

SURVEILLANCE REPORT



Influenza in Europe Season 2013–2014

ECDC SURVEILLANCE REPORT

Influenza in Europe

Season 2013–2014



This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated and written by Cornelia Adlhoch, Eeva Broberg, René Snacken, Julien Beauté, Phillip Zucs and Pasi Penttinen.

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Abbreviations

ARI	Acute respiratory infection
EEA	European Economic Area
ERLI-Net	European Reference Laboratory Network for Human Influenza
EISN	European Influenza Surveillance Network
EU	European Union
ILI	Influenza-like illness
RSV	Respiratory syncytial virus
SARI	Severe acute respiratory infection
TESSy	The European Surveillance System
VE	Vaccine effectiveness

Summary

The 2013–14 influenza season was mild and dominated by influenza A viruses, with a co-circulation of A(H1N1)pdm09 and A(H3N2) viruses in most countries. Only two countries reported higher syndromic notification rates compared with the previous season.

Only a few countries reported widespread influenza transmission and high influenza intensity during the season although the percentage of influenza-positive sentinel specimens was above 10% over 20 weeks, which was comparable to what was observed in previous seasons. The proportion of influenza-positive sentinel specimens peaked at 44% during week 03/2014.

A total of 4 786 hospitalised and laboratory-confirmed cases were reported by eight countries with surveillance of severe influenza; 2 402 (50%) of these cases were infected by A(H1N1)pdm09 virus.

A total of 430 deaths due to influenza were reported by five countries that report data for severe influenza to ECDC. Infections with A(H1N1)pdm09 were detected in 249 (58%) of the 430 cases with a fatal outcome, mostly in persons 40 years of age and older.

None of the characterised viruses differed substantially from the current vaccine viruses recommended by WHO, and only a few viruses showed antiviral resistance.

1 Background

The European Influenza Surveillance Network (EISN) combines epidemiological and virological surveillance of influenza to provide decision-makers and public health experts in EU/EEA Member States with the necessary information to assess influenza activity in Europe and take appropriate action. Virological surveillance activities are coordinated through the European Reference Laboratory Network for Human Influenza (ERLI-Net), a sub-network within EISN.

The objectives of influenza surveillance are:

- to describe the epidemiology of influenza;
- to monitor intensity, geographic spread and trends;
- to identify the influenza virus types and subtypes in circulation, check whether they are susceptible to antiviral treatment and how well they match the vaccine strains recommended by WHO, thereby providing information relevant to vaccine updates; and
- to monitor the burden, spectrum of influenza disease and associated clinical risk factors.

These surveillance objectives are linked to specific public health actions (Table 1).

Table 1: Objectives and public health purpose of seasonal influenza surveillance in Europe

Objectives	Public health purpose
Early detection of influenza viruses	Supplying information on start of season and circulating viruses
Determining duration, shape, number and tempo of the waves of infection across Europe	Informing countries yet to be affected
Determining antigenic type and phenotype	Supplying isolates to WHO to collectively review and update the annual vaccine composition. Detect new variants (untypable) that might emerge as pandemic strains
Monitoring susceptibility to antiviral drugs	Detecting the emergence of resistant viruses and amending recommendations for the use of antiviral drugs
Monitoring age and clinical groups most affected	Reviewing and adapting recommendations on the groups to be targeted for immunisation and antivirals
Measuring susceptibility in the population by determining the age groups with the most infections (seroepidemiology)	Reviewing and adapting recommendations on the groups to be targeted for immunisation and antivirals
Describing the clinical presentation of severe disease and how it complicates other infections and underlying diseases	Informing testing and case-detection policies; alerting clinicians to new clinical presentations
Assessing impact and severity of the epidemic (a complex variable best seen as a matrix)	Alerting clinicians and managers on whether to implement contingency plans
Evaluating effectiveness of interventions and counter-measures, including influenza vaccines and antiviral pharmaceuticals	Informing decisions on vaccines and antivirals for regulatory agencies, clinicians, the public, researchers and industry

2 Methods

This report describes surveillance data for the period from week 40/2013 to week 20/2014 (data as of 17 June 2014). 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.

