

Economic Report into the Cost of Influenza to the Australian Health System

Report to the Influenza Specialist Group

MARCH 2007

Anthony T Newall

National Centre for Immunisation Research and Surveillance,
University of Sydney, Westmead, NSW

Professor Paul A Scuffham

School of Medicine, Griffith University, Brisbane, Qld



Brent Hodgkinson

Research and Practice Development Centre, University of
Queensland and Blue Care, Brisbane, Qld

Executive summary

Introduction

Influenza is a largely preventable communicable viral illness. Treatment of influenza and its complications consume considerable resources that could otherwise be used for other essential healthcare resources. The costs to the health system, largely borne by the Australian Government (state/territory and federal), could be used more efficiently for the prevention of influenza. This study seeks to estimate the direct health care costs to Government for the treatment of influenza. The purpose is to establish a baseline against which the effects from future interventions can be compared, and to estimate the parameters necessary as a first step in undertaking a full economic evaluation.

Methods

A cost-of-illness study is developed from the perspective of costs to the Australian Government. Key inputs are the numbers of GP consultations and admissions to hospital for influenza/pneumonia, other respiratory conditions, and circulatory illnesses, and the associated costs for each of these events. GP consultation data was obtained from a continuous randomised study of general practice activity and the numbers of hospital admissions associated with influenza activity (i.e. excess hospitalisations) were estimated from national hospital data (i.e. the AIHW National Hospital Morbidity Database). Statistical models using laboratory reports defining influenza activity plus a range of other explanatory variables were developed to estimate the number of excess hospitalisations. Cost data were derived from Medicare for GP consultations and from Australian Refined Diagnosis Related Group (AR-DRGs) for each admission to hospital. All costs are reported in 2005 values.

Results

Over the last five years there was an annual average of 310,000 GP consultations and 18,000 admissions to hospital caused by influenza. These events cost Government \$85 million annually. From a sensitivity analysis around the key parameters, there are between 282,000 and 339,000 GP consultations, and 10,000 to 30,000 admissions to hospital annually. The costs for these events range from \$52 million up to \$137 million annually. The most important factors affecting results were the numbers of admissions to hospital for influenza/pneumonia and for other respiratory conditions. The numbers and costs associated with GP consultations accounted for approximately 12% of the total cost.

Discussion

The costs to Government of treating influenza are substantial. Moreover, the true costs of influenza are even greater as there are many additional costs that have not been included in the analysis. Costs to Government, such as the costs of pharmaceuticals, x-rays and laboratory tests, were not included. In addition, there are costs to individuals for out-of-pocket expenses (Medicare and pharmaceutical gap payments), plus a range of associated costs for travel and informal care. Furthermore, time off work and lost production imposes a large cost to employers and the economy as a whole.

This study improves on previous cost estimates and develops the groundwork for future comparative studies and for assessing the relative cost-effectiveness of the interventions that can be used to gain better control on influenza epidemics.

Table of Contents

INTRODUCTION	3
OVERVIEW OF THE LITERATURE	5
Effectiveness of vaccination	5
Vaccination coverage	5
Costs and cost-effectiveness of influenza and vaccination	6
METHODS	8
Estimation of GP consultations for influenza	8
Estimation of hospitalisations due to influenza	8
Assigning costs to health resource use	9
Sensitivity analyses	9
RESULTS	10
GP consultations for influenza	10
Hospitalisations due to influenza	10
Estimated costs	10
Sensitivity Analysis	11
DISCUSSION	13
ABOUT THE AUTHORS	15
ABOUT THE ISG	15
REFERENCES	16

Introduction

Influenza is the result of a viral infection that affects the respiratory system causing acute bouts of myalgia, cough and headaches¹. It is considered a seasonal epidemic disease due to the high level of infection and transmission that occurs in colder months in temperate climates and throughout the year in tropical and subtropical climates with seasonal spikes of increased occurrence².

In at risk populations – such as those with heart conditions, asthma and other lung conditions, diabetes, kidney problems, those with weakened immune systems, residents of nursing homes and other long-term care facilities, as well as anybody aged 65 and over regardless of their health status – the complications that can arise from influenza (such as pneumonia) can be life threatening. Therefore, in most developed countries national annual vaccination programs have been instituted for high risk

populations^{3,4}. However, in the adult “healthy” working population (considered as 18 to 64 years) there is generally a lower risk of complications. Although the disease burden in this population would seem to be small with most symptoms lasting a median of 3 days, the cough and malaise associated with influenza can last for several weeks¹. In addition, it is also important to be mindful that 1.2 million of people considered “healthy” working adults have underlying conditions that could result in severe and even life-threatening consequences if they contract influenza⁵.

The number of laboratory confirmed notifications of influenza in Australia in 2006 was 3096 cases. Of these, 43.4% were in people aged between 20 and 64 years, 42.1% in children 0–19 years (21% ≤4 years of age), and 14.5% ≥65 years of age⁶. In Australia in 2002, hospitalisation rates with a primary diagnosis of influenza were highest in children aged under five years (49.5 per 100,000) and ranging from 15 per 100,000 for those aged 60–64 years to 52 per 100,000 for those aged 85 years or more⁷.

In the two year period (2001 to 2002), a total of 87 deaths (rate 0.2 per 100,000) were recorded in which influenza was signified as the direct cause of death⁷. The majority of these deaths occurred in the ≥60 year age group (73 deaths or 84%, rate 1.1 per 100,000), with 13% in the 25 to 59 year age group and 3% in the 0 to 4 year age group. The complications of influenza such as pneumonia and effects on the cardiovascular system are not included and therefore the true number of deaths *attributable* to influenza is known to be considerably higher^{8,9}.

