RISK ASSESSMENT

# Seasonal influenza 2011–2012 in Europe (EU/EEA countries)

9 March 2012

## Contents

# Executive summary

## Situation as of week 8

- The 2011/12 seasonal influenza epidemics in Europe started unusually late, and unlike the last few winters have not followed any particular geographical progression.
- Countries that are only just experiencing the start of transmission can expect increased influenza activity irrespective of their location in Europe, though transmission may be truncated where spring comes early.
- The epidemics have so far been dominated by the A(H3N2) viruses, but recently the proportion of B viruses has been on the increase. There are some A(H1N1)pdm09 viruses. Although these are far lower in numbers than the last two seasons, they are over-represented among the most severely affected hospitalised cases with confirmed infection.
- Resistance to neuraminidase inhibitors (oseltamivir, zanamivir and newer NIs) is reportedly very low this year, but resistance to adamantenes seems total, and there is no scientific basis for the use of the latter.
- There are reasons to believe that national seasonal influenza vaccine coverage has not improved since the 2009 EU Council Recommendation on seasonal influenza vaccination, but it has not declined much either, even in countries where there were controversies in the 2009 pandemic.
- While there may be some concern due to a genetic drift in the A(H3N2) and some B viruses (which have led to other viruses being recommended for the seasonal vaccine in the 2012–13 season), it is too early to reach any conclusions on the implications for vaccine effectiveness this season. Statements on actual vaccine effectiveness need to await the results of field effectiveness studies.
- Scientific evidence suggests there would be advantages to continuing the availability of seasonal vaccines for older people, those with chronic disease, and especially healthcare workers in countries still experiencing significant transmission.
- There are no indications of excessive pressures on primary care in the first affected countries.
- There are some indications of local pressures on secondary and higher levels of care in some areas, justifying preparation for mutual help within countries, but not for the general alerting of services.
- Outbreaks in nursing homes for older people and among those with chronic illness are a feature this season in some of the first affected countries. Immunisation of staff and patients is recommended. There is also a case for early treatment with neuraminidase inhibitors when outbreaks occur.
- Clinicians should be made aware of the greater likelihood of influenza manifesting itself this year in other presentations in older patients – pneumonias, cardiovascular and cerebrovascular pathology.
- A rise in all-cause mortality has been reported by three EU countries plus Switzerland for older age groups although at this stage it cannot be determined whether this is due to cold weather, influenza A(H3N2) or other causes.
- An early forward look risk assessment by Norway based on seroepidemiology is proving accurate with its prediction of an A(H3N2)-dominated season with older people especially affected. There are good reasons for the increased use of standardised seroepidemiology in Europe. At current, only two countries routinely use standardised seroepidemiology this season.
- This season, there are no new concerns over the safety of pharmaceutical interventions.
- Three remaining uncertainties are a) the role of B viruses towards the end of the season, b) vaccine effectiveness, and c) premature mortality in older people due to A(H3N2).
- ECDC will review this risk assessment periodically and update it either as the need arises or after the end of the season.

# Abbreviations

| | |
|---|---|
| ARDS | Acute respiratory distress syndrome |
| EISN | European influenza surveillance network |
| EuroMOMO | The European mortality monitoring project |
| GP | General practitioner |
| ILI | Influenza-like illness |
| IQR | Interquartile range |
| NI | Neuraminidase inhibitors |
| RSV | Respiratory syncytial virus |
| WHO | World Health Organization |

# Introduction

It is now ECDC practice to produce an annual risk assessment for the seasonal influenza epidemics in Europe. This is following both a recommendation in the report on the handling of the 2009 pandemic adopted by the World Health Assembly in May 2011 and the model developed by ECDC during that pandemic [1,2,3]. The first EU seasonal influenza risk assessment was published in January 2011, following the start of the influenza season in late November 2010 [4]. In 2012, the season started later than in most years, with the first five countries exceeding their epidemic threshold in week 3/2012 [5].

## Scope and purpose

The objectives of the risk assessment are as previously:

- to give an early description of the epidemics of seasonal influenza in the European Union and European Economic Area countries, especially in the states affected earliest in the influenza season;
- to identify the special features of the current season, especially areas where public health or clinical actions are justified; and
- to highlight areas of uncertainty and therefore priorities for further work.

## Methodology

Experiences passed on through routine reporting are looked at, along with the first affected countries in the EU/EEA. We are looking at key features that are known to differ from year to year (and between pandemics), especially those that may have implications for public health and clinical action (see Table 1). This focus on key operational decisions is essential to ECDC's approach to the assessment of the severity of the influenza season [3,6].

Three sources of information are combined, namely:

- routine reporting to ECDC through the European Influenza Surveillance Network (EISN);
- a short questionnaire relating to the impact of the epidemics (sent to and completed by the official competent body in the first affected countries this season: Belgium, Bulgaria, France, Greece, Iceland, Italy, Norway, Romania and Spain); and
- other information that is available from WHO, through publications, from the EuroMOMO projects and from epidemic intelligence.

A full list of the assessed evidence can be found in the Annex.

A draft of the initial risk assessment was sent to a group of experts for rapid review and improvement and then finalised and published. The initial risk assessment is kept under periodic review and is, if necessary, modified in season. A final risk assessment is published after the end of the season. The annual cycle is completed by ECDC convening a meeting of experts in autumn in preparation for the next season.

The initial and final risk assessments replace the previous early and late descriptions of the influenza season produced for the European Influenza Surveillance Network and the European Influenza Surveillance System. The final risk assessment feeds into ECDC's Annual Reports. At the same time, in-season academic publications are produced by ECDC and its collaborators as justified by the situation.

## Source and type of request

ECDC internal decision – routine and planned risk assessment.

## Main questions

- What are the main features of the 2011/2012 influenza season in Europe, what are the risks to human health, and what was the initial experience in the first affected countries in comparison to earlier seasons with special reference to a) the pattern of infection and disease, b) the virology, and c) the impact on the health services?
- Which is the expected pattern of influenza activity during the rest of the season in EU/EEA countries?
- What countermeasures and actions by public health authorities, if any, do the scientific and public health data and analyses support?
- What uncertainties remain and what further investigations should be prioritised?

# More specific questions

- When and where has the influenza activity started? Is the geographical spread similar/different? How intense the influenza activity now?
- What is comparable or different in comparison with previous seasons (e.g. intensity, age of patients)?
- Is the impact on primary healthcare stonger/weaker?
- Is the activity of respiratory syncytial virus (RSV) concomitant?
- In countries reporting in previous year(s) and now, is the pattern of reported severe cases different (e.g. age)? Are there differences in severe cases according to the infecting influenza virus? Are there influenza subtypes causing more severe disease? Is the pressure on ITU's more important? Is there an excess related mortality?
- Which influenza viruses are circulating in the community? Has there been any change in the virology of the A(H1N1)2009 virus? Which are the genetic and antigenic characteristics of the circulating viruses? How distant/close are they compared with previous seasons? Is there a good match between circulating and vaccine strains? How important is the resistance to antiviral medications? Are serological studies available? If yes, how to interpret them?
- Which is the vaccine effectiveness? Which is the vaccine coverage in the EU/EEA; are there any changes in comparison with previous seasons? What risk groups should be offered seasonal vaccines to for the 2011/2012 season in the Member States?
- What is the situation elsewhere (rest of EU, Asia, North America) and how was the influenza activity in the Southern hemisphere in 2011?
- What can be anticipated for the rest of the season?

