ECDC FORWARD LOOK RISK ASSESSMENT

Likely scenarios and uncertainties in the 2010/2011 influenza season in Europe and beyond

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Contents

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Executive summary

This is an update of a March 2010 ECDC publication with identical objectives, namely to inform EU stakeholders about the more likely scenarios for inter-pandemic (seasonal) influenza transmission in Europe in the coming winter 2010/2011. It takes into account information and analyses that have been published or have come to ECDC since.

Specifically, this work looked at what can most reasonably be expected in Europe until the end of the 2010/11 influenza season. It has also identified further information that needs to be elucidated through surveillance and research in order to determine vaccine strategies, as they are relevant to the implementation of the 2009 EU Health Council Recommendation on seasonal influenza immunisation. This work will continue as more is learnt about the new inter-pandemic (seasonal) influenza and its similarities and differences from the previous seasonal influenza.

Since the March 2010 publication, further evidence, data and information came from the experience of five Southern Hemisphere temperate countries (Argentina, Australia, Chile, New Zealand and South Africa) in their 2010 winter (May to September 2010). There were also contributions from limited seroepidemiological data and analyses from Europe and elsewhere in the world.

One almost entirely consistent picture in the Southern Hemisphere was that the second winter following the start of the pandemic in 2010 saw lower levels of reports of influenza than was experienced in 2009. This came from combined community surveillance and virology. Also reports of severe cases and deaths associated with influenza were noticeably lower in number than in 2009. This is a contrast with the experience of the preceding A(H3N2) pandemic (1968–70), in which a number of European countries saw higher levels of transmission and deaths during the second winter in comparison to the first due to a change in the behaviour of the virus. That now seems an unlikely scenario for Europe, though it cannot be entirely ruled out given the unpredictability of influenza.

However, there are some important points to attend to in the detailed reports from the Southern Hemisphere. While the pandemic virus A(H1N1) predominated in some countries, A(H3N2) and B influenza viruses were also seen in almost all countries. In South Africa, they were almost the only influenza viruses present. Two countries (Australia and Chile) experienced late season rises in influenza and one other country (New Zealand) had considerable local epidemics of influenza, in some areas reaching higher levels of reports than in the pandemic winter in those localities, straining the local hospitals. This risk from A(H3N2) and B viruses supported the World Health Organization's (WHO) recommendation of using a trivalent seasonal vaccine and a conservative approach to risk and target groups for immunisation this season, while further information is gathered. WHO advises that those recommended for vaccination this season should accept immunisation, even those who had had the pandemic vaccine in 2009. It was noticed that there was a case for adding pregnant women to the groups for recommending seasonal influenza immunisation though the data relating to this view from Europe is sparse because of weak surveillance of severely affected individuals.

Fortunately, the pandemic A(H1N1) virus has, as yet, changed little since its emergence and there are few reports of antiviral resistance and even fewer cases of transmission of a resistant virus.

ECDC concludes that, as in all winters, epidemic transmission of influenza is highly likely in the next (2010/2011) winter season but the intensity cannot be predicted. Transmission of A(H1N1) seems very likely at least in very young children and other susceptible individuals. The major uncertainty in Europe stems from not knowing the proportion of the population that remains susceptible. Only a handful of serological surveys (measuring the levels of immunity in the community) have been published and these results may be misleading because of the unknown contribution of pre-existing cellular immunity. Data on the use of pandemic vaccines are being gathered but are not yet available, though there are informal reports of widely varying coverage across EU countries, from near zero up to over 60% of the population. Some data on the likely levels of seasonal vaccination in recent years is available through a VENICE survey for the largest risk group, older people.

Given the very different levels of protection from immunisation, it is possible that countries with high coverage of pandemic and seasonal vaccines will have little influenza transmission this season. However, it has to be remembered that other respiratory infections are still likely to cause pressure on primary and secondary care. Also, high immunity against the pandemic A(H1N1) may make transmission of A(H3N2) and B viruses more prominent in some countries.

The annual meeting of the European Influenza Surveillance Network (EISN) identified priority work for Member States and ECDC to undertake. Following that, ECDC has identified eight priority areas for surveillance and development research where it advises work should be undertaken to clarify uncertainties.

Influenza viruses are notorious for their unpredictability and so this forward look risk assessment must not be seen as representing anything more than the most likely scenarios.

This document represents guidance from ECDC and does not necessarily represent the opinions of those who contributed to the work or their employing institutions. Comments on this forward look are welcomed and should be sent to influenza@ecdc.europa.eu.

Rationale of this risk assessment

The revision of an earlier forward look risk assessment [1] was needed for a number of planning purposes, notably to inform decisions on short- and long-term influenza vaccination strategies. It is required because, given the WHO declaration that the pandemic was over at the global level, a 'new' seasonal influenza is expected this coming winter in Europe and health authorities in Europe are preparing for this [2,3].

Source, date and type of request

ECDC internal decision informed by discussion at the ECDC Advisory Forum No. 20 (December 2009) and the Health Security Committee Influenza Section (October 2010).

Objectives

Specific objectives of the work are:

- to inform Member States, the European Commission, the European Medicines Agency and others as to possible scenarios for inter-pandemic (seasonal) influenza transmission that can reasonably be expected or excluded in the 2010/2011 influenza season.

To determine:

- to what extent the new seasonal influenza will be alike or different from the pattern of infection and disease seen in the 2009 pandemic or the preceding seasonal influenza [2].
- who are likely to be in the risk and target groups for immunisation in the EU, as the ones for the previous seasonal influenza may no longer entirely apply [4].
- what further information and work is needed to determine vaccine strategies, including implementation of the 2009 EU Health Council Recommendation on seasonal influenza immunisation [5].

