World Health Organization

REGIONAL OFFICE FOR Europe

Epidemiological and virological situation update of the 2012/2013 influenza season in the WHO European Region

EuroFlu data week 40/2012 to week 04/2013

8 February 2013

ABSTRACT

Current overview of the 2012/2013 influenza season

- From week 40/2012 to week 04/2013 49 out of 53 Member States reported data to EuroFlu, of which 26 Member States shared clinical specimens and/or isolated viruses with a WHO Collaborating Centre.
- The 2012/2013 influenza season began earlier with most of countries in the Region reporting higher influenza-like illness (ILI)/acute respiratory infection (ARI) consultation rates and higher percentage of specimens positive for influenza compared with the same period of the previous season.
- Influenza A(H1N1) pdm09, A(H3N2) and influenza B viruses co-circulated. The majority of the influenza viruses detected during this period were influenza A(H1N1) pdm09 and influenza B, of which 89% were of the Yamagata lineage.
- Most of the antigenically characterized influenza viruses were closely related to viruses recommended by WHO for inclusion in the influenza vaccine for the northern hemisphere 2012/2013 season.
- There is no indication of wide spread resistance to the neuraminidase inhibitors oseltamivir and zanamivir during the winter of 2012/2013. All influenza viruses screened for susceptibility to adamantanes were found to be resistant.
- While the proportion of respiratory specimens testing positive from ILI and ARI patients has most likely reached its peak in several countries, patients with SARI testing positive for influenza are still increasing, possibly due to the later start of the season in the eastern European countries that conduct sentinel SARI surveillance.

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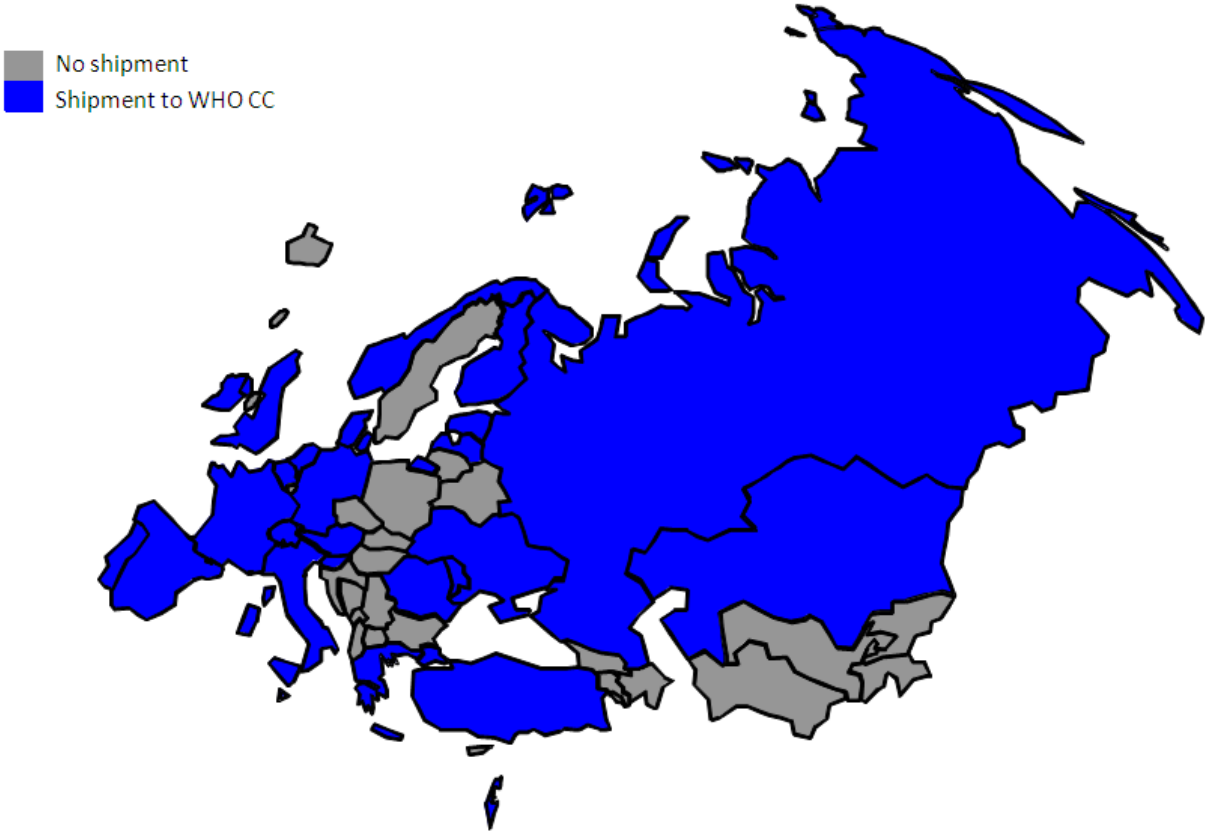
WHO Consultation on the Composition of Influenza Virus Vaccines (VCM)

This overview has been submitted for consideration during the WHO Consultation on the Composition of Influenza Virus Vaccines for the Northern Hemisphere 2013/2014, to be held 18–21 February 2013. It complements the data generated by the WHO Collaborating Centre for Reference and Research on Influenza at the National Institute for Medical Research, London, the United Kingdom (WHO CC London), from analyses performed on influenza viruses provided by the WHO European Member States.

