

Start of the 2014/15 influenza season in Europe: drifted influenza A(H3N2) viruses circulate as dominant subtype

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The influenza season 2014/15 started in Europe in week 50 2014 with influenza A(H3N2) viruses predominating. The majority of the A(H3N2) viruses characterised antigenically and/or genetically differ from the northern hemisphere vaccine component which may result in reduced vaccine effectiveness for the season. We therefore anticipate that this season may be more severe than the 2013/14 season. Treating influenza with antivirals in addition to prevention with vaccination will be important.

Influenza activity started increasing in the western part of the World Health Organization (WHO) European Region during week 50 2014, when Malta, the Netherlands and Sweden reported medium intensity of influenza activity which refers to usual activity of influenza season [1]. Rates of influenza-like illness (ILI) and/or acute respiratory infection (ARI) have continued to increase, and in week 2 2015, 13 countries (Albania, Finland, France, Greece, Iceland, Malta, the Netherlands, Portugal, Slovenia, Spain, Sweden, Switzerland, the United Kingdom (UK)) in the WHO European Region reported medium intensity and Albania, the Netherlands, Portugal, Spain and Switzerland had ILI rates above the epidemic threshold for the pre-season [2]. Of the 13 countries reporting medium intensity, six (Finland, the Netherlands, Portugal, Slovenia, Sweden and the UK (England)) reported patterns of widespread activity with laboratory-confirmed influenza cases in 50% or more of their administrative units (or reporting sites).

Influenza surveillance in Europe

Since October 2014, all 53 Member States of the WHO European Region report their epidemiological and virological influenza surveillance data to The European Surveillance System (TESSy), hosted by the European Centre for Disease Prevention and Control (ECDC) [1]. The data are jointly published with the WHO European Regional Office to describe the annual occurrence of

influenza (timing and spread), its impact and severity (groups which are most affected), the predominating influenza type and subtype, as well as analyses of virus strains to support the WHO recommendations for the composition of seasonal influenza vaccines (www.flunewseurope.org). The northern hemisphere influenza vaccine composition recommendation is given by WHO at the end of February each year.

Influenza surveillance in Europe is mainly based on primary care sentinel sites collecting specimens from patients with ILI and/or ARI [1,3]. Data are collected at the national level and reported to the European level according to standardised case definitions [4,5]. The national influenza centres perform antigenic and genetic characterisation of influenza viruses as well as antiviral susceptibility testing of a representative sample of virus isolates.

In addition to the primary care surveillance, particularly since the 2009 influenza A(H1N1) pandemic, hospital surveillance of laboratory-confirmed influenza cases has been conducted, including for this season, in Finland, France, Ireland, Spain, Sweden and the UK. Additionally, sentinel severe acute respiratory infection (SARI) surveillance is in place in 13 countries [1].

