

RESPIRATORY INFECTIOUS  
DISEASE BURDEN IN AUSTRALIA

Edition 1, March 2007

We are pleased to present to you the first edition of The Australian Lung Foundation's Case Statement on Respiratory Infectious Disease Burden in Australia.

This Case Statement integrates relevant information across the breadth of respiratory medicine in Australia and makes an evidence based case for Respiratory Infectious Disease to be identified as a major Health Priority for Australia.

Both The Australian Lung Foundation and Thoracic Society of Australia and New Zealand are committed to reducing the large burden of disease and impact of Respiratory Infectious Disease. It is a challenge that will require a collaborative effort from the community, research institutions, health professionals, government and other stakeholders. In order to influence health outcomes, the effort to combat Respiratory Infectious Disease will have to be sustained and it will likely be costly. However the costs of inaction, both individually and for the community, mandate this concerted approach.

The Australian Lung Foundation Respiratory Infectious Disease initiatives warrant our serious attention. We strongly encourage you to support The Australian Lung Foundation's Respiratory Infectious Disease initiatives and commend to you this first edition of the Respiratory Infectious Disease Burden in Australia case statement.

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National Chairman  
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March 2007

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# “RESPIRATORY INFECTIOUS DISEASE BURDEN IN AUSTRALIA”

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## FOREWORD

The Respiratory Infectious Disease (RID) Case Statement summarises the full impact of respiratory infection in Australia as (1) multiple specific disease entities that are significant factors in their own right and as (2) a major complicating factor that cuts across all areas of respiratory health. The Statement serves the dual purpose of:

1. Raising the public awareness of the total burden of disease associated with respiratory infection across the breadth of respiratory medicine;
2. Providing a platform to launch policy initiatives that could help alleviate the mismatch between the enormity of the total disease burden and the paucity of current effective management strategies.

The Case Statement has been developed by the RID group of The Australian Lung Foundation. The key motivation behind the formation of both this multi-disciplinary group and the Case Statement was concern over the apparent complacency regarding RID. The RID group wanted to capture relevant information across the breadth of respiratory medicine in order to highlight the large mismatch between total respiratory infection disease burden and current management inefficiencies, and to identify common themes and important areas worthy of closer focus.

The Case Statement summarises the evidence that justifies RID to be identified as a major Health Priority for Australia. RID should be a major Health Priority for a number of reasons including:

- RID affects all sections of the community – young or old, chronically ill or well, socially disadvantaged or not.
- The disease burden associated with RID is the major contributor to the burden of infectious disease around the world.
- The management of RID is sub-optimal. Widely acknowledged inefficiencies in RID treatment are greatly compounded by inadequate diagnostic tools and lack of knowledge.
- There are serious threats posed by specific respiratory pathogens.

Respiratory infections have an enormous diversity, both in their epidemiology and likely severity. These infections range from the commonplace to the exotic and from the trivial to the very severe. Respiratory infections may involve the upper airway, the lower airway and / or the lung itself – the latter, by definition, constituting pneumonia. Rarely, the key factors in determining specific outcomes may threaten to combine with potentially disastrous consequences, as in the risks associated with pandemic influenza. In all these cases, an accurate diagnosis

is key to optimising management strategies for specific infections, avoiding unnecessary antibiotic use, and prioritising the need for ongoing antimicrobial drug development.

Each year in Australia, pneumonia results in several hundred thousand general practice consultations and more than 40,000 hospital admissions. Pneumonia is the sixth leading cause of death in Australia and is a major cause of hospital-acquired morbidity and mortality. The very young and the elderly are particularly vulnerable to pneumonia.

Viral infections of the upper airway touch the lives of nearly every Australian. Although these infections are usually just an irritation for the individual, they are associated with substantial costs to the community in terms of absenteeism and loss of productivity. However, viral infections can be serious, especially in children. In this population, viral infections such as croup, bronchiolitis and pneumonia can be major causes of morbidity and hospitalisation.

Respiratory infections can also aggravate common chronic respiratory conditions, such as asthma and chronic obstructive pulmonary disease (COPD), and chronic medical conditions, such as heart failure. In addition to impacting the very young and the elderly, RID has a major impact on: patients already suffering from chronic illness (e.g. young patients with cystic fibrosis); patients with immunosuppression caused by disease or treatment; indigenous Australians; and newly arrived refugees and migrants.

Specific respiratory infections such as influenza and tuberculosis have major public health implications and costs for Australia. These infections also have considerable implications in terms of our relationships and responsibilities in the Asia Pacific region.

Finally, various respiratory infections have the potential to become problems on a nightmare scale. These problems include the threat of: increasing antibiotic resistance, with some infections becoming 'untreatable'; pandemics from emerging viral illnesses, such as avian influenza and severe acute respiratory syndrome (SARS); and bioterrorism, using infections spread by the aerosol route.

In summary, RID is common and can be a direct or indirect cause of illness. Management of RID is largely sub-optimal and the problems posed by respiratory infections are greatly compounded by severe limitations in diagnostic techniques and a relatively poor understanding of pathogenic mechanisms. In particular, there is a lack of effective diagnostic and therapeutic strategies for most viral pathogens and an increasing number of multi-resistant bacteria. The threats posed by emerging respiratory infections and limited development of new antimicrobial drugs can only worsen this situation.

**Viral infections of the upper airways touch the lives of nearly every Australian.**

**Respiratory Infectious Disease should be a National Health Priority.**

The identification of RID as a major health priority for Australia will simultaneously raise awareness of the unmet clinical need posed by respiratory infection across many areas of medicine and offers a clear path forward to efficiently focus and co-ordinate future clinical science research and health policy initiatives directed at reducing the current and future burden of respiratory infectious disease on the Australian population.

Investing in reducing the burden of RID today will pay off many times in the future for all Australians – whether they become ill or not.

## “WE MUST DO BETTER, AND WE CAN”



Foreword by: Associate Professor Tom Kotsimbos, MD, FRACP  
Chairman, “The Australian Lung Foundation Respiratory Infectious Diseases Consultative Group.”

March 2007

## EXECUTIVE SUMMARY

### Acute respiratory infections in Australia

- Upper respiratory tract infections account for three to four million visits to general practitioners (GPs) each year in Australia. This represents more than 6 per 100 of all GP consultations. Each year, upper respiratory tract infections cost Australian taxpayers more than A\$150 million in direct cost and considerably more in indirect costs (i.e. costs due to absenteeism and loss of productivity).
- Lower respiratory tract infections account for almost three million visits to GPs each year in Australia. Croup and bronchiolitis account for the majority of winter hospitalisations in children. Between 50 to 90% of hospital admissions for bronchiolitis and 5 to 40% of hospital admissions for pneumonia are due to respiratory syncytial virus infection.
- The combined death rate for pneumonia and influenza positions these respiratory infections as the sixth leading cause of death in Australia. In 2002, pneumonia and influenza accounted for 3084 deaths (2.34% of all deaths in Australia) and 43,953 hospital admissions (average length of stay = 6.3 days).
- Each year in Australia, community-acquired pneumonia is associated with an overall mortality rate of 11.8% for hospitalised patients aged greater than 65 years. This mortality rate increases to 19.2% if two or more co-morbid diseases (e.g. chronic obstructive pulmonary disease, congestive cardiac failure, diabetes) are present.
- The direct and indirect cost burden of community-acquired pneumonia in Australia is estimated to be more than A\$500 million each year.

### Respiratory infections in ‘at risk’ individuals

- In 2003 / 2004, there were approximately 14,000 cases of hospital-acquired pneumonia in Australia. The median length of hospital stay was 18 days and, in patients aged more than 65 years, the mortality rate was 27.1%. Each year in Australia, hospital-acquired pneumonia costs more than A\$500 million – in direct costs alone.
- Each year in Australia, up to 30,000 hospital admissions for asthma and up to 40,000 hospital admissions for chronic obstructive pulmonary disease are precipitated by viral infections. Viral infections are therefore implicated in 50 to 80% of all hospitalisations for asthma and chronic obstructive pulmonary disease.
- Indigenous Australians are disproportionately affected by respiratory tract infections. Compared to the non-indigenous population, indigenous Australians have a 4-fold greater hospitalisation rate from pneumonia and a 9 to 11-fold greater mortality rate from respiratory infections.

**Upper respiratory tract infections account for 3 - 4 million visits to GPs each year.**

**Pneumonia and influenza are the sixth leading cause of death in Australia.**

**Treatment of hospital-acquired pneumonia costs more than \$500 million each year.**

**The impact of inter pandemic influenza can be minimised by an adequate vaccination strategy.**

**Bacterial resistance to antibiotics is becoming more widespread.**

## Respiratory infections and public health

- Inter pandemic influenza causes an annual increase in respiratory morbidity and mortality; this increase can be greatly minimised by an adequate vaccination strategy. In the event of an influenza pandemic, the best conservative estimates of the likely impact in Australia include six million clinically ill. Of these six million, three million could require outpatient care, 80,000 could require hospitalisation and there could be 35,000 deaths. The direct and indirect cost burden is estimated to be up to 14.5 billion dollars.
- Each year in Australia, approximately 1000 new cases of tuberculosis are diagnosed. The majority of patients with tuberculosis were born overseas (particularly in the Asia Pacific and African regions). The overseas-born patients also account for nearly all of the 10% of *Mycobacterium tuberculosis* isolates that are resistant to any of the common first line treatments.
- Bacteria resistant to many or most of the commonly used antibiotics are becoming more widespread in both the hospital and the community. This level of resistance greatly compounds the adverse impact from an international reduction in the development of new antibiotics.