National Influenza Centres (NICs) in the WHO European Region routinely perform real-time monitoring of the characteristics of circulating viruses by performing antigenic characterizations with post-infection ferret sera distributed by WHO CC London, genetic characterizations and antiviral susceptibility testing. The results of this monitoring are reported to the EuroFlu platform on a weekly basis. The European Region Member States annually contribute to the vaccine consultation meetings (VCMs) for the northern and southern hemispheres by sharing the selection of their clinical specimens and/or isolated viruses, supplemented with associated epidemiological information, with a WHO CC. Of the 53 Member States in the European Region, 38 performed shipments during the 2011/2012 season and 35 during the 2012/2013 season. As of week 04/2013 29 NICs from 26 Member States shipped clinical specimens and/or isolated viruses to WHO CC London (Fig. 1). The majority of the shipments were from countries in the western part of the Region, which reflects the west to east pattern of influenza activity in the Region during the winter of 2012/2013.

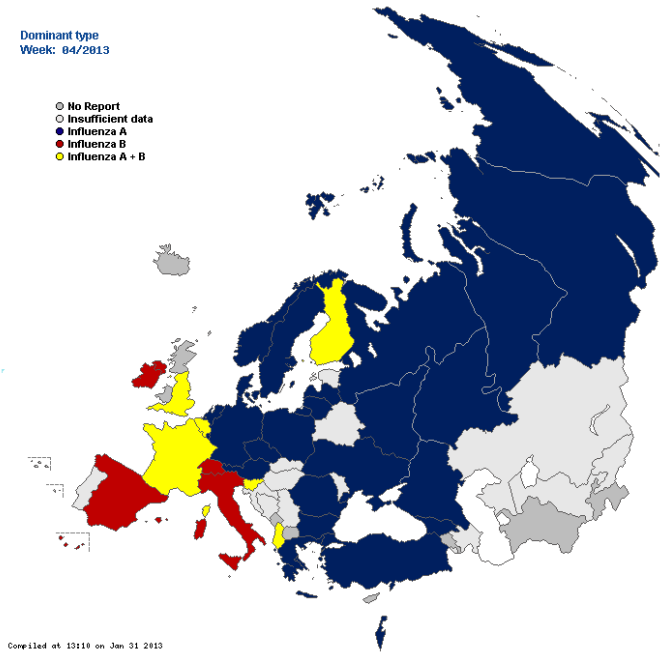
Fig. 1 Map of specimens/isolates shipped from NICs to WHO CC London, week 40/2012 – 04/2013



1. Current virological overview of the 2012/2013 influenza season

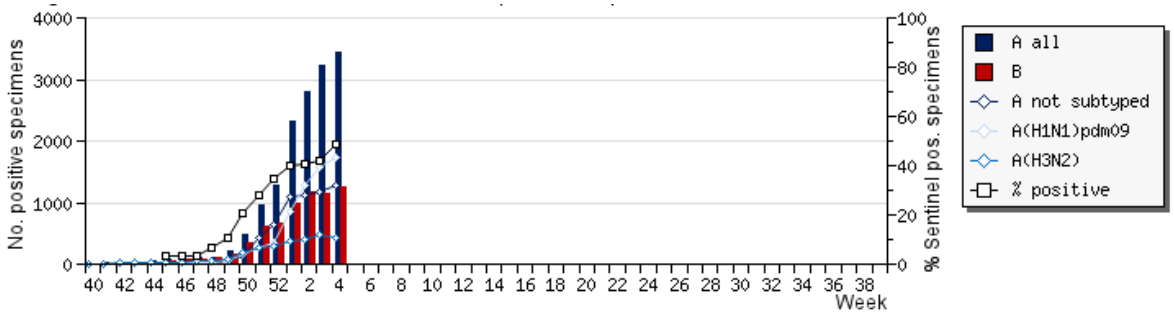
Circulation of influenza viruses is diverse in the WHO European Region with co-circulation of influenza A(H1N1)pdm09, A(H3N2) and influenza B. An increase in the prevalence of influenza A(H1N1)pdm09 viruses has been observed during the last several weeks (Fig. 3). The number of sentinel specimens collected from patients meeting case definition of influenza-like illness (ILI) or acute respiratory infection (ARI) testing positive for influenza in the Region increased to 49% in week 04/2013. The per cent positive respiratory specimens from patients with severe acute respiratory infections (SARI) testing positive for influenza continued to rise to 30% in week 04/2013.

Fig. 2 Map of influenza virus dominant type



During this week influenza A(H1N1)pdm09 was reported as the dominant virus in Turkey and several countries in northern, eastern and central Europe, while influenza B was reported as the dominant virus in some countries in the southern and western parts of the Region (Fig. 2). Between these areas, co-circulation of influenza A(H1N1)pdm09, A(H3N2) and influenza B was reported. This is a noticeable difference from the 2011/2012 season when high prevalence of influenza A(H3N2) circulation was observed across the Region.

Fig. 3 Combined sentinel and non-sentinel specimens positive for influenza A and B, week 40/2012 – 04/2013



Since the beginning of the season (week 40/2012), 23 200 influenza viruses from sentinel and non-sentinel sources have been typed: 16 158 (70%) were influenza A and 7042 (30%) influenza B. Of the influenza A viruses, 9858 were subtyped: 6843 (69%) as A(H1N1)pdm09 and 3015 (31%) as A(H3N2). In addition, the lineage for 1035 influenza B viruses has been determined: 921 (89%) belonged to the B/Yamagata lineage and 114 (11%) to B/Victoria. This situation is very different from the last influenza season where A(H1N1)pdm09 and influenza B were detected in less than 10% of circulating viruses. Table 1 gives a detailed overview of cumulative influenza virus detections by type and subtype/lineage since week 40/2012.