In comparison, a study in the USA reported that the rate of influenza associated hospitalisation in people aged younger than 5 years was between 26.3 and 114 per 100,000 person years, in 5 to 49 years the rate was between 11.5 and 28 per 100,000 person years, in 50 to 64 year olds between 53 and 111 per 100,000 person years, in 65 to 69 year olds between 106 and 230 per 100,000 person years rising to between 777 to 1669 per 100,000 person years in people 85 years and over¹⁰. In the 1990s the number of deaths in the USA attributable to influenza was estimated at 92 per year (0.4 deaths per 100,000) in children aged <5 years and 32,651 per year (98.3 per 100,000) in adults ≥65 years³.

The costs associated with these events can be substantial. In countries with publicly-funded health systems, the direct healthcare costs for treating cases of influenza and its associated complications are largely borne by the tax payer. This study seeks to establish and quantify these costs for two reasons. First, quantifying these costs allows comparisons over different time periods to be made such that significant trends can be identified in both the epidemiology of influenza and the trends in the associated costs. This also allows the effects of any intervention to reduce the incidence of influenza to be identified. Second, establishing a baseline of these costs is the first step for undertaking a cost-effectiveness analysis. A cost-effectiveness analysis then provides information on the relativity of investments in healthcare such that the intervention with the greatest return can be selected over other interventions which offer less value for money.

The next section provides a brief overview of the literature. After this, the methods used in this study are presented followed by the results. A discussion of the results then follows.

Overview of the literature

Effectiveness of vaccination

The effectiveness of vaccination with inactivated influenza vaccines, of the type used in Australia, depends largely on two factors: **a)** the age and health status of the vaccine recipient; and **b)** the degree of antigenic relatedness between the viruses in the vaccine and those circulating in the population. Vaccine effectiveness has been assessed by a variety of measures including reduction in acute respiratory illness, prevention of influenza or pneumonia-associated hospitalisations or deaths and prevention of culture or serologically-proven influenza virus illness.

High post-vaccination antibody levels develop in the majority of vaccinated children and young adults¹¹⁻¹³ and these antibodies are protective against illness caused by strains that are antigenically similar to the strains included in the vaccine¹²⁻¹⁵. Young children aged between 6 months and 9 years of age require 2 vaccine doses, usually administered a month apart on initial vaccination, to provide protective antibody levels.

In a recent review, Ruben¹⁶ concluded that influenza vaccination was effective in preventing respiratory disease and otitis media due to influenza in children; findings which are supported by epidemiologic studies¹⁷. Langley and Faughnan¹⁸ reviewed the literature for protection against influenza in the general population and concluded that the protection afforded by influenza vaccines for healthy adults and children varied from moderate to high, dependent on vaccine immunogenicity and antigenic match with circulating virus strains. The American Advisory Committee on Immunisation Practices (ACIP) cites a typical effectiveness of 70–90% against influenza illness in healthy adults aged less than 65 years when there is a good strain match between vaccine and circulating viruses¹⁹. ACIP also cites evidence demonstrating decreased work absenteeism and decreased use of health-care resources including antibiotics among this group¹⁹.

Importantly, influenza vaccination has also been shown to be effective in preventing illness and subsequent complications in older populations, resulting in numerous countries including Australia publicly funding vaccination programs for those aged 65 or over. In one such review, vaccinated residents of nursing homes experienced significant reductions in cases of pneumonia (46%), hospital admissions (45%), and influenza and pneumonia related deaths (42%) when there was a good match between the vaccine and circulating viruses²⁰. The same review also found that influenza vaccination in community dwelling older persons significantly reduced hospital admissions for influenza and pneumonia (26%), and all cause mortality (42%), despite no clear link with reducing influenza like illness or pneumonia²⁰.

Studies of influenza vaccine in other sub-groups of the population also report significant benefits from vaccination. For example, a recent systematic review of influenza vaccination in “healthy” children aged 2 years or older, concluded that live vaccine and inactivated vaccine reduce the incidence of influenza by 33% and 36% respectively²¹. Similarly, a review of vaccine effectiveness in people with chronic obstructive pulmonary disease suggested that vaccination reduced influenza-related exacerbation of COPD²², but there was limited evidence on those with asthma²³.

Vaccination coverage

In Australia, vaccination coverage in the over 65 years of age population has been estimated at nearly 80%²⁴. Data on the coverage of vaccination in Australian children is not available as influenza vaccination

is not routinely provided to children. In a recent report by the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases the authors state that “Whilst available Australian data also suggest that there is a significant burden of illness in this (6 to 23 month) age group, examination of the feasibility of recommending influenza vaccination for all children and cost-effectiveness analysis are required before recommending and implementing such a population level strategy”⁷.

In a recent survey, uptake of vaccine by “healthy” adults aged 18 to 64 years was estimated to be 18.8%²⁴. In comparison, vaccination coverage in the USA of “not high risk” adults was between 16.6% in those aged 18–49 years and 32.1% in those aged 50–64 years in 2004³.

Uncertainty by health practitioners and health policy makers as to the effectiveness of vaccination in the healthy working age adult population, and perceived low effectiveness by the target population themselves are likely to be the reasons for variable and generally low uptake of influenza vaccination.

