

**Clinical Guidelines for Patients with an
Influenza like illness during
an Influenza Pandemic**

**British Thoracic Society
British Infection Society
Health Protection Agency**

Version 5.0

Last updated: 15 October 2005

DRAFT FOR CONSULTATION

CONTENTS

Section

- 1 Introduction
- 2 Epidemiology and Health Impact Projections

Chapter i – Clinical Management of Adults

- 3 Clinical Features
- 4 General Management in the Community
- 5 Severity assessment and criteria for hospital admission
- 6 General investigations
- 7 Microbiological investigations
- 8 General management in Hospital
- 9 Antiviral therapy
- 10 Antibiotic therapy

Chapter ii – Clinical Management of Children

- 11 Clinical Features in children
- 12 Severity assessment in children
- 13 General investigations for children admitted to hospital
- 14 Microbiological investigations for children admitted to hospital
- 15 General management for children in hospital
- 16 Antiviral therapy in children
- 17 Antibiotic therapy in children

Chapter iii – Summary and Synopses of Recommendations

- 18 Primary Care Summary
- 19 Management of hospitalised adults – Synopsis of recommendations
- 20 Management of children – Synopsis of recommendations
- 21 Acknowledgements, declarations of interests, affiliations and addresses of committee members
- 22 References

Appendix

- 1 International Phases and UK Alert Levels
- 2 Patients at high risk of influenza-related complications
- 3 Initial investigations for adults referred to hospital
- 4 Initial management of adults referred to hospital
- 5 Initial assessment and management of children
- 6 Management of children referred to hospital
- 7 Antibiotic doses for children

1 INTRODUCTION

1.1 Scope and Purpose

This document contains guidance for health professionals regarding the treatment of pandemic influenza, agreed by experts from the British Thoracic Society, the British Infection Society and the Health Protection Agency. It is published as official UK guidance by the Department of Health in England and covers treatment in hospitals and the community, of both adults and children. It is intended for use in the UK in event that the World Health Organisation declares that an influenza pandemic has started,(1) and the Department of Health in England (UK-wide lead agency on pandemic influenza, including the devolved administrations) has declared UK Pandemic Alert Level 2 (cases of pandemic influenza identified within the UK – see Appendix 1).(2)

This guidance should be read in conjunction with UK Infection Control Guidance for Pandemic Influenza,(3) (document to be published) the Department of Health UK Pandemic Influenza Contingency Plan,(2) Operational Guidance for Health Service Planners,(4) and the Operational Framework for stockpiling, distributing and using antiviral drugs in the event of pandemic influenza.(5)

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, based on the best evidence available from previous pandemic and interpandemic periods. Thus the guidance may evolve as clinico-pathological information on the eventual pandemic virus emerges. Therefore, once an influenza pandemic is underway, users are strongly urged to ensure that they refer to the most up-to-date version of these guidelines (from web-based access points).

1.2 Context

Seasonal influenza is a familiar infection in the UK, especially during winter. Every year strains of influenza (type A or B) circulate, giving rise to clinical consultations in primary care (age-specific impact varies by season), episodes of hospital treatment (mainly in older persons and young children, but occasionally in working age adults), and deaths (mainly in the elderly). Treatment in primary care and hospital may be required due to the direct effects of influenza virus infection or its possible complications, most commonly secondary bacterial pneumonia. Increases in GP consultations for influenza-like illness and winter bed pressures are frequently associated with periods of known community influenza activity.(6)

Pandemic influenza occurs when a new influenza A virus subtype emerges which is markedly different from recently circulating subtypes and strains, and is able to:

- infect humans;
- spread efficiently from person to person;
- cause significant clinical illness in a high proportion of those infected.

Because the virus is novel in humans, a high proportion of the population will have little or no immunity, producing a large pool of susceptible persons; accordingly the disease spreads widely and rapidly.

Influenza pandemics occur sporadically and unpredictably. In 1918 a devastating and unusual pandemic caused by influenza A/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/H2N2 ('Asian flu') emerged in 1957 and H3N2 ('Hong Kong flu') in 1968; both produced roughly 1 million excess deaths worldwide.(7)

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 (1918-1957). The unpredictability of the timing of the next pandemic is underlined by the occurrence of several large outbreaks of highly pathogenic avian influenza associated with epizootic transmission to humans.(8) By far the most serious has been the massive and unprecedented outbreak of highly pathogenic influenza (A/H5N1) affecting poultry in East and South East Asia in late 2003, which is still continuing. This outbreak has so far been associated with a small number of human cases but a high proportion of deaths. Recently, epidemiological and virological changes have been reported from northern Viet Nam which may indicate that the virus is beginning to adapt to humans.(9) Although the emergence of an A/H5N1 strain with capacity to spread efficiently between humans is neither inevitable nor imminent, international concern has increased regarding the possibility that avian influenza A/H5N1 may evolve to produce the next pandemic.

