RAPID RISK ASSESSMENT

# Risk assessment for seasonal influenza, EU/EEA, 2017–2018

20 December 2017

## Main conclusions and options for response

- The influenza season started in week 48/2017 with 11 EU/EEA countries reporting 10% or more sentinel specimens positive for influenza.
- First detections indicated circulation of A(H3N2) and B/Yamagata viruses. As the former subtype dominated last season, a high proportion of the population should be protected. However, the emergence of variant strains, as in the US, cannot be excluded and this would increase the likelihood of severe outcomes in the elderly.
- At this stage, it is impossible to predict the intensity or the peak of the influenza epidemic across Europe.
- Vaccine effectiveness against A(H1N1)pdm09 is expected to be high, whereas effectiveness against A(H3N2), the most prevalent type A virus, is likely to be low.
- B/Yamagata viruses are dominant so far, and vaccine effectiveness against this virus will be low as it is not included in the most widely used trivalent vaccine. Some effectiveness could be expected from cross-protection as a result of vaccination against B/Victoria virus.
- Regardless of vaccination status, the use of neuraminidase inhibitors and non-pharmaceutical measures in accordance with national guidelines or policy is encouraged.

## Source and date of request

ECDC Internal Decision, 12 December 2017.

## Public health issue

Early rapid risk assessment on seasonal influenza.

## Consulted experts

ECDC (in alphabetical order): Cornelia Adlhoch, Pasi Penttinen, René Snacken

External: Aristotle University of Thessaloniki - Angeliki Melidou.

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# Objectives

Since the 2009 influenza pandemic, ECDC has regularly produced early-season risk assessments for EU/EEA countries to inform national public health authorities of key features during the ongoing season. These risk assessments can be used to guide local public health authorities – for example, when reinforcing vaccination programmes in certain age groups or frail people, or deciding on antiviral policies and allocating appropriate healthcare resources.

The main objectives of the early season risk assessment 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 (NA).

# Sources of evidence

As the main sources of evidence, this risk assessment is based on clinical (influenza like-illnesses (ILI) and acute respiratory infections (ARI)), epidemiological and virological data from primary and secondary healthcare settings. The data are routinely 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 sources include situation reports from countries, especially those in the northern hemisphere, peer-reviewed literature and data from the European Monitoring of Excess Mortality for Public Health Action (EuroMOMO) project.

Any risks related to the influenza epidemic currently getting underway, for instance the risk of severe outcomes in particular age groups, have been assessed with regard to likelihood and potential impact.

# Primary care situation in the first affected countries

By week 48/2017, low intensity of influenza activity had been reported by 29 countries and ILI/ARI rates were at baseline level or below the Moving Epidemic Method (MEM) threshold [1]. However, 11 countries (Austria, Croatia, Denmark, France, Hungary, Italy, Norway, Poland, Portugal, Spain and the UK) reported > 10% of respiratory specimens testing positive for influenza which signalled the start of epidemic influenza activity in these countries (Figure 1).

This overall epidemic threshold was exceeded two weeks later than in the previous season but within the same range (weeks 47–51) as in all seasons since 2010–2011.

