INFLUENZA VACCINATION AMONG THE ELDERLY IN BANGKOK

Valaikanya Plasai[1], Somrat Lertmaharit[2], Ong-arj Viputsiri[2], Sathirakorn Pongpanich[1], Usa Panichpathompong[3], Veerachai Tarnmaneewongse[4], Florence Baron-Papillon[5] and Sunate Cheunkitmongkol[4]

[1]College of Public Health, [2] Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok; [3] Formerly at Sanofi Pasteur Ltd., Bangkok; [4] Sanofi Pasteur Ltd, Bangkok, Thailand; [5]Sanofi Pasteur, Lyon, France

Abstract. This study aimed to determine the effectiveness of influenza vaccinations among the elderly in Bangkok in reducing influenza-like illness (ILI) and influenza-related complications. Using a non-randomized, controlled, prospective methodology, healthy, active people aged 60 years or more, living in the Bangkok Metropolitan Administration (BMA) area, were studied. The two study cohorts comprised 519 persons in the vaccinated group and 520 in the non-vaccinated group. The outcome under study was influenza-like illness (ILI), as reported by the study volunteers. The two groups were comparable for most socio-demographic characteristics, except for gender, level of education, marital status, and smoking habit. The age range was 60-88 years (mean: 68 years). Females outnumbered males in both groups, with ratio of female to male of 2.6:1 and 1.9:1 in the vaccinated and non-vaccinated groups, respectively. The top three co-morbidities among these groups were hypertension, diabetes mellitus, and heart disease, in that order. Only 1% of the volunteers reported lung disease as co-morbidity. During the 12-month study period, a total of 107 volunteers reported ILI in both groups, with 38 persons in the vaccinated group and 69 persons in the non-vaccinated group. There were 46 ILI episodes in the vaccinated group, and 86 in the non-vaccinated group, for a total of 132 episodes. The incidence rates rates of influenza in this population, therefore, were 8.9% for the vaccinated and 16.9% for the non-vaccinated groups; with a reduction in the rate of reported ILI and doctor visits of 8%. Vaccine effectiveness was rated at 47.6%, crude risk ratio at 1.9 (1.33-2.75), and adjusted risk ratio at 1.92 (95% CI: 1.25-2.95), after adjustment for gender, marital status, education, and smoking habit. No complications due to ILI were observed in this population during the study period. Hospitalizations during this period were due to non-ILI related causes, such as cancer and accident.

INTRODUCTION

Influenza is largely a preventable disease that is still plaguing Thailand with economic losses due to illness and death. In 2003, morbidity due to influenza still ranked as the ninth leading cause of illness, with an incidence rate of 47.54 per 100,000 population in all age groups (Bureau of Epidemiology, 2004). Even though no death due to influenza was reported in that year, such morbidity may lead to economic loss and inflict unnecessary reduction in quality of life. Moreover, the incidence rate may reflect only severe cases, resulting in underestimation of the real situation (Simmerman *et al*, 2004).

Influenza vaccine has been proven to be safe and effective in preventing influenza-like illness (ILI) in various population groups (Anonymous, 1993; Mullooly *et al,* 1994; Nichol *et al,* 1994). The US CDC recommends such vaccination in adults aged 65 and over. Moreover, the American Academy of Family Physicians has now lowered the age for routine vaccination to 50 (Zimmerman, 1999). In Thailand, the age distribution of reported influenza cases revealed higher risk among the older age group, 55 and above (Simmerman *et al,* 2004). Despite this evidence and these current recommendations, most elderly Thais, a vulnerable population, are not vaccinated against influenza.

This study, therefore, aimed to determine the effectiveness of influenza vaccination among the elderly in Bangkok in reducing influenza-like illness (ILI) and influenza -related complications. Evaluation of the effectiveness and benefits of such vaccination among the elderly in Bangkok can support public health policy decisions concerning vaccination, and also help influence medical practice to better serve the aging population of Thailand.