Table 1 Number and percentage of sentinel and non-sentinel respiratory specimens positive for influenza A and B, week 40/2012 – 04/2013

Specimens tested and viruses detected	Sentinel				Non-sentinel		Total	
	ILI/ARI		SARI					
Specimens tested	20093		2570					
Influenza +	***5362***	***27%***	***191***	***7%***	***17647***		***23200***	
Influenza A	**2930**	**55%**	**113**	**59%**	**13115**	**74%**	**16158**	**70%**
Influenza A subtyped	2614		95		7149		9858	
A (H1N1)pdm09	*1691*	*65%*	*59*	*62%*	*5093*	*71%*	*6843*	*69%*
A (H3N2)	*923*	*35%*	*36*	*38%*	*2056*	*29%*	*3015*	*31%*
Influenza B	**2432**	**45%**	**78**	**41%**	**4532**	**26%**	**7042**	**30%**
Influenza B lineage determined	477		0		558		1035	
B/Yamagata lineage	*421*	*88%*	*0*		*500*	*90%*	*921*	*89%*
B/Victoria lineage	*56*	*12%*	*0*		*58*	*10%*	*114*	*11%*

Figures 4, 5 and 6 present proportion of influenza virus detections by type and subtype/lineage by type of surveillance system (non-sentinel, sentinel ILI/ARI and sentinel SARI). The proportion of influenza A viruses was highest (74%) in non-sentinel specimens with only 26% of specimens being positive for influenza B. The proportions of influenza A and B viruses in sentinel ILI/ARI detections were 55% and 45%, while this was 59% and 41% in SARI detections respectively. Influenza A virus was not subtyped in 34% of the non-sentinel influenza A detections compared to 6% and 9% in sentinel ILI/ARI and SARI detections. Among viruses from all settings (non-sentinel, sentinel ILI/ARI and sentinel SARI) the proportion of influenza A(H1N1)pdm09 viruses was higher than A(H3N2) viruses. The proportion of B/Yamagata lineage viruses was higher than B/Victoria lineage viruses.

Fig. 4 Number and percentage of non-sentinel respiratory specimens positive for influenza A and B, week 40/2012 – 04/2013

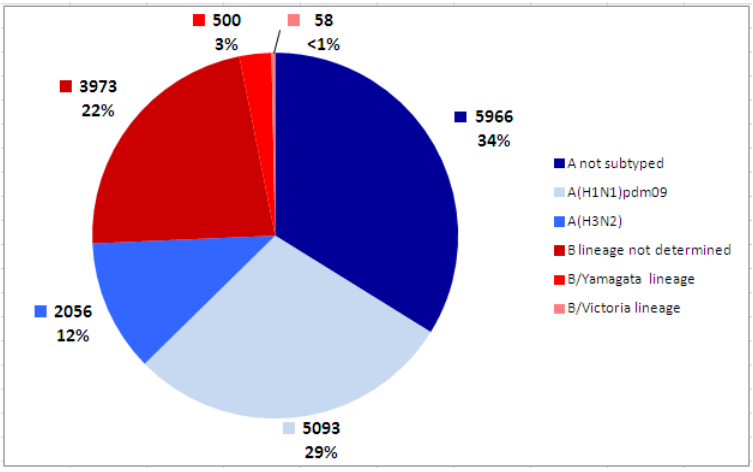


Fig. 5 Number and percentage of sentinel ILI/ARI specimens positive for influenza A and B, week 40/2012 – 04/2013

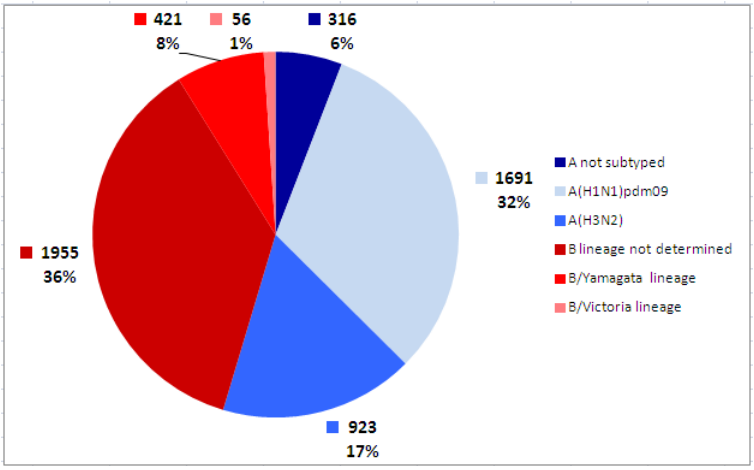
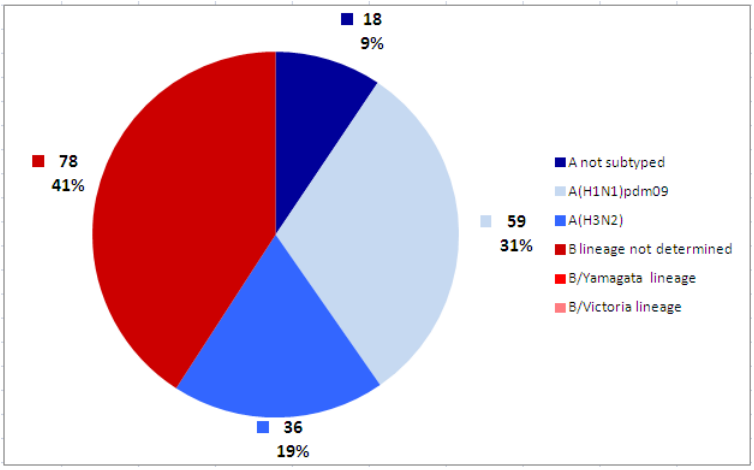


Fig. 6 Number and percentage of sentinel SARI specimens positive for influenza A and B, week 40/2012 – 04/2013



Virus strain characterizations

For the 2012/2013 northern hemisphere influenza season, WHO recommends inclusion of A/California/7/2009 (H1N1)pdm09-like, A/Victoria/361/2011 (H3N2)-like and

B/Wisconsin/1/2010-like (from the B/Yamagata lineage) viruses in vaccines[1]. The antigenic and genetic characterizations performed on influenza isolates by NICs in the WHO European Region are presented in Fig. 7 and 8, respectively.

