INFLUENZA PANDEMIC CONTINGENCY PLAN

Version 7.0/February 2005

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Abbreviations

ACDP	Advisory Committee on Dangerous Pathogens
CCC	Civil Contingencies Committee
CDSCNI	Communicable Disease Surveillance Centre, Northern Ireland
CEO	Chief Executive Officer
CEPR	Centre for Emergency Preparedness and Response
CMO	Chief Medical Officer
CfI	Centre for Infections
CSG	Core Strategic Group
DEFRA	Department of Environment, Food and Rural Affairs
DH	Department of Health
ECDC	European Centre for Disease Control
EISS	European Influenza Surveillance Scheme
GP	General Practitioner
GMP	Good Manufacturing Practice
HPA	Health Protection Agency
HEPO	Health Emergency Planning Officer
HPU	Health Protection Unit
HSE	Health and Safety Executive
ITU	Intensive Therapy Unit
LaRS	Local and Regional Services
MOSA	Medical Officers of Schools Association
NAW	National Assembly of Wales
NHS	National Health Service
NIBSC	National Institute of Biological Standards and Control
NIMR	National Institute of Medical Research
NIPC	National Influenza Pandemic Committee
NPHS	National Public Health Service (Wales)
ONS	Office for National Statistics
PCT	Primary Care Trust
PWG	Pandemic Working Group
R&D	Research and Development
RCGP	Royal College of General Practitioners
RDsPH	Regional Directors of Public Health
SARS	Severe Acute Respiratory Syndrome
SCIEH	Scottish Centre for Infection and Environmental Health
SECC	Strategic Emergency Co-ordinating Centre
SECT	Strategic Emergency Co-ordinating Team
SHA	Strategic Health Authority
SitRep	Situation Report
SOP	Standard Operating Procedure
UK	United Kingdom
WHO	World Health Organisation

Introduction

This document outlines the Health Protection Agency's plan for responding to an influenza pandemic. It replaces the Public Health Laboratory Service Pandemic Influenza Plan of July 2001.

Influenza is a familiar infection in the UK, especially during winter. Almost every year new drifted strains of influenza emerge giving rise to morbidity and mortality, mainly in older persons and young children. Pandemic influenza is different: its emergence and potential impact are both difficult to predict.

A pandemic of influenza is the result of a new influenza A virus subtype emerging which is markedly different from recently circulating strains and is able to:

- infect people (rather than, or in addition to, animals or birds)
- spread from person to person, and
- cause illness in a high proportion of the people infected,

and also

- spread widely, because a high proportion of the population is susceptible (most people will have little or no immunity to the new virus because they will not have been infected or vaccinated with it or a similar virus before).

New subtypes of influenza have emerged sporadically over the last century. In 1918 a devastating and unusual pandemic caused by influenza A, subtype H1N1 ('Spanish flu') killed between 20 and 40 million people worldwide. Other pandemics that followed had a less devastating impact but were nevertheless severe. Influenza A, subtype H2N2 ('Asian flu') emerged in 1957 and H3N2 ('Hong Kong flu') in 1968.

The circumstances still exist for a new influenza virus with pandemic potential to emerge and spread and the longest interval so far recorded between pandemics is 39 years. The unpredictability of the timing of the next pandemic is underlined by the occurrence of several large outbreaks of highly pathogenic avian influenza since the early 1980s. Large outbreaks in poultry were described in Pennsylvania in 1982 (A/H5N2), Mexico in 1993 (A/H5N2), Hong Kong in 1997 (A/H5N1), Hong Kong again in 2003 (A/H9N2) and The Netherlands in 2003 (A/7N7). Both the Hong Kong and Netherlands outbreaks were associated with epizootic transmission to humans. However, by far the most serious was the massive and unprecedented outbreak of highly pathogenic influenza (A/H5N1) affecting poultry in East and South East Asia in late 2003 and again in 2004. This outbreak has so far been associated with a small number of human cases and a high proportion of deaths. Whether these outbreaks presage the emergence of an A/H5N1 strain with capacity to spread efficiently between humans is unknown.

Other events and developments that inform the creation of this plan are:

- The creation of a new organisation, the Health Protection Agency from the Public Health Laboratory Service, the Centre for Applied Microbiological Research (CAMR), the National Radiological Protection Board, and Consultants in Communicable Disease Control and their Health Protection Teams formerly employed by the NHS.
- The emergence and successful control of Severe Acute Respiratory Syndrome (SARS) using aggressive infection control methods combined with standard public health interventions.
- The development and licensing of a new class of drug (neuraminidase inhibitors) active against influenza A and B.

AIMS AND OBJECTIVES

Aim

The aim of this publication is to provide a framework for the Health Protection Agency's response to an influenza pandemic, in the context of the overarching national arrangements laid out in the UK Health Departments' UK Influenza Pandemic Contingency Plan. Clear guidance is given in order that individual Divisions of the HPA can develop more detailed operational plans for their own parts of the response, including the development of local and regional arrangements with NHS colleagues.

Objectives

To ensure that the resources of the Health Protection Agency are effectively mobilised to support the national response to an influenza pandemic, led by the Department of Health, in the areas of detection, diagnosis, management, control and prevention. Specific HPA objectives are to:

- Recognise rapidly the emergence of a novel influenza virus and/or its introduction into England and Wales
- Produce timely and accurate information and advice for the public and health professionals
- Produce regular, timely and accurate surveillance information for central government and other partner organisations
- Provide expert advice regarding the detection, isolation and management of cases
- Develop and validate tests for diagnosis of the new virus and provide a national diagnostic reference service
- Support clinical and laboratory diagnosis locally and regionally
- Provide expert advice and assistance in the targeting and use of antivirals
- Support the rapid development of an effective pandemic vaccine
- Provide expert advice and assistance in the targeting and use of vaccine
- Quantify the overall magnitude and burden of the pandemic and characterise its impact
- Collaborate effectively with both national and international partner organisations, and in particular with the Department of Health in respect of its overarching arrangements for dealing with an influenza pandemic in the UK

The HPA will maintain its capability and capacity to meet these responsibilities at all times. This will necessitate the implementation of programmes for service development and improvement, and for research, in order that the necessary expertise is maintained and practiced.

Scope

1. The Health Protection Agency has specific responsibilities within England and Wales and this document refers to arrangements in those administrations. However, the HPA cooperates closely with the equivalent agencies in Scotland and Northern Ireland and in the event of a pandemic would collate UK surveillance data for the purpose of providing daily updates to the Department of Health Operations Room and Civil Contingencies Committee.

2. The Department of Health is the lead government agency in England for coordinating the response to a pandemic. However it will also perform many lead agency functions for the devolved administrations of Scotland, Wales and Northern Ireland and take overarching responsibility for the UK response. The Health Protection Agency Pandemic Plan should be interpreted in the context of the Department's overall Contingency Plan, being in effect a sub-plan of the Department of Health's plan.

3. In developing this plan account has been taken of the "NHS Doctrine for Handling Major Incidents" and the wider government arrangements "Dealing with Disaster": both of which are generic approaches to a wide range of threats.

4. The overall aim of the plan is to ensure that the resources of the HPA can be brought to bear effectively in the provision of advice, specialist capabilities and supporting services to DH, the NHS and others with responsibilities in responding to an Influenza Pandemic.

5. In order to ensure clarity in the scope of the plan, the overall roles and responsibilities of HPA divisions are set out in the context of the overarching HPA Strategic Emergency Response Arrangements, and the interaction with the wider Command and Control structure that would come into play.

6. The uncertainties in the nature and scope of any pandemic are very large. To address this, the plan is based on certain Planning Assumptions and Control Principles. These in turn are underpinned by an assessment of the possible burden of illness.

7. The structure of the plan utilises the WHO phases of a pandemic and the UK Alert Levels as described in the Department of Health Contingency Plan, and provides a matrix of integrated responses at the local, regional and national levels set against these phases and levels.

8. The above matrix should be regarded as a default set of actions. The previously mentioned uncertainties in any pandemic mean that the actual characteristics of the pandemic may be different from the planning assumptions. Similarly, whilst public health is at the core of the plan, it has to have the flexibility to deal with situations where the pandemic could have, or has had, a major impact on the national infrastructure. Thus in addition to specifying a set of default actions the plan provides a framework for decision making that will enable flexibility to deal with the specific needs of the situation.

Epidemiology of pandemic influenza and possible burden of illness

Seasonal influenza

Influenza is an acute viral infection characterised by the sudden onset of fever, chills, headache, muscle pains, prostration and usually cough, with or without a sore throat or other respiratory symptoms. The acute symptoms last for about one week, although full recovery may take longer. In most years, influenza occurs predominantly in a six to eight week period during the winter. For most people, this 'seasonal' influenza is an unpleasant but self-limiting and not life-endangering illness, but in some people it may be more severe, or complicated by secondary bacterial infections such as bronchitis and pneumonia. The very young, the elderly and people with other underlying diseases such as heart or chest disease are particularly at risk of serious illness from influenza. Without interventions such as annual influenza vaccination, the elderly and those of all ages in disease-based risk groups suffer significant morbidity and mortality even in a non-pandemic year. Deaths from influenza have been estimated to be around 12,000 per year in England and Wales and occur predominantly in the elderly[1].

Pandemic influenza

In the case of an influenza pandemic a substantial proportion (possibly all) of the population is likely to be non-immune. In past pandemics, the scale and severity of illness (and hence consequences) have been variable but broadly of a higher order than even the most severe winter epidemics. Typically, there are also changes in the age-distribution of cases compared with non-pandemic years. Mortality, which in typical seasonal influenza is usually confined to older age groups, tends to be increased in younger age groups. The size of any increase in morbidity and mortality and the extent to which a shift in age distribution occurs will depend on a variety of factors including the nature of the pandemic virus and pre-existing immunity.