# 1. ACUTE RESPIRATORY INFECTION SYNDROMES

## 1.1 Upper Respiratory Tract Infection

Upper respiratory tract infections (URTIs) are usually defined on the basis of the anatomical structure involved (e.g. rhinitis - nose; pharyngitis - throat; laryngitis - larynx; sinusitis - sinuses; otitis media - middle ear). It is also possible to define URTIs based on the microbiological cause: most are caused by viruses such as rhinovirus, adenovirus, parainfluenzavirus, influenzavirus, respiratory syncytial virus or coronavirus. Bacteria can be the primary cause of URTI (e.g. Streptococcal pharyngitis, *Mycoplasma pneumoniae* otitis media) but can also act as secondary pathogens (e.g. otitis media caused by pneumococcus or *Moraxella catarrhalis*).

Respiratory illnesses are the most common problems managed in general practice, accounting for about one seventh of all consultations. The burden of respiratory illness in Australian general practice has been identified in the BEACH (Bettering the Evaluation And Care of Health) study from AIHW (Australian Institute of Health and Welfare) General Practitioner Statistics and Classification Centre at the University of Sydney [1]. Key points from the BEACH study are summarised below:

- From March 2002 to March 2004, Australians made seven million visits to their general practitioner (GP) because of an URTI. This visit rate means that URTIs account for more than 6 of every 100 clinical presentations to GPs.
- Women were more likely than men to visit their GP because of an URTI.
- 31% of URTI patients were aged less than 15 years; 17% were less than 5 years and 10% were aged 65 years and above.
- Cough was the most common presenting symptom, reported at a rate of 30 per 100 consultations.
- Medications were prescribed at a rate of 59 medications per 100 URTIs, and supplied by the GP at a rate of 3 medications per 100 URTIs.
- Antibiotics were prescribed at a rate of 40 per 100 URTIs (likely to have been unnecessary in most cases) and comprised two thirds of all prescriptions. More than half of the antibiotics prescribed were betalactam antibiotics (penicillins or cephalosporins). In most instances the antibiotics were probably not clinically necessary and frequently had a broad spectrum of activity which may have contributed to antimicrobial resistance in the community [2, 3].

**Upper respiratory tract infections account for more than 6 out of 100 presentations to GPs.**

### The impact of URTIs on society is considerable.

- Approximately 30% of URTI patients received advice about issues other than medication including clinical observation, health education, certificates and counselling.
- In terms of additional tests, 1.6% of URTI patients had a blood test and 1.3% had an imaging procedure.
- Less than 1% of URTI patients were referred to another health care professional.

The economic impact of URTIs is difficult to estimate because of imprecise diagnosis and reporting. Influenza is responsible for 10 – 12% of all absenteeism from work [4] and is estimated to cost the Australian economy A\$600 million per annum [5, 6]. Influenza can slow reaction times by 20 – 40% for those who continue to work while they are ill, increasing the potential for errors and injuries [7].

The majority of URTIs represent an inconvenience to individuals, with minor discomfort for a few days. However, the associated cumulative impact of URTIs on society is considerable, due to absenteeism and loss of productivity. In addition, there are certain high risk individuals in whom URTIs can cause severe illness, a need for hospitalisation or even death. The 'high risk' people include those with chronic lung or heart disease, diabetes, immunosuppressing conditions (e.g. malignancy) or immunosuppressive therapy (e.g. corticosteroids). Furthermore, URTIs can have potentially devastating effects when virulent organisms infect communities; examples include the Asian and Hong Kong flu pandemics of 1957 and 1968 – 1969 respectively, severe acute respiratory syndrome (SARS), and, more recently, avian influenza or "bird flu". Patients with URTIs can also suffer from secondary complications such as glue ear, chronic sinusitis, exacerbations of chronic bronchitis or asthma, pneumonia, septicaemia and meningitis.

The upper respiratory tract is also a major site of primary bacterial infections. These bacterial infections may be very localised or extend to involve the lower respiratory tract.

Society tends to take URTIs for granted: a minor problem that runs through communities in wintertime, which is quickly forgotten. However, the impact of URTIs on society and strategies for minimising URTI transmission require further emphasis, publicity and research.

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**Viral pathogens are the most common cause of respiratory tract infections in children.**

**25 - 40% of respiratory syncytial virus infections lead to pneumonia and bronchiolitis in Australian infants.**

**Croup is the most common form of acute upper airway obstruction in children.**

## 1.2 Respiratory Tract Infections in Children

Viral pathogens are the most common cause of both upper and lower respiratory tract infections in children in Australia and the world. The most common pathogens are rhinovirus and respiratory syncytial virus (RSV) (the latter being more likely to cause severe infection). There is increasing evidence that influenza and metapneumovirus may also account for many respiratory infections. The full impact of viral respiratory infections has not been well understood due to the combination of current diagnostic limitations and few therapeutic options. Until now, the incentives to change this situation have been limited.

One of the more easily identifiable viruses that cause lower respiratory tract infections (LRTI) in children is RSV. Based on a study in the USA in 1991, approximately 100,000 children were hospitalised due to RSV, resulting in a cost of US\$300 million [1]. Extrapolation of these data to the Australian environment would mean that approximately 10,000 children would be hospitalised each year due to RSV, resulting in a cost of A\$20 million. Infection due to RSV is most common in young children, with a peak incidence occurring in infants aged one to six months [2]. Infection from RSV does not cause lasting immunity and, as a result, RSV infection often occurs repeatedly. Each year, approximately 3% of each year's birth cohort are admitted to hospital with RSV infection in Europe, Australasia and North America [3].

The major clinical illnesses produced by RSV are bronchiolitis, tracheobronchitis and pneumonia [2]. In Australia, approximately 25 to 40% of RSV infections lead to pneumonia and bronchiolitis in infants aged less than 12 months [2]. In terms of hospital admissions for children, RSV is responsible for 50 to 90% of admissions for bronchiolitis, 5 to 40% of admissions for pneumonia and 10 to 30% of admissions for tracheobronchitis [1]. Infants hospitalised with RSV bronchiolitis also have an increased risk of developing asthma in later life [4].

Given the considerable morbidity of RSV infection, an effective RSV vaccine is obviously a high priority. However, no effective RSV vaccine is currently available. Although passive immunisation with a monoclonal RSV antibody can reduce hospital admissions in high-risk infants [5], the treatment is expensive. The cost-effectiveness of passive immunisation with a monoclonal RSV antibody has not been established for otherwise healthy infants and this treatment is not available through the Australian Pharmaceutical Benefits Scheme. Consequently, the treatment of RSV infection in hospital remains supportive, with fluids and supplemental oxygen. Bronchodilators, corticosteroids and antibiotics have no routine role in the management of uncomplicated RSV infection in children.

Croup (also known as laryngotracheobronchitis or LTB) is the most common form of acute upper airway obstruction in children [6]. Acute viral croup is most commonly caused by parainfluenza virus infection. Spasmodic croup is another form of the illness that occurs in the absence of diagnosed viral infection.

The clinical illness and management for viral and spasmodic croup, however, are identical.

Hospitalisation for croup is highest for infants in the first year of life, and admission rates peak in autumn and trough in summer [6]. Corticosteroids are the most effective treatment for upper airway obstruction in croup. Before the widespread use of steroids, as many as 31% of patients with croup required hospitalisation [7], and 1.7% required intubation for life-threatening upper airway obstruction [8]. In Australia, steroid therapy for croup has resulted in significant reductions in rate of intubation, admission to intensive care and length of stay in hospital [9]. Corticosteroid treatment is also effective in the out-patient management of croup [10]. Currently, there is no effective vaccine available that can prevent parainfluenza virus infection.

Epiglottitis is an acute bacterial infection of the upper airway caused by *Haemophilus influenzae* type B (HIB). This infection can cause life-threatening upper airway obstruction. Before the introduction of the HIB vaccination in 1992, the annual HIB attack rate in children less than 5 years of age was 40 to 60 per 100,000. This rate was higher (450 per 100,000) in Aboriginal children in the Northern Territory [11]. Since 1992, incorporation of the HIB vaccine into the routine immunisation schedule in Australia has led to a dramatic reduction in paediatric cases of epiglottitis; most cases now occur in adults [12].

Whooping cough is primarily an acute bacterial infection of the upper airways that rapidly involves the lower airways. Whooping cough is caused by *Bordetella pertussis*. An effective vaccine has been available for many years. However, as immunity wanes over time, there has been an increased incidence of whooping cough in adults. Currently, most notifications for whooping cough are in the 12 to 16 year old age group [13]. The increased incidence and notification pattern for whooping cough is of concern. Adolescents and adults may transmit the infection to very young infants, who are unimmunised or partially immunised, and thus more vulnerable to severe or even fatal disease [14]. A 'booster' pertussis vaccine for adolescents is needed to target this source of infection. In NSW, a federally funded program has administered vaccines for pertussis, diphtheria and tetanus to more than 100,000 teenagers through school-based vaccination clinics in an effort to overcome this problem [15].

**Epiglottitis can cause life-threatening upper airway obstruction.**

**The incidence of whooping cough is increasing.**

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## 1.2 Pneumonia - Community-Acquired and Hospital-Acquired

Pneumonia is a clinical-radiological diagnosis based on an infection in the lung. Pneumonia may be:

- Community-acquired: usually due to *Streptococcus pneumoniae*, atypical bacteria (such as *Mycoplasma*, *Chlamydia* and *Legionella*), or viral pathogens. In approximately 50% of community-acquired pneumonia cases no organism is identified.
- Hospital-acquired: associated with a much greater spectrum of pathogens, particularly bacterial pathogens that are usually more difficult to treat.

