ECDC INTERIM RISK ASSESSMENT

Influenza A(H1N1) 2009 pandemic

20 July 2009

Table of contents

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Executive summary

The interim ECDC risk assessment for Europe is that the 2009 pandemic influenza A(H1N1) virus will continue to spread, but many uncertainties remain. Though it seems that most of those infected in the US and in Europe experience a mild and self-limiting infection, this picture is still unclear as there has not been enough transmission to judge the effects, especially in those more at risk. The indications from Europe and North America are that there are significant differences between the pandemic and the seasonal influenzas as regards more severe disease: there seems to be an underrepresentation of older people and a prominent representation of adults under the age of 60 with chronic ill health (including very obese persons), pregnant women, and very young children. If confirmed this will have important implications for early treatment and vaccination policies. Key features to note to date are:

- There are no reports as yet of unusual presentations or transmission routes for this influenza compared to normal seasonal influenza viruses. There is no indication of risk of infection through food or potable drinks.
- If the pandemic behaves like previous ones, cumulative clinical attack rates over the first major wave of infection in 2009–10 might be expected to be in the range of 20% to 30%, with a reasonable planning assumption of 30%.
- Based on experience in North America, clinical attack rates will be highest in children and younger adults.
- Adults over 60 years seem, at present, to be the least affected age group, though there are indications from the USA that those few that are affected experience the highest risk of severe disease of any age group.
- The groups experiencing most of the severe disease and death are those in the risk groups of people with chronic underlying medical conditions (this includes morbid obesity), pregnant women and young children (especially under two years of age).
- Most of those infected experience a mild self-limiting illness, even in people in risk groups. However, as for seasonal influenza there are some people who experience more severe disease and some of these die despite medical care. These include a few people without any known underlying condition and outside other risk groups.
- 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 may rise because of the presence of other respiratory infections.
- Local experience from the USA (New York City) indicates that, without preparation, this pandemic can severely stress healthcare systems.
- The observed case fatality rate based on the largest population reported to date, from the USA, is 0.4%. While in Europe the observed rate in the earliest affected country (the United Kingdom) is 0.3%. However, this is likely to be higher than the true figure, which may at present be more than the range of 0.1% to 0.2% of all clinical cases.
- As in seasonal influenza, case fatality rates are high in the very young, low in children and young adults and then increase with age.
- At the individual level the highest risk of hospitalisation for an affected person is: a) in the risk groups; and b) for young children and those over 60.
- As yet almost all the viruses have been sensitive to the antivirals known as neuraminidase inhibitors (oseltamivir and zanamivir) but they are resistant to adamantenes (amantidine and rimantidine). There have been a few pandemic virus isolates that have showed resistance to oseltamivir (though sensitive to zanamivir).
- The current seasonal influenza vaccine that contains a component effective against another A(H1N1) virus is not effective against the new pandemic A(H1N1) 2009 virus.
- It is impossible to predict when European countries will be affected, but a proper first wave seems inevitable for the autumn. The experience in one country (the United Kingdom) suggests that countries could be affected considerably earlier in the autumn than happens with seasonal influenza.
- It is too early to predict what the mix of pandemic and seasonal influenza viruses will be this autumn, although there will also be B influenza viruses, as they do not compete with A viruses.
- Pandemic viruses are unpredictable, and can change their characteristics as they evolve. Even pandemics usually slow down in summer, only to pick up in autumn, and the virus may even then come back, perhaps in a more aggressive form, like it happened in 1918–19.
- ECDC will work with Member States, other European Agencies, the European Commission, WHO and its other international partners to gather more information to update this Risk Assessment at intervals. Special attention will be paid to how the pandemic is developing in the first affected European countries and the temperate Southern Hemisphere countries.

Source, date and type of request

ECDC internal decision, 18 May 2009, latest revision 16 July 2009.

Specific question

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

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), the Public Health Agency for Canada and the Ministry of Health of Mexico.

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 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 important are dealt with in section 2. 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 [3,19,4].