As Australia has no policy for vaccination of the “healthy” adult population the decision of whether to promote and pay for vaccination of individuals is generally left to the discretion of the employer or the individual. The strongest rationale for employers desiring to vaccinate their workforce is the prevention of absenteeism due to illness. In a single Australian study of healthy adult volunteers who were administered with a monovalent influenza B vaccine the number of working days lost due to clinically defined cases of influenza was 2.25 ± 4.11 days²⁵. This is compared with a mean range of 0.12 to 2.03 days in placebo treated healthy adults in studies outside Australia^{26,27}. In a meta-analysis of three parenteral inactivated vaccine studies (of unmatched strains) results showed that vaccination resulted in an average reduction in work days lost of 0.4 days^{1,28}. In a recent report, absenteeism (defined as requiring a minimum of 3 days sick leave) acting as a non-specific index of influenza activity was reported to run as high as 1.2% of the Australian postal workforce in some one week periods, up from a baseline absentee rate of 0.8%²⁹.

Costs and cost-effectiveness of influenza and vaccination

The cost of influenza in Australia has been estimated to be between \$828 million and \$884 million per year (CPI adjusted from 1994 values)³⁰. These costs included indirect costs from days of work lost due to influenza. However, direct costs dominated those estimates contributing 68–70% of the total costs. Direct costs in the study included out-of-pocket costs to patients, GP costs, costs to Medicare and other health insurers, laboratory and diagnostic costs and costs for hospitalisation. The costs for admissions to hospital accounted for 82% of direct costs (i.e. \$500 million^a); this was clearly the greatest factor contributing to the total costs of influenza in the study. Although the costs for hospital admissions were based on the Australian average cost per day, the number of hospital admissions were estimated from USA reports dating back to 1985 and 1994. These hospital admission rates may not be applicable to Australia not only because the USA has a different health care system with different incentives to admit patients to hospital, but the reports used to estimate admissions in Australia were produced following relatively large influenza epidemics. Moreover, the methods and case definition used to estimate the rates were not reported. Most data (cases, events, and costs) were derived from studies conducted in the USA dating back to 1973. Therefore, the costs estimated in that study are generally not applicable to Australia today.

a Mills and Yapp reported an estimate of 30,000 admissions to hospital based on the 1985 and 1994 USA data. Each admission cost, on average \$12,221 in 1995 dollars. Inflated to 2005 values, this is equivalent to \$16,800 per admission. The average cost for admissions under the Major Diagnostic Category “Diseases and disorders of the respiratory system” (MDC 04) in 2004-05 was \$4,136⁴⁰.

While economic analyses in the USA include indirect costs (i.e. days off work for parents), the Pharmaceutical Benefits Advisory Committee in practice considers only the direct costs of illness and therefore the resulting cost-effectiveness ratios are unlikely to be favourable³¹.

The cost-effectiveness of influenza vaccines in the “healthy” population has been of particular interest and the subject of numerous studies^{26,30,32–36}. In Australia, modelling the vaccination of “at risk” adults aged 18 to 64 years was shown to be cost saving with the incremental cost of vaccination to be \$59.7 million and the cost-offsets to be \$57.7 million without accounting for societal costs of increased risk of mortality³⁷.

In five identified cost-effectiveness studies, a program of employee vaccination was found to be cost-effective^{32–36}. In two studies a net savings of US\$2.58³⁴ and US\$2.21³² for every dollar spent on the vaccination program was realised. In two studies the cost savings of the evaluated vaccination programs were US\$13.66³⁵ and US\$35.45³³ per person vaccinated. A final study found that breakeven point for the cost of the vaccine and its administration was US\$43.07 per person vaccinated³⁶.

In comparison, a US study of “healthy” young adults undertaken in mid to late 1990s concluded that influenza vaccination may not provide overall economic benefits in most years²⁶. The incremental costs to society per person vaccinated were US\$65.59 when the vaccine was not well matched with circulating influenza strains and US\$11.17 when the vaccine was well matched. However, the study found that in years when there is a good match between the vaccine and the circulating influenza strains, vaccination programs could significantly reduce rates of influenza like illness, lost work days and physician visits.

Despite some disagreement in the results between studies, what is clear from these studies is that any cost savings resulting from a vaccination strategy for “healthy” working adults is heavily related to inclusion of indirect costs (i.e. averted production losses and days absent), the cost of the vaccine and the match between the vaccine virus antigens and the predominant circulating virus.

In the USA, influenza vaccination has been found to be cost effective in children aged 6–23 months not at risk with cost-effectiveness ratios of US\$12,000 per QALY^b ³⁸. In children not at risk aged 12–17 years the cost per QALY was US\$119,000³⁸. Where vaccination in children was found to be highly effective was in children considered “at risk” with a realised cost savings in 6–35 month old infants and cost per QALY ranging from \$1,000 to \$10,000 in children aged 3 to 17 years.