Consulted experts

Internal ECDC experts, ECDC Advisory Forum members or individuals nominated by them, World Health Organization (Headquarters and Regional Office for Europe), relevant experts and specialists from EU and other countries, notably from WHO and EU pandemic modelling groups (Annex 1).

Background, terminology and assumptions

This document is an update of a March 2010 ECDC publication. It incorporates further work from ECDC's Advisory Forum or their nominated representatives [1] and follows on from the declaration of a post pandemic phase by the WHO in August 2010 [6]. The members of the group that initially advised ECDC are listed in Annex 1 along with consulted ECDC experts, ECDC Advisory Forum members or individuals nominated by them, persons from the World Health Organization, relevant experts and specialists from EU and other countries, notably from WHO and EU pandemic modelling groups.

Historically, pandemic influenzas 'settle down' and can dominate the new pattern of inter-pandemic influenza (more commonly known as *seasonal influenza*), which may then be somewhat or significantly different in its characteristics from what was experienced prior to the pandemic (Table 1, Figure 1). Certainly there were at least 10 important differences between the 2009 pandemic and the preceding inter-pandemic (seasonal) influenza (Table 1) [2]. It should not be assumed that those differences will persist into the new seasonal influenza. Some, like the high transition rates and the appearance 'out of season', will certainly not endure but others may.

The timeframe for the transition from a pandemic to a seasonal pattern is uncertain. It can happen quite quickly (such as in the 1957 pandemic) (Figure 2) or take two seasons (the 1918 and 1968 pandemics) (Figure 3 for the 1968–70 pandemic) [7]. The pandemic of 1968–70 was striking in Europe in that its second winter was worse than its first, when transmissibility of the virus increased [7,8].

The formal name of the transition phase (which is still in the pandemic period) is 'post-peak' and it is followed by a post-pandemic phase [9]. Pandemic phases are global, i.e. they apply in all regions of the world. Hence although there was very little influenza transmission in Europe in 2010 after March, because of enduring transmission in equatorial regions and uncertainty over what the 2010 winter would be like in the Southern Hemisphere temperate countries, it was not until August 2010 that WHO declared that the world was in post-pandemic phase [6].

Methodology, available information and evidence assessment

The methodology used was an adaptation of that used for the March 2010 publication, namely to consider three data sources or types of analyses. These are only noted in detail where there are new data or analyses since March:

- Observations of what was reported and published from five Southern Hemisphere temperate countries with moderate or good routine influenza surveillance using published data (Table 2).
- Estimations of the likely proportions of people who are immune due to prior immunity, by having been infected during this pandemic or from being immunised, hence, whether there are sufficient susceptible individuals to sustain transmission. Because of the difficulties of dealing with overlapping estimations and the indeterminate sizes of the overlap, particular attention was paid to the limited serological data that has been becoming available.
- Estimations of the proportions of the population that need to be immune for transmission to terminate, given the transmission characteristics (especially the values for R) observed to date [10].

In addition, there is important information on the apparent risk group and mortality data, which differ somewhat from that seen for the previous seasonal influenza [11–15]. To determine the risk and target groups for immunisation, data will be needed from the experience with the 2009 pandemic A(H1N1) and the following inter-pandemic (seasonal influenza) concerning risk factors associated with experiencing severe disease and death from this infection [4]. A formal project reviewing publications on this is being undertaken by ECDC following a call for tender [16].

The experience since March 2010 in Europe

Rates of influenza transmission reported in Europe continued to decline in early 2010 as shown by both syndromic surveillance in primary care and laboratory reporting. Numbers of reports of pandemic influenza A(H1N1) declined and after about week 10 some B viruses were reported by a number of laboratories. This is evidenced by national primary care and virological reports from Member States, reporting to the European Influenza Surveillance Network (EISN) with outputs in successive Weekly Influenza Surveillance Overviews (WISO), which have continued over the summer in Europe at fortnightly intervals and have now resumed weekly publication [17]. The experience of the pandemic has been described by ECDC [18]. Active Epidemic Intelligence Scanning for national announcements of influenza deaths stopped at week 17 after 12 months of surveillance [19].

The evidence

Observations from the Southern Hemisphere winter 2010

Surveillance reports from the five Southern Hemisphere temperate countries whose data and analyses were used (Table 2) indicate that in April and May 2010, before they entered their 2010 winter, there were no additional waves of influenza transmission following the end of their 2009 winter. What influenza transmission there was involved the 2009 pandemic A(H1N1) virus, but at very low level.

The evidence from the five Southern Hemisphere countries for their 2010 winter shows some important consistencies while at the same time there are notable country-specific patterns and differences (Table 3). The most relevant surveillance analyses are summarised in Table 3 and have been illustrated graphically in a series of ECDC global updates over the summer the last published on 14 October 2010. Across all the countries, levels of transmission in the community as evidenced by primary care surveillance were considerably down on what was seen in the pandemic winter. This is unlikely to be simply due to fewer people seeking care as the number of influenza-related hospitalisations reported and deaths were also considerably down on what was seen in 2009 (Table 3). The previous oseltamivir-resistant seasonal influenza A(H1N1) was not observed. However, beyond that there are a number of important variations.

