RISK ASSESSMENT

Seasonal influenza 2012/13 in Europe (EU/EEA countries)

February 2013

Executive summary

The 2012/13 seasonal influenza epidemics in Europe started earlier than in 2011/12 (a particularly late and mild season) in western EU/EEA countries and Scandinavia. South-western European countries (Spain and Portugal) have been less affected to date.

Countries in central and eastern Europe are advised to prepare for a similar pattern of transmission and intensity to that seen in the western Scandinavian countries.

Overall, there is no clear dominance of any particular influenza viruses. A(H3N2), A(H1N1)* and both lineages of B viruses (Yamagata and Victoria) are all circulating in substantial numbers with different countries reporting different dominant viruses. This differs from what is observed in the United States where influenza A(H3N2) viruses have predominated among the A viruses.

As one group of influenza B viruses circulating (B Victoria-lineage) has not been included in the current trivalent vaccine, the antigenic match this season between the circulating strains and the vaccine components is imperfect. However, the B Victoria-lineage accounts for only a small proportion of all viruses circulating this season.

Following replacement of the A(H3N2) component of the 2011/12 vaccine, the vaccine effectiveness of the 2012/-13 influenza vaccine is expected to be higher against influenza A(H3) infection than the especially low levels observed in Europe for the 2011/12 season. First indications from the UK confirm this although the estimates are in the range of 45% to 55%.

Informal reports suggest that national seasonal influenza vaccine coverage is similar to last season, although the VENICE data show there have been some small declines in coverage in older people in a number of countries since 2009.

There were some indications that pressure on primary care and emergency room services in the first affected countries was higher than during the equivalent period of the 2011/12 epidemic. However, this increased pressure maybe partly due to the fact that the epidemics started before the Christmas and New Year holidays when primary care services scale down in some countries.

There are some indications of local pressures on secondary healthcare services and intensive care units in some areas justifying preparation for surge capacity, but these are not strong enough to support putting hospital services on general alert.

To date only one oseltamivir-resistant A(H1N1) virus with the H275Y mutation has been reported. It was detected in the Netherlands in an immuno-compromised patient after treatment with oseltamivir. All other viruses tested

* Throughout this document 'A(H1N1)' refers to the pandemic 2009 virus strain officially designated A(H1N1)pdm09. This is now one of the circulating seasonal influenza viruses.

have been susceptible to the neuraminidase inhibitors. All screened influenza A viruses are resistant to adamantanes and there is no basis for the use of these drugs.

There is some indication of excess mortality from all causes in older people in some countries in temporal association with influenza epidemics. This applies especially in Denmark where influenza A(H3N2) virus is dominant. It is too early to determine whether this excess mortality is associated with cold weather, influenza virus infection or other causes.

In the UK in recent weeks, there has been an apparent rise in the number of cases of severe pneumonia due to toxin-producing strains of *Staphylococcus aureus* (PVL-SA), possibly associated with influenza. It remains to be seen whether this phenomenon will occur in other EU countries. Health practitioners should therefore be vigilant and clinicians are encouraged to report cases to their national authorities.

There are no concerns over the safety of seasonal influenza vaccines in use this season.

The main uncertainties are the impact that the substantial circulation of influenza A(H1N1) will have among younger patients, especially as regards the severity of disease, and if and how circulating B Victoria-lineage viruses might affect vaccine effectiveness.

ECDC's scientific and public health advice

It should be remembered that influenza can cause severe disease and death, especially in older patients and patients with underlying conditions and this is being seen from hospital surveillance this season. Even young healthy persons are at some risk of experiencing severe disease.

The scientific and public health data support an emphasis on traditional methods of reducing transmission: respiratory hygiene, regular hand-washing and early self-isolation when ill.

In view of the continued circulation of influenza viruses in Europe, countries still experiencing significant transmission should continue to offer seasonal vaccines to those recommended by national authorities. VENICE* surveys have indicated that the most commonly recommended groups are older people, those with chronic disease, healthcare workers and (in many but not all countries) pregnant women. Vaccination remains the most effective single method of protecting people against influenza.

Influenza A(H3N2) outbreaks in nursing homes for older people and among those with chronic illness were observed during the late stages of the previous season in some of the first affected countries. Immunisation of both staff and patients is recommended if that has not been done already.

Neuraminidase inhibitors should be used, as prophylaxis or early treatment, according to national guidance, especially in outbreaks among vulnerable groups such as in care homes.

* Vaccine European New Integrated Collaboration Effort. http://venice.cineca.org/

Introduction

Since the 2010/11 season, ECDC has produced an annual risk assessment of the seasonal influenza epidemics in Europe. This follows the model developed by ECDC during the 2009 pandemic and a recommendation in the report on the handling of the 2009 pandemic adopted by the World Health Assembly in 2011 [1,2].

Europe is sufficiently large geographically that epidemics progress across the region over a matter of months. Hence, the experience in the first affected countries can guide and inform preparations and action in countries that are yet to be affected. Particular emphasis is placed on the features where public health or clinical action can be taken.

Scope and purpose

The geographic scope is the European Union and European Economic Area for the season 2012–2013. The specific objectives of the risk assessment are:

- To give an early description of the epidemics of seasonal influenza in the Member States that have been affected earliest,
- To identify the special features of this year particularly where public health or clinical actions are justified, but also reminding authorities of default actions that are likely to apply each year,
- To highlight areas of uncertainty and therefore priorities for further work.

Methodology

The risk assessment focuses on features of influenza that are known to differ from year to year, focusing on those that may have implications for public health and clinical action (see Table 1). It uses the same methodology as for analysing pandemics. It does not replace other more quantitative approaches [2,3,4], but rather it complements them.

This risk assessment is based on:

- data routinely reported to ECDC through the European Influenza Surveillance Network (EISN);
- responses to a short questionnaire on the impact of the epidemics in the first affected countries this season (Belgium, Denmark, France, Germany, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Spain and the UK (England, Scotland));
- other information that is publicly available. For a full list of the evidence assessed, see Annex 2.

A draft of the risk assessment was reviewed by an external group of experts (see Annex 1). The draft was also sent for comment to the countries that completed the questionnaire. After publication, the risk assessment will be kept under review and modified later in the season if necessary. A final descriptive analysis will be published after the end of the season.

The risk assessment and later descriptive analysis replace the previous early and late descriptions of the influenza season produced on behalf of the European Influenza Surveillance Network and before that the European Influenza Surveillance Scheme.

Source and type of request

ECDC internal decision and planned risk assessment.

