Contents

Foreword 1
Summary 2
Introduction 3

Section 1
The Community Perspective 4

Section 2
A General Practice Perspective 6

Section 3
Hospital Perspective 16

Section 4
Impact on Mortality 19

Section 5
The Laboratory Perspective 22

Section 6
Issues for Health Services 26

Section 7
The Surveillance Perspective - How Does Surveillance Help? 34

Selected Reading 36
Acknowledgments 36

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Foreword

This report is the brainchild of Richard Wise, a clinician and non-executive Board member of the Health Protection Agency. When he first suggested to the Board that such a report would be valuable, Christmas decorations were beginning to appear and pharmacies were stacked with winter cold “remedies” - paracetamol, aspirin, lemon drinks and the rest. It was also a time for 'flu vaccinations for the over 65s and for younger groups at special risk. General Practitioners’ surgeries and hospitals were gearing up for winter pressures. Since then, the threat of an influenza pandemic has been increased as a result of avian 'flu infection in south east Asia enhancing the importance of his proposal.

But just what do we know and what do we understand by winter infections? What organisms are involved, when do they peak and what are their effects? This report gives you information about the plethora of infectious agents which cause particular problems in winter.

Effective surveillance is essential to keep on top of winter illnesses and the activities of the Health Protection Agency and organisations such as the Royal College of General Practitioners, Birmingham Research Unit, enable us to predict their arrival, monitor their progression and recommend appropriate advice on how to contain them. The Agency’s diagnostic laboratories are central in diagnosing and characterising the agents; the Agency’s local and regional services have to work with and provide support for NHS and other frontline healthcare staff. This is a well-honed annual exercise in support of NHS and government’s departmental needs.

A Winter’s Tale provides information on the prevalence of such winter ailments and emphasises just how effective national surveillance systems are in monitoring what is happening and when. It is part of the broad base of public health protection in which the Agency’s plays a national and indeed international key role.

I thank the authors for the time and effort that they have put in to preparing this report and I warmly commend it to you.
Summary

1. Respiratory infections always peak in mid-winter. The peak is predictable in timing but not always in size. A separate peak as a result of an influenza epidemic may also occur.

2. The youngest and most elderly are at greatest risk. Though there are many young children who need admission because of respiratory illnesses during winter, the maximum admission pressures come from the oldest and frailest sections of the population who usually need to stay in hospital much longer than younger people. Increasing numbers of elderly people, the proportions living alone, the limitations of nursing care availability in residential homes, all suggest the demand for hospital admission due to respiratory infections is likely to increase.

3. Influenza is unpredictable in timing. The threat of an influenza pandemic is always with us. Influenza vaccination is an essential part of winter health service management, but however efficiently administered it will never completely remove the demand placed on health services by the most elderly population. Influenza adds a level of unpredictability to winter planning but, once it arrives, demands on the health service will increase over succeeding weeks. These demands will depend on the age groups where influenza has the greatest impact, which in turn depends mainly on the strain of influenza circulating.

4. The impact of acute bronchitis is at least as great as influenza yet the cause is not known. This is an immediate priority for research. A general increase in respiratory infections at the end of August also justifies further research.

5. Community based support care and hospital surge requirements are highest in mid-winter. Sickness absence amongst staff and travel difficulties are greatest when respiratory infections and weather conditions are at their worst.

6. The importance of surveillance needs to be better recognised. Sampling needs to be more representative of the population and the principles of surveillance need to be extended to other viruses and to the whole year.

7. The ethical framework for conducting surveillance programmes is different from that for individual patient management and for clinical research. There is a strong argument for separating the ethical supervision of surveillance from the arrangements made for research.

8. Where effective treatments are available for targeted use, ways of delivering these treatments in the early stages of these illnesses need to be sought as a matter of urgency.

9. Near patient tests for Influenza and Respiratory Syncytial Virus are of high enough quality that their potential for aiding decision-making in people presenting for admission should now be evaluated systematically in typical clinical settings.
Introduction

Twenty-four percent of the population consults a general practitioner at least once a year because of respiratory problems; this proportion exceeds those reported for any other major group of diseases. With few exceptions these problems are caused by infection.

The incidence of respiratory problems varies seasonally and pressurises health service provision. This was particularly noticeable over the millennium winter when national newspapers were filled with reports of problems for patients in hospital A&E departments, who could not be found a bed. The Department of Health introduced initiatives to address this problem including: increased provision of hospital beds, modification of surgical schedules, reducing discharge delays, improving influenza vaccine uptake, more rapid response in A&E departments, improvements in out of hours services in primary care and drawing attention to issues concerning household heating (Winter and the NHS 2003-2004).

We welcome these initiatives and here, provide more detailed information about general respiratory problems in winter. This report is primarily concerned with the situation in England and Wales.

“Twenty-four percent of the population consults a general practitioner at least once a year because of respiratory problems: such conditions can occur at any time of year although respiratory infections are concentrated in the colder winter months.”
Terms such as ‘a cold’, ‘the flu’, ‘bronchitis’ or ‘chest infection’ are in everyday use to describe a range of respiratory infections, and mean something to most people. There is also a general understanding that, although such conditions can occur at any time of year, respiratory infections are concentrated in the colder winter months. There is also a wide understanding that these illnesses are largely caused by viruses and are caught through contact with other people in the home, at work, or at school. That is to say they are transmissible from person to person.

People who succumb to winter respiratory illness experience a range of symptoms. Some suffer such a minor illness that they do not need to take time off work or contact health services. This type of illness is almost impossible to measure accurately except in research projects, such as the community based studies of respiratory infection performed in the USA in the mid 1960s to mid 1970s. These studies involved large numbers of families with children, monitored over several winters, and showed how common respiratory infections were. In Seattle, 149 families were studied between 1965 and 1969 and on average, people reported four respiratory illnesses each year. This rate was highest in children under 5 years (five respiratory illnesses each year); mothers suffered much more illness than fathers, perhaps reflecting increased contact time with their children. A large variety of organisms were recovered, of which the vast majority were viruses. Both in this study and in a similar study in Tecumseh (USA) swabs were taken routinely from all patients experiencing respiratory illness.