In **Australia** in 2010, the age distribution of influenza laboratory reports were intermediate between those of 2008 and 2009 being relatively consistent across all age groups but decreasing with increasing age, so that as in both the pandemic winter and 2010 winter older people were underrepresented, at least in laboratory reports. After a quiet initial period, the rates of consultations with influenza-like illness, confirmations and the proportion of samples from sentinel physicians all rose in parts of Australia in late winter, suggesting a late season rise in transmission. To date (October 2010) there are few deaths reported associated with influenza, predominately (15 out of 18) people with underlying health conditions. There was higher use of seasonal vaccines than usual (G Grohman, personal communication) and it is unclear how this affected the observed epidemiology [20].

Chile is one of the few countries worldwide that reports on testing for respiratory syncytial virus (RSV). As in some other seasons, it experienced early winter season epidemics of RSV in young children resulting in considerable illness in the community and hospital admissions. As in Australia, there was a quiet early season but followed by a late season rise associated with influenza A(H3N2) viruses.

New Zealand had a particularly interesting pattern. While, like other countries, overall rates of transmission in the community were lower than in the pandemic winter (as were reported hospital admissions associated with influenza), there was intense influenza transmission in places with numbers of hospital admissions. Overall there were considerable numbers of hospital transmissions but the reduction was not as notable as in the four other countries. It was observed that these 'hot spots' tended to be areas that had had less influenza transmission in the pandemic. Some support for this came from a national serosurvey, which showed heterogeneity of immunity more so than in other countries [21, 22]. Unlike Australia and Chile, there has been no late season rise in transmission.

A **South African** publication provided more limited data but the pattern there was unusual in that there were hardly any isolations of the pandemic influenza A(H1N1). Influenza A(H3N2) and B viruses predominated, a pattern that WHO reported as consistent at last for A(H3N2) in the few other parts of Southern and Eastern Africa for which data are available.

Relevance for Europe – the relevance of this diversity of experiences is hard to speculate on. It is a reminder of the important differences between the Northern and Southern temperate zones, and especially Europe. The Southern Hemisphere temperate countries are somewhat isolated from each other and can, like this, show different patterns; in

contrast, such variation is less common within Europe, although it can be seen between Europe and North America or China and Japan.

Estimations of numbers and proportions of people likely to be immune in Europe now (seroepidemiology)

Whether or not transmission increases in the autumn and winter depends on whether there are enough people to sustain transmission, given the observed low transmissibility ('R' value) of pandemic A(H1N1) or sufficient people lacking immunity for A(H3N2) [22]. There are at least three possible sources or types of immunity to the pandemic viruses:

- pre-existing immunity – principally in people born before the mid-1950s;
- immunity after infection during the current pandemic;
- immunisation.

In addition, there is also the possibility of non-specific immunity such as being mediated through T-cells [23]. These groups overlap to varying extent, and particular attention needs to be paid to serological data to overcome that difficulty. However, those data are uncommon in Europe, and an additional difficulty arises because, for a key group (children and adolescents), it is especially difficult to obtain serological data at a population level and data obtained on them from outbreaks can be misleading [1–26].

Estimations of the numbers and proportions of population groups that have been immunised with the pandemic vaccine are being gathered by a survey undertaken by the VENICE[1] consortium and ECDC, for the European Member States, and WHO. However, those data are not yet available. Data on vaccines administered have also been gathered by the European Medicines Agency but are not yet publicly available as country-specific information. A VENICE survey on this is underway but will not report until later in the year. Estimates of the proportions of the population immunised, especially the crucial younger populations are not yet available for most countries. However, enough countries have reported to indicate major differences, with a few countries achieving high coverage of the population (60–70%) and others immunising hardly any people with the specific pandemic vaccines [1]. Previous VENICE surveys of seasonal influenza immunisation also show much country-to-country variation so that, with some important exceptions, countries that immunised few people with seasonal influenza vaccine tend also to have immunised few with the pandemic vaccine (Figure 4). However the converse is not the case. There are countries that usually have considerable success with seasonal vaccination where pandemic vaccination proved surprisingly difficult [1].

There are limited serological data becoming available from Europe with published survey results from Finland, Norway and the UK. In addition, data collated by WHO and surveys from the Southern Hemisphere are relevant [21–28]. These all show considerably more immunity than would be recognised by syndromic surveillance which fits with the observations on pre-existing immunity (including that due to non-humoral immunity, e.g. due to T-cells) and the high proportion of mild and asymptomatic infections in this pandemic [23]. However some surveys show considerable heterogeneity of the prevalence of immunity in the community, while at least one in a densely populated area (Hong Kong) shows much more homogeneity [21,25-27].

A specific forward-look analysis has been undertaken for Italy which also looks at the Southern Hemisphere data as well as Italian data. That considered the numbers of influenza-like illness cases, the number of protected individuals (vaccinated and previously exposed as assessed from a pre-pandemic seroprevalence study) and an underreporting factor (estimated by a mathematical model) of the INFLUNET sentinel surveillance system. It was estimated that approximately 50% of those aged < 65 years old and 33% of those aged > 65 remain susceptible to the pandemic virus. This approximates to 46% of the Italian population of all ages. Considering these estimates, it is believed by the authors that for the forthcoming season a basic reproductive number (R_0) higher than 1.8 would be needed to produce severe epidemics of A(H1N1) in Italy. Considering that the observed R_0 for the pandemic virus has been 1.4–1.5, the authors expert opinion was that it was unlikely that Italy will face a severe A(H1N1) season unless there is a change in that virus [29].

[1] Vaccine European New Integrated Collaboration Effort.