Main questions

What are the main features, risks to human health and course of the 2012/13 influenza season in Europe and what has been the initial experience in the first affected countries in comparison to earlier seasons with special reference to areas where clinical and public health activity may be indicated, (Table 1) as well as a) the pattern of infection and disease, b) the virology and c) the impact on the health services?

What is the expected pattern of influenza activity during the rest of the season in EU/EEA countries?

What countermeasures and actions (Table 1) that could be taken by authorities and clinicians 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? How does the geographical spread compare to previous seasons? How intense is the influenza activity now?

What is comparable to or different from previous seasons (intensity, age of patients, etc)?

Is the impact on primary healthcare larger or smaller?

Is the activity of RSV concomitant with the influenza outbreaks?

In countries reporting previous year(s) and now, is the pattern of reported severe cases different (age, for instance)? Are there differences in severe cases according to the infecting influenza virus? Are there influenza sub-types that are causing more severe disease? Is the pressure on intensive care units higher? Is there a related excess 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 circulating viruses? How distant or close are they to those circulating during the previous season? Is there a good match between the circulating and vaccine strains? How high is the level of resistance to antiviral medication? Are serological studies available? If yes, how should they be interpreted?

What is the vaccine effectiveness? What is the vaccine coverage in the EU/EEA; are there any changes in comparison with previous seasons? To which risk groups should countries plan to offer seasonal vaccines for the 2011/12 season?

What is the situation elsewhere in the northern hemisphere (rest of Europe, Asia, North America) and what was the influenza activity in the southern hemisphere in 2012?

What can be anticipated for the rest of the season?

Epidemiology and impact on primary healthcare services

The 2012/13 season started around week 49/2012 and influenza activity has been increasing since then. During week 3/2013, 14 of 26 countries reporting clinical data stated that they were experiencing medium or high intensity of influenza activity.

In weeks 52/2012, 1/2013, 2/2013 and 3/2013, geographical spread of influenza activity was reported as regional or widespread by 7, 13, 15 and 16 countries, respectively, mainly in western and northern Europe (with the exception of Portugal and Spain) (see Maps 1–3). In week 3/2013, many countries were still reporting rising trends of ILI or ARI. The majority of the 13 countries which returned the questionnaire mentioned that it was too early to estimate any particular pressure on primary healthcare services. Some noted that the epidemics had started before the Christmas and New Year holidays, putting pressures on emergency rooms that were operating at reduced capacity over the holiday period.

In the majority of countries, the most affected age group as reported from primary care services has been 0–4 year-olds, even though in Belgium, Iceland, Ireland, Malta and Norway, rates of influenza-like illness and acute respiratory infection (ILI/ARI) have been higher among 15–64 year-olds. In all countries but Iceland and parts of the UK (Northern Ireland and Scotland), a lower incidence of cases with mild illness seeking primary care was observed in the older age groups (>64 years old). This is the distribution of care-seeking by age group that is typically observed and may not necessarily represent the incidence of infection and disease. From the questionnaire, Denmark reported much higher percentages of ILI consultation in the Capital region putting pressure on the on-call service over Christmas compared with other regions.

The respiratory syncytial virus (RSV) activity had already peaked in week 51/2012 and has continuously declined since then. RSV may have contributed to an observed increase in respiratory symptoms, especially in children.

Epidemiology and impact on secondary healthcare services

Epidemiology

Countries reporting severe influenza surveillance data have applied case definitions for laboratory-confirmed influenza requiring hospitalisation or severe acute respiratory infection sometimes without laboratory confirmation. For the purpose of this report, and following the reporting preference of most EU/EEA countries, only those reporting laboratory-confirmed hospitalised influenza were included in the analysis.

From week 40/2012 to week 3/2013, 593 laboratory-confirmed hospitalised influenza cases were reported by eight countries (Belgium, France, Ireland, Romania, Slovakia, Spain, Sweden and the UK). Of these cases, 320 (54%) tested positive for influenza type A and 273 (46%) for type B. Of 162 subtyped influenza A viruses, 91 (56%) were A(H1) and 71 (44%) were A(H3) viruses.

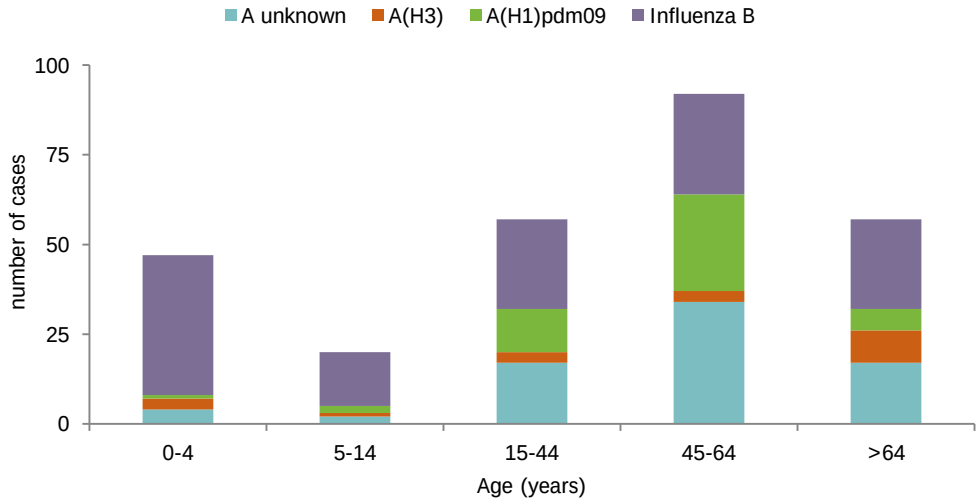
The male-to-female ratio was 1:1. Of 273 cases with reported age, 92 (34%) were in the 45–64 year-old group (Figure 1). This distribution differs from the one observed in the 2011/12 season where the largest proportion of cases had been in the youngest and oldest age groups and A(H3) had dominated.

Of the 226 hospitalised influenza cases with known outcome, 18 died; giving a hospitalised case–fatality rate of 8%. Out of the 18 cases with a fatal outcome, one was reported with influenza A(H3), seven with influenza A with an unknown subtype, six with influenza A(H1), and four with influenza B virus. The median age of the 18 fatal cases was 60 years (range: 3–102 years).

Of 164 hospitalised laboratory-confirmed influenza cases with information on underlying conditions, 69 (42%) had at least one recognised risk factor for severe disease, most commonly obesity (18/69). Five cases were pregnant women, which is about 3% of the cases with known underlying conditions.

Of 122 cases with known vaccination status, 113 (93%) were reported as not vaccinated.

