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Executive summary

1. Introduction

a. This revised guidance, prepared in November 2008, replaces the draft version for consultation published in January 2007, and all other documents previously published by the Pandemic Influenza Expert Group (PIEG).

b. The aim of the document is to provide timely, authoritive information on pandemic influenza, to provide clinical guidance for health professionals, and to provide public health advice for the public, public health professionals, and policy makers in the Department of Health and Children and other government Departments and agencies, all of whom will be involved in the response to an influenza pandemic.

2. Pandemic Phases

a. The phases of a pandemic are subdivided as per WHO advice, with the addition of EU and Irish alert levels, allowing for a graded response to be planned.

3. Impact

a. It is not possible to predict when the next pandemic will occur, which influenza strain will cause it, and how severely it will affect the world's population. However, when planning for a pandemic, PIEG recommends that the UK Health Protection Agency's model be used, and that a range of scenarios are considered, ranging from a clinical attack rate of 25%, with a hospitalisation rate of 0.55% of clinical cases, and a death rate of 0.37% of clinical cases; to a worst case scenario, with a clinical attack rate of 50%, a hospitalisation rate of 3.7% and a death rate of 2.5% of clinical cases.

4. Surveillance and situation monitoring

a. Surveillance is an essential component of preparedness for pandemic influenza, and efforts are being made to continuously strengthen clinical and virological surveillance for seasonal influenza and for novel viruses. During the planning phase the PIEG advises that it is important to focus also on the development of template "situation monitoring" reports, i.e. reports that measure the health and non-health impact, and which contain for example information on absenteeism due to illness, use of healthcare and other resources etc.

b. With regard to surveillance of antiviral and vaccine effectiveness, side effects and toxicity, PIEG recommends that this work be done in conjunction with ECDC, who is tendering for this work at present.
c. During a pandemic, timely information on the number of deaths occurring will be essential. Recent changes to the Civil Registration Act, which allows for registration of deaths for up to 3 months following its occurrence, may jeopardise the capacity of the system to accurately and quickly measure the impact of a pandemic using mortality information. PIEG therefore recommends that consideration should be given to reviewing this Act, with a view to shortening the timeframe for death registration to 5 days.
d. When the initial cases of pandemic influenza occur in Ireland, PIEG recommends that detailed case based enhanced surveillance is carried out, in order to accurately describe the epidemiology, clinical features and outcome. In addition information on contacts of pandemic influenza cases will need to be gathered. PIEG recommends that a national electronic contact tracing system is developed for this purpose.
e. During the pandemic sentinel weekly GP and hospital surveillance will need to continue. In the interim, the sentinel hospital surveillance system needs to be strengthened. A system for active surveillance among a subset of hospitalised patients should be developed too.
f. As a vital component of the response to pandemic influenza, PIEG recommends that planning for surveillance surge capacity be undertaken and resources are allocated to these tasks.

5. Public Health Response: Antiviral drugs

a. Antiviral drugs are essential components of a comprehensive pandemic response. Pending the availability of virus specific vaccines, and assuming that they will be effective against the pandemic strain, they will be the only influenza-specific medical intervention available for use in a pandemic. PIEG recommends that they are used to prevent or reduce deaths and hospitalisations, to prevent morbidity, and to maintain essential services during a pandemic.
b. Ireland has a stockpile of oseltamivir sufficient to treat 25% of the population, and of zanamivir sufficient to treat 20% of the population aged over 7 years. The emergence of resistance of A (H1N1) to oseltamivir during the 2007/2008 season is a cause of concern, and warrants ongoing review.

c. During the pandemic alert period, PIEG recommends that oseltamivir treatment is used for any avian influenza cases. If an outbreak of highly pathogenic avian influenza occurs in birds in Ireland, PIEG recommends that antivirals should be used for prevention and control of avian influenza in occupational groups and other contacts exposed to dead or diseased birds.
d. At the start of a pandemic, when isolated cases or small outbreaks are occurring in Ireland, PIEG recommends that contact tracing of family and health care worker contacts be carried out and that short term post exposure prophylaxis be offered.
e. Later on, when cases are widespread in Ireland, PIEG recommends that all early symptomatic cases are treated, but that contact tracing and post exposure prophylaxis are discontinued.
f. If the clinical attack rate is very high and stockpiles are not sufficient to treat all symptomatic persons, PIEG recommends that the following groups are prioritised for treatment: Persons hospitalised with influenza, ill health-care and emergency service workers, ill high risk persons in the community (those with chronic illnesses,) and high risk residents of institutions.
g. PIEG, noting that significant logistical problems will arise in achieving timely and appropriate distribution and delivery of antiviral drugs, recommends that sufficient resources are put into planning a robust capacity in delivering antiviral drugs as needed as quickly as possible.

6. Public Health Response: Vaccines

a. Vaccination is the ideal primary public health response in the event of an influenza pandemic. However there are significant delays, of at least 6 months, before a pandemic specific vaccine can be produced.
b. Vaccination against seasonal influenza has 2 benefits, namely reducing the burden of influenza each year, and increasing vaccine production capacity. PIEG recommends that every effort is made to increase seasonal influenza vaccination coverage of all people at high risk in all settings (e.g. healthcare clinics, GP surgeries and workplaces) and to achieve the WHO target of 75% uptake of seasonal vaccination by older people by 2010.
c. The goals for vaccination during a pandemic are to prevent and reduce death and hospitalisations, to prevent and reduce influenza related morbidity and to maintain essential services by protecting the health of essential service workers.

d. PIEG recommends that Ireland should enter into an advanced purchase agreement with vaccine manufacturer(s) for sufficient vaccine to vaccinate the whole population, in the event of a pandemic emerging.
e. PIEG recommends that initial supplies of the pandemic specific vaccine be prioritised to the following subgroups of the population:
    i. Health care staff with patient contact (including ambulance staff), and staff in residential care homes for the elderly
    ii. Providers of essential services e.g. fire, utilities, Gardaí, security, communications, defence forces, undertakers and essential healthcare staff without direct patient contact
    iii. Those with high medical risk e.g. chronic respiratory or heart disease, renal failure, diabetes or immunosuppression due to disease or treatment, women in the last trimester of pregnancy, and children aged from 6 months to 23 months
    iv. All over 65 years of age
    v. Selected industries – maintenance of essential supplies e.g. pharmaceuticals
    vi. Selected age groups, depending on advice from WHO e.g. children
    vii. Offer to all

Please note that these priorities are subject to change as the epidemiology becomes evident.

f. PIEG recommends that protocols for timely assessment of vaccine effectiveness should be drawn up in advance of a pandemic and that options for measuring vaccine uptake among priority groups and in the general population are examined as part of the planning process.
g. Scientific data is emerging to demonstrate that “pre-pandemic” H5N1 vaccination might have a significant impact on the size, duration, morbidity and mortality of the pandemic, if the next pandemic were H5N1 derived. However there is no guarantee that the next pandemic will be H5N1 derived. PIEG recommends that the Department of Health and Children considers commissioning a cost-benefit analysis looking a various options for use of pre-pandemic H5N1 vaccine.
h. Given that Streptococcus pneumoniae is one of the main pathogens responsible for secondary bacterial infection

following influenza infection, PIEG recommends that the benefits of pneumococcal vaccine is promoted among at risk groups and healthcare professionals.

7. **Public health Response: Non pharmaceutical interventions in the pandemic alert period (WHO Phases 3, 4 and 5)**
    a. Non pharmaceutical public health interventions include public health information, communications, personal measures such as respiratory hygiene and self isolation when sick, increasing social distance (school closures), measures at ports of entry, travel restrictions etc. In the pandemic alert period, PIEG recommends that the WHO approach to outbreak communications be adopted for all communications about influenza. The principles of the WHO approach include developing trust, announcing information early, being transparent, engaging and talking to the public and integrating risk communication into preparedness planning.
    b. PIEG recommends that information on respiratory hygiene should be promoted, including public campaigns and respiratory hygiene in healthcare settings, from Phase 3 on. A universal respiratory hygiene strategy should be adopted in all health care facilities now.
    c. In order to prevent spread of illness, PIEG recommends that cases of illness due to novel virus occurring during the pandemic alert period should be isolated and assessed in hospital. Cases should be interviewed in depth, and all contacts traced.
    d. PIEG recommends that all schools should have ready access to information on influenza and how to reduce the risk of infection, now, at Phase 3.
    e. PIEG recommends that closure of schools, universities and educational institutions could be considered during Phases 4 and 5 of the pandemic alert period, but only if clusters of cases due to novel virus were occurring in Ireland at that time, if transmission was occurring in these settings, and if the case fatality was high.
    f. Similarly, if during Phase 5, Ireland was experiencing clusters of cases, and the case fatality was high, PIEG recommends that population wide measures such as closing workplaces, discouraging mass gatherings etc should be considered.
    g. PIEG recommends that at Phase 4 and 5; a national medical helpline should be established to deal with individual queries or

concerns, and to direct those with symptoms to the appropriate location for care and treatment.

h. PIEG recommends that from Phase 3 on, advice and information on avoiding contact with high risk environments should be available for travellers to areas where outbreaks of novel influenza are occurring. From Phase 4 on, PIEG recommends that travellers should be advised to defer non-essential travel to affected areas.

i. From Phase 4 on, PIEG recommends that international travellers coming from, or going to affected areas, should be provided with Health alert Notices, be asked to self-report if they are ill, and to postpone travel if ill. Exit screening for travellers via questionnaire should be implemented.

j. From Phase 4 on, PIEG recommends that passengers who become ill on board, should be separated from other travellers, and the Public Health authorities in the destination and transit countries should be informed, so that contact tracing and control measures can be implemented.

k. PIEG recommends that consideration be given to the significant human resource implications of implementing these recommendations, and that manpower planning for pandemic influenza also includes planning for a robust public health infrastructure and sufficient surge capacity for public health.

8. Public health response: Non pharmaceutical interventions during the Pandemic (Phase 6)

a. During the pandemic, the aims of non-pharmaceutical interventions are to slow the spread of infection, gaining time for the development of pandemic specific vaccine and other pharmaceutical measures, to decrease the size of the epidemic peak, and to reduce the total number of cases.

b. PIEG recommends that the Pandemic Severity Index, a planning tool developed in the USA to characterise the severity of a pandemic in terms of numbers of cases and case fatality ratio, is used in order to implement interventions according to the levels of severity experienced in the population. Category 5 is the most severe category.

c. During Phase 6, PIEG recommends that the WHO outbreak communications approach be taken to all risk communication activities in relation to pandemic influenza.

d. PIEG recommends that information on respiratory hygiene should be promoted, including public campaigns and respiratory

hygiene in healthcare settings. A universal respiratory hygiene strategy should be adopted in all healthcare facilities.

e. PIEG recommends that during Phase 6, voluntary isolation of pandemic influenza cases when symptomatic.
f. PIEG advises that the evidence at this point does not support a recommendation for public use of facemasks during Phase 6 as a measure to prevent transmission of disease.
g. PIEG recommends that initial cases seen in Phase 6 should be interviewed in depth and all contacts identified, contact traced and asked to go into voluntary home quarantine by the local Department of Public Health.
h. As for the pandemic alert period, PIEG recommends that all schools should have ready access to information on influenza and how to reduce the risk of infection. All schools and day care institutions should have a plan for how they could close during an emergency. For Pandemic Index category 4 and 5 pandemics, PIEG recommends that school/college/institution closure should be strongly considered on a national basis.
i. PIEG recommends that population wide measures to reduce mixing of adults (close workplaces, initiate leave of absence for non essential workers, discourage mass gatherings) should be strongly considered on a national basis for category 4 and 5 pandemics.
j. In order to encourage prompt self-diagnosis, PIEG recommends that the public should be informed of the symptoms of influenza, how to recognise if they might have it, and advised of practical issues such as the value of having a thermometer at home
k. In addition, PIEG recommends that a national medical helpline be established to deal with individual queries and concerns, and to direct those with symptoms to the appropriate location for care and treatment.
l. During the pandemic, PIEG recommends that travellers be advised to defer non-essential international travel to affected areas.
m. PIEG recommends that health alert notices are provided to all travellers to and from affected areas, travellers are advised to check themselves for fever and to report any illness, and to defer travel if ill. Exit screening for at-risk travellers should be implemented.
n. During Phase 6, PIEG recommends that passengers who become ill on board, should be separated from other travellers, and the Public Health authorities in the destination and transit countries should be informed

9. **Health system response: Clinical management of patients with influenza like illness during an influenza pandemic.**
    a. The aim will be to treat as many people as possible at home during the pandemic. People may be treated at home with appropriate advice and treatment from health professionals, or in hospitals if too ill, or lacking the social supports to be able to manage at home. PIEG recommends that all patients who are more than one year of age, with an acute influenza like illness, fever and symptomatic for less than 48 hours should be considered for treatment with antivirals (neuraminidase inhibitors). This is subject to having sufficient antivirals to treat all those clinically ill, and evidence that antivirals are effective against the pandemic strain.
    b. There is no validated severity assessment tool for influenza related pneumonia. PIEG recommends that the CRB-65 score, which has been validated for community acquired pneumonia, is used to aid management of influenza related pneumonia. The Pandemic Medical Early Warning Score (PMEWS) could be used as an alternative measure in the community. In hospital settings PIEG recommends that the CURB-65 severity assessment tool is used to categorise disease severity, and guide investigations and management.

10. **Health system response: infection control**
    a. In advance of a pandemic strain emerging, it is not possible to know its infectivity, pathogenicity, mode(s) of transmission, virulence etc. PIEG is assuming in the guidance that the modes of transmission, incubation period and period of communicability are similar to seasonal influenza.
    b. The balance of evidence points to droplet and direct and indirect contact as the most important routes of transmission. Airborne transmission may also occur. PIEG recommends that standard infection control precautions and droplet precautions are the principal infection control strategies that should be rigorously followed for pandemic influenza. In certain circumstances (during aerosolising procedures) these control measures need to be augmented by the use of airborne precautions.
    c. As nebulisation is an aerosolising procedure, PIEG recommends that the use of nebuliser therapies should be minimised wherever feasible without compromising patient care.

d. PIEG recognises that full implementation of infection control guidance will be challenging, particularly in primary care settings. It recommends that adequate resources are provided by the system to facilitate implementation of the recommendations.

11. Influenza in animals and human health implications

a. Avian influenza has become a disease of great importance for animal and human health. Surveillance is very important not only for animal health, but also to provide early warning of new strains in animals that might pose a risk to human health. The Department of Agriculture, Fisheries and Food has had a serological monitoring programme in place for avian influenza since 1995.
b. PIEG recommends that close collaboration between veterinary and public health authorities continues at all levels, with ongoing development and review of protocols and joint working.

Changes to Pandemic Influenza Preparedness for Ireland: Advice of the Pandemic Influenza Expert Group

The following chapters of the EG advice have been updated on 22nd May, 2009 as follows:

Chapter 2, "Phases of a pandemic: WHO, EU and Irish" has been changed to reflect the new WHO pandemic phases, published on 30th April, 2009.

Chapter 5, "Public Health Response: antivirals" has been changed to incorporate advice from the European Medicines Evaluation Agency (EMEA) on the use of oseltamivir and zanamivir in pregnancy and in children aged less than one year of age, in the case of a pandemic being declared. The priority groups for antiviral treatment during an influenza pandemic, if stockpiled supplies are not sufficient to treat all symptomatic patients, have been amended.

Chapter 9, "Health System Response: Clinical Management of Patients with influenza like Illness during an Influenza Pandemic" has been updated and revised following a review by the Infectious Disease Society of Ireland.

Chapter 1 Table of Contents

1 Introduction

1.1 Background

The circulation of influenza viruses typically follows a seasonal pattern and influenza epidemics are frequent during the winter months in temperate regions of the world. These epidemics cause an increase in morbidity and mortality, particularly among the elderly and persons with decreased immunity. Occasionally a new strain of influenza virus appears to which the overall population has no immunity. Such strains may produce an influenza pandemic.

Unlike influenza epidemics, pandemics are very severe outbreaks that rapidly spread to involve all parts of the world. During a pandemic, disease often occurs outside of the usual influenza season, including the summer months, and multiple waves of disease occur before and after the main outbreak. Mortality during a pandemic is very high and is not confined to the usual risk groups: high attack rates can occur in all age groups with particularly high mortality among healthy young adults, as happened in the 1918-1919 pandemic.

It is estimated that a quarter of the world's population were ill with influenza in the influenza pandemic of 1918-1919, and that 40-50 million people died. The mortality was highest among the 20-40 year age group, and contemporary reports described a very rapid onset of disease with death often occurring within hours. The impact of the 1918-1919 pandemic was so severe that the average life expectancy in the USA was reduced by 10 years. Since then there have been a further two influenza pandemics: 1957 (severe), and 1968 (moderate). The fact that the last severe pandemic was in 1957 makes it more likely that the world's population would have little or no immunity to a new pandemic influenza strain, thus making a severe pandemic more likely.

It is almost inevitable that another influenza pandemic will occur. It is impossible to predict when this might occur, but a pandemic has the potential to cause widespread human suffering. The impact of a pandemic will be measured not only by the morbidity and mortality from influenza and its complications but also by the resulting economic and social disruption. A severe influenza pandemic would result in a global health and economic crisis, the scale and impact of which would be greater than either of the two world wars fought in the previous century.

With the ease of global travel a novel virus has the potential to spread rapidly across countries and continents. Expert Guidance is required to enable an informed and coordinated response to be mounted, thereby minimising the effects as far as possible.

1.2 Terms of Reference of the National Pandemic Influenza Expert Group

The National Pandemic Influenza Expert Group has been in existence since 1999, when it was established by the Minister for Health and Children. It works under the Chairmanship of Professor William Hall, Director of the National Virus Reference Laboratory. Current members of the Expert Group and subcommittees established by the Expert Group are listed in Appendix A. In addition to the committee members, expert opinion has been sought on certain specialised issues.

"A Model Plan for Influenza Pandemic Preparedness" was first circulated in 2001 and further revised in 2002.[1] Since that time the Pandemic Influenza Expert Group has met regularly to discuss developments in influenza pandemic preparedness. This document, "Pandemic Influenza Preparedness for Ireland: Advice of the Pandemic Influenza Expert Group, 2008", supersedes all previous publications of the Expert Group.

The terms of reference of the National Pandemic Influenza Expert Group were revised in 2005 to the provision of expert advice as follows:

- To function as a standing Expert Group that will monitor and review national and international research and developments in relation to pandemic influenza, and provide expert advice to the Minister of Health and Children and the Health Service Executive.

- To review current advice and guidance on pandemic influenza preparedness and response, identify gaps, and update and provide clear, evidence-based expert advice on pandemic influenza preparedness and response.

1.3 Aim

The aim of this document, "Pandemic Influenza Preparedness for Ireland: Advice of the Pandemic Influenza Expert Group, 2008", is to provide timely authoritative information on pandemic influenza, and to provide clear clinical guidance and public health advice to health professionals and others involved in pandemic influenza preparedness and response in line with the revised WHO Global Influenza Preparedness Plan.[2] It is relevant to many agencies and groups. This includes Government Departments, health service agencies, health professionals, the pharmaceutical industry, the media and the public.

The Department of Health and Children and the Health Service Executive produced the National Pandemic Influenza Plan 2007.[3] The National Plan is based on the framework recommended by the World Health Organisation for national pandemic plans, and reflects the expert advice contained in this document. It concentrates on the health response to pandemic influenza, but also provides the basis for planning which must take place across all sectors of society.

Within the Health Service Executive strategic, tactical and operational plans in accordance with the National Plan and Expert Group Advice, are being developed at local and area level, based on detailed action checklists that have been circulated to all locations and services. Intersectoral issues are

being addressed by an Interdepartmental Committee chaired by the Department of Health and Children.

The National Pandemic Influenza Plan and the HSE strategic, tactical and operational plans now supersede the influenza pandemic appendix of the National Public Health Emergency Plan (NPHEP), 2004.[4] Section 5 of the National Pandemic Influenza Plan outlines the roles and responsibilities of those involved in pandemic response. It is currently being expanded and will replace the generic national framework contained in the NPHEP.

The remaining appendices of the NPHEP dealing with SARS and bio threats remain in force until updated by the Department of Health and Children and the HSE.

1.4 Structure of the document

The phases of an influenza pandemic are described in Chapter 2. Chapter 3 describes the epidemiology of pandemic influenza and its potential impact. Chapter 4 describes surveillance, detection and situation monitoring. Chapters 5, 6 7 and 8 outline the public health response to pandemic influenza, dealing with antivirals (Chapter 5), vaccines (Chapter 6) non-pharmaceutical public health interventions in the pandemic alert period (Chapter 7) and during the pandemic (Chapter 8). Chapter 9 deals with case management and Chapter 10 with infection control. Chapter 11 summarises the situation with regard to avian influenza and the implications for human health.

There is also a series of supplements to a number of chapters (3, 10 and 11), dealing with more operational guidance.

1.5 Changes in this document versus A Model Plan for Influenza Pandemic Preparedness, 2002

This document replaces the previous Expert Group advice “A Model Plan for Influenza Pandemic Preparedness 2002. The WHO pandemic phases have been updated in line with the revised WHO Global Influenza Preparedness

plan: “The role of WHO and recommendations for national measures before and during pandemics.”

The Chapters on Action Plan, Communications and Legislation have been removed, as these are addressed within the National Pandemic Influenza Plan, 2007. Legal issues that might arise in a pandemic such as implementing non pharmaceutical public health interventions, quarantine etc are considered outside the remit of this Expert Group.

The chapters on antivirals, avian influenza, vaccines, case management and surveillance have been updated. Modelling information on the impact of the pandemic has been updated. A new chapter and supplement on infection control has been added.

In January 2007 a draft version of this document “Pandemic Influenza Preparedness for Ireland: Advice of the Pandemic Influenza Expert Group”, was put out for public consultation. A total of 18 submissions were received and reviewed by the Expert Group. The document was amended in light of these submissions and it was also updated to reflect the latest international research and developments.

1.6 Ethical Issues in Pandemic Influenza

Difficult issues will arise in healthcare during a pandemic. These could include prioritisation of scarce resources and conflicts between personal and professional obligations of staff. Some of these issues are addressed in this document e.g. priority groups for vaccines and antivirals.

The World Health Organisation initiated a project in 2006 to aid countries in addressing ethical issues in pandemic planning and response. The focus is on fairly prioritising access to scarce prophylactic and therapeutic measures and clarifying the ethical obligations of public health authorities and healthcare workers. The project is also addressing issues arising in border control,

isolation, quarantine and social distancing measures and international obligations. The initial report on these discussions has been published.(5)

In October 2006, the Irish Council for Bioethics discussed ethical issues in relation to pandemic planning at a conference in Dublin and the findings have been published.(6)

The Expert Group has advised that ethical issues should be addressed at a national level now in advance of a pandemic. This recommendation has been accepted. The Department of Health and Children has convened a steering group to oversee the production of a discussion paper on ethical issues and to advise on public consultation.

1.7 Appendix A Membership of the National Pandemic Influenza Expert Group

Professor William Hall, Director, National Virus Reference Laboratory (NVRL) (Chair)

Dr Darina O'Flanagan, Director, Health Protection Surveillance Centre (HPSC)

Dr Derval Igoe, Specialist in Public Health Medicine, HPSC

Dr Joan Gilvarry, Medical Director, Irish Medicines Board

Dr Jeff Connell, Assistant Director, NVRL

Dr Anna Beug, ICGP (resigned Autumn 2006)

Dr David Hanlon, ICGP (since Autumn 2006)

Dr Colm Bergin, Consultant in Infectious Diseases, St James's Hospital

Dr Gerard Sheehan, Consultant in Infectious Diseases, Mater Misericordiae Hospital

Dr John Ryan, Consultant in Emergency Medicine, St Vincent's University Hospital

Dr Brendan Crowley, Consultant Microbiologist, St James's Hospital

Dr Charles Gallagher, Respiratory Physician, St Vincent's University Hospital (resigned May 2005)

Dr Brenda Corcoran, Specialist in Public Health Medicine, HSE National Immunisation Office

Dr Elizabeth Keane, Director of Public Health, HSE South

Mr Gavin Maguire, Assistant National Director HSE, with responsibility for Emergency Management (since February 2006))

Dr Kevin Kelleher, Assistant National Director of Population Health - Health Protection (since March 2006)

Ms Mary O'Connell, HSE Assistant Chief Officer

Ms Winifred Ryan, HSE National Hospitals Office (resigned July 2005)

Mr Frank McClintock, HSE Assistant National Director, National Hospitals Office (since February 2006)

Ms Sally Gaynor, Superintending Veterinary Inspector, Department of Agriculture and Food

Dr Eibhlín Connolly, Deputy Chief Medical Officer, Department of Health and Children (DOHC)
Ms Teresa Cody, Assistant Principal, Public Health Division, DOHC (resigned June 2008)
Ms Mary McCarthy, Chief Nursing Officer, DOHC (resigned Sept 2007)
Mr Brian Mullen, Principal Officer, Public Health Division (resigned December 2005) DOHC
Ms Noreen Quinn, Acting Chief Pharmacist, DOHC
Ms Mary Day, Nurse Advisor, DOHC (from Sept 2007)

Sub-committees

Infection Control
Dr Derval Igoe, Specialist in Public Health Medicine, HPSC
Dr Peter Finnegan, Specialist in Public Health Medicine, Chair of Infection Control Implementation Group, HSE
Dr Gerard Sheehan, Consultant in Infectious Diseases, Mater Hospital
Ms Siobhan Flanagan, Infection Control Nurses Association

Case Management
Dr Deirdre Murray, Specialist in Public Health Medicine, HSE South
Dr Fidelma Fitzpatrick, Consultant Microbiologist, HPSC
Dr Gerard Sheehan, Consultant in Infectious Diseases, Mater Hospital
Dr John Ryan, Consultant in Emergency Medicine, St Vincent's University Hospital

Avian Influenza
Dr Derval Igoe, Specialist in Public Health Medicine, HPSC
Dr Peter Finnegan, Specialist in Public Health Medicine, HSE NE
Dr Imelda Lynskey, Senior Medical Officer, HSE NE
Ms Mary Maguire, Occupational Health Nurse, Office of Chief Medical Officer of Civil Service
Dr Renee Moloney, Occupational Health Physician, Office of CMO of Civil Service

Dr Paul Gueret, Occupational Health Physician, Health and Safety Authority
Dr Jeff Connell, Assistant Director, NVRL
Ms Sally Gaynor, Superintending Veterinary Inspector, Department of Agriculture and Food
Dr Áine McNamara, Specialist Registrar in Public Health Medicine, HPSC (until Dec 2005)
Dr Kevin Kelleher, Assistant National Director of Population Health - Health Protection
Mr Brendan McInerney, Principal Officer, DAF (until June 2006)
Dr Tom O'Connell, Chief Medical Officer of Civil Service,
Dr Miriam Owens, Senior Medical Officer, HPSC (until June 2007)

Non pharmaceutical public health interventions
Dr Darina O'Flanagan, Director, HPSC
Dr Derval Igoe, Specialist in Public Health Medicine, HPSC
Dr Elizabeth Keane, Director of Public Health, HSE South
Dr Brenda Corcoran, Specialist in Public Health Medicine, National Immunisation Office
Dr Mai Mannix, Specialist Registrar, Department of Health and Children (until June 2005)
Dr Eibhlin Connolly, Deputy Chief Medical Officer, Department of Health and Children

Acknowledgements
Professor Shane O'Neill, Consultant Respiratory Physician, Beaumont Hospital
Dr Anita Menon, Consultant Paediatrician, Our Lady's Hospital for Sick Children
Dr Miriam Owens, Senior Medical Officer, HPSC
Ms Kate Hunter, Statistician, HPSC
Dr Joan O'Donnell, Specialist in Public Health Medicine, HPSC
Ms Sarah Jackson, Surveillance Scientist, HPSC
Dr Lisa Domegan, Surveillance Scientist, HPSC
Ms Orla Bannon, Senior Executive-Corporate Services, HPSC

Dr Karina Butler, Consultant in Paediatric Infectious Diseases, Our Lady's Hospital for Sick Children

Ms Kirsty MacKenzie, PA to Director, HPSC

1.8 References

(1) National Influenza Pandemic Committee. A Model Plan for Influenza Pandemic Preparedness. www.doh.ie . 2002.

(2) Department of Communicable Disease Surveillance and Response Global Influenza Programme. WHO global influenza preparedness plan. 2005.

(3) HSE, DOHC. National Pandemic Influenza Plan, 2007. 2007.

(4) Department of Health and Children. Public Health Emergency Plan. 2006.

(5) WHO. Global consultation on addressing ethical issues in pandemic influenza planning. Summary of discussions. 1-27. 2007. Geneva, WHO.

(6) The Irish Council for Bioethics. Ethical Dilemmas in a Pandemic. Proceedings of the Irish Council for Bioethics Conference 17th October 2006, Dublin. 2007. The Irish Council for Bioethics.

Chapter 2 Table of Contents

2 Phases of a pandemic: WHO, EU, and Irish

2.1 Introduction

A phased approach to planning preparedness and response for pandemic influenza is recommended. WHO has defined pandemic phases, and these are described below. In addition the EU has defined four levels of alert to be used during WHO Phase 6. Within Ireland, a four point Ireland-specific alert mechanism will also be used during WHO Phase 6. These are described in this chapter.

2.2 WHO phases

The WHO pandemic phases were developed in 1999 and first revised in 2005. The phases provide a structure to aid countries in preparedness and response planning for pandemic influenza. The 2009 WHO guidance document Pandemic Influenza Preparedness and Response has retained the use of a six-phased approach but has regrouped and redefined the phases to more accurately reflect pandemic risk and the epidemiological situation based upon observable phenomena.(1) These revised phases are outlined in Figure 1 and Table 1. Ireland is adopting these revised phases in this updated guidance document.

The 2009 WHO guidance document recommends actions for national authorities and WHO during each of these phases.(1) To facilitate planning at national and global levels, Phases 1-3 and 5-6 were grouped to include common action points (Table 1). Phases 1-3 correlate with preparedness while Phases 4-6 signal the need for response and mitigation efforts. The time after the first pandemic wave has been elaborated into post peak and post pandemic periods (Table 1). The focus during the post-peak period includes preparation for a possible future pandemic wave(s).

The 2009 pandemic phases are:

- a planning tool;
- simpler, more precise, and based on verifiable phenomena;

- will be declared in accordance with the International Health Regulations (2005);
- only loosely correspond to pandemic risk;
- identify sustained human-to-human transmission as a key event;
- better distinguish between time for preparedness and response; and
- include the post-peak and post-pandemic periods for recovery activities.

The new phases are NOT:

- designed to predict what will happen during a pandemic; and
- always going to proceed in numberical order.

Figure 1. WHO Pandemic influenza phases (2009)

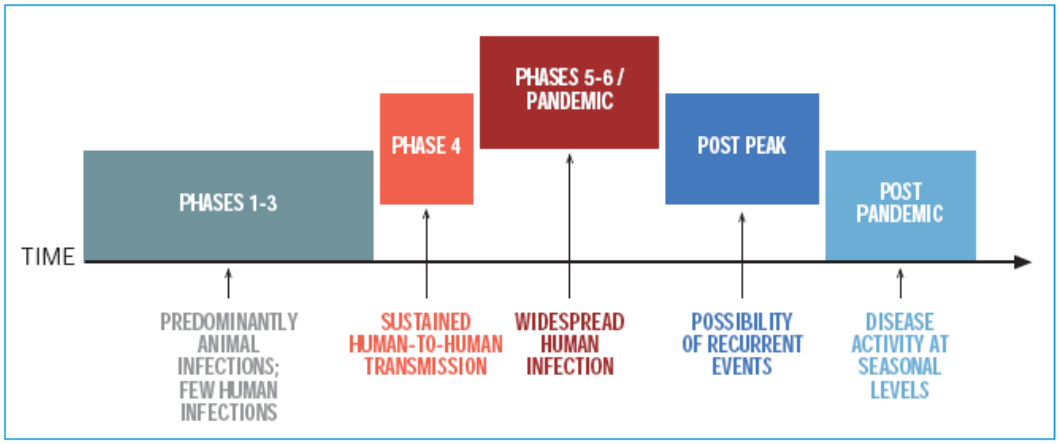


Table 1. WHO pandemic phase descriptions and main actions by phase (2009).

	Estimated Probability of Pandemic	Description	Main Actions in Affected Countries	Main Actions in Not-Yet-Affected Countries
Phase 1	Uncertain	No animal influenza virus circulating among animals has been reported to cause infection in humans.	Producing, implementing, exercising, and harmonizing national pandemic influenza preparedness and response plans with national emergency preparedness and response plans.	
Phase 2		An animal influenza virus circulating in domesticated or wild animals is known to have caused infection in humans and is therefore considered a specific potential pandemic threat.		
Phase 3		An animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks.		
Phase 4	Medium to high	Human-to-human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified.	Rapid containment.	Readiness for pandemic response.
Phase 5	High to certain	The same identified virus has caused sustained community level outbreaks in at least two countries in one WHO region.	Pandemic response: Each country to implement actions as called for in their national plans.	Readiness for imminent response.
Phase 6	Pandemic in progress	In addition to the criteria defined in Phase 5, the same virus has caused sustained community level outbreaks in at least one other country in another WHO region.		
Post-Peak Period		Levels of pandemic influenza in most countries with adequate surveillance have dropped below peak levels.	Evaluation of response; recovery; preparation for possible second wave.	
Possible New Wave		Level of pandemic influenza activity in most countries with adequate surveillance is rising again.	Response	
Post-Pandemic Period		Levels of influenza have returned to the levels seen for seasonal influenza in most countries with adequate surveillance.	Evaluation of response; revision of plans; recovery.	

2.3 Designation of WHO phases

The Director-General of WHO designates the phases. Designation of a phase will be made consistent with applicable provisions of the International Health Regulations (2005)[2] and is done in consultation with other organisations, institutions and affected Member States. With every announcement of a new phase, the Director General will set a time period at which the designation will be reviewed. The current WHO pandemic phase is Phase 5.

In the event of simultaneous situations posing different levels of risk, e.g. different new influenza subtypes occurring simultaneously, the highest level of risk will determine the phase.

2.4 EU alert levels

The European Commission has published four levels of alert to be used in the European context during WHO pandemic Phase 6 in the EU.[3-5] These alert levels are needed due to the specific circumstances of the European Union, which is characterised by the absence of internal borders and the free circulation of persons and goods.

EU alert levels in Phase 6

EU alert level	**Description**
EU Alert Level One	No confirmed human cases infected with the pandemic virus in any EU Member State
EU Alert Level Two	One or more confirmed human case(s) infected with the pandemic virus in any EU Member State
EU Alert Level Three	A confirmed outbreak (transmission) with the pandemic virus in any EU Member State
EU Alert Level Four	Widespread transmission in EU Member States

2.5 Ireland specific alert levels

Once the pandemic is declared (WHO Phase 6), a four point Ireland specific alert mechanism has been developed. This subdivision of WHO Phase 6 will

help in planning responses that are appropriate to a specific time within Phase 6.

Irish alert levels in WHO Phase 6

Irish Alert Level	**Description**
Irish Alert Level 1	Cases only outside Ireland (in a country or countries with or without extensive Irish travel/trade links
Irish Alert Level 2	New virus isolated in Ireland
Irish Alert Level 3	Outbreak(s) in Ireland
Irish Alert Level 4	Widespread activity in Ireland

To summarise, the WHO Phases, combined with the EU and Irish alert Levels will be used in describing the current status with regard to pandemic influenza.

2.6 References

(1) WHO. Pandemic influenza preparedness and response: a WHO guidance document. www.who.int. 2009. Available from URL: http://www.who.int/csr/disease/influenza/PIPGuidance09.pdf

(2) WHO. International health regulations (2005) -- 2nd ed. www.who.int. 2005. Available from URL: http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf

(3) EU Committee on the Environment. Public Health and Food Safety. Commission communication to the Council, the European Parliament, the European Economic and Social Committee and the Committee of the Regions on pandemic influenza preparedness and response planning in the European Community. www.europa.eu. 2006. Available from URL: http://europa.eu/bulletin/en/200511/p104062.htm

(4) EU Committee on the Environment. Public Health and Food Safety. Report on pandemic preparedness and response planning in the European Community. 2006.

(5) EU Committee on the Environment. Public Health and Food Safety. Pandemic influenza preparedness planning. Report on the second joint WHO/European Commission workshop, Copenhagen, 24-26 October 2005. 2005.

Chapter 3 Table of Contents

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]

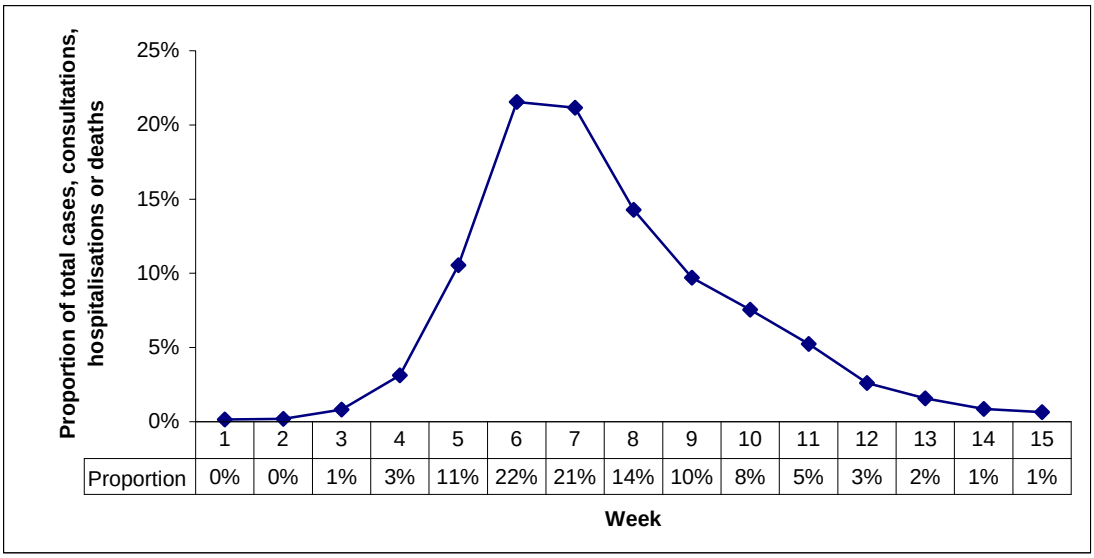
More detailed reports on these models are available in Supplement 3.

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.

3.11 References

(1) Cunha BA. Historical aspects of infectious diseases, part I. Infect Dis Clin North Am 2004; 18(1):XI-XV.

(2) Taubenberger JK, Morens DM. 1918 Influenza: the mother of all pandemics. Emerg Infect Dis 2006; 12(1):15-22.

(3) Smith W, Andrews CH, Laidlaw PP. A virus obtained from influenza patients. Lancet , 66-68. 1933.

(4) Fouchier RA, Munster V, Wallensten A, Bestebroer TM, Herfst S, Smith D et al. Characterization of a novel influenza A virus hemagglutinin subtype (H16) obtained from black-headed gulls. J Virol 2005; 79(5):2814-2822.

(5) Wiselka M. Influenza: diagnosis, management, and prophylaxis. BMJ 1994; 308(6940):1341-1345.

(6) Fleming DM. The contribution of influenza to combined acute respiratory infections, hospital admissions, and deaths in winter. Commun Dis Public Health 2000; 3(1):32-38.

(7) Atkinson W, Humiston S, Nelson R. Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Washington DC: Public Health Foundation, 2006.

(8) HPSC. HPSC, 2006 Weekly influenza Report. www.stanford.edu . 2006.

(9) Nguyen-Van-Tam J.S, Hampson AW. The epidemiology and clinical impact of pandemic influenza. Vaccine 2003; 21(16):1762-1768.

(10) HMSO. Report on the mortality from influenza in England and Wales during the epidemic of 1918-1919. Supplement to the 81st annual report of the Registrar General. [81], 1-47. 1920.

(11) Glezen WP. Emerging infections: pandemic influenza. Epidemiol Rev 1996; 18(1):64-76.

(12) Thompson WJ. Mortality from influenza in Ireland. SSISI 1919; xiv:1919-1920.

(13) WHO. Avian Influenza: Assessing the pandemic threat. www.who.int . 2005.

(14) ECDC. The public health rIsk from highly pathogenic avian influenza viruses emerging in Europe with specific reference to type A/H5N1. 2006.

(15) Mounts AW, Kwong H, Izurieta HS. Case-Control Study of Risk Factors for Avian Influenza A (H5N1) Disease, Hong Kong, 1997 . J Infect Dis 2006.

(16) OIE. Update on Avian Influenza in Animals (Type H5). www.oie.int . 2007.

(17) WHO. Cumulative number of confirmed human cases of avian influenza (A/H5N1) reported to WHO. 2007.

(18) Ungchusak K, Auewarakul P, Dowell SF, Kitphati R, Auwanit W, Puthavathana P et al. Probable person-to-person transmission of avian influenza A (H5N1). N Engl J Med 2005; 352(4):333-340.

(19) Beigel JH, Farrar J, Han AM, Hayden FG, Hyer R, de Jong MD et al. Avian influenza A (H5N1) infection in humans. N Engl J Med 2005; 353(13):1374-1385.

(20) Buxton BC, Katz JM, Seto WH, Chan PK, Tsang D, Ho W et al. Risk of influenza A (H5N1) infection among health care workers exposed to patients with influenza A (H5N1), Hong Kong. J Infect Dis 2000; 181(1):344-348.

(21) Vong S, Coghlan B, Mardy S, Holl D, Seng H, Ly S et al. Low frequency of poultry-to-human H5N1 virus transmission, Southern Cambodia, 2005. Emerg Infect Dis [serial on the Internet] 2006; 12(10).

(22) Apisarnthanarak A, Kitphati R, Thongphubeth K, Patoomanunt P, Anthanont P. Atypical avian influenza (H5N1). Emerg Infect Dis 2004; 10(7):1321-1324.

(23) Dinh PN, Long HT, Tien NTK, Hien NT, Mai LTQ, Phong LH et al. Risk factors for human infection with avian influenza A H5N1, Vietnam, 2004. Emerg Infect Dis [serial on the Internet] . 2006.

(24) Human cases of influenza A (H5n1) infection in eastern Turkey, December 2005 - January 2006. www.who.int/wer 81[43], 410-416. 2006.

(25) Yang Yang M.Elizabeth Halloran JSIL. Detecting Human-to-human transmission of Avian influenza A(H5N1). Emerg Infect Dis 2007; 13(9):1348-1353.

(26) Bureau of Epidemiology DoDCMoPHT. Avian Influenza surveillance in human. http://thaigcd.ddc.moph.go.th/AI_case_report_060802.html . 2006.

(27) Koopmans M, Wilbrink B, Conyn M, Natrop G, van der NH, Vennema H et al. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. Lancet 2004; 363(9409):587-593.

(28) WHO. Epidemiology of WHO confirmed human cases of avian influenza A (H5N1). www.who.int/wer 81[26], 249-260. 2006.

(29) Beigel JH, Farrar J, Han AM, Hayden FG, Hyer R, de Jong MD et al. Avian influenza A (H5N1) infection in humans. N Engl J Med 2005; 353(13):1374-1385.

(30) Health Protection Agency. Influenza Pandemic Contingency Plan. www.hpa.org.uk . 2005.

(31) 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.

(32) 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.

(33) Health Protection Agency. Pandemic Influenza Contingency Plan. www.hpa.org.uk . 2006.

(34) Census 2006. Preliminary Report. www.cso.ie . 2006.

Chapter 4 Table of Contents

4 Surveillance, detection and situation monitoring

4.1 Overview

This chapter describes surveillance, detection and situation monitoring activities needed in preparing for a pandemic. Good surveillance is essential as an early warning system for the emergence of novel viruses, and also for identifying those most at risk of serious disease and death from the pandemic strain. This information will be used to identify vaccine and antiviral priority groups for early intervention. Detailed plans for situation monitoring reporting are essential so that absenteeism rates, occupancy by healthcare setting, essential supplies, consumption of antivirals and vaccines, and non health impact intelligence information will be available to those charged with managing and coordinating the response to the pandemic. Pandemic surveillance and situation monitoring planning needs to build on existing activities as well as introducing new sources and types of information that will be needed to monitor impact.

4.2 Introduction

Surveillance of influenza activity is important. It provides information on the prevalence of influenza in the community, including in select populations and groups; and on factors that may be involved in transmission. It can also be used to measure the efficacy of potential control measures. In the Northern Hemisphere (Europe, North America, Canada, Asia), community based surveillance of seasonal influenza and influenza-like illness (ILI) is conducted all year round with particular emphasis placed on the period from October (week 40) to May (week 20) when activity peaks. This involves surveillance of clinical conditions i.e. influenza-like illness (ILI) and also virological surveillance of laboratory confirmed cases of influenza.

During a pandemic, all experience of pandemic exercises and planning suggest that the requirements and expectations of influenza surveillance in the pandemic period will be considerably greater than during a normal influenza season. Surveillance may be expected to deliver reports that have

not been produced previously; reports that are far more timely and precise; and also to deliver parameters, which are outside the scope of routine seasonal surveillance. In particular, there will be increased requests for information from health and political decision makers and the media. In conjunction with this, the technical capacity to deliver even routine influenza surveillance data will be compromised by staff illness and increased workload.

The national influenza surveillance system, which monitors seasonal influenza, will be used to provide clinical and virological disease surveillance data needed to guide response efforts during a pandemic.

When a pandemic begins, enhancements will need to be instituted to improve demographic and geographical coverage, and to increase the amount of detail captured by particular components of the system. **The Expert Group advises that enhancements to the national influenza surveillance system should be designed and developed now during the pandemic alert period so that baseline data for interpreting information gathered during the pandemic will be available and users will have experience and familiarity with new methodologies.**

Testing the resilience of existing seasonal influenza surveillance, and further development and expansion of components of the surveillance system, are critical in order to strengthen surveillance capacity during a pandemic. A pragmatic approach to developing surveillance will however be needed e.g. it will be pointless to identify a desired surveillance output, which could not be delivered even in optimal conditions.

Situation monitoring reports may present even more of a challenge. Timely information that will be needed by health and policy decision makers on absenteeism, use of healthcare and other resources, are not currently collated rapidly nationally, and procedures to collate, analyse and report on this key information are not currently in place. This will require unprecedented efforts both within the health system, and also cross sectorally to achieve this. Appropriate monitoring systems to assess the health and non-health impact

and need for resources during the pandemic are needed. **The Expert Group advises that template situation reports should be developed now in the pandemic alert period so that situation monitoring information requirements are identified and sourced in advance of the pandemic.**

Pandemic influenza surveillance objectives:

The objectives of pandemic influenza surveillance are summarised here, and described in more detail in the subsequent sections by WHO and Irish pandemic alert phases. These objectives are:

1. To serve as an early warning system to detect increases in ILI[1] in the community
2. To rapidly detect the introduction and early cases of a novel influenza virus or strains with pandemic potential, to assess the extent of human to human transmission and determine pandemic risk
3. To monitor the epidemiology, morbidity and mortality caused by pandemic influenza and from this to identify populations, which are severely affected, and to whom interventions can be targeted.
4. To track the pandemic virus's introduction into local areas
5. To monitor changes in the pandemic virus, including development of antiviral resistance

During a pandemic, virological and clinical surveillance data, supplemented by data from outbreak investigations and special studies, can help decision makers identify effective control strategies and re-evaluate recommended priority groups for vaccination and antiviral therapy. They can also facilitate efforts to mathematically model disease spread during the pandemic.

Outbreak investigations and special studies e.g. to address questions related to viral transmission or the clinical course of disease may include the following:

[1] * Influenza-like illness (ILI) is defined as the sudden onset of symptoms with a temperature of 38^0C or more and two or more of the following: headache, sore throat, dry cough and myalgia.

- Early on, studies of humans who are in close contact with animal reservoirs or human cases in the case of the pandemic, to assess both cross-species transmission and subsequent human-to-human transmission. Such studies detect sub-clinical, asymptomatic cases.
- Studies to determine the impact of antiviral drugs and the evolution of resistance
- Studies to measure the impact of social distancing measures and the behaviour of individuals during an outbreak.
- Telephone surveys for the impact of pandemic i.e. morbidity and burden of illness measured by use of healthcare services and absenteeism from work and school.

The European Centre for Disease Control (ECDC) is reviewing and consulting with Member States on surveillance activities to be carried out during the pandemic. This includes the likelihood that ECDC will issue calls for tender to develop protocols for surveillance of antivirals and vaccine effectiveness, side effects and toxicity within the EU.

The Expert Group advises that Ireland supports ECDC now during the pandemic alert period in its call for tender to develop protocols for surveillance of antivirals and vaccine effectiveness, side effects and toxicity within the EU

Pandemic Influenza Situation Monitoring objectives:

The objectives of pandemic influenza situation monitoring are summarised here, and described in more detail in the subsequent sections by WHO and Irish pandemic alert phases. These objectives are:

1. To assess on a timely basis the impact of the pandemic and resource needs during the pandemic, in health and in the wider public system.
2. To provide regular up to date summarised information including information on absenteeism, use of healthcare resources (beds, staff, supplies etc) and other resources (food supply, fuel etc) for use by the

National Public Health Emergency Team (NPHET) and the HSE National and Area Crisis Management Teams.

4.3 Situation monitoring and surveillance requirements by WHO and Irish Alert Phases

The WHO Global Influenza Preparedness Plan outlines situation monitoring and assessment objectives, and actions that countries should be undertaking by pandemic phase.[(1)] This approach will be used when examining the objectives and actions needed in Ireland.

Pandemic Alert Period: WHO Phase 3 (current situation)

4.4 National objectives

Surveillance

1. To have available up to date information on trends in human infection with seasonal strains of influenza
2. To be able to detect animal and human infections with new influenza virus strains, identify potential animal sources of human infection and assess the risk of transmission to humans.
3. To report information internationally to WHO rapidly

Situation monitoring

4. To develop plans for ongoing assessment of impact and resource needs during the pandemic

There are several systems in place in Ireland that can meet most of the objectives above.

A. The Irish national influenza surveillance system meets objective one.

B. National human virological surveillance and national reporting of clusters of unusual illness are in place, as well as veterinary surveillance and protocols for assessment, investigation and reporting of avian influenza outbreaks in Ireland. Mechanisms are in place for rapid international alerting of the detection of novel viruses. These systems meet objectives two and three.

C. The health system has initiated work on identifying and monitoring resource needs during a pandemic. This partly addresses objective four.

Each of these systems will now be described briefly.

4.5 The National Influenza Surveillance System

The Health Protection Surveillance Centre (HPSC) maintains and co-ordinates the national influenza surveillance system, which monitors disease activity during interpandemic influenza seasons and identifies circulating influenza viruses. This is done in collaboration with the National Virus Reference Laboratory (NVRL) and the Irish College of General Practitioners (ICGP).

The components of the national influenza surveillance system include:

1. Reporting of clinical data/influenza-like illness (ILI) by sentinel GPs
2. Virological reporting (NVRL)
3. Hospital surveillance comprising weekly data on total admissions, total Emergency Department (A&E) admissions and total respiratory admissions (upper respiratory tract infection, lower respiratory tract infection, pneumonia, asthma, chronic bronchitis, and exacerbations of chronic obstructive pulmonary disease) from sentinel hospitals
4. Surveillance of absenteeism rates in sentinel schools
5. Reports on outbreaks due to influenza or ILI
6. Mortality data (weekly review of all cause and pneumonia and influenza registered deaths (uncoded)) from the General Registrar's Office (GRO)
7. Weekly regional influenza indices based on clinical activity, virological activity and outbreak activity. This is defined as no report, no activity, sporadic activity, localised activity, and widespread activity. (Appendix A).

These components help to determine when, where and which influenza viruses are circulating; details of the various types of disease surveillance; and provide an overall national level assessment of influenza activity. They are described in more detail in Appendix B.

Mortality data is potentially a very important source of information during a pandemic, and the quality of the information provided from the General Registrar's Office is good. However the main difficulty is the timeliness of registration of deaths. Up to December 2005, there was a requirement to register a death within five days of its occurrence. The legislation then changed to allow persons to register deaths up to three months following death, thus potentially limiting the value of this data source as a timely early warning of the impact of the pandemic. **The Expert Group advises that consideration should be given to reviewing the Civil Registration Act, with a view to shortening the timeframe for death registration to five days, so that timely mortality surveillance during the pandemic can be achieved**.

In Europe, the surveillance of ILI and influenza is presently co-ordinated by the European Influenza Surveillance System (EISS). Ireland participates in EISS.

4.6 National human virological surveillance, national veterinary Avian Influenza (AI) surveillance

4.6.1 Monitoring for novel strains of influenza

During the pandemic alert period enhanced surveillance to identify patients at increased risk for infection with a novel influenza virus is being implemented. Novel influenza strains include avian influenza (influenza A/H5N1) that can infect humans, other animal influenza viruses that can infect humans or new or re-emergent human influenza strains that cause cases or clusters of human disease.

There are national, European Centre for Disease Prevention and Control (ECDC) and WHO case definitions and criteria for cases of avian influenza A/ (H5N1). Ireland is using the WHO case definition. (Appendix C) Guidance on the screening, detection, reporting and surveillance of persons potentially infected with avian influenza A/ (H5N1) has been circulated to the health system and is available in Supplement 11.

4.6.2 Reporting of novel strains

Clinicians should immediately contact the Medical Officer of Health (MOH) once they suspect a human case of infection with an avian or animal strain of influenza virus or with any other novel human influenza virus strain. Following epidemiological and laboratory investigation HPSC will report probable and confirmed cases to ECDC and to WHO. HPSC has been nominated as the National Focal Point for the new International Health Regulations, which have been implemented (Sept 2006) for avian and pandemic influenza. These regulations require countries to rapidly investigate and report internationally any public health emergency of international concern, and also to rapidly disseminate within the country any information relating to a public health emergency of concern that has arisen abroad.

4.6.3 Veterinary Surveillance

The Department of Agriculture, Fisheries and Food (DAFF) (in collaboration with the poultry industry and Birdwatch Ireland) undertakes active and passive surveillance for avian influenza in wild birds and poultry. This is outlined in detail in Chapter 11. Notification procedures have been agreed between the Department of Agriculture, Fisheries and Food and the HSE in the event of avian influenza being identified or highly suspected.

4.7 Plans for situation monitoring during the pandemic

As well as information on the epidemiology of the disease in terms of who is most at risk, locations where outbreaks are occurring, morbidity in those affected, and response to interventions etc, considerable additional information will be needed to monitor the situation. **The Expert Group advises that systems are put in place in the pandemic alert period to**

ensure availability of the following types of situation monitoring information:

- **Daily health, and other essential sector absenteeism and availability rates**
- **General workplace absenteeism rates**
- **School absenteeism rates**
- **Daily bed occupancy, admissions, attendances by flu care setting, mortuary capacity etc**
- **Real time monitoring of essential supplies and resources**
- **Consumption, uptake and impact of antivirals, vaccines and other countermeasures**
- **Vaccine and antiviral efficacy, safety and emergence of antiviral resistance**
- **Non health impact e.g., status on fuel, food supply, maintenance of essential services**

Pandemic alert period: WHO Phases 4 and 5

4.8 National objectives

Surveillance

1. To assess the extent of human-to-human transmission and determine pandemic risk
2. To detect, notify and characterise additional clusters (including the identification of risk factors and other data concerning transmission as requested by WHO).
3. To assess the threat to human health and the impact of any control measures

Situation monitoring

4. To identify resources required for enhanced control.
5. To determine and monitor public health resources required for pandemic response

If, as is likely, Ireland is not an affected country at WHO Phases 4 and 5, then the actions needed are to enhance surveillance to the maximum extent in order to detect any possible cases that might be imported into the country. The methods are the same as those described at Phase 3.
If however, Ireland is an affected country, then the surveillance and protocols described for Phase 3 need to be implemented fully, and in addition, the following should be done:

- Attempt to assess the impact of containment measures via epidemiological investigation of cases and contacts, and review and refine the case definition
- Enhance surge capacity for surveillance
- Assess the sustainability of human-to-human transmission
- Report cases internationally
- Adjust modelling forecasts of the likely impact of both infection spread and control measures, using data from real cases
- Monitor the development of antiviral resistance

HPSC will coordinate the national epidemiological investigation, reporting and modelling work. The NVRL will analyse samples from potential cases and when appropriate monitor for development of antiviral resistance. The health system will develop public health surge capacity plans to cater for the considerable public health requirements during these phases.

The system will need to put in place the mechanisms to determine and monitor the public health resources required for pandemic response

Also, during WHO Phase 4 and 5 it will be important to monitor the global situation (vaccine, antiviral availability, best practice recommendations) and estimate the impact of antiviral programmes (and vaccination programmes if used) elsewhere.

Pandemic period: WHO Phase 6

4.9 National objectives

Surveillance

1. To monitor the epidemiological, virological and clinical features of the pandemic at the national level, in order to forecast trends, identify those most at risk, and hence indicate where interventions could be targeted

Situation Monitoring

2. To monitor the impact of the pandemic, and to assess the use and effectiveness of interventions used, in order to guide future actions and optimise the use of finite resources

4.10 Early – Ireland not yet affected

Initiate enhanced surveillance and laboratory testing procedures to detect any possible early imported cases. Guidance for surveillance and laboratory procedures are outlined in Appendix D.

4.11 Once Ireland is affected (Irish alert level 2, 3 and 4)

As soon as the first cases of pandemic influenza are detected in the country the surveillance activities will be focused on detecting community outbreaks, tracking trends in influenza disease activity and identifying populations that are severely affected. Real-time reporting between healthcare institutions, clinicians and public health will be crucial in order to obtain daily influenza information. It will also be important to monitor the pandemic's impact on health, the health system, and on society.

4.11.1 Surveillance activities

The Expert Group advises that enhanced (detailed case based) surveillance be undertaken on all initial cases of pandemic influenza in order to describe accurately the epidemiology of the disease, the clinical features and outcome. This information will be used to guide policy decisions regarding priority groups for interventions.

The enhanced surveillance and case management database facility in the national electronic database Computerised Infectious Disease Reporting (CIDR) can be used to identify initial cases and track initial geographic spread. For case/contact management to be effective:

- The MOH should be notified immediately of all cases fulfilling the agreed case definition.
- Surveillance data should be reported on a daily basis as required by all partners
- HPSC should collate and disseminate case data nationally and internationally to ECDC and WHO.
- Clinicians and general practitioners should also be encouraged to report any unusual clusters of cases of influenza-like illness or other acute respiratory illness to the Department of Public Health
- Pathologists should be asked to notify any deaths due to unusual causes or any clusters of unexplained deaths to the MOH

This initial detailed case based data should be used as the main means to clarify the epidemiology, age specific incidence, clinical presentation, outcome and virological features of the pandemic virus.

Once the numbers of cases increase and disease activity becomes widespread, detailed enhanced surveillance for all cases should discontinue and the focus should move to more standard data collection, which will provide information on age groups affected, and on morbidity and mortality. HPSC will advise on the timing of this change. Further work is needed on how best to sustain this activity which will be needed throughout the pandemic period.