Other events and developments that inform the creation of this guidance are the development and licensing of a new class of drug (neuraminidase inhibitors) active against influenza, and UK government's recent announcement of plans to procure 14.6 million treatment courses of oseltamivir (Tamiflu®)(10) for use in the UK in the event of a pandemic.

1.3 Who are these guidelines aimed at?

These guidelines are offered for the guidance of all UK 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 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, lower respiratory tract infections or community acquired pneumonia (CAP).

1.4 Grading of recommendations

The recommendations offered in the current guidelines are based on a matrix of evidence centred mainly around seasonal influenza, expert opinion and group consensus. Grading of these recommendations based on the strength of the evidence base was deemed inappropriate.

Summary

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 will take less than one month for the virus to reach the UK.
5. Once cases begin to occur in the UK it will take only 2 – 3 weeks before activity is widespread and roughly a further 3 weeks (6 weeks after initial cases in UK) until activity peaks.
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.
8. Increases in demand for health care services are likely to be very substantial in both primary care and hospital settings.

2.1 Introduction

When an influenza pandemic occurs, a substantial proportion (possibly all) of the population is likely to be non-immune, producing a large pool of susceptible persons. 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. It is reasonable to expect this to be the case with the next pandemic as well.

2.2 Excess Mortality

Excess mortality due to influenza occurs in most winter seasons but is especially marked during epidemics. The average annual excess mortality attributable to influenza in recent years is around 12,000 deaths per annum in England and Wales,(11) although there is considerable yearly variation and some years are notably much higher than the average (est. 26,000 in 1989/90 epidemic). 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 civilians in 1918/19, and 37,500 in 1957/58. In 1968/69 and 1969/70 (both seasons considered to be associated with the influenza A/H3N2 pandemic) there were an estimated 31,000 and 47,000 deaths respectively.(7) Therefore the extent of mortality associated with the next pandemic cannot be reliably predicted although it is reasonable to plan for a scenario worse than a severe winter epidemic of normal influenza.

2.3 Age distribution of morbidity and mortality

Typically, there are changes in the age-distribution of cases compared with seasonal influenza. Mortality, which in typical seasonal influenza is usually confined to age groups over 65 years, 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 depends on a variety of factors including the nature of the pandemic virus and pre-existing immunity but appears to be a consistent phenomenon.(12) Therefore clinicians can expect to see relatively larger amounts of influenza-related illness in younger adults compared with normal winter

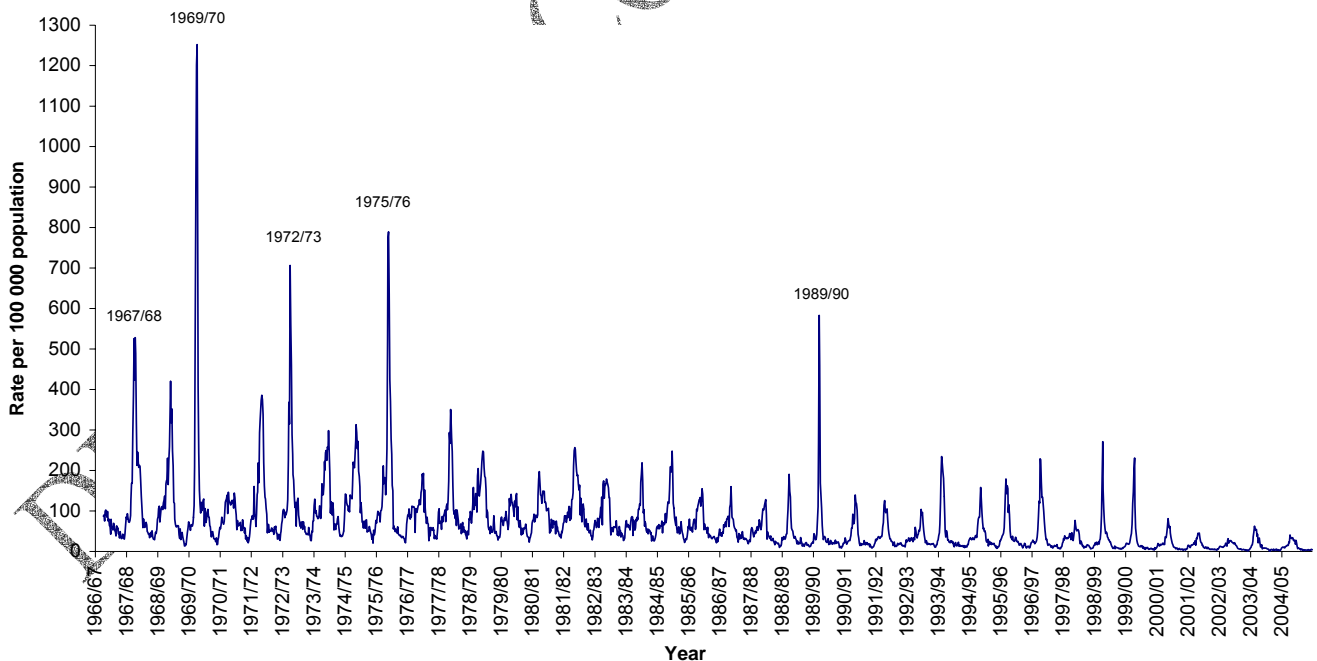
activity. At least one third of all excess deaths may be expected in persons under 65 years of age.