Some people however suffer more serious disease: respiratory infections are one of the commonest causes of sickness absence both from work and school. In the UK there are no current information systems that routinely monitor sickness absence from work. National statistical data are available on certified incapacity from work, though medical certification for social security purposes does not involve the first five days of sickness absence. The impact of most respiratory infections is not sufficient to cause sickness absence of more than one week and thus data derived from sickness certificates have only a limited potential to inform on respiratory illness. Children of school age commonly experience winter respiratory infections and school absence records are also a potential source of information on their impact. However, these data are also not available contemporaneously and are not available by cause. Furthermore, school absence is influenced by many factors other than the illness of the pupil.

For many people affected by a respiratory infection, the first source of advice may be a community pharmacist. Sales of
over-the-counter cold and ‘flu’ remedies have been studied to give an idea of the level of respiratory infections in the community. However, these data are commercially sensitive, not always readily available and subject to the variability associated with marketing strategies. Hence they have only limited value in the context of disease surveillance.

NHS Direct is a telephone helpline that started in 1997. It provides health information and directs callers to the appropriate NHS service according to their reported symptoms. The entire population of England and Wales now has access to this service. NHS Direct offices use a computerised clinical decision support system which allows calls to be grouped into broad symptom categories and classifies them according to outcome such as simple advice or referral to another part of the NHS. Between December 2001 and April 2004 NHS Direct received on average approximately 70,000 calls per week about health problems of which between 0.5% and 2% were allocated to ‘cold/flu’ symptoms depending on the time of year (figure 1). A winter surge in the proportion of calls attributed to ‘cold/flu’ was well matched by the numbers of influenza virus reports to the Health Protection Agency. A weekly, daily or even hourly analysis of calls received is available to provide an immediate indicator of ‘cold/flu’ activity.

“The NHS Direct helpline provides health information and directs callers to the appropriate NHS service according to their reported symptoms. A weekly, daily or even hourly analysis of calls received is available to provide an immediate indicator of ‘cold/flu’ activity.”
The impact of respiratory illnesses in general practice is routinely monitored by the Royal College of General Practitioners (RCGP) national network of sentinel general practitioners known as the Weekly Returns Service (WRS). This service:

- monitors numbers of patients consulting with new episodes of illness classified by diagnosis
- was established in 1964 at the RCGP Birmingham Research Unit
- is funded by Department of Health
- provides weekly incidence rates per 100,000 population for new episodes of illness
- has archived all data since 1967 providing an unrivalled opportunity to look at long-term trends of disease

Clinical diagnoses are usually described according to the parts of the respiratory tract in which the symptoms are dominant though most respiratory pathogens (especially viral) affect both upper and lower respiratory airways.

### TABLE 1.

<table>
<thead>
<tr>
<th>Clinical diagnoses associated with upper and lower respiratory tract infections (URTI and LRTI)</th>
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<tbody>
<tr>
<td><strong>URTI</strong></td>
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<tr>
<td>Tonsillitis</td>
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<tr>
<td>Sore throat</td>
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<tr>
<td>Otitis media</td>
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<td>Common cold</td>
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<tr>
<td>Sinusitis</td>
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<tr>
<td><strong>LRTI</strong></td>
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<tr>
<td>Influenza-like illness</td>
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<tr>
<td>Pneumonia</td>
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<tr>
<td>Bronchitis</td>
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<td>Laryngitis</td>
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<tr>
<td>Pleurisy</td>
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</table>

Clinical diagnoses are usually described according to the parts of the respiratory tract in which the symptoms are dominant though most respiratory pathogens (especially viral) affect both upper and lower respiratory airways.

### FIGURE 2.

Upper and lower respiratory tract infection (URTI and LRTI) percent proportion: average by age over years 1994-2003.
In figure 2, the relative proportions of upper and lower respiratory tract infections (URTI, LRTI) are given by age (table 1). These distributions are compiled from accumulated data reported to the WRS over the years 1994-2003. The figure shows more upper respiratory diagnoses in young children and lower respiratory diagnoses in the elderly.

The overall impact of respiratory diseases on primary care is shown in figure 3 in which all new episodes of respiratory disease are averaged over the years 1994-2003. More than 95% of new episodes of respiratory disease are due to infection. As in many of the figures included in this report, the New Year is denoted at the centre of the horizontal axis since the emphasis is on winter activity. Each of the 52 points on these graphs represent the average weekly incidence of respiratory illness per 100,000 population. Regardless of age, the incidence of respiratory disease is high in winter especially in December and January. Increased winter incidence is particularly noticeable in young children. In the critical mid-winter period incidence in all age groups is more than double that in summer.

“Regardless of age, the incidence of respiratory disease in winter, especially in December and January, is more than double that in summer.”
The incidence of respiratory infections presenting to general practitioners in the WRS has been falling in recent years. The decrease is evident at all times of the year and is illustrated in figure 4 in which the mean weekly incidence in each quarter of the year over the period 1994-2003 in all ages combined is presented separately for males and females. The decreasing trend is seen in both URTI and LRTI and is evident in males and females. The female rates are higher than the male rates; these trends are also seen in each of eight age groups for which data are available (not presented).

In the paragraphs that follow, information is given about the common clinical syndromes as diagnosed in general practice. Diagnoses made by general practitioners are not based on rigid criteria. It is difficult to apply rigid guidelines across all age groups and when consulting patients in differing phases of their illness. Many people consult at a time when the most important criteria are only apparent from the history and not from objective findings.

**Acute bronchitis**

Acute bronchitis is the most important respiratory syndrome diagnosed in general practice. Incidence in male children less than 1 year is about 25% higher than in females; in age group 1-4 years 10% higher; between 15-64 years incidence is higher in females; in the elderly (65 years and over) incidence rates are similar in both genders.