MATERIALS AND METHODS

Sample size calculation used incidence rate at 5%, vaccine efficacy at 65%, with α at 0.5 (two-tailed test) and power of 80%, yielding a sample size of 474 in each study arm. Considering dropout rate of 5%, 520 volunteers in each arm was planned. in all, we enrolled 1,039 health, active adults (Canadian Center for Activity

Correspondence: Valaikanya Plasai, College of Public Health, Chulalongkorn University, Bangkok 10330, Thailand.
Tel: 66 (0) 2218-8199; Fax: 66 (0) 2255-6046
E-mail: valaikanya@yahoo.com

and Aging, 2004) aged 60 years and above in Bangkok, from the Elderly Co-ordination Centers (ECC) of the Bangkok Metropolitan Administration (BMA) were enrolled (519 vaccinated and 520 non-vaccinated). Exclusion criteria were egg allergy or allergy to any vaccine component; influenza vaccination within the previous year, or other vaccination within the previous 30 days; past history of Guillain Barre syndrome; or current immunosuppressive treatment. The studied product was trivalent split inactive influenza vaccine, given as a single dose at 0.5 ml (Vaxigrip®, Sanofi Pasteur). The virus strains were the southern strains, A/New Caledonia/20/99(H1N1)-like virus, A/Fujian/411/2002(H3N2)-like virus, and B/Shandong/7/99-like virus. The vaccination period was the last two weeks of May 2004. Outcome, ILI—Influenza-like illness, was defined as the occurrence of febrile illness lasting for 3.5 days, involving fever (higher than 38°C) for one day minimum and two or more of the following symptoms: chills, headache, runny nose, sore throat, cough, muscle aches, tiredness and weakness. The elderly volunteers were followed up every 30 days for 12 months for self-reported ILI symptoms. Those vaccinated were also followed on Day 7 for any adverse event. Binary logistic regression was employed in statistical analysis of the results to control for confounding.

RESULTS

In all, 515 volunteers in the vaccinated group, and 496 volunteers in the non-vaccinated group, remained with the study until its conclusion. The mean duration of follow-up in both groups of participants was

Table 1
Socio-economic characteristics of the study volunteers.

Characteristics	Vaccinated (n = 519)		Non-vaccinated (n = 520)		p-value[a]
	n	%	n	%	
Age (year)					p = 0.203
60-65	199	38.3	207	39.8	
66-70	165	31.8	140	26.9	
> 70	155	29.9	173	33.3	
Mean (SD)		67.9 (5.34)		68.3 (6.07)	
Gender					p = 0.039
Female	375	72.3	344	66.2	
Male	144	27.7	176	33.8	
Female: Male ratio		2.6: 1		1.9: 1	
Marital status					p < 0.001
Single	56	10.8	23	4.4	
Married	272	52.4	273	52.5	
Widowed	191	36.8	224	43.1	
Education					p < 0.001
No	82	15.9	19	3.6	
Primary school	345	66.8	395	76.0	
Secondary school	75	14.6	91	17.5	
Certificate	2	0.4	1	0.2	
University	11	2.1	14	2.7	
Not in system	1	0.2	0	0	
Missing data	4				
Current smoker					p = 0.002
Yes	37	7.1	67	12.9	
< 20 cigs/day	28		53		
≥ 20 cigs/day	6		12		
Unknown	3		2		
No	482	92.9	453	87.1	

[a] Chi-square test

similar: the NV group 11.72 months (min-max: 1-12); vaccinated group 11.96 months (min-max: 2-12).

Socio-demographic characteristics of the study population

The two groups were comparable for most socio-demographic characteristics, except for gender, marital status, level of education, and smoking habit. The volunteers in both groups were aged 60-88 years, with the non-vaccinated being slightly older, with a maximum age of 88, and mean age 68.3, while those of the vaccinated were 87 and 67.9 years. Their reported health status was also comparable, with about 40% of the volunteers in both groups having moderate health status, 25% good, and about 20% poor. The majority of the group also reported that health status had improved from last year, with only 30% or less reporting deteriorated health (Table 1). Over 65% of all volunteers reported having similar chronic health conditions, hypertension, diabetes mellitus, and heart conditions, in that order. Only one vaccinated and six non-vaccinated volunteers reported lung disease (Table 2).

The two study groups differed in four characteristics-gender, marital status, level of education, and smoking habit ($p<0.05$). Females outnumbered males in both groups. The gender ratios between the two groups were different; with a female to male ratio of 2.6:1 in the vaccinated group and 1.9:1 in the non-vaccinated group. This appearsed to be a normal characteristic of the study population, because females were more likely to visit the BMA's elderly clubs regularly for such activities as aerobic exercise.

Although half of each group (about 52% in both) were married, the volunteers in the non-vaccinated group were more likely to be single than those in the vaccinated group (4.4% versus 10.8%), and more were widowers (43.1% *vs* 36.8%).