Formulation: Likely scenarios for the influenza season 2010/2011 in Europe

At present the published European serological data are sparse and as such do not rule out the possibility of extensive A(H1N1) transmission in the coming season [22]. However, the experience in the Southern Hemisphere, specifically the lower levels of disease in the community and hospitals due to influenza, suggests that the experience of the last pandemic in Europe is not likely to reoccur. Some caution must be expressed in interpreting lower levels of reports of influenza-like illness and laboratory reports as these are likely to be influenced by reductions in care-seeking and testing. More reliance should probably be placed on the reductions in numbers of severe cases and deaths. However, those data and specific analyses like those of Italy imply that the experience of the preceding A(H3N2) pandemic (1968–70), when a number of European countries saw higher levels of transmission and deaths in the second than the first winter, is unlikely unless there is a change in the behaviour of the virus [8] (Figure 3).

Because of the widely varying proportions of the population that have been offered and have accepted 2009 pandemic vaccine in European countries (from over 60% to zero), it is likely that there is a heterogeneous set of risks of reappearing transmission of the pandemic virus across Europe in the coming season [1]. The amount of A(H1N1) transmission overall will depend on how extensive immunity is in countries where there has been no or very little vaccination.

However, there are several important points to attend to in the detailed reports from the Southern Hemisphere. While the pandemic virus A(H1N1) predominated in some countries, A(H3N2) and B influenza viruses were also seen, thus providing a scientific case for use of a trivalent seasonal vaccine (as recommended by WHO's expert consultation early in the year) rather than any remaining monovalent pandemic vaccines [30]. A lack of transmission early in the European season may be misleading since at least two countries (Australia and Chile) experienced late season rises in influenza (Table 3). Also, there may be local higher levels of transmission since one country (New Zealand) had considerable local epidemics, in some areas reaching higher levels of reporting than in the pandemic winter [21].

Given the Southern Hemisphere experience, the presence of some influenza A(H3N2) and B viruses seems also likely this coming season in Europe. What is unclear is what will be their relative importance. A(H3N2) viruses are especially important as they are a main cause of preventable morbidity and deaths in older people. The Southern Hemisphere experience suggests that, unlike most earlier pandemics, the pre-existing A viruses (the previous seasonal A(H1N1) and the A(H3N2) viruses) have not been entirely displaced (Figure 1). The old seasonal A(H1N1) which were mostly resistant to oseltamivir have seemingly gone but the A(H3N2) viruses seem likely to persist. It will be especially interesting and important to see how the latter fare in countries with and without pandemic and seasonal vaccination (Figure 4).

Another uncertainty is over the clinical picture for this coming winter. If pandemic influenza A(H1N1) continues, what will be its characteristics? If some of the more troubling ones persist (Table 1), notably severe disease including acute respiratory distress syndrome in young healthy adults and pregnant women, then Europe might experience a different spectrum of disease and a different set of risk groups than now, albeit overlapping with the current ones [1,31,32]. It is noticeable that in preparation for this some EU countries at least have extended recommending routine seasonal influenza immunisation to pregnant women.

One important implication of these findings is that, from this conservative forward look, it is most likely that transmission of the pandemic virus will return in the winter of 2010. But whether or not this virus will be the predominant influenza A virus causing seasonal influenza in the winter of 2010/2011 is unknown and unknowable. That is not forgetting influenza B viruses. A likely group to experience transmission will be young children born recently, but other uninfected and unimmunised persons will also be at risk of infection. The possibility of major outbreaks cannot be excluded because of the paucity of seroepidemiological information available in Europe. Unless the virus changes, the patterns of some severe morbidity and mortality can be expected to be similar to that of the pandemic virus, at least in the first few winters (Table 1). Certainly, this winter it will be especially important to have early indications of what the experience is in the first affected Member States if the common West to East progression of seasonal and pandemic influenza returns [18,33].

It is known that the vaccines based on the new A(H1N1) viruses are effective in the field. An estimate of effectiveness is around 70%, normal for seasonal influenza vaccines [34,35]. The vaccine has also been found to be very safe [36]. However, as it is to be expected with such unprecedented intense post-marketing surveillance, some safety 'signals' are now being investigated. Therefore, for Member States following the 2009 EU Health Council recommendations to protect their citizens for the 2010/2011 winter, the case for offering the recommended trivalent seasonal vaccine in 2010 to their chosen risk and target groups is strong. ECDC's advice to EU citizens remains to accept influenza vaccination should it be recommended and offered to them.

Risk and target groups for immunisation

Given the uncertainty over what will be the picture for transmission this coming winter, it is impossible to undertake a completely evidence-based approach. The position of ECDC has not changed since the spring, noting the likelihood that A(H3N2) and B viruses will circulate as well as the new pandemic viruses and hence the case for retaining a conservative approach of immunising the traditional risk and target groups while waiting for more data [4]:

- older people;
- people with chronic ill health, including children over six months of age;
- healthcare workers.

Where there is a lack of unanimity in Europe is over whether to offer immunisation to pregnant women. The recommendation of WHO was to do this in the pandemic for the pandemic vaccine and now some EU Member States are doing so for seasonal influenza [4]. However, the burden of disease in pregnant women in Europe is unclear. Conversely, there is a strong record of experience of effectiveness and safety with the seasonal influenza in pregnant women in the United States and some evidence of how vaccination of the pregnant mother protects the newborn child in the first six months of life [35].

