ECDC RISK ASSESSMENT

Pandemic H1N1 2009

Version 6 - 6 November 2009

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Stockholm, November 2009

What's new or different in this update?

This update is informed by the first experiences from this autumn in Europe and North America as well as further analyses from the Southern Hemisphere's temperate countries during their winter season.

It also includes:

- details of the clinical experience of people who are becoming severely ill;
- the first adjusted planning assumptions for European countries not significantly affected by the earlier wave;
- the basic parameters of the pandemic, drawing on work undertaken with WHO and ECDC Advisory Forum;
- confirmation that many older people possess prior immunity, but that those who are not immune are more at risk of severe disease than any other age group;
- more information on the extent of asymptomatic and very mild cases and;
- first estimates of the relative risk for those who, if they have certain risk factors, become severely ill with this infection (pregnant women, people with asthma and other chronic respiratory diseases and massively obese people).

Executive summary

This update of ECDC pandemic risk assessment for Europe is based on data and analyses available in early November 2009. It draws on the experience in European countries, North America and the Southern Hemisphere's temperate countries, which have already passed through a winter with the new virus.

After transmitting heterogeneously but at low levels over the summer in European countries, epidemics of the pandemic virus are now affecting almost all EU countries. At this stage, it cannot be predicted exactly how intense the peaks of transmission will be. However, in this update, ECDC has issued reasonable worse case planning assumptions (see Figure 7, pg 14) to assist Member States that were not significantly affected by the first wave over the summer in their final preparations. It is important not to see these as predictions of what will happen.

All indications are that this pandemic will be a significant health event for European countries and will put stress on some health services, especially hospitals and their intensive care capacity. However the same experience shows that well prepared health care services should be able to cope and there should be no special strain on the essential services outside the health sector if they have undertaken robust business continuity planning.

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

- Europeans are being affected by transmission waves earlier in the season than 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 a minority of 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 are taking place they are resulting in more cases at once;
  - there is 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 are experiencing the highest rates of severe disease and death of any age group;
  - the spectrum of severe disease includes cases of primary viral pneumonia causing severe acute respiratory distress syndrome (ARDS); this is difficult to manage and will put special strain on intensive care services
  - secondary bacterial infection may be less prominent than usual, except in children;
  - deaths in adults are occurring at a considerably younger age than normally seen with seasonal influenza;
  - there are many asymptomatic or very mild infections.
- Because of the large number of cases occurring at once, it is important that they are dealt with at home or in primary care if hospitals are not to be overwhelmed.
- If only a small proportion of cases result in severe illness that will still be enough to stress some hospital healthcare systems, especially intensive care units. A number of Member States have expanded their intensive care services accordingly.
- 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, following that, 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 (although the individual risk of a pregnant woman experiencing severe disease is low) and young children (younger two years of age).
- From Southern Hemisphere and American data it is estimated that the risk of an infected person requiring intensive care rises if they have a series of well recognised risk factors: pregnancy (ten fold rise), asthma or other chronic respiratory disease (three fold), massive obesity (six fold). (In all these cases, the comparison is with a person without any risk factors.)
- 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. These comprise between 20 and 30% of the deaths attributed to influenza.

- The number of deaths due to this pandemic may be similar to what is seen in some ordinary influenza seasons, though they will be in different groups of people than usual.
- The number and proportions of infected 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 completed.
- Almost all the isolates of the pandemic viruses analysed 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.
- Although the current seasonal influenza vaccine contains a component effective against another A(H1N1) virus, it 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 season. The experience in the Southern Hemisphere is that the pandemic A(H1N1) influenza has, on the whole, reduced the proportion of other influenza A and B viruses and entirely replaced the seasonal A(H1N1). There are some other influenza A viruses circulating, notably A(H3N2), and there remains a possibility of influenza A(H3N2) and B epidemics early in 2010 when the pandemic waves have passed .

There remain a number of important areas of uncertainty or topics where trends need a degree of quantification. These include:

- **the extent of asymptomatic infections;**
- **the absolute level of risk of severe outcome for healthy people and those in most of the risk groups and;**
- **the exact degree of effectiveness of pharmaceutical countermeasures such as antivirals.**

ECDC will work with Member States, other European Agencies–notably EMEA and EFSA, the Commission, WHO and its other international partners to gather more information to update this risk assessment at intervals.

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.

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. Last revision, 25 September 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 over the summer, the analyses of the pandemic waves in countries in the Southern Hemisphere during their winter and the second wave now affecting Europe and North America. 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.

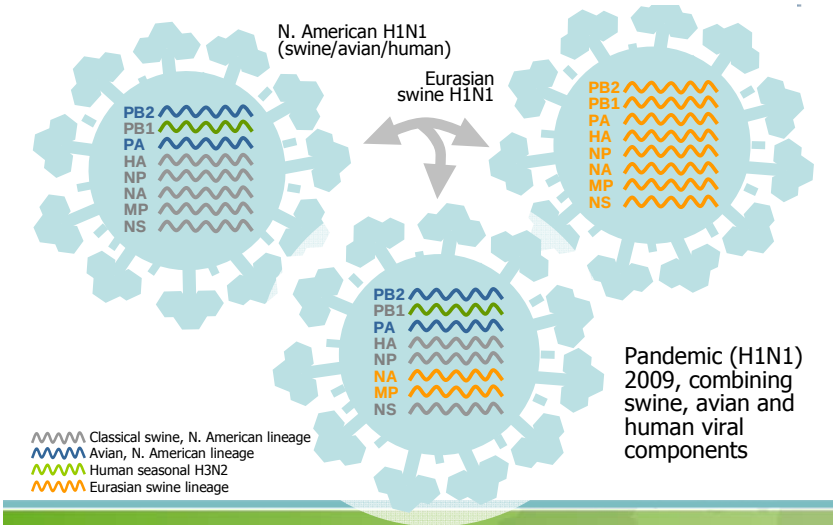
Risk assessment

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 [1–3].