Level of education was also significantly different in the two groups, although the majority of both groups reported having primary education, with 66.8% among the vaccinated, and 76.0% in the other, group. More volunteers in the vaccinated group reported having no education, with 15.9% compared with 3.6%, and fewer volunteers in the vaccinated group reported having secondary education, with 14.6% compared with 17.5%. The volunteers in the non-vaccinated group, therefore, appeared to have higher levels of education.

Smoking status and smoking habits also appeared to be different between the two study groups. The non-vaccinated group appeared to have more smokers, and smoked more cigarettes per day, with 12.9% in the non-vaccinated, compared to 7.1% in the vaccinated, group. The majority of smokers in both groups, almost 80% in

Table 2
Self-reported co-morbidity.

Co-morbidity	V (519)		NV (520)		
	No.	%	No.	%	p-value
No	167	32.2	176	33.8	
Yes	351	67.8	344	66.2	p = 0.628
Missing information	1	-	0	-	
Hypertension	197	38.1	178	34.4	p < 0.001
DM	112	21.8	111	21.4	p < 0.001
Heart disease	43	8.3	45	8.7	p < 0.001
Rheumatoid	24	4.6	30	5.8	NA
Allergy	17	3.3	8	1.5	NA
GI-tract disease	12	2.3	13	2.5	NA
Renal disease	2	0.4	4	0.8	NA
CVS	1	0.2	0	0	NA
Cancer	1	0.2	4	0.8	NA
Immunology	2	0.4	0	0	NA
Lung disease	5	1	6	1.2	NA
Others[a]	84	16.2	56	10.8	NA

Note: NA = Not available; [a] Mostly hyper-cholesterolemia

the non-vaccinated group and about 75% in the vaccinated group, reported smoking > 20 cigarettes per day. More of the non-vaccinated group also reported having ever smoked, witht 27.8% compared with 20.7%.

About 20% of the study population reported that they still earned an income, with 24.2% and 22.6% in the vaccinated and non-vaccinated groups, respectively.

Adverse events among those vaccinated

At day 7 post-vaccination, no serious adverse event was found among the vaccinated; only 18.7% of the vaccinated volunteers reported insignificant adverse events, mostly mild muscle aches, but they did not interfere with their normal course of life.

Reported ILI during the follow-up period (12 visits every 30 days)

During the follow-up period, 107 people reported having ILI, 38 vaccinated, and 69 non-vaccinated, with 132 total ILI episodes (vaccinated 46; non-vaccinated 86). Our study showed that vaccination is associated with a reduction in ILI, with incidence rates of 8.9% and 16.9% in vaccinated and non-vaccinated groups, respectively, with a reduction of ILI and doctor visits of 8%, and vaccine effectiveness at 47.6%. Our study shows a risk ratio of 1.9 (95% CI: 1.29-2.75). After adjusting for gender, marital status, education, and smoking habit, the adjusted risk ratio was 1.92 (95% CI: 1.25-2.95), Table 3.

The monthly distribution of the ILI cases is illustrated in Fig 1, with peak incidence for both groups during months 6-8, October-December 2004. No volunteer in either group reported hospitalization due to ILI or complications during the study period.

DISCUSSION

This study aimed to determine whether influenza vaccination is beneficial to the elderly in Bangkok in

Table 3
Attack rates, risk ratios and estimated vaccine effectiveness among the elderly in Bangkok, Thailand, 2005.

	V (519)	NV (520)	Total
No. of volunteers with ILI	38	69	107
ILI episodes	46	86	132
1 episode	32	56	88
2 episodes	4	10	14
3 episodes	2	2	4
4 episodes	0	1	1
Person-month	518.08	507.83	
Incidence rate (%)	8.9	16.9	
Reduction in rate of ILI and doctor visits (%)			8
Vaccine effectiveness (%)			47.6
Crude risk ratio (95% CI)			1.9 (1.33-2.72)
Adjusted risk ratio (95% CI)			1.92 (1.25-2.95)

