

SEASONAL INFLUENZA IN THE WHO EUROPEAN REGION, 2017–2018 EARLY SEASON

Situational analysis



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Contents

Summary and recommendations.....	1
Objectives	3
Methods.....	4
Trigger for analysis.....	4
Data sources.....	4
Findings	5
Viruses detected in sentinel-source specimens (ILI and ARI)	6
Viruses detected in non-sentinel-source specimens	7
Hospital data	8
Mortality monitoring	12
Characterization of viruses	12
Antiviral susceptibility testing.....	13
Conclusion.....	14
References	15

Summary and recommendations

- The influenza epidemic period for the European Region started in week 48/2017 and by week 1/2018 one third of Member States reported that 30% or more of their sentinel specimens were testing positive for influenza viruses[1].
- Both influenza types B and A viruses are co-circulating in the Region. Influenza B viruses are almost exclusively B/Yamagata-lineage and mixed patterns of influenza A virus subtype circulation (A(H3N2) and A(H1N1)pdm09) are being observed.
- The timing of influenza is similar to previous seasons and levels of transmission are as expected for this time of the year. However, this season is unusual in that influenza type B activity is occurring earlier and in higher proportions than typically observed.
- Member States located in the north, west and south of the Region are experiencing increasing influenza activity with excess mortality in the elderly (aged over 65 years) reported for United Kingdom (Scotland), Portugal and Spain as of week 1/2018[2]. Excess mortality is generally observed during an influenza season, but a meaningful comparison to previous seasons can only be made when more data become available in coming weeks.
- Limited influenza transmission has been reported in Member States located in the eastern part of the Region. These, together with Member States that have passed their epidemic threshold might experience increased pressures on primary and secondary care in coming weeks. The activation of contingency plans to preserve and release capacity in acute care should be considered based on the local epidemiological picture.
- Vaccine effectiveness against A(H1N1)pdm09 and the influenza B viruses is expected to be good, whereas effectiveness against A(H3N2) tends to be lower, similar to that seen in the 2016–2017 influenza season. While B/Yamagata viruses, which have dominated so far this season, are only included in the quadrivalent vaccines, some cross-protection may be conferred by the B/Victoria lineage virus component in the trivalent vaccine.
- Vaccination is the most effective measure available to prevent severe disease caused by influenza. Annual influenza vaccination is particularly important for persons at higher risk of severe consequences following influenza infection – including older persons, people with pre-existing chronic diseases, such as cardiovascular and respiratory diseases and immune deficiencies, pregnant women, and young children. Vaccination against influenza among health care workers, especially frontline workers caring for vulnerable patient groups, is also recommended to decrease their risks of infection and potential transmission of influenza to patients. However, according to most recently available data, influenza vaccination uptake remains suboptimal in the Region; trends of vaccination in high-risk groups between 2008–2009 and 2014–2015 seasons are declining in a number of Member States with only one achieving the goal of vaccinating 75% of persons over 65 years of age by the end of this period[3].
- Post-exposure antiviral treatment with oseltamivir or zanamivir should be encouraged for treating severely ill patients with suspected Influenza infection, particularly for high-risk patients and regardless of vaccination status[4, 5]. In closed settings, such as nursing homes, prophylactic use of neuraminidase inhibitors should be considered following the first detected case in the setting.

Situational analysis of the 2017–2018 early influenza season in the WHO European Region

- Non-pharmaceutical measures, such as good respiratory hygiene, early self-isolation and avoiding close contact with sick people should be encouraged throughout the season[6].

The influenza season in the Region will continue to be monitored over the coming period and weekly updates will become available on FluNewsEurope[1].

Objectives

The main objectives of this situation analysis are:

- to provide a description of the epidemiological pattern of seasonal influenza in the first affected Member States;
- to estimate the progression of influenza activity and the possible impact on susceptible and at-risk populations for the rest of the season; and
- to compare circulating viruses with current vaccine strains and describe susceptibility to neuraminidase inhibitors (NAI).