Excess Mortality

Excess mortality occurs as a result of most winter seasonal influenza epidemics. The average annual excess mortality attributable to influenza in recent years is around 12,000 deaths per annum in England and Wales, although there is considerable year on year variation and some years are notably much higher than the average (est. 26,000 in 1989/90)[1]. Excess mortality in England and Wales associated with the three pandemics of the 20th century has also varied widely; this was estimated at 198,000 in 1918/19[2], and 37,500 in 1957/58[3]. In the 1968/69 and 1969/70 pandemic seasons associated with influenza A/H3N2 there were an estimated 31,000 and 47,000 deaths respectively[4].

It is impossible to predict with precision the level of excess mortality that will be experienced in the next pandemic. However the table below illustrates the broad range of excess mortality that needs to be considered based on various combinations of case fatality rate and clinical attack rates.

Range of possible excess deaths based on various permutations of case-fatality rates and clinical attack rate

Case fatality rate	Clinical attack rate		
	10%	25%	50%
0.37%	19,300	**48,400**	96,700
1.00%	51,700	129,200	258,400
1.50%	77,100	192,700	385,400
2.50%	129,200	323,000	645,900

A case fatality rate of 0.37% corresponds to the approximate rate observed in interpandemic years and a clinical attack rate of 25% corresponds to the approximate clinical attack rate seen in all three previous pandemics. These make a figure of at least 50,000 excess deaths seem reasonably possible. These assumptions have been used for all modelling illustrated in this plan.

Age-specific mortality and consultations

In the 1918/19 influenza A/H1N1 pandemic there was evidence that in relative terms elderly persons were spared (almost certainly because of prior exposure to the A/H1N1 virus) whereas mortality was extremely high in young adults aged 15-44 years and children less than 5 years[2,5]. However, the 1957 A/H2N2 pandemic excess mortality occurred largely in persons aged 55 years and over[3,5]. Finally, in the A/H3N2 pandemic of 1968/9 excess mortality in the USA was observed in children under 5 years and persons aged 55 years and over[5]; but this contrasts with the fact that in the UK, GP consultations were highest in persons under 5 years and in working age adults, yet far lower in persons aged 65 years and over[4].

At the time of emergence of each previous pandemic the proportion of excess deaths occurring in persons under 65 years of age has always been higher than in subsequent seasons once the virus has become established[6]. This is illustrated in the table below.

Alterations in age-specific mortality in past pandemics

Proportion of P&I excess deaths occurring in persons <65 years (%)

	1918	**1944**	**1957**	**1967**	**1968**	**1994**
A/H1N1	**98**	**31**	**-**	**-**	**-**	
A/H2N2	**-**	**-**	**36**	**3**	**-**	**-**
A/H3N2	**-**	**-**	**-**	**-**	**47**	**4**

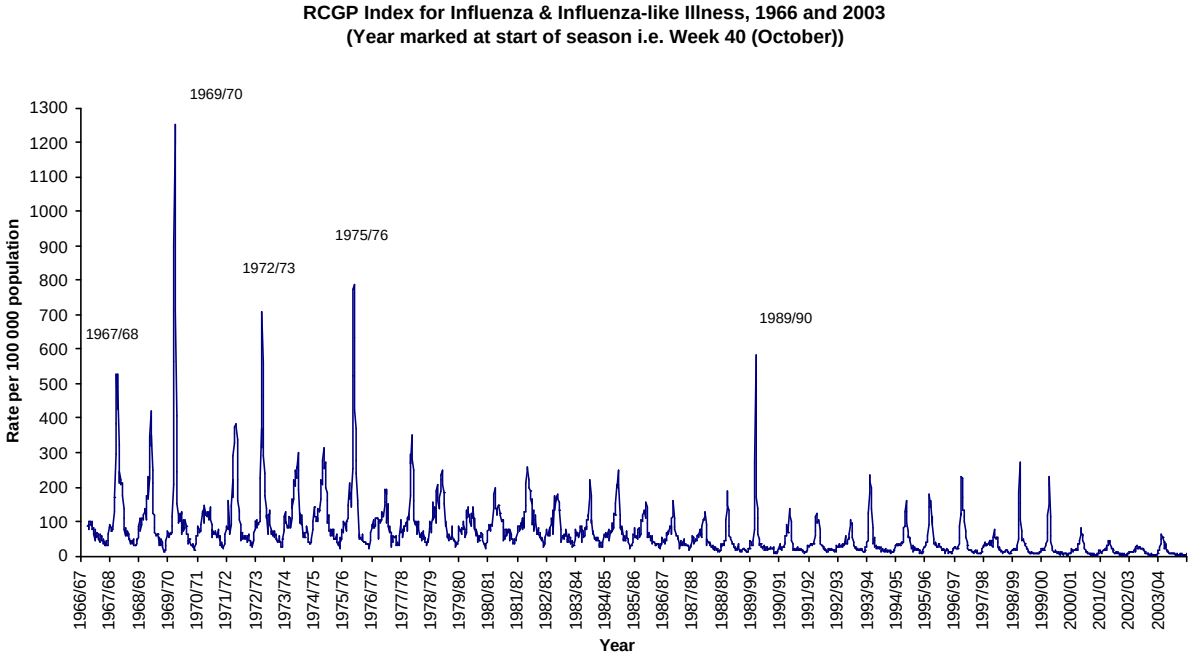
Therefore it is likely that a substantial proportion of excess deaths will occur in persons <65 years during the next pandemic (compared with only 5% during

interpandemic periods). From modelling studies this has been predicted to be 20% but it may be higher.

Geographical and temporal spread

Virological and clinical surveillance of influenza have improved markedly since the last pandemic in 1968. However the extent of international travel has also grown. Modelling studies using transmission characteristics based on the 1968/69 pandemic and international air-traffic data from 2002 indicate that the approximate delay between a first case in Hong Kong and first introduction to UK might be in the order of 2-4 weeks. In terms of the spread within the UK, past experience of pandemics suggests that it would only take a few weeks from the initial introduction(s) to widespread influenza activity across the country. Modelling further suggests that it would only take a further 7-9 weeks before peak influenza activity was in all regions of the UK.

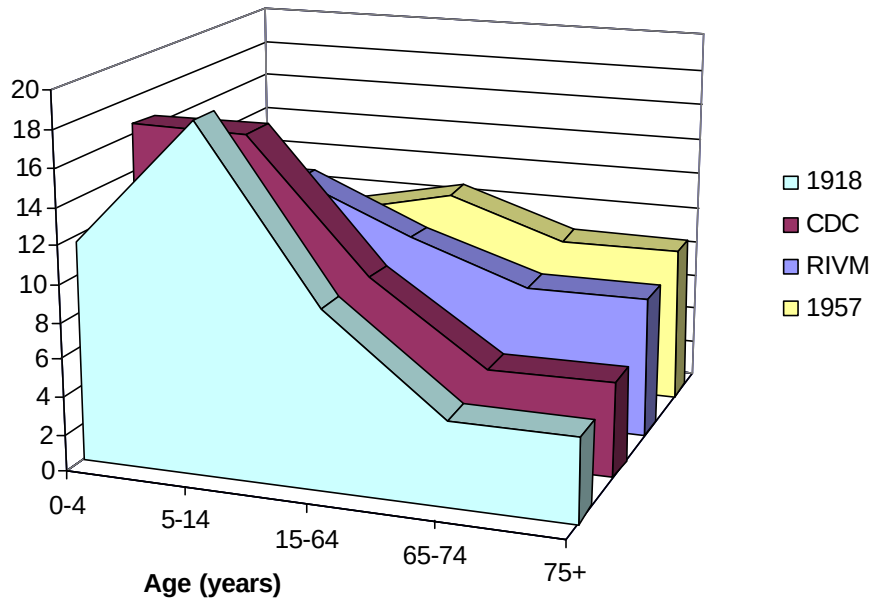
The temporal and spatial spread of a pandemic strain is important, particularly in terms of the demand placed on healthcare services. Pandemic activity taking the form of a brief but severe peak in cases will be more difficult for all services to cope with, compared with an identical number of cases distributed over a longer time course. Such was the observation in the 1968/9 A/H3N2 pandemic when a long first wave occurred in the winter of 1968/9 with morbidity and mortality approximately at the same level as the previous seasonal influenza; however in the following winter of 1969/70 a short and more severe epidemic occurred with a three-fold higher peak in general practice consultation rates and a four-fold higher peak in mortality attributed to influenza, bronchitis and pneumonia[4]. The high peak in consultation rates is well illustrated by the consultation data shown in the figure below.



Attack rates

In an average interpandemic year approximately 5% of adults and 20% of children develop symptomatic (clinical) influenza and similar proportions show serological evidence of infection without symptoms[7]. In past pandemics roughly 25% of the population (cumulative across all waves) has suffered a clinical illness and roughly

50% (cumulative) has shown evidence of infection on serology[8]. Both clinical and serological attack rates are typically higher in school-age groups[9]. It should be noted that age specific clinical attack rates have differed markedly between pandemics (see figure below).