**Table 1. Severity and guidance matrix**

| Feature | Known unknown | Result: unusual this season? | Implications and guidance: possible public health and clinical actions |
|---|---|---|---|
| **Geographical pattern of infection** | The duration, shape, number and tempo of the waves of infection | Late start of the season; appearing simultaneously in a number of countries without clear west-to-east progression. | Alerting clinicians and services; creating awareness that even if the season starts late, the intensity of the outbreak will be unpredictable. |
| **Dominant viruses** | Relative prevalence of different seasonal influenza viruses | A(H3N2); few A(H1N1)pdm09, B viruses now appearing. | Expected to affect older people, but children are also at risk from B viruses. Alert clinicians to the abnormal appearances of influenza viruses. |
| **Vaccine fit and effectiveness** | Antigenic type and phenotype; likely effectiveness of existing vaccines | A(H3N2) and B: antigenically heterogeneous and some lack of fit to the current vaccine antigens; A(H1N1)pdm09 has good fit. | Emphasise the use of antivirals, even in Member States with a high vaccination coverage; need to review vaccine effectiveness rapidly as planned under I-MOVE. |
| **Antiviral resistance** | Susceptibility/resistance to antivirals | No resistance to neuraminidase inhibitors. All viruses are resistance to adamantenes. | At present no need to consider antiviral resistance in most cases. No role for adamantenes. |
| **Risk groups for mild disease** | Susceptibility in the population; age-groups with most transmission | Children 0 to 4 have highest rates of consulting. Limited seroepidemiology (two countries only) suggest high risk of predominance of A(H3N2) and disease in older people. | Remind clinicians to be aware of the circulation of the virus and the risk of severe outcome in older people. |
| **Primary care pressures** | Impact report (questionnaire) | None out of nine countries experiencing notable pressures. | No case for alerting and preparing primary care surge capacity this season. |
| **Secondary care pressures** | Impact report (questionnaire) | From nine countries: some indications in some countries of particular local pressure. | Some case alerting; preparation of secondary care for the possibility of local pressures and the subsequent need for mutual support. |

| Feature | Known unknown | Result: unusual this season? | Implications and guidance: possible public health and clinical actions |
|---|---|---|---|
| **Risk groups for severe disease** | Age and clinical groups most affected | Depending on the causative virus: the very youngest and the eldest with A(H3N2), the 14-to-64 age group with A(H1N1)pdm09, and children with B viruses. | Alerting clinicians to the likelihood of unrecognised influenza in older people. Particular emphasis on immunising staff and patients in residential care homes for older people and those with chronic illness; aggressive treatment of outbreaks with antivirals and infection control. |
| **Mortality** | Pathogenicity (case/infection-fatality rates); excess premature deaths | Some indications of excess mortality in older people. Some confounding from extreme cold weather in some countries. | As last item. Also need to use planned mechanisms for estimating excess premature mortality, but controlling for confounding effects. Please note that this is expected with A(H3N2). |
| **Cross-sectoral pressures** | Level of ill health | No cross-sectoral pressures in any country. | No action needed. |
| **Special features** | Precise clinical case definition and sub-clinical infections and unusual features. What are the complicating conditions (super-infections, etc.)? | No special features aside from above. | No action needed. |

# Risk assessment

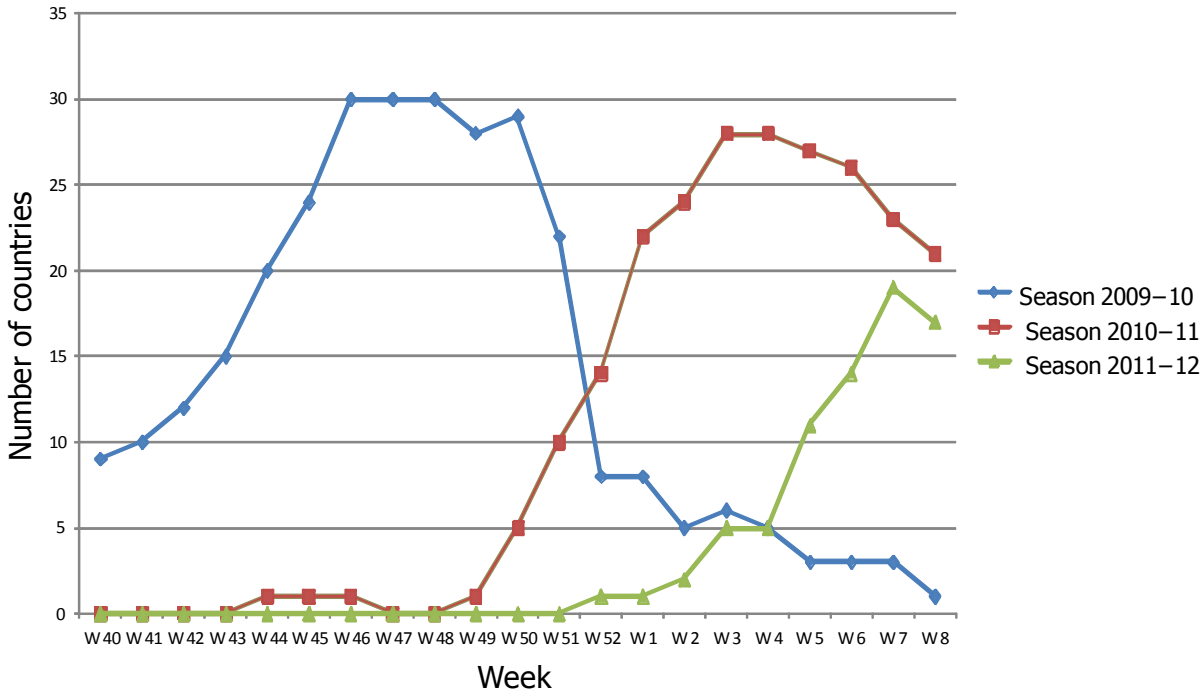
## Epidemiological situation and impact on primary healthcare services

This season started five weeks later than the 2010–2011 season (Figure 1). Week 3/2012 was the first week when more than three countries reported medium intensity, i.e. above the levels seen outside the influenza virus circulation period. That week, five countries (Bulgaria, Iceland, Italy, Malta, and Spain) reported medium intensity. In the following weeks, more countries reported medium intensity. By week 6/2012, 14 countries reported medium intensity. By week 8/2012, 17 countries reported medium or high intensity (see Figure 2, end of document).

For the geographic spread by week 3/2012, five countries reported local and four regional spread. By week six, 21 countries reported local, regional or widespread geographical spread. At week 8/2012, thirteen countries reported increasing trends. By then, two of the first affected countries reported declining trends for three weeks and so were considered to have peaked. The respiratory syncytial virus activity had already peaked in week 52/2011 and has been continuously declining since then [5].

The age group most attending primary care consultation have been the 0- to 4-year-olds as is often observed, followed by the 5- to 14-year-old age group. The least consulting group are adults aged 65 years and older, although they constitute the majority of the laboratory-confirmed hospitalised cases. In most countries, rates for influenza-like illness (ILI) and acute respiratory infection (ARI) are lower than in 2010–2011, except for Spain, where the ILIs were similar to the previous season.

**Figure 1: Distribution of countries reporting medium or higher intensity, by week, last three seasons**




There was no particular pressure on primary healthcare reported by **Iceland**, **Italy**, **Norway**, and **Romania**.

In **Belgium**, 86% of questioned GPs said that the pressure on primary care was lower or at the same level as in 2010–2011; 95% conformed this in comparison with the 2009 pandemic.

In **Bulgaria**, unusual pressures were observed in primary healthcare services, but they were weaker than during the two previous seasons.

In **France**, 'normal' influenza activity was observed by sentinel GPs. There are reports of an increased number of ILI cases among vaccinated people. The incidence rate of ILI consultation is still increasing, and the peak will probably be above the 2010–2011 peak. In nursing homes, the number of ARI has never been so high since the beginning of the surveillance (2005): attack rate and observed fatality rates are similar to what was observed in previous years.

In **Greece**, no particular pressure on primary healthcare was observed. In addition, the circulation of influenza started about four weeks later than last year, close to what used to be peak influenza season before the 2009 pandemic. A conventional pattern of geographical progression from north to south was not observed.

In **Spain**, the pressures on primary care in the 2011–2012 season were less than in 2010–11 and the 2009 pandemic.

