Modelling impact of pandemic influenza: Interim report for Pandemic Influenza Expert Group

January 2006

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1 Summary

- The pandemic predictions of three different mathematical models have been explored[1]. For estimating health impact, an empirical model of pandemic influenza devised by the HPA, based on the profile of previous UK pandemics, has been used in Ireland for interim planning purposes.

- The HPA model has been used to predict the number of clinical cases, hospitalisations and deaths that will occur in Ireland during each week of a 15-week single wave pandemic, in the absence of any interventions.

- A 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 Ireland during an influenza pandemic, in the absence of any interventions.(1)

- An epidemiological model created by Gani et al in the UK has been used to predict the number of clinical cases and hospitalisations that will occur in Ireland during each week of an influenza pandemic.(2) This model has also be used to explore the effect of different antiviral therapy strategies on the weekly numbers of clinical cases and hospitalisations.

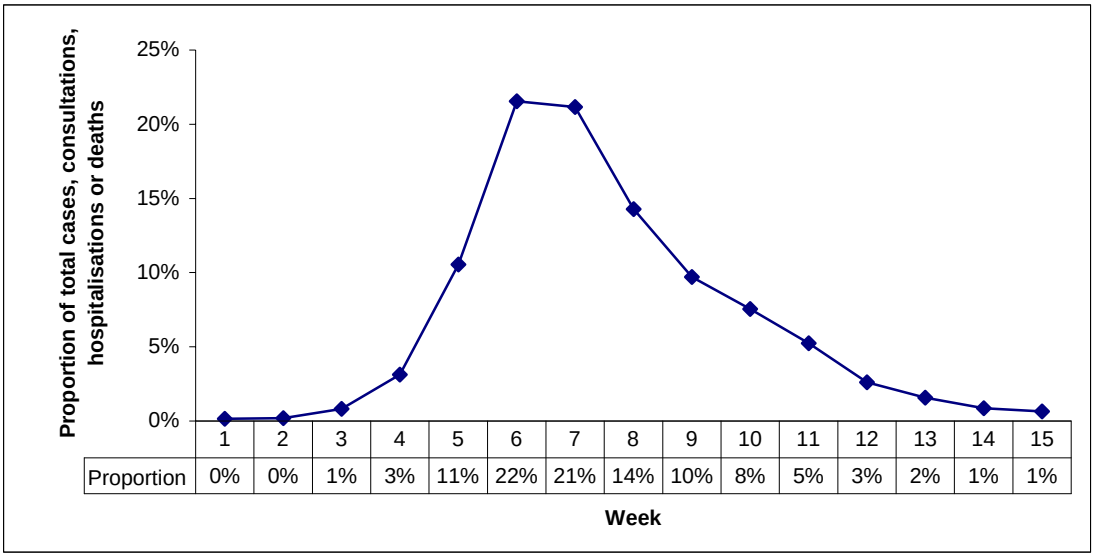
2 HPA Model

The Health Protection Agency (HPA) in the United Kingdom has adopted an empirical model of pandemic influenza for planning purposes. (3-5) The model was derived using data from three previous UK pandemics (1918, 1957, 1969/70).

[1] Note: all figures in this interim report are based on data from the 2002 census, which indicated a total Irish population of 3,917,203. Models in this report use age-specific data, which is not yet available from the 2006 census preliminary report.

2.1.1 HPA Model Structure

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 2.1 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 of 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 2.1 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.

2.2 HPA Model predictions when applied to Irish situation

2.2.1 Clinical Attack Rate

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).

2.2.2 Clinical Cases

Assuming a 25% clinical attack rate yields a total of 979,301 cases in the Irish population. When the total number of cases is broken down by week in accordance with the proportions shown in Figure 2.1, the number of cases in one week peaks during week six at 211,069 (Table 2.1). The number of weekly cases rises sharply from 30,562 in week four to 103,324 in week five.

Week	% total cases	Cases per week	Cases per 100,000 pop	Hospitalisations per week	Deaths per week
1	0.1%	1,407	36	8	5
2	0.2%	2,001	51	11	7
3	0.8%	8,024	205	44	30
4	3.1%	30,562	780	168	113
5	10.6%	103,324	2,638	568	382
6	21.6%	211,069	5,388	1,161	781
7	21.2%	207,228	5,290	1,140	767
8	14.3%	139,754	3,568	769	517
9	9.7%	95,127	2,428	523	352
10	7.5%	73,871	1,886	406	273
11	5.2%	51,231	1,308	282	190
12	2.6%	25,505	651	140	94
13	1.6%	15,336	392	84	57
14	0.9%	8,443	216	46	31
15	0.7%	6,419	164	35	24
Total	**100%**	**979,301**	**25,000**	**5,386**	**3,623**

Table 2.1: Weekly numbers 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

2.2.3 Hospitalisations

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 interpandemic years; the actual rate may be higher than 0.55%.

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 5,386 over the 15-week period (Table 2.1). The model predicts that approximately 1,150 hospitalisations would occur during both weeks six and seven of the pandemic (Table 2.1).

2.2.4 Deaths

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 3,623 deaths in Ireland during a pandemic with a 25% clinical attack rate (Table 2.1).

2.3 HPA Model evaluation

2.3.1 Limitations

- No attempt is made to quantify the impact of antivirals on the pandemic profile – it is likely that the use of antivirals would flatten the peak and widen the curve.
- 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.
- It assumes that the next pandemic will mirror previous pandemics.

- Death rate may be too low – 2.5% used in worst case scenarios in comparison to 0.37% here.
- No allowance is made for a time lag between becoming clinically ill and being hospitalised/dying. All peak during week six whereas we may expect there to be a time 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 HPA Influenza Pandemic Contingency Plan states that the numbers of hospitalisations and deaths predicted by the model should be considered the minimum expected for pandemic flu.

2.3.2 Strengths

- Straightforward to use for different attack rates, hospitalisation and death rates.
- No assumptions with regard to the nature of the virus itself in terms of infectivity etc.

3 Meltzer model

Meltzer et al devised an economic model of pandemic influenza. It differs from the empirical model in that only the total impact of the pandemic in terms of hospitalisations and deaths is estimated – numbers are not broken down by week.[(1)] The purpose of Meltzer's original paper was to assess the economic effectiveness of different intervention strategies and provide a dollar estimate of the impact of an influenza pandemic in the USA. During the HPSC modelling exercise, the Meltzer model was applied to the Irish population to produce estimates of the hospitalisations and deaths that would occur under varying clinical attack rates. At this stage, the economic cost of a pandemic in Ireland has not been explored.