There is currently is no electronic contact tracing system in place in Ireland, to facilitate contact tracing and management. **The Expert Group advises that a national electronic contact tracing system for monitoring and managing initial contacts of patients with pandemic influenza be developed**.

4.11.2 Maintain GP sentinel surveillance

The Expert Group advises that during the pandemic it will be important to maintain weekly GP sentinel surveillance of the community incidence of ILI and influenza. The existing system uses computerised practices and is fairly highly automated and robust, thus facilitating its continuation during the pandemic. In addition, it is proposed that the planned development to use CIDR for sentinel surveillance will facilitate further automation and assist in increased geographical completeness, frequency of reporting and sustainability of ILI data. Currently it is proposed that reporting from sentinel GPs will continue on a weekly basis during a pandemic. This will allow ongoing measurement of the age specific incidence during the pandemic. The weekly reports will combine this data with all virology results from the NVRL (sentinel and non sentinel) to provide an up to date epidemiological picture.

4.11.3 Continue and strengthen monitoring of hospital admissions in sentinel hospitals to estimate morbidity and impact

Data on age specific hospitalisation rates for influenza will be needed on a frequent basis nationally and regionally in order to monitor disease severity and to determine the most severely affected age groups. At present surveillance of data in relation to hospitalisations associated with influenza is limited to sentinel hospitals (nine nationally) and is not timely. This system is being strengthened at present, and will serve as the means for measuring age specific hospitalisation rates for influenza in sentinel hospitals during the pandemic. Alternative methods will need to be considered for measuring hospital admissions overall, as a measure of impact.

The Expert Group advises that the existing sentinel system for surveillance of influenza in hospitals be improved so that it will have the capacity to provide robust age specific hospitalisation rates for influenza in sentinel hospitals during the pandemic.

The Expert Group advises that a system for active hospitalisation surveillance including virological investigation of a subset of hospitalised patients in all age groups in a limited number of sites be

developed. This method will also be developed for bacterial super infection surveillance.

Additional types of hospital surveillance are currently under review, including:

- Emergency Department surveillance of ILI and acute respiratory infection
- ICU occupancy with influenza/pneumonia cases
- Surveillance of age profile, risk factors, and clinical outcome in a subset of ICU admitted patients
- Mortality surveillance in hospital

4.11.4 Continue Mortality surveillance

The Expert Group advises that weekly mortality surveillance reporting be continued and supported during the pandemic. If timely death reporting is reintroduced, as advised by this Group, GRO based mortality data will be used to help monitor the severity of the pandemic and to determine the areas and age groups in which the highest mortality rates are occurring. This data, which will be analysed and reported on weekly by HPSC, will guide decisions on control and response measures. It will be important during the pandemic that death registration is viewed as essential work that will need to be maintained, and that relatives are encouraged to register deaths promptly.

4.11.5 Implement surveillance surge capacity plans

There is a need to ensure that surveillance activities continue during the pandemic, as the information provided will be essential to an appropriate response. This information for action will allow decisions to be made that will save lives and trigger essential actions. As there will be massive demands within the system, and more immediate activities may seem more relevant locally to response, these activities must be planned for and protected. Therefore, **the Expert Group advises that the system plans for surge capacity for surveillance and that it ensures that adequate resources (personnel and financial) are allocated to these tasks.**

If the surveillance activities outlined above are implemented, they will provide information on the impact of the pandemic in terms of age specific incidence rate of ILI in the community, hospitalisations for respiratory illness, ICU admissions for influenza and the morbidity, clinical outcome and risk factors associated with illness for a subset of these patients, as well as mortality by location and age group.

4.11.6 Virological surveillance

Virological surveillance of influenza will enable detection of the introduction and early cases of a pandemic influenza virus in Ireland, including tracking the virus's introduction into local areas and monitoring changes in the pandemic virus including development of antiviral resistance.

There will be a need to rapidly and accurately identify the influenza type and to subtype influenza A virus haemagglutinin to determine whether it is the pandemic strain. Hence it is important that tests with high sensitivity and specificity are used in order to ensure accurate identification of the strain.

During the pandemic the volume of requests for laboratory testing is expected to increase dramatically. The most intense testing will be required during the early stages of the pandemic, when detecting the introduction of the virus into the country is the primary objective. In an area with known high pandemic activity, diagnostic testing will usually not be needed at all.

However, highly accurate testing is still necessary whenever pandemic activity is detected in a previously unaffected area or when it is critical to the management of individual patients or in the public health management of the pandemic. Throughout this period, there may be ongoing cell culture of a proportion of samples at the NVRL in order to allow antigenic and genetic monitoring of the strain. During the late phases of the pandemic, there will be a return to the routine testing so that the end of the pandemic can be confidently identified.

The NVRL is responsible for initial identification and characterisation of novel influenza strains. If however numbers increase, other laboratories have been identified to supplement the diagnostic testing for the pandemic strain. The NVRL will be the agency at a national level to decide on the introduction of new diagnostic assays and remain responsible for resistance testing and detailed analysis of resistant strains. A protocol for the involvement of other laboratories in diagnostic testing is being developed by an operational laboratory implementation committee within HSE.

***Note*:** During a pandemic as the burden of disease increases and health services and public health face multiple competing demands, it might be necessary to adjust surveillance strategies and to reassess the need for daily reporting from the laboratory. Reporting on the pandemic virus will be via CIDR.

If the care settings differ from usual care settings during the pandemic, e.g. with use of telephone triage etc., then the feasibility of surveillance in these settings should also be considered and planned for.

4.12 Situation monitoring during the pandemic

The situation monitoring information requirements to be planned in Phase 3 now need to come into operation. The situation monitoring information needs include:

- Daily health, and other essential sector absenteeism and availability rates
- General workplace absenteeism rates
- School absenteeism rates
- Daily bed occupancy, admissions, attendances by flu care setting, mortuary capacity etc
- Real time monitoring of essential supplies and resources
- Consumption, uptake and impact of antivirals, vaccines and other countermeasures

- Vaccine and antiviral efficacy, safety and emergence of antiviral resistance
- Non health impact e.g., status on fuel, food supply, maintenance of essential services

The Expert Group advises that standardised situation reports, which are customised for each organisation that is responding to the pandemic, and which contain appropriate and relevant up to date information, are used during the pandemic.

4.13 References

1. WHO. WHO Global Influenza Preparedness Plan. www.who.int . 2005.

2. Kyncl J, Prochazka B, Goddard NL, Havlickova M, Castkova J, Otavova M et al. A study of excess mortality during influenza epidemics in the Czech Republic 1982 - 2000. Eur J Epidemiol 2005; 20:365-371.

3. Centers for Disease Control and Prevention. 122 Cities Mortality Reporting System. Manual of Procedures. 2004. Atlanta,USA.

4.14 Appendix A: Influenza Activity Index

The influenza activity index is based on weekly data on influenza-like illness, laboratory confirmed cases of influenza, and/or outbreaks associated with influenza/influenza-like illness. The index is analogous to that used by the WHO global influenza surveillance scheme and the European Influenza Surveillance Scheme www.eiss.org. The index (0-5) is described in Table 1.

Table 1: Irish Influenza Activity Code, Name and Description

Index Code	**Index Name**	**Index Description***
0	No Report	No reports received.
1	No Activity	No ILI or laboratory confirmed influenza cases and no influenza/ILI outbreaks in a HSE-Health Area.
2	Sporadic Activity	Isolated case(s) of ILI or laboratory confirmed influenza case(s) in a HSE-Health Area, or an influenza/ILI outbreak in a single institution.
3	Localised Activity	Increases in ILI in local areas (such as a city, county, or district) within a HSE-Health Area, or outbreaks in two or more institutions within an area, with laboratory confirmed cases of influenza infection. Levels of activity in the remainder of the HSE-Health Area would be sporadic or have no activity.
4	Regional Activity	Increases in ILI in one or more regions with a population comprising less than 50% of the HSE-Health Area's total population, with laboratory confirmed influenza cases in the affected region(s). Levels of activity in the remainder of the HSE-Health Area would be sporadic or have no activity.
5	Widespread activity	Increases in ILI in one or more regions with a population comprising 50% or more of the HSE-Health Area's total population, with laboratory confirmed influenza infections.

*ILI=Influenza-like illness

4.15 Appendix B: The National Influenza Surveillance System

The Health Protection Surveillance Centre (HPSC) maintains and co-ordinates the national influenza surveillance system, monitors disease activity during interpandemic influenza seasons, and identifies circulating influenza viruses, in collaboration with the National Virus Reference Laboratory and the Irish College of General Practitioners (ICGP).

The objectives of seasonal influenza surveillance are outlined as follows:

1. To serve as an early warning system to detect increases in ILI[2] in the community
2. To monitor the morbidity and mortality caused by seasonal influenza including monitoring trends in influenza disease activity and identifying populations, which are severely affected.
3. To identify and characterise influenza viruses that are circulating; Note: Each season these data are used for updating the formulation of the next season's vaccine

The role of HPSC as influenza surveillance co-ordinator is to:

1. Maintain and develop the current sentinel influenza surveillance network
2. Oversee enhancements as outlined e.g. year round surveillance, surveillance of hospitalised cases.
3. Promote year round surveillance of influenza
4. Maintain close working relationship with the National Virus Reference Laboratory (NVRL) and the Irish College of General Practitioners (ICGP).

The components of the national influenza surveillance system include:

8. Reporting of clinical data/influenza-like illness (ILI) by sentinel GPs

[2] * Influenza-like illness (ILI) is defined as the sudden onset of symptoms with a temperature of 38^0C or more and two or more of the following: headache, sore throat, dry cough and myalgia.

9. Virological reporting (NVRL)
10. Hospital surveillance comprising weekly data on total admissions, total Emergency Department (A&E) admissions and total respiratory admissions (upper respiratory tract infection, lower respiratory tract infection, pneumonia, asthma, chronic bronchitis, and exacerbations of chronic obstructive pulmonary disease) from sentinel hospitals
11. Surveillance of absenteeism rates in sentinel schools
12. Reports on outbreaks due to influenza or ILI
13. Mortality data
14. Weekly regional influenza indices based on clinical activity, virological activity and outbreak activity. This is defined as (no report, no activity, sporadic activity, localised activity, widespread activity). (Appendix A).

These components help to determine when, where and which influenza viruses are circulating; details of the various types of disease surveillance; and provide an overall national level assessment of influenza activity.

4.15.1 Reporting of clinical data by sentinel GPs

In Ireland clinical surveillance of ILI and influenza is conducted by sentinel general practices distributed throughout all HSE areas. At present 52 general practices (comprising116 general practitioners) participate which cover over 4.8% of the population (2006 census). These GPs report, on a weekly basis, the number of flu-like illnesses seen (defined as the sudden onset of symptoms with a temperature of 38^0C or more and two or more of the following: headache, sore throat, dry cough and myalgia) and include date of birth, sex, the date of consultation and the diagnosis. Virological confirmation is sought by supplying combined nose (preferably nasopharyngeal swabs) and throat swabs on at least one patient in whom ILI was diagnosed from each practice per week.

ILI surveillance is undertaken all year round with weekly reports produced by HPSC between weeks 40 (October) and 20 (May) and monthly reports produced from June through to September. Year round surveillance during the summer provides information on the baseline level of influenza activity

during the summer and these data have the potential to become an important component in the surveillance of novel strains of influenza e.g. influenza A (H5N1) or in the early detection of a pandemic.

This is a collaborative project between ICGP, NVRL, HSE Departments of Public Health and HPSC. HPSC is the co-ordinating centre for all these data. In Europe, the surveillance of ILI and influenza is presently co-ordinated by the European Influenza Surveillance System (EISS), though it is moving to ECDC later in 2008.

4.15.2 Virological Reporting

Year-round virological monitoring for influenza in Ireland is undertaken by the NVRL in the form of routine detection of influenza viruses. The NVRL is a member of the WHO Global Influenza Surveillance Network. The aim of this laboratory network is to monitor influenza trends and to compare seasonal differences rather than to record all influenza tests performed.

Data obtained on virological specimens include sex, date of birth, date of onset of illness, dates sample taken and received, vaccination status, test applied, brief clinical history and history of antiviral drug use in the previous 14 days. For any confirmed positive sample, preliminary sequence analysis and virus characterisation occurs at the NVRL. When appropriate the isolate and viral sequences are referred to the WHO Collaborating Centre, London, UK for further characterisation.

4.15.3 Hospital Surveillance

There are 10 sentinel hospitals throughout the country, which monitor the following on a weekly basis: Total admissions, total A&E admissions and total respiratory admissions. Ideally, sampling for influenza virus should also be carried out in these populations. These data are reported to HPSC on a weekly basis between weeks 40 and 20. It is proposed to extend this to year-round surveillance.

Enhanced surveillance is also undertaken on all children aged 14 years and under who are hospitalised with influenza (probable or confirmed). This surveillance examines clinical presentation and complications, risk factors, vaccination and outcome status.

4.15.4 Surveillance of absenteeism rates in sentinel schools

The sentinel school network monitors absenteeism rates in both primary and secondary schools between weeks 40 and 20. This network represents approximately 1% of the school population in Ireland. HSE Departments of Public Health collate data on weekly absenteeism rates for the sentinel schools. These data comprise the average number of pupils absent on a given week. If more than 10% of the school's population is absent on any one day in the week for any cause this should be recorded. These data are collected and combined with data from hospitals and nursing homes in each HSE Department of Public Health area to allow assessment of the impact of influenza on the community and the health services.

4.15.5 Surveillance of outbreaks due to influenza or ILI

Under the Infectious Diseases (Amendment) (No.3) Regulations 2003 (SI No.707 of 2003) medical practitioners and clinical directors of laboratories are required to notify to the Medical Officer of Health (MOH) any unusual clusters or changing pattern of illness, and individual cases thereof, that may be of public health concern. This would include outbreaks of influenza or ILI. These data are notified to HPSC who include them in the weekly influenza surveillance report. Most of these outbreaks to date have been identified in schools or residential settings e.g. nursing homes for older people.

4.15.6 Mortality Surveillance

Since December 2004, HPSC has received a weekly electronic file from the General Registrar's Office (GRO) on all causes of death in the previous week. HPSC checks the number of deaths caused by influenza on a weekly basis. However, this is not an accurate estimate, as the literature would indicate that influenza as a cause of death is under reported.[(2)]

Currently a pilot study is underway exploring the benefits of using these data. It is proposed to use these data in future to estimate excess deaths from pneumonia and influenza (P&I). A model to estimate baseline and excess thresholds for P&I deaths will be developed thus allowing for the detection of excess deaths due to P&I which is a proxy for increased influenza activity. This is similar to the 121 City Mortality System, which is used by the Centres for Disease Control in Atlanta (USA).[3] However, several years data are required in order to calculate the thresholds and at present, there are only two years data available. The Central Statistics Office (CSO) collects mortality data, however, these data are not available for at least 6 to 12 months after the date of death and so are not sufficiently timely for this purpose.

4.15.7 Regional influenza activity by HSE area

Weekly regional influenza indices based on clinical activity, virological activity and outbreak activity. This is defined as no report, no activity, sporadic activity, localised activity, and widespread activity. (Appendix A).

4.15.8 Weekly Notifications of Influenza

Under the Infectious Diseases (Amendment) (No.3) Regulations 2003 (SI No.707 of 2003) medical practitioners and clinical directors of laboratories are required by law to notify to the MOH a list of 77 notifiable diseases, one of which is influenza.

However, while influenza is notifiable, it is not possible to provide an absolute case count for influenza or to determine population-based rates of infection or illness on a national level because many infected persons are asymptomatic or experience only mild illness and do not seek medical care.

Nevertheless the national influenza surveillance system comprising weekly data on GP sentinel surveillance, sentinel hospital and schools data, weekly ID notifications, and mortality data, allows HPSC to monitor regional and national disease trends and to compare the timing and intensity of the current influenza season with previous seasons.

4.16 Appendix C WHO case definitions for A(H5N1) (August 2006)

Person under investigation

A person whom public health authorities have decided to investigate for possible H5N1 infection.

Suspected H5N1 case

A person presenting with unexplained acute lower respiratory illness with fever (>38 ºC) and cough, shortness of breath or difficulty breathing.

AND

One or more of the following exposures in the 7 days prior to symptom onset:

a. Close contact (within 1 metre) with a person (e.g. caring for, speaking with, or touching) who is a suspected, probable, or confirmed H5N1 case;

b. Exposure (e.g. handling, slaughtering, defeathering, butchering, preparation for consumption) to poultry or wild birds or their remains or to environments contaminated by their faeces in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month;

c. Consumption of raw or undercooked poultry products in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month;

d. Close contact with a confirmed H5N1 infected animal other than poultry or wild birds (e.g. cat or pig);

e. Handling samples (animal or human) suspected of containing H5N1 virus in a laboratory or other setting.

Probable H5N1 case (notify WHO)
Probable definition 1:
A person meeting the criteria for a suspected case

AND

One of the following additional criteria:

a. Infiltrates or evidence of an acute pneumonia on chest radiograph plus evidence of respiratory failure (hypoxemia, severe tachypnea)

OR

b. positive laboratory confirmation of an influenza A infection but insufficient laboratory evidence for H5N1 infection.

Probable definition 2:
A person dying of an unexplained acute respiratory illness who is considered to be epidemiologically linked by time, place, and exposure to a probable or confirmed H5N1 case.

Confirmed H5N1 case (notify WHO)

A person meeting the criteria for a suspected or probable case

AND

One of the following positive results conducted in a national, regional or international influenza laboratory whose H5N1 test results are accepted by WHO as confirmatory:

a. Isolation of an H5N1 virus;

b. Positive H5 PCR results from tests using two different PCR targets, e.g. primers specific for influenza A and H5 HA;

c. A fourfold or greater rise in neutralization antibody titer for H5N1 based on testing of an acute serum specimen (collected 7 days or less after symptom onset) and a convalescent serum specimen. The convalescent neutralizing antibody titer must also be 1:80 or higher;

d. A microneutralization antibody titer for H5N1 of 1:80 or greater in a single serum specimen collected at day 14 or later after symptom onset and a positive result using a different serological assay, for example, a horse red blood cell haemagglutination inhibition titer of 1:160 or greater or an H5-specific western blot positive result.

4.17 Appendix D

A. Guidance for surveillance in WHO Phase 6, Irish Alert Level 1 (Ireland not yet affected)

1. Establish surveillance of clinical conditions which have been linked to the novel virus abroad, but which are not necessarily part of the clinical criteria for routine influenza investigation
2. Travellers returning from areas with pandemic activity should be provided with information and advised to seek medical attention if they become unwell.
3. All doctors should be advised to ask patients presenting with respiratory illnesses about overseas travel. Samples should be collected for influenza detection and sent to the NVRL from all patients with respiratory illness who have:
   - Fulfilled the case definition for pandemic influenza or
   - Been hospitalised with viral pneumonia or
   - Travelled to areas of known or potential pandemic influenza activity in the week preceding onset of illness or;
   - Have a flu-like illness and are family members or other close contacts of either of the above.
4. Departments of Public Health must immediately be notified of:
   - All cases who have been hospitalised with viral pneumonia (or other particular clinical features associated with the pandemic strain that form part of the case definition); and who have travelled to areas of known or potential influenza activity in the week preceding onset of illness and
   - Those who have a flu-like illness and are family members or other close contacts of a person in either of these categories.

B. Guidance on Laboratory procedures when pandemic influenza is present outside Ireland (Irish Alert Level 1)

1. Samples should be collected for influenza investigation (including viral culture when advised by WHO) from all patients who:

- Have been hospitalised with viral pneumonia;
- Have travelled to areas of known or potential influenza activity in the week preceding onset of illness and have symptoms associated with the pandemic influenza strain
- Have a flu-like illness and are family members or other close contacts of either of the above.

2. All samples from “highly suspicious cases” must be promptly referred to NVRL for investigation, as per agreed procedures. Any influenza strains detected should be provisionally characterised at the NVRL urgently and referred with available phylogenetic data urgently to the WHO Collaborating Centre in London for confirmation and sub typing.
3. NVRL should validate any novel diagnostic tests to ensure that “best practice” methodologies are utilised and can be introduced immediately
4. NVRL should monitor the developments regarding the laboratory diagnosis and “bedside” diagnosis of the new influenza strain.

Chapter 5 Table of Contents

5 Public Health Response: Antivirals

5.1 Introduction

Antiviral drugs are essential components of a comprehensive pandemic response. There is evidence that, when given rapidly (within 12 hours of onset of symptoms) they can reduce infectivity and, when given within 48 hours of onset of symptoms, they are effective in treating seasonal influenza. They are also effective in preventing it. Pending the availability of virus-specific vaccines, antivirals will be the only influenza-specific medical intervention available for use in a pandemic. It is hoped that the effectiveness of antivirals against seasonal influenza will also apply to pandemic influenza. However, many countries have no or very limited supplies. There is a global shortage of antivirals, and it takes several years to construct new production facilities and significantly increase production capacity. Only those countries with stockpiles of antivirals drugs will have them in the event of a pandemic. Each country also has to consider which groups will have first call on scarce supplies. WHO has advised countries to set goals and priorities for the use of antivirals during a pandemic, which should reflect the particular circumstances of each country. **The Expert Group advises that the goals for Ireland for use of antiviral drugs should be, in order of priority:**

- **To prevent or reduce deaths and hospital admissions from influenza**
- **To prevent and reduce morbidity from influenza**
- **To maintain essential services**

This chapter outlines the drugs used in treatment and prophylaxis of influenza, their effectiveness, the potential uses of antivirals during a pandemic; recommendations on use of antivirals in Ireland during a pandemic; as well as outlining the other requirements needed for an effective public health antiviral treatment implementation strategy.

5.2 Types of antiviral agents

5.2.1 Neuraminidase inhibitors (Zanamivir and oseltamivir)

Zanamivir and oseltamivir are neuraminidase inhibitors (NAI), which interfere with replication of both influenza A and B viruses.

5.2.2 M2 Inhibitors (Amantadine and rimantadine)

These agents are inhibitors of the M2 ion channel protein contained within the influenza virus. They are effective against influenza A virus. Currently, only amantadine is licensed for use in Ireland, and only as prophylactic treatment against influenza A virus.

Up to date details, including the summary product characteristics (SPC) on these drugs are available at www.medicines.ie. A summary table of the properties of antiviral agents, extracted from a recent review on influenza antiviral medicinal products for potential use during a pandemic by the European Medicines Agency (EMEA, 2005) is presented in Appendix A.(1)

5.3 Review of effectiveness of antivirals in the treatment and prevention of influenza, antiviral resistance, and stability of oseltamivir

5.3.1 Neuraminidase inhibitors (NAI) in treatment

NAI treatment: Key points

Treatment with NAI (within 48 hours) for seasonal influenza leads to reduction of:

- 0.4 -1 days in duration of symptoms
- 25-43% of complications requiring antibiotics
- 55% in Lower Respiratory Tract Infections
- 34% in need for antibiotics
- 59% in hospitalisations
- 44% in otitis in children

A systematic review and meta-analysis of randomised controlled trials, based on studies published prior to December 2001, was carried out on the effectiveness of neuraminidase inhibitors in treatment and prevention of Influenza A and B.[2] It found that treating otherwise healthy adults and children with zanamivir and oseltamivir, when given within 48 hours of onset of symptoms, reduced the duration of symptoms in the intention to treat population by between 0.4 and 1.0 days, and provided a 29% to 43% relative reduction in the likelihood of complications requiring antibiotics. In high-risk populations, the results were less conclusive.

There is also evidence from a more recent study that oseltamivir treatment leads to a reduction in secondary lower respiratory tract complications (Lower Respiratory Tract Infections (LRTI), bronchitis, pneumonia) and hospitalisations.[3] Those receiving oseltamivir were 55% less likely than those on placebo to develop an influenza-related LRTI requiring antibiotic treatment. In patients with an increased risk of these complications, there was a 34% reduction in LRTIs requiring antibiotics and a 59% reduction in hospitalisation.

In children aged one year of age or older, oseltamivir treatment resolved illness 36 hours earlier than placebo, and it reduced the incidence of otitis by 44%.[4]

Oseltamivir was used to control the transmission of H7N7 in the outbreak of avian influenza in the Netherlands in 2003. All cases were treated, and prophylaxis (oseltamivir 75mg/day) was given to all people handling potentially infected poultry, to be continued for two days after their last exposure.[5] More recently, they have reported that oseltamivir was found to have a protective effect. It protected against conjunctivitis (OR=0.14; 95% CI 0.08-0.27) and against infection without specific symptoms (OR=0.47: 95% CI 0.25-0.88).[6]

Gani et al have modelled the effect of using antiviral stockpiles for treatment on hospitalisation with pandemic influenza.[7] A stockpile that covers 20-25% of the population would be sufficient to treat most of the clinical cases in the

first wave of infection and could lead to 50-77% reductions in hospitalisations. Treating all sick patients was the best strategy in reducing hospitalisations and transmission.

5.3.2 Neuraminidase inhibitors (NAI) as prophylaxis for seasonal influenza

NAI prophylaxis for seasonal influenza: Key points

Oseltamivir 75mg/d for 7-42 days as prophylaxis:

Reduces incidence of seasonal influenza by 81%

In children reduces incidence of febrile illness in contacts by 55%

Modelling studies show that:

Providing prophylaxis to 80% of population for 8 weeks contains an epidemic similar to the 1957/1958 pandemic, reducing the attack rate from 33% to 2%

Very early geographically targeted prophylaxis and social distancing could eliminate an emergent pandemic strain

Antiviral prophylaxis of household contacts reduces cumulative attack rates by one third and peak attack rates by 50%, but needs large stockpile to do this

Influenza antiviral agents can be used prophylactically as follows:

- To prevent infection given exposure,
- To reduce the probability of clinical illness given infection,
- To reduce the probability of transmission to others given infection.

In a 2005 review article which summarised the outcomes of studies on the use of oseltamivir in prophylaxis, the conclusions were that when oseltamivir was prescribed at a dose of 75mg/day once daily for 7-42 days, it reduced the incidence of laboratory confirmed clinical influenza by 81% [range 58%-92%]; reduced the proportion of patients shedding influenza virus; reduced the incidence of clinically diagnosed complications of influenza; did not prevent the formation of a specific antibody response to influenza infection; and did not result in the development of resistance.[8] There was no evidence that the protective efficacy of oseltamivir in adults and children >= 13 years was

altered by age, gender, geographic region, or the existence of pre-existing co-morbidity.

In 2004, Hayden et al determined the efficacy of post exposure prophylaxis (PEP) and treatment of ill index cases with oseltamivir in an attempt to prevent influenza transmission in households.[9] In this study, involving 277 households with 298 index cases, and 812 contacts aged >= one year, contacts were randomised by household to receive treatment for five days if illness developed, or PEP for 10 days. The number of households with at least one contact developing laboratory confirmed influenza was measured. They found that PEP with oseltamivir was 58.5% more effective in reducing secondary cases of influenza illness in households, and 68% more effective in individuals, compared with treating index cases alone. PEP must be initiated early however for optimal protection. They also investigated the efficacy of oseltamivir prophylaxis in children aged 1-12 years old. The overall incidence of influenza was three times higher in those paediatric contacts managed expectantly over those given PEP (24%-8%). PEP reduced the incidence of febrile influenza illness by 55% among paediatric contacts. The number of households given prophylaxis (number needed to treat) to prevent one household reporting a secondary case was six. Among individual contacts, the number needed to treat to prevent one secondary case was 11.

Longini et al investigated the use of targeted antiviral prophylaxis as a method for controlling pandemic influenza.[10] They modelled an influenza pandemic for an agent similar to influenza A virus (H2N2) that caused the Asian influenza pandemic of 1957-1958. In the absence of intervention, the model predicted an influenza illness attack rate of 33% of the population and an influenza death rate of 0.58 deaths /1000 persons. With the use of targeted antiviral prophylaxis, if 80% of the persons maintained prophylaxis for up to eight weeks, the epidemic could be contained, and the model predicted a reduction to an illness attack rate of 2% (95% CI: 0.2,16) and a death rate of 0.04/1000 persons (95% CI 0.0003, 0.25). If you extrapolate their data to the US population, this would require 1.9 billion doses of antiviral agent. This is equivalent to 27 million doses in the Irish population. These figures seem

unrealistically large, and the authors acknowledged this. They stated that using a targeted antiviral strategy using whatever stocks are available would save many lives and constitute the most prudent use of influenza antiviral agents. They also acknowledged that a successful strategy would require the identification of the index cases in households, preschools, schools, and other institutional settings. It would also be effective for healthcare personnel, other essential workers and first responders. They concluded that targeted antiviral prophylaxis has potential as an effective measure for containing influenza until adequate quantities of vaccine are available.

In 2005 Ferguson et al reported on strategies for containing an emerging influenza pandemic in Southeast Asia using targeted mass prophylactic use of antiviral drugs as a containment strategy.(11) A combination of geographically targeted prophylaxis and social distancing measures could eliminate an emergent pandemic strain, provided the reproductive number (average number of secondary cases generated by a typical primary case) is less than 1.8. The effectiveness of this strategy was critically dependent on rapid early identification of the original cluster of cases, rapid sensitive case detection, and ability to deliver drugs to the target groups rapidly, i.e. within 48 hours. Since publication of this article, WHO has developed a pandemic influenza draft protocol for rapid response and containment.(12)

In 2006, Ferguson, Cummings et al further investigated the use of various strategies, including antivirals for mitigating an influenza pandemic.(13) Using an individual based simulation model of pandemic transmission for the UK and the US, they found that treatment of clinical cases can reduce transmission, but only if antivirals are given within a day of symptoms starting. Antiviral prophylaxis of household members when a case is identified in a household is effective in reducing cumulative attack rates by at least one third and peak attack rates by a half, but requires an antiviral stockpile large enough to treat 46% or 57% of the population, at Ro of 1.7 and 2.0 respectively. In addition if classmates or close work colleagues of a clinical case are targeted for antiviral prophylaxis, this also has a dramatic impact on

attack rates but this requires stockpiles of 72% or 102% of the population size for Ro of 1.7 and 2.0 respectively.

5.3.3 NAI: Antiviral Resistance

Up to the 2007/2008 flu season, the frequency of resistance emergence was low during treatment with NA inhibitors. Resistance to zanamivir has been observed only in an immunocompromised host to date.[14] With oseltamivir, less than one per cent of immunocompetent adults and from 8 to 18% of infected children shed resistant viruses during or immediately after treatment.[15] Until the 2007/2008 season, these resistant variants mainly showed decreased virulence and infectivity.

In late January 2008 antiviral drug susceptibility surveillance of seasonal influenza viruses in Europe (the EU-EEA-EFTA countries) revealed that some of the A (H1N1) viruses circulating this season (winter 2007-8) were resistant to the antiviral drug oseltamivir through mutation at position 274 in the viral neuraminidase gene.[16] Analysis of 2499 A/H1N1 viruses from 24 European (European Union, EEA/EFTA) countries isolated between November 2007 and early April (data archived on April 23rd) showed that 577 were resistant to oseltamivir, but retained sensitivity to zanamivir and amantadine. The proportion of A(H1N1) viruses that are oseltamivir resistant varied significantly across Europe. The highest proportion of resistant viruses to date have been in Norway where 168 (67%) of the 252 samples are resistant to oseltamivir, whereas no resistant viruses have been detected in five of the 24 countries. In Ireland, 9.1% are resistant. There is also evidence of similarly resistant viruses in North America and the Far East.

There is no evidence that the appearance of these new viruses is related to use of oseltamivir. The 07/08 winter season is the first time there has been widespread and sustained transmission of such viruses in the community. Similar viruses have been seen before, but usually following treatment. Such viruses previously have not been able to readily transmit and have rapidly disappeared. At this stage the significance of these findings remains

uncertain. The emergence of drug resistance in the context of limited drug use is unexpected, and the extent of future circulation is difficult to predict.

In 2005, Mai Le et al reported isolation of drug resistant H5N1 virus from a Vietnamese girl.[17] This 15-year-old girl was treated with a prophylactic dose for three days, and then subsequently was given a therapeutic dose for seven days. She recovered. She had not had any direct contact with poultry, but had cared for her brother who had documented H5N1 infection. Although the virus was resistant to oseltamivir, it was sensitive to zanamivir. Since that report, there have been two additional cases reported where H5N1 virus, which is resistant to oseltamivir, was isolated.[18] In these patients, the viruses were isolated during or shortly after a course of oseltamivir at therapeutic doses. Both of these patients died. The authors stated that at least in some patients with A(H5N1) infection, treatment with recommended doses of oseltamivir incompletely suppresses viral replication, and that this can allow the infection to proceed, but also provides opportunities for drug resistance to develop.

Ferguson et al have modelled the potential spread of drug resistant influenza infections during community-based use of antivirals.[19] Looking at different scenarios of usage of oseltamivir, ranging from treatment of 6% of symptomatic infections, to treatment of 40% of symptomatic infections and PEP following 5% of exposure events, they found that the currently isolated strains of influenza exhibiting resistance are unlikely to be transmitted in a frequency that would significantly interfere with the efficacy of even high levels of drug usage. However, this work pre-dated the emergence of resistance of A(H5N1) to oseltamivir in the 2007/2008 season.

The potential human-to-human transmissibility of these variants is a major public health concern. If the A(H1N1) resistance to oseltamivir seen in the 2007/2008 season persists, it could affect our ability to use antiviral drugs during a pandemic, if this resistance were present also in the pandemic strain.

5.3.4 M2 inhibitors (amantadines) in treatment

In 2004, a Cochrane review of the effectiveness and safety of amantadine and rimantadine in healthy adults was carried out. All controlled trials registered up to September 2003 were included. Amantadine prevented 25% of influenza like illness (ILI) cases (95% confidence interval (CI) 13% to 36%), and 61% of influenza A cases (95% CI 35% to 76%). Amantadine reduced duration of fever by one day (95% CI 0.7 to 1.3). Rimantadine demonstrated comparable effectiveness, but there were fewer trials and the results for prevention were not statistically significant. Both amantadine and rimantadine induced significant gastrointestinal adverse effects. Adverse effects of the central nervous system and study withdrawals were significantly more common with amantadine than rimantadine. They concluded that amantadine and rimantadine have comparable effectiveness in the prevention and treatment of influenza A in healthy adults, although rimantadine causes fewer adverse effects than amantadine.

Several placebo controlled prospective studies, during the 1968 H3N2 pandemic and 1977 H1N1 pandemic reappearance, showed that amantadine and rimantadine provided therapeutic benefit in uncomplicated illness in previously healthy adults with reductions in fever, symptom severity and time to resuming normal activities.[20;21] No prospective trials to date have documented reductions in complications, antibiotic use or hospitalisations.[22]

5.3.5 M2 inhibitors (amantadines) as prophylaxis

Placebo controlled, prospective studies of seasonal prophylaxis with amantadine and rimantadine during the 1968 H3N2 pandemic and the 1977 H1N1 reappearance established that these agents are effective for chemoprophylaxis in naïve adult populations. The level of protection against illness averages approximately 60-70%, slightly lower than that achieved with inter-pandemic influenza.[20] However one study during the 1968 pandemic of short-term (10 days) post exposure amantadine prophylaxis in families, along with treatment of the index case, found low protective efficacy against illness (6%) and none against infection.[23] This may have been due to emergence of resistant variants, though this was not studied at the time.

5.3.6 M2 inhibitors: Antiviral Resistance

As the amantadines block the M2 ion channel protein, single nucleotide changes in any one of several sites within the transmembrane region of M2 can lead to high-level antiviral resistance. These variants are resistant to all M2 inhibitors, but seem to retain full virulence, infectivity and ability to transmit.[9] M2 inhibitors emerge rapidly when these drugs are used for treatment, and roughly 30% of treated children or adults will shed resistant variants from two to five days after initiation of treatment. In immunocompromised patients, this frequency is higher. In addition, in nursing home populations, resistant variants have caused failures of chemoprophylaxis and severe illness. Stilianakis et al developed a model for the emergence of drug resistant influenza viruses in a closed population single wave epidemic.[24] This model, based on treatment with amantadine and rimantadine, predicted that chemoprophylaxis of susceptibles (without treatment of symptomatic cases) led to lower levels of infection and that the emergence of drug resistance would be low. If treatment was combined with chemoprophylaxis, there was a similar effect on the number of infections and low likelihood of emergence of resistant variants. Treatment alone of symptomatic persons did not slow the epidemic and had a variable risk of developing drug resistance. However this model assumed that variant viruses were less transmissible than wild type viruses, and if this is not the case, then prophylaxis failures are expected to be common due to resistant virus. Ferguson et al, when modelling the potential spread of drug-resistant influenza stated that because amantadine resistance mutations in the M2 virus protein are not associated with a detectable loss in viral function, and that transmissibility, experimental infectivity and pathogenesis of resistant mutants are comparable to wild type, their analysis predicts that widespread use of amantadines for the treatment of symptomatic influenza could result in substantial transmission of resistant virus.[19] Recently H5N1 isolates recovered from children and adults in Viet Nam and Thailand have been resistant to M2 inhibitors.[22]

5.3.7 Oseltamivir----- side effects

Hypersensitivity to oseltamivir is listed as a contraindication. Side effects of oseltamivir are listed in appendix A, with nausea and vomiting the most commonly reported.

More recently there have been reports mostly from Japan of neuropsychiatric events including delirium, convulsions, and encephalitis mainly in children and adolescents who were taking oseltamivir. Japan has the highest usage of oseltamivir worldwide.[25] In March 2007, Tokyo's Ministry of Health and Welfare instructed the Japanese distributor of oseltamivir to include a warning not to give the drug to patients aged between 10 and 19, after reports that at least 18 Japanese children taking Tamiflu have died as a result of irrational behaviour. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMEA) reviewed these reports. The relative contribution of the drug to these events is unknown. The EMEA's Committee for Medicinal Products for Human Use (CHMP) reviewed adverse drug reactions to the drug in 2005 and in 2007.[26;27] In 2007, it recommended an update of the product information to inform healthcare professionals and patients about neuro-psychiatric side effects. The recommended wording for patients is that "Convulsion, depressed level of consciousness, abnormal behaviour, hallucinations and delirium have been reported during Tamiflu administration, leading in rare cases to accidental injury. Patients, especially children and adolescents, should be closely monitored and their healthcare professional should be contacted immediately if the patient shows any signs of unusual behaviour". The current package leaflet[28] states the following for adults and adolescents "Influenza can be associated with a variety of neurologic and behavioural symptoms which can include events such as hallucinations, delirium, and abnormal behaviour, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease. During Tamiflu treatment, events like convulsions and delirium (including symptoms such as altered level of consciousness, confusion, abnormal behaviour, delusions, hallucinations, agitation, anxiety, nightmares) have been reported, in a very few cases resulting in accidental injury, in some instances with fatal outcome. These events were reported primarily among children and adolescents and

often had an abrupt onset and rapid resolution. The contribution of Tamiflu to those events is unknown. Such neuropsychiatric events have also been reported in patients with influenza who were not taking Tamiflu."

5.3.8 Oseltamivir in pregnancy and for those <1 year of age

On 7th May, 2009, following a review of all the available evidence by the CHMP of the EMEA, that seems to show that no new safety risks to the foetus are connected to the use of oseltamivir in pregnant women, the CHMP concluded that overall the data suggest that the benefit of using oseltamivir in pregnant or breastfeeding women outweighs the risk in the context of novel influenza A (H1N1) in a pandemic situation.[29] (For seasonal influenza epidemics oseltamivir should not be used during pregnancy/breast feeding unless the potential benefit to the mother justifies the potential risk to the foetus/nursing infant.[1;29])

The CHMP of the EMEA acknowledged that limited data are available supporting the use of oseltamivir in children below 1 year of age. However considering the urgent need for recommendations to treat this population, in case of pandemic influenza being declared by WHO in the context of the novel influenza A (H1N1) outbreak, the CHMP recommends <u>treating</u> children below 1 year of age with oseltamivir.[29] The appropriate dosage to treat children below 1 year of age is 2-3mg/kg twice daily during 5 days. The paediatric suspension or dilution of the capsules of Tamiflu can be used to prepare the dose in children below 1 year of age. Children below 1 year of age should be treated under medical supervision. However in case of pandemic influenza, this recommendation could potentially place huge burden on hospital resources and therefore, the CHMP strongly recommends that at least children below 3 months of age are treated under medical supervision in hospital. The post-exposure prophylaxis of children below 1 year of age should be very carefully considered by prescribers. If it is decided to prescribe oseltamivir to prevent influenza for children below 1 year of age who have been exposed to the virus, the appropriate dose should be 2-3mg/kg once a day during 10 days. (For seasonal influenza oseltamivir is only indicated for children aged one year and older.)

5.3.9 Zanamivir in pregnancy

Zanamivir (Relenza) has in animal studies been shown to cross the placenta and to be secreted in breast milk. The non-clinical data are not indicative of any relevant cause for concerns regarding the safe use of zanamivir at recommended doses. The CHMP of the EMEA states that taken together the overall data suggest that the benefit of using zanamivir in pregnant or breastfeeding women outweighs the risk in the context of a novel influenza A (H1N1) in a pandemic situation.[29] (For seasonal influenza epidemics zanamivir should not be used during pregnancy unless the expected benefit to the mother is thought to outweigh any possible risk to the foetus and is not recommended in mothers who are breast feeding.[1;29])

5.3.10 Oseltamivir stability

Due to the public health emergency linked to the current risk of pandemic influenza (as a result of the recent outbreak of the novel influenza virus A (H1N1)), and based on data made available regarding the stability of oseltamivir 30mg, 45mg and 75mg capsules for an additional period of 2 years, the CHMP of the EMEA recommends that boxes of Tamiflu capsules should not be discarded where the expiry date has already passed.[29] For these batches an updated expiry date should be determined by adding a further period of 2 years to the stated expiry date. The conditions of storage play a role in the stability of medicinal products. It is of great importance that these boxes have always been kept and remain stored below 25^{o}C.

5.4 Expert Group recommendations on use of antivirals in the pandemic alert period and during a pandemic

5.4.1 Phases 2-5 (Present Position)

Oseltamivir has been used to treat avian influenza cases in Thailand, Viet Nam,Turkey and other affected countries, and to prevent infection in close contacts. The drug has also being given prophylactically to health care workers, family members and close contacts of cases. WHO has recently

published evidence based Rapid Advice Guidelines on the pharmacological management of humans infected with avian influenza A (H5N1) virus.[30] **The Expert Group advises that Ireland follows the WHO recommendations for treatment of cases as described below:**

Where neuraminidase inhibitors are available:

- **Clinicians should administer oseltamivir treatment (strong recommendation); zanamivir might be used as an alternative (weak recommendation). The quality of evidence if considered on a continuum is lower for the use of zanamivir compared to oseltamivir.**
- **Clinicians should not administer amantadine or rimantadine alone as a first-line treatment (strong recommendation).**

Recommendations regarding the use of antivirals for prophylaxis in contacts of human cases are detailed in the avian influenza Chapter 11.

If an outbreak of highly pathogenic avian influenza occurs in birds in Ireland, **the Expert Group advises that antivirals should be used in the prevention and control of avian influenza in occupational groups and other contacts exposed to dead or diseased birds. Antivirals should be used for personal protection of these workers and also to protect against transmission.** This is detailed further in Chapter 11 and Supplement 11.

Pandemic period

Antivirals may be used for treatment or prophylaxis of influenza. In a pandemic situation antivirals will **primarily** be used for treatment of influenza cases. Antivirals will have great importance as the only influenza-specific medical intervention for reducing morbidity and mortality. It is recognised that pandemic planning is a dynamic process. As the definition of risk is likely to change over time, recommendations for use of antivirals must be kept under review. In particular, the Expert Group will need to review the epidemiological data before final recommendations are decided in the setting of an imminent

pandemic, and during its course. The decision making process will be guided by relevant expert advice from the European Commission and the World Health Organization.

Antivirals will only be used in a community once the pandemic virus is detected in the community. The initial antiviral drug of choice for use will be oseltamivir. If however, evidence emerges that resistance is developing to oseltamivir and/or the clinical attack rate is very high, zanamivir will then be used. If the attack rate is very high, then it might be best to use zanamivir in those age groups where administration of the inhaled drug would not pose a problem, such as workers, including healthcare workers, and in the community rather than the hospital setting. Detailed guidance on indications for use will be developed if this situation arises, based on experience of treatment of the pandemic virus at the time.

5.4.2 Antiviral use in Ireland at the start of a pandemic

Antivirals have a role in trying to contain infection or slow transmission at a stage when isolated cases or small outbreaks are occurring, and when transmission is not occurring efficiently. **The Expert Group advises that at the start of the pandemic when isolated cases or small outbreaks are occurring, influenza cases should be treated with antivirals, and that contact tracing and short-term post-exposure prophylaxis to prevent infection developing in close contacts including family members and health care workers be carried out**. See treatment algorithms (Appendix B and C).

5.4.3 Antiviral use in Ireland during the pandemic

In the event of a pandemic, and a clinical attack rate of 25%, as per the HPA empirical model recommended for use in Ireland, it is likely that there will be sufficient quantities of antiviral drugs to be able to treat all early symptomatic cases. Antivirals should only be used where there is surveillance evidence or laboratory confirmation of influenza in the community/region.

If however the clinical attack rate is high (50% as per the worst case scenario outlined in Chapter 3) it will be necessary to prioritise or target specific groups for treatment. In advance of a pandemic, based on current knowledge of risk of mortality and morbidity due to influenza, the following priorities have been identified. **This is subject to change, once the epidemiology of the pandemic strain is known.**

Expert Group advice on priority groups for antiviral treatment during an influenza pandemic – *if stockpiled supplies are not sufficient to treat all symptomatic persons*

Group 1: Treatment of persons hospitalised for influenza (if hospitalised within 48 hours of onset of symptoms). To be consistent with the goal of reducing morbidity and mortality and considering the optimal use of antiviral drugs in relation to onset of illness, those who are hospitalised within the first 48 hours of onset of illness should be highest priority for treatment. Treatment with oseltamivir may be considered in those who are hospitalised more than 48 hours after onset of symptoms, although its effectiveness in this situation is not established.

Group 2: Treatment of ill health care and emergency services workers. Considering the essential role that health care workers and emergency service workers will have in the pandemic response, influenza infection in these groups, identified within the first 48 hours of onset of illness, should be high priority for treatment.

Group 3: Treatment of ill high risk persons* in the community. Persons with underlying heart and lung conditions or those who are immunocompromised, and who present for medical care within 48 hours of onset of symptoms, will also be considered high priority for treatment since they are at high risk of complications.

***NOTE: during a pandemic the definition of high risk persons may change based on epidemiological evidence.*

This categorisation is based partly on the priority groups outlined in the Canadian Pandemic Plan (February 2004) and reflects general guidance from the World Health Organisation.[31]

5.5 Planning requirements for an effective antiviral strategy

Identifying the antivirals to be stockpiled, the goals and the priority groups are only part of an effective antiviral strategy. For an effective antiviral strategy, a secure supply, with a well planned distribution and monitoring system, and the ability to target priority groups (if necessary) will be essential. In addition, it will require the availability of diagnostic tests (particularly in the early stages), and clinical case definitions to distinguish influenza from other respiratory symptoms, as well as enhanced surveillance to identify changes in the epidemiology of the virus, emergence of resistance to antivirals, and for drug related adverse events. Also, there is a requirement to develop clinical guidelines on their appropriate use, and study protocols to assess the effectiveness in treatment and prophylaxis, as well as effective materials for communication with the public and health care workers on antivirals.

The Expert Group advises that it is critical that sufficient attention is given to the significant logistical problems that will arise in achieving timely and appropriate distribution and delivery of antiviral drugs, and that sufficient resources are put into planning a robust capacity to deliver antiviral drugs as needed as quickly as possible.

5.5.1 Decision on stockpiling of antivirals

In February 2005, the National Pandemic Influenza Expert Group reviewed recommendations for the use of antivirals in line with international guidance.

Based on this assessment, it advised that pandemic planning be based on the assumption that the virus most likely to cause an influenza pandemic will be an avian influenza virus or avian influenza derived.

It also advised that oseltamivir should be stockpiled in view of its effectiveness against avian/avian-related influenza. The possibility of recommending the

use of amantadine in future if the evidence on the potential pandemic virus changes has not been ruled out.

The Expert Group also advised that a supply of the Active Pharmaceutical Ingredient (API), oseltamivir phosphate powder, should be purchased to treat young children between the ages of one and five years. Arrangements have been put in place so that API powder will be converted to paediatric capsules, which will be used for all children aged one to 11 years of age.

Following consideration of the expert advice, Ms Mary Harney T.D, then Tánaiste and Minister for Health and Children decided that one million treatment packs of Oseltamivir (Tamiflu) should be stockpiled. This quantity is sufficient to treat 25% of the population and is in line with international trends. 63kg of the API has also been purchased.

Subsequently, the Expert Group reviewed recommendations with regard to stockpiling of zanamivir (Relenza) in addition to oseltamivir. This was in light of a case report of suspected resistance to oseltamivir, detailed earlier in this chapter. The Expert Group advised that it would be prudent to stockpile a second antiviral agent that would allow for treatment of 20% of the population. The Minister for Health and Children accepted this advice.

Zanamivir has been shown to be effective against seasonal influenza. This antiviral agent could be used if resistance to oseltamivir developed in significant numbers of cases. However it cannot be used in young children and in some adults, due to the drug's method of administration (inhalation).

706,000 packs of zanamivir (Relenza) have now been ordered. This is sufficient to cover 20% of the population over the age of seven. This stockpile is now complete.

5.6 References

(1) EMEA. Updated review of influenza antiviral medicinal products for potential use during pandemic by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA). EMEA 2007 December 13 Available from: URL: http://www.emea.europa.eu/pdfs/human/pandemicinfluenza/59210207en.pdf

(2) Cooper NJ, Sutton AJ, Abrams KR, Wailoo A, Turner D, Nicholson KG. Effectiveness of neuraminidase inhibitors in treatment and prevention of influenza A and B: systematic review and meta-analyses of randomised controlled trials. BMJ 2003 Jun 5;326(7401):1235.

(3) Kaiser L, Wat C, Mills T, Mahoney P, Ward P, Hayden F. Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations. Arch Intern Med 2003 Jul 28;163(14):1667-72.

(4) Whitley RJ, Hayden FG, Reisinger KS, Young N, Dutkowski R, Ipe D, et al. Oral oseltamivir treatment of influenza in children. Pediatr Infect Dis J 2001 Feb;20(2):127-33.

(5) Koopmans M, Wilbrink B, Conyn M, Natrop G, van der NH, Vennema H, et al. Transmission of H7N7 avian influenza A virus to human beings during a large outbreak in commercial poultry farms in the Netherlands. Lancet 2004 Feb 21;363(9409):587-93.

(6) Bosman A, Mulder YM, de Leeuw JRJ, Meijer A, Du Ry van Beest Holle M, Kamst RA. Avian Flu Epidemic 2003: Public Health Consequences. http://www rivm nl/en/ 2004Available from: URL: http://www.rivm.nl/bibliotheek/rapporten/630940004.html

(7) 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 Sep;11(9):1355-62.

(8) Ward P, Small I, Smith J, Suter P, Dutkowski R. Oseltamivir (Tamiflu) and its potential for use in the event of an influenza pandemic. J Antimicrob Chemother 2005 Feb;55 Suppl 1:i5-i21.

(9) Hayden FG, Belshe R, Villanueva C, Lanno R, Hughes C, Small I, et al. Management of influenza in households: a prospective, randomized comparison of oseltamivir treatment with or without postexposure prophylaxis. J Infect Dis 2004 Feb 1;189(3):440-9.

(10) Longini IM, Jr., Halloran ME, Nizam A, Yang Y. Containing pandemic influenza with antiviral agents. Am J Epidemiol 2004 Apr 1;159(7):623-33.

(11) Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley S, Meeyai A, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature 2005 Sep 8;437(7056):209-14.

(12) WHO. WHO pandemic influenza draft protocol for rapid response and containment. 2006.

(13) Ferguson NM, Cummings DA, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. Nature 2006 Apr 26.

(14) Gubareva LV. Molecular mechanisms of influenza virus resistance to neuraminidase inhibitors. Virus Res 2004 Jul;103(1-2):199-203.

(15) Kiso M, Mitamura K, Sakai-Tagawa Y, Shiraishi K, Kawakami C, Kimura K, et al. Resistant influenza A viruses in children treated with oseltamivir: descriptive study. Lancet 2004 Aug 28;364(9436):759-65.

(16) ECDC. Resistance to oseltamivir (tamiflu) found in some European influenza virus samples. 2008 May 7.

(17) Le QM, Kiso M, Someya K, Sakai YT, Nguyen TH, Nguyen KH, et al. Avian flu: isolation of drug-resistant H5N1 virus. Nature 2005 Oct 20;437(7062):1108.

(18) de Jong MD, Tran TT, Truong HK, Vo MH, Smith GJ, Nguyen VC, et al. Oseltamivir resistance during treatment of influenza A (H5N1) infection. N Engl J Med 2005 Dec 22;353(25):2667-72.

(19) Ferguson NM, Mallett S, Jackson H, Roberts N, Ward P. A population-dynamic model for evaluating the potential spread of drug-resistant influenza virus infections during community-based use of antivirals. J Antimicrob Chemother 2003 Apr;51(4):977-90.

(20) Galbraith AW, Oxford JS, Schild GC, Potter CW, Watson GI. Therapeutic effect of 1-adamantanamine hydrochloride in naturally occurring influenza A 2 -Hong Kong infection. A controlled double-blind study. Lancet 1971 Jul 17;2(7716):113-5.

(21) Van Voris LP, Betts RF, Hayden FG, Christmas WA, Douglas RG, Jr. Successful treatment of naturally occurring influenza A/USSR/77 H1N1. JAMA 1981 Mar 20;245(11):1128-31.

(22) WHO. WHO consultation on priority public health interventions before and during an influenza pandemic. www who int 2004Available from: URL: http://www.who.int/csr/disease/avian_influenza/consultation/en/

(23) Galbraith AW, Oxford JS, Schild GC, Watson GI. Study of 1-adamantanamine hydrochloride used prophylactically during the Hong Kong influenza epidemic in the family environment. Bull World Health Organ 1969;41(3):677-82.

(24) Stilianakis NI, Perelson AS, Hayden FG. Emergence of drug resistance during an influenza epidemic: insights from a mathematical model. J Infect Dis 1998 Apr;177(4):863-73.

(25) Maxwell SRJ. Tamiflu and neuropsychiatric disturbance in adolescents. BMJ 2007 Jun 16;334(7606):1232-3.

(26) EMEA. Press release: European Medicines Agency recommends no changes for Tamiflu safety information. EMEA 2005 December 15 [cited 2009 May 20];Available from: URL: http://www.emea.europa.eu/pdfs/human/press/pr/42008705en.pdf

(27) EMEA. Press release: European Medicines Agency statement on safety of Tamiflu. EMEA 2007 March 23 [cited 2009 May 20];Available from: URL: http://www.emea.europa.eu/pdfs/general/direct/pr/13456607en.pdf

(28) Tamiflu (Oseltamivir) 75 mg hard capsules [Package leaflet: Information for the user] Roche. www medicines ie 2009 May [cited 2009 May 19];Available from: URL: www.medicines.ie

(29) EMEA. Opinion of the Committee for Medicinal Products for Human Use Pursuant to Article 5(3) of Regulation (EC) No 726/2004, on Novel Influenza (H1N1) outbreak Tamiflu (oseltamivir) Relenza (zanamivir). EMEA 2009Available from: URL: http://www.emea.europa.eu/humandocs/PDFs/EPAR/tamiflu/27883809en.pdf

(30) WHO. WHO Rapid Advice Guidelines on Pharmacological Management of Humans Infected with Avian Influenza (H5N1) Virus. www who int 2006Available from: URL: http://www.who.int/csr/disease/avian_influenza/guidelines/pharmamanagement/en/index.html

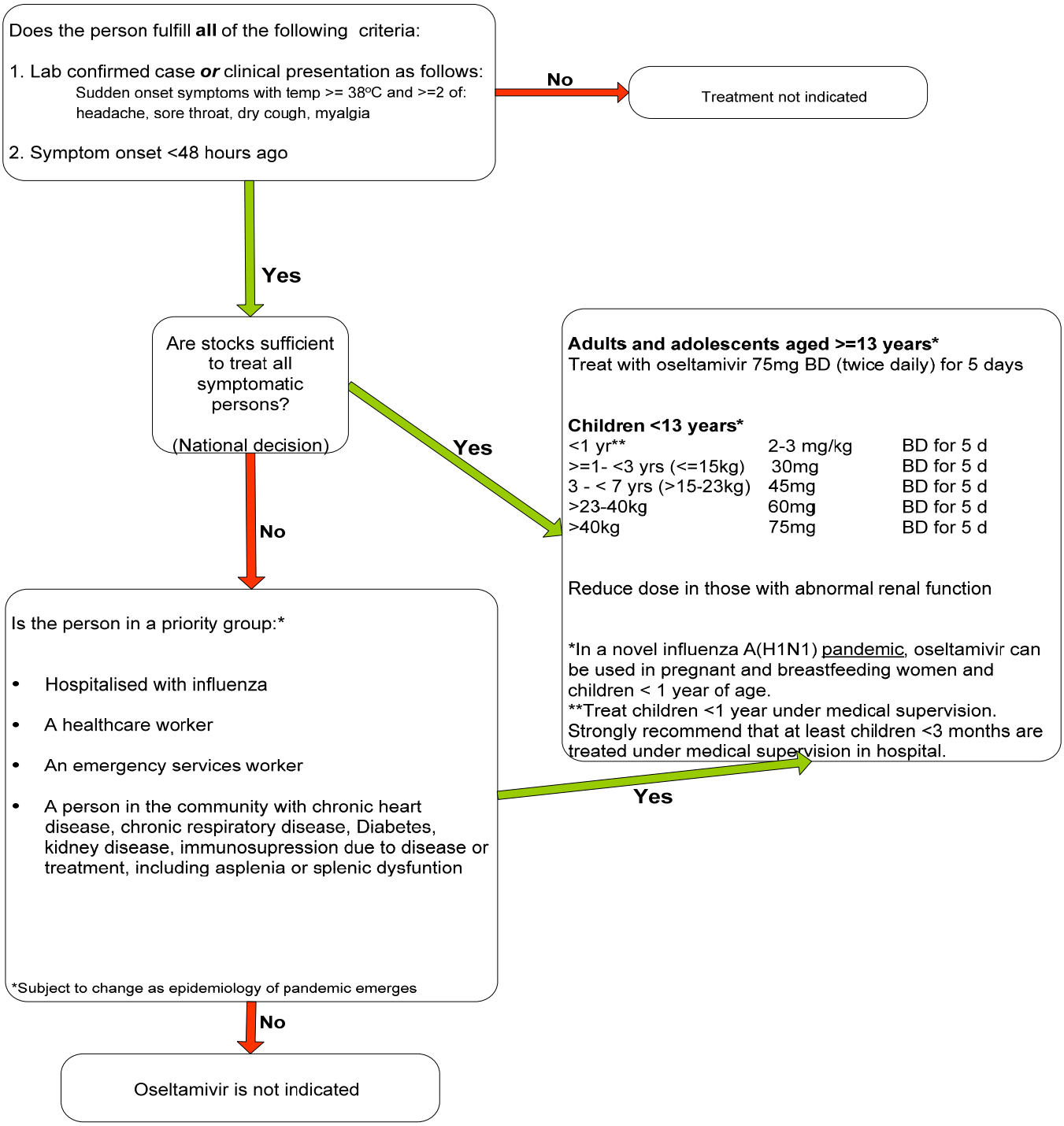
(31) Health Canada. Canadian Influenza Pandemic Plan. Public Health Agency of Canada 2004

Appendix A Properties of the relevant influenza antiviral medicinal products
(taken from the EMEA report entitled Updated review of influenza antiviral medicinal products for potential use during pandemic[1])

Property	Amantadine	Oseltamivir	Zanamivir
Mode of action	M2 ion channels blockade	Neuraminidase inhibition	Neuraminidase inhibition
Adverse effects	Common-uncommon: CNS effects, nausea, vomiting, palpitation Rare. Cardiac arrhythmias, seizures	Common: Nausea, vomiting, headache Rare to very rare: hypersensitivity skin reactions hepatitis, elevated liver enzymes, neuro-psychiatric events	Very rare: bronchospasm, allergic-type reaction, dyspnoea, throat tightness or constriction and rash, urticaria
Warnings (some variation at the member state level)	Prostatic hypertrophy Narrow angle glaucoma Agitation and confusion History of seizure, psychosis or delirium Severe hepatic or renal dysfunction	Hypersensitivity reactions Observation of oseltamivir-treated children	Bronchospasm and/or decline in respiratory function
Use during pregnancy*	Not recommended	Only if the risk of infection exceeds the risk to the foetus*	Only if the risk of infection exceeds the risk to the foetus*
Use in children*	Very limited data	Used in children from one year of age Not recommended for children < 12 Mo.* Studies are ongoing to establish posology and safety in these children.	Limited data on children Not suitable for children <5 years
Contraindications (some variation at the member state level)	Hypersensitivity to the product Severe renal failure History of convulsions History of gastric ulcerations Severe heart disease	Hypersensitivity to the product	Hypersensitivity to the product
Drug-drug interactions	Anticholinergic agents Several medicinal products affecting CNS Combination diuretics Quinine, quinidine	Not known	Not known
Effect: treatment prophylaxis	Modest Good initially, may be lost due to resistance	Modest Good	Modest Good
Route of administration	Oral	Oral	Inhalation with a device
Site of action	Systemic	Systemic	Respiratory tract
Effect on past pandemic strains	Yes (*in vitro and in vivo*)	Yes (*in vitro*)	Yes (*in vitro*)
Effect on H5N1 "bird flu"strains	Questionable	Yes (*in vitro*, experimentally *in vivo*)	Yes (*in vitro,* experimentally *in vivo*)
Resistance	Common during treatment Primary resistance by many H5N1 strains	Rare (except in treatment of children)	Very rare
Formulations	Tablets	Capsules, powder for solution, extemporaneous formulations	Powder for inhalation

*On the 7th May 2009 the CHMP of the EMEA recommended that, in the case of a pandemic influenza declared by the WHO in the context of the novel influenza A (H1N1) outbreak, oseltamivir and zanamivir can be used in women who are pregnant or breastfeeding and oseltamivir can be used in children <1 year of age (see sections 5.3.8 - 5.3.9).[29]

Appendix B Oseltamivir treatment algorithm for pandemic influenza



Appendix C Algorithm for public health doctors prescribing oseltamivir as prophylaxis for human contacts of novel influenza

Please see www.hpsc.ie for most up to date version.