Figure 1. Number of hospitalised laboratory-confirmed influenza cases in Belgium, France, Ireland, Romania, Slovakia, Spain and Sweden, by type, subtype and age group, weeks 40/2012 to 3/2013 (n=273)



Impact

In **Belgium**, paediatric surveillance of influenza activity started when RSV was still present, while in the previous season, the epidemics were dissociated. This may have had a significant impact on the perception of paediatricians. Many more respiratory samples were collected from hospitals than last season, at the same period of the epidemic (i.e. week 1/2013). So far, in 29 confirmed cases, no ICU admission, no critical state on admission, no acute respiratory distress syndrome and only one fatality in a very old patient (102 years old) with co-morbidities were noted. The age distribution of severe influenza cases is similar to the last season.

In the **Czech Republic**, up to the end of week 1/2013, a cumulative total of 33 severe-illness patients with laboratory-confirmed influenza A(H1N1) or influenza A (not subtyped), including four deaths, were reported by intensive and resuscitation care units. These high numbers of severe influenza caused a similar pressure as in the two previous years.

In **Denmark**, some regions reported more hospitalisations in press releases than in previous years, but according to the national surveillance system of ICU admissions due to influenza, there are fewer cases than in the two previous seasons. However, the burden of influenza among the elderly seems to be higher this season.

In **France**, the mean age of laboratory-confirmed influenza patients admitted to ICU is lower than the previous season (34 years versus 51).

In **Ireland**, more influenza B cases have been observed this season, but no further details on the impact or the virus lineage are available as yet.

In **Spain**, only 29 severe hospitalised cases have been reported up to week 3/2012, compared to 65 cases during a similar period in the previous season. Of these cases, 70% were influenza B virus and their median age was 35 years (IQR: 5–55), which is comparable to the median age among severe hospitalised influenza B cases in the season 2011/12 (30; IQR: 3–61).

In the **UK (England)**, a surveillance system with comparable data for both hospital admissions and ICU admissions was established in 2011/12, but reporting through similar systems in 2010/11 showed larger pressures. Chronic respiratory conditions are to date the most frequently reported underlying clinical risk factor in 2012/13 for ICU admissions reported through the sentinel network. There has been an apparent rise in Panton–Valentine leukocidin (PVL) pneumonia cases and possible association with influenza. PVL cytotoxin-producing strains of *Staphylococcus aureus* (PVL-SA) typically cause skin and soft tissue infections. They can sometimes cause more severe invasive infections and the association with severe community-acquired pneumonia (CAP) is recognised with high (50–75%) mortality rates reported. Over the four–week period 6 December 2012 to 7 January 2013, the national UK reference laboratory confirmed 18 cases of severe CAP caused by PVL-SA; all have been admitted to intensive care units and four (22%) have died. This compares to a national figure of 30–40 PVL-CAP cases per year across England, usually peaking in the winter months. Fourteen have been due to meticillin-sensitive *S. aureus* infection and four due to meticillin-resistant *S. aureus*, associated with a variety of strains. Most cases have reported an influenza-like prodrome with at least six confirmed with an influenza B co-infection. Influenza has been circulating in the community in England, with the dominant strain being influenza B. Cases have been distributed

around the country with at least two small household clusters identified. Patients were aged from four to 63 years (median 41 years) and 11 (61%) were female. Further epidemiological and microbiological work is underway*.

The **UK (Scotland)** has reported 20 ICU cases of confirmed seasonal influenza despite only being a few weeks into the season. During the previous season, 17 cases were admitted to ICU in total. However, there are no reports of any severe pressure on general admission to hospitals. Geographically, these ICU cases are representative of the population distribution. So far, there have been three deaths among the 20 ICU cases (two with influenza A(H3N2) and one with influenza A, not subtyped). The mean age is lower than for the previous season (45 years versus 62). RSV co-infection in an infant and an invasive group A streptococcal infection in an adult ICU case who died have been documented. An increase in the number of invasive meningococcal infections or invasive group A streptococcal infections has been noticed in those geographical areas in which cases of influenza are being reported.

Virology

Circulating viruses from sentinel sources

Of the 2 948 influenza virus detections in sentinel specimens from week 40/2012 to week 3/2013, 1 430 (48.5%) were type A, and 1 518 (51.5%) were type B viruses. Of 1 253 influenza A viruses subtyped, 732 (58%) were A(H1) and 521 (42%) were A(H3), showing the return of A(H1N1) which hardly circulated in Europe last season. Of the 269 type B viruses ascribed to a lineage, 231 (86%) were Yamagata and 38 (14%) were Victoria. The latter lineage is not included in the 2012/13 vaccine. [5]

Circulating viruses from non-sentinel sources

Of the 11 719 influenza viruses detected from non-sentinel sources from week 40/2012 to week 3/2013, 8 440 (72%) were type A, and 3 279 (28%) were type B. Of 4 368 type A viruses subtyped, 3 110 (71%) were A(H1) and 1 258 (29%) were A(H3). Of the 456 B viruses ascribed to a lineage, 412 (90%) were Yamagata and 44 (10%) were Victoria. The higher proportion of influenza A viruses is not surprising, as non-sentinel specimens are collected for diagnostic purposes, e.g. in hospitals, suggesting that specimens were taken from more severe cases. [5]

Antigenic and genetic characteristics

From week 40/2012 to week 3/2013, 168 antigenic characterisations of influenza viruses from sentinel and non-sentinel specimens were reported: the majority (92) have been characterised as A(H3)/Victoria/361/2011-like, 16 as A(H1) A/California/7/2009 (H1N1)-like, 42 as B/Wisconsin/1/2010-like (B/Yamagata/16/88-lineage), one as B/Florida/4/2006-like (B/Yamagata/16/88 lineage), 13 as B/Brisbane /60/2008-like (B/Victoria/2/87 lineage) and three strains have not been attributed to any category. [5]

Of the 143 genetic characterisations of influenza viruses reported for sentinel and non-sentinel specimens from week 40/2012 to week 3/2013, 58 were A(H3) clade representative A/Victoria/208/2009 and fell in groups 3A, 3C and 5; 40 were A(H1) from groups 6 and 7; 18 were B(Yam)-lineage clade representing B/Estonia/55669/2011; 12 were B(Yam)-lineage clade representing B/Wisconsin/1/2010; 11 were B(Vic) lineage clade representing B/Brisbane/60/2008 and three strains were not attributed to any clade/group. [5]

