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# 3 Epidemiology and potential impact

## *3.1 Introduction*

Influenza commonly called the “flu” is one of the oldest and most common diseases known to man. Hippocrates first described influenza in 412 BC. The first well-described pandemic of influenza occurred in 1580. Since then, there have been 31 documented influenza pandemics, including three in the 20th century: 1918, 1957 and 1968.(1) The 1918 pandemic (“Spanish Flu”) was particularly virulent, resulting in as many as 50 million deaths worldwide.(2)

## *3.2 Virology and capability for mutation*

There are three types of influenza virus, A, B and C. Influenza C is rarely a cause of human illness. Whereas influenza B changes very little from year to year, influenza A can undergo considerable antigenic change resulting in new infections. Influenza A, therefore, is the most clinically important of the three viruses, responsible for both epidemics and pandemics.

Influenza A Flu virus was first isolated in 1933.(3) Flu viruses are enveloped viruses of the family Orthomyxoviridae that contain a segmented RNA genome. Influenza A viruses can be subtyped according to the antigenic and genetic nature of their surface glycoproteins. 16 haemagglutinin (HA) and nine neuraminidase (NA) have been identified to date.(4) Influenza is a zoonosis. All subtypes exist in avian hosts, but so far, only viruses of H1, H2 and H3 have been found to cause pandemics in humans. The three pandemics in the 20th century were due to A/H1N1 in 1918-1919, A/H2N2 in 1957-58 and A/H3N2 in 1968-69. Human disease has also been caused by three additional HA subtypes, H5, H7 and H9.

Influenza viruses are unstable in their structure and are continually evolving. Antigenic variation takes place on an ongoing basis in the two surface glycoproteins of the virus (HA and NA). Point mutations in the HA and NA genes occur, called antigenic drift. These changes mean that a person becomes susceptible to new strains despite previous infection with influenza,

or vaccination. The constant antigenic drift in influenza A and B viruses is responsible for frequent epidemics and regional outbreaks and necessitates annual reformulation of the influenza vaccine. If a new strain differs only slightly from a previous strain, there is likely to be some immunity amongst the general population. The greater the difference between previous strains and the emerging strain, the higher the risk of the virus causing an epidemic as there will be little pre-existing immune recognition.(5)

A second type of change, called antigenic shift can also occur. This change, which is a major change, occurs when a virus with a new HA is introduced into the human population. Antigenic shift can occur in one of two ways:

- An animal or avian influenza A virus changes/adapts and is transmitted without reassortment to humans
- Genetic reassortment between animal and human influenza A viruses occurs leading to a new virus with a new HA

The emergence of these completely new subtypes occurs at irregular and unpredictable intervals and only with type A viruses.

### *3.3 Reservoir*

The natural reservoirs for influenza virus strains are avian species, particularly waterfowl and other aquatic wild bird species. Other animals, e.g. horses, pigs, whales, seals, cats, leopards and tigers can also be affected.

Pandemic influenza happens when a novel virus emerges against which the vast majority of the world's population has no immunity. There are two other requirements for a pandemic to arise. The strain must cause disease in humans and spread easily from person to person. The pandemic strain then sweeps worldwide within months and causes repeated waves of infection. The pandemic strain can arise via adaptation or reassortment, or in addition, via re-emergence of viruses similar to those which circulated in previous eras, known as antigenic re-cycling.

## *3.4 Epidemiology*

### *3.4.1 Inter pandemic (seasonal) influenza*

Influenza constitutes an ongoing threat to public health outside of pandemics. An increase in mortality typically accompanies an influenza epidemic. Over a 10 year period, Fleming estimated that in the UK, an average of 12,554 excess deaths occurred in each year when a seasonal influenza epidemic occurred.[6] An estimated 20,000 or more excess deaths occurred in each of five influenza epidemics in the years 1972 through to 1995 in the United States of America. It is estimated that 90% of these deaths occurred in the elderly. The deaths may be directly related to viral pneumonia, secondary bacterial pneumonia or due to worsening of pre-existing chronic medical conditions. In inter pandemic years, the majority of deaths occur in the elderly, though they also occur in young children and infants. Approximately 110,000 hospitalisations per year are related to influenza in the United States.[7]

Influenza viruses circulating globally in the year 2007/2008 include influenza B and two subtypes of influenza A, H1N1 and H3N2. In temperate regions, there is extremely low-level transmission in the summer months, followed by an annual upsurge in activity in winter months. This upsurge is variable in intensity and duration, but usually produces clinically recognisable disease in the population for eight to twelve weeks.[8] In tropical and sub-tropical regions, the disease usually occurs year round.