The basic genetic structure of the virus has been described and this information is available through publicly accessible websites [4–6]. 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)[5,7,8].

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 [7, 8]. However, those infections have not transmitted efficiently from human to human. In contrast, this new virus is transmitting efficiently from human to human*. Since the disease spread widely to all continents it met WHO's predetermined criteria for a pandemic influenza strain and is a human influenza†[9]. The infection has been global for some time [10].

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 [11]. Pandemic influenza A(H1N1) 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*'[12,13] (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, the Southern Hemisphere and 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 pandemic virus, what can and cannot initially 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

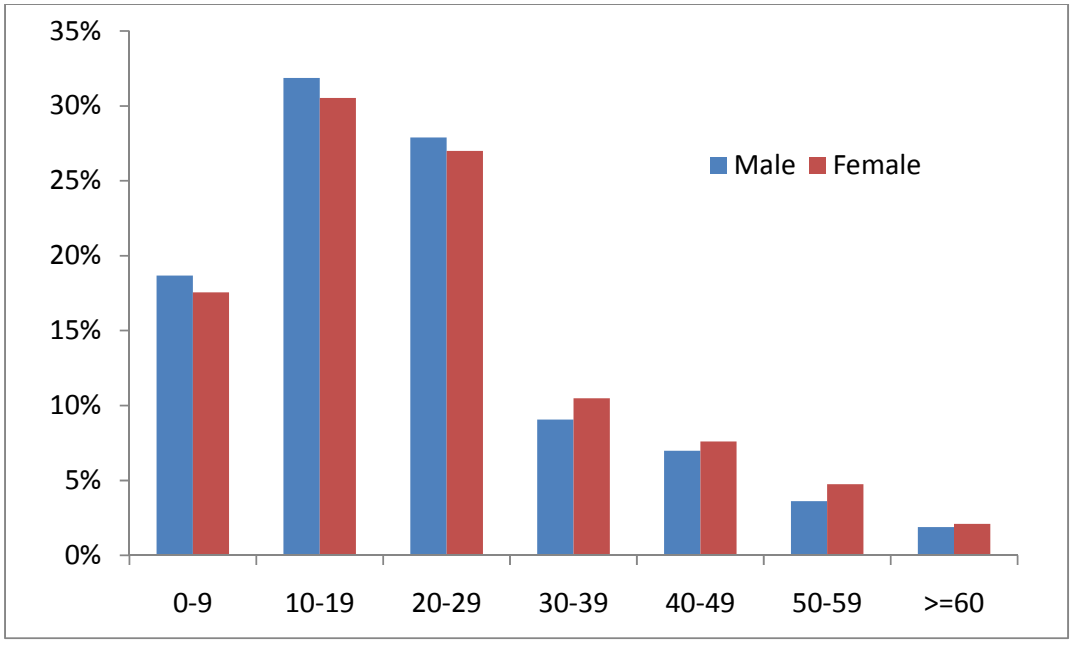
- Antigenic type and phenotype.
- Prior immunity in population.
- Resistance to antivirals.
- Age-groups and clinical groups most affected.
- Age-groups with most transmission.
- Clinical attack rates.
- Pathogenicity (case-fatality rates).
- 'Severity' of the pandemic.
- Precise parameters needed for 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.
- Exactly how safe are pharmaceutical interventions?

2.1 Basic epidemiology and basic parameters

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 [14–16]. There is a marked underrepresentation of infections in people over 65 years of age, who made up only 2% of the initial 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 [14-17] (Figure 3).

Figure 3: Distribution by age and gender of individual case reports of influenza A(H1N1)v infection, 28 EU/EEA countries, from 19 April–22 September 2009 (n=9813)



2.1.2 Prior Immunity

Broadly speaking, males and females are equally affected [18]. However, the age pattern is more than could be explained by initial case findings focusing on returning travellers in the 20–29-year-old age group and secondary spread in schools [15]. There are consistent serological laboratory results indicating that older people are less affected due to some enduring immunological memory of an earlier influenza A(H1N1) infection with a similar phenotype [19].

In Finland, a retrospective seroprevalence analysis of more than 1000 serum specimens collected in 2005 has been carried out to determine the presence and level of cross-reactive anti-pandemic 2009 H1N1 virus-specific antibodies. Haemagglutination inhibition (HI) analysis revealed that 15–20% of individuals born from 1930–1944 have detectable anti-pandemic H1N1 virus-specific antibodies. The prevalence of antibodies is higher in older generations and individuals born from 1920–1929 and from 1909–1919 show 57% and 96% seroprevalence, respectively. It is noteworthy that in the oldest generations (born from 1909–1929), approximately 50% of the seropositive individuals have relatively high cross-reactive antibody levels (HI titer ≥40). These data indicate that infections caused by the Spanish flu and its descendant viruses are likely to have given immunity against the present influenza A(H1N1)v virus. This is supported by the epidemiological findings in Europe and elsewhere (Figure 3) from all around the world that individuals presently older than 65 years of age are underrepresented among those who have contracted the pandemic 2009 virus*.

