



Influenza

A guide for general practitioners

Vaccination against influenza safely and effectively reduces the risk of infection, and treatments are now available to alleviate the duration and severity of symptoms if infection occurs. Yet while Australia has made excellent progress in targeting those aged 65 and older, the majority of younger at-risk individuals remain unprotected. This publication, from the Influenza Specialist Group, reviews current issues in the prevention and treatment of influenza – at a time when awareness of viral respiratory infections has been heightened by the occurrence of SARS and the recent spread of avian influenza, originating in South-East Asia and highlighting the threat of a potential worldwide pandemic.

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PLANNING VACCINES FOR THE INFLUENZA SEASON

The formulation of influenza vaccines for Australians is based on information from an international surveillance and monitoring program coordinated by the World Health Organization. Four Collaborating Centres for Influenza, in Atlanta, London, Melbourne and Tokyo, integrate information from 110 centres in 80 different countries. Mr Alan Hampson, Convener of the ISG, said the network meets twice yearly to make recommendations for vaccines for the following Northern and Southern hemisphere seasons.

“Influenza is a ‘moving target’ for vaccines,” Mr Hampson said. “Continuing antigenic drift, which is an evolutionary response by this easily-mutated RNA virus to host immunity, means that we have to make a prediction each year about the strains that will be most prevalent.”

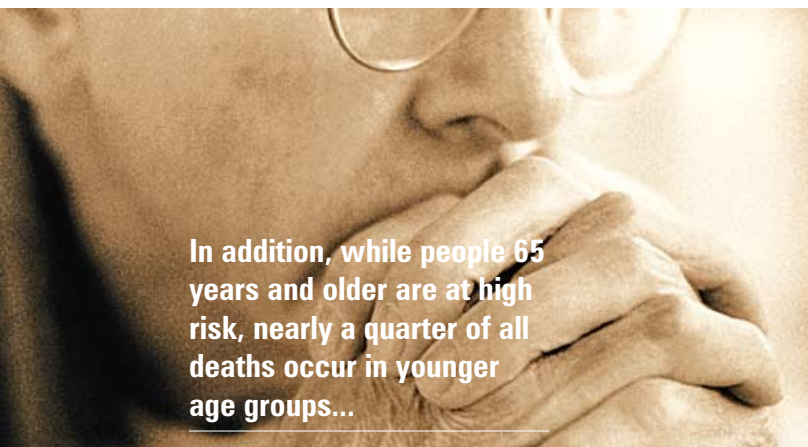
Recommendations from WHO are taken to the Australian Influenza Vaccine Committee, within the Therapeutic Goods Administration, in October each year for approval and implementation, allowing manufacture of vaccines to commence. Vaccines normally contain two influenza A strains and one influenza B strain, and are developed from clearly-characterised laboratory stocks of the virus.

RISKS OF INFLUENZA AND BENEFITS OF VACCINATION

Risks

Influenza is a potentially fatal disease, and a number of studies have shown that deaths directly attributed to the infection are a substantial under-estimate of the true mortality. A Dutch study, for example, estimated the mortality rate was four times higher than that recorded in death certificates, with many deaths attributed to secondary cardiovascular and respiratory complications.¹ An actuarial study in Australia suggested the death rate could be eight times higher than that officially recorded.² In addition, while people 65 years and older are at high risk, nearly a quarter of all deaths may occur in younger age groups (Table 1).

An Australian study estimated that influenza was responsible for a million medical consultations, 20,000-40,000 hospitalisations, 1,500 deaths and 1.5 million days off work each year, and a total economic cost of about \$600 million annually.³



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Benefits of vaccination

Influenza vaccination is about 70% effective against laboratory-proven, symptomatic disease, according to Dr Heath Kelly, Head of the Epidemiology Unit at the Victorian Infectious Diseases Reference Laboratory. "There are special difficulties in assessing the effectiveness of influenza vaccination in 'real world' settings, and data from studies need careful interpretation," Dr Kelly said. Vaccinations against other viral infections such as measles are targeted at a stable antigen, while the match between the vaccine and circulating strains of influenza virus is not always perfect. In addition, only about 40% of 'influenza-like' respiratory viral infections, characterised by rapid onset, fever and malaise, are in fact caused by the influenza virus. Outcome measures and techniques for identifying infection also vary markedly between studies.

