ECDC INTERIM RISK ASSESSMENT

Pandemic H1N1 2009

25 September 2009

Table of contents

Stockholm, September 2009

What is new or different in the September update?

This update is informed by the experience from the Southern Hemisphere's temperate countries during their winter season.

Descriptions from those countries suggest that well prepared essential services are not overly taxed by this pandemic in its current form but that there are pressures experienced by hospital services, especially intensive care units.

The difference between the experience of most people who are infected by the pandemic virus (mild disease) and the few who experience very severe disease has become more apparent.

Planning assumptions (reasonable worst-case scenarios) for clinical attack, hospitalisation and case fatality rates have been reduced.

There are a number of indications of there being asymptomatic infections.

Moreover, there are descriptions of unusual and very severe clinical conditions experienced by some individuals, especially primary viral pneumonias leading to Acute Respiratory Distress Syndrome (ARDS), as well as single and multiple organ failure.

The additional individual risk of severe disease experienced by pregnant women because of infection with the pandemic infection has now been roughly quantified.

Executive summary

The interim ECDC risk assessment for Europe is based on data and analyses available in mid-September 2009. It draws on the experience in the affected European Countries, North America and more recent data from the Southern Hemisphere's temperate countries, which have passed through a winter with the new virus.

After transmitting heterogeneously but at low levels over the summer in European countries, the influenza A(H1N1)v virus has started to show increased transmission in a few EU countries. It is inevitable that this will be followed by a wave of transmission in the autumn and winter of 2009–10 and planning should be undertaken on that basis. However, at this stage, it cannot be predicted when the transmission will start in individual countries or how intense the peaks of transmission will be. The indications from the effects of the pandemic in temperate Southern Hemisphere countries is that this will be a significant event for European countries and put stress on some health services, especially some hospitals and their intensive care capacity. However the same experience shows that well prepared services will be able to cope and there should be no special strain on the essential services outside the health sector if they have undertaken business continuity planning.

To date, important features of the pandemic H1N1 2009 include the following:

- The continuing transmission over the summer in European countries indicates that Europeans will be affected by transmission waves earlier in the season than as is common with seasonal influenza.
- The large majority of those infected experience a mild, self-limiting illness or an asymptomatic infection.
- As for seasonal influenza, there are some people who will experience more severe disease and some of these will die despite medical care.
- While there is much that is similar between the pandemic H1N1 2009 and the seasonal influenza that affects Europe each year, there are also important differences:
  - when the pandemic waves take place they will result in more cases at once;
  - there will be an under-representation of older people in the pandemic relative to seasonal influenza since many, but not all, have some immunity against the pandemic virus; paradoxically older people who are infected will experience the highest rates of severe disease and death of any age group;
  - the spectrum of severe disease includes cases of primary viral pneumonia causing sever acute respiratory distress syndrome (ARDS); secondary bacterial infection may be less prominent than usual, except in children;
  - deaths in adults are occurring at a younger age than normally seen with seasonal influenza;
  - there are some indications that there are many asymptomatic or very mild infections.
- Because of the large number of cases occurring at once, if only a small proportion of these result in severe illness that will still be enough to stress some hospital healthcare systems, especially intensive care units.
- There are no reports of unusual transmission routes for this influenza compared with normal seasonal influenza viruses and there is no indication of risk of infection through food.
- Clinical attack rates are highest in children and young adults.
- The groups experiencing severe disease and requiring hospitalisation the most—those in the *risk groups*—are people with chronic underlying medical conditions, pregnant women and young children (under two years of age).
- Pregnancy increases the risk of a woman experiencing severe disease to about four-fold, although the individual risk of a pregnant woman experiencing severe disease is low.
- Most young children going into hospital experience short illnesses and spend little time in hospital. In contrast, hospitalised adults spend much longer periods there.
- The underlying conditions putting people at risk are different for adults and children but very similar to those for seasonal influenza. In adults, the major risk groups—apart from pregnant women—include those with chronic respiratory or metabolic disorders. Children most at risk are those with neurological or developmental conditions.
- There are adults and children who experience severe disease or even death without any obvious underlying condition. Limited data from deaths due to the pandemic indicate these comprise between 20 and 30% of deaths.
- Planning estimates based on '*reasonable worst-case*' scenarios have declined and it is now considered that cumulative clinical attack rates over the first year of the pandemic of more than 30% of the population are unlikely.
- A reasonable planning estimate for hospitalisation rates in Europe using the overall clinical attack rate as a base is in the in the 1% range. However, in the winter, rates could seem higher because of other respiratory infections such as respiratory syncytial virus.

- Case fatality rates for Europe remain difficult to estimate at this stage. A reasonable worst-case upper limit case fatality rate will be 0.1% of people with symptoms but the actual rate will probably be lower.
- The number of deaths due to this pandemic may be similar to or even lower than what is seen in some influenza seasons, though they will be in different groups of people
- The number of people with symptoms will be especially difficult to estimate as there will be many people with mild disease and it will not be possible to estimate all those infected until serological studies are undertaken.
- Almost all the pandemic viruses have been sensitive to the antivirals known as neuraminidase inhibitors (oseltamivir and zanamivir), but they are resistant to the adamantenes (amantidine and rimantidine).
- There have been a few pandemic virus isolates that have been resistant to oseltamivir (though sensitive to zanamivir). To date none of these have transmitted efficiently.
- The current seasonal influenza vaccine contains a component effective against another A(H1N1) virus but this is not effective against the new influenza A(H1N1)v virus.
- It is difficult to predict what the mix of pandemic and seasonal influenza viruses will bring this autumn. The experience in the Southern Hemisphere is that A(H1N1)v influenza has, on the whole, reduced the proportion of other influenza A and B viruses. Still, there are some other influenza A viruses circulating.

There remain a number of important areas of uncertainty or topics where trends need a degree of quantification. These include the following: the extent of asymptomatic infection; the actual additional level of risk of severe outcome for healthy people and those in most of the risk groups and; the degree of effectiveness of pharmaceutical countermeasures such as antivirals. ECDC will work with Member States, other European Agencies, the Commission, WHO and its other international partners to gather more information to update this risk assessment at intervals. Special attention will be paid to the way the pandemic is developing in the first affected European countries and further analyses from the temperate Southern Hemisphere countries.

Pandemic viruses are unpredictable and can change their characteristics as they evolve and perhaps reassort with other influenza viruses, though there is no evidence that this has happened yet. It therefore remains possible that the pandemic virus could acquire resistance to neuraminidase inhibitors or even become more pathogenic.

This risk assessment will be updated at intervals as new information becomes available.

Comments on the risk assessment and details of further relevant data and analyses are most welcome and should be sent to PHE-incoming@ecdc.europa.eu preferably marked *ECDC Pandemic Risk Assessment 2009*

Source, date and type of request

ECDC internal decision, 18 May 2009. Latest revision, 20 August 2009.

Specific question

Health implications for Europe regarding the pandemic H1N1 2009 influenza.

Consulted experts

Internal ECDC experts. ECDC Advisory Forum.

Evidence assessment

The evidence underlying this risk assessment comes from published data, studies, routine reports and other technical documents of public health organisations and agencies including the World Health Organization (WHO), the United States Centers for Disease Control and Prevention (CDC), and official sources in a number of other affected countries including those in Europe. Unpublished data and analyses are noted but not referenced.

The current evidence comes mostly from early observations of the pandemic and reported cases in Europe and the US and from the initial analyses of the pandemic waves in countries in the Southern Hemisphere during their winter. A particular difficulty arises from the mild nature of the disease, which means that many infections are undetected and unreported while more severe disease and deaths are likely to be captured in surveillance systems. This means that observed rates or ratio percentages (numbers of hospitalisations or deaths per 100 reported cases) are likely to be biased upwards. They are correct observations, but can be misleading for planning purposes.

Topics of prime public health importance are dealt with in Section 2 and areas of particular uncertainty are listed in Section 3.

