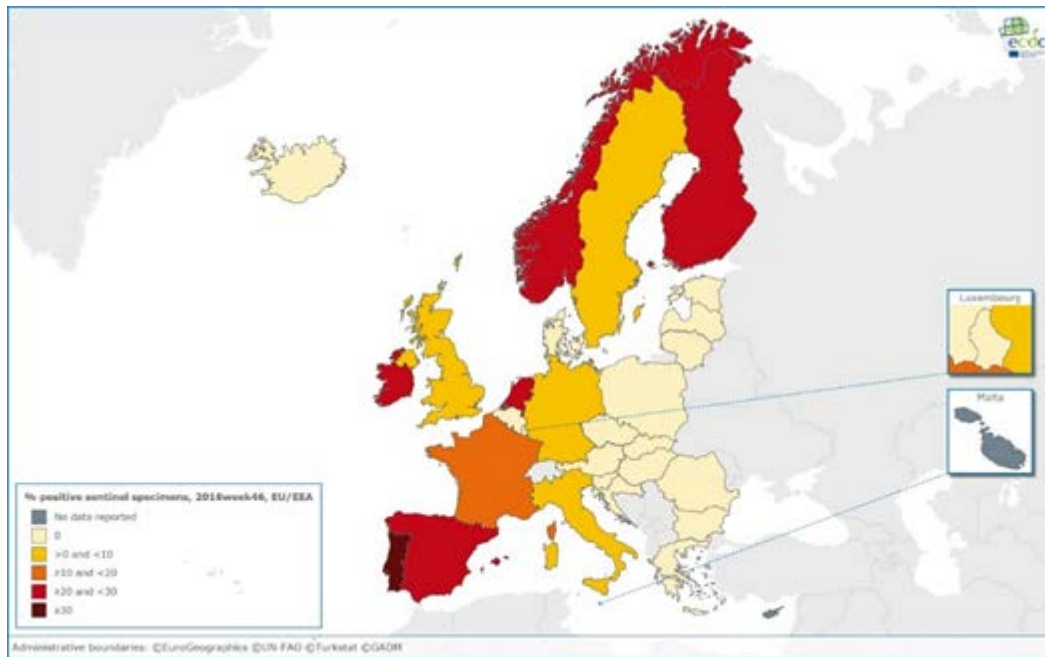# Event background information

Data sources

This risk assessment is based on the weekly clinical (influenza-like illnesses - ILI and acute respiratory infections - ARI), epidemiological and virological data from primary and secondary healthcare settings, 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). Other information used includes situation reports from other countries, peer-reviewed literature and data from the European Monitoring of Excess Mortality for Public Health Action (EuroMOMO) project.

Different risks related to the influenza epidemic (for instance the risk of severe outcomes in particular age groups) were assessed with regard to likelihood and potential impact.

Primary care situation in the first affected countries

Compared to clinical indicators (ILI/ARI rates), the proportion of detected viruses in primary care is a very sensitive indicator for estimating influenza activity in a region. By week 46/2016, 28 countries had reported low influenza intensity based on clinical indicators. However, seven countries (France, Finland, Ireland, the Netherlands, Norway, Spain and Portugal) (Figure 1) had reported ≥10% of respiratory specimens from ILI patients in sentinel general practitioners' (GP) practices testing positive for influenza. Pooled data across all EU/EEA countries reported for week 46/2016 yielded 11% positivity of sentinel specimens, indicating the start of the European influenza season based on the indicator crossing the 10% threshold (Figure 2). This was earlier than the last six seasons, when the threshold was not exceeded before week 48 (Figure 3.)