### *3.4.2 Pandemic influenza*

Most experts agree that another pandemic is likely to occur, although the exact timing or severity cannot be predicted. Increases in global travel and in the world population during the past century will probably accelerate the rapid spread of the virus. The average time between each of the last three pandemics was 25 years; the last pandemic was 40 years ago in 1968.

Pandemic influenza is less constrained by season than inter pandemic influenza. It can occur at any time of the year. It has occurred in multiple waves in each of the three pandemics of the 20th century. In the 1918 pandemic, the first wave occurred in spring 1918 in the USA and in US troops in France. It was also reported at that time in Asia. In August 1918 the second wave occurred in Europe and in spring 1919 the third wave occurred. All populations of the world were affected within 10 months. It is not possible to say where this pandemic originated because the first wave occurred more or less simultaneously in Asia, Europe and the US. The 1957 pandemic started in China in February 1957 and spread to all continents by mid 1957. The 1968 pandemic started in July in China and spread via US troops to the US in September of that year. Although it was isolated in Europe in that winter, significant disease was not apparent in the EU until the winter of 1969/1970. It had effectively spread globally within 6 months.(9)

### *3.4.3 Mortality in pandemics*

Mortality in each of the three pandemics of the 20th century has varied markedly. In the 1918-1919 pandemic there were 198,000 excess deaths in England(10) and 550,000 excess deaths in USA.(11) Excess deaths are defined as the number of deaths observed during an epidemic of influenza like illness in excess of the number expected. On the island of Ireland, in 1918 there were 10,651 influenza deaths registered, a rate of 243 per 100,000 population. (The mortality rate in England and Wales for 1918 was 313 per 100,000).(12) This compared with an annual rate of between 16 and 41 per 100,000 for the previous ten years. Of the 10,651 deaths registered, 5,591 were males and 5,060 were females. The mortality rate varied by region, being 304 per 100,000 in Leinster, 302 per 100,000 in Ulster, 159 per 100,000 in Munster and 114 per 100,000 in Connaught. The deaths per 100,000 by age group were as follows: under 5 years 295, 5-10 years 120, 10-15 years 103, 15-20 years 223, 20-25 years 329, 25-35 years 380, 35-45 years 239, 45-55 years 222, 55-65 years 226, 65-75 years 221 and more than 75 years, 256. In addition to influenza-registered deaths, excess deaths from pneumonia rose in 1918 by circa 2000.

The 1957 pandemic was milder and worldwide the death toll was estimated to be more than two million deaths.[13] In the US, a total of 115,700 excess deaths occurred for the pandemic period. Death rates were highest at the extremes of age, i.e. in the young and the elderly. The overall impact was one tenth that of the 1918/1919 pandemic.[11] The 1968 pandemic was milder again, the excess deaths being about half of that observed in the Asian pandemic. Most of the excess deaths occurred in those aged 65 years and older.

### *3.4.4 Clinical attack rates*

The clinical attack rate in 1918 was estimated to be approximately 25% with 50% of the world's population becoming infected. In the 1957 pandemic, attack rates of 25-30% were reported. The clinical attack rate in 1968/1969 was 20%. Rates were higher in school groups.

### *3.4.5 Symptoms of pandemic flu*

In 1918 pandemic influenza presented with severe typical flu like symptoms: high fever, headache, myalgia/arthralgia, anorexia, nausea, vomiting and cough lasting 2-4 days. Some died very quickly, being overwhelmed by a tracheo-bronchitis associated with dyspnoea and mahogany spots around the mouth, coalescing into a violacious heliotrope cyanosis. Up to 18% developed pneumonia. In 1957 and 1968 the symptoms were that of seasonal flu, with a higher than usual incidence of primary viral pneumonia, and this mainly occurred in those with underlying illnesses.