3.1 Meltzer Model structure

Scenarios

Two pandemic scenarios are defined which differ in two key areas:

1. The age-specific attack rate
2. The proportion of the population who are classed as "being at a higher risk of contracting an influenza-related illness with a serious health outcome"

3.1.1 Age-specific attack rate

In scenario A, the majority of cases (53%) occur in the 20-64 year age group, with 40% in the 0-19 year age group and 7% in the 65+ age group. Figure 3.1 below shows that the main difference between Scenarios A and B is that a larger proportion of cases fall into the 0-19 year age group in Scenario B.

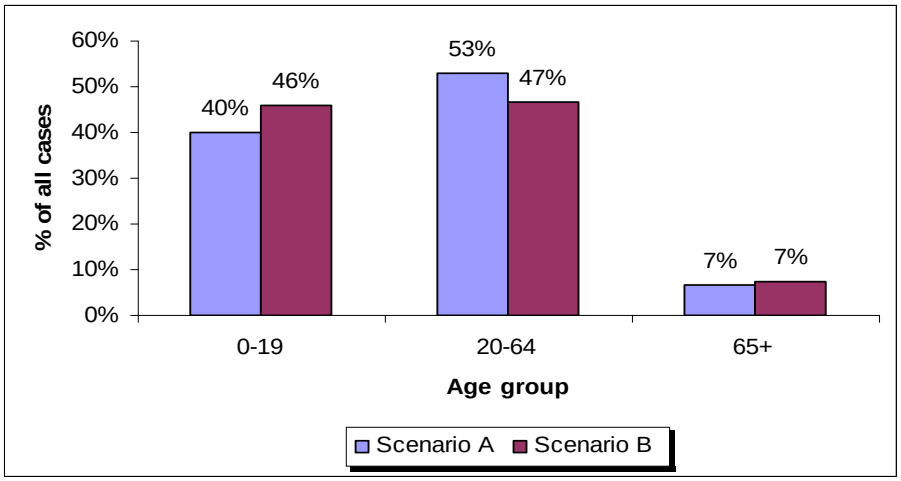


Figure 3.1: Proportion of total cases within each age group in 2 scenarios

The age distribution of the cases within the two scenarios was derived using the upper and lower estimates of age-specific attack rates in data from 1918, 1928-29 and 1957.

3.1.2 Percentage of the population at high risk

In Scenario B, a higher percentage of each age group is defined as high risk. The high-risk percentages used in Scenario A are lower across all age groups, as can be seen in Figure 3.2.

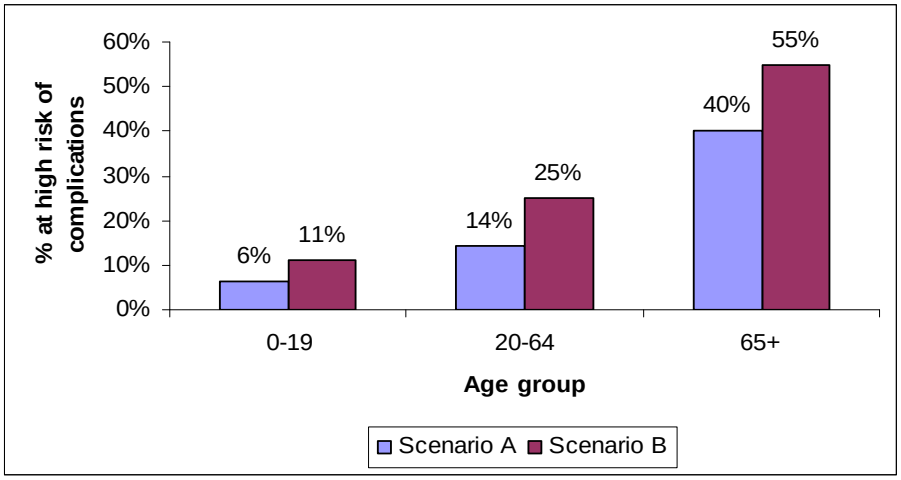


Figure 3.2: Proportion at high risk within each age group in 2 scenarios

It is apparent that Scenario B is a worse case scenario, with 24.3% of the total Irish population defined as high risk compared to 14.9% in Scenario A.

The US Working Group on Influenza Pandemic Preparedness and Emergency Response (GRIPPE, unpublished data) provided Meltzer with both scenario estimates of the high-risk proportion within the 0-19 year age group and also the scenario A estimate for the 20-64 age group. Both high-risk estimates for the 65+ age group and the scenario B estimate for the 20-64 year age group were obtained from expert opinion.

3.1.3 Deriving profile of cases

The parameters as defined in a particular scenario can be used to classify the population of clinical cases from a particular attack rate into age and risk group as in Figure 3.3.

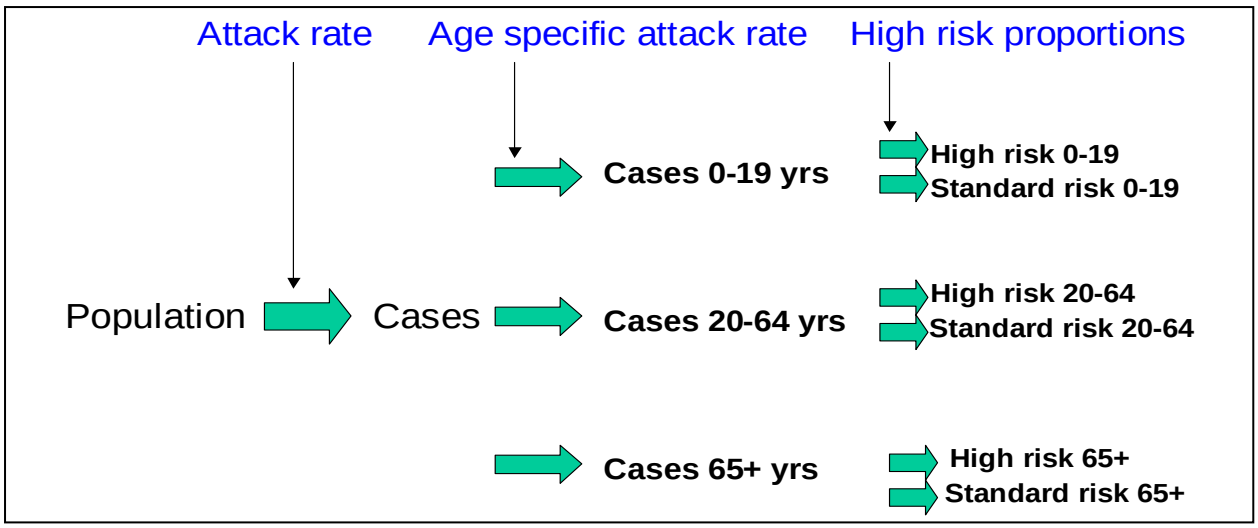


Figure 3.3: Flowchart showing method for calculating total number of cases and then dividing cases by age and risk group