In populations over the age of 65 years, studies of the cost effectiveness of influenza vaccination have been mixed. In a cost-benefit analysis in the UK routine vaccination of 65 to 74 year olds was not found to be cost-effective^{39,40}. As no significant difference in the frequency of influenza was found between the vaccine and placebo treatment arms, the corresponding cost-effectiveness ratios were found to be unacceptably high. The cost per GP consultation avoided was \$4,320 (PPP 2004 figures OECD^c). The cost per hospital admission avoided and cost per death avoided was \$131,760 and \$4,104,000 respectively. The incremental cost per QALY was as high as \$656,640. However, in a USA study in which a birth cohort aged 65 and older were followed for their lifetime, the cost-effectiveness of influenza vaccine was found to be favourable⁴¹. Vaccination resulted in a cost per QALY of only US\$980 including cost-offsets of US\$17 per person vaccinated.

b QALY = Quality Adjusted Life Year

c PPP = purchasing power parities, 2004 data from the Organisation for Economic Co-operation and Development

Methods

A cost-analysis was undertaken. This combines estimates of the epidemiology of influenza with the costs associated health care resource use. The epidemiology used here is focussed on events that require use of health care services; these are general practitioner (GP) consultations for influenza/influenza-like illness, and admissions to hospital associated with influenza. Through these, as well as healthcare reimbursement agencies (i.e. the Pharmaceuticals Benefits Scheme) the Australian Government (state/territory and federal) covers the majority of costs for most acute healthcare needs in Australia. The cost to Government for the treatment of influenza and its associated complications is taken as the perspective for this study.

Estimation of GP consultations for influenza

Data were supplied by the Australian General Practice Statistics and Classification Centre, the University of Sydney, a collaborating unit of the Australian Institute of Health and Welfare, about all encounters at which the GP had recorded influenza/influenza like illness (ICPC-2 rubrics "R80") between April 2000 and March 2006 inclusive in the Bettering the Evaluation and Care of Health (BEACH) database⁴². The BEACH program is a continuous national study of general practice activity in Australia in which random samples (utilising a rolling sample, or ever changing GPs) of approximately 1,000 GPs participate per year. Each GP records details of 100 consecutive GP/patient encounters (see Reference 43 for details of methodology and validation). It is the only continuous national randomised study of general practice activity in the world⁴³.

Estimation of hospitalisations due to influenza

Excess hospitalisations were determined by a GLM regression model⁴⁴, using a similar methodology to those used in other countries^{45,46}. The GLM procedure specified Poisson models with a log-link function; where over dispersion existed a negative-binomial regression was undertaken (also in the GLM procedure using a log-link function). The model utilised hospitalisation data for the period July 1998 to Jun 2005, supplied by the Australian Institute of Health and Welfare (AIHW). The AIHW National Hospital Morbidity Database collects administrative, demographic and clinical information about all patients admitted to public and private hospitals in Australia. All data with ICD-10 code J (respiratory) or I (circulatory) were extracted and restricted to principal hospitalisation. Analysis was conducted to determine the hospitalisations attributable to influenza in the following categories:

- influenza/pneumonia (ICD J1.X)
- other respiratory illness excluding influenza/pneumonia (ICD J, excluding J1.X), and
- all circulatory (ICD I).

Influenza activity (A and B) and Respiratory Syncytial Virus (RSV) were obtained from The Laboratory Virology and Serology Reporting Scheme (LabVISE). LabVISE is a national system of sentinel laboratories which analyses specimen all year round. The number of laboratories participating varies from year to year and in 2005 there were 11 laboratories from all states and territories except Western Australia and the Northern Territory²⁹. These data, indicating when influenza epidemics occurred, were used as an explanatory variable in the model with the GLM procedure.

The excess numbers of hospitalisations were then estimated from the models. Three steps were involved:

1. Predicting the numbers of hospitalisations from the models based on the observed number of LabVISE reports
2. Predicting the numbers of hospitalisations from the models with the number of influenza LabVISE reports set to zero
3. Calculating the difference between steps 2 and 1.

This gives the number of hospitalisations that could be averted if influenza epidemics did not occur or the population was completely protected by a 100% efficacious vaccination.

Assigning costs to health resource use

To determine the average cost per GP consultation for influenza we attached the 2005 Medicare Benefits Scheme (MBS) consultation costs for the appropriate level of consultation as reported in the BEACH database⁴². In situations where we could not determine the exact MBS cost to attach we utilised the most plausible cost that could be applicable (e.g. consultations listed as 'home visits' were assumed to be for a level B consultation; i.e. attendance involving taking a selective history, examination of the patient with implementation of a management plan in relation to 1 or more problems, or an attendance of less than 20 minutes duration).

Hospitalisation costs were determined by examining the Australian Refined Diagnosis Related Group (AR-DRG) recorded for each patient hospitalised under the appropriate ICD category (i.e. influenza/pneumonia, all respiratory excluding influenza/pneumonia, or all circulatory) in the period of review. The appropriate AR-DRG (version 5.1) cost for each of these hospitalisations was then applied, taking into account if the patient was in a public or a private hospital^{47, 48}. Through this process we determined the total cost for all hospitalisations in each ICD category, and subsequently the average cost of a hospitalisation for each of the categories of hospitalisation.

Sensitivity analyses

A one-way sensitivity analysis was undertaken to determine the key parameters driving the costs. The 95% Confidence Intervals (CI) around the number of GP consultations and excess hospitalisations were used; because unit costs are a point estimate only, these were varied around a plausible range. GP costs were all set to a level A (short consultation) and level C consultation costs for the lower and upper range. Hospital costs were varied by +/- 20% for each category.

Results

In this section we present the results for the number of GP consultations and the number of hospitalisations associated with influenza epidemics. The costs to the Australian Government (state/territory and federal) are then presented followed by the sensitivity and scenario analyses. All costs are reported in 2005 A\$.

GP consultations for influenza

The BEACH database estimated an annual total of 310,650 (95% CI: 282,300-338,950) encounters nationally at which influenza (ICPC-2 rubrics “R80”) was managed.