The basic genetic structure of the virus has been described and this information is available through publicly accessible websites [41,30]. 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 [30]. However, it is unclear if 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 avian, human and swine genes have previously been circulating in pigs in the US, and have occasionally been transmitted to humans [37,34,42]. 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].

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

Since the disease has now spread massively 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] [45].

WHO and other 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 still causes deaths in the region. However, human-to-human transmissions of A(H5N1) and other avian influenza have been very limited [10]. The 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 becomes a pandemic. ECDC refers to the most important of these as the 'known unknowns' [11,13,29,46] (see Figure 1). A few of these are still unknown, but for several of the unknowns data are becoming available, both from North America — through the authorities in Canada, Mexico and USA — and from the Southern Hemisphere. Analyses from these data need to be relied on for now, though at a later stage data from Europe and other Northern Hemisphere countries will be used, as the pandemic spreads and data become available.

Figure 1. For any future pandemic virus – what can and cannot be assumed?

What probably can be assumed:

Known knowns

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

What cannot be assumed:

Known unknowns

- Antigenic type and phenotype
- Susceptibility/resistance to antivirals
- Age-groups and clinical groups most affected
- Age-groups with most transmission
- Clinical attack rates
- Pathogenicity (case-fatality rates)
- 'Severity' of the pandemic
- Precise parameters needed for modelling and forecasting (serial interval, R_o)
- 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

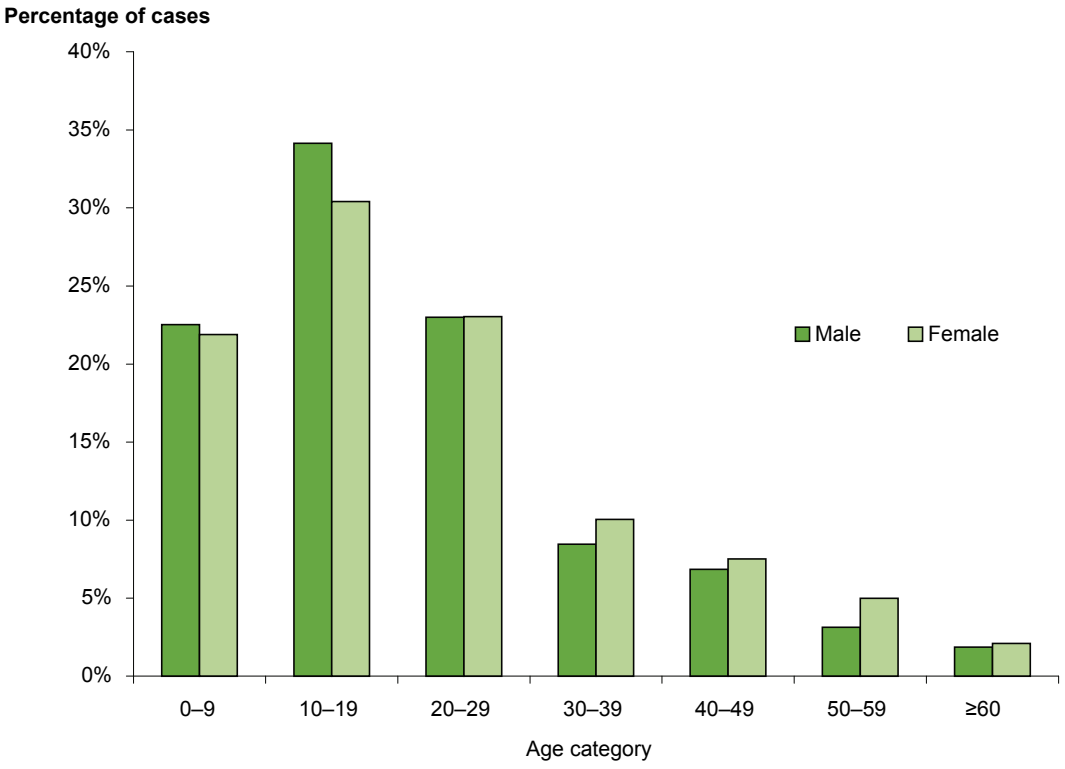
The observed age distribution is unusual and different from seasonal influenza, being skewed towards younger age groups [36,13]. There is a marked underrepresentation of infections in people over 60 years of age, who make up only 2% of reported cases, even among those being hospitalised. In European reported cases, most patients are young, median age being 25 years in those who acquired the infection during travel and 13 years in

[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://www.ecdc.europa.eu/en/Health_topics/novel_influenza_virus/2009_Outbreak/).

those domestically infected. Nearly 80% of cases are in individuals under 30 years of age [36,40,13,14] (see Figure 2).