3.1.4 Hospitalisation Rates

Age group (years)	Hospitalisation rate per 1,000 cases	
	Standard risk	High risk
0-19	0.6 – 6.9	6.0 – 21.4
20-64	1.5 – 12.0	6.9 – 22.3
65+	12.5 – 15.8	33.3 – 68.4

Table 3.1: Hospitalisation rates for each age and risk group combination

The rates used by Meltzer, as shown in Table 3.1 and Figure 3.4, were derived from two studies carried out in Oregon by Mullooly [6] and Barker [7] and a Delphi study of expert opinion published by Schoenbaum et al.[8]

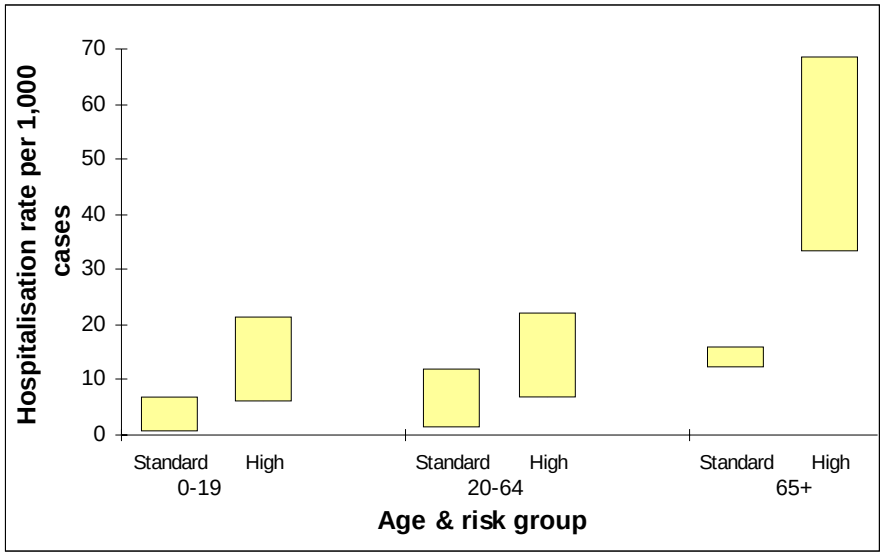


Figure 3.4: Range of hospitalisation rates for each age & risk group combination

It can be seen in Figure 3.4 that there is a considerable difference between the hospitalisation rates within an age group, depending on if the patient is considered high risk. This is most noticeable within the 65+ age group.

3.1.5 Death Rates

Age group (years)	Death rate per 1,000 cases	
	Standard risk	High risk
0-19	0.04– 0.3	0.4 – 21.9
20-64	0.2 – 0.4	0.8 – 24.9
65+	2.3 – 4.5	23.0 – 29.6

Table 3.2: Death rates for each age and risk group combination

Meltzer derived the death rates shown in Table 3.2 and Figure 3.5 using a variety of published sources including the Mullooly and Barker and Schoenbaum studies used to calculate the hospitalisation rates. Data were also used from a paper by Serfling [9] and an Office of Technology report.[10]

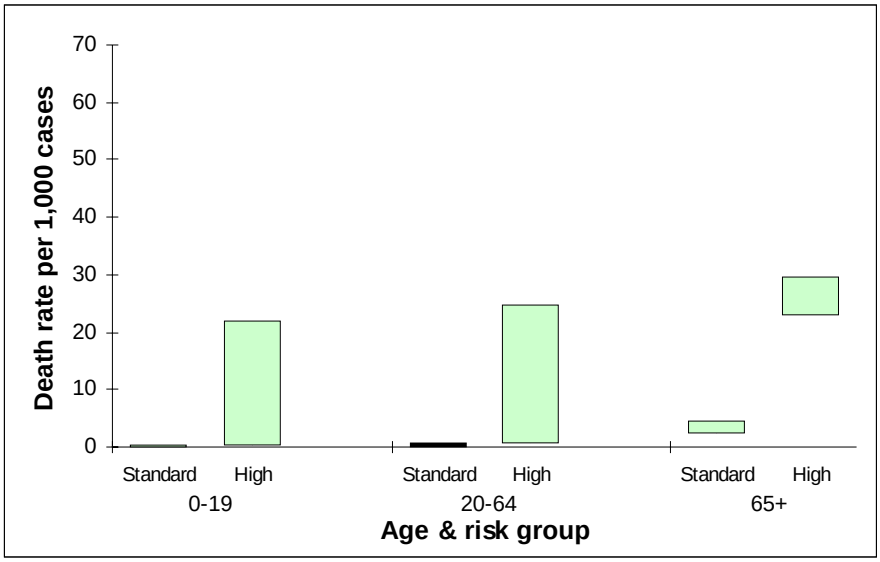


Figure 3.5: Range of death rates for each age & risk group combination

3.2 Meltzer Model predictions when applied to Irish situation

3.2.1 Hospitalisations

Under a defined clinical attack rate, when the relevant hospitalisation rates in Table 3.1 above are applied to the corresponding numbers of cases within each age/risk group combination, the following predictions are derived.