2.4 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 will be less than one month.⁽¹³⁾ In terms of the spread within the UK, it will probably take only 2-3 weeks from the initial introduction(s) until activity is widespread and a further 3 weeks (6 weeks from initial UK cases) until activity peaks

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. For example, during the A/H3N2 pandemic 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; but 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. The high peak in consultation rates is well illustrated in the figure below.

Figure 2.1 RCGP Index for Influenza & Influenza-like Illness, 1966 and 2005 (Year marked at start of season i.e. Week 40 (October))



2.5 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. The A/H3N2 pandemic caused an

epidemic wave in the winter of 1968/69 but a more severe one in 1969/70. In contrast, the second wave of the 1957/58 pandemic in the UK was very small in comparison to the first.(7) Thus it should be considered a possibility that more than one wave of influenza will occur within a few months of the emergence of a pandemic virus and a subsequent wave could be worse than the first.

2.6 Health impact projections

It is impossible to reliably predict with precision the level of excess mortality that will be experienced in the next pandemic. However Table 2.1 illustrates the broad range of excess mortality that it is reasonable to consider, based on various realistic combinations of case fatality rate and clinical attack rates derived from previous pandemics and epidemics.

Table 2.1a Range of possible excess deaths based on various permutations of case-fatality rates and clinical attack rate for England and Wales.

Overall 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
1.5%	77,100	192,700	385,400
2.5%	129,200	323,000	645,900

Table 2.1b Range of possible excess deaths based on various permutations of case-fatality rates and clinical attack rate for the U.K.

Overall case fatality rate	Clinical attack rate		
	10%	25%	50%
0.37%	21,500	53,700	107,500
1.00%	56,700	141,800	283,700
1.5%	85,100	212,800	425,500
2.5%	141,800	354,600	709,300

A case fatality rate of 0.37% corresponds to the aggregate rate observed in recent epidemic seasons (1989/90, 1991/92, 1993/94, 1995/96, 1996/97, 1997/98 and 1998/99) and the 1957 pandemic, although the overall case-fatality rate observed in the 1918-19 pandemic was in the region of 1-2%. A clinical attack rate of around 25% corresponds to the approximate clinical attack rate seen in all three previous pandemics of the 20th century. Thus, a figure of at least 50,000 excess deaths is likely.

Using mathematical projections it is possible to illustrate the potential impact of the next pandemic, but these do not amount to accurate predictions. The table below summarises the number of events that might be expected by a GP with 1,000 patients on his/her list and by a PCT serving a population of 100,000 persons.

Table 2.2 Estimated burden of illness attributable to pandemic influenza over the entire pandemic based on a 25% clinical attack rate and illustrative case hospitalisation and case fatality rates of 0.55% and 0.37% respectively. Health Care Contacts represent the equivalent of GP consultations outside the pandemic period. It is envisaged that individuals experiencing symptoms will be diverted away from GPs in a pandemic. GP consultations represent the remaining contacts required to deal with complications and with young children (see text for explanation). Figures are rounded and represent work additional to normal background health service activity. (Figures in parentheses illustrate the range from 10% (lower limit) to 50% (upper limit) attack rates.)