The relatively low attack rates overall for a pandemic (see Figure 6) and the distinct age-distribution are consistent with significant background levels of immunity in the adult population that increases with age. Hence clinical attack rates are twice as high in people under 16 years than in older people. This is also consistent with serological information from Australia as well as the studies in Finland. The limited immunity in younger adults is considered to arise from earlier exposure to the seasonal H1N1 virus while the higher levels in older adults due to exposure to the pre-1957 seasonal H1N1 virus (which was replaced by the 1957 pandemic virus).

2.1.3 Basic parameters†

Incubation period (the period from exposure to symptoms appearing): The indications are that the incubation period is little different from other human influenza though the distribution may have a longer tail than is usually observed; the results to date are a median of 1.5 to 2 days with a range of 1–7 days [20].

Generation time – serial interval (the interval between successive generations of infection): Between 2.5 and 3 days.

Reproduction number (R_0) (the average number of secondary infections caused by an index case): There have been a number of estimates for this ranging from 1.1 to 1.8 but with higher values observed in groups with close proximity, notably in school settings [21].

At the early stages of the pandemic during high susceptibility rates in populations, the basic reproduction number ranged from 1.4–1.6 in Mexico [22] and 1.2–1.7 in Peru [23] to 1.80–2.15 in New Zealand [21]. Higher values have been observed in countries where transmission is intense [14,23,26], with even higher figures in some closed communities, such as schools[13]. Lower values of what is then called the "Effective Reproduction Number" are observed in populations which have prior immunity, have already experienced significant waves of pandemic or after effective vaccination uptake. The derived reproduction number also depends on the modelling approach used; for example, analysis based on confirmed cases in Australia in the period of exponential growth of the pandemic (i.e. the second half of May 2009) indicated a reproduction number of 2.4 (95% CI: 2.1-2.6), but when undetected transmission was also taken into account, this estimate was reduced to 1.6 (95% CI: 1.5-1.8) [24].

Secondary attack rates (the percentage of people showing clinical disease among close contacts in home and other enclosed settings): These have ranged from 7–13%, though it must be noted that because of mild and asymptomatic infections true secondary infection rates may be considerably higher.

Proportions of symptomatic and asymptomatic infections: For reasons mentioned above and in section 2.2.2 (Asymptomatic and mild cases), this may be especially difficult to determine for this pandemic.

Period of infectivity: This has yet to be determined. There are anecdotal reports of detection of expressed virus through polymerase chain reaction (PCR) beyond symptomatic periods, but detection of virus by such sensitive tests does not necessarily imply infectiousness. With a mild infectious disease, decisions on exclusion periods need therefore to be undertaken with a degree of pragmatism and exercising judgment [25].

* For further information: Professor Ilkka Julkunen at National Institute for Health and Welfare (THL), Finland (ilkka.julkunen@thl.fi).

† This section especially draws on a review undertaken by the World Health Organization

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. other than by droplets from coughing and sneezing and direct and indirect contact with respiratory secretions from infected persons [26]. There is no evidence suggesting unusual transmission routes for influenza and no reason to suggest transmission through food [27].

2.2.2 Spectrum of disease

Asymptomatic and mild cases

The finding of test positive cases without symptoms in contacts of known cases—during field epidemiology studies and serological findings—have demonstrated that there are numerous asymptomatic cases in this pandemic. This is seen for seasonal influenza and all pandemics. However, a notable feature of this pandemic is the numbers of mild cases that do not fit classical case definitions of influenza-like illness (ILI) or even acute respiratory infections (ARI). This is also suggested by baseline data from clinical trials in Australia [28]. Hence the precise proportions of asymptomatic cases among all infections are going to be more difficult to determine than usual (Figure 5). Equally, clinical attack rates will be exceptionally difficult to determine and highly sensitive to the case definition used.

Uncomplicated mild disease—clinical features

Among the cases reported early on, the only notable clinical feature that differs to date from seasonal influenza is seen in some reports of more gastroenteric symptoms than are common for seasonal influenza [29]. But these gastrointestinal symptoms have almost always been accompanied by other more usual signs of influenza. The distribution of symptoms in Europe is similar to that described from the USA, with the proportion of patients reporting gastrointestinal symptoms being around 14% [15].

Severe disease—clinical features

A considerable amount of data have now become available on the clinical characteristics of the severe cases of influenza A(H1N1)v [16, 30–33] and was recently reviewed at a global consultation organised by WHO[34].

The median interval between symptoms onset and hospital admission varied between six days in Mexico and four days in Canada [31,35]. Delay in seeking care and especially in the late use of antivirals—or not using antivirals at all—was associated with a poor outcome [34]. Almost half of 722 reported cases requiring intensive care unit (ICU) admission in New Zealand and Australia had a distinct acute respiratory distress syndrome (ARDS) or viral pneumonitis that is unusual for seasonal influenza. Pathological investigation indicates diffuse alveolar damage, haemorrhagic interstitial pneumonitis with lymphocyte proliferation and few neutrophils, which are consistent with viral pneumonitis and ARDS.