	Number of hospitalisations predicted by model			
Attack Rate	Scenario A lower limit **Minimum**	Scenario B lower limit	Scenario A upper limit	Scenario B upper limit **Maximum**
10%	1,172	1,417	5,012	5,479
15%	1,758	2,126	7,519	8,218
20%	2,344	2,835	10,025	10,957
25%	2,930	3,543	12,531	13,697
30%	3,516	4,252	15,037	16,436
35%	4,102	4,960	17,543	19,175
40%	4,688	5,669	20,050	21,915
45%	5,274	6,378	22,556	24,654

Table 3.3: Hospitalisations predicted under both scenarios and varying clinical attack rates using the Meltzer model

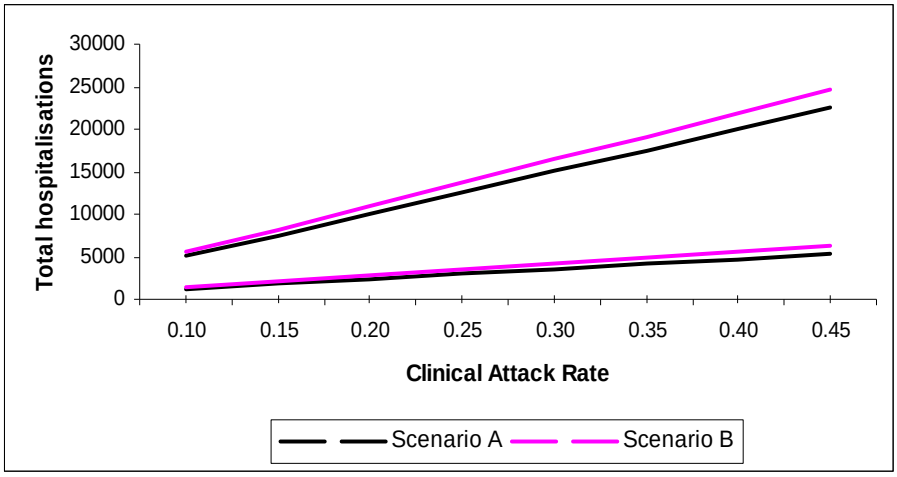


Figure 3.6: Upper and lower estimates of number of hospitalisations in Ireland under varying clinical attack rates and two pandemic Scenarios

Table 3.3 and Figure 3.6 show that the predicted number of hospitalisations in Ireland varies according to the clinical attack rate and which assumptions are adopted (Scenario A or B). As Scenario B is based on a larger proportion of the population being at high risk and the high risk group has a greater hospitalisation rate, the predicted number of hospitalisations is higher in the Scenario B setting.

A clinical attack rate of 25% has been used for planning purposes in Ireland. The number of hospitalisations predicted by the Meltzer model for a clinical attack rate of 25% ranges from 2,930 to a maximum of 13,697 (Table 3.3).

3.2.2 Deaths

The number of deaths predicted by the model can be derived analogously to the hospitalisations, using the death rates shown in Table 3.2. The model predictions can be seen in Table 3.4:

	Number of deaths predicted by model			
Attack Rate	Scenario A lower limit **Minimum**	Scenario B lower limit	Scenario A upper limit	Scenario B upper limit **Maximum**
10%	353	471	1,470	2,205
15%	530	707	2,205	3,307
20%	706	943	2,940	4,410
25%	883	1,178	3,675	5,512
30%	1,060	1,414	4,410	6,614
35%	1,236	1,650	5,145	7,717
40%	1,413	1,885	5,880	8,819
45%	1,589	2,121	6,615	9,922

Table 3.4: Minimum and maximum deaths predicted under both scenarios and varying clinical attack rates using the Meltzer model

Again, the highest number of deaths is predicted under the Scenario B assumptions. If the 25% clinical attack rate is considered, the estimated number of deaths ranges from 883 using Scenario A and the lower limit of the death rate to a maximum of 5,512 using Scenario B and the upper limit of the death rate.

Figure 3.7 illustrates that there is considerable difference between the Scenario A and Scenario B death estimates, particularly when the highest death rate is applied (See Table 3.2 for the range of death rates).

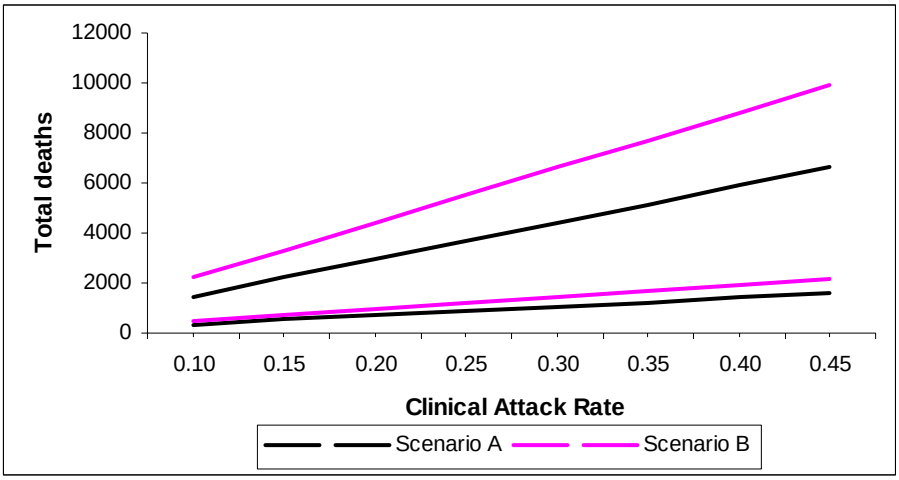


Figure 3.7: Upper and lower[2] estimates of number of deaths in Ireland under varying clinical attack rates and two pandemic scenarios

[2] While considering figure 3.7, it cannot be assumed that the most likely estimate for the number of deaths would fall half way between the upper and lower estimates. Meltzer hypothesises a distribution that is weighted toward the lower end of the death rate ranges.

3.3 Evaluation of Meltzer model

An advantage of the Meltzer model is that it makes no explicit assumptions about the duration of the pandemic although this makes it less useful from a planning perspective. Meltzer did not devise this model to provide a unique estimate of the impact of a pandemic but more to create a range of potential scenarios for discussion. The model was devised primarily to explore the cost effectiveness of vaccination against influenza rather than to make pandemic predictions.

Two software packages (Flu Aid and Flu Surge) developed by Meltzer are available on the web and are straightforward to use for calculations of pandemic impact at a local, regional or national level.

The high risk proportions used in Meltzer's model may not be applicable to the Irish population – a larger overall proportion of the population are defined as high risk in Meltzer's model than e.g. the high risk proportions found in UK data and used in Gani's paper.

4 Gani model

An epidemiological model devised in the UK by Ray Gani et al can be used to predict the impact of pandemic influenza on Ireland and also to assess the benefits of various antiviral intervention strategies.[(2)] The Gani model is useful for planning purposes as it provides estimates of the situation at defined time points e.g. weekly/daily intervals unlike the Meltzer model which gives an end stage total figure.

4.1 Gani Model structure

The Gani model postulates that members of the population exist in one of four states during a single wave influenza pandemic: Susceptible, Exposed, Infectious, Removed. Figure 4.1 below depicts the direction of movement and time spent in each of the states as defined by Gani.