## ***3.5 Avian Influenza (AI), the risk to human health and its pandemic potential***

Much has been written on this subject in the past two years. The European Centre for Disease Prevention and Control (ECDC) and WHO have produced comprehensive overviews of the risks posed.[13;14]

Avian influenza viruses are present in the bird population all the time, and have the potential to cross the species barrier and infect humans and cause illness. They also have the potential to mutate to a form that could easily

transmit from person to person. This mutation could occur without mixing with a human influenza virus, or could occur if human and avian viruses mix in an infected host and mutate. This would allow such a virus to be the cause of the next pandemic.

What has caused concern over the past few years is the emergence of one particular avian influenza subtype A/H5N1 which has caused multiple outbreaks in birds, and which has crossed the species barrier to infect humans.

### *3.5.1 Evolution of A/H5N1 as a pandemic threat*

In 1997, a series of poultry outbreaks of Highly Pathogenic Avian Influenza (HPAI) occurred in Hong Kong. Eighteen human cases of A/H5N1 were identified. The high mortality, mainly among previously healthy young adults, (six died from acute respiratory distress or multiple organ failure) caused major concern. Exposure to live poultry in the week before onset was associated with human disease.[15] The virus was successfully eliminated from Hong Kong at the time by the rapid culling of infected and at risk poultry and biosecurity measures.

Influenza A/H5N1 reappeared in humans in Hong Kong in February 2003 (five cases, two fatalities). The infection was again controlled in poultry by culling, biosecurity measures and poultry vaccination.

Since then there has been a massive unprecedented increase in infection in the poultry populations of many countries of the Far East, and also more recently spreading to countries in Europe and Africa. For an up to date list of affected countries, visit the OIE website [16]

This has been accompanied by an increase in the number of human cases of disease. As of 10th September 2008, 387 cases and 245 deaths have been reported in 15 countries: Azerbaijan, Bangladesh, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Lao Peoples' Democratic Republic, Myanmar, Nigeria,

Pakistan, Thailand, Turkey, and Viet Nam. For an up to date list of the number of human cases, visit the WHO website [17].

The risk to human health from A/H5N1 is twofold:

- Risk of human infection, disease and death following contact with infected birds or contaminated environment
- Pandemic potential for a new virus to emerge either directly from H5N1, or from recombination of H5N1 with a human virus, so that it can spread easily from person to person.

All evidence to date indicates that the H5N1 virus does not easily spread from birds to infect humans. Although millions of persons have been exposed in the countries affected by AI, only a tiny proportion of people have become infected or ill. Human exposure to AI viruses occurs through contact with infected tissues, excretions and secretions of infected birds, especially faeces and respiratory secretions. Most cases have been related to close direct contact with live or dead infected poultry or occasionally wild birds. AI could also be transmitted via inhalation of contaminated dust, inhalation of fine water droplets, aerosols, hand to mucous membrane transfer of infected faeces or respiratory secretions, or via consumption of raw or undercooked blood, organs or meat.

Those at risk therefore are those who have close and intense contact with sick A/H5N1 infected domestic poultry or their droppings. Infections have tended to occur in small household clusters involving family members, so if one person is infected, the rest of the household is deemed to be at high risk. The increased risk may be related to shared exposures rather than potential human-to-human transmission. There is also a theoretical risk to those who via their work have exposure to potentially infectious materials, e.g. vets, and those involved in outbreak control activities, healthcare workers dealing with sick A/H5N1 infected patients, laboratory workers, others with close contact with wild birds etc.

In September 2004, Thailand reported a probable case of human-to-human H5N1 transmission, but this and any other suspected cases of human-to-human transmission so far have been mainly limited to family members.[18] In these cases, intimate contact without the use of precautions was implicated and so far no case of human-to-human transmission by small particle aerosol has been implicated. Serological surveys have not found evidence of asymptomatic infections among contacts.[19] In a report on the outbreak in Hong Kong in 1997, where a retrospective cohort study was done to compare the prevalence of H5N1 antibody among healthcare workers (HCW) exposed to H5N1 case patients with the prevalence among non exposed HCWs, it found that eight (3.7%) of 217 exposed and two (0.7%) of 309 non exposed HCWs were H5N1 seropositive. Two exposed HCWs, in whom paired samples had been taken, were shown to have seroconverted. Since this report, despite several studies, there have been no reports of seropositivity in HCWs.[20]