Incidence of acute bronchitis usually peaks in children just before Christmas whereas in the elderly it peaks in the first week of the year (figure 5). The figure compares incidence in the age range 0-4 years with that in persons over 65 years in mid-winter weeks for alternate winters since 1995/96 and illustrates how consistently episodes of acute bronchitis occurred each winter. Social mixing at Christmas time probably accounts for the spread of many respiratory infections from children to grandparents. However winters in which there is a particularly high incidence in one age group do not necessarily give rise to particularly high incidence in another. In the millennium winter (1999/00), the incidence of
acute bronchitis in the elderly over the New Year period was the highest reported for 20 years, but incidence rates in young children were not exceptional; the opposite was seen in the winter of 1997/98.

“Acute bronchitis is the most important respiratory syndrome diagnosed in general practice; incidence usually peaks in children just before Christmas whereas in the elderly it peaks in the first week of the year.”
In children 0-4 years infection by respiratory syncytial virus (RSV) is probably the major cause of acute bronchitis. Incidence rates match virus reports submitted to the Health Protection Agency as illustrated in figure 6 for some recent winters. Of the total reports submitted more than 95% are in this age group. The cause in the elderly is less clear and is an important gap in our knowledge.

“In children 0-4 years old, infection by respiratory syncytial virus is probably the major cause of acute bronchitis; in the elderly the cause is less clear and represents an important gap in our knowledge.”

**Asthma**

From a general practice management perspective it is often difficult to distinguish new episodes of acute bronchitis from new episodes of asthma. Respiratory illnesses with cough and wheeze tend to be diagnosed as acute bronchitis unless occurring in known asthmatics. In children less than one year asthma is rarely diagnosed; in those aged 1-4 years there are on average about 39 episodes of asthma for every 100 of acute bronchitis, in adults 15-44 years 34 episodes and in the elderly 65 years and over, 9 episodes. In figures 7a and 7b, the mean weekly incidence of asthma averaged over the years 1994-2003 is contrasted with the incidence of total respiratory system diseases in children aged 0-4 and 5-14 years respectively (note the differing scales on the two graphs). Asthma attacks follow the same pattern as respiratory diseases generally. A pre-Christmas peak is particularly evident in young children.
FIGURE 7a.
Respiratory system diseases (RSD) and asthma: weekly incidence in 0-4 year olds averaged over years 1994-2003

FIGURE 7b.
Respiratory system diseases (RSD) and asthma: weekly incidence in 5-14 year olds averaged over years 1994-2003
**Influenza-like illness**

The term influenza-like illness (ILI) is commonly applied by general practitioners to an acute illness with a high fever and a dry cough usually appearing at a time in which several cases are presenting. Seasonal trends of ILI are highly consistent with influenza virus isolations obtained from a subset of the WRS general practices (figure 8).

The weekly incidence of ILI (all ages) over alternate winters (1993/94-2001/02) is shown in figure 9. Whilst in recent years ILI has frequently occurred around Christmas, the timing of influenza outbreaks varies winter by winter. As a rule of thumb, influenza outbreaks caused by influenza A viruses usually establish themselves before the New Year and those caused by influenza B after it. However, an exception to this pattern occurred in 1997/98 when influenza A appeared in February and March, mainly affecting the elderly. Influenza B generally does not have as great an impact as influenza A except in young children, where it is sometimes equally severe. Outbreaks of influenza usually last about eight weeks in England and Wales. Background levels of the incidence of ILI reported when there are limited numbers of influenza virus detections are less than 30 per 100,000 population per week.

“Whilst in recent years influenza-like illness has frequently occurred around Christmas, the timing of influenza outbreaks varies winter by winter.”

**FIGURE 8.**

Influenza-like illness (ILI): weekly incidence compared with influenza virus isolations from RCGP/Agency surveillance scheme in selected winter outbreak periods.
The incidence rates of ILI by age group reported in WRS data for the winters 1969/70 (pandemic year), 1989/90, 1993/94 and 1999/00 are compared in figure 10. Attention is first drawn to the noticeably different peak incidence rates: the all age peak in 1969/70 was 1252 per 100,000 in week 1; in 1989/90, 583 in week 49; in 1993/94, 235 in week 45; and in 1999/00, 233 in week 2. Examining the data separately by age group the maximum impact in 1969/70 was in the working population (age range 15-44 and 45-64 years); in 1989/90 and 1993/94 in children; and in 1999/00 in older adults (45-64 and 65 years and over). Note also the rates of ILI reported in a pandemic (1969/70) and even in a serious epidemic winter (1989/90) are many times those reported in other winters. The highly variable incidence rates of ILI both between winters and between age groups contrast with those of most other respiratory diseases.

This is partly because immunity to influenza lasts only a comparatively short time because influenza viruses are constantly changing, a process known as antigenic drift.

“The highly variable incidence rates of influenza-like illness both between winters and between age groups contrast with those of most other respiratory diseases.”
"Upper respiratory tract infections show the same weekly pattern of incidence as lower respiratory tract infections."

Otitis media is not usually thought of as a respiratory disease. It is generally diagnosed on the basis of a feverish illness with earache, usually with signs of inflammation on inspection of the eardrum or of excess fluid in the middle ear. The weekly incidence of otitis media in children less than 5 years is contrasted with that for children presenting with common cold in 1999 as an example year (figure 11). The similarity of incidence is evident every year. In this age group there is one child with otitis media presenting to a general practitioner for every two with a common cold. Comparisons like this, in which the incidence of diseases match so closely, indicate a common cause. There has been much debate about the use
of antibiotics for otitis media. Though it can be complicated by secondary bacterial infection, most children with otitis media have a viral infection and are unlikely to benefit from an antibiotic.