Post-exposure Prophylaxis (PEP) for close contacts of probable[1] or confirmed[2] human case(s) of Influenza A(H1N1) in WHO Pandemic Alert Phase 5

PEP for close contacts of probable and confirmed cases is a control measure to be applied before there is a wide spread sustained transmission within Ireland. Therefore this policy may be modified if the situation changes.

Post exposure prophylaxis is indicated for close contacts that were exposed to a probable or confirmed case during the period when the case was symptomatic and for 24 hours before onset of symptoms AND the contact's last exposure occurred no more than 7 days previously.
Any probable or confirmed human case of Influenza A(H1N1) should be notified to the local DPH as soon as possible.

Category of Contact		Actions
1	Household members of a case	YES → *Voluntary Quarantine of Contact

THEN

Quarantine Unnecessary

			Actions
2	Roommates of cases in hospitals or institutions e.g. nursing homes	Yes →	• Start Antiviral PEP[3] as soon as possible unless more than 7 days have elapsed since last exposure. Post exposure prophylaxis should be taken for 10 days.[3] • Provide information leaflets • Coordinate active follow up for 7 days after last exposure to the case.[4] • Taking serology may be relevant in certain circumstances in order to better understand transmission. In these circumstances paired samples should be taken (first sample when identified as a contact and second sample 14 days later). • Contacts who work on pig farms should remain off work for 7 days as soon as diagnosis is suspected • **If contacts are in a school, contact HPSC directly**
3	People occupying the same room with a case (<1metre) for at least 4 hours	Yes →	
4	Contact with fomites contaminated with respiratory secretions (e.g. touching used tissues or hands of infectious person)	Yes →	
5	Travellers by plane sitting in the same row or in the 2 rows ahead or behind on flight of ≥ 4 hours of a symptomatic (sneezing and coughing) case OR persons caring for such a passenger	Yes →	
6	Health or social care workers who provided direct clinical/personal care or who or who examined a symptomatic patient without wearing appropriate PPE**	Yes →	
7	All others not classified as contacts	→	Information leaflets may be helpful but no other action is required.

If a contact becomes unwell, they should contact local DPH and s/he should liaise with HPSC

***Duration of Voluntary Quarantine:**
Should last 7 days from last unprotected contact
****Appropriate PPE is:**
Routine care: (including taking nasal and throat swabs for viral testing) Surgical mask, Plastic Apron, Gloves (and goggles if risk of splashing/spraying)
Aerosolising generating procedures: FFP2 or FFP3 respirator mask, goggles, long-sleeved gown and gloves.

Footnotes:
1. Probable case: Any person meeting the clinical and epidemiological criteria AND with a positive test for influenza A (see Algorithm for the management of persons with acute febrile respiratory illness).
2. Confirmed case: Any person with laboratory confirmation of influenza A(H1N1).
3. Refer to relevant dosing schedule for antiviral prophylaxis in Advice of the Pandemic Influenza Expert Group
4. Active follow up: contacts to self-monitor for symptoms for 7 days, check temp twice daily. Staff from local office of Director of Public Health will make contact daily to ensure asymptomatic.

In case of uncertainty, discuss with your Director of Public Health

Adapted from material provided by HPA London

Chapter 6 Table of Contents

6 Public Health Response: Vaccines

6.1 Introduction

Ideally, vaccination would be the primary public health response in the event of an influenza pandemic. However, a pandemic vaccine can only be developed once the pandemic virus is identified and the first vaccine doses will only begin to appear four to six months after that. The first pandemic wave may well have passed before a pandemic vaccine becomes available.

This chapter outlines the benefits of seasonal influenza and pneumococcal vaccination, and how maximising uptake in target groups now will aid pandemic preparedness. It explains how vaccines are produced and supplied in the inter-pandemic and pandemic period. It outlines current vaccine priority groups for pandemic vaccine and also describes the rationale and plans for procurement of A/H5N1 vaccine for essential healthcare and other workers.

6.2 Global Vaccine Action Plan

Current world manufacturing capacity of influenza vaccine covers just 5% of the world's population. In September 2006 the WHO published a Global Vaccine Action Plan with strategies aimed at increasing influenza vaccine production and surge capacity before and during an influenza pandemic.[(1)] Three main approaches were identified: a) an increase in seasonal vaccine use; b) an increase in production capacity; and c) further research and development. It will not be possible to bridge the expected gap between vaccine demand and supply in the short term. Implementation of the Action Plan will require a sustained global effort and commitment by countries, the vaccine industry, the research community and donors over a period of five to ten years.

6.3 Benefits of seasonal vaccination

In the inter-pandemic period, influenza vaccination remains the most effective way to reduce the impact of influenza, especially in high-risk groups. This requires annual vaccination with the current recommended strains, as advised by WHO.

Vaccination is recommended for two groups of individuals[2]:

- Any individual older than six months of age who is at increased risk of influenza related complications
- Those at increased risk of transmitting influenza to a person at high risk for influenza complications.

The high-risk groups are adults and children with any of the following:

- Chronic illness requiring regular medical follow-up (e.g. chronic respiratory disease, including cystic fibrosis, moderate or severe asthma, chronic heart disease, bronchopulmonary dysplasia, diabetes mellitus, Haemoglobinopathies, chronic renal failure etc.)
- Immunosuppression due to disease or treatment, including asplenia or splenic dysfunction
- Persons aged 50 years or older, as recommended by WHO
- Children on long term aspirin therapy (because of the risk of Reyes Syndrome)
- Children with any condition (e.g. cognitive dysfunction, spinal cord injury, seizure disorder, or other neuromuscular disorder) that can compromise respiratory function
- Residents of nursing homes, old peoples' homes, and other long stay facilities where rapid spread is likely to follow the introduction of infection.

Vaccines that are well matched to the current circulating strains are 70-90% effective in preventing illness in healthy adult volunteers.[3] Annual vaccination offered to all older people, irrespective of whether they have any underlying disease, is cost effective.[4-6] Influenza vaccine has been shown to prevent severe complications and death due to influenza in elderly nursing home residents. Hospitalisation rates, cases of pneumonia and respiratory illness and death rates were reduced by over 50% in one elderly residential population that had been vaccinated.[7] The vaccine is also effective in

reducing mortality in older people living in the community and those who are not classed as high risk.[4-6]

The ideal time for vaccination in the Northern Hemisphere is from September to mid-October as influenza activity increases from October onwards. On average, it takes two weeks for the vaccine to induce a protective antibody response.

Increasing seasonal vaccination uptake is important not only for reducing the impact of influenza each year, but also as it increases vaccine production capacity, for increasing the capacity to respond when a pandemic strain is detected. In addition it improves national capacity and experience in implementing vaccination programmes. It also fosters increased familiarity with and public confidence in influenza vaccines. The aim is to increase uptake in all high-risk populations with a target of 75% uptake in older people by 2010.[8]

In this context, the National Immunisation Advisory Committee (NIAC) has recommended the extension of routine influenza vaccination to everyone aged 50 years and over on a phased basis.

The Expert Group advises that every effort should be made to increase seasonal vaccination coverage of all people at high risk in all settings, (e.g. healthcare clinics, GP surgeries and workplaces), and to achieve the WHO target of 75% uptake of seasonal vaccination by older people by 2010.

6.4 Inter-pandemic vaccine production and supply

During the inter-pandemic period, trivalent influenza vaccine is manufactured according to WHO recommendations released in February each year for the Northern Hemisphere. Suitable seed viruses that grow well in eggs are identified and developed. Vaccine viruses are grown in embryonated hens' eggs and the infected allantoic fluid is then harvested. The viruses are purified, inactivated and further treated to produce either a whole virus, split or

subunit virus. The lead-time for vaccine production is approximately six months. Vaccines for human use are not manufactured in Ireland.

6.5 Pandemic vaccine production and supply

At the beginning of a pandemic, a vaccine whose efficacy and safety are clearly established will not be available against the pandemic virus strain. The vaccine needs to match the unique genetic and antigenic characteristics of the pandemic virus strain, and will need to be developed once the pandemic strain has been recognised. Following a lead-time of at least four to six months to produce the first doses of vaccine, the subsequent increase in supply will be progressive. It is unlikely that pandemic-specific vaccine will be available before the end of the first pandemic wave.

There are a number of rate limiting steps involved in the manufacturing process, not least the ability to develop seed viruses in a timely fashion. Other difficulties include the availability of fertilised hen's eggs, and the growth rate of the virus in hen's eggs, especially if the pandemic occurs outside of the usual production season.

6.6 Advance Purchase Agreement for pandemic vaccine

The Global Vaccine Action Plan notes that countries may be required to pay for under-used capacity to assure that sufficient pandemic vaccine doses are produced within the required time frame. This is the rationale behind the advance purchase agreements (or sleeping contracts), which a number of countries are making with vaccine manufacturers. **The Expert Group has advised that Ireland should take this approach and provide for the purchase of sufficient pandemic vaccine to vaccinate the whole population, in the event of a pandemic emerging.**

6.7 Research and development

The third approach in the Global Vaccine Action Plan focuses on efforts being undertaken by researchers, including the vaccine industry, to design more potent and effective vaccines that: a) are capable of inducing protective

responses after one dose, and/or b) induce broad spectrum and long-standing immunity against both seasonal and pandemic influenza strains.

Investigation continues into the best method of delivering the vaccine during a pandemic and studies are being undertaken to define the formulation and dosage regimens that will make the best possible use of available vaccine antigen at the time of a pandemic.

Recent experience with H5N1 vaccine trials indicate that split-product or sub-unit vaccines (the types in use in the EU as seasonal influenza vaccines) are likely to require very high doses of haemagglutinin antigen per dose (90µg) without an adjuvant, 30µg or more if using alum adjuvant, but potentially in the range of 3.8 – 7.5µg if newer adjuvants are used. Data from a whole virus non-adjuvented vaccine (using wild-type H5N1 strain and grown in ell culture) suggest that 7.5µg will be needed.[9]

Presently it is assumed that in the pandemic all those vaccinated will lack previous exposure and will require two doses of vaccine, three weeks apart to confer maximum protection.[10]

6.8 Pandemic vaccine licensing

The new vaccine will be licensed centrally within Europe on the recommendation of the European Medicines Evaluation Agency (EMEA).

As already outlined, at the beginning of a pandemic, no vaccine will be available whose efficacy and safety is clinically established against the pandemic strain. In order to cater for the urgency of the situation and in the interests of public health, it may be necessary for the EMEA to recommend the granting of a marketing authorisation on the basis of less than complete data but subject to specific obligations to subsequently complete the data. This type of an authorisation is called a “conditional marketing authorisation” (CMA).

A conditional marketing authorisation may be granted where:

1. The risk-benefit balance of the vaccine is positive;
2. It is likely that the applicant will be in a position to provide comprehensive clinical data;
3. Unmet medical needs will be fulfilled;
4. The benefit to public health of the immediate availability of the vaccine outweighs the risk inherent in the fact that additional data are still required.

The authorisation is not intended to remain conditional indefinitely.

To date the European Medicines Evaluation Agency (EMEA) has approved marketing authorisations for two human pandemic influenza vaccines using a 'core dossier' approach – Focetria and Daronrix. This is a novel European approach that is intended to speed up the eventual process for obtaining an authorisation for a pandemic vaccine. It allows the submission, before the outbreak of a pandemic, of a core pandemic vaccine dossier based on a "mock-up" vaccine containing a pandemic influenza candidate virus. This mock-up vaccine can be evaluated and a Marketing Authorisation granted before a pandemic. In an officially declared pandemic situation (WHO Phase 6), the pandemic vaccine would be approved for use following a variation, which will contain only the quality data specific to strain replacement.

In 2005 the EMEA introduced a number of incentives to encourage companies to use the core dossier approach. These include a commitment of the Agency's Committee for Medicinal Products for Human Use (CHMP) to accelerate the scientific evaluation of applications for scientific advice and marketing authorisations for pandemic vaccines 'core dossiers'. Work on pandemic influenza preparedness began in 2003 and the EMEA issued its draft pandemic crisis management plan in 2005 for public consultation. The

plan aims to establish efficient procedures for the assessment and authorisation of pandemic vaccines via the centralised procedure and for the surveillance of vaccines and antiviral medicines used in a potential pandemic.

6.9 Pandemic vaccine administration

The Expert Group advises that a mechanism for the storage, distribution and administration of pandemic vaccine should be developed as part of the planning response.

Childhood immunisation is an extremely beneficial and cost effective public health intervention. Interruption to the delivery of routine scheduled immunisation could lead to children's health being put at risk.

The Expert Group advises that the primary childhood immunisation programme should continue during a pandemic unless clinical circumstances dictate otherwise.

6.10 Expert Group advice on pandemic vaccine priority groups

WHO has advised countries to set goals and priorities for the use of vaccines during a pandemic. These goals should reflect the particular circumstances of each country.

Priorities on who should receive influenza vaccination during a pandemic may differ from interpandemic recommendations as follows:

- The target population for vaccination will extend beyond the typical high-risk groups;
- Simultaneous occurrence of disease and vaccination programme.
- Limitations set by the availability and quantity of vaccine will determine who receives the vaccine initially.
- Vaccine will need to be distributed and administered as rapidly as possible in a much shorter timeframe
- It is likely that there may be no vaccine available during the first wave of the pandemic, and in the second wave there may be vaccine shortages

In prioritising target groups for vaccination, the Expert Group advises that the goals for Ireland in a pandemic should be as follows:

- **To prevent or reduce deaths and hospital admissions due to influenza**
- **To prevent and reduce influenza related morbidity**
- **To maintain essential services by protecting the health of essential service workers.**

In order to address the first two goals, the epidemiology of the particular novel virus, including information on who is most frequently affected, the clinical severity of the disease and the age specific mortality rates will be used to help determine who the priority groups for early vaccination should be. In addition, it is likely that WHO will give advice on priority groups for immunisation.

The Expert Group advises that the following population sub-groups are prioritised to receive initial supplies of the pandemic virus vaccine:

Priority groups for vaccination during an influenza pandemic

1. Healthcare staff with patient contact (including ambulance staff) and staff in residential care homes for the elderly
2. Providers of essential services e.g. fire, utilities, Gardaí, security, communications, defence forces, undertakers, and essential healthcare staff without direct patient contact
3. Those with high medical risk e.g. chronic respiratory or heart disease, renal failure, diabetes or immunosuppression due to disease or treatment, women in the last trimester of pregnancy, and children aged from 6 months to 23 months
4. All over 65 years of age
5. Selected industries – maintenance of essential supplies e.g. pharmaceuticals
6. Selected age groups, depending on advice from WHO e.g. children
7. Offer to all

Please note that these priorities are subject to change as the epidemiology becomes evident.

6.11 Surveillance of pandemic vaccination

6.11.1 Vaccine effectiveness

There will be at best limited data on efficacy of the pandemic vaccines in advance of their use. Therefore their effectiveness in the field will need to be assessed rapidly. This may be done by comparing rates of influenza like illness, hospitalisation, and/or death among vaccinated and unvaccinated persons, and by vaccine product.

The Expert Group advises that protocols for timely assessment of vaccine effectiveness should be drawn up in advance of a pandemic.

6.11.2 Vaccine uptake

Once the priority groups for vaccination have been identified the denominator populations of these groups will need to be determined to allow uptake targets to be established, and progress towards achieving them to be monitored. This presents a logistical challenge, given the limitations in current systems for monitoring vaccination uptake, and the lack of chronic disease registers and universal primary care registration.

Influenza vaccine uptake is currently measured using GMS data based on returns by GPs to the HSE Primary Care Reimbursement Service, allowing measurement among only those patients in the population with a GMS card i.e. all patients over 70 years but only 50% of the population aged 65 – 69 years. There is no routine way of measuring uptake in at risk populations less than 65 years old at present. Therefore measurement of vaccine uptake during a pandemic will be very difficult.

The Expert Group advises that options for measuring vaccine uptake among priority groups and generally should be examined as part of the planning process.

6.12 Monitoring adverse events related to vaccination

Safety is critical for pandemic vaccines for the following reasons:

- Vaccination of the whole population (different age groups, risk groups, pregnant women);
- Unknown safety profile;
- Concomitant disease;
- Public confidence in the vaccination programme can only be maintained by the perception that competent authorities will rapidly and adequately assess the safety of vaccines;
- Communication of safety is essential to respond to public concerns, starting in the inter-pandemic phase.

The Irish Medicines Board (IMB) is the regulatory body for human and veterinary medicines in Ireland and is the national competent authority under EU Regulations and Directives. One of its main roles is pharmacovigilance and drugs safety monitoring. Of particular importance are all suspected reactions to newly authorised products, serious reactions to established products and suspected reactions to vaccines or medicines in pregnancy.

The EMEA received a proposal from EVM (European Vaccine Manufacturers) for a pharmacovigilance plan for pandemic vaccines, to which the Agency's Pharmacovigilance Working Party (PhVWP) responded in December 2005. In its response, the PhVWP discussed four major requirements of such a pharmacovigilance plan:

- Routine pharmacovigilance activites (spontaneous reporting of adverse drug reactions (ADRs), with a focus on severe ADRs to enable signal detection)
- Additional pharmacovigilance activities i.e. prospective cohort study of an adequate number of vaccines.

- Shared responsibilities of companies and competent authorities in risk management.
- Feasibility – adequate tools should be in place to handle the enormous workload.

It is envisaged that there will be a harmonised approach of risk management by vaccine manufacturers.

The IMB will monitor adverse events related to vaccination with pandemic vaccine. During the pandemic, the IMB will produce regular reports on vaccine safety. The IMB may direct changes in the vaccine, the vaccination schedule or the program during the pandemic in response to immunogenicity, effectiveness and safety data received during the pandemic.

6.13 H5N1 Vaccines

6.13.1 Potential benefit of stockpiling H5N1 vaccines

A/H5N1, which has caused unprecedented outbreaks in poultry in Southeast Asia since late 2003, and more recently in Europe and Africa, could be the source of the next pandemic, in other words, the next pandemic virus strain may originate from A/H5N1.

WHO has told Member States that, for affluent countries, stockpiling vaccines against H5N1 may be a viable option.(1) It may offer some protection against a future human pandemic strain for healthcare and other essential workers pending development of the precisely matched pandemic strain vaccine. If however a future pandemic strain diverges significantly from this strain, then the H5N1 vaccine will not match the pandemic strain, and it would be ineffective. This is the rationale behind the EMEA's 'core dossier' approach as previously discussed. Further opportunities exist, however, with use of A/H5N1 pre-pandemic or 'mock-up' vaccines as follows:

- Allows the establishment of a collaborative approach between stakeholders including public health, industry, regulatory agencies and clinical service providers, in advance of a pandemic.

- Allows the exploration of likely scenarios in a mass vaccination program.

- Allows for the development of pharmacovigilance systems for a medicinal product with limited clinical data before market authorisation

6.13.2 Pre-Pandemic Vaccination

In August 2007, the European Centre for Disease Prevention and Control published two Technical Reports produced by Expert Advisory Groups on Human H5N1 Vaccines - the first dealing with scientific questions and the second dealing with public health and operational questions.(9;11) The purpose of these reports is to create a common understanding of the scientific and public health rationale for these vaccines. The reports were presented at the 4th Joint EC/ECDC/WHO Workshop on Pandemic Influenza Preparedness in September 2007.(12)

The Expert Group on Scientific Questions found that the data on the developmental H5N1 vaccines are promising with regard to cross-protection and cross-reactivity *provided* the pandemic virus is a H5 strain. However if the next pandemic arises from a non –H5 subtype, a H5N1 vaccine will offer no protection. Modelling data does suggest that public health benefits from an appropriate vaccine given before the pandemic, even if poorly matched to the pandemic strain, will be greater than from a vaccine of much higher efficacy, but not widely available until after a pandemic is underway.

The Public Health Expert Group notes that the group that would most benefit from vaccination with an H5N1 vaccine will change with the evolving profile of the developing pandemic and also depend on the timing and use of the vaccine. Should infection of domestic birds with H5N1 become more widespread in Europe, while remaining predominantly an animal infection, it would be reasonable to consider poultry workers and veterinarians for vaccination with an H5N1 vaccine. However, if the situation develops so that

human-to-human transmission becomes more important poultry workers and veterinarians would probably no longer be a priority.
The four groups that were considered for targeted use of H5N1 vaccine and the rationale for this are:

1. Healthcare workers and laboratory staff – more likely to be exposed
2. Social care and other "front-line" staff (having face to face contact with the public) – more likely to be exposed.
3. Vulnerable populations (similar to those currently recommended for seasonal vaccine, i.e. the elderly, those with chronic medical conditions) – can be anticipated to be especially vulnerable.
4. Children – may be the most potent spreaders of influenza in the community and vaccinating them may influence the size and duration of the pandemic.

There are epidemiological and ethical considerations regarding all of these groups which need to be examined further.

The report also states that an H5N1 vaccine should not be administered to any large population groups prior to the emergence of a H5 –based pandemic. Early vaccination is scientifically reasonable, but this has to be balanced against logistic, economic and political considerations. Substantial continuous investment (in order of tenths of 1% of GDP) is needed in order to reduce the impact of a pandemic through H5N1 vaccines, but this may be cost effective if an H5N1 pandemic does occur.

6.13.3 Recommendations for use of H5N1 vaccine

There is scientific data published that demonstrates that H5N1 vaccines can induce immunity and provide cross protection against clades/subclades of circulating strains. In addition, modelling data shows that even a poorly matched pre-pandemic vaccine of limited effectiveness (20%) could have a significant impact on size, duration and morbidity and mortality during a H5 derived pandemic. **The Expert Group advises that the Department of**

Health and Children considers commissioning a cost-benefit analysis looking at various options for use of pre-pandemic H5N1 vaccine.

The Expert Group advised in August 2005 that a limited amount of H5N1 vaccine should be stockpiled to provide for vaccination of healthcare and other essential workers. This advice was accepted by the Minister for Health and Children.

The priority groups recommended for H5N1 vaccine were:

Priority Group 1: Healthcare staff, with direct patient contact (including ambulance staff) and staff in residential care homes for the elderly

Priority Group 2: Providers of essential services e.g. fire, utilities, Gardaí, security, communications, armed forces, undertakers, and essential healthcare staff, without direct patient contact.

Health care workers with direct patient contact are defined as:

> *Persons who provide or assist in provision of direct health care (within 1 metre) to potential or known influenza cases with or without personal protective equipment*.

The Expert Group will advise on use of this vaccine when the pandemic is declared. Recommendations regarding priority groups will also be kept under review.

6.14 Pneumococcal vaccination in the pandemic alert period

Streptococcus pneumoniae is one of the main pathogens responsible for secondary bacterial infection following influenza infection, especially in the elderly or those who have underlying medical conditions. The vaccine is currently recommended for use in persons who are at increased risk of pneumococcal disease and its complications, particularly those with[13]:

- Asplenia or splenic dysfunction including surgical splenectomy sickle cell disease and coeliac syndrome

- Chronic renal disease or nephrotic syndrome
- Chronic heart, lung or liver disease, including cirrhosis
- Diabetes mellitus
- Complement deficiency (particularly early component deficiencies C1, C2, C3, C4)Immunosuppressive conditions (e.g. some B- and T-cell disorders, HIV infection, leukaemia, lymphoma, Hodgkin's disease) and those receiving immunosuppressive therapies CSF leaks, either congenital or complicating skull fracture or neurosurgery
- Intracranial shunt
- Candidate for, or recipient of a cochlear implant
- Persons aged 65 years of age and older
- Children < five years of age with history of invasive pneumococcal disease, irrespective of vaccine history

Increased use of pneumococcal vaccine in the pandemic alert period may decrease rates of secondary bacterial infections during a pandemic. Because large-scale pneumococcal vaccination might not be feasible once a pandemic occurs, the pandemic alert period is the ideal time to promote and deliver this preventive measure.

The Expert Group advises that the benefits of pneumococcal vaccine for at risk groups should be promoted among at risk groups and healthcare professionals.

6.15 References

(1) WHO. Global pandemic influenza action plan to increase vaccine supply. 2006.

(2) National Advisory Committee Royal College of Physicians of Ireland. Immunisation Guidelines for Ireland. 2006.

(3) WHO. Availability of new H5N1 prototype strain for influenza pandemic vaccine development. www.who.int . 2006.

(4) Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. N Engl J Med 1994; 331(12):778-784.

(5) 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.

(6) NHS Centre for Reviews and Dissemination. Influenza Vaccination and Older People. 1996. University of York.

(7) Gross PA, Hermogenes AW, Sacks HS, Lau J, Levandowski RO. The efficacy of influenza vaccine in elderly persons. A meta-analysis and review of the literature. Ann Intern Med 1995; 123(7):518-527.

(8) Resolution of the World Health Assembly. Prevention and control of influenza pandemics and annual epidemics. 2003.

(9) ECDC. Technical Report: Expert Advisory Groups on Human H5N1 vaccines. Scientific Questions. 1-8-2007.

(10) Department of Health U. Pre-pandemic and pandemic influenza vaccines: Summary of the evidence. 2007.

(11) ECDC. Technical Report: Expert Advisory Groups on Human H5N1 vaccines: Public Health and operational questions. 1-8-2007.

(12) 4th joint EC/WHO/ECDC workshop on pandemic influenza preparedness. Luxembourg, 25-27 September 2007. 27-9-2007.

(13) Immunisation Advisory Committee of the Royal College of Physicians of Ireland. Immunisation Guidelines for Ireland. www.hpsc.ie . 2002.

Chapter 7 Table of Contents

7 Public health response: Non-pharmaceutical interventions in the Pandemic Alert Period (WHO Phases 3, 4 and 5)

7.1 Introduction

This chapter outlines the rationale for implementing non-pharmaceutical public health interventions against a novel influenza virus in the Pandemic alert period, and some of the difficulties posed by planning these interventions in advance of knowing the characteristics of novel influenza strains, such as infectivity, clinical severity etc. Chapter 8 deals with the use of non-pharmaceutical interventions during the Pandemic Period.

The purpose of this guidance is to promote a consistent approach to population based measures which might be taken at WHO Pandemic Phases 4 and 5, such as school closures, and also measures aimed at individuals in the community to reduce their risk of infection. Some of these measures are appropriate to implement now, at Phase 3, for seasonal influenza.

The non-pharmaceutical public health interventions recommended by the World Health Organisation are reviewed, and recommendations are made on the interventions that are appropriate to implement in Ireland, in the Pandemic Alert Period (Phases 3 (current situation), 4 and 5).[1;2]

Implementation of these recommendations, if adopted, will not only apply within the health services, but also across other government departments and services. It is recognised that there is a need for flexibility as to which public health interventions are appropriate to implement. This will be dependent on the severity of the novel viruses encountered.

7.2 Aim of non-pharmaceutical interventions

The principal aim of non-pharmaceutical public health interventions during the Pandemic Alert Period is to limit transmission, illness and deaths, and to slow or stop the spread of infection with novel viruses, if possible.

One constraint with their use is the fact that it is unclear how long the world will remain in each of the WHO Phases, and how rapidly progression will occur from one phase to the next. At Phase 4 and 5, there will be evidence of human-to-human transmission, with increasing adaptation to humans, but as yet the novel virus will not be fully transmissible. Many of the interventions may have their greatest potential role during these phases, rather than during the pandemic (Phase 6) when human-to-human transmission is highly efficient.

During Phases 4 and 5, it's important to note that interventions may not be undertaken in isolation, and that strategies may be adopted of using several pharmaceutical and non pharmaceutical public health interventions in combination.

7.3 WHO recommendations for non-pharmaceutical public health interventions

The WHO undertook a broad ranging consultation exercise in 2004 on the public health interventions that could be used during an influenza pandemic.[(2)] The aims of these interventions are:

- To prevent further human-to-human cases caused by a virus that has not yet established efficient human-to-human transmission
- To slow pandemic spread and thus gain time for strengthening preparedness measures, including the augmentation of vaccine supplies
- To reduce the impact of the first wave of a pandemic

The consultation group agreed that once efficient and sustained human-to-human transmission was established, there would be no possibility of averting a pandemic or appreciably slowing its spread. Also at some point, efforts to prevent international spread through travel related measures would also

become ineffective. In addition, as mortality and morbidity increase during the pandemic, contact tracing and quarantine of contacts would not be effective or feasible.

From this consultation process, the WHO identified and categorised non-pharmaceutical public health interventions as follows:

1. Public health information, communications
2. Measures to reduce the risk that cases transmit infection
3. Measures to reduce the risk that contacts (of cases) transmit infection
4. Measures to increase social distance e.g. school closures
5. Measures to decrease interval between symptom onset and patient isolation
6. Disinfection measures
7. Measures for persons entering or exiting an infected area within the country
8. Measures at borders for persons entering or exiting a country
9. Measures at borders for international travellers coming from or going to affected areas
10. Entry screening
11. Exit screening
12. Measures for travellers on board international conveyances from affected areas

The use of non-pharmaceutical interventions categorised as above has been considered where appropriate for each Pandemic Alert Phase (3, 4 and 5).

The first seven interventions apply to persons living or travelling within an affected country, and the next two relate to travel advice. The remainder apply at international level.

7.3.1 Public health information, communications

The Expert Group advises that the WHO approach as outlined in the WHO Outbreak communications guidelines, 2005, be taken to all risk

communication activities in relation to influenza in the Pandemic Alert Period 9.[3] This guidance contains a short list of best practice for outbreak communication as follows:

Trust

The overriding goal for outbreak communication is to communicate with the public in ways that build, maintain or restore trust. This is true in every type of system.

Announcing early

Trust is established in the first official announcement of the outbreak. This message's timing, candour and comprehensiveness make it the most important of all communications.

Transparency

Maintaining the public's trust throughout an outbreak requires transparency. This means communication that is candid, easily understood, complete and factually accurate. Transparency allows the public to view the information gathering, risk assessing and decision making processes associated with outbreak control

Talking with the public

Understanding the public is critical to effective communication. It is usually difficult to change pre-existing beliefs unless those beliefs are explicitly addressed. It is nearly impossible to design successful messages that bridge the gap between the expert and the public without knowing what the public thinks

Planning

The decisions and actions of public health officials have more effect on trust and public risk perception than communication. In what you do, and what actions you take, you have a risk communication impact. Risk communication is therefore most effective when it is integrated with risk analysis and risk management. Risk communication should be

integrated into preparedness planning for major events and outbreak response.

7.3.1.1 Information for the public and health professionals on risks and risk avoidance (tailored to target populations)

The Expert Group advises that during the pandemic alert period (from Phase 3 on) information should be available for the public and for health professionals on risks and risk avoidance in the Pandemic Alert Period. Preparatory material should also be available for the next Phase. This information should be tailored to different target populations and should include general information on the pandemic, its phases, and how to reduce the risk of infection.

7.3.1.2 Advice on universal hygiene behaviour

The Expert Group advises that information on respiratory hygiene should be promoted, including public campaigns and respiratory hygiene in healthcare settings, from Phase 3 on. This includes advising the public to cover the nose and mouth with a tissue when coughing or sneezing, and to dispose of tissues promptly in bins after use. Hand washing using soap and warm water is effective in reducing the risk of respiratory diseases, and should be encouraged. Alternatively alcohol based hand rubs can be used.

7.3.2 Measures to reduce the risk of cases transmitting infection

7.3.2.1 Confinement/isolation of cases

Patients with seasonal influenza should be asked to isolate themselves at home, unless hospitalisation is required. Isolation of cases is an important measure to prevent transmission of infection by reducing contact between cases in their most infectious phase and uninfected persons. **For initial cases of influenza due to a novel virus, the Expert Group advises that the patients are assessed and isolated in hospital**

An algorithm for the management of persons with acute febrile respiratory illness who may have avian influenza is available in Supplement 11, Appendix 3)

7.3.2.2 Measures to reduce transmission of infection in healthcare facilities

A universal respiratory hygiene strategy is a series of measures designed to reduce transmission of infection in healthcare facilities. These are outlined in Appendix A. These measures are not specific to influenza, but will also reduce the incidence of other respiratory pathogens. They include the use of facemasks by symptomatic patients when waiting for assessment in waiting rooms. **The Expert Group advises that a universal respiratory hygiene strategy should be adopted now in the Pandemic Alert Period (Phases 3, 4 and 5) in all health care facilities.**

7.3.3 Measures to reduce the risk that contacts of cases transmit infection

7.3.3.1 Contact tracing and quarantine

In the pandemic alert period, efficient human-to-human transmission of novel, potentially pandemic strains of influenza may not yet have been established. In this context, there is merit in aggressively tracing contacts and isolating and treating them with antiviral drugs if available in order to prevent wider spread. The potential difficulties with successful contact tracing include the fact that if the novel virus behaves similarly to seasonal influenza, with its short incubation period, being infectious for 24 hours prior to onset of symptoms, and a high rate of asymptomatic illness, this could lead to a limited ability to identify all contacts in the time required.

The Expert Group advises that all cases of influenza due to novel influenza virus occurring during the pandemic alert period should be interviewed in depth and all contacts should be identified and contact traced by the Department of Public Health.

A protocol for the management of contacts identified in the pandemic alert period is available in Supplement 11.

7.3.4 Measures to increase social distance

The Expert Group advises the voluntary confinement of symptomatic persons throughout the pandemic alert phases. For initial cases, this

confinement will be in hospital. Mandatory quarantine and curfews are not considered necessary.

7.3.4.1 Closure of educational facilities

The aim of this intervention is to reduce spread in those settings where transmission is occurring, and would only be considered in Phases 4 and 5 **if clusters of cases due novel influenza virus were occurring in Ireland.**

The Expert Group advises that in the Pandemic Alert Period, all schools should have ready access to information on influenza, and how to reduce the risk of infection. This information should also be available in the workplace and other settings where groups of people spend time together and use communal facilities.

The Expert Group advises that closure of schools, universities and educational institutions could be considered during Phases 4 and 5 of the Pandemic Alert Period, but only if clusters of cases due to novel influenza virus were occurring in Ireland at that time, if transmission was occurring in these settings, and if the case fatality ratio was high. All schools and day care institutions should have a plan for how they could close in an emergency. This plan should have input and involvement of teachers, parents and carers.

If a decision were taken to close a school, then ideally, criteria for reopening the school should as far as is possible be agreed in advance.

7.3.4.2 Population-wide measures to reduce mixing of adults

The Expert Group advises that population-wide measures to reduce mixing of adults (close workplaces, initiate leave of absence for non essential workers, discourage mass gatherings) should be considered in Phase 5 of the pandemic alert period, if Ireland was experiencing clusters of cases at that time and the case fatality ratio was high.

7.3.5 Measures to decrease the interval between symptom onset and patient isolation

7.3.5.1 Public campaign to encourage prompt self-diagnosis

The Expert Group advises that the public should be informed of the symptoms of influenza, how to recognise if they might have it, and advised of practical issues such as the value of having a thermometer at home, in the pandemic alert period .

7.3.5.2 Public advice and medical help lines

The Expert Group advises that at Phase 4 and 5, a national medical helpline should be established to deal with individual queries or concerns, and to direct those with symptoms to the appropriate location for care and treatment.

7.3.6 Disinfection measures

The Expert Group advises that disinfection measures which are effective in preventing the transmission of influenza should be promoted during the Pandemic Alert Period (Phases 3, 4 and 5)

Information on respiratory hygiene should be promoted, including public campaigns and respiratory hygiene in healthcare settings, from Phase 3 on. Hand washing using soap and warm water is effective in reducing the risk of respiratory diseases, and should be encouraged. Alternatively alcohol based hand rubs can be used.

Influenza viruses survive in the environment, and can pass from surfaces to the hands and cause infection. They can survive on tissues also, and cause infection. Tissues should be disposed of after use. Potentially contaminated surfaces should be cleaned using household disinfectants.

Widespread environmental decontamination or air decontamination is not recommended. Further guidance on infection control and disinfection can be found in the infection control supplement (Supplement 10).

7.3.7 Measures for persons entering or exiting an affected area in Ireland during Phases 4 and 5

The Expert Group advises that in the event of clusters of cases due to novel virus influenza (e.g. A/H5N1 infection of poultry) occurring in Ireland (Phases 4 and 5), persons should avoid contact with high-risk environments (such as infected poultry farms, live poultry markets) in areas affected.

The Expert Group advises that during WHO Phases 4 and 5 of the pandemic alert period, if outbreaks of influenza due to a novel virus are occurring at the time, non-essential travel to affected areas within Ireland should be deferred

It is anticipated that during pandemic Phases 4 and 5 most persons will voluntarily restrict travel to and from affected areas. Enforcement of travel restrictions is considered impractical, as is the imposition of a cordon sanitaire around affected areas. For public health purposes, disinfection of clothing, shoes or other objects of persons exiting an affected area is not recommended.

7.3.8 Measures at the international level

7.3.8.1 Travel Advice

The Expert Group advises that from pandemic alert Phase 3 on, advice and information on avoiding contact with high-risk environments should be available for travellers travelling to areas where outbreaks of novel influenza are occurring (e.g. the current international outbreak of A/H5N1 see Appendix B).

The Expert Group advises that from Phase 4 on, travellers should be advised to defer non-essential international travel to affected areas.

7.3.9 Measures at borders for international travellers coming from or going to affected areas

The Expert Group advises the following measures from Phase 4 onwards at borders for international travellers coming from or going to affected areas

1. **Health Alert Notices should be provided to all travellers**
2. **Travellers to and from affected areas should be advised to self-report if they have illness.**
3. **Exit screening for at-risk travellers – identified via health questionnaires or declaration notices - should be implemented**
4. **All intending travellers who are ill should be recommended to postpone travel**

Entry screening such as screening for symptoms (visual detection of symptoms), health screening questionnaires, thermal screening, and medical examination should not be necessary. There is a lack of proven health benefit with these measures. However, if there is evidence that exit screening at the point of embarkation does not meet the standards expected, it may be considered, following consultation with WHO and EU colleagues.

7.3.10 Measures for travellers on board international conveyances from affected areas

The Expert Group advises the following measures for travellers on board international conveyances coming from affected areas **from Phase 4 on**:

1. **Travellers should be asked to self-report flu like illness, and sick travellers should be separated on board, if possible.**
2. **The public health authorities in the destination and transit countries should be informed that there is an ill person on board so that appropriate contact tracing and control procedures can be initiated.** In addition, appropriate arrangements for medical assessment and treatment of the sick traveller need to be in place**.**

Interim Guidance for Aircraft Cabin Staff on Management of Suspected Human Cases of Avian Influenza is available in Appendix C.

7.4 Public Health Surge capacity

Non-pharmaceutical public health interventions may be the only tools available to slow spread of an emerging novel virus in advance of sufficient quantities of antivirals and pandemic strain vaccine becoming available.

The Expert Group considers it is crucial that consideration is given to the significant human resource implications of implementing these recommendations and that manpower planning for pandemic influenza also includes planning for a robust public health infrastructure and sufficient surge capacity for public health.

7.5 Reference List

(1) WHO. WHO global influenza preparedness plan. www.who.int . 2005.
Ref Type: Electronic Citation

(2) WHO. WHO consultation on priority public health interventions before and during an influenza pandemic. www.who.int . 2004.
Ref Type: Electronic Citation

(3) WHO Expert Consultation. Outbreak Communication. Best practice for communicating with the public during an outbreak. www.who.int . 2005.
Ref Type: Electronic Citation

Appendices

7.6 Appendix A Universal Respiratory Hygiene

The following are components of a universal respiratory hygiene strategy to be adopted in all health care facilities.

- The posting of visual alerts at the entrances to all healthcare facilities, instructing patients and those who accompany them to:
    - Inform healthcare personnel of symptoms of a respiratory infection when they first register for care
    - Practice respiratory hygiene
    - Advise visitors with respiratory symptoms to defer their visit until symptoms have resolved
- All patients and visitors who have symptoms of an infectious respiratory illness (cough, runny nose, sore throat or sneezing) should be provided with a surgical mask and instructions on their proper use and disposal. They should also be provided with instructions on hand hygiene.
- For those who cannot wear a mask, provide tissues and instructions on when to use them (i.e. when coughing, sneezing, or controlling nasal secretions), where they should be disposed of, and on the importance of hand hygiene after using them
- Waste bins should be readily available for disposal of tissues.
- Provide hand hygiene materials in the waiting room areas and encourage persons with respiratory symptoms to perform hand hygiene i.e. wash hands with soap and water and/or alcohol based hand disinfectants
- Instruct registration, reception and triage staff of their risk of exposure to infections spread by droplets and to consider wearing masks whenever

registering or assessing patients who have respiratory symptoms and are not wearing a mask. Instruct them to remain at least 3 feet from unmasked patients.

- Consider the use of Plexiglas barriers at the point of triage or registration to protect healthcare personnel from contact with respiratory droplets.
- Where possible, designate an area, cubicle or separate room in waiting areas where patients with respiratory symptoms can be segregated (ideally by at least 3 feet) from others without respiratory symptoms.
- Commonly used surfaces such as door handles, handrails, table surfaces etc. should be cleaned twice daily with disinfectant.
- Use droplet precautions to manage patients with respiratory symptoms until it is determined that the cause of the symptoms is not an infectious agent that requires more than standard precautions.

7.7 Appendix B: Advice for travellers going to and returning from travel to areas affected by avian influenza

The World Health Organisation (WHO) has not recommended travel restrictions to countries affected by avian influenza, including countries that have reported cases in humans. If the WHO changes its assessment of the risks of travel to an increased threat level, you will be advised accordingly.

Pre travel

- Always educate yourself and others who may be travelling with you about any disease risks in areas you plan to visit. A full list of countries with outbreaks of highly pathogenic avian influenza in avian species is available on the HPSC website.
- See your doctor before you travel to get any information on travel risks to the area you are going to.
- Include a thermometer and alcohol-based hand rub for hand hygiene in your travel health kit.

During travel

- Avoid all direct contact with poultry, including touching well-appearing, sick, or dead chickens and ducks. Avoid places such as poultry farms and bird markets where live poultry are raised or kept, and avoid handling surfaces contaminated with poultry faeces or excretions. Large amounts of the virus are known to be excreted in the droppings of infected birds
- One of the most important preventive practices is careful and frequent hand washing. Cleaning your hands often, using either soap and water or waterless alcohol-based hand rubs, removes potentially infectious materials from your skin and helps prevent disease transmission.
- Influenza viruses are destroyed by heat; therefore, as a precaution, all foods from poultry, including eggs and poultry blood, should be thoroughly cooked.
- If you become sick with symptoms such as a fever, difficulty breathing, cough, or any illness that requires prompt medical attention, it is advisable that you defer travel until you are free of symptoms unless your travel is health-related.
- Don’t attempt to bring any live poultry or other avian products back to Ireland

Post travel

For 7 days following travel to an affected area:

- If you become ill with fever, difficulty breathing, cough, or any illness during this period, consult your GP

Before you visit your GP, or seek medical attention, tell your GP about your symptoms and recent travel history so that he or she can be aware you have travelled to an area reporting avian influenza.

October 2005

7.8 Appendix C - Interim Guidance for Aircraft Cabin Staff on Management of Suspected Human Cases of Avian Influenza

7.8.1 Introduction

This guidance is intended to inform airline crews on the appropriate management of an ill passenger who has recently been in an area affected by avian influenza outbreaks in poultry and other birds.

7.8.2 Background

Avian influenza is an infectious disease of birds caused by type A strains of the influenza virus. The disease, which was first identified in Italy more than 100 years ago, occurs worldwide and mainly affects wild birds.
http://www.who.int/mediacentre/factsheets/avian_influenza/en/index.html

Avian influenza also affects domestic and wild avian species such as chickens, turkeys, ducks, geese, shorebirds, gulls and others Avian influenza outbreaks associated with highly pathogenic H5N1 have occurred in several countries since 2003.

Information on countries currently affected by avian influenza outbreaks in animals is available on the World Organisation for Animal Health and the WHO websites. The spread of H5N1 to poultry in new areas is of concern as it increases opportunities for further human cases to occur. However, all evidence to date indicates that the H5N1 virus does not spread easily from birds to infect humans.

Regular updates on the numbers of confirmed cases, and situation updates from the affected countries are available on the WHO website and also on the HPSC website countries affected by highly pathogenic avian influenza.

Although avian influenza A (H5N1) virus is highly pathogenic in humans, it is not transmitted efficiently from one human to another and human outbreaks have been short-lived. The 2004/2005 human influenza A (H5N1) infections were associated with close contact with infected poultry. These infections were thought to have been directly transmitted from the poultry. In September 2004, the Thai government 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 limited to family members. There is currently no evidence of sustained person-to-person

transmission of avian influenza. However it is prudent to consider that individuals who are ill with H5N1 are potentially infectious.

7.8.3 Clinical presentation of avian influenza

The main presenting clinical symptoms during the 2004 avian influenza epidemics in Thailand and Viet Nam were fever, cough, widespread aches, sore throat, runny nose, shortness of breath and diarrhoea. Transmission of H5N1 viruses from infected individuals, if it does happen, could occur through the spread of large respiratory droplets, which usually requires close contact (<1 metre/3 feet) with an infected person or contact with contaminated hands or inanimate objects (e.g., armrests).

An **algorithm** outlining guidance for health professionals on the assessment and management of cases of respiratory illness in travellers returning from areas affected by avian influenza is available.

Any respiratory illness is more likely to be caused by the usual circulating respiratory pathogens but evaluation by a health care provider should take place.

7.8.4 Measures to control spread of infectious diseases while travelling

Many infectious diseases can be spread by human hands. Soiled hands are an effective means of delivering infectious material (e.g., saliva or other body fluids that may contain viruses) to the nose or eyes, where they can enter the body. Hand washing is an important way to reduce exposure to common infectious diseases. Cleaning one's hands with soap and water removes potentially infectious material from one's skin. Hands should be cleaned before preparing food, eating or touching one's face, and after handling soiled material (e.g., used tissues, lavatory surfaces), coughing or sneezing, and using the toilet. Waterless alcohol-based hand rubs may be used when soap is not available and hands are not visibly soiled.

7.8.5 In-flight care of suspected case of Avian Influenza

If a passenger travelling from an affected area becomes noticeably ill with a fever and respiratory symptoms, the following action is recommended for cabin crew:

1. The passenger should be, as far as possible, isolated from other passengers and crew (1-2 metres). Designate one cabin crew to look after the sick passenger.

2. The passenger should be asked to wear a protective (surgical) mask to reduce the number of droplets coughed into the air. If a surgical mask is not available, provide tissues and ask the ill patient to cover his/her mouth and nose when coughing and to put the used tissues into a waste bag. If the ill person is unable to wear a mask, the designated crew should wear a surgical mask.

3. The designated crew should wear disposable gloves for direct contact with blood or body fluids of any passenger. Immediately after activities involving contact with body fluids the gloves should be discarded into a wastebasket and hands should be cleaned with liquid soap and water or an alcohol based hand rub. Dispose of soiled materials in a biohazard bag, if one is available. If not use a sealed plastic bag.

4. The captain should radio ahead to the airport of destination so that local Director of Public Health can be alerted to the arrival of a suspect human case of Avian Influenza.

5. On arrival, the ill passenger should be placed in isolation and medically assessed.

7.8.6 Contacts

1. All contacts of the ill passenger should have already been identified during the flight. For the purposes of air travel a contact is defined as:

    - Passengers sitting in the same seat row or within at least 3 rows in front or behind the ill passenger
    - All flight attendants on board
    - Anyone having intimate contact, providing care or otherwise having contact with respiratory secretions of the ill passenger
    - Any one on the flight living in the same household as the ill passenger

2. Contacts should provide, to the local Department of Public Health, identification and details of address/contact details valid for 14 days.
3. Contacts should be given information about avian influenza and a public Health contact number. They should be advised to seek immediate medical attention, according to local Public Health protocols, if they develop any symptoms of avian influenza within seven days of the flight. In seeking medical attention they should ensure that all those treating them are aware that they have been in contact with a suspect case of avian influenza

4. Contacts should be allowed to continue to travel.
5. If over time it becomes apparent that the suspect case is a probable case of avian influenza the health authority where the case is being cared for should inform other health authorities in those areas in which contacts reside that active surveillance of each contact (daily temperature check and interview by health care worker) should be undertaken until seven days after the flight.

7.9 Aircraft Cleaning - General Guidelines for Cleaning Crew issued by IATA

The following are general guidelines for Cleaning Crew who has to clean an arriving aircraft with a suspected case of communicable disease. During an outbreak of a specific communicable disease, the World Health Organization (WHO) or member states may modify or add further procedures to these general guidelines. However, these general guidelines would always provide a basic framework of response that would reassure the cleaning crew and help them through any unplanned incident.

1. Wear non-sterile impermeable disposable gloves.
2. Remove and discard gloves if they become soiled or damaged, and after cleaning.
3. Wash hands with soap and water immediately after gloves are removed. An alcohol-based hand sanitizer can be used if the hands are not visibly soiled.
4. Surfaces to be cleaned (affected seat, adjacent seats same row, back of the seats in the row in front),
   - Armrests
   - Seatbacks (the plastic and/or metal part)
   - Tray tables and trays if still in place
   - Light and air controls
   - Adjacent walls and windows
   - Individual video monitor
   - Lavatory(ies) used by the sick traveller: door handle, locking device, toilet seat, faucet, washbasin, adjacent walls and counter.
5. Disinfection of upholstery, carpets, or storage compartments is only indicated when they have been soiled by body fluids. In such cases, disinfect before vacuuming to eliminate the risk of re-aerosolization.
6. Use only cleaning agents and disinfectants that have been approved by aircraft manufacturers.
7. Dispose of soiled material and gloves in a biohazard bag if one is available. If not, use a sealed plastic bag and label it as biohazard.
8. Do not use compressed air. It might re-aerosolize infectious material.

Source:
http://www.iata.org/whatwedo/safety_security/safety/health_safety/aviation_communicable_diseases.htm

Chapter 8 Table of Contents

8 Public health response: Non-pharmaceutical interventions during the Pandemic (Phase 6)

8.1 Introduction

This chapter provides advice on the non-pharmaceutical public health interventions to implement during Phase 6 of an influenza pandemic. It is recognised that there are difficulties in planning interventions in advance of knowing the characteristics of novel influenza strains, such as infectivity, clinical severity etc. As information on the epidemiology of influenza transmission, the effectiveness of non-pharmaceutical public health interventions and their costs are developed, the guidance will be updated. The purpose of this advice however, is to promote a consistent approach to population based measures to be taken at WHO Pandemic Phase 6 such as school closures and other social distancing measures, and also to measures aimed at individuals in the community to reduce their risk of infection.

The nature and duration of the interventions recommended by the Expert Group will depend on the severity of the pandemic. **The Expert Group advises that Ireland adopts the Pandemic Severity Index, a planning tool developed in the United States to characterise the severity of a pandemic, and that interventions are implemented according to the levels of severity experienced.**[(1)]

In deriving this guidance, the non-pharmaceutical public health interventions recommended by the World Health Organisation were reviewed, as well as the "ECDC Menu".[(2)]

It is important to note that implementation of these recommendations, if adopted, will not only apply within the health services, but also across other government departments and services.

8.2 Aim of non-pharmaceutical interventions

The principal aims of non-pharmaceutical public health interventions are to:

- slow the spread of infection, thereby gaining some time to allow for development, production and administration of vaccine and antiviral agents against the pandemic strain
- decrease the epidemic peak
- reduce the total number of cases

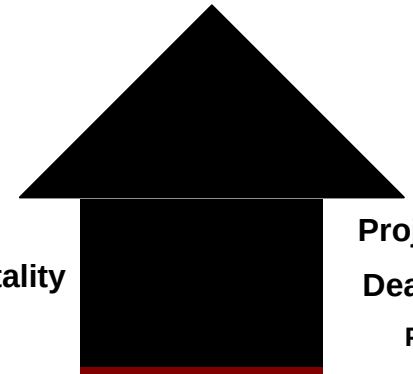
It is recognised that many of the interventions may have their greatest potential role during Phases 4 and 5 when there will be evidence of human-to-human transmission, with increasing adaptation to humans, but as yet the novel virus will not be fully transmissible. Their effectiveness during Phase 6 when human-to-human transmission is highly efficient may be less.

During a pandemic, its also likely that interventions will not be undertaken in isolation, and that strategies will be adopted of using several pharmaceutical and non pharmaceutical public health interventions in combination, so called **defense in depth**, or **layering of measures**. Combining several partially effective interventions may have an overall greater effect than each one on its own.

8.2.1 The Pandemic Severity Index

This index is designed to enable estimation of the severity of a pandemic on a population level. Pandemics are assigned to one of five discrete categories of increasing severity (Category 1 to Category 5). The category the pandemic is classified as largely determines the type of interventions to implement, and their duration of implementation. For category 4 or category 5 pandemics (Scenario 1), all available non pharmaceutical interventions are recommended and for up to 12 weeks duration. For category 2 and category 3 pandemics, social distancing measures should be implemented only if local crisis management teams determine that their use is warranted due to the characteristics of the pandemic in their community. If social distancing measures are to be used, then they should last for 4 weeks or less. For category 1 pandemics, voluntary home isolation of sick patients is the only community wide recommendation, though again local communities may

choose to apply some social distancing measures, if local epidemiology, surge capacity issues etc indicate that this would be beneficial.



Case Fatality Ratio		Projected Number of Deaths (based on Irish Population, 2006)
>= 2%	Category 5	>= 21,000
1.0% - < 2.0%	Category 4	10,600 - <21,200
0.5% - < 1.0%	Category 3	5300 - < 10, 600
0.1% - < 0.5%	Category 2	1060 - < 5300
<0.1%	Category 1	< 1060

Scenario 1: Clinical attack rate 25%

Note: The Pandemic Severity Index is based on a clinical attack rate of 25%. If the clinical attack rate was higher, this would lead to more deaths in the population at a given case fatality ratio, and the index would need to be adjusted accordingly.

8.3 Triggers for initiating use of non-pharmaceutical interventions

Timing of initiation of these measures is difficult. Implementation needs to be early enough to prevent the initial steep upsurge in cases and long enough to cover the peak of the epidemic curve, whilst avoiding being so long as to be no longer feasible to maintain. The primary trigger for intervention is the

arrival and transmission of the pandemic virus. This is defined as a laboratory confirmed cluster of infection with a novel virus, and evidence of community transmission. It is recognised that defining what is meant by a community is not necessarily easy to do, given commuting patterns, and other non geographical links that exist.

8.4 Recommendations for non-pharmaceutical public health interventions

8.4.1 WHO priority Public Health interventions

The WHO undertook a broad ranging consultation exercise in 2004 on the public health interventions that could be used before and during an influenza pandemic, and from this [(3)] consultation process, it identified 12 possible non pharmaceutical interventions which could be used, and the stage(s) and circumstances during which it would be appropriate to use them. These measures were described in more detail in Chapter 7.

8.4.2 ECDC Menu

ECDC published 3 documents in 2007 outlining a Menu of the public health measures that can be taken to reduce the impact of a pandemic during Phase 6.[(2)] These measures are grouped into personal actions (hand washing and mask wearing) and pharmaceutical interventions (antivirals, human avian influenza vaccines and late in the pandemic specific vaccines) as well as community social distancing measures. The ECDC document sets out the public health and scientific information on what is known or can be said about their likely effectiveness, costs (direct and indirect), their acceptability, public expectations and other practical considerations.

8.4.3 Irish guidance on use of non-pharmaceutical interventions at Phase 6

The Irish guidance has been developed, taking into consideration both the WHO recommendations and ECDC menu. It also incorporates the US Pandemic Severity Index. The Expert Group considers that this tool helps planners to predict the impact, and to recommend interventions matched to the severity of the pandemic.