Age specific attack rate profiles of past pandemic and interpandemic years

1918 & 1957: distributions in England and Wales[2,3]
CDC: average of distributions in the USA during the 1918 & 1957 pandemics and the epidemic in 1928-29[10]
RIVM: estimated from epidemic influenza in the Netherlands[11]

Pandemic waves

In 1918/19 the A/H1N1 pandemic occurred in three distinct epidemic waves: early spring 1918, autumn 1918 and late winter 1919. The second wave was by far the largest and case-fatality rates were also higher than in the first wave[12]. The A/H3N2 pandemic caused an epidemic wave in the winter of 1968/69 but a more severe one in 1969/70[4]. In contrast, the second wave of the 1957/58 pandemic in the UK was very small in comparison to the first[3]. Thus all planning should assume that more than one wave is possible (but not inevitable) and that a second wave could be worse than the first.

Summary of Epidemiology

1. The scale and severity of illness (and hence consequences) caused by pandemic influenza generally exceed those of even the most severe winter epidemics.
2. Mortality in the UK is likely to exceed 50,000 deaths, possibly appreciably higher.
3. Besides the elderly, excess mortality is also likely in younger adults and children.
4. Modelling studies suggest that after a case occurs in Hong Kong, because of international travel, it may take 2-4 weeks for the virus to reach the UK.
5. Once cases begin to occur in the UK it will take only a few weeks before activity is widespread
6. It is possible that there will be more than one epidemic wave (with an interval of several months) and, if a second wave occurs, it may be more severe than the first.
7. Cumulative clinical and serological attack rates across all waves together may be in the order of 25% and 50% respectively.

Modelling results (health impact)

Using the results of mathematical modelling it is possible to gain a broad understanding of the likely impact of the next pandemic. The table below summarises the number of events that might be expected by a GP with 1,000 patients on his/her list, a PCT serving a population of 100,000 persons, a Strategic Health Authority covering a population of 1 million persons and England and Wales as a whole.

Summary of estimated cumulative burden of illness attributable to pandemic influenza (based on a 25% clinical attack rate and 0.37% case fatality rate)

Population	**Clinical cases**	**GP* consultations**	**Minimum hospitalisations required***	**Excess deaths**
A GP list (1,000)	**250** (200-300)	**50** (40-60)	**2** (0-2)	**1** (0-2)
A Primary Care Trust (population 100,000)	**25,000** (20,000-30,000)	**5,000** (4,000-6,000)	**150** (120-180)	**100** (80-120)
A Strategic Health Authority (population 1,000,000)	**250,000** (200,000-300,000)	**50,000** (40,000-60,000)	**1500** (1,200-1,800)	**1000** (800-1,200)
England and Wales total population (population 52,041,916 Census 2001)	**13,000,000** (10m – 16m)	**2,600,000** (2.1m – 3.1m)	**72,000** (58,000-86,000)	**48,000** (38,000–58,000)

All figures are approximate
Figures in parentheses illustrate scenarios for 20% (lower limit) and 30% (upper limit) attack rates
*These figures are in addition to background health service activity

Using the same assumptions, the table below illustrates the number of events by week over an assumed 17-week (single wave) pandemic period in England and Wales.

Estimated clinical cases, excess GP consultations, minimum excess hospitalisations required, number of excess deaths, and beds needed to be occupied in England and Wales during an influenza pandemic, distributed by week of pandemic activity.

Week	GP consultations per 100,000	GP consultations	Clinical cases	Minimum hospitalisations required	Excess deaths	Bed occupancy at the end of the week
1	40	20,700	103,300	600	400	400
2	67	35,000	175,100	1,000	700	900
3	112	58,400	292,000	1,600	1,100	1,500
4	182	94,800	474,000	2,600	1,800	2,500
5	283	147,300	736,700	4,100	2,700	3,900
6	412	214,300	1,071,700	5,900	4,000	5,800
7	546	284,000	1,420,000	7,800	5,300	7,900
8	642	333,900	1,669,500	9,200	6,200	9,700
9	658	342,600	1,712,900	9,400	6,400	10,600
10	589	306,700	1,533,400	8,500	5,700	10,300
11	468	243,400	1,216,900	6,700	4,500	8,900
12	337	175,600	878,000	4,800	3,300	7,100
13	227	118,300	591,300	3,300	2,200	5,200
14	146	76,000	380,000	2,100	1,400	3,600
15	91	47,400	237,000	1,300	900	2,400
16	56	29,000	145,100	800	500	1,600
17	34	17,600	87,800	500	300	1,000

The same can also be demonstrated for a typical PCT as laid out below.

Estimated clinical cases, excess GP consultations, minimum excess hospitalisations required, number of excess deaths, and beds needed to be occupied in an average Primary Care Trust population of 100,000 during an influenza pandemic, distributed by week of pandemic activity.

Week	GP consultations per 100,000	GP consultation	Clinical cases	Minimum hospitalisations required	Excess deaths	Bed occupancy at the end of the week
1	40	40	200	1	1	1
2	67	67	300	2	1	2
3	112	112	600	3	2	3
4	182	182	900	5	3	5
5	284	284	1,400	8	5	7
6	413	413	2,100	11	8	11
7	547	547	2,700	15	10	15
8	643	643	3,200	18	12	18
9	659	659	3,300	18	12	20
10	590	590	2,900	16	11	19
11	468	468	2,300	13	9	17
12	337	337	1,700	9	6	13
13	227	227	1,100	6	4	10
14	146	146	700	4	3	7
15	91	91	500	2	2	5
16	56	56	300	2	1	3
17	34	34	200	1	1	2

The final table illustrates the likely demand for hospitalisation by age group over time, for England and Wales.

Estimated minimum excess hospitalisations required by age group in England and Wales during an influenza pandemic, distributed by week of pandemic activity.

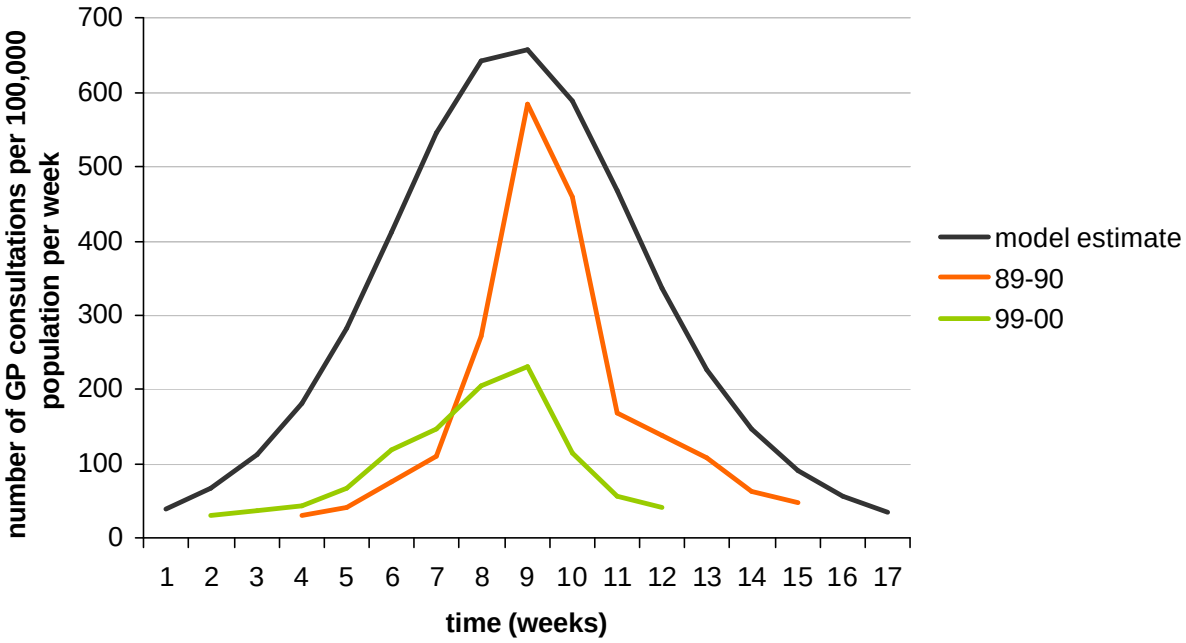
Week	Age (years)				Total
	0-4	5-14	15-64	65+	
1	50	10	120	390	570
2	80	10	200	660	960
3	130	20	340	1,110	1,600
4	220	40	550	1,790	2,600
5	340	50	860	2,790	4,040
6	490	80	1,250	4,060	5,880
7	660	110	1,650	5,380	7,790
8	770	120	1,940	6,320	9,160
9	790	130	1,990	6,490	9,390
10	710	110	1,780	5,810	8,410
11	560	90	1,410	4,610	6,670
12	410	60	1,020	3,320	4,810
13	270	40	690	2,240	3,240
14	180	30	440	1,440	2,080
15	110	20	280	900	1,300
16	70	10	170	550	800
17	40	10	100	330	480

(totals do not exactly match earlier tables due to rounding effects)

Comparison with normal winter activity

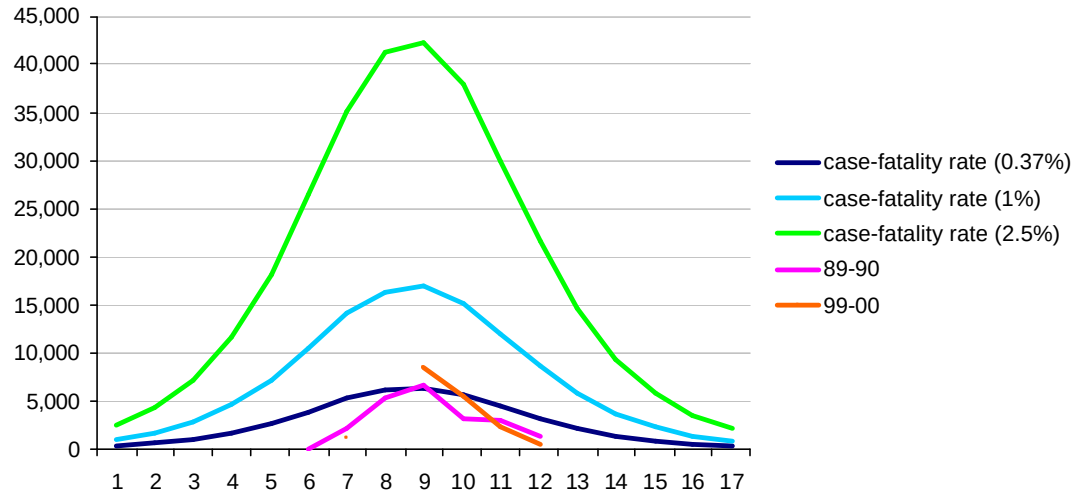
The figure below illustrates the likely impact on GP consultation compared with two interpandemic influenza seasons, which were considered to be sizeable epidemics.