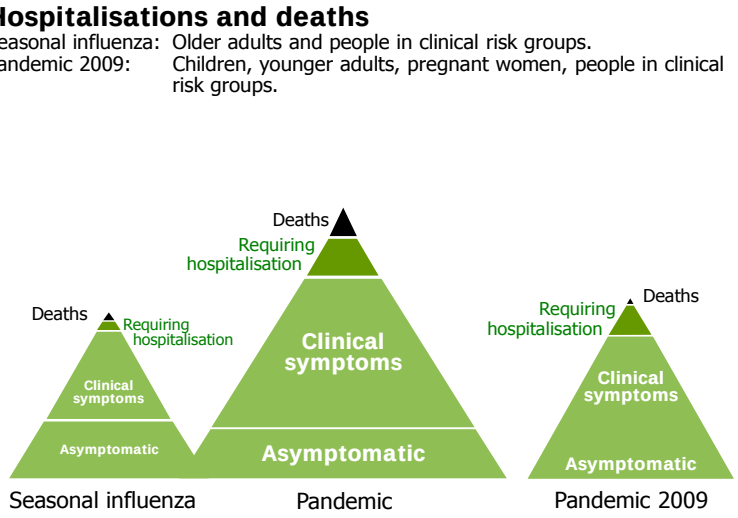
Supra-infection (secondary infection) with bacteria and bacterial pneumonias has been seen but is less common than in seasonal influenza. The WHO review meeting reported that supra-infection with bacteria has been documented in post-mortems in the USA and Canada. In New Zealand and Australia, 20% of cases admitted to ICU had secondary bacterial pneumonia. This is very similar to the data reported from Canada, where 24% of ICU cases had evidence of bacterial pneumonia. The most frequently isolated pathogens were *Staphylococcus aureus* and *Streptococcus pneumoniae*. Nosocomial (healthcare-associated) infections, such as ventilator-associated pneumonia, have been identified in critically ill cases with a prolonged hospital stay. Multiple pulmonary emboli have been observed in several very severe cases in patients admitted to ICUs with refractory ARDS in the USA.

These viral pneumonias and ARDS are difficult to manage and ventilate and can require highly specialised care. The most common cause of death in these cases is progressive organ failure [36]. 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 [37].

In various countries, extracorporeal membrane oxygenation (ECMO) has been used to treat patients with ARDS not responding to mechanical ventilation. The largest published experience comes from Australia and New Zealand [38]. The use of ECMO very much depends on its availability. In Australia and New Zealand, it was used at a rate of 2.6 cases per million population. A similar incidence of ECMO use in Europe would mean a rough estimate of 1300 cases during the 2009/10 winter. The median age of patients treated with ECMO in Australia and New Zealand was 34.4 years. Among the 68 cases observed, many had pre-existing conditions of which the most common were obesity (BMI>30) present in 50% of cases, followed by asthma (28%) and diabetes (15%). A secondary bacterial infection was identified in 28% of cases. The majority of the patients receiving ECMO survived (mortality rate was 21%). This is lower than the mortality rate observed for patients receiving ECMO for other reasons. Data on the effectiveness of ECMO treatment are difficult to obtain as it would be unethical to study a

control group of patients with similar clinical severity not receiving ECMO. However the positive outcome of the majority of patients requiring ECMO suggests that the treatment is likely to have reduced mortality.

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



*2.2.3 Clinical attack rate**

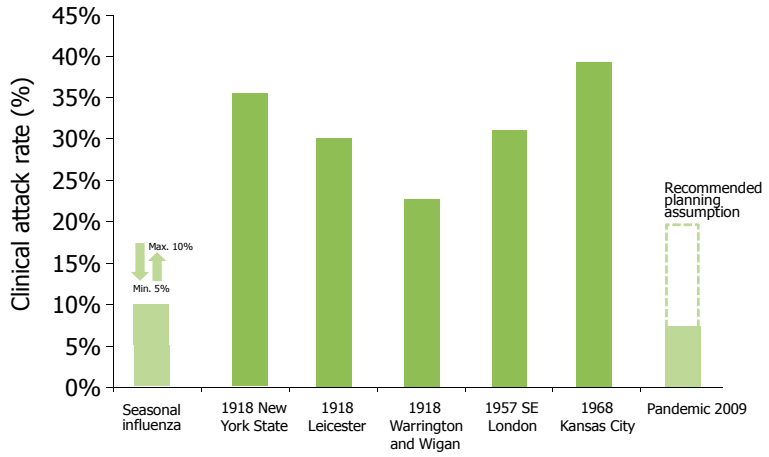
In previous pandemics it was unusual to observe population clinical attack rates of less than 20%, while for seasonal influenza, rates are usually between 5 and 10% [39]. However, this pandemic is unusual because of the prior immunity, especially in older people. Because of the mild nature of many cases (see Figure 5) clinical attack rates are hard to determine and vary from study to study. One using ILI as a criterion will result in a low rate, while one including more mild disease will result in higher figures. Experience from the Southern Hemisphere, where there were stringent criteria, resulted in low rates of 10% or less [30]. In a study conducted in Mexico, a figure of 30% was observed in one community [13]. While lower figures have been observed in North America—notably in New York City where a telephone survey in May gave a figure of 7% [40]—this transmission took place in the Northern Hemisphere's spring, 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 6). An estimate of the attack rate of clinical infections in New Zealand was 8% for the 2009 season which rises to 11% if assumptions are made for asymptomatic infections [26]. This is little different from a normal influenza season [30,39,41,42].

In Europe, higher clinical attack rates were observed in focal outbreaks in closed communities. In school outbreaks in the UK and France, figures of around 30 and 50% have been reported [43,44]. As is the case with other human influenza infections, there will probably be many mild and asymptomatic cases [15,39]. Certainly in New York most of those affected did not consult a doctor [45].

This notwithstanding, for planning purposes it is safest to assume population attack rates of up to 20% in the first year of the pandemic (planning assumptions represent reasonable worst-case scenarios). Attack rates will naturally be considerably lower during second waves in European localities which have already experienced significant first waves over the summer.