8.5 Measures at the national level

8.5.1 Public Health information, communications

There is good evidence that risk communication during outbreaks can affect outbreak control. In 2005, the WHO published evidence based field-tested communication guidance.[4] This guidance contains a short list of best practice for outbreak communication as follows:

Trust

The overriding goal for outbreak communication is to communicate with the public in ways that build, maintain or restore trust. This is true in every type of system.

Announcing early

Trust is established in the first official announcement of the outbreak. This message's timing, candour and comprehensiveness make it the most important of all communications.

Transparency

Maintaining the public's trust throughout an outbreak requires transparency. This means communication that is candid, easily understood, complete and factually accurate. Transparency allows the public to view the information gathering, risk assessing and decision making processes associated with outbreak control

Talking with the public

Understanding the public is critical to effective communication. It is usually difficult to change pre-existing beliefs unless those beliefs are explicitly addressed. It is nearly impossible to design successful messages that bridge the gap between the expert and the public without knowing what the public thinks

Planning

The decisions and actions of public health officials have more effect on trust and public risk perception than communication. In what you do, and what actions you take, you have a risk communication impact. Risk communication is therefore most effective when it is integrated with risk analysis and risk

management. Risk communication should be integrated into preparedness planning for major events and outbreak response.

The Expert Group advises that the WHO outbreak communications approach be taken to all risk communication activities in relation to pandemic influenza in Phase 6.

8.5.1.1 Information for the public and health professionals on risks and risk avoidance (tailored to target populations)

The Expert Group advises that information should be available for the public and for health professionals on risks and risk avoidance during the pandemic. This information should be tailored to different target populations and should include general information on the pandemic, its phases, and how to reduce the risk of infection.

8.5.1.2 Advice on universal hygiene behaviour

The Expert Group advises that information on respiratory hygiene should be promoted, including public campaigns and respiratory hygiene in healthcare settings, during Phase 6. This includes advising the public to cover the nose and mouth with a tissue when coughing or sneezing, and to dispose of tissues promptly in bins after use. Hand washing using soap and warm water is effective in reducing the risk of respiratory diseases, and should be encouraged. Alternatively alcohol based hand rubs can be used.

8.5.2 Measures to reduce the risk of cases transmitting infection

8.5.2.1 Confinement/isolation of cases

Voluntary confinement of ill patients to a single dedicated room for the duration of their symptoms reduces transmission by reducing contact between cases and uninfected persons. There is no published evidence on effectiveness available from trials, though it is supported in modelling studies by Ferguson.[5] There are practical implications in implementing this and consideration needs to be given to ensuring that support(social, physical and other) is available to patients and their caregivers. It is likely that compliance with a recommendation to voluntarily confine oneself if sick would be high.

The Expert Group advises voluntary isolation of pandemic influenza cases when symptomatic. For those who do not require hospitalisation this will usually at home, but could be elsewhere if the circumstances at home are not suitable.

8.5.2.2 Measures to reduce transmission of infection

Simple infection control advice can help reduce transmission of infection. This advice is:

- Cover nose and mouth with disposable single-use tissues when sneezing, coughing, wiping and blowing nose
- Dispose of used tissues in the nearest waste bin
- Wash hands after coughing, sneezing, using tissues, or contact with respiratory secretions and contaminated objects
- Keep hands away from the mucous membranes of the eyes and mouth
- If sick with flu, stay at home to avoid spreading infection to others

The advice aims to reduce transmission from person to person by indirect contact, and also to interrupt droplet transmission. Hand washing using soap and warm water is effective in reducing the risk of respiratory diseases, and should be encouraged. Alternatively alcohol based hand rubs can be used. Influenza viruses survive in the environment, and can pass from surfaces to the hands and cause infection. They can survive on tissues also, and cause infection. Tissues should be disposed of after use. Potentially contaminated surfaces should be cleaned using household disinfectants. Widespread environmental decontamination or air decontamination is not recommended. [Further guidance on infection control and disinfection can be found in the infection control supplement (Supplement 10)].

In many settings it is quite difficult to wash hands regularly and to increase hand washing would require considerable investment in schools and other settings. This might be the main limiting factor in implementing this recommendation. With regard to use of tissues, supplies are available, and it

is likely that this practical measure would be accepted and implemented by the community.

8.5.2.3 Respiratory hygiene in healthcare facilities

A universal respiratory hygiene strategy is a series of measures designed to reduce transmission of infection in healthcare facilities. These are outlined in Appendix A. These measures are not specific to influenza, but will likely also reduce the incidence of other respiratory pathogens. They include the use of facemasks by symptomatic patients when waiting for assessment in waiting rooms. There is however no evidence from trials regarding the effectiveness of respiratory hygiene strategies. This intervention would probably be well accepted by the public.

The Expert Group advises that infection control measures (hand washing and respiratory hygiene) are promoted for the public during the pandemic, and that a universal respiratory hygiene strategy should be adopted in all health care facilities.

8.5.2.4 Public use of facemasks

The aim of this intervention is the reduction of transmission in public places, the workplace and schools. There is very little evidence on the effect of use of facemasks in public (e.g. when in close contact with others on crowded public transport, cities etc) in preventing influenza transmission. There is some limited evidence of their effectiveness from two case-control studies carried out in Beijing and Hong Kong during SARS. In these studies, wearing masks in public was independently associated with protection from SARS in a multivariate analysis.[6;7] WHO has recommended that mask use by the public should be based on risk, including frequency of exposure and closeness of contact with potentially infectious persons. This could be interpreted as supporting mask use in crowded settings such as public transport. Although the unit cost is low, if used for the duration of the pandemic, the supply costs would be huge, and security of supply might be an issue. There would also need to be training in the proper use of masks

The Expert Group advises that the evidence at this point does not support a recommendation for public use of facemasks during Phase 6 as a measure to prevent transmission of disease.

8.5.3 Measures to reduce the risk that contacts of cases transmit infection

8.5.3.1 Contact tracing and quarantine

In the early stages of Phase 6, efficient human-to-human transmission of the pandemic strain of influenza may not yet have been established in Ireland. In this context, there is merit in aggressively tracing initial contacts and isolating and treating them with antiviral drugs if available in order to prevent wider spread. The potential difficulties with successful contact tracing include the short incubation period, being infectious for 24 hours prior to onset of symptoms, and a high rate of asymptomatic illness, leading to a limited ability to identify all contacts in the time required.

The Expert Group advises that initial cases occurring during the pandemic should be interviewed in depth and all contacts should be identified, contact traced and asked to go into voluntary home quarantine by the local Department of Public Health.

If this measure were continued during the pandemic, modelling studies suggest that it would result in significant numbers of people being quarantined, on several occasions during the pandemic. This would have huge costs and adverse effects in the wider economy. Once efficient transmission has been demonstrated in Ireland, consideration should be given to continuing voluntary home quarantine, and other social distancing measures, where feasible, particularly in a category 4 or 5 pandemic.

8.5.4 Measures to increase social distance

8.5.4.1 Closure of educational facilities

The aim of this intervention is to reduce spread in those settings where transmission is occurring. Despite the propensity of influenza epidemics to be amplified in primary schools, data on the effectiveness of school closures are

limited. [8] The knowledge base in this area consists primarily of historical and contemporary observations and modelling studies, rather than controlled studies of evaluation interventions. A recent review article on non-pharmaceutical interventions for pandemic influenza by a WHO Writing Group concluded that no data or analyses exist for recommending illness thresholds or rates of change that should lead to considering closing or reopening schools.[9]

Some quantitative evidence is available from Israel where a recent retrospective cohort study of 186,094 children aged 6-12 years was undertaken during a flu outbreak. As a result of a national strike, elementary schools closed for a period of two weeks. Children were cared for mainly at home. There were significant reductions in visits to the doctor, and in diagnoses of respiratory tract infections during the strike. School closure was temporally associated with decreased morbidity from respiratory infections.[10]

The Expert Group advises that all schools should have ready access to information on influenza, and how to reduce the risk of infection. This information should also be available in the workplace and other settings where groups of people spend time together and use communal facilities.

All schools and day care institutions should have a plan for how they could close in an emergency. This plan should have input and involvement of teachers, parents and carers.

The Pandemic Severity Index will be used when considering implementing school closure. **For Category 4 and 5 pandemics, the Expert Group advises that school/college/educational institution closure should be strongly considered on a national basis.** For category 2 and 3 pandemics, decisions to implement school closures locally may be made taking the following factors into consideration:

- Epidemiology of cases: age groups affected, where infected, attack rate by age group, by institution, time since index case first identified, number of transmission cycles, severity of cases etc.
- Evidence of recent transmission occurring in a school or institution, and there is otherwise no widespread transmission in the community.
- The morbidity and mortality among children
- Urban versus rural school. In a rural setting, it could be the main mode of transmission, but less likely to be in urban settings
- The potential consequences to the workforce of closing schools, as working parents might need to take time off work to care for their children

For category 1 pandemics, school closure is not recommended.
If a decision is taken to close a school, then ideally, criteria for reopening the school should as far as is possible be agreed in advance.

8.5.4.2 Population-wide measures to reduce mixing of adults

The Expert Group advises that population-wide measures to reduce mixing of adults (close workplaces, initiate leave of absence for non essential workers, discourage mass gatherings) should be strongly considered on a national basis for category 4 and 5 pandemics. In addition, other political and economic considerations will influence these decisions. For category 2 and 3 pandemics, decisions may be taken on a local level if local characteristics of the pandemic determine that their use is warranted. For category 1 pandemics, these interventions are not recommended.

> *Mass gatherings are settings or situations where there is the potential for transmission of infection to many persons, and where it may be possible to delay or slow the spread of infection if they are restricted.*

Mass gatherings may provide opportunities for transmission and dissemination of influenza, and may leave patients sick, when away from home. Cancellation of all events would however be very costly. The

discouragement or banning of mass gatherings is under consideration and may be reviewed following guidance from the World Health Organisation, and others.

8.5.5 Measures to decrease the interval between symptom onset and patient isolation

8.5.5.1 Public campaign to encourage prompt self-diagnosis

The Expert Group advises that the public should be informed of the symptoms of influenza, how to recognise if they might have it, and advised of practical issues such as the value of having a thermometer at home.

8.5.5.2 Public advice and medical help lines

The Expert Group advises that a national medical helpline should be established to deal with individual queries or concerns, and to direct those with symptoms to the appropriate location for care and treatment. This helpline will be resource intensive, as was seen during the SARS outbreak in Toronto.[11] However its implementation will be critically important to reducing the burden on primary care and will reduce face to face contacts.

8.5.6 Measures for persons entering or exiting an affected area in Ireland during Phase 6

It is anticipated that during pandemic Phase 6 most persons will voluntarily restrict travel to and from affected areas. Enforcement of travel restrictions is considered impractical, as is the imposition of a cordon sanitaire around affected areas. For public health purposes, disinfection of clothing, shoes or other objects of persons exiting an affected area is not recommended.

8.5.7 Measures at the international level

In a recent WHO review of international non-pharmaceutical public health interventions, it concluded, based on experience from past influenza pandemics, that screening and quarantine of entering travellers at international borders did not substantially delay introduction of pandemic influenza, except in some island countries.[12] In addition it also stated that

similar policies, even if they could be implemented in time and regardless of expense, are unlikely to be more effective given extensive international air travel. **WHO does not recommend at any Phase that individual countries be quarantined or that international borders be closed.**[13] This is further supported by Ferguson's modelling work which showed that border restrictions and/or internal travel restrictions were unlikely to delay spread by more than 2 to three weeks unless more than 99% effective.[5]

8.5.7.1 Travel Advice

The Expert Group advises that during the pandemic, travellers should be advised to defer non-essential international travel to affected areas.

8.5.8 Measures at borders for international travellers coming from or going to affected areas

The Expert Group advises:

1. **Health Alert Notices should be provided to all travellers to and from affected areas**
2. **Travellers to and from affected areas should be advised to check themselves for fever and to self-report if they have illness.**
3. **Exit screening for at-risk travellers – identified via health questionnaires or declaration notices - should be implemented**
4. **All intending travellers who are ill should be recommended to postpone travel**

Entry screening such as screening for symptoms (visual detection of symptoms), health screening questionnaires, thermal screening, and medical examination should not be necessary. There is a lack of proven health benefit with these measures. However, if there is evidence that exit screening at the point of embarkation does not meet the standards expected, entry screening may be considered, following consultation with WHO and EU colleagues.

8.5.9 Measures for travellers on board international conveyances from affected areas

The Expert Group advises the following measures for during phase 6:

1. **Travellers should be asked to self-report flu like illness, and sick travellers should be separated on board, if possible.**
2. **The public health authorities in the destination and transit countries should be informed that there is an ill person on board**

8.6 Public Health Surge capacity

Non-pharmaceutical public health interventions may be the only tools available to slow spread of a pandemic virus in advance of sufficient quantities of antivirals and pandemic strain vaccine becoming available.

The Expert Group considers it is crucial that consideration is given to the significant human resource implications of implementing these recommendations and that manpower planning for pandemic influenza also includes planning for a robust public health infrastructure and sufficient surge capacity for public health.

	Category 1	Category 2	Category 3	Category 4	Category 5
Measures at the national level					
Public health information, communications					
Information for the public and health professionals	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Advice on universal hygiene behaviour	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Measures to reduce the risk of cases transmitting infection					
Confinement/isolation of cases	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Measures to reduce transmission of infection					
Measures for the public	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Respiratory hygiene in healthcare facilities	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Measures to reduce the risk that contacts of cases transmit infection					
Contact tracing and quarantine of early cases	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Quarantine of contacts during the pandemic	**Generally not recommended**	**Generally not recommended**	**Generally not recommended**	**Consider**	**Consider**
Measures to increase social distance					
Closure of educational facilities	**Generally not recommended**	**Consider <= 4 weeks**	**Consider <= 4 weeks**	**Recommend**	**Recommend**
Population wide measures to reduce mixing of adults	**Generally not recommended**	**Consider <= 4 weeks**	**Consider <= 4 weeks**	**Recommend**	**Recommend**
Measures to decrease the interval between symptom onset and patient isolation	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Public campaigns to encourage prompt self diagnosis	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Public advice and medical helplines	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Measures for persons entering or exiting an affected area in Ireland					
Measures at the international level					
Travel advice					
Advice to defer non essential international travel to affected areas	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Measures at borders for international travellers coming from or going to affected areas					
Health alert notices for all travellers to and from an affected area	**Consider**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Travellers to and from an affected areas should be advised to check themselves for fever and to self report if they have illness	**Consider**			**Recommend**	**Recommend**
Exit screening for at risk travellers - identified via HAN or declaration notices - should be implemented	**Consider**			**Recommend**	**Recommend**
All intending travellers who are ill should be advised to postpone travel	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
Measures for travellers on board international conveyances from affected areas					
Travellers should be asked to report illness, and separated on the plane	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**
PH authorities to be informed of ill person(s) on board	**Recommend**	**Recommend**	**Recommend**	**Recommend**	**Recommend**

8.7 Reference List

(1) CDC. Interim Pre-pandemic planning Guidance: community strategy for pandemic influenza mitigation in the United States. 1-108. 1-2-0008.
Ref Type: Report

(2) ECDC. ECDC Pandemic Public Health Measures Menu. 1-1-2008.
Ref Type: Report

(3) WHO. WHO consultation on priority public health interventions before and during an influenza pandemic. www.who.int . 2004.
Ref Type: Electronic Citation

(4) WHO Outbreak Communication Guidelines. www.who.int . 2005.
Ref Type: Electronic Citation

(5) Ferguson NM, Cummings DA, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. Nature 2006.

(6) Lau JT, Tsui H, Lau M, Yang X. SARS transmission, risk factors, and prevention in Hong Kong. Emerg Infect Dis 2004; 10(4):587-592.

(7) Wu J, Xu F, Zhou W, Feikin DR, Lin CY, He X et al. Risk factors for SARS among persons without known contact with SARS patients, Beijing, China. Emerg Infect Dis 2004; 10(2):210-216.

(8) Neuzil KM, Hohlbein C, Zhu Y. Illness among schoolchildren during influenza season: effect on school absenteeism, parental absenteeism from work, and secondary illness in families. Arch Pediatr Adolesc Med 2002; 156:986-991.

(9) World Health Organization Writing Group. Nonpharmaceutical interventions for pandemic influenza, national and community measures. Emerg Infect Dis [serial on the Internet] 2006; 12(1):88-94.

(10) Heymann A, Chodick G, Reichman B, Kokia E, Laufer J. Influence of school closure on the incidence of viral respiratory diseases among children and on health care utilization. Pediatr Infect Dis J 2004; 23(7):675-677.

(11) Svoboda T, Henry B, Shulman L, Kennedy E, Rea E, Ng W et al. Public health measures to control the spread of the severe acute respiratory syndrome during the outbreak in Toronto. N Engl J Med 2004; 350(23):2352-2361.

(12) World Health Organization Writing Group. Nonpharmaceutical interventions for pandemic influenza, international measures. Emerg Infect Dis [serial on the Internet] 2006; 12(01).

(13) World Health Organization Writing Group. Nonpharmaceutical interventions for pandemic influenza, international measures. Emerg Infect Dis [serial on the Internet] 2006; 12(01).

Appendices

8.8 Appendix A Universal Respiratory Hygiene

The following are components of a universal respiratory hygiene strategy to be adopted in all health care facilities.

- The posting of visual alerts at the entrances to all healthcare facilities, instructing patients and those who accompany them to:
    - Inform healthcare personnel of symptoms of a respiratory infection when they first register for care
    - Practice respiratory hygiene
    - Advise visitors with respiratory symptoms to defer their visit until symptoms have resolved
- All patients and visitors who have symptoms of an infectious respiratory illness (cough, runny nose, sore throat or sneezing) should be provided with a surgical mask and instructions on their proper use and disposal. They should also be provided with instructions on hand-hygiene.
- For those who cannot wear a mask, provide tissues and instructions on when to use them (i.e. when coughing, sneezing, or controlling nasal secretions), where they should be disposed of, and on the importance of hand-hygiene after using them.
- Waste bins should be readily available for disposal of tissues.
- Provide hand-hygiene materials in the waiting room areas and encourage persons with respiratory symptoms to perform hand-hygiene.
- Instruct registration, reception and triage staff of their risk of exposure to infections spread by droplets and to consider wearing masks whenever registering or assessing patients who have respiratory symptoms and are not wearing a mask. Instruct them to remain at least 3 feet from unmasked patients.
- Consider the use of Plexiglas barriers at the point of triage or registration to protect healthcare personnel from contact with respiratory droplets.

- Where possible, designate an area, cubicle or separate room in waiting areas where patients with respiratory symptoms can be segregated (ideally by at least 3 feet) from others without respiratory symptoms.
- Commonly used surfaces such as door handles, handrails, table surfaces etc. should be cleaned twice daily with disinfectant.
- Use droplet precautions to manage patients with respiratory symptoms until it is determined that the cause of the symptoms is not an infectious agent that requires more than standard precautions.

Chapter 9 Table of Contents

9 Health System Response: Clinical Management of Patients with influenza like Illness during an Influenza Pandemic

9.1 Scope and purpose

This chapter contains guidance for health professionals regarding the treatment of pandemic influenza. It covers treatment in hospitals and the community of both adults and children. It is intended for use in Ireland in event that the World Health Organisation declares that an influenza pandemic has started,[1] and cases of pandemic influenza have been identified within Ireland.

It has been adapted with kind permission from Guidance produced by the Department of Health, UK, British Infection Society, British Thoracic Society, and Health Protection Agency, in March 2006.[2] [3] It has also been reviewed by the Infectious Diseases Society of Ireland in May 2009. It should be read in conjunction with the National Plan for Pandemic Influenza 2007. The chapter contains synopses on:

- Clinical management in the community (adults and children)
- Clinical management of adults referred to hospital
- Clinical management of children referred to hospital

To facilitate preparedness planning, this document has been written in advance of the emergence of the next influenza pandemic, at a time when the identity of the causative virus remains unknown.

These Guidelines are based on the best evidence available from previous pandemic and interpandemic influenza periods. An influenza pandemic will not be "business as usual" and the way the healthcare system functions will need to be altered to accommodate exceptional arrangements. The guidance may evolve as clinico-pathological information on the eventual pandemic virus emerges. **Once an influenza pandemic is**

underway, users are strongly urged to refer to the most up-to-date version of these Guidelines (from web-based access points).

9.2 Who are these guidelines aimed at?

These guidelines are offered for the guidance of all hospital doctors and primary care physicians. In the event of a pandemic, it is envisaged that all health care practitioners, regardless of individual specialisation, may be involved in the management of patients with influenza. It is intended that these guidelines will also be of value to health care practitioners who do not usually manage patients with influenza but may be called upon to do so in a pandemic situation. Modification of some recommendations at a local level may be necessary in specific instances.

These guidelines are not relevant for the management of patients affected by seasonal influenza, sporadic acute exacerbations of chronic obstructive pulmonary disease (AECOPD), lower respiratory tract infections or community-acquired pneumonia (CAP).

9.3 Health care delivery modes

Even though it is impossible to predict with certainty the impact of the next pandemic, based upon the available epidemiological and modelling information, it is clear that it will generate demands for health care which may saturate or overwhelm normal acute services for a period of time, perhaps several weeks or months. Accordingly, it should be anticipated that the Health Service Executive (HSE) (in common with all health systems around the world) will need to revert to emergency arrangements.

The aim will be to treat as many people as possible at home. The following care settings may apply:

- Self-care with appropriate advice and treatment from healthcare professionals
- GP treatment of community patients 'well' enough to be managed in the community

- Hospital care in acute medicine for persons considered too ill or lacking the social supports to be managed at home.
- Treatment of patients in the community (who would normally receive care from a GP) by other health care professionals (community health and public health doctors, nurses, paramedics, pharmacists etc.) following treatment guidance laid out in this publication
- Treatment of patients in their own homes or in temporary intermediate care facilities/ alternative care settings under the care of a GP or other healthcare professional, following treatment guidance laid out in this publication when, under normal circumstances, such patients would have been admitted for hospital care
- Using hospitals who normally deal with mainly elective work (e.g. orthopaedic hospitals) to treat patients who require hospital care but do not need High Dependency Unit care (HDU) or Intensive Care (ICU)
- Treatment of severely ill patients in hospital by medical and nursing teams who do not normally manage patients with influenza or community acquired pneumonia, in areas of the hospital not normally used for providing medical care (for example, surgical teams and bed space diverted from routine elective work towards pandemic response).

The aim will be to consider for treatment with antivirals (neuraminidase inhibitors) all patients if they have all of the following:

1) An acute influenza-like illness
2) Fever (≥ 38°C/100. 4°F in adults, or ≥ 38.5 °C/101.3°F in children) and
3) Been symptomatic for 48 hours or less.

This is subject to having sufficient antivirals to treat all those clinically ill, and also demonstration that antivirals are effective against the pandemic strain.

9.4 General management and investigations in the community

Box 1.1 Clinical Case Definition

The presence of fever and new (or, in those with chronic lung disease, worsening) cough of acute onset when influenza with pandemic potential is circulating in the community.
(**Important note** - This definition may be modified once a pandemic occurs.)

9.4.1 Initial assessment and triage

Management decisions regarding patients with influenza should be based primarily on:

- an assessment of illness severity
- identification of whether the individual is in an at risk group
- age, if the patient is a child(children aged less than 3 years should be seen by a doctor)
- current advice from Health Protection Surveillance Centre (HPSC)/local Medical Officer of Health (MOH) based on the epidemiology of the pandemic

Patients (including children aged over 3 years of age) who are not considered to be at high risk and who have no features suggesting severe disease or complications may be seen in a community health facility staffed by healthcare professionals other than GPs.

Patients at high risk of complications (Appendix 1) should be seen and assessed by a GP or at the designated flu assessment centre of the acute hospital.

A series of algorithms have been developed to aid and summarise initial assessment and management of pandemic influenza. These are outlined in Appendices 2, 3, 4 and 6.

9.4.2 Criteria for Hospital Referral (Adults) (Appendices 2 and 3)

Patients with clinically defined uncomplicated influenza infection would be expected to make a full recovery. They require good symptomatic management, access to antiviral treatment, information about the natural history, and advice as to when to re-consult. Patients with **new or worsening symptoms** - particularly shortness of breath or recrudescent fever not responding to treatment - **should be examined to assess the presence** and severity **of influenza-related pneumonia.**

There is no validated severity assessment tool validated for influenza-related pneumonia, but the CRB-65 score has been validated for community acquired pneumonia. The **CRB-65 score** (Table 9.1) is recommended for use in the **community setting** to determine the management of influenza related pneumonia. It does not replace clinical judgment.

- Patients with influenza-related pneumonia who have a CRB-65 score of 2 are at increased risk of death and should be considered for hospital admission, or at a minimum, hospital supervised outpatient treatment

    - Patients with influenza-related pneumonia clinically, who have a CRB-65 score of 1 or 2 (particularly score 2) AND require oxygen, IV fluids, IV antibiotics, nursing care or NG tube feeding, BUT do not have a pre-existing co-morbid medical condition as outlined in Appendix 1, should be referred to hospital. If available locally, an elective, rather than an acute hospital should be used.

    - Patients with influenza-related pneumonia clinically, who have a CRB-65 score of 1 or 2 (particularly score 2) AND require oxygen, IV fluids, IV antibiotics, nursing care or NG tube feeding, AND have a pre-existing co-morbid medical condition as outlined in Appendix 1, should be referred to an acute hospital

- Patients with CRB-65 score of 3 or more should be referred to an acute hospital for urgent admission.

- Patients with worsening of pre-existing co-morbid medical conditions should be managed according to best practice for that condition with reference to published disease-specific guidelines, if available. If such patients have progression of their flu symptoms such that they require hospital treatment, they should be referred to an acute hospital.

- Patients with bilateral chest signs of pneumonia (crackles) should be referred to an acute hospital for further assessment regardless of CRB-65 score (Table 9.1).

Table 9.1 Severity assessment used to determine the management of influenza-related pneumonia in patients in the community (CRB-65 score)

CRB-65 score*	Recommended action
0	Likely suitable for home treatment
1 or 2	Consider hospital referral, particularly with score 2
3 or more	Urgent acute hospital referral
Any(0 to 4) in the presence of bilateral chest signs of pneumonia	Consider acute hospital referral

*Score 1 point for each feature present:
- **C**onfusion (Mental Test Score of ≤ 8, or new disorientation in person, place or time.)
- **R**espiratory rate ≥ 30/min
- **B**lood pressure (SBP < 90mmHg or DBP ≤ 60mmHg)
- Age ≥ **65** years

The Pandemic Medical Early Warning Score (PMEWS) is an alternative to CRB 65 which could also be used in the community. [4] It was developed in the UK for use in primary and secondary care, with the aim of identifying patients who need hospital admission. They modified an existing hospital Medical Early Warning score to include transcutaneous oxygen saturation and added supplementary scoring features of co-morbidity and social factors. The score adds an extra point for age over 65 years and another for any of social isolation, chronic disease or having a performance status of limited

activity or worse. The threshold score for admission can be altered locally, depending on demand.

9.4.3 Criteria for Hospital Referral (Children) - (Appendix 4)

- Children who are severely ill should be referred for assessment for admission to an acute hospital. Indicators of severe disease are any of these below:
    1) cyanosis
    2) severe dehydration
    3) altered conscious level
    4) complicated or prolonged seizures
    5) signs of sepsis such as extreme pallor, hypotension, a floppy infant
    6) persistent signs of respiratory distress such as markedly raised respiratory rate, grunting, intercostal recession or breathlessness with chest signs. (A useful severity assessment tool for respiratory distress taken from the BTS pneumonia guidelines is given in Appendix 5)
- Children who have progression of their flu symptoms AND require oxygen, IV fluids, IV antibiotics, nursing care or NG tube feeding BUT do not fit the criteria for acute hospital referral above, may be referred to an elective hospital.

9.4.4 General Management of both adults and children in the Community

9.4.4.1 Initial management

All patients presenting with symptoms suggestive of influenza (except perhaps those in whom urgent admission is required) should be given general advice and advice on antipyretics, fluids and infection control, and be considered for antiviral therapy.

There is little scientific evidence for most symptomatic and self-help treatment, but experience suggests that some of the following may help, and are unlikely to cause harm.

- Treatment of fever, myalgia and headache with paracetamol or ibuprofen
- Rest
- Drink plenty of fluids
- Avoid smoking
- Consider: steam inhalation, short course of topical decongestants, throat lozenges, saline nose drops

Aspirin is contraindicated in children less than 16 years of age

9.4.4.2 Investigations

- Where possible, **early** in a pandemic (i.e. when cases are not widespread throughout Ireland: WHO Phase 6, Irish Alert levels 2-3), nose and throat swabs, or nasopharyngeal swabs (in children), in virus transport medium should be submitted to the local laboratory.
- Once a pandemic is established (i.e. widespread cases throughout the country; WHO Phase 6, Irish Alert level 4), microbiological investigations are not recommended.
- General investigations, including a chest x-ray, are not necessary for the majority of patients managed in the community.
- Routine testing for bacterial pathogens is not recommended at any stage.

9.4.4.3 Use of antivirals

- Ideally, individuals should be considered for treatment with antivirals (neuraminidase inhibitors) if they have all of the following:
    1) An acute influenza-like illness
    2) Fever (≥ 38°C/100. 4°F in adults, or ≥ 38.5 °C/101.3°F in children) and
    3) Been symptomatic for 48 hours or less.

The antiviral treatment of choice is oseltamivir (Tamiflu ™). Liquid paediatric suspension is available for children and dilution of the capsules of Tamiflu can also be used to prepare the dose. **Note**: Paediatric capsules (30mg, 45mg) are also available.

Treatment Schedule:

Adults - Oseltamivir 75mg every 12 hours for 5 days

(Dose to be reduced by 50% if creatinine clearance is less than 30ml/minute i.e. 75mg once daily)

Children

Child aged < 1 year	Oseltamivir 2-3mg/kg twice daily for 5 days
Child aged ≥1yr; body weight 15kg or lower (≥1yr-<3yrs)	Oseltamivir 30mg 12-hourly for five days
>15-23kg (3yr-<7yrs)	Oseltamivir 45mg 12-hourly for five days
>23-40kg	Oseltamivir 60mg 12 hourly for five days
Child >40kg	Oseltamivir 75mg 12-hourly for five days

(Dose to be reduced by 50% if creatinine clearance is less than 30ml/minute)

The European Medicines Evaluation Agency's (EMEA) Committee for Medicinal Products for Human Use (CHMP) recommends, in the case of pandemic influenza being declared by WHO in the context of the novel influenza A (H1N1) outbreak, treating children below 1 year of age with oseltamivir.[5] Children below 1 year of age should be treated under medical supervision. It is strongly recommended that at least children below 3 months of age are treated under medical supervision in hospital.

Although there is no strong evidence to support antiviral use outside the above circumstances, antiviral treatment should be considered for:

- Patients who are unable to mount an adequate febrile response e.g. the immunocompromised or very elderly may still be eligible for antiviral treatment despite lack of documented fever.
- Hospitalised patients who are severely ill, particularly if also immunocompromised, may benefit from antiviral treatment started more than 48 hours from disease onset, although there is no evidence to demonstrate benefit, or lack of, in such circumstances.

9.4.4.3.1 Antivirals in Pregnancy

On 7th May, 2009, following a review of all the available data by its Scientific Committee (CHMP), the EMEA concluded that the benefit of using oseltamivir (Tamiflu) in pregnant or breastfeeding women outweighs the risk in the context of novel influenza A (H1N1) in a pandemic situation.(5) Zanamivir (Relenza) has in animal studies been shown to cross the placenta and to be secreted in breast milk. The non-clinical data are not indicative of any relevant cause for concerns regarding the safe use of Relenza at recommended doses. Taken together, EMEA states that the overall data suggest that the benefit of using Relenza in pregnant or breastfeeding women outweighs the risk in the context of a novel influenza A (H1N1) in a pandemic situation.

9.4.4.4 Antibiotic management in adults with influenza managed in the community (see also Appendix 7)

The use of antibiotics in adults with influenza **not complicated by pneumonia** is determined by (a) the presence of any co-morbid illnesses (see Appendix 1) and (b) the timing of first consultation with respect to the onset of symptoms.

Table 9.2: Recommendations on use of antibiotics in adults with influenza managed in the community

Patient group	**Recommendation**
(A) **Not complicated by influenza-related pneumonia**	
Previously well	Antibiotics not routinely required
Previously well, but who have developed significant worsening of symptoms (particularly recrudescent fever or	Consider antibiotic use

increasing breathlessness)	
Patients at high risk of complications (see Appendix 1)	*Strongly consider a prescription for 'delayed prophylactic' antibiotics to be used if the illness is not starting to improve after 24 hours or there is worsening of symptoms (recrudescent fever or increasing breathlessness).
(B) Complicated by influenza-related pneumonia	
All patients	Antibiotics recommended

Table 9.3 below outlines the empirical antibiotic treatment regimens for adults with pneumonic and non-pneumonic lower respiratory tract infections (including exacerbations of COPD and acute bronchitis) complicating influenza managed in the community.

- Those with features of severe infection (i.e. bilateral chest signs or C-RB-65 score of 3 or more) should be urgently referred to hospital.
- For those referred to hospital, GPs should consider administering antibiotics immediately where the illness is considered life-threatening or where delays (>2 hours) in admission are likely.
- Reference should be made to a specialist text (e.g. IMF/BNF, or IPHA Compendium of Medicines, available at www.medicines.ie) for the antibiotic management of women who are pregnant or lactating and for those with renal or hepatic impairment.

Table 9.3. Empirical antibiotic treatment regimens for adults with pneumonic and non pneumonic lower respiratory tract infection complicating influenza managed in the community

Preferred	Alternative[a]
Doxycycline[b] 200mg stat and 100mg orally, once daily for 1 week **or** Co-amoxiclav 625mg orally,3 times daily for 1 week **or** Cefuroxime 500mg orally, 2 times daily for 1 week	Clarithromycin 500 mg orally, 2 times daily for 1 week Or Clarithromycin LA 500mg orally, once daily for 1 week

a) An alternative regimen is provided for those intolerant of or hypersensitive to preferred regimen
b) Doxycycline contraindicated in pregnancy

9.4.4.5 Antibiotic management in children with influenza managed in the community (see also Appendix 7)

Secondary bacterial infections particularly pneumonia and otitis media are common in children with influenza. S *pneumoniae*, S *aureus* and H *influenzae* are the most common pathogens encountered during influenza outbreaks.

- Children in any one of the following groups should be treated with an antibiotic that will provide cover against *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae:*
    1) those at risk of complications of influenza (see Appendix 1)
    2) those with one or more of the following adverse features
        a. breathing difficulties
        b. severe earache
        c. vomiting > 24 hours
        d. drowsiness, *or*
    3) those with disease severe enough to merit hospital admission during an influenza pandemic
- Empirical antibiotic treatment regimens recommended for children in the community in the above categories are detailed below:
- Reference should be made to a specialist text (e.g. IMF/BNF, or IPHA Compendium of Medicines, available at www.medicines.ie) for the antibiotic management of children with renal or hepatic impairment.

Preferred	Alternative[a]
Co-amoxiclav orally for 1 week	Clarithromycin orally for 1 week Or Cefuroxime orally for 1 week

a) An alternative regimen is provided for those intolerant of or hypersensitive to preferred regimen

- For children less than 12 years co-amoxiclav is the drug of choice and is preferred for children up to 18 years

Co-amoxiclav (orally for 7 days)*

Age	Dose	Frequency	Formulation
0-12 months	0.25ml/Kg	3 times daily	of 125/31 suspension
1-6 years*	5mls	3 times daily	of 125/31 suspension
7-12 years*	10mls	3 times daily	of 125/31suspension
12-18 yrs	1 tablet	3 times daily	250/125

***** Double the dose in severe infection

- Equivalent twice daily formulations of Co-amoxiclav (*Augmentin Duo*) are presented below:

Augmentin Duo* (orally for 7 days)

Age	Dose	Frequency	Formulation
2 months -2 years	0.15ml /kg	2 times daily	400/57 suspension
2-6 years (13-21 kg)	2.5mls	2 times daily	400/57 suspension
7-12 years (22-40kgs)	5 mls	2 times daily	400/57 suspension

***** Double the dose in severe infection

- Clarithromycin or cefuroxime should be used in children allergic to penicillin.

Clarithromycin (orally for 7 days)

Age	Dose	Frequency	Formulation
<8kg	7.5mg/kg	2 times daily	125mg in 5ml suspension
8-11kg	2.5ml	2 times daily	125mg in 5 ml suspension
12-19kg	5ml	2 times daily	125mg in 5 ml suspension
20-29kg	7.5ml	2 times daily	125mg in 5 ml suspension
≥30kg	5ml	2 times daily	250mg in 5 ml suspension
>10years	250mg	2 times daily	Tablet

Cefuroxime (orally as cefuroxime axetil for 7 days)

Age	Dose	Frequency	Formulation
3-24 months	10mg/kg (up to a max. of 125mg)	2 times daily	125mg in 5 ml suspension
2-12 years	15mg /kg (up to a max. of 250mg)	2 times daily	125mg in 5 ml suspension
13-18 years	500mg	2 times daily	Tablet

- For children over 12 years, doxycycline 100mg orally daily is an alternative (should be swallowed whole with adequate fluids). Note: Doxycycline is contraindicated in pregnancy.

9.4.4.6 When should patients re-consult?

Examples of what should prompt patients to re-consult are given in table 9.4.

Table 9.4: Examples of what should prompt patients to re-consult

Examples of what should prompt patients to re-consult
➢ Shortness of breath at rest or while doing very little
➢ Painful or difficult breathing
➢ Coughing up bloody sputum
➢ Drowsiness, disorientation or confusion
➢ Fever for 4-5 days and not starting to get better (or getting worse)
➢ Starting to feel better then developing high fever and feeling unwell again
➢ If taking antiviral drugs, symptoms should start to improve within two days. Lack of any improvement after two days from starting antiviral drugs is an indication to re-consult
Note: This information may be modified once a pandemic occurs

To summarise:

- Any rapid deterioration following first consultation should prompt a patient to re-consult.

- Failure to improve 2 days after starting an antiviral agent is an indication to re-consult.
- If the first consultation did not involve contact with a physician, re-consultation should preferably involve a physician, usually a GP.

9.5 Clinical management of adults in the hospital setting

9.5.1 Severity assessment when presenting to hospital

- Patients with uncomplicated influenza infection would be expected to make a full recovery and do not require hospital care.
- In uncomplicated infection, the illness usually resolves in 7 days although cough, malaise and lassitude may persist for weeks.
- Patients with worsening of pre-existing co-morbid medical conditions should be managed according to best practice for that condition with reference to published disease-specific guidelines, if available.

9.5.1.1 Assessment of those with Influenza-related pneumonia

There is no validated severity assessment tool developed specifically for influenza-related pneumonia. The **CURB-65** severity assessment tool is recommended for the stratification of **hospital patients** with influenza-related pneumonia (see Table 9.5) into disease severity groups. In addition, the presence of diffuse bilateral lung infiltrates on chest radiography consistent with primary viral pneumonia is an adverse prognostic feature. Such patients should be treated as for severe pneumonia.

Table 9.5: Severity assessment used to determine the management of influenza-related pneumonia in patients admitted to hospital (CURB-65 score)

CURB-65 score*	Recommended action
0	Likely suitable for home treatment
1 or 2	Consider elective hospital stay, particularly with score 2, or hospital supervised outpatient stay
3 or more	Manage in acute hospital as severe pneumonia

*Score 1 point for each feature present:

- **C**onfusion (Mental Test Score of ≤ 8, or new disorientation in person, place or time.)
- **U**rea > 7mmol/L
- **R**espiratory rate ≥ 30/min
- **B**lood pressure (SBP < 90mmHg or DBP ≤ 60mmHg)
- Age ≥ **65** years

*NOTE: ***New bilateral lung shadowing on CXR* consistent with primary viral pneumonia should be taken as a feature of severe pneumonia regardless of CURB-65 score.**

9.5.1.2 High Dependency or Intensive Care Unit referral

- Patients with primary viral pneumonia *or* a CURB-65 score of 4 or 5 should be considered for HDU/ICU referral.
- General indications for HDU/ICU referral include:
    1) persisting hypoxia with PaO_2 <8Kpa despite maximal oxygen administration
    2) progressive hypercapnia
    3) severe acidosis (pH<7.26)
    4) septic shock
- Patients with influenza admitted to Intensive Care Unit should be managed by specialists with appropriate training in Intensive Care, Respiratory Medicine and/or Infectious Diseases.

9.5.2 General Investigations for Adults in Hospital

- The following investigations are recommended in patients referred to hospital:

Test	Who this applies to
Full blood count	**All patients**
Urea and electrolytes	**All patients**
Liver function tests	**All patients**
Chest x-ray	**All patients**
Pulse oximetry	**All patients. If <92% on air, then arterial blood gases.**
ECG	**Patients with cardiac and respiratory complications or co-morbid illnesses.**
C-reactive protein	**If influenza-related pneumonia is suspected***

- In those patients who are subsequently followed up in a hospital outpatient clinic or by a general practitioner a repeat chest X-ray should

be obtained at around 6 weeks if respiratory symptoms or signs persist or where there is a higher risk of underlying malignancy (especially smokers and those over 50 years of age).

- Further investigations including a CT thoracic scan and bronchoscopy should be considered if the chest X-ray remains abnormal at follow up.

9.5.3 Microbiological investigations

9.5.3.1 Early in a pandemic (i.e. the virus has been isolated in Ireland and there are outbreaks, but there is not, as yet, widespread activity across Ireland: WHO Phase 6, Irish Alert level 3)

- All patients should have virological tests.
    1) Nose and throat swabs in virus transport medium.
       If presentation is more than 7 days after onset of illness, an 'acute' serum (5-10mLs clotted blood) should be collected and a 'convalescent' sample (5-10mLs clotted blood) obtained after an interval of not less than 7days.
- Patients with influenza-related pneumonia should also have the following bacteriological tests:

1) **Blood culture** (preferably before antibiotic treatment is commenced)
2) **Pneumococcal urine antigen** (20 mls urine sample)
3) **Legionella urinary antigen** (20 mls urine sample)
4) **Sputum Gram stain, culture** and antimicrobial susceptibility tests on samples obtained from patients who:
    i. are able to expectorate purulent samples, *and*
    ii. have not received prior antibiotic treatment.
5) **Paired serological examination for influenza/other agents**. Acute serum should be collected and a 'convalescent' sample obtained after an interval not less than 7days (both 5-10mLs clotted blood).

9.5.3.2 Once a pandemic is established (i.e. widespread activity across Ireland: WHO Phase 6, Irish Alert Level 4)

- Virological tests are not routinely recommended.

- Patients with influenza-related pneumonia should have bacteriological tests in accordance to the severity of illness.

a. Non-severe pneumonia (CURB-65 Score 0, 1 or 2)

No routine testing. In patients who do not respond to empirical antibiotic therapy, sputum samples should be sent for Gram stain culture and antimicrobial susceptibility tests.

b. Severe pneumonia (CURB-65 Score 3, 4 or 5, or bilateral CXR changes)

- **Blood culture,** preferably before antibiotic treatment is commenced
- **Pneumococcal urine antigen** (20mls urine)
- **Legionella urine antigen** (20mls urine)
- **Sputum Gram stain, culture** and antimicrobial susceptibility tests on samples obtained from patients who are able to expectorate purulent samples, *and* have not received prior antibiotic treatment.
- **Paired serological examination** for influenza/other agents. 'Acute' serum should be collected and a 'convalescent' sample obtained after an interval not less than 7 days (both 5-10mLs clotted blood).
- **Tracheal or endotracheal aspirate samples**, if available, should be sent for Gram stain, culture and antimicrobial susceptibility testing.

9.5.4 General Management of adults admitted to hospital

9.5.4.1 Initial management

- All patients should be managed in accordance with the infection control guidelines outlined in Guidance for Pandemic Influenza: Infection Control in Hospitals, Community and Primary Care settings
- Hypoxic patients should receive appropriate oxygen therapy with monitoring of oxygen saturations and inspired oxygen concentration with the aim to maintain $PaO_2 \geq 8$ Kpa and $SaO_2 \geq 92\%$. High concentrations of oxygen can safely be given in uncomplicated pneumonia.

- Oxygen therapy in patients with pre-existing chronic obstructive pulmonary disease complicated by ventilatory failure should be guided by repeated arterial blood gas measurements. Non-invasive ventilation may be helpful.
- Patients should be assessed for cardiac complications and also volume depletion and their need for additional intravenous fluids.
- Nutritional support should be given in severe or prolonged illness.

9.5.4.2 Monitoring in hospital

- Temperature, respiratory rate, pulse, blood pressure, mental status, oxygen saturation and inspired oxygen concentration should be monitored and recorded initially at least twice daily and more frequently in those with severe illness or requiring regular oxygen therapy.
- In patients who are not progressing satisfactorily a full clinical reassessment and a repeat chest radiograph are recommended.

9.5.4.3 Discharge and follow up

- Patients should be reviewed 24 hours prior to discharge home. Those with 2 or more of the following unstable clinical factors should be considered for continuing care in hospital:
    1) temperature > 37.8^{o}C
    2) heart rate > 100/min
    3) respiratory rate > 24/min
    4) systolic blood pressure <90mmHg
    5) oxygen saturation < 92% on room air
    6) inability to maintain oral intake
    7) abnormal mental status or mental status not returned to baseline.
- Follow up clinical review should be considered for all patients who suffered significant complications or who had significant worsening of their underlying disease, either with their general practitioner or in a hospital clinic.

- At discharge or at follow up, patients should be offered access to information about their illness, take home medication and any follow up arrangements.
- **It is the responsibility of the hospital team to arrange the follow up plan with the patient and the general practitioner.**

9.5.5 Use of antivirals in hospitalised adult patients

Individuals should be considered for treatment with antivirals (neuraminidase inhibitors) if they have all of the following:

1. An acute influenza-like illness
2. Fever (>38^{0}C/100.4^{0}F) and
3. Are symptomatic for 48 hours or less.

Treatment Schedule:

Adults - Oseltamivir 75mg every 12 hours for 5 days (Dose to be reduced by 50% if creatinine clearance is less than 30ml/minute i.e. 75mg once daily)

- Patients who are unable to mount an adequate febrile response e.g. the immunocompromised or very elderly, may still be eligible for antiviral treatment despite lack of documented fever.
- Hospitalised patients who are severely ill, particularly if also immunocompromised, may benefit from antiviral treatment started more than 48 hours from disease onset, although there is no evidence to demonstrate benefit, or lack of, in such circumstances.

9.5.6 Use of antibiotics in hospitalised adults (see also Appendix 7)

- Guidelines for inpatient management should be according to the existing hospital policy for the management of Community Acquired Pneumonia (CAP). Special attention should be made to ensure that adequate *S. aureus* coverage is included in the regimen. When a pathogen has been identified local microbiological advice should always be sought regarding specific therapy.

- Reference should be made to a specialist text (e.g. BNF, or IPHA Compendium of Medicines, available at www.medicines.ie) for the antibiotic management of women who are pregnant or lactating and for those with renal or hepatic impairment.

9.5.6.1 Bronchial complications without influenza-related pneumonia

- Previously well adults with acute bronchitis complicating influenza, in the absence of pneumonia, do not routinely require antibiotics.
- Antibiotics should be considered in those previously well adults who develop worsening symptoms (recrudescent fever or increasing dyspnoea).
- Patients at high risk of complications or secondary infection (see Appendix 1) should be considered for antibiotics in the presence of lower respiratory features.
- Patients with chronic lung disease, including COPD, should receive antibiotics in the presence of increased purulent sputum.
- Most patients can be adequately treated with oral antibiotics.

- The preferred choice includes:

Co-amoxiclav 625mg orally, 3 times daily for 7 days **or** Doxycyline* 200mg stat and then 100mg orally, 2 times daily for 7 days

*Contraindicated in pregnancy

- Alternatives include: Clarithromycin (500mg orally, 2 times daily for 7 days), cefuroxime (500mg orally, 2 times daily for 7 days), or a fluoroquinolone active against *S. pneumoniae and S. aureus* where required e.g. for those intolerant of penicillins (moxifloxacin 400mg orally, once daily for 5 days or levofloxacin 750mg orally, once daily for 5 days).

9.5.6.2 Non-severe influenza-related pneumonia

- Most patients can be adequately treated with oral antibiotics.
- Antibiotics should be administered within 4 hours of admission.

- Oral therapy with co-amoxiclav or a tetracycline as outlined above is preferred. Alternatives include: Clarithromycin (500mg orally, 2 times daily for 7 days), cefuroxime (500mg orally 2 times daily for 7 days), or a fluoroquinolone active against *S. pneumoniae and S. aureus* where required e.g. for those intolerant of penicillins (moxifloxacin 400mg orally once daily for 5 days or levofloxacin 750mg orally, once daily for 5 days).

- When oral therapy is contra-indicated, recommended parenteral choices include:

Co-amoxiclav 1.2g IV 3 times daily **or** Cefuroxime 1.5g IV 3 times daily

- If the above antibiotics are unavailable, ceftoxamine 1g IV 3 times daily, or ceftriaxone 1g IV once daily are acceptable alternatives, although they are less active against *S. aureus.*

9.5.6.3 Severe influenza-related pneumonia

- Patients with severe pneumonia should be treated immediately after diagnosis with parenteral antibiotics.
- The following is recommended:

Co-amoxiclav 1.2g IV 3 times daily **or** Cefuroxime 1.5g IV 3 times daily **PLUS** Clarithromycin 500mg IV/orally 2 times daily

- If co-amoxiclav or cefuroxime are unavailable, ceftoxamine 1g IV 3 times daily, or ceftriaxone 1g IV once daily are acceptable alternatives, although they are less active against *S. aureus.*
- In patients where outpatient antibiotic treatment has failed and patient requires hospitalization, an alternative regimen includes a fluoroquinolone with enhanced activity against pneumococci together with a broad spectrum β-lactamase stable antibiotic or a macrolide.

- In critically ill patients (i.e. ICU admission required) when Methicillin Resistant *S. aureus* (MRSA) is suspected (or confirmed), Vancomycin (15mg/kg IV 2 times daily) or linezolid (600mg IV or orally, 2 times daily) should be added.
- Antibiotic therapy should be directed at the pathogen and thus therapy should be modified once the results from cultures are obtained.

9.5.6.4 Route and duration of antibiotic

- Patients treated initially with parenteral antibiotics should be transferred to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 hours, providing there is no contra-indication to the oral route.
- For most patients admitted to hospital with non-severe and uncomplicated pneumonia, **7 days** of appropriate antibiotics is recommended.
- **For those with severe, microbiologically undefined pneumonia**, **10 days treatment** is proposed. Longer therapy may be required depending on the patient's clinical response, especially where *S. aureus* or Gram negative enteric bacilli pneumonia is suspected or confirmed.

9.5.6.5 Failure of empirical antibiotic therapy

- If the patient fails to improve on empirical antibiotic therapy, the consultant medical microbiologist or infectious diseases physician should be consulted in all cases for advice on appropriate antimicrobial therapy
- For those with non-severe pneumonia in hospital on combination therapy, changing to a fluoroquinolone with effective pneumococcal and staphylococcal cover is an option.
- Adding further antibiotics effective against MRSA is an option for those with severe pneumonia not responding to combination antibiotic therapy. Consult with local Consultant Microbiologist or Infectious Disease Consultant.

9.6 Clinical management of children presenting to hospital

9.6.1 Severity assessment in children (see Appendices 4, 5 and 6)

- Coughs and mild fevers ---

  Treat at home by parents with antipyretics and fluids

  (Note: aspirin should not be used in children < 16 years)

- High fever (>38.5°C/101.3°F) and cough or influenza like symptoms ---
  - Seek medical advice.
  - If there are no features which put them at high risk of complications (Appendix 1 and below) they should be treated with oseltamivir, and given advice on antipyretics and fluids.
  - Children at risk of complications, and all children aged less than 3 years should be seen by a GP.

- High fever (>38.5°C/101.3°F) and cough or influenza like symptoms PLUS at-risk group. These children should be seen by their GP or in an Emergency Department.

Children may be considered at increased risk of complications if they have cough and fever (or influenza like illness) and temperature >38.5°C/101.3°F AND either chronic disease or one of following features:

- **Breathing difficulties**
- **Severe earache**
- **Vomiting > 24 hours**
- **Drowsiness**

These children should be offered an antibiotic as well as oseltamivir and advice on antipyretics and fluids.

Criteria for hospital referral for admission are any of the following:

1) Signs of persistent respiratory distress.
    - markedly raised respiratory rate
    - grunting
    - intercostal recession
    - breathlessness with chest signs
2) Cyanosis
3) Severe dehydration
4) Altered conscious level
5) Complicated or prolonged seizure
6) Signs of septicaemia – extreme pallor, hypotension, floppy infant

- Most children admitted to hospital are likely to need oxygen therapy and/or intravenous support as well as antibiotics and oseltamivir.

Indications for referral to High Dependency or Intensive Care are:

1) the child is failing to maintain a SaO2 of >92% in FiO2 of >60%
2) the child is shocked
3) there is severe respiratory distress and a raised PaCO2 (> 6.5 Kpa)
4) there is a rising respiratory rate and pulse rate with clinical evidence of severe respiratory distress with or without a raised PaCO2
5) there is recurrent apnoea or slow irregular breathing
6) there is evidence of encephalopathy

- When there are no PICU beds available, children will have to be triaged on the basis of the severity of their acute and co-existing disease, and the likelihood of their achieving full recovery.

9.6.2 General investigations for children in hospital

- A full blood count with differential, urea, creatinine and electrolytes, liver enzymes and a blood culture should be done in all severely ill children.
- A CXR should be performed in children who are hypoxic, have severe illness or who are deteriorating despite treatment.
- Pulse oximetry should be performed in every child being assessed for admission to hospital with pneumonia.

9.6.3 Microbiological/virological investigations in hospital

Early pandemic recommendations. (i.e. the virus has been isolated in Ireland and there are outbreaks, but there is not, as yet, widespread activity across Ireland: WHO Phase 6, Irish Alert levels 2 and 3)

A. **Virology – all children**

1) Nasopharyngeal aspirate or nose and throat swabs
2) If presentation is more than 7 days after onset of illness, an 'acute' serum (2-5 ml clotted blood) should be collected and a 'convalescent' sample (2-5 ml clotted blood) obtained after an interval of not less than 7 days.

B. **Bacteriology – children with influenza related pneumonia**

1) Blood culture (before antibiotic treatment is commenced)
2) Sputum samples obtained from older children
3) Paired serological examination for influenza/other agents.

Established pandemic recommendations (i.e. widespread activity across Ireland: WHO Phase 6, Irish Alert level 4)

A. **Virology** – not routinely recommended

B. **Bacteriology – children with influenza related pneumonia**

1) Blood culture (before antibiotic treatment is commenced)
2) Sputum samples obtained from older children
3) Paired serological examination for influenza/other agents

9.6.4 General management of children admitted to hospital

- All patients should be managed in accordance with the infection control guidelines outlined in Guidance for Pandemic Influenza: Infection Control in Hospitals, Community and Primary Care settings
- Patients whose oxygen saturation is 92% or less while breathing air should be treated with oxygen given by nasal cannulae, head box, or face mask to maintain oxygen saturation above 92%.
- When children are unable to maintain oral intake supplementary fluids should when possible be given by the enteral route. Intravenous fluids in those with severe pneumonia should be given at 80% basal levels.
- Children can be safely discharged from hospital when they
    1) are clearly improving
    2) are physiologically stable
    3) can tolerate oral feeds
    4) have a respiratory rate < 40/min (<50/min in infants)
    5) have an awake oxygen saturation of >92% in air.

9.6.5 Antiviral therapy in children

- In the setting of a pandemic, children should be considered for treatment with antivirals if they have <u>all</u> of the following:
    1) an acute influenza-like illness (see definition in clinical section)
    2) fever (>38.5^{0}C/101.3^{0}F) and
    3) been symptomatic for 2 days or less
- Oseltamivir is the anti-viral agent of choice.

Child aged < 1yr	Oseltamivir 2-3mg/kg twice daily for 5 days
Child aged ≥1yr; body weight 15kg or lower	Oseltamivir 30mg 12-hourly for 5 days
>15kg-23kg	Oseltamivir 45mg 12-hourly for 5 days
>23kg-40 kg	Oseltamivir 60mg 12-hourly for 5 days
> 40kg	Oseltamivir 75mg 12 hourly for 5 days

- In children who are severely ill in hospital oseltamivir may be used if the child has been symptomatic for <6 days (but there is no evidence to demonstrate benefit or lack of it in such circumstances)

9.6.6 Use of Antibiotics in hospitalised children (see also Appendix 7)

- Guidelines for inpatient management should be according to the existing hospital policy for the management of Community Acquired Pneumonia (CAP) in children.
- Preferred and alternative initial treatment regimens are summarised below.
- Children who are hospitalised during an influenza pandemic should be treated with an antibiotic that will provide cover against S. *pneumoniae*, *S. aureus* and *H. influenzae.*
- Reference should be made to a specialist text (e.g. IMF/BNF, or IPHA Compendium of Medicines, available at www.medicines.ie) for the antibiotic management of children with renal or hepatic impairment.
- Once susceptibility results are available the drug regimen should be rationalized if possible.

9.6.6.1 Non severe-secondary bacterial respiratory infection in children

- Where clinically appropriate, oral antibiotics should be given provided oral fluids are tolerated.

Preferred	Alternative[a]
Co-amoxiclav orally for 1 week	Clarithromycin orally for 1 week Or Cefuroxime orally for 1 week

a)An alternative regimen is provided for those intolerant of or hypersensitive to preferred regimen

- For children less than 12 years oral co-amoxiclav is the drug of choice and is preferred for children up to 18 years

Co-amoxiclav* (orally for 7 days)..

Age	Dose	Frequency	Formulation
0-12 months	0.25ml/Kg	3 times daily	of 125/31 suspension
1-6 years	5ml	3 times daily	of 125/31 suspension
7-12 years	10ml	3 times daily	of 125/31suspension
12-18 yrs	1 tablet	3 times daily	250/125

***** Double the dose in severe infection

- Equivalent twice daily formulations of co-amoxiclav (Augmentin Duo) are presented overleaf:

Augmentin Duo* (orally for 7 days)

Age	Dose	Frequency	Formulation
2 months -2 years	0.15ml / kg	2 times daily	400/57 suspension
2-6 years (13-21 kg)	2.5mls.	2 times daily	400/57 suspension
7-12 years (22-40kgs)	5 mls	2 times daily	400/57 suspension

***** Double the dose in severe infection

- Clarithromycin or cefuroxime should be used in children allergic to penicillin.