“Though it can be complicated by secondary bacterial infection, most children with otitis media have a viral infection and are unlikely to benefit from an antibiotic.”
National data on hospital admissions are collected routinely in England and Wales. They are available by diagnosis as recorded when patients are discharged. The main respiratory diagnoses are pneumonia and influenza, chronic obstructive pulmonary disease (which includes asthma) in adults and acute asthma, bronchitis and bronchiolitis in children.

Admissions for respiratory and cardiac disease (all ages) presented as weekly rates per 100,000 population for winter weeks 44-08 are given for winters 1995/96-1999/00 in figure 12. Admission rates for respiratory disease peak consistently over Christmas and New Year but no such peak is evident for cardiac admissions. Age-specific rates of admission for respiratory disease are presented as the weekly average in each of 13 four-weekly periods over the years 1994-2000 in figure 13. The graph shows large winter surges in the oldest and youngest age groups and illustrates the difference between winter rates and those at other times of the year. It is also evident from the graph that rises in respiratory admissions begin in August (4 weekly period 9), especially in children. Bed stay also increases with age: for respiratory admissions average bed stay in 1999/00 was 3.0 days in children less than 1 year and less than 2 days in older children; in adults 1.9 days per person aged 20-24 years, 3.7 days for those 50-54 years, but 10.7 days per person aged 80-84 years.

“Admission rates for respiratory disease peak consistently over Christmas and New Year but no such peak is evident for cardiac admissions.”

**FIGURE 12.**
Respiratory and cardiac admissions : rates by winter week over years 1995-2000
The respiratory admission rate has increased slightly in recent years especially in the elderly (figure 14). A large increase in admissions occurs during periods of influenza activity. Winter admissions for respiratory disease in adults in three age groups 45-64, 65-74 and 75 years and over are plotted by week against a background of periods of influenza activity in figure 15. Superficial examination might prompt us to think that all the surges of admission are due to influenza but closer inspection shows that surges are sometimes present at a slightly different time than is readily explained by influenza, e.g. 1997/98. Furthermore, surges can still be substantial even when the type of influenza which is circulating is causing comparatively mild illness in the community. Admissions in the age group 75+ during influenza periods have been increasing despite increasing uptake of influenza vaccination. Influenza and RSV are commonly circulating in the community at the same time and it is not easy to disentangle the impact of these viruses.

“A large increase in respiratory admissions occurs during periods of influenza activity.”
A WINTER'S TALE: COMING TO TERMS WITH WINTER RESPIRATORY ILLNESSES

FIGURE 14.
Respiratory admissions: winter rate in age groups 65-74 and 75+ over years 1994-2000

FIGURE 15.
Respiratory admissions: rates and influenza epidemic periods: years 1994-2000 by age
Impact on Mortality

In western countries winter mortality exceeds that in the summer. This is not the case in the undeveloped world nor historically in western countries. Momiyama (1977) observed two seasonal peaks: a summer peak probably associated with intestinal infections and a winter peak associated with winter respiratory infections (Figure 16). The figure illustrates seasonal mortality in Chicago over selected years from 1867-1925. (The complex scaling of this graph was chosen by Momiyama to display the respective peaks in as clear a manner as possible. Also it is important to note the horizontal axis is centred on the summer months in contrast to the majority of other figures in this report). Between 1887 and 1925 the summer mortality peak declined dramatically and the relative importance of the winter peak increased. Clean water and improvements in hygiene have eliminated the summer peak in western countries, but we have not yet eliminated the winter peak.

When considered in broad groups of diseases, rates of mortality follow similar seasonal patterns. In figure 17 the death rates in each winter week averaged over years 1993-2000 certified due to respiratory, circulatory or other cause are displayed. This common pattern implies at least some degree of common cause. Acute respiratory infections, and on present evidence especially influenza and RSV infection, are a large part of that cause.

“...rates of mortality follow similar seasonal patterns, peaking in mid-winter.”

In figure 18 the average death rate (all ages and all causes) in each winter over the period 1993-2000 is shown, and against that background we superimpose the weekly numbers of deaths during four substantial influenza outbreaks (1989/90, 1993/94, 1996/97, and 1999/00). The figure demonstrates that influenza impacts on death at whichever period during the winter it occurs. In 1989/90 and 1993/94 influenza occurred well before the Christmas and New Year period and before the coldest part of the winter.
“Influenza impacts on mortality at whichever period during the winter it occurs.”

Cold weather does have an effect on mortality especially for cardiac disease. Death rates increase slightly following decreases in temperature: it has been estimated that a one degree fall in daily temperature is responsible for approximately 50 extra deaths per day. It remains uncertain whether the effect of cold weather is direct or mediated through respiratory infections. Because excess winter mortality seems to be higher in UK than in some other colder countries, it has been suggested that standards of home heating and household insulation may be poorer in the UK, therefore contributing to the high levels of excess winter mortality. It has also been noted that countries with a relatively large concentration of the population living not too distant from the sea (such as in the UK, Portugal and Italy) have higher excess winter mortality than countries in Eastern Europe where the population live far from the sea and the climate is much colder. It is possible that the transmission of viruses between people is influenced by climatic conditions and that the ambient temperature or other characteristics of typical British winters may encourage transmission.

Figure 19 discloses differences in the seasonal patterns of mortality according to age, under 45, 45-64, 65-74 and 75 years and over. The figure is based on aggregated data over years 1993-2000 and shows the disproportionate effect of age. Most deaths occur in elderly people, particularly over 75 years, but the mid-winter surges are almost confined to people in the oldest age groups. It should be noted in passing that average temperature in the UK is lower in February than December and commonly also than in January.