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

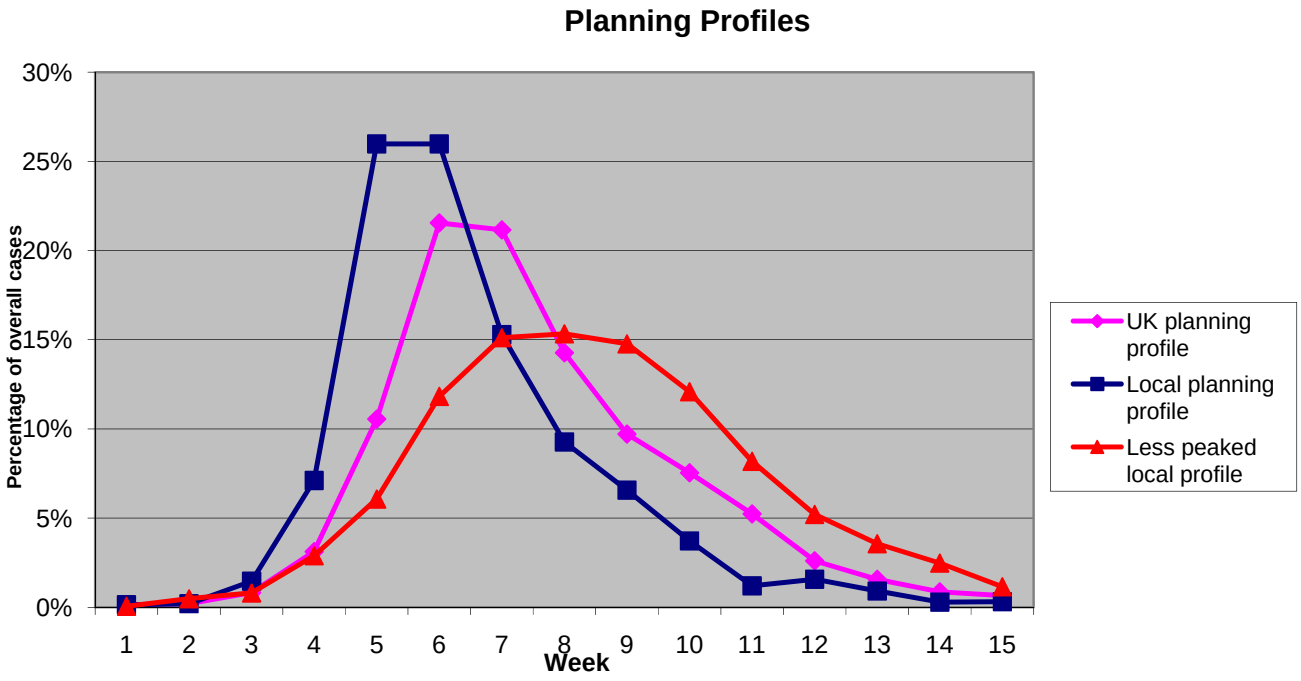
* Technically, the three 'rates' (clinical attack, hospitalisation and case fatality rates) should be called 'ratios' as they are proportions and do not have a time component as all rates should. The 'clinical attack rate' is the proportion of the population that is infected and has symptoms (i.e. asymptomatic 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.



2.2.4 The pattern of epidemics

There is no reason to expect a different epidemic curve for this pandemic than for others. Reasonable national and local planning curves are shown in Figure 6. It is important to note that again the height of the curve this is not a prediction. It is a reasonable worse case scenario. Also different considerations and lower peaks will apply in European populations where there were significant numbers of infections over the summer.

Figure 6: National and local planning profiles (UK). Proportion of local population becoming ill per week.



No pandemic has ever behaved in quite so neat a way as shown here. It is especially important to note the difference between national and local 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. Different European countries and different

parts of countries experience waves at different times. The duration of a winter wave is usually 16 weeks in all though it may be longer for large and countries with scattered populations. At times of low transmission, such as in the summer, the pattern of the waves has been especially sensitive to school closures.

For planning purposes, there are four components of a pandemic wave: Initiation, Acceleration, Peak and Decline. After the decline influenza can be expected to settle back down to its seasonal pattern again. The seasonal flu may be 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 were small outbreaks. It is not clear exactly when each country will enter their acceleration phase though by now (November 2009) most countries have done so.

2.2.6 Hospitalisation rates

The data from the United Kingdom up to early July (with an observed hospitalisation rate of 1–2%) is advantageous in 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 [18]. However, more recent estimates of case hospitalisation rates have limited value at the moment given the influence of various numerator and denominator biases that are likely to occur. Therefore only a selected number of suspected cases are currently laboratory tested and they mainly represent those hospitalised. However, for reasons previously stated, the overall number of clinical cases is unknown [17]. It is therefore best to rely on population estimates of hospitalisation rates. In the southern hemisphere, rates ranged from 9–25 per 100 000 population. Except for the UK figures above, data on hospitalisation rates are not yet available for Europe. Eventually the rates will be sensitive to the capacity of European hospital services, the ability of primary care to absorb care and traditions of populations to bypass primary care and go directly to hospital emergency departments. For these reasons, recommended planning assumptions will tend to be generous and higher than have been observed in the Southern Hemisphere (see section 2.2.8).

