ECDC INTERIM RISK ASSESSMENT

Pandemic (H1N1) 2009 influenza

21 August 2009

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Executive summary

This interim ECDC risk assessment for Europe points out that the 2009 pandemic influenza A(H1N1) 2009 virus will continue to transmit in a heterogeneous manner but at a low level over the summer in European countries. It is most likely that this will be followed by the proper first wave of a pandemic that will take place in the autumn and winter of 2009–10 and planning should be undertaken on that basis. Exactly what this will mean for Europe is unclear, though there are enough indications from the effects of the pandemic in temperate countries in the southern hemisphere that this will be a serious event for European countries and put particular stress on some health services, especially hospitals. Notable features of the pandemic to date:

- It is impossible to predict exactly when European countries will be affected but a proper first wave seems inevitable for the autumn. The experience in one country (the UK) suggests that countries could be affected considerably earlier in the autumn than happens with seasonal influenza.
- There is much that is similar between the pandemic A(H1N1) and the seasonal influenza that affects Europe each year. However, there are two important differences:
  – when the pandemic waves come to European countries they will result in many more cases at once;
  – there is an under-representation of older people in the pandemic, many, but not all, of whom seem to have some immunity against the pandemic virus (although those few older people that are affected experience the highest rate of severe disease and death of any age group).
- Most of those infected experience a mild self-limiting illness. However, as for seasonal influenza there are some people who experience more severe disease and some of these die despite medical care.
- 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 hospital healthcare systems.
- There are no reports of unusual presentations or 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 younger adults.
- The groups experiencing most of the severe disease, those in the *risk groups*, are people with chronic underlying medical conditions, pregnant women and very young children (under 2 years).
- As for seasonal influenza there are a few people without any known underlying condition and outside other risk groups who are experiencing severe disease.
- Cumulative clinical attack rates over the first major wave of infection in 2009–10 are expected to be in the range of 20% to 30%.
- A reasonable planning estimate for hospitalisation rates in Europe using the overall clinical attack rate as a base is in the in the range 1% to 2%. However, in the winter this seems to rise because of the presence of other respiratory infections.
- Initial experience from countries outside Europe indicates that without preparation this pandemic could severely stress healthcare systems, especially the hospital sector.
- Case fatality rates for Europe are not yet clear. The most accurate observed case fatality rate reported to date from the USA is 0.4%, while in Europe the observed rate in the earliest affected country is 0.3%. However, this is likely to be higher than the true figure which may at present be more in the range of 0.1% to 0.2% of all clinical infections.
- As yet, almost all the pandemic viruses have been sensitive to the antivirals known as oseltamivir and zanamivir (neuraminidase inhibitors) but they are resistant to the adamantanes (amantidine and rimantidine). There have been a few pandemic virus isolates that have been resistant to oseltamivir (though they remain sensitive to zanamivir).
- The current seasonal influenza vaccine which contains a component effective against another A(H1N1) virus is not effective against the new pandemic A(H1N1)v virus.
- It is too early to predict what the mix of pandemic and seasonal influenza viruses will be this autumn, although there will almost certainly be B influenza viruses as they do not compete with the A viruses.

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 as yet. It remains possible that the pandemic virus could acquire resistance to neuraminidase inhibitors or even become more pathogenic. 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 the temperate southern hemisphere countries.

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

Source, date and type of request

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

Specific question

Health implications for Europe of the pandemic (H1N1) 2009 influenza.

Consulted experts

Internal ECDC experts.

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 Prevention and Control (CDC), and official sources in a number of other affected countries including those in Europe.

ECDC assesses the overall evidence as weak at present as it comes mostly from early observations of the pandemic and reported cases. The proper first wave of the pandemic is only now being observed in the temperate southern hemisphere. 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 ratios (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 import 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 [3,24,4].

The basic genetic structure of the virus has been described and this information is available through publicly accessible websites [51,41]. 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 [41,12].