# Epidemiology and impact in secondary healthcare services

**Epidemiology.** Countries reporting severe influenza surveillance data have applied one of two different case definitions: laboratory-confirmed influenza requiring hospitalisation, or severe acute respiratory infection (SARI). For the purpose of this report, only countries reporting laboratory-confirmed hospitalised influenza cases were included in the analysis.

From week 40/2011 to week 5/2012, 263 laboratory-confirmed hospitalised influenza cases were reported by four countries (France, Ireland, Spain and the UK). Of these, 176 had undergone typing and subtyping, revealing that 144 (81.8%) were associated with A(H3) infection, 20 (11.4%) with A(H1N1)pdm09, and 12 (6.8%) with B viruses.

Of the 141 hospitalised influenza cases with known outcome in season 2011–2012, 14 died. This was lower compared to season 2010–2011 in the same countries (18.4%, p = 0.01). Out of the 14 cases with a fatal outcome, nine were reported with influenza A(H3), three with influenza A with unknown subtype, one with influenza A(H1N1)pdm09, and one with influenza B virus. A formal publication on this has been published in Eurosurveillance. [7].

Severe disease was observed mostly among the youngest and oldest age groups (<5 year and >64 years). The proportion of severe cases aged between 15 and 64 years was significantly lower as compared to the previous season in the same countries (28.5% vs. 67.0%, p<0.01).

Of 101 severe cases with known underlying condition status, only seven (6.9%) had no underlying condition. Of 134 cases with known vaccination status, 85 (63.4%) were reported as not vaccinated.

**Impact.** Few countries have mechanisms for centrally monitoring pressures on hospitals. Therefore the information from the questionnaires is inevitably impressionistic. It is notable that infections and severe disease in very old people and care facilities were mentioned in the reports, although that was not asked for. This was also a feature in some national reports on official websites (see Annex).

The questionnaire completed by **Bulgaria** indicated no pressure observed in hospitals and/or ITUs.

In **France,** some hospital overloads were described. One explanation might be influenza, but also school holidays (and hence less GPs working and not enough staff for the entry screening at the hospital). The proportion of influenza consultations hospitalised for influenza, observed through an emergency unit network, is already higher than in 2008–2009 and 2010–2011, but not 2009–2010. The proportion of seniors (>=65 years) is increasing. Last week, they represented almost 50% of the influenza hospitalisation. The number of cases admitted to ICUs is increasing but still far from what was observed last season (92 cases four weeks after the start of the epidemic vs. 374 last season). The proportion of vaccinated people has also increased compared to the previous year (28% [when the vaccine status is known] vs. 12%). The mean age is 53 years vs. 45 last season. A full virological status is available for 31/93 cases: 6% B, 13% H1N1 and 80% H3N2. Community distribution is 6%, 6% and 88%, respectively.

In **Greece**, there were fewer severe influenza cases needing ICU admission compared with 2010–2011 (which was a severe year) and the age pattern resembles the one observed before the pandemic (mean age 63.5 in 2012 vs. 42 in 2009). The percentage of patients without underlying conditions was lower this season (23% vs. 30%). Acute respiratory distress syndrome (ARDS) was observed in patients infected with A(H3N2) virus, while other bacterial infections, e.g. staphylococcal infections, were more common in patients infected by B viruses. Two paediatric deaths have been reported: one in an infant due to A(H1N1)pdm09 (imported case from Libya) and one in a five-year-old child with influenza A (not further subtyped) with necrotic encephalitis.

**Iceland** reported some mild additional stress on higher-level services in one or two hospitals and, in one case, needed some reorganising of services in the hospital.

This is the third consecutive season since the pandemic that the **Italian** Ministry of Health and the 'Istituto Superiore di Sanità' have recommended the collection of clinical and epidemiological information on severe confirmed influenza cases and deaths. To date for this season, approximately 30 cases have been reported. Results will be available at the end of the season.

In **Norway**, age groups are different in comparison with the two previous seasons. More elderly people have been affected this year compared with the last two seasons. Intensive care surveillance shows that this year a larger

part of the patients are above 65 years compared with 2010–2011. Severe disease and fatal cases were also reported among people in long-term care facilities (where staff were also affected).

In **Romania**, compared with the previous season and the 2009 pandemic, an increase in severe cases was observed through week 06/2012 in the proportion of SARI cases/confirmed SARI cases in the 0- to 4-year-old age group. Compared with previous seasons, an increased number of secondary bacterial pneumonia was observed in both confirmed and not confirmed SARI cases. No increased number of ARDS was observed.

In **Spain,** the youngest and eldest age groups are the most affected age groups this season, with 34% (younger than five years of age) and 36% (above 64 years of age) of hospitalised severe influenza cases. The median age of hospitalised severe influenza cases in season 2011–2012 (45 years) was similar than in season 2010–2011 (47 years); IQR 2–73 and IQR 29–60, respectively. By contrast, median age was higher than in the pandemic season 2009–2010 (38 years, IQR 0–94). The proportion of cases with the most severe complications (ARDS or deaths) was lower in comparison with previous seasons.

# Virology

## Circulating viruses in from sentinel and non sentinel sources [5,9,10]

The dominant virus subtype of this season so far has been A(H3N2). Only a small portion of the detected influenza viruses have been of subtype A(H1N1)pdm09 and of type influenza B viruses, but in week 8 the proportion of the latter was the highest yet observed this season (11%).

Of the 15 103 influenza virus detections in sentinel and non-sentinel specimens since week 40/2011, 14 453 (95.7%) were type A and 650 (4.3%) were type B viruses. Of 7 840 influenza A viruses subtyped, 7 646 (97.5%) were A(H3) viruses and 194 (2.5%) were A(H1)pdm09. The lineage of 90 influenza B viruses has been determined: 51 (56.7%) were B-Victoria and 39 (43.3%) were B-Yamagata lineage.

## Antigenic and genetic characteristics [5,9,10]

Since week 40/2011, 249 antigenic characterisations of viruses have been reported: 221 (88.4%) were A/Perth/16/2009 (H3N2)-like; 16 B/Brisbane/60/2008-like (Victoria lineage); four B/Florida/4/2006-like (Yamagata lineage); five B/Bangladesh/3333/2007-like (Yamagata lineage), and three A/California/7/2009 (H1N1)-like.

Since week 40/2011, 530 genetic characterisations of viruses have been reported, of which 306 (57.7%) were A(H3) viruses falling within the A/Victoria/208/2009 clade (genetic group 3 represented by A/Stockholm/18/2011). Viruses falling within this genetic group are antigenically diverse and there is accumulating evidence of altered antigenicity compared to the vaccine virus, A/Perth/16/2009.

Since week 40/2011, 466 (86.9%) of the genetically characterised and reported viruses have been A(H3) viruses.

More details on the antigenic and genetic characteristics of circulating viruses can be found in the February report [10] prepared by the Community Network of Reference Laboratories (CNRL) coordination team.

An analysis of a broader representation of influenza viruses circulating recently was considered at the WHO strain selection meeting (in February) with the following outcome:

### *Influenza A(H1N1)pdm09 viruses*

The A(H1N1)pdm09 viruses remained antigenically homogeneous and closely related to the earlier vaccine virus A/California/7/2009. The sequence analysis of the HA genes of A(H1N1)pdm09 viruses indicated that the viruses fell into at least eight genetic groups which were antigenically indistinguishable.

### *Influenza A(H3N2) viruses*

The recently circulating A(H3N2) viruses were antigenically heterogeneous. An increasing proportion of viruses circulating in 2012 showed reduced reactivity with ferret antisera raised against earlier vaccine virus A/Perth/16/2009. Recent A(H3N2) viruses showed higher titres with ferret antisera raised against A/Victoria/361/2011-like reference viruses. The HA genes of recent viruses fell into two phylogenetic groups represented by A/Victoria/361/2011 (genetic group 3) and A/Brisbane/299/2011 (genetic group 6), with the majority falling within genetic group 3.