Work to be undertaken in 2010 and beyond

Arising from the above considerations and uncertainties, as demonstrated both in this document and the ECDC Risk Assessment on the 2009 Pandemic [14], surveillance, research and other work could be recommended in the following areas, among others, with varying degrees of ECDC and WHO coordination and support:

- continue primary care and virological surveillance in the EU throughout the whole of 2010, with particular emphasis on looking for significant changes in the 2009 virus – *all countries;*
- conduct serological studies to determine age group-specific immunity after the autumn/winter wave and share the analyses with other Member States ahead of publication – *as many countries as possible with ECDC and WHO coordination;*
- retrospectively review risk groups in EU Member States through surveillance data on severe acute respiratory infection and deaths so as to review the previous recommendations on risk and target groups. Special attention may need to be paid to the 'new' risk groups: young children, pregnant women and those with morbid obesity – *as many countries as possible*; *ECDC literature review;*
- establish and strengthen surveillance for severe acute respiratory infection and deaths so that it is found routinely on a sentinel basis in more countries in the EU – *as many countries as possible*; *ECDC and WHO coordination,*
- determine whether there are any additional deaths attributable to influenza in specific age groups through routine death monitoring – *individual Member States and EU level work;*
- estimate the actual levels of additional risk of illness for the individual citizen from the pandemic – *volunteering countries;*
- determine the mortality in age group and risk groups and compare this with previous seasonal influenza using parameters like 'years of potential life lost' – *volunteering countries and ECDC;*
- closely monitor the global situation as it is relevant to Europe – *ECDC and WHO.*

Tables and figures

Table 1: Differences between prior seasonal influenza and 2009 pandemic influenza in Europe

	Seasonal influenza (to 2008/9 season)	2009 pandemic influenza
Circulating influenza viruses	Two A viruses [(H1N1) and (H3N2)] and some B viruses – blend varied with season	Almost exclusively the pandemic (H1N1), a few (H3N2) and increasing numbers of B viruses latterly
When waves occurred	In season – mostly starting after Christmas in recent years	Started out of season with spring/summer wave then an early autumn/winter wave in Europe
Intensity of transmission	Variable year on year with local heterogeneity but estimated to be 5% to 15% per annum	Hard to estimate, local heterogeneity, estimated to be over 15% through serological studies reviewed by WHO and in New Zealand and Hong Kong
Setting for transmission	Probably any setting where people come together	Schools are considered especially important, along with household transmission
Experiencing severe disease	Those in clinical risk groups and older people	Young children, pregnant women and those in clinical risk groups. About 30% with severe disease were outside risk groups. Many born before mid-1950s were immune, but those not experienced severe disease (Donaldson et al)
Premature deaths	Considered that around 90% were in those aged 65 years or older (Thompson et al)	In confirmed reported deaths, around 80% were under age 65 years (reports to ECDC). Increase in all-cause deaths in children detected across eight EU countries by EuroMOMO system
Mortality and years of potential life lost (YPLL)	Few confirmed deaths reported each year in official statistics. Have been estimates of up to 40 000 in a bad year using statistical methods	Substantial numbers of confirmed deaths announced by EU/EFTA Member States (n=2 900) but recognised to be an underestimate. Not estimated in any EU Member States but estimated in the US
Acute respiratory distress syndrome	Extremely rare	Uncommon but has been recorded in many countries, even in young fit adults. This is partially explained by the tropism of the pandemic virus for epithelial receptors that predominate in the lung alveoli while the previous seasonal viruses bind best to receptors found predominately in the upper airways (WHO Clinical summary)
Pathological findings	Viral pneumonia rare but secondary bacterial infections more common in fatal cases	Fatal viral pneumonias relatively common with alveolar lining cells, including type I and type II pneumocytes, the primary infected cells. In fatalities more than 25% also had bacterial infections (WHO Clinical summary, Shieh et al)
Antiviral resistance	Common and transmissible oseltamivir resistance in A(H1N1) emerged in season 2007/8 (Meijer et al)	Observed most often following antiviral treatment of susceptible individuals. However, to date (July 2010) only transmitting very rarely in certain circumstances (see WHO). Resistant seasonal A(H1N1) seemingly displaced by the new influenza, at least for now.

Table 2: Sources of epidemic intelligence information for Southern Hemisphere temperate countries

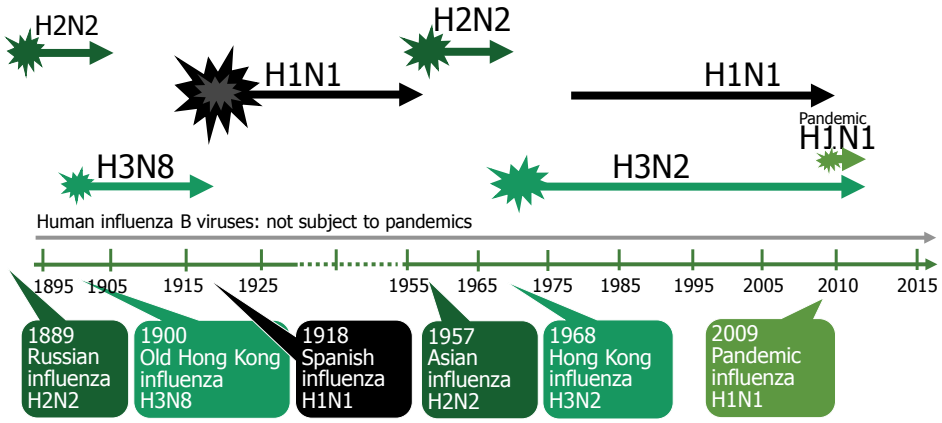
Argentina	Epidemiological reports for respiratory diseases
Australia	Australian Influenza Surveillance 2010 – Latest report
Chile	General A(H1N1) pandemic page Full report on the 2009 pandemic for 2009 (see pages 21 and 22 of this document for comparison back to 2005)
New Zealand	Influenza Weekly Surveillance Update Ministry of Health Influenza Page
South Africa	National Institute for Communicable Diseases (NICD)