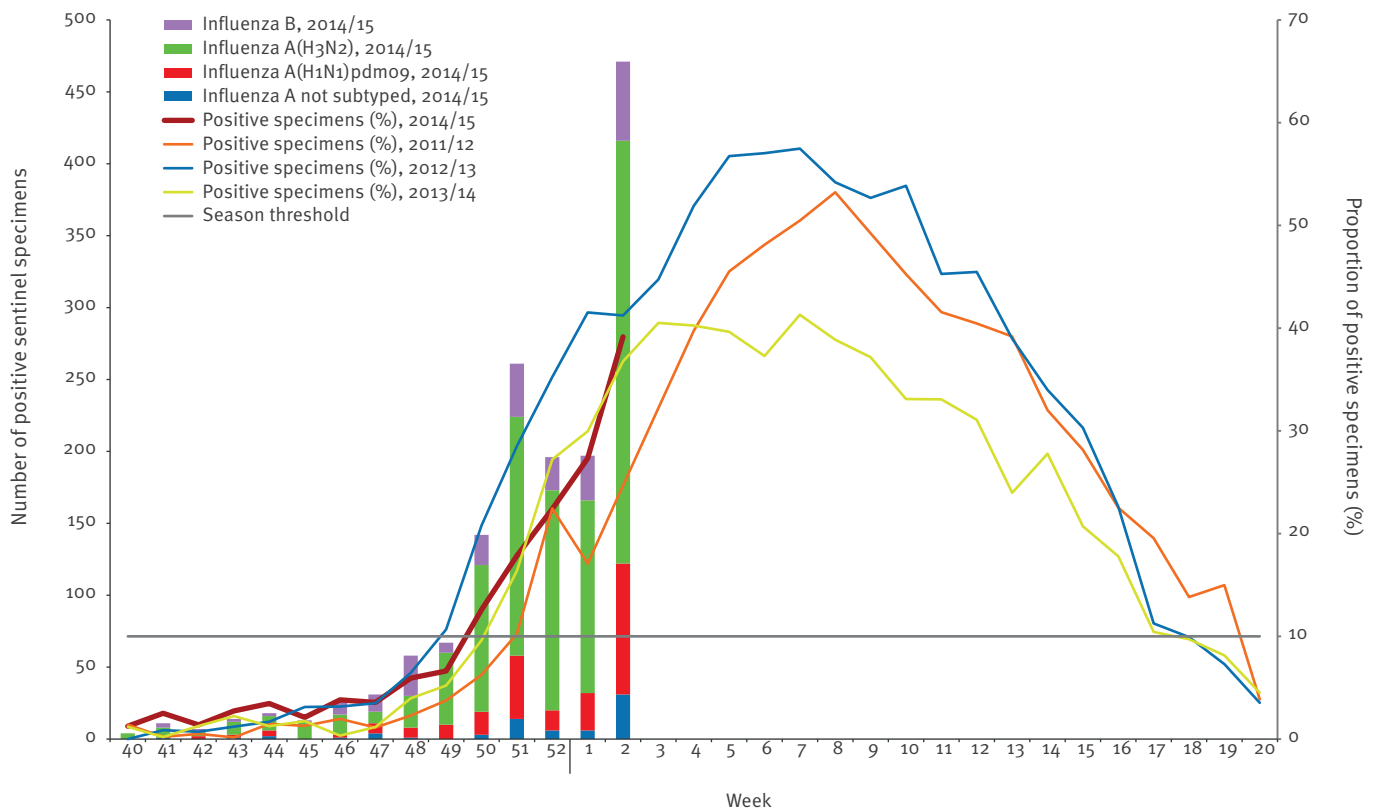
Virological situation in primary healthcare

The overall proportion of influenza-positive sentinel specimens increased from 4% to 39% from week 47 2014 to week 2 2015, indicating the start of the season at a similar time to the previous season (Figure 1). The season threshold of 10% was exceeded in season 2011/12 and 2013/14 in week 51, in 2012/13 in week 49, and in the current season during week 50 (Figure 1).

In most countries, influenza A(H3N2) virus was the dominant subtype in both sentinel and non-sentinel specimens in week 2 2015. In the sentinel systems, since week 40, 1,134 (10%) of the 11,854 specimens

FIGURE 1

Number of influenza virus-positive sentinel specimens by (sub)type and week, and proportion of positive specimens compared to three previous seasons, World Health Organization European Region, weeks 40 2014–2015 for season 2014/15



collected in 35 countries tested positive for influenza, 901 (79%) for type A influenza virus and 233 (21%) for type B (Figure 1). Of the 831 type A viruses subtyped, 688 (83%) were A(H3N2) and 143 (17%) were A(H1N1)pdm09 by week 2 2015 (Figure 1). The lineage of 87 type B viruses was determined: six were B/Victoria lineage and 81 B/Yamagata lineage.

The antigenic characteristics of 117 influenza viruses and the genetic characteristics of 202 influenza viruses were reported to TESSy by 16 countries mainly in the western countries of the Region. Of 68 influenza A(H3N2) viruses antigenically characterised, 40 were reported by the national influenza centres as A(H3N2) A/Texas/50/2012-like (vaccine-like) and 26 were A/Switzerland/9715293/2013-like (antigenically different from the vaccine); two viruses could not be ascribed to an antigenic category. All 21 A(H1N1)pdm09 viruses characterised were A/California/7/2009-like (vaccine strain). Of the 30 influenza B viruses characterised, 28 were of the B/Yamagata/16/88-lineage (10 were reported as B/Massachusetts/02/2012-like viruses, one B/Wisconsin/1/2010-like and 17 B/Phuket/3073/2013-like) and two were B/Brisbane/60/2008-like viruses of the Victoria lineage.