Population	People with clinical symptoms/ Health Care contacts	GP consultations	A&E presentations	Minimum excess hospitalisations	Minimum excess deaths
Population of 1,000	250 (100-500)	25 (10-50)	13 (5-25)	1 (0-3)	1 (0-2)
Population of 100,000	25,000 (10,000-50,000)	2,500 (1,000-5,000)	1,250 (500-2500)	140 (50-300)	90 (40-180)

*approximate figures.

Using the same assumptions, the table below illustrates the number of events by week over an assumed 15-week (single wave) pandemic period in a typical PCT population of 100,000. Most major acute trusts receive patients from a catchment area spanning several PCTs and the figures below require pro-rata adjustment before applying to individual hospitals.

Table 2.3 Demand for Health Care Contacts by primary care unit: The table shows weekly totals for the number of new clinical cases, and thus potential demand for Health Care Contacts, per 100,000 population, and per PCT, community pharmacy, GP practice or GP list of various sizes (see footnote for definition of 'small', 'medium' and 'large' as they are used in the table)

Period	Clinical cases	Cases per 100,000	% of total cases	Cases per PCT			Cases per pharmacy			Cases per GP practice			Cases per GP		
				Small	Medium	Large	Small	Medium	Large	Small	Medium	Large	Small	Medium	Large
Week 1	21,367	36	0.1%	28	54	109	1	2	3	1	2	3	0	1	1
Week 2	30,400	51	0.2%	40	77	155	2	3	4	2	3	5	1	1	1
Week 3	121,886	205	0.8%	162	310	620	7	11	18	8	13	19	3	3	4
Week 4	464,219	780	3.1%	617	1,181	2,360	28	41	67	29	49	72	10	12	15
Week 5	1,569,434	2,638	10.6%	2,086	3,992	7,977	94	137	226	99	166	242	33	42	52
Week 6	3,206,019	5,388	21.6%	4,261	8,155	16,295	192	280	462	203	339	494	67	85	106
Week 7	3,147,669	5,290	21.2%	4,183	8,007	15,999	189	275	454	199	333	485	66	84	105
Week 8	2,122,779	3,568	14.3%	2,821	5,400	10,790	127	185	306	134	224	327	44	56	70
Week 9	1,444,925	2,428	9.7%	1,920	3,676	7,344	87	126	208	91	153	223	30	38	48
Week 10	1,122,055	1,886	7.5%	1,491	2,854	5,703	67	98	162	71	119	173	23	30	37
Week 11	778,167	1,308	5.2%	1,034	1,980	3,955	47	68	112	49	82	120	16	21	26
Week 12	387,404	651	2.6%	515	985	1,969	23	34	56	25	41	60	8	10	13
Week 13	232,944	392	1.6%	310	593	1,184	14	20	34	15	25	36	5	6	8
Week 14	128,240	216	0.9%	170	326	652	8	11	18	8	14	20	3	3	4
Week 15	97,498	164	0.7%	130	248	496	6	9	14	6	10	15	2	3	3
All weeks	14,875,000	25,000	100%	19,770	37,839	75,606	891	1,299	2,145	942	1,572	2,292	311	396	494

Note:

In the above table, 'small', 'medium' and 'large' refer to the 2.5th, 50th and 97.5th percentiles for the population served by a PCT, community pharmacy, GP practice or GP list, as follows:

Population	PCT	Pharmacy	GP practice	GP list
small	80,000	3,600	3,800	1,200
medium	150,000	5,200	6,300	1,600
large	300,000	8,600	9,200	2,000

2.7 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 NHS acute services for a period of time, perhaps several weeks or months. Accordingly, it should be anticipated that the NHS (in common with all health systems around the world) will need to revert to emergency arrangements. These are laid out in further detail in Operational Guidance for Health Service Planners,(4) and the UK Operational Framework for stockpiling, distributing and using antiviral drugs in the event of pandemic influenza.(5) With regard to the delivery of medical care for patients with influenza this is normally achieved through:

- GP treatment of community patients 'well' enough to be managed in the community
- Hospital care in acute medicine for persons considered too ill to be managed at home.

In the event of a pandemic the following additional care settings may have to be considered as the threshold for hospital admission rises:

- Treatment of patients in the community (who would normally receive care from a GP) by other health care professionals (nurses, paramedics, pharmacists etc.) following treatment guidance laid out in this publication and using Prescription-only medicines according to Patient Group Directives (PGDs)
- Treatment of patients in their own homes or in temporary intermediate care facilities by a GP, following treatment guidance laid out in this publication when, under normal circumstances, such patients would have been admitted for hospital care
- 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).