A retrospective survey of poultry deaths and a sero-epidemiological investigation concluded that transmission of H5N1 from infected poultry to humans was low in a rural Cambodian population with confirmed and suspected H5N1 poultry outbreaks, and where a human fatal case occurred during 2005.[21] This finding was consistent with a study of healthcare workers in Thailand, who were exposed to a case of H5N1 without using appropriate personal protective equipment. All were monitored for two weeks for temporally related influenza like illness and all remained well.[22]

A case-control study to evaluate the risk factors for human infection with H5N1 undertaken in Viet Nam, reported that preparing sick or dead poultry for consumption in an H5N1-affected area is a risky practice.[23]

All 106 persons selected as controls in this study from communities with at least one confirmed human H5N1 case were negative for H5N1 antibodies and adds further evidence to the belief that widespread subclinical H5N1 infection has not yet occurred in Southeast Asia as described by Vong et al.[21]

The largest family cluster to date of cases of A/H5N1 occurred in 2006 in Karo, Sumatra. In this cluster of eight cases, seven died. One of the cases, the index case, died before specimens were taken and so her illness was not laboratory confirmed. The family gathered together when the index case was symptomatic. A WHO review of this cluster was held, and confirmed that human-to-human transmission probably occurred in this cluster. The index case transmitted infection to six blood relatives, one of whom transmitted the disease to another blood relative. There was no spread of disease beyond the family.

Epidemiological investigation of human cases of H5N1 in Turkey (eight cases, including three family clusters) found no evidence of human-to-human transmission between households, which were all located in a limited geographical area of approximately 2 $km^2$.[24]

In a recent paper by Yang Yang et al, statistical methods were used to test whether these two observed clusters were due to human-to-human transmission. They concluded that there was statistical evidence of human-to-human transmission in Sumatra but not in Turkey. For Sumatra, the estimated secondary attack rate was 29%([25]).

Since the beginning of 2006, health authorities in Thailand have investigated over 2,300 clinical influenza or pneumonia patients as part of their surveillance activities, and until the occurrence of a fatal case in the Phichit province, none of these had been found to be H5N1 infected.[26]

To conclude, A (H5N1) has demonstrated considerable pandemic potential, and the virus is now entrenched in the poultry populations of parts of Asia. However despite exposure of millions to the virus, there have been relatively few human cases, and the virus does not transmit easily from person-to-person. It remains uncertain whether A/(H5N1) will be the source of the next pandemic.

### *3.5.2 Human illness due to non H5N1 A/HPAI subtypes*

Although internationally the focus of concern has been with A/H5N1, it must be remembered that other HPAIs can cause human illness, and indeed could be the source of the next human pandemic. An outbreak of HPAI H7N7 in the Netherlands in 2003 resulted in 89 human infections, mostly resulting in conjunctivitis. Only seven had respiratory illness. However a previously healthy 57-year-old veterinarian who visited an affected poultry farm contracted H7N7 and died from multi-organ failure and respiratory insufficiency.(27)

### *3.5.3 Epidemiology of confirmed human cases of A/H5N1*

The epidemiology of human cases of AI was recently summarised by WHO.(28) This described all laboratory confirmed human cases of H5N1 (PCR on >= 1 respiratory tract specimens and/or microneutralisation assay on serum specimens) with an onset date between 1st December 2003 and 30th April 2006. Asymptomatic cases were not included. During this time period, nine countries (Vietnam, Thailand, Cambodia, Indonesia, China, Turkey, Iraq, Azerbaijan, Egypt) reported a total of 205 laboratory confirmed human cases of H5N1 avian influenza to WHO. Two of these were asymptomatic and were excluded from further analysis. Each year from 2003 to 2006 there was a northern hemisphere winter and spring peak in the number of cases. The number of countries reporting human cases increased dramatically after October 2005, and mirrored the geographical extension of AI outbreaks in birds at that time. The mean age of cases was 20 years (range 3 mths-75 years). Half of the cases occurred in persons aged less than 20 years. This might however reflect the age distribution of the populations in which the cases arose. The overall sex ratio of males to females was 0.9. The median duration from onset of illness until hospitalisation was four days (range 0-18). The overall case fatality rate was 56%. The highest rate was reported in those aged 10-19 years at 73% and the lowest was reported in those aged 50 and over at 18%. The median duration from onset of symptoms until death was nine days (range 2-31).