Due to diagnostic limitations, empirical antibiotic therapy, at least initially, is routine. Patients with mild community-acquired pneumonia may be managed as outpatients. However, patients with more severe disease may require hospitalisation, which may also involve support from the intensive care unit. Patients with hospital-acquired pneumonia experience increased morbidity and mortality compared to hospitalised patients who do not contract pneumonia. Hospital-acquired pneumonia greatly increases the direct and indirect costs of hospital care.

The incidence and impact of both community-acquired pneumonia and hospital-acquired pneumonia can be estimated based on the International Classification of Disease [1] 'codes at discharge' data from AIHW and the Victorian Department of Human Services [2 – 4]. These data sources use common coding practices and modelling systems, which have been adopted from those used in global burden of disease studies conducted by the World Health Organization.

In developed countries, pneumonia tends to occur more frequently, and is associated with increased severity and poorer outcomes in the elderly (who often have other co-morbidities) and in indigenous communities (who often have poor socioeconomic status). In lower income countries, the incidence and impact of pneumonia tends to be highest in the very young. The use of disability-adjusted life years as a major summary measure for disease burden tends to downplay the impact of pneumonia syndromes in the elderly. For this reason, pneumonia is not in the current top 10 causes of disease burden in most developed countries, although it remains the sixth leading cause of death. However, the use of disability-adjusted life years amplifies the impact of pneumonia in the very young. For this reason, pneumonia is a leading cause of disease burden in the developing world [5 – 6]. Although trends in these data can be used to make some extrapolations of the future disease burden associated with respiratory infections, highly specialised models are required to deal with the potentially dramatic impact of future pneumonia epidemics (e.g. due to influenza or SARS) [7].

**Due to diagnostic limitations, empirical antibiotic therapy is routine.**

**Pneumonia is associated with increased severity and poorer outcomes in the elderly.**

**Increasingly, elderly patients with community acquired pneumonia require hospitalisation.**

### Pneumonia burden in Australians

Based on data from AIHW, there were 3,084 deaths attributable to pneumonia and influenza in 2002 (2.34% of all deaths) [8]. Pneumonia accounted for a total of 43,953 hospital admissions (i.e 22 per 10,000 hospital admissions), with an average length of stay of 6.3 days. During the same period, the AIHW BEACH study identified that there were 337,200 GP consultations each year for pneumonia [9].

More detailed measures of the incidence of community-acquired pneumonia requiring hospitalisation and hospital-acquired pneumonia can be sourced from the Victorian Hospital Morbidity database (Victorian Admitted Episodes Dataset – VAED) [4]. This database is a comprehensive repository of hospital-related information in Victoria, but can be used to extrapolate findings for the Australian population. The Victorian Hospital Morbidity data show that during the last seven years there has been an increase in the number of patients in Victoria with community-acquired pneumonia requiring hospitalisation (Table 1). In each year examined, the major impact was in the group aged greater than 65 years old. Patients in this age group with co-morbid disease also had a higher mortality rate. For example, in 2003 / 2004, patients with two or more co-morbid diseases (such as chronic obstructive pulmonary disease, congestive cardiac failure, diabetes) who were hospitalised for community-acquired pneumonia had a mortality rate of 19.2%; patients without two or more co-morbid diseases had a mortality rate of 11.8% [10 – 12].

**Table 1: Community-Acquired Pneumonia in Victoria [4]**

| Age Group (years) | 1998/1999<br>n = 22,158         |           |              |            | 2001/2002<br>n = 24,613         |           |              |            | 2003/2004<br>n = 27,655         |           |              |            |
|-------------------|---------------------------------|-----------|--------------|------------|---------------------------------|-----------|--------------|------------|---------------------------------|-----------|--------------|------------|
|                   | Proportion within age group (%) | Death (%) | LOS (median) | Severe (%) | Proportion within age group (%) | Death (%) | LOS (median) | Severe (%) | Proportion within age group (%) | Death (%) | LOS (median) | Severe (%) |
| 0 - 18            | 11.9                            | 0.5       | 2            | 2.5        | 10.9                            | 0.3       | 2            | 4.3        | 10.7                            | 0.3       | 2            | 4.3        |
| 19 - 64           | 27.2                            | 3.7       | 5            | 7.6        | 25.9                            | 3.7       | 4            | 9.6        | 25.3                            | 3.4       | 4            | 9.2        |
| > 65              | 60.9                            | 13.8      | 7            | 5.5        | 63.2                            | 13.2      | 7            | 7.1        | 64.1                            | 11.8      | 7            | 6.9        |

\*LOS = Length of Stay in hospital

There are no robust economic data on the costs of community acquired pneumonia in Australia. A recent evaluation of the economic cost of community-acquired pneumonia in New Zealand adults identified that the major generators of cost were the number of hospitalisations (especially for patients aged greater than 65 years) and loss of productivity [13]. This study documented that between 2000 – 2001, an average of 26,826 New Zealand adults were hospitalised per year (85.9 per 10,000 hospital admissions). This hospitalisation rate was associated with an annual cost estimate of NZ\$63 million, comprising \$29 million direct medical costs, \$1 million in direct non-medical costs, and \$33 million in loss of productivity costs [13]. Scaling the data from New Zealand to the Australian population indicates that the annual total cost burden of hospitalised community-acquired pneumonia in Australia would be between A\$300 – 350 million [14]. These estimates are in keeping with US hospitalisation costs from community-acquired pneumonia of between USA\$7,000 – 8,000 per admission (US\$4 million per 100,000 population) [15, 16].

Based on an extrapolation of data from the VAED, there would have been 100,000 patients hospitalised for community-acquired pneumonia throughout Australia in 2003 / 2004 (55 per 10,000 admissions). These Australian estimates are similar to data from the USA, with community-acquired pneumonia accounting for 1.3 million hospitalisations in 2001 (National Hospital Discharge Survey (NHDS), Centres for Disease Control and Prevention (CDC), USA) (47.3 per 10,000 admissions) [15]. Additional data from the USA indicate that community-acquired pneumonia affects approximately 4.8 million people in the USA each year and accounts for 8% of hospital deaths. In the USA, pneumonia is ranked as the seventh leading cause of death [5]. The extrapolation of VAED data suggest that the AIHW estimate of 43, 953 hospital admissions in Australia for community-acquired pneumonia may indeed be an underestimate.

**Table 2: Hospital-Acquired Pneumonia in Victoria [4]**

| Age Group (years) | 1998/1999<br>n = 3,505          |           |              |            | 2001/2002<br>n = 3,777          |           |              |            | 2003/2004<br>n = 4,104          |           |              |            |
|-------------------|---------------------------------|-----------|--------------|------------|---------------------------------|-----------|--------------|------------|---------------------------------|-----------|--------------|------------|
|                   | Proportion within age group (%) | Death (%) | LOS (median) | Severe (%) | Proportion within age group (%) | Death (%) | LOS (median) | Severe (%) | Proportion within age group (%) | Death (%) | LOS (median) | Severe (%) |
| 0 - 18            | 1.5                             | 11.3      | 13           | 37.7       | 1.6                             | 5.0       | 13           | 38.3       | 1.5                             | 4.9       | 14           | 57.4       |
| 19 - 64           | 27.6                            | 12.6      | 15           | 43.3       | 25.6                            | 15.0      | 16           | 46.4       | 26.2                            | 13.2      | 19           | 56.7       |
| > 65              | 70.9                            | 28.6      | 17           | 26.8       | 72.8                            | 28.6      | 18           | 29.1       | 72.3                            | 27.1      | 18           | 31.5       |

\*LOS = Length of Stay in hospital

Data from the VAED can also be used to estimate the incidence and impact of hospital-acquired pneumonia. In Victoria, the incidence of hospital-acquired pneumonia has increased during the last seven years, affecting approximately 4,000 patients in 2003 / 2004 (Table 2). As expected, the incidence and the severity of hospital-acquired pneumonia were greatest in patients aged more than

**Hospitalised community-acquired pneumonia costs A\$300 - 500 million each year.**

65 years of age and in those with co-morbidities. An extrapolation of the VAED data indicates that there would have been approximately 14,000 patients in Australia each year with hospital-acquired pneumonia (7 per 10,000 admissions); this estimate is consistent with data from the USA (8 per 10,000 admissions) [15]. In the USA, pneumonia accounts for approximately 15% of all hospital associated infections with an attributable mortality between 20 to 33% [15]. The associated direct and indirect costs have been estimated to be greater than US\$450 million [16].

The quality of the data from the VAED has been validated by comparing the findings to extensive audit data of approximately 14,000 patients over a two-year period [17]. Therefore, data from the VAED provide excellent information regarding hospitalisation and mortality rates related to community- and hospital-acquired pneumonia in Australia. In contrast, an estimate of the total socio-economic burden of these diseases remains difficult. A systematic analysis of the problem based on Australian data is required as international comparisons may be dramatically confounded by differences in health care delivery models.

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## 2. CHRONIC AIRWAYS DISEASE AND RESPIRATORY INFECTION

Asthma and chronic obstructive airways disease are major causes of both acute and chronic respiratory morbidity, and impact greatly on the total burden of ill health in Australia [1, 2]. Respiratory infection is a leading cause of acute exacerbations in these diseases. Furthermore, respiratory infection remains under-recognised as a contributor to the progression of these diseases.

### 2.1 Asthma

Respiratory infection is a common cause for deterioration in asthma, which can lead to GP consultations or hospital admissions. In 2000-2001, the total health expenditure on asthma in Australia was A\$693 million, with 41% of this cost due to GP consultations and hospital admissions [1].