Of the 160 genetically characterised A(H3N2) viruses, 110 (69%) fall in two genetic subgroups

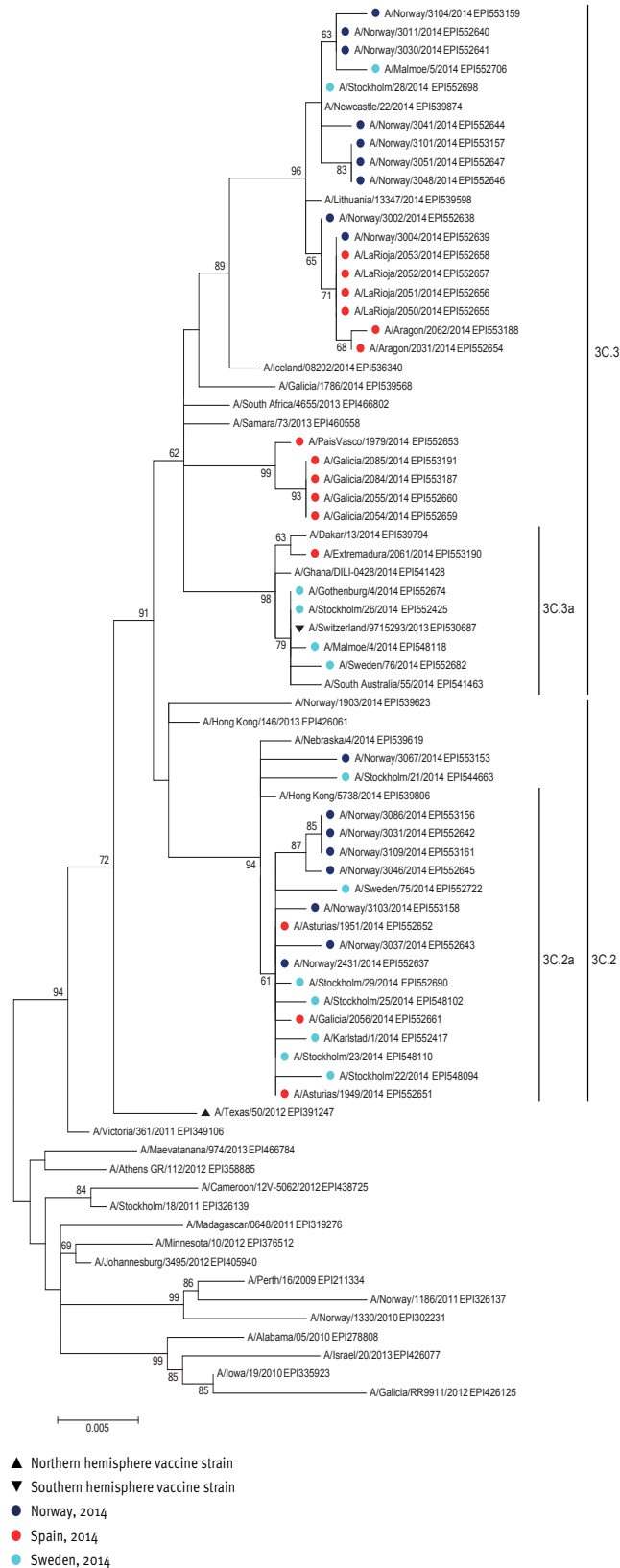
containing antigenic drift variants compared with A/Texas/50/2012, the vaccine component for the northern hemisphere 2014/15 season [6].