Since week 40/2012, 1154 influenza viruses characterized antigenically by 11 countries (Denmark, Germany, Greece, Latvia, Portugal, Romania, the Russian Federation, Slovakia, Slovenia, Switzerland and the United Kingdom (England and Scotland)) corresponded with the viruses recommended by WHO for inclusion in the current northern hemisphere seasonal influenza vaccine (Fig. 7). The United Kingdom characterized the majority of these viruses (837/73%) and of these, 70% of the A/Victoria/361/2011 (H3N2)-like viruses characterized this season were characterized by Scotland. The data reported by Scotland heavily influenced the antigenic characterization ratio of influenza A virus subtypes in the Regional data. The ratio of subtypes in the antigenic characterization data was 18:72 [A(H1N1)pdm09:A(H3N2)], compared to the ratio of 69:31 observed in detections. The influenza B viruses of B/Yamagata and B/Victoria lineages were antigenically characterized in ratio of 85:15 similar to the ratio of 89:11observed in detections.

Twelve countries (Austria, Belgium, Denmark, Finland, Germany, Greece, Norway, Portugal, Scotland, Spain, Sweden, Switzerland) characterized 321 influenza viruses genetically (Fig. 8). No country submitted more than 20% of the total number of genetic characterizations reported to EuroFlu. A higher proportion of A(H3N2) viruses were genetically characterized compared to A(H1N1)pdm09. During the season 69% of the influenza A detections were A(H1N1)pdm09, but influenza A(H1N1)pdm09 made up only 41% of the influenza A characterizations. Similarly, the influenza B viruses of B/Victoria lineage were 37% of influenza B characterizations, but made up only 11% of influenza B detections.

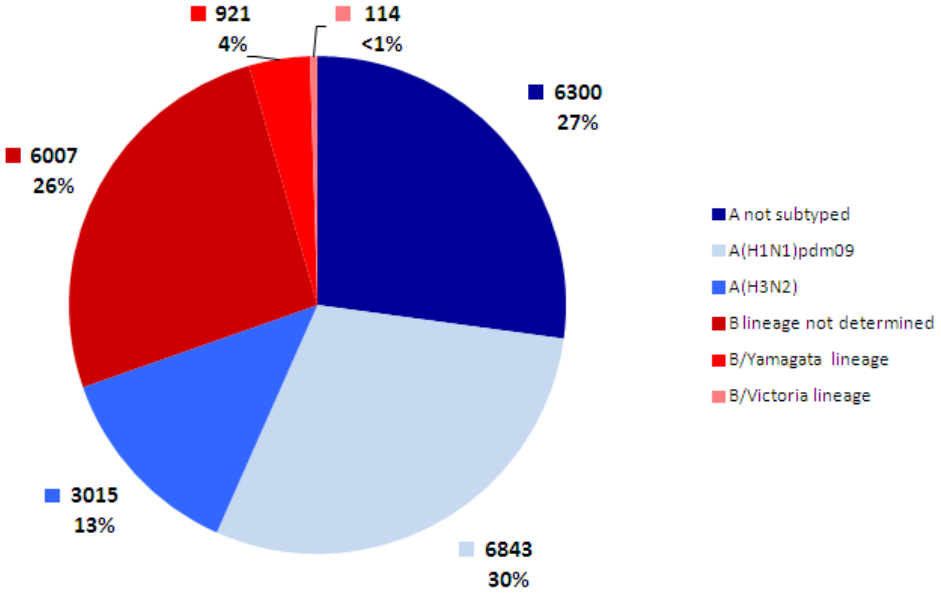
The virus strain characterizations reported to EuroFlu may not be truly representative of viruses circulating in the Region during the winter of 2012/2013. The antigenic and genetic characterization data were provided by less than 10% of countries in the Region and a relatively small number of viruses were characterized. The data from individual countries may also have disproportionately influenced the Regional results.

The results show that both A(H1N1)pdm09 and A(H3N2) viruses have evolved to fall into some different genetic groups, which are all antigenically similar to their vaccine viruses, A/California/7/2009 and A/Victoria/361/2011, respectively. Influenza B viruses of the B/Victoria/2/87 and the B/Yamagata/16/88 lineages are co-circulating with the clear dominance of the B/Yamagata lineage viruses this season (90%). Influenza B viruses of the B/Victoria lineage, that are not included in the trivalent vaccine, all fall within the B/Brisbane/60/2008 clade and are antigenically indistinguishable. B/Yamagata lineage viruses in circulation clearly fall into two distinct genetic clades, represented by B/Estonia/55669/2011 (Clade 2) and B/Wisconsin/1/2010 (Clade 3) respectively. Viruses in these clades can be distinguished antigenically from each other, but the antigenic differentiation of these clades is not clear-cut as post-infection ferret antisera raised against Clade 2 viruses are more clade-specific than are antisera raised against clade 3 viruses. Nevertheless, viruses within these clades remain antigenically similar to the current vaccine virus, B/Wisconsin/1/2010.