This analysis can be used to guide local public health authorities, for instance in reinforcing vaccination programmes in certain risk groups, directing antiviral policies or allocating appropriate health care resources.

Methods

Trigger for analysis

WHO Regional Office for Europe internal decision, 11 January 2018, in response to changing characteristics of the 2017–2018 season epidemic since the publication of the European Centre for Disease Prevention and Control (ECDC) “Risk assessment for seasonal influenza, EU/EEA, 2017–2018”[7].

Data sources

This situation analysis is based on clinical (influenza like-illness (ILI) and acute respiratory infection (ARI)), epidemiologic and virologic data from primary and secondary health care settings. These data are routinely reported by public health institutes and national influenza centres (NICs) through a single collection mechanism to the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control, who jointly coordinate regional influenza surveillance activities. This information is published in the weekly Flu News Europe bulletin[1]. Other information sources include situation reports from Member States, peer-reviewed literature and data from the European Monitoring of Excess Mortality for Public Health Action (EuroMOMO) project[2].

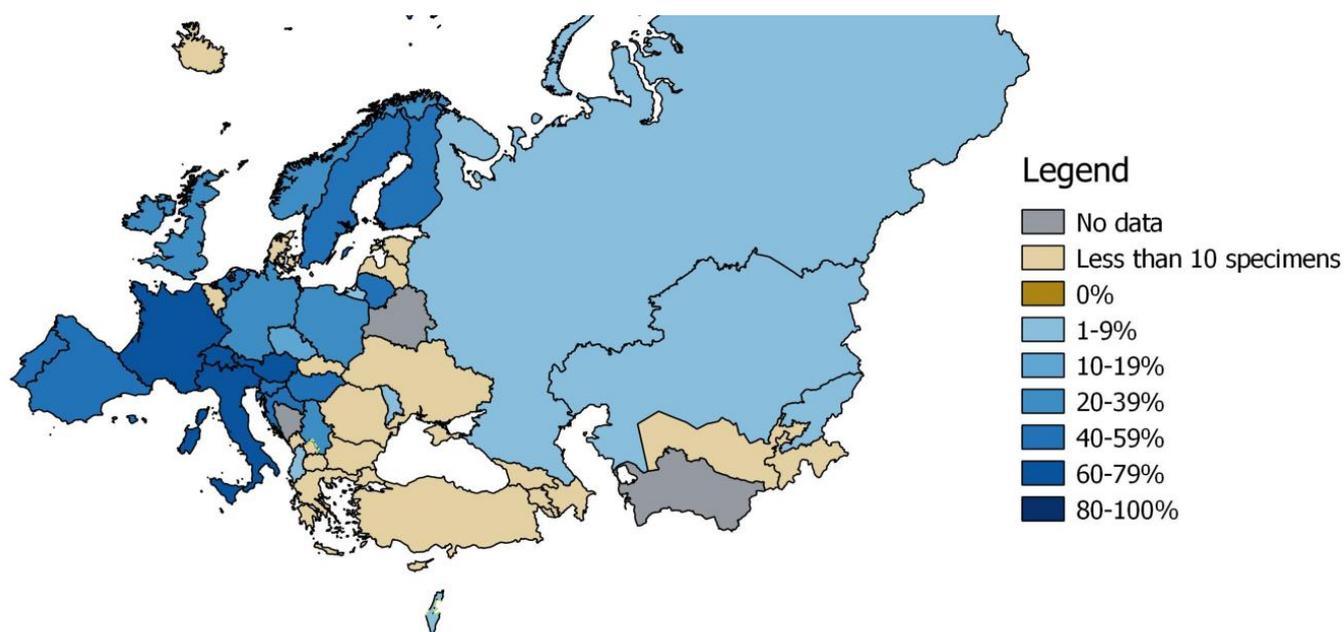
Findings

Primary care data

Data reported for week 1/2018 showed 12 Member States in northern, western and southern areas of the WHO European Region (Croatia, France, Ireland, Israel, Italy, the Netherlands, Norway, Portugal, Spain, Switzerland, Turkey and the United Kingdom (Northern Ireland, Scotland)) to be experiencing increased levels of influenza activity (according to the qualitative indicators “intensity” and “geographic spread”). Such geographic distribution of the virus early in the influenza season, with increased activity later in the eastern part of the Region, has been reported previously[8].