### *Influenza B viruses*

The B/Victoria/2/87 and the B/Yamagata/16/88 lineages were observed in similar proportions in some countries, suggesting an increase in the prevalence of viruses of the B/Yamagata/16/88 lineage. In China, however, viruses of the B/Victoria/2/87 lineage predominated, except in Hong Kong (SAR: Hong Kong Special Administrative Region of the People's Republic of China) where the two lineages were present in approximately equal proportions. The majority of viruses of the B/Yamagata/16/88 lineage were antigenically distinguishable from the previous vaccine virus of the B/Yamagata/16/88 lineage, B/Florida/4/2006, and antigenically similar to recent reference viruses, e.g. B/Wisconsin/1/2010. In addition, the majority of viruses of the B/Victoria/2/87 lineage were antigenically closely

related to the current vaccine virus B/Brisbane/60/2008 and the HA gene sequences of the viruses. This is consistent with the global findings reported by WHO for this season [9].

## Resistance to antivirals [5,10]

From week 40/2011 to week 5/2012, antiviral susceptibility data from Germany, Italy, the Netherlands, Norway, Portugal, Romania and Sweden have been reported to the TESSy and EUROFLU antiviral databases. None of the A(H1N1)pdm09, A(H3N2) and B viruses tested for neuraminidase inhibitor susceptibility were resistant, but all of A(H1N1)pdm09 and A(H3N2) viruses screened were resistant for M2 blocker drugs. This is consistent with the global findings reported by WHO for this season [9].

## Susceptibility and seroepidemiology

### *Serological studies*

Serological studies provide important information on the groups that are likely to be susceptible to infection in countries [11]. Norway and Poland are the only countries performing annual serological influenza studies in Europe.

**Norway.** Based on 1976 convenience samples from weeks 31 to 35 (August 2011 [8]), the prevalence of protective antibodies to A(H3N2) influenza viruses was noted to be very low (4%) in 25- to 59-year-old adults. Therefore it was felt that the adult population would be especially prone to A(H3N2) infection during the present influenza season. However, the prevalence of antibodies to A(H3N2) viruses was relatively high (31%) in school-aged children, whose immunity may limit the spread of the A(H3N2) viruses. This was one of the reasons for the conclusion of the Norwegian risk assessment that this season would be dominated by A(H3N2) [8].

The prevalence of protective antibodies to A(H1N1)pdm09 remained around 30% both in children and in young adults. B/Brisbane/60/08 (B/Victoria lineage) was the dominating virus in season 2010–2011. This was reflected by a substantial antibody prevalence (average for all ages: 17%) to this virus in the Norwegian population in 2011.

In **Poland**, antibody titres were defined in 1451 serum samples in autumn 2011 (personal communication[1]). The percentage of persons with a protective haemagglutination titre (≥40) against A(H3N2) influenza viruses was highest in the age group 15 to 25 (40.5%) and 8- to 14-year olds (33.8%). Of the adult population older than 25 years, an average of 27% had antibodies against A(H3N2). In infants and toddlers 0 to 3 years old, 14% had protective levels of A(H3N2) antibodies. There was a marked increase of A(H3N2) antibodies in all age groups in Poland compared with the 2010–2011 season. The percentage of persons with protective levels of antibodies against A(H1N1)pdm09 influenza virus also increased compared with the 2010–2011 season, particularly in children up to 14 years of age (mean 40% in age groups 0 to 3, 4 to 7, and 8 to 14 years). In young adults and adults, the protective antibodies against A(H1N1)pdm09 were at the same or a slightly higher level than in 2010–2011.

An increase of B influenza infections later this year would particularly affect the 0- to 7-year-old age group and younger and middle-aged adults (between 15 and 44 years): in these groups, fewer than 15% have protective antibodies against the B/Victoria lineage viruses that are currently circulating outside of Europe.

These results seem to suggest a greater susceptibility for A(H3N2) infection in the adult population of Norway. However, making comparisons and predictions based on the results of serological studies from different countries is difficult because of the lack of standardisation of serological tests [12].

# Influenza vaccine

## Vaccine coverage (VENICE)

Seasonal vaccine coverage data are now available from VENICE for the 2010–2011 season but are not yet finalised for publication. They show a strong gradient across EU/EEA countries, with much lower vaccination coverage in those EU countries that joined after 2003 compared with the old EU countries [13], although there seems to have been only limited negative impact on coverage in some countries from the controversies in the pandemic on the need for vaccination. Romania (by questionnaire) reported very low vaccination coverage this year, reflecting specific national vaccination production difficulties. In Greece, the vaccination coverage was estimated at 10% (telephone survey). In addition, the percentage of immunised persons with underlying conditions was 23%, while only 17% of healthcare workers were immunised.

[1] Summary report sent to Eeva Broberg by Aleksandra Malicka (on behalf of Lidia Brydak), Department of Influenza Research, National Influenza Center, National Institute of Public Health – National Institute of Hygiene, Warsaw, Poland.

## Match between circulating and vaccine strains [9]

While A(H3N2) viruses collected since 1 February 2011 fall into seven genetic groups, all recent viruses analysed in ECDC-affiliated countries fall within genetic group 3, with some evidence of altered antigenicity compared to the vaccine virus A/Perth/16/2009. Viruses falling within this genetic group are antigenically diverse but remain antigenically similar to the current vaccine virus A/Perth/16/2009.

As to A(H1N1) viruses, the season has been dominated by the A(H1N1)pdm09 virus, and the current vaccine will raise immunity against the circulating A(H1N1) influenza strains. Currently, there are not enough data to assess the vaccine match of the influenza B viruses as only one B/Yamagata virus (B/England /254/2011) has been reported to ECDC to have been characterised by HI assay against the reference viruses at WHO CC London [9]. However, global data suggest that there is some movement away from the vaccine strain [9].

## Vaccine effectiveness

In a season dominated by A(H3N2), and now by a rising number of B viruses, there has to be some concern because based on antigenicity data the reported match between the vaccine and circulating A(H3N2) viruses has declined to the point where there may be a decline in effectiveness. The same may also be true for B viruses. However this cannot be assumed, and it will be important to wait for the I-MOVE ECDC data to appear to arrive at any conclusion on effectiveness [14]. That said, clinicians should be made aware of this possibility in order to inform their management of people who report that they were vaccinated but still display influenza-like symptoms.

# Mortality from all causes

A number of countries undertake their own monitoring of death returns. In addition, all-cause mortality by age group in 16 EU/EEA countries is monitored by the former EuroMOMO project, using a common algorithm to standardise excess mortality estimates across Europe. Monitoring of early mortality data is useful for detecting the impact on mortality of unusual severe events like some influenza epidemics, heat waves, or cold weather. During February 2012 (up to week 8), excess mortality was observed in the age group >65 years in at least three EU countries (Belgium, Netherlands, Portugal) plus Switzerland. Both a period of cold weather that prevailed from 29 January to 12 February 2012 as well as influenza A(H3N2) may have contributed to the excess of mortality from all causes during this period.

During weeks 5, 6 and 7, a specific all-cause excess of mortality was observed in Portugal. During and prior to this period, Portugal experienced both low temperatures and the start of the influenza epidemic period. As reported by the national surveillance systems, the ILI rate increased above the baseline from week 4/2012 onwards, and as of week 8 was still continuing to increase. At week 7/2012, influenza activity was medium with an increasing trend. The dominant type of virus is the A(H3N2). A preliminary analysis shows that the excess mortality was concentrated in the age group over 74 years of age. That trend started in the northern region and then progressed to the south. Impact was observed in the centre and in Lisbon and the Tagus valley, and there is informal information from hospitals indicating an increase in hospitalisations [15]. In two or three other countries an excess of mortality was also observed, especially among those older than 75 years of age. It should be emphasised that this pattern has previously been observed with A(H3N2) viruses, for example in Portugal in 2008–2009 [16].