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 [36,13]. 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 [14].

Figure 2. 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)



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 from the Americas or elsewhere suggesting unusual transmission routes for influenza and no reason to suggest transmission through food [26].

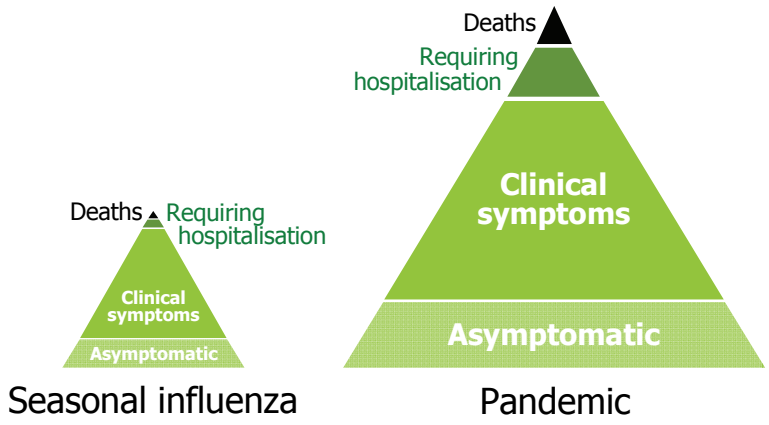
2.2.2 Spectrum of disease – clinical features

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 [36]. But these gastrointestinal symptoms have always been accompanied by other more usual signs of influenza [36]. The distribution of symptoms in Europe is very similar to what is described from the USA, with the proportion of patients reporting gastrointestinal symptoms being 24% [14]. 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 [47].

2.2.3 Asymptomatic cases

There are some indications of asymptomatic cases from contact tracing in Europe [14]. However, it will be some time before it is known what proportion of infected people develop the disease [20]. That will best be assessed from future serological studies.

Figure 3. Seasonal influenza compared to pandemic — proportions of types of cases



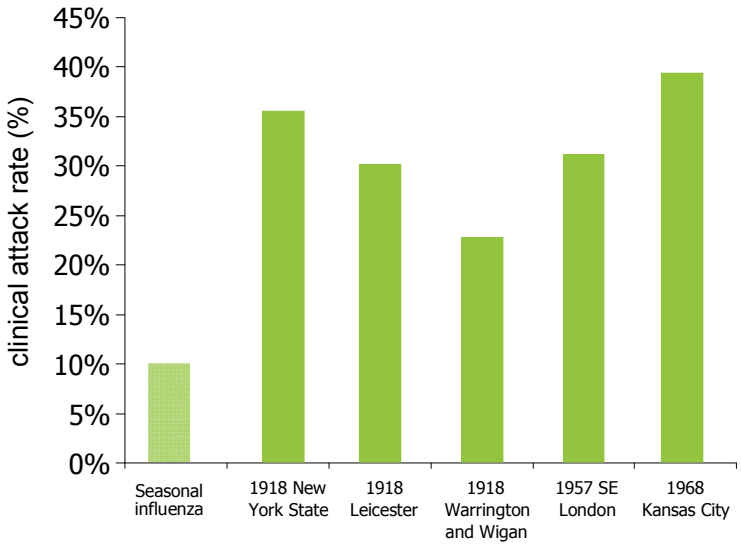
2.2.4 Ease of transmission – effective reproductive number

There have already been estimates of the basic reproductive rate (Ro), which all lie between 1 and 2 (with some outliers); the range 1.4 to 1.6 being most probable [19]. As would be expected for a pandemic, this is higher than the value observed for seasonal influenza but in line with previous pandemics [11,22]. Effective reproductive number will be a more important parameter than Ro and that is being measured or monitored in some countries. At a population level, it has rarely risen above 2 [19,20], though higher figures should be expected in closed communities such as schools.