Estimated weekly number of GP consultations for influenza-like illness per 100,000 population in England and Wales and actual weekly numbers from two past epidemics, 1989/90 and 1999/2000



A similar comparison can be drawn for excess deaths.

Estimated weekly number of deaths in England and Wales during next pandemic and actual weekly numbers from two past epidemics, 1989/90 and 1999/2000



*Some data in 99-00 curves appear 'missing' due to negative values

Deaths in the UK normally occur at rate of 10,000 per week rising to 15-20,000 per week at the height of each normal winter period. Using a case-fatality estimate of 0.37%, excess deaths are predicted to peak at a similar level to that experienced in 1989/90 and 1999/2000. However the period during which excess deaths occur will be sustained over a far longer period. Higher case-fatality rates (illustrated in the figure for 1% and 2.5%) would result in correspondingly higher number of deaths (figure).

Modelling assumptions

See Appendix 3

Planning assumptions

Pandemic potential
There were three pandemics in the 20th century; in 1918, 1957, and 1968. The emergence of another pandemic is unpredictable but the probability is considered sufficiently high to warrant detailed planning.

Place of emergence
The most likely place of emergence for the next pandemic is China or South East Asia.

Time of onset
The pandemic may not follow the normal seasonal winter pattern of interpandemic influenza

Point of entry into the UK
This may be through multiple locations either directly from the pandemic source country or via intermediate countries in Europe or elsewhere.

Length of first wave
Between 3-5 months, depending on seasonal timing of first wave activity[13].

Mode of transmission
Droplet transmission (>5 μm) occurs[14]
Airborne or aerosol transmission (<5 μm particle size) occurs[15,16,17]
Role of transmission through contact with live virus particles on surfaces unclear.

Environmental factors
Virus survival is considerably enhanced in conditions of cold temperature and low relative humidity[18].

Incubation period
One to three days, typically two[19].

Period of communicability
Up to 6 days from exposure to the virus[19,20], but typically 3-5 days from onset of fever[19]. Virus shedding may be detectable 24 hours before onset of illness in some adults[19]. Children generally shed the virus for longer periods – up to 6 days prior to onset of symptoms and up 14 days afterwards, or 21 if immunocompromised[21,22,23].

Likely R_0 in UK setting
In the absence of vaccination and control measures the reproduction number is approximately 3 in a susceptible UK population.[24]

Clinical attack rate
25-30% cumulative[4,9,25].

Sub-clinical infectious cases
50% of all influenza infections are sub-clinical[8,9].

Case-fatality rate
At least 0.37%

Time to availability of vaccine
The time from first virus isolation to production of large quantities of standardised monovalent vaccine will be between six to eight months (assuming a prior commitment to funding for vaccine development and production)[26].

Supply of vaccine
In the short term, production capacity and delivery of the vaccine in the UK may be limited.

Number of doses of vaccine required
For novel subtypes (e.g. H5N1) in completely unprimed populations a single dose of vaccine is likely to provide incomplete protection. Two standard doses may be necessary for complete clinical protection. The most likely dose regimen will be 2 x 15mcg with adjuvant or 2 x 7.5mcg with adjuvant, but studies are needed to explore this issue.

Effectiveness of neuraminidase inhibitors
Prophylaxis: Likely to be effective in preventing illness (efficacy 80%).
Treatment: Likely to be effective in shortening illness, lessening morbidity and reducing hospital admissions if given within 48 hours after onset of symptoms (shortens average illness period by one day). Limited data from epidemic influenza suggests treatment to have an efficacy of around 50% for the prevention of severe outcomes if administered within 48 hours of symptom onset[14].

Resources
In common with many other government agencies, the Health Protection Agency is likely to exceed normal budgetary allocations during the response to a pandemic. Some specific costs, for example those associated with vaccine development, are likely to be very high and will need to be incurred during the early phases of preparation, before it is even clear that a pandemic is inevitable. These expenditures will need to be specifically sanctioned.

Control principles

- Individual control measures aimed at detecting cases (or giving sufficient information to individuals for them to diagnose themselves) and minimising their contact with other individuals may help slow the spread of the pandemic. These measures may include:

    - Information distributed at ports of entry
    - Detection of symptomatic cases on entry into the UK
    - General education messages
    - Voluntary home isolation of infected cases and their contacts
    - Effective infection control measures in hospitalised cases
    - Intense post-exposure prophylaxis around early cases

- Measures to reduce contact between large numbers of susceptible individuals, such as school and university closures, may be effective in preventing further individual cases and slowing the evolution of the epidemic.

- Neuraminidase inhibitors are likely to play an important role during a pandemic but their optimal use, for both treatment and prophylaxis, will need to be determined in light of the specific characteristics of the pandemic. However, it is likely that they may have a role to play in containing spread from early cases, thereby slowing the introduction of the pandemic into the UK or slowing the early development of pandemic activity within the UK.

- Vaccination with a pandemic vaccine is probably the most effective intervention in the medium to long term. Optimal vaccination strategies (in the likely event of initial vaccine scarcity) will need to be determined in light of the specific characteristics of the pandemic.

Roles and responsibilities of HPA Divisions

The Health Protection Agency (HPA)

The Health Protection Agency provides specialist advice and operational support to the Department of Health (DH), Strategic Health Authorities (SHAs), the NHS, and other organisations whose formal responsibilities include responding to an influenza pandemic. Operational support at local, regional and national level will be provided for the development and implementation of interagency contingency plans for pandemic influenza.

The main roles of the divisions within the HPA in the event of a pandemic are summarised as follows:

The Centre for Infections (CfI), Colindale will provide specialist advice; coordinate the provision of clinical and epidemiological surveillance data; provide infection control advice; undertake epidemiological analyses; disseminate relevant information to the public and healthcare professionals; undertake modelling studies. Specific advice will be offered to DH regarding strategy and policy for use of antivirals and vaccine. The CfI will also obtain and characterise the new virus; conduct virological surveillance; provide advice on biological safety; develop and validate new diagnostic tests; rollout new tests as appropriate; provide antiviral susceptibility testing. In discharging its responsibilities, the CfI will be able to draw on the expertise, resources and containment facilities available at CEPR, including the Special Pathogens Reference Unit.

The Local and Regional Services Division (LaRS) will discharge the HPA's responsibilities at local and regional levels by supporting local and regional emergency planning arrangements. This will include working with PCTs, SHAs and Government Offices regarding pandemic planning; reviewing the availability of appropriate laboratory containment facilities; reviewing local diagnostic capacity; communicating with professional colleagues in primary care and acute trusts; assisting with coordination of control measures including use of antivirals and vaccine; gathering local epidemiological information.

The Centre for Emergency Preparedness and Response (CEPR) will be responsible for the integration of pandemic planning with other emergency planning measures. In particular, the HPA's Strategic Emergency Response Plan will require the establishment of a Strategic Emergency Co-ordination Centre (SECC). The primary functions of the SECC would be to take a strategic overview, provide a forward look on potential development and provide co-ordinated briefings and liaise with DH and other agencies. CEPR will work with National Institute of Biological Standards and Control (NIBSC) towards vaccine development, standardisation and production and will liaise with vaccine manufacturers. On request from DH, and supported by appropriate funding, CEPR will lay down Good Manufacturing Practice (GMP) seed stocks, to develop a manufacturing process, and manufacture small vaccine lots. CEPR will also make available its containment laboratories and expertise at the Special Pathogens Reference Unit, in support of the plan. The modelling unit of CEPR will model the impact of pandemic influenza and the potential impact of control measures. In conjunction with modellers at CfI, they will contribute to the overall HPA modelling of pandemic influenza.

Communications Division will provide information and appropriate spokespersons for the media; draft information for informing the general public; liaise with government departments and the NHS to ensure that regular, clear, consistent and timely messages are given to both the media and the general public.

Roles and responsibilities of the Department of Health and the National Health Service

The following responsibilities have been identified in other plans with which the HPA's plan must integrate. They are recorded here in order to clarify responsibilities.

The Department of Health will be responsible for national oversight and monitoring of the pandemic influenza response. It will establish a national 'Operations Room' to support SHA management of incidents and to act as a focal point for links across Government and for coordination of health services, vaccine distribution and the prioritisation, purchase and distribution of antiviral drugs.

Regional Public Health Groups led by Regional Directors of Public Health will maintain a 24 hour capability to support both the SHAs and the rest of the Department of Health, and where necessary to co-ordinate the work of PCTs and NHS Trusts in responding to public health emergencies. The RDsPH will provide the Department of Health link to Regional Resilience mechanisms and act as the regional nominated co-ordinator in public health emergencies.