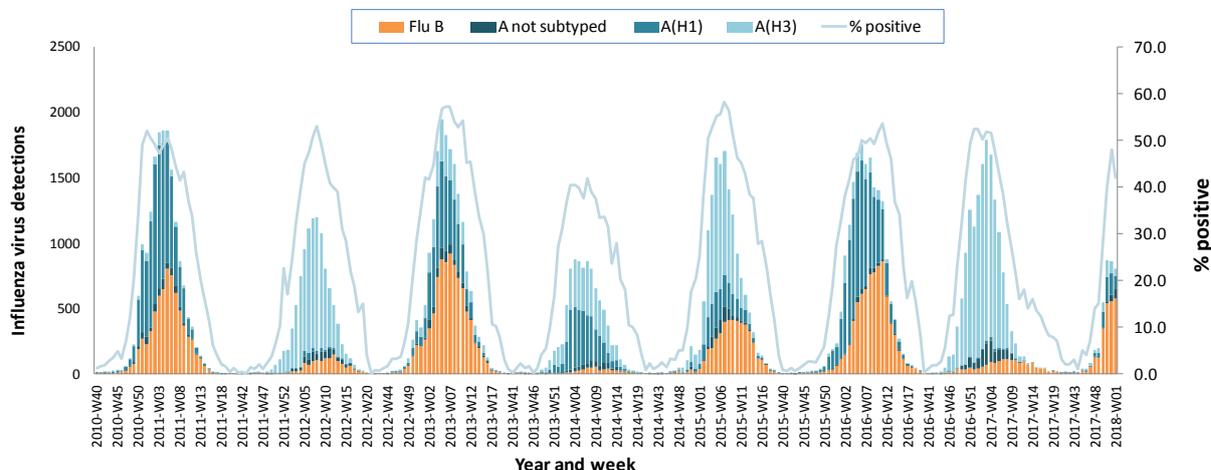
A similar geographic pattern has been observed with other clinical and virological data. 29 Member States each tested at least 10 sentinel specimens in week 1/2018. Of these, 16 Member States (in northern, western and southern areas of the Region) reported a percentage of specimens from sentinel sources positive of at least 30% or more (median of 44%, range of 30% to 100%; **Figure 1**) and included five of the Member States with increased clinical activity.

Figure 1. Percentage of specimens from sentinel sources positive for influenza virus by country, WHO European Region, week 1/2018



The epidemic period this influenza season began in week 48, two weeks later than in the 2016–2017 season, but within the range (weeks 48-51) observed during all other seasons since the post-2009 pandemic seasons (**Figure 2**). The start of the influenza season has been defined by use of a 10% threshold of regional sentinel specimens testing positive for influenza viruses and has been demonstrated to be an appropriate indicator for the start of a regional epidemic (WHO unpublished data).

Figure 2. Influenza virus detections in sentinel-source specimens by season (weeks 40 to 20 only), type and subtype, WHO European Region, season 2010–2011 until week 1/2018



Viruses detected in sentinel-source specimens (ILI and ARI)

Since week 40/2017, more influenza type B (65.1%) than type A (34.9%) viruses have been detected in specimens from sentinel sites. Of 1 127 subtyped A viruses, 60% were A(H1N1)pdm09. The majority of type B viruses were reported without lineage, but of the 729 ascribed to a lineage, 96% were B/Yamagata (**Table 1**).