Hospitalisations due to influenza

The Poisson/Negative-Binomial regression procedure outlined above provided a good predictive fit for the three hospitalisation data series modelled using the LabVISE data as an explanatory variable. From these models, 11% of influenza/pneumonia hospitalisations were associated with influenza epidemics (Table 1). Similarly, 4% of hospitalisations for all other respiratory illnesses were associated with influenza epidemics. There was no statistically significant association between hospitalisations for circulatory illnesses associated with influenza epidemics. However, it is unlikely that influenza epidemics offer a protective effect (indicated by the negative lower 95% CI) but it is plausible that these epidemics increase hospital admissions for circulatory illness.

TABLE 1. EXCESS ADMISSIONS TO HOSPITAL

	Percentage of hospitalisations for the ICD category associated with influenza (95% CI)	Annual no. of excess hospitalisations (95% CI)	Excess hospitalisations per 100,000 population (95% CI)
Influenza/pneumonia	0.109 (0.076-0.139)	6973 (4723-9225)	35.705 (24.18-47.23)
Other respiratory illness	0.042 (0.020-0.063)	11039 (5259-16820)	56.520 (26.92-86.12)
Circulatory	-0.003 (-0.016-0.010)	-1228 (-6786 - 4329)	-6.289 (-34.74-22.16)

Estimated costs

Based on the BEACH consultation categories we found an average cost per consultation of \$33.32. After excluding the records where consultation-type was missing (8.7%), the majority of the consultations (92%) were listed as Level B. For the purpose of costing we also removed the small number of

consultations listed as “workers compensation”, “other items”, “no charge”, “other paid”, “indirect”, together these categories made up of 2.5% of the total GP consultations. Determining a realistic range of uncertainty for GP costs is difficult, the lowest cost for a consultation Level A (Professional attendance for an obvious problem characterised by the straightforward nature of the task that requires a short patient history and, if required, limited examination and management) is \$14.40, however only 0.6% of the consultations surveyed were given this coding by the recording GP. Given the total number of GP visits (310,650; 95% CI: 282,300-338,950) we estimate that the total cost of GP visits for influenza was \$10,349,600 (Table 2).

Using the AR-DRGs to calculate the national average cost for each hospital admission over the period of review, we estimated the average cost of an influenza/pneumonia hospitalisation to be \$5,245 and the average cost of other respiratory hospitalisations (excluding influenza/pneumonia) to be \$3,460. Similarly, the cost for a circulatory admission was \$4,412 (this cost is the national average cost for these admissions). However, we cannot state there were any admissions to hospital for circulatory illness associated with influenza epidemics, and therefore, the cost of these admissions must be zero.

Multiplying the numbers of excess hospitalisations by the average cost for each class of hospitalisation gives the total cost for hospitalisations as \$74,776,035. The sum of costs for hospitalisations and GP consultations is estimated at \$85,125,636.

TABLE 2. COSTS OF EVENTS

Event	Unit cost (\$)	Total cost (\$)
GP consultations	33.32	10,349,600
Admissions to hospital:		
Influenza/pneumonia	5,245	36,576,844
Other respiratory	3,460	38,199,191
Circulatory	4,412	0
Total		85,125,636

Sensitivity Analysis

Variation in the number of admissions to hospital for influenza/pneumonia had the greatest effect on total costs (Table 3), followed by the numbers of admissions to hospital for other respiratory illnesses. Varying the costs of admissions to hospital by +/- 20% for influenza/pneumonia resulted in an 11% change in total costs; this factor was the largest cost factor. The effects of varying the hospital costs for other respiratory illness had a relatively small effect on total costs (i.e. a 7% change). When the upper limit of admissions to hospital for circulatory illness was used, total costs increased by 17% and when the upper estimate of the cost of these admissions was used, total cost increased further to 120% of the base case estimate.

TABLE 3. SENSITIVITY ANALYSIS

Variable	Parameter value	Total cost (\$)
Base case		85,125,636
Number of events		
GP consultations		
Lower	282,300	84,181,128
Upper	338,950	86,068,477
Influenza/pneumonia hospitalisations		
Lower	4,723	73,320,218
Upper	9,225	96,932,532
Other respiratory hospitalisations		
Lower	5,259	65,123,899
Upper	16,820	105,127,849
Circulatory hospitalisations		
Upper	4,329	104,224,837
Upper value of range *		136,976,789
Lower value of range *		52,373,974
Cost of events		
GP consultations		
Lower (level A surgery consultation)	14.70	79,342,590
Upper (level C, 90% surgery consultation and 10% home visits)	63.20	94,407,562
Influenza/pneumonia hospitalisations		
Lower (-20%)	4,196	77,810,267
Upper (+20%)	6,294	92,441,004
Other respiratory hospitalisations		
Lower (-20%)	2,768	77,485,797
Upper (+20%)	4,152	92,765,474
Circulatory hospitalisations **		
Lower (-20%)	3,530	100,404,997
Upper (+20%)	5,294	108,044,678

* All epidemiological variables were set to their upper or lower 95% CI (at the average cost per event)

** The upper 95% CI limit on numbers admitted to hospital was used

The sensitivity analysis revealed that the number of GP consultations had relatively little effect on the total cost (i.e. when the upper or lower 95% CI was used, total costs changed by 0.8%). However, when the cost of a GP consultation was varied from the lowest to an upper cost within the plausible range (the upper cost included home visits for 10% of consultations) the total costs varied by -5% to 8%.