For 63 viruses, Norway, Spain and Sweden reported the haemagglutinin gene sequence accession number for the Global Initiative on Sharing All Influenza Data (GISAID) EpiFlu database. The maximum likelihood phylogenetic tree of these viruses together with the A(H3N2) reference viruses shows that the current circulating viruses cluster mainly with the genetic subgroups 3C.3, 3C.3a together with the A/Switzerland/9715293/2013, and 3C.2a with the A/Hong Kong/5738/2014, and show genetic drift from the current vaccine virus (Figure 2). The antigenic drift of viruses clustering with the A/Newcastle/22/2014 has not yet been shown.

Ninety-three influenza A(H3N2) viruses, 20 A(H1N1)pdm09 and four influenza B viruses have been tested phenotypically or genotypically for neuraminidase inhibitor susceptibility. None showed evidence of reduced susceptibility to either oseltamivir or zanamivir.

FIGURE 2

Maximum likelihood phylogenetic tree of haemagglutinin nucleotide sequences (1,063 nucleotides) from influenza A(H3N2) viruses reported to the European Surveillance System and reference A(H3N2) viruses, weeks 40 2014–1 2015



All sequences have been retrieved from GISAID EpiFlu database (accession numbers indicated in the tree)

Laboratory-confirmed hospitalised influenza cases

Current surveillance systems reporting laboratory-confirmed hospitalised influenza cases to TESSy, while not being representative on a population basis in all countries, provide information on groups being hospitalised due to influenza as well as risk factors for severe disease. This season, as of week 40 2014, six countries with a monitoring system for laboratory-confirmed hospitalised influenza cases reported 719 laboratory-confirmed hospitalised cases. In intensive care units (ICU), 671 cases were reported: three in Finland, 101 in France, 20 in Spain, five in Sweden and 542 in the UK. In comparison, for season 2013/14, by week 2 2014, France had reported 77, Ireland two, Spain 227 and Sweden 11 ICU cases. The UK had not reported a single severe case by week 2 2014 and the surveillance system there has not changed.

Of the 719 laboratory-confirmed hospitalised influenza cases, 682 (95%) were positive for influenza A virus (197 subtyped: 149 A(H3N2) and 48 A(H1N1)pdm09) and 37 (5%) for influenza B virus, which reflects the overall predominance of A(H3N2) and co-circulation of the A(H1N1)pdm09 and B viruses.

Of the 671 cases admitted to ICU, 642 (96%) were positive for influenza A virus (170 subtyped: 126 A(H3N2) and 44 A(H1N1)pdm09) and 29 (4%) for influenza B virus. Half of the cases admitted to ICU for which information on age was available (61/128) were aged 65 years or older. The median age at admission to ICU was 64 years (mean 61.6 years, range 1–93 years). In the 2013/14 influenza season (up to week 2 2014 and during the whole season), the majority of ICU cases had been 40–64 years old, with influenza A(H1N1)pdm09 virus as the dominating subtype [7].

Discussion and conclusions

The influenza season in Europe has started and continues to expand according to the clinical, epidemiological and virological indicators. The season is dominated by influenza A(H3N2) viruses, although both A(H1N1)pdm09 and B viruses co-circulate. This is similar to the influenza activity in the other parts of northern hemisphere, e.g. the United States (US), where the influenza activity has continued to increase with influenza A(H3N2) viruses predominating [8].

The last influenza seasons in Europe dominated by A(H3N2) viruses were seasons 2011/12 [9,10] and 2012/13 [3,11], when A(H1N1)pdm09 and A(H3N2) viruses co-dominated. These seasons were estimated as moderately severe based on ILI/ARI consultation rates, although the European Union/European Economic Area (EU/EEA) still lacks agreed criteria for severity of influenza. The current season has started earlier in the US where higher influenza-related hospitalisation rates are being reported as compared with the past A(H3N2)-dominated seasons [12]. As shown for Europe, the 2014/15 season has started at a similar time and

with similar impact in primary care as the previous season. Since A(H3N2)-dominated seasons usually cause more severe outcomes among the elderly and other risk groups than A(H1N1)pdm09 or B seasons [13,14], the current influenza epidemic in Europe is expected to cause an increased number of severe infections, hospitalisations, ICU admissions and deaths in the elderly than the 2013/14 influenza season. This has already been observed in ICU admissions reported from the UK this season in comparison with the previous season.