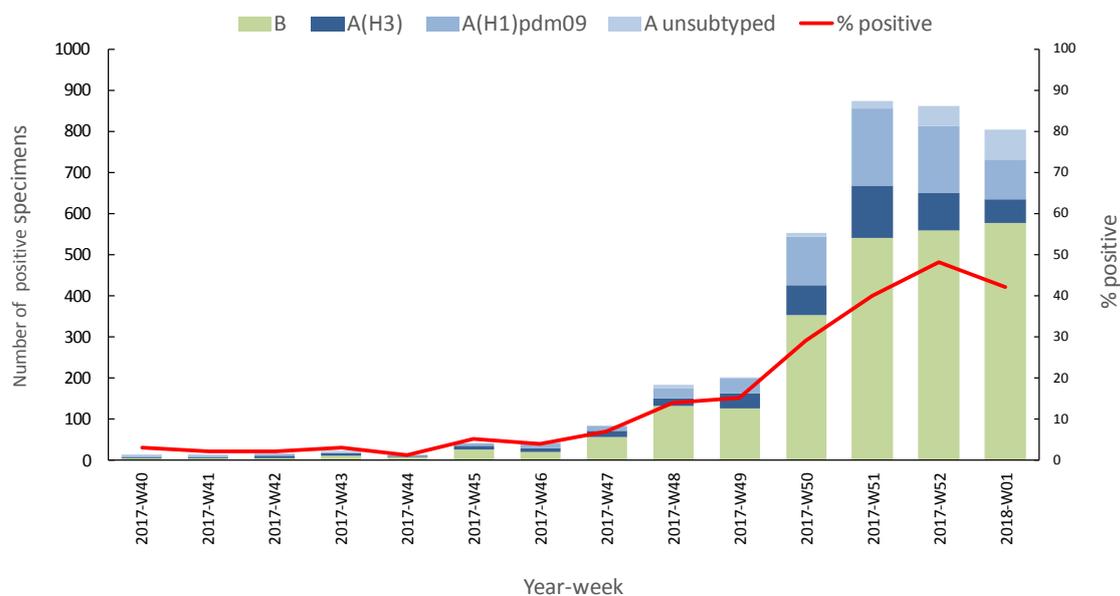
Table 1. Influenza virus detections in sentinel-source specimens by type and subtype, weeks 40/2017–1/2018[1]

Virus type and subtype	Week 40/2017-1/2018	
	Number	% ^a
Influenza A	1 293	34.9
A(H1N1)pdm09	672	59.6
A(H3N2)	455	40.4
A not subtyped	166	-
Influenza B	2 413	65.1
B/Victoria lineage	33	4.5
B/Yamagata lineage	696	95.5
Unknown lineage	1 684	-
Total detections (total tested)	3 706 (16 841)	22.0

^a For influenza type percentage calculations, the denominator is total detections; for subtype and lineage, it is total influenza A subtyped and total influenza B lineage determined, respectively; for total detections, it is total tests.

Since the start of the season all three influenza types and subtypes/lineages have been circulating, with influenza B being most commonly detected, followed by influenza A(H1N1)pdm09 and A(H3N2). (Figure 3). Within Member States a mixed pattern of influenza viruses has been observed.

Figure 3. Weekly influenza virus detections in sentinel-source specimens by type and subtype, week 40/2017–1/2018[1]



The detection of this level of influenza type B viruses this early in the influenza season is unusual for the Region. While seasons with substantial circulation of influenza type B viruses have been observed after the pandemic of 2009–2010, influenza B virus activity typically started later in the season and peaked after the peak for influenza type A viruses. The 2012–2013 season is the only season similar to what we have observed so far this season, with initial co-dominance between the two virus types.

Viruses detected in non-sentinel-source specimens

Among typed influenza viruses detected from non-sentinel sources (such as hospitals, schools, primary care facilities not involved in sentinel surveillance, nursing homes and other institutions), 51% were type A and 49% were type B. While less than 21% of the viruses detected in non-sentinel sources have been ascribed to a subtype or lineage, 68% of all subtyped A viruses were A(H3N2) and 98% of the type B viruses ascribed to a lineage were B/Yamagata (Table 2).