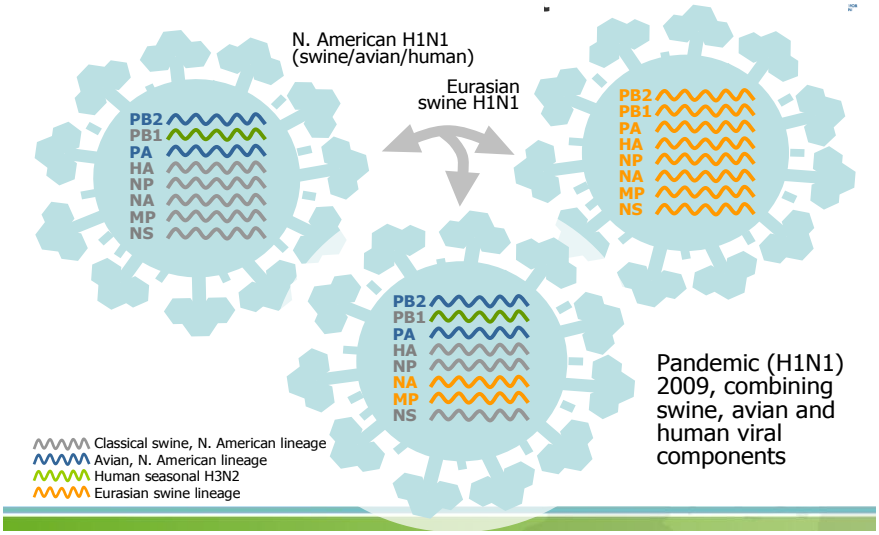
Risk assessment

1 Background

A new influenza A virus was identified by the United States CDC in April this year in samples from two cases and retrospectively in cases in Mexico [4,27,5].

The basic genetic structure of the virus has been described and this information is available through publicly accessible websites [58,47]. The virus has a number of genetic elements from two different types of swine influenza, but also elements originally from avian and human influenzas that were incorporated into other swine influenza viruses (Figure 1) [47,13].

Figure 1. Genetic origins of the pandemic (H1N1) 2009 virus combining swine, avian and human



It is unclear whether the specific reassortment leading to the new virus took place in pigs or humans. In recent years, occasional swine influenza infections in humans have been detected through surveillance of humans, especially in North America. Swine influenza viruses with genes from avian, human and swine influenzas have previously been circulating in pigs in the US, and have occasionally been transmitted to humans [54,49,59]. However, those infections have not transmitted efficiently from human to human. In contrast, this new virus is not only infecting humans and causing some disease but it is also transmitting efficiently from human to human[*]. Since the disease has now spread widely to all continents causing a number of deaths, it has clearly met WHO's criteria for a pandemic influenza strain and should be regarded as a human influenza[†] [64]. Internationally speaking, the infection is now spreading widely [89].

WHO and other international agencies are now calling the disease 'pandemic H1N1 2009'. The term 'swine flu' is inaccurate and confusing. An acceptable shorthand for the virus is influenza A(H1N1)v (where v indicates variant), which has been used by WHO's Global Influenza Surveillance Network for specific nomenclature of viruses to distinguish them from seasonal influenza A(H1N1) viruses and A(H1N1) swine influenza viruses. Increasingly, however, the preferred nomenclature is A(H1N1) 2009.

There are several recent examples where influenza viruses of animal origin have occasionally transmitted to humans. Some have also transmitted occasionally from human to human. The most obvious example being the avian A(H5N1) influenza 'bird flu', which has been circulating in East and Southeast Asia for more than a decade, and which has caused severe infections and deaths in the region. However, human-to-human transmissions of A(H5N1) and other avian influenza have been very limited [17]. Influenza A(H1N1)v is the first animal influenza for some years to have adapted sufficiently to be referred to as a human influenza.

2 Important features

Each pandemic is different and there are always a series of unknowns when a new influenza virus emerges and causes a pandemic. ECDC refers to the most important of these as the 'known unknowns' [18,19,41,65] (see Figure 2). Some of these remain unknown or at least unclear but for several of the unknowns, data are becoming available from many affected countries; notably from North America, countries in the Southern Hemisphere experiencing the pandemic and, increasingly, European countries.

[*] The virus is not genetically related to the single human swine flu infection recently detected in a human in Europe [http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19120, Personal communication to ECDC A Hay WHO Influenza Collaborating Centre, May 2009]

[†] Information on the spread of the pandemic is being updated regularly on WHO websites (http://www.who.int/csr/disease/swineflu/en/index.html) and information on the spread in the European Union/EEA countries can be found on ECDC website (http://ecdc.europa.eu/en/healthtopics/Pages/Influenza_A(H1N1)_Outbreak.aspx).

Figure 2. For any future pandemic virus, what can and cannot be assumed?

What probably can be assumed:

Known knowns

- Modes of transmission (droplet, direct and indirect contact)
- Broad incubation period and serial interval
- At what stage a person is infectious
- Broad clinical presentation and case definition (what influenza looks like)
- The general effectiveness of personal hygiene measures (frequent hand washing, using tissues properly, staying at home when you get ill)
- That in temperate zones transmission will be lower in the spring and summer than in the autumn and winter

What cannot be assumed:

Known unknowns

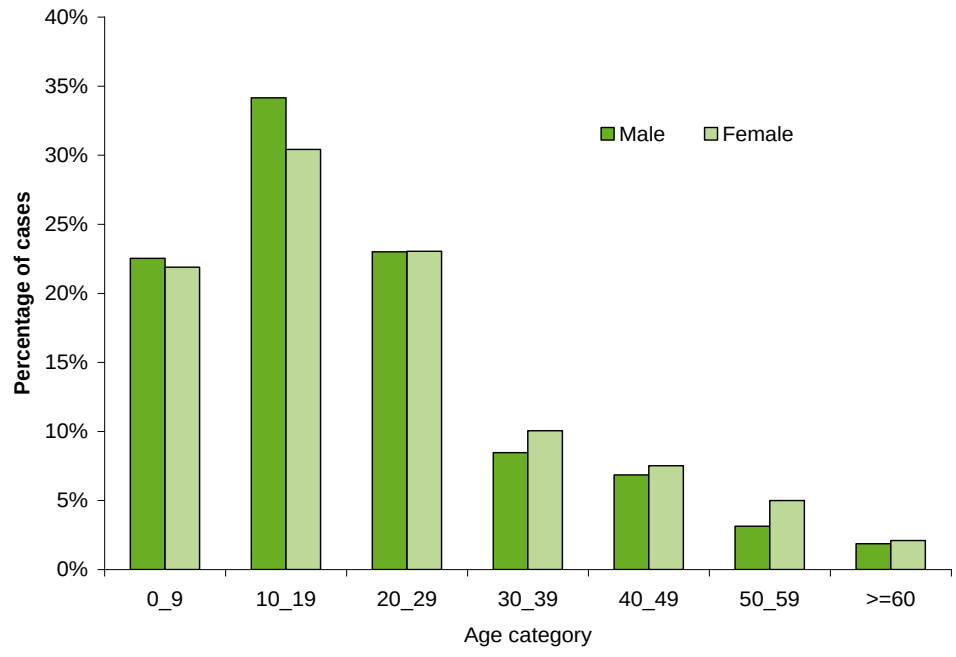
- Antigenic type and phenotype
- Susceptibility/resistance to antivirals
- Age-groups and clinical groups most affected
- Age-groups with most transmission
- Clinical attack rates
- Pathogenicity (case-fatality rates)
- 'Severity' of the pandemic
- Precise parameters needed for modelling and forecasting (serial interval, R_0)
- Precise clinical case definition
- The duration, shape, number and tempo of the waves of infection
- Will new virus dominate over seasonal type A influenza?
- Complicating conditions (super-infections)
- The effectiveness of interventions and counter-measures including pharmaceuticals
- The safety of pharmaceutical interventions

2.1 Basic epidemiology

2.1.1 Age and sex

Among reported cases, the observed age distribution is unusual and different from seasonal influenza, being skewed towards younger age groups [52,20,7,77]. There is a marked underrepresentation of infections in people over 65 years of age, who make up only 2% of reported cases. In Europe, the reported cases tend to be young: median age being 25 years in those who acquired the infection during travel, and 13 years in those domestically infected. Nearly 80% of all cases are in individuals under 30 years of age [52,57,7,20,21] (see Figure 3).

Figure 3. Distribution by age and gender of individual case reports of influenza A(H1N1)v infection, 28 EU/EEA countries, as of 6 July 2009 (n=6560)



This is more than can be explained by initial case findings focusing on returning travellers in the age group of 20–29-year-olds, and secondary spread in schools [52,20]. There are also some laboratory results from serology consistent with a finding that older people may be less affected due to some enduring immunological memory of an earlier influenza A(H1N1) infection with a similar phenotype [6]. Males and females are equally affected [21].