Age differences in hospitalisation

Some estimates are available from the United States where a population-based surveillance system network (the Emerging Infections Program (EIP)) is in place. In conjunction with the steep increase of outpatient visits for ILI observed between weeks 38 and 41/2009 in the US, hospitalisation rates for laboratory-confirmed influenza increased steeply. From September 1, 2009–October 17, 2009, cumulative rates for children aged 0–4 years and 5–17 years were 19–30 and 9–16 per 100 000 population, respectively. Rates for adults aged 18–49 years, 50–64 years and ≥ 65 years were 6, 6 and 5 per 100 000 population, respectively. These cumulative rates will further increase in the coming weeks as the current pandemic wave in the USA was still in the acceleration phase; however the age differential pattern is an important one for planning of hospital services.

Hospitalisation rates reported in countries in the Southern Hemisphere vary considerably and are difficult to compare given the different criteria used for hospital admission which, in turn, may reflect differences in the availability of services. In Australia (New South Wales), a total of 1 214 confirmed cases were admitted to hospital which gives an incidence of 17.2 per 100 000 population [46].

In Brazil, using a case definition of severe acute respiratory infection (SARI), the overall incidence of SARI was 3 per 100 000 inhabitants with two peaks: one in the group of up to five-year-olds (3.8 per 100 000) and one in the group of 20–29 year-olds (4.6 per 100 000) [47].

Epidemiological reports from Northern America indicate a significant burden on hospitals though relatively moderate number of morbidities. In the United States, among 13 217 influenza A(H1N1)v reported cases there were 1 082 (8.2%) hospitalisations [16], while in Canada, among 7 107 reported cases there were 1 441 (20.3%) hospitalisations [31].

Use of intensive care services

A crucial parameter for planning includes the requirements for critical or intensive care. Some information comes from the Southern Hemisphere (Australia and New Zealand). Based on the analysis of all (722) confirmed influenza A(H1N1)v cases requiring ICU admission over a period of three months (June–August 2009), the estimated incidence of ICU admission was 2.9 (95%C.I. 2.65-3.1) per 100 000 population [33]. For planning purposes, another approach is to consider that 15% of hospital admissions will require intensive care. However, because patients going into intensive care will stay in hospital longer, in prevalence surveys up to 25% of cases hospitalised for influenza may be found occupying intensive care beds on any given day[48]. There are important age differences for this, with younger children more rarely going into intensive care.

2.2.7 Case fatality rates (CFR)

Estimated rates are coming down and most estimates for industrialised countries are less than 0.02% [49]. Earlier published estimates are highly variable and reflect the various factors that can influence its measurement and its actual value including, among others, social and healthcare related factors [50]. An overall CFR of 0.6% was calculated based on deaths reported worldwide and analysed by an epidemic intelligence team. However, the range of CFR varied from 0.1–5.1% depending on the country [51]. In Mexico, case ascertainment 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 probably misleadingly high case fatality rate [52]. An indirect method gave a value of 0.4%[52] while initial estimates for the United States give a figure ranging from 0.5–1% [53]. This is somewhat above what is considered normal for seasonal influenza. In Europe, the initial figure was also around 1%, but again that was certainly an overestimate [18]. 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) [54]. This is not that different from what has been observed in modelling studies [55]. Given the seeming immunity to the pandemic strain in older age groups (whom 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. The mortality trend data from Australia shows little difference from their 2008 winter. In contrast, in the United States, the rates for deaths from influenza and pneumonia have risen steeply this autumn [56].

Of more relevance for public health planning are estimates of mortality per 100 000 population. The data available from the Southern Hemisphere (Oceania, South America and Africa/Indian Ocean) has been recently summarised in an editorial published in Eurosurveillance [57]. With a few outliers, population mortality was estimated to have been between 0.4 and 1.5 deaths per 100 000 population. The review by WHO gave a range of 0.2–1.4 per 100 000, with the high value (for Argentina) being an outlier and the next highest being 0.9 per 100 000 for Australia .

Data on mortality among severe cases has also recently become available. These were very similar in Australia/New Zealand and Canada (14% and 17% respectively) [31, 33], but higher in Mexico (41%) [35]. The study in Mexico was however smaller and a selection bias for the inclusion of the most severe cases might have occurred. This is due to the fact that the Mexican study was conducted in the six reference hospitals that specialised in the treatment of severe influenza cases. In the US, 7% of 272 hospitalised patients with confirmed pandemic influenza are known to have died [58].

Contrast with seasonal influenza

It remains the case that because influenza-associated deaths are in a younger population than usual and involve people who might normally be expected to die from seasonal influenza in such numbers (pregnant women, previously healthy people), these deaths are regarded as unusual and commented upon. For example, the number of children dying from pandemic influenza has risen steeply in countries experiencing their first pandemic wave, therefore age-specific mortality will be important to measure. Though calculations have yet to be undertaken, it is likely that the number of life years lost will be more than would be accounted for by seasonal influenza. Where attributable, mortality is normally focused on people in their 70s and older.

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 [39,49]. In both cases, the assumed rates of disease, hospitalisations and deaths declined in the light of data such as in this document. Working with a series of countries and advised by WHO specialists ECDC has produced some planning estimates for EU/EEA (Figure 7).

Figure 7: EU Reasonable worst-case planning assumptions for the 2009 pandemic first year to mid-May 2010

Planning assumptions to mid-May 2010: potential effects of A(H1N1) infection for the general population in countries and populations that have not experienced significant transmission in a first wave over the summer	
Clinical Attack Rate	up to 20% of population
Hospitalisation Rate	up to 100 per 100,000 population of whom up to 25% could require intensive care at any given time
Case Fatality Rate	up to 3 per 100,000 population
Peak Absence Rate	No different from what is seen in normal winters

Note: These estimates should not be used for predictions.