Clarithromycin (orally for 7 days)

Age	Dose	Frequency	Formulation
<8kg	7.5mg/kg	2 times daily	125mg in 5ml suspension
8-11kg	2.5ml	2 times daily	125mg in 5 ml suspension
12-19kg	5ml	2 times daily	125mg in 5 ml suspension
20-29kg	7.5ml	2 times daily	125mg in 5 ml suspension
≥30kg	5ml	2 times daily	250mg in 5 ml suspension
>10years	250mg	2 times daily	Tablet

Cefuroxime (orally as cefuoroxime axetil for 7 days)

Age	Dose	Frequency	Formulation
3-24 months	10mg/kg (up to a	2 times daily	125mg in 5 ml

	max.of 125mg)		suspension
2-12 years	15mg /kg (up to a max. of 250mg)	2 times daily	125mg in 5 ml suspension
13-18 years	500mg	2 times daily	Tablet

- For children over 12 years, doxycycline 100mg orally daily is an alternative (should be swallowed whole with adequate fluids). Note: Doxycycline is contraindicated in pregnancy.

9.6.6.2 Severe secondary bacterial respiratory infection in children

- In children who require intravenous antibiotics, any one of the following schedules can be used.

Co-amoxiclav IV **or** Cefuroxime IV

- If co-amoxiclav or cefuroxime are unavailable, ceftoxamine IV or ceftriaxone IV are acceptable alternatives, although they are less active against *S. aureus.*
- Children who are severely ill with pneumonia complicating influenza should have a second agent added to the regime (e.g. clarithromycin) and the drugs should be given intravenously to ensure high serum and tissue antibiotic levels.
- Intravenous to oral switch should also be considered if the child has made sufficient clinical improvement.

Co-amoxiclav IV

Age	Dose	Frequency
< 7 days	30mg/kg	2 times daily
7-28 days	30mg/kg	3 times daily
1-3 months	30mg/kg	3 times daily
3-12 months	30mg/kg	3 times daily (4 times daily in severe cases)

12-18 years	1.2g 3 times daily	3 times daily (4 times daily in severe cases)

Cefuroxime IV

Age	Dose	Frequency
< 7 days	25mg/kg	2 times daily*
7-21 days	25mg/kg	3 times daily*
21-28 days	25mg/kg	4 times daily*
1month-18 years	20-30mg/kg	3 times daily*

*Dose can be doubled in severe infection

Cefotaxime IV

Age	Dose	Frequency
< 7 days	25mg/kg	2 times daily*
7-21 days	25mg/kg	3 times daily*
21-28 days	25mg/kg	4 times daily*
1month-18 years	50mg/kg	3 times daily (4 times daily in severe infection)

*Dose can be doubled in severe infection

Ceftriaxone IV

Age	Dose	Frequency
Do not give to Neonates		
<50kg	50mg/kg	once daily
>50 kg	1g	once daily

Clarithromycin IV

- If possible give orally, but if it must be given intravenously

Age	Dose	Frequency
1 month-12 years	7.5mg/kg	2 times daily
12-18 years	500mg	2 times daily

In children who are critically ill (i.e. requiring ICU admission), when Methicillin Resistant *S. aureus* is suspected (or confirmed), Vancomycin IV or linezolid IV should be added. Expert advice should be sought from a medical microbiologist or infectious disease physician.

9.7 References

(1) WHO. Pandemic influenza preparedness and response: a WHO guidance document. www.who.int. 2009. Available from URL: http://www.who.int/csr/disease/influenza/PIPGuidance09.pdf

(2) British Thoracic Society, British Infection Society, Health Protection Agency for the Department of Health. Clinical guidelines for patients with an influenza like illness during an influenza pandemic. Version 10.5 March 2006. Available from URL: http://www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/DH_4121753

(3) Lim WS. Pandemic flu: clinical management of patients with an influenza-like illness during an influenza pandemic. Thorax 2007 Jan 1;62(suppl_1):1-46.

(4) Challen K, Bright J, Bentley A, Walter D. Physiological-social score (PMEWS) vs, CURB - 65 to triage pandemic influenza: a comparative validation study using community - acquired pneumonia as a proxy. BMC Health Services Research 2007. 7:33.

(5) EMA. Opinion of the Committee for Medicinal Products for Human Use Pursuant to Article 5(3) of Regulation (EC) No 726/2004, on Novel Influenza (H1N1) outbreak Tamiflu (oseltamivir) Relenza (zanamivir). EMA 2009. Available from URL: http://www.emea.europa.eu/humandocs/PDFs/EPAR/tamiflu/27883809en.pdf

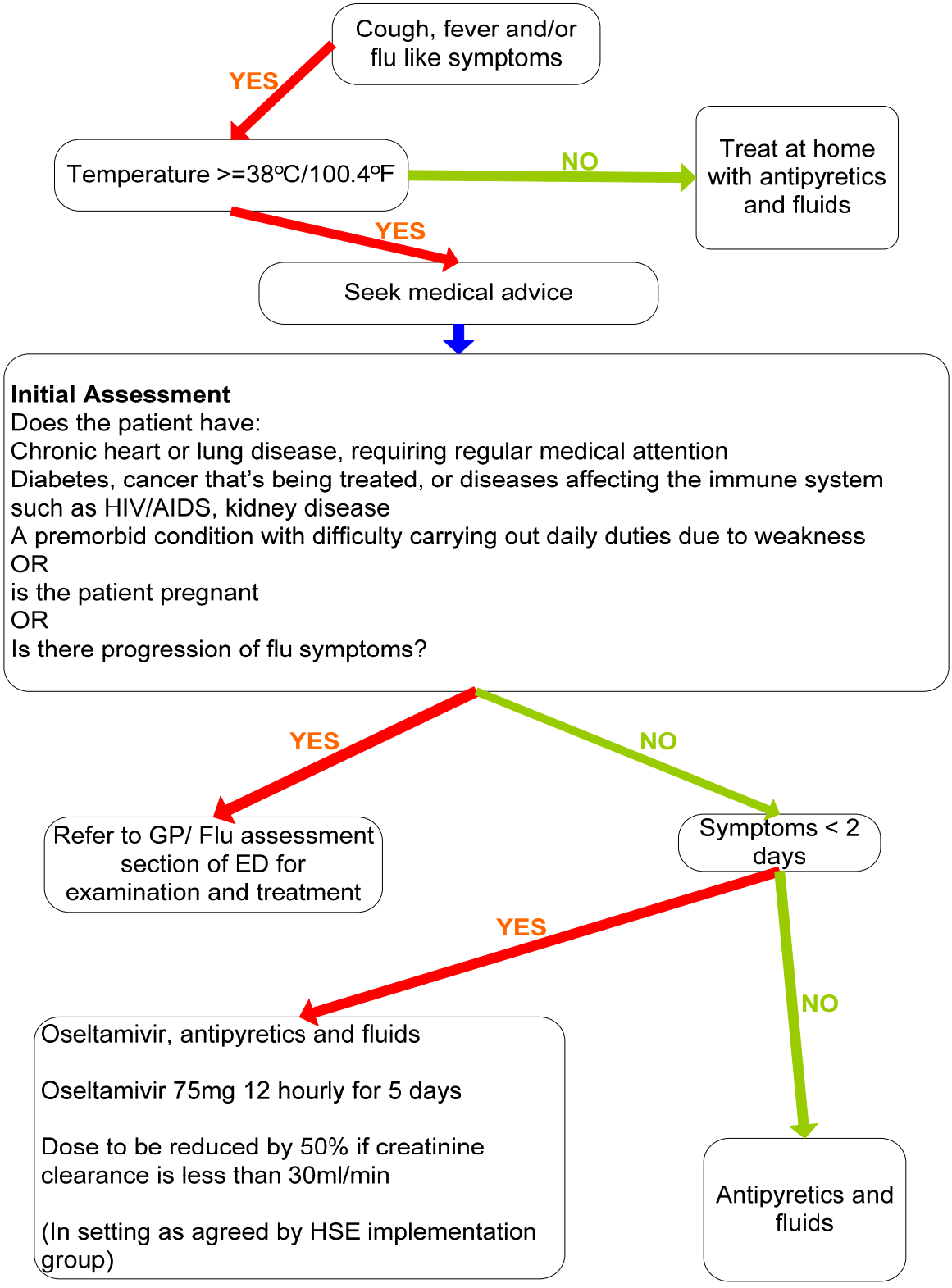
Appendix 1 Patients at high risk of influenza related complications

Clinical risk category	Examples
Aged 65 years or older	
Chronic respiratory disease, including asthma	This includes chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and brochopulmonary dysplasia (BPD). Asthma requiring continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospital admission. Children who have previously been admitted to hospital with lower respiratory tract disease
Chronic heart disease	This includes congenital heart disease, hypertension with cardiac complications, chronic heart failure and individuals requiring regular medication and/or follow up for ischaemic heart disease
Chronic renal disease	Including nephrotic syndrome, chronic renal failure, renal transplantation
Chronic liver disease	Including cirrhosis, inflammatory bowel disease
Diabetes and chronic metabolic disorders	Diabetes mellitus requiring insulin or oral hypoglycaemic drugs
Immunosuppression and malignancy	Due to disease or treatment. Including Asplenia or splenic dysfunction, HIV infection at all stages, malignancy. Patients undergoing chemotherapy leading to immunosuppression. Individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age) or for children under 20kg a dose of 1mg per kg per day
Long-stay residential care homes residents	This does NOT include prisons, young offender institutions, university halls of residence, boarding schools
Others	Doctors retain discretion in identifying additional individual patients who they recognize as at high risk of serious complications should they develop influenza; for example patients with haemoglobinopathies, neurological diseases with muscle weakness, cerebral palsy or children on long term aspirin who are at increased risk of Reyes syndrome

The high risk groups described in this appendix are largely based on data from interpandemic influenza. During the course of a pandemic, the definition of high risk groups may differ. If so, details of the high risk patient group will be altered according

to relevant clinico-epidemiological data. Users are strongly advised to refer to the latest edition of these guidelines at all times

Appendix 2 Initial assessment and management of adults with pandemic influenza



Appendix 3 Guidance on GP assessment and management of adults with pandemic influenza

GP should assess those with:
Chronic heart or lung disease, requiring regular medical attention
Diabetes, cancer that's being treated, or diseases affecting the immune system such as AIDS/HIV, kidney disease
A premorbid condition with difficulty carrying out daily duties due to weakness
OR
if the patient is pregnant
OR
Is there progression of flu symptoms (particularly shortness of breath or fever not responding to treatment)

Assess clinical severity using CRB-65 score
Score 1 point for each feature present:

Confusion (Mental test score <=8, or new disorientation in person, place or time)
Respiratory rate >= 30/min
Blood pressure (SBP <90mmHg or DBP <= 60mmHg)
Age >= **65** years

CRB-65 Score	**Recommended action**
0	Likely suitable for home treatment
1 or 2	Consider hospital referral, particularly with score 2
3 or more	Acute hospital referral
Any (in the presence of bilateral Chest signs of pneumonia)	Consider acute hospital referral

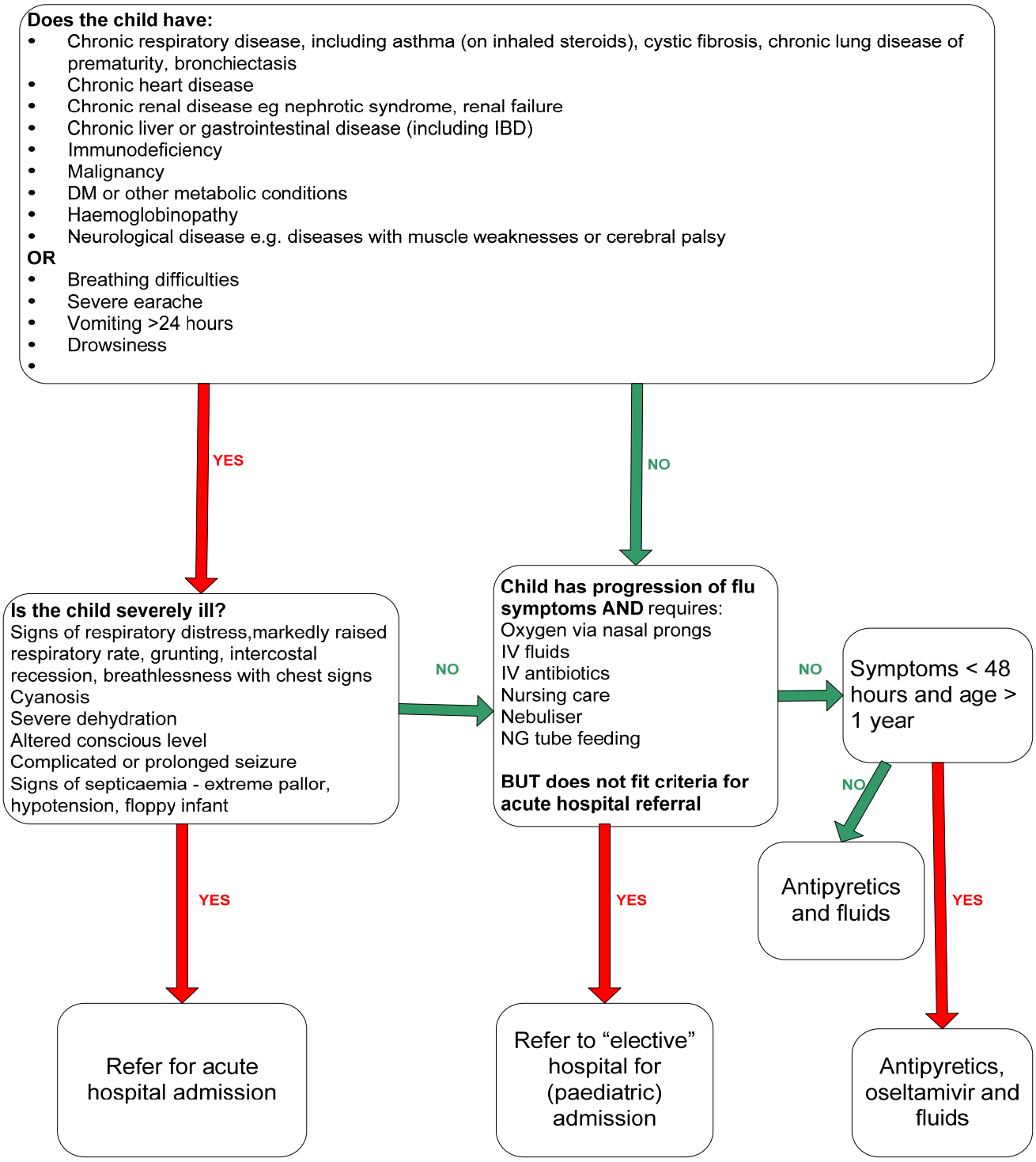
NOTE: Those with a pre-morbid medical condition and progression of flu symptoms should be referred to an acute hospital, rather than an elective hospital

For those suitable for home treatment:

- **Prescribe antivirals** if fever >= 38ºC/100.4ºF and symptomatic for <48 hours: Oseltamivir 75mg every 12 hours for 5 days (Dose to be reduced by 50% if creatinine clearance is less than 30ml/minute)
- **Consider prescription for "delayed prophylactic" antibiotics** to be used if no improvement after 24 hours or there is worsening of symptoms: Doxycycline 200mg stat and 100mg od PO or Co-amoxiclav 625mg tds PO (for one week)
- **Provide advice** on infection control, use of antipyretics, when there is a need to re-consult and fluid intake

If medically suitable for home treatment, but inadequate social supports are in place, refer to HSE communal home

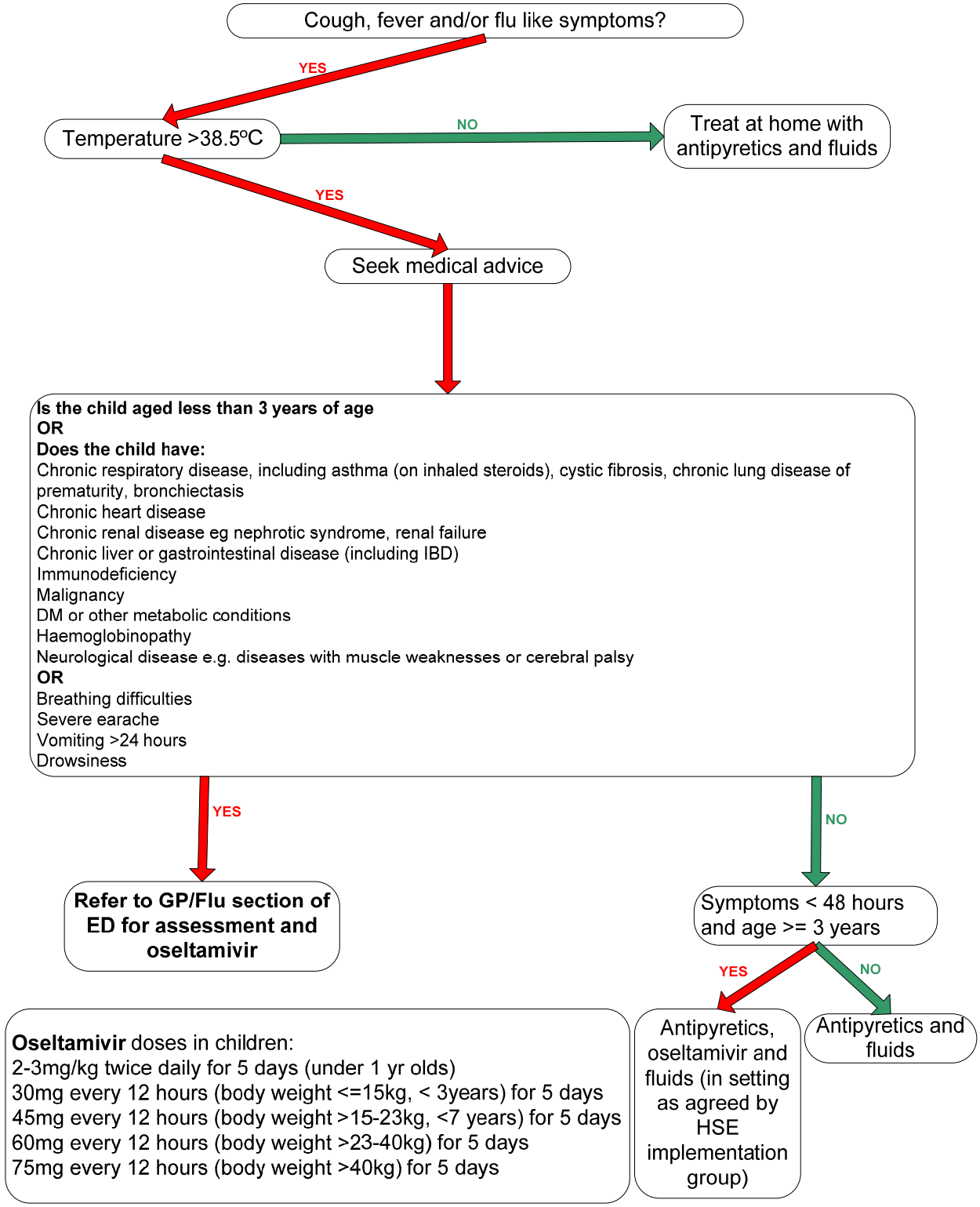
Appendix 4 GP/Emergency Department assessment and management of children



Appendix 5 Paediatric Respiratory Distress Severity Assessment

	Mild	**Severe**
Infants	Temperature <38.5^{o}C	Temperature >38.5^{o}C
	Respiratory rate <50 breaths per min	Respiratory rate >70 breaths per min
	Mild recession	Moderate to severe recession
	Taking full feeds	Nasal flaring
		Cyanosis
		Intermittent apnoea
		Grunting respiration
		Not feeding
Older children	Temperature <38.5^{o}C	Temperature > 38.5^{o}C
	Resp rate < 50 breaths per min	Resp rate > 50 breaths per min
	Mild breathlessness	Severe difficulty in breathing
	No vomiting	Nasal flaring
		Cyanosis
		Grunting respiration
		Signs of dehydration

Appendix 6 Initial assessment and management of children



Appendix 7 Summary of Antibiotic guidelines for adults and children

- The most common causes of secondary bacterial pneumonia in patients with influenza are S. pneumoniae and S. aureus. Other bacterial causes include Haemophilus influenzae and group A Streptococci.

- These are empirical guidelines only. When a pathogen has been identified, local microbiological advice should always be sought and therapy should be modified once the results from cultures are obtained.

- Reference should be made to a specialist text (e.g. BNF, or IPHA Compendium of Medicines, available at www.medicines.ie) for the antibiotic management of women who are pregnant or lactating and for those with renal or hepatic impairment.

  In case of severe or complicated infection, expert advice should be sought.

1. Adult Recommendations

1.1 Oral Antibiotic management of adults in the community

One of the following:

- Co-amoxiclav 625mg orally, 3 times daily for 7 days
- Cefuroxime 500mg orally, 2 times daily for 7 days
- Doxycycline 200 mg stat and 100mg orally 2 times daily, for 7 days

Alternative (for those intolerant or hypersensitive to preferred regimen above)

Clarithromycin 500mg orally, 2 times daily for 7 days

1.2 Oral Antibiotic management of hospitalised adults:

Guidelines for inpatient management should be according to the existing hospital policy for the management of Community Acquired Pneumonia (CAP). Special attention should be made to ensure that adequate S. aureus coverage is included in the regimen.

Suggestions include the following:

- Co-amoxiclav 625 orally, 3 times daily for 7 days
- Doxycycline 200mg orally stat, then 100mg orally 2 times daily for 7 days.

Alternatives include:

- Clarithromycin 500 mg orally, 2 times daily for 7 days
- Cefuroxime 500mg orally, 2 times daily for 7 days
- Moxifloxacin 400mg orally, once daily for 5 days or
- Levofloxacin 750mg orally, once daily for 5 days.

1.3 Intravenous Antibiotic management of hospitalized adults

One of the following:

- Co-amoxiclav 1.2g IV, 3 times daily
- Cefuroxime 1.5g IV, 3 times daily
- Cefotaxime 1g IV, 3 times daily
- Ceftriaxone 1g IV, once daily

PLUS Clarithromycin 500mg IV or orally, 2 times daily

In critically ill patients (i.e. ICU admission) when Meticillin Resistant S. aureus (MRSA) is suspected (or confirmed) one of the following should be added:

- Vancomycin 15mg/kg IV, 2 times daily or
- Linezolid 600mg IV or orally, 2 times daily

2. Paediatric Recommendations

2.1 Oral Antibiotic management of children in the community

(symbolises that you can double the dose in severe infections)*

One of the following:

Co-amoxiclav (orally for 7 days)

- 0-12 months — 0.25ml/kg of 125/31 suspension, 3 times daily
- 1-6 years — 5ml of 125/31 suspension*, 3 times daily
- 7-12 years — 10mls of 125/31 suspension*, 3 times daily
- 12-18 years — one tablet of 250/125 strength, 3 times daily

Co-amoxiclav *Augmentin Duo* formulation (orally for 7 days)

- 2 months- 2 years — 0.15ml/kg of 400/57 suspension*, 2 times daily
- 2-6 years (13-21kg) — 2.5mls of 400/57 suspension*, 2 times daily
- 7-12 years (22-40kg) — 5mls of 400/57 suspension*, 2 times daily

Clarithromycin (orally for 7 days)

- <8 kg — 7.5mg/kg of 125mg in 5ml suspension, 2 times daily
- 8-11 kg — 62.5mg of 125mg in 5ml suspension, 2 times daily
- 12-19 kg — 125mg 125mg in 5ml suspension, 2 times daily
- 20-29 kg — 187.5mg 125mg in 5ml suspension, 2 times daily
- ≥ 30 kg — 250mg of 250mg in 5 ml suspension, 2 times daily
- >10 years — 250 mg tablet, 2 times daily

Cefuroxime as *cefuroxime axetil* (orally for 7 days)

- 3-24 months — 10mg/kg (to a maximum of 125mg) 2 times daily
- 2-12 years — 15mg/kg (to a maximum of 250mg) 2 times daily
- 12-18 years — 500mg tablet, 2 times daily

Alternatives (should be swallowed whole with adequate fluids)

Doxycycline (for those >12yo, orally for 7 days)

- 12-18 years — 200mg on first day and then 100mg daily.

2.2 Oral Antibiotic management of children who are hospitalised:

Recommendations are as above.

2.3 Intravenous Antibiotic Management of children who are hospitalised:

- Guidelines for inpatient management should be according to the existing hospital policy for the management of Community Acquired Pneumonia (CAP).
- Special attention should be made to ensure that adequate S. aureus coverage is included in the regimen. Once susceptibility results are available the drug regimen should be rationalised, if possible.
- Intravenous to oral switch should also be considered if the child has made sufficient clinical improvement.

Any one of the following schedules can be used:

Paediatric intravenous dosing schedules
(* symbolises that you can double the dose in severe infection)

- Co-amoxiclav IV
  - < 7 days 30mg/kg, 2 times daily
  - 7-28 days 30mg/kg, 3 times daily
  - 1-3 months 30mg/kg, 3 times daily
  - 3-12 months 30mg/kg, 3 times daily (severe cases: 4 times daily)
  - 12-18 years 1.2g, 3 times daily (severe cases: 4 times daily)

- Cefuroxime IV
  - < 7 days 25mg/kg, 2 times daily*
  - 7-21 days 25mg/kg, 3 times daily*
  - 21-28 days 25mg/kg, 4 times daily*
  - 1 month-18 years 20-30mg/kg, 3 times daily*

- Cefotaxime IV
  - < 7 days 25mg/kg, 2 times daily*
  - 7-21 days 25mg/kg, 3 times daily*
  - 21-28 days 25mg/kg, 4 times daily*
  - 1 month-18 years 50mg/kg, 3 times daily (severe cases: 4 times daily)

- Ceftriaxone IV
  - Do not give to neonates
  - <50kg 50mg/kg, once daily
  - >50 kg 1g, once daily

- Clarithromycin IV
  - if possible give orally, but if it must be given intravenously
  - 1 month-12 years 7.5mg/kg, 2 times daily
  - 12-18 years 500mg, 2 times daily

In children who are critically ill (i.e. requiring ICU admission), when Methicillin Resistant S. aureus is suspected (or confirmed), Vancomycin or linezolid should be added. Expert advice should be sought from a medical microbiologist or infectious disease physician.

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10 Health system response: Infection Control

10.1 Introduction

This chapter provides an overview of current information regarding influenza infectivity, modes of transmission and best practice for infection control for pandemic influenza in the acute care, primary care, and other institutional settings. Adherence by all health care workers to good infection control practices is extremely important to prevent and limit transmission of influenza as well as many other infectious diseases. Key infection control precautions such as hand hygiene, use of appropriate personal protective equipment (PPE), separation or cohorting of symptomatic patients, and appropriate environmental cleaning are applicable for all infectious diseases. Detailed guidance to accompany this chapter is provided in the appendix titled "Guidance for Pandemic influenza: Infection control in hospitals, community and primary care settings". Information for the public on prevention and control of infection is detailed in Chapter 7.

Infection control guidance for avian influenza and other novel virus infections is dealt with separately in Chapter 11.

10.2 Limitations to the infection control guidance

In advance of a pandemic virus emerging, it is not possible to know its infectivity, pathogenicity, mode(s) of transmission, virulence, susceptibility of subgroups of the population, or period of communicability (infectious period).

We are assuming that:
The modes of transmission, incubation period and period of communicability are similar to seasonal influenza.

10.3 Key facts

10.3.1 Identification of Influenza

Influenza is an acute viral illness of the respiratory tract characterised by fever, headache, myalgia, prostration, coryza, sore throat and cough. Cough is often severe and protracted. Recovery usually occurs within 2-7 days. Gastrointestinal symptoms, such as nausea, vomiting and diarrhoea can accompany the illness particularly in children. The most common complication is pneumonia.

10.3.2 Incubation period

The incubation period is short, typically two days with a range of one to four days.(1)

10.3.3 Period of communicability

Persons are infectious from 24 hours pre onset of symptoms and during the most symptomatic period, usually three to five days from clinical onset in adults and up to seven days or longer in young children. Peak shedding occurs during the first 24-72 hours of illness and declines within several days. Shedding does not usually continue once the clinical illness has resolved. Duration of shedding is likely to be shorter with the use of antivirals. There is very limited information on transmission of infection in those who are in the incubation period of the disease. In a recent review article, the WHO writing group identified only one published report in which transmission occurred during the incubation period in a group of adults in New Zealand in 1991.(2)

10.3.4 Survival of virus

Studies have shown that it survives for 24-48 hours on hard, non-porous surfaces, eight to 12 hours on cloth, paper and tissue and five minutes on hands. When it is cold and humidity is low, survival of the virus is enhanced.(3)

10.3.5 Susceptibility

Susceptibility is general. It is expected that no one will have any immunity to the pandemic virus. It is not possible to predict in advance which subgroups of

the population will be at higher risk of infection. For planning purposes, WHO has recommended that planners aim for an infection rate of 50% and a clinical attack rate of 25%.

10.3.6 Mode of transmission

Animal studies and most influenza outbreaks amongst humans suggest that virus laden large droplets generated when infected persons cough or sneeze are the predominant mechanism of influenza virus transmission.(4) There is also some evidence for transmission via contaminated hands, other surfaces or fomites, and for transmission via droplet nuclei (airborne transmission). Overall information on transmission is limited, and there are no human experimental studies published in English delineating person-to-person transmission of influenza.

Salgado et al summarised the findings of 12 outbreaks of nosocomial influenza outbreaks.(5) In each of the outbreaks, the droplet and/or contact precautions, in conjunction with the use of antivirals, vaccines, and isolation were used to control spread. Airborne precautions were not used.

Bean et al investigated the transmission of influenza viruses via hands and environmental surfaces.(3) They found that human influenza viruses survived for 24-48 hours on hard non-porous surfaces such as stainless steel and plastic, but survived less than 8-12 hours on cloth, paper and tissues. They calculated that persons shedding significant quantities of virus could transmit infection via stainless steel surfaces for two hours and possibly up to eight hours, and via paper tissues for a few minutes (essentially before drying of the tissue). They also found that viruses survived on hands for up to five minutes after transfer from environmental surfaces. In an outbreak in Hawaii, transmission of oral secretions from patient to patient by staff not wearing gloves explained transmission in the outbreak.(6)

There is some limited evidence showing possible airborne transmission. In a point source outbreak due to an infected passenger on a delayed airplane with a non-functioning ventilation system, there was a 72% clinical attack rate

among those sitting throughout the cabin, the risk related to the amount of time spent on the airplane.[7] However as passengers moved freely around the cabin at that time, it's possible that large droplet transmission also occurred.

Recently a systematic review of the (English language) literature on modes of transmission of influenza A was carried out[8] Following initial searching, and consideration, 32 articles, including 8 relating to virus survival, 15 experimental and 9 outbreak reports were reviewed. They concluded that existing data are limited with respect to the identification of specific modes of transmission in the natural setting, but that transmission occurs at close range rather than over long distances, suggesting that airborne transmission is unlikely to be of significance in most clinical settings. Most natural influenza transmission occurs primarily through the droplet and contact routes.

10.4 Recommended infection control measures

The balance of evidence points to droplet and direct and indirect contact as the most important routes of transmission. Airborne, or fine droplet transmission, may also occur.

The Expert Group advises that Standard Infection Control Precautions and Droplet Precautions are the principal infection control strategies that should be rigorously followed for pandemic influenza.

In certain circumstances (during aerosolising procedures) these control measures will need to be augmented with higher levels of respiratory protection i.e. through the use of Airborne Precautions. This approach is the same as the approach being promoted by WHO and the UK.

As nebulisation is an aerosolising procedure, the Expert Group advises that the use of nebuliser therapies should be minimised wherever feasible without compromising patient care. To avoid unnecessary exposures, only those health care workers needed to perform the procedure should be present. See Supplement 10:5.3.3

Prevention of influenza transmission in healthcare settings is based on:

- Strict adherence to infection control practices especially hand hygiene, containment of respiratory secretions and the use of personal protective equipment (PPE)
- Adherence to Standard Infection Control Principles and Droplet Precautions
- Administrative controls e.g., separation or cohorting of patients with pandemic influenza.
- Restriction of symptomatic workers and visitors
- Education of staff, patients and visitors

Hand hygiene is the single most important practice to reduce the transmission of infectious agents in the healthcare and the community setting. A universal respiratory hygiene strategy is an essential component of any healthcare organisation's preparedness plan for pandemic influenza. This strategy, which is outlined in Appendix A, includes the following elements:

- Posting of visual alerts for all patients or visitors to inform staff and take precautions if they have respiratory symptoms
- Providing a surgical mask for those with respiratory symptoms, or tissues if unable to use mask, and separating them from other patients
- Providing adequate handwashing facilities in the waiting area, tissues and disposal bins
- Using barriers at registration to protect staff from symptomatic patients' respiratory secretions

The Expert Group advises that a universal respiratory hygiene strategy is adopted in all healthcare facilities.

In the community setting it is very important that the public is aware of how to minimise potential influenza transmission through the following:

- Cover nose and mouth with disposable single-use tissues when sneezing, coughing, wiping and blowing nose
- Dispose of used tissues in the nearest waste bin
- Wash hands after coughing, sneezing, using tissues, or contact with respiratory secretions and contaminated objects
- Keep hands away from the mucous membranes of the eyes and mouth
- If sick with flu, stay at home to avoid spreading infection to others

The Expert Group advises that the communications materials for the public contain these important messages on minimising transmission of influenza.

The use of PPE is detailed in Supplement 10. PPE should be worn to protect staff from contamination with body fluids and thus reduce the risk of transmission of pandemic influenza between patients and staff and from one patient to another. It is very important that staff are trained in the proper use of PPE, including fit testing of respirators, if they will be carrying out aerosolising procedures.

In order to minimise the risk of spread of infection, patients with influenza should be separated from other non-influenza infected patients. This will require considerable planning in advance.

Education of staff, patients and visitors on influenza, its symptoms and prevention of transmission is essential. In addition, staff need to be familiar with the pandemic influenza plans for their healthcare institution, and his/her role in them.

The Expert Group recognises that full implementation of the infection control guidance will be challenging, particularly in primary care settings, and advises that adequate resources are provided by the system to facilitate implementation of these recommendations.

Detailed guidance providing specific recommendations, planning strategies, and tools for local public health and healthcare staff are provided in Supplement 10. This guidance includes sections on preparedness planning, occupational health, infection control precautions, and environmental infection control, as well as sections focusing on hospital, community and primary care specific-issues separately. This guidance is based on and adapted from Guidance developed by the Department of Health, England and the Health Protection Agency, with permission.

10.5 Reference List

(1) Morris JA, Kasel JA, Saglam M, Knight V, Loda FA. Immunity to influenza to antibody levels. N Engl J Med 1966; 274(10):527-535.

(2) World Health Organization Writing Group. Nonpharmaceutical interventions for pandemic influenza, international measures. Emerg Infect Dis [serial on the Internet] 2006; 12(01).

(3) Bean B, Moore BM, Sterner B, Peterson LR, Gerding DN, Balfour HH, Jr. Survival of influenza viruses on environmental surfaces. J Infect Dis 1982; 146(1):47-51.

(4) Bridges CB, Kuehnert MJ, Hall CB. Transmission of influenza: implications for control in health care settings. Clin Infect Dis 2003; 37(8):1094-1101.

(5) Salgado CD, Farr BM, Hall KK, Hayden FG. Influenza in the acute hospital setting. Lancet Infect Dis 2002; 2(3):145-155.

(6) Morens DM, Rash VM. Lessons from a nursing home outbreak of influenza A. Infect Control Hosp Epidemiol 1995; 16(5):275-280.

(7) Moser MR, Bender TR, Margolis HS, Noble GR, Kendal AP, Ritter DG. An outbreak of influenza aboard a commercial airliner. Am J Epidemiol 1979; 110(1):1-6.

(8) Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. Lancet Infect Dis 2007; 7(4):257-265.

Appendix A Universal Respiratory Hygiene

The following are components of a universal respiratory hygiene strategy to be adopted in all health care facilities.

- The posting of visual alerts at the entrances to all healthcare facilities, instructing patients and those who accompany them to:
    - Inform healthcare personnel of symptoms of a respiratory infection when they first register for care
    - Practice respiratory hygiene
    - Advise visitors with respiratory symptoms to defer their visit until symptoms have resolved
- All patients and visitors who have symptoms of an infectious respiratory illness (cough, runny nose, sore throat or sneezing) should be provided with a surgical mask and instructions on its proper use and disposal. They should also be provided with instructions on hand-hygiene.
- For those who cannot wear a mask, provide tissues and instructions on when to use them (i.e. when coughing, sneezing, or controlling nasal secretions), where they should be disposed of, and on the importance of hand-hygiene after using them
- Waste bins should be readily available for disposal of tissues.
- Provide hand-hygiene materials in the waiting room areas and encourage persons with respiratory symptoms to perform hand-hygiene
- Instruct registration, reception and triage staff of their risk of exposure to infections spread by droplets and to consider wearing masks whenever registering or assessing patients who have respiratory symptoms and are not wearing a mask. Instruct them to remain at least three feet from unmasked patients.
- Consider the use of Plexiglas barriers at the point of triage or registration to protect healthcare personnel from contact with respiratory droplets.
- Where possible, designate an area, cubicle or separate room in waiting areas where patients with respiratory symptoms can be segregated (ideally by at least 3 three feet) from others without respiratory symptoms.

- Commonly used surfaces such as door handles, handrails, table surfaces etc. should be cleaned first and then disinfected with a chlorine releasing disinfectant (1000 ppm) twice daily.
- Use droplet precautions to manage patients with respiratory symptoms until it is determined that the cause of the symptoms is not an infectious agent that requires more than standard precautions.

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11 Influenza in animals and human health implications

11.1 Introduction

Avian influenza (AI) has become a disease of great importance for animal and human health. The number of outbreaks of AI in poultry has increased sharply over the past five years compared to the number reported for the previous 40 years. Between 1999 and 2005 more than 200 million birds have been involved in outbreaks.(1) These outbreaks have lead to major consequences for the poultry industry in affected countries. There is also growing concern about the pandemic threat posed by AI. This risk posed to human health and the epidemiological features of confirmed human cases have been discussed in Chapter 3 (section 3.5).

This chapter describes AI, surveillance activities, agriculture contingency plans for dealing with an outbreak, as well as the public health management of an avian outbreak. It provides guidance on surveillance and management of human cases and their contacts. Finally it also provides information on influenza in other animals.

11.2 Avian Influenza in birds

AI can occur in most, if not all species of birds. Waterfowl (wild and domesticated) are the major natural reservoir of influenza viruses. All available evidence suggests that primary introduction of influenza viruses into an area is a result of waterfowl activity. Wild waterfowl are usually asymptomatic, may excrete virus for long periods, may be infected with more than one type, and often do not develop a detectable antibody response.

Commercial ducks have frequently been shown to be infected with influenza viruses, but this has rarely been associated with disease in the ducks because of the marked resistance these birds show, even to strains that are highly virulent for chickens and turkeys (e.g. Ireland influenza outbreak in 1983).

Influenza A viruses that infect poultry can be divided into two groups, according to the severity of the disease that they cause. These groups are Highly Pathogenic Avian Influenza (HPAI) and Low Pathogenic Avian Influenza (LPAI). HPAI viruses cause high mortality (>75%) in poultry, whereas LPAI cause only mild symptoms. HPAI viruses so far have been restricted to A/H5 and A/H7 A subtypes, although not all A/H5 and A/H7 are highly pathogenic. While HPAI is lethal in domestic birds (chickens and turkeys) it has a variable clinical effect in domestic waterfowl and wild birds. HPAI has only been associated with mortalities in wild birds in the case of A/H5N3 in common terns (South Africa, 1961) and in various species but particularly waterfowl and some scavenging birds during the current A/H5N1 panzootic (Asia, Africa and Europe, 2004-2007). LPAI viruses exist in nature and wild bird populations, particularly waterfowl. They can be of any subtype A/H1-16. They cause a localised infection that results in sub-clinical or mild disease, primarily respiratory disease, depression, and egg production problems. However, some low pathogenic strains of A/H5 and A/H7 have mutated to become HPAI following circulation among domestic poultry.

11.3 Surveillance of AI: international and national prevalence data

Comprehensive surveillance of AI is necessary not only for animal health, but also to provide early warning of new strains in animals, which might pose a threat to human health. Internationally and nationally, much work is underway to strengthen animal surveillance.

11.3.1 Worldwide surveillance

The World Organisation for Animal Health (OIE) collects analyses and disseminates information on animal diseases from 169 countries worldwide, with the aim of increasing transparency globally. Up until 2006, only HPAI outbreaks were notifiable to the OIE. In 2006 the OIE Code was amended to make LPAI H5 and H7 outbreaks notifiable.

Table 11.1 below lists the outbreaks of HPAI in poultry that are known to have occurred from 1959 to date (October 2007). Of all the HPAI outbreaks recorded worldwide, the most recent HPAI H5N1 panzootic is unprecedented

in terms of severity of disease in birds, range of bird and other animal species affected and geographical extent of disease. Sixty countries on three continents (Asia, Europe and Africa) have been affected by the disease.

Table 11.1. Known outbreaks of HPAI in poultry 1959-2007 (adapted from WHO)

Year	Area	Affected	Strain
1959	Scotland	chicken	H5N1
1963	England	turkey	H7N3
1966	Ontario (Canada)	turkey	H5N9
1976	Victoria (Australia)	chicken	H7N7
1979	Germany	chicken	H7N7
1979	England	turkey	H7N7
1983	Pennsylvania (USA)*	chicken, turkey	H5N2
1983	Ireland	turkey	H5N8
1985	Victoria (Australia)	chicken	H7N7
1991	England	turkey	H5N1
1992	Victoria (Australia)	chicken	H7N3
1994	Queensland (Australia)	chicken	H7N3
1994	Mexico*	chicken	H5N2
1994	Pakistan*	chicken	H7N3
1997	New South Wales (Australia)	chicken	H7N4
1997	Hong Kong (China)*	chicken	H5N1
1997	Italy	chicken	H5N2
1999	Italy*	turkey	H7N1
2002	Hong Kong (China)	chicken	H5N1
2002	Chile	chicken	H7N3
2003	Netherlands*	chicken	H7N7
2003 (ongoing)	Asia, Europe, Africa*	multiple species	H5N1
2004	British Columbia (Canada) Pakistan	chicken	H7N3
2006	South Africa	ostrich	H5N2
2007	Saskatchewan (Canada)	Chicken	H7N3
2008	England	Chicken	H7N7

**Outbreaks with significant spread to numerous farms, resulting in great economic losses. Most other outbreaks involved little or no spread from the initially infected farms.*

Table 11.2 below shows the number of outbreaks of HPAI H5N1 that have been detected in poultry and wild birds in EU Member States since the virus it was first introduced in February 2006.

Table 11.2 Outbreaks of HPAI H5N1 detected in poultry and wild birds in the EU during 2006 and 2007

	HPAI H5N1 in poultry 2006	**HPAI H5N1 in poultry 2007**	**HPAI H5N1 in wild birds 2006**	**HPAI H5N1 in wild birds 2007**
Austria			117	
Belgium				
Bulgaria				
Cyprus				
Czech Republic		4	14	1
Denmark	1		43	
Estonia				
Finland				
France	1		62	3
Germany	1	6	331	227
Greece			32	
Hungary	29	2	16	
Ireland				
Italy			16	
Latvia				
Lithuania				
Luxembourg				
Malta				
Netherlands				
Poland		9	64	1
Portugal				
Romania	172			
Slovakia			2	
Slovenia			28	
Spain			1	
Sweden	1		21	
UK		3	1	
	205	**24**	**748**	**233**

The Food and Agriculture Organisation (FAO) provides policy advice, strategy design, technical information and guidelines, contingency planning and technical assistance, training, equipment and supplies such as laboratory equipment, vaccines, agency and donor coordination and public advocacy in relation to AI. It works hand in hand with the OIE and, because of the threat to human health, the WHO. FAO has carried out many missions to HPAI H5N1 affected countries and produces regular bulletins on the situation worldwide.

11.3.2 EU surveillance

The EU introduced active surveillance for AI in poultry in 2003, with the initial aim of determining the prevalence of LPAI A/H5 and A/H7 subtypes. Surveillance in wild birds was initially voluntary, but became compulsory in September 2005, when HPAI H5N1 spread from Asia into Eastern Europe. In September 2005 the EU surveillance programme was extended to include healthy wild birds and a list of target species - in which HPAI H5N1 had been detected, was created - with the additional objective of having an early warning system for the introduction of H5N1 into poultry.

The results of the EU surveillance programmes may be found on the website of DG SANCO at the following address: http://ec.europa.eu/food/animal/diseases/controlmeasures/avian/eu_resp_surveillance_en.htm

11.3.3 Surveillance in Ireland

The Department of Agriculture Fisheries and Food (DAFF) has had a serological monitoring programme for avian influenza in place since 1995. The programme is part of the Poultry Health Programme, and monitors commercial breeding poultry just before they come into lay, and when they move between sites. In addition all blood samples from clinically affected poultry are sent for serological testing. Approximately 20,000 samples are tested each year. Since 2003, DAFF has also taken part in the annual EU survey for avian influenza in poultry and wild birds. The survey in poultry includes turkeys and ducks reared for meat, free-range broilers, commercial

egg layers and breeding flocks. The wild bird survey includes birds found dead and birds that have been shot. The results of the surveys from 2003 to 2007 are shown in **Tables 11.3** and **11.4** below.

Table 11.3. Results of AI survey in commercial poultry in Ireland (2003-2007)

	No. poultry holdings sampled	**No. poultry holdings positive for A/H5 or A/H7**
2003	248	0
2004	321	0
2005	305	0
2006	306	0
2007	302	0

Table 11.4. Results of AI survey in wild birds in Ireland (2003-2007)

	No. wild birds sampled	**No. samples positive**
2003	449	1 pool (H10)
2004	360	H6, H10, H11
2005	757	12 (not H5 or H7)
2006	1070	2(H11) 1 (H5)
2007	728	3 (H5), 1 (not H5 or H7)

The last outbreak of HPAI occurred in 1983. Since 1987, there have been several outbreaks of LPAI in poultry in Ireland. A number of LPAI isolates of have also been detected in wild birds as a result of the EU survey. To date none of these has been an A/H7 subtype. A/H5 subtypes have been detected in two wild shot teal submitted as part of the active survey in hunted birds during the winters of 2006/2007 and 2007/2008. The list of isolates is set out in **Table 11.5** below:

Table 11.5: Avian Influenza Isolates Detected in Ireland (1983 to June 2007)

Year	Subtype	Pathogenicity	Isolated from
1983	H5N8	HPAI	2 commercial turkey flocks 1 broiler flock 1 breeding/commercial duck flock
1987	H9N2	LPAI	1 turkey breeder flock
1989	H7N7	LPAI	1 broiler breeder flock 1 commercial turkey flock
1991	H6N2	LPAI	1 broiler breeder flock
1993	H3N8 H9N3	LPAI LPAI	1 imported mallard duck consignment in quarantine
1995	H7N7	LPAI	2 commercial turkey flocks
1997	H9N2	LPAI	1 breeding pheasant flock
1998	H7N7	LPAI	28 commercial turkey flocks 1 broiler breeder flock
2003*	H10N5	LPAI	wild mallards
2004	H6N6 H10N7 H11N9	LPAI LPAI LPAI	wild widgeon wild mallards wild mallards
2005	Not H5 or H7	LPAI	
2006	H11 H5	LPAI LPAI	exotic duck in private collection wild teal
2007	H5	LPAI	wild teal

*first year of survey in wild birds

11.4 Laboratory testing of avian and mammalian influenza viruses

The Central Veterinary Research Laboratory (CVRL), Backweston, Co. Kildare maintains a capability for virus isolation and identification of avian and mammalian influenza viruses. It also has the capacity and expertise for serological identification of antibodies to these viruses in the different species. Virus isolates from avians are submitted to the EU reference laboratory (Weybridge) in accordance with Directive requirements for further biotyping. Isolates from pigs are submitted to specialist laboratories for additional typing. Thus effectively a monitoring programme for all animal viruses is in operation from the CVRL. This allows for accurate diagnosis and the implementation of appropriate control measures.

The CVRL is the EU National Reference Laboratory for Avian influenza and at an international level participates in proficiency tests organized by the European (EU) Reference Laboratory for Avian Influenza.

11.5 Veterinary Control Measures for AI in birds

EU legislation exists for the control of avian influenza in birds. The specific control measures that must be applied will depend on whether the virus is confirmed in poultry/captive birds or in wild birds, whether the virus is a highly pathogenic or low pathogenic strain, and whether or not the subtype involved is H5N1.

Council Directive 2005/94/EC lays down the rules for the control of HPAI and LPAI in poultry or captive birds.

Avian influenza is defined as *"an infection of poultry or other captive birds caused by any influenza A virus of the subtypes H5 or H7, or with an intravenous pathogenicity index (IVPI) in six-week old chickens greater than 1.2".*

HPAI is defined as an infection caused by *"avian influenza viruses of the subtypes H5 or H7 with genome sequences codifying for multiple basic amino acids at the cleavage site of the haemagglutinin molecule similar to that observed for other HPAI viruses, indicating that the haemagglutinin molecule can be cleaved by a host ubiquitous protease or avian influenza viruses with an intravenous pathogenicity index in six-week old chickens greater than 1.2".*

LPAI is defined as an infection caused by "*avian influenza viruses of subtypes H5 or H7 that do not come within the definition of HPAI*".

11.5.1 Controls when HPAI is confirmed

When HPAI is confirmed in poultry or other captive birds, the Directive requires that certain measures are applied on the infected premises and

additional measures are applied in a *protection zone* and *surveillance zone* in the area immediately surrounding the infected premises:

Infected premises

- Killing and disposal of all poultry/captive birds
- Cleaning and disinfection of the premises
- Destruction or treatment of manure, slurry and bedding
- Tracing and destruction of poultry meat and eggs produced during risk period
- Epidemiological investigation and tracing of high-risk contacts
- Prohibition on birds entering or leaving
- Controls on people, vehicles and other things entering or leaving
- Controls on re-stocking

Protection zone (minimum of 3 km radius from the infected premises)

- Identification of all poultry/captive bird holdings
- Clinical examination and testing of all commercial holdings
- Clinical examination of all non-commercial holdings
- Confinement of all poultry indoors
- Prohibition on bird fairs, markets, shows or other gatherings
- Prohibition on the release of game birds
- Controls on the movement of live poultry and eggs
- Controls on poultry meat originating from birds in the zone
- Biosecurity measures to be taken when people or vehicles are in contact with poultry, poultry carcases and eggs

Surveillance zone (minimum of 10 km radius from the infected premises)

- Identification of all poultry holdings
- Prohibition on bird fairs, markets, shows or other gatherings
- Prohibition on the release of game birds
- Controls on the movement of live poultry and hatching eggs
- Biosecurity measures to be taken when people or vehicles are in contact with poultry, poultry carcases and eggs

Controls must be kept in place for at least 30 days. Where movements are controlled, specific derogations are allowed, but only after a risk assessment and if appropriate biosecurity precautions are taken.

Additional measures such as a standstill on movements of poultry, preventive culling and vaccination in high-risk areas or in high-risk compartments (e.g. categories such as free-range birds, integrated companies) are also allowed for.

11.5.2 Controls when LPAI is confirmed

If LPAI is confirmed in poultry or captive birds, the Directive requires that some or all of the following measures are applied on the infected premises (as determined by a risk assessment), and measures are applied within a *restricted zone* around the infected premises:

LPAI infected premises

- Killing and disposal, or slaughter following testing, of all poultry
- Killing and disposal captive birds
- Cleaning and disinfection of the premises
- Destruction or treatment of manure, slurry and bedding
- Epidemiological investigation and tracing of high-risk contacts
- Tracing of hatching eggs produced during risk period, and official supervision of birds hatched from these
- Prohibition on birds entering and controls on birds leaving
- Controls on people, vehicles, table eggs and other things entering or leaving

Restricted zone (minimum of 1 km radius from the infected premises)

- Identification of all commercial poultry/captive bird holdings
- Clinical examination and testing of all commercial poultry holdings
- Prohibition on bird fairs, markets, shows or other gatherings
- Prohibition on the release of game birds

- Controls on the movement of live poultry and eggs
- Biosecurity measures to be taken when people or vehicles are in contact with poultry, poultry carcases and eggs

The controls apply for at least 21 days where the birds are killed and testing has been completed and no further risk exists, and 42 days if the birds are not killed.

11.5.3 Controls when HPAI H5N1 is confirmed

If H5N1 is confirmed in **poultry**, Commission Decision 2006/415/EC requires that a *protection zone and surveillance zone* are declared as for HPAI. These zones become *Area "A".* In addition a buffer zone must be declared between area "A" and the disease-free area of the country. This buffer zone is called *Area "B".* Movements of poultry, other captive birds, wild game birds, wild feathered game meat, poultry by-products and hatching eggs between and from these areas are controlled.

If H5N1 is confirmed in **wild birds**, Commission Decision 2006/563/EC requires that initially a *control area* (minimum 3 km radius) and *monitoring area* (minimum 10 km) are declared. The limits of the areas must then be re-assessed when the species of bird, its normal habitat, range etc. and the local environmental conditions are known. The size may then be decreased or increased accordingly.

11.5.4 Contingency Plan for AI in birds

In order to carry out the control measures as quickly as possible, a Contingency Plan has been prepared by DAF. The plan includes an operation manual, which contains chapters on the following:

- Suspect avian influenza
- Confirmed avian influenza
- Public health aspects
- Slaughter
- Disposal

- Cleaning and disinfection
- Slaughter plants
- Forms
- Advice leaflets
- Restriction notices
- Protocols for sampling
- Licensing

11.6 Public Health Management of AI outbreaks in birds

With progression of AI in wild birds into the EU, and occasional poultry outbreaks, considerable effort has gone into agreeing combined veterinary and public health working protocols for the public health management of an outbreak of avian influenza in Ireland. In Supplement 11, Guidance on Public Health Actions to be taken on Notification of Avian Influenza in Animals in Ireland is provided. This guidance is based on international guidance from WHO, ECDC, CDC and Canada. The guidance includes the agreed notification procedure between Agriculture and Public Health, management of contacts; guidance for those involved in avian influenza outbreak control activities, surveillance protocols, and public health advice leaflets for those affected and for the general public. These protocols have been tested in multi-agency exercises throughout Ireland, and are subject to ongoing review.

The Expert Group advises that close collaboration between veterinary and public health authorities at all levels, and joint working, protocol development etc. continue on an ongoing basis.

11.6.1 Prevention and clinical management

The possibility of A/H5N1 should be considered in all patients with severe acute respiratory illness. This includes travellers and visitors to AI affected countries as well as those with close contact with sick poultry or wild birds. An algorithm for assessment, referral and laboratory investigation has been prepared and is available in Supplement 11. Patients with suspected or proven A/H5N1 should be hospitalised in isolation for clinical monitoring,

appropriate diagnostic testing and antiviral therapy. Supportive care with provision of supplemental oxygen and ventilatory support is the foundation of management.

WHO recently produced rapid advice guidelines on pharmacological management of humans infected with A/H5N1.[2] The evidence was assessed according to the methodology described by GRADE, a methodological guideline process, which included evaluation of existing systematic reviews, literature searches and expert consultation. The quality of evidence was classified as high, moderate, low or very low based on the methodological characteristics of the available evidence. In addition recommendations were graded as strong or weak, where strong recommendations mean that most individuals should receive the intervention and weak evidence means that most would want the intervention, but many would not. These recommendations are:

- In patients with confirmed or strongly suspected H5N1 infection, clinicians should administer oseltamivir treatment as soon as possible (strong recommendation, very low quality evidence)
- In patients with confirmed or strongly suspected H5N1 infection, clinicians might administer zanamivir (weak recommendation, very low quality evidence)
- In patients with confirmed or strongly suspected H5N1 infection, who do not need mechanical ventilation and have no other indication for antibiotics, clinicians should not administer prophylactic antibiotics (strong recommendation, no quality grading provided)
- In patients with confirmed or strongly suspected H5N1 infection, who need mechanical ventilation, clinicians should follow clinical practice guidelines for the prevention or treatment of ventilator associated or hospital acquired pneumonia (strong recommendation, no quality grading provided)
- In pregnant patients with confirmed or strongly suspected infection with avian influenza A (H5N1) virus, clinicians should not administer

11.7 Infection control

Guidance for AI is based on that recommended by WHO, which should be consulted for detailed information.[3] A summary of some of the aspects is given below:

1. *All healthcare facilities should take standard infection control precautions, which include:*
   - Hand hygiene
   - PPE based on risk assessment and to avoid contact with blood, body fluids, excretions and secretions
   - Appropriate handling of patient care equipment and soiled linen
   - Prevention of needlestick/sharp injuries
   - Appropriate environmental cleaning and spills management
   - Appropriate handling of waste
2. *All healthcare facilities should implement respiratory hygiene*
   - Persons with respiratory infection should be educated to:
     - Cover their mouth and nose with a tissue when coughing and dispose of used tissue in waste containers
     - Use a mask if coughing, when a mask can be tolerated
     - Perform hand hygiene after contact with respiratory secretions
     - Sit or stand at least 1 metre (3 feet) from other persons if possible
   - Healthcare facilities should promote respiratory hygiene by:
     - Educating HCWs, patients, family members and visitors on the importance of containing respiratory aerosols and secretions to help prevent the transmission of influenza and other respiratory viruses
     - Posting signs requesting that patients and family members with acute febrile respiratory illness use respiratory hygiene

- Posting signs requesting that persons with acute febrile respiratory illness refrain from visiting the healthcare facility
- Considering making tissues and masks available so that source control measures can be used in common areas and areas used for the evaluation of patients with acute febrile respiratory illness. Areas where people gather such as waiting rooms should be prioritised
- Providing resources for hand hygiene in common areas. Areas where people gather such as waiting rooms should be prioritised.

3. *Early recognition, isolation and reporting of possible AI cases*

- Healthcare facilities should
  - Make it a priority to establish methods to ensure early recognition and investigation of possible AI cases (Algorithm, Supplement 11)
  - Initiate IC precautions promptly when AI is suspected
  - Report all possible cases immediately to the Medical Officer of Health, and provide all essential available information requested

- In Ireland, currently **without** known AI infections in animals or humans:
  - **Query** patients with severe acute febrile respiratory illness about travel to AI affected countries within the 2 weeks prior to symptom onset
  - **Consider** the diagnosis of AI in patients with severe acute febrile respiratory illness who have travelled to an AI affected country within the 2 weeks prior to symptom onset and who have had exposure to birds, to known or suspected AI infected patients, or to other severely ill people while in an AI affected country.

- If symptoms, travel and exposure history support the possibility of AI infection, such patients should be put under isolation precautions immediately

4. *Isolation precautions for suspected or confirmed AI-infected patients* (See WHO guidance for detailed description)[4]
   - Patient placement
     - Place the patient in an adequately ventilated (>= 12 air changes per hour) room (airborne infection isolation room) if available
     - If a single room is not available, suspected and confirmed AI patients may be cohorted separately in designated multi-bed rooms or wards
   - Cohorting
     - If single rooms are not available, patients infected with the same organisms can be cohorted. These rooms should be in a well-defined area that is clearly segregated from other patient-care areas used for uninfected patients. Suspected and confirmed cases should be housed separately
     - The distance between beds should be at least one metre.
     - HCWs assigned to cohorted patient care units should be experienced, and should not be assigned to other non-infected areas.
     - The number of persons entering the cohorted area should be limited to the minimum number necessary for patient care and support
     - HCWS should be aware that cohorted patients may be concurrently infected or colonised with other pathogens and should use standard and pathogen specific transmission based precautions where applicable
   - Barrier precautions for the care of patients with respiratory illness or suspected or confirmed AI

- In addition to standard precautions, all HCWs providing care for patients with acute febrile respiratory illness or suspected or confirmed AI should use PPE as per **Table 11.6**

5. *Duration of infection control precautions*
   - For adolescents > 12 years of age, and adults, implement precautions at the time of admission and continue for 7 days after resolution of fever.
   - For infants and adolescents <=12 years of age, implement precautions at time of admission and continue for 21 days after symptom onset.

