

Influenza in Singapore: Assessing the Burden of Illness in the Community

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Abstract

Introduction: Influenza infection has significant morbidity and mortality. The social and economic costs from work absence in the working population and from hospitalisations in the elderly are considerable. Meta-analyses of cohort and randomised controlled studies indicate that influenza vaccination is effective in preventing respiratory illness, hospitalisation, pneumonia and death in 50% to 68% of cases. In Singapore, data on the disease burden from influenza are sparse and no official recommendation on influenza vaccination exists. **Method:** We estimated the disease burden of influenza-like illness (ILI), influenza infection in the general adult population, and hospitalisations and deaths from pneumonia and influenza, from routine official and published sources, ad hoc community sample surveys, national virological surveillance, hospitalisation and mortality data. **Results:** In a resident population of 3 million people, there were 4.2 million cases of ILI in a typical non-epidemic year, 3.5 million visits to the doctor and 2.1 million days of work absence due to ILI. Data from the National Influenza Surveillance Programme indicated that about 15% of patients with ILI were positive for influenza isolates. We therefore estimated 630,000 cases of influenza virus infection cases a year, giving rise to 520,000 sick visits and 315,000 days of sick absence from work. About 4200 elderly (65+) persons were hospitalised for pneumonia and influenza, resulting in about 1450 deaths every year. The literature suggests a vaccine efficacy of about 50% of preventing influenza and its complications, including hospitalisations and deaths. This indicates that at least 315,000 cases of influenza virus infection, 258,000 sick visits, and 157,000 lost days from work in the whole population, and 2100 hospitalisations and 600 deaths from pneumonia in the elderly are potentially preventable by vaccination each year. **Conclusion:** Influenza poses a considerable burden of illness in the community and the potential benefits from influenza vaccination are substantial.

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Introduction

Influenza is a major cause of morbidity and mortality worldwide. Morbidity in the working age group gives rise to frequent doctor visits and considerable sickness absence from work. Influenza in the elderly population and in high-risk groups results in hospitalisations and deaths due to complications of pneumonia.

The primary preventive measure against influenza infection is annual vaccination with a trivalent inactivated vaccine.¹ The safety and efficacy of the influenza vaccine in the elderly and working populations has been demonstrated in case-control, cohort and randomised controlled studies.²⁻⁸ A recent meta-analysis estimated an overall vaccine efficacy of 56% of preventing influenza and its complications resulting in hospitalisation and death

in the elderly.⁹ The efficacy in preventing pneumonia, hospitalisation and death ranged from 50% to 68%. Several cost-effectiveness analyses of the use of influenza vaccine have demonstrated that influenza immunisation is cost effective;^{8,10,11} in some studies, cost savings were demonstrated. Annual influenza vaccination is recommended in many countries for all persons aged 65 years and older and for those who are at high risk of developing serious complications as a result of influenza infection.¹² Despite national health policy recommendations, the influenza vaccine is, however, under-utilised worldwide.¹³

In Singapore, no official uniform recommendation on influenza vaccination exists. Although the vaccine is now available in some health care facilities, there are no uniform recommended guidelines for its uses in specific population

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groups. Recommendation for a public health programme of influenza vaccination should be based on formal assessment of the health-care technology, using empirical data for informed decision-making. Epidemiological and health care utilisation data related to influenza are sparse and scattered. The objective of this study was to assess the burden of illness from influenza infection in Singapore. The burden of illness study should provide a basis on which better-informed decisions regarding the adoption of a vaccination programme can be recommended.

Materials and Methods

We estimated the total number of persons with influenza virus infection (influenza cases) in a year from estimates of the total number of upper respiratory infection (URTI) and influenza-like illnesses (ILI) using the following sources of data:

1. Routine official administrative and other published sources. These are:
 - a) Survey data extracted from the National One-Day Morbidity Surveys of Outpatient Care Providers in both the private and public sectors (i.e. private clinics and government polyclinics) which had been conducted in 1988 and 1993.^{14,15}
 - b) Administrative data from the most recent (1998) published reports of the Singapore Family Health Service of the Ministry of Health.¹⁶
 - c) National hospitalisation data from the Central Claims Processing System (CCPS) of the Ministry of Health which commenced data collection in 1991.
 - d) Mortality data from the Registry of Births and Deaths, National Registration Department, Singapore.¹⁷
 - e) Virological surveillance data from the National Influenza Surveillance Programme.^{18,19} In this programme, random throat swabs are routinely obtained at weekly intervals from patients with influenza-like symptoms attending 3 sentinel polyclinics (Clementi, Bedok and Ang Mo Kio) and influenza viruses were detected by isolation and/or immunofluorescence and serology at the Department of Pathology, Singapore General Hospital. The weekly number of attendances at government polyclinics for acute respiratory infections (URTI) and the percentage of respiratory specimens positive for influenza virus are monitored by the Quarantine and Epidemiology Department, Ministry of the Environment.¹⁹
2. Ad hoc data from community-based sample survey to estimate incidence of ILI in the adult general population conducted in 1999. An interviewer-administered, questionnaire-based survey was carried out from April

to June of 1998 (April to June being one of the two seasonal peaks in Singapore). The survey sample was a random, disproportionately stratified sample of 500 adults, aged 20 and above, from the electoral register for Bishan-Toa Payoh constituency. The sample was disproportionately stratified by age and ethnicity to enhance precision of estimates for age- and ethnic-specific rates. The response rate in the survey was 82% based on 410 responses. The questionnaire sought information on:

- i. demographic data,
- ii. systemic and respiratory tract symptoms of influenza within the past two weeks,
- iii. whether the symptoms required a visit to a doctor and, if so, how many, and
- iv. whether the symptoms caused absence from work and, if so, how many days of absence.

Definition of Illness

As actual respiratory illness due to influenza virus infection can only be serologically established, influenza defies precise clinical definition. The term “upper respiratory tract infection” (URTI) is used in both the National One-Day Morbidity Surveys and the Ministry of Health administrative data source to identify cases. It encompasses a range of acute symptomatic respiratory illnesses that are caused by pathogens other than influenza, such as coronaviruses, respiratory syncytial virus and adenovirus. A prospective study by Nicholson et al²⁰ on community-living elderly suggested that only 5 out of 179 episodes of acute URTI (3%) in the community were caused by the influenza virus. “Influenza-like illness” has been used as a more precise clinical term in some studies^{7,8} as it includes a higher proportion of influenza virus positive identification. A French prospective study of general practice patients with ILI identified 12% of isolates as positive for influenza A and 15% as positive for influenza B.²¹

For the community questionnaire survey, we adopted the definition of ILI as proposed by Campbell et al^{7,8} in their study of the cost effectiveness of the influenza vaccine in a healthy, working-age population. An ILI was defined as the occurrence of a respiratory illness of at least 2 days duration and one consisting of 1) at least one of the systemic symptoms of fever, chills or myalgia (muscle ache or pain); and 2) at least one of the following respiratory tract symptoms: coryza (stuffy or runny nose), sore throat, unusual cough or hoarseness.

Estimation of Influenza Infection

We derived and compared two separate estimates of the total yearly number of influenza infection in Singapore

using two different original sources of data (the routine published and ad hoc survey data). For the estimate based on ad hoc community sample survey data, we used the age-group specific two-week incidence of ILI to estimate the overall incidence rate corrected to the age distribution of the general population. Published estimates of the proportion of positive influenza A isolates in patients with influenza-like symptoms were used to derive an estimate of actual influenza infection.

Results

1. Population Estimates of ILI and Impact Using Published Data Sources

One-year estimates of doctor visits for URTI: The one-day morbidity survey of primary care doctors in 1993 showed that URTIs were the most common disease condition among all outpatient 'sick visits'. In adults above

15 years of age, they accounted for 36.3% of all 'sick visits'. This gives an estimated total of 5.4 million doctor visits and 1.97 million medical certificates of sick absences for URTI in a year. (Table I). In the 60+ years age group, 13.2% of all sick visits were for URTI, giving a total of about 220,000 doctor visits. The majority of visits (88%) took place in private general practice clinics: 4.78 million attendances, representing 37.7% of 'sick visits' and 45.7% of total medical certificates for sick absences (Table II). Government clinics handled 610,000 attendances for URTI (27.7% of all 'sick visits' and 45.9% of total medical certificates).