Susceptibility to antivirals

From week 40/2012 to week 3/2013, 196 influenza A and B viruses from Denmark, Germany, the Netherlands, Norway, Spain, Sweden and the UK have been tested for neuraminidase inhibitor (oseltamivir and zanamivir) susceptibility and none showed genetic (markers) or phenotypic (IC50) evidence for (highly) reduced inhibition. All 19 influenza A viruses screened for M2-blocker susceptibility were resistant. Recently in the Netherlands, an oseltamivir-resistant A(H1N1) virus with the H275Y amino acid substitution was detected in a hospitalised immuno-compromised patient. This resistant variant emerged during oseltamivir therapy and was detected shortly after oseltamivir was stopped and before zanamivir therapy was started. The patient was also treated with antibiotics for pneumonia due to *Haemophilus influenzae*, improved rapidly and was discharged 20 days after onset of respiratory symptoms (A. Meijer, personal communication). Hence it remains the case that no oseltamivir-resistant infections have been found to be circulating in Europe. [5]

* For further information, see http://www.hpa.org.uk/hpr/news/#pvlsa and for clinical guidance see http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1267551719486 and http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1218699411960

Susceptibility – seroepidemiology

As in previous years, the only country undertaking an early annual seroepidemiological survey was Norway. In contrast to the two previous years, no particular virus type or subtype could be identified as likely to predominate this season [6]. With respect to age distribution, the results are highly compatible with the age-specific incidence of laboratory-confirmed influenza in Norway with lower incidence in the 5–24 year age group for A(H1N1), in the 0–24 year-olds for A(H3N2), and in the 15–24 year-olds for Yamagata-lineage influenza B. The apparently good immunity in the 5–24 year-olds against A(H1N1) is corroborated by the relatively few numbers of laboratory-confirmed cases in this age group in Norway. Even so, Norway experienced a significant incidence of influenza in weeks 1 and 2/2013, with A(H1N1) as the predominant virus. The Norwegian reporter commented that other age groups (e.g. infants and/or adults above 25) may play a larger role in the spread of this virus than commonly thought. There have been deaths, including in younger persons, associated with A(H1N1) in Norway this season and in the Czech Republic.

Influenza vaccine

Vaccine coverage

Seasonal vaccine coverage data are not yet available from the VENICE project* for the 2012/13 season. From the questionnaire, Latvia reported a lower proportion of people vaccinated while the UK (England) reported vaccination coverage comparable to 2011/12. Preliminary results from England estimate an uptake of >70% among those aged ≥65 years and around 50% in those under 65 years old in a clinical risk group, with a much higher uptake among pregnant women than during the previous season. Among the nursing homes affected by ARI outbreaks in France, the vaccine coverage (81%) was the lowest observed since 2003/04. This proportion is still to be confirmed, but it could reflect a lower national vaccine coverage among older people this season. The UK (Scotland) reported an increased uptake by pregnant women; 48.3% in those without risk factors and 64.6% in those with risk factors. Norway mentioned low vaccination coverage in risk groups. There is no information on immunisation of healthcare workers. Overall, it should be noted that there have been small declines in vaccine coverage in older age groups (the only risk group with consistent data) in a number of EU countries since the 2007/08 season [7].

Match between circulating and vaccine strains

Notwithstanding the absence of influenza B Victoria lineage from the composition of the vaccine [8], the remaining viruses circulating this season seem to be well-matched with the components of the 2012/13 seasonal vaccine viruses. Nevertheless, this match does not necessarily mean that the vaccine effectiveness is as high as would be desirable [9,10].

Characterisation of A(H3N2) viruses collected in Denmark, Germany, Norway, Sweden and the UK (England) from 1 September to 31 December 2012 have shown antigenic similarity to the vaccine strain A/Victoria/361/2011. A(H1N1) viruses continued to show genetic drift from the vaccine virus A/California/07/2009, but the vast majority remained antigenically similar [11].

Vaccine effectiveness

A recent American study [9] published an early estimate of influenza vaccine effectiveness non-adjusted for age of 62% (95% CI: 51%–71%) for 2012/13 which is better than for the previous season in the United States. A study from Canada showed somewhat lower levels [12]. However, it is essential to note that the US estimates were not adjusted for age, risk groups and other confounders and the proportions of circulating viruses in the USA and the EU are quite different this season: there are few A(H1N1) viruses circulating in the USA. Also, the analytic approach is different; in Europe the focus is more on effectiveness in the high risk groups. Hence, the US percentage should be interpreted with caution and may not reflect the vaccine effectiveness in Europe or for high risk groups. Early estimates of vaccine effectiveness in the UK have shown an overall adjusted vaccine effectiveness of 51% (CI: 27%–68%) with 49% against influenza A alone and 52% against influenza B [13]. Further results from the I-MOVE consortium are expected in the coming weeks.

In France, none of the 24 cases admitted to ICU had been vaccinated.

In the UK (Scotland), an ICU case had been infected by an influenza B Victoria-lineage not included in the trivalent vaccine. There have been a further three recent vaccine failures in ICU cases – all influenza A infections (results from detailed molecular testing are awaited).

* Vaccine European New Integrated Collaboration Effort. http://venice.cineca.org/

Mortality

A number of countries undertake their own monitoring of death statistics. In addition, all-cause mortality by age group in 16 EU/EEA countries is monitored in a timely manner by the EUROMOMO* project, using a common algorithm to standardise excess mortality estimates across Europe. Monitoring early mortality data is useful for detecting the impact on mortality of unusual severe events like influenza epidemics, heatwaves or cold weather.

Pooled analysis for week 3/2013 [14] does not show any excess of all-cause mortality so far this season. However, two of the 16 reporting countries, Denmark and the UK (Scotland & England) saw increased mortality in people 65 years of age and above. The increase was particularly evident in Denmark, where influenza A(H3N2) transmission is predominant and peaked around Christmas.

Due to reporting delays, excess mortality associated with influenza may also appear after an interval. It has been estimated that there may be up to 38 500 premature deaths in the EU/EEA associated with influenza in a single influenza season [15].

Situation in other temperate countries in the northern hemisphere [16]

In **Canada**, some regions have reported widespread and localised influenza activity and 107 additional influenza outbreaks have been reported. Influenza virus detections by type/subtype to date have been as follows: 97.5% influenza A (33.2% A(H3), 1.2% A(H1N1) and 65.6% A(not subtyped)) and 2.5% influenza B. [17]

In the **United States**, influenza activity has remained elevated, but may have peaked in some regions. The virological pattern has been considerably different to that in Europe as there have been very few influenza A(H1N1) viruses. The proportions of influenza A and B viruses have been 80% and 20%, respectively. Among subtyped influenza A viruses, the proportion of A(H1N1) has been 1%. [18]

In **China**, influenza activity has remained at a low level in the south but has continued to increase in the north. The distribution of circulating viruses has been 82% to 99% of influenza A and 1% to 18% of influenza B. Among subtyped influenza A viruses, 67% to 75% have been A(H3N2) and 15% to 18% have been A(H1N1) viruses. No resistance to neuraminidase inhibitors has been observed. [19]

In **Japan**, A(H3) virus has largely dominated, followed by a few B(Victoria lineage) and some A(H1N1) viruses [20].