An exacerbation of asthma, secondary to a respiratory viral infection, affects between 50 to 80% of patients with asthma who present to hospital [3]. In Victoria, at least 37% of all asthma admissions were estimated to have been associated with a viral respiratory tract infection [4].

As most infective exacerbations of asthma are caused by a virus, antibiotics are rarely indicated and should only be used for specific infections [1].

As well as being a major cause of asthma exacerbations, viral infections have also been implicated in the initiation and progression of asthma. The respiratory virus-asthma interaction is multifaceted - further investment in research that focuses on this interaction is likely to result in considerable health benefits [5, 6].

### 2.2 Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a major, chronic disease that is very common in Australia. For Australians aged 45 years and over, the prevalence rate of COPD is as high as one person in six [7]. Due to increased smoking and worsening air pollution, the illness burden associated with COPD is increasing internationally at alarming rates [2].

In 2000 / 2001, 50,779 patients with COPD were admitted to hospital in Australia; viral or bacterial exacerbations caused the majority of these admissions [8]. Patients with COPD accounted for 16% of all respiratory diagnoses and the average length of stay in hospital was 7.2 days or 366,516 beds days [8]. During the same period of time, COPD was associated with 635,782 consultations to GPs [8].

**In 2000 - 2001 Australian health expenditure on asthma was \$693 million.**

**At least 37% of asthma admissions are associated with a viral respiratory tract infection.**

Acute and chronic respiratory infections are major complicating factors in COPD.

Both acute and chronic respiratory infections are major complicating factors in COPD, and therefore are major cost drivers in the healthcare system [2]. As bacterial infection may have either a primary or secondary role in 50% of exacerbations of COPD [9], antibiotics are frequently indicated in the management of acute infective exacerbations [10]. Recent studies examining the community management of COPD have also identified that preventative strategies such as influenza and pneumococcal vaccination are under-utilised in this 'high risk' group of patients [11].

In addition to being a major cause of COPD, cigarette smoking has been shown to independently increase the risk of a wide range of respiratory infections and their severity including invasive pneumococcal pneumonia [12 - 15].

### 2.3 Bronchiectasis: Cystic Fibrosis and Non-Cystic Fibrosis Related

Bronchiectasis is a disorder of the major bronchi and bronchioles that is characterised by permanent abnormal dilatation and destruction of bronchial walls. Bronchiectasis is usually due to a combination of impaired airway defences (e.g. immunodeficiency, mucociliary clearance abnormalities or local obstruction) and an infectious insult. Although the prevalence and impact of bronchiectasis associated with specific disorders such as cystic fibrosis can be determined relatively easily, the overall prevalence and health burden of bronchiectasis in Australia is unknown.

Cystic fibrosis (CF) is the most common, life-limiting, genetic disorder in western societies. There are approximately 3,000 patients with CF in Australia [16, 17]. The estimated annual cost to the Australian community is more than A\$22,000 per patient, resulting in a cost of approximately \$70 million to the national health budget. As the life expectancy of patients with CF increases, the number of adults with the disease will soon exceed the number of paediatric and adolescent patients with CF [16]. In the USA, more than 300 of the nearly 25,000 patients with CF die each year [18]. After adjusting for population differences, the mortality rate in Australia is similar [17]. In Australia at least 75% of CF deaths are due to respiratory failure caused by bronchiectasis [17]. Therefore, lung transplantation is a life saving procedure for many patients with CF. Indeed, patients with CF account for 30 to 40% of the patients who have this expensive procedure worldwide [19]. In Australia, this translates to 40 to 50 lung transplants each year, with the short-term (i.e. first 12 months) costs for each transplant exceeding A\$100,000 per transplant (A / Prof. T. Williams, Alfred Hospital, Melbourne; personal communication).

The prevalence and health burden of bronchiectasis in Australia is unknown.

Other chronic respiratory diseases that are complicated by infection include muco-purulent bronchitis and non-cystic fibrosis bronchiectasis. Both of these diseases are relatively under-recognised and are associated with significant morbidity due to chronic airflow limitation [20, 21].

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### 3. 'AT RISK' POPULATIONS AND RESPIRATORY INFECTION

All Australians are potentially at risk from respiratory infection. However, specific groups of individuals are recognised as being particularly at risk due to their increased susceptibility to infection, their reduced physiological reserve to cope with infection if it occurs, and their poor access to health care services.

#### 3.1 Indigenous Australians

Indigenous Australians are disproportionately affected by respiratory tract infections. Compared to the non-indigenous population, indigenous Australians have a 4-fold greater hospitalisation rate from pneumonia and a 9 to 11-fold greater mortality rate from respiratory infections [1, 2]. Based on GP consultation rates, the top two conditions affecting indigenous Australians are acute URTIs and acute bronchitis [1, 3]. In addition, chronic infections of the ear, airway and lung are very common in indigenous children [1, 4]. Clinical bronchiectasis is present in 1 to 2% of indigenous children in central Australia [4]. Infection with *Streptococcus pneumoniae* is a major cause of bacterial pneumonia and meningitis in indigenous children [5, 6].

Factors contributing to the higher rates of these diseases in indigenous population include poor nutrition and housing, lower socio-economic status and poor access to health care. These same factors are also largely responsible for the much higher rate of tuberculosis in indigenous communities (Figure 1). The annual incidence of tuberculosis for indigenous Australians (8.5 cases per 100,000 people) is considerably higher than the incidence for the Australian-born, non-indigenous population (1.1 cases per 100,000 people) [7 - 9].

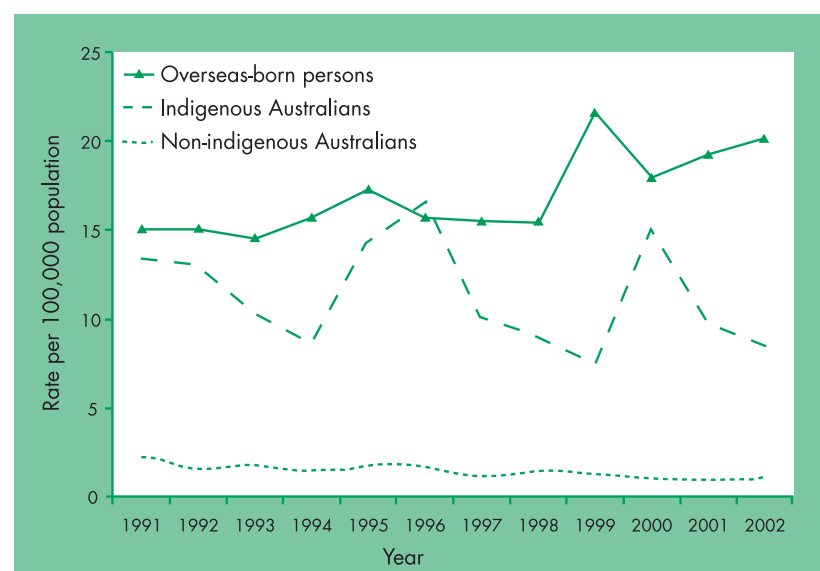


Figure 1: Tuberculosis notifications in Australia in 2002 [9]

Indigenous Australians are disproportionately affected by respiratory tract infections.

#### 3.2 Refugees and Migrants

Refugees and other migrant groups are at least ten times more likely to develop tuberculosis than the Australian-born population (Figure 1). The annual incidence of tuberculosis for refugees and other migrant groups (20.2 cases per 100,000 people) is considerably higher than the incidence for the Australian-born population (1.1 cases per 100,000 people) [7 - 9]. Most cases represent reactivation of tuberculosis infection acquired in the country of origin, rather than new disease acquired in Australia [10]. The increased risk for refugees relates to the high prevalence of tuberculosis in the country of origin, coupled with the risk of poor nutrition. Multiple drug resistant tuberculosis is common within countries bordering Australia, and represents a considerable public health risk to Australia for the future.

#### 3.3 The Ageing Population

As people age, their normal resistance to lung infection is reduced. Elderly people, particularly those over the age of 65, are also more likely to suffer from other medical conditions such as diabetes or COPD [11], which further reduce that individual's ability to fight respiratory infection. For this reason, pneumonia and other serious lung infections are more common in the elderly, and cause more deaths [12].

#### 3.4 People with Compromised Immune Systems

People with compromised immune systems include those who (a) have general or specific abnormalities that impair their host defence systems or (b) are being treated with medications that affect the immune system, either intentionally or as a side effect. Anecdotally, the number of people with compromised immune systems is increasing. Many factors are contributing to this increase, including our ageing population, the increased prevalence of chronic disease and relatively good access to health care options, such as new immunosuppressive drugs and organ transplantation. Although each of these factors is associated with a general increase in the susceptibility of the body to infection, the lungs are more frequently affected than other sites [13, 14]. In addition, these 'at risk' patient groups may be infected with unusual organisms not seen in people with normal immune systems, and may develop more severe illness [13, 14].

At one end of the 'immunocompromised host' spectrum, patients who are unwell enough to require hospital care for any reason may develop pneumonia as a complication of their hospital admission. This translates to a large number of patients and a huge economic burden (refer page 17: Pneumonia Burden in Australians). Organisms causing pneumonia in hospitalised patients are frequently resistant to the types of antibiotics used for community-acquired pneumonia, require more expensive antibiotics, and are associated with a much higher mortality rate.

Refugees and migrants are ten times more likely to develop tuberculosis.

The number of people with compromised immune systems is increasing.