In 1997, the number of visits for URTI recorded in government Family Health Service clinics (polyclinics) was 536,673 (20.1% out of a total of 2,676,353 attendances). If the 1993 public-private sector proportions for URTI attendances have been maintained, this gives an estimate of 4.75 million doctor visits for URTI in 1997 for the whole of Singapore.

Combining these two sources of information, it is thus reasonable to estimate that about 5 million doctor visits and 1.8 million medical certificates of sick absences a year are made for URTI in Singapore.

One-year estimates of URTI and ILI episodes in the community: The majority of persons with URTI did not seek treatment from a health care provider. Ad hoc data from the community-based sample survey showed that only 38% of adults who experienced an episode of URTI symptoms sought treatment from a doctor. The total number of URTI illnesses in the community may therefore be estimated to be about 13 million. During seasonal peak periods in the year, about 48% of cases of URTI in the community may be expected to be cases of ILI (using data from the ad hoc community survey, see below). Assuming that two-thirds of the total yearly number of URTI episodes occur during 6 months in the year with two seasonal peaks, the total number of ILI in a year is estimated to be about 4.10 million. Data from the community survey indicated that for every 100 persons with ILI, 82 visits were made to the doctor and 50 days were lost from work. There are therefore approximately 3.36 million visits to the doctor

TABLE I: OUTPATIENT ATTENDANCES FOR UPPER RESPIRATORY TRACT INFECTION (URTI) BY SECTOR, ADULT AGE GROUPS, SEX AND RACE (1993)

	Sick attendances (millions)	Percentage with URTI	Attendances for URTI (millions)
Private GP clinics	12.69	37.7%	4.78
Government polyclinics	2.19	27.7%	0.61
Public & private sector	14.88	36.3%	5.40
Age group (y)			
15-24	2.38	42.1%	1.00
25-44	5.57	36.6%	2.04
45-59	2.11	21.5%	0.45
>60	1.65	13.2%	0.22
Sex			
Male	7.02	37.0%	2.60
Female	7.87	35.6%	2.80
Race			
Chinese	11.25	37.2%	4.19
Malay	2.08	34.9%	0.73
Indian	1.07	31.1%	0.33

Information in this table was derived from: Emmanuel S C, Tan B Y, Choo K W. 1993 morbidity survey of outpatients. Singapore Family Physician 1994; 20:75-91.¹⁵

TABLE II: MEDICAL CERTIFICATES (MC) GIVEN FOR UPPER RESPIRATORY TRACT INFECTION (URTI) BY SECTOR (1993)

	Total (sick and well) attendances (millions)	% of attendances given MCs	No. of attendances given MCs (millions)	% of MCs for URTI	Total no. of MCs for URTI (millions)
Private GP clinics	13.62	27.3%	3.72	45.7	1.70
Government polyclinics	2.97	19.8%	0.59	45.9	0.27
Public & private sector	16.58	26.0%	4.31	45.8	1.97*

* sum of number in private GP clinics and government polyclinics

Information in this table was derived from: Emmanuel S C, Tan B Y, Choo K W. 1993 morbidity survey of outpatients. Singapore Family Physician 1994; 20:75-91.¹⁵

and 2.05 million lost days of work due to ILI in the community each year.

2. Population Estimates of ILI and Impact Using Data From Community Survey Data

One-year estimates of ILI in the Community: Table III shows the results of the survey with stratum-specific incidences of ILI by age, race and sex. A total of 128 episodes of acute URTI were found among the survey subjects. Of these, 62 (48%) were ILI. The reported two-week incidence of ILI was 15.8 ILI episodes per 100 persons in adults (aged 20 years and above) in the Bishan-Toa Payoh constituency during the seasonal peak period from April to June in 1998. Among the elderly (aged 65+ years), the incidence was highest at 20 ILI episodes per 100 persons. An estimated 355,000 of the general population

could be expected to have an ILI over a two-week period during the April to June influenza season (Table IV).

Tables V and VI show the average number of visits to the doctor and the average work days absent for survey respondents who had ILI, by age group, over two weeks. There were an estimated 293,000 visits to the doctor and 179,000 days of work absence due to ILI over a two-week period in the April to June influenza season.