Table 3: Influenza pattern in five Southern Hemisphere temperate countries in their 2010 winter

Country	Community epidemiology and impact	Virology
Argentina (few data)	Lower observed rates than in 2009 – fewer severe cases	Mostly A(H1N1)
Australia	Lower observed rates than in 2009 – fewer severe cases Late season rise due to a mix of viruses	A(H1N1) then some B & A(H3N2)
Chile	Lower observed rates than in 2009 – fewer severe cases Late season rise mostly due to A(H3N2)	A(H1N1) then B & A(H3N2) Early epidemics of RSV
New Zealand	Local observed rates higher than in 2009 – fewer severe cases than in 2009 but straining hospital services in some areas	Almost entirely A(H1N1)
South Africa	Lower observed rates than in 2009 – fewer severe cases	A(H3N2) & B – no A(H1N1)

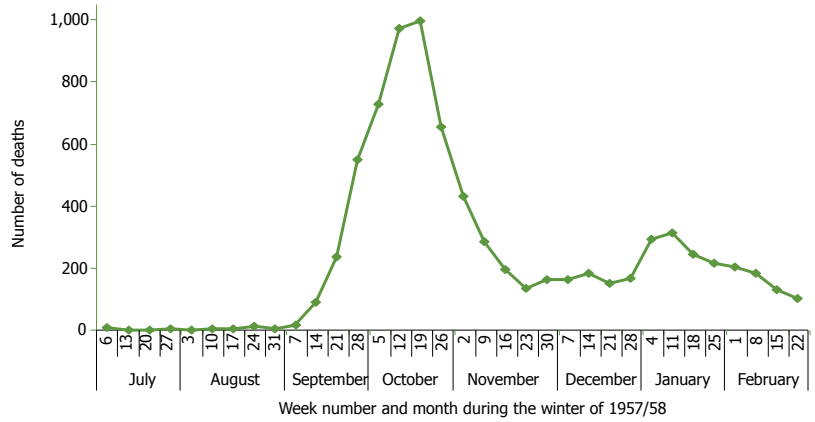
Detailed analyses and visual representations of the experience in these countries are available in the ECDC Global Analyses for Europe – most recent and last published on 14 October.

Figure 1: Previous pandemics and inter-pandemic (seasonal) influenza



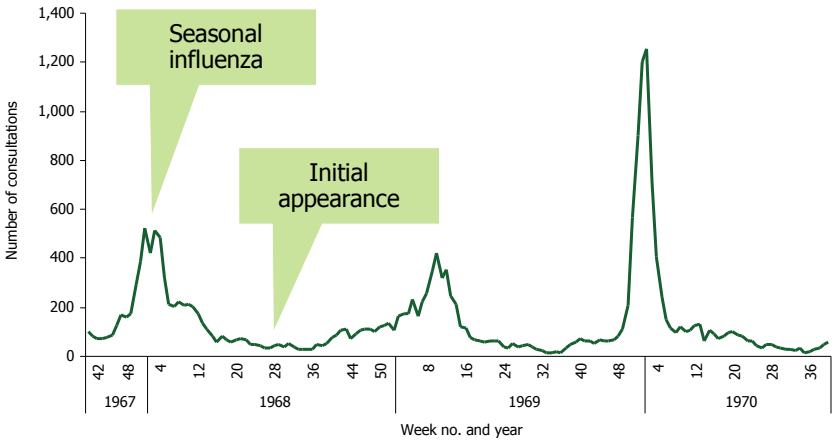
The major current seasonal influenzas in any season are represented by the arrows running horizontally at the time, so that in 1960 it was A(H2N2) viruses, in 1970 A(H3N2) viruses, and in 1980 onwards until 2008/9 A(H3N2) and A(H1N1) viruses. There are also influenza B viruses each year as indicated. Reproduced and adapted (2009) with permission of Dr Masato Tashiro, Director, Center for Influenza Virus Research, National Institute of Infectious Diseases (NIID), Japan.