At the other end of the spectrum, patients may be immunocompromised due to chronic illness (e.g. cardiac, lung or renal disease etc), specific diseases such as human immunodeficiency virus infection / acquired immunodeficiency syndrome (HIV / AIDS) or specific immunosuppressive medication being taken for a wide variety of diseases, including organ transplantation and auto-immune disease. Patients living with HIV infection are particularly vulnerable to respiratory infection from organisms that do not normally cause lung disease in the general population. In third world countries, the combination of tuberculosis and HIV is a common cause of mortality [15]. Although increasingly potent immunosuppressive agents may be more effective in controlling certain immunological diseases, they can be a double-edged sword. These potent immunosuppressive agents can simultaneously increase the patient's risk for infection. For example, a recent new class of drugs, which block tumour necrosis factor, has been developed for patients with severe rheumatoid arthritis. However, these drugs also significantly increase the risk of reactivation of tuberculosis, even in patients who had previously been thought to be at low risk [16].

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## 4. SPECIFIC RESPIRATORY INFECTIONS AND PUBLIC HEALTH

### 4.1 Influenza

Each year, interpandemic or annual influenza viruses can cause epidemic respiratory illness. The sporadic epidemics and periodic worldwide pandemics of influenza are characteristic of this disease; epidemics occur each year during winter and pandemics occur approximately every 20 to 30 years [1, 2]. Although pandemic outbreaks of influenza are responsible for episodes of devastating global morbidity and mortality (e.g. the 1918 - 1919 Spanish flu pandemic), the cumulative impact of interpandemic influenza over the centuries is likely to be significantly greater [1].

During a 'normal' winter influenza epidemic, approximately 5% to 20% of the population can become ill [1, 3]. However, during severe influenza A epidemics, illness can affect approximately 30% to 50% of the population. The highest rates of infection and clinical illness occur in children, but serious complications and death occur mainly in the elderly and in patients with chronic diseases. Outbreaks in closed communities (e.g. nursing homes, schools, prisons, health care facilities) are also important causes of morbidity and mortality [4, 5]. Each year in Australia, influenza causes approximately 1,000 deaths in adults and children and this represents only the tip of the iceberg in terms of influenza-related morbidity, hospitalisations and economic cost [2, 3, 6].

Particular features of influenza epidemiology and transmission are:

- Repeated infections throughout a patient's lifetime.
- Rapid spread with short-lived epidemics.
- Concurrent outbreaks in remote areas.
- Frequent high morbidity.
- Regular epidemics and occasional pandemics.
- Epidemic influenza:
  - Seasonal in temperate zones.
  - Year round in tropics.
- Pandemic influenza:
  - Less seasonal in temperate zones.
  - Frequently originates in China.

**Each year in Australia, influenza causes approximately 1,000 deaths in adults and children.**

**Measuring the full impact of interpandemic influenza is difficult, primarily due to diagnostic limitations.**

Influenza causes an acute febrile illness that is usually associated with prominent systemic symptoms (e.g. sore muscles), respiratory symptoms (e.g. cough) and occasional complications (e.g. pneumonia, encephalitis, unusual neurological syndromes such as Guillain-Barré syndrome). Influenza virus subtypes A and B cause nearly all serious disease in Australia, with influenza A subtype H3 causing the most recent influenza epidemics. The incubation period is two to four days, although cough and malaise frequently persist for one to two weeks [1, 4].

Measuring the full impact of interpandemic influenza in Australia is difficult, primarily due to diagnostic limitations. However, estimates of the impact can be made using influenza surveillance and notification data, 'excess mortality' data during the winter months and societal-economic impact modelling. These sources of information can also be used to help forecast the potential impact of pandemic influenza (see Future Threats, Section 5).

Australia has a national vaccination program for influenza, targeting people aged greater than 65 years and people with medical risk factors. The latest national surveys indicate that nearly 80% of the population aged greater than 65 years receives an annual flu vaccination. However, these surveys also indicate that less than 50% of the population with medical risk factors receives an annual flu vaccination [3, 7]. Furthermore, less than 50% of health care workers have an annual influenza vaccination – this is of great concern as health care workers can potentially transmit infection to many others who have a high risk of complications.

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## 4.2 Mycobacterial Infection

### *M. tuberculosis*

Each year in Australia, approximately 1000 patients are newly diagnosed with tuberculosis [1]. There has been no significant decline in the number of new cases per year since the mid-1980s. The number of annual reported cases has ranged from 863 in 1986 to 1,117 in 1999 [1-6] with the number in 2004 being 1076 [1]. Of the 1076 cases of tuberculosis reported in 2004, 82.3% occurred in overseas-born people; the proportion of cases due to overseas-born people has been gradually increasing over the years. On a global scale, the annual incidence of tuberculosis has been estimated as eight million, with an annual mortality rate of two million [7]. Relevant to Australia, the majority (2.7 million) of the tuberculosis cases notified to the WHO (3.8 million) from 1989 to 1991 came from two neighbouring regions, Southeast Asia and the Western Pacific [7]. Australia only contributed 1,000 cases to the 2.7 million regional total. These neighbouring regions are a continuing source of migration to Australia, together with increasing waves of migrants and refugee intakes from Eastern Europe, the former Soviet States, East Timor, Somalia, Ethiopia and, most recently, from the Sudan. As a consequence of these migration patterns, adequate management of tuberculosis in recently arrived migrants has considerable implications for Australia.

Even within Australian-born people, there is a disparity in the incidence of tuberculosis between non-indigenous, Australian-born people (with rates varying between 0.9 and 1.2 per 100,000 population in the five years 2000-2004) and the indigenous population (with rates varying between 8.1 and 15.3 per 100,000 population in the five years 2000-2004) [1 – 5]. The increased rates of tuberculosis in the indigenous population are related to increased transmission (i.e. due to case clusters within communities) and to the increased risk of progression from latent infection to active disease (i.e. due to chronic diseases and lower general health status).

The estimated costs for nursing (including travel) and pharmaceutical treatment for each patient with tuberculosis susceptible to first line anti-tuberculosis drugs varies between A\$460 and \$1,000. The costs vary depending on whether or not treatment is being fully supervised by nursing staff or whether nursing staff merely visit on a regular basis (A Konstantinos, Queensland Tuberculosis Control Centre; personal communication). Additional costs are incurred for diagnosis, hospital admission (requiring respiratory isolation during the infectious phase), medical consultations and follow-up pathology testing. Unfortunately, clinical practice varies from setting to setting, and a direct estimate cannot be made of these costs. However, these additional costs are likely to be considerable, given that treatment duration can vary from 6 months in uncomplicated cases to more than 18 months in drug-resistant cases [8].

**Each year in Australia, 1000 patients are newly diagnosed with tuberculosis.**

**Tuberculosis affects more indigenous people than non-indigenous, Australian-born people.**

**Treatment of patients with infectious tuberculosis is the primary strategy for prevention of tuberculosis.**

**Screening in high risk situations minimises transmission.**

Treatment of patients with infectious tuberculosis remains the primary prevention strategy for tuberculosis, as infectious patients transmit the disease to others. Therefore, ensuring patients adhere to the prescribed treatment regimen until cure is an important public health activity. Treatment costs can escalate considerably if there is a need to use a non-standard tuberculosis drug regimen (i.e. due to intolerable side effects or because of resistance to standard anti-tuberculosis antibiotics). Multi-drug resistant-tuberculosis has been estimated to increase the cost of diagnosis and treatment 20 to 100 times [7]. In 2003, approximately 10% of all tuberculosis isolates in Australia were resistant to isoniazid, rifampicin or ethambutol. Between 1993 and 2003, only 0.9% (range 0.3 to 2.0%) of isolates were multi-drug resistant (i.e. resistant to at least isoniazid and rifampicin) [9].

In addition to diagnosis and treatment costs there are patient-related costs related to travel expenses and loss of work, even in uncomplicated cases. Screening for tuberculosis in high risk situations, with the aim of diagnosing disease early to minimise transmission, also results in major social costs. The most obvious screening activity is contact screening, which is conducted for notified case of tuberculosis. In Queensland, there are approximately nine contacts screened for each patient with tuberculosis (A Konstantinos, Queensland Tuberculosis Control Centre). However, the number of individual contact screens can vary greatly. During the last 10 years in Queensland, the largest contact screen required 2,500 contacts of a health care worker, who had infectious tuberculosis of long duration [Queensland Tuberculosis Control Centre]. These contact screening data are representative of costs in other Australian states. Recently, 15,000 subjects in the Netherlands underwent contact screening related to a multi-drug resistant tuberculosis outbreak in which transmission was linked to a large supermarket [10].

Australia also carries out targeted active screening of special populations. These populations include migrant screening (carried out by the Department of Immigration and Multicultural Affairs), screening of health care workers (as part of infection control policies), and screening of various high risk communities according to State and Territory-based surveillance (e.g., indigenous communities, institutional communities, refugee resettlement programmes). Appropriately targeted screening can provide considerable cost savings by reducing diagnostic delays for infectious tuberculosis. Early diagnosis averts the cost of large and costly contact screening. More importantly, such screening detects subjects with latent tuberculosis infection who may be candidates for treatment of latent tuberculosis infection or surveillance (with appropriate educational support).

Each State and Territory government provides resources for tuberculosis control activities and the Commonwealth Government provides resources for meetings of the National Tuberculosis Advisory Committee (comprised of State Directors of Tuberculosis Control Units). Because of the public health implications of poorly controlled tuberculosis, State and Territory Health Department fund

public tuberculosis units within their jurisdictions to ensure patients are managed adequately and adhere to treatment. This model also enables appropriate transfer between jurisdictions and internationally when patients who are being treated need to move. These units are also responsible for:

- Surveillance of tuberculosis.
- Provision of accessible and equitable clinical services (particularly for subjects at high risk of tuberculosis who may not have ready access to routine health care delivery services).
- Maintenance of expertise in the diagnosis and management of tuberculosis.
- Provision of Bacillus of Calmette and Guérin (BCG) vaccination.
- Accrediting and training staff for tuberculin skin testing.