Table 2. Influenza virus detections in non-sentinel-source specimens by type and subtype, week 40/2017–1/2018[1]

Virus type and subtype	Week 40/2017 - 1/2018	
	Number	% ^a
Influenza A	17 022	51.4
A(H1N1)pdm09	2 056	32.3
A(H3N2)	4 310	67.7
A not subtyped	10 656	-
Influenza B	1 6065	48.6
B/Victoria lineage	14	2.1
B/Yamagata lineage	655	97.9
Unknown lineage	15 396	-
Total detections (total tested)	33 087 (227 879)	-

^a For influenza type percentage calculations, the denominator is total detections; for subtype and lineage, it is total influenza A subtyped and total influenza B lineage determined, respectively; as not all Member States have a true non-sentinel testing denominator, no percentage calculations for total tested are shown.

Hospital data

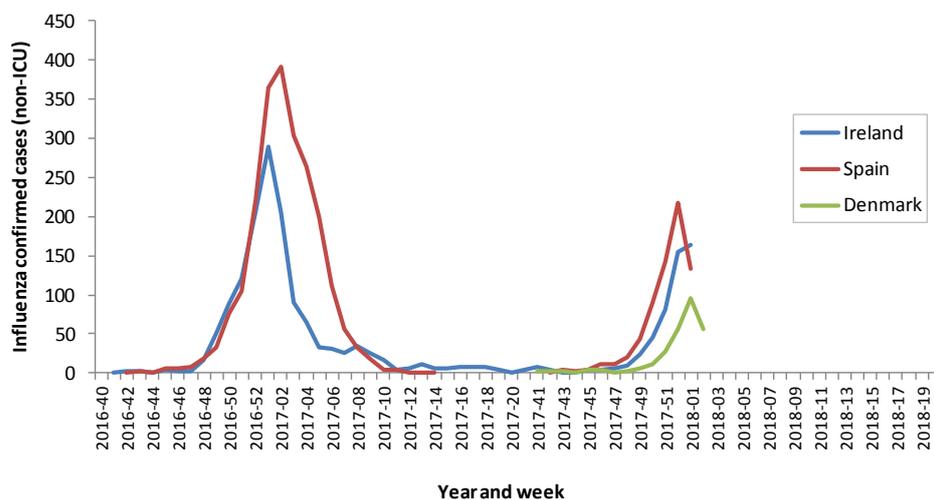
Severe disease related to influenza virus infection is monitored in some Member States by surveillance of hospitalised, laboratory-confirmed influenza cases or severe acute respiratory infections (SARI). Increasing numbers of severe cases were reported since week 50/2017 by some European Union (EU) Member States. There has been relatively little severe disease activity reported from the eastern part of the Region.

Hospitalised laboratory-confirmed influenza cases

Since week 40/2017, nine Member States (Denmark, Czech Republic, Ireland, France, Romania, Spain, Sweden, Slovakia and the United Kingdom) have reported laboratory-confirmed hospitalised influenza cases in intensive care units (ICU) or other (non-ICU) wards.

For non-ICU wards, Ireland and Spain reported most of the influenza-confirmed cases. The numbers have been steadily increasing in recent weeks (**Figure 4**).