“Most deaths occur in elderly people, particularly over 75 years, but the mid-winter surges are almost confined to people in the oldest age groups.”
FIGURE 18.
All-cause mortality rate (8 year average 1993-2000) with specific influenza seasons superimposed

FIGURE 19.
Deaths: all-cause weekly rate by age group: winter weeks averaged over years 1993-2000
Laboratory confirmation of clinical diagnoses, by identifying viral and bacterial causes greatly strengthens our understanding of seasonal infectious diseases and provides the evidence to rationalise management. It is unrealistic to expect that more than a very small proportion of clinical illness diagnoses are accompanied by virological confirmation because of the costs involved and the limited value of a virological diagnosis which is either too late to influence management, or for which no specific treatment is available. This situation may be challenged by the arrival of simple bedside tests for influenza and RSV, and the availability of safe and effective antiviral drugs. However, the costs of performing these tests, including the professional time involved are such that they are only likely to be used in people with comparatively severe illness. This is an area where operational research is needed to define best use.

“There are no systems in place that enable comprehensive virological data capture from all potential sources.”

In England and Wales the majority of the available data are assembled by the Health Protection Agency. For influenza, special programmes of virological sampling have been established based on the RCGP/WRS network, on peripheral public health laboratories and on selected independent boarding schools. For RSV, reports are mainly obtained from hospital-based laboratories and relate to children admitted with LRTI. Data about some other pathogens such as Mycoplasma pneumoniae are reported by hospital laboratories to the Health Protection Agency, though the underlying laboratory investigation of respiratory illnesses is highly variable. Data on most other viruses are obtained largely from outbreak investigations.

“In England and Wales the majority of the available virological data are assembled by the Health Protection Agency.”
In relation to virological sampling, there are several problems that limit the acquisition of good data for epidemiological purposes. Of primary importance is the timing of sampling during the early stages of a respiratory infection. To maximise the likelihood of isolating virus from the patient, specimens should be taken within 48 hours of symptom onset. However, it has been recently demonstrated that in England, many patients do not present within this critical 48 hour time period, reducing the potential for isolating pathogens of interest. The majority of virus surveillance schemes in England and Wales use the national postage system to transport clinical specimens from the primary care source to the laboratory. Samples are transported under conditions that are far from ideal, with delays for up to three days. Consideration of these factors shows how the extent of the virological burden of illness is likely to be greatly underestimated.

Advances in laboratory techniques e.g. multiplex polymerase chain reaction (PCR) have provided more sensitive methods of detection when compared to “gold standard” techniques such as virus culture, for the detection of respiratory viruses. These developments have increased the potential for the identification of specific pathogens in poor quality specimens that previously would have yielded negative results. These will improve both the diagnosis of infections, and the quality of surveillance systems. Though there has been significant commercialisation of PCR tests for diagnosis of blood borne viral infections such as hepatitis and HIV there has been little equivalent activity for respiratory virus infections. Also, the relationship between pathology services, virology laboratory provision, clinical management budgets and financial investment in hospital laboratories is complex. Development of standard tests, and testing algorithms, which can be applied widely in a variety of different hospital settings, is extremely difficult given the wide divergence of equipment and skills and local investment policies. The Health Protection Agency is working with the NHS and academic virology laboratories to extend the use of molecular diagnostic techniques in laboratories in England.

Key objectives for the development of virological laboratory data for modelling of morbidity, planning health care provision and improving the diagnostic quality of respiratory illness include:

- consideration of year round linked clinical virological respiratory disease surveillance in primary care including detection of a range of viruses
- development of antiviral resistance monitoring
- continued investment in the infrastructure of reference and regional virology laboratories enabling swift response to emergencies such as SARS (severe acute respiratory syndrome) and avian influenza

During the recent emergence of SARS and avian influenza, molecular biology techniques were used in both diagnostic and research laboratories to help in defining strategies to limit the spread of infection, to guide efficient patient management, to develop diagnostic tests and towards developing new vaccines and treatments. In the last few years we have become well aware of the dangers, threats and unpredictability posed by the emergence of new respiratory virus infections. As well as SARS and avian flu, two new viruses (a new variant of coronavirus and human metapneumovirus) have been identified illustrating the fast pace of pathogen discovery and the continuing necessity for capability to develop diagnostic tools through which the impact of viral pathogens on illness in the community can be assessed. A high proportion of patients from whom virological samples are investigated remain undiagnosed in virological terms and present a continuing challenge to our understanding of disease in the community. Many respiratory viruses are capable of mutating rapidly and evading immune responses. The potential for transmission of avian influenza from birds to humans should not be underestimated; it poses a real threat of a pandemic.
“A high proportion of patients from whom virological samples are investigated remain undiagnosed in virological terms and present a continuing challenge to our understanding of disease in the community.”

Laboratories responsible for supporting surveillance activities; for providing quality assurance of tests in current use; for deploying new tests in an intelligent and cost efficient manner; and for investigating novel viruses are at the cutting edge of microbiological science. A high skill base and high quality scientific environment are essential; these activities go well beyond those associated with the basic provision of routine diagnostic services which we expect from a national health service.

Aside from routine surveillance, specific research enquiries provide valuable information on the nature of the disease processes. For example, two community-based studies investigated the contribution of viral respiratory infections to exacerbation of symptoms in asthmatics and found associations in more than 85% and 44% of cases in children and adults respectively. Many different respiratory viruses were identified. For asthma in particular, it has been suggested that underlying infection with RSV is a predisposing factor to acquiring asthma in childhood. Whether it has much bearing on asthma extending on into adult life is less certain. There has also been the contrary argument that exposure to respiratory infections as a young child leads to higher levels of immunity and relative protection for ongoing asthma.

For some clinical syndromes there are clear links to specific viruses (table 2). Parainfluenza is particularly associated with croup, RSV with acute bronchiolitis in young children and also with conditions causing wheeze in the elderly. Rhinovirus has been particularly linked with the common cold; adenovirus and coronavirus are all recognised causes of respiratory infection. Most commonly these viruses cause only minor illness and this means that their contribution to respiratory disease occurring in the community is severely underestimated. However, the impact of frequently circulating viruses is serious for a few people and the relative minority with illness severe enough to prompt hospital admission or even cause death can be significant in their total number and in terms of their impact on health services.