2.2 Disease characteristics

2.2.1. Modes of transmission

There is no evidence to date suggesting that the virus spreads in any different way from other human influenza, i.e. by droplets from coughing and sneezing and direct and indirect contact with respiratory secretions from infected persons [77]. There is no evidence suggesting unusual transmission routes for influenza and no reason to suggest transmission through food [38].

2.2.2 Spectrum of disease

Uncomplicated mild disease—clinical features

Among the cases reported early on, the only notable clinical feature that differs to date from seasonal influenza is some reports of more gastroenteric symptoms than are common for seasonal influenza [52]. But these gastrointestinal symptoms have always been accompanied by other more usual signs of influenza [52]. The distribution of symptoms in Europe is very similar to that described from the USA, with the proportion of patients reporting gastrointestinal symptoms being 24% [21]. There are some indications from baseline data in clinical trials of vaccine that there may have been more very mild episodes than expected. There are also reports that the incubation period may have a longer tail than is usually observed; the results to date are median of 3–4 days with a range of 1–7 days [66].

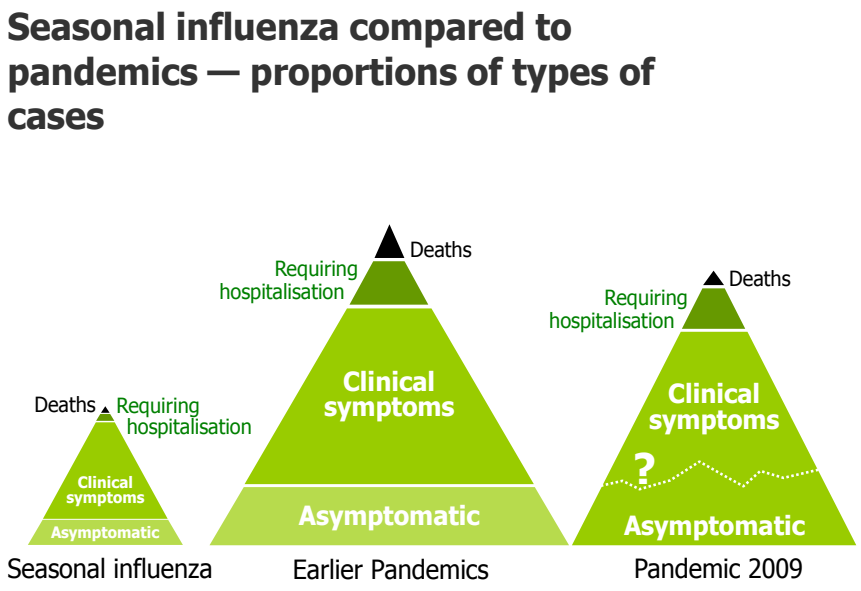
Severe disease—clinical features

There are important differences from seasonal influenza for the severe cases in adults [78]. An important reason for hospitalisation and severe disease in adults is primary viral pneumonia (viral pneumonitis) due to direct viral invasion in lung tissues. Pathological investigation indicates diffuse alveolar damage, haemorrhagic interstitial pneumonitis with lymphocyte proliferation and few neutrophils which are consistent with viral pneumonitis and acute respiratory distress syndrome (ARDS). Supra-infection (secondary infection) with bacteria and pneumonia has been seen in adults but is less common than in seasonal influenza when it causes severe disease. A WHO summary reported that supra-infection with bacteria has been documented in post-mortems in the USA and Canada. Nosocomial (healthcare associated) infections, such as ventilator-associated pneumonia, have been identified in critically ill cases with a prolonged hospital course. Multiple pulmonary emboli have been observed in several very severe cases in patients admitted to intensive care units (ICUs) with refractory ARDS in the USA. These viral pneumonias and ARDS are difficult to manage or ventilate. The most common cause of death in these cases is progressive organ failure [78]. In children severe disease is less common, with most hospitalisations being short. However as with seasonal infection, there are cases of supra-infection in children with bacterial infections [83].

2.2.3 Asymptomatic cases

There are some indications of asymptomatic cases from contact tracing in Europe [21]. However, it will be some time before it is known what proportion of infected people develop the disease [29]. Two plausible assumptions based on previous experience are 33 and 50% of infections being asymptomatic [22,31]. More precise estimates will best be derived from serological studies now underway.

Figure 4. Seasonal influenza compared to pandemic — proportions of types of cases



2.2.4 Ease of transmission—effective reproductive number

There have already been estimates of the basic reproductive rate ($R^{\ddagger}$), which all lie between one and two (with some outliers); the range 1.4–1.6 being most probable [27]. As would be expected for a pandemic, this is higher than the value observed for seasonal influenza but in line with previous pandemics [18,32]. Higher values up to two have been observed in countries where transmission is intense [27,29,51] with even higher figures in some closed communities, such as schools.

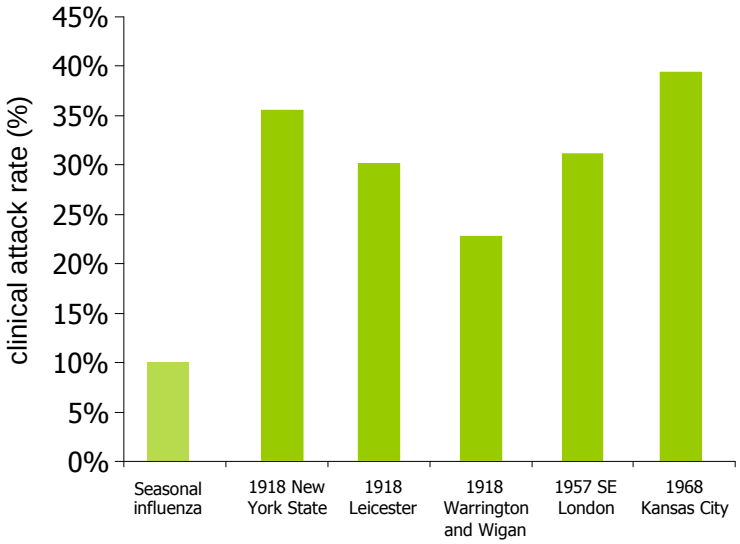
2.2.5 Clinical attack rate[§]

In previous pandemics it was unusual to observe population clinical attack rates of less than 20%, while for seasonal influenza, rates are usually between 5 and 10% [31]. However, this pandemic may be unusual since it seems that older people may be missing from those infected. This notwithstanding, it will be safer to assume higher attack rates of up to 20% in the first year of the pandemic as planning assumptions represent reasonable worst-case scenarios [23]. However, attack rates may be considerably lower this autumn in localities where there have been significant epidemics in the spring and summer, especially if substantial numbers of asymptomatic infections have taken place.

[‡] Technically, it is preferable to refer to 'R' (the effective reproductive number) rather than 'Ro' (the basic reproductive number) since the latter assumes a fully susceptible population when it is already apparent that there are some persons who are immune to infection.

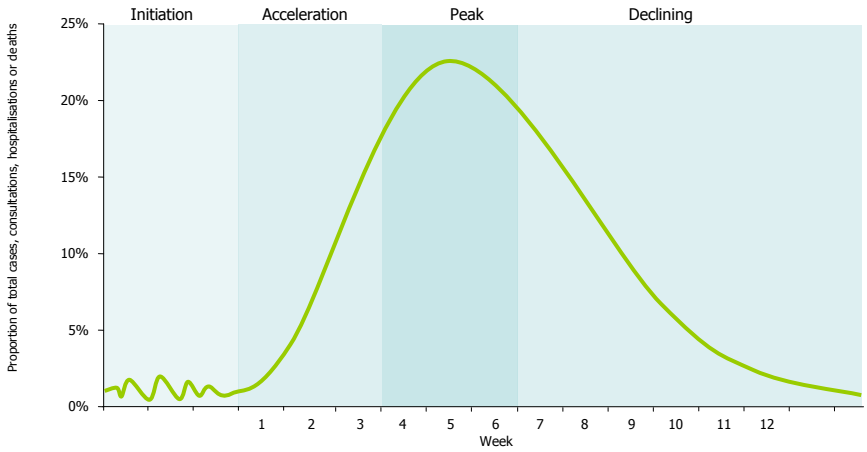
[§] Technically, the three 'rates' (clinical attack, hospitalisation and case fatality rates) should be called 'ratios' as they are proportions and do not have a time component as all rates should. The 'clinical attack rate' is the proportion of the population that is infected and has symptoms (i.e. asymptomatic infections are excluded). When considered for a pandemic, it can extend over the whole first wave period and mean the 'cumulative attack rate'. The 'hospitalisation rate' is the proportion of those affected (with symptoms) that are ill enough to go to hospital, while the 'case fatality rate' is the proportion of those affected who die as a direct or indirect consequence of their infection.