In September 2014, the WHO consultation and information meeting on the composition of influenza virus vaccines indicated an emergence of two new genetic clades of A(H3N2) viruses (clades 3C.2a and 3C.3a) containing antigenic drift viruses of previously circulating viruses [15]. The US Centers for Disease Control and Prevention subsequently posted a health alert network notification [16], and ECDC issued a risk assessment [17] concerning the continued circulation and transmission of these viruses.

Based on our analysis and the current knowledge of the circulating viruses [18], the northern hemisphere vaccine may not offer desired protection against the circulating A(H3N2) viruses. However, for the A(H1N1)pdm09 and B/Victoria lineage viruses, only limited drift has been observed and protection against the circulating influenza A(H1N1)pdm09 viruses is still conferred by the vaccine.

The vaccine effectiveness for this season for the A(H3N2) and possibly the B component is expected to be reduced as already seen in the US [19] and in previous seasons in Europe [20,21]. However, the vaccine is anticipated to prevent some infections, improve the course or shorten the duration of influenza in infected individuals, and is likely to reduce the number of severe outcomes and mortality. It therefore remains the measure of choice to prevent severe illness and possibly fatal outcomes in risk groups. The circulating viruses are susceptible to the antiviral drugs oseltamivir and zanamivir and these drugs are therefore an important adjunct in the treatment of influenza.

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Conflict of interest

None declared.

Author's contributions

Broberg E: influenza surveillance data maintenance, data analysis and draft of the manuscript; Snacken R: influenza surveillance data maintenance and analysis and seasonal risk assessment, review of the manuscript; Adlhoch C, Beauté J, Galinska M and Pereyaslov D: influenza surveillance data maintenance and analysis, review of the manuscript; Brown C and Penttinen P: surveillance strategy, critical review of the manuscript.