<table>
<thead>
<tr>
<th>TABLE 2.</th>
<th>Common respiratory viruses and their associated clinical syndromes</th>
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<tbody>
<tr>
<td><strong>Respiratory Virus</strong></td>
<td><strong>Clinical Manifestations</strong></td>
</tr>
<tr>
<td>Influenza</td>
<td>Illness usually with fever, cough, sore throat, muscle pains</td>
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<tr>
<td>Parainfluenza</td>
<td>Wide range of symptoms ranging from “common cold” to croup</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>A feverish ILI with cough and wheeze</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>Common cold</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>Common cold symptoms with vomiting</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>Usually a mild form of ILI</td>
</tr>
</tbody>
</table>
“The impact of frequently circulating viruses is serious for a few people and the relative minority with illness severe enough to prompt hospital admission or even cause death can be significant in their total number and in terms of their impact on health services.”

The average number of reports to the Health Protection Agency of selected common viruses in four-week periods over the last five years is given in figure 20 (it is important to note the differing scale for RSV). RSV and influenza are the only clearly identified winter viruses while some viruses e.g. parainfluenza have clearly defined periods of circulation at other times of the year. Ninety percent of RSV is reported in people aged less than 2 years and a further 5% in those 2-4 years. For influenza the situation is almost opposite: less than 10% of influenza viruses are identified in children aged 0-5 years. These data reflect sampling bias rather that the true distribution of pathogens by age.

“Respiratory syncytial virus and influenza are the only clearly identified winter viruses. Other viruses circulate at other times of the year”
Rates of respiratory disease as found in new episodes of illness in general practice, and admissions to hospital are contrasted with all-cause death rates using weekly data averaged from years 1994-2004 over the winter period (weeks 44-08) in figure 21. The mid-winter surges are evident in all three indices and management from the health service perspective involves them all.

As previously shown in figures 3, 5, 10, 13, 15 and 19, age impacts on all three indices to differing extents. Numerically, deaths are almost all limited to persons over 65 years and mainly over 75 years. In an analysis of influenza associated respiratory admissions, the average number in each adult five year age group over the winters 1989-2001 increased dramatically with age so that more than 50% of the estimated excess winter admissions associated with influenza outbreaks occurred in persons over 75 years and they were responsible for 69% of total bed occupancy (figure 22).

“Mid-winter surges are evident in General Practitioners episodes, hospital admissions and all-cause death rates; management from the health service perspective involves them all.”
“More than 50% of the estimated excess winter admissions associated with influenza outbreaks occurred in persons over 75 years and they were responsible for 69% of total bed occupancy.”

It is difficult to make estimates of the persons consulting general practitioners, admitted to hospital or dying because of respiratory infection, because of the lack of individual patient specific data (especially including virological data). Excesses attributable to influenza, RSV and cold weather have been estimated using a variety of methods. At the simplest however, we are able at least to distribute events over time periods.
In Table 3 data are given about the proportion of new respiratory episodes presenting to general practitioners (WRS data), respiratory admissions (data for England and Wales) and respiratory deaths (national data for England) in four-week periods from 1994-2000. As in the figures already presented in this report the mid-winter values (periods thirteen and one) are presented in the middle of the table. If the impact on health services was the same throughout the year 7.7% of the impact would be evident in each four-week period, but this is clearly not the case. In the table, values over 10% have been identified by red highlighting; it is clear that the highest proportions of respiratory episodes occur in all ages in midwinter although a shift in timing can be seen from the young to the elderly as previously demonstrated with acute bronchitis (figure 5). The highest proportions of respiratory admissions are limited to the young and old, and respiratory deaths are limited only to the elderly. This pattern is accentuated during influenza outbreak periods.

“The highest proportions of respiratory admissions are limited to the young and old, and respiratory deaths are limited exclusively to the elderly. This pattern is accentuated during influenza outbreak periods.”

The maximum surge impact on admissions is seen at opposite ends of the age spectrum. Figure 23 contrasts the proportions of respiratory episodes, admissions and deaths in each of the 13 four-weekly periods in the age groups 0-4 years and 65 years and over. 27% of infant admissions and 24% of admissions in the age group 65 years plus are concentrated in periods thirteen and one (December and January) compared with the 15% which would be expected if admissions were equally distributed. From accumulated clinical incidence and virological data the December peak in

**TABLE 3**

<table>
<thead>
<tr>
<th>Seasonal period</th>
<th>GP episodes</th>
<th>Admissions</th>
<th>Deaths*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-4</td>
<td>5-14</td>
<td>15-44</td>
</tr>
<tr>
<td>June</td>
<td>6.6</td>
<td>9.5</td>
<td>9.0</td>
</tr>
<tr>
<td></td>
<td>4.7</td>
<td>7.0</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>3.4</td>
<td>5.7</td>
<td>5.1</td>
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<td>3.7</td>
<td>6.0</td>
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<td>10.1</td>
<td>12.4</td>
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<td>11.2</td>
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<td></td>
<td>7.0</td>
<td>7.8</td>
<td>9.5</td>
</tr>
<tr>
<td>May</td>
<td>7.0</td>
<td>8.2</td>
<td>9.6</td>
</tr>
</tbody>
</table>

* no data were available for the 15-44 age group
FIGURE 23.
Proportion of respiratory episodes, admissions and deaths in the young (0-4 years) and elderly (65+ years) in 4-weekly periods averaged over years 1994-2000

0-4 years

65+ years

4-weekly period

proportion (%) proportion (%)
A WINTER'S TALE : COMING TO TERMS WITH WINTER RESPIRATORY ILLNESSES

children is likely to be primarily caused by RSV infection and the peak in the elderly in January primarily by influenza with RSV making a significant additional contribution. Public health management strategy therefore focuses particularly on influenza-like illness and acute bronchitis or alternatively influenza and RS viruses.