Figure 2: Recorded deaths from influenza, England and Wales, 1957/58



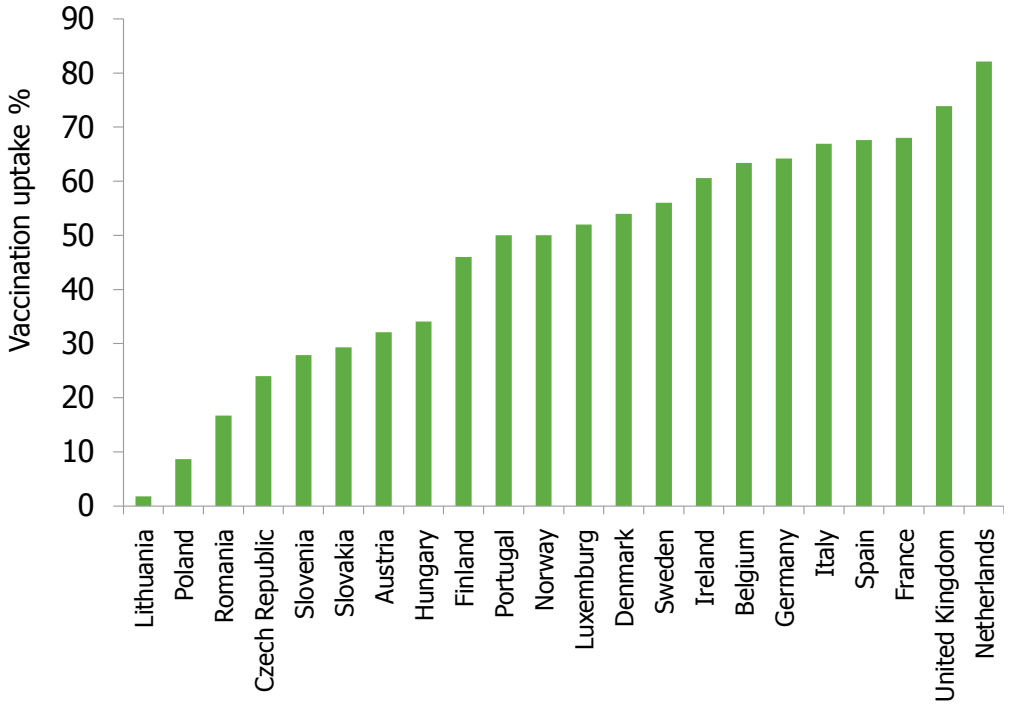
Source: Health Protection Agency, UK.

Figure 3: Number of GP consultations with influenza-like illness per week, England and Wales, 1968/69



Source: Health Protection Agency, UK.

Figure 4: Vaccination coverage for seasonal influenza vaccine in the elderly (65 years and older) in EU and EEA countries - Latest data available in spring 2008. Source VENICE survey.



Data not available for: Bulgaria,Cyprus, Estonia, Greece, Iceland, Latvia, Malta.
Data from VENICE Survey and other sources 2008, version 18 March 2008. Available at:
http://venice.cineca.org/Influenza_Study_Report_v1.0.pdf and http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19017

References

1. European Centre for Disease Prevention and Control (ECDC). ECDC forward look risk assessment. Likely scenarios for influenza in 2010 and the 2010/2011 influenza season in Europe and the consequent work priorities. March 2010. Available from: http://www.ecdc.europa.eu/en/healthtopics/H1N1/Documents/1003_RA_forward_look_influenza.pdf
2. Nicoll A, Sprenger M. The end of the pandemic – what will be the pattern of influenza in the 2010-11 European winter and beyond? Euro Surveill 2010;15(32):pii=19637. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19637
3. Nicoll A. A new decade, a new seasonal influenza: the Council of the European Union Recommendation on seasonal influenza vaccination. Euro Surveill 2010;15(1):pii=19458. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19458
4. Nokleby H, Nicoll A. Risk groups and other target groups – preliminary ECDC guidance for developing influenza vaccination recommendations for the season 2010-11. Euro Surveill 2010;15(12):pii=19525. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19525
5. Council of the European Union. Council Recommendation of 22 December 2009 on inter-pandemic influenza vaccination (Text with EEA relevance)(2009/1019/EU). Official Journal of the European Union 2009; L 348/71. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:348:0071:0072:EN:PDF
6. World Health Organization (WHO). H1N1 in post-pandemic period. 10 Aug 2010. Available from: http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html
7. ECDC. Visual presentations of previous pandemics in one country. ECDC web presentation 2009. Available from: http://ecdc.europa.eu/en/healthtopics/pandemic_preparedness/basic_facts/Pages/historical_pandemics.aspx and http://ecdc.europa.eu/en/healthtopics/Documents/0905_Pandemic_Influenza_Pandemics_of_Influenza.pdf
8. Jackson C, Vynnycky E, Mangtani P. Estimates of the transmissibility of the 1968 (Hong Kong) Influenza Pandemic: Evidence of Increased Transmissibility Between Successive Waves. Am J Epidemiol 2010;171(4):465-478. doi: 10.1093/aje/kwp394. Available from: http://aje.oxfordjournals.org/content/171/4/465.full
9. WHO. Pandemic influenza preparedness and response: a WHO guidance document. Geneva: WHO; 2009. Available from: http://www.who.int/csr/disease/influenza/PIPGuidance09.pdf
10. WHO. Mathematical modelling of the pandemic H1N1 2009 – Background and objectives of an informal network coordinated by WHO. Weekly Epidemiological Record 2009;34(84):341–352. Available from: http://www.who.int/wer/2009/wer8434.pdf
11. Donaldson LJ, Rutter PD, Ellis BM, Greaves FEC, Mytton OT, Pebody RG et al. Mortality from pandemic A/H1N1 2009 influenza in England: public health surveillance study. BMJ 2009;339:b5213. Available from: http://www.bmj.com/content/339/bmj.b5213.full
12. Santa-Olalla Peralta P, Cortes-García M, Vicente-Herrero M, Castrillo-Villamandos C, Arias-Bohigas P, Pachon-del Amo I et al, on behalf of the Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control Team in Spain. Risk factors for disease severity among hospitalised patients with 2009 pandemic influenza A (H1N1) in Spain, April–December 2009. Euro Surveill 2010;15(38):pii=19667. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19667
13. ECDC. Comparison between the 1957 and 2009 pandemics – a close but imperfect fit. ECDC Scientific Advance 1 October 2009
14. ECDC. Risk Assessment – 2009 influenza A(H1N1) pandemic. 17 December 2009. Available from: http://ecdc.europa.eu/en/healthtopics/Documents/0908_Influenza_AH1N1_Risk_Assessment.pdf
15. Mazick A, Gergonne B, Wuillaume F, Danis K, Vantarakis A, Uphoff H et al. Euro Surveill 2010;15(5):pii=19480. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19480
16. ECDC. Call for tender: ECDC yearly review of seasonal influenza vaccine recommendations for the EU/EEA countries. Available here.
17. ECDC and European Influenza Surveillance Network (EISN). Weekly Influenza Surveillance Overviews. Available from: http://ecdc.europa.eu/en/healthtopics/seasonal_influenza/epidemiological_data/Pages/Weekly_Influenza_Surveillance_Overview.aspx
18. ECDC. The 2009 A(H1N1) pandemic in Europe: A review of the experience. Stockholm: ECDC; in press.
19. ECDC. Pandemic fatal cases as announced by EU/EFTA Member States. ECDC 2009 Pandemic website. Available from: http://ecdc.europa.eu/en/healthtopics/H1N1/Pages/index.aspx
20. WHO. Southern Hemisphere influenza vaccine recommendations for winter 2011. Available from: http://www.who.int/csr/disease/influenza/recommendations2011south/en/index.html
21. Bandaranayake D, Huang QS, Bissielo A, Wood T, Mackereth G, et al. 2010 Risk Factors and Immunity in a Nationally Representative Population following the 2009 Influenza A(H1N1) Pandemic. PLoS ONE 5(10): e13211. doi:10.1371/journal.pone.0013211
22. WHO. Seroepidemiological studies of pandemic influenza A(H1N1) 2009 virus. Weekly Epidemiological Record;2010;24(85):229–236. Available from: http://www.who.int/wer/2010/wer8524.pdf