Figure 5. Numbers affected in seasonal influenza epidemics and pandemics (overall clinical attack rate in previous pandemics)



In a study conducted in Mexico, a figure of 30% was observed in one community [27]. While lower figures have been observed in North America—notably in New York City where a telephone survey gave a figure of 7% [48]—transmission took place in May 2009 in the Northern Hemisphere when the United States in particular was still in the initiation phase of its pandemic wave. Given the time of year, this probably does not represent the final cumulative clinical attack rate, which is always higher for pandemic than seasonal viruses (see Figure 5). An estimate of the attack rate of clinical infections in New Zealand was 8% for the 2009 season which comes up to 11% if assumptions are made for asymptomatic infections [81].This is little different from a normal influenza season [1,56,55,7,8,31].

Figure 6. Idealised national curve for planning, Europe 2009



Single-wave profile showing proportion of new clinical cases, consultations, hospitalisations or deaths by week. Based on London, second wave 1918.

For planning purposes, there are four components of a pandemic wave: Initiation, Acceleration, Peak and Decline. The percentage on the vertical axis represents the proportion of all those infected in the first wave that are infected in the different phases. After the decline there may be a second and even a third wave before influenza settles back down to its seasonal pattern again. The seasonal flu is usually worse than the years before the pandemic because it is invigorated with new genetic material. The same four phases actually apply to epidemics as well. This particular wave has been given an erratic initiation

phase representing what happened in Europe in the summer and early autumn, when there have small outbreaks. It is not clear when each country will enter their acceleration phase. However, no pandemic has ever behaved in quite so neat a way as shown here. Pandemics do not follow set patterns and each one is different. It is also important that this is a national curve. The local curves are narrower and with a higher central peak, i.e. local pandemic spread is shorter and sharper but also highly variable.

In Europe, focal outbreaks in closed communities observed higher attack rates. In school outbreaks in the UK and France, figures of around 30 and 50% have been reported [35,30]. No serological data are yet available. As is the case with other human influenza infections, there will probably be many mild and asymptomatic cases [20,31]. Certainly in New York most of those affected did not consult a doctor [63].

2.2.6 Hospitalisation rate

As yet, this is a difficult figure to derive for Europe. A case hospitalisation rate of 11% (of clinical cases) was initially calculated out of the total number of reported cases in the United States. This rate should not be used for planning purposes as it is likely to represent an overestimate of the true rate because of the mild nature of most cases [7]. A more recent estimate of population hospitalisation rates in the United States derived from the Emerging Infections Program (EIP) (a population-based surveillance network) shows that hospitalisation rates for laboratory-confirmed influenza in children aged 0–23 months, 2–4 years, and 5–17 years were 2.5, 1.0, and 0.8 per 10 000, respectively. Rates in adults aged 18–49 years, 50–64 years, and ≥ 65 years, were 0.5, 0.6, and 0.5 per 10 000, respectively [79, 82].

In some European countries, initial cases were isolated in hospital as a way of preventing onward transmission and this practice resulted in seeming high rates [21]. Many of those people would not have needed hospital care in normal circumstances. In making estimates for Europe, it has been observed that the denominators (total number of cases) are especially sensitive to how intensively surveillance is being undertaken. An overall hospitalisation rate for Europe at present is around 5–6% [21]. The data from the United Kingdom up to early July (with an observed hospitalisation rate of 1–2%) has the advantage that patients have generally not been hospitalised for infection control purposes. The denominator is also likely to be more complete than most, as it is derived from vigorous case finding and contact tracing [21]. Generally, as the focus of reporting moves from all cases to hospitalised cases, it can be expected that hospitalisation rates will seem to rise, but without any change in the underlying data. Therefore, at present, a 1% rate (applied to the clinical attack rate) is a reasonable one to use for planning purposes. However, it always needs to be remembered that, while national pandemic waves are spread out over three months, local waves are shorter and higher. This needs to be considered for planning local responses [40].

2.2.7 Case fatality rates (CFR)

These remain difficult to estimate with accuracy given the various factors that can influence its measurement and its actual value, including, among others, social and healthcare related factors [70]. An overall CFR of 0.6% was recently calculated based on deaths reported worldwide and analysed by an epidemic intelligence team. However the range of CFR varied from 0.1 to 5.1% depending on the country [88] In Mexico, case ascertainment has favoured detecting patients with more severe illness, hence a report of a CFR of just over 1% (119 deaths among 10 962 cases) gives a misleadingly high case fatality rate [67]. An indirect method gave a value of 0.4% [27], while estimates for the United States give a figure ranging from 0.5 to 1% [18]. This is somewhat above what is considered normal for seasonal influenza. In Europe, the initial figure was also around 1%, but again that is certainly an overestimate [21]. In the first affected country in Europe (the United Kingdom) the observed rate, with data as of 15 July 2009, was 0.3% (28 deaths in 10 649 confirmed cases) [36]. This is not that different from what has been observed in modelling studies [27]. This rate will have been quite accurate given that the UK's initial policy of very active case finding is likely to have given a more complete denominator than in countries with less active case finding. Equally, the rate can now be expected to seem to rise as case finding and laboratory testing have become less active in the UK. Even so, the figure of 0.3% will be an overestimate since the denominator will be incomplete due to very mild cases and a figure of 0.1% or less will be nearer the true figure at this stage. Given the seeming immunity to the pandemic strain in older age groups (that usually experience higher risk of severe disease and death), it is quite possible that the overall CFR for this pandemic will be lower than the one for seasonal influenza. Whether there will be more actual deaths than experienced in seasonal influenza winter remains to be seen. Certainly the unpublished mortality trend data from Australia shows little difference from their 2008 winter. However it remains the case that because the influenza-associated deaths will be in younger adults than usual, they will be regarded as unusual and commented upon.

2.2.8 Planning assumptions, including pressures on hospitals

From the above considerations, it is possible to revise previous generic *reasonable worst-case* planning assumptions and this has been published by at least two European countries in July and then updated in September [22,23]. In both cases, the assumed rates of disease, hospitalisations and deaths declined in the light of data such as in this document (Figure 7).

Figure 7. Revised reasonable worst-case planning assumptions for the pandemic—first wave A(H1N1) 2009 to mid-May 2010

Planning assumptions to mid-May 2010: potential effects of A(H1N1) infection for the general population	
Clinical Attack Rate	up to 30% of population
Peak Clinical Attack Rate	up to 6.5% (local planning assumptions 4.5%-8%) of population per week
Complication Rate	up to 15% of clinical cases
Hospitalisation Rate	up to 1% of clinical cases, of whom up to 25% could require intensive care at any given time
Case Fatality Rate	up to 0.1% of clinical cases
Peak Absence Rate	up to 12% of workforce

These assumptions apply to one European Country (the United Kingdom) with data available as of early September 2009. ***They should not be used for predictions.***

Courtesy of Department of Health, UK, http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_104843.pdf

Pressures on hospitals

The proportion of hospitalised cases requiring intensive care and respiratory support is especially important information for determining the needs for higher levels of care in European countries. Initial estimates in the figures above have been derived from experience in the UK and the Southern Hemisphere. They require careful interpretation bearing in mind that the figure from the UK estimates (25%) represent the proportion at any one time. The risk of a hospitalised patient going into ITU will be lower since the period of time that patients going into ITU stay in hospital is longer than for simple hospitalisation. An area that requires particular clarification is the position for children (see below).

2.2.9 Risk groups for hospitalisation and severe disease

- **People with underlying chronic diseases**: In an initial published study from California, of 553 probable and confirmed infections with A(H1N1)v virus, 30 people were hospitalised needing care. Nineteen of the 30 patients had underlying chronic conditions, which have been in decreasing frequency: asthma or chronic obstructive airways disease; diabetes; being immunocompromised; chronic cardiovascular disease (not simple hypertension); chronic renal failure; epilepsy (seizure disorders) and; malignancy [8]. Another published study highlighted massive or morbid obesity in adults though it is increasingly considered that massive obesity is a proxy for other chronic medical conditions, such as respiratory insufficiency [9]. The largest dataset reported to date (n=302) is based on deaths reported to CDC in the United States and this defines the current risk groups as pregnant women, children under two years of age and people with the chronic underlying conditions listed above, plus chronic neurological and neuromuscular disorders. These underlying conditions are present in 70% of the people dying or experiencing severe disease [7].
- **Pregnant women**: A published study from the USA has identified pregnant women infected with A(H1N1) 2009 as being four to five times as likely to be hospitalised than pregnant women not suffering from infection; though the absolute risk for infected pregnant women being hospitalised remains low, at around 0.32 per 100 000.This is somewhat higher than the heightened risk noted for women experiencing seasonal influenza [41].
- **Young children**: There are limited published studies focusing on this group as yet but it is noticeable that, in association with the pandemic affecting the USA, the group that has shown the highest hospitalisation rates is children under two years of age [10]. Similarly, children aged 1–4 years had the highest ILI consultation rates in New Zealand, followed by those ages <1 year, according to the national sentinel surveillance system data [80,1].