Figure 1. **Genetic origins of the pandemic (H1N1) 2009 virus combining swine, avian and human**
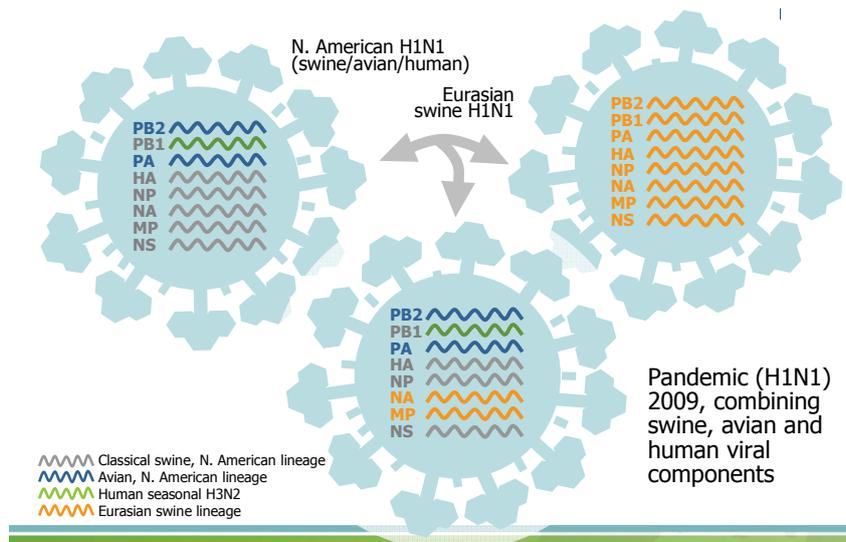
However, it is unclear whether the specific reassortment leading to the new virus took place in pigs or humans. In recent years occasional swine influenza infections in humans have been detected through surveillance of humans, especially in North America. Swine influenza viruses with genes from avian, human and swine influenzas have previously been circulating in pigs in the US, and have occasionally been transmitted to humans [47,43,53]. 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[1]. Since the disease has now spread widely to all continents, causing a number of deaths, it clearly meets WHO's criteria for a pandemic influenza strain and should be regarded as a human influenza[2] [56].

WHO and other international agencies are now calling the disease 'pandemic (H1N1) 2009'. The term 'swine flu' is inaccurate and confusing. A shorthand for the virus is influenza A(H1N1)v (where v indicates variant), which has been chosen 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.

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 causes severe infections and deaths in the region. However, human-to-human transmissions of A(H5N1) and other avian influenza have been very limited [14]. 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' [15,16,37,57] (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, but also from countries in the southern hemisphere experiencing the pandemic and now increasingly from European countries.

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[1] 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]

[2] 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:	What cannot be assumed:
Known knowns	**Known unknowns**
• Modes of transmission (droplet, direct and indirect contact)	• Antigenic type and phenotype
• Broad incubation period and serial interval	• Susceptibility/resistance to antivirals
• At what stage a person is infectious	• Age-groups and clinical groups most affected
• Broad clinical presentation and case definition (what influenza looks like)	• Age-groups with most transmission
	• Clinical attack rates
• The general effectiveness of personal hygiene measures (frequent hand washing, using tissues properly, staying at home when you get ill)	• Pathogenicity (case-fatality rates)
	• 'Severity' of the pandemic
	• Precise parameters needed for modelling and forecasting (serial interval, R_o)
• That in temperate zones transmission will be lower in the spring and summer than in the autumn and winter	• 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