Each Strategic Health Authority (SHA) must be able to assume strategic control of any incident that affects or seems likely to affect several hospitals. Every SHA must ensure that the NHS within its area has unequivocal command and control structures, that escalation policies are clearly described, that capacity plans are available and that links within the NHS, with neighbouring SHAs, with Regional Directors of Public Health (RDsPH), the HPA and across into others sectors - including social care - are effective and durable. As part of this, many SHAs will have 'lead' PCTs to work with.

All hospital and ambulance services trusts are responsible for deploying the right healthcare resources to care for those affected by pandemic influenza. Each service must be able to mobilise local resources flexibly and to the maximum extent consistent with maintaining essential care. Each trust must also plan to offer effective support to any neighbouring service that is substantially affected and in return should be able to rely on such mutual support if it is needed.

All Primary Care Trusts (PCTs) must be able to mobilise and direct healthcare resources to local hospitals at short notice to support them and to sustain patients in the community should these hospital services be reduced or compromised for a period. They must also plan to harness and effectively utilise primary care resources where needed to support. They must also have agreed systems in place to enable them to work as 'lead' PCT with others or, as appropriate, in support of the 'lead' PCT.

Other partner organisations

The WHO Influenza Collaborating Centre at Mill Hill has an international role as one of the four WHO international collaborating centres in the surveillance of new influenza strains, obtaining or sharing new virus isolates, properly characterising the new virus isolates and working on providing agreed diagnostic methods.

The World Health Organisation will announce the onset of the various pandemic phases, coordinate international efforts to characterise and diagnose new viruses, coordinate international efforts to develop a new vaccine, and promote uniform international surveillance through the development of guidelines.

The European Influenza Surveillance Scheme will continue to monitor influenza activity across the EU and exchange timely information between the 23 participating national centres.

The European Union will coordinate a response between the member states of Europe including where possible sharing of surveillance strategies, entry screening processes and stocks of vaccine and antiviral medications. The European Centre for Disease Control (ECDC) may play a role in sharing and coordinating surveillance information from member states.

The Department of Environment, Food and Rural Affairs (DEFRA) is responsible for surveillance and control of influenza in animal populations in the case of a contemporaneous or initial pandemic in animal populations.

The National Institute for Biological Standards and Control (NIBSC) has a key role in the development, quality assurance and testing of influenza vaccines. It is working with the WHO in developing candidate vaccines against avian influenza viruses using reverse genetics and other technologies.

NHS Direct provides a confidential 24 hour telephone health advice service staffed by trained nurses using standard algorithms to provide advice on self-treatment and direct people to treatment services as necessary. In addition, data on calls received for relevant clinical syndromes will be supplied to CfI for the purposes of integrating into daily SitReps sent to DH and CCC.

The Royal College of General Practitioners through their Birmingham Research Unit Weekly Returns Service contributes to national surveillance by reporting new episodes of influenza and other respiratory infections.

The Medicines and Healthcare Products Regulatory Agency (MRHA) will carry out the licensing of candidate influenza vaccines in preparation for a pandemic.

The UK Vaccine Industry Group (UVIG) will collaborate with the DH and other government agencies over the supply of pandemic vaccines for the UK.

WHO International phases and implications

WHO Phase	Phase short description	Description
Phase 0 (0.0)	No new virus types	No new virus types reported; inter-pandemic influenza activity with established influenza types or drift variants may continue
Phase 0 preparedness level 1 (0.1)	Novel virus type isolated	Isolation of a novel virus subtype from a single human case without any evidence of further human cases or human-to-human transmission
Phase 0 preparedness level 2 (0.2)	Human infections	Two or more human infections have occurred with a new virus subtype but ability of the virus to spread directly from person-person remains in doubt
Phase 0 preparedness level 3 (0.3)	Human-to-human transmission	Human-to-human transmission confirmed either by spread to close contacts of an index case, spread in the general population, clusters of secondary cases or identification of novel subtypes in several countries with no explanation other than contact between infected people
Phase 1	Onset of pandemic	A new pandemic will be declared by WHO when a new virus subtype has been shown to cause several outbreaks in one country and spread to another country, with consistent disease patterns indicating that serious morbidity and mortality is likely
Phase 2	Regional and multiregional outbreaks	Outbreaks are occurring in multiple countries and spreading across the world region by region
Phase 3	End of first pandemic wave	The increase in outbreak activity in the initially affected countries or regions has stopped or reversed, but outbreaks and epidemics of the new virus are still occurring elsewhere
Phase 4	Second wave	Second or later wave of the pandemic usually in the following influenza season
Phase 5	End of the pandemic	WHO will report when the pandemic period is over when morbidity and mortality have returned closer to baseline levels. This will usually be 2-3 years after onset of the pandemic

Implications for the UK

A pandemic is thought most likely to start outside the UK, and to become established in other countries before reaching the UK. For the UK, three alert levels are described in the DH Contingency Plan:

Alert level 1	Cases due to pandemic virus only outside the UK
Alert level 2	New pandemic virus isolated in the UK (pandemic imminent in the UK)
Alert level 3	Outbreak(s) due to new pandemic subtype in the UK
Alert level 4	Widespread pandemic activity across UK

The hierarchy may change if influenza due to the pandemic strain is occurring close to UK, for example, in Western Europe. The DH Plan also covers the contingency that the UK becomes involved earlier than this but in both DH and HPA plans, in terms of specific action, UK alert levels 1-4 are assumed to occur within WHO phase 2.

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Transition between phases

Transition between phases may be rapid and the distinction blurred. The crucial interval is between phases 1 and 2, which will determine to a large extent whether vaccine will be available in time for the first wave of illness in the UK.

The Influenza Team of the HPA Centre for Infections, which continuously monitors global influenza activity, will convene a meeting of the HPA Rapid Assessment Group for Pandemic Influenza to review changes in influenza activity that might presage a pandemic threat. The Group includes experts from the WHO UK Collaborating Centre (Mill Hill) and NIBSC and a representative of the DH. The Group advises the HPA on the need to convene the HPA Pandemic Working Group (PWG).

HPA involvement in mechanisms for changing Alert Status in the UK

On being informed by WHO of the isolation of a new influenza virus with pandemic potential (normally when person to person spread has been confirmed, i.e. Phase 0.3), the Secretary of State, on the advice of the Chief Medical Officer, will convene the National Influenza Pandemic Committee (NIPC). The DH will inform the Devolved Administrations and the Civil Contingencies Committee. The Civil Contingencies Secretariat will inform other Government Departments.

On receipt of confirmation from WHO of the onset of a likely pandemic, the DH will immediately cascade this information to the Devolved Administrations, **the HPA**, the Civil Contingencies Secretariat, other Government Departments and Agencies and the NHS.

In exceptional circumstances, the DH **may convene the NIPC on the strength of advice from the HPA** [or the National Expert Panel on New and Emerging Infections/NEPNEI) in the absence of, or where this differs from, advice from WHO, on the grounds of national interest. The UK may also implement its pandemic plans in the absence of a WHO declaration, on the advice of the NIPC, and after consultation with other European Member States through the European Communicable Diseases Network.

Should a potential pandemic subsequently fail to evolve, the NIPC will be stood down and other bodies including the HPA informed.

Relation of UK Alert levels to WHO international Phases

<table>
<tr><th colspan="2">International Phases</th><th colspan="2">UK Alert levels</th></tr>
<tr><td>0</td><td>No cases worldwide</td><td>No cases worldwide</td><td>Level 0</td></tr>
<tr><td>0.1</td><td>First report of new virus</td><td rowspan="5">Virus/cases only outside the UK

Virus isolated in the UK

Outbreak(s) in the UK

Widespread activity across the UK</td><td rowspan="5">Alert level 1

Alert level 2

Alert level 3

Alert level 4</td></tr>
<tr><td>0.2</td><td>Two or more human cases</td></tr>
<tr><td>0.3</td><td>Human to human spread</td></tr>
<tr><td>1</td><td>Several outbreaks with spread to more than one country</td></tr>
<tr><td>2</td><td>Outbreaks/epidemics in more than one WHO Region</td></tr>
<tr><td>3</td><td>End of first wave</td><td></td><td></td></tr>
<tr><td>4</td><td>Second or later waves</td><td></td><td>Alert levels as above according to activity in UK</td></tr>
<tr><td>5</td><td>End of pandemic</td><td></td><td></td></tr>
</table>

PHASE 0: INTERPANDEMIC PERIOD

Definition

No new virus types reported

Key planning assumptions for the United Kingdom

- Cases do not exceed system capacity to cope
- First cases in the new pandemic occur outside the UK and evolution of the pandemic allows an orderly escalation through WHO phases

Phase 0, Preparedness Level 0

Key issues: maintain and strengthen routine activity

Detect emergence of drift variants and new influenza strains
Detect onset of annual or biannual outbreak
Describe patterns of morbidity and mortality and influenza burden
Contribute to annual vaccination strategy

Responses

The following ongoing surveillance and preparedness actions will continue:

At national level	**Responsibilities**
• Royal College of General Practitioners Weekly Returns: - Every week the RCGP supplies CfI with data on new consultations for respiratory illness diagnosed by general practitioners in 74 practices, mostly in England.	**RCGP/CfI**
• NHS Direct. Weekly reports of number of calls for flu-like illness by age group and region.	**NHS Direct/CfI**
• Mortality surveillance. The Office for National Statistics provides CfI with provisional weekly mortality data for all deaths, 'influenza' and total respiratory deaths (Pneumonia, bronchitis and influenza).	**ONS/CfI**
• The Medical Officers of Schools Association (MOSA):- MOSA provides information on influenza like illness in a population of approximately 9,500 boarding school children aged 5-18 years.	**MOSA/CfI**
• Emergency Bed Service. Obtain weekly data on the number of applications for emergency admission to hospitals in London.	**CfI/EBS**
• Weekly collation of reports from NHS and HPA laboratories of numbers of serological or respiratory specimens positive for influenza by age and sex.	**CfI**
• Develop and maintain microbiology guidelines and sampling advice.	**CfI**
• Antigenic and genetic characterisation of all influenza strains received through active and passive virological surveillance.	**CfI**
• Perform antiviral susceptibility testing.	**CfI**
• Directed virological surveillance using specimens from the RCGP network and HPA network.	**CfI**
• Collect data on co-pathogens (bacteria) associated with influenza infection	**CfI**

• Draw together influenza surveillance information from devolved administrations.	**CfI**
• Contribute to WHO and EU influenza surveillance activities	**CfI**
• Assess threat to UK posed by influenza activity abroad	**CfI**
• Undertake modelling studies to support pandemic influenza contingency planning and pandemic exercise planning. Including modelling to assess possible therapeutic, public health and social interventions.	**CEPR/CfI**
	CEPR
• Conduct pandemic planning exercises in conjunction with other agencies.	**CEPR**
• Develop and implement programme to exercise the HPA Plan.	**CEPR**
• On an annual basis assess whether plan remains fit for purpose or needs updating.	**CEPR**

At regional level

• Regional (LaRS) and NHS clinical laboratories send isolates to the CfI Influenza Laboratory.	**LaRS**
• Operate regional sentinel surveillance schemes.	**LaRS**
• Annual serological surveillance conducted by LaRS (Preston) - age-stratified geographically representative collection of serum conducted annually.	**CfI/LaRS**
• Conduct formal annual review of influenza contingency plans and pandemic arrangements.	**LaRS (Regional Directors)**
• Regional Health Emergency Planning Officer (HEPO) undertakes an annual audit of NHS Trusts against quality assurance standards including pandemic preparedness.	**LaRS**

At local level

• Support annual PCT plans to immunise elderly and high-risk groups against influenza.	**LaRS**
• Provide local support and guidance for use of antivirals including any local decisions about thresholds and usage in outbreaks.	**LaRS**
• Outbreak detection and response in schools and nursing homes.	**LaRS**
• Review local Health Protection Team incident/outbreak plans on an annual basis including pandemic arrangements.	**LaRS**

Phase 0, Preparedness Level 1

First report of new influenza subtype from a single human case outside UK*

Definition

Isolation of a novel virus subtype from a single human case without any evidence of further human cases or human-to-human transmission

Key issue
Review likely diagnostic capability

Responses

At national level	**Responsibilities**
• Monitor and disseminate international reports.	**CfI**
• In conjunction with WHO and other laboratories involved in typing influenza isolates, review reagents and prepare status report of reagents and diagnostic activity.	**CfI**
• Maintain capability for animal and laboratory containment work, and vaccine development.	**CEPR**
• Liaise with NIBSC & DH over vaccine development plans.	**CEPR**
At the regional level	**As in Phase 0.0**
At the local level	**As in Phase 0.0**

*NB: In the unlikely circumstance that the first report of a new influenza subtype were to occur in the UK, the actions above would be superseded by a full clinical, epidemiological and virological investigation and risk assessment.

Phase 0, Preparedness Level 2

Confirmation of two or more human infections outside UK

Definition

Two or more human infections have occurred with a new virus subtype but there is no evidence of human-to-human transmission

Key issues
Ensure enhanced surveillance activities are in place to detect imported human cases of the new virus subtype Ensure CfI Influenza Laboratory has resources to diagnose new virus subtype

Responses

At national level	**Responsibility**
• The HPA CfI (Influenza Team) convenes a meeting of the HPA Rapid Assessment Group to review the current situation and advise the HPA on the need to convene the full HPA PWG.	**Rapid Assessment Group**
• Prepare website information for the general public and professionals.	**CfI**
• Prepare interim surveillance definition, guidelines and case-management algorithms.	**CfI**
• CfI Influenza Laboratory obtains new virus for antigenic analysis and reagent preparation and liaises with NIBSC/WHO.	**CfI**
• Review and update HPA Pandemic Plan	**CEPR/CfI/LaRS**
• Submit protocols for pandemic related R&D projects	**ALL**
• Activate the communications plan o Work with CfI to ensure website material is adequate o Prepare press briefing material	**Communication Division**

At regional level

• Laboratories in areas with travel-related contact with the site of initial identification of the novel virus to enhance virological sampling of patients, regardless of timing in relation to normal "influenza season"	**LaRS/CfI**
• Health Protection Units (HPUs) and laboratories to report possible clusters or outbreaks of influenza-like illness to CfI.	
• Brief RDsPH and Regional Government Offices and activate regional communications plans.	**LaRS**

At the local level

• Ensure local pandemic plans are up-to-date.	**LaRS**
• Advise port health authorities based on national entry-screening advice.	**LaRS**
• Liaise with emergency departments; Intensive Therapy Units (ITUs) and other first line services that may see imported cases.	**LaRS**
• Ensure infection control teams are fully alerted.	**LaRS**

Phase 0, Preparedness Level 3

Occurrence of human-to-human transmission confirmed outside the UK

Definition

Human-to-human transmission confirmed either by spread to close contacts of index cases, spread in the general population, clusters of secondary cases or identification of novel subtypes in several countries with no explanation other than contact between infected people.

Key issues

Surveillance capacity to detect as early as possible importation of cases
Distributed diagnostic capacity to detect new strain subtype
Effective communication to public and professionals

Responses

At national level	**Responsibility**
• CEO of the HPA convenes the PWG for coordination of HPA tactical response activities in providing advice, guidance and services (see appendix for membership). Optimal configuration of this group may be into two task groups – public health and virology.	**CEO**
• CEO considers need to establish Core Strategic Group (CSG led by CEPR) to assess potential impact of pandemic on HPA business continuity and resource options to deliver plan, together with liaison with government and other agencies.	**CEO**
• Through WHO and EISS, gather epidemiological, clinical and virological information about cases occurring in countries where transmission is already taking place.	**CfI**
• Participate in WHO/EISS-led discussions and activities	**CfI**
• Advise DH on vaccine policy, use of neuraminidase inhibitors, and other public health and social interventions.	**CfI**
• In liaison with Communication Division, web-publish surveillance case definitions for suspected cases.	**CfI/Communication Division**
• Activate enhanced clinical surveillance in hospital and primary care settings using alerting systems.	**CfI**
• Issue national guidance on Infection Control Measures.	**CfI**
• Negotiate with NHS Direct Board to ensure that protocols are in place for structured enhanced clinical and virological surveillance using agreed algorithms.	**CfI/NHS Direct**
▪ Activate case-management database.	**CfI/LaRS**
• Ensure adequate and appropriate central reference resources/literature.	**CfI**
• Liaise with DEFRA/Health and Safety Executive (HSE)/Advisory Committee for Dangerous Pathogens (ACDP) and clinical virology network with respect to guidelines for handling novel virus agent.	**CfI**
• Collaborate with DH, Industry and others to support rapid development of new vaccine(s).	**CEPR**
• Develop contingency plans for delivery of antivirals to critical staff groups within HPA.	**CEPR/ Corporate Services**
• Review existing occupational health guidelines for laboratory	**CfI**

• staff.	
• Review strategy for diagnostic investigations in non-reference laboratories (including provision of centralised service if required).	**CfI**
• Begin production of diagnostic reagents for new strain.	**CfI**
• Ensure provision and distribution of diagnostic reagents.	**CfI**
• Provide guidelines and SOPs for safe-handling and identification of novel virus in non-reference laboratory setting.	**CfI**
• Evaluate commercial and non-commercial rapid tests for sensitivity and specificity against the virus.	**CfI**
• Obtain structured random sample of sera from the anonymised Residual serum collection administered by the CfI seroepidemiology unit and held at Preston, for determining age and sex specific immunity to possible pandemic strain.	
• Develop robust serological tests for assessment of Susceptibility and immunity to new virus	**CfI**
• Develop antiviral susceptibility testing for new strain.	**CfI**
• Communications	**Communication Division**
* Identify national and regional spokespeople	
* Ensure information for public and journalist inquiries is in place and daily updates are issued.	
* Ensure channels of communication are functioning	
▪ Identify mechanisms for re-deployment of staff from 'non-influenza' areas	**Corporate Services Executive Directors**
▪ Identify mechanisms for supporting staff required to work extended hours during phase 1 and 2.	**Corporate Services**
▪ Rehearse daily reporting to Civil Contingencies Committee and DH Operating Room	**CfI/devolved Partner organisations**

At regional level

LaRS

- Develop and rehearse standardised regional method of collating aggregate case information

Support RDsPH in the SHA and Government Office response.

At local level

- Local HPUs to convene local Influenza Pandemic Control Committees (or equivalent body). **LaRS**
- Work with PCTs and NHS Trusts to contact all primary care physicians and emergency departments to ensure surveillance guidance is in place. **LaRS**
- Set up local enhanced surveillance especially in at-risk communities (e.g. communities with close links with geographic area of origin of pandemic). **LaRS**
- Update all staff contact information to facilitate rapid communication. **LaRS**
- Develop local methods for collating aggregate case information by residence, sex and age. **LaRS**
- Assist NHS colleagues in developing framework for delivery of mass vaccination to target groups. **LaRS**
- Develop local vaccine monitoring framework based on national template. **LaRS**

PHASE 1: CONFIRMATION OF ONSET OF PANDEMIC

Definition

The pandemic will be declared by WHO when the new virus subtype has been shown to cause several outbreaks in one country and spread to another country, with consistent disease patterns indicating that serious morbidity and mortality is occurring or is likely.