Although the proportion of deaths attributed to pneumonia and influenza did not exceed what was expected in the summer in the USA, 47 paediatric deaths associated with laboratory-confirmed A(H1N1)v influenza occurred during April 26–August 29, 2009. [83] A more in-depth analysis of 36 of these children revealed that 19% were <5 years old and 67% had one or more underlying conditions. Of the 24 children with underlying conditions, 92% had a neurodevelopmental condition often associated with co-morbid pulmonary conditions. Forty-three per cent of all children who died had a documented bacterial infection [83]. However, the children who died with no underlying condition were older than what is usually experienced with seasonal influenza [83]. It was also observed that hospitalised younger children without underlying conditions often experienced a short stay in hospital; far shorter than their adult counterparts.

From these data and analyses it is possible to derive a list of risk groups, i.e. groups experiencing more severe infections than the general population.

Figure 8. Risk groups for the pandemic H1N1 2009

Risk groups for the A(H1N1) pandemic 2009

The following groups are considered more at risk of experiencing severe disease due to influenza A(H1N1)v virus 2009 than the general population:

- People with chronic conditions in the following categories:
  - chronic respiratory diseases;
  - chronic cardiovascular diseases (though not isolated mild hypertension);
  - chronic metabolic disorders (notably diabetes);
  - chronic renal and hepatic diseases;
  - persons with deficient immunity (congenital or acquired);
  - chronic neurological or neuromuscular conditions; and
  - any other condition that impairs a person's immunity or prejudices their respiratory (breathing) function, including severe or morbid obesity.

Note: These categories will be subject to amendment and development as more data become available. These are very similar underlying conditions that serve as risk factors for seasonal influenza. What is especially different from seasonal influenza is that the older age groups (over the age of 60 years) without underlying conditions are relatively unaffected by the pandemic strain.

- Pregnant women.
- Young children (especially those under two years).

Sources:
ECDC Pandemic 2009 Risk Assessment. Available from: http://www.ecdc.europa.eu/en/Health_topics/novel_influenza_virus/2009_Outbreak
Finelli L. CDC Influenza Surveillance. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jun09/15-2-inf.pdf
Nicoll A et al. Eurosurveillance, Volume 13, Issue 43, 23 October 2008. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19018
Jamieson D et al. Lancet 2009; July 29, 2009 DOI:10.1016/S0140-6736(09)61304-0
CDC 2009 ACIP Meeting, 31 July 2009. Novel influenza A(H1N1) epidemiology update. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jul09-flu/02-Flu-Fiore.pdf
CDC 2009 ACIP Meeting, 31 July 2009. Vaccine workgroup considerations. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jul09-flu/11-Flu-Fiore.pdf

2.2.10 Older people:

There are a number of analyses indicating that people 65 years of age and older are noticeably underrepresented in reported infections and hospitalisations compared to what is seen for seasonal influenza [57,50]. Normally, in the United States, people 65 years of age and older would account for nearly 50% of hospitalisations with confirmed seasonal influenza, but with A(H1N1)v influenza, the figure has so far been less than 5% [7]. This is consistent with the fact that many older people are immune due to prior exposure to a similar virus in the early 1950s or earlier [6]. However, as might be expected, when one of the minority of older people who is susceptible becomes infected with A(H1N1) 2009, they seem to have a high likelihood of needing hospital care and a higher case fatality rate than any other age group [7].

2.2.11 People without risk factors:

There are consistent reports of severe disease and deaths in people without any reported underlying disease or other conditions. It should be remembered that these also occur with seasonal influenza [57,7,84]. In the series of deaths reported to be attributable to or associated with the pandemic influenza in the UK in the first sixty to seventy cases where investigations had been undertaken, between 20 and 30% of the cases (of all ages) were in those with either no reported underlying condition (20%) or only mild conditions (10%) (Department of Health London, unpublished data).

The United States has published analyses concerning children based on the first 36 deaths. This found 10 children (28%) with no reported underlying condition. The age-span of these children was also surprising: four of the ten were two years of age or under (ages of 2–4 months and one and two years). However, the other six were between nine and fifteen years of age, indicating that older, healthy children are also at risk of death from this virus. Pathological reports on these children are awaited.

2.3 Features of the virus

2.3.1 Genetic stability

To date, all the isolates of the pandemic virus have shown little genetic variation and no indication of reassortment with other viruses [10,13,37].

2.3.2 Susceptibility to antivirals and antiviral resistance

Based on genetic evidence, the indications are that the neuraminidase inhibitors oseltamivir and zanamivir will provide effective treatments, but that the virus will be resistant to adamantenes (amantidine). With many people on antivirals, it is to be expected that some viruses will appear with markers of antiviral resistance as it has been seen with other human influenzas (ECDC 2009f, WHO 2009e). Indeed, somewhere between 20 and 30 isolates of the pandemic virus have been reported resistant to oseltamivir (WHO unpublished data) with a few cases of verified primary resistance—i.e. a virus acquired by a person who was seemingly on oseltamivir [68,69,13]. All of the isolates have been susceptible to zanamivir. Three secondary cases were detected in Europe and four in Japan, where there is particularly close surveillance [24,13]. There must, however, be concern that genetic reassortment could take place with circulating oseltamivir-resistant viruses, as has happened with at least one other virus of swine origin [24].

2.3.3 Pathogenicity of the virus

There are no reports of known genetic markers associated with severe disease. Initial animal challenges show that, although the virus does cause disease, the results are considerably less severe than, for instance, the highly pathogenic influenza A(H5N1), but somewhat more pathogenic than seasonal influenza A(H1N1) [26,44,45,13].

2.3.4 Prior immunity in humans

Laboratory studies are being undertaken and show some cross-reactivity in sera from older people. Epidemiological data from the US also indicate that older age groups may be less affected. Viruses of the same subtype, A(H1N1), have been responsible for seasonal influenza during several years, but that subtype is quite different from the current one. It is very unlikely that the current influenza vaccine against seasonal A(H1N1) will give any protection against A(H1N1)v influenza . Equally, the first study from Australia showed that seasonal vaccination neither decreased or increased risk of pandemic disease in the 2009 season[85]. Most of the genes of the novel virus are similar to genes that have developed in pigs—independently of human H1N1 viruses—probably since 1918 [6].

2.4 Severity of the pandemic

Many national authorities consider it important to have an assessment of the 'severity' of a pandemic so as to determine a proportionate response [70,71]. However, it is difficult to classify pandemics as the experience and perception of people, organisations and societies may differ because severity can vary from country to country and even from place to place within a country. It can also change over time and there are important social and societal factors, including the vulnerability of populations, capacity for response, the available healthcare and the level of advance planning and preparedness. Severity can also be seen either from the individual perspective (people who are infected experience a severe disease—even though they may be only a few), or from a societal view (many people are away from work and essential services are threatened—even though the disease may be relatively mild).