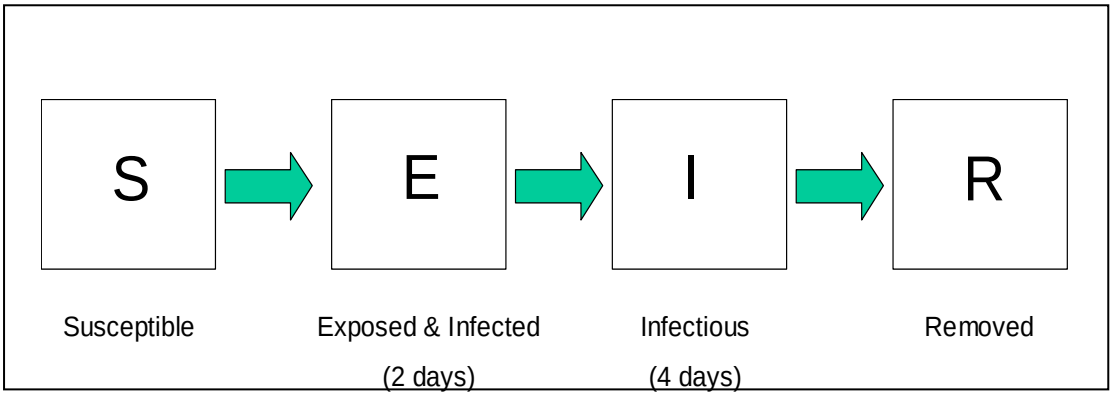


Figure 4.1: Structure of Gani model

The four states are defined thus:

State	Definition
Susceptible	Have not been infected by virus
Exposed & Infected	Have been infected by virus No viral shedding No symptoms
Infectious	Now shedding virus May also be symptomatic
Removed	No longer infectious, either recovered or dead

Table 4.1: Description of states within Gani model

4.1.1 Determinants of movement between states

Initially, it is assumed that the entire population is susceptible to the pandemic influenza virus. When a number of infectious individuals are seeded into the population they pass on the virus to others who then move out of the susceptible state and along the S-E-I-R sequence. The rate of infection and the subsequent transitions between states depend on a number of variables as shown in Figure 4.2.

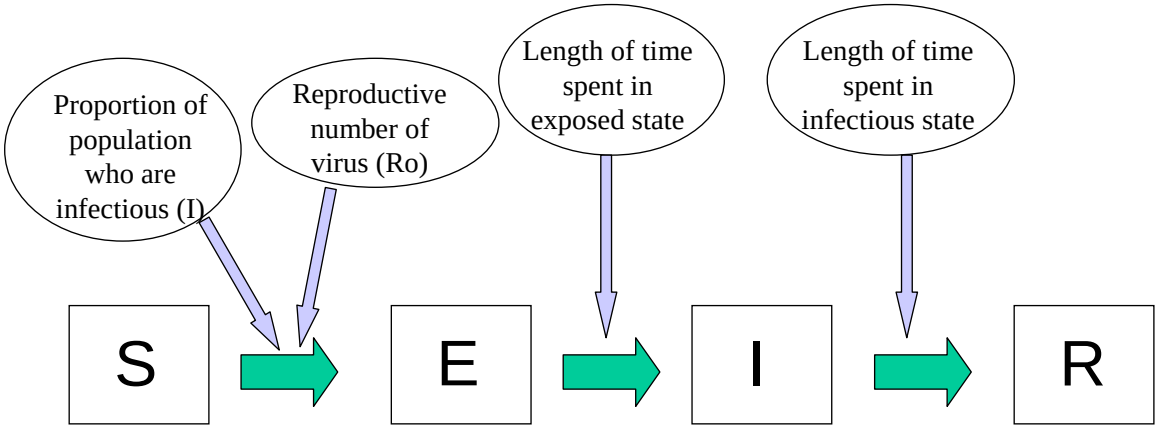


Figure 4.2: Determinants of movement between states

There are two factors shown in Figure 4.2 that influence the progression of an individual from susceptible to exposed and infected. One of these factors is Ro, the reproductive number of the virus. Ro is defined as the number of secondary infections produced by one infectious person in a completely susceptible population.

It is Ro that determines the Serological Attack Rate (SAR) of the epidemic. Table 4.2 outlines some values of Ro and the corresponding SAR and Clinical Attack Rates (CAR). Gani assumes that 50% of infections are non-clinical i.e. the CAR is 50% of the SAR.[11]

Ro	Clinical Attack Rate	Serological Attack Rate
1.19	15%	30%
1.28	20%	40%
1.39	**25%**	**50%**
1.52	30%	60%
1.72	35%	70%
2	40%	80%

Table 4.2: Values for Ro and corresponding Clinical and Serological Attack Rates

The HPA and WHO have used a CAR of 25% for planning purposes, this corresponds to a Ro of 1.39.

4.2 *Gani Model predictions when applied to Irish situation*

4.2.1 Pandemic progression: Initial importations

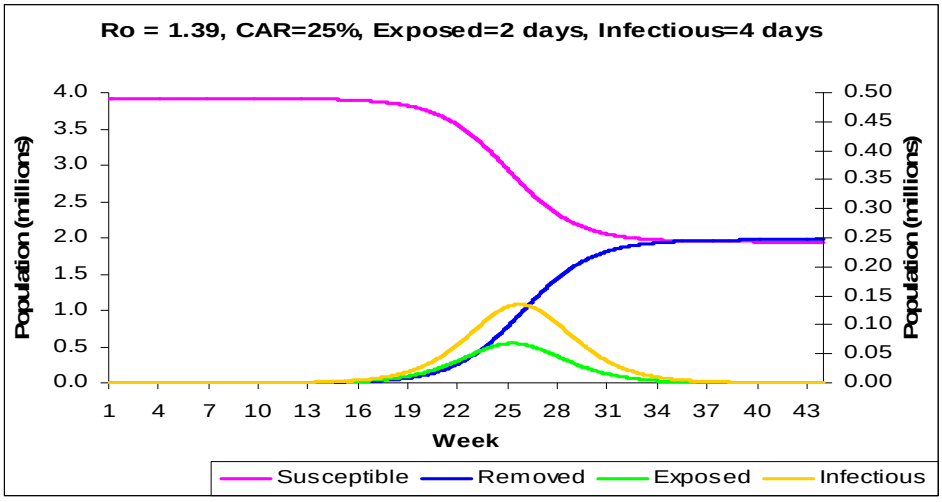


Figure 4.3: Number of persons in states S, E, I, R over time after 10 infectious cases imported in week 1, Ro=1.39 LHS axis: Susceptible and Removed curves, RHS axis: Exposed and Infectious curves

The predicted number of cases begins to noticeably increase during week 16, 15 weeks after the first ten cases enter the Irish population. The pandemic peaks in week 25, at which point there are 135,214 infectious cases in the population (Figure 4.3). It is important to remember that half of these cases are asymptomatic thus the peak number of clinical cases is 67,607. At the end of the single wave pandemic, which takes approximately 37 weeks to reach a conclusion, 50% of the population have been infected with the virus and have either recovered or died.