Studies have highlighted the important role of good surveillance in tuberculosis control activities. Failure to ensure appropriate treatment can have major adverse effects on public health [11], including the development of multi-drug resistant tuberculosis [12].

#### Pulmonary diseases caused by non-tuberculous mycobacteria

As pulmonary diseases caused by non-tuberculous mycobacteria (NTM) are not uniformly notifiable in all States and territories, accurate estimates of incidence and prevalence in Australia do not exist. In Queensland, pulmonary NTM disease is more common than tuberculosis [13]. However, there is still much debate about diagnostic criteria for active disease. In general, NTM is also important as a confounder of tuberculosis. In Queensland, more than 50% of newly reported positive sputum smears for acid-fast bacilli (AFB) are eventually culture-positive for NTM (C Gilpin, Chief scientist, Mycobacterium Reference Laboratory, Queensland Health Pathology and Scientific Services; personal communication). The confounding effects of NTM impacts the overall utilisation of resources for tuberculosis and confounds decision making related to the treatment and isolation of patients.

Ongoing evaluation of patients with NTM isolates contributes to considerable diagnostic costs as computed tomography (CT) scans and repeat endoscopic examinations are frequently required [14]. Major costs are involved in treating these patients as treatment often needs to be prolonged (at least 18 months for most patients) and treatment failures and relapses are common, as are reinfections among those with disease due to *Mycobacterium avium*-complex isolates [15]. Additionally, the continuing debate about the role of these organisms in chronic respiratory infections (especially bronchiectasis) as opposed to a 'classic tuberculosis presentation' and the lack of diagnostic clarity in these situations leads to diagnostic delays. Consequently, patients present with advanced disease that

**Good surveillance is important for controlling tuberculosis.**

may be more difficult and costly to treat. Notably, further research is required to clearly determine whether early treatment of such patients does deliver beneficial long-term outcomes. The need for this research is accentuated by the direct and indirect (related to side effects) costs of the drugs used to treat these patients.

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## 5. FUTURE THREATS

There is no doubt that respiratory infectious diseases pose an enormous potential threat to the health of Australians during the next three to four decades. These threats include the:

- Emergence of new viral pathogens – a problem compounded by the relative paucity of antiviral treatment options.
- Increasing rates of antibiotic resistance amongst common bacterial pathogens - a problem compounded by the relatively limited development of new antibiotics.
- Potential disasters that may result from the deliberate use of biological agents – a threat that has increased markedly in recent years due to increased terrorist activities.

### 5.1 New Viral Threats

#### Pandemic influenza

The potential for a new pandemic of influenza, either a mutated form of conventional influenza A or B or avian influenzae, has been recognised for decades [1, 2]. Ideal conditions for a potentially devastating influenza pandemic have been created due to:

- An ageing population.
- Increased high density living.
- The speed with which pathogens can circulate the globe due to the large numbers of people travelling by air.

To combat this threat, substantial resources will continue to be needed for vaccine development, antiviral research and public health initiatives.

Influenza A viruses undergo major antigenic shift at unpredictable intervals and, as a result, may cause worldwide pandemics with high morbidity and mortality. The largest pandemic was in 1918 and is estimated to have caused 30 million deaths [1, 2]. Typically, new shifted strains of influenza virus emerge in southern China and spread via Asia or Australia to the USA and Europe [1 – 8].

Despite uncertainty about the magnitude of the next pandemic, estimates of the health and economic impact remain important. These estimates can aid public health policy decisions and can guide pandemic planning for health and emergency sectors.

**The potential for a new influenza pandemic has been recognised for decades.**

During a pandemic more than 50% of a population may become infected.

### Impact of an influenza pandemic

The impact of the next influenza pandemic is difficult to predict, and is dependent on the following factors:

- How virulent the virus is.
- How rapidly it spreads from population to population.
- The effectiveness of prevention and response efforts.

Historic data show that during a pandemic more than 50% of a population may become infected with the novel virus [1, 2, 9, 10]. The age-specific morbidity and mortality may be quite different from the annual epidemics, with a higher proportion of deaths in persons under 65 years of age [1 – 3, 9]. In the 1918 / 1919 pandemic, young adults had the highest mortality rates, with nearly half of the influenza-related deaths occurring in patients aged between 20 and 40 years [1, 2]. During the 1957 / 1958 and 1968 / 1969 pandemics in the USA, patients aged less than 65 years accounted for 36% and 48% of influenza-related deaths, respectively [1, 2].

In the USA, a model has been used to show the effect of assumptions (based on epidemiological and previous pandemic data) on various population health outcomes (e.g. death, hospitalisation, outpatient treatment, ill but no formal care) for severe influenza A epidemics [10]. The model does not include the potential impact of antiviral drugs or an effective vaccine. Although this model may over- or under-estimate the potential impact in Australia, it can provide some guidance for planning purposes. Using this model, estimates of the magnitude and potential impact of the next influenza pandemic in Australia have been calculated (Figure 2, Table 3). These estimates do not take into account the differences between Australia and the USA in terms of the health care systems, practice patterns and health care seeking behavior. The economic impact (direct and indirect costs) on the Australian health care system is estimated to be between A\$6.0 to 14.5 billion.

**Table 3. Estimated impact of different attack rates of pandemic influenza in Australia**

| Attack Rate | DEATHS         |                | HOSPITALISATION |                | OUTPATIENT VISITS |                |
|-------------|----------------|----------------|-----------------|----------------|-------------------|----------------|
|             | Lower Estimate | Upper Estimate | Lower Estimate  | Upper Estimate | Lower Estimate    | Upper Estimate |
| 10%         | 2,763          | 12,483         | 7,641           | 30,009         | 753,978           | 893,640        |
| 20%         | 5,529          | 24,969         | 15,285          | 60,018         | 1,507,953         | 1,787,280      |
| 30%         | 8,355          | 37,452         | 22,926          | 90,027         | 2,261,931         | 2,680,920      |
| 40%         | 11,061         | 49,938         | 30,570          | 120,036        | 3,015,909         | 3,574,560      |
| 50%         | 13,821         | 62,424         | 38,211          | 150,045        | 3,769,887         | 4,468,200      |

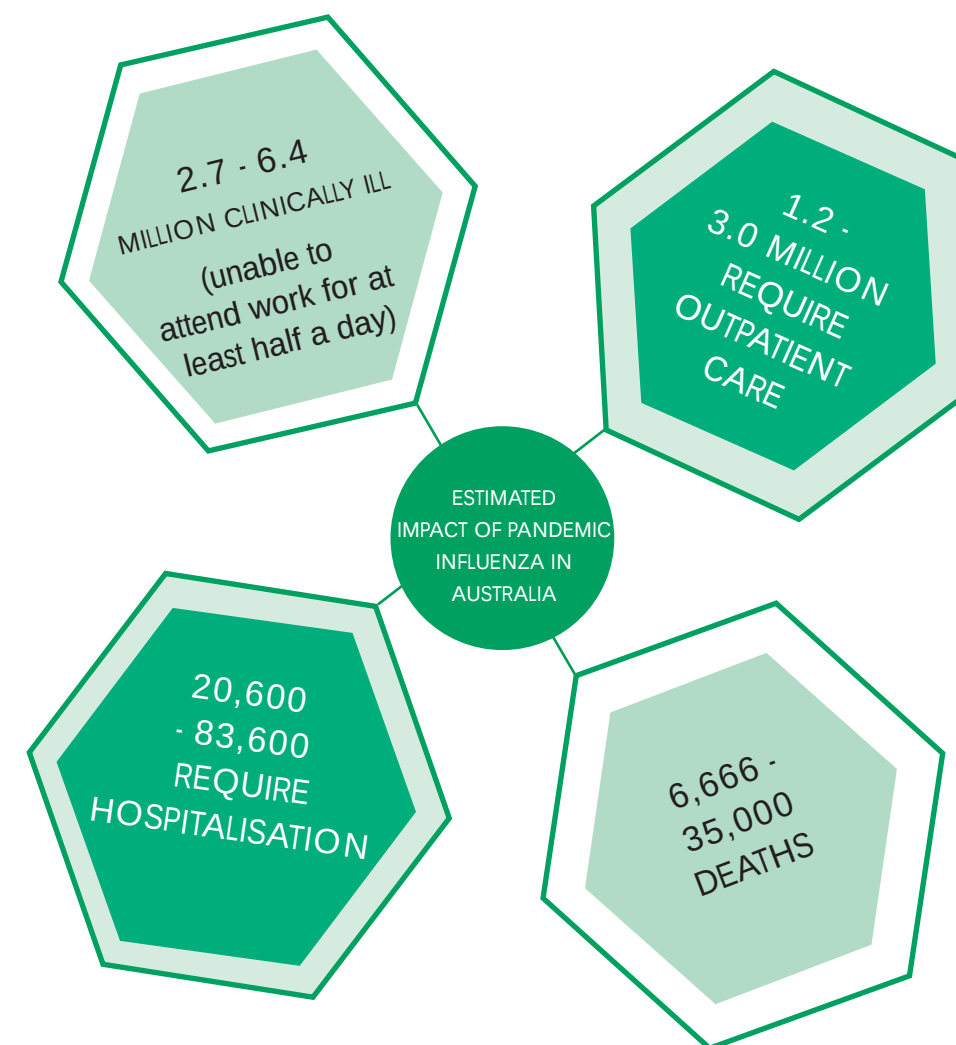


**Figure 2: Estimated impact of pandemic influenza in Australia**

### Improve influenza surveillance network

To enable the public health system to respond to a pandemic threat there must be adequate surveillance of influenza before, as well as during, the pandemic. The principal role of surveillance is to provide virological and epidemiological data to guide national decisions on:

- The choice and deployment of diagnostic tests.
- Provision of candidate vaccine strains.
- Availability, deployment and use of antiviral agents.
- Appropriate clinical and public health responses (including organization of health care services).