Some important points have to be made about these assumptions and are enlarged on in a supporting document. The clinical attack rate and the other rates will be lower in countries and populations that have not experienced significant transmission in a first wave over the summer. Also it has to be remembered that many of the disease episodes will be very mild and certainly will not need to be seen by doctors. The hospitalisation rate is higher than is observed but that reflects differing traditions on who goes to hospital in some European countries. Though the absenteeism rates will not be higher than usual, it should be remembered that in ordinary winters other respiratory viruses combine with influenza to put people off of work.

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. Strong evidence of this has recently become available from the Southern Hemisphere (Australia and New Zealand). Based on the analysis of all (722) confirmed influenza A(H1N1)v cases requiring ICU admission over a period of three months (June–August 2009), the estimated incidence of ICU admission was 28.7 (95%C.I. 26.5-30.8) per million inhabitants [33].

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; this is because patients going into ITU stay in hospital longer than those that are in for simple hospitalisation. An area that requires particular clarification is the position for children (see below).

Experience from the United States shows that, in contrast to seasonal influenza—when influenza hospitalisations are more common among the elderly—hospitalisations due to A(H1N1)v influenza are more common in those under the age of 18 years (44%) than in the group over the age of 65 years (5%) [16]. This observation suggests that hospitals should be well prepared with paediatric care facilities. In case these facilities are absent, proper adult care units can be adjusted for paediatric demand [59].

Christmas and New Year's holidays may represent a period of vulnerability for countries still experiencing waves in December if primary care services are less available in the holiday. This could present special burdens on emergency services and hospitals if they have to deal with people who would normally only go to primary care. Some European countries have planned for this.

2.2.9 Risk groups for hospitalisation, severe disease and death

There is a range of experience with the risk groups for severe disease since, as we move along, the spectrum of disease regarding clinical risk groups becomes more and more important. There are limited data as yet from Europe, but when considering mortality from influenza, the best estimates reflect 70–80% of deaths in people with chronic underlying conditions and pregnant women.

So far, there is only one large, published study that attempts to compare the prevalence of risk factors among severely ill pandemic influenza cases with the prevalence of the same risk factors in the general population. This study was conducted among all confirmed 2009 influenza A(H1N1)v cases requiring ICU admission in Australia and New Zealand. It showed that the following risk factors were much more frequent among cases with confirmed severe influenza disease than the general population (See Figure 8):

- Pregnant women (9% vs 1%)
- Obesity (defined as BMI greater than 35) (29% vs 5%)
- Asthma or other chronic pulmonary disease (33% vs 13%)

In New Zealand, another important finding showed that indigenous populations were at a higher risk of severe disease: For Pacific Islanders, 9.7% of their populace contracted severe disease versus 2.5% of the rest of New Zealand population and for the Maori the rates were 25% versus 13.6%. The accuracy of data concerning risk factors collected from influenza cases is likely to be better than the information from the general population. This may have led to an overestimation of the role of risk factors (ascertainment bias). Even taking into consideration the possible influence of bias, these findings represent the strongest available evidence pointing towards specific risk factors for severe A(H1N1)v influenza.

In addition, these findings are consistent with what has been reported so far from other parts of the Southern Hemisphere, US and Canada

- **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 [27]. 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 [60]. 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 [9,59].

- **Pregnancy**: There is consistent evidence showing that pregnancy is a risk factor for severe disease during pandemic H1N1 2009. In addition to the data described above from Australia and New Zealand, among 272 hospitalised patients in the USA, pregnant women represented 7% of cases and 16% of fatal cases [58]. A published study from the USA has identified pregnant women infected with influenza A(H1N1)v as being four to five times as likely to be hospitalised as pregnant women not suffering from infection, even though the absolute risk for infected pregnant women being hospitalised remains low (around 0.32 per 100 000). This is somewhat higher than the heightened risk noted for women experiencing seasonal influenza [61]. When considering the risk for going into intensive care, the relative risk rises to ten [62].
- **Age**: Children under the age of 15 have experienced higher rates of infection than other age groups and, as a consequence, this age-group also accounts for the largest proportion of hospital admissions in most of the available reports. In Australia and New Zealand, the highest age-specific incidence of ICU admission was among infants (0 to 1 year of age), whereas the highest number of ICU admission was among patients 25–49 years [33]. In the USA, a total of 95 deaths in children (0–17 years) associated with influenza A(H1N1)v virus have been reported to CDC[37]. 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 [37]. However, the children who died with no underlying condition were older than what is usually experienced with seasonal influenza [37]. It was also observed that hospitalised younger children without underlying conditions often experienced a short stay in hospital; far shorter than their adult counterparts.
- **Obesity:** The data from Australia, New Zealand and the United States indicate that obesity is a strong risk factor for severe A(H1N1)v influenza. However, it remains unclear whether this is only because of the high prevalence of co-morbidities in obese individuals. The analysis of hospitalised cases in the US seems to confirm the latter hypothesis. In a series of 100 adults admitted to hospital for confirmed A(H1N1)v influenza, 29 (29%) were obese, and 26 (26%) were morbidly obese; 26 of the obese patients (90%) and 21 of the morbidly obese patients (81%) had an underlying medical condition. The association of obesity and other underlying conditions seems less strong among children. Of 61 children, 18 were obese (30%); of the obese children, 12 (67%) had an underlying medical condition.

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) 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).