The observed age distribution is unusual and different from seasonal influenza, being skewed towards younger age groups [46,17,6]. There is a marked underrepresentation of infections in people over 65 years of age, who make up only 2% of reported cases. In Europe, among the reported cases the 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 cases are in individuals under 30 years of age [46,50,6,17,18] (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 (n=6560)
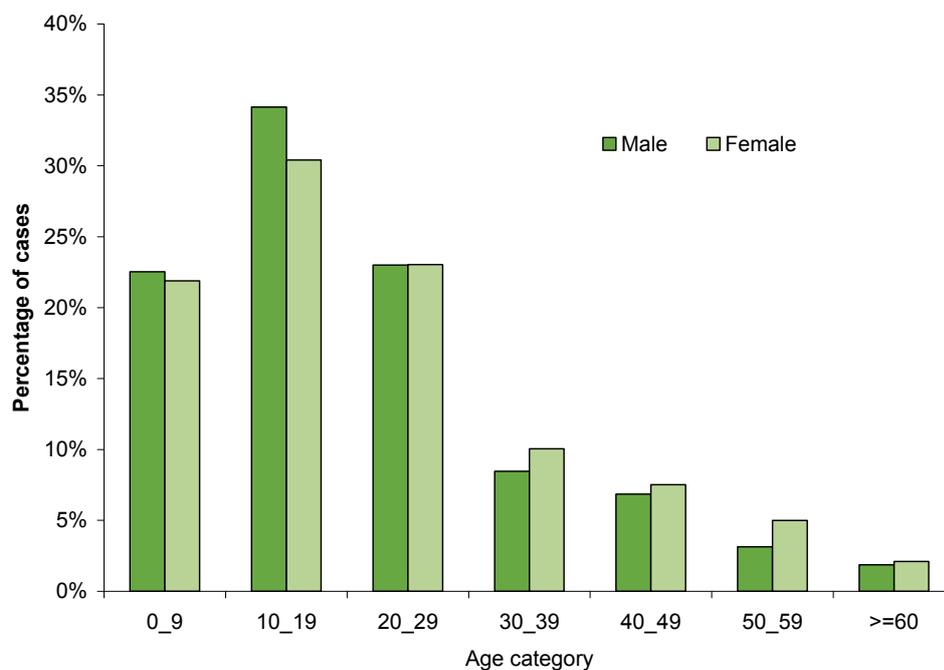
This is more than can be explained by initial case finding focusing on returning travellers in the age group of 20–29 year-olds, and secondary spread in schools [46,17]. There are also some laboratory results from serology consistent with a finding that older people may be less affected due to some enduring immunological memory of an earlier influenza A(H1N1) infection with a similar phenotype [5]. Males and females are equally affected [18].

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 [1]. There is no evidence suggesting unusual transmission routes for influenza and no reason to suggest transmission through food [34].

2.2.2 Spectrum of disease – clinical features
Among the simple cases reported early on, the only notable clinical feature that differs to date from seasonal influenza are some reports of more gastroenteric symptoms than are common for seasonal influenza [46]. But these gastrointestinal symptoms have always been accompanied by other more usual signs of influenza [46]. 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% [18]. There are also preliminary reports that the incubation period may have a longer tail than usually observed. The results to date are: median 3–4 days, range 1–7 days [58].

2.2.3 Asymptomatic cases
There are some indications of asymptomatic cases from contact tracing in Europe [18]. However, it will be some time before it is known what proportion of infected people develop the disease [26]. Two plausible assumptions based on previous experience are 33% and 50% of infections being asymptomatic [19,28]. A more precise figure will best be derived from planned serological studies.

Figure 4. **Seasonal influenza compared to pandemic — proportions of types of cases**
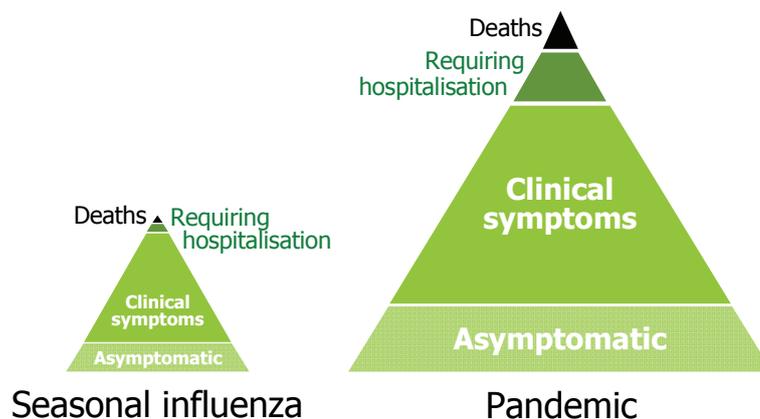
2.2.4 Ease of transmission – effective reproductive number
There have already been estimates of the basic reproductive rate (R[3]), which all lie between 1 and 2 (with some outliers); the range 1.4 to 1.6 being most probable [24]. As would be expected for a pandemic, this is higher than the value observed for seasonal influenza but in line with previous pandemics [15,29]. Effective reproductive number is being measured or monitored in some countries and values up to 2 have been observed in countries where transmission in intense, notably in southern hemisphere temperate countries [24,26,45], though higher figures should be expected in closed communities such as schools.