**Figure 1. Percentage of sentinel specimens positive for influenza virus by country, EU/EEA, week 48/2017**

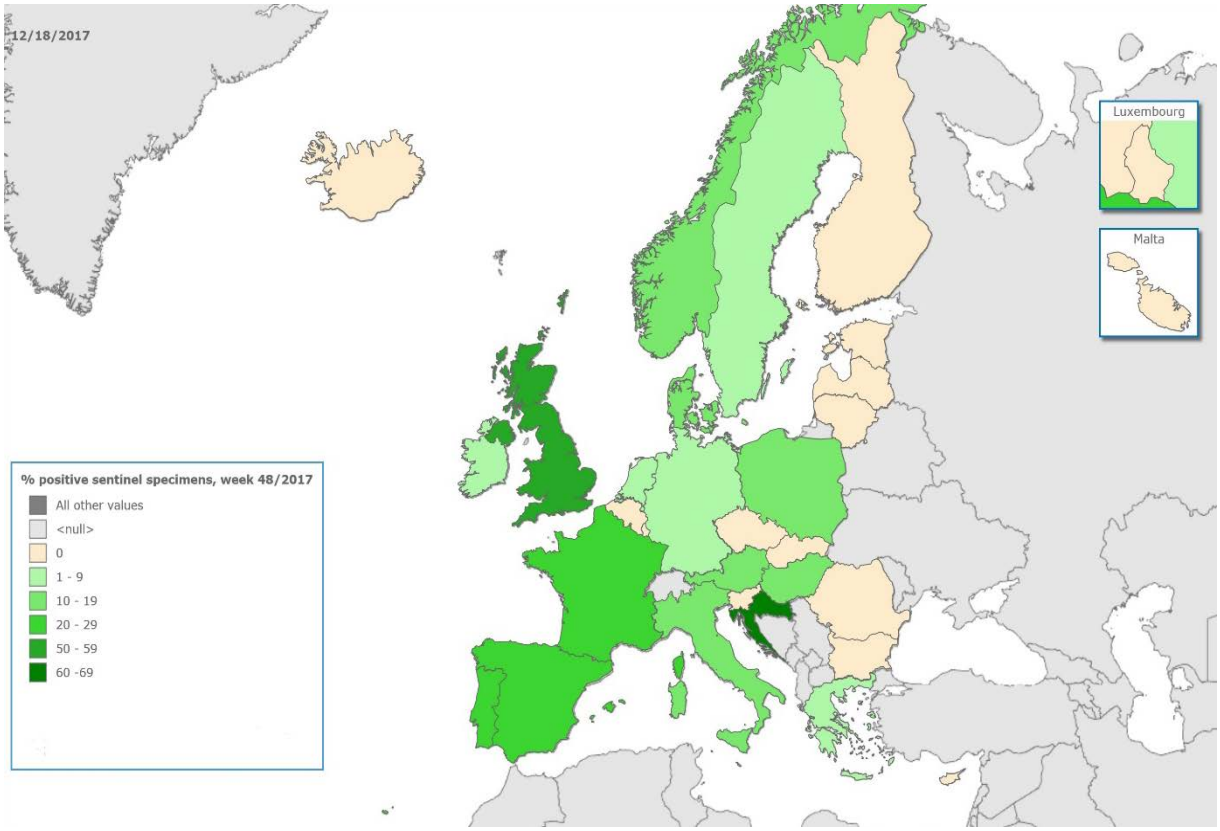
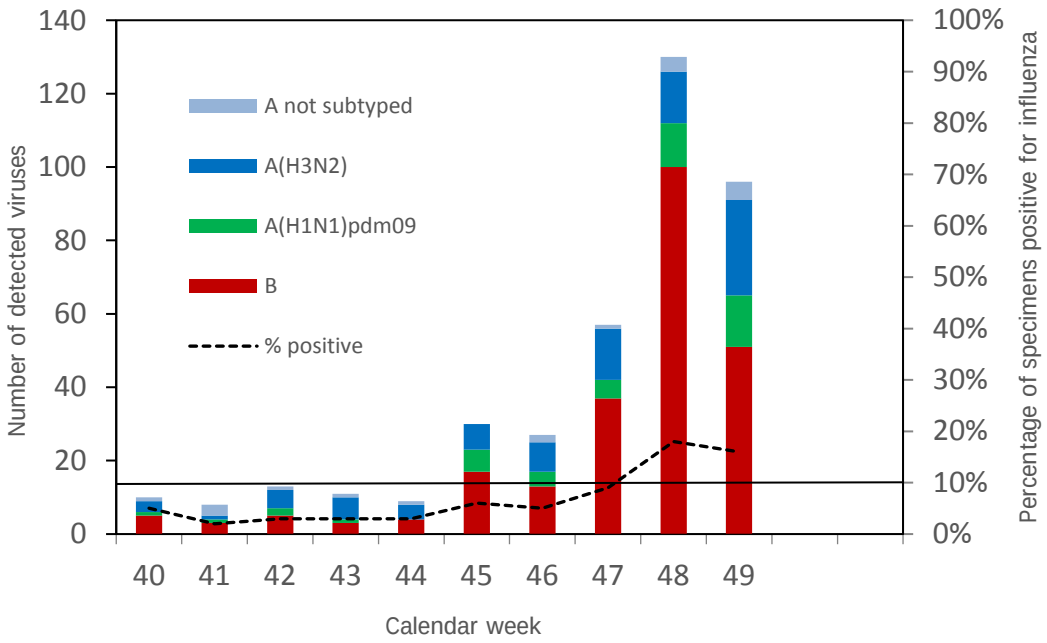