23. McVernon J, Laurie K, Nolan T, Owen R, Irving D, Capper H, et al. Seroprevalence of 2009 pandemic influenza A(H1N1) virus in Australian blood donors, October–December 2009. Euro Surveill 2010;15(40):pii=19678. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19678

24. Health Protection Agency. Pandemic (H1N1) 2009 in England: an overview of initial epidemiological findings and implications for the second wave. 2 December 2009. Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1258560552857

25. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet 2010;375(9720):1100–1108. doi:10.1016/S0140-6736(09)62126-7. Available from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)62126-7/fulltext

26. Waalen K, Kilander A, Dudman SG, Krogh GH, Aune T, Hungnes O. High prevalence of antibodies to the 2009 pandemic influenza A(H1N1) virus in the Norwegian population following a major epidemic and a large vaccination campaign in autumn 2009. Euro Surveill. 2010;15(31):pii=19633. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19633

27. Neels P. Report from the Belgian H1N1 workshop on vaccination campaigns, Brussels, 22 March 2010. Presentation at the Belgian Presidency Conference, Brussels 2 July 2010. Available from: http://www.health.belgium.be/internet2Prd/groups/public/@public/@mixednews/documents/ie2divers/19061406.pdf

28. Wu JT, Ma ESK, Lee CK, Chu DKW, Ho P-L, Shen AL, et al. The Infection Attack Rate and Severity of 2009 Pandemic H1N1 Influenza in Hong Kong. Clinical Infectious Diseases 2010;51(10):1184-1191. Available from: http://www.journals.uchicago.edu/doi/pdf/10.1086/656740

29. Rizzo C, Merler S, Riccardo F, Declich S, Salmaso S. Epidemiological del'influenza A(H1N1)v: previsioni per las stagione 2010. National Center for Epidemiology, Surveillance and Health Promotion, Istituto Superiore di Sanità, Roma, Italy. Unpublished.

30. WHO. Northern Hemisphere influenza vaccine recommendations for winter 2010-2011. Available from: http://www.who.int/csr/disease/influenza/recommendations2010_11north/en/index.html

31. Falagas ME, Koletsi PK, Baskouta E, Rafailildis PI, Dimpoulos G, Karageorgopoulos DE. Pandemic A(H1N1) 2009 influenza: review of the Southern Hemisphere experience. Epidemiol Infect 2010. doi:10.1017/S0950268810002037. Available from: http://journals.cambridge.org/download.php?file=%2FHYG%2FS0950268810002037a.pdf&code=4690adf8befd0b77892e95a86818a91c

32. Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza. Clinical Aspects of Pandemic 2009 Influenza A (H1N1) Virus Infection. N Engl J Med 2010;362:1708-17. Available from: http://content.nejm.org/cgi/content/full/362/18/1708

33. Paget J, Marquet R, Meijer A, van der Velden K. Influenza activity in Europe during eight seasons (1999–2007): an evaluation of the indicators used to measure activity and an assessment of the timing, length and course of peak activity (spread) across Europe. BMC Infect Dis 2007;7(1):141. Available from: http://www.biomedcentral.com/1471-2334/7/141

34. ECDC. Effectiveness of seasonal and pandemic vaccines. Executive Science Update 11, April–June 2010. Available from: http://www.ecdc.europa.eu/en/publications/Publications/1006_COR_Executive_Science_Update.pdf

35. Fiore AE, Shay DK, Broder K, Iskander JK, Uyeki TM, Mootrey G, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Recomm Rep 6 August 2010;59(rr08):1-62. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5908a1.htm?s_cid=rr5908a1_e

36. European Medicines Agency. Pandemic Pharmacovigilance Summaries. Available from: http://www.ema.europa.eu/influenza/updates.html

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