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[3] 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.

2.2.5 Clinical attack rate[4]

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% [28]. 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 30% as planning assumptions recognising that planning assumptions represent the reasonable worse-case scenarios [20,52].

Figure 5. Numbers affected in seasonal influenza epidemics and pandemics (overall clinical attack rate in previous pandemics)
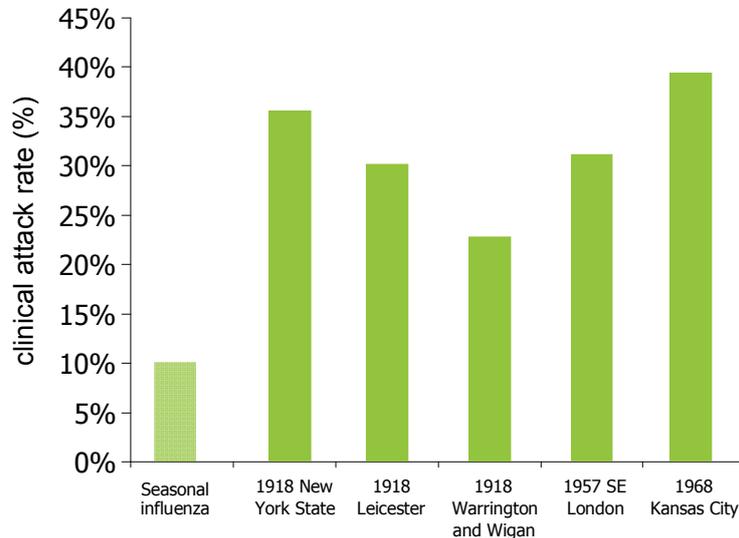
In a study conducted in Mexico, a figure of 30% was observed in one community [24]. While lower figures have been observed in North America, notably in New York City, where a telephone survey gave a figure of 7% [42], transmission took place in May 2009 in the northern hemisphere when the United States in particular was still in the initiation phase of its pandemic wave.

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[4] 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 6. Idealised national curve for planning, Europe 2009
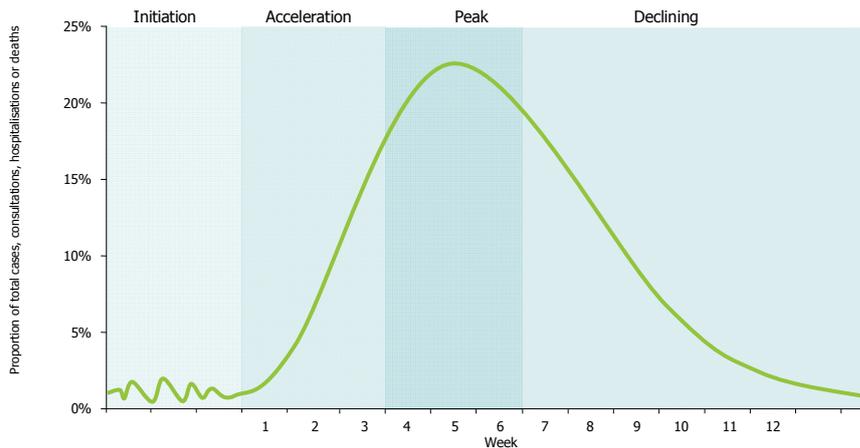
Single-wave profile showing proportion of new clinical cases, consultations, hospitalisations or deaths by week. Based on London, second wave 1918.