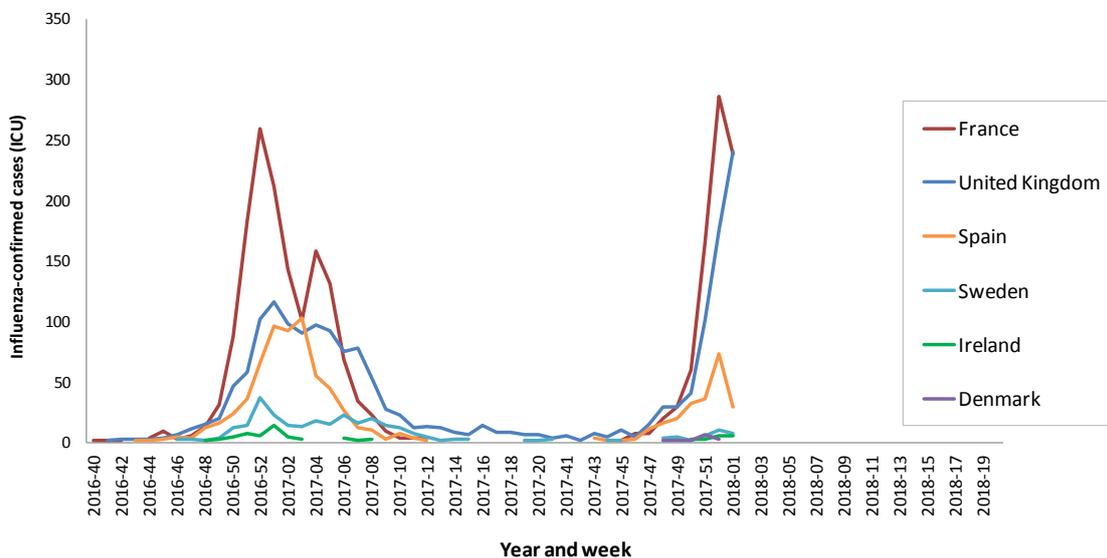
Figure 4. Number of hospitalised patients admitted to non-ICU wards by country, weeks 40/2017–1/2018*



* Data should be interpreted with care as the holiday period may have had an effect on health care seeking behaviour and data reporting; Member States with five or less specimens detected in a season were not included in the graph; Denmark started to report data as of the 2017–2018 season.

For ICU wards, France, Spain and the United Kingdom reported most of the influenza-confirmed cases. An increase in cases was also observed as of week 50/2017, with a steep increase in cases for France and the United Kingdom, surpassing last year’s peaks (**Figure 5**). The dip observed in week 1/2018 for non-ICU and ICU based surveillance is likely to be related to the holiday period.

Figure 5. Number of hospitalised patients admitted to ICU wards by country, weeks 40/2017–1/2018*



* Data should be interpreted with care as the holiday period may have had an effect on health care seeking behaviour and data reporting; Member States with five or less specimens detected in a season were not included in the graph; Denmark started to report data as of the 2017–2018 season.

Information about age and virus (sub)type was available for 1 080 patients in ICU and 795 patients in other wards. However, these data should be interpreted with caution, as the ages of the patients in the reporting hospitals may not be representative of the Member States’ population age distribution.

For the patients in non-ICU wards, influenza type B was more commonly detected (55%) and, among the four age groups, patients of 65 years and older accounted for the largest number of cases (49%) (**Figure 6**). This pattern of older adults being more often admitted to hospital is common and has also been observed in previous seasons.

The majority (86%) of the patients in ICU were 40–65 years of age (42%) and 65 years and older (44%). Influenza type A was most often detected (67%) (**Figure 7**). A relatively high proportion of persons aged 40–64 was admitted to ICU, more data in the coming weeks will reveal if this is a consistent trend.

Figure 6. Number of hospitalised patients admitted to non-ICU wards by age group and influenza virus type and subtype, weeks 40/2017–1/2018 (n=795)