### *3.5.4 Clinical features*

The Writing Committee of the WHO Consultation on Human Influenza A/H5 reviewed the clinical features, management and prevention of A/H5N1 at a meeting in May 2005.[29]

They reported that the incubation period for A/H5N1 might be longer than for other known human influenzas. In 1997, most cases occurred within two to four days of exposure. More recent cases had similar intervals, but with a wider range, up to eight days. Most patients had initial symptoms of high fever (> 38$^{o}$C), and flu like illness with lower respiratory tract symptoms. Patients rarely had conjunctivitis. Diarrhoea, vomiting, abdominal pain, pleuritic pain and bleeding from the nose and gums were reported to occur in some patients early in the onset of the disease. Watery diarrhoea could occur, and may precede respiratory symptoms by up to one week. Two patients were reported to present with encephalopathic illness and diarrhoea but no respiratory symptoms. Lower respiratory symptoms developed early in the course of the disease, respiratory distress, tachypnoea, and inspiratory crackles were common. Almost all patients had clinically apparent pneumonia. Radiological changes were seen a median of seven days following onset of fever. This process was a primary viral pneumonia. Progression to respiratory failure occurred a median of six days from onset of illness. Multiorgan failure with renal dysfunction, cardiac dilatation, and supraventricular tachyarrhythmias was common. Other complications included ventilator-associated pneumonia, pulmonary haemorrhage, pneumothorax, pancytopenia, Reye's syndrome and sepsis syndrome without documented bacteraemia.

## *3.6 Lessons from past pandemics*

Key lessons from the three pandemics of the last century have been identified by the WHO and are summarised below.[13]

- The unpredictable behaviour of a pandemic strain of influenza, and its capacity to cause severe disease in non-traditional age groups, namely young adults, are major determinants of a pandemic's overall impact.

- Virological surveillance has performed a vital function in rapidly confirming the onset of pandemics, alerting health services, isolating and characterising the virus, and making it available to vaccine manufacturers.
- In parts of Asia where dense populations of humans live in close proximity to ducks and pigs, surveillance for both animal influenza and clusters of unusual respiratory disease in humans perform an important early warning function.
- Some public health interventions may have delayed the international spread of past pandemics, but could not stop them. Quarantine and travel restrictions have shown little effect. As spread within countries has been associated with close contact and crowding, the temporary banning of public gatherings and closure of schools are potentially effective measures.
- The impact of vaccines on a pandemic, though potentially great, remains to be demonstrated. In 1957 and 1968, vaccine manufacturers responded rapidly, but limited production capacity resulted in the arrival of inadequate quantities too late to have an impact.
- A pandemic similar to the 1957 and 1968 pandemics will cause excess mortality at the extremes of life and in persons with underlying chronic disease. As these risk groups are the same as during seasonal epidemics**,** countries with good programmes for yearly vaccination will have experience in the logistics of vaccine administration to at least some groups requiring priority protection during a pandemic. While such a strategy can reduce excess mortality, sudden and large increases in morbidity, and a correspondingly high demand for medical care, should nonetheless be anticipated. [(13)]

### *3.7 Potential impact of a pandemic*

The potential impact of a future pandemic on morbidity and mortality can be estimated using mathematical modelling techniques. The Pandemic Influenza Expert Group has reviewed several types of models to model the impact of

pandemic influenza and of the potential effects of different intervention strategies.