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 is happening in Europe in the summer and perhaps early autumn, when there are small outbreaks and 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 the United States, generally, attack rates have been lower than in Mexico, at around 7% to 10% at the population level in affected areas and 20% in confined outbreaks. This is no different from seasonal influenza [49,48,6,7,28]. 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).

In Europe focal outbreaks in closed communities observed attack rates have been higher. In school outbreaks in the UK and France figures of around 30% and 50% have been reported [31,27]. No serological data are yet available. As is the case with other human influenza infections, there will probably be many mild and asymptomatic cases [17,28]. Certainly in New York most of those affected did not consult a doctor [55].

2.2.6 Hospitalisation rate

As yet this is a difficult figure to derive for Europe. A rate observed from reported cases for the United States (11%) is correct but should not be used for planning, as it will be an overestimate because of the mild nature of most cases [6]. In some European countries, initial cases were offered isolation in hospital as a way of preventing onward transmission resulting in seeming high rates [18]. Many of those people would not have needed hospital care in normal circumstances. In making planning estimates for Europe, 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% [18]. The data for 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 [18]. 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, the 1–2% rate would seem 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 [36].

2.2.7 Case fatality rate (CFR)

This is difficult to estimate with great accuracy at this stage and it should anyway be remembered that it is a measure that is sensitive to social factors [62]. In Mexico, case ascertainment has favoured detecting patients with more severe illness, so a report of a CFR of just over 1% (119 deaths among 10 962 cases) gives a misleadingly

high case fatality rate [59]. An indirect method gave a value of 0.4% [24], while estimates for the United States give a figure of 0.5% to 1% [13]. This is somewhat above what is considered normal for seasonal influenza. In Europe, the initial figure is also around 1%, but that is again 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) [32]. This is not that different from what has been observed in modelling studies [24]. This rate will have been quite accurate given that the UK's initial policy of very active case 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 between 0.1% and 0.2% may 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. However, it needs to be borne in mind that because of this being a pandemic strain — and therefore many more people will be affected than for seasonal flu — it remains most likely that there will be higher numbers of actual deaths (and hospitalisations) than experienced in even a bad seasonal influenza winter.

2.2.8 Planning assumptions

From the above considerations, it is possible to revise previous generic planning assumptions and this has been done by two European countries [19,20].

Figure 7. Revised planning assumptions for the pandemic – first wave A(H1N1) 2009
Note: These figures should not be used for predictions

Clinical attack rate	30%
Peak clinical attack rate	6.5% (local planning assumptions 4.5% to 8%) per week
Complication rate	15% of clinical cases
Hospitalisation rate	2% of clinical cases
Case fatality rate	0.1% to 0.2% (cannot exclude up to 0.35%) of clinical cases
Peak absence rate	12% of workforce

These assumptions represent a reasonable worst case applying to one European country (the United Kingdom) with data available as of July 2009. They should not be used for predictions.

Courtesy of Department of Health, UK, http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_102892

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), 30 people were hospitalised because of needing care. Nineteen of the 30 patients had underlying chronic conditions, which have been in decreasing frequency: asthma or chronic obstructive airways disease, diabetes, immunocompromise, chronic cardiovascular disease (not simple hypertension), chronic renal failure, epilepsy (seizure disorders) and malignancy [7]. 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 [8]. The largest dataset reported to date (n=302) is based on deaths reported to CDC in the United States and this finds 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 [6].

- **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 as pregnant women overall, though the absolute risk for infected pregnant women being hospitalised remains low, at around 0.32 per 100 000 [37].

- **Young children:** There are no published studies of 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 [9].

- **Older people:** There are a number of analyses indicating that people of 65 years and older are noticeably underrepresented in reported infections and hospitalisations compared to what is seen for seasonal influenza [50,44]. Normally, in the United States people of 65 years and older would account for nearly 50% of hospitalisations with confirmed seasonal influenza, but with A(H1N1) 2009 the figure is less than 5% [6]. 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 [5]. However, as might be expected when one of the minority of older people who is susceptible is infected with A(H1N1) 2009, they seem to have a high likelihood of needing hospital care and a high case fatality rate [6].