A meta-analysis by Dr Kelly and his colleagues found influenza vaccine prevented 35% of all influenza-like illness in people aged 65 or more living in the community, 33% of hospitalisations for pneumonia and influenza, and 47% of deaths following hospitalisation.⁴ "The less specific the outcome measure, the lower the apparent efficacy," he said. "In general, though, the finding of 70% protection against proven infection is a robust one, in different countries, different populations and different years."

A number of meta-analyses have addressed specific outcomes, and identified pronounced benefits in terms of proven influenza infection:

Table 1: Estimated influenza deaths in the United Kingdom - 10 year period

65 years and older	21,900
40-64	6,100
15-39	280

Table 2: Efficacy of influenza vaccination in preventing outcomes in elderly patients⁵

All respiratory diseases	56%
Pneumonia	53%
Hospitalisation for any cause	50%
Death from any cause	68%

Table 2 provides a representative example. The most appropriate outcome measure can be influenced by the population being studied. In the frail elderly and those with underlying conditions, prevention of hospitalisation and death may be the main aim, while in younger healthy people the focus may be on decreasing time off work or reducing complications from pre-existing chronic diseases.

Contraindications to vaccination include hypersensitivity to the vaccine components and current febrile illness.

ANTIVIRAL TREATMENTS FOR EXISTING INFECTION

Two specific antiviral drugs are now available for the treatment of established influenza infection. Zanamivir ('Relenza') and oseltamivir ('Tamiflu') both inhibit the influenza neuraminidase, interfering with the replication of influenza virus by preventing the escape of replicated virus from cells. Zanamivir is administered as a twice daily inhalation to adults and children aged five years and over. Oseltamivir is administered as a twice daily capsule to those aged 13 years and over and as a suspension formulation for children one year and older, and adult patients who cannot swallow capsules.

Dr Dominic Dwyer, medical virologist at Westmead Hospital in Sydney, said the drugs are effective for laboratory-confirmed influenza infection, reducing the severity and duration of infection.^{6,7} "Both treatments need to be commenced within 36-48 hours of the first symptoms, and they are not effective against other viruses such as RSV, adenovirus, parainfluenza and metapneumovirus which can cause similar symptoms," Dr Dwyer said. "Ideally, influenza should be confirmed in the laboratory before starting treatment. Although rapid diagnostic tests are improving and becoming more widely available, this is often difficult in practice and empirical treatment may be necessary. We also need to educate patients about the need to seek early treatment, rather than just spending the first few days at home in bed."

Decisions by GPs to recommend antiviral treatment will be influenced by the prevailing patterns of influenza, as awareness of the potential benefits and opportunities for timely treatment is likely to increase when the disease becomes more common. "The efficacy of these antivirals against novel strains of influenza is not yet known, but they are targeted

at a stable component of the neuraminidase enzyme," Dr Dwyer said.

The neuraminidase inhibitors can also be used as prophylaxis in those exposed to influenza, for example in a household where someone has just developed influenza, or in outbreaks in nursing homes or other 'closed' environments.

Most trials of zanamivir and oseltamivir have been in relatively healthy people without comorbid conditions. The benefits in preventing complications are likely to be greater in the frail elderly who are at most risk, Dr Dwyer said. Effects in reducing the duration of illness are also more pronounced in people with additional risk factors.

AUSTRALIAN VACCINATION RATES: GOOD PROGRESS BUT ROOM FOR IMPROVEMENT

Dr Rosemary Lester, Manager of the Prevention and Perinatal Health Section at the Department of Human Services in Victoria, said there has been good progress in vaccinating older Australians against influenza but room for significant improvement in protecting younger people considered at risk.

"There is no vaccination register for influenza, but vaccination rates in Australians over 65s are fairly stable with latest research from the AIHW demonstrating uptake rates of 79% in this group," Dr Lester said.