Key planning assumptions for the UK

- The pandemic has commenced elsewhere and sustained pandemic activity in the UK is still several weeks away

Key issues

Enhanced surveillance capacity to detect first importation of infected cases
Distributed diagnostic capacity to detect new strain subtype
Efforts to support production of a vaccine and strategy for vaccination

Responses

At national level	**Responsibility**
• CEO establishes or enhances Core Strategic Group (CSG) to co-ordinate HPA resources and liaises with government and other agencies in assessing forward projections and response options. The CSG will establish with PWG a daily 'battle rhythm' for meetings and information flows to meet HPA and government needs.	**CEO**
• PWG coordinates HPA responses and discusses progress and action through daily teleconference and situation reports.	**PWG**
• Implement enhanced surveillance and case investigation procedures.	**CfI/LaRS**
• Validate novel diagnostic tests including rapid tests.	**CfI**
• Intensify production of reagents for non-reference diagnosis, including rapid detection.	**CfI**
• Develop guidelines for use of rapid tests.	**CfI**
• Test representative sample of all influenza specimens for new virus.	**CfI**
• Develop guidelines for vaccination based on emerging epidemiology.	**CfI/DH/JCVI**
• Develop guidelines for use of antivirals based on emerging epidemiology and clinical information.	**CfI/DH/ LaRS**
• Rapidly disseminate information about emerging clinical and virological surveillance data.	**CfI**
• Communications o review staffing levels o review briefing materials o liaise closely with colleagues in the DH and the Cabinet Office o convene press conference (as appropriate).	**Corporate Services/ Communication Division**

At regional level

- Activate SHA level teams. **LaRS**
- Ensure regional laboratories are prepared. **LaRS**
- Develop aggregate activity reporting from hospitals to SHAs based on national template. **LaRS**

At local level

- Continue work with/through local Influenza Pandemic Control Committees. **LaRS**
- Support PCTs in compiling registers of at-risk or high priority groups for vaccination. **LaRS**
- Support PCTs in developing local vaccination action plan based on national guidance. **LaRS**
- Support PCTs to identify vaccination teams and delivery points. **LaRS**
- Work with PCTs to develop local distribution strategy for antiviral medication. **LaRS**
- Work with PCTs to identify secure antiviral distribution points. **LaRS**
- Work with PCTs to develop aggregate reporting methods for primary care according to national template. **LaRS**
- Work with Acute NHS Trusts to ensure local preparedness. **LaRS**

PHASE 2: REGIONAL AND MULTIREGIONAL OUTBREAKS

Definition

Outbreaks are occurring in multiple countries and spreading across the world region by region

Key planning assumption

During this phase the first wave of the pandemic takes its course in the UK from first detection of domestically acquired cases to maximum morbidity and mortality
Vaccine may become available but initial lots may need to be rationed or prioritised

Key issues

Prompt detection through intensive surveillance
Measures to reduce transmission
Protection of the population through vaccination
Rapid detection of any changes in the virus
Reducing and modifying surveillance activity as pandemic peaks

Phase 2, UK Alert Level 1

No virus isolated yet in the UK

Definition

Phase 2 has been declared by WHO but there have been no confirmed cases in the United Kingdom.

Preparedness activities are as for Phase 1 plus:

At regional level

- Support PCTs in coordination of antiviral distribution (as supplies are allocated by DH). **LaRS**
- Support PCTs in coordination of vaccination (as supplies are allocated by DH). **LaRS**

At local level

- Support PCTs in distributing antivirals to high-priority groups (as supplies are allocated by DH) **LaRS**
- Support PCTs in coordination of vaccination (as supplies are allocated by DH). **LaRS**

Phase 2, UK Alert Level 2

First reports of virus isolates in the UK

Definition

The pandemic strain is first isolated from a person(s) in the UK. Subsequent cases are isolated; cases are sporadic and may be predominantly imported. Sustained chains of domestic transmission are not yet confirmed.

At national level	**Responsibilities**
• CEO activates full Strategic Emergency Response Plan, led by Strategic Emergency Co-ordinating Team (SECT). Daily 'battle rhythm' is reviewed in light of HPA and government needs.	**CEO**
• PWG coordinates HPA tactical responses and discusses progress and action through daily teleconference and situation reports.	**PWG**
• Ensure all key HPA staff are vaccinated (if vaccine available and if stipulated in national policy) and criteria for vaccination clearly explained.	**PWG/Executive/ Corporate Services**
• Ensure all key HPA staff are offered antiviral prophylaxis if stipulated in national policy.	**PWG/Executive/ Corporate Services**
• Inform WHO of first case.	**CfI**
• Activate pandemic module through NHS Direct ensuring that information collation enables assessment of vaccine efficacy (if appropriate)	**CfI/DH**
• Open case-management database.	**CfI/LaRS/CEPR (modellers)**
• Implement HPA R&D priorities directed by nominated coordinator.	**CfI/LaRS/CEPR**
• Begin monitoring of vaccine uptake in nominated target groups as vaccine supplies become available	**CfI**
• Implement data collection and review information on co-pathogens in influenza cases (community and hospital).	**CfI**
• Refine antibiotic and symptomatic treatment guidelines based on data collection above.	**CfI**
• Produce detailed antigenic and genetic characterisation for all novel UK influenza viruses for preparation of candidate vaccine strains.	**CfI**
• Develop UK specific serological and diagnostic reagents.	**CfI**
• Compare virological data from UK and international sources.	**CfI**
• Monitor antiviral susceptibility of virus isolates, including any treatment failures and compare data with other international sources.	**CfI**

At regional level

- Support coordination of antiviral distribution (as supplies are allocated by DH). **LaRS**
- Support coordination of vaccination (as supplies are allocated by DH). **LaRS**
- Support vaccine uptake monitoring arrangements **LaRS**
- Collate local reports of aggregate influenza activity. **LaRS**

At local level

- Continue work with/through local Influenza Pandemic Control Committees. **LaRS**
- Support PCTs in coordinating distribution of antivirals to high-priority groups. **LaRS**
- Support PCTs in coordination of vaccination (as supplies are allocated by DH). **LaRS**
- Support vaccine uptake monitoring arrangements **LaRS**

Phase 2, UK Alert Level 3

Outbreaks in the UK

Definition

Clear evidence of sustained chains of transmission forming local and/or regional outbreaks

Responses

At the national level	**Responsibilities**
• SECT review experience to date in dealing with the resource demands within HPA and the profile of experience from countries that have suffered / are suffering the pandemic and refine strategy. Work with Government to ensure that appropriate data and advice is supplied and to act as the conduit for downward tasking.	**SECT**
• PWG co-ordinates HPA tactical responses through daily teleconference and Situation Reports.	**PWG**
• Consider closure of national case-management database and substitution of aggregate reporting.	**CfI**
• Monitor systematically collected and anecdotal reports of influenza activity across the country and in population subgroups.	**CfI**
• Investigate and document outbreaks including efficacy of any appropriate control measures and clinical and microbiological results.	**CfI**
• Carry out rapid vaccine efficacy studies using case control or other methods.	**CfI/LaRS**
• Review information on co-pathogens in influenza cases (community and hospital).	**CfI**
• Refine antibiotic and symptomatic treatment guidelines based on data collection above.	**CfI**
• Produce detailed antigenic and genetic characterisation for all UK influenza novel viruses for preparation of candidate vaccine strains.	**CfI**
• Develop UK specific serological and diagnostic reagents.	**CfI**
• Compare virological data from UK and international sources.	**CfI**
• Monitor antiviral susceptibility of virus isolates, including treatment failures and compare data with other international sources.	**CfI**
• Collate information from all data sources to provide daily Situation Report of overall impact and burden of pandemic on community and hospitals to support the work of other agencies and the Civil Contingencies Committee (as convened).	**CfI/SCIEH/NPHS Wales/CDSC NI**
• Reduce virological surveillance when pandemic reaches peak to avoid overwhelming laboratories.	**CfI**
• Concentrate on identification of antigenic drift in novel strain, antiviral resistance or emergence of other variants.	**CfI**
• Continue surveillance of secondary bacterial infections to inform treatment guidelines.	**CfI**
• Liaise with the central DH Operations Room and Civil Contingencies Committee.	**Communication Division**

At regional level

- Support aggregate reporting arrangements. **LaRS**
- Support investigation and response of outbreaks and efficacy of control measures. **LaRS**
- Support coordination of antiviral and vaccine distribution. **LaRS**

At local level

- Continue work through/with local Influenza Pandemic Control Committees. **LaRS**
- Collate local aggregate reports of influenza cases in primary care. **LaRS**
- Support PCTs in distribution of antivirals and vaccine in accordance with national policy. **LaRS**

Phase 2, UK Alert Level 4

Widespread pandemic activity in the UK

Definition

Clear evidence of sustained chains of transmission with outbreaks now merging into confluent UK-wide activity

Responses

<u>All responses as for Alert level 3, EXCEPT:</u>

At the national level	**Responsibilities**
• Because of scale of occurrence, reduce or cease investigation and documentation of individual outbreaks, including efficacy of any appropriate control measures and clinical and microbiological results.	**CfI**
• Development of UK specific serological and diagnostic reagents no longer applies: assume completed during Alert Level 3.	**CfI**

PHASE 3: END OF FIRST PANDEMIC WAVE

Definition

The increase in outbreak activity in the initially affected countries or regions has stopped or reversed, but outbreaks and epidemics of the new virus are still occurring elsewhere