Discussion

This study shows the direct healthcare cost to the Australian Government (state/territory and federal) for the treatment of influenza-related illnesses in a typical season is \$85 million. Due to variance in the data, these costs range from a minimum of \$52 million to \$137 million. These costs cover GP consultations and admissions to hospital only. As such, these costs are relatively conservative as they do not include some healthcare costs that are incurred by Government (e.g. the cost of examination/autopsy and preparation of death certificates for those who die as a consequence of influenza). In addition, these cost estimates do not include the costs associated with emergency department (ED) visits – these may be substantial. However, the lack of a national data collection system makes calculating the true cost of ED visits problematic. As with hospitalisations, one would expect that the true number of ED visits attributable to influenza would be far greater than the number specifically coded as influenza. Similarly, tests and diagnostics costs associated with influenza consultations have not been included due to the lack of detailed data to correctly identify and associate pathology tests with influenza. Thus, the costs estimated here are likely to understate the true costs to Government.

Moreover, the costs to Government may be a small fraction of the true costs to society. That is, costs to society include the value of lost production from time off work due to illness and premature death, the costs of reduced productivity from working at lower levels of efficiency when at work with illness and the value of pain and suffering incurred by those infected with influenza. These social costs apply to voluntary/unpaid work as well as paid employment. However, these societal costs largely depend upon the theoretical approach taken – that is, either the conservative “cost friction” or the traditional “human capital” approach.

There are also direct out-of-pocket costs to patients with influenza for over-the-counter medicines, travel-related costs for GP visits and for relatives to visit hospital inpatients, and gap payments (the extra costs that GPs and private hospitals charge that is above the Medicare reimbursement fee) as well as the payments for prescription medications not covered by the Pharmaceutical Benefits Scheme (PBS). The costs of the vast majority of pharmaceuticals are out of pocket costs as these are less than the \$30.70 threshold after which attracts the subsidy by the PBS (with the exception of DVA and concession card holders, where the threshold is \$4.90).

This study does have some limitations mainly due to data limitations. The AR-DRG costs attached to excess influenza-attributable hospitalisations were based on the assumption that these excess cases do not differ from the average cost for the respective DRG category. It is possible that admissions to hospital associated with influenza systematically have greater or lower costs compared with the mean AR-DRG cost. We have provided a range of estimates in the sensitivity analysis by increasing/decreasing the respective costs by +/- 20%.

A second limitation is the LabVISE data were based on absolute counts, rather than the proportion positive. Thus, variation may not only be due to the changes in influenza activity but also to changes in the number of samples tested. We developed Poisson and negative-binomial regression models to make the best use of these data. Those models were good predictors of admissions to hospital.

Finally, we have assumed that all cases of influenza (ICPC-2 rubrics “R80”) managed at GP encounters were the result of an influenza infection. A proportion of these consultations may be the result of other infections. However, we expect that our estimate is conservative given that the true estimate of GP encounters attributable to influenza would also include a proportion of GP visits for other causes, such

as complications of influenza, that we have not included (e.g. a proportion of GP visits for pneumonia would be the result of an influenza infection).

Compared with the only other study identified which estimated the costs of influenza in Australia, the estimates from our study are substantially lower. There are two reasons for this: first, our estimate of admissions to hospital is lower than the estimate from Mills and Yapp³⁰. Their estimate of 30,000 admissions annually was based on a relatively old USA study whereas we estimated 18,000 admissions annually directly from Australian hospital data. Our upper 95% CI extends to 30,374, admissions; therefore, there is a small overlap between studies. Second, the cost of admissions to hospital in Mills and Yapp was \$16,800; this is more than four times greater than the mean cost of \$4,136 for admissions in the Major Diagnostic Category “Diseases and disorders of the respiratory system” (MDC 04) in 2004–05⁴⁷. We stratified admissions into influenza/pneumonia and other respiratory illnesses and obtained a mean cost per admission of \$4151 (weighted by the proportion in each group stratified). Therefore, our study presents more realistic estimates using Australian data and is a substantial improvement on previous work.

The implications of this study suggest that a proportion of the costs to Government for the treatment of influenza could be redirected to prevention of influenza. The optimal proportion and the best use of those funds is the subject of further study. Nevertheless, multiple strategies to prevent influenza do exist – including increasing vaccine use in high risk groups^{20,37}, vaccination in children^{38,49}, vaccination in healthy / working adults by employers^{32–36}, and the use of anti-viral medications for prevention and/or treatment in adults⁵⁰. These interventions have all been shown to be effective, and some of those with cost-effectiveness analyses have been shown to be good value for money. However, the best approach for Australia, given the current uptake rates of vaccination in the various sub-groups, is currently unknown and requires urgent and ongoing research.

About the authors

Anthony T Newall

Anthony Newall is a PhD student at the University of Sydney, situated at the National Centre for Immunisation Research and Surveillance (NCIRS). He recently completed a Masters of Public Health (Honours) and his PhD focuses on the economic evaluation of vaccination programs in Australia.

Professor Paul A Scuffham

Paul Scuffham is a Professor of Health Economics at Griffith University. He has wide experience in economic evaluation of medical interventions, including medical devices, pharmaceuticals, and health services. His previous posts include Director of the Queensland Evaluation Group and senior staff member at York Health Economics Consortium in the prestigious University of York, England. He has consulted for a wide range of international organisations, including pharmaceutical, biotechnology, and medical device companies and the UK Health Department. His research interests include the economics of medical decision making of health care interventions; public health (especially infectious disease, cardiology, injury, and telemedicine); valuing health outcomes; and comparing the effectiveness, efficiency and equity of health systems.