The NHMRC recommends vaccination in adults and children older than 6 months with chronic pulmonary or circulatory disease, including severe asthma, and other chronic illness that required regular medical follow-up or hospitalisation in the preceding year. In these at risk groups, latest research has shown that only 42% of people are getting vaccinated annually.

"I strongly encourage GPs to recommend vaccination in at-risk groups, and to support it in people who seek it for other reasons," Dr Lester said.

HEALTH AUTHORITIES SUPPORT VACCINATION IN CHRONIC ILLNESS

Representatives of three leading health authorities have supported the benefits of influenza vaccination in people with an underlying chronic illness that increases their vulnerability to the infection and its complications.

Greg Johnson, Chief Executive Officer of Diabetes Australia in Victoria, noted that NHMRC guidelines recommend vaccination for adults and children older than 6 months who have chronic illnesses that require regular medical follow-up. This includes diabetes. "We believe all people with diabetes, regardless of their age, should be aware of this recommendation and discuss their individual needs with their doctors," Mr Johnson said. "Diabetes is a rapidly growing problem, affecting Australians of all ages. Influenza can exacerbate the problems of diabetes, and it is sensible to take steps to avoid it."

The NHMRC also recommends vaccination for people with severe asthma. Kristine Whorlow, Chief Executive Officer of the National Asthma Council, said the effects of influenza and the risks of complications could be more problematic in the presence of underlying asthma and other

chronic respiratory illnesses. "We define 'severe' asthma as asthma which causes persistent or frequent symptoms including night-time asthma, limits physical activity, needs emergency department visits or hospital admission, or requires treatment with high doses of inhaled corticosteroids or oral corticosteroids," Ms Whorlow said. "There are a number of myths about influenza vaccination in people with asthma. It does not trigger asthma attacks, although it may cause a slight increase in symptoms in a minority of people. If this occurs, then it's appropriate to increase the use of a preventer medication in line with the individual's written asthma management plan. Most people, though, notice no difference in their asthma symptoms after influenza vaccination."

The National Heart Foundation also encourages people with a range of cardiovascular diseases to have an annual influenza vaccination. "It's been estimated that up to two-thirds of people hospitalised with influenza are younger than 65 and have conditions such as heart disease, lung disease or diabetes," according to Dr Andrew Boyden, the Foundation's Medical Affairs Manager. "Although this group suffers a significant proportion of the total burden of the disease, only about 40% of Australians aged between 40 and 65 who have such high-risk conditions are protected through immunisation." An acute influenza infection predisposed people with heart disease not just to a higher risk of respiratory complications, but also risked exacerbating their underlying cardiovascular problem.

IMPLEMENTING INFLUENZA PREVENTION IN GENERAL PRACTICE

Some simple steps can facilitate influenza vaccination programs in general practice, according to Dr John Litt, Senior Lecturer from the Department of General Practice at Flinders University in Adelaide. They include:

- Flagging patient records (whether computerised or paper) early in the year, of all risk groups identified by the NHMRC, not just those patients aged 65 or older. "The flag can be used to identify who has had the flu injection, leaving a residue of patients who then need following up," Dr Litt said.
- Using annual influenza vaccination as a prompt to check whether patients have also received five-yearly pneumococcal vaccination, which remains significantly under-used and can be administered at the same time (and is government funded for those 65 and over).
- Reminding patients of the benefits of vaccination, including substantial reductions in hospitalisation and all-cause mortality in the elderly.
- Organising vaccination clinics, with appropriate publicity and staff support, to minimise the disruption to normal practice during the vaccination and influenza season.

"Recommendations from a GP are known to be one of the most powerful influences on whether patients have an influenza vaccination," Dr Litt said. "GPs have a vital role in prompting patients to consider the benefits, and in addressing any concerns about safety and efficacy. A GP recommendation often overcomes patients' concerns."

Dr Litt reinforced the need to improve vaccination rates in younger patients with chronic conditions such as ischaemic heart disease, diabetes and renal disease - representing about two million Australians. "One effect of influenza is to exacerbate pre-existing illness. The efficacy against this type of complication has not been emphasised sufficiently," he said.