**Figure 2. Weekly proportion of sentinel specimens positive for influenza virus and number of detections by type and subtype, EU/EEA, season 2017–2018**



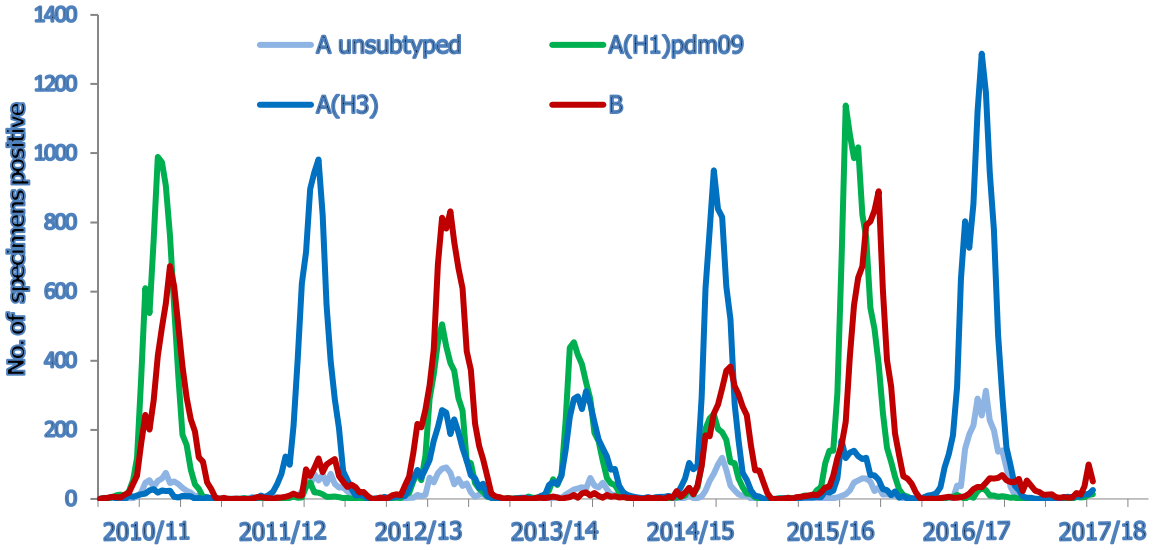
# Circulating viruses from sentinel sources

Since week 40/2017, influenza type B has predominated (61%) over type A (39%), and the number of type B viruses has been increasing, especially since week 45/2017 (Figure 2).

In total, 66% of subtyped A viruses have been A(H3N2), while 34% have been A(H1N1) pdm09 viruses. Of B viruses ascribed to a lineage, B/Yamagata predominated almost exclusively (96%) over B/Victoria (4%).

Since the 2009 influenza pandemic, seasons with high B virus circulation have occurred every two to three years (Figure 3). In most seasons, the circulation of B viruses tends to peak slightly later than the circulation of A viruses.