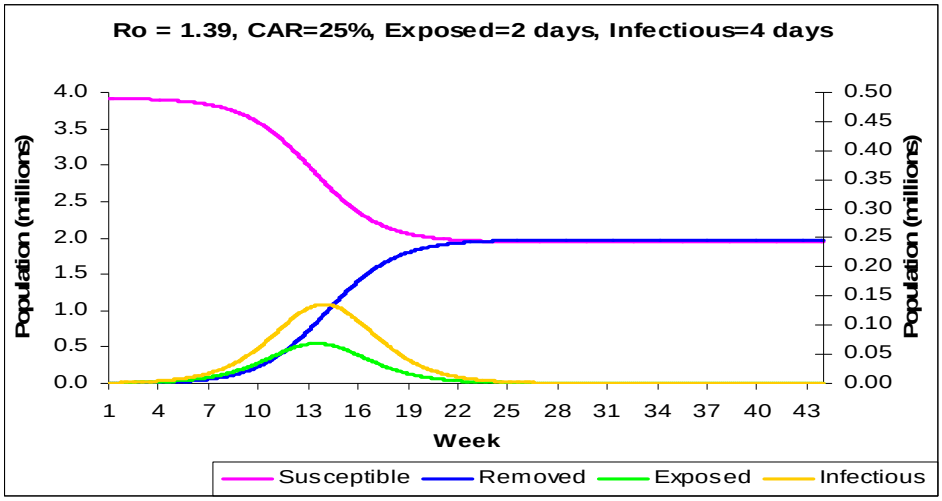


Figure 4.4: Number of persons in states S, E, I, R over time after 250 infectious cases imported daily during week 1, Ro=1.39 LHS axis: Susceptible and Removed curves, RHS axis: Exposed and Infectious curves

Figure 4.3 is based on the situation in which 10 infectious cases enter the country and there are no further importations of the disease. The length of time between entry of the disease and the epidemic peak is dependent on both the reproductive number (Ro) of the virus and also on the number of initial cases that arrive into Ireland. The situation in which 250 new infectious cases arrive into the country every day for one week is shown in Figure 4.4.

There is a clear difference in pandemic progression when 250 cases are imported daily during week one compared to the situation when 10 infectious cases enter the population in week one and there are no further importations. The peak number of infectious cases is similar in both scenarios (136,085 vs. 135,214 in the 10 importation scenario) however the time taken for the epidemic to peak is considerably shortened when there are multiple importations. The epidemic peak is reached 12 weeks after the initial cases enter the country in the multiple importations scenario compared to 24 weeks after 10 infectious cases enter the country.

4.2.2 Pandemic progression: Ro

A Ro of 1.39 has been used for planning purposes. This produces a CAR of 25%, as proposed by the WHO and also used by Meltzer et al and the HPA in their planning literature. It can be seen that varying Ro has a significant impact on the pandemic predictions from the Gani model. Figure 4.5 shows the model predictions when a Ro of 2 (corresponding to a CAR of 40%) is used.

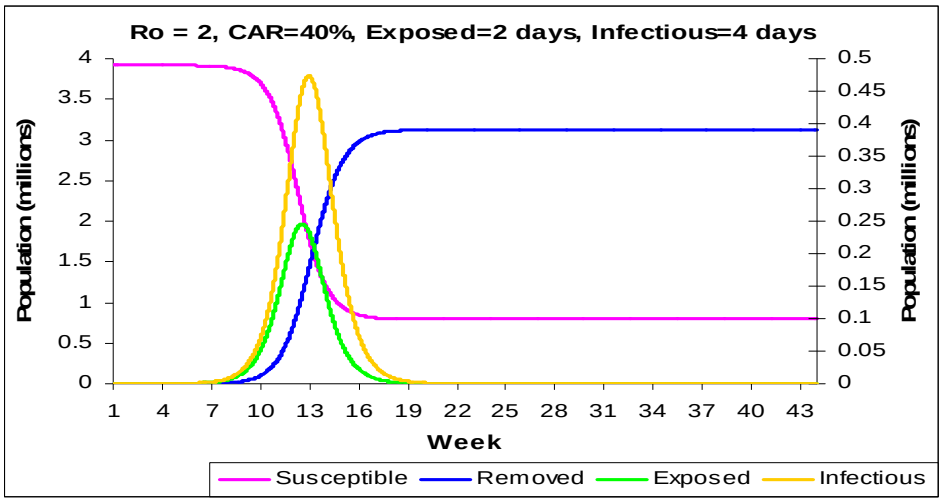


Figure 4.5: Number of persons in states S, E, I, R over time after 10 infectious cases imported in week 1, Ro=2 LHS axis: Susceptible and Removed curves, RHS axis: Exposed and Infectious curves

When Ro is 2, the peak number of 473,099 infectious cases occurs during week 12 compared to a peak of 135,214 during week 25 in the scenario in which Ro is 1.39. Again it should be noted that 50% of infectious cases are presumed to be symptomatic therefore the peak number of clinical cases in this scenario is 236,550.

4.2.3 Pandemic progression: Hospitalisations

As in the Meltzer model, hospitalisation rates differ within an age group according to risk status. The proportion of the population at high risk of a severe outcome was derived from a UK study of primary care patients and includes immunosuppressed individuals and those with chronic conditions e.g. diabetes, heart disease.[12]

Age group (yrs)	% at high risk of complications*
0-4	8.79
5-14	7.76
15-64	5.82
65-74	26.10
75+	33.80

Table 4.3: Percentage at high risk within age groups

The hospitalisation rates derived by Gani for each age and risk group combination are shown in Table 4.4 below.

Age group (yrs)	Hospitalisation Rates per 100,000 clinical cases	
	High risk	Low risk
0-4	3,562	509
5-14	274	39
15-64	873	125
65-74	4,235	605
75+	8,797	1,257

Table 4.4: Hospitalisation rates within each age/risk group

Assuming that there is a uniform attack rate across all age and risk groups and that 50% of infectious cases are clinically ill, hospitalisation numbers can be calculated and are displayed, with varying Ro in Figure 4.6.