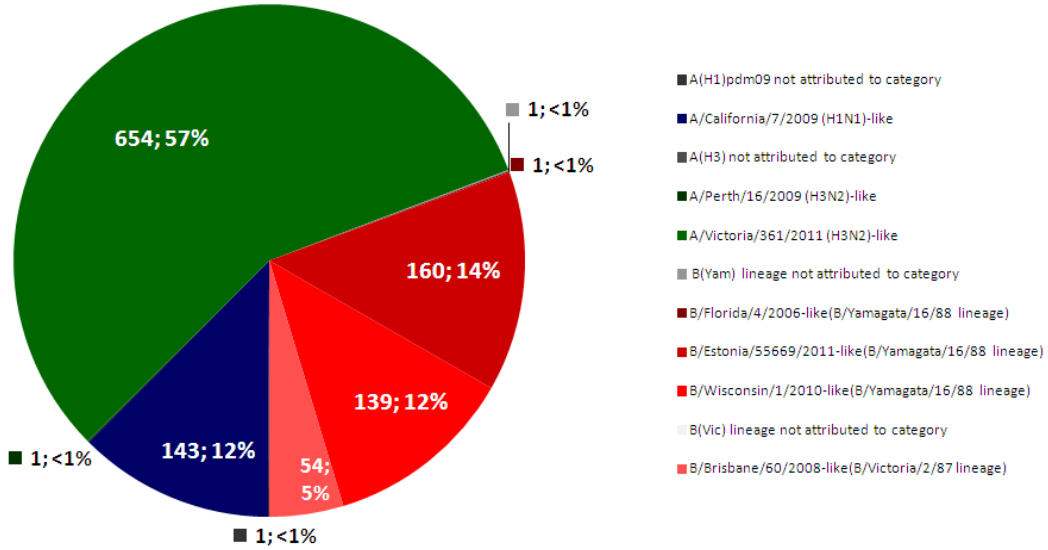
[1] http://www.who.int/influenza/vaccines/virus/recommendations/en/

Fig. 7 Number and percentage of sentinel and non-sentinel respiratory detections (A) compared with antigenic strain characterizations (B), week 40/2012 – 04/2013

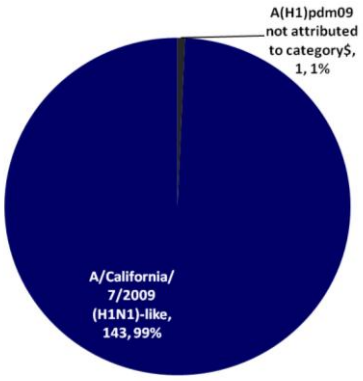
A. Sentinel and non-sentinel respiratory specimens positive for influenza



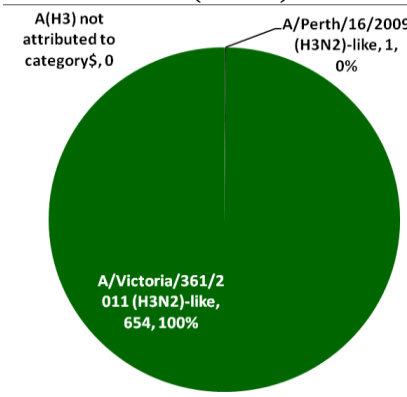
B. Cumulative virus strain characterizations – antigenic



C. Influenza A(H1N1)pdm09



D. Influenza A(H3N2)



E. Influenza B

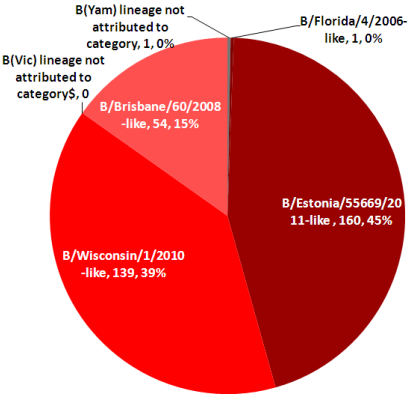
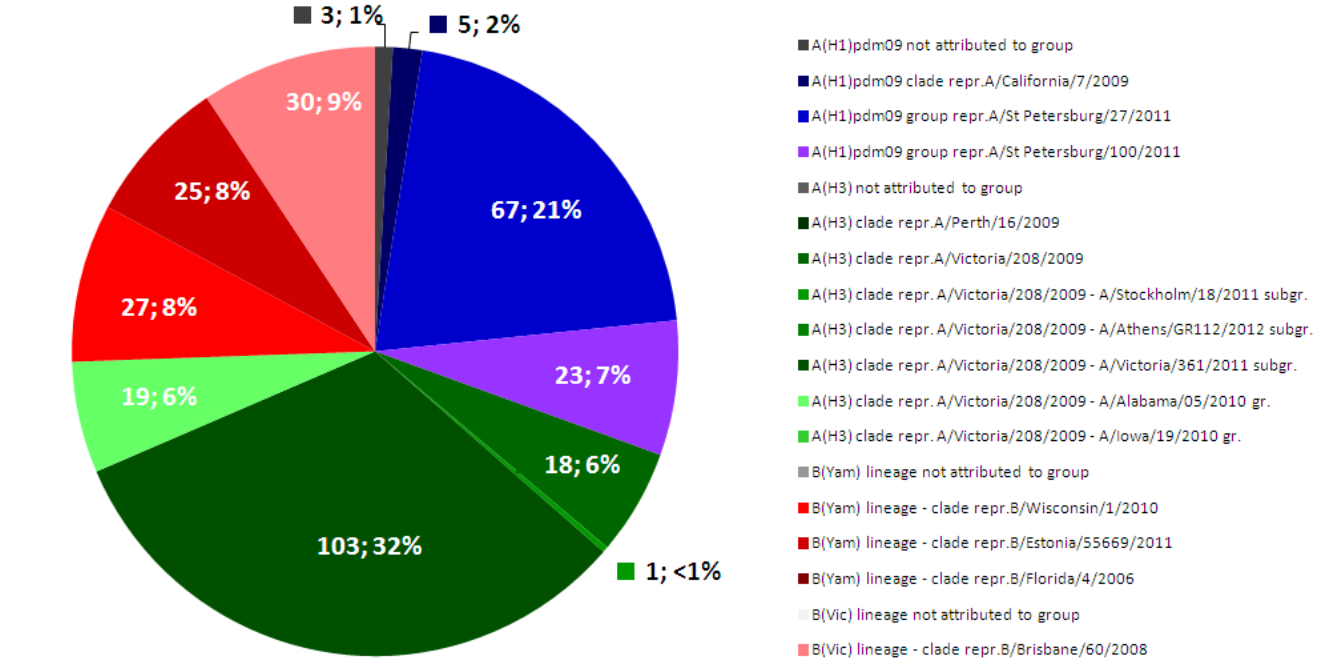
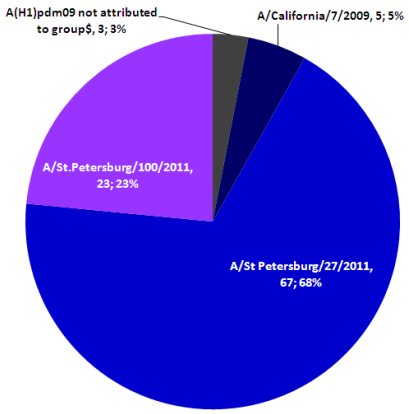