In Belgium, the first excesses of mortality were observed in December 2011 and in the beginning of January 2012 when winter weather conditions were moderate. An excess of mortality was then reported in a period of cold weather for the period 29 January to 20 February 2012. During this period the upper limit of mortality was exceeded in the general population, with an excess of mortality observed in the general population of 11%. This effect was more marked in the population aged 85 and older (19% over expected) and in the population aged 65 to 84 years (9% over expected). The Be-MOMO model [17] which, after corrections for delays of reporting, predicts excesses of mortality, estimated an excess of mortality of 19% in the general population, 27% in the population aged 85 and older, 17% in the population aged 65 to 84, and 8% in the population aged under 65. Up to the date of this report, there is a large overlap between the influenza epidemic and the cold wave so that no comment on the influenza epidemic and mortality can be provided at this moment. (Personal communication, Francoise Wuillaume, Scientific Institute of Public Health (WIV-ISP), Brussels, Belgium, 6 March 2012.)

# Situation in the northern hemisphere

In **Canada**, in week 6/2012, influenza activity has slightly increased compare to the previous week: one region reported widespread influenza activity, 10 regions reported localised influenza activity, and 22 regions reported sporadic influenza activity.

The proportions of the isolated influenza viruses were: 31% A(H3), 12% A(H1)pdm09, 16% unsubtyped, and 41% influenza B viruses. All viruses tested for antiviral resistance were susceptible to oseltamivir and zanamivir.

In the **United States**, the percentage of positive specimens for influenza in week 08/21012 was 18.4% (apparently still increasing). Of 726 typed viruses, 96% were type A and 4% were type B. Of 377 subtyped influenza A viruses, 81% were A(H3) and 19% were A(H1)pdm09. Among B viruses, 46% belonged to the B/Victoria lineage and 54% belonged to the Yamagata lineage. No tested circulating viruses were resistant to neuraminidase inhibitors. During the same period, the percentage of deaths due to pneumonia and influenza was below the epidemic threshold. One paediatric death was related to an influenza B infection.

In **China** in week 8/2012, influenza activity was at its peak in both south and north China. Influenza B viruses were still the predominant strain. Among antigenically characterised influenza B viruses, 76% were B/Victoria viruses, related to B/Brisbane/60/2008-like.

In **Japan**, during five weeks from week 1 to week 7/2012, influenza A(H3) and B/Victoria were dominating.

In summary, the intensity of influenza activity in northern hemisphere countries outside Europe continues to increases but is heterogeneous. There are some similarities to the pattern observed in EU/EEA countries, though in North America there was a higher proportion of A(H1N1) viruses than in Europe. In China, influenza B viruses are dominant. There are no clear indications of particular impact (stress) on healthcare services or other essential services this season.

# Situation in the southern hemisphere

From May to October 2011, ECDC monitored the influenza situation in five temperate southern hemisphere countries in terms of virology, epidemiology, and impact on healthcare of influenza and other respiratory viruses. Monitoring included reports on websites (e.g. ministries of health, public health institutes), details on the impact of influenza on healthcare services, risk factors associated with severe cases, complicating conditions, and vaccine coverage. Influenza experts in these five countries reported their information via a simple questionnaires prepared by ECDC. The process and the findings are described in a 'rapid communication' published in Eurosurveillance [18].

## Implications for Europe

The virological influenza pattern observed was not consistent enough to make a clear prediction for the 2011–2012 season in Europe. In general, the findings on the impact of influenza in the southern hemisphere in 2011 were reassuring for Europe, and the match of the A(H3N2) viruses with the vaccine was considered good. There was only limited evidence of freely circulating oseltamivir resistant A(H1N1)pdm09 [18].

# Safety of interventions

There are no indications of any new adverse events following immunisation (AEFI). The AEFI surveillance system related to the 2010–2011 trivalent seasonal influenza vaccines used in EU countries did not detect any adverse events. There have been no convincing adverse event signals reported for the neuraminidase inhibitors, the group of antivirals thought to be most used in Europe [19].

# ECDCs scientific and public health advice

What countermeasures do these scientific and public health data and analyses support?

Vaccination: Even late in the season it is worthwhile to immunise unvaccinated people for whom vaccination is recommended, especially in the countries where transmission is continuing [13]. Although a reduction in effectiveness against the main circulating A viruses (H3N2) and B viruses (Yagamata strain) is possible, no final conclusions can be drawn [9].

Antivirals: Despite the controversies over the interpretation and re-analysis of historical trials, the available data all in all continue to support the early use of antiviral treatment in all those presenting with severe influenza-like illness pending virological confirmation, and in those with milder disease but risk factors [20,21].

This season, hardly any antiviral resistance against the neuraminidase inhibitors was detected. Because of the observed drift in the predominating A(H3N2) and some B viruses it is more likely this season than last that an immunised person with symptoms of an influenza-like illness actually has influenza and will possibly benefit from a neuraminidase inhibitor. The evidence suggests that older people, especially those in residential care, will benefit from this approach [20,21].

Higher-level care: So far, there is only limited reason this year to alert hospital services, especially intensive healthcare services, of potentially increased numbers of influenza patients needing hospital care/intensive care in the next few weeks.

Clinical care: Given the increased burden in older people from A(H3N2) there will be advantages if clinicians are aware of the greater likelihood of influenza manifesting itself this year in 'atypical' presentations in older people (pneumonias and cardiovascular pathology) [22].

Special groups, e.g. older people in nursing homes and those with chronic illness: Outbreaks in these settings were reported as a feature this year in at least two of the countries affected early. This supports the approach of prevention through immunisation of patients (and in particular staff) and treatment of outbreaks of influenza-like illness with antivirals [23,24].

## Interpretation of the current situation, specific questions, remaining uncertainties, and priorities for further investigation

- This season started late and shows no clear geographic progression, making it unlike most recent seasons and the 2009 pandemic.
- An early forward look risk assessment from Norway using seroepidemiology is proving accurate though it will be important to evaluate the long-term accuracy of risk assessments based on seroepidemiology. If quality assurance can be developed, there will be advantages for Europe having more countries undertaking this work, both for the seasonal risk assessments and as a basis for work in a pandemic.
- There is no special burden on primary care and secondary care services so far this season. However, experiences in the first affected countries show that local intensity on the hospital health services can occur.
- Based on limited seroepidemiological data, initial experiences, and the fact that this is an A(H3N2)-dominated season, it seems most likely that there will be a considerable burden of infection and disease among older people [11,12].
- There is a likelihood of excess premature mortality especially due to A(H3N2) in older people in some countries but the extent of this is yet to be determined, particularly in view of the impact of the late-January cold spell.
- The effectiveness of the 2011–2012 vaccines against this season's A(H3N2) and B viruses is yet to be determined.

## What can be anticipated for the rest of the season 2011/2012?

The influenza activity in the community started later in comparison with the two previous seasons but the intensity looks similar or somewhat less. The classical geographical pattern of first cases in western countries moving to eastern countries has not been observed.

The circulation of influenza A(H1N1)pdm09 was much lower in comparison with previous seasons, and A(H3N2) dominates largely. In addition, based on the serological studies from two countries (Norway and Poland) the adult population would be prone to A(H3N2) infection during the present influenza season, should the number of B viruses continue to rise as they did in week 8; this may have a stronger impact on the younger population.

Hospitalised severe influenza cases were reported by some countries. The mean age of these patients seems to be older (Greece, Norway and Spain) and this will continue to be an issue in the countries with continuing transmission.