* Provisional proportions, currently under discussion with Ray Gani

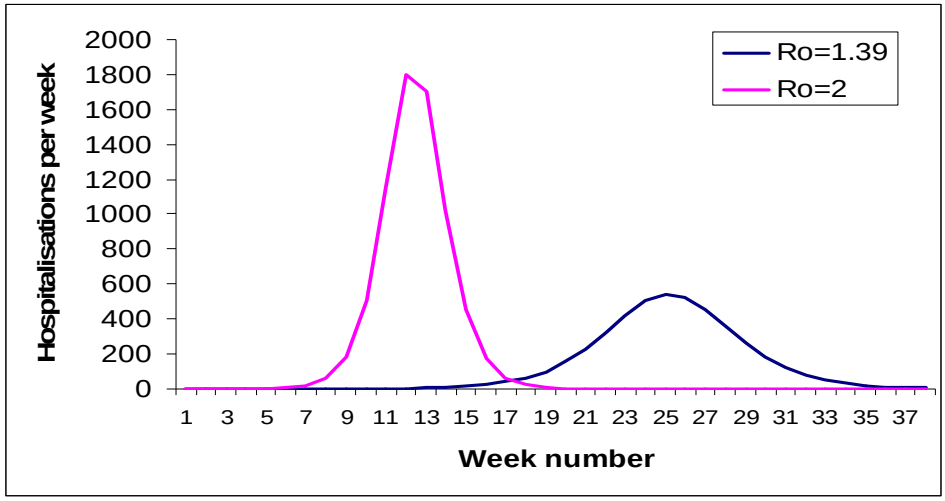


Figure 4.6: Hospitalisations per week as predicted by Gani model with varying Ro after 10 infectious cases imported in week 1

The model predicts that weekly hospitalisations in the case where Ro=1.39 (CAR=25%) would peak in the 25th week of the pandemic at 541. A larger Ro of 2 would result in an earlier and larger peak in weekly hospitalisations than the Ro=1.39 situation. A peak in weekly hospitalisations of 1,800 in the Ro=2 case is predicted to occur in week 12.

4.2.4 Effect of antiviral therapy on total hospitalisation volumes

The Gani model can also be used to assess the effect of interventions such as Antiviral Therapy (AVT) on the number of clinical cases and hospitalisations that would occur during the pandemic. Gani assumes that AVT reduces the infectious period from 4 days to 2.5 days and lessens the risk of hospitalisation by 50%.[13]

Figure 4.7 depicts the effect of AVT on total hospitalisations in the course of the pandemic. The treatment strategy used here has been to treat all clinical cases over 1 year old. The model offers the possibility of investigating other treatment strategies e.g. AVT to high risk patients only or particular age groups.

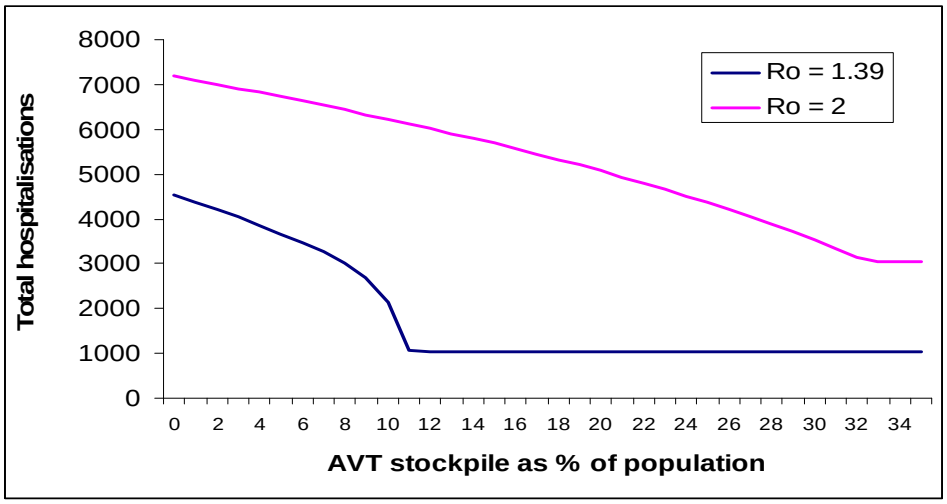


Figure 4.7: Total hospitalisations as predicted by Gani model with varying stockpile sizes and Ro

The interaction between AVT stockpile size and the number of hospitalisations can be clearly seen in Figure 4.7. The point at which the curves level out and become horizontal is where the stockpile is of sufficient size to treat all clinical cases. In the case where Ro is 1.39, a stockpile of around 12% is enough to treat all cases and produce the minimum number of hospitalisations. Administering AVT to all clinical cases over 1 year old is predicted to reduce the total number of hospitalisations from 4,500 (when there is no AVT available) to 1,000 when there is a sufficient stockpile to treat all eligible cases.

The figures relating to the effect of AVT represent a best-case scenario in terms of AVT distribution and compliance. In the real situation it is unlikely that all eligible cases would receive AVT in the first 2.5 days of their illness and also unlikely that all those who are given AVT would follow the course through to completion.

The assumptions made with respect to the AVT shortening the infectious period and reducing the likelihood of hospitalisation are based on the premise that AVT will have the same effect on the pandemic strain as on seasonal influenza viruses and this may not be the case.

When Ro is 2, the total number of hospitalisations is reduced from 7,200 in the absence of AVT to 3,000 when there is a stockpile of 33% (Figure 4.7).