In **summary**, the intensity of influenza activity in northern hemisphere countries outside Europe is high, but heterogeneous. Similar to the previous season in the EU/EEA, the proportion of A(H1N1) is very low in North America and Japan. It is higher in China, but not dominant.

Except in some areas of North America, there are no clear indications of particular impact (stress) on healthcare services or other essential services this season.

Situation in the temperate countries of the southern hemisphere in the 2012 season [16,21]

In **Australia** there were very few notifications of influenza A(H1N1). Influenza A(H3N2) was the predominant circulating virus, along with increasing co-circulation of influenza B. [22]

Of 2 330 detected influenza viruses in **New Zealand** with known subtype or lineage, 1 526 (65%) were influenza A(H3N2), 244 (10%) A(H1N1), 252 (11%) B (Victoria-lineage) and 69 (3%) B (Yamagata-lineage). [23]

In **South Africa** 116 A(H3N2) viruses, 1 A(H1N1) virus and 115 B viruses were detected. [24]

The influenza A(H3N2) virus was predominant in **Chile** and **Uruguay**, while in **Paraguay** and **Argentina** transmission was essentially associated with A(H1N1). Few influenza B were detected. [21]

Influenza A(H1N1) was dominant in **Brazil** with fewer A(H3) and B viruses. Towards the end of the season, A(H3) became dominant. [25]

* The European Mortality Monitoring Project. http://www.euromomo.eu/

The intensity of reported influenza-like illness was similar to the previous season in almost all countries of the southern hemisphere.

Implications for Europe

The virological influenza pattern observed on other continents was not consistent enough to make a clear prediction for the 2012/13 season in Europe. However, in general, the findings on the impact of influenza in the southern hemisphere in 2012 are reassuring. The match of the A(H3N2) viruses with the vaccine was considered good and there was no evidence of resistance to neuraminidase inhibitors.

Safety of interventions in Europe

In the trivalent Novartis vaccine, flocculation was observed which was not considered unsafe, but was responsible for a limited shortage. Other than that, there were no indications of any new adverse event following immunisation (AEFI) safety signals related to the 2012/13 trivalent seasonal influenza vaccines being used in the EU. Likewise, no convincing adverse event signals have been reported for the neuraminidase inhibitors, the antivirals used the most in Europe [26].

ECDC's scientific and public health advice

Simple protective measures

While the scientific base on effectiveness for measures like early self-isolation, hand-washing and good respiratory hygiene is not that strong for influenza, such evidence that exists supports a recommendation of these simple measures.

Vaccination

Many people for whom influenza vaccination is recommended by their national health authorities are still unvaccinated. Although it is late for immunisation, it is advantageous to immunise these risk groups, especially in countries where transmission is not yet declining in a convincing manner [27]. After the replacement of the A(H3N2) strain, vaccine effectiveness is somewhat higher this season than last [28]. Vaccination is recommended by Member States for older people, those in medical risk groups and for healthcare workers. The majority of countries also recommend immunising pregnant women. Vaccination remains the most effective single way of protecting individuals and their families against influenza infection and disease, but more effective vaccines are needed [10].

Antivirals

Notwithstanding controversies over interpretation and re-analysis of historic trials against different earlier influenza viruses, the available data on balance continue to support the early use of antiviral treatment in all those presenting with severe influenza-like illness pending virological confirmation, in those with risk factors with milder disease and those in risk groups and thought to have been exposed [29,30]. This has been confirmed by recent observational analyses of effectiveness against influenza A(H1N1) which now accounts for a sizeable proportion of the seasonal viruses in Europe. This season, no reduced antiviral susceptibility or resistance has been detected in screened circulating strains, unless one oseltamivir-resistant strain in an immuno-compromised patient treated with oseltamivir was very recently detected in the Netherlands. The evidence suggests that older people and especially those in residential care will especially benefit from early antiviral treatment or prophylaxis, even immunised persons when outbreaks occur in those settings [29–31].

Higher-level care

The early experience from western Europe indicates that there is only limited reason to alert hospital services of potentially increased numbers of influenza patients needing hospital/intensive care in the next few weeks. This may, however, not be the case in countries were A(H1N1) predominates and vaccine coverage in risk groups is low.

Clinical care

With the return of A(H1N1), the mean age of patients, compared to previous seasons, will probably decrease in affected countries, but classical underlying conditions and old age remain the main risk factors for severe influenza disease, particularly due to A(H3N2) infection.

Special groups

Outbreaks in nursing homes for older people and those with chronic illness were reported last season. This supports prevention through immunisation and/or prophylactic use of antivirals in patients and in particular in staff, if that has not been done already, and treatment of outbreaks of influenza-like illness with antivirals [31–33].

Conclusions

The 2012/13 season started early, being most apparent in north-western Europe with a suggestion of the west-to-east geographic progression seen in earlier years. This may allow non-affected countries, especially in central and eastern Europe, to be better prepared.

The single available sero-survey (Norway) suggests that a wide range of viruses is likely to circulate, but it is difficult to anticipate what will happen in other countries as Norway had a very high coverage with A(H1N1) monovalent vaccine.

While there are some indications of particular pressures in ICUs in some countries, the pattern is heterogeneous, making it difficult to estimate the possible workload for ICUs in individual countries.

With the replacement of the A(H3N2) component, the effectiveness of the 2012/13 vaccines among risk groups is somewhat better than in the 2011/12 season, but further vaccine effectiveness studies, such as I-MOVE* field effectiveness studies using the ECDC-developed standard protocols, are needed to confirm this hypothesis.