2.2.5 Clinical attack rate[3]

In previous pandemics it was unusual to observe population clinical attack rates of less than 20%. 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 [16].

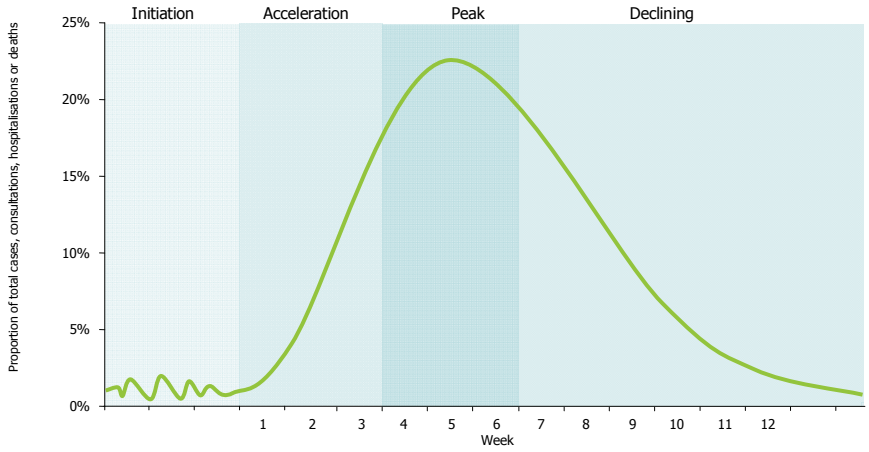
Figure 4. Numbers affected in seasonal influenza epidemics and pandemics (overall clinical attack rate in previous pandemics)



[3] 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.

In a study conducted in Mexico, a figure of 30% was observed in one community [19]. Lower figures have been observed in North America — notably in New York City, where a telephone survey gave a figure of 7% [33]. 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.

Figure 5. 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 [39,38,6,7]. 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 4).

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 [24,21]. No serological data are yet available. As is the case with other human influenza infections, there will probably be many mild and asymptomatic cases [13]. Certainly in New York most of those affected did not consult a doctor [43,44].

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 [14]. 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% [14] (see Table 1). 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 [14]. 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 [28].

Table 1. Reported number of cases of influenza A(H1N1)v infection, travel association and hospital admission, 29 EU/EEA countries, as of 6 July 2009 [14]

	Aggregated case reports	Individual case reports			
Country	**Cumulative number of confirmed cases**	**Total cases(2)**	**Travel-related(2)**	**Hospitalised(2, 3)**	**Last reporting date**
Austria	19	18	15	16	5/7
Belgium	54	54	43	12	4/7
Bulgaria	13	8	4	8	29/6
Cyprus	117	82	10	20	3/7
Czech Republic	15	15	15	3	2/7
Denmark	66	65	37	6	5/7
Estonia	13	13	11	8	26/6
Finland	62	43	38	3	2/7
France	318	318	231	182	3/7
Germany	527	521	217	82	3/7
Greece	151	–	–	–	
Hungary	21	12	10	3	3/7
Iceland	4	4	3	0	22/6
Ireland	74	63	55	1	3/7
Italy	146	100	87	26	30/6
Lithuania	1	2	1	0	3/7
Luxembourg	3	6	4	1	30/6
Latvia	6	1	1	1	25/6
Malta	16	2	2	0	2/7
Netherlands	142	75	41	1	3/7
Norway	41	27	23	1	2/7
Poland	25	19	16	13	1/7
Portugal	45	18	18	15	2/7
Romania	44	44	27	44	6/7
Slovakia	19	18	17	15	6/7
Slovenia	14	7	7	0	3/7
Spain	776	113	74	-	28/5
Sweden	87	84	59	5	3/7
United Kingdom	7 447	5 974	414	90	3/7
Total	10 266	7 706	1 480	556	