**Australia plays a pivotal role in monitoring new influenza virus strains in the Asia Pacific.**

This continuing surveillance requires centralised resources to maintain diagnostic expertise as well as national reference capacity in laboratories and epidemiological surveillance. Additional resources must be available for rapid deployment in the event of a potential pandemic.

Australia plays a pivotal role in monitoring the emergence of new influenza virus strains in the Asia Pacific region [3 – 8]. Specifically, Australia:

- Is geographically part of the Australasian region, engaging in active trade, education and tourism exchange with Asian countries.
- Is the fifth continent, containing within the country tropical, subtropical and temperate regions, thus enabling the monitoring of samples from a variety of climatic conditions.
- Allows continuity in influenza surveillance during off-peak seasons in the Northern hemisphere due to its geographic location.
- Has a population with a wide variety of different ethnic backgrounds who frequently travel overseas.
- Has a well-developed public health infrastructure, providing reliable epidemiological data.
- Has the laboratory capacity to perform influenza virus isolation and typing in various centers.
- Has three active World Health Organisation (WHO) National Influenza Centres located in Melbourne, Perth and Sydney and a WHO Collaborating Centre.

The active participation of Australia in the global influenza surveillance network is of paramount importance. Similarly, the critical importance of new diagnostic strategies for respiratory viral infections and intervention strategies utilizing up-to-date vaccines and antiviral treatments necessitates that Australia remains at the forefront of developments in these areas as well [9 – 14].

#### Milestones for efficient pandemic planning and surveillance

##### 1. Improve avian surveillance

- Define the avian influenza gene pool.
- Integrate with human influenza surveillance (predominantly an international initiative).

##### 2. Establish influenza surveillance as a national priority

- Expand surveillance into new and poorly covered geographical areas.
- Improve pandemic preparedness.

##### 3. Coordinate existing laboratories

- Standardise laboratory methods, reagents, competency testing and laboratory manuals.
- Expand networks and regular forums of information exchange.

##### 4. Improve capture of surveillance data

- Agree on inclusion criteria and case definitions.
- Expand the data management system.
- Prepare inventories of available data sources.
- Improve epidemiological analysis of data and staff training.

##### 5. Annual studies on current vaccines and outbreaks

- Ascertain whether current vaccines induce satisfactory antibody levels to new epidemic strains.
- Undertake studies on outbreak strains, epidemiology, and vaccine efficacy.

##### 6. Expand the objectives and scope of influenza surveillance

- Expand drug resistance surveillance.
- Facilitate study of the evolution of variant strains (established protocols at the WHO Collaborating Centre in Melbourne).

**SARS is not  
an isolated  
or uncommon  
phenomenon.**

### National pandemic influenza plan

Australia has already made a considerable investment in developing National and State Pandemic Influenza plans which focus on containment in the early phases and maintenance of essential services in the later stages [15, 16]. These plans however will require ongoing review and modification as new knowledge and management options become available.

### New emerging viruses

The recent outbreak of the SARS virus and its impact on the population and health care resources (particularly in China, Hong Kong, Toronto and Singapore) is an example of the potential effect of viruses that transition from animal to human hosts. SARS is not an isolated or uncommon phenomenon – there is strong evidence of several viruses having made the same transition in recent times [17]. Resources will continue to be needed to monitor the arrival of new viral threats, to enable effective liaison with international health partners and for coordinating the Australian response.

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## 5.2 Increasing Antibiotic Resistance

Increasing antibiotic resistance is a natural consequence of the use of antibiotics to treat bacterial infections. However, the rate of resistance development is dramatically increased when antibiotics are used inappropriately. Hence there is a strong need for ongoing health professional and community education regarding appropriate antibiotic use particularly as it applies to empirical treatment settings [1, 2]. The clinical impact of any resistance development is markedly increased if it involves common pathogenic bacteria for which there are limited antibiotic alternatives. The problem of increasing antibiotic resistance is further compounded by the recent world wide trend of decreasing investment in the development of new antibiotics [3 – 5].

### *Streptococcus pneumoniae*

As yet penicillin resistance in pneumococci has not reached the same levels in Australia as that seen in the USA and Europe [5]. There is increasing evidence that penicillin resistance is adversely affecting patient outcomes, including mortality [6].

### *Staphylococcus aureus*

Multi-antibiotic resistant *Staphylococcus aureus* (MRSA) is already a problem in many hospitals in Australia, where it causes wound infections, bacteraemia and pneumonia. Increasing reports from Australia, USA, and Europe of community-acquired lung infections with MRSA are a major cause for concern [7, 8].

### *Multi-antibiotic resistant gram-negative pathogens*

Due to increasing antibiotic resistance, it has become more difficult to treat hospital-acquired pneumonias (i.e. caused by *Pseudomonas aeruginosa*, *Acinetobacter* species and other gram-negative pathogens). Intensive care units in the USA and Europe have encountered antibiotic strains that are resistant to all known antibiotics [9,10].

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**Respiratory pathogens  
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used in a terrorist attack**

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### 5.3 Bioterrorism

Respiratory pathogens account for more than 50% of the pathogens classed as 'most likely to be used in a terrorist attack' (Class A) by the USA Center for Disease Control and Prevention (CDC) [1]. These pathogens include the plague, anthrax, smallpox and tularaemia. Although conventional terrorist attacks with explosive devices are likely to remain far more likely for many reasons, the potential disruption (and cost) to society of a biological weapons attack is vastly greater. The potential impact of a biological weapons attack was highlighted by the simulated smallpox attack in the US 'Dark Winter' exercise in 2001.

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## 6. WHERE TO FROM HERE? STRATEGIES TO REDUCE THE BURDEN OF RESPIRATORY INFECTIOUS DISEASE IN AUSTRALIA

The case has been made that respiratory infectious diseases, as a group, are a major burden on the health of Australians over their whole lifetime. Although many respiratory infection syndromes and respiratory pathogens have been discussed, the overwhelming theme is that of inefficiencies in treatment, compounded by problems of inadequate diagnostic tools and lack of knowledge. This Case Statement provides a unifying platform from which to strategically plan for the future – for respiratory infectious diseases in general and for specific case scenarios.

### Acute respiratory infection

The current management of acute respiratory infections is heavily reliant on a strategy of empirical antibiotic use to cover likely bacterial pathogens. This approach, which is driven by the current diagnostic limitations for respiratory infection syndromes, requires balanced decision-making. The need to use antibiotics to benefit the individual (i.e. to avoid under treatment of bacterial infection) must be balanced against the need to limit antibiotic use to benefit the community (i.e. to avoid overuse of antibiotics and the risk of antibiotic resistance). This need for balance is recognised in the ever-increasing efforts to formulate syndrome-specific antibiotic guidelines for respiratory infections. The key goal of antibiotic guidelines for respiratory infection syndromes is to optimise appropriate antibiotic use in the community. The aim is to avoid using antibiotics in settings where major bacterial infection is unlikely (e.g. viral URTIs), but to use antibiotics effectively to treat specific bacterial infections (e.g. in severe pneumonia or exacerbations of COPD). In the short-term, the acceptance of these guidelines must be consolidated, and the effectiveness of such guidelines must be evaluated. In the long-term, however, there is a need to move away from an almost absolute requirement for empirical antibiotics and move toward targeted antibiotic strategies.

A major pre-requisite for targeted antibiotic treatment strategies is the development of markedly improved diagnostic tools for respiratory infection. These diagnostic tools would need to be quick, reliable and, preferably, available at the point of care. Improvements in the sensitivity and specificity of diagnostic assays for specific respiratory pathogens are also required. Improved sensitivity would enhance the ability to make the correct decision to not use antibiotics to treat specific infections. Improved specificity would enhance the ability to make the correct decision to use specific antibiotics in the first instance and to use them to their maximum potential according to pharmacodynamic principles. Although the recent developments of enzyme-linked immunosorbent assays for some bacterial

**Respiratory infectious  
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Australians.**

**Antibiotic use must  
benefit the individual  
and the community.**

**Targeted antibiotic  
strategies are needed.**



### Improved diagnostic tests enable optimally tailored treatment.

antigens (e.g. *Legionella*, *Streptococcus pneumoniae* and multiplex polymerase chain reaction assays for viral and atypical bacterial organisms are promising, this area requires considerably more research.

Realistically, the logistical issues associated with obtaining a test sample and an immediate test result will mean that empirical antibiotics will continue to be used, at least initially, in several scenarios. If empirical antibiotics are used, then the benefits from improved diagnostic tests are clear. There would be an immediate benefit, as patients could receive optimally tailored treatment. There would also be a longer-term benefit as epidemiological data on local respiratory infections could enhance decision-making regarding empirical antibiotic use. For example, 'state of the art' diagnostic testing is being used in the recently concluded Australia-wide, community-acquired pneumonia study (ACAPS); this study will identify the aetiology of community-acquired pneumonia, on a large scale, in Australia for the first time (P Charles, L Grayson *et al.*, February 2007, unpublished). As data collection becomes more organised and routine, ongoing surveillance for local epidemiology alerts and early dissemination of information to clinicians will be enhanced. Dissemination of clinically-relevant information is currently being performed only by (a) State-designated infectious disease reference laboratories, which focus on specific infections that have major public health implications, such as influenza (sentinel network surveillance program) or (b) microbiology laboratory special interest groups (AGAR- Australian Group on Antimicrobial Resistance). Another potential spin off from enhanced data collection would be a better understanding of the problems associated with specific virus or bacterial infections. This information may influence the development of the antimicrobial pipeline of pharmaceutical companies.