Given a two-week incidence of 15.8 ILI episodes per 100 persons (355,000 cases every fortnight) during the April to June period, and assuming two three-month influenza seasons a year, we estimated that there will be about (355,000 x 12) 4.26 million cases of ILI in a typical non-epidemic year. In the same manner, there will be an estimated yearly number of (293,000 x 12) 3.50 million visits to the doctor and (179,000 x 12) 2.15 million days of work absence.

Thus, combining the separate estimates from two different data sources, we have, in Table VII, the one-year estimates (million) of ILI in the community from routine and survey data sources. They are remarkably similar.

TABLE III: TWO-WEEK INCIDENCE OF INFLUENZA-LIKE ILLNESS (ILI) BY AGE GROUP, RACE AND SEX IN ADULTS AGED 20 YEARS AND OVER (BISHAN-TOA PAYOH SURVEY FROM APRIL TO JUNE 1998)

	No. of subjects	ILI episodes	ILI episodes per 100 (95% CI)
Age group (y)			
20-34	110	21	19.1 (11.7 - 26.4)
35-49	167	24	14.4 (9.0 - 19.7)
50-64	91	9	9.9 (3.8 - 16.0)
>65	35	7	20.0 (6.7 - 33.3)
Race			
Chinese	225	24	10.7 (6.6 - 14.7)
Malay	154	30	19.5 (13.2 - 25.7)
Indian	24	7	29.2 (11.0 - 47.3)
Sex			
Male	204	20	9.8 (5.7 - 13.9)
Female	201	41	20.4 (14.8 to 26.0)
Total	410	62	15.8 (11.7 - 18.6)*

* Standardised to the age distribution of the whole general population

The numbers do not add up to 410 due to missing data.

TABLE IV: ESTIMATED NUMBERS AND INCIDENCE IN THE SINGAPORE GENERAL POPULATION WITH INFLUENZA-LIKE ILLNESS (ILI) OVER A TWO-WEEK PERIOD FROM APRIL TO JUNE 1998

Age group (y)	ILI episodes per 100 adults	1998 mid-year Singapore adult resident population* (thousands)	Estimated population with influenza-like illness (thousands)
20-34	19.1	785.0	149.9
35-49	14.4	843.7	121.5
50-64	9.9	388.7	38.5
>65	20.0	225.9	45.2
Total	15.1†	2243.3	355.1

* Source: Department of Statistics, Singapore (1999)

† Incidence of ILI episodes per 100 adults adjusted to the age distribution of the 1998 mid-year Singapore adult resident population

TABLE V: NUMBER OF SURVEY RESPONDENTS WITH INFLUENZA-LIKE ILLNESS (ILI) AND ESTIMATED NUMBER OF PHYSICIAN VISITS FOR ILI IN THE SINGAPORE GENERAL POPULATION OVER A TWO-WEEK PERIOD FROM APRIL TO JUNE 1998

Age group (y)	No. of survey respondents with ILI	No. of physician visits	Average visits per person with ILI	Estimated population with ILI (thousands)	Estimated number of physician visits for ILI in population (thousands)
20-34	21	15	0.71	149.9	106.4
35-49	24	21*	0.88	121.5	106.9
50-64	9	5	0.56	38.5	21.6
>65	7	9*	1.29	45.2	58.3
Total					293.2

* Includes 1 subject with 5 or more visits. For calculation purposes, a conservative estimate of 5 visits has been used.

TABLE VI: NUMBER OF SURVEY RESPONDENTS WITH INFLUENZA-LIKE ILLNESS (ILI) AND ESTIMATED NUMBER OF CERTIFIED WORK-DAYS ABSENT FOR ILI IN THE SINGAPORE GENERAL POPULATION OVER A TWO-WEEK PERIOD FROM APRIL TO JUNE 1998

Age group (y)	No. of survey respondents with ILI	No. of days absent	Average days absent	Estimated population with ILI (thousands)	Estimated number of days absent for ILI (thousands)
20-34	21	16	0.76	149.9	113.9
35-49	24	12	0.50	121.5	60.8
50-64	9	1	0.11	38.5	4.2
> 65	7	0	0.0	45.2	0.0
Total				355.1	178.9