Key planning assumption

Phase 3 actions in UK begin when circulation of virus reduces to low levels in the UK
Larger quantities of vaccine are becoming available for the first time

Key issues

Evaluation and assessment
Preparation for second wave including orderly vaccination of remaining susceptible groups

At national level	**Responsibilities**
• SECT will debrief in the light of PWG report (see below) and experiences of the interfaces with government. It will produce a Strategic Overview of the effectiveness of the HPA's plans, identify lessons to be learned and propose to the CEO revision of plans as appropriate for the possible second wave.	**SECT**
• PWG will debrief and prepare a report for the Director of the HPA.	**PWG**
• The Director of the HPA will decide if and when the PWG should stand down.	**CEO/Executive**
• Review progress of current R&D and need for further activities.	**CfI/LaRS**
• Evaluate national experience in comparison with other countries through international liaison.	**CfI**
• Prepare reports for HPA use, publication and public domain.	**CfI**
• Consider how to foster international research collaborations on pandemic influenza.	**CfI**
• Carry out a national serological survey to determine age-specific patterns of susceptibility and age-specific attack rates.	**CfI**
• Monitor uptake of vaccine as supply meets demand and mass vaccination gets underway.	**CfI**
• Manage transition of communications from DH Operations Room/CCC back to HPA.	**Communication Division**
• Consider deployment of HPA resources/expertise to support countries still in Phase 2.	

At regional level	
• Ensure restocking of laboratories.	**LaRS/CfI**
• With RDsPH and SHAs, account for regional stocks of vaccine and estimate remaining demand.	**LaRS**

At the local level	
• Support PCTs in vaccinating remaining susceptible groups.	**LaRS**

PHASE 4: SECOND OR SUBSEQUENT WAVES

Definition

Based on past experience, a second wave of outbreaks caused by the new virus may be expected to occur in many countries

Key planning assumptions

The second wave occurs within 3 to 9 months of the initial epidemic in the winter following the first wave
Majority of population are, by now, vaccinated
The virus may have evolved
Impact may be equal or worse than first phase

Key issue
Early detection of second wave

Responses

At national level	**Responsibilities**
• Continue monitoring global impact and spread of virus.	**CfI**
• Maintain national surveillance mechanisms for evidence of resurgence in activity.	**CfI/LaRS**
• Monitor any antigenic drift in the virus and assess potential significance.	**CfI**
• Reconvene the PWG and SECT as needed.	**CEO**
• **Reactivate Phase 2 Level 3 of HPA Plan at all levels as needed**	**SECT/PWG**

PHASE 5: END OF PANDEMIC

Definition

WHO will announce when the pandemic period is over. In the UK the pandemic will be deemed to have ceased when the epidemiological indices have returned to background levels.

Planning assumptions

- This or a similar virus is likely to remain in circulation
- It may take months or even several years for some national services to recover

Key planning assumptions

Key issues

Assessment and evaluation

Responses

National, regional and local	**Responsibilities**
• Assessment of overall health impact of pandemic.	**CfI**
• Assessment of effectiveness of Strategic Emergency Response Plan and Influenza Pandemic Plan.	**CEPR**
• Evaluation of lessons learned.	**Whole organisation**
• Update Pandemic Plan.	**CfI/LaRS/CEPR**
• Prepare HPA report.	**CfI/LaRS/CEPR**

Plan References

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Appendices

Appendix 1

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Proposed Pandemic Working Group membership

Chief Executive Officer or designated Director
Director of CfI or designated representative
Director of CEPR or designated representative
Head of Influenza Laboratory
Head of Respiratory Department CfI
Members of HPA Influenza Team including one who acts as Scientific Secretary
Regional Epidemiologist from Local and Regional Services
Regional Virology/Microbiology Representative from Local and Regional Services
DEFRA representative
NIMR representative
NIBSC representative
Communications / Press Office
Representatives from NPHS Wales, Scotland (SCIEH) and CDSC Northern Ireland
HSE representative
Representative from the Clinical Virology Network
Representative from the RCGP
Representative from clinical department of an Infectious Diseases Unit
Representative from the Department of Health

Appendix 2

Glossary of terms

Antigenic drift	Point mutations leading to changes in antigenicity of the major H and N antigen subtypes of an influenza virus
Antigenic shift	Change in circulating major antigen (H and N) determinants either through exchange and reassortment of genetic material or adaptation to human transmission
Haemagglutinin	One of the two major surface proteins. Important for virus attachment to cells of the respiratory epithelium. Subtypes include H1 to H15. H1, H2 and H3 are the only described determinants involved in sustained human to human transmission
Neuraminidase	One of the two major surface proteins of the influenza virus. Less important for attachment but probably important for propagation and virulence. Subtypes N1 to N9.
Pandemic	Worldwide spread of a new influenza virus subtype
R_0	The basic reproduction number R_0 is the number of secondary cases produced by one case in a completely susceptible population. It depends on the duration of the infectious period, the probability of infecting a susceptible individual during one contact, and the number of new susceptible individuals contacted per unit of time. It varies between populations because of different contact rates.

Appendix 3

Assumptions used in modelling estimated health impact

1. There will be no large-scale interventions such as vaccine or antiviral use on a population basis

2. The total population of England and Wales (52,041,916) and age distribution are as according to the 2001 National Census.

3. Mixing within the population is assumed to be homogeneous.

4. Individuals considered to be high risk are those currently recommended for annual influenza vaccination.

5. The proportion of each age group in risk categories is as reported by Fleming et al[1].

6. The pandemic is modelled to take the form of a single wave.

7. The activity threshold used to signify the start/end of the pandemic for descriptive purposes is that described by Goddard et al[2]. (2003) (greater than or equal to 30 GP consultations for influenza-like illness per 100,000 population per week).

8. The clinical attack rate applied is 25%. This is the overall clinical attack rate, describing the total number of clinical cases in England and Wales over the course of the entire pandemic. (The epidemic curve produced by the model describes a total of 24.6% of the total population developing clinical symptoms whilst influenza levels are above the 'baseline', the remainder occurs in the tails, when 'flu activity is below baseline levels.)

9. Age-specific clinical attack rate is assumed to be constant. Although this will not be the case in reality, previous pandemic and interpandemic years have shown such a large degree of variation in this parameter that there is no sense in being more specific.

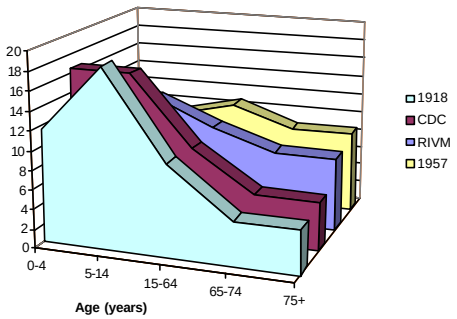

Figure: Age specific attack rate profiles of past pandemic and interpandemic years

1918 & 1957: distributions in England and Wales as reported by Ministry of Health[3,4].
CDC: average of distributions during the 1918 & 1957 pandemics and the epidemic in 1928-29[5].
RIVM: estimated from epidemic influenza in the Netherlands[6].

10. There are no definitive values for the length of latent and infectious periods for influenza infection, which can vary from person to person. Approximate values of 2 days latency (time between infection and viral shedding, which may be before onset of symptoms) and 2.5 days infectivity were used; these are comparable to previous research and modelling[7-13].

11. Half of all influenza infections are assumed to be asymptomatic resulting in a 25% clinical attack rate, and an overall 50% serological attack rate.

12. The derivation of hospitalisation and death rates for different age and risk groups has been calculated using data from interpandemic years, taking vaccination coverage into account (data from past pandemics is of limited quality and quantity and may not be comparable to the current day situation with regards to factors such as the NHS and medical technology/expertise).

Table: Derived hospitalisation and excess death rates per 100,000 clinical cases

Age (Years)	**0-4**	**5-14**	**15-64**	**65-74**	**75+**	**Overall**
Probability of hospitalisation **in Low Risk individuals per 100,000 clinical case**	**509**	**39**	**125**	**605**	**1,257**	**550 (0.55%)**
Probability of hospitalisation **in High Risk individuals per 100,000 clinical case**	**3,562**	**274**	**873**	**4,235**	**8,797**	
Probability of excess death **in Low Risk individuals per 100,000 clinical cases**	**27.2**	**12.2**	**70.4**	**494.6**	**797.0**	**370 (0.37%)**
Probability of excess death **in High Risk individuals per 100,000 clinical cases**	**223.7**	**100.1**	**579.8**	**4071.2**	**6559.4**	

13. The proportion of clinical cases that consult a GP has been estimated using weekly returns data on excess consultations for Influenza-Like Illness (ILI) and Acute Respiratory Infections (ARI) and ONS data for the relevant population sizes[14]. Again, these were data from interpandemic years. A value between those calculated for ILI and ARI was selected as most appropriate following expert consultation and it is therefore assumed that 20% of clinical cases consult a GP.

14. It was assumed that age-specific consultation rates would be constant across all age groups. The proportion of each different age group attending a GP for ILI has varied between interpandemic years and it has not been established whether this is due to true differences in consultation rates (patient behaviour) or to differences in age-specific clinical attack rates.

15. The model makes a simplifying assumption that there is no delay between the development of clinical illness and the need for hospitalisation or progression towards death.

16. Bed occupancy has been calculated under the assumptions that 5% of those admitted require ventilation/ intensive care and so spend 28 days as inpatients[15]. The remaining 95% are assumed to remain in hospital for 8 days[16].

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