2.2 Primary care surveillance

2.2.1 Syndromic surveillance

Surveillance of influenza-like illness (ILI) and/or acute respiratory infection (ARI) is carried out by national sentinel networks of physicians, mostly general practitioners, covering between 1% and 6% of the population in their countries. Depending on the country's choice, every sentinel physician reports the weekly number of patients seen with ILI, ARI or both to a national hub (Table 2). Most countries use population denominators while some use the number of physician consultations as the denominator. From the national level, both numerator and denominator data are reported to The European Surveillance System (TESSy) database on a weekly basis. In addition to ILI/ARI rates, semi-quantitative and only partly standardised indicators of intensity, geographic spread and trend of influenza activity are reported. The intensity is assessed by comparing current ILI/ARI rates with country-specific baseline rates outside of the influenza season and with historical values. The intensity can range from low (below or at baseline), medium (above baseline but still within the range previously seen), high (higher than previously seen) to very high (much higher than observed during previous years).

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

No activity is characterised by baseline or below baseline ILI/ARI rates with no laboratory confirmations.

Sporadic activity is reported if there are isolated cases of laboratory-confirmed influenza in a region or an outbreak in a single institution, with clinical activity remaining at or below baseline.

Local activity refers to locally increased ILI/ARI rates or outbreaks in two or more institutions within a region, in conjunction with laboratory-confirmed cases of influenza, while levels of activity in the remainder of the region and other regions of the country remain at or below baseline.

Regional activity is defined by ILI/ARI rates above baseline – and laboratory-confirmed influenza infections above baseline – in one or more regions, comprising less than 50% of the country's total population, while levels of activity in other regions of the country remain at or below baseline. Regional activity generally does not apply to countries with a population of less than five million, unless the country is large and features geographically distinct regions.

Finally, widespread activity is reported if one or more regions comprising 50% or more of the country's population experience ILI/ARI rates above baseline, in conjunction 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.

Table 2: Syndromic influenza surveillance numerator and denominator by country

Country	Numerator	Denominator
Austria	ARI, ILI	Population
Belgium	ILI, ARI	Population
Bulgaria	ARI	Population
Croatia	ILI	Unknown
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

Country	Numerator	Denominator
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
UK-England	ILI, ARI	Population
UK-Northern Ireland	ILI, ARI	Population
UK-Scotland	ILI, ARI	Population
UK-Wales	ILI	Population

2.2.2 Virological surveillance

In accordance with nationally defined sampling strategies, sentinel physicians take nasal and/or pharyngeal swabs from a subset of their ILI/ARI patients. The specimens are sent to the respective country's ERLI-Net laboratory, or regional laboratory coordinated by the ERLI-Net laboratory, for influenza virus detection, typing and subtyping, antigenic and/or genetic characterisation and antiviral susceptibility testing. Influenza viruses detected in specimens collected in non-sentinel healthcare settings are also reported. Laboratory results, including those obtained for non-sentinel specimens, are reported to TESSy every week.

Non-systematically selected viruses are either characterised by the respective laboratories or sent for further characterisation to the WHO Collaborating Centre in London. A subset of viruses is also tested for susceptibility to neuraminidase inhibitors (NAIs: oseltamivir and zanamivir) by genetic and/or phenotypic methods.

2.3 Hospital surveillance

A subset of EU countries reports case-based severe influenza data to ECDC every week. Case definitions, populations under surveillance and data formats differ among these countries (Table 3). In order to make the data more comparable and pool them at EU level, only hospitalised, laboratory-confirmed influenza cases are included in this report.

Table 3: Main characteristics of surveillance systems for severe influenza

Country	Case definition	Population under surveillance	Type of surveillance	Data format
Finland	Lab confirmed, hospitalised	ICU**	Comprehensive	Case based
France	Lab confirmed, hospitalised	ICU	Comprehensive	Case based
Ireland	Lab confirmed, hospitalised	All wards	Comprehensive	Case based
Romania	SARI*, hospitalised	All wards	Sentinel	Case based
Spain	Lab confirmed, hospitalised	All wards	Sentinel	Case based
Sweden	Lab confirmed, hospitalised	ICU	Comprehensive	Case based
United Kingdom	Lab confirmed, hospitalised	ICU	Comprehensive	Aggregated

* Severe acute respiratory infection

** Intensive care unit

2.4 Data analysis

Syndromic, virological and severe influenza surveillance data were retrieved from TESSy. The intensity of influenza activity was colour-coded and displayed by country and week of reporting. Numbers of tested sentinel swabs, crude and (sub)type-specific numbers of influenza-positive sentinel swabs were plotted by week of reporting. (Sub)type-specific numbers of influenza-positive non-sentinel swabs were listed. Cumulative absolute and relative frequencies of antigenic virus characterisation results were determined. Basic demographic characteristics of severe influenza cases were described, and age-specific case-fatality ratios were calculated.