TABLE VII: ONE-YEAR ESTIMATES OF INFLUENZA-LIKE ILLNESS IN THE COMMUNITY FROM ROUTINE AND SURVEY DATA SOURCES

	Routine and published data sources (millions)	Ad hoc community survey data source (millions)
ILI episodes	4.10	4.26
Doctor visits	3.36	3.50
Days of work absence	2.05	2.15

3. Estimates of Influenza Virus Infection and its Impact

Data from the Ministry of Health influenza surveillance programme show that influenza A and B viruses were detected throughout the year with two peak periods in most years, during April to June and November to January/February. In most non-epidemic years, approximately 15% of specimens from polyclinic patients with ILI have been positive for influenza A virus and also for influenza B virus (although much less frequent) during the seasonal influenza peaks. This compares well with the data obtained in a French prospective study of general practice patients with ILI, in which 12% of isolates were positive for influenza A and 15% were positive for influenza B.²¹ During inter-nodal months, much lower rates of positive isolates were found. During the influenza season, isolates may be expected to be more selective for patients with ILI.

Using an average of 15% positive influenza isolates from government outpatient clinic surveillance of patients with ILI during peak seasons, we therefore estimated 630,000 cases of influenza virus infection cases a year, giving rise to 520,000 sick visits and 315,000 days of sick absence from work.

The literature suggests a vaccine efficacy of 50% to 60% of preventing influenza and higher estimates of efficacy in younger age groups. Using the conservative estimate of 50% efficacy, this implies there are at least 315,000 cases of influenza virus infection, or 258,000 sick visits, and 157,000 lost days from work that are potentially preventable each year.

4. Hospitalisations for Pneumonia in the Elderly (65+) Population

We obtained national data from the Central Claims Processing System of the Ministry of Health on the number of hospitalisations for pneumonia (ICD-9: 480-486) and influenza (ICD-9: 487) for the elderly population aged 65 years and over. These were obtained for the period 1991 to 1999, the years when such data became available. There were a yearly average of 4256 hospitalisations for pneumonia and 20 hospitalisations for 'influenza'. Based on the results of meta-analyses,⁹ about 50% of pneumonia hospitalisations could potentially be prevented by influenza vaccine. It may hence be estimated that about 2100 cases of pneumonia hospitalisations may be prevented by influenza vaccine in Singapore.

5. Deaths from Pneumonia and Influenza

Every year, less than 3 deaths are registered as influenza being the cause of death. Pneumonia is the fourth commonest cause of death in Singapore, with a mortality rate of 47 per 100,000 population. The yearly average number of pneumonia deaths in persons aged 65+ years in the recent 5 years period from 1995 to 1999 was 1456, representing about 80% of all pneumonia deaths (Registry of Births and Deaths, National Registration Department, Singapore). The pooled estimates from meta-analyses indicated that 40% of pneumonia deaths are preventable by vaccination. Hence, about 600 pneumonia deaths in the elderly could potentially be prevented by influenza vaccination.

Discussion

In developed countries, annual influenza vaccination is recommended for all elderly persons, those six months of age and older with chronic pulmonary, cardiovascular, renal, metabolic or immunosuppressive diseases, persons who are in contact with chronically ill patients, such as health care providers and home care providers, and residents of nursing homes and other chronic care facilities. In Singapore, and in other countries in the region, no official uniform recommendations have been made with regard to

influenza vaccination. Although the vaccine is available, it is not widely used. This has also been observed in many countries. In the US, for example, the rate of influenza vaccination among the elderly is only 42%,¹³ despite national recommendations for its use. Despite the growing literature evidence of the safety and benefits of influenza vaccination, there is continuing ambivalence in national recommendations on influenza vaccination in many countries. International variations^{22,23} in national recommendations for influenza vaccination are partly explained by uncertainties in the level of benefits expected in the elderly with different levels of risk, and differences in national reimbursement policy. Experience in Australia²⁴ have shown that a low level of influenza vaccine use has been persisting despite official recommendations and offer of free vaccine, largely reflecting the beliefs of the medical profession and the public about the efficacy and reactogenicity of the vaccine. On technical and practical grounds, the frequent emergence of new antigenic variants required that the vaccine be updated each year by close antigenic matching between the vaccine and the circulating strains, hence, the need for repeated annual vaccinations. However, this did not appear to be a major issue in preventing national bodies on immunisation to recommend influenza vaccination.