**Figure 3. Influenza virus detections in sentinel-source specimens by season, type and A subtype, EU/EEA, season 2010-11 until week 49/2017**




# Circulating viruses from non-sentinel sources

Among influenza viruses detected from non-sentinel sources (such as hospitals, schools, primary care facilities not involved in the sentinel surveillance, nursing homes and other institutions) and typed, two thirds (64%) were type A, while one third (34%) was type B. This differs from the distribution of virus types among sentinel specimens and probably reflects differences in underlying populations and the severity of clinical illness caused by the different subtypes. However, similar to the sentinel specimens, influenza A(H3N2) virus largely dominated (80%) among subtyped influenza A viruses and 95% of B viruses ascribed to a lineage were B/Yamagata.

# Hospital data

Since week 40/2017, seven countries (Czech Republic, Denmark, France, Ireland, Spain, Sweden, and the United Kingdom) have reported hospital surveillance data from 166 patients with laboratory-confirmed influenza admitted to intensive care units (ICU) and 122 patients admitted to other wards. The United Kingdom reported the majority (58%) of cases in ICU. Of the 166 patients in ICU, 121 (73%) were infected with influenza A virus (76 unsubtyped, 23 A(H3N2) and 22 A(H1N1)pdm09) and 45 (27%) with influenza B. The distribution of virus types and subtypes was approximately the same in the three countries (France, Spain and the United Kingdom) reporting the majority of cases. In patients admitted to other wards, more B virus infections were detected than in ICU cases (46% against 27%).

Information about age and virus (sub)type was available for 66 patients in ICU with the majority (79%) of the viruses being influenza A (Figure 4). The proportion of patients above 65 years of age admitted to ICU is higher than in other wards (47% against 32%; Figure 5). These data should be interpreted with caution as ECDC does not have information on whether the catchment of the reporting hospitals is representative of the underlying population age distribution (e.g. if paediatric and neonatal ICUs are included).

Up to week 49/2017, seven fatal cases following influenza infection had been reported: six from Spain and one from France. Four had been admitted to ICUs and three to other wards.

During the same period in the 2016–17 season, where early influenza activity was observed, seven countries reported 185 patients to have been admitted to ICU, slightly more than the 166 cases this season.

**Figure 4. Number of hospitalised patients admitted to intensive care units by age group and influenza virus type and subtype, seven EU countries, 2017–18, weeks 40–49 (n=66)**