3 Results

3.1 Primary care

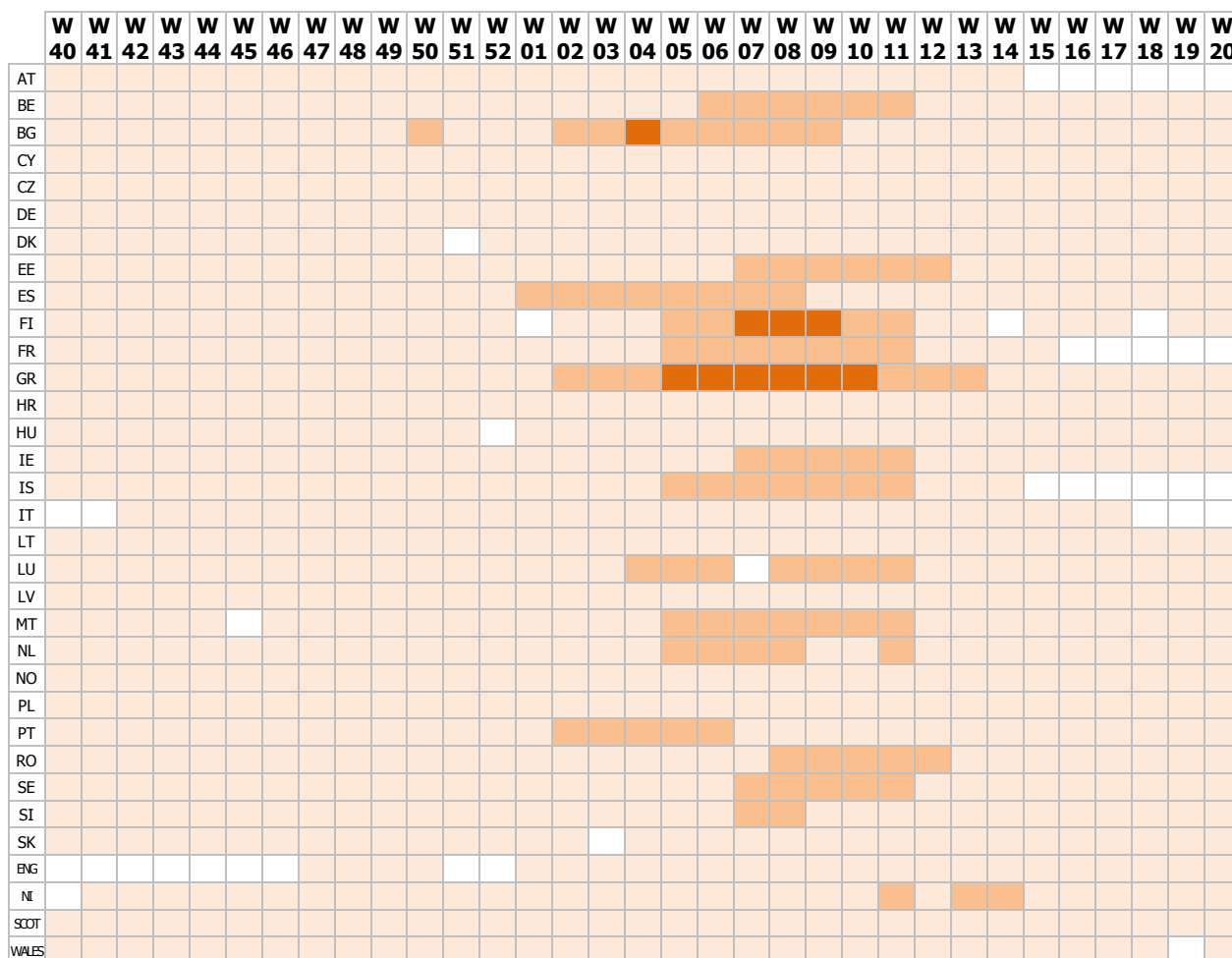
3.1.1 Syndromic surveillance

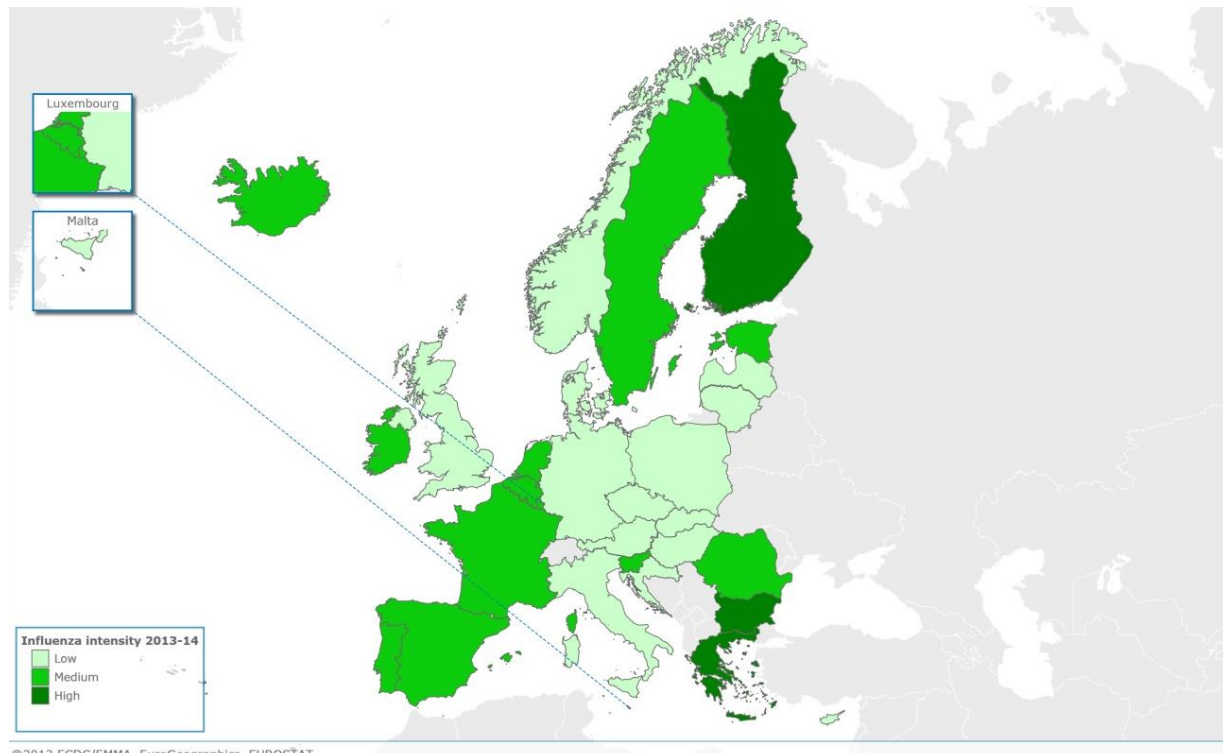
Widespread circulation of influenza was reported by 20 countries between weeks 1 and 15/2014, with a range between two (Luxembourg) and ten weeks (Croatia and Greece). Local or sporadic activity during the whole season was reported in nine countries.

Only three countries (Bulgaria, Finland and Greece; Figure 1 and Map 1) reported high influenza intensity during the 2013–14 season. A total of 16 countries reporting clinical data experienced low-intensity activity throughout the season.

During the 2013–14 influenza season, the reported ILI/ARI rates in most countries were lower than those reported in previous seasons, with the exception of Greece, Portugal and Spain where ILI rates in 2013–14 were similar or higher to those reported in recent seasons. These three countries were also the first affected countries this season [1,2].

Figure 1: Influenza intensity reported by week, EU/EEA, weeks 40/2013–20/2014



Map 1: Influenza intensity during the 2013–14 season, EU/EEA countries, weeks 40/2013–20/2014

3.1.2 Virological surveillance

The overall proportion of influenza-positive sentinel specimens started to increase in week 49/2013 and peaked at 44% in week 3/2014 (Figure 2). The proportion exceeded the season threshold of 10% between weeks 51/2013 and 17/2014 and again in week 19/2014, indicating a duration of the season of 20 weeks, which is comparable to the length of previous seasons. The highest positivity rate of 44% in the sentinel system was lower than in the previous seasons (2011–12: 58% and 2012–13: 60%).