Brent Hodgkinson

Brent Hodgkinson is the Research Fellow at the UQ/Blue Care Research and Practice Development Centre where he coordinates Centre research projects with specific focus on best practice in palliative and continence care. Previously he was an evaluator for the Pharmaceutical Benefits Advisory Committee assessing the cost-effectiveness of drugs under application for listing on the Pharmaceutical Benefits Schedule, and a research officer performing Health Technology Assessments for the Medical Services Advisory Committee. His interests are in Health Economics and Health Technology Assessment and he is currently pursuing his PhD in Health Economics measuring the utility and quality of life in older adults with particular emphasis on patients receiving palliative care.

About the ISG

The Influenza Specialist Group (ISG) consists of medical and scientific specialists and includes representatives of professional and patient groups from around the country. It cooperates with state and federal governments in educational activities regarding 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 conducts an annual Influenza Awareness Program. The Program, launched in 1992, informs key audiences regarding the consequences of influenza and the importance of preventing and treating infection. The ISG receives support as educational grants from industry organisations; however the ISG, through its executive, maintains full control over all of its activities and published materials.

References

1. Demicheli V, Rivetti D, Deeks JJ *et al.* Vaccines for preventing influenza in healthy adults. *Cochrane Database Syst Rev* 2004(3): CD001269
2. Hampson AW, Mackenzie JS. The influenza viruses. *Med J Aust* 2006; **185**(10):S39-43
3. Smith NM, Bresee JS, Shay DK *et al.* Prevention and control of influenza: Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2006;**55**(RR10):1-42
4. Tay-Teo K, Carter R. "Influenza vaccination for 'at risk' Australian adults aged between 18 to 64. Part 1: Literature review of influenza vaccination for the 'at risk' Australian adults" in *NICS Evidence Report*. 2006; National Institute of Clinical Studies: Canberra
5. National Institute of Clinical Studies. *Flu Facts* (factsheet). February 2007. Available at: <http://www.fightflu.com.au/asp/index.asp?sid=2118&page=facts>
6. Australian Department of Health and Ageing. *National Notifiable Diseases Surveillance System: Number of notifications of influenza (laboratory confirmed), Australia, 2006 by age group and sex*. 2006 [cited 2007 20/02/07]. Available at: http://www9.health.gov.au/cda/Source/Rpt_5.cfm.
7. Brotherton J, McIntyre P, Puech M *et al.* Vaccine preventable diseases and vaccination coverage in Australia 2001 to 2002. *Commun Dis Intell* 2004;**28** (Suppl 2):vii-S116
8. Simonsen L, Clarke MJ, Williamson GD *et al.* The impact of influenza epidemics on mortality: introducing a severity index. *Am J Public Health*. December 1997;**87**(12):1944-1950
9. Sprenger MJW, Beyer WEP, Kempen BM *et al.* Risk factors for influenza mortality? Published in: *Options for the Control of Influenza II*. Edited by Hannoun C *et al.* 1993; Elsevier Science Publishers: 15-23
10. Thompson WW, Shay DK, Weintraub E *et al.* Influenza-associated hospitalizations in the United States. *JAMA* 2004;**292**(11):1333-40
11. La Montagne JR, Noble GR, Quinnan GV *et al.* Summary of clinical trials of inactivated influenza vaccine – 1978. *Rev Infect Dis* 1983;**5**:723-36
12. Oxford JS, Schild GC, Potter CW *et al.* The specificity of the anti-haemagglutinin antibody response induced in man by inactivated influenza vaccines and by natural infection. *J Hyg Lond* 1979;**82**:51-61
13. Neuzil KM, Dupont WD, Wright PF *et al.* Efficacy of inactivated and cold-adapted vaccines against influenza A infection, 1985 to 1990: the pediatric experience. *Pediatr Infect Dis J* 2001;**20**(8):733-40
14. Potter CW, Oxford JS. Determinants of immunity to influenza infection in man. *Br Med Bull* 1979;**35**:69-75

15. Hirota Y, Kaji M, Ide S *et al.* Antibody efficacy as a keen index to evaluate influenza vaccine effectiveness. *Vaccine* 1997;**15**(9):962-7
16. Ruben FL. Inactivated influenza virus vaccines in children. *Clin Infect Dis* 2004;**38**(5):678-88
17. Wright PF. The use of inactivated influenza vaccine in children. *Semin Pediatr Infect Dis* 2006;**17**(4):200-5
18. Langley JM, Faughnan ME. Prevention of influenza in the general population. *CMAJ* 2004;**171**(10):1213-22
19. Smith NM, Bresee JS, Shay DK *et al.* Prevention and Control of Influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;**55**(RR-10):1-42
20. Rivetti D, Jefferson TO, Thomas R *et al.* Vaccines for preventing influenza in the elderly. *Cochrane Database Syst Rev* 2006. 3: CD004876
21. Smith S, Demichili V, Di Pietrantonj C *et al.* Vaccines for preventing influenza in healthy children. *Cochrane Database Syst Rev* 2006;1: CD004879
22. Poole PJ, Chacko E, Wood-Baker RW *et al.* Influenza vaccine for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2000;4:CD002733
23. Cates CJ, Jefferson TO, Bara AI *et al.* Vaccines for preventing influenza in people with asthma. *Cochrane Database Syst Rev* 2004;2:CD000364
24. Australian Institute of Health and Welfare, 2004 *Adult vaccination survey: summary results*. 2005, AIHW and DOHA: Canberra
25. Edmonson KW, Graham SM, Warburton MF. A clinical trial of influenza vaccine in Canberra. *Med J Aust* 1970;**4**: p. 6-13
26. Bridges CB, Thompson WW, Meltzer MI *et al.* Effectiveness and cost-benefit of influenza vaccination of healthy working adults: A randomized controlled trial. *JAMA* 2000;**284**(13):1655-63
27. Nichol KL, Lind A, Margolis KL *et al.* The effectiveness of vaccination against influenza in healthy, working adults. *N Engl J Med* 1995;**333**(14):889-93
28. Jefferson T, Bianco E, Demicheli V. Influenza vaccines in adults. *Occup Med (Lond)* 2002;**52**(5):255-8
29. Firestone SM, Barr G, Roche PW *et al.* Annual report of the National Influenza Surveillance Scheme, 2005. *Commun Dis Intell* 2006;**30**:189-200
30. Mills J, Yapp T. *An Economic Evaluation of Three CSIRO Manufacturing Research Projects*. 1996; CSIRO: Australia