“Public health management strategy focuses particularly on influenza-like illness and acute bronchitis or alternatively influenza and respiratory syncytial viruses.”

In the paragraphs that follow we consider a number of questions relevant to public health management. These emphasise the importance of the actions already undertaken as a result of the Department of Health's winter pressures plan, but also raise some further issues.

1. Can the surges of respiratory illness be predicted and by what time margin?

Surges in health service use and mortality over Christmas and New Year periods are predictable well in advance. They may be modulated to a limited extent by weather conditions. Influenza epidemics may cause additional surges in demand in the winter in some years. The relative impact by age will vary but some data may be available if influenza is already circulating in other countries. Surges clinically attributable to influenza will be more closely related to the time of year that influenza strikes and existing surveillance strategies provide at least 4 weeks notice of peak demand in severe epidemics.

In most winters, there is usually one dominant strain of influenza and one of RSV, but persons can be infected by both viruses and have additional infections if more than one strain is circulating.

The likelihood that a new influenza strain substantially different from that occurring elsewhere in the world might first appear in the UK is very remote. The emergence of a drug resistant virus strain capable of transmission between humans remains a theoretical possibility.

“Surges in health service utilisation and mortality over Christmas and New Year periods are predictable well in advance. Surges clinically attributable to influenza will be more closely related to the time of year that influenza strikes and existing surveillance strategies provide at least 4 weeks notice of peak demand in severe epidemics.”

2. Can more be done to prevent influenza and RSV and their transmission?

Pre-season vaccination has been shown to be effective in reducing the more serious manifestations of influenza. So, in target groups where it is known that there is a risk of a greater number of severe attacks of influenza and their complications, it is appropriate to pursue a programme of vaccination vigorously. There are also arguments in favour of vaccinating selected persons who might particularly influence transmission. It is widely thought that influenza spreads particularly from outbreaks in children though this has not been UK experience. However, influenza spreads rapidly in close-knit communities and schools are an obvious example. Vaccination of health care workers is important to limit spread in hospitals and also to minimise sickness from influenza among risk groups of workers and consequent sickness absences in influenza active periods. Extension of influenza
vaccination target groups might also be considered but it is unlikely and probably economically unjustifiable to vaccinate a sufficient proportion of the population to stop the spread of influenza altogether.

"Pre-season vaccination has been shown to be effective in reducing the more serious manifestations of influenza. Extension of influenza vaccination target groups might also be considered but it is unlikely and probably economically unjustifiable to vaccinate a sufficient proportion of the population to stop the spread of influenza altogether."

There has been considerable investment by the pharmaceutical industry in the preparation of an RSV vaccine. At present a preventative treatment is available but with very limited application at considerable cost. Whilst it is reasonable to hope that an effective vaccine, suitable for widespread use and at reasonable cost will eventually be available, this is not anticipated within the next five years.

The incidence of respiratory infections presenting to general practitioners has fallen in recent years. We can only speculate about the cause, but improvements in air quality, reduced smoking, improved standards of hygiene and changing thresholds for consultation and antibiotic prescribing may all be relevant. In a study of the spread of the common cold amongst soldiers, the distance between beds in a dormitory was critical. The implications for the effects of overcrowding are obvious. Though limitations on the freedom of meeting and on the opening of places of entertainment may be important parts of pandemic planning strategy, they are not appropriate for usual winter respiratory epidemic management. However, temporary school closures might be a consideration in a serious epidemic even if not involving a pandemic strain.
Nursing homes and residential institutions pose particular problems for containing the spread of influenza. We need to recognize that influenza vaccination though very effective in the healthy elderly is less effective in the very aged and frail elderly. Therefore, it is particularly important to recognize influenza early in residential institutions and to institute appropriate prophylaxis with neuraminidase inhibitor (NI) antivirals. If introduced promptly this intervention is likely to be effective in curtailing the spread of influenza in institutional environments, which include boarding schools, military barracks and prisons as well as residential institutions and nursing homes for the elderly.

"Nursing homes and residential institutions pose particular problems for containing the spread of influenza."

The transmission of influenza virus infections is mainly by airborne droplet, but for RSV contact spread is important. Basic hand washing therefore applies in the nursing context of RSV infected patients as for other and perhaps better-recognized bacterial pathogens.

3. What can be done to minimise the pressures on hospital admissions?

Until now patients have been admitted to hospital chiefly via a general practitioner referral. The situation is changing partly because general practitioners are less involved in emergency care and partly because freedom of choice gives patients other ways of accessing health care. In earlier days many general practitioners were likely to revisit sick elderly persons but current management for emergency care limits this availability. Changes in the delivery of primary health care impact on secondary care and though we cannot forecast the likely impact on pressures for hospital admissions in winter, a decrease seems unlikely.

"Changes in the delivery of primary health care impact on secondary care and though we cannot forecast the likely impact on pressures for hospital admissions in winter, a decrease seems unlikely."

Extra factors that need to be borne in mind include:

- there are increasing numbers of elderly people
- welfare/residential homes are not approved to provide nursing care
- the public generally is less willing to see relatives dying at home. In 1998, 19.6% of deaths occurred at home, in 2000 19.0% and in 2002 18.3%. In the elderly (75 years and over) these proportions were and it was 15.3%, 14.9% and 14.3% respectively
- doctors are increasingly cautious about looking after patients at home with serious illness if vulnerable to criticism for not admitting them to hospital where oxygen and resuscitation facilities are more immediately available

Diagnosis at the potential point of admission might help. Near patient diagnostic tests are available for both influenza and RSV. Management is improved by firm diagnosis and two examples illustrate how near patient tests might be used to minimise admission.

"Diagnosis by near patient tests at the point of admission might help patient management."

Case 1: A child with an acute lower respiratory infection.