An empirical model devised by the Health Protection Agency (HPA) is based on previous UK pandemics and can be used to predict the number of clinical cases, hospitalisations and deaths that will occur during each week of a 15-week single wave pandemic.[30] An economic model devised by Meltzer et al in the US has been used to predict the total number of hospitalisations and deaths that will occur in the absence of any interventions.[31] Gani et al in the UK created a model to predict the weekly number of clinical cases and hospitalisations that may occur and enables the effect of interventions to be assessed.[32]

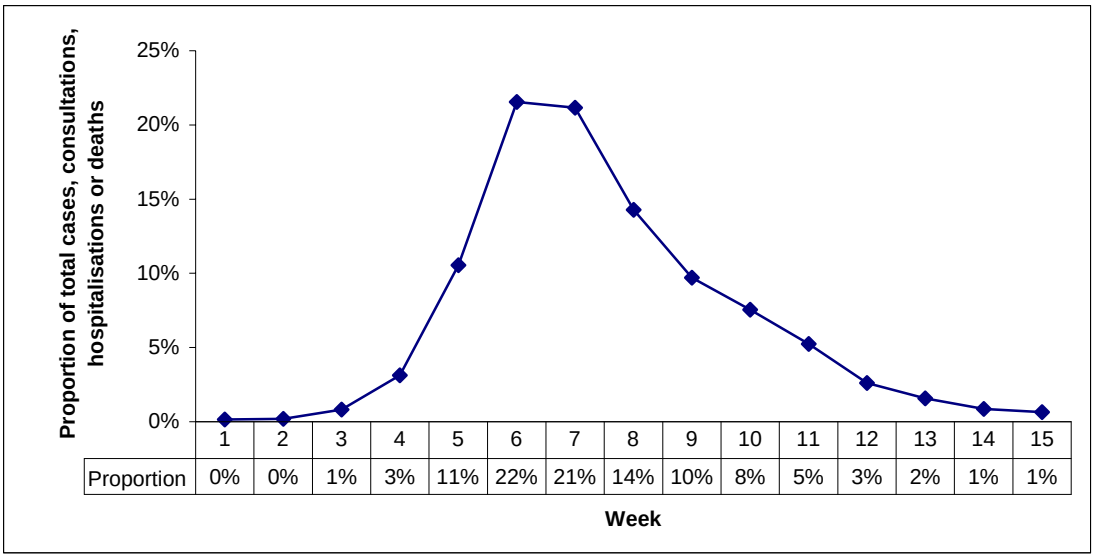
More detailed reports on these models are available in Supplement 3.

For planning purposes, the Pandemic Influenza Expert Group recommends that the HPA empirical model, which is based on the profile of previous UK pandemics be used for planning purposes in Ireland.

### *3.7.1 HPA Empirical model*

The Health Protection Agency (HPA) in the United Kingdom has adopted an empirical model of pandemic influenza for planning purposes.[33] The model is derived using data from three previous UK pandemics (1918, 1957, 1969/70). The pandemic is modelled over a single wave, rather than over multiple waves.

The main assumption of the empirical model is that the next influenza pandemic will take place over a single wave of 15 weeks and will have a profile similar to what has occurred during previous pandemics. The shape of the modelled epidemic curve can be seen in Figure 1 below:




| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Proportion | 0% | 0% | 1% | 3% | 11% | 22% | 21% | 14% | 10% | 8% | 5% | 3% | 2% | 1% | 1% |

**Figure 1 Pandemic profile as predicted by empirical model: Proportion of total cases, consultations, hospitalisations and deaths that will occur each week during single wave pandemic**

The profile is a weighted average of influenza deaths in England and Wales during the 1969/70 and 1957 pandemics and London during the 1918 pandemic. The weights used were based on the overall mortality rate of each pandemic. The 1918 pandemic therefore had a strong influence on the shape of the curve since the highest death rate occurred in this pandemic.

Figure 1 is a generic curve that can be applied to break down by week the total number of cases, GP consultations, hospitalisations and deaths that would be expected in the course of the pandemic. For example, the model predicts that 22% of all cases will occur during week six of the pandemic and 8% of cases will occur during week ten. Similarly, 22% of total hospitalisations and deaths will occur during week six and 8% of hospitalisations and deaths will occur during week ten.

### *3.8 Model applied to Irish situation*

In applying this empirical model to the Irish situation two scenarios have been considered. The first considers a clinical attack rate of 25%, a hospitalisation rate of 0.55% and a mortality rate of 0.37%. Predictions based on these parameters are described in section 3.8.2 to 3.8.4.