Fig. 8 Number and percentage of genetic strain characterizations, week 40/2012 – 04/2013

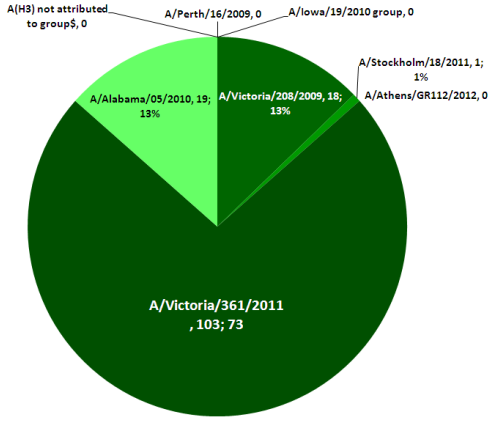
A. Cumulative virus strain characterizations – genetic



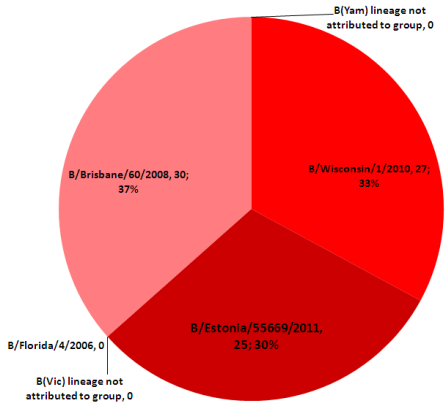
B. Influenza A(H1N1)pdm09



C. Influenza A(H3N2)



D. Influenza B



Monitoring of susceptibility to antiviral drugs

From week 40/2012 to week 04/2013, 7 countries (Denmark, Germany, the Netherlands, Norway, Spain, Sweden and the United Kingdom (England)) screened 262 viruses for susceptibility to the neuraminidase inhibitors oseltamivir and zanamivir. The 95 influenza A(H3N2) and 67 influenza B viruses showed susceptibility to both drugs. Of the 100 A(H1N1)pdm09 viruses tested, 99 showed susceptibility to both drugs and 1 virus carrying the neuraminidase H275Y amino acid substitution, causing resistance to oseltamivir, was detected in the Netherlands in a hospitalized, immunocompromised patient exposed to oseltamivir through

treatment. There is no indication of widely spreading resistant strains of influenza viruses during the winter of 2012/2013.

The 14 influenza A(H3N2) and 10 influenza A(H1N1)pdm09 viruses screened for susceptibility to adamantanes were carrying the S31N amino acid substitution in the M2 protein associated with resistance to adamantanes.

2. Current epidemiological overview of the 2012/2013 influenza season

Results from outpatient surveillance for ILI and ARI

The 2012/2013 influenza season arrived 3-4 weeks earlier than the 2011/2012 season in the WHO European Region (Fig. 9) with a distinct west to east pattern in the spread over the Region (Fig.10), as has been seen in several previous seasons 2008/2009, 2009/2010, and 2010/2011. Consultation rates were generally higher than during the 2011/2012 season.