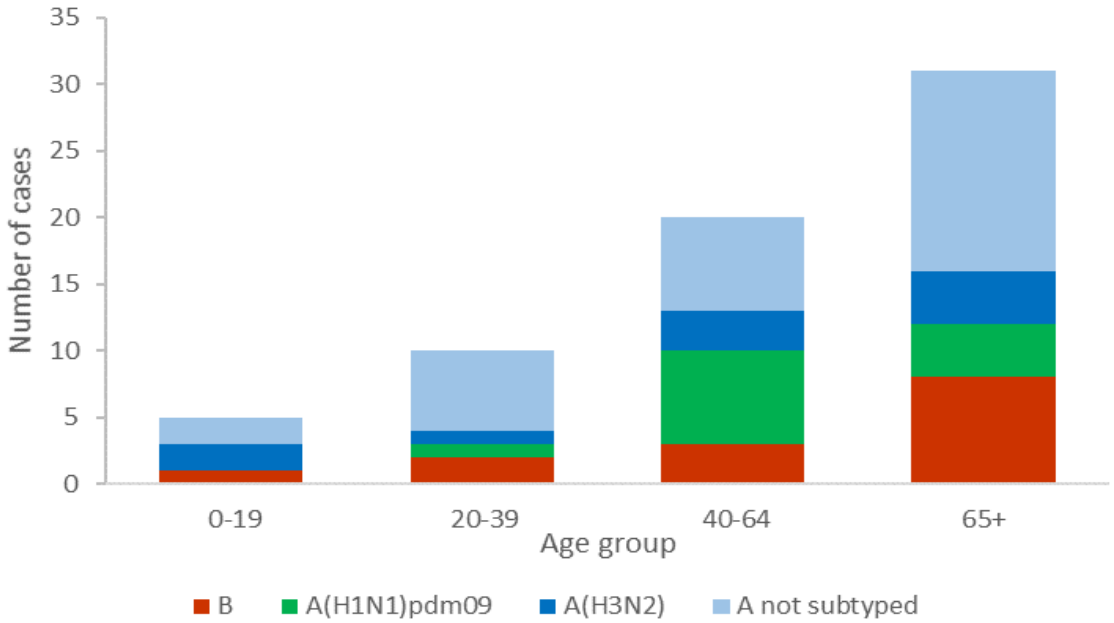
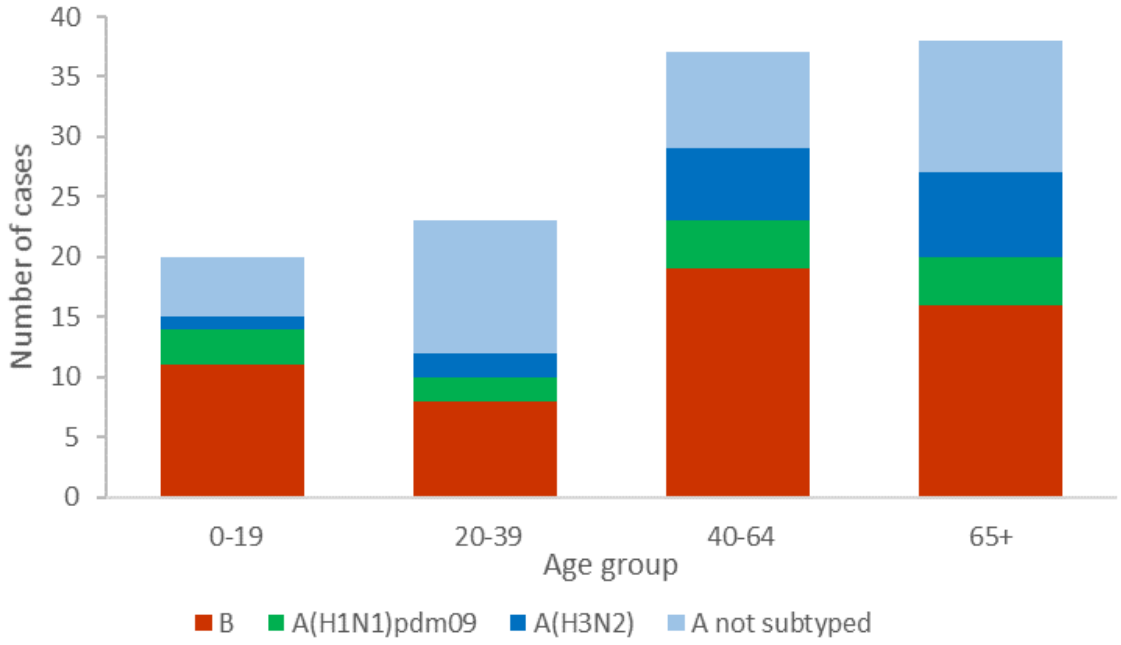



**Figure 5. Number of hospitalised patients admitted to other wards (except ICUs) by age group and influenza virus type and subtype, six EU countries, 2017–18, weeks 20–49 (n=122)**



# Mortality

Levels of all-cause mortality from 19 EU countries were within normal ranges until week 49/2017 [2].

# Virus characteristics

By week 49/2016, all 26 A(H1N1)pdm09 viruses that were genetically characterised fell in clade 6B and in subclade 6B.1, like the vaccine virus A/Michigan/45/2015 (Table 1) [3].

Eighty-eight circulating A(H3N2) viruses belonged mainly to two genetic groups: the majority (65%) belonged to clade A/Hong Kong/4801/2014 3C.2a (vaccine virus) and the rest (35%) to subclade A/Singapore/INFIMH-16-0019/2014 3C.2a1 (Table 1). Though viruses from both groups accumulated amino acid substitutions, the majority of circulating variant viruses tested until now were well recognised by the vaccine virus (80% of 3C.2a viruses and 60% of 3C.2a1 viruses).