Figure 1. Distribution of sentinel specimens' positivity for influenza, from primary care, EU/EEA countries, week 46 of 2016

Note: Germany, Italy, Norway, Sweden and the UK tested <10 specimens

Figure 2. Weekly proportion of sentinel specimens positive for influenza virus and number of detections, by type and subtype, from primary care, EU/EEA, 2016-2017
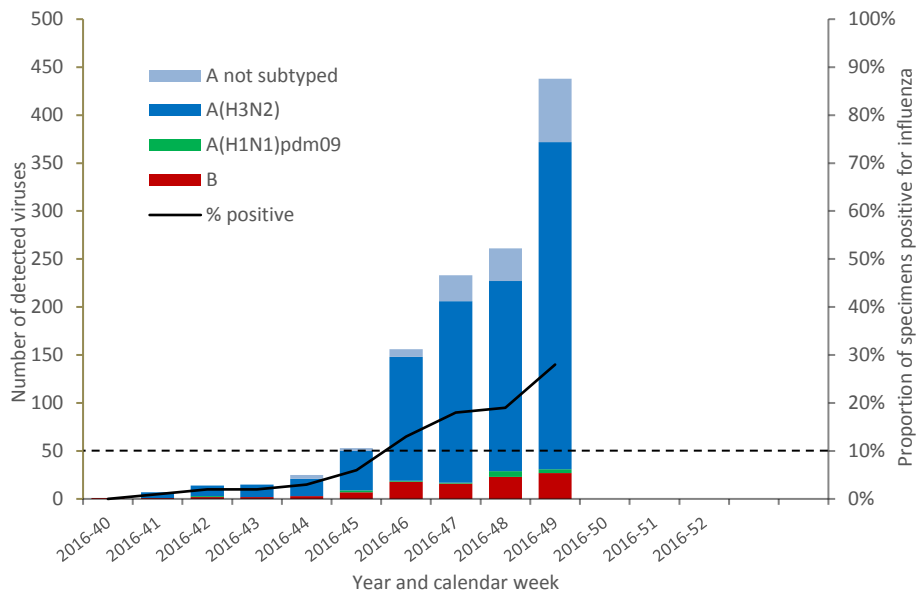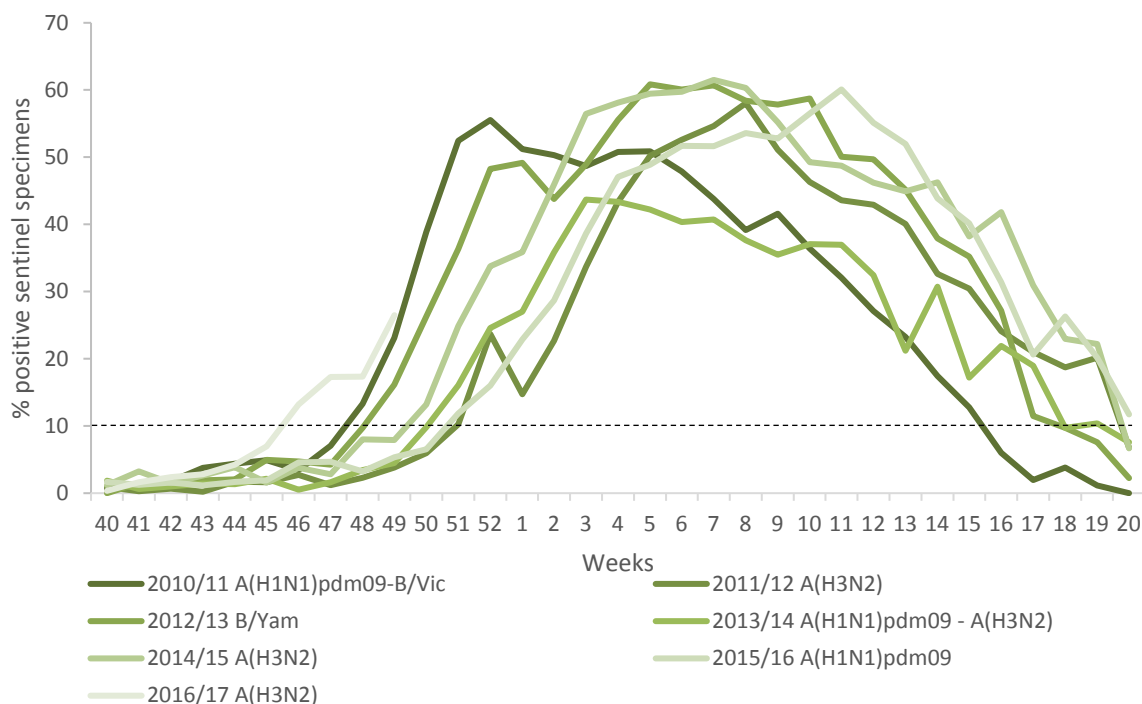
Figure 3. Weekly proportions of sentinel specimens positive for influenza and threshold of 10% positivity, from primary care, EU/EEA, seasons 2010-2011 to 2016-2017