Fig. 9 Percentage of sentinel ILI/ARI specimens testing positive for influenza by season

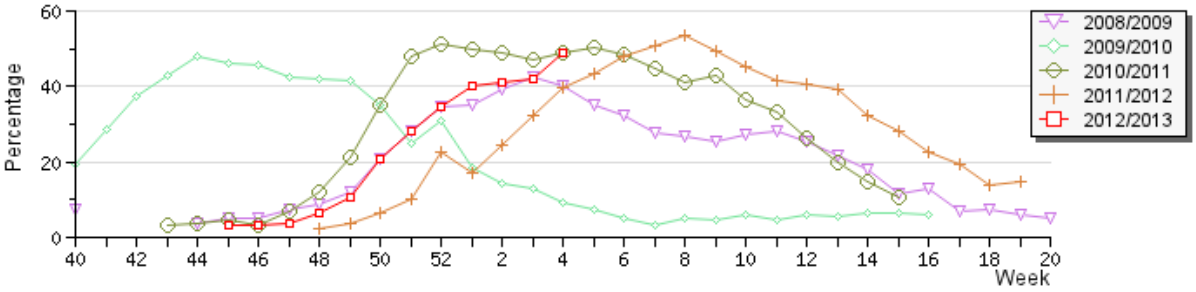
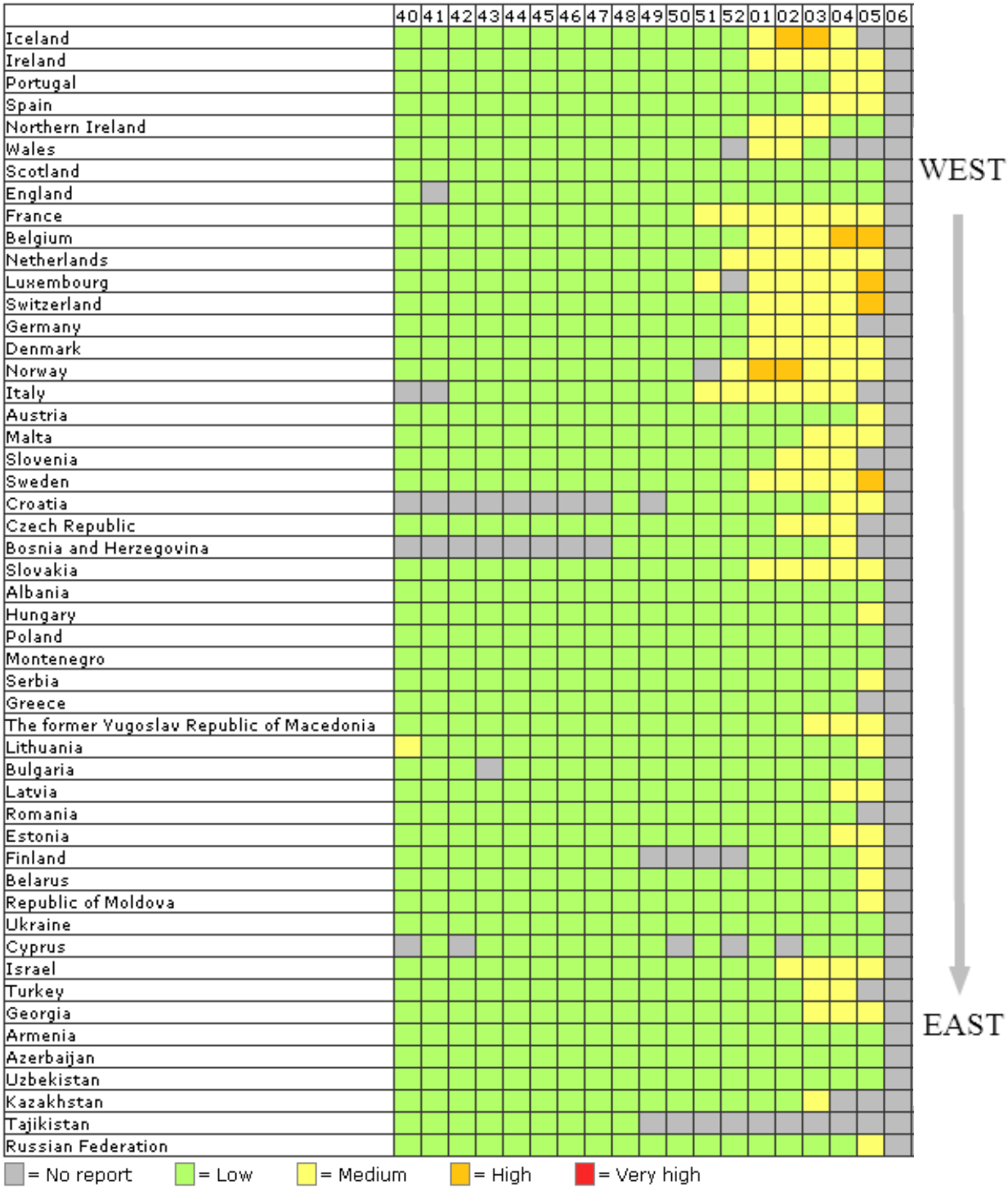


Fig. 10 Weekly intensity for season 2012/2013 by country[2]



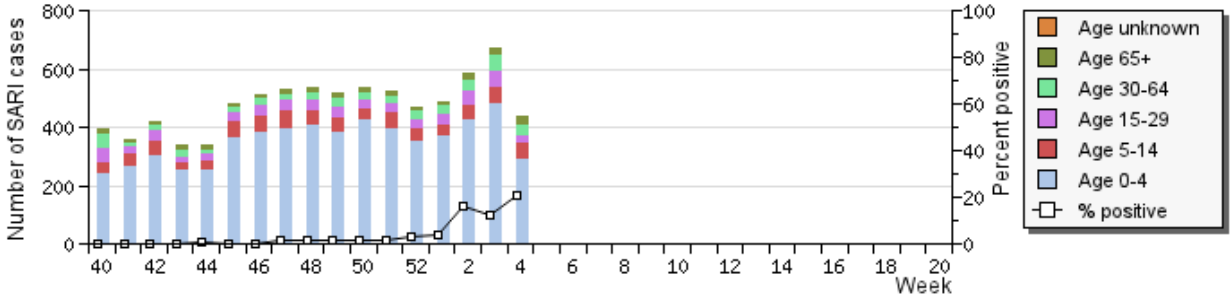
[2] https://www.euroflu.org/html/tables.html

Results from inpatient surveillance for SARI

During the 2012/2013 influenza season, data on sentinel SARI were reported to EuroFlu from 13 Member States located in the central and eastern parts of the Region.