Of sentinel specimens, 98% tested positive for influenza type A virus and 2% for type B (Table 4). Among all subtyped influenza A viruses, A(H1)pdm09 and A(H3) were co-circulating with a slightly higher percentage of A(H1N1)pdm09 viruses detected. At the beginning of the season, A(H1N1)pdm09 viruses dominated, whereas in the last weeks of the season, A(H3) viruses were more prevalent (Figure 2).

In non-sentinel specimens, a slightly higher proportion of B viruses were detected compared to sentinel surveillance (5% vs. 2%). Among the subtyped influenza A viruses, a higher proportion of A(H1)pdm09 viruses (70%) than A(H3) viruses (30%) were detected, but the percentage of viruses not subtyped was much higher. In both surveillance systems, influenza B Yamagata was found to be the major circulating B virus lineage (Table 4).

Figure 2: Number and percentage of influenza-positive sentinel specimens by type, subtype and week, EU/EEA, weeks 40/2013–20/2014

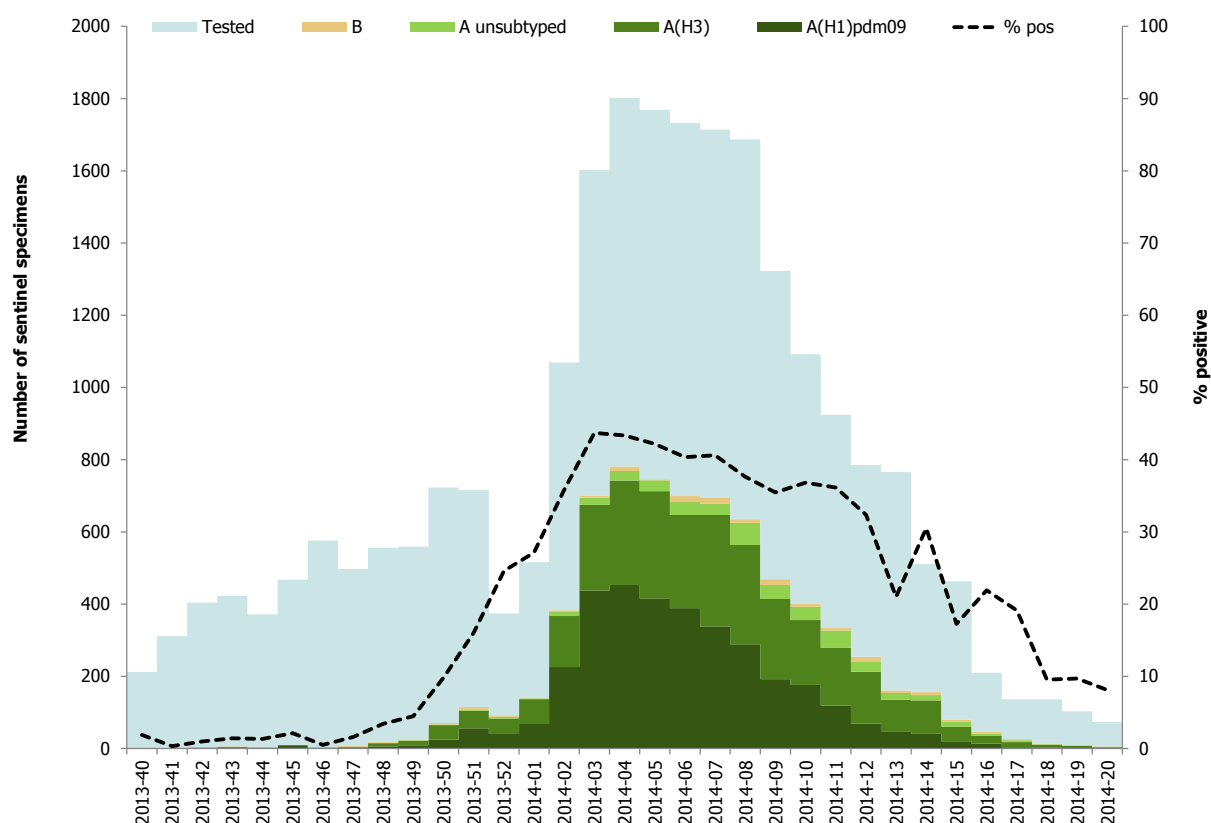


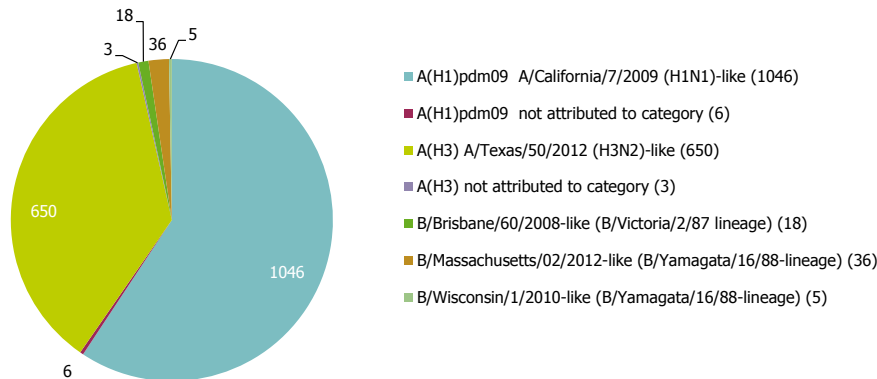
Table 4: Influenza detections by surveillance system, virus type and subtype/lineage, EU/EEA, weeks 40/2013–20/2014

Virus type/subtype	Sentinel detections	Non-sentinel detections
Influenza A	6 924 (98%)	27 380 (96%)
A(H1)pdm09	3 458 (53%)	11 329 (70%)
A(H3)	3 021 (47%)	4 773 (30%)
A(subtype unknown)	445	11 278
Influenza B	176 (3%)	1 282 (5%)
B(Vic) lineage	11 (15%)	7 (4%)
B(Yam) lineage	61 (85%)	176 (96%)