This early influenza circulation contrasted with low clinical surveillance indicators in primary care settings. In week 49/2016, ILI and ARI rates were still at baseline level in most countries and increasing in Finland, France, Ireland, Italy, Luxembourg, the Netherlands, Norway and Portugal. Of 734 influenza viruses detected from sentinel sources in week 49/2016, 713 (97%) were type A and 21 (3%) type B. The vast majority (98%) of subtyped influenza A viruses were A(H3N2). Very few A(H1N1)pdm09 viruses (14) were detected in Croatia, Denmark, Italy, Portugal, Spain and the United Kingdom. Of 21 B viruses detected, 10 were ascribed to a lineage and equally distributed between B/Victoria and B/Yamagata lineages. In non-sentinel specimens, 6 497 influenza A viruses (96%) and 164 B viruses (4%) were detected. The majority (98%) of type A viruses were A(H3N2). Of 24 B viruses ascribed to a lineage, 15 (62%) were B/Yamagata and nine B/Victoria (38%).

Secondary care situation in the first affected countries

Since week 40/2016, seven countries, mostly France, Spain and the United Kingdom, have reported hospitalised laboratory-confirmed influenza cases. Thirty-six cases were reported to have been admitted to intensive care units (ICU) and 117 to regular wards. Restricting analysis to the same reporting countries and time period (weeks 40 to 49/2016), the number of cases in ICU are slightly higher than in the previous two seasons (35 vs. 22 and 24). The majority (95%) of hospitalised cases were infected by influenza type A virus and 58 (91%) of 64 subtyped A viruses were A(H3N2) viruses. The distribution of influenza virus types and subtypes in hospitalised patients reflects the proportions observed in primary care.

Virus characteristics

By week 49/2016, circulating A(H3N2) viruses belonged mainly to two genetic groups: the pre-existing clade A/Hong Kong/4801/2014 3C.2a (vaccine virus) and a new emerging clade A/Bolzano/7/2016 3C.2a1 (Table 1), both matching well with the reference viruses (data not shown), with this new clade being found to be antigenically similar to the vaccine strain. Of six genetically characterised B viruses, four belonged to the B/Victoria-lineage B/Brisbane/60/2008 included in both trivalent and quadrivalent vaccine [1]. Twelve viruses (eight A(H3N2), one A(H1N1), two B/Yamagata and one B/Victoria) were antigenically characterised and reported. Five of the eight A(H3N2) viruses belonged to the vaccine A/Hong Kong/4801/2014 -like antigenic group, while three were A/Switzerland/9715293 (H3N2)-like (2015-2016 vaccine virus).

Seventy-four circulating viruses, mainly A(H3N2) viruses, have been tested for antiviral susceptibility and none showed reduced inhibition by neuraminidase inhibitors.

Table 1. **Influenza viruses attributed to genetic and antigenic groups, weeks 40 to 49**

Phylogenetic group	Number of viruses
B/Brisbane/60/2008 (Victoria lineage clade 1A)b	4
A(H1N1)pdm09 A/Michigan/45/2015 (subgroup 6B.1)	3
A(H3N2) A/Bolzano/7/2016 (subgroup 3C.2a1)	82
A(H3N2) A/Hong Kong/4801/2014 (subgroup3C.2a)a	61
A(H3N2) A/Switzerland/9715293/2013 subgroup (3C.3a)a	1
B/Phuket/3073/2013 (Yamagata lineage clade 3)a	2

Antigenic group	Number of viruses
A(H3) A/Switzerland/9715293 (H3N2)-like	3
A(H3) A/Hong Kong/4801/2014 (H3N2)-like	5
B/Phuket/3073/2013-like (B/Yamagata/16/88-lineage)	2
B/Brisbane/60/2008-like (B/Victoria/2/87 lineage)	1
A(H1)pdm09 A/California/7/2009 (H1N1)-like	1

ECDC threat assessment for the EU

High numbers of influenza-positive sentinel specimens signal the circulation of influenza virus in primary care in the first affected countries, however low ILI/ARI rates were reported. The proportion of detected viruses in primary care is a more sensitive indicator than the reported ILI/ARI rates and is hence considered the best indicator for estimating influenza activity in a region [2]. At this stage of the season, it is impossible to estimate the intensity of influenza activity based on ILI/ARI rates in individual EU/EEA countries.