As of week 04/2013, the proportion of respiratory specimens from patients with SARI testing positive for influenza has increased since week 01/2013 (Fig. 11). Overall, the majority of countries reported cases mainly in the group aged 0–4 years. Since week 40/2012, 191 influenza virus detections were reported of which: 113 (69%) were influenza A and 78 (41%) influenza B. Of the influenza A viruses, 95 were subtyped: 59 (62%) as A(H1N1)pdm09 and 36 (38%) as A(H3N2).

Fig. 11 SARI cases by age group (years) and percentage of specimens positive for influenza at sentinel hospitals



Among the countries reporting on hospitalization of severe laboratory-confirmed influenza cases to the European Centre for Disease Prevention and Control, 714 such cases were reported since week 4/2013, 384 (54%) were influenza A and 330 (46%) influenza B. Of the influenza A viruses, 205 were subtyped: 122 (60%) as A(H1N1)pdm09 and 83 (40%) as A(H3N2). This reflects the higher levels of influenza activity in the western part of the Region[3]. To date, A(H1N1)pdm09, A(H3N2) and influenza B have been detected among hospitalized patients.

3. Description of influenza surveillance in the WHO European Region

Most of the 53 Member States of the WHO European Region monitor influenza activity through surveillance of ILI and/or ARI in primary care clinics, with some countries also conducting hospital-based surveillance for severe disease. Surveillance data in the Region are collected from sentinel and non-sentinel systems. Sentinel data come from a network of designated clinicians who routinely and systematically collect respiratory specimens from ILI, ARI or SARI cases according to standard case definitions. Non-sentinel data come from a variety of other sources, including community outbreaks, general practitioners and hospitals that are not part of the sentinel surveillance system for influenza and may not use a standard case definition for ILI, ARI or SARI. The WHO European Influenza Surveillance Network (EuroFlu[4]) presents data from the different surveillance systems in the Region on a weekly basis. Data from the European Union (EU) and the European Economic Area (EEA) Member States are automatically transferred to EuroFlu from the European Centre for Disease Prevention and Control

[3] http://ecdc.europa.eu/en/Pages/home.aspx/
[4] www.euroflu.org

Surveillance System (TESSy)[5]. The data included in this report are publicly available at www.euroflu.org, where WHO Regional Office for Europe publishes a weekly surveillance report in English and Russian that is based on data covering the Region's total population of 896 million.

Outpatient surveillance

In most countries of the Region, outpatient surveillance is performed by clinician networks represented by a group of primary care physicians that cover a representative sample of the general population (sentinel surveillance). In some countries, nation-wide surveillance systems are in place, whereby all cases of ILI or ARI are reported. The primary care physicians report the weekly number of clinical cases of ILI and/or ARI to a central registry and take respiratory specimens according to a nationally defined sampling strategy or plan. The specimens are sent to a national influenza laboratory for testing to obtain information on types, subtypes and characterization of influenza viruses circulating.

Inpatient surveillance

Several Member States have also established hospital-based surveillance of SARI and influenza in recent years, using different methodologies, e.g. reporting of all-cause SARI hospitalizations and proportion of cases testing positive for influenza (sentinel SARI[6]) or only laboratory-confirmed hospitalized cases of influenza[7]. These systems contribute to providing epidemiologic and virological data on more severe influenza infections in the Region, such as the identification of the viruses associated with severe disease and risk factors associated with severe illness.

The description of the sentinel SARI systems can be found at:
http://euroflu.org/documents/Overview_of_SARI_Surveillance_Systems_13.02.2012.pdf

Laboratory network

The WHO European Region influenza laboratory network (Fig.1) is part of the Global Influenza Surveillance and Response System (GISRS)[8] and consists of national influenza laboratories in 50 Member States of the Region, a WHO collaborating centre for reference and research on influenza (WHO CC) in the United Kingdom and two WHO H5 reference laboratories in France and the Russian Federation. National influenza laboratories in 40 countries are formally recognized by WHO as National Influenza Centres (NICs), of which laboratories in 29 countries of the EU/EEA participate in the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL)[9]. NICs receive appropriate clinical specimens from outpatient and inpatient surveillance in their countries during the influenza season, undertake virus isolation and initial identification of virus type and subtype using the WHO reagents kit provided through the GISRS. Representative clinical specimens and/or isolated viruses are sent to a WHO CC in time

[5] http://ecdc.europa.eu/en/activities/surveillance/tessy/pages/tessy.aspx
[6] WHO Regional Office for Europe guidance for sentinel influenza surveillance in humans
http://www.euro.who.int/__data/assets/pdf_file/0020/90443/E92738.pdf
[7] Weekly Influenza Surveillance Overview (WISO) ECDC
http://ecdc.europa.eu/en/healthtopics/seasonal_influenza/epidemiological_data/pages/weekly_influenza_surveillance_overview.aspx
[8] http://www.who.int/influenza/gisrs_laboratory/en/

[9] http://ecdc.europa.eu/en/activities/surveillance/eisn/laboratory_network/pages/laboratory_network.aspx

prior to the WHO Consultation on the Composition of Influenza Virus Vaccines for more in depth analyses, notably relating to fuller antigenic analysis with panels of post-infection ferret sera raised against reference influenza viruses including the current vaccine candidates.

Fig. 12 Laboratory network for influenza surveillance in the WHO European Region