Of 55 genetically characterised B viruses, six belonged to the B/Victoria-lineage B/Brisbane/60/2008 clade 1A, included in both the trivalent and quadrivalent vaccine, and 49 belonged to the B/Yamagata-lineage B/Phuket/3073/2013 clade 3, included in the quadrivalent vaccine. Three B/Yamagata-lineage viruses were not attributed to any clade. With regard to the B/Victoria virus, none of the characterised viruses carried the HA1 amino acid deletions Δ162-163 or Δ162-164, characteristic of the new antigenically distinct subcluster of genetic clade 1A viruses that are circulating in Canada, Trinidad, USA and Hong Kong [4].

Nineteen viruses (four A(H3N2), eight A(H1N1) and seven B/Yamagata) were antigenically characterised. The eight A(H1N1)pdm09 viruses were characterised as being similar to the vaccine component, A/Michigan/45/2015. Two of the A(H3N2) viruses belonged to the vaccine A/Hong Kong/4801/2014-like antigenic group, while two were A/Singapore/INFIMH-16-0019/2016(H3N2)-like (2018 southern hemisphere vaccine virus) [5]. The seven B/Yamagata viruses belonged to the B/Phuket/3073/2013- like group.

**Table 1. Influenza viruses attributed to genetic groups for weeks 40–49/2017**

| Phylogenetic group | Number of viruses |
|---|---|
| A(H1N1)pdm09 A/Michigan/45/2015 (clade 6B.1) [a] | 26 |
| A(H3N2) A/Hong Kong/4801/2014 (clade 3C.2a) [b] | 57 |
| A(H3N2) A/Singapore/INFIMH-16-0019/2014 (clade 3C.2a1) [c] | 31 |
| B/Brisbane/60/2008 (Victoria lineage clade 1A) [b, d] | 6 |
| B/Phuket/3073/2013 (Yamagata lineage clade 3) [c, e] | 49 |
| B/Yamagata lineage not attributed to any clade | 3 |

[a] Vaccine component of vaccines for 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] Vaccine component of quadrivalent vaccines for use in northern hemisphere 2017–2018 season

**Table 2. Influenza viruses attributed to antigenic groups for weeks 40–49/2017**

| Phylogenetic group | Number of viruses |
|---|---|
| A(H1)pdm09 A/Michigan/45/2015 (H1N1)-like [a] | 8 |
| A(H3) A/Hong Kong/4801/2014 (H3N2)-like [b] | 2 |
| A(H3) A/Singapore/INFIMH-16-0019/2016 (H3N2)-like [c] | 2 |
| B/Phuket/3073/2013-like (B/Yamagata/16/88-lineage) [c, e] | 7 |

[a] Vaccine component of vaccines for 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] Vaccine component of quadrivalent vaccines for use in northern hemisphere 2017–2018 season

## Antiviral resistance

Up to week 49/2017, four EU/EEA countries had reported on the antiviral susceptibility of 87 circulating viruses (16 (H1N1)pdm09, 52 A(H3N2), one B/Victoria and 18 B/Yamagata viruses) from sentinel and non-sentinel sources. Viruses have been tested for antiviral susceptibility by phenotypic and/or genotypic methods. Only one A(H3N2) virus with R292K mutation in neuraminidase showed highly reduced inhibition by oseltamivir and reduced inhibition by zanamivir.

## Vaccination coverage

Vaccination trends in high-risk groups are declining in most of the EU/EEA countries [6] and the EU target of 75% coverage has only been reached by Northern Ireland (UK) for people with chronic conditions, the Netherlands and the UK (Northern Ireland and Scotland) for older age groups.