# References


1. WHO. Report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza A (H1N1) 2009 (Fineberg Report). Final version submitted to the World Health Assembly 2011. Geneva: WHO; 2011. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf
2. European Centre for Disease Prevention and Control. Pandemic 2009, risk assessments source page. Available from: http://ecdc.europa.eu/en/healthtopics/H1N1/risk_threat_assessment/Pages/risk_threat_assessment.aspx
3. Nicoll A, Ammon A, Amato Gauci A, Ciancio B, Zucs P, Devaux I, et al. Experience and lessons from surveillance and studies of the 2009 pandemic in Europe. Public Health 2010 124:14–23.
4. European Centre for Disease Prevention and Control. Risk assessment: seasonal influenza 2010–2011 in Europe (EU/EEA countries). Stockholm: ECDC; 2012. Available from: http://ecdc.europa.eu/en/publications/Publications/110125_RA_Seasonal_Influenza_EU-EEA_2010–2011 .pdf
5. European Influenza Surveillance Network. Weekly influenza surveillance overview (WISO).
6. Nicoll A. Planning for uncertainty: a European approach to informing responses to the severity of influenza epidemics and pandemics. Bulletin of the World Health Organization 2011;89:542-544. doi: 10.2471/BLT.11.089508. Available from: http://www.who.int/bulletin/volumes/89/7/11-089508/en/index.html
7. Beauté J, Broberg E, Plata F, Bonmarin I, O'Donnell J, Delgado C, et al. Overrepresentation of influenza A(H1N1)pdm09 virus among severe influenza cases in the 2011/12 season in four European countries. Euro Surveill. 2012;17(9):pii=20105. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20105
8. Norwegian Institute of Public Health. Rapport om scenarioer for influensaepidemi i 2012, 23. Januar 2012. Oslo: Folkehelseinstituttet; 2012. Available from: http://www.fhi.no/dokumenter/042f3a2a9d.pdf
9. WHO. Recommended composition of influenza virus vaccines for use in the 2012–2013 northern hemisphere influenza season. Report of strain selection meeting, February 2012. http://www.who.int/influenza/vaccines/virus/recommendations/201202_recommendation.pdf
10. CNRL-ECDC influenza virus characterisation, February 2012. Available from: http://ecdc.europa.eu/en/publications/Publications/1203_TED_CNRL_report_Feb2011.pdf
11. Broberg E, Nicoll A, Amato-Gauci A. Seroprevalence to influenza A(H1N1) 2009 virus – Where are we? Clin Vaccine Immunol. August 2011 vol. 18 no. 8 1205-121. Available from: http://cvi.asm.org/content/18/8/1205.full.pdf+html.
12. Wood JW, Major D, Heath A, RW Newman, Höschler K, Stephenson I, et al. Reproducibility of serology assays for pandemic influenza H1N1: Collaborative study to evaluate a candidate WHO International Standard, Vaccine, Volume 30, Issue 2, 5 January 2012, 210-17, ISSN 0264-410X, 10.1016/j.vaccine.2011.11.019. Available from: http://www.sciencedirect.com/science/article/pii/S0264410X11017865
13. Mereckiene J, Cotter S, D'Ancona F, Giambi C, Nicoll A, Lévy-Bruhl D, et al., on behalf of the VENICE project gatekeepers group. Differences in national influenza vaccination policies across the European Union, Norway and Iceland 2008–2009. Euro Surveill. 2010;15(44):pii=19700. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19700
14. Valenciano M, Kissling E, Ciancio BC, Moren A. Study designs for timely estimation of influenza vaccine effectiveness using European sentinel practitioner networks. Vaccine. 2010 Oct 8;28(46):7381-8. Epub 2010 Sep 17.
15. Portuguese Ministry of Health/Institute Síndroma gripal Vigilância epidemiológica semanal, clínica e laboratorial Portugal, época 2011/2012 Semana 08 – de 20/02/2012 a 26/02/2012 http://www.insa.pt/sites/INSA/Portugues/Documents/Gripe2.pdf
16. Nogueira PJ, Nunes A, Machado E, Rodrigues E, Gómez V, Sousa L, et al. Early estimates of the excess mortality associated with the 2008–9 influenza season in Portugal. Euro Surveill. 2009 May 7;14(18). pii: 19194. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19194
17. Cox B, Wuillaume F, Van Oyen H, Maes S. Monitoring of all-cause mortality in Belgium (Be-MOMO): a new and automated system for the early detection and quantification of the mortality impact of public health events. Int J Pub Health 2010 Aug;55(4):251-9. Epub 2010 Apr 8.
18. Lopez Chavarrias V, Broberg E, Nicoll A. Preliminary implications for Europe of the 2011 influenza season in five temperate southern hemisphere countries. Euro Surveill. 2011;16(50):pii=20044. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20044

19. European Medicines Agency. Pandemic influenza pharmacovigilance safety updates. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000246.jsp&murl=menus/special_topics/special_topics.jsp&mid=WC0b01ac058004bf57
20. Moscona A. Neuraminidase inhibitors for influenza. N Engl J Med. 2005;353:1363-1373
21. Hernan MA, Lipsitch M. Oseltamivir and risk of lower respiratory tract complications in patients with flu symptoms: a meta-analysis of eleven randomized clinical trials. Clin. Infect. Diseases. Published online: June 15, 2011. Available from: http://cid.oxfordjournals.org/content/early/2011/06/14/cid.cir400.full
22. Warren-Gash C, Smeeth L, Hayward AC. Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review. The Lancet infectious diseases. 2009 Oct;9(10):601-10.
23. Hayward AC, Harling R, Wetten S, Johnson AM, Munro S, Smedley J, et al. Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. BMJ. 2006 Dec 16;333(7581):1241. Epub 2006 Dec 1.
24. Hayward AC, Watson J. Effectiveness of influenza vaccination of staff on morbidity, and mortality of residents of long-term care facilities for the elderly. 2011 Mar 16;29(13):2357-8. Epub 2011 Feb 2.

# Consulted experts

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ECDC is very grateful for the expert input from the persons above. They were consulted as individuals on the basis of their expert knowledge and experience rather than as representatives of their institutions or countries. It should also be noted that responsibility for the content of this risk assessment lies with ECDC rather than with these individuals. Declarations of interest were collected for those listed above.

The WHO Regional Office for Europe was consulted on this document. The views in this document do not necessarily represent the views of the WHO Regional Office for Europe.

Other contributors were those who completed questionnaires or who contributed subsidiary data and analyses, notably:

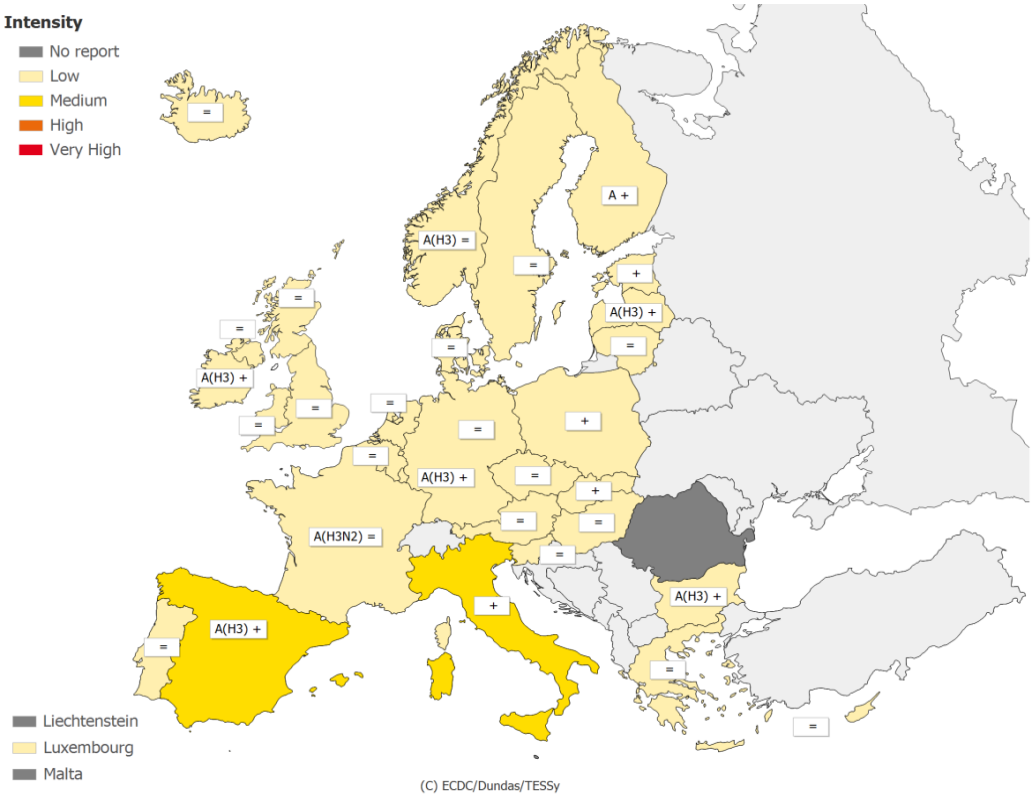
Agoritsa Baka, Isabelle Bonmarin, Siri Helene Hauge, Rania Kalkouni, Mira Kojouharova, Odette Nicolae, Florin Popovici, Caterina Rizzo, Guðrún Sigmundsdottir, Françoise Willaume, Georgia Spala, Amparo Larrauri (Spanish Influenza Surveillance System and National Epidemiological Surveillance Network) and the collaborators in the EuroMOMO project, especially Drs Kåre Mølbak and Anne Mazic.