A CASE FOR VACCINATION

Vera, aged 67, is active and healthy apart from some osteoarthritis. She cares for her husband who has early Alzheimer's disease. Vera was concerned about possible side effects of influenza vaccination but, reassured by her GP, she has agreed to annual vaccination funded under the National Influenza Vaccine Program for Older Australians.

David, aged 56, is overweight, an ex-smoker and suffers from diabetes and chronic obstructive pulmonary disease. David had not previously considered the need for influenza vaccination, but appreciated the offer using a PBS-funded prescription for high-risk patients younger than 65.

Kellie, aged 38, is an IT manager in a firm currently undergoing significant restructuring. She is concerned about having time off work because of illness, and the high rate of 'colds and flu' in her workplace. Kellie agreed it was worthwhile for her to fund the cost of a vaccination.

AVIAN INFLUENZA

Epidemics of influenza among poultry flocks in Asia have made headline news, but the implications for human infection are still uncertain. Influenza A is fundamentally a virus of birds, with infection of humans and the establishment of distinct and self-perpetuating human strains an incidental occurrence, according to Alan Hampson. Influenza A has 16 H (haemagglutinin) types and nine N (neuraminidase) types. Only three H types (H1, H2 and H3) and three N types (N1, N2, N8) have been known to occur as self-perpetuating infections in humans.

Recent outbreaks originating in Asian countries have involved an H5N1 type, and human infections and deaths have been reported. "The concern is that the virus will adapt to the human host, either through mutation or genetic reassortment by mixing with a human strain," Mr Hampson said. "This type of antigenic shift is the basis of influenza pandemics." A vaccine seed virus has been produced by the UK. This is a Vietnamese strain of the H5N1. Trials testing this vaccine strain have commenced in the USA and Australia will also trial vaccines using this same strain. A concern is that if the virus changes considerably in adapting to humans that this vaccine may no longer be immunogenic.

The ongoing spread of the Avian influenza into Mongolia and Russia continues to heighten the threat that a pandemic may result. WHO is sponsoring the effort to prepare and coordinate an international response.

The threat of avian influenza does not lessen the benefits of routine vaccination against known human strains. "In fact, there may be extra benefits from following the usual indications for vaccination," Mr Hampson said. "It can reduce the reservoir of human viruses available for mixing with the avian strain. For travellers, it will help in resolving diagnostic confusion if they do appear to develop influenza. In addition, if you avoid a case of normal influenza while travelling, you will also avoid the inconvenience of quarantine and other control measures that may be imposed on people with influenza-like illnesses."

PLANNING FOR A PANDEMIC

Influenza pandemics occurred in 1918, 1957 and 1968, and it is thought to be inevitable that another pandemic will occur in the future. The Australian government has developed an action plan to coordinate an organised and effective response in the event of a pandemic, through the National Influenza Pandemic Action Committee under the chairmanship of the Australian government's Chief Medical Officer.

The action committee has developed strategies ranging from the stockpiling of antiviral medications through to plans coordinating the activity of hospitals and other health care facilities. A special working committee is also reviewing the issues and developing strategies for primary care. In addition Australia is working closely with manufacturing companies, CSL Ltd and Sanofi Pasteur to ensure rapid development of a pandemic vaccine if it is required. "We can't avert a future pandemic, but we can aim to minimise its impact and make the best use of the resources we have at our disposal," Mr Hampson said.

INFLUENZA SPECIALIST GROUP

The Influenza Specialist Group consists of medical and scientific specialists as well as professional and patient groups from around the country. It cooperates with state and federal governments in educational activities about influenza. In conjunction with other organisations including the Australian Medical Association, Royal Australian College of General Practitioners, WHO Collaborating Centre for Reference and Research on Influenza, Pharmaceutical Society of Australia, National Asthma Council, Diabetes Australia and the National Heart Foundation it runs the annual Influenza Awareness Program. The Program, launched in 1992, informs key audiences about the consequences of influenza and the importance of preventing and treating infection.

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