Unknown lineage	105	1 099
Total influenza	7 100	28 662

Antigenic and genetic characterisation of circulating viruses

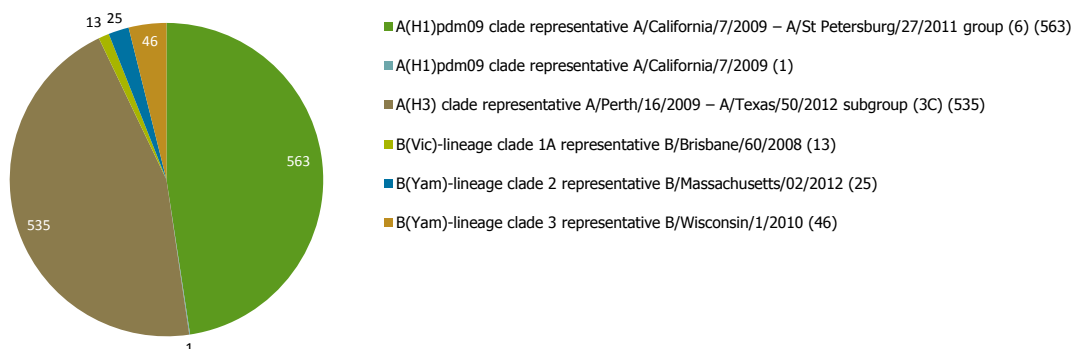
A total of 1 764 virus isolates were antigenically characterised (Figure 3), with six A(H1N1)pdm09 and three A(H3N2) viruses not attributed to any category. Sixty percent of the viruses were A(H1)pdm09 A/California/7/2009 (H1N1)-like and 37% A(H3) A/Texas/50/2012 (H3N2)-like. Among the influenza B viruses, two B(Yamagata)-lineage viruses were detected.

Figure 3: Number of specimens characterised antigenically, EU/EEA, weeks 40/2013–20/2014



A total of 1 183 virus isolates were genetically characterised (Figure 4), most of them influenza A viruses. A(H1)pdm09 clade representative A/California/7/2009 – A/St Petersburg/27/2011 group (6) and A(H3) clade representative A/Perth/16/2009 – A/Texas/50/2012 subgroup(3C) were evenly distributed. For the B lineages slightly more isolates of B(Yamagata)-lineage clade 3 representative B/Wisconsin/1/2010 were characterised than B(Yamagata)-lineage clade 2 representative B/Massachusetts/02/2012.

Figure 4: Number of specimens characterised genetically, EU/EEA, weeks 40/2013–20/2014



Viruses characterised at the WHO Collaborating Centre in London mirrored the distribution of types and subtypes in the EU/EEA, with influenza type A viruses dominating and similar percentages of A(H3N2) and A(H1N1)pdm09 viruses.