The detailed guidance also covers recommendations regarding visits by family member/visitors, pre-hospital care and transport, waste disposal, environmental cleaning and disinfection, patient care equipment occupational health recommendations for HCWs, and care of the deceased.

11.8 Public health management of human cases of avian influenza A/H5N1 and their contacts

Guidance for the public health management of human cases of avian influenza A/H5N1 and their contacts has been prepared and are detailed in Supplement 11. This guidance includes case definitions of AI, the notification procedures to be followed when a case is suspected, establishment of outbreak control teams, media management, provision of information to the public and others, case surveillance requirements, and contact tracing.

Table 11.6. Barrier precautions for persons providing care for patients with acute febrile respiratory illness (AFRI, including patients with suspected or confirmed AI infection

Barrier precautions	**Application of barrier precautions depending on type of patient contact**			
	Close contact (<1 m/3ft) with patients with AFRI with no known AI risk factors*	Entry to AI isolation room/area, but no anticipated patient contact	Close contact (<1 m/3ft) with AI infected patient in or out of isolation room/area	Performance of aerosol generating procedure on AI patient [a, b]
Hand Hygiene [c]	Yes	Yes	Yes	Yes
Gloves	Not routinely [d]	Risk assessment	Yes	Yes
Apron	Not routinely	Risk assessment [e]	Not routinely [e]	Not routinely [f]
Gown	Not routinely	Risk assessment [e]	Yes [f]	Yes [f]
Hair cover	Not routinely	Not routinely	Not routinely	Optional
Surgical mask (on HCW)	Yes	Not routinely	Yes	Not routinely
Surgical mask (on patient)	Not routinely [i]	No	Not routinely[i]	No
Particulate respirator (min FFP2 or FFP3)	Not routinely	No	No	Yes[g]
Eye protection	Risk assessment	Risk assessment [h]	Yes	Yes

* Bird exposure in regions with AI infections in animals or exposure to AI-infected patients

a. Aerosol generating procedures create aerosols of different sizes (large and small-particle aerosols) Examples of aerosol-generating procedures include endotracheal intubation, aerosolised or nebulised medication administration, diagnostic sputum induction, bronchoscopy, airway suctioning, tracheostomy care, chest physiotherapy, nasopharyngeal aspiration, positive pressure ventilation via face mask (BiPAP, CPAP), high frequency oscillatory ventilation, post-mortem excision of lung tissue.
b. Where possible aerosol-generating procedures should be performed in adequately ventilated (>= 12 exchanges per hour) rooms, side rooms or other closed single-patient areas with minimal staff present. PPE should cover the torso, arms and hands as well as the eyes nose and mouth
c. Standard precautions are the minimum level of precautions indicated for all persons at all times
d. Gloves should be worn in accordance with standard precautions.
e. Gloves and gown or apron should be worn during cleaning procedures
f. If splashing with blood or other bodily fluids is anticipated, and gowns that are not fluid resistant are used, a waterproof apron should be worn over the gown.
g. If particulate respirator is not available, avoid aerosol-generating procedures as much as possible.
h. Use eye protection if close contact (<1 metre) with patient is possible
i. Provide surgical mask for patient (if tolerated) when patient is outside the isolation room/area.

11.9 H5N1 in other animals

11.9.1 A/H5N1 in cats

A number of papers have reported on avian influenza in cats. Keawcharon et al demonstrated that H5N1 caused severe pneumonia in tigers and leopards that fed on infected poultry carcasses.[5] Kuiken et al experimentally inoculated cats with H5N1 virus intrathecally and fed them virus-infected chickens.[6] The cats developed severe diffuse alveolar damage and transmitted the virus to sentinel cats. Rimmelzwaan et al reported that domestic cats can be infected by eating infected birds, and that infected cats can spread infection to other cats, most likely through faeces, urine and other secretions from the respiratory tract.[7]

However, cats probably have little or no contribution to the spread of the disease because the number of infected poultry is much higher than the number of infected cats; poultry shed much more virus than other animals. During an H5N1 outbreak it is recommended that domestic animals should be monitored for infection.

11.9.2 Equine Influenza

This disease is caused by two subtypes of virus H7N7 also known as A/equine 1 (prototype Prague/56), which is a H7N7 and A/equine 2 (Prototype Miami/63), which is a H3N8. The former does not appear to be prevalent currently and has not been isolated, since about 1979 although antibodies to this type have been detected in non-vaccinated horses born since that year. The H3N8 appears to have arisen from recombination from avian strains.

Equine influenza is endemic in most countries with significant equine populations, except Australia. Vaccination is widely practiced, using the H3N8 strains of virus in the vaccines. Antigenic shift continues and major epidemics occur, despite vaccination and the incorporation of recent isolates into vaccines.

Equine influenza is considered a production disease i.e. occurrences of the disease are not notifiable and there are **no official** measures specifically designed to control this disease in Ireland. Specific control measures, in the event of an outbreak are the responsibility of attending private veterinary practitioners.

Mandatory industry rules apply regarding vaccination and revaccination for competition horses in the thoroughbred industry. Vaccination in the presence of maternal antibodies appears not only to inhibit the serological response but also inhibits the response to future vaccinations. Vaccination reduces clinical disease due to the virus but does not prevent circulation of the virus or disease occurrence in the non-responders.

Major epidemics of equine influenza occur at periodic intervals e.g. Eastern Europe 1956; USA 1963; North America and Europe 1978-81, South Africa 1986, India 1987; China 1989 and 1993/94. The epidemic in China in 1989 involved an avian influenza virus A/Equine/Jilin/1/89 (H3N8), which had lost its ability to replicate in birds when it became infective for horses.
Equine influenza has never been known to infect man.

11.9.3 Swine Influenza

This disease is a scheduled and notifiable disease in Ireland (Class B). Two subtypes generally affect pigs - namely H1N1 and H3N2. Two main types of swine viruses are currently in circulation in Europe - the avian like H1N1 and a human/avian like H3N2. More recently a H1N2 has been detected in pigs in the UK, France, Italy and the Netherlands. These latter isolates contain a haemagglutinin, which is closely related to a human type of the early 80's. H1N7 has also been isolated from pigs in the UK associated with clinical disease.
Two types of virus have been isolated in Ireland - a H1N1 was isolated for the first time in November 1991, and H3N2 was isolated for the first time in June 1993. The H1N1 isolated in Ireland, is different from the strains circulating in Europe and elsewhere, and probably represents a separate introduction of an avian strain into Irish pigs. It is serologically related to Weybridge 79 and OMS/2899/82. The H3N2 virus isolated is serologically related to OMS/3633/84.
No evidence for the existence of H1N2 in Irish pigs has so far been detected.

11.9.4 Other Mammals

Other mammals can and do respond clinically to influenza infections notably mink, which have been affected with H10N4 in Sweden. H5N1 infection was confirmed in a Stone Marten that was found in the Rugen area of Germany where three cats were previously confirmed as having H5N1.
A mink infected with an H5 virus was found in late March 2006 in the Blekinge region of Southern Sweden, where several infected birds had also been found. It was thought to have contracted the virus by consuming infected wild birds, the suspected mode of transmission to felines as well.

11.10 References

(1) Capua I, Marangon S. Control of avian influenza in poultry. Emerg Infect Dis 2006; 12(9).

(2) WHO. WHO Rapid Advice Guidelines on Pharmacological Management of Humans Infected with Avian Influenza (H5N1) Virus. www.who.int . 2006.

(3) World Health Organisation. Avian Influenza, including Influenza a (H5N1), in humans: WHO interim infection control guideline for health care facilities. 2007.

(4) WHO Regional Offices for South East Asia and the Western Pacific. Practical Guidelines for Infection Control in Health Care Facilities. SEARO Regional Publication No 41. 2004.

(5) Keawcharoen J, Oraveerakul K, Kuiken T, Fouchier RA, Amonsin A, Payungporn S et al. Avian influenza H5N1 in tigers and leopards. Emerg Infect Dis 2004; 10(12):2189-2191.

(6) Kuiken T, Rimmelzwaan G, van Riel D, van Amerongen G, Baars M, Fouchier R et al. Avian H5N1 influenza in cats. Science 2004; 306(5694):241.

(7) Rimmelzwaan GF, van Riel D, Baars M, Bestebroer TM, van Amerongen G, Fouchier RAM et al. Influenza A Virus (H5N1) Infection in Cats Causes Systemic Disease with Potential Novel Routes of Virus Spread within and between Hosts. Am J Pathol 2006; 168(1):176-183.

Supplement 3

Modelling and Potential Impact

Supplement 3

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Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

hpsc

Modelling impact of pandemic influenza: interim report on use of empirical model in Ireland

December 2006

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Executive summary

- Various different mathematical models can be used in preparing for an influenza pandemic. For estimating health impact, an empirical model of pandemic influenza, based on the profile of previous UK pandemics, can be used in Ireland.

- This model can be 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.

- In the first scenario considered, a 25% clinical attack rate is assumed, yielding a total of 1,058,731 clinical cases in Ireland in the course of the pandemic with a peak of 228,200 predicted during week six.

    - Under scenario 1 assumptions, the model predicts a minimum total of 5,800 influenza-related hospitalisations over the 15 weeks with a peak of 1,250 predicted during week six.

    - Under scenario 1 assumptions, the model predicts a minimum total of 3,900 influenza-related deaths over the 15 weeks with a peak of 840 predicted during week six.

- In the second or worst case scenario, a 50% clinical attack rate is assumed, yielding a total of 2,117,463 clinical cases in Ireland in the course of the pandemic with a peak of 456,400 predicted during week six.

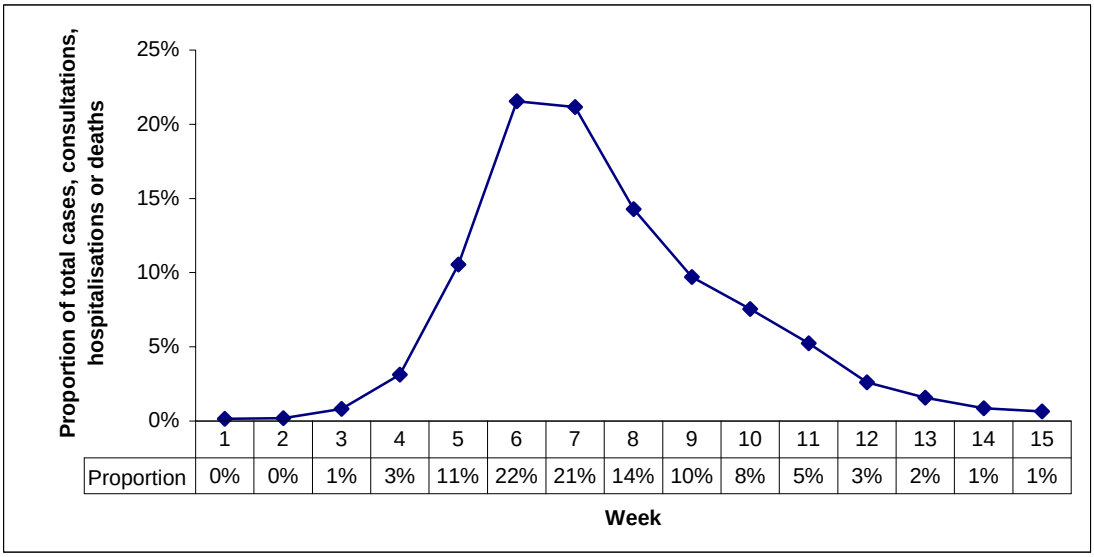
    - Under scenario 2 assumptions, the model predicts a minimum total of 78,300 influenza-related hospitalisations over the 15 weeks with a peak of 16,900 predicted during week six.

    - Under scenario 2 assumptions, the model predicts a minimum total of 52,937 influenza-related deaths over the 15 weeks with a peak of 11,400 predicted during week six.

1 Background

The Health Protection Agency (HPA) in the United Kingdom has adopted an empirical model of pandemic influenza for planning purposes.[1] The model is derived using data from three previous UK pandemics (1918, 1957, 1969/70).

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 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.

2 Model applied to Irish situation

Two different scenarios have been considered when deriving predictions from the empirical model. The first considers a clinical attack rate of 25%, a hospitalisation rate of 0.55% and a mortality rate of 0.37%. 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. All calculations in this section are based on the preliminary results of the 2006 census, which indicated a total Irish population of 4,234,925

2.1 Clinical Attack Rate: Scenario 1

A clinical attack rate of 25% has been assumed in scenario 1 to derive the predictions from the model. This is approximately equal to the clinical attack rates of the last three pandemics (1918, 1957, 1969).

2.1.1 Clinical Cases: Scenario 1

Assuming a 25% clinical attack rate yields a total of 1,058,731 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 228,189 (Table 1). The number of weekly cases rises sharply from 33,041 in week four to 111,705 in week five.

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**

Table 1: Weekly numbers of cases, hospitalisations and deaths as predicted by the empirical model assuming a 25% attack rate, a hospitalisation rate of 0.55% and a mortality rate of 0.37%

2.1.2 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 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 5,823 over the 15-week period (Table 1). The model predicts that approximately 1,250 hospitalisations would occur during both weeks six and seven of the pandemic (Table 1).

2.1.3 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 deaths in Ireland during a pandemic with a 25% clinical attack rate (Table 1).

2.2 Clinical Attack Rate: Scenario 2

A worst case clinical attack rate of 50% has been assumed in scenario 2 to derive the predictions from the model.

2.2.1 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 2). The number of weekly cases rises sharply from 66,082 in week four to 223,410 in week five.

Week	% of total cases	No. cases	Cases per 100,000 pop	Hospitalisations	Deaths
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
All weeks	**100%**	**2,117,463**	**50,000**	**78,346**	**52,937**

Table 2: Weekly numbers of cases, hospitalisations and deaths as predicted by the empirical model assuming a 50% attack rate, a hospitalisation rate of 3.7% and a mortality rate of 2.5%

2.2.2 Hospitalisations: Scenario 2

The HPA Influenza Pandemic Contingency Plan states that the numbers of hospitalisations and deaths predicted by the model under Scenario 1 should be considered the minimum expected for pandemic flu.[(3)]

Based on a worst case 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 15-week period (Table 2). The model predicts that

approximately 16,700 hospitalisations would occur during both weeks six and seven of the pandemic (Table 2).

2.2.3 Deaths: Scenario 2

If 2.5% of cases result in death there would be 52,937 deaths in Ireland during a pandemic with a 50% clinical attack rate (Table 2).

3 Model evaluation

3.1 Limitations

Limitations to this model include the following

- The pandemic is modelled as a single wave, and in reality more than one wave might occur.
- No attempt is made to quantify the impact of anti virals on the pandemic profile – it is likely that the use of anti virals would flatten the peak and widen the curve.[(2)] Other interventions may 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.
- This model assumes that 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.

3.2 Strengths

- This model is straightforward to use for different attack rates, hospitalisation and death rates.
- No assumptions are made regarding the nature of the virus itself in terms of infectivity etc.

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

4 References

1. Health Protection Agency. Influenza Pandemic Contingency Plan. www.hpa.org.uk . 2005.

2. Department of Health. UK operational framework for stockpiling, distributing and using antiviral medicines in the event of pandemic influenza. 2006.

3. Department of Health. UK Health Departments' Influenza pandemic contingency plan. www.doh.gov.uk/pandemicflu . 2005.

Modelling impact of pandemic influenza: Intensive Care Unit Requirements

December 2006

Table of Contents

1 Summary

- The figures shown in this report are estimates of the daily Intensive Care Unit (ICU) requirements in the event of an influenza pandemic. These estimates are based on predictions from the Health Protection Agency (HPA) empirical model.

- It is assumed that a 15-week single wave pandemic will involve a 25% Clinical Attack Rate (CAR) and that 0.55% of cases will require hospitalisation. Consideration is given to a range of Intensive Care Unit (ICU) admissions (5%, 15%, 25%) as a proportion of overall hospitalisations.

- Adopting an ICU rate of 15% of hospitalised cases, daily ICU bed requirements are considered, assuming varying length of ICU stay ranging from 2-10 days.

- Daily numbers of ventilators in use are considered over a range of ventilation requirements (25% -100% of ICU patients) and length of ICU stay (2 – 10 days) assuming that 15% of influenza-related hospitalisations require ICU care.

- A range of estimates is produced, depending on which assumptions are adopted. Assuming that 15% of influenza-related hospitalisations require critical care, new ICU admissions per day peak at 33 during week 6.

- Assuming that 15% of influenza-related hospitalisations require critical care, the peak number of ICU beds required nationally ranges from 64 (assuming 2 days length of stay) to 284 (10 days length of stay).

- The peak number of ventilators required per day ranges from 16 (assuming 25% of ICU patients require ventilation for a 2 day stay) to 284 (assuming 100% of ICU patients require ventilation for a 10 day stay).

- It is important to consider these estimates alongside the ICU resources available in Ireland in a pandemic situation.

- It is important to remember that all figures in this report are derived from a hospitalisation rate of 0.55%. This is the minimum rate that can be expected and therefore could be an underestimate of the true pandemic hospitalisation rate. Estimated daily hospitalisations based on a CAR of 50% and hospitalisation rate of 3.7% (a worst case scenario) are given in Appendix II.

2 Introduction

The report presented to the Pandemic Influenza Expert Group in January 2006 outlined three models used to estimate the impact of pandemic influenza in Ireland.([1]) The Health Protection Agency (HPA) empirical model has been adopted for planning purposes and provides estimates of weekly hospitalisations based on a 25% CAR and hospitalisation rate of 0.55% of cases.([1-3])

It is important to consider the ICU service requirements in the event of a pandemic. This report provides weekly and daily estimates of the number of ICU beds and ventilators required during a pandemic. The estimates provided are derived from applying various rates of ICU admission and ventilation to the weekly hospitalisation figures generated from the HPA empirical model.([1]) Daily hospitalisations have been approximated from the weekly totals suggested by the HPA model and used to derive daily ICU requirements using various assumptions relating to length of ICU stay.

The figures in this document have been derived based on the HPA assumption that the pandemic situation lasts for 15 weeks. It is assumed that the Clinical Attack Rate (CAR) is 25% and that 0.55% of clinical cases will be hospitalised[1].

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

3 Weekly ICU admissions and ventilation requirements

Meltzer estimates that 33% of influenza patients hospitalised in the US during a pandemic will require a stay in the ICU.([4]) Other papers have applied different ICU rates; ranging from 5% to 25% of influenza-related hospitalisations. ([5;6])Various ICU admission rates (5%, 10%, 25%) have been applied to the weekly pandemic hospitalisations in Ireland (as predicted by the HPA empirical model) to produce estimates of the weekly ICU admissions.

After considering the number of ICU admissions in a week, different ventilation rates (25%, 50%, 75%) were used to derive estimated ventilation requirements. This ventilation rate range was also used in an Australian and New Zealand Intensive Care Society (ANZICS) paper to estimate ventilation requirements and is based on ventilation rates for community-acquired pneumonia.([6])

3.1 Assuming 5% of influenza-related hospitalisations require an ICU stay

Week No	Hospitalisations	New admissions to ICU	Number requiring ventilation		
			25%	50%	75%
1	8	0	0	0	0
2	12	1	0	0	0
3	48	2	1	1	2
4	182	9	2	5	7
5	614	31	8	15	23
6	1,255	63	16	31	47
7	1,232	62	15	31	46
8	831	42	10	21	31
9	566	28	7	14	21
10	439	22	5	11	16
11	305	15	4	8	11
12	152	8	2	4	6
13	91	5	1	2	3
14	50	3	1	1	2
15	38	2	0	1	1
	5,823				

Table 1: Weekly ICU admissions and ventilation requirements assuming 5% critical care rate within hospitalised patients and varying ventilation rate from 25% to 75%

3.2 Assuming 15% of influenza-related hospitalisations require an ICU stay

Week No	Hospitalisations	New admissions to ICU	Number requiring ventilation 25%	50%	75%
1	8	1	0	1	1
2	12	2	0	1	1
3	48	7	2	4	5
4	182	27	7	14	20
5	614	92	23	46	69
6	1,255	188	47	94	141
7	1,232	185	46	92	139
8	831	125	31	62	93
9	566	85	21	42	64
10	439	66	16	33	49
11	305	46	11	23	34
12	152	23	6	11	17
13	91	14	3	7	10
14	50	8	2	4	6
15	38	6	1	3	4
	5,823				

Table 2: Weekly ICU admissions and ventilation requirements assuming 15% critical care rate within hospitalised patients and varying ventilation rate from 25% to 75%

3.3 Assuming 25% of influenza-related hospitalisations require an ICU stay

Week No	Hospitalisations	New admissions to ICU	Number requiring ventilation 25%	50%	75%
1	8	2	1	1	2
2	12	3	1	1	2
3	48	12	3	6	9
4	182	45	11	23	34
5	614	154	38	77	115
6	1,255	314	78	157	235
7	1,232	308	77	154	231
8	831	208	52	104	156
9	566	141	35	71	106
10	439	110	27	55	82
11	305	76	19	38	57
12	152	38	9	19	28
13	91	23	6	11	17
14	50	13	3	6	9
15	38	10	2	5	7
	5,823				

Table 3: Weekly ICU admissions and ventilation requirements assuming 25% critical care rate within hospitalised patients and varying ventilation rate from 25% to 75%

4 Daily Hospitalisations

The HPA model predicts weekly total influenza-related hospitalisations. Daily hospitalisations are useful from a service planning perspective.

Estimates of the number of influenza-related hospitalisations per day (Table 4, Figure 1) were obtained from the HPA model weekly totals using 2 constraints:

- Daily hospitalisations for each 7-day period sum to the weekly total
- The number hospitalised per day is non-decreasing until the last day of week 6 and non-increasing from the first day of week 7.

Week	Hospitalisations	Hospitalisations by Day						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	8	1	1	1	1	1	1	2
2	12*	2	2	2	2	2	2	2
3	48	3	4	6	7	8	9	11
4	182*	14	18	22	26	30	34	37
5	614*	50	63	75	88	100	113	126
6	1255	139	152	166	179	193	206	220
7	1232	203	194	185	176	167	158	149
8	831*	139	133	126	119	112	105	98
9	566	91	88	84	81	77	74	71
10	439	67	66	64	63	61	60	58
11	305	57	52	48	44	39	35	30
12	152	26	24	23	22	20	19	18
13	91	16	15	14	13	12	11	10
14	50	8	8	8	7	7	6	6
15	38*	5	5	5	5	5	5	5

Table 4: Estimated daily hospitalisations generated from the HPA Model weekly totals, based on 25% CAR and 0.55% hospitalisation rate among clinical cases

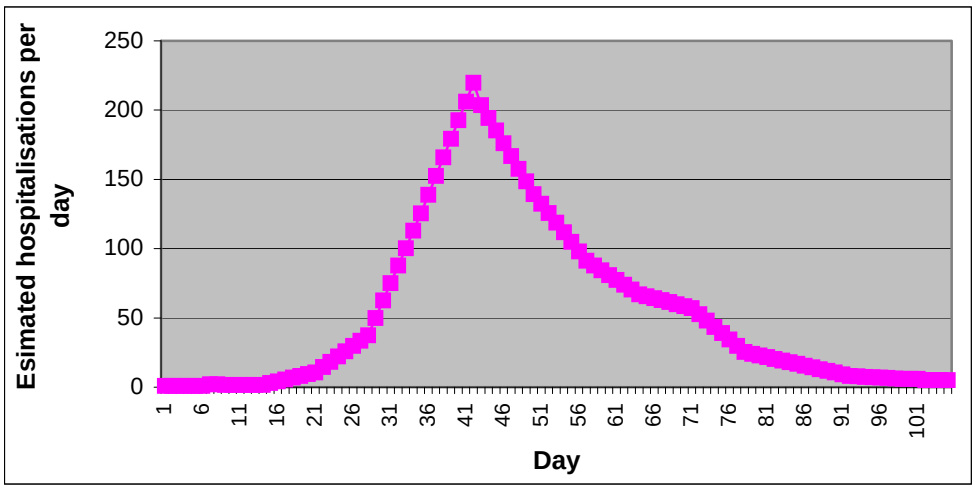


Figure 1: Estimated daily hospitalisations (generated from HPA Model) based on 25% CAR and 0.55% hospitalisation rate among clinical cases

* These rows do not sum to the exact weekly total due to rounding effects

5 Daily ICU and ventilation requirements

5.1 Daily ICU admissions

Assuming that 15% of influenza-related hospitalisations require critical care, daily admissions to ICU are estimated as♣:

Week	ICU admissions	ICU admissions by Day						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	1	1	1	1	2
4	27	2	3	3	4	4	5	6
5	92	8	9	11	13	15	17	19
6	188	21	23	25	27	29	31	33
7	185	31	29	28	26	25	24	22
8	125	21	20	19	18	17	16	15
9	85	14	13	13	12	12	11	11
10	66	10	10	10	9	9	9	9
11	46	9	8	7	7	6	5	5
12	23	4	4	3	3	3	3	3
13	14	2	2	2	2	2	2	1
14	8	1	1	1	1	1	1	1
15	6	1	1	1	1	1	1	1

Table 5: Daily ICU admissions derived from HPA model assuming that 15% of daily hospitalisations require ICU facilities

5.2 Daily ICU bed requirements

Based on the assumptions made in the previous sections (25% CAR over a 15 week period, 0.55% of cases hospitalised) and adopting the idea that 15% of hospitalised patients require a stay in ICU, the daily totals of ICU beds required can be predicted. It is likely that a patient's stay in ICU will be longer than one day.([7;8]) A rolling total is needed in order to estimate the total number of ICU beds required per day.

Tables 6,7 and 8 show the estimated ICU bed requirements assuming that 15% of hospital admissions require a stay in ICU and that the length of ICU stay is 2, 7 or 10 days.

♣ICU admissions per day calculated as 15% of estimated daily hospitalisations (Table 4) therefore may not sum to exact weekly totals due to rounding effects

5.2.1 Length of stay in ICU – 2 days

Week	ICU admissions	No. ICU beds required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	2	2	2	2	3
4	27	4	5	6	7	8	9	11
5	92	14	17	20	24	28	32	36
6	188	40	44	48	52	56	60	64
7	185	64	60	57	54	51	49	46
8	125	43	41	39	37	35	33	31
9	85	29	27	26	25	24	23	22
10	66	21	20	20	19	18	18	18
11	46	18	17	15	14	13	11	10
12	23	9	8	7	6	6	6	6
13	14	5	4	4	4	4	4	3
14	8	2	2	2	2	2	2	2
15	6	2	2	2	2	2	2	2
16	0	1	0	0	0	0	0	0

Table 6: Daily totals of ICU beds required derived from HPA model assuming that 15% of daily hospitalisations require a 2 day stay in ICU

5.2.2 Length of stay in ICU – 7 days

Week	ICU admissions	No. ICU beds in use						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	2	3	4	5	7
4	27	9	11	13	16	19	23	27
5	92	33	39	47	56	67	79	92
6	188	105	119	133	147	161	175	189
7	185	199	205	208	207	203	196	185
8	125	175	166	157	149	141	133	126
9	85	119	112	106	100	95	90	86
10	66	82	79	76	73	70	68	66
11	46	65	63	60	58	55	51	47
12	23	42	38	34	30	27	25	23
13	14	21	19	18	17	16	15	13
14	8	12	11	10	9	8	7	7
15	6	7	7	7	7	7	7	7
16	0	6	5	4	3	2	1	0

Table 7: Daily totals of ICU beds required derived from HPA model assuming that 15% of daily hospitalisations require a 7 day stay in ICU

5.2.3 Length of stay in ICU – 10 days

Week	ICU admissions	No. ICU beds in use						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	2	3	4	5	7
4	27	9	12	15	19	22	26	31
5	92	38	46	55	66	78	92	107
6	188	124	142	161	180	200	220	240
7	185	256	268	277	282	284	283	278
8	125	270	259	245	232	220	208	197
9	85	186	175	166	157	149	141	134
10	66	127	121	116	111	107	103	100
11	46	97	94	90	87	83	78	74
12	23	69	64	58	52	47	43	39
13	14	35	32	29	27	25	24	22
14	8	20	18	16	15	14	13	12
15	6	11	10	10	10	10	10	10
16	0	9	8	7	6	5	4	3

Table 8: Daily totals of ICU beds required derived from HPA model assuming that 15% of daily hospitalisations require a 10 day stay in ICU

5.3 Daily ventilation requirements

Published literature assumes a range of ventilation requirements. The February 2005 HPA plan [5]assumed that 100% of ICU patients would require ventilation and that ICU admissions would make up 5% of influenza-related hospitalisations.[8]The HPA plan ICU rate of 5% of all admissions is lower than 15% rate used in this report.

Meltzer [4] assumed that 50% of ICU patients would require ventilation. The ANZICS paper considered ventilation rates of 25%, 50% and 75% within ICU patients.[6]

A range of ventilation requirements (25%, 50%, 75%, 100% of ICU patients) and ICU length of stay (2, 7, 10 days) have been considered in the figures below. A detailed breakdown of the daily totals depicted in Figures 2, 3 and 4 can be seen in Appendix I.

5.3.1 Length of stay in ICU - 2 days

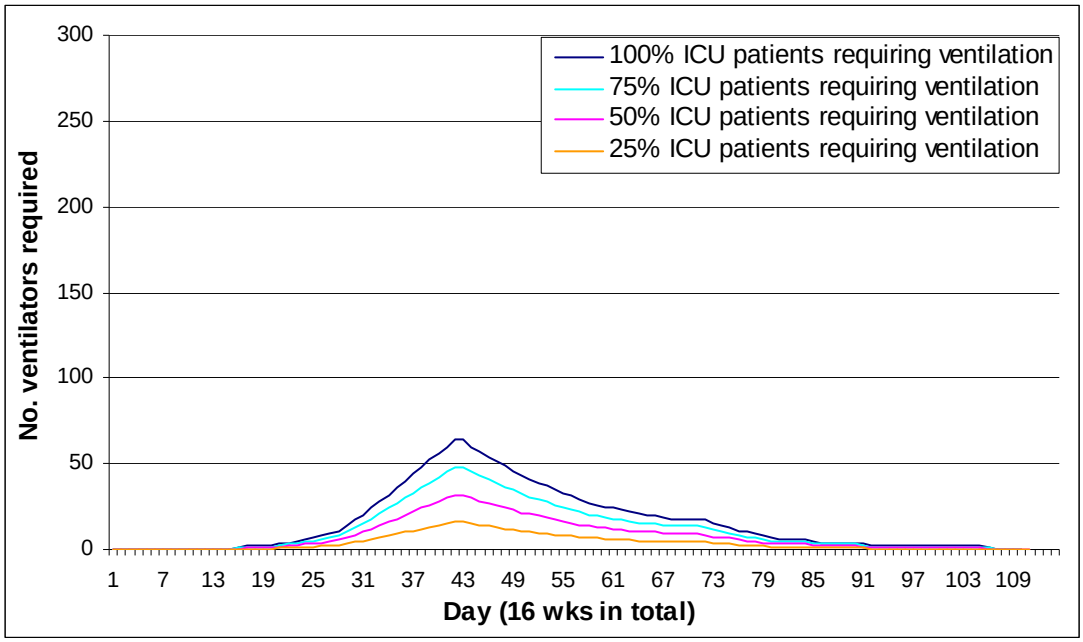


Figure 2: Daily ventilation requirements based on a range of ventilation rates and assuming that 15% of hospitalised patients enter ICU for a 2 day stay

5.3.2 Length of stay in ICU - 7 days

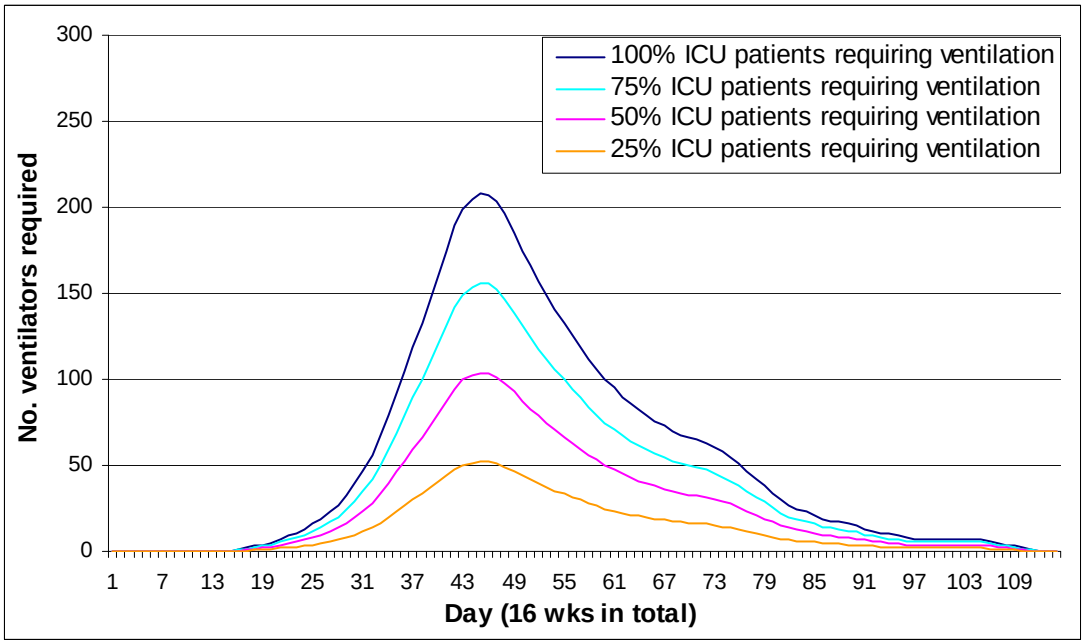


Figure 3: Daily ventilation requirements based on a range of ventilation rates and assuming that 15% of hospitalised patients enter ICU for a 7 day stay

5.3.3 Length of stay in ICU - 10 days

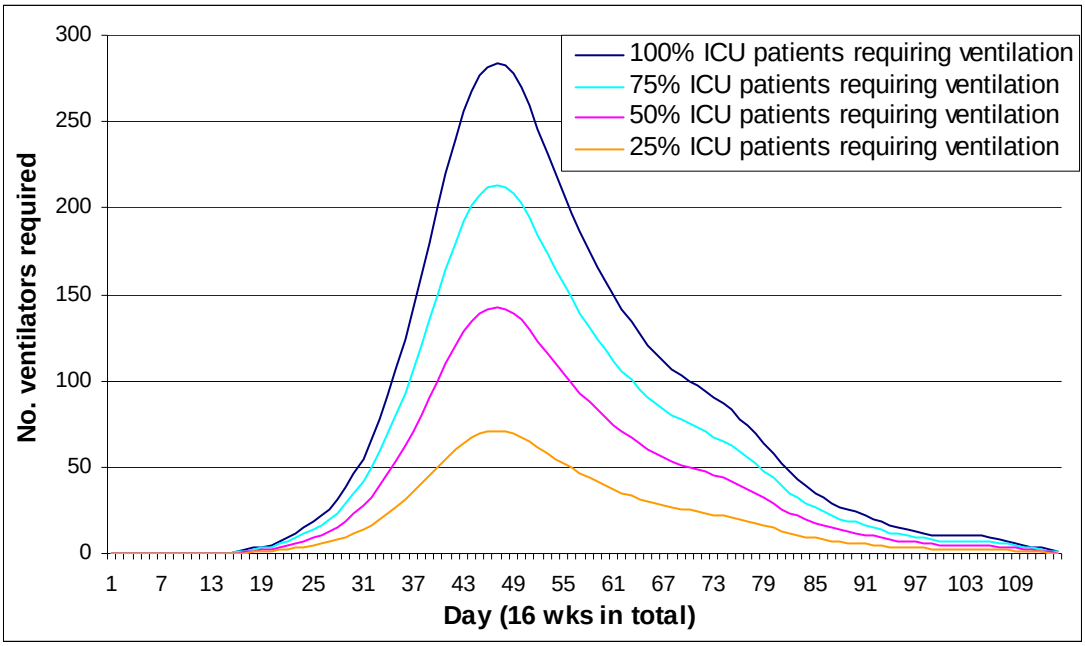


Figure 4: Daily ventilation requirements based on varying ventilation rates and assuming that 15% of hospitalised patients enter ICU for a 10 day stay

6 References

1. Hunter K, Igoe I, Mannix M, O'Flanagan D. Modelling Impact of Pandemic Influenza. Report presented to Pandemic Influenza Expert Group. Jan 2006. 2006.

2. Health Protection Agency. Influenza Pandemic Contingency Plan. www.hpa.org.uk . 2005.

3. Health Protection Agency. Pandemic Influenza Contingency Plan. www.hpa.org.uk . 2006.

4. 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.

5. Health Protection Agency. Influenza Pandemic Contingency Plan October 2005. www.hpa.org.uk . 2005.

6. Anderson AA, Hart GK, Kainer MA. Pandemic influenza - Implication sfor critical care resources in Australia and New Zealand. Journal of Critical Care 2003; 18(3):173-180.

7. Oliveira EC, Marik PE, Colice G. Influenza Pneumonia: A descriptive study. Chest 2001; 119(6):1717-1723.

8. Turner D, Wailoo Aea. Systematic review and economic decision modelling for the prevention and treatment of influenza A and B. Health Technol Assess 2003; 7(35 iii-iv, xi-xii):1-170.

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

7 Appendix I – numbers depicted in Figures 2, 3 and 4

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	0	1	1	1	1	1
4	27	1	1	2	2	2	2	3
5	92	4	4	5	6	7	8	9
6	188	10	11	12	13	14	15	16
7	185	16	15	14	14	13	12	12
8	125	11	10	10	9	9	8	8
9	85	7	7	7	6	6	6	6
10	66	5	5	5	5	5	5	5
11	46	5	4	4	4	3	3	3
12	23	2	2	2	2	2	2	2
13	14	1	1	1	1	1	1	1
14	8	1	1	1	1	1	1	1
15	6	1	1	1	1	1	1	1
16	0	0	0	0	0	0	0	0

Table A1: Daily ventilation requirements assuming 2-day stay in ICU, 25% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	1	1	1	1	2
4	27	2	3	3	4	4	5	6
5	92	7	9	10	12	14	16	18
6	188	20	22	24	26	28	30	32
7	185	32	30	29	27	26	25	23
8	125	22	21	20	19	18	17	16
9	85	15	14	13	13	12	12	11
10	66	11	10	10	10	9	9	9
11	46	9	9	8	7	7	6	5
12	23	5	4	4	3	3	3	3
13	14	3	2	2	2	2	2	2
14	8	1	1	1	1	1	1	1
15	6	1	1	1	1	1	1	1
16	0	1	0	0	0	0	0	0

Table A2: Daily ventilation requirements assuming 2 day stay in ICU, 50% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	2	2	2	2	2
4	27	3	4	5	5	6	7	8
5	92	11	13	15	18	21	24	27
6	188	30	33	36	39	42	45	48
7	185	48	45	43	41	38	37	35
8	125	32	31	29	28	26	25	23
9	85	22	20	20	19	18	17	17
10	66	16	15	15	14	14	14	14
11	46	14	13	11	11	10	8	8
12	23	7	6	5	5	5	5	5
13	14	4	3	3	3	3	3	2
14	8	2	2	2	2	2	2	2
15	6	2	2	2	2	2	2	2
16	0	1	0	0	0	0	0	0

Table A3: Daily ventilation requirements assuming 2 day stay in ICU, 75% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	0	1	1	1	1	2
4	27	2	3	3	4	5	6	7
5	92	8	10	12	14	17	20	23
6	188	26	30	33	37	40	44	47
7	185	50	51	52	52	51	49	46
8	125	44	42	39	37	35	33	32
9	85	30	28	27	25	24	23	22
10	66	21	20	19	18	18	17	17
11	46	16	16	15	15	14	13	12
12	23	11	10	9	8	7	6	6
13	14	5	5	5	4	4	4	3
14	8	3	3	3	2	2	2	2
15	6	2	2	2	2	2	2	2
16	0	2	1	1	1	1	0	0

Table A4: Daily ventilation requirements assuming 7 day stay in ICU, 25% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	1	2	2	3	4
4	27	5	6	7	8	10	12	14
5	92	17	20	24	28	34	40	46
6	188	53	60	67	74	81	88	95
7	185	100	103	104	104	102	98	93
8	125	88	83	79	75	71	67	63
9	85	60	56	53	50	48	45	43
10	66	41	40	38	37	35	34	33
11	46	33	32	30	29	28	26	24
12	23	21	19	17	15	14	13	12
13	14	11	10	9	9	8	8	7
14	8	6	6	5	5	4	4	4
15	6	4	4	4	4	4	4	4
16	0	3	3	2	2	1	1	0

Table A5: Daily ventilation requirements assuming 7 day stay in ICU, 50% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	2	2	3	4	5
4	27	7	8	10	12	14	17	20
5	92	25	29	35	42	50	59	69
6	188	79	89	100	110	121	131	142
7	185	149	154	156	155	152	147	139
8	125	131	125	118	112	106	100	95
9	85	89	84	80	75	71	68	65
10	66	62	59	57	55	53	51	50
11	46	49	47	45	44	41	38	35
12	23	32	29	26	23	20	19	17
13	14	16	14	14	13	12	11	10
14	8	9	8	8	7	6	5	5
15	6	5	5	5	5	5	5	5
16	0	5	4	3	2	2	1	0

Table A6: Daily ventilation requirements assuming 7 day stay in ICU, 75% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	0	1	1	1	1	2
4	27	2	3	4	5	6	7	8
5	92	10	12	14	17	20	23	27
6	188	31	36	40	45	50	55	60
7	185	64	67	69	71	71	71	70
8	125	68	65	61	58	55	52	49
9	85	47	44	42	39	37	35	34
10	66	32	30	29	28	27	26	25
11	46	24	24	23	22	21	20	19
12	23	17	16	15	13	12	11	10
13	14	9	8	7	7	6	6	6
14	8	5	5	4	4	4	3	3
15	6	3	3	3	3	3	3	3
16	0	2	2	2	2	1	1	1

Table A7: Daily ventilation requirements assuming 10 day stay in ICU, 25% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	1	2	2	3	4
4	27	5	6	8	10	11	13	16
5	92	19	23	28	33	39	46	54
6	188	62	71	81	90	100	110	120
7	185	128	134	139	141	142	142	139
8	125	135	130	123	116	110	104	99
9	85	93	88	83	79	75	71	67
10	66	64	61	58	56	54	52	50
11	46	49	47	45	44	42	39	37
12	23	35	32	29	26	24	22	20
13	14	18	16	15	14	13	12	11
14	8	10	9	8	8	7	7	6
15	6	6	5	5	5	5	5	5
16	0	5	4	4	3	3	2	2

Table A8: Daily ventilation requirements assuming 10 day stay in ICU, 50% ventilation rate

Week	New ICU admissions	No. ventilators required						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	1	0	0	0	0	0	0	0
2	2	0	0	0	0	0	0	0
3	7	0	1	2	2	3	4	5
4	27	7	9	11	14	17	20	23
5	92	29	35	41	50	59	69	80
6	188	93	107	121	135	150	165	180
7	185	192	201	208	212	213	212	209
8	125	203	194	184	174	165	156	148
9	85	140	131	125	118	112	106	101
10	66	95	91	87	83	80	77	75
11	46	73	71	68	65	62	59	56
12	23	52	48	44	39	35	32	29
13	14	26	24	22	20	19	18	17
14	8	15	14	12	11	11	10	9
15	6	8	8	8	8	8	8	8
16	0	7	6	5	5	4	3	2

Table A9: Daily ventilation requirements assuming 10 day stay in ICU, 75% ventilation rate

8 Appendix II - Daily hospitalisations assuming 3.7% of cases are hospitalised

The weekly total hospitalisations in Table A10 are based on the assumption that there is a 50% CAR and that 3.7% of cases are hospitalised. Using the same constraints as described in section 4, daily estimates of hospitalisations have been produced and are displayed below.

Week	Hospitalisations	Hospitalisations by Day						
		Mon	Tue	Wed	Thu	Fri	Sat	Sun
1	113	10	11	14	16	18	21	23
2	160*	23	23	23	23	23	23	23
3	642*	40	57	74	92	109	126	143
4	2445	195	246	298	349	401	452	504
5	8266	673	842	1012	1181	1350	1519	1689
6	16886	2168	2250	2331	2412	2494	2575	2656
7	16579	2738	2615	2492	2368	2245	2122	1999
8	11181*	1876	1783	1690	1597	1504	1411	1319
9	7610*	1226	1180	1133	1087	1041	995	949
10	5910	903	883	864	844	825	805	786
11	4099	767	706	646	586	525	465	404
12	2040	344	327	309	291	274	256	239
13	1227	221	206	191	175	160	145	129
14	675	114	108	102	96	91	85	79
15	514*	73	73	73	73	73	73	73
	78,346							

Table A10: Estimated daily hospitalisations generated from the HPA Model weekly totals, based on 50% CAR and 3.7% hospitalisation rate among clinical cases

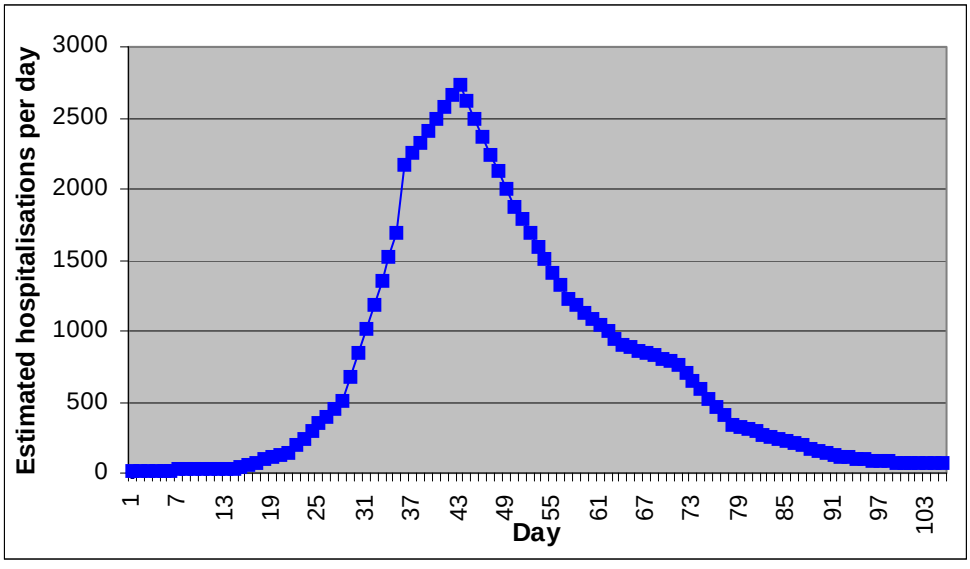


Figure A1: Estimated hospitalisations per day (HPA Model), based on 25% CAR and 3.7% hospitalisation rate among clinical cases

* These rows do not sum to the exact weekly total due to rounding effects

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

January 2006

Table of Contents

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.

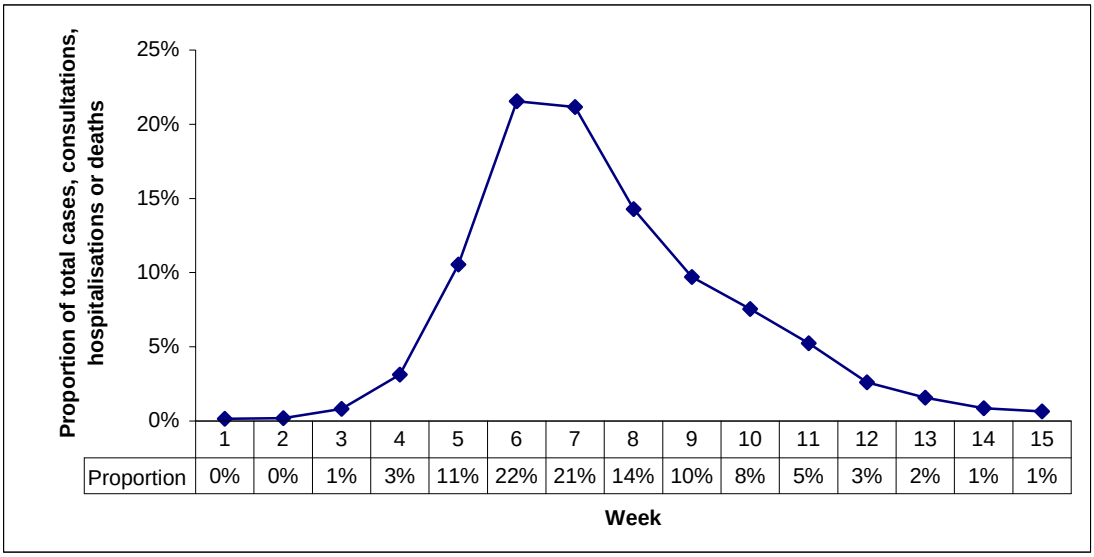
2 HPA Model

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.

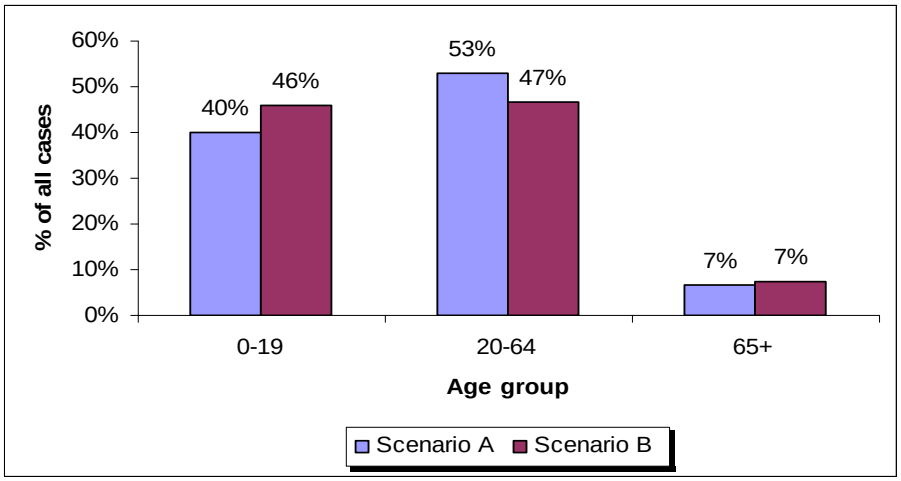


Figure 3.1: Proportion of total cases within each age group in 2 scenarios

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.

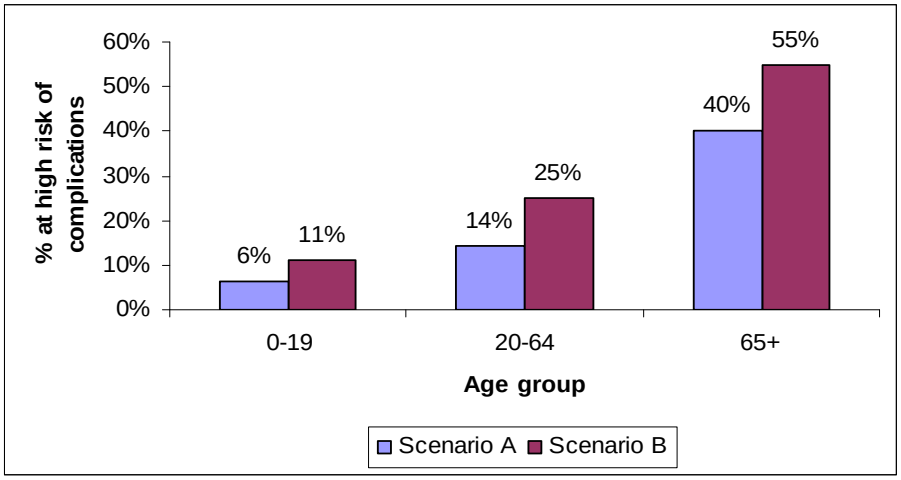


Figure 3.2: Proportion at high risk within each age group in 2 scenarios

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.

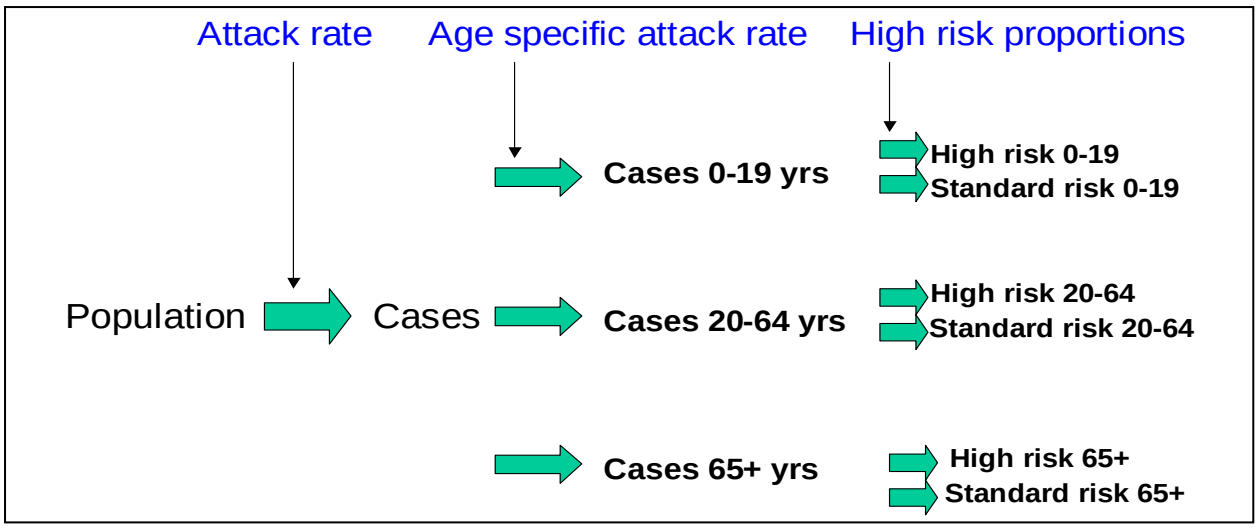


Figure 3.3: Flowchart showing method for calculating total number of cases and then dividing cases by age and risk group

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]

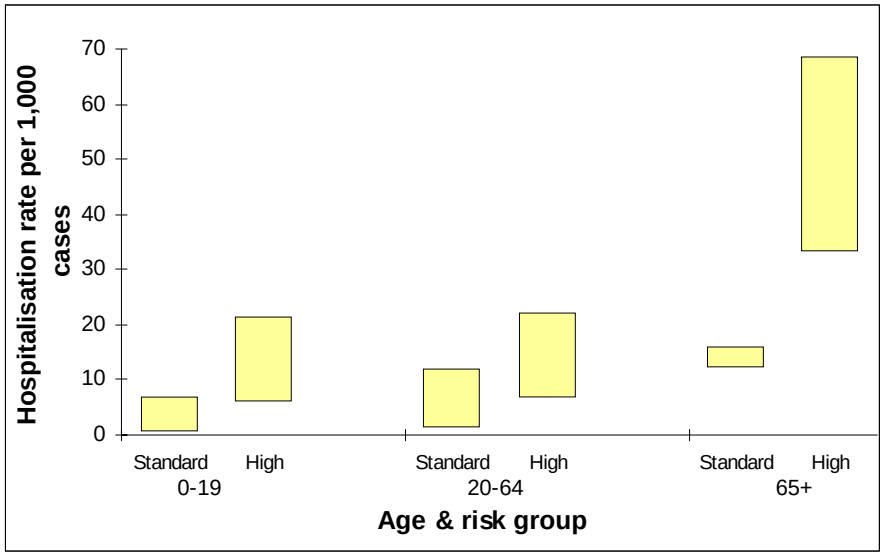


Figure 3.4: Range of hospitalisation rates for each age & risk group combination

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]

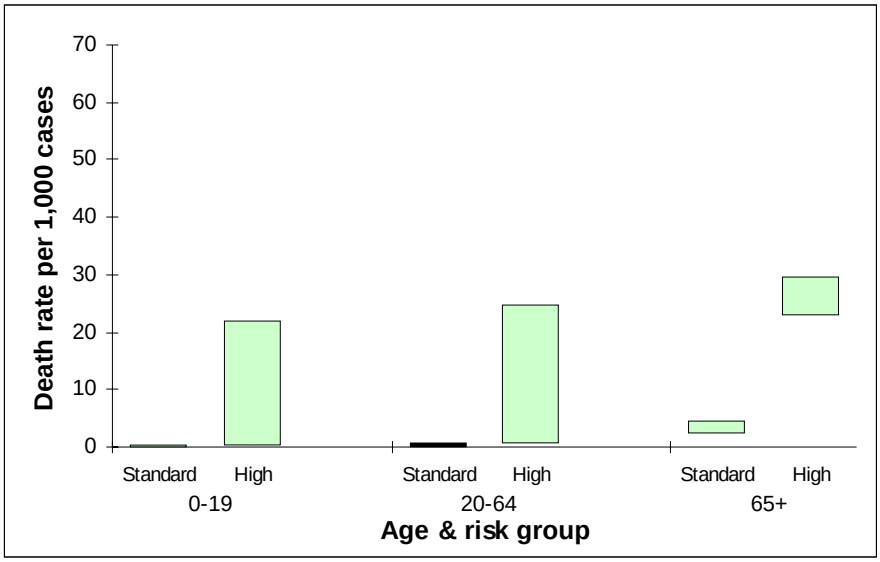


Figure 3.5: Range of death rates for each age & risk group combination

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

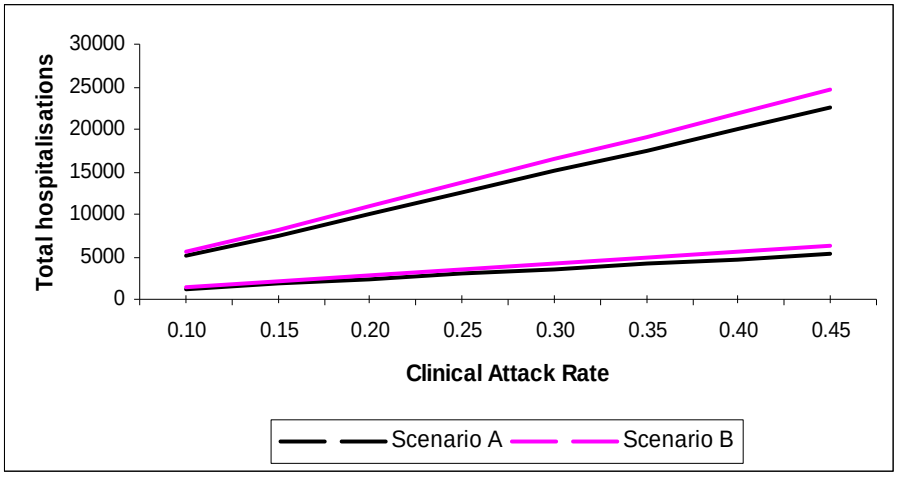


Figure 3.6: Upper and lower estimates of number of hospitalisations in Ireland under varying clinical attack rates and two pandemic Scenarios

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).