Since the 2009 influenza pandemic, one sub-type of influenza A virus most often largely predominated over other circulating viruses. In the influenza seasons 2011/2012 and 2014/2015, A(H3N2) virus predominated over A(H1N1)pdm09, and conversely, the latter was dominant in 2010/2011, 2012/2013 and in 2015/2016. However, during the season 2013/2014, both A viruses were co-circulating with 62% of A(H1N1)pdm09 and 38% of A(H3N2) [3] (Figure 3).

In A(H3N2)-dominated seasons, older people have been affected the most, resulting in a high number of hospitalised cases and an increase in fatal outcomes in this age group. This was also seen during the 2014—2015 season, with a high number of outbreaks in long-term care facilities and excess all-cause mortality reported by the EuroMOMO project [4]. Should the A(H3N2) virus remain predominant in most countries, as currently also observed in the US [5], older age groups would likely be the most affected and the most at risk of severe disease and outcomes [6].

A late co-circulation of A(H1N1)pdm09 virus during this season cannot be excluded, since low but increasing numbers of detections have already been reported by six countries. As observed since the 2009 pandemic, influenza A(H1N1)pdm09 virus mainly affects middle-aged adults [7].

There are early indications that viruses of both detected B lineages may be circulating this season, but it is not currently possible to predict which lineage of circulating B viruses will dominate. However, irrespective of the lineage that will predominate, the clinical impact of B viruses is expected to be moderate and similar to previous seasons. If Victoria-lineage predominates, the trivalent influenza vaccine would offer sufficient protection as the B/Victoria lineage is included, and the trivalent vaccine is the most widely used vaccine.

More than half of the detected characterised A(H3N2) viruses belong to a new genetic clade, but all are antigenically similar to the vaccine strain [8]. A preliminary adjusted vaccine effectiveness (VE) estimate from Stockholm county in Sweden suggests a VE of 56% (95% CI: 11-78%) for preventing laboratory-confirmed influenza A(H3N2) infection in people 65 years and above [9]. A Finnish study reported a preliminary VE of 60% against ILI and 46% against laboratory-confirmed influenza [10]. Between 2011 and 2015, VE estimates against A(H3N2) have ranged from 11% to 42% [11].

There is no evidence of an emergence of reduced susceptibility to NAIs this season. The use of antiviral treatment is therefore a viable option and should be considered, particularly in high-risk patients.

Conclusions and options for response

Influenza viruses, mainly A(H3N2), started circulating early in the EU/EEA this season. It is too early to anticipate the intensity in primary care and severity in secondary care, but if A(H3N2) continues to predominate then there is a risk that people over 65 years will be the most severely affected, possibly putting some healthcare systems under pressure. Influenza A(H1N1)pdm09 may dominate in a few countries where A(H3N2) was dominant last season (Slovenia and Italy).

Although just over half of the A(H3N2) viruses characterised at this early stage of the season belong to a new genetic clade, they all are antigenically less than four-fold different from the vaccine strain in the haemagglutination inhibition test. Preliminary vaccine effectiveness (VE) estimates from Scandinavia suggest levels of effectiveness towards the upper range of those seen between 2011—2015. Given the early epidemiological and VE data, vaccination of the elderly and other high-risk individuals remains a priority, in line with the national recommendations of the EU/EEA Member States, to prevent more severe cases. Given the partial effectiveness of influenza vaccines, rapid use of neuraminidase inhibitors for laboratory-confirmed or probable cases of influenza should be considered for vaccinated and non-vaccinated at-risk patients.

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