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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 [34,63]. 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%[55]. This is consistent with the fact that many older people are immune due to prior exposure to a similar virus in the 1950s or earlier [19] . **However, older people are more likely to be in clinical risk groups and, as might be expected, when one of the minority of older people who is susceptible becomes infected with influenza A(H1N1)v virus, they have a high likelihood of needing hospital care, stay in hospital longer and a higher case fatality rate than any other age group.** For this reason, when considering who is hospitalised for influenza on any particular day in a hospital, the age-pattern is more even than would be expected from the age pattern of cases seen in Figure 3 [19].

2.2.11 People without risk factors:

There are significant numbers of cases 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 [64–66]. In deaths reported to be attributable to or associated with the pandemic influenza in the UK (England), in the first ninety or so cases, 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%) (Chief Medical Officers Confidential Investigation of A(H1N1)v Deaths, Department of Health London, unpublished data).

The United States has published analyses concerning children based on the first 36 deaths. These findings showed 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. Moving back into the cases on intensive care units and then into people receiving conventional hospital care the proportion of cases without any clinical risk factors tends to increase.

2.3 Features of the virus

2.3.1 Genetic stability

To date, all of the isolates of the pandemic virus have shown little genetic variation and no indication of reassortment with other viruses [64,65,67].

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. Indeed, somewhere over 40 isolates of the pandemic virus have been reported resistant to oseltamivir. 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 [8]. 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 [8].

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) [4, 65,66,68].

2.3.4 Impact of seasonal immunisation

As indicated above, laboratory studies show some cross-reactivity in sera from older people. Viruses of the same subtype—A(H1N1)—have been responsible for seasonal influenza for several years, but that subtype is quite different from the current one. It is considered 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 nor increased risk of pandemic disease in the 2009 season [14]. 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 [19].

2.4 Severity of the pandemic in Europe

Many national authorities consider it important to have an assessment of the 'severity' of a pandemic so as to determine a proportionate response [50,69]. 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 5—25/10 000 [70]. The limited information to date for Europe (mostly from the UK) suggests similar rates [18]. Because of the seeming underrepresentation of older people among those infected, the overall fatality rate in Europe may be less or similar to a moderate influenza season, like 2008–09. However, age-specific rates are expected to show a very different picture, with higher mortality in younger age-groups. Also the absolute numbers of hospitalisations could be higher, especially because of the short hospitalisations of young children. Experience from Southern Hemisphere countries shows that particular pressures will be felt by hospital services , specifically: paediatric services, the services for critically ill patients who might benefit from intensive care, artificial ventilation and extracorporeal membrane oxygenation (ECMO) [71].
- **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 [51] . What will be more difficult in the autumn and winter in Europe is when there are steep local peaks of transmission, 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. A particular problem can arise when numbers of people bypass primary care and go to hospitals;

this happened for a short time in New York City [45,64]. If the pandemic waves in Europe extend to Christmas and the New Year, it will be important to ensure that primary care services extend through the holiday period in order to protect hospital services

- **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 in the winter that the pressure will come in Europe, and there is a need for final preparations in the healthcare sector for this season [61].

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). Severity will need to be monitored, especially given the possibility of the virus acquiring genetic material associated with pathogenicity or antiviral resistance in humans [71].

3 Areas of particular uncertainty

3.1 Mix of influenza and other viruses that will be circulating this coming 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 [53]. In Australia and New Zealand, there were contributions by both influenza A(H3N2) and the pandemic influenza A(H1N1), 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 and European national authorities that plans for immunising conventional risk groups with the seasonal vaccine go ahead in Northern Hemisphere countries [42,63]. 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.

In the Northern Hemisphere, the proportion of cases related to seasonal influenza A(H3N2) continues to decline in Asia (apart from China where significant numbers are still being reported) while the proportion related to influenza A(H1N1)v virus increases significantly [72]. The trend of supplanting seasonal influenza subtypes with pandemic influenza strain is evidently visible in Europe and United States, where in October, the percentage of influenza A(H1N1)v virus samples tested constituted over 80% in relation to other influenza subtypes† [73].

That said, what cannot be ruled out are late epidemics of A(H3N2) and B viruses in the late winter after the pandemic waves have passed.

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

The exact timing is becoming more possible to predict. This pandemic virus has been transmitting in Europe in the warmer months. A number of European countries experienced initiation phase outbreaks over the summer months despite it being the summer months [54]. Schools have been especially associated with outbreaks and equally transmission was blunted by the closure of schools over the summer. School amplification has now resumed [74]. Given the experience in the Southern Hemisphere, it was predictable that pandemic waves would affect countries and now a general West to East trend is noted. What remains uncertain is exactly how high peak attack rates will be though these will be lower where there has been prior transmission. 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 which are underway. It has been prudent of European countries to prepare for early pandemic waves, even if they do not eventually come until later in the autumn and winter [70,74]. Countries in their final

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

† See http://www.cdc.gov/h1n1flu/updates/international/map.htm

planning stages 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 being unavailable for work) [71,75] (see also section 2.2.4).

3.3 Shedding the virus and infectivity

As yet there are no published data on how long infected people shed the virus and the shorter period of 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 new estimates of relative, attributable risk or absolute risk from Europe. More is known about the risk for pregnant women [61]. 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.

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 [63]. Population data and especially age-specific data are not yet available for European countries.

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 and the collective experience of those treating cases with the pandemic strain point to the success of early treatment with oseltamivir in preventing severe outcomes [36,76].

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 [30]. 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 [37].

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

Late-November 2009 – if important changes take place these will be incorporated earlier.

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