Table 1. Guidance matrix

Feature	2012/13 season	Public health implications and guidance for possible action
Geographical and temporal pattern of infection	Early start of the season appearing simultaneously in a number of western countries except Spain and Portugal	Alert clinicians and services in central and eastern countries to prepare for similar epidemics
Dominant viruses	As of week 03/2012, the proportions in sentinel samples of A and B viruses were respectively 48% and 52%, with different viruses dominating at national level. The latter proportion of B viruses is unusual at the beginning of an influenza season. Proportions of A(H1N1) and A(H3N2) were respectively 58% and 42%, showing the return of A(H1N1) which hardly circulated last season (2%). Recently, A(H1N1) viruses have become more dominant than A(H3N2).	In countries where A(H1N1) or B viruses are dominant, higher incidences may be expected in young age groups.
Vaccine match and effectiveness	A(H3N2) has shown antigenic similarity to the vaccine strain A/Victoria/361/2011. A(H1N1) viruses have continued to show genetic drift from the vaccine virus A/California/07/2009, but the majority have remained antigenically similar to the vaccine strain. B/Yamagata has been the dominant circulating B virus (85%) which matches the vaccine strain well. However, there is a significant proportion of B/Victoria viruses (15%) that are not included in the trivalent vaccine.	Emphasise the therapeutic use of antivirals, where clinically indicated, especially in persons with risk factors for severe disease, even if vaccinated. MS that have the resources should rapidly review vaccine effectiveness following the ECDC–I-MOVE protocols as planned by national institutes. Data should be pooled by countries participating in I-MOVE.
Antiviral resistance	The first oseltamivir-resistant A(H1N1) virus with H275Y mutation was detected very recently in the Netherlands in an immuno-compromised patient treated with oseltamivir.	At present, there is no need to consider antiviral resistance to neuraminidase inhibitors in most cases. Seeming antiviral failures should be rapidly investigated virologically to detect any emerging antiviral resistance. As usual, there is no basis for the use of adamantanes.

* Influenza - Monitoring Vaccine Effectiveness. https://sites.google.com/site/epiflu/

Feature	2012/13 season	Public health implications and guidance for possible action
Risk groups for mild disease	In the majority of countries, children under 5 years have been the most affected age group, even if in some countries, ILI/ARI rates have been highest in 15–64-year-olds. In countries where the B virus is dominant, 5–14-year-olds have been the main age group affected.	Remind clinicians to be aware of circulation of influenza viruses in children.
Pressure on primary care	From seven countries reporting, Denmark, Ireland and the UK (England and Scotland) experienced higher pressure on primary care than in the previous season, although activity occurred much later in 2011/12. France, Luxembourg and Norway experienced a similar pressure to last season and the UK (Scotland) less pressure than in 2011/12. A complication this season may have been that the epidemics started before the Christmas and New Year holidays when primary care services scale down in some countries.	Alert and prepare primary care services that they may possibly need surge capacity this season.
Pressure on secondary care	Four countries (Belgium, Denmark, Ireland, and the UK (England, Scotland)), have indicated particular local pressure on secondary care. France has experienced a similar pressure compared to the previous season.	Alert and prepare secondary care for the possibility of local pressures and thus the need for mutual support. To be expected in all countries not yet affected.
Risk groups for severe disease	Risk groups as observed in hospitalised patients with severe confirmed infection were similar to previous season with old age and underlying conditions as the main risks. However, there were also cases reported in healthy younger people with no known risk factors.	Particular emphasis on immunising staff and patients in residential care homes for older people, health care workers and those with chronic illness. Aggressive treatment of outbreaks with antivirals and infection control. Reminders to clinicians that they may be seeing influenza causing mild or severe disease in young healthy children and adults.
Mortality	Excess mortality from all causes in older people has increased in association with the influenza epidemics in a few countries, especially where A(H3N2) predominates.*	Use planned mechanisms to estimate excess premature mortality. Excess mortality is expected with A(H3N2) infection, especially in the elderly, but there are case reports of deaths in young patients infected by A(H1N1).
Cross-sectoral Pressures	No cross-sectoral pressures in any country	No action needed
Clinical presentation, sub-clinical infections and unusual features	Severe PVL-SA pneumonia associated with influenza has been reported from the UK†	Clinicians outside the UK should also be look for and urgently report this phenomenon to national authorities.

* It should be noted that apparent links of seasonal influenza epidemics with excess premature all-cause mortality are imprecise and subject to confounding factors. Also, the lack of an increase in all-cause mortality does not rule out substantial numbers of deaths associated with influenza. See link here for a discussion.

† Health Protection Agency. Apparent rise in PVL pneumonia and possible association with influenza Health Protection Report. Volume 7 No 2; 11 January 2013 http://www.hpa.org.uk/hpr/archives/2013/news0213.htm

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Annex 1. Consulted experts

Internal to ECDC: Epidemic intelligence, influenza and communication functions.
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Declarations of Interest have been received for all of the Expert Group. They have been reviewed by ECDC and none are considered to represent a conflict of interest.

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 rests with ECDC rather than with these individuals.

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

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

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Annex 2. Global and European data and analyses accessed

WHO. Global Influenza updates available from http://www.who.int/influenza/surveillance_monitoring/en

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: http://www.euroflu.org/index.php

CNRL–ECDC Influenza virus characterisation.
http://ecdc.europa.eu/en/publications/surveillance_reports/influenza/Pages/influenza_virus_characterisation.aspx

First affected countries (Belgium, Bulgaria, France, Greece, Iceland, Italy, Norway, Romania and Spain) to week 3/2013 including their early publications (like France, Portugal)

More information and detailed data from EU/EEA countries reporting on severe disease and impact:
Ireland (Health protection Surveillance Centre: http://www.hpsc.ie)
France (Institut de Veille Sanitaire: http://www.invs.sante.fr)
UK (England) (Health Protection Agency: http://www.hpa.org.uk)
Spain (Sistema de Vigilancia de la Gripe en España: http://vgripe.isciii.es/gripe/inicio.do)
Romania (Institutul National de Sanatate Publica: http://www.insp.gov.ro/)
Slovakia (Public Health Authority: http://www.uvzsr.sk/en/).

More specific EUROMOMO – European monitoring of excess mortality for public health action. Pooled results are available from http://www.euromomo.eu/results/pooled.html