References

1. European Centre for Disease Prevention and Control (ECDC)/ World Health Organization Regional Office for Europe (WHO/ Europe). Flu News Europe. System description. ECDC/ WHO. [Accessed 22 Jan 2015]. Available from: <https://www.flunewseurope.org/SystemDescription>
2. 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 Other Respir Viruses*. 2013 Jul;7(4):546-58. doi: 10.1111/j.1750-2659.2012.00422.x
3. Snacken R, Broberg E, Beauté J, Lozano JE, Zucs P, Amato-Gauci AJ. Influenza season 2012-2013 in Europe: moderate intensity, mixed (sub)types. *Epidemiol Infect*. 2014;142(09):1809-12. <http://dx.doi.org/10.1017/S0950268814001228> PMID:24814635
4. European Centre for Disease Prevention and Control (ECDC). Influenza case definitions. Stockholm: ECDC. [Accessed 22 Jan 2015]. Available from: http://ecdc.europa.eu/en/activities/surveillance/eisn/surveillance/pages/influenza_case_definitions.aspx.
5. European Commission. Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. *Official Journal of the European Union*. 2008/426/EC.
6. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2014-2015 northern hemisphere influenza season. Geneva: WHO. 20 Feb 2014. Available from: http://www.who.int/influenza/vaccines/virus/recommendations/2014_15_north/en/.
7. Adlhoch C, Broberg E, Beauté J, Snacken R, Bancroft E, Zucs P, et al.; European Influenza Surveillance Network (EISN). Influenza season 2013/14 has started in Europe with influenza A(H1)pdm09 virus being the most prevalent subtype. *Euro Surveill*. 2014;19(4):20686. <http://dx.doi.org/10.2807/1560-7917.ES2014.19.4.20686> PMID:24507465
8. World Health Organization (WHO). Influenza Update N° 228. 12 January 2015. Geneva: WHO. Available from: http://www.who.int/influenza/surveillance_monitoring/updates/2015_01_12_surveillance_update_228.pdf?ua=1.
9. European Centre for Disease Prevention and Control (ECDC). Surveillance report. Influenza in Europe – Season 2011-2012. Stockholm: ECDC. October 2012. Available from: <http://www.ecdc.europa.eu/en/publications/Publications/Influenza-Europe-2011-2012-surveillance-report.pdf>.
10. World Health Organization (WHO) Regional Office for Europe. Summary of the 2011-2012 influenza season in the WHO European Region. Copenhagen: WHO. [Accessed 22 Jan 2015]. Available from: <http://www.euro.who.int/en/health-topics/communicable-diseases/influenza/publications/2012/summary-of-the-2011-2012-influenza-season-in-the-who-european-region>.
11. World Health Organization (WHO) Regional Office for Europe. Summary of the 2012-2013 influenza season in the WHO European Region. Copenhagen: WHO. [Accessed 22 Jan 2015]. Available from: <http://www.euro.who.int/en/health-topics/communicable-diseases/influenza/publications/2013/summary-of-the-2012-2013-influenza-season-in-the-who-european-region>.
12. Centers for Disease Control and Prevention (CDC). CDC: Flu Activity Expands; Severity Similar to Past H3N2 Seasons. Atlanta: CDC. 5 Jan 2015. Available from: <http://www.cdc.gov/flu/news/flu-activity-expands.htm>.
13. Lee BE, Mukhi SN, Drews SJ. Association between patient age and influenza A subtype during influenza outbreaks. *Infect Control Hosp Epidemiol*. 2010;31(5):535-7. <http://dx.doi.org/10.1086/652159> PMID:20334548
14. Kaji M, Watanabe A, Aizawa H. Differences in clinical features between influenza A H1N1, A H3N2, and B in adult patients. *Respirology*. 2003;8(2):231-3. <http://dx.doi.org/10.1046/j.1440-1843.2003.00457.x> PMID:12753540
15. World Health Organization (WHO). WHO Consultation and Information Meeting on the Composition of Influenza Virus Vaccines for the Northern Hemisphere 2014-2015. Geneva: WHO. 17-19 Feb 2014. Available from: <http://www.who.int/influenza/vaccines/virus/recommendations/consultation201402/en/>
16. Centers for Disease Prevention and Control (CDC). CDC Health Advisory Regarding the Potential for Circulation of Drifted Influenza A (H3N2) Viruses. Atlanta: CDC. 3 Dec 2014. Available from: <http://emergency.cdc.gov/HAN/HAN00374.asp>
17. European Centre for Disease Prevention and Control (ECDC). Rapid risk assessment: circulation of drifted influenza A(H3N2) viruses in the EU/EEA. Stockholm: ECDC. 22 Dec 2014. Available from: <http://www.ecdc.europa.eu/en/publications/Publications/RRA-InfluenzaA-H3N2-Dec-2014.pdf>
18. European Centre for Disease Prevention and Control (ECDC). Surveillance report. Influenza virus characterisation - Summary Europe - November 2014. Stockholm: ECDC. Nov 2014. Available from: <http://www.ecdc.europa.eu/en/publications/Publications/ERLI-Net%20report%20November%202014.pdf>
19. Flannery B, Clippard J, Zimmerman RK, Nowalk MP, Jackson ML, Jackson LA, et al.; Centers for Disease Prevention and Control. Early estimates of seasonal influenza vaccine effectiveness - United States, January 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(1):10-5. PMID:25590680
20. Rondy M, Launay O, Puig-Barberà J, Gefenaite G, Castilla J, de Gaetano Donati K, et al. 2012/13 influenza vaccine effectiveness against hospitalised influenza A(H1N1)pdm09, A(H3N2) and B: estimates from a European network of hospitals. *Euro Surveill*. 2015;20(2):pii=21011.
21. Castilla J, Martínez-Baz I, Navascués A, Fernandez-Alonso M, Reina G, Guevara M, et al.; Primary Health Care Sentinel Network; Network for Influenza Surveillance in Hospitals of Navarre. Vaccine effectiveness in preventing laboratory-confirmed influenza in Navarre, Spain: 2013/14 mid-season analysis. *Euro Surveill*. 2014;19(6):20700. <http://dx.doi.org/10.2807/1560-7917.ES2014.19.6.20700> PMID:24556347