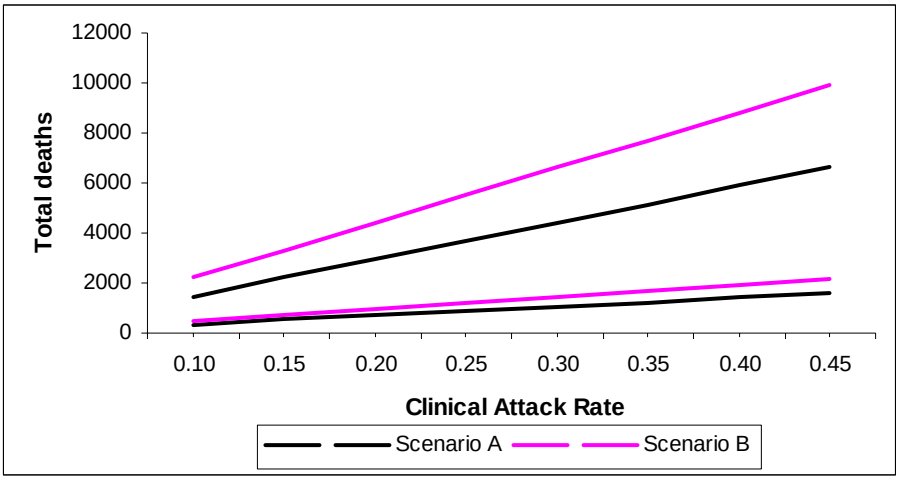


Figure 3.7: Upper and lower[2] estimates of number of deaths in Ireland under varying clinical attack rates and two pandemic scenarios

[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.

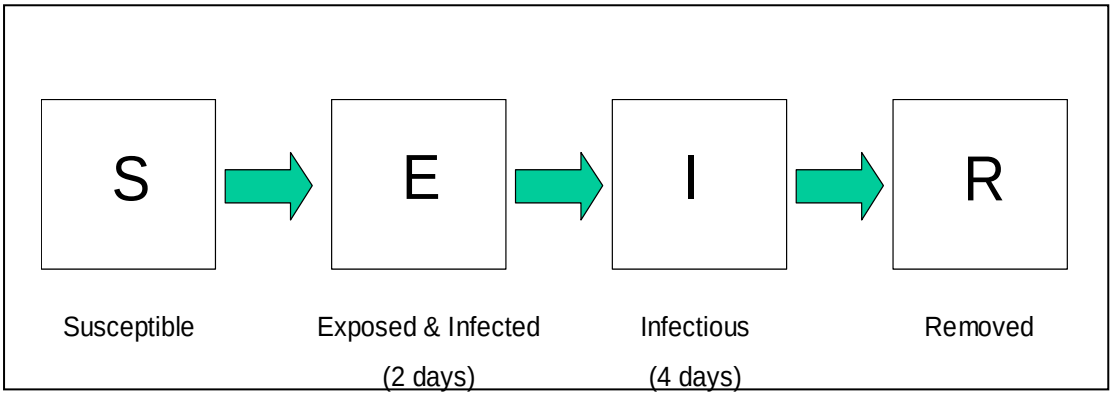


Figure 4.1: Structure of Gani model

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.

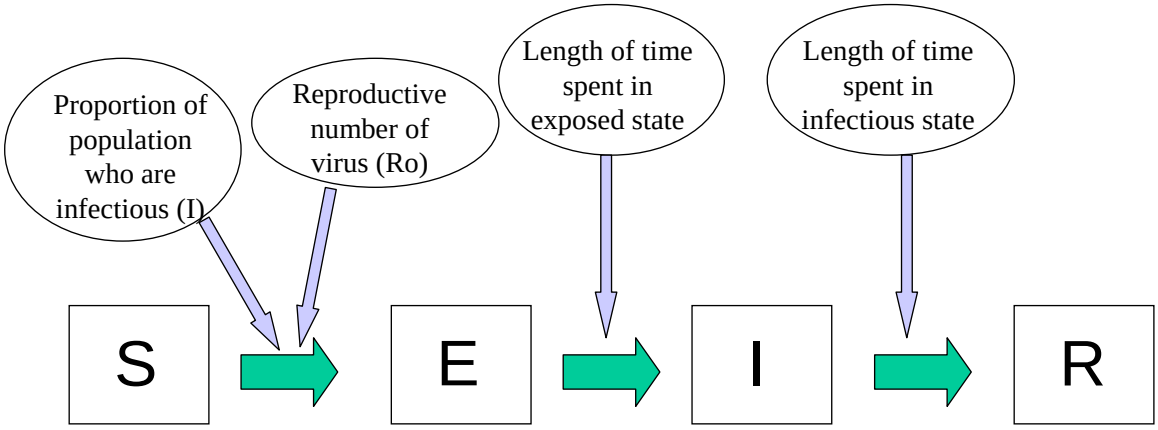


Figure 4.2: Determinants of movement between states

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

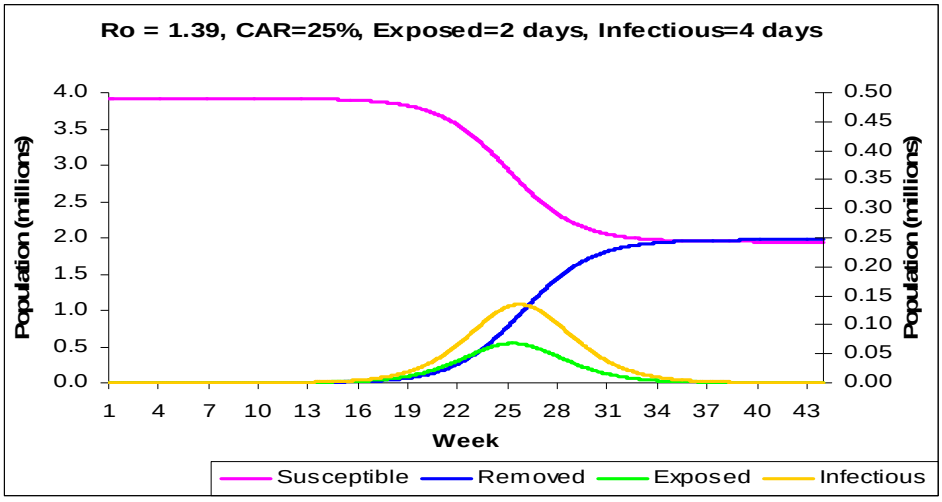


Figure 4.3: Number of persons in states S, E, I, R over time after 10 infectious cases imported in week 1, Ro=1.39 LHS axis: Susceptible and Removed curves, RHS axis: Exposed and Infectious curves

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.

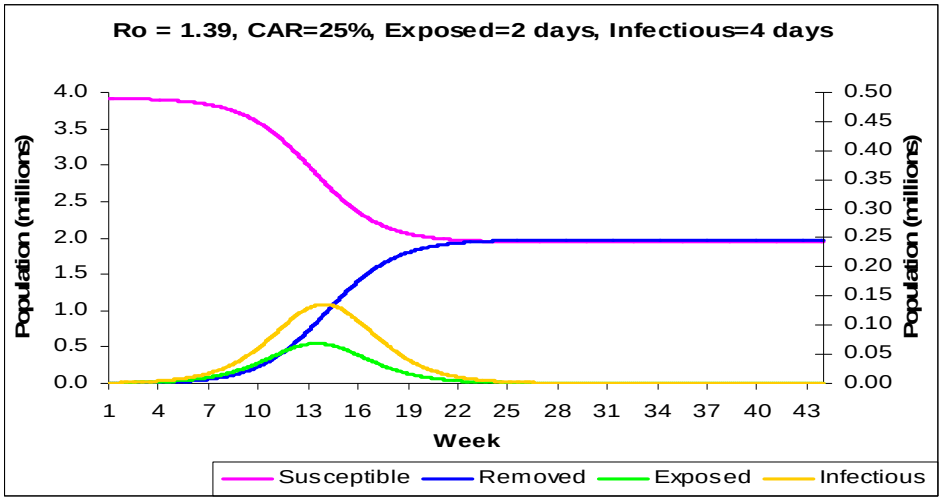


Figure 4.4: Number of persons in states S, E, I, R over time after 250 infectious cases imported daily during week 1, Ro=1.39 LHS axis: Susceptible and Removed curves, RHS axis: Exposed and Infectious curves

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.

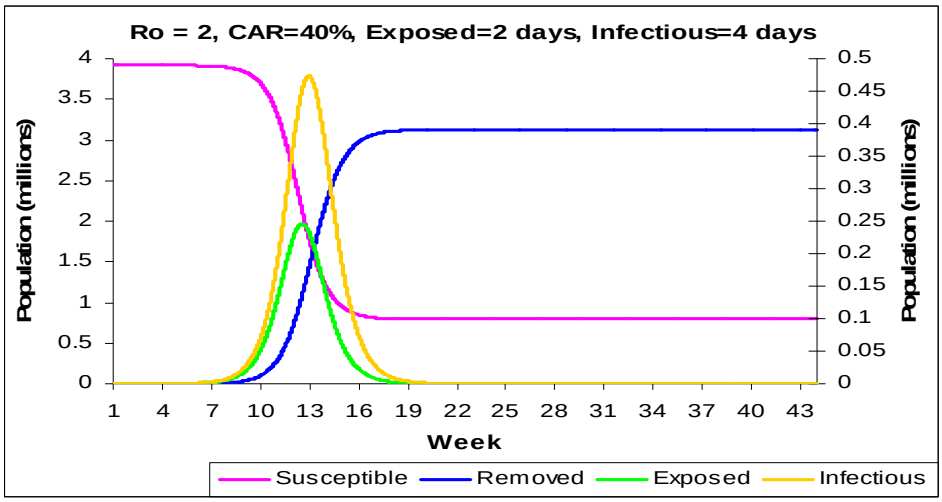


Figure 4.5: Number of persons in states S, E, I, R over time after 10 infectious cases imported in week 1, Ro=2 LHS axis: Susceptible and Removed curves, RHS axis: Exposed and Infectious curves

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

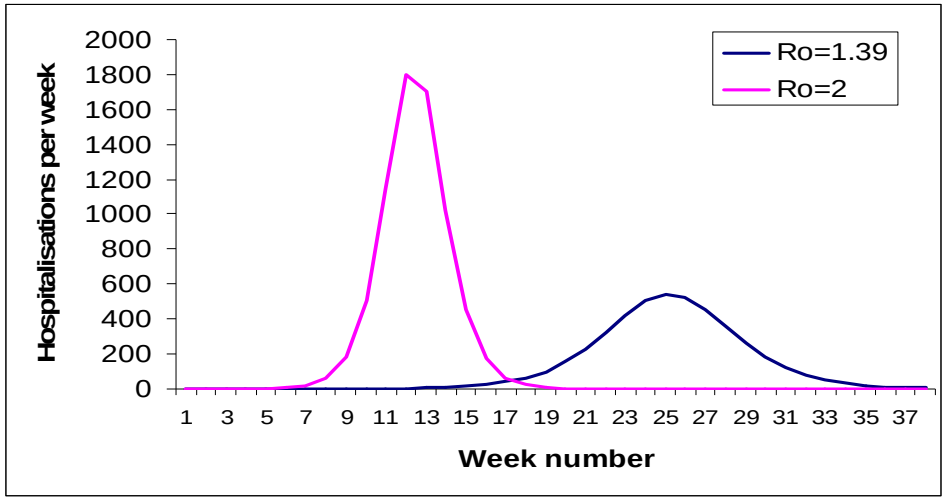


Figure 4.6: Hospitalisations per week as predicted by Gani model with varying Ro after 10 infectious cases imported in week 1

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.

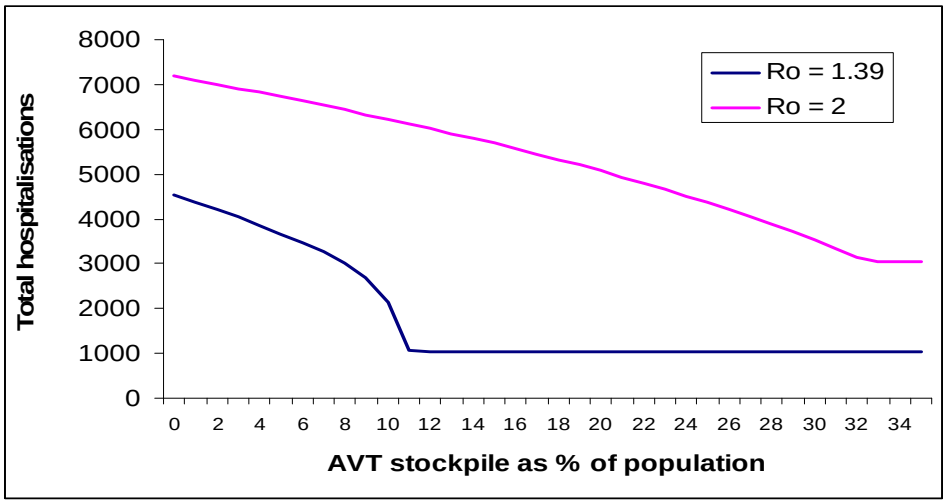


Figure 4.7: Total hospitalisations as predicted by Gani model with varying stockpile sizes and Ro

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

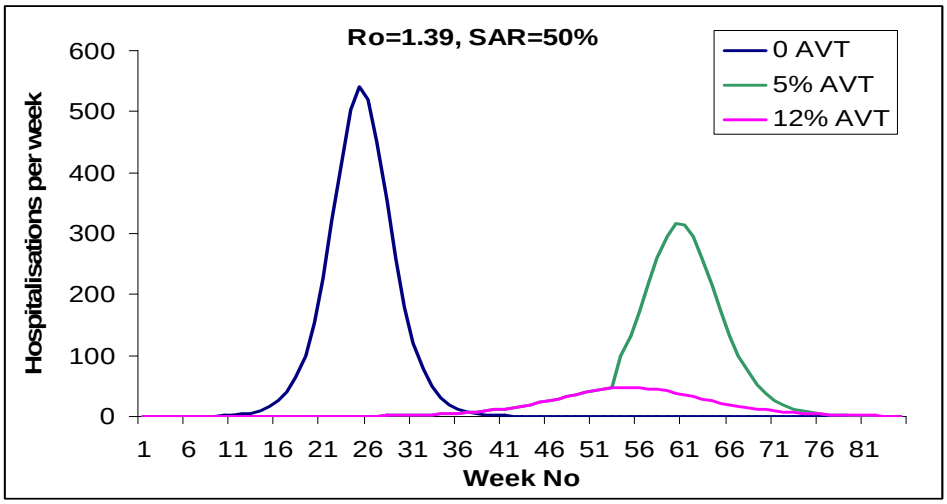


Figure 4.8: Weekly hospitalisations when Ro=1.39 as predicted by Gani model with varying stockpile sizes

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.

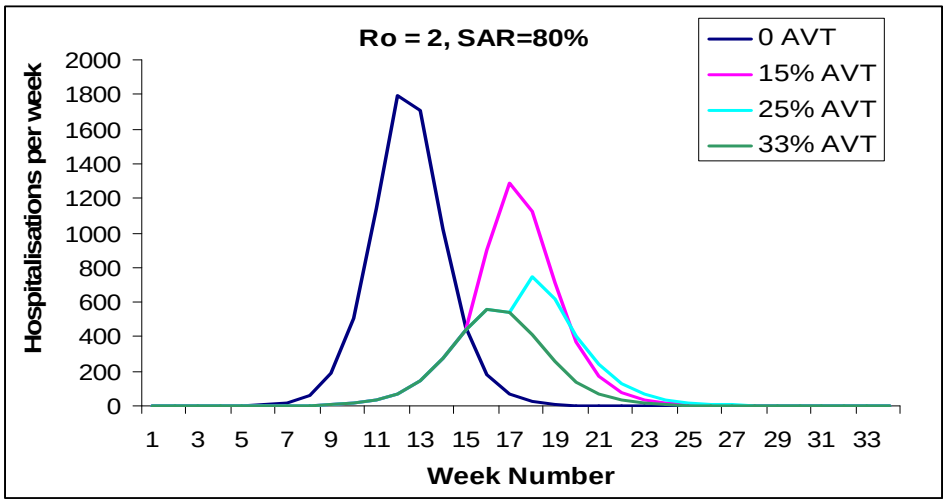


Figure 4.9: Weekly hospitalisations when Ro=2
as predicted by Gani model with varying stockpile sizes

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.

Guidance on public health actions to be taken on notification of Avian Influenza (AI) in birds in Ireland

October 2012

Produced by the avian influenza subcommittee of the Pandemic Influenza Expert Group

This guidance is subject to change, due to the evolving situation regarding avian influenza. Please see www.hpsc.ie for the latest information and guidance

Contents

Interim guidance on public health actions to be taken on notification of Avian Influenza (AI) in animals in Ireland

Introduction

The purpose of this document is to outline the Public Health actions in the event of Avian Influenza being notified in poultry or wild birds in Ireland. It has been updated in light of experience this year (2012) of low pathogenic H5N2 in pheasants in Clonakilty, Cork.

If AI is suspected on clinical grounds both veterinary and public health action will be required, and this may likely be in advance of knowing full details of the subtype of influenza involved. The veterinary actions, laid down in EU Directives, detail the control measures necessary from an animal health perspective.

Animal Health Actions

Under EU legislation, if there is **a suspected outbreak of avian influenza in poultry flocks**, all poultry on the farm must be kept indoors or confined in an isolated area where they will have no contact with other poultry.

Measures will be put in place to restrict movement of animals and humans and the Department of Agriculture Fisheries, Food and the Marine (DAFM) will institute biosecurity measures (1). These control measures focus on animal health issues and aim to prevent any further spread of the disease among animals. Pending confirmation of the outbreak, if deemed necessary, all the poultry in the holding may be culled and destroyed.

Once **highly pathogenic avian influenza (HPAI) is confirmed**, all poultry must be culled and destroyed immediately. All egg and poultry products must also be destroyed. The meat from poultry from the holding, which were slaughtered within the period presumed to cover the incubation of the disease, shall also be traced and destroyed, as should hatching and table eggs laid in the incubation period.

A protection zone with a radius of 3km around the site of infection and a **surveillance zone** with a minimum radius of 10 km around the protection zone will be established.

Within the **protection zone** the following will apply:

- Identification of all poultry and other bird holdings
- Periodic documented clinical inspections (& sampling if necessary) of all commercial poultry holdings
- On-farm biosecurity measures
- Active monitoring of wild birds
- Awareness campaigns for bird owners, hunters and bird watchers
- Ban on assembly of birds
- Ban on hunting wild birds
- Movement controls on poultry, etc.

Within the **surveillance zones** the following measures will apply:

- Identification of all poultry and other bird holdings

- On-farm biosecurity measures
- Ban on assembly of birds
- Ban on hunting wild birds
- Movement controls on poultry, etc.

If HPAI H5N1 is confirmed in poultry

The Restricted Zone is divided into two Areas:

Area A consists of:
- The Protection Zone with a radius of at least **3 km** around the infected premises
- The Surveillance Zone which is outside the Protection Zone and has a radius of at least **10 km** around the infected premises.

Area B consists of:
- An additional buffer zone around Area A. The size of this will depend on the number and location of the outbreaks.

Measures in the Area A Surveillance Zone:
- A census of all premises containing commercial poultry will be carried out
- Movements of **poultry, wild game birds, other animals from poultry farms, litter/ manure from poultry farms, wild feathered game meat, eggs, bird carcases and other animal by-products derived from poultry/birds** are prohibited (except under certain conditions and under licence)
- Bird gatherings are banned
- The release of game birds is banned
- Biosecurity measures must be implemented in the case of people and vehicles moving to and from premises containing poultry or captive birds

Measures in Area B:
- Movements of **poultry, wild game birds, other captive birds, wild feathered game meat, hatching eggs, bird carcases and other animal by-products derived from poultry/birds** are prohibited (except under certain conditions and under licence)
- Bird gatherings are banned

Period for which movement controls remain in place
- The Protection Zone must stay in place for at least **21 days** after the preliminary cleaning and disinfection of the infected premises has been carried out, and then the Zone becomes part of the Surveillance Zone
- The Surveillance Zone must stay in place for at least **30 days** after the preliminary cleaning and disinfection of the infected premises has been carried out.
- Area B will stay in place until a risk assessment has determined that it is safe to remove it.

If HPAI H5N1 is suspected or confirmed in wild birds, they will not be culled, as this is likely to lead to dispersal of the disease.

A **Wild Bird Restricted Zone** will be established which will consist of two Areas:
- A Control Area with a radius of at least **3 km** around the location where the wild bird was found
- A Monitoring Area with a radius of **10 km** around the location where the wild bird was found

The limits of the Areas will be decided in conjunction with ornithology experts who will assist the Department of Agriculture in assessing the area at risk.

Measures in the Control Area:

- A census of all poultry will be carried out
- Commercial poultry and targeted poultry/captive bird flocks at particular risk will be examined by a veterinary inspector and samples may be taken for avian influenza testing
- Increased surveillance will be carried out at wild bird habitats
- Warning notices will be placed around the area where the infected wild bird carcases were found
- Checks on biosecurity in poultry flocks will be carried out by Department of Agriculture staff
- Movements of **poultry, wild game birds, other captive birds, poultry and wild feathered game meat, hatching eggs, bird carcases and other animal by-products derived from poultry/birds** are prohibited (except under certain conditions and under licence)
- Gatherings of birds are banned
- Hunting of wild birds is banned
- Release of game birds is banned

Measures in the Monitoring Area:

- A census of all poultry will be carried out
- Increased surveillance will be carried out at wild bird habitats
- Checks on biosecurity in poultry flocks will be carried out by Department of Agriculture staff
- Movements of **poultry and other captive birds** are prohibited (except under certain conditions and under licence)
- Gatherings of birds are banned
- Hunting of wild birds is banned
- Release of game birds is banned

If there is **confirmed low pathogenic avian influenza (LPAI) in poultry,** the following measures will be taken:

Measures on the infected premises:

- All infected poultry and captive birds will be slaughtered (in certain cases a derogation from this may be allowed – this would be decided of a case-by-case basis)
- The carcases of slaughtered birds and eggs will be destroyed
- An investigation will be carried out by the veterinary inspector (to identify the possible source of infection and all contact premises)
- The premises must be cleaned and disinfected
- The premises may not be re-stocked for 21 days after the cleaning and disinfection has been completed

Measures within the Low-Pathogenic Avian Influenza Restricted Zone (LPAI RZ):

- A census of all premises containing commercial poultry or captive birds will be carried out
- All commercial poultry flocks will be examined by a veterinary inspector and samples taken for avian influenza testing
- Movements of **poultry, other captive birds, other animals from poultry farms, eggs** and **poultry litter/manure** are prohibited (except under certain conditions and under licence)
- Bird gatherings are banned
- The release of game birds is banned

- Biosecurity measures must be implemented in the case of people and vehicles moving to and from premises containing poultry or captive birds (see **Section 9**)

The LPAI RZ will normally be within a radius of **1 km** from the infected premises. **Check points** to control movements of vehicles transporting poultry or poultry-related products into/out of the Zones may or may not be put in place, depending on the particular circumstances.

The LPAI RZ will remain in place for at least **21 days** after the preliminary cleaning and disinfection of the infected premises has been completed. In the event that the infected flock is not slaughtered, this period must be extended to at least 42 days.

Human Health Actions

As AI is mainly an animal health issue, the risk to the human population is confined to those who have been in close contact with infected birds or their droppings, or to those involved in outbreak control activities.

The response to AI will need to be flexible, and dependent not only on the pathogenicity of the AI strain, and also on any evidence for human infection and person-to-person spread. Dynamic risk assessments will need to be undertaken, so that the level and intensity of response is appropriate to the risks identified.

Protective measures are necessary in two groups of people:

1. **Contacts, i.e. persons with significant exposure to infected poultry or droppings (e.g. owners of infected or suspected poultry farms and their families) or persons involved in handling infected (sick or dead) wild birds.**

2. **All persons involved in carrying out outbreak control activities.**

Public Health will work closely with DAFM in the protection of the two groups listed above.

- DAFM will identify all those potentially exposed to infected poultry or droppings (e.g. workers, families etc). Only those persons authorised by DAFM will be allowed to have continued contact with potentially infected poultry or droppings.
- Those potentially exposed to infected wild birds will also be identified by DAFM. These may include veterinary workers who handled sick or dead wild birds or members of the public who inadvertently handled sick or dead birds.
- Movement of workers and families between farms under investigation and non-infected farms will be restricted.
- Close collaboration between local veterinary personnel and Public Health will be required to ensure that protective measures are put in place and that surveillance of workers is undertaken.

Management of contacts of sources of Avian Influenza

The first tasks facing Public Health will be the management of contacts of sources of Avian Influenza. Assessment of their level of exposure will be done in conjunction with the local DAFM veterinary personnel.

Public Health management of persons considered to have had significant exposure is set out in this document. This may change depending on the emerging outbreak situation and on local circumstances. Those who will have an ongoing role in outbreak control activities will be need to be identified as their level of exposure may differ from those who may have had a one off exposure. They will move from being regarded as a contact to someone requiring occupational surveillance.

It may be useful to collate a number of the Appendices, which will be of use when dealing with this group of people.

Appendix 3: Algorithm for the management of persons with acute febrile respiratory illness who may have AI
Appendix 6: Contact Surveillance Form
Appendix 7: Information leaflet for those who have been in contact with infected poultry
Appendix 8: Template letter for contact's GP
Appendix 9: Algorithm for doctors prescribing oseltamivir as prophylaxis
Appendix 13: Information leaflet on oseltamivir
Appendix 17: DAFM list of personnel who are contacts of suspected avian influenza case /outbreak
Appendix 19: Algorithm for management of public health consequences of AI in poultry/wild birds: Strict versus standard approach
Appendix 20: Information leaflet on Bird Flu

Management of personnel involved in outbreak control measures

The second group of people, who will require Public Health management, include all personnel involved in the outbreak control measures such as culling and disposal of carcases.
More than 200 DAFM veterinary and other personnel who may be involved in control measures have already been identified and assessed as to their suitability to undertake this type of work. They have all been offered seasonal influenza vaccine on an annual basis.
It may be necessary to employ other workers (such as the Farm Relief Service, Civil Defence, rendering plant and gas company staff) in outbreak controls. . The DAFM has arranged with an occupational health consultant to assess these workers as to their suitability for outbreak control activities and offer them seasonal influenza vaccine, and organises occupational health workshops for these workers annually.
DAFM will be responsible for the provision of PPE and training their staff in its use.

There are three aspects to Public Health management of persons involved in outbreak control activities:

- Occupational surveillance
- Administration of antiviral prophylaxis
- Ensuring mechanisms are in place for the administration of seasonal influenza vaccine

Again it may be useful to collate a number of the Appendices, which will be of use when dealing with this group of people.

Appendix 5: Guidance for protection of persons involved in AI outbreak control & eradication activities
Appendix 9: Algorithm for doctors prescribing oseltamivir
Appendix 10: Information leaflet for those under occupational surveillance
Appendix 11: Interim Occupational Surveillance Form
Appendix 12: Template letter to GP of those under occupational surveillance
Appendix 13: Information leaflet on oseltamivir
Appendix 17: DAF list of personnel who are contacts of suspected avian influenza case /outbreak
Appendix 19: Algorithm for management of public health consequences of AI in poultry/wild birds: Strict versus standard approach
Appendix 20: Information leaflet on Bird Flu

Notification Process

The veterinary service will contact Public Health when a case of avian influenza is confirmed, or when a highly suspicious case is being considered. (See Appendix 1 for notification procedure and contact numbers). This will be in advance of knowing further details on the subtype of influenza involved.

In these early stages of an incident, prior to definitive epidemiological and laboratory information being available it is appropriate to adopt an intensive "Strict Approach". All the actions outlined below should be undertaken.

However when the laboratory and epidemiological information becomes clearer and this information combined with the risk assessments show reduced risk, this Strict Approach can be modified to a Standard Approach. The Standard Approach involves stopping (or not starting) chemoprophylaxis and passive rather than active follow up of contacts. Its important to undertake the risk assessments on an ongoing basis, as if for example in an outbreak of LPAI evidence of human to human transmission was present; there would be a need to move back to a Strict Approach.

Strict Approach to an outbreak of Avian Influenza

On first notification to HSE Area Director of Public Health/Medical Officer of Health (MOH), he / she will carry out the following actions:

- Notify Health Protection Surveillance Centre (HPSC), and Assistant National Director Health Protection
- Contact National Virus Reference Laboratory (NVRL) and review arrangements for laboratory testing
- Consider need to put on standby alert or activate Regional Public Health Emergency Plan and Regional Crisis Management Team

- Depending on the scale of the incident, set up Health Service Executive (HSE) area outbreak control team:
    - Invite Regional Senior Superintending Veterinary Inspector (RSSVI) or nominee, and HPSC representative onto Outbreak Control Team (OCT)
    - HSE Occupational Health Physician should be invited onto the OCT
- Undertake a health risk assessment of the public health impact of the incident. Recognising that the risk assessment will change over time, this will need to be repeated at intervals during the incident. (The HPZone Dynamic Risk Assessment model can be used – see Appendix 18)
- Working with the local Department of Agriculture officials, identify and manage contacts of an avian source of avian influenza
- For poultry workers involved in outbreak control activities make arrangements for:
    - Occupational surveillance of workers involved in outbreak control activities for symptoms of AI
    - Administration of antiviral prophylaxis
    - And ensure mechanisms are in place for the administration of seasonal influenza vaccine, if influenza is circulating
- Advise Local Disease Control Centre on infection control issues. The provision of Personal Protective Equipment (PPE) and training their staff in the use of PPE is the responsibility of the Department of Agriculture Food and the Marine. (See worker protection guidance, Appendix 5)
- Plan the media and public communications campaign in conjunction with HPSC. Provide information on avian influenza for those directly affected, for health professionals and for the public
- Refine case definition for human cases (Appendix 2)
- Initiate active surveillance and case finding for cases in humans
- Disseminate case definition, notification mechanisms and algorithms for clinical assessment to all relevant stakeholders, including PH, OH, GPs, hospital physicians
- If human cases identified, follow algorithm for investigation (Appendix 3)
- **Report any human cases immediately to HPSC.** This information will need to be reported internationally to WHO, European Centre for Disease Control and the European Commission.
- Complete case investigation forms (Appendix 4). Where possible, use CIDR for case management, reporting, and analysis
- Liaise with HPSC and NVRL re evidence of human influenza strains currently circulating in or near the affected area
- In consultation with HPSC and NVRL, consider need for special epidemiological and laboratory studies which may require data collection or laboratory specimen collection during or following the outbreak
- Where practical, it may be preferable for the link Public Health doctor(s) to be based in the Local Veterinary Disease Control Centre liaising with the local DAFM team. This facilitates the sharing of information and collaboration in risk assessment of personnel involved in outbreak control activities.

- In conjunction with the National Assistant Director of -Health Protection, consider public health surge capacity and need for additional resources and/or redeployment of resources: e.g. obtaining additional public health resources from other HSE areas or divisions.
- Review need for Strict Approach in light of laboratory and epidemiological information, and ongoing risk assessments, and change to Standard Approach if appropriate.

On first notification to HSE HPSC

1. HPSC to notify:
    a. Director of Public Health /MOH in the affected area
    b. Assistant National Director of -Health Protection
    c. Assistant National Director of Emergency Planning
    d. Chief Medical Officer
    e. National Virus Reference Laboratory
    f. Public Health Agency, Health Protection division (depending on scale)
    g. National Pandemic Influenza Expert group
2. Discuss with Assistant National Director, Health Protection,re convening a National Outbreak Investigation Group
3. HPSC to
    a. Review communications materials and information available on website for public, health professionals, affected farmers etc.
    b. Review case definitions for human cases, data collection questionnaires, and methods of data collation, analysis and presentation
    c. Institute enhanced surveillance for potential cases nationally
    d. Review laboratory testing protocols in collaboration with NVRL
    e. If human cases occur, coordinate the epidemiological investigation nationally.
4. HPSC personnel to attend HSE area outbreak control team
5. HPSC staff to be seconded to aid in field investigation, if human cases occur, and upon request

Communications

Agreement will be required in advance between Department of Agriculture, Food and the Marine, and the HSE as to who will deal with specific issues. Designated spokespersons/ experts should be identified. If this has not been done in advance, agree this as soon as possible.

The Communications contact for HSE (including HSE HPSC) is: press@hse.ie
telephone: 6352840
The Communications Officer for the Department of Agriculture, Food and the Marine is:
Martina Kearney: Telephone 01 607 2190, email: martina.kearney@agriculture.gov.ie

Regional and local communications departments in each agency should ensure that their communications strategies include measures that will be activated in the event of an outbreak of AI. These measures should ensure that accurate, factual and relevant information is conveyed to the public, using methods appropriate to target audiences.

Procedures will be required to ensure that timely information is communicated to HSE staff so that they can comply fully with what they are required to do in outbreak control measures and that they minimise risk to themselves and the public.

Public health personnel involved in management of contacts/workers involved in outbreak control should have access to real time information, which they can use in dealing with particular queries. This information should be in multilingual format taking account of variations in literacy levels.

The main public health messages that need to be communicated at the time are:

- Avian influenza is mainly an animal health issue
- Who is at risk? The potential risk to the human population is confined to those who have been in close contact with infected birds or their droppings, or to those involved in outbreak control activities
- Precautions are being taken for those at risk, i.e. use of PPE and Oseltamivir
- Good personal hygiene, i.e. washing your hands with soap and water will protect against infectious diseases, including AI
- Careful preparation and eating properly cooked poultry and eggs do not pose a threat to human health
    - When handling raw poultry, the person involved in the food preparation should always wash their hands thoroughly with soap and warm water. Surfaces and utensils in contact with uncooked poultry products should also be thoroughly cleaned.
    - The Food Safety Authority of Ireland and Safefood also emphasise longstanding advice about the importance of thoroughly cooking poultry. Poultry should be cooked, so that it reaches temperatures of at least 70˚C in all parts of the item, ensuring that it is piping hot all the way through, with no pink meat left, and until the juices run clear.
    - Consumers are advised to continue to cook eggs as normal.

Public health management of contacts of sources of Avian Influenza (AI)

A contact is an asymptomatic person who has been in direct contact (within 1 metre – three feet) with an avian source or potential avian source of avian influenza virus, within the past seven days.

An avian source of avian influenza virus is dead or alive domestic fowl or wild bird(s) or domestic duck(s) **or** settings in which domestic fowl were confined or had been confined within the past six weeks, in whom the diagnosis of avian influenza is highly suspected or confirmed

On notification of a case of Avian Influenza, the Department of Public Health should carry out a ***risk assessment*** in conjunction with veterinary epidemiologists at the Local Disease Control Centre, and the Regional Senior Superintending Veterinary Inspector. This will include the ***identification*** of all possible contacts and the ***assessment of their level of exposure.*** The use of PPE and reported adherence to correct use of PPE by contacts (e.g. vets, laboratory staff) should form part of the risk assessment, and will influence the assessment of level of exposure.

The Local Veterinary Inspector will supply contact details of all persons who are potential contacts (Appendix 17).

The following categories of people may need to be assessed if the outbreak is at a poultry farm:

1. Poultry flock owners, their families and household members
2. Visitors to affected premises in the risk period between 48 hours before clinical onset and date of restriction of premises (e.g. fieldsmen, catchers, advisors etc.)
3. Personnel handling live birds, poultry meat, eggs that originated from affected premises in risk period (e.g. in slaughter plant, hatchery, packing centre, rendering plant, litter processor / spreader)
4. If the notification date is significantly later than the onset of clinical signs then those persons, who may have been exposed further back than the 7 days as set out in the definition of a contact, will also need to be identified to see if they have been ill or perhaps are still unwell.

These categories cover a large number of potential contacts, who in a specific time span may have visited the farm or lived and/or worked on it.

A more comprehensive list of possible visitors to poultry farms may be found in Appendix 14.
Levels of exposure for these groups may differ depending on the nature of the activity or business undertaken.

The risk assessment should include consideration of the following:

- The likelihood that the virus is circulating at a particular location (e.g. laboratory confirmation in a poultry flock or in wild birds)
- The nature of the bird/animal interactions e.g. whether or not the live birds needed to be caught and restrained during a cull

- The physical environment e.g. the presence of large exhaust fans blowing air out of a barn

The greatest risk will be from large numbers of infected birds in enclosed, intensive accommodation especially if there is inadequate ventilation. The highest risk of exposure is to those working in the same environment as live infected birds, and increases with the amount of time spent in this environment. Any work that stirs up litter or dust, e.g. culling or cleaning and disinfection of poultry sheds will increase the risk of infection by inhalation or ingestion. For those contacts that have been in contact with wild birds, physical handling of the birds, rather than contact within 1 metre of a dead bird is a significant contact warranting oseltamivir prophylaxis.

For those contacts considered to have had a significant exposure and to be defined as contacts, the following actions should be taken by public health:

- Record demographic details, contact details and the exposure history, using contact surveillance form (Appendix 6)
- Provide all contacts with clear public health recommendations – see information for contacts (Appendix 7)
- Notify the contact's GP that the person is being monitored as a contact and what measures are being taken (Appendix 8)
- Ask contacts to self-monitor for the development of fever (twice daily), respiratory or other symptoms for seven days after the last exposure to a known or suspected source of avian influenza virus. Provide a contact number for Public Health. Ask contacts to contact Public Health by telephone if any symptoms occur.
- Provide digital thermometer for twice daily oral temperature readings
- Provide a small supply of surgical masks to be used if symptomatic, when contacting health care services.
- Contacts should be provided with a public health contact number for queries and also if they develop symptoms. (Standard information leaflet Appendix 7)

- If they develop **any** of the following:
    - Temperature ≥ 38^{o}C
    - Cough
    - Shortness of breath
    - Sore throat, runny nose
    - Watery diarrhoea, stomach pain, nausea or vomiting

They need to be assessed urgently. Local arrangements will need to be in place for assessment in a suitable location (hospital/clinic etc.) as per algorithm (Appendix 3). (Remember to phone in advance)

- Evaluate all contacts for antiviral prophylaxis. (Oseltamivir 75mg daily for 10 days (see Appendix 9)
- Arrange that all contacts are immunised with current human influenza vaccine, if influenza is circulating at the time; local arrangements with GPs may be required
- Advise all contacts to strictly adhere to all Infection Control precautions as follows:

    - Avoid touching their faces, including their eyes and mucous membranes with their hands
    - Wash hands frequently: this means washing with soap and running water for a minimum of 15-20 seconds or the use of an alcohol based hand sanitizer if the hands are not visibly soiled
- Identify source of water supply to holding or farm (mains, group scheme, private well etc.)
- Check that water is treated as per WHO Guidelines (chlorinated etc.) (2)
- If water has not been treated as per guidelines, a risk assessment will be necessary to determine any potential human health risk. The result of the risk assessment will inform decisions about the issuing of "boil water notices" in consultation with national bodies (2-4).

Contacts should not visit other farms or unaffected agricultural locations with poultry or other birds, to avoid spread of contaminated materials – this is subject to review depending on the situation during the outbreak. More strict controls may be introduced.

Public Health management of persons involved in outbreak control activities

There are three aspects to public health management of persons involved in outbreak control activities for avian influenza:

- Occupational surveillance of workers involved in outbreak control activities for symptoms of AI
- Administration of antiviral prophylaxis
- Ensuring mechanisms are in place for the administration of seasonal influenza vaccine, if influenza is circulating

More than 200 DAFM veterinary and ancillary personnel have already been assessed as medically fit for outbreak control activities and have all been offered seasonal influenza vaccine. Additional DAFM and contract workers employed for outbreak control measures will be assessed /screened by Occupational Health Physicians contracted by DAFM.

The DAFM, UCD School of Public Health and Population Sciences and an Occupational Health Physician have carried out a risk assessment of emergency response personnel who may be involved in outbreak control activities. Workers have been categorised according to their level of potential exposure (Levels 1 to 6). The categorisation guidance and risk assessment may be seen in Appendix 15.

Workers involved in outbreak control activities are workers entering environments in which potentially infected poultry is kept, or who are in close contact with potentially infected birds or bird products. They need appropriate PPE (Appendix 5), information on AI, on the need to monitor for

symptoms, to be under surveillance, and to be offered prophylaxis. They should also be vaccinated with seasonal influenza vaccine.

Checklists

A. Occupational Surveillance

1. This will be led by Public Health
2. DAFM will supply names and contact details of all those who will be involved in outbreak control activities. Appendix 17.
3. DAFM will appoint a liaison manager to work with Public Health Doctor(s) regarding occupational surveillance. He/she will contact the Public Health Doctor immediately if a worker becomes ill, or is absent from work. Such workers need to be followed up urgently by public health. If these workers require clinical assessment, public health is to refer them as arranged locally (hospital/clinic etc.).
4. Provide each worker with information on avian flu and its symptoms*, how to self-monitor for symptoms, and what to do if symptoms develop (Appendix 10).
5. Provide digital thermometer for twice daily oral temperature readings
6. Provide a small supply of surgical masks
7. All those under occupational surveillance need to self monitor daily during culling activities and for **7 days** after last exposure.
8. Notify the worker's GP that the person is under occupational surveillance and what measures are being taken (Appendix 12)
9. A 1-2 months serum sample (flu serology) may be taken, following discussion with the NVRL. This will be carried out by DAFM occupational health staff.

*Those at risk of occupational exposure should be aware of the early clinical signs of H5N1 infection, but also understand that many other common diseases – of far less health concern – will show similar early symptoms. Most patients infected with the H5N1 virus show initial symptoms of fever (38^0 C or higher) followed by influenza-like respiratory symptoms, including cough, rhinorrhoea, sore throat, and (less frequently) shortness of breath. Watery diarrhoea is often present in the early stages of illness, and may precede respiratory symptoms by up to one week. Gastrointestinal symptoms (abdominal pain, vomiting) may occur and headache has also been reported. To date, one report has described two patients who presented with an encephalopathy and diarrhoea without apparent respiratory symptoms.

B. Administration of antiviral prophylaxis

10. Check that Oseltamivir is available locally
11. Assess each worker's duties with regard to need for Oseltamivir chemoprophylaxis (Appendix 9), and provide the Tamiflu leaflet if appropriate (Appendix 13).

C. Seasonal Influenza Vaccination

12. Vaccinate with seasonal influenza vaccine, if influenza is circulating, and if not already vaccinated. This may require local arrangements between GPs and public health. (The majority of Department of Agriculture staff have been vaccinated)

Contingency arrangements need to be considered for provision of translation services (oral and written), as some poultry workers come from different countries and have may have limited understanding of English.

Strict and Standard approaches to management of an AI incident

The approach adopted by the Health Protection Agency in the UK to the management of AI incidents is that the risk in an incident is assessed and reassessed as new information becomes available, so that the incident management can be tailored to the prevailing risk. This is known as dynamic risk assessment (DRA), and DRA tools are available to support these assessments, such as the one developed by HPZone. This approach is also to be adopted in Ireland.

On initial notification, a precautionary "Strict Approach" to management should be adopted, until further information becomes available with which to further refine the risk assessment. For some situations, the Strict Approach will need to remain throughout the incident, but for others, a change to a Standard Approach might be possible. A Standard Approach might also need to be modified to a Strict Approach in the light of emerging epidemiological, clinical or virological information and expert advice.

The Strict Approach

- Keep the numbers of persons likely to be exposed during the response to an absolute workable minimum
- Significant efforts should be made to ensure that prophylaxis for persons already exposed (contacts) when the incident is first reported is started with the minimum avoidable delay
- Prophylaxis for those who are going to be involved in outbreak control activities must be started in advance of the commencement of such duties.
- Follow up may not just be confined to persons directly exposed (contacts), but might also include close/family contacts of these contacts. Follow up arrangements must be comprehensive and robust, so that cases in contacts (and their contacts if under surveillance) can be picked up rapidly and so that person-to-person transmission can be ruled out.

The Standard Approach

- Keep the numbers of persons likely to be exposed during the response to an absolute workable minimum
- Prophylaxis for contacts, and for those involved in outbreak control activities ,may be stopped if already started as part of the strict approach (or need not be started) provided that, in the current incident and in the worldwide literature, there have been:
    - No human deaths
    - No serious human illnesses
    - No person-to-person transmission (lab confirmed)
    - No large numbers of humans affected by common clinical syndrome suspected or confirmed to be linked to that subtype

  If any of these occur, then a strict approach must be adopted
- Follow up of contacts and workers involved in outbreak control activities should be passive through provision of information and advice to report any suspicious illnesses without delay

Circumstances which qualify for a strict approach

- The initial period of any incident when the DAFM has contacted Public Health indicating strong suspicion or confirmed AI where the specific influenza subtype is completely unknown
- Any period during an incident when the only information available at the time relates to the H subtype (N is unknown, high path/low path is unknown) and that H subtype is confirmed by DAFM to be H5 H7 or H9
- Any period during an incident when the H subtype is confirmed by DAFM to be H5, H7 and in addition DAFM has made a provisional identification of a high pathogenicity virus
- Any incident in which associated human deaths are already apparent
- Any incident in which AI-associated serious human illness is already apparent or strongly suspected
- Any incident in which person-to-person transmission of a relevant influenza subtype is already confirmed by laboratory tests
- Any incident in which widespread person-to-person transmission of a relevant AI-associated clinical illness is already suspected
- Any incident (in addition to the above) in which the expert virological/epidemiological view is that the currently identified virus has significant pandemic potential

Circumstances which may also qualify for a strict approach (need to seek expert virolovial and epidemiological advice)

- An incident in which the influenza subtype is confirmed by Dept Ag to be H2 (not currently circulating, and cause of previous pandemic)
- An incident in which the influenza subtype is confirmed by Dept Ag to be H10 (documented cases of human disease)

Other agreed triggers for upgrading from a standard to a strict approach

- Any incident in which AI-associated human death(s) are discovered
- Any incident in which AI-associated serious human illnesses becomes apparent or strongly suspected
- Any incident in which person-to-person transmission of a relevant influenza subtype is discovered by confirmed laboratory tests

Any incident in which the expert virological/epidemiological evidence based advice is that the currently identified virus has significant pandemic potential. An algorithm, summarising the management of the public health consequences of avian influenza in poultry/wild birds is available in Appendix 19

Public Health management of contacts of human cases of AI

Please refer to the document *"Irish Guidelines for the Public Health Management of Human Cases and of Influenza A/H5N1 and their contacts." This is available in supplement 11, Part 2.*

References

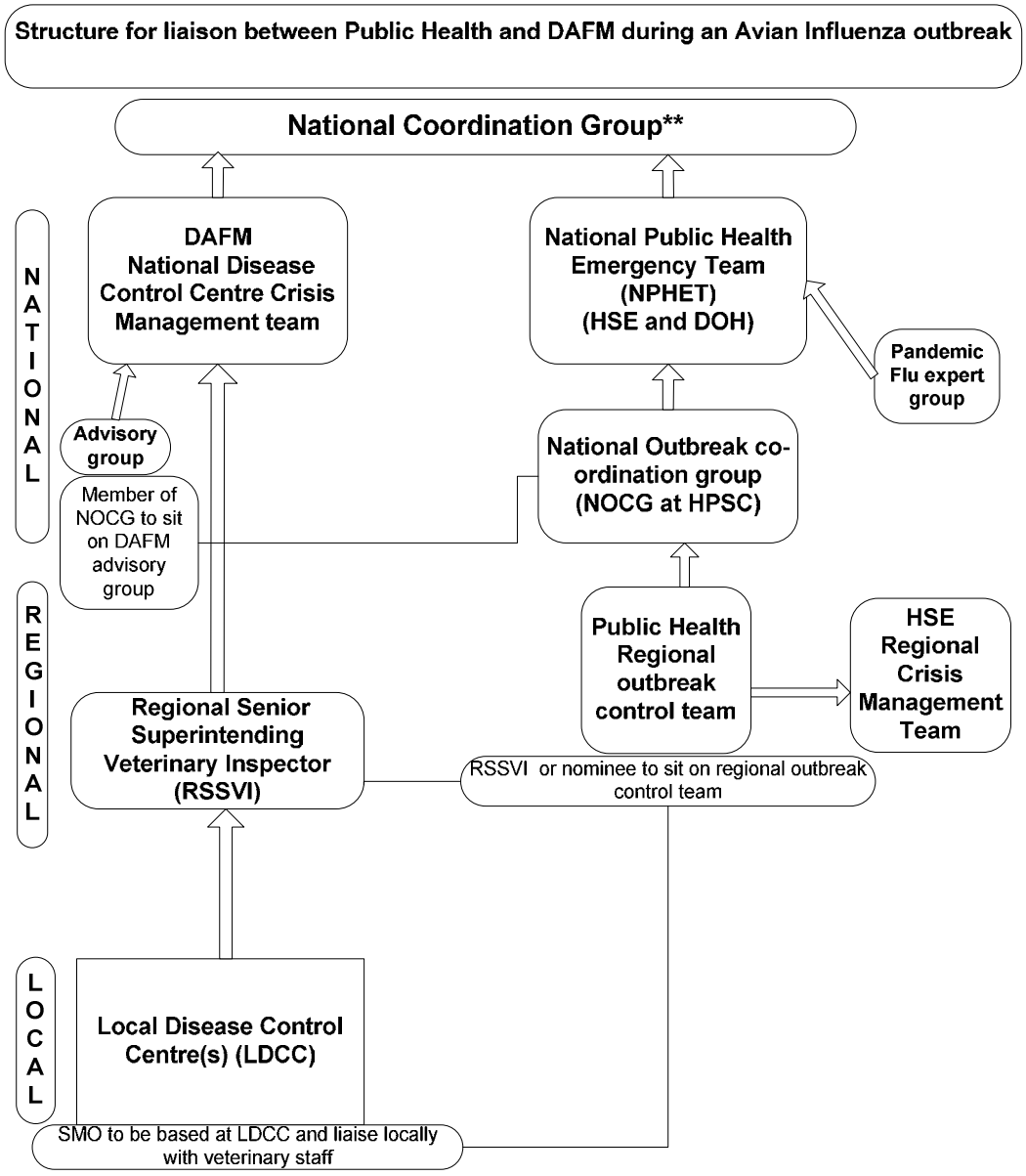
1. EU. Commission Decision on biosecurity measures. 2005.

2. WHO. Guidelines for Drinking-Water Quality. 3rd Edition. 2006.

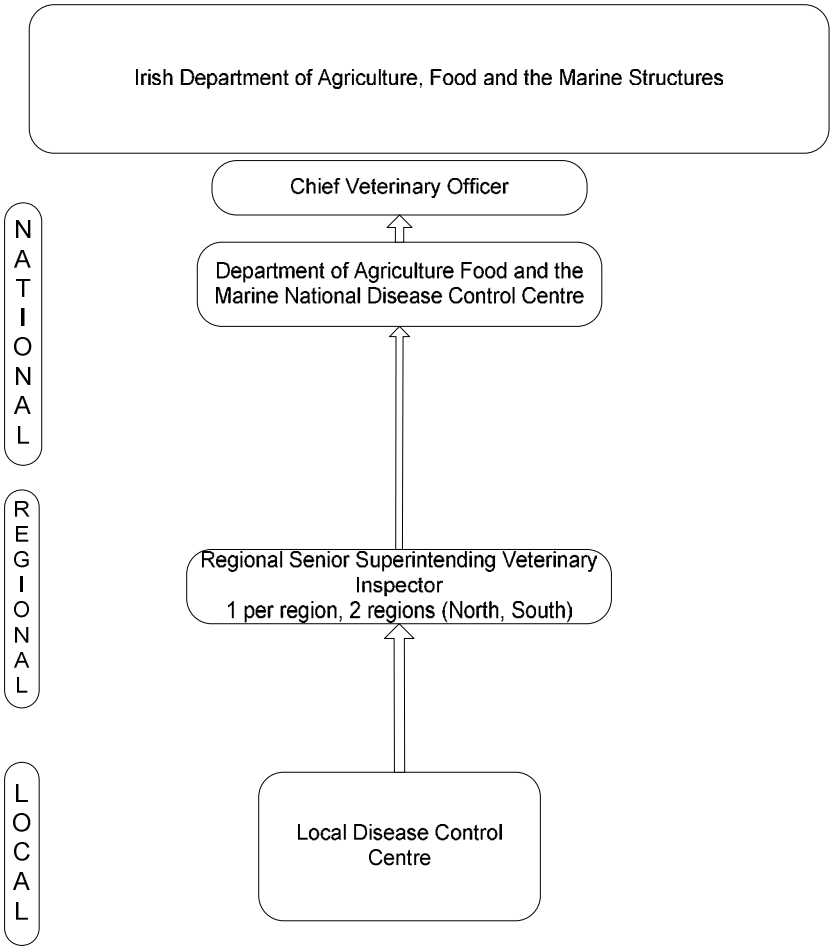
3. ECDC. Avian influenza A/H5N1 in bathing and potable (drinking) water and risks to human health. 2006.

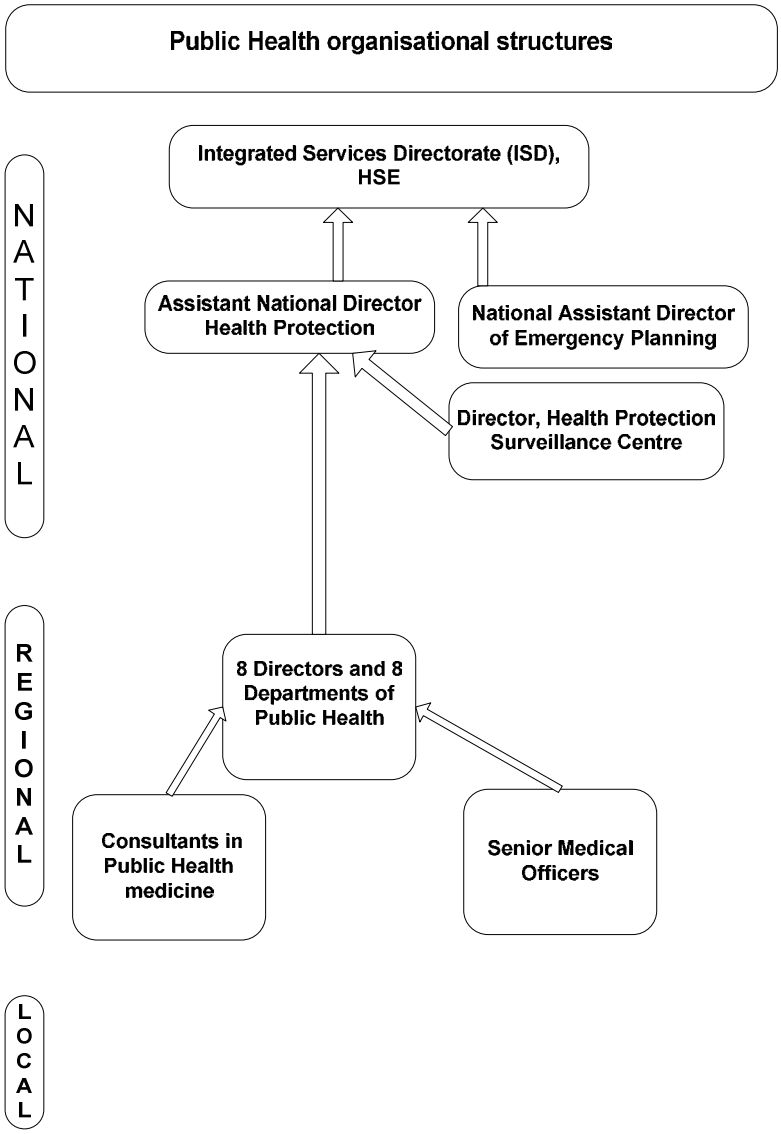
4. WHO. Review of the latest available evidence on risks to human health through potential transmission of avian influenza (H5N1) through water and sewage. 2006.

Appendix 1 Notification procedure



** Led by DAFM or DOH, depending on whether mainly AI, or if there are human cases. See Guidelines for Coordinating a national level emergency/crisis response, 2011.


Irish Department of Agriculture, Food and the Marine Structures
Chief Veterinary Officer
NATIONAL
Department of Agriculture Food and the Marine National Disease Control Centre
REGIONAL
Regional Senior Superintending Veterinary Inspector
1 per region, 2 regions (North, South)
LOCAL
Local Disease Control Centre


Public Health organisational structures
NATIONAL
REGIONAL
LOCAL
Integrated Services Directorate (ISD), HSE
Assistant National Director Health Protection
National Assistant Director of Emergency Planning
Director, Health Protection Surveillance Centre
8 Directors and 8 Departments of Public Health
Consultants in Public Health medicine
Senior Medical Officers

Appendix 2: Case Definition for Influenza A/H5N1 in Humans (WHO)

The case definition for influenza A/H5N1 used in Ireland is the case definition developed by the World Health Organisation and issued in August 2006. It is notable that this case definition applies to the current phase of pandemic alert (phase 3) and may change as new information about the disease or its epidemiology becomes available.

This case definition is defined by a set of clinical, epidemiological and microbiological criteria and is classified as Person under Investigation (PUI), suspected case, probable case and confirmed case. These definitions are outlined as follows:

Person Under Investigation

A person whom public health authorities have decided to investigate for possible influenza A/H5N1 infection.

Suspected case of Influenza A/H5N1

A person presenting with unexplained acute lower respiratory illness with fever (>38 ºC) and cough, shortness of breath or difficulty breathing.

AND

One or more of the following exposures in the 7 days prior to symptom onset:

a. Close contact (within 1 metre /3 feet) with a person (e.g. caring for, speaking with, or touching) who is a suspected, probable, or confirmed H5N1 case

b. Exposure (e.g. handling, slaughtering, defeathering, butchering, preparation for consumption) to poultry or wild birds or their remains or to environments contaminated by their faeces in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month

c. Consumption of raw or undercooked poultry products in an area where H5N1 infections in animals or humans have been suspected or confirmed in the last month

d. Close contact with a confirmed H5N1 infected animal other than poultry or wild birds (e.g. cat or pig)

e. Handling samples (animal or human) suspected of containing H5N1 virus in a laboratory or other setting.

Probable case of Influenza A/H5N1
Probable definition 1:
A person meeting the criteria for a suspected case

AND

One of the following additional criteria:

a. Infiltrates or evidence of an acute pneumonia on chest radiograph plus evidence of respiratory failure (hypoxemia, severe tachypnoea)

OR

b. Positive laboratory confirmation of an influenza A infection but insufficient laboratory evidence for H5N1 infection.

Probable definition 2:
A person dying of an unexplained acute respiratory illness who is considered to be epidemiologically linked by time, place, and exposure to a probable or confirmed H5N1 case.