31. Isaacs D. Should all Australian children be vaccinated against influenza? Questions of cost-effectiveness, vaccine efficacy and feasibility are yet to be answered. *Med J Aust* 2005;**182**(11):553-4
32. Berg GD, Thomas E, Silverstein S *et al.* Reducing medical service utilization by encouraging vaccines: randomized controlled trial. *Am J Prev Med* 2004;**27**(4):284-8
33. Burckel E, Ashraf T, de Souza Filho JP *et al.* Economic impact of providing workplace influenza vaccination. A model and case study application at a Brazilian pharma-chemical company. *Pharmacoeconomics* 1999;**16**(5 Pt 2):563-76
34. Campbell DS, Rumley MH. Cost-effectiveness of the influenza vaccine in a healthy, working-age population. *J Occup Environ Med* 1997;**39**(5):408-14
35. Nichol KL. Cost-benefit analysis of a strategy to vaccinate healthy working adults against influenza. *Arch Intern Med* 2001;**161**(5):749-59
36. Nichol KL, Mallon KP, Mendelman PM. Cost benefit of influenza vaccination in healthy, working adults: an economic analysis based on the results of a clinical trial of trivalent live attenuated influenza virus vaccine. *Vaccine* 2003;**21**(17-18):2207-17
37. Colgan S, Tay-Teo K, Shik S *et al.* Influenza vaccination for 'at risk' Australian adults aged between 18 to 64. Part 2 of the cost-of-illness study of current practice and cost analysis of extending vaccination to all 'at risk' Australian adults. In NICS Evidence Report. 2006, National Institute of Clinical Studies: Canberra
38. Prosser LA, Bridges CB, Uyeki TM *et al.* Health benefits, risks, and cost-effectiveness of influenza vaccination of children. *Emerg Infect Dis* 2006;**12**(10):1548-58
39. Allsup S, Gosney N, Haycox A *et al.* Cost-benefit evaluation of routine influenza immunisation in people 65–74 years of age. *Health Technol Assess* 2003;**7**(24):iii-x, 1-65
40. Allsup S, Haycox A, Regan M *et al.* Is influenza vaccination cost effective for healthy people between ages 65 and 74 years? A randomised controlled trial. *Vaccine* 2004;**23**(5):639-45
41. Maciosek MV, Solberg LI, Coffield AB *et al.* Influenza vaccination health impact and cost effectiveness among adults aged 50 to 64 and 65 and older. *Am J Prev Med* 2006;**31**(1):72-9
42. Family Medicine Research Centre. BEACH (*Bettering the evaluation and care of health*) report – influenza among patients in general practice 2000–2006. 2006; The University of Sydney at Westmead Hospital: Westmead
43. Britt H, Miller GC, Knox S *et al.* *General practice activity in Australia 2004–05*, in *AIHW Cat. No. GEP 18*. 2005; Australian Institute of Health and Welfare: Canberra
44. Newall A *et al.* *Estimating excess hospital admissions associated with influenza*. Unpublished manuscript, 2007

45. Dushoff J, Plotkin JB, Viboud C *et al.* Mortality due to influenza in the United States – an annualised regression approach using multiple-cause mortality data. *Am J Epidemiol* 2006;**163**:181-187
46. Thompson WW, Shay DK, Weintraub E *et al.* Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA* 2003;**289**:179-186
47. Commonwealth Department of Health and Aged Care. *National Hospital Cost Data Collection: Cost Report Public hospital (Round 9, 2004-2005)*. 2006; Commonwealth Department of Health and Aged Care: Canberra
48. Commonwealth Department of Health and Aged Care. *National Hospital Cost Data Collection: Cost Report Public hospital (Round 7, 2002-2003)*. 2004; Commonwealth Department of Health and Aged Care: Canberra
49. Jefferson TO, Smith S, Demicheli V *et al.* Assessment of the efficacy and effectiveness of influenza vaccines in healthy children: systematic review. *Lancet* 2005;**365**(9461):773-80
50. Lynd L, Goeree R, O'Brien B. Antiviral agents for influenza – A comparison of cost-effectiveness data. *Pharmacoeconomics* 2005;**23**(11):1083-1106

Acknowledgements

Information in this report has been drawn from data collected by the General Practice Statistics and Classification Unit, the University of Sydney in collaboration with the Australian Institute of Health and Welfare (AIHW). Hospitalisation data were provided by the AIHW. We thank the AIHW for provision of data. LabVISE data were provided by the Australian Government Department of Health and Ageing.

Anthony Newall's PhD research is supported by a Public Health Postgraduate Scholarship (402920) from the National Health and Medical Research Council (NHMRC) of Australia, and by a GlaxoSmithKline Australia Support Grant.