The characterised A(H1N1)pdm09 viruses belonged to genetic subgroups 6B and 6C, with viruses in genetic subgroup 6B predominating. Viruses in subgroups 6B and 6C were antigenically similar to the vaccine virus, A/California/07/2009.

The characterised A(H3N2) viruses fell within genetic group 3C represented by the recommended vaccine virus for the 2013–14 and 2014–15 seasons, A/Texas/50/2012, with viruses of genetic subgroup 3C.3 predominating. Antigenic analysis using antisera raised against cell-propagated H3N2 viruses indicates that the circulating viruses were antigenically similar to those in circulation in the 2012–13 influenza seasons.

The circulating influenza B type belonged to two genetic clades of B/Yamagata-lineage viruses: clade 3 represented by B/Wisconsin/1/2010 and clade 2 represented by B/Massachusetts/02/2012, with clade 3 predominating in samples collected in 2014. The few B/Victoria-lineage viruses belonged to clade 1A. The viruses were antigenically similar to the prototype virus B/Brisbane/60/2008 and genetically similar to this prototype virus. B/Brisbane/60/2008 has been recommended by WHO as a component in quadrivalent influenza vaccines for the 2013–14 and 2014–15 influenza seasons [3,4].

Antiviral susceptibility

During the 2013–14 influenza season, 1 216 A(H1N1)pdm09 viruses, 419 A(H3N2) and 78 influenza B viruses were tested for susceptibility to neuraminidase inhibitors (NAIs) by genetic and/or phenotypic methods. Fifteen (1.3%) A(H1N1)pdm09 viruses carried the NA-H275Y amino acid substitution associated with highly reduced inhibition by oseltamivir. One of these viruses showed highly reduced inhibition by oseltamivir and normal inhibition by zanamivir. However, in 11 of the 15 cases, mixtures of wild-type NA-275H (showing normal inhibition by oseltamivir) and NA-H275Y substitution viruses were detected in the corresponding clinical specimens. The median proportion of NA-H275Y was 35% (range 18–80%). One A(H3N2) virus carrying the NA-E119V amino acid substitution showed reduced inhibition by oseltamivir in phenotypic testing and normal inhibition by zanamivir.

3.2 Hospitalisations and deaths due to influenza

During the influenza season 2013–14, eight Member States (Finland, France, Ireland, Romania, Slovakia, Spain, Sweden and the United Kingdom) reported hospitalisations or deaths due to influenza to ECDC. These countries reported 4 786 hospitalised cases with laboratory-confirmed influenza infection, 430 of them fatal (Table 5). In 2 402 (50%) of these hospitalised cases, A(H1N1)pdm09 virus was detected, whereas influenza A(H3) (1 473; 31%) and B virus (59; 1%) were reported less frequently; 18% of the specimens were reported as 'influenza A virus unsubtype'. Of the 3 860 cases with known age, 1 437 (37%) were between 40 and 64 years old and 1 431 (37%) were 65 years and older. In 45% of patients between 40 and 64 years of age, influenza A(H1)pdm09 was detected, while infections with influenza A(H3) virus were more likely in those 65 years and older. Ventilator support was required for 661 (14%) of the 4 786 hospitalised cases with confirmed influenza.

Of the reported 4 786 hospitalised cases with confirmed influenza, 2 563 patients admitted to intensive care units (ICU) were reported with influenza A(H1N1)pdm09 as dominant virus, particularly in the age group 40–64 years.

Overall, 430 deaths due to influenza were reported up to 16 June 2014 (Table 5). Infections with A(H1N1)pdm09 were detected in 249 (58%) of the fatal cases, mostly in persons 40 years of age and older (Table 6).

Vaccination status was known for 333 of the fatal cases: 101 (30%) were vaccinated with the seasonal vaccine and 82 (81%) of the latter were older than 64 years. Spain reported 294 fatal cases, which is a 153% increase compared to the last A(H1N1)pdm09-dominated season, 2010–11, with 191 fatal cases.