It is difficult at this stage to comment on severity in EU Member States when there has been so little experience in Europe. It is especially difficult to place the impact and effect of this pandemic virus into the mild, moderate and severe categories preferred by WHO. However, what is known so far from the North American and limited European experience is as follows:

- **Hospitalisation and case fatality rate.** Recent data from the United States suggest hospitalisation rates varying with age in the range of 0.5—2.5/10 000 [81]. The limited information to date for Europe (mostly from the UK) suggests similar rates [21]. Because of the seeming underrepresentation of older people among those infected, the fatality rate in Europe may be less than for a moderate influenza season, like 2008–09, though the absolute numbers of hospitalisations could be higher. Experience from the Southern Hemisphere countries shows that particular pressures may be felt by the hospital services and, within those, the services for critically ill patients who might benefit from intensive care, artificial ventilation and extracorporeal membrane oxygenation (ECMO) [40].
- **Number of people being ill with respiratory illnesses at any one time.** This correlates to the pressure on the health services to deal with these patients. The limited experience from North America suggests this is manageable as long as the public are not alarmed into coming forward and there are not other epidemics of illness taking place [62]. What will be more difficult in the autumn and winter in Europe is when there are steep local peaks of transmission and especially when epidemics of the pandemic virus are laid on top of other seasonal respiratory viruses—influenza and otherwise—as happened in Chile, for example.
- **Critical services functioning.** So far there have been no reports of the peak prevalence of ill people or those caring for others as causing any problems in any affected countries globally.
- **Certain groups experiencing severe illness or dying unexpectedly.** There have been unexpected findings as there is both an underrepresentation of older people and three groups who are suffering more

than would be expected with seasonal flu: namely people under age 65 with chronic but treatable illnesses, pregnant women and very young children (see Figure 8). These three groups are overrepresented in those falling ill and dying in the United States.

Given this experience, it would seem that most well-prepared European Member States should be able to cope with this pandemic in its present form in the summer months. However, it is during autumn and winter in Europe that the pressure will come and there is a need for final preparations in the healthcare sector for these seasons [40].

2.4.1 Potential worsening of severity

Historically however, it must also be remembered that pandemic viruses are quite capable of worsening their impact over time (this happened in 1918–19 and 1968–69 in some European countries) and so severity will need to be monitored, especially given the possibility of the virus acquiring genetic material associated with pathogenicity or antiviral resistance in humans [40].

3 Areas of particular uncertainty

3.1 Mix of influenza and other viruses that will be circulating this coming autumn and winter in Europe

Some predictions can now be made about this. The pattern in the Southern Hemisphere in their winter has been mixed. In a number of countries, the pandemic virus has increasingly predominated while in others the pattern is more mixed [69,14]. In Australia and New Zealand, there were contributions by both influenza A(H3N2) and the influenza A(H1N1)v, but the latter came to predominate. Also it is not clear what sampling and testing strategies are being used by the countries concerned (for example whether B viruses are being included). Current data are regularly published by the United States CDC and WHO[**]. It is recommended by WHO that plans for immunising conventional risk groups with the seasonal vaccine go ahead in Northern Hemisphere countries [50,12]. In at least one Southern Hemisphere country (Chile), respiratory viruses apart from influenza (such as respiratory syncytial viruses) added to the pressure on health services as sometimes happens in all winters.

3.2 Likely timing and pattern of spread of the virus in Europe in the summer, autumn and winter

The exact timing is impossible to predict, especially for individual countries. This pandemic virus has been transmitting in Europe in the warmer months. A number of European countries have experienced initiation phase outbreaks over the summer months, at least for a while, despite it being the summer months [36]. Schools have been especially associated with outbreaks and transmission was probably blunted by the closure of schools over the summer. School amplification will now be resumed [3]. Given the experience in the Southern Hemisphere, it is certain that pandemic waves will affect countries though it is uncertain when these will come, which countries will be affected first and how high peak attack rates will be. An important determinant will be the level of asymptomatic infection or very mild disease that has been experienced. This will only be determined by serological studies. It would be prudent for European countries to prepare for early pandemic waves, even if in fact they do not eventually come until later in the autumn and winter [40,69]. Countries in their final planning will need to recall that local epidemics may be shorter but sharper than the overall pandemic wave in the country (having higher incidence of people needing care and unavailable for work) [40,23].

3.3 Shedding the virus and infectivity

As yet there are no published data on how long infected people shed the virus or regarding how long they remain infectious (the latter will be a shorter period of time than the former). This is important for informing infection control activities in healthcare settings and the community.

3.4 Relative and attributable risk of more severe disease

While the risk groups are becoming clearer, there are as yet no estimates of relative, attributable risk or absolute risk. The one exception is concerning pregnant women [41]. The attributable individual risk—'how much more likely am I (or my child) to be hospitalised if I am infected with this virus?'—is especially important for allowing the public and clinicians to make informed choices on early treatment with antivirals or vaccination when specific pandemic 2009 vaccines become available.

[**] See http://www.cdc.gov/h1n1flu/updates/international/map.htm

3.5 Pathological processes underlying severe disease and individual vulnerability

There is no information as yet as to whether the causes of death and responses to the infections in humans are the same as for seasonal influenza or otherwise, though the numbers of severe viral pneumonias suggest some people are experiencing unusual illnesses. This is important for informing treatment strategies and for determining why most people experience mild disease but some even previously healthy people get so ill.

3.6 Population level mortality attributable to the pandemic virus in Europe

With seasonal influenza there are significant numbers of deaths attributable to influenza each year. The groups most affected are older people and people with chronic medical conditions [86].

3.7 Protective value of early treatment with antivirals:

No trials can be undertaken in these circumstances but it is noticeable that in the patients that have been hospitalised, most patients have not received the effective antivirals, oseltamivir and zanamivir (Department of Health, London UK—unpublished data). Thorough, controlled analyses remain to be undertaken. However, observational studies of seasonal influenza point to the success of early treatment in preventing severe outcomes [87, 82].

3.8 Data and analyses concerning patient numbers in hospitals and information on children

Though some information has come from Southern Hemisphere countries, there are few details that allow European countries to undertake planning[1].There are also a number of anecdotal reports indicating that the clinical course in children may be different from adults and from the experience with seasonal influenza [15].

Next steps for ECDC

In addition to close surveillance of cases in the EU, ECDC will continue to closely monitor the situation in North America and the temperate countries of the Southern Hemisphere. It is from these countries that further information for the parameters listed above will come, in addition to the information from the European Union. ECDC will continuously provide information through its website and update this risk assessment as needed. For rapid updates, please see the Daily Updates published on weekdays on the ECDC Pandemic 2009 website: http://ecdc.europa.eu/en/healthtopics/Pages/Influenza_A(H1N1)_Outbreak.aspx

Date of next planned update

Mid-October 2009.

References

1. Baker M, Wilson N, Huang Q, Paine S, Lopez L, Bandaranayake D et al. Pandemic influenza A(H1N1)v in New Zealand: the experience from April to August 2009. Eurosurveillance 2009 August 27;14(34). pii. 19319. Available from http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19319
2. Brankston G, Gitterman G, Hirji J, Lemieux C, Gardam M. Transmission of influenza A in human beings. Lancet Infectious Diseases 2007; 7 (4):257–265.
3. Cauchemez S, Ferguson NM, Wachtel C, Tegnell A, Saour G, Duncan B, et al. Closing schools during an influenza pandemic: A review. Lancet Infectious Diseases 2009(9)8;473-481. Available from: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(09)70176-8/abstract.
4. Centers for Disease Control and Prevention. Swine influenza A (H1N1) infection in two children — Southern California, March–April 2009. MMWR Morb Mortal Wkly Rep. 2009 Apr 24;58(15):400–2.
5. Centers for Disease Control and Prevention. Novel Influenza A (H1N1) Virus Infections — Worldwide, May 6, 2009 MMWR May 8, 2009 / 58(17);453-458.
6. Centers for Disease Control and Prevention. CDC Serum Cross-Reactive Antibody Response to a Novel Influenza A (H1N1) Virus After Vaccination with Seasonal Influenza Vaccine. MMWR May 22, 2009/58(19);521–524.
7. Centers for Disease Control and Prevention. ACIP Meeting July 31. Fiore A. Novel influenza A(H1N1) Epidemiology update. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jul09-flu/02-Flu-Fiore.pdf
8. Centers for Disease Control and Prevention. Hospitalized Patients with Novel Influenza A (H1N1) Virus Infection — California, April–May, 2009. MMWR May 22, 2009/58(19);536-541.
9. Centers for Disease Control and Prevention. Intensive-Care Patients With Severe Novel Influenza A (H1N1) Virus Infection — Michigan, June 2009. MMWR 58.
10. Centers for Disease Control and Prevention. FluView – a weekly influenza surveillance report. Available from: http://www.cdc.gov/flu/weekly/
11. Centers for Disease Control and Prevention. Press briefing transcript May 28th 2009. Available from: http://www.cdc.gov/media/transcripts/2009/t090528.htm.
12. Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines. MMWR 2009;58:1-52 . Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5808a1.htm
13. Centers for Disease Control and Prevention. ACIP Meeting July 31. Klimov A. Virology and immunology update. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jul09-flu/04-Flu-Klimov.pdf
14. Centers for Disease Control and Prevention. ACIP Meeting July 31. Mott J. Novel influenza epidemiology update – International. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jul09-flu/03-Flu-Mott.pdf
15. CDC, Surveillance for Pediatric Deaths Associated with 2009 Pandemic Influenza A (H1N1) Virus Infection - United States, April - August 2009, MMWR Morb Mortal Wkly Rep. 2009 September 4; 58(34):941-7
16. Centers for Disease Control and Prevention. International situation update September 18th Available from: http://www.cdc.gov/h1n1flu/updates/international/ including up to date map http://www.cdc.gov/h1n1flu/updates/international/map.htm
17. ECDC. The public health risk from highly pathogenic avian influenza viruses emerging in Europe with specific reference to influenza type A/H5N1. June 1 2006 (online). Available from: http://ecdc.europa.eu/en/publications/Publications/0606_TER_The_Public_Health_Risk_from_Highly_Pathogenic_Avian_Influenza_Viruses_Emerging_in_Europe.pdf
18. ECDC. Working Group Influenza Surveillance in a Pandemic, August 2007. Available from: http://ecdc.europa.eu/en/healthtopics/Documents/0708_Pandemic_Influenza%20_Influenza_Surveillance_in_a_Pandemic.pdf
19. ECDC. Surveillance and studies in a pandemic in Europe, June 2009. Available from: http://ecdc.europa.eu/en/publications/Publications/0906_TER_Surveillance_and_Studies_in_a_Pandemic_in_Europe.pdf
20. ECDC working group on influenza A(H1N1)v. Preliminary analysis of influenza A(H1N1)v individual and aggregated case reports from EU and EFTA countries. Eurosurveillance 2009, 14(23). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19238
21. ECDC. Analysis of influenza A(H1N1)v individual case reports in EU and EEA countries. Update 9 July 2009. Available from: http://ecdc.europa.eu/en/healthtopics/Documents/090709_Influenza_A(H1N1)_Analysis_of_individual_data_EU_EEA-EFTA.pdf
22. ECDC. Public Health Development Planning Assumptions for the First Wave of Pandemic A(H1N1) 2009 in Europe, July 29 2009. Available here.
23. ECDC. Meeting Report: European pandemic planning assumptions. January 2009. Available from: http://ecdc.europa.eu/en/publications/Publications/0901_MER_European_Pandemic_Influenza_Planning_Assumptions.pdf
24. ECDC. First isolation of a secondary oseltamivir-resistant A(H1N1)v strain in Denmark, 1 July 2009. Available from: http://ecdc.europa.eu/en/healthtopics/Documents/0906_Influenza_AH1N1_ECDC_Threat_Assessment_First_isolation_