- **People without risk factors:** There are limited reports of severe disease and deaths in people without any underlying disease or other condition though it should be remembered that these occur also with seasonal influenza [50,6].

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

The following groups are considered more at risk of experiencing severe disease through infection with influenza A(H1N1) 2009 :

- 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).

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 [9,12,33].

2.3.2 Susceptibility to antivirals and antiviral resistance
Based on genetic evidence, the indications are that the neuraminidase inhibitors oseltamivir and zanamivir will be 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, a few isolates of the pandemic virus have been reported resistant to oseltamivir with a few cases of verified primary resistance — i.e. a virus acquired by a person who was seemingly on oseltamivir [60,61,12]. All of the isolates have been susceptible to zanamivir. One of the secondary cases was detected in Europe and four were in Japan, where there is particularly close surveillance [21,12]. 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 [21].

2.3.3 Pathogenicity of the virus
There are no reports of known genetic markers associated with severe disease, and initial animal challenges show that although the virus does cause disease, the results are considerably less severe than, for instance, for the highly pathogenic influenza A(H5N1), but somewhat more pathogenic than seasonal influenza A(H1N1) [23,39,40,12].

2.3.4 Immunity
Laboratory studies are being undertaken and they 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 the pandemic A(H1N1). 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 [5].

2.4 Severity

Many national authorities consider it important to have an assessment of the 'severity' of a pandemic so as to determine a proportionate response [62,63]. However, it is difficult to classify pandemics, as the experience 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 angle (people who are infected experience a severe disease — even though they may be few), or from a societal angle (many people are away from work and critical 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.** From the United States' initial observed experience, about 11% of the confirmed cases have been hospitalised and the case fatality rate is 0.4% [6]. The limited information to date for Europe (mostly from the UK) suggests lower rates [18,52]. 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. However, it is important to realise that only because of the high numbers that will be infected, the absolute number of people requiring hospital care and/or dying in the first wave in the autumn and winter will probably be higher than seen in any normal winter. 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 ECMO [36].
- **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 [54]. 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.
- **Critical services functioning.** So far there have been no reports of the peak prevalence of people off ill or caring for others as causing any problems in any affected countries globally.
- **Certain groups experiencing severe illness or dying unexpectedly.** Here there have been unexpected findings as there is both an underrepresentation of older people and three groups who are suffering more than it 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 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 [36].

2.4.1 Potential worsening of severity
However, it must also be remembered that, historically, 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 for humans [36].

3 Areas of particular uncertainty

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

No prediction can be made about this at present. The pattern in the southern hemisphere in their winter is mixed. In some countries the pandemic virus is predominating while in others the pattern is more mixed [61,13]. Also it is not clear what sampling and testing strategy is being used by the countries concerned (for example whether B

viruses are being included). It is important that plans for immunising the conventional risk groups with the seasonal vaccine go ahead in Europe [44,11].

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 is transmitting in Europe in the warmer months and though its transmission may be blunted by the closure of schools some of that effect may be offset by children mixing elsewhere [2]. Also seeming declines in the reporting of numbers of cases in affected countries will now become more difficult to interpret as affected countries follow WHO's and ECDC's guidance to move to different indicators [64,24]. It seems likely that in the summer there will be outbreaks in a number of countries and that transmission will continue in the affected countries, as it is doing in the USA [9]. Given the experience in the southern hemisphere, it is certain that pandemic waves will affect countries though it is uncertain when these will come and in which countries first. 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 [32]. 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 [36,61]. 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) [36,20].

3.3 Shedding of viruses and infectivity

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

3.4 Proportion of hospitalised cases requiring intensive care and respiratory support

This is especially important information for determining the needs for intensive care in European Member States.

3.5 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 [37]. The the absolute risk — 'how 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.

3.6 Pathological processes underlying severe disease

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. This is important for informing treatment strategies.

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 Situation Reports published on the ECDC Pandemic 2009 website: http://ecdc.europa.eu/en/healthtopics/Pages/Influenza_A(H1N1)_Outbreak.aspx

Date of next planned update

1 September 2009

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