Table 5: Number of hospitalised cases with laboratory-confirmed influenza, by week and country; EU/EEA, weeks 40/2013–20/2014

Country	Alive (%)	Dead (%)	Unknown outcome (%)	Total
Spain	1 702 (70)	294 (12)	422 (18)	2 418
Finland	0 (0)	0 (0)	30 (100)	30
France	545 (86)	87 (14)	0 (0)	632
Ireland	654 (97)	19 (3)	0 (0)	673
Romania	51 (80)	13 (20)	0 (0)	64
Sweden	35 (57)	17 (27)	10 (16)	62
Slovakia	3 (75)	0 (0)	1 (25)	4
UK	0 (0)	0 (0)	903 (100)	903
Total	2 990 (62)	430 (9)	1 366 (29)	4 786

Table 6: Number of fatal cases reported by France, Ireland, Romania, Spain and Sweden; by age group, virus type and subtype; EU/EEA, weeks 40/2013–20/2014

	A unsubtype	A(H3)	A(H1N1)pdm09	B	Total
<19 years	1	0	11	0	12
20–39 years	5	2	22	1	30
40–64 years	41	10	102	1	154
≥ 65 years	68	48	111	3	230
Total	115 (27%)	60 (14%)	246 (58%)	5 (1%)	426

Discussion and conclusions

Judging by the epidemiological and virological indicators, the 2013–14 influenza season was mild and only low virus activity was reported in most countries. Syndromic notification rates were low in most of the countries and lower compared to previous seasons, suggesting a low circulation of respiratory pathogens in general. Influenza A viruses dominated with a co-circulation of A(H1N1)pdm09 and A(H3N2) viruses.

After several seasons dominated by influenza A(H3N2) and B viruses, 2013–14 was the first season in Europe since 2010–11 where the proportion of influenza A(H1N1)pdm09 in all subtyped viruses was above 50%. The circulation of A(H1N1)pdm09 viruses may have been responsible for the higher number of hospitalised cases affecting mostly adults compared with previous seasons.

These findings are comparable with the US, where A(H1N1)pdm09 viruses dominated, although a higher proportion of circulating B viruses was observed later in the season [5]. Syndromic rates and mortality were lower overall compared to A(H3N2)-dominated seasons although the hospitalisation rate among people between 50 and 64 years of age was higher. All-cause mortality monitored in the EuroMOMO project was also within the normal range for all reporting countries during the 2013-14 season [6]. As in Europe, only few of the characterised viruses differed antigenically from the components in the current vaccine [5].

In south-east Asia and China, the proportion of circulating influenza A(H1N1)pdm09 and A(H3N2) viruses differed between countries; overall, a higher proportion of circulating influenza B viruses was reported [7].

Data from Europe showed no increase in resistant viruses, and characterised viruses matched the recommended vaccine components [3]. A moderate to low vaccine effectiveness (VE) was reported from different countries.

A Canadian study showed 71% VE against any influenza and 74% against A(H1)pdm09 [4,8]. Another Canadian study was based on hospitalised cases and estimated an overall VE of 59% and 58% for confirmed influenza A(H1N1)pdm09 [9]. A US study estimated adjusted VE against influenza A and B virus infection with medically attended ARI at 61% and VE against A(H1)pdm09 virus at 62% [5,10]. Studies from Spain showed an overall VE of 24–35%, 33–40% VE against A(H1)pdm09 and 13–28% VE against influenza A(H3) [11,12]. In the United Kingdom, VE against confirmed influenza A(H3N2), A(H1N1)pdm09 and B virus infection, adjusted for age, sex, surveillance scheme (i.e. setting) and month of sample collection was 26%, 73% and 51%, respectively [13]. The high vaccination rate in fatal cases older than 64 years seen in the EU/EEA surveillance data this season also suggests low vaccine effectiveness against A(H3N2) in older age groups, underlining the urgent need for more effective influenza vaccines in the future.

The fact that only a few countries across Europe are reporting hospitalised and fatal influenza cases limits the representativeness of the related findings. Another limitation derives from the higher proportion of untyped influenza A viruses in both the non-sentinel and the severe disease surveillance systems.

Overall, the season's evolution was in line with the early projection of the season [1] in the annual risk assessment and an earlier analysis of EU/EEA influenza surveillance data [2]. Even when facing seemingly mild influenza seasons, comprehensive epidemiological and virological surveillance – as well as monitoring of vaccine coverage, effectiveness and impact – is essential. It allows for a better understanding of the disease's epidemiology and for the detection of any unusual features, which may help minimise the population impact of an ongoing season and can aid preparation for coming seasons and pandemics.

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