Regional and national influenza websites in temperate Northern hemisphere countries outside of WHO European Region:
Canada (PHAC-Fluwatch: http://www.phac-aspc.gc.ca/fluwatch/)
China (CCDC: http://www.cnic.org.cn/eng/)
Japan (NIID: http://idsc.nih.go.jp/index.html)
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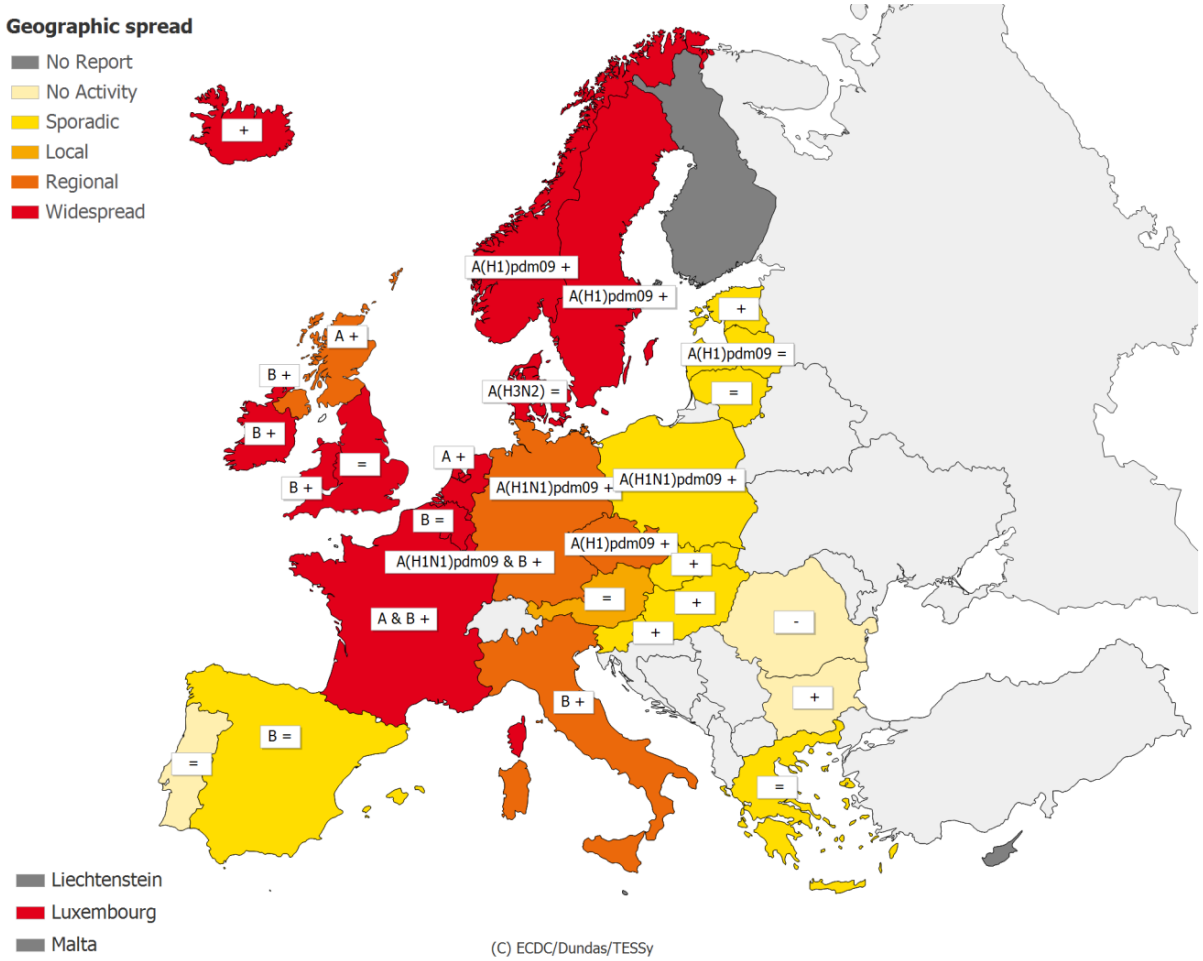
Map 1. Geographic spread for week 1/2013



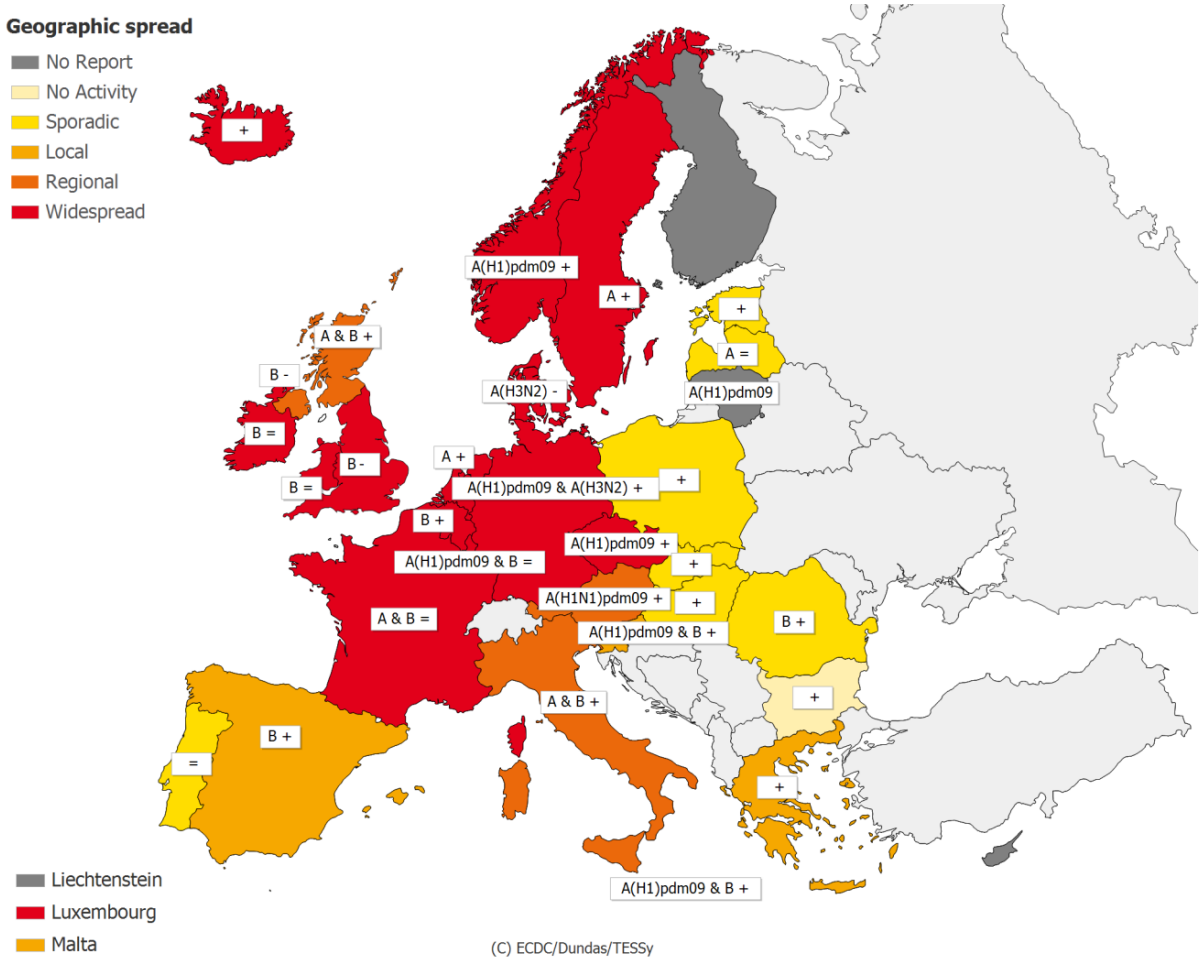
* A type/subtype is reported as dominant when at least ten samples have been detected as influenza positive in the country and of those > 40 % are positive for the type/subtype.