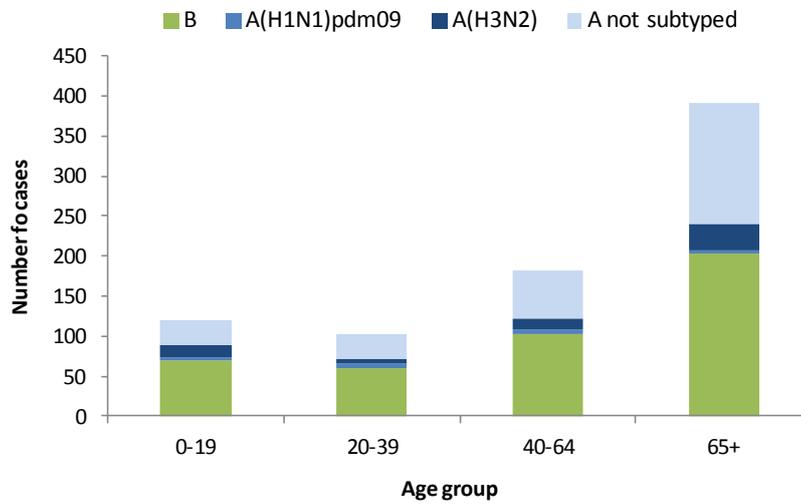
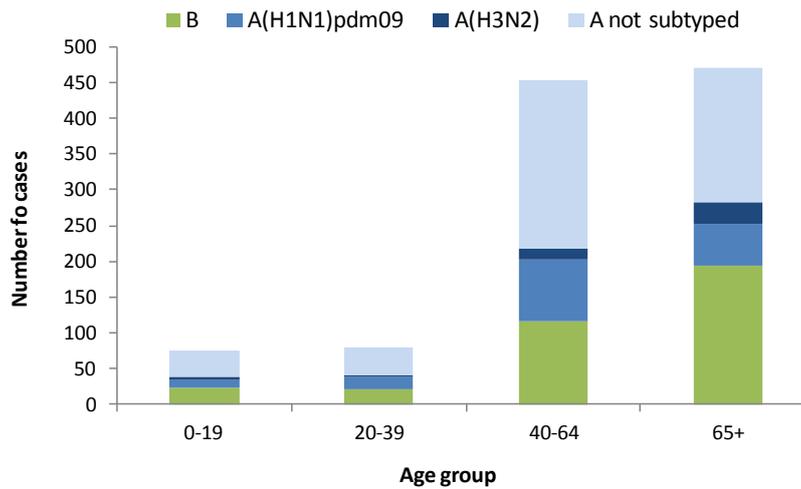


Figure 7. Number of hospitalised patients admitted to ICU by age group and influenza virus type and subtype, weeks 40/2017–1/2018 (n=1 080)



SARI surveillance

Hospital-based SARI surveillance has been implemented in 15 Member States in the eastern part of the Region.

Since week 40/2017, 13 768 SARI cases have been reported and 3 265 specimens tested for influenza viruses of which only 113 (3%) were positive for influenza virus (Albania (n=3), Armenia (n=57), Belarus (n=2), Kazakhstan (n=13), Kosovo (in accordance with Security Council resolution 1244 (1999)) (n=1), the Russian Federation (n=2), Serbia (n=6), Tajikistan (n=4), Ukraine (n=23) and Uzbekistan (n=2). In these Member States influenza type B was most often reported (80%) followed by equal proportions of influenza A(H1N1)pdm09 and A(H3N2).

Mortality monitoring

Data from 16 Member States or regions reporting to the EuroMOMO project were received for week 1/2018 and included in the pooled analyses of all-cause excess mortality[2]. Over the past weeks, there has been increased mortality among the elderly, notably in the southwest of the Region (Portugal and Spain) and the United Kingdom (Scotland).

Characterization of viruses

For specimens collected between weeks 40/2017 and 1/2018, genetic characterization of 298 viruses has been reported (**Table 3**). 32 A(H1N1)pdm09 viruses fell in clade 6B within the 6B.1 subclade, as does the current season's vaccine virus, A /Michigan/45/2015[9]. One A(H1N1)pdm09 virus was not attributed to any clade.

Table 3. Viruses attributed to genetic groups, cumulative for weeks 40/2017–1/2018[1]

Phylogenetic group	Number of viruses
A(H1N1)pdm09 A/Michigan/45/2015 (clade 6B.1) ^a	32
A(H1N1)pdm09 not attributable to any clade	1
A(H3N2) A/Hong Kong/4801/2014 (clade 3C.2a) ^b	88
A(H3N2) A/Singapore/INFIMH-16-0019/2016 (clade 3C.2a1) ^c	49
A(H3N2) not attributable to any clade	1
B/Brisbane/60/2008 (Victoria lineage clade 1A) ^{b, d}	8
B/Norway/2409/2017 (Victoria lineage clade 1A Δ162-163) ^e	6
B/Phuket/3073/2013 (Yamagata lineage clade 3) ^{c, f}	110
B/Yamagata lineage not attributed to any clade	3

^a Vaccine component of vaccines for both northern (2017–2018 season) and southern (2018 season) hemispheres

^b Vaccine component for northern hemisphere 2017–2018 season

^c Vaccine component for southern hemisphere 2018 season

^d Vaccine component of quadrivalent vaccines for use in southern hemisphere 2018 season

^e Deletion of K162 and N163 in the HA1 subunit of the hemagglutinin and antigenically different from the vaccine component.