The potential benefits of influenza vaccination is based on published evidence of vaccine efficacy of 50% in preventing influenza and its complication from studies conducted in temperate countries in the West. There are very limited data of vaccine efficacy from studies in tropical countries. Data from such studies may be more relevant and useful to the present assessment. Also, in assessing the place of influenza vaccination in the population, one has to consider the importance of the disease in the population in terms of its economic and social impact. The costs of providing medical care for hospitalised patients with complications from influenza and the loss of productivity are the two main economic impacts of influenza. Western countries typically report that influenza results in 5 to 6 days of restricted activity, 3 to 4 days of disability in bed and 3 days of absenteeism from work or school.²⁵ About 50% of influenza episodes resulted in a visit to a doctor. In Singapore, however, the effects on doctor visits and sick absence from work are considerably more muted. This is not unexpected and has been frequently noted. Nevertheless, the social and economic costs of influenza are still considerable. The results of a randomised controlled trial of influenza vaccination in healthy working adults⁸ have shown considerable cost savings in direct and indirect costs. Nearly 86% of the net savings were due to productivity losses averted, while about 15% were due to direct savings in medical care costs. The degree to which

vaccination is cost effective or cost saving depends on the burden of the diseases, the vaccination rates achieved, pattern of health care use, the cost of the vaccine and the costs of treating influenza and its complications, including costs of hospitalisation. Although the same extent of cost saving does not apply to Singapore because of a different health care system and financing, increasing costs of health care and doing business will make this cost saving possibility more evident. The rapidly increasing proportion of the population who are over 65 years of age will also make this issue more deserving of close scrutiny.

The assessment of the burden of influenza in the elderly is not straightforward because severe complications following influenza infection, such as bacteria pneumonia, are often diagnosed well after the influenza virus has been cleared. It is well-known that many influenza-related hospitalisations and deaths are incompletely ascertained. Furthermore, the impact of influenza on hospitalisations and deaths in the elderly were under-estimated to the extent that only one direct complication, pneumonia, was considered, and hospitalisations and deaths due to other respiratory conditions, congestive heart failure or from all causes were ignored. For example, it has been shown that the vaccine effectiveness for preventing death from any cause among the elderly is as high as 70%.⁹

There are methodological limitations in deriving estimates of influenza virus infection in the present study. Given that influenza virus infection can only be serologically established, influenza defies precise clinical definition. The estimates of actual influenza infection were derived from two independent primary data sources: URTI consultations in primary care clinics and ad hoc survey of ILI in the community; as well as a number of assumptions based also on other published evidence, such as the proportion of positive influenza A isolates in patients with influenza-like symptoms. The different definitions from different published data sources and the survey data may influence the results of our estimation. In consideration of this, we have found that the one-year estimates of ILI in the community from routine and survey data sources were in fact remarkably similar. The ad-hoc community survey of 500 adults in the Bishan-Toa Payoh area was based on a random population sample taken during a specific time period from April to June, one of the two seasonal peaks in Singapore. In deriving our estimates of influenza infection, we have taken this into account, and adjusted for this accordingly. The sample response rate (82%) (including 'non-contactables', actual 'refusals' being less than 4%) was reasonably high. Data on the non-responders were available for 'housing types', and the non-responders in the survey were similar to the responders in terms of this characteristic. Also we think it is unlikely that for an illness

like influenza, there would be any social or other negative response bias in self-reports of symptoms in respondents and non-respondents. The two-week incidence rate of ILI in those aged 65+ years (20 ILI per 100 persons) was based on 7 cases out of 35 subjects, and as reflected by the 95% confidence intervals, was not precise. The combined estimate for those aged 50 to 64 and 65+ years was 12.7 (95% CI, 6.9-18.5), and is probably a more accurate reflection of the incidence rate in the older age group. In any case, the contribution by persons in the oldest age groups in terms of the total number of ILI cases in the whole population is small, and is over-shadowed instead by the number of actual cases of hospitalisations and deaths from pneumonia and other related causes of deaths.

In conclusion, taking into consideration the methodological limitations, assumptions and indirect estimates made in the study, influenza poses a considerable burden of illness in the community and the potential benefits from influenza vaccination are substantial.

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