4.2.5 Effect of antiviral therapy on weekly hospitalisation volumes

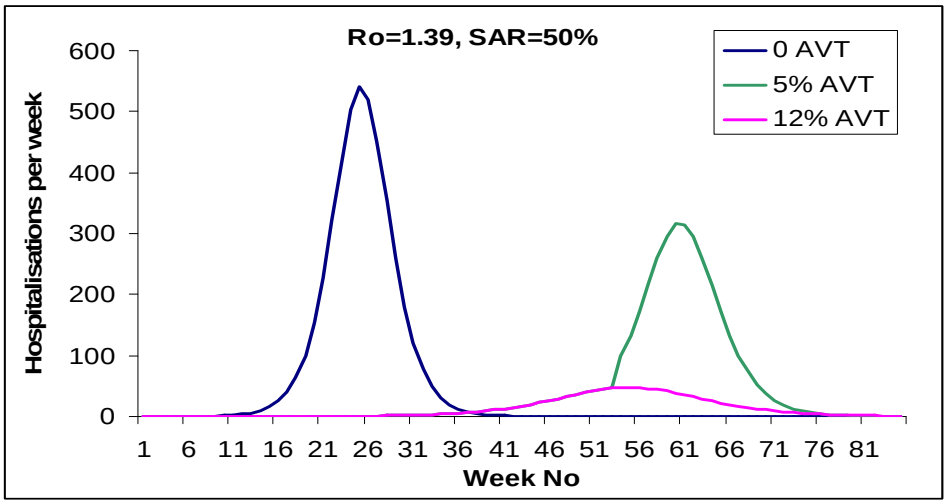


Figure 4.8: Weekly hospitalisations when Ro=1.39 as predicted by Gani model with varying stockpile sizes

The model predicts that a stockpile size equal to 12% of the total Irish population is required to keep hospitalisations to a minimum in a situation where the pandemic virus has a Ro of 1.39. When there is no AVT available, hospitalisations are predicted to peak during week 25 at 541 whereas when there is a 12% stockpile, the predicted peak number of weekly hospitalisations is 48 and occurs in week 55 (Figure 4.8).

The situation in which the stockpile is 5% of the population size is illustrated in Figure 4.8. Weekly hospitalisations follow the pattern in the 12% stockpile case until week 54, at which point the stockpile is exhausted and AVT ceases. Hospitalisations increase sharply after this point.

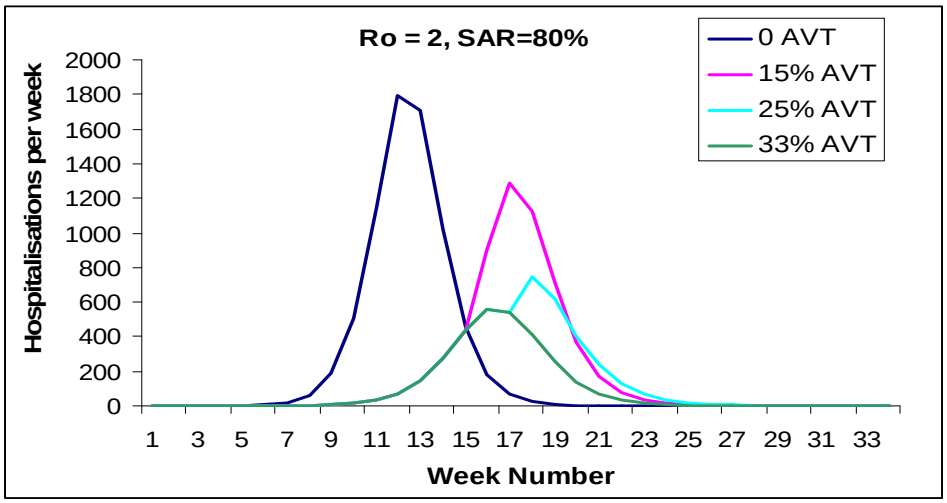


Figure 4.9: Weekly hospitalisations when Ro=2
as predicted by Gani model with varying stockpile sizes

In the Ro=2 scenario, if AVT is given to all eligible clinical cases, the peak number of weekly hospitalisations is reduced from 1,800 in week 12 to 559 in week 16 (Figure 4.9). This would require a stockpile of enough doses of AVT to treat 33% of the Irish population.

Stockpile sizes of 15% and 25% would not be enough in this situation to treat all clinical cases, as is evident in Figure 4.9. However, the use of AVT in each of these scenarios is sufficient to delay and lower the peak number of weekly hospitalisations.

4.3 Evaluation of Gani model

A very useful aspect of the Gani model is that it can be used to assess the effectiveness of antiviral interventions on pandemic progression, the Meltzer and HPA models do not allow this. The fact that the model provides weekly numbers is useful from a planning perspective.

The biggest weakness of the model is the number of assumptions within it – if one of these is incorrect then the validity of the model predictions is called into question. However, there is the capacity to adjust any parameter that is considered faulty and create a new set of predictions based on another estimate. This feature could prove most useful in the event of a pandemic; as

information on the virus strain becomes known it can be fed into the model and used to produce updated predictions.

Another weakness is that uniform behaviour in terms of duration of illness and antiviral efficacy is assumed across all age and risk groups. This is unlikely to be true in reality.

This report was prepared by Kate Hunter, Dr Derval Igoe, Dr Mai Mannix and Dr Darina O'Flanagan, HPSC.

5 References

1. Meltzer MI, Cox NJ, Fukuda K. The economic impact of pandemic influenza in the United States: priorities for intervention. Emerg Infect Dis 1999; 5:659-671.
2. Gani R, Hughes H, Fleming D, Griffin T, Medlock J, Leach S. Potential impact of antiviral drug use during influenza pandemic. Emerg Infect Dis 2005; 11(9):1355-1362.
3. Department of Health. UK operational framework for stockpiling, distributing and using antiviral medicines in the event of pandemic influenza. 2006.
4. Health Protection Agency. Influenza Pandemic Contingency Plan. www.hpa.org.uk . 2005.
5. Health Protection Agency. Influenza Pandemic Contingency Plan October 2005. www.hpa.org.uk . 2005.
6. Mullooly JP, Bennett MD, Hornbrook MC, Barker WH, Williams WW. Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintenance organization. Ann Intern Med 1994; 121(12):947-952.
7. Barker WH, Mullooly JP. Impact of epidemic type A influenza in a defined adult population. Am J Epidemiol 1980; 112(6):798-811.
8. Schoenbaum SC, McNeil BJ, Kavet J. The swine-influenza decision. N Engl J Med 1976; 295(14):759-765.
9. Serfling RE, Sherman IL, Houseworth WJ. Excess pneumonia-influenza mortality by age and sex in three major influenza A2 epidemics, United States, 1957-58, 1960 and 1963. Am J Epidemiol 1967; 86(2):433-441.
10. Cost effectiveness of influenza vaccination. Office of Technology Assessment, US Congress. 1981. Washington. D.C., Government Printing Office.
11. Mann PG, Pereira MS. A five-year study of influenza in families. Joint Public Health Laboratory Service/Royal College of General Practitioners working group. J Hyg (Lond) 1981; 87(2):191-200.

12. Fleming D, Charlton J, McCormick A. The population at risk in relation to influenza immunisation policy in England and Wales. Health Trends 1997.
13. Stiver G. The treatment of influenza with antiviral drugs. CMAJ 2003; 168(1):49-56.