# Annex. Global and European data and analyses accessed

- WHO. Global Influenza updates available from here.
- National data from EU/EEA Member States as reported to ECDC and appearing in the Weekly Influenza Surveillance Overviews (WISO).
- WHO Regional Office for Europe – specifically reports for counties in the WHO European Region but outside the EU/EEA group of countries from Euroflu.
- CNRL-ECDC Influenza virus characterisation, February 2012, available here.
- First affected countries (Belgium, Bulgaria, France, Greece, Iceland, Italy, Norway, Romania and Spain) to week 7/2012 including their early publications (France, Portugal).
- More information and detailed data from EU/EEA countries reporting on severe disease and impact: Ireland (Health Protection Surveillance Centre), France (Institut de Veille Sanitaire), UK (England: Health Protection Agency), Spain (Sistema de Vigilancia de la Gripe en España), Romania (Institutul National de Sanatate Publica) and the Slovak Republik (Public Health Authority).
- More specific EuroMOMO – European monitoring of excess mortality for public health action. Pooled results are available here.
- Regional and national influenza websites in temperate northern hemisphere countries outside of WHO European Region: Canada (PHAC-Fluwatch), China (CCDC), Japan (NIID), USA (CDC-FluView).
- WHO strain selection meeting: http://www.who.int/influenza/vaccines/virus/recommendations/201202_recommendation.pdf

## Figures 2a–2d: Intensity trends for weeks 2/2012 to 8/2012

Intensity for week 2/2012

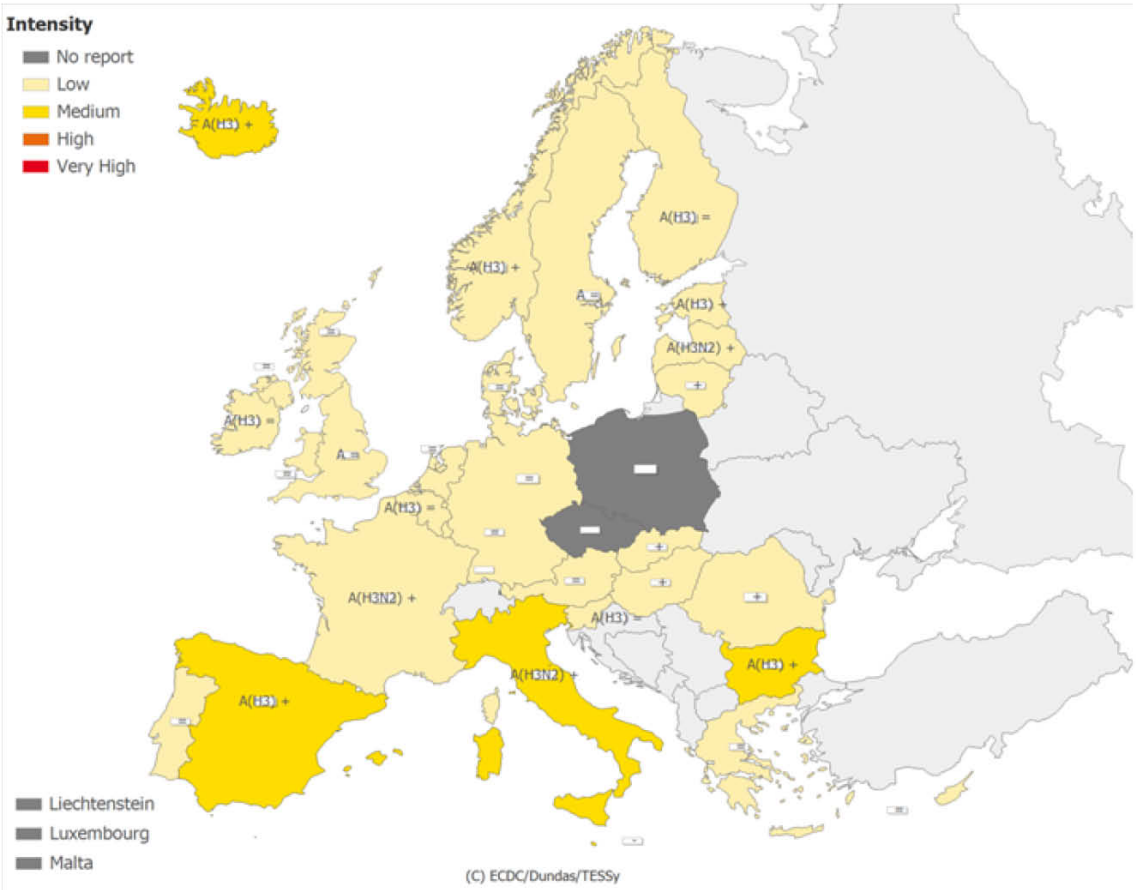



* A type/subtype is reported as dominant when at least ten samples have been detected as influenza positive in the country and of those > 40 % are positive for the type/subtype.

Legend:

| | | | |
|---|---|---|---|
| **No report** | Intensity level was not reported | **+** | Increasing clinical activity |
| **Low** | No influenza activity or influenza at baseline levels | **-** | Decreasing clinical activity |
| **Medium** | Usual levels of influenza activity | **=** | Stable clinical activity |
| **High** | Higher than usual levels of influenza activity | **A** | Type A |
| **Very high** | Particularly severe levels of influenza activity | **A(H3)** | Type A, Subtype H3 |
| | | **A(H3N2)** | Type A, Subtype H3N2 |