Legend:

No report	Activity level was not reported
No activity	No evidence of influenza virus activity (clinical activity remains at baseline levels)
Sporadic	Isolated cases of laboratory confirmed influenza infection
Local outbreak	Increased influenza activity in local areas (e.g. a city) within a region, or outbreaks in two or more institutions (e.g. schools) within a region (laboratory confirmed)
Regional activity	Influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population (laboratory confirmed)
Widespread	Influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population (laboratory confirmed)

+	Increasing clinical activity
-	Decreasing clinical activity
=	Stable clinical activity
A	Type A
A & B	Type A and B
A(H1)pdm09	Type A, Subtype (H1)pdm09
A(H1N1)pdm 09	Type A, Subtype (H1N1)pdm09
A(H1N1)pdm 09 & B	Type B and Type A, Subtype (H1N1)pdm09
A(H3N2)	Type A, Subtype H3N2
B	Type B

Map 2. Geographic spread for week 2/2013



* 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:

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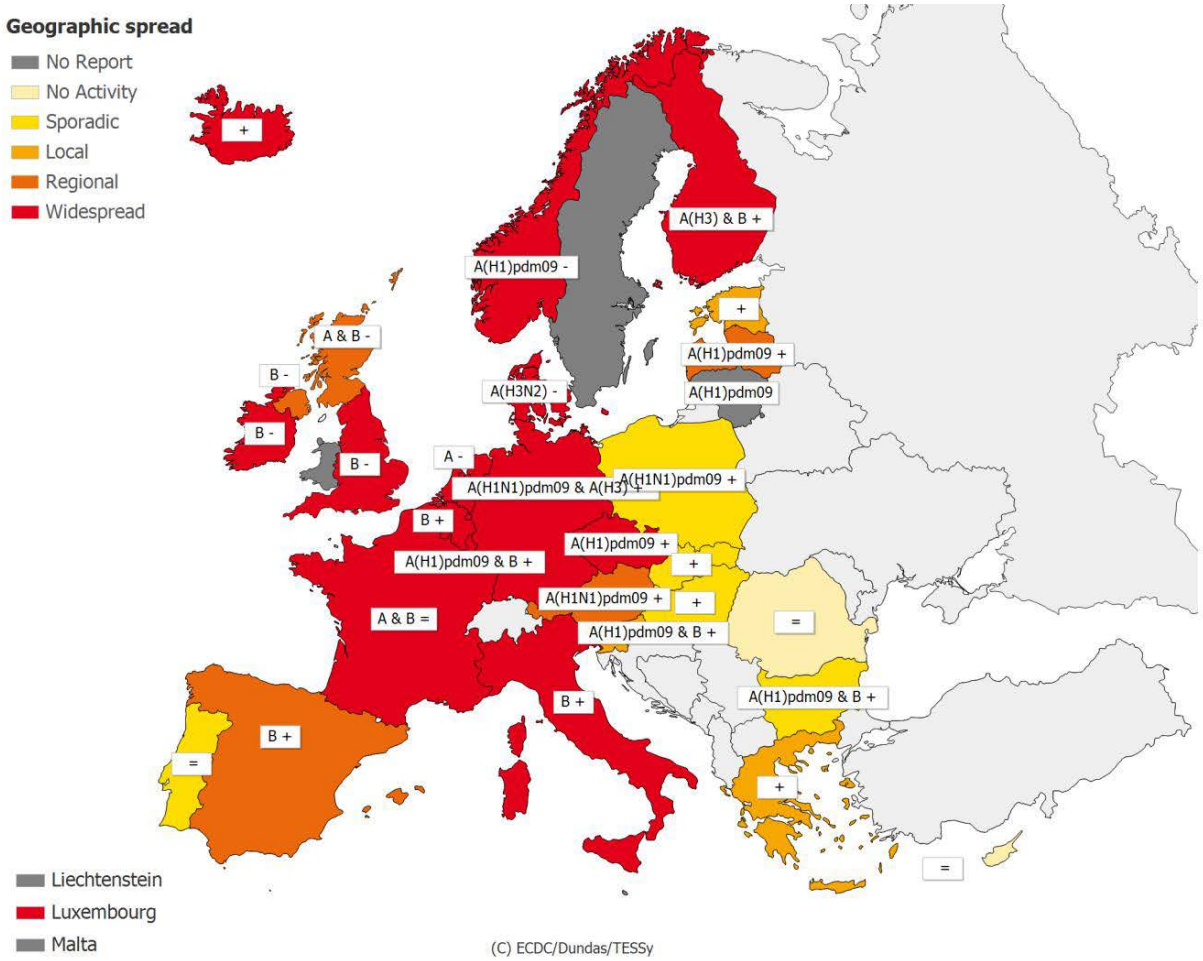
Regional activity	Influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population (laboratory confirmed)
Widespread	Influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population (laboratory confirmed)

+	Increasing clinical activity
-	Decreasing clinical activity
=	Stable clinical activity
A	Type A
A & B	Type A and B
A(H1)pdm09	Type A, Subtype (H1)pdm09
A(H1)pdm09 & A(H3N2)	Type A, Subtype (H1)pdm09 and H3N2
A(H1)pdm09 & B	Type B and Type A, Subtype (H1)pdm09
A(H1N1)pdm09	Type A, Subtype (H1N1)pdm09
A(H3N2)	Type A, Subtype H3N2
B	Type B

Map 3. Geographic spread for week 3/2013



* 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	Activity level was not reported
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Regional activity	Influenza activity above baseline levels in one or more regions with a population comprising less than 50% of the country's total population (laboratory confirmed)
Widespread	Influenza activity above baseline levels in one or more regions with a population comprising 50% or more of the country's population (laboratory confirmed)

+	Increasing clinical activity
-	Decreasing clinical activity
=	Stable clinical activity
A	Type A
A & B	Type A and B
A(H1)pdm09	Type A, Subtype (H1)pdm09
A(H1)pdm09 & B	Type B and Type A, Subtype (H1)pdm09
A(H1N1)pdm 09	Type A, Subtype (H1N1)pdm09
A(H1N1)pdm 09 & A(H3)	Type A, Subtype (H1N1)pdm09 and H3
A(H3) & B	Type B and Type A, Subtype H3
A(H3N2)	Type A, Subtype H3N2
B	Type B