If a near patient test with a positive result within 20 minutes supports the diagnosis of influenza and the child has not shown signs of breathing difficulties indicating the need for
admission, it is reasonable to begin treatment with neuraminidase inhibitor (NI) antivirals immediately and not admit. Conversely if the same patient were diagnosed by near patient test with RSV, management decisions would have to recognise that there is no curative treatment and the risk of developing breathing problems would be different and would influence the decision to admit. Current guidance from the National Institute for Clinical Excellence (NICE) on the use of antivirals for influenza restricts use in children to those with chronic diseases such as asthma. As experience of using these drugs grows and the potential of near patient tests is realised, guidance in the use of these drugs should be reviewed.

“As experience of using neuraminidase inhibitor drugs grows and the potential of near patient tests is realised, guidance in the use of these drugs should be reviewed.”

Case 2: An elderly person presenting with acute febrile respiratory illness (whether vaccinated against influenza or not).

If influenza viruses are circulating there is a high probability that the illness is due to this virus. The sensitivity of near patient tests for influenza is such that a positive test can be accepted as a reasonable basis for managing this patient. Provided the patient has presented early, the introduction of treatment with NI antivirals straight away is desirable whether or not admission takes place. In some cases, administration of this treatment may justify a decision not to admit.

A second factor affecting admission relates to the availability of community-based care. As was evident in the analyses presented in table 3 there was increased respiratory disease in people of working age. Nurses and care workers are commonly also pressurised from nursing their own children. Since the need for community caring staff in some months is much greater than in others, seasonally based contracts such as are common in retail and holiday enterprises might be considered.

Flexibility of working arrangements is desirable not only among the staff but also in the allocation of hospital beds between specialities. There will always be more beds needed for acute admissions in winter. Some initiatives have already been taken (Winter and the NHS 2003-2004) with regard to the timing of admissions for elective surgery. The allocation of beds to specific specialities, to work programmes and the concept of 5 day wards limits the possibility of an overflow from the acute admission wards. The preservation of these working arrangements must be weighed against the pressure of admission during times of crisis, often from patients whose bed stay requirements is likely to exceed 5 days.

“Greater flexibility of working arrangements is desirable not only among the staff but also in the hospital allocation of beds between specialities.”
Much of our understanding of the occurrence of the impact of acute respiratory infections on society comes from routine surveillance.

Most of these surveillance data have been generated by the management of the patient within the health service. This includes clinical diagnosis made by health carers on presentation in a general practice and the results of laboratory testing of specimens taken either in the community or in hospital. Other sources of information, such as data derived from death certificates, contribute to routine surveillance information. Information derived from surveillance can be used to understand new infection problems as they occur including the underlying causative organisms and the extent of spread, and contribute to the more effective management of these problems by the health service. To be most effective in this aim, surveillance information needs to be both timely and representative. While intensive efforts have been put into the surveillance of influenza including the timely provision of information about current influenza activity levels, surveillance of other respiratory infections is generally very limited. Two examples illustrate current shortcomings:

1. Acute bronchitis is common in adults each winter but the cause of this illness is largely unknown. The epidemic character of the appearance of acute bronchitis in the winter period strongly suggests a viral origin but, if the illness is investigated at all, bacteria rather than viral pathogens are sought. It is likely, however, that bacterial infections are secondary to the initial virus infection.

2. A rise in respiratory infections in all age groups is seen every year at the end of August and the beginning of September. This may be due to the return of children to school and spread of infections among this group. Although this explanation is plausible it has not been demonstrated and does not explain the fact that the increase at this time of year occurs as much in adults as in children.

“A rise in respiratory infections in all age groups is seen every year at the end of August and the beginning of September.”

Most routine surveillance data are received from separate sources. For example, counts are made of episodes of illness presenting to general practitioners, patients admitted to hospital, laboratory specimens examined and numbers of deaths. Routine surveillance does not currently link information between these episodes i.e. between presenting clinical illness, admission to hospital, results of laboratory testing, and (if relevant) cause of death. Although much can be understood about respiratory illnesses in the community based on independent sources of information, the power of surveillance would be greatly enhanced by linking these data sources using the facilities offered by modern information technology and the use of a unique identifier such as the NHS number.

The need to maintain patient confidentiality and other ethical considerations present problems for the development and maintenance of surveillance. Information for individual patient management requires identifying the patient by name: information for the purpose of surveillance does not. However, mechanisms are needed which preserve information links and these can be achieved by using unique patient code...
numbers. Surveillance requirements include patient linked information on related illnesses, recent antibiotic use, vaccination status, hospitalisation, other pathology results etc. Provided that stringent safeguards are adhered to, patient confidentiality can be strictly maintained. It should be accepted practice that information, derived from patient consultation and investigation within the health service should also be used for the benefit of the whole population.

At present individuals have the right to bar the use of personal data, (even in an anonymised form), from being passed to any other person other than those involved in their direct clinical care. Routine surveillance, however, cannot function effectively if patients can opt out in this way. This use of information about patients differs substantially from the information collected in investigative clinical research in which health care interventions are used. An ethical framework for surveillance which recognises the differences from clinical research is needed so that effective and appropriate surveillance can be conducted.

“For effective management of epidemics and even of the usual winter surges of respiratory illness, more representative sampling of patients developing illness is required.”

A new pandemic of influenza is generally believed likely at some time in the future. During such a pandemic, there will be substantial legitimate demands from surveillance systems for information about the impact of the pandemic. This will require the collection of comprehensive information much of which is not collected routinely. On the other-hand, in the face of a pandemic the development of new surveillance systems will be difficult in view of the competing pressures on the time of health professionals and the possibility that many health professionals will themselves be unable to work because of sickness. Robust surveillance at the time of a pandemic or other major epidemic, is therefore dependent on the development of robust surveillance systems during the inter-pandemic period.

“Robust surveillance at the time of a pandemic or other major epidemic, is therefore dependent on the development of robust surveillance systems during the inter-pandemic period.”
Selected Reading


The referenced text of this report is available at: www.hpa.org.uk

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Notes