(1) Reported daily through epidemic intelligence.
(2) Reported as individual data.
(3) Some hospitalisations were for isolation purposes.
(–) no information available

2.2.7 Case fatality rate (CFR)

It is difficult to estimate this with great accuracy at this stage and it should anyway be remembered that it is a measure that is sensitive to social factors [51]. 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 of 1% [48]. An indirect method gave a value of 0.4% [19], while estimates for the United States give a figure of 0.4% [6]. 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 [14]. In the first affected country in Europe (United Kingdom) the observed rate, with data as of 15 July 2009, was 0.3% (28 deaths in 10 649 confirmed cases) [25]. This is not that different from what has been observed in modelling studies [19]. This rate will have been quite accurate given 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. Again as for the hospitalisation rate, the CFR can now be expected to seem to rise without any change in the underlying data 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. 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 from seasonal influenza and pandemics), 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 a many higher numbers of actual deaths (and hospitalisations) than experienced in even a bad seasonal influenza winter.

2.2.8 Risk groups for hospitalisation and severe disease

In an initial published study from California of 553 probable and confirmed infections with the pandemic virus, 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, seizure disorder and malignancy [7]. Another published study highlighted massive or morbid obesity in adults [8]. The largest dataset reported to date 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 and massive or morbid obesity [6]. There are limited reports of severe disease and deaths in people without any underlying disease, though it should be remembered that these occur also with seasonal influenza [40,25].

Figure 6. Risk groups for the A(H1N1)v pandemic 2009

The following groups are considered more at risk of experiencing severe disease than the general population should they become infected with the pandemic A(H1N1)v virus 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)

Sources:
ECDC Pandemic 2009 Risk Assessment.
Finelli L. CDC Influenza Surveillance. Available from: http://www.cdc.gov/vaccines/recs/ACIP/downloads/mtg-slides-jun09/15-2-inf.pdf
Nicoll A et al. Eurosurveillance, Volume 13, Issue 43, 23 October 2008. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19018

2.3 Features of the virus

2.3.1 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 and rimantidine). 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. though usually these viruses are not capable of efficient human-to-human transmission and rapidly disappear once therapy stops in the individual [16]. Indeed, a few isolates of the pandemic virus have been reported resistant to oseltamivir with reports of three isolates to date (13 July 2009), one of which seems to be a case of primary resistance — i.e. a virus acquired by a person who was seemingly not on oseltamivir [49,50]. 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 [17].

2.3.2 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) [18,30,31].

2.3.3 Immunity and effectiveness of the current seasonal A(H1N1) vaccine

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 [51,52]. However, it is difficult to classify pandemics, as there is as yet no consensus over what is meant by 'severity' and the experience of people, organisations and societies may differ because severity of pandemics does 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' 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 that they may be even lower. 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 will probably be higher than seen in any normal winter [28].
- **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 [43]. 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 6). 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. There is, however, an urgent need for final preparations in the healthcare sector for the autumn and winter [28].

2.4.1 A potential for a 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 [28].

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 [50]. It is important that plans for immunising the conventional risk groups with the seasonal vaccine go ahead in Europe [35].

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 quite capable of transmitting in 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. 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. Parts of one European country (the UK) are already in an acceleration phase, at least for a while, despite it being the summer months [25]. 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 [28,50]. 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) [28,16].

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 important information for determining the needs for intensive care in Member States. There are such cases but no useful estimates for calculating the need for intensive care and ventilatory support and the only comment that can be made is that there are likely to be severe pressure on these services when the pandemic affects countries

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 latter — '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 yes at 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.

3.7 Patients with severe disease but outside the risk groups

As is the case with seasonal influenza, there are now sporadic reports of cases like this in North America and the UK — i.e. people with severe disease and dying due to the pandemic strain but not being in the recognised risk groups. It will be important to investigate these cases to a standard protocol to determine if there are new risk groups, to determine underlying pathologies and to monitor the proportion of these cases as a proxy for severity.

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://www.ecdc.europa.eu/en/Health_topics/novel_influenza_virus/2009_Outbreak/

Date of next planned update

5 August 2009

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