In the second or worst case scenario a clinical attack rate of 50%, a hospitalisation rate of 3.7% and a mortality rate of 2.5% are considered. This higher mortality rate reflects the mortality rate observed in 1918. The higher hospitalisation rate of 3.7% is assumed, to ensure that the hospitalisation: mortality ratio is consistent across both scenarios. Predictions based on these parameters are described in section 3.8.6 to 3.8.8.

In both instances all calculations are based on the Census 2006 Preliminary Report (July 2006), in which the Irish population is 4,234,925, an increase of 8.1% on the 2002 figure.[34]

### *3.8.1 Clinical Attack Rate: Scenario 1*

A clinical attack rate of 25% has been assumed to derive the predictions from the model. This is approximately equal to the clinical attack rates of the last three pandemics (1918, 1957, 1969).

### *3.8.2 Clinical Cases: Scenario 1*

Assuming a 25% clinical attack rate yields a total of 1,058,731 cases in the Irish population[1]. When the total number of cases is broken down by week in accordance with the proportions shown in Figure 1, the number of cases in one week peaks during week six at 228,189 (Table 3.1). The number of weekly cases rises sharply from 33,041 in week four to 111,705 in week five.

### *3.8.3 Hospitalisations: Scenario 1*

The HPA have used a hospitalisation rate of 0.55% of clinical cases. This should be considered as the minimum rate of hospitalisations associated with pandemic influenza as it was derived using hospitalisation data from inter pandemic years; the actual rate may be higher than 0.55%.

[1] All calculations based on the 2006 census which indicated a total Irish population of 4,234,925

| Week | % Total cases | Cases per week | Cases per 100,000 pop | Hospitalisations per week | * Deaths per week |
|---|---|---|---|---|---|
| 1 | 0.1% | 1,521 | 36 | 8 | 6 |
| 2 | 0.2% | 2,164 | 51 | 12 | 8 |
| 3 | 0.8% | 8,675 | 205 | 48 | 32 |
| 4 | 3.1% | 33,041 | 780 | 182 | 122 |
| 5 | 10.6% | 111,705 | 2,638 | 614 | 413 |
| 6 | 21.6% | 228,189 | 5,388 | 1,255 | 844 |
| 7 | 21.2% | 224,036 | 5,290 | 1,232 | 829 |
| 8 | 14.3% | 151,089 | 3,568 | 831 | 559 |
| 9 | 9.7% | 102,843 | 2,428 | 566 | 381 |
| 10 | 7.5% | 79,863 | 1,886 | 439 | 295 |
| 11 | 5.2% | 55,386 | 1,308 | 305 | 205 |
| 12 | 2.6% | 27,574 | 651 | 152 | 102 |
| 13 | 1.6% | 16,580 | 392 | 91 | 61 |
| 14 | 0.9% | 9,128 | 216 | 50 | 34 |
| 15 | 0.7% | 6,939 | 164 | 38 | 26 |
| Total | 100% | 1,058,731 | 25,000 | 5,823 | 3,917 |

*(It is assumed that 0.37% of all clinical cases will die but not all of these deaths will occur among hospitalised cases.)

**Table 3.1 Weekly number of cases, hospitalisations and deaths as predicted by the empirical model assuming a 25% clinical attack rate, 0.55% cases hospitalised and 0.37% cases die. (Scenario 1)**

Based on the minimal hospitalisation rate of 0.55%, the total number of hospitalisations expected during a pandemic with a clinical attack rate of 25% would be 5,823 over the 15-week period (Table 3.1). The model predicts that approximately 1,250 hospitalisations would occur during both weeks six and seven of the pandemic (Table 3.1).

### *3.8.4 Deaths: Scenario 1*

The empirical model as defined by the HPA assumes that 0.37% of clinical cases will die (similar to UK rates in 1990s epidemics and the 1957 pandemic). It is emphasised that this assumption will predict the minimum

number of deaths that would occur, as the mortality rates seen in other pandemics were markedly higher than 0.37%.

If 0.37% of cases result in death there would be 3,917 influenza deaths in Ireland during a pandemic with a 25% clinical attack rate (Table 3.1).

### *3.8.5 Clinical Attack Rate: Scenario 2*

A clinical attack rate of 50% is assumed in predictions of a worst case scenario.