of_a_secondary_oseltamivir_resistant_strain_in_Denmark.pdf
25. ECDC. Reassortment seasonal influenza virus and swine influenza virus in Saskatchewan, Canada, 9 July 2009. Available from: http://ecdc.europa.eu/en/healthtopics/Documents/0907_TA_Swine_influenza_Canada.pdf
26. ECDC. Pathogenicity and transmissibility of pandemic influenza A(H1N1)v – results from an animal model. Available here.
27. ECDC. Meeting report: Surveillance and studies in a pandemic: Fourth meeting of the SSiaP working group. July 2009. available from: http://ecdc.europa.eu/en/publications/Publications/0908_MER_Surveillance_and_Studies_in_a_Pandemic_Meeting_Report.pdf
28. Fraser C, Donnelly CA, Cauchemez S et al. Pandemic potential of a strain of influenza A(H1N1): early findings. Science Express, 11 May 2009, doi 10.1126/science.1176062.
29. Garske T, Legrand J, Donnelly CA, Ward H, Cahchemez S, Fraser C, Ferguson NM, Ghani AC. Assessing the severity of the novel influenza A/H1N1 pandemic. BMJ. 2009 14; 339:b2840. Available from: http://www.bmj.com/cgi/content/full/339/jul14_3/b2840
30. Guinard A, Grout D, Durand C, Schwoebel V. Outbreak of influenza A(H1N1)v without travel history in a school in the Toulouse district, France, June 2009. Eursurveillance 2009; 14(27). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19265
31. Hayward AC, Kovar J, Bermingham A, Edmunds J, Johnson AM, Knott F et al. The community burden of influenza and influenza like illness in England – Early results from the MRC Flu Watch Study. Poster 5-011, Third ESWI Conference, Portugal 14–17 Sept 2008. Programme book 114. Available from: http://www.eswi.org/userfiles/files/TEIC_programmebook
32. Hall IM, Gani R, Hughes HE, Leach S. Real-time epidemic forecasting for pandemic influenza. Epidemiol Inf. 2007 Apr;135(3):372-85. Epub 2006 Aug 24
33. Hanshaoworakul W, et al. Severe human influenza infections in Thailand: oseltamivir treatment and risk factors for fatal outcome. PLoS ONE, June 25 2009
34. Health Protection Agency. Epidemiology of new influenza A(H1N1) virus infection, United Kingdom, April–June 2009. Eurosurveillance 2009; 14(22). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19232
35. Health Protection Agency West Midlands. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. Eurosurveillance 2009, 14:27. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19264
36. Health Protection Agency. HPA Weekly National Influenza Report 16 July 2009 (Week 29). Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1247728935374
37. Health Protection Agency. HPA Weekly National Influenza Report 30 July 2009 (Week 31). Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1248940851283
38. INFOSAN. Information Note No. 2/2009 — Human-animal interface aspects of Influenza A/H1N1. Available from: http://www.who.int/foodsafety/fs_management/No_02_influenza_Apr09_en_rev1.pdf
39. Irvine RM, Brown IH. Novel H1N1 influenza in people: global spread from an animal source. Vet Rec 2009; 5777–8.
40. Jakab Z. Pandemic 2009–10. ECDC's future look and risk assessment. Briefing to the Swedish Presidency Informal Council, Jönköping, Sweden, July 6th 2009. Speaking notes. Available from: http://ecdc.europa.eu/en/press/news/Documents/0907_ZJ_Pandemic_2009_2010_Future_Look_and_Risk_Assessment.pdf . Presentation available from: http://ecdc.europa.eu/en/press/news/Documents/0907_ZJ_Presentation_on_the_2009_2010_Pandemics.ppt
41. Jamieson D, Honein M, Rasmussen S, Williams J, Swerdlow D, Biggerstaff M et al. H1N1 2009 influenza virus infection during pregnancy in the USA. Lancet 2009; July 29, 2009. doi:10.1016/S0140-6736(09)61304-0. Available from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)61304-0/abstract
42. Kelly H, Grant K. Eurosurveillance 2009 Aug ; 14(31) Available at : http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19288
43. Lipsitch M, Riley S, Cauchemez S, Ghani AC, Ferguson NM. Managing and Reducing Uncertainty in an Emerging Influenza Pandemic. NEJM. 2009. doi 10.1056/nejmp0904380 Available from: http://content.nejm.org/cgi/reprint/NEJMp0904380.pdf
44. Maines TR et al. Transmission and Pathogenesis of Swine-Origin 2009 A(H1N1) Influenza Viruses in Ferrets and Mice. Science 2009. Published online July 2 2009. Abstract available at: http://www.scienceonline.org/cgi/content/abstract/1177238
45. McGeer A, Green KA, Plevneshi A, Shigayeva A, Siddiqui N, Raboud J et al. Antiviral therapy and outcomes in influenza requiring hospitalisation in Ontario. Canada. Clin Infect Dis 2007 Dec 15;45(12):1568-75
46. Munster VJ et al. Pathogenesis and Transmission of Swine-Origin 2009 A(H1N1) Influenza Virus in Ferrets. Science 2009. Science. 2009 Jul 24;325(5939):481-3 Published online July 2 2009. Abstract available at: http://www.scienceonline.org/cgi/content/abstract/1177127
47. Nava GM, Attene-Ramos MS, Ang JK, Escorcia M. Origins of the new influenza A(H1N1) virus: time to take action. Eurosurveillance 2009; 14(22). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19228
48. New York City Department of Health and Mental Hygiene. Results of Survey, June 10th 2009. Available from: http://www.nyc.gov/html/doh/html/pr2009/pr041-09.shtml