^f Vaccine component of quadrivalent vaccines for use in northern hemisphere 2017–2018 season

Among 137 influenza A(H3N2) viruses, 88 (64%) fell in the vaccine virus component clade (3C.2a)[9], and 49 (36%) in subclade 3C.2a1. Viruses in these two groups are antigenically similar, but both clade and subclade have been evolving rapidly with the emergence of several new virus clusters which require continued monitoring of antigenic characteristics. One influenza A(H3N2) virus was not attributed to any reportable clade.

Of 127 genetically characterized type B viruses, eight belonged to the B/Victoria-lineage B/Brisbane/60/2008 clade 1A included in trivalent vaccines and 110 belonged to the B/Yamagata-lineage B/Phuket/3073/2013 clade 3 that is included in quadrivalent vaccines[9]. Three B/Yamagata-lineage viruses were not attributed to any reportable clade. Six of the fourteen B/Victoria-lineage viruses belonged to a subgroup of clade 1A viruses, represented by B/Norway/2409/2017, which carry the HA1 double amino acid deletion, $\Delta 162-163$, characteristic of the new antigenically distinct subgroup of genetic clade 1A viruses that are circulating in several countries (Canada, China including Hong Kong Special Administrative Region, Finland, Spain, Trinidad and Tobago, and the United States of America [10, 11]).

Antiviral susceptibility testing

Neuraminidase inhibitor susceptibility has been reported for 124 viruses (60 A(H3N2), 29 A(H1N1)pdm09 and 35 type B) from sentinel and non-sentinel sources with collection dates between weeks 40/2017 and 52/2017. Viruses have been tested for antiviral susceptibility by phenotypic and/or genotypic methods. Only one A(H3N2) virus showed evidence of reduced inhibition by neuraminidase inhibitors oseltamivir and zanamivir.

Conclusion

Both influenza types A and B viruses are co-circulating in the Region. Influenza B viruses are almost exclusively B/Yamagata-lineage and mixed patterns of influenza A virus subtype circulation (AH3N2) and A(H1N1)pdm09) are being observed. Influenza B/Victoria viruses, including the antigenically divergent Δ 162-163 subgroup, have limited circulation to date and give no indication of emerging to compete with B/Yamagata viruses. Because all seasonal influenza viruses are circulating, severe influenza cases can be expected among all ages.

This season's vaccines are expected to provide good protection against circulating A(H1N1)pdm09 viruses. The vaccine effectiveness against A(H3N2) viruses is expected to be lower compared to the protection against A(H1N1)pdm09, but similar to the previous season (low to moderate)[12-14].

Similar to A(H1N1)pdm09, the quadrivalent vaccine will likely provide good protection against B/Yamagata viruses. However, this virus strain is not included in the more widely used trivalent inactivated vaccine. Some cross-protection against B/Yamagata may, nonetheless, be conferred by the B/Victoria lineage viruses included in the trivalent vaccine. It should, however, be noted that while this year's vaccine effectiveness against B/Victoria viruses is anticipated to be good, a newly emerged deletion variant subclade of B/Victoria viruses was detected in Norway during the summer months of 2017[15]. This variant has also been detected elsewhere in Europe (Finland and Spain) and outside the continent[10, 11]. These viruses, which are circulating in limited numbers at present, are antigenically different from the B/Victoria vaccine component and the effectiveness of the current B/Victoria component of this season's vaccine is not yet known.

Although vaccine effectiveness against the different circulating viruses may be suboptimal for some strains, annual vaccination is the best prevention measure available against influenza infection and can prevent a substantial number of influenza-related illnesses even with low to moderate effectiveness.

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