### *3.8.6 Clinical Cases: Scenario 2*

Assuming a 50% clinical attack rate yields a total of 2,117,463 cases in the Irish population. When the total number of cases is broken down by week in accordance with the proportions shown in Figure 1, the number of cases in one week peaks during week six at 456,377 (Table 3.2). The number of weekly cases rises sharply from 66,082 in week four to 223,410 in week five.

### *3.8.7 Hospitalisations: Scenario 2*

Based on a hospitalisation rate of 3.7%, the total number of hospitalisations expected during a pandemic with a clinical attack rate of 50% would be 78,346 over the fifteen-week period (Table 3.2). The model predicts that approximately 16,700 hospitalisations would occur during both weeks six and seven of the pandemic.

### *3.8.8 Deaths: Scenario 2*

With a mortality rate of 2.5% there would be 52,937 deaths in Ireland during a pandemic with a 50% clinical attack rate.

| Week | % Total cases | Cases per week | Cases per 100,000 pop | Hospitalisations per week | * Deaths per week |
|---|---|---|---|---|---|
| 1 | 0.1% | 3,042 | 72 | 113 | 76 |
| 2 | 0.2% | 4,327 | 102 | 160 | 108 |
| 3 | 0.8% | 17,351 | 410 | 642 | 434 |
| 4 | 3.1% | 66,082 | 1,560 | 2,445 | 1,652 |
| 5 | 10.6% | 223,410 | 5,275 | 8,266 | 5,585 |
| 6 | 21.6% | 456,377 | 10,777 | 16,886 | 11,409 |
| 7 | 21.2% | 448,072 | 10,580 | 16,579 | 11,202 |
| 8 | 14.3% | 302,178 | 7,135 | 11,181 | 7,554 |
| 9 | 9.7% | 205,686 | 4,857 | 7,610 | 5,142 |
| 10 | 7.5% | 159,725 | 3,772 | 5,910 | 3,993 |
| 11 | 5.2% | 110,772 | 2,616 | 4,099 | 2,769 |
| 12 | 2.6% | 55,147 | 1,302 | 2,040 | 1,379 |
| 13 | 1.6% | 33,160 | 783 | 1,227 | 829 |
| 14 | 0.9% | 18,255 | 431 | 675 | 456 |
| 15 | 0.7% | 13,879 | 328 | 514 | 347 |
| Total | 100% | 2,117,463 | 50,000 | 78,346 | 52,937 |

*(It is assumed that 0.37% of all clinical cases will die but not all of these deaths will occur among hospitalised cases.)

**Table 3.2 Weekly number of cases, hospitalisations and deaths as predicted by the empirical model assuming a 50% clinical attack rate, hospitalisation rate of 3.7% and a mortality rate of 2.5%. (Scenario 2)**

### *3.9 Model evaluation*

Limitations to this model include the following

- The pandemic is modelled as a single wave, whereas in reality more than one wave might occur.
- No attempt is made to quantify the impact of antivirals on the pandemic profile – it is likely that the use of anti virals would flatten the peak and widen the curve. Other interventions might also have an effect on the model.

- No information is provided as to what proportion of deaths will occur in hospitals versus elsewhere i.e. the degree of overlap between hospitalisations and deaths is not addressed.
- The model assumes that the next pandemic will mirror previous pandemics. Scenario 1, which incorporates the average clinical attack rate seen in the past three pandemics, is simple to apply and useful for planning purposes. However, it is important not to rely solely on this scenario, as it is not possible to predict what the clinical attack rate, hospitalisation rate or mortality will be. A range of impacts, up to the worst case scenario should be considered and planned for.
- No allowance has been made for the time lag between becoming clinically ill and being hospitalised/dying. All peak during week six whereas we may expect there would be a lag between the maximum number of cases and the maximum number of deaths.
- The curve is based on mortality data and in reality peak mortality may occur slightly later than the clinical peak.

The strengths of this model however are that it is straightforward to use for different attack rates, hospitalisation and death rates, and no assumptions have been made with regard to the nature of the virus itself in terms of infectivity etc.

### *3.10 Recommendations*

**The Pandemic Influenza Expert Group advises that the HPA empirical model be used for planning purposes, with consideration being given both to scenario one, based on previous pandemics, and also to the worst case scenario.**

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