# ECDC threat assessment for the EU

## Dominant strains

In some of the first affected EU/EEA countries, B/Yamagata viruses account for the majority of circulating influenza viruses but they may co-circulate with A(H3N2) virus. As A(H3N2) circulated almost exclusively last year, albeit in different proportions across the EU/EEA countries, population immunity should be high, but even circulation to a lesser extent may still result in severe outcomes in the elderly. In addition, the emergence of A(H3N2) variants, as observed in the US, cannot be excluded. The low reported level of A(H1N1)pdm09 virus at the beginning of influenza activity this season is probably an indicator that its high prevalence during previous seasons conferred a high immuno-protection in the population, with the exception of very young children who may be susceptible to the virus. There are early indications that B/Victoria virus is barely circulating in the first affected countries and it is considered unlikely that it will emerge later and compete with B/Yamagata.

## Vaccine match

The vaccine effectiveness against the circulating H1 viruses will probably be high. Should A(H1N1)pdm09 viruses co-circulate to an appreciable extent with A(H3N2) viruses, this will contribute to an overall increased vaccine effectiveness.

The vaccine effectiveness against A(H3N2) viruses is expected to be similar to the previous season (low to moderate) [7, 8, 9]. Similar to the situation last season, influenza A(H3N2) viruses belonging to different phylogenetic subclusters within 3C.2a or 3C.2a1 are likely to predominate in different proportions across countries, possibly causing variable levels of protection. Paradoxically, the WHO Collaborating Centre in London showed that almost 80% of 3C.2a and 60% of 3C.2a1 circulating viruses were well covered by the vaccine during the previous influenza season (WHO CC southern hemisphere VCM report). Antigenic drift in the A(H3N2) virus, as shown recently in the US with the emergence of a new variant [10], would probably lead to suboptimal vaccine effectiveness against A(H3N2) with a major impact among the elderly.

The vaccine effectiveness against B/Yamagata viruses will probably be good, however this virus strain is only included in the rarely-used quadrivalent vaccine and is not included in the most widely used trivalent vaccine. Some cross-protection with B/Victoria, which is included in the trivalent vaccine, may occur.

Vaccine effectiveness against B/Victoria viruses will be high. However, this influenza type seems less prevalent this season. A newly emerged deletion variant subgroup of B/Victoria viruses was observed in Norway during the summer months [11]. These viruses are antigenically different from the vaccine virus, so if they would spread, the vaccine would only offer limited protection.

# Conclusions and options for response

At this stage of the current influenza season, it is too early to pass judgement on the intensity of the season or the timing of the peak in virus circulation.

Overall, vaccination is the most effective measure for preventing severe influenza in population groups at risk of serious consequences following influenza infection (the elderly, people with pre-existing chronic diseases and people with immune deficiencies). Vaccination of pregnant women is probably the best way to protect new-born infants. Vaccination of healthcare workers against influenza, especially frontline workers caring for the most vulnerable, should decrease their risk of infecting their patients.

As the currently dominant B/Yamagata virus is not included in the trivalent vaccines and there is no evidence of any reduced susceptibility, post-exposure of antiviral treatment with oseltamivir or zanamivir should be encouraged, particularly in high-risk patients [12]. In closed settings, such as nursing homes, prophylactic use of neuraminidase inhibitors should be considered following the first detected case in the setting.

Non-pharmaceutical measures, such as strict personal and cough hygiene, and social distancing measures should be encouraged during the whole season [13].

EU/EEA Member States that have already passed the epidemic threshold might experience heavy pressure during the upcoming Christmas holiday period, especially in doctor's practices and paediatric wards, as B viruses tend to circulate more intensively among children. Only a few EU/EEA Member States offer vaccinations for children. The activation of contingency plans to preserve and release capacity in acute care should be considered, depending on the local epidemiological picture.

As this is the fourth consecutive year in which the B virus included in the trivalent vaccine has not matched the circulating B viruses, EU/EEA Member States might consider increasing the availability and use of the quadrivalent influenza vaccine in their countries for the next season.

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