#### 'At risk' populations

All of the issues related to acute respiratory infections in otherwise healthy individuals apply to an even greater degree to 'at risk' populations. These people are 'at risk' because of underlying lung disease (e.g. asthma, COPD) or immune impairment (e.g. elderly, malnourished, chronic renal impairment, immunodeficiency-innate, acquired, iatrogenic). Compared to the rest of the population, the 'at risk' population is susceptible to a wider spectrum of infections and more severe disease from any given infecting organism. Improvements in the sensitivity and specificity of diagnostic assays for respiratory infection would offer dramatic benefits to the everyday clinical management of 'at risk' patients.

In addition to diagnostic improvements, the treatment of 'at risk' patients could be enhanced by obtaining disease susceptibility information in well-defined 'at risk' populations. This information could aid decision making in terms of whether to use prophylactic or pre-emptive antibiotics to avoid specific acute infection syndromes in certain 'at risk' patient groups. This information could also provide insights into host-pathogen interactions in conditions such as pneumonia (community- and hospital-acquired, immunocompromised hosts) as well as asthma and COPD (where acute exacerbations and chronic progression are a major burden of

**Disease susceptibility information obtained from 'at risk' groups will improve treatment.**



respiratory disease). The obvious extension of this research would be to gain a greater understanding of the heterogeneity in host-pathogen interactions. This type of research might explain why patients vary in their susceptibility to respiratory infectious disease and why the clinical expression of disease differs between patients. Ultimately, this research could enable better management of all respiratory infectious diseases.

#### Public health

Australia has a national vaccination program for influenza and pneumococcal disease; the program targets people aged greater than 65 years and those with medical risk factors. The latest national surveys indicate that nearly 80% of the population aged greater than 65 years receives an annual flu vaccination. However, these surveys also indicate that less than 50% of the population with medical risk factors receives an annual flu vaccination. Clearly, further efforts are required to increase influenza and pneumococcal coverage in people with medical risk factors, particularly as they have a high risk of suffering from serious disease.

The influenza vaccination strategy also targets health care workers. Health care workers have the potential to transmit influenza to many others who could have a high risk of complications. However, it is estimated that only 40% of this group receive yearly vaccinations. Although an improvement in the vaccination rate of health care workers is required, there are barriers that need to be overcome. This population, in particular, raises the issue of ethical decision-making and how to balance autonomy against public responsibility. The clinical, ethical and societal impact of inter-pandemic influenza will be dramatically increased in the event of a future pandemic influenza outbreak.

Australia has made a considerable investment in a National Pandemic Influenza plan, which focuses on containment in the early phases and maintenance of essential services in the later stages. The plan also focuses on the race to develop and distribute a protective vaccine. The success of this plan is likely to depend on the degree to which it is understood and embraced by all health care providers and the community. Therefore, it is critical that sufficient research and resources are specifically targeted toward the implementation of the National Pandemic Influenza plan.

A major component of the National Pandemic Influenza plan is the focus on an appropriately staged plan of action, which is underpinned by thorough epidemiological surveillance on a local, regional (Asia Pacific) and global basis. The more that Australia invests in epidemiological surveillance in the Asia Pacific region, the more forewarned Australia would be of any emergent viral threat, particularly as any new influenza pandemic (e.g. the potential for an avian influenza pandemic) is likely to originate in the Asia Pacific region.

Notifiable bacterial respiratory infections include not only tuberculosis, but also infections from organisms such as *Legionella* and *B. pertussis*. Again, however,

**Greater influenza and pneumococcal vaccine coverage is needed.**

**Implementation of a National Pandemic Influenza plan.**

**Notification strategies are only a first step.**



**There is a strong case for ongoing commitment to health care initiatives.**

adequate notification strategies are only the first step in reducing the impact of these diseases on the Australian community. Additional steps include: a national tuberculosis management program (incorporating diagnosis, treatment and contact screening); maintenance of cooling towers (well known sources of Legionella outbreaks); and adequate *B. pertussis* vaccination programs. Each of these initiatives would require ongoing health professional education as well as ongoing program support, development and quality review. Additional steps would also be required for tuberculosis control in Australia. These steps include improved migrant screening strategies and improved regional control (the majority of patients with tuberculosis in Australia are overseas-born).

Indeed, Australia's island nation status, its proximity to the Asia Pacific region, and the explosive public health implications of specific respiratory infection problems, which are endemic in this region, make a strong case for an ongoing commitment to health care initiatives. Ultimately, investing in surveillance, preventative strategies and adequate treatment and adopting a long-term perspective will greatly help our regional neighbours and our nation.

#### RID as a major health priority for Australia

The identification of RID as a major health priority for Australia will simultaneously raise the awareness of the unmet clinical need posed by respiratory infection across many areas of medicine and offer a clear path forward to efficiently focus and co-ordinate ongoing health professional education, future clinical science research and health policy initiatives directed at reducing the current and future burden of respiratory infectious disease on the Australian population (Figure 3).

Investing in reducing the burden of Respiratory Infectious Disease today will pay off many times in the future for all Australians – whether they become ill or not.

### *WE MUST DO BETTER, AND WE CAN!*

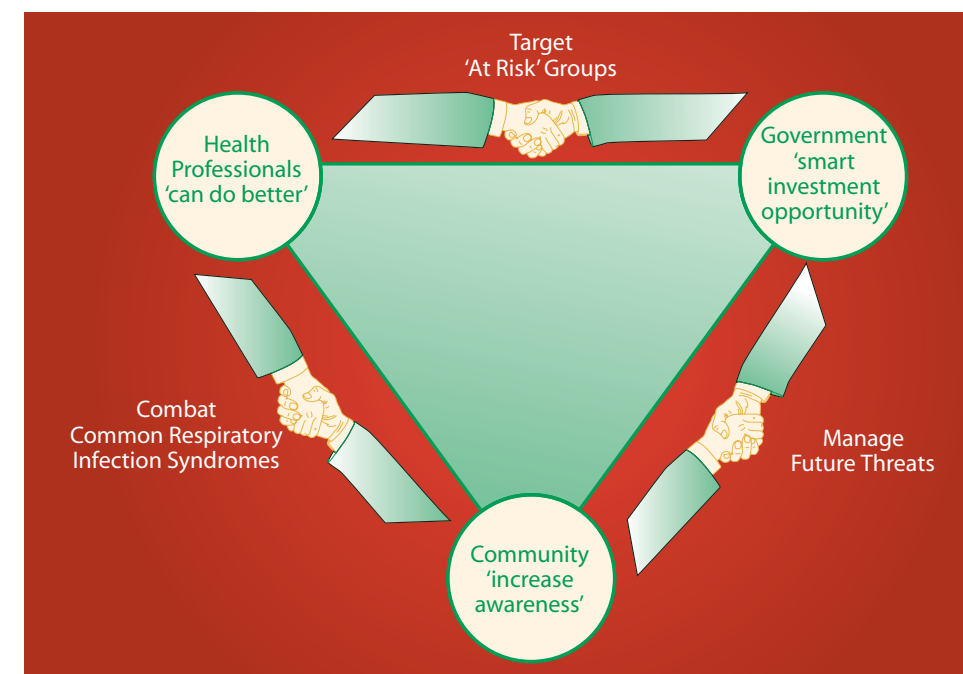


Figure 3: 'Call to arms summary recommendations'

## THE AUSTRALIAN LUNG FOUNDATION

The Australian Lung Foundation's mission is to reduce the burden of respiratory infectious diseases and promote awareness through research, education, advocacy and patient support.

The Australian Lung Foundation was established in 1990. Its national office is in Brisbane and it has a committee in every state. It is linked to The Thoracic Society of Australia and New Zealand, which is the peak professional body for medical and scientific knowledge on respiratory disease.

A cross-disciplinary Respiratory Infectious Diseases Consultative Group was established in 1998 and assists The Australian Lung Foundation to improve prevention, management and community awareness of respiratory infectious disease.

How can The Australian Lung Foundation help people with respiratory infectious diseases? By calling The Australian Lung Foundation's toll free number (1800 654 301), patients and their carers will be offered:

### 1) Respiratory information

- LungNet News – a free magazine for patients and carers published quarterly
- To subscribe to LungNet News on line, email: [enquiries@lungnet.com.au](mailto:enquiries@lungnet.com.au)
- Educational leaflets on a range of issues related to respiratory health. Relevant titles include:
  - Better Living with COPD
  - Bronchiectasis
  - COPD: Chronic Bronchitis and Emphysema
  - The Common Cold
  - Corticosteroid Therapy in Respiratory Disorders
  - Influenza
  - Tuberculosis

### 2) Support groups

The Australian Lung Foundation co-ordinates LungNet, a national network of lung support groups. There are currently over 100 groups throughout metropolitan, regional and rural Australia supporting people with lung and respiratory disease. To find out about a support group in your area, call 1800 654 301.

Relevant titles include:

- Quality of Life Through Patient Support
- How to Start a LungNet Patient Support Group

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