Confirmed Case of Influenza A/H5N1

A person meeting the criteria for a suspected or probable case

AND

One of the following positive results conducted in a national, regional or international influenza laboratory whose H5N1 test results are accepted by WHO as confirmatory:

a. Isolation of an H5N1 virus
b. Positive H5 PCR results from tests using two different PCR targets, e.g. primers specific for influenza A and H5 HA
c. A fourfold or greater rise in neutralization antibody titre for H5N1 based on testing of an acute serum specimen (collected 7 days or less after symptom onset) and a convalescent serum specimen. The convalescent neutralising antibody titre must also be 1:80 or higher;
d. A microneutralisation antibody titre for H5N1 of 1:80 or greater in a single serum specimen collected at day 14 or later after symptom onset and a positive result using a different serological assay, for example, a horse red blood cell haemagglutination inhibition titre of 1:160 or greater or an H5-specific western blot positive result.

Algorithm for the management of persons with acute febrile respiratory illness who may have avian influenza

i.e. returning travellers and visitors from countries affected by avian influenza and people with close contact with sick poultry and/or wild birds

1 Screening

As soon as the patient mentions a febrile respiratory illness and travel in the last 2 weeks[1] to an area of the world affected by H5N1[2] **OR** contact with sick, dying or dead poultry and/or wild birds, the following precautions should be taken before continuing with the assessment:

YES

2 Assessment

Clinical

Acute onset of fever (temperature ≥38°C) with signs and symptoms of an acute respiratory infection.

AND

Epidemiological

At least one of the following exposures (a, b, c) within 7 days prior to onset of symptoms:

A. Contact with poultry or wild birds: Reside in or have visited an area of a country where influenza A/H5N1 is currently suspected or confirmed as reported on the HPSC web-site **AND**

Having been in close contact (within one metre) with sick or dead domestic poultry and/or wild birds in the affected area; **OR**

Having been in a home or farm where sick or dead domestic poultry have been reported in the previous six weeks in the affected area;

B. Human Contact: Having been in close contact (within one metre) with a person reported as a probable or confirmed case of influenza A/H5N1;

C. Laboratory Contact: Having worked in a laboratory where there is potential exposure to influenza A/H5N1;

If patient doesn't meet the above criteria and you are still concerned regarding avian influenza please contact HSE-HPSC 01-8765300.

NO

Unlikely to be Influenza A (H5N1). Treat as indicated.

YES

Refer to Hospital for Treatment & Investigation

Treatment & Investigations (treat samples as "high risk")

Consider treatment with oseltamivir

- Combined nose/throat swab in virus transport medium for immediate H5N1 PCR at the NVRL. Seasonal influenza A/B rapid test will be done in parallel at NVRL.
- FBCs with differential (lymphopenia is a prominent feature of AI)
- LFTs (liver function frequently deranged with AI)
- Legionella & pneumococcal urinary antigens
- Serology mycoplasma, influenza A & B, adenovirus, RSV & 20mls reserve
- CXR
- Blood culture
- Pulse Oximetry
- Sputum culture ± gram stain

3

Negative H5N1

Treat as appropriate AND remove from strict respiratory isolation if appropriate

Positive H5N1

Inform local MOH immediately. Local MOH to inform HSE-HPSC immediately of result and discuss prophylaxis.

Infection Control & Reporting[3]

Strict hand hygiene

Primary care / community

Location: At patient's home if possible
Patient to wear mask (surgical)
Staff to wear mask, gown, gloves and eye protection

Hospital

Location: Side room
Patient to wear mask (surgical)
Staff to wear mask (surgical), gown, gloves and eye protection

Inform Director of Public Health (MOH) immediately

Inform hospital infection control & occupational health

Standard, Contact & Droplet Precautions

Patient: Single room adequately ventilated (≥12 air changes per hour)

Staff:
Routine care – barrier precautions[4]

Aerosolizing procedures – barrier precautions[4] & correctly fitted high filtration mask – minimum standard FFP2.

1. Includes the possibility of a long incubation and late presentation
2. For countries affected by avian influenza see HPSC website http://www.hpsc.ie/hpsc/A-Z/Respiratory/AvianInfluenza/AffectedCountries/
3. For infection control advice see http://www.who.int/csr/resources/publications/AI_Inf_Control_Guide_10May2007.pdf
4. Barrier precautions = adequate hand hygiene, use of gowns, clean gloves, medical mask and eye protection if splashes are anticipated

Please check HPSC website www.hpsc.ie for further updates.

HSE-HPSC Version 2.5 December 19th 2007 *Originally adapted with permission from material produced by HPA UK*

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Avian Influenza Case Surveillance

Report of Suspect, Probable or Confirmed Case of Influenza A (H5 or H5N1)

hpsc

Date of Notification to Public Health Department:
Notifying Clinician: | Notifying Institute / Organisation:

Date of Report to WHO: | Date of Report to HPSC:
Name of Reporter to HPSC: | Position of Reporter:
HSE Area / Region of Reporter: | County of Reporter:
Reporter's Telephone: | Reporter's Fax:
Reporter's E-mail:

PATIENT INFORMATION

Case ID | Surname: | Forename:

Sex: F ☐ M ☐ NK* ☐ | Date of Birth: | Age (years): | Age (months):

Current Address: | County:

Telephone (Home): | Telephone (Mobile):

Country of Residence : | Country of Infection:
Ethnicity: | Occupation:

GP Surname:
GP Forename:
GP Work Phone:
GP Mobile Phone:
GP Fax:
GP Address:
GP E-mail:

CLINICAL DETAILS

Date of 1st diagnosis:
Date of onset of symptoms:

Current Health Status: Recovering ☐ | Moderately ill ☐ | Severely ill ☐ | Died ☐

If the patient died: Due to this ID ☐ | Not Due to this ID ☐ | Not Known ☐ | Not Specified ☐

Date of death: | Autopsy: Yes ☐ No ☐ Not Known ☐

Symptoms:	Yes	No	Not Known		Yes	No	Not Known
High fever (≥38ºC)	☐	☐	☐	Cough	☐	☐	☐
Dyspnoea / Difficulty breathing	☐	☐	☐	Sore throat	☐	☐	☐
Diarrhoea	☐	☐	☐	Conjunctivitis	☐	☐	☐
Myalgia	☐	☐	☐	Other, please specify:			

INVESTIGATION STATUS

Patient under investigation ☐
Investigated, not a case ☐
Investigated, suspect influenza A H5N1 ☐
Investigated, probable influenza A H5N1 ☐
Investigated, confirmed influenza A H5N1 ☐

** NK = Not Known*

Please forward this form to your local Department of Public Health, who will forward the information to:
Director of Health Protection Surveillance Centre (Fax: 01 - 856 12 99)

Version 2.3 - 16/11/2007

Avian Influenza Case Surveillance

HOSPITAL ADMISSION

Admitted to hospital? **Yes** ☐ **No** ☐ **Not Known** ☐

Please complete the following table for any hospital admission (including transfers):

	Name of Hospital	Date of Admission	Was person isolated / cohorted? **Yes / No / NK**	Date Isolated / Cohorted	Date of Discharge
Hospital 1					
Hospital 2					

	Yes	No	Not Known
During any hospital admission, was the person mechanically ventilated?	☐	☐	☐
During any hospital admission, was the person admitted to ICU?	☐	☐	☐

TRAVEL RELATED

In the 7 days prior to the onset of symptoms, did the case travel or reside **OUTSIDE** Ireland? **Yes** ☐ **No** ☐ **Not Known** ☐

If **YES**, please give details below:

Initial City / Port of Departure:

City / Port of Arrival	Country	From (dd/mm/yy)	To (dd/mm/yy)	Primary Mode of Transport
1.				
2.				
3.				

In the 7 days prior to the onset of symptoms did the case travel or reside in areas **WITHIN** Ireland? **Yes** ☐ **No** ☐ **Not Known** ☐
(excluding their own home if resident in Ireland)

If YES, please give details:

Address	From (dd/mm/yy)	To (dd/mm/yy)	Primary Mode of Transport
1.			
2.			
3.			

EXPOSURE HISTORY

	Yes	No	Not Known
a) During the 7 days prior to onset of symptoms was the case working: In an at-risk animal-related occupation*?	☐	☐	☐
In a laboratory where samples are tested for influenza A/H5 viruses?	☐	☐	☐
As a health care worker (HCW)	☐	☐	☐

** see Appendix A for list of at-risk animal-related occupations*

b) During the 7 days prior to onset of symptoms did the case have close contact (within 1 metre/3 feet), in any setting, with live or dead: Domestic fowl?	☐	☐	☐
Wild birds?	☐	☐	☐
Swine?	☐	☐	☐
c) During the 7 days prior to onset of symptoms did the case have exposure to a setting where the following were confined in the previous 6 weeks? Domestic fowl?	☐	☐	☐
Wild birds?	☐	☐	☐
Swine?	☐	☐	☐

*If **YES, to any of sections a, b or c** please give address details of each location:*

Address
1.
2.
3.

Date 1st Exposed | Date Last Exposed | Duration of Total Exposure (Hours)

Please forward this form to your local Department of Public Health, who will forward the information to:
Director of Health Protection Surveillance Centre (Fax: 01 - 856 12 99)

EXPOSURE HISTORY *(continued)*

If HCW, please specify type:

If HCW, did case have direct patient care responsibilities? **Yes** ☐ **No** ☐ **Not Known** ☐

If the case had been exposed to potentially infected poultry in the 7 days prior to onset of symptoms were they wearing Personal Protective Equipment (PPE)? **Yes** ☐ **No** ☐ **Not Known** ☐

If YES, date when they started wearing it?

Were they wearing any of the following during that exposure? **Please tick all that apply**

Gloves ☐	Safety glasses ☐	Impermeable overalls ☐	Disposable shoes or shoe covers ☐
Mask ☐	Head and hair cover ☐	Disposable outer garments ☐	Boots that are disinfected and worn again ☐
			Outer garments that are worn repeatedly ☐

During the 7 days prior to onset of symptoms, had the case been in close contact with: **Yes** **No** **Not Known**

A confirmed case of influenza A/H5? ☐ ☐ ☐

A person with an unexplained acute respiratory illness that later resulted in death? ☐ ☐ ☐

Any other person for whom the diagnosis of influenza A/H5 is being considered? ☐ ☐ ☐

If YES, please give details:

Exposure history unknown or undetermined: **Yes** ☐ **No** ☐

Is this case linked to an avian influenza outbreak? **Yes** ☐ **No** ☐ **Not Known** ☐

If YES, is the outbreak: Already known ☐ Newly identified ☐

If already known, please give outbreak code:

What is the setting of this outbreak?

Household/Private House ☐	Extended Family ☐	Recreational Camp ☐
Hospital ☐	Military Barracks ☐	Other Residential Institution ☐

Other, please specify:

SUMMARY OF LABORATORY RESULTS

	Yes	No	Not Known
Positive RT-PCR for influenza A/H5 or A/H5N1?	☐	☐	☐
Positive viral culture for influenza A/H5N1?	☐	☐	☐
Positive immunofluorescence antibody (IFA) test using influenza A/H5 monoclonal antibodies?	☐	☐	☐
4-fold rise in influenza A/H5 specific antibody titre in paired serum samples?	☐	☐	☐

	Yes	No	Not Known
Were samples or isolates sent to a WHO reference laboratory for further confirmation of diagnosis of influenza A/H5 infection?	☐	☐	☐

If YES, please specify which reference laboratory:

Please specify influenza A/H5 N subtype: N unknown ☐ N1 ☐ N2 ☐

If known, please specify influenza A/H5 strain:

Version 2.3 - 16/11/2007

Please forward this form to your local Department of Public Health, who will forward the information to:
Director of Health Protection Surveillance Centre (Fax: 01 - 856 12 99)

PROPHYLAXIS AGAINST INFLUENZA

Was the case vaccinated against seasonal influenza in the 6 months prior to the onset of symptoms? Yes ☐ No ☐ Not Known ☐

If YES, in which country did the case receive it? _____

Was the case vaccinated against influenza A (H5N1)? Yes ☐ No ☐ Not Known ☐

Date case was vaccinated against influenza A (H5N1)? _____

During the **7 days** prior to onset of symptoms, was the case taking any antiviral medication? Yes ☐ No ☐ Not Known ☐

If YES: Name of Antiviral: Oseltamivir phosphate (Tamiflu) ☐ Zanamivir (Relenza) ☐ Dosage (mg) _____

Start Date _____ Stop Date _____

Did the case take antivirals everyday? Yes ☐ No ☐ Not Known ☐

TREATMENT

Was antiviral treatment commenced? Yes ☐ No ☐ Not Known ☐

If YES: Name of Antiviral:

- Oseltamivir phosphate (Tamiflu) ☐
- Zanamivir (Relenza) ☐
- Oseltamivir phosphate (Tamiflu) & Zanamivir (Relenza) ☐
- Other antiviral ☐

If Other antiviral, please specify: _____

	Start Date	Stop Date	Dosage (mg)
Oseltamivir phosphate (Tamiflu)			
Zanamivir (Relenza)			
Other antiviral			

How soon after the onset of symptoms did the case begin antiviral treatment?

	Yes	No	Not Known
Less than 12 hours	☐	☐	☐
Less than 24 hours	☐	☐	☐
Less than 48 hours	☐	☐	☐
More than 48 hours	☐	☐	☐
Did the case take antivirals every day?	☐	☐	☐

CASE CLASSIFICATION

Case Classifications:

- Person under investigation ☐
- Suspect influenza A (H5N1) ☐
- Probable influenza A (H5N1) ☐
- Confirmed influenza A (H5N1) ☐

If Other, please specify _____

Date of final case classification _____

FINAL CASE OUTCOME (COMPLETE ONCE FINAL OUTCOME IS KNOWN)

Date of final case outcome: _____

Recovered ☐ Still ill ☐ Died ☐ Lost to follow-up ☐

Please forward this form to your local Department of Public Health, who will forward the information to:
Director of Health Protection Surveillance Centre (Fax: 01 - 856 12 99)

AVIAN INFLUENZA PERSONAL CONTACTS [1]

Reporting Region / Area:		Region / Area AI Case ID:	

Please give details of all people with whom you have had close contact since the onset of your symptoms.
This includes people who:

1	Live with you
2	Work in the same environment as you
3	Friends / family / others who have visited you / whom you have visited
4	Other close contacts

***Please use numbers (1-4) in table above for 'Type of Contact'**

Name & Address of Contact	Phone Number	Type of Contact*	Date of Last Contact	Is this person ill with influenza like-illness? (If YES, please indicate Onset Date)		
1.		☐		Yes / No / NK	☐	
2.		☐		Yes / No / NK	☐	
3.		☐		Yes / No / NK	☐	
4.		☐		Yes / No / NK	☐	
5.		☐		Yes / No / NK	☐	
6.		☐		Yes / No / NK	☐	
7.		☐		Yes / No / NK	☐	
8.		☐		Yes / No / NK	☐	
9.		☐		Yes / No / NK	☐	
10.		☐		Yes / No / NK	☐	

[1] A contact of a human case is defined as a person who shared a defined setting
- household
- extended family
- hospital or other residential institution
- military barracks or recreational camps

with a person for whom the diagnosis is being considered, while the case was in their infectious period (i.e. from 1 day before onset of symptoms to 7 days after onset of symptoms, or to the date prescribed by public health).

If more contacts, please add in AI contact sheet and staple to this form. Thank you.

Please forward this form to your local Department of Public Health, who will forward the information to:
Director of Health Protection Surveillance Centre (Fax: 01 - 856 12 99)

MISCELLANEOUS COMMENTS

Appendix A - List of occupations likely to have close contact with live poultry or poultry carcasses

1. Poultry flock owners and their families
2. Poultry veterinary practitioners
3. Poultry advisors
4. DAF veterinary inspectors and other personnel involved in outbreak control measures
5. Laboratory personnel involved in poultry post mortems or poultry virology
6. Catching teams
7. Poultry transporters
8. Carcass transport and rendering plant personnel
9. Workers in the hang-on, stunning and plucking areas in slaughter plants
10. Fieldsmen
11. Vaccinators / selectors etc.
12. People involved in cleaning & disinfection of poultry houses or poultry transport
13. Personnel involved in litter removal and litter processing.

Appendix 5: Guidance for protection of persons involved in avian influenza outbreak control and eradication activities in Ireland

October2012

Introduction

Avian influenza is a disease of birds and poultry caused by influenza A viruses. Other animals can become infected, such as pigs, horses etc, but may remain asymptomatic. It can also rarely affect humans.

Routes of infection

Birds that are infected with influenza can shed virus in saliva, nasal secretions and faeces. Transmission from sick or dead birds can occur via these routes to other birds or to humans. Faeces contain high concentrations of virus and are an important factor in spreading disease. The viruses can survive in the environment for up to 3 months in cool and moist conditions.

Clinical symptoms in humans

Infection with Avian influenza in humans can cause flu like symptoms, i.e. cough, temperature, sore throat and coughing as well as diarrhoea. Avian influenza can also cause conjunctivitis, i.e. red watery itching painful eyes, with a purulent discharge. It can cause serious respiratory complications and death.

Activities that could result in exposure to avian influenza-related poultry outbreaks include euthanasia (culling of birds), carcass disposal, and cleaning and disinfection of premises affected by avian influenza.

These recommendations aim to protect individuals involved in the response to an outbreak of Highly Pathogenic Avian Influenza (HPAI) from illness. These should also be considered for all outbreaks of avian influenza.

Efforts must be made to limit exposure of persons to outbreaks of infected avian influenza. Technical and organisational measures must be taken to minimise the risk posed to those who will be required to work on outbreak control activities.

1. Hand hygiene

All workers who have been in close contact with infected animals should know the importance of and the need to adhere to proper use of hand hygiene after the following activities:

- Contact with infected or exposed poultry
- Contact with contaminated surfaces
- Removal of gloves

Hand hygiene consists of:

Washing with soap and water for 15-20 seconds

Or use of alcohol based hand rub/wipes.

Hand hygiene is **the most important measure in preventing the spread of infection** after contact with infected or exposed poultry, contact with contaminated surfaces or after removing gloves.

There should be no eating, drinking, smoking, applying cosmetics or putting on/taking off contact lenses in high-risk areas. Used wipes must be disposed of appropriately.

2. Personal Protective Equipment

All workers should have access to:

- Appropriate personal protective equipment (PPE)
- Instructions and training in PPE use
- Respirator fit-testing

Disposable **gloves** made of lightweight nitrile or vinyl, or heavy-duty rubber work gloves that can be disinfected, should be worn. A thin cotton glove may be worn inside the external glove to protect against contact dermatitis. Change gloves immediately if they become torn or damaged. Remove gloves promptly after use, before touching non-contaminated surfaces and items.

Protective clothing, preferably disposable outer garments or overalls with hoods, or surgical gowns with long cuffed sleeves. This includes protective cover for the hair. (Mop cap or hair net)

Disposable **protective shoe covers** or rubber or polyurethane boots that can be cleaned and disinfected should be worn.

Safety goggles should be worn to protect the mucous membrane of the eyes. They should comply with EN standards[4] and be the anti-mist type to allow prolonged periods of use. It's really important to avoid touching or rubbing eyes with hands after removing the goggles.

Disposable particulate respirators (e.g. European EN149: 2001 FFP2; or European EN149: 2001 FFP3;) are the minimum level of respiratory protection that should be worn. Prior to undertaking any outbreak eradication and control activities, **workers must be fit-tested to the respirator model that they will wear** and know how to check the face-piece to face seal. Workers who cannot wear a disposable

particulate respirator due to facial hair, should wear a loose-fitting (i.e. helmeted or hooded) powered air purifying respirator equipped with high-efficiency filters.

Disposable PPE should be **properly discarded (sealed plastic bags)** and non-disposable PPE should be cleaned and disinfected as specified. The sealed plastic bags need to be disposed of appropriately. **Hand hygiene should be performed after removal of PPE**.

Instructions and training in PPE use.

Workers should be trained in proper techniques of donning, removing and disposing of PPE, without contaminating him/herself. Prior to use of respirators, workers must be fit-tested to the model of respirator that they will wear.

Summary of order of removal of protective attire/equipment

1. Remove gloves* - use technique that avoids touching the outside surface of the gloves with bare hands
2. Remove gown* - use technique that minimises the risk of touching the outside surface of the gown
3. Wash/decontaminate hands
4. Remove eye protection
5. Remove mask/respirator
6. Wash/decontaminate hands again

* Order may vary according to local protocol

3. Use of oseltamivir

Unless medically contraindicated, workers should receive oseltamivir 75mg daily prophylactically for the duration of time during which contact with infected poultry or contaminated surfaces occurs. This should be continued for 7 days following last exposure. If oseltamivir has not been given prophylactically, and workers then present with symptoms suggestive of avian influenza, treatment with oseltamivir 75mg twice daily for 5 days should be initiated. The Director of Public Health as Medical Officer for Health for the affected area will make arrangements for supply and distribution of oseltamivir as prophylactic treatment.

4. Vaccination with seasonal influenza vaccine

If human influenza is circulating, unvaccinated workers should receive the current seasons influenza vaccine[5] to reduce the possibility of dual infection with avian and human influenza viruses.

5. Surveillance and monitoring of workers

All those in contact with potentially infected materials should be given information about avian influenza, and its symptoms, and should monitor their health for any suggestive symptoms. (Appendix 7)

Workers should be asked to report any relevant health problems when undertaking outbreak control and eradication activities, and for one week following their last exposure to avian influenza-infected birds or contaminated environmental surfaces as follows:

- Cough, shortness of breath
- Fever
- Flu-like illnesses: sore throat, myalgia/arthralgia (painful muscles or joints), or headache
- Watery diarrhoea – This is often present in the early stages of illness and may precede respiratory symptoms by up to one week
- Abdominal pain and vomiting
- Headache

Before seeking medical assistance, they should inform them that they might have been exposed to avian influenza. Suspected cases should be placed in isolation. If these symptoms develop, the attending doctor should notify the Director of Public Health/ MOH immediately.

Persons at high risk for severe complications of influenza (e.g. immunocompromised) those over 60 years old, or with chronic heart or lung disease or those for whom oseltamivir is contraindicated should avoid working with infected chickens. Those on medications such as steroids should seek medical advice prior to working with infected chickens.

A blood sample may be taken 1-2 months after outbreak control activities have commenced in exposed animal workers and veterinarians. This will be done by the occupational health staff.

6. Contacts should not visit other farms or unaffected agricultural locations with poultry or other birds to avoid spread of contaminated materials.

References

1. WHO interim recommendations for the protection of persons involved in the mass slaughter of animals potentially infected with highly pathogenic avian influenza viruses. 26 January 2004. http://www.who.int/csr/disease/avian_influenza/guidelines/interim_recommendations/en/index.html. Last accessed 26th August 2005
2. CDC Interim Guidance for protection of persons involved in US avian influenza outbreak disease control and eradication activities, February 17 2004 http://www.cdc.gov/flu/avian/professional/protect-guid.htm. Last accessed 26th August 2005
3. Human Health Issues related to Domestic Avian Influenza Outbreaks. Canadian Pandemic Influenza Committee and affiliated Working Groups, May 2005. http://www.phac-aspc.gc.ca/publicat/daio-enia/index.html Last accessed 26th August 2005.
4. http://www.hse.gov.uk/lau/lacs/68-7.htm. Last accessed 29th August 2005
5. http://www.who.int/csr/disease/influenza/vaccinerecommendations1/en/. Last accessed 29th August 2005

Surveillance Form for Contact of Avian source of Avian Influenza A (H5N1)

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

hpsc

Incident ID

Name of Reporter | Position
Institution / organisation | HSE Area | County

Telephone | Mobile
E-mail: | Fax

CONTACT DETAILS

Contact ID | Date identified as a potential contact
Forename | Surname

DOB | Age | Age Type *(please tick box)* Years Months Weeks Days | Sex: Female Male
Nationality
Home Address

HSE Area | CCA / LHO | Number in household
Home Contact Details: Home | Mobile
E-mail

Occupation

If Healthcare Worker, involved in clinical care or examination of the case? **Yes** **No** **Not Known**

Work Address

HSE Area | CCA / LHO
Work Contact Details: Phone | Mobile
E-mail

GP Name: | GP Phone
GP Address

Vaccinated against most recent seasonal influenza vaccine? **Yes** **No** **Not Known**
If YES, in which country was vaccine received?

SYMPTOMS

	Yes	No	Not Known
Does the contact have symptoms?			
Conjunctivitis			
Cough			
Diarrhoea			
Dyspnoea / difficulty breathing			
Headache			
High fever (≥38ºC)			
Myalgia			
Sore throat			
Other			

If **YES**, date of onset of symptoms

Medications:

If **Other**, please specify:

Surveillance Form for Contact of Avian source of Avian Influenza A (H5N1)

CONTACT EXPOSURE ASSESSMENT - CONTACT WITH AN AVIAN SOURCE OF H5N1

During the risk period* has the person had any contact with poultry, poultry products, poultry manure or sick / dead wild birds? ☐ ☐ ☐

If **YES**, when was the first contact / exposure?
When was the last contact / exposure?
Date of onset of clinical symptoms in birds

Nature of exposure:

AT RISK? **Yes** ☐ **No** ☐

If YES, proceed to Action Plan below
If NO, sign and date the form below

** 2 days before onset of clinical signs in birds until date of restriction*

ACTION PLAN *(TICK ALL THAT APPLY)*

	Yes	No	Not Known
Self-monitoring (temp check twice daily)	☐	☐	☐
Antiviral chemoprophylaxis	☐	☐	☐
GP contacted	☐	☐	☐
Passive surveillance	☐	☐	☐
Quarantine	☐	☐	☐
Vaccination with seasonal influenza vaccine	☐	☐	☐
Refer to hospital for further assessment / investigation	☐	☐	☐
Serology sample (at 1 month)	☐	☐	☐
Other actions	☐	☐	☐

Result ☐ Date

Other actions, please specify:

Details of medication:

Brand name
Generic name
Route of administration
Dose (quantity)
Dose (unit of measurement)
Frequency of administration

OUTCOME

	Yes	No	Not Known
Symptomatic?	☐	☐	☐
Avian Influenza diagnosed?	☐	☐	☐

Name (PRINTED)
Telephone:

Appendix 7: Bird flu (Avian influenza): Information for those who have been in contact with infected poultry or wild birds

What is a contact of bird flu?

A person who is a contact of bird flu is someone who has been in direct contact (within three feet or 1metre) with a source or potential source of bird flu virus, within the past seven days.

This means direct handling of birds, or sharing the same confined airspace as the birds or their droppings.

This can happen if you live on a poultry farm, or work with poultry, or keep poultry at home, and the poultry are infected or suspected of having bird flu. The virus is present in large amounts in the droppings of poultry with bird flu.

You have been identified by public health doctors and vets as being a contact.

What happens now that I am identified as a contact?

A Public Health Doctor will contact you will ask you a number of questions about your health and the type of work you do, and give the following advice

1. Take a drug to prevent bird flu

- You will be offered a course of Tamiflu. This is an antiviral medicine used to prevent or treat bird flu. If you do become infected with the virus, this medicine may prevent you from becoming ill or reduce the severity of the illness. This will be free of charge. Please read the Tamiflu leaflet provided by Public Health, which explains this in more detail.

2. Check your temperature twice a day and look out for flu like symptoms:

- Fever (38^0C or 100.4^0F or higher)
- Flu like symptoms (cough, runny nose, sore throat, temperature or aches and pains)
- Diarrhoea, stomach pains

You will be given a thermometer to measure your temperature regularly. If you develop any of the symptoms listed here during the seven days after your last contact with poultry, contact the Public Health Doctor using the phone number below. You will be given a small supply of masks to wear if you are unwell when seeking medical assistance. Make sure you ring first, and tell them about the type of work you do. Avoid contact with others until you have been checked out.

3. Get vaccinated against seasonal flu (regular flu vaccine)

If it's the flu season (September to May) and you have not already been vaccinated against ordinary flu, you should get this year's flu vaccine as soon as possible. This will stop you from having human and bird flu at the same time. Having bird flu and human flu together could lead to changes (mutations) in the bid flu virus to become more infectious for humans. The Public Health Doctor will tell you where you can get this vaccine. Like Tamiflu the vaccine will be free.

4. Wash your hands frequently

Always wash your hands with soap and water after any contact with poultry, manure or contaminated surfaces. Hand washing is one of the most important protections against bird flu, and should be carried out frequently with soap and water for at least 15-20 seconds. Avoid touching your eyes, nose or mouth with your hands.

5. Avoid all contact with potentially infected poultry or manure.

If a farm is infected with bird flu, only persons authorised by the Department of Agriculture, Food and the Marine will be allowed into close contact with potentially infected poultry or manure. Those allowed must comply with requirements laid down by the Department of Agriculture, Food and the Marine.

If I live in an affected area but haven't been identified as a contact, what should I do?

If you are assessed and found not to have had close contact with infected or ill birds with bird flu, or their manure, then no other action is needed except to watch out for flu like symptoms (cough, runny nose, sore throat, temperature or aches and pains) and seek immediate medical care if they occur.

6. Do not visit other farms or unaffected agricultural locations with poultry or other birds, to avoid spread of contaminated materials.

Your Public Health Contact details are:

Name: _____

Telephone number: _____

Appendix 8: Template letter to GP for close contacts of avian source

<Insert Department of Public Health address>

PRIVATE AND CONFIDENTIAL

Dear Doctor,

Re:
Date of Birth:
Address:

The above named patient has been in close contact with poultry, which have been or may be potentially infected with avian influenza. Avian Influenza may cause a range of human illnesses, the severity of which is determined by the particular subtype involved. Symptoms may include fever, and acute respiratory symptoms. With some types of avian influenza conjunctivitis may also be a symptom.

Oseltamivir protects against this infection when taken as post exposure prophylaxis (PEP) and can also be used to treat the disease. Your patient has been given a supply of oseltamivir by Public Health as post exposure prophylaxis, (75mg/day for 10 days) as he/she has been identified as a contact of an avian source of avian influenza. He/she is being asked to monitor for symptoms suggestive of avian influenza, and is being monitored daily by Public Health. Please let me know if he/she contacts you with symptoms

For further information on avian influenza, please see guidance at the HPSC website www.hpsc.ie and also the enclosed algorithm for assessment of febrile patients with possible avian influenza.

Yours etc

Appendix 10:

Bird flu (Avian influenza): Information for those involved in outbreak control activities

Only those who are needed to control outbreaks of AI should be exposed. The Department of Agriculture will take all measures possible to minimise the risk posed to those who will be required to work on outbreak control activities. Prior to starting work on outbreak control, you will be assessed initially to see if you are suitable for undertaking culling activities. Persons at high risk for severe complications of flu (e.g. those with problems with their immune system) those over 60 years old, with chronic heart or lung disease or those for whom oseltamivir (Tamiflu) is contraindicated should avoid working with infected chickens. Those on medications such as steroids should seek medical advice prior to working with infected chickens. For over 200 Department of Agriculture staff, this assessment has already taken place.

Routes of infection with bird flu
Birds infected with bird flu can shed the virus in saliva, nasal secretions and droppings. Transmission from sick or dead birds can occur via these routes to other birds or to humans. Droppings contain high concentrations of virus and are an important factor in spreading disease. The viruses can survive in the environment for up to 3 months in cool and moist conditions.

Clinical symptoms in humans
Infection in humans with bird flu can cause flu like symptoms, i.e. cough, temperature, sore throat and coughing as well as diarrhoea. It can cause serious respiratory complications and death.

When working on outbreak control activities, please take the following precautions:

1. Wash your hands

When you have been in close contact with infected animals you should wash your hands with soap and water for 15-20 seconds or use an alcohol based hand rub after:

- Contact with infected or exposed poultry or their droppings
- Contact with contaminated surfaces
- Removal of gloves

This is the most important measure you can take to prevent the spread of infection

Do not eat, drink, smoke, apply cosmetics or insert / remove contact lenses in high-risk areas.

Used wipes must be disposed of appropriately.

2. Use the Personal Protective Equipment (PPE) provided by the Department of Agriculture; this includes:

Disposable **gloves** made of lightweight nitrile or vinyl, or heavy-duty rubber work gloves that can be disinfected. You can wear a thin cotton glove inside the external glove to protect against contact dermatitis. Change your gloves immediately if they become torn or damaged. Remove gloves promptly after use, before touching non-contaminated surfaces and items.

Protective clothing, preferably disposable outer garments or overalls with hoods, or surgical gowns with long cuffed sleeves. This includes protective cover for the hair. (Mop cap or hair net)

Disposable **protective shoe covers** or rubber or polyurethane boots that can be cleaned and disinfected should be worn

Safety goggles to protect the mucous membrane of the eyes. It's really important to avoid touching or rubbing eyes with hands after removing the goggles.

Respirators (masks). Before starting working on the outbreak, you need to be fitted with the correct type of mask that will form a correct seal. This is known as fit testing.

Disposable PPE should be **properly discarded in sealed plastic bags** and non-disposable PPE should be cleaned and disinfected as specified by the Department of Agriculture. Always wash your hands after disposing of PPE.

Make sure you have got instructions and training in how to use PPE

Summary of order of removal of protective attire/equipment

1. Remove gloves* - use technique that avoids touching the outside surface of the gloves with bare hands
2. Remove gown* - use technique that minimises the risk of touching the outside surface of the gown
3. Wash/decontaminate hands
4. Remove eye protection
5. Remove mask/respirator
6. Wash/decontaminate hands again

3. Take a preventive drug called oseltamivir (Tamiflu)

You should take oseltamivir 75mg daily as a preventive measure for all of the time that you have contact with infected poultry or contaminated surfaces, and for 7 days after last contact. If you do become infected with bird flu, this medicine may prevent you from becoming ill or reduce the severity of the illness. Please read the Tamiflu leaflet provided by Public Health, which explains this in more detail. Tamiflu is provided free of charge.

4. Get vaccinated against seasonal influenza vaccine

Most workers involved in outbreak control activities have already been vaccinated. If you have not already been vaccinated against ordinary flu, you should get this year's flu vaccine as soon as possible. This will stop you from having human and bird flu at the same time. Having bird flu and human flu together could lead to changes (mutations) in the bid flu virus to become more infectious for humans. The Public Health Doctor will tell you where you can get this vaccine. Like Tamiflu the vaccine will be free.

5. Check your temperature twice a day and look out for flu like symptoms:

- Fever (38^0C or 100.4^0F or higher)
- Flu like symptoms (cough, runny nose, sore throat, temperature or aches and pains)
- Diarrhoea, stomach pains, vomiting

You will be given a thermometer to measure your temperature. .

If you develop any of the symptoms listed here for up to seven days after your last contact with poultry, contact the Public Health Doctor using the phone number supplied. You may be referred to a medical assessment clinic or Accident and Emergency. Make sure you ring first, and tell them about the type of work you do. Avoid contact with others until you have been checked out. You will be given a small supply of masks to wear if you are unwell when seeking medical assistance

You may be asked have a blood test one to 2 months after you start outbreak control activities to check for any signs of infection with bird flu.

Do not visit other farms or unaffected agricultural locations with poultry or other birds, to avoid spread of contaminated materials.

If you have any further queries, contact the public health doctor named by the Department of Agriculture liaison manager.

Your Public Health Contact details are:

Name: _____

Telephone number: _____

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Interim Avian Influenza Surveillance Form for persons under Occupational Surveillance

hpsc

Date of initial report | Name of Reporter

Position | Institution / organisation
County | HSE Area

Telephone | Fax
E-mail:

Personal Details:

Worker ID | Date first identified as worker under surveillance

Forename initials | Surname initials

DOB | Age | Sex: Female ☐ Male ☐

Home Address

HSE Area | CCA / LHO

Home Contact Details: Home | Mobile
E-mail

Work Address

HSE Area | CCA / LHO

Work Contact Details: Phone | Mobile
E-mail

GP Name: | GP Phone

GP Address

Occupational Exposure Assessment

Occupational Surveillance Plan:

	Yes	No
Assessed by occupational health as medically suitable for outbreak control activities	☐	☐

If **YES**, please complete the following:

	Yes	No
Oseltamivir chemoprophylaxis prescribed?	☐	☐
Vaccinated against seasonal flu?	☐	☐
Information leaflet provided?	☐	☐
GP informed?	☐	☐

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Interim Avian Influenza Surveillance Form for persons under Occupational Surveillance

hpsc

Outcome:

Date started outbreak control activities

Date occupational surveillance (OS) commenced

Date OS finished

Symptomatic during surveillance — Yes ☐ No ☐

If **YES**, classified as:
Person under investigation ☐
Suspect AI case ☐
Probable AI case ☐
Confirmed AI case ☐
Other illness ☐

If **Other illness**, please specify

Side effects from Oseltamivir — Yes ☐ No ☐
If **YES**, please specify

Serology taken at 1 month — Yes ☐ No ☐ Result:

Lost to follow up — Yes ☐ No ☐

Date

Name (Printed)

Contact Phone Number

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Interim Avian Influenza Surveillance Form for persons under Occupational Surveillance

hpsc

Date of initial report | Name of Reporter

Position | Institution / organisation
County | HSE Area

Telephone | Fax
E-mail:

Personal Details:

Worker ID | Date first identified as worker under surveillance

Forename initials | Surname initials

DOB | Age | Sex: Female ☐ Male ☐

Home Address

HSE Area | CCA / LHO

Home Contact Details: Home | Mobile
E-mail

Work Address

HSE Area | CCA / LHO

Work Contact Details: Phone | Mobile
E-mail

GP Name: | GP Phone

GP Address

Occupational Exposure Assessment

Occupational Surveillance Plan:

	Yes	No
Assessed by occupational health as medically suitable for outbreak control activities	☐	☐

If **YES**, please complete the following:

	Yes	No
Oseltamivir chemoprophylaxis prescribed?	☐	☐
Vaccinated against seasonal flu?	☐	☐
Information leaflet provided?	☐	☐
GP informed?	☐	☐

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Interim Avian Influenza Surveillance Form for persons under Occupational Surveillance

hpsc

Outcome:

Date started outbreak control activities

Date occupational surveillance (OS) commenced

Date OS finished

Symptomatic during surveillance — Yes ☐ No ☐

If **YES**, classified as:
Person under investigation ☐
Suspect AI case ☐
Probable AI case ☐
Confirmed AI case ☐
Other illness ☐

If **Other illness**, please specify

Side effects from Oseltamivir — Yes ☐ No ☐
If **YES**, please specify

Serology taken at 1 month — Yes ☐ No ☐ Result:

Lost to follow up — Yes ☐ No ☐

Date

Name (Printed)

Contact Phone Number

Appendix 12: Template letter to GP for occupational contact

<Insert Department of Public Health address>

PRIVATE AND CONFIDENTIAL

Dear Doctor,

Re:
Date of Birth:
Address:

The above named patient works with poultry, which have been or may be potentially infected with avian influenza. Avian influenza may cause a range of human illnesses, the severity of which is determined by the particular subtype involved. Symptoms may include fever, and acute respiratory symptoms.

Oseltamivir protects against this infection when taken as prophylaxis and can also be used to treat the disease. Your patient has been given a supply of oseltamivir by Public Health as prophylaxis, as he/she is involved in outbreak control activities associated with avian influenza. While working he/she is using Personal Protective Equipment. He/she is being asked to monitor for symptoms suggestive of avian influenza, and to report any symptoms to Public Health.

For further information on avian influenza, please see guidance at the HPSC website www.hpsc.ie and also the enclosed algorithm for assessment of febrile patients with possible avian influenza.

Yours etc

Before taking Oseltamivir (*Tamiflu*), is there anything I should let the doctor know?

Please remember to inform the doctor before taking this antiviral:

- If you are taking any other medication including those you may have bought without a prescription. Oseltamivir can be taken with paracetamol, ibuprofen or acetylsalicylic acid (Aspirin)
- If you have any drug allergies.
- If you have any kidney problem.
- If you are pregnant or breast-feeding.

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

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Email: info@ndsc.ie **www.ndsc.ie**

OSELTAMIVIR (TAMIFLU)

for the prevention of avian influenza

What is OSELTAMIVIR (TAMIFLU)?

The antiviral you have been advised to take is called Oseltamivir (*Tamiflu*). It comes as a tablet. It is a well-known antiviral medicine used to prevent or treat influenza ("the flu"). It has been used successfully in many countries for several years.

Why have I been advised to take it?

You have been in close contact with birds suspected to be infected with the avian influenza ("bird flu") virus. As a result, there is a very small risk that you may become infected with this virus. People infected with avian influenza ("bird flu") virus can become seriously ill.

What is the benefit of taking this medication?

The risk of becoming infected with avian influenza ("bird flu") virus is very small. But if you take Oseltamivir (*Tamiflu*) it can prevent the virus from spreading inside your body. If you become infected with the virus, this antiviral medicine may prevent you from becoming ill or may reduce the severity of the illness that follows.

What is the risk of taking this medication?

Most people who take Oseltamivir (*Tamiflu*) do not experience any difficulties with it. But like most medications, Oseltamivir (*Tamiflu*) can have possible side effects. Nausea, vomiting and stomach pains are the most common complaints. If these side effects occur, they mostly occur after the first dose and will usually improve over time. Diarrhoea, bronchitis, dizziness, tiredness, headache and sleeping difficulties are less common side effects. Side effects are like the symptoms of influenza ("the flu"). So it is very important that you contact your doctor if you develop any of these symptoms while taking Oseltamivir (*Tamiflu*).

Will Oseltamivir (*Tamiflu*) remove the possibility of becoming ill?

If you were to become infected with avian influenza ("bird flu") virus, taking antiviral medicine should reduce the possibility of becoming ill. But it will not completely remove the possibility, and so you should be on your guard and contact your doctor if you feel unwell in any way.

How should I take the antiviral medicine?

You will be given one tablet to take each day while you are in contact with infected birds, and one tablet to take each day for a further 10 days. It is important that you take the tablets as directed.

- The tablets should be swallowed whole with a full glass of water. You should not break or chew the tablets
- It is best to take the tablet in the morning with your breakfast.
- If you forget to a tablet, take it as soon as you remember. Do not take a double dose.

These antiviral medicines work to protect you against becoming ill. It is very important that you continue to take the tablets until the course is finished, even if you feel well.

Appendix 14 Possible Visitors to Poultry Farms

In an effort to categorise visitors to farms the following groupings have been devised. There may be overlap between some of these groups.

Delivery Services for the following:

- Day old/point of lay/brooded birds
- Animal feed
- Oil/ gas
- Shavings
- Farm equipment

Advisers:

- Feed company advisers
- Company advisers/selectors/management
- Teagasc
- Health and Safety Authority inspectors

Routine Animal Health Activities:

- Vaccinating team
- Beak trimming team
- Artificial inseminating team
- Private veterinary practitioner /lay assistant
- DAF staff (vets, poultry officers, egg marketing)
- Blood samplers (DAF or company)

Farm Maintenance Activities:

- Litter / slurry removal
- Fumigating personnel
- Rentokill
- Equipment Maintenance personnel
- Cleaning and disinfection of poultry houses or poultry transport

Miscellaneous Activities

- Other visitors (e.g. personnel from other companies, other farmers, relations, ESB, postman, Bord Gais etc

In the case of the other categories of poultry and other birds specific human contacts will need to be assessed if the outbreak occurs involving wild birds or poultry in a geographical region.

Avian Category
Commercial poultry (supplying hatcheries, approved slaughter plants, packing centres)
Small poultry flocks supplying local markets, farm gate, local abattoirs
Back yard poultry (own consumption only)
Open farms (+ visitors)
Fancy fowl (pure bred species)
Game birds
Pigeon lofts
Zoos, game parks (+ visitors)
Quarantine premises (only 1 in Mayo)
Laboratory/research establishments
Pet shops (+ visitors)
Caged and aviary birds
Bird reserves, public parks etc (+ visitors)
Pets in dwelling houses

Appendix 17 PERSONNEL CONTACTS TO SUSPECTED AVIAN INFLUENZA CASE/OUTBREAK

Name & address of suspect avian influenza infected premises:	**NDCC Reference No.** **AI R _____/ 20____**	**Date premises restricted:** **Date of onset of clinical signs:**
Location & species of suspected avian influenza infected wild bird:	**Laboratory Reference No.** **_____/06/_____**	**Date bird collected:**

Name	Address & telephone/mobile number	Date & type of contact

Poultry/captive birds: Notify all contacts from **2 days** before onset of clinical signs in the birds, until date of restriction

Wild birds: Notify all contacts that handled the bird

Signed: _____ VI Date: _____

Copy to local Department of Public Health

Appendix 18: Dynamic Risk Assessment (DRA) model

Severity

The seriousness of the incident in terms of the intrinsic propensity in the specific circumstances to cause harm to individuals or to the population.

Severity and prognosis of known cases

The degree of harm already incurred, or likely to be incurred by those already affected including, course, complications, death and morbidity rates as obtained from established knowledge, and the speed of onset and duration of illness.

Grade	Qualifier	Description	Examples
0	*Very Low*	Seldom causing severe illness.	• Hand, foot and mouth disease in a nursery. • MRSA in a domestic setting. Head lice.
1	*Low*	Occasional serious illness rarely with long term effects or death.	• Hepatitis A in a primary school.
2	*Moderate*	Often severe illness occasionally with long term effects or death.	• Toxigenic E. Coli 0157. • Pulmonary Tuberculosis. • MRSA infection in a high dependency unit. • Hepatitis B or C infection. • Legionnaires' Disease.
3	*High*	Usually severe illness often with long term effects or death.	• Meningococcal disease. • MDRTB.
4	*Very High*	Severe illness almost invariably fatal.	• Rabies. • Ebola. • VCJD

Confidence

The level of confidence, epidemiologically, clinically, statistically and from laboratory evidence, that the diagnosis is correct in the set of circumstances.

Confidence in the hypothesis

Extent of confidence in and consistency of the clinical picture in terms of available laboratory diagnostic results and associated confounding factors including ambiguity and uncertainty.

Grade	Qualifier	Description	Examples
0	***Very Low***	Available evidence suggests that the hypothesis is correct with an empirical probability of less than 10%.	• Hunch.
1	***Low***	Available evidence suggests that the hypothesis is correct with an empirical probability in the range of 10% to 25%.	• Alternative hypothesis more likely but cannot exclude the working hypothesis.
2	***Moderate***	Available evidence suggests that the hypothesis is correct with an empirical probability in the range of 25% to 50%.	• Alternative hypotheses equally likely.
3	***High***	Available evidence suggests that the hypothesis is correct with an empirical probability in the range of 50% to 85%.	• Typical incident picture without conflicting information.
4	***Very High***	Available evidence suggests that the hypothesis is correct with an empirical probability higher than 85%.	• Typical incident picture with increasing confirmation.

Spread

The intrinsic temporal and spatial potential for spread including the infective dose, the virulence of the organism the availability of the route(s) of spread, the observed spread and the susceptibility of the population (e.g. lack of immunity) in the set of circumstances.

Potential of the organism to spread given the circumstances

The transmissibility of the organism, its characteristics (virulence and infective dose), its mode(s) of transmission and the availability of the routes of infection.

The susceptibility of population at risk i.e. the state of immunity, general health and nutrition of population under consideration and the extent to which normal defence mechanisms will protect that population.

Grade	Qualifier	Description	Examples
0	***Very Low***	Very low likelihood of spread with very few new cases.	• A single case of Campylobacter.
1	***Low***	Low likelihood of spread with few new cases.	• A single case of meningococcal disease. • A smear negative culture positive case of TB.
2	***Moderate***	Moderate likelihood of spread with new cases. May develop into a limited outbreak.	• Viral gastro-enteritis in a nursing home. • A handful of cases of Hepatitis A occurring over a prolonged period of time in a large community. • A smear positive case of TB.
3	***High***	High likelihood of spread with many new cases. May develop into a large outbreak	• Multiple cases of Dysentery in a deprived population of children under 8 years old. • Epidemic of influenza in an army camp.
4	***Very High***	Spread almost inevitable.	• Measles in an non-immune sub-population.

Intervention

The feasibility to intervene to alter the course and influence the outcome of the event in terms of containing, reducing or eliminating the transmission of the organism, or assuaging public anxiety. The feasibility of delivering what is needed, to whom it is needed and when and where it is needed, considering the extent to which interventions are intrinsically simple, effective, available, affordable, cost-effective, acceptable, accessible, timely and well targeted.

Grade	Qualifier	Description	Examples
0	***Very easy***	Intervention well established with clear benefits and no anticipated difficulties to implement.	• Hand washing advice.
1	***Easy***	Intervention with clear beneficial effects and few difficulties to implement.	• Withdrawal of contaminated food in a closed institution. • Measles or Hepatitis A immunisation to a small group of vulnerable contacts of a case. • A case of meningococcal infection in a child with contacts confined to the household.
2	**Passable**	Intervention with some beneficial effects and some difficulties to implement.	• Prophylaxis to immediate family and close contacts in a meningococcal case where they are dispersed.
3	**Difficult**	Some remedial intervention possible but either difficult to implement, relatively ineffectual or other significant problems.	• National food withdrawal. • Urgent mass immunisation campaign. • Response to rabid dog on the loose.
4	***Very difficult***	Remedial intervention very difficult.	• Response to a cluster of vCJD. • MRSA in a busy high dependency unit.

Context

The broad environment, including public concern and attitudes, expectations, pressures, strength of professional knowledge and the overall setting of external factors including politics, in which events are occurring and decisions on responses are being made.

5.1. Media, parents and local concern
The degree to which media, parents, local concern, politics aggravate and raise the profile of the event under consideration.

5.2. Historical problems
Influence of local experience of similar interests and previous events, the way they were handled, associated consequences and expectations arising.

5.3. Peer group practice
Extent to which an established approach or recommended best practice is tested and documented (national guidelines).

5.4. What is happening elsewhere
Extent to which other similar incidents are being managed and publicised, with resultant effect on public attitudes and expectations.

Grade	Qualifier	Description	Examples
0	***Very Calm***	No raised level of interest.	• Apathy. Public / media are supportive of immunisation. • Common adverse problems are fairly well understood.
1	***Calm***	A small degree of increased interest with a low level of conflicting factors. Little public concern.	• Misunderstanding corrected by routine information. • Head-lice control campaign. • A few cases of diarrhoea in a nursery school.
2	***Passable***	A degree of unease and anxiety on the part of the public and the media. The context could deteriorate if the event is mis-handled.	• A series of gastro-enteritis cases associated with an outdoor centre to which school children are sent. • TB in a school in a low incidence area.
3	***Difficult***	Context is sensitive with significant difficulties, press interest and local people (unaffected) involved. The incident could go very wrong unless carefully handled. The event could have re-occurred in spite of preventive actions.	• Surgeon is found to have HIV / AIDS. • Wide spread food poisoning affecting several schools. • Unjustified allegation about the safety of childhood vaccines with media coverage.
4	***Very Difficult***	Significantly raised public concern and political and emotional pressure with the public and the media declaring antagonistic and unhelpful views.	• If BSE-like illness linked to new source e.g. pork. • If MMR immunisation was shown to have serious unsuspected side effects.

Dynamic Risk Assessment Model

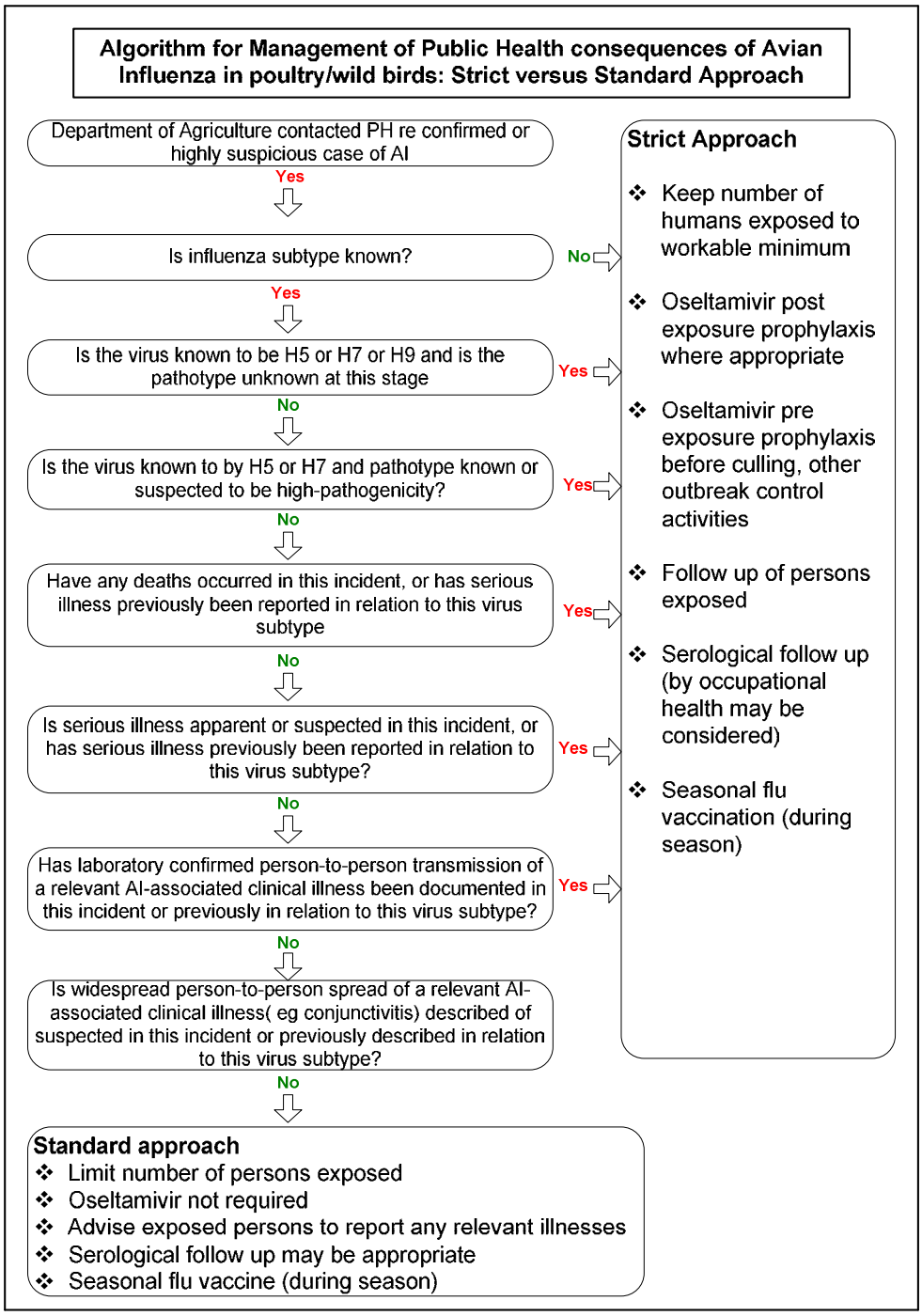
Incident ID: _____

Date __ / __ / ____ **Time:** ___.____ (24 hour clock)

Completed by: _____

	0	1	2	3	4
Severity					
Confidence					
Spread					
Intervention					
Context					

Latest analysis and observations



Appendix 19 (avian): Algorithm for management of PH consequences of AI in poultry/wild birds: Strict versus Standard approach October 2012

I am travelling to a country affected by bird flu. What should I do?

Check the HPSC website www.hpsc.ie for the latest travel advice

- Avoid any contact with live poultry and wild birds
- Avoid visiting live animal markets and poultry farms
- Avoid contact with surfaces contaminated with animal droppings
- Don't handle dead birds
- Don't handle or eat undercooked or raw poultry, egg or duck dishes
- Exercise good personal hygiene with frequent hand washing
- Don't bring any live poultry or poultry products (e.g. feathers) back to Ireland

For further information call 1850 24 1850 or visit www.hpsc.ie

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Avian influenza
(Bird flu)

What is bird flu?

Bird flu is an infectious disease of birds caused by influenza viruses. There may be little or no obvious disease in wild waterfowl. However, but sometimes large outbreaks of highly infectious disease occur in domestic poultry leading to large numbers of deaths.

Are there different types of bird flu?

There are many different strains of bird flu viruses. The H5N1 strain has caused most of the outbreaks since late 2003 and is currently the strain of greatest concern to human health.

Can bird flu viruses cause infections in people?

Up to now, human infection with bird flu has been very rare. It has mainly been caused by close contact with live infected birds or their droppings, or following slaughtering, plucking, butchering or preparing diseased poultry for eating. There have been reports of a limited number of cases in which it may have spread from person-to-person.

What are the symptoms?

Most people infected with bird flu get fever (38ºC or higher) followed by flu-like symptoms, including cough, runny nose, sore throat, and shortness of breath. Diarrhoea is often present early on in the illness, but may start up to one week before the flu-like symptoms. People can also have stomach pain or vomiting or headache.

Why is it so important to prevent bird flu infections in people?

It is still very unusual for people to catch bird flu. However, when somebody does catch it, they become very ill and more than half of those who have picked up the disease from birds have died. Flu viruses are by their nature very changeable. The virus can change so that it becomes easilly spread from person-to-person.It can also change if a person catches bird flu when they already ill with normal flu. This could allow the two viruses to mix. The bird flu virus could then change to a form that allows it to spread easilly from person-to-person. If this happens it could start a world-wide outbreak, known as pandemic flu.

What can the public do to prevent bird flu?

- Avoid touching live poultry or their droppings
- Don't handle any dead poultry or wild birds
- Wash your hands well with soap and water for about 20 seconds immediately after contact with live poultry, birds or their droppings. Avoid touching your eyes, nose or mouth with your hands. Washing your hands regularly is one of the most important ways to protect yourself against bird flu.

Is there a vaccine against bird flu?

No. For now there is no vaccine to prevent bird flu in humans.

Can regular flu vaccine prevent bird flu?

No. Regular flu vaccine doesn't prevent bird flu. The vaccine prevents infection with human flu and can cut the risk of a person becoming sick with human flu and bird flu at the same time. This can prevent the two types of flu mixing and becoming more easilly spread from person-to-person.

Glossary

CIDR	Computerised Infectious Disease Reporting
Clinical attack rate	The percentage of the total population who become infected and show symptoms of influenza
CSO	Central Statistics Office
CVRL	Central Veterinary Research Laboratory
DAF	Department of Agriculture and Food
DOHC	Department of Health and Children
DPH	Director of Public Health
ECDC	European Centre for Disease Prevention and Control
EISS	European Influenza Surveillance System
EMEA	European Medicines Agency
FAO	Food and Agriculture Organisation of the United Nations
GRO	General Registrar's Office
HCW	Health Care Worker
HPA	Health Protection Agency
HPAI	Highly Pathogenic Avian Influenza
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
ICGP	Irish College of General Practitioners
IHR	International Health Regulations
ILI	Influenza-like illness
LPAI	Low Pathogenic Avian Influenza
LRTI	Lower Respiratory Tract Infection
Mathematical modelling	The application of mathematical methods to create pandemic predictions
MOH	Medical Officer of Health
NAI	Neuraminidase inhibitor
NVRL	National Virus Reference Laboratory
OIE	World Health Organisation for Animal Health
PEP	Post-exposure prophylaxis
PPE	Personal Protective Equipment
SPC	Summary Product Characteristics
WHO	World Health Organisation