49. Newman AP, Reisdorf E, Beinemann J, Uyeki TM, Balish A, Shu B, et al. Human case of swine influenza A(H1N1) triple reassortant virus infection, Wisconsin. Emerg Infect Dis. 2008 Sep;14(9):1470-2.
50. Nicoll A, Ciancio B, Tsolova S, Blank PR, Yilmaz C. The scientific basis for offering seasonal influenza immunisation to risk groups in Europe. Eurosurveillance. 2008;13(43). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19018
51. Nishiura H, Wilson N, Baker M. Estimating the reproduction number of the novel influenza A virus (H1N1) in a Southern Hemisphere setting: preliminary estimate in New Zealand. New Zealand Med J 2009;122, No. 1299. Available from: http://www.nzma.org.nz/journal/122-1299/3722/
52. Norwegian Institute of Public Health Planning assumptions for Influenza A(H1N1) September 2009 http://www.fhi.no/eway/default.aspx?pid=233&trg=MainLeft_6129&MainArea_5661=6129:0:15,5004:1:0:0:::0:0&MainLeft_6129=5544:79652::1:6130:7:::0:0
53. Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans. N Engl J Med 2009;360 (doi 10.1056/NEJMoa0903810). Available from: http://content.nejm.org/cgi/content/full/NEJMoa0903810?resourcetype=HWCIT
54. Olsen CW, Karasin AI, Carman S, Li Y, Bastien N, Ojkic D, et al. Triple reassortant H3N2 influenza A viruses, Canada, 2005. Emerg Infect Dis. 2006;12(7):1132–5.
55. Public Health Agency of Canada 2009. Surveillance. Pandemic (H1N1) 2009 outbreak epidemiological update. Available from: www.phac-aspc.gc.ca/alert-alerte/swine-porcine/surveillance-eng.php.
56. Secretaria de Salud Mexico. Situación actual de la epidemia. Available from: http://portal.salud.gob.mx/descargas/pdf/influenza/situacion_actual_epidemia_250609.pdf.
57. Thompson WW, Shay DK, Weintraub E, Brammer L, et al. Influenza-associated hospitalizations in the United States. JAMA 2004 Sep 15;292(11):1333–40.
58. Trifonov V, Khiabanian H, Greenbaum B, Rabadan R. The origin of the recent swine influenza A(H1N1) virus infecting humans. Euro Surveill. 2009;14(17):pii=19193
59. UK Cabinet Office and Department of Health. Swineflu UK Planning Assumptions September 2009 http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_104843.pdf
60. United States HHS Assessment of the 2009 Influenza A (H1N1) Outbreak on Selected Countries in the Southern Hemisphere August 2009. Available from: http://www.flu.gov/professional/global/southhemisphere.html
61. Van Reeth K, Nicoll A. A human case of swine influenza virus infection in Europe – implications for human health and research. EuroSurveill. 2009;14(7):pii=19124. Available from: http://www.eurosurveillance.org/images/dynamic/EE/V14N07/art19124.pdf
62. Weisfuse I. Presentation to ECDC on Outbreak of Influenza A(H1N1)v in New York. Webcast available from: http://ecdc.europa.eu/en/press/Pages/ECDC_Webcast.aspx
63. Weifuse I. Personal communication (e-mail). 8 July 2009.
64. WHO. Pandemic influenza preparedness and response. WHO guidance document April 2009. Available from: http://www.who.int/csr/disease/influenza/pipguidance2009/en/index.html
65. WHO. Global surveillance during an influenza pandemic April 2009. Available from: http://www.who.int/csr/resources/publications/swineflu/surveillance/en/index.html
66. WHO. Media Briefing Dr Keiji Fukuda, Assistant Director-General for Health Security and Environment, World Health Organization May 9th 2009. Available from: http://www.who.int/mediacentre/swineflu_presstranscript_2009_05_04.pdf
67. WHO. Situation Report No 58. July 7th 2009. Available from: http://www.who.int/csr/don/2009_07_06/en/index.html
68. WHO. Viruses resistant to oseltamivir (Tamiflu) identified. Available from: http://www.who.int/csr/disease/swineflu/notes/h1n1_antiviral_resistance_20090708/en/index.html
69. WHO. Virtual press conference July 7th (transcript). Available from: http://www.who.int/mediacentre/Pandemic_h1n1_presstranscript_2009_07_07.pdf
70. WHO. Considerations for assessing the severity of an influenza pandemic WER 29 May 2009; vol. 84:(22)197–202. Available from: http://www.who.int/wer/2009/wer8422.pdf
71. WHO. Summary report of a High-Level Consultation: new influenza A (H1N1) May 18th 2009. Available from http://www.who.int/csr/resources/publications/swineflu/High_Level_Consultation_18_May_2009.pdf
72. WHO. Human infection with pandemic (H1N1) 2009 virus: updated interim WHO guidance on global surveillance. 10 July 2009. Available from: http://www.who.int/csr/disease/swineflu/WHO_case_definition_swine_flu_2009_04_29.pdf
73. WHO Human infection with pandemic A (H1N1) 2009 influenza virus: clinical observations in hospitalized patients, Americas, July 2009 – update Weekly Epidemiological Report 2009 84: 305-8 http://www.who.int/wer/2009/wer8430.pdf
74. WHO Preparing for the second wave: lessons from current outbreaks Pandemic (H1N1) 2009 briefing note 9 http://www.who.int/csr/disease/swineflu/notes/h1n1_second_wave_20090828/en/index.html
75. WHO Preparing for the second wave: lessons from current outbreaks Pandemic (H1N1) 2009 briefing note 9 http://www.who.int/csr/disease/swineflu/notes/h1n1_second_wave_20090828/en/index.html
76. WHO Pandemic Update 66 September 18th http://www.who.int/csr/don/2009_09_18/en/index.html
77. Surveillance for the 2009 pandemic influenza A (H1N1) virus and seasonal influenza viruses - New Zealand, 2009.

MMWR Morb Mortal Wkly Rep. 2009 Aug 28;58(33):918-21.
78. Human infection with pandemic A (H1N1) 2009 influenza virus: clinical observations in hospitalized patients, Americas, July 2009 - update. Wkly Epidemiol Rec. 2009 Jul 24;84(30):305-8.
79. Centers for Disease Control and Prevention. FluView – 2008-2009 Influenza Season Week 35 ending September 5, 2009. Available from: http://www.cdc.gov/flu/weekly/weeklyarchives2008-2009/weekly35.htm
80. Surveillance for the 2009 pandemic influenza A (H1N1) virus and seasonal influenza viruses - New Zealand, 2009. MMWR Morb Mortal Wkly Rep. 2009 Aug 28;58(33):918-21.
81. L Finelli LB, L Blanton, S Epperson, R Dhara, A Fowlkes, et al. Update: Influenza Activity --- United States, April--August 2009. MMWR Morb Mortal Wkly Rep. 2009;58(September 10, 2009 / (Early Release);):1-4.
82. Hanshaoworakul W, Simmerman JM, Narueponjirakul U, Sanasuttipun W, Shinde V, Kaewchana S, et al. Severe human influenza infections in Thailand: oseltamivir treatment and risk factors for fatal outcome. PloS one. 2009;4(6):e6051.
83. Surveillance for pediatric deaths associated with 2009 pandemic influenza A (H1N1) virus infection - United States, April-August 2009. MMWR Morb Mortal Wkly Rep. 2009 Sep 4;58(34):941-7.
84. Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, Hernandez M, Quinones-Falconi F, Bautista E, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. N Engl J Med. 2009 Aug 13;361(7):680-9.
85. Kelly H, Grant K. Interim analysis of pandemic influenza (H1N1) 2009 in Australia: surveillance trends, age of infection and effectiveness of seasonal vaccination. Euro Surveill. 2009;14(31).
86. Nicoll A, Ciancio B, Tsolova S, Blank P, Yilmaz C. The scientific basis for offering seasonal influenza immunisation to risk groups in Europe. Euro Surveill. 2008 Oct 23;13(43).
87. McGeer A, Green KA, Plevneshi A, Shigayeva A, Siddiqi N, Raboud J, et al. Antiviral therapy and outcomes of influenza requiring hospitalization in Ontario, Canada. Clin Infect Dis. 2007 Dec 15;45(12):1568-75.
88. Vaillant L, La Ruche G, Tarantola A, Barboza P. Epidemiology of fatal cases associated with pandemic H1N1 influenza 2009. Euro Surveill. 2009;14(33).
89. WHO. Recommended composition of influenza virus vaccines for use in the 2010 southern hemisphere influenza season. Available at: http://www.who.int/csr/disease/influenza/200909_Recommendation.pdf

Contact for further information and comment: PHE.H1N1v@ecdc.europa.eu (preferably marked in the subject field "Interim Risk Assessment").