Intensity for week 4/2012

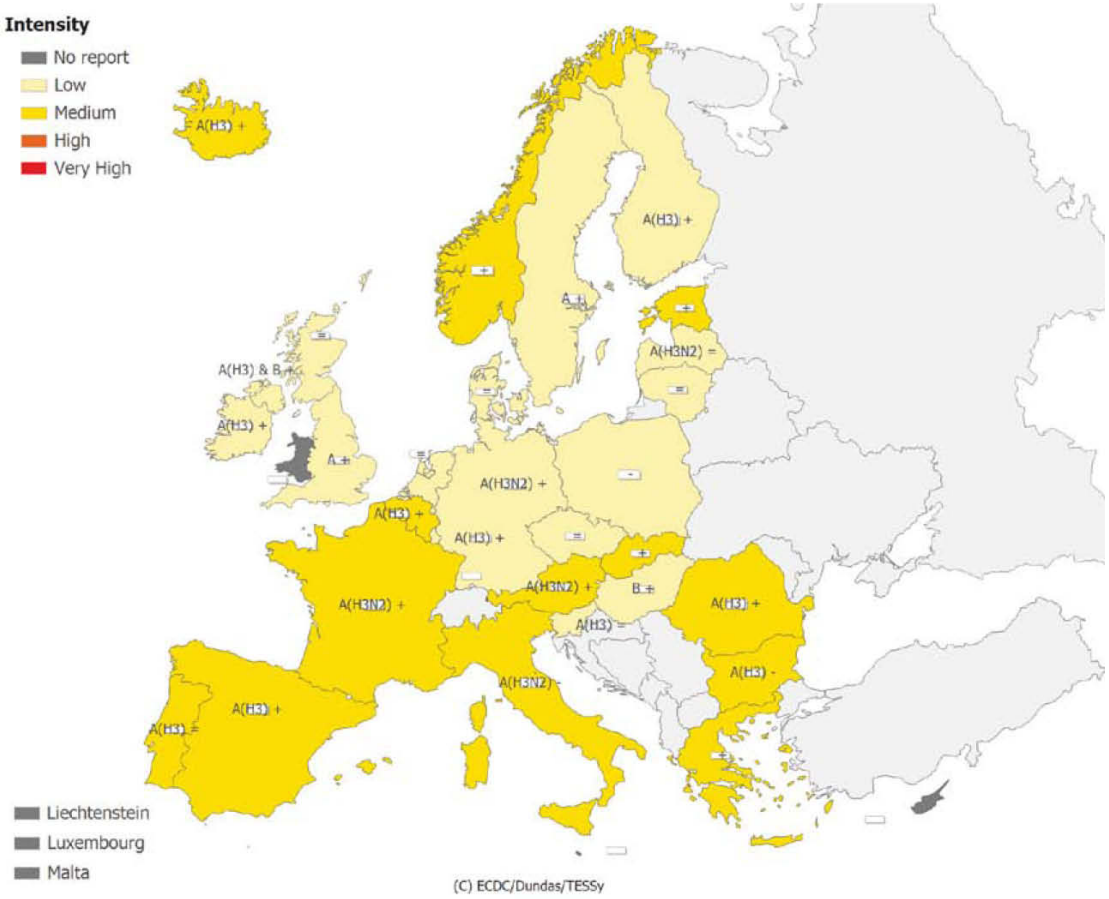



* A type/subtype is reported as dominant when at least ten samples have been detected as influenza positive in the country and of those > 40 % are positive for the type/subtype.

Legend:

| | | | |
|---|---|---|---|
| **No report** | Intensity level was not reported | **+** | Increasing clinical activity |
| **Low** | No influenza activity or influenza at baseline levels | **-** | Decreasing clinical activity |
| **Medium** | Usual levels of influenza activity | **=** | Stable clinical activity |
| **High** | Higher than usual levels of influenza activity | **A** | Type A |
| **Very high** | Particularly severe levels of influenza activity | **A(H3)** | Type A, Subtype H3 |
| | | **A(H3N2)** | Type A, Subtype H3N2 |

Intensity for week 6/2012

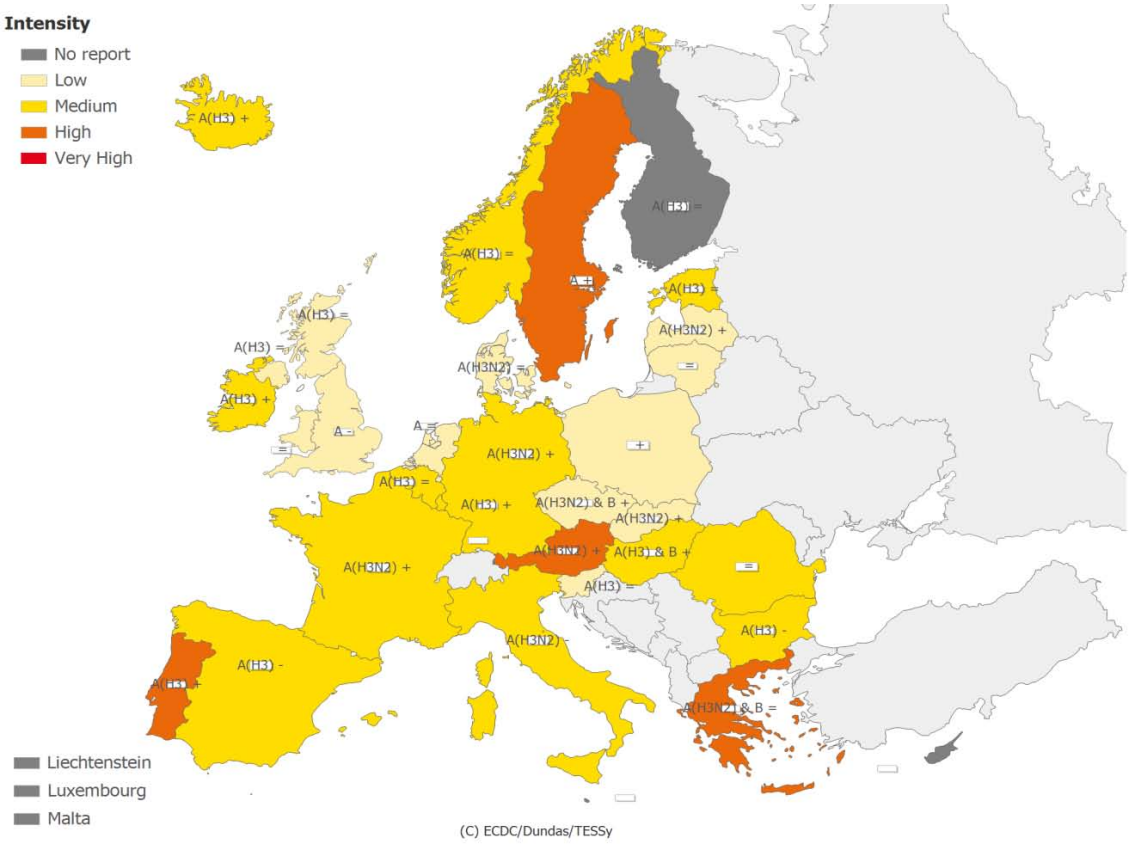



* A type/subtype is reported as dominant when at least ten samples have been detected as influenza positive in the country and of those > 40 % are positive for the type/subtype.

Legend:

| | | | |
|---|---|---|---|
| **No report** | Intensity level was not reported | **+** | Increasing clinical activity |
| **Low** | No influenza activity or influenza at baseline levels | **-** | Decreasing clinical activity |
| **Medium** | Usual levels of influenza activity | **=** | Stable clinical activity |
| **High** | Higher than usual levels of influenza activity | **A** | Type A |
| **Very high** | Particularly severe levels of influenza activity | **A(H3)** | Type A, Subtype H3 |
| | | **A(H3) & B** | Type B and Type A, Subtype H3 |
| | | **A(H3N2)** | Type A, Subtype H3N2 |
| | | **B** | Type B |

Intensity for week 8/2012




* A type/subtype is reported as dominant when at least ten samples have been detected as influenza positive in the country and of those > 40 % are positive for the type/subtype.

Legend:

| | | | |
|---|---|---|---|
| **No report** | Intensity level was not reported | **+** | Increasing clinical activity |
| **Low** | No influenza activity or influenza at baseline levels | **-** | Decreasing clinical activity |
| **Medium** | Usual levels of influenza activity | **=** | Stable clinical activity |
| **High** | Higher than usual levels of influenza activity | **A** | Type A |
| **Very high** | Particularly severe levels of influenza activity | **A(H3)** | Type A, Subtype H3 |
| | | **A(H3) & B** | Type B and Type A, Subtype H3 |
| | | **A(H3N2)** | Type A, Subtype H3N2 |
| | | **A(H3N2) & B** | Type B and Type A, Subtype H3N2 |