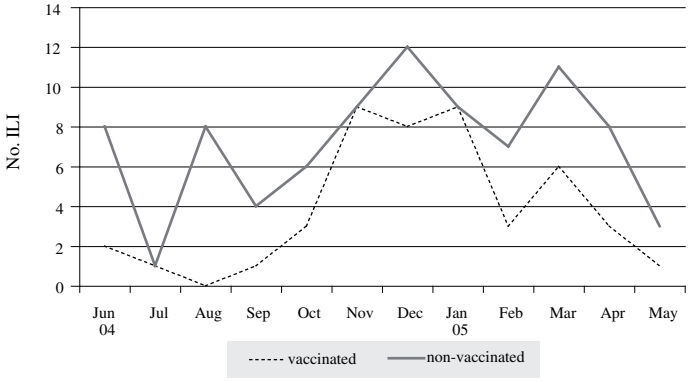

Fig 1- Distribution of ILI among the elderly in Bangkok, 2004-02005.

reducing influenza-like illness and influenza-related complications. This was a community-based research study, relying on volunteers' self-reporting of influenza signs and symptoms; serological determination was not performed. In general, the volunteers in the vaccinated and non-vaccinated groups were similar for age and co-morbidity, but differences were statistically significant for gender, marital status, education, and smoking habit.

ILI case distribution during the 12-month study period peaked between the months of October 2004 and January 2005, which coincided with the second and smaller peak of Thailand's seasonal distribution (Bureau of Epidemiology, 2004). It was also noted that during the months of June-October 2004, the normal influenza peak season in Thailand (Bureau of Epidemiology, 2004; Thawatsupha *et al,* 2005), there was less influenza activity among our volunteers. The reason for this variation requires further investigation by comparing our finding with the influenza seasonal distribution for the year 2003, as reported by the Bureau of Epidemiology of the Ministry of Public Health. A plausible explanation for this discrepancy may be that the influenza season for 2004 was several months later than the usual peak. This information, however, will be made public by the Bureau of Epidemiology in due course. Another probable explanation may be that our case distribution reflected the Bangkok situation, since our volunteers lived in Bangkok, while the Bureau of Epidemiology reports influenza cases for the whole country.

The results of this study showed that the non-vaccinated group was almost twice as likely to suffer ILI than the vaccinated. Binary logistic regression on age, gender, marital status, and smoking habit, showed no confounding effect. Influenza vaccination was also well-tolerated by the elderly, as they reported negligible adverse events, such as mild muscle aches, that did not interfere with their normal course of life. Vaccine effectiveness in our study was 47.6%. Our finding thus supports the report by Praditsuwan *et al* (2005). We therefore recommend vaccination against influenza as beneficial to the elderly living in the community. A policy to support this finding will enhance the well-being of those who receive vaccination.

In addition to this epidemiological report, we await results from the economic evaluation section of the study, to conclude whether vaccination among the elderly in Bangkok is cost-effective, for further policy recommendations.

ACKNOWLEDGEMENTS

We thank all of the elderly who volunteered to participate in this study for their valuable time and contributions. We wish to thank the health workers at all study sites for their time and efforts in data collection. Dr Wantanee Wattana, Dr Panrudee Manomaipibul, Dr Chatchai Wacharapruksadee and Dr Eiam Vimuttisunthorn of the Bangkok Metropolitan Administration are thanked for their kind advice, assistance and hospitality in the field. Professor Chaivej Nuchprayoon provided valuable comments and advice to the researchers during the initial phase of the study; we thank him for that.

REFERENCES

Anonymous. Final results: Medicare influenza vaccine demonstration: Selected states, 1988-1992. *MMWR Morb Mortal Wkly Rep* 1993;42:601-4.

Bureau of Epidemiology, Ministry of Public Health, Thailand, 2004. Annual summary of surveillance for 2003. [Cited 2006 Apr 6]. Available from: URL: http://epid.moph.go.th/dssur/respir/influenza.htm

Canadian Center for Activity and Aging. About the active living coalition for older adults. [Cited 2004 Apr 1]. Available from: URL:www.uwo.ca/actage/proceedings

Mullooly JP, Bennett MD, Hornbrook MC, *et al*. Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintenance organization. *Ann Intern Med* 1994;121:947-52.

Nichol KL, Margolis KL, Wuorenma J, von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med* 1994;22:778-84.

Simmerman JM, Thawatsupha P, Kingnate D, Fukuda K, Chaising A, Dawell SF. Influenza in Thailand: a case study for middle income countries. *Vaccine* 2004;23:182-7.

Thawatsupha P, Chittaganpit M, Waicharoen S. Identification and seasonal distribution of influenza virus strains in Thailand: January 2001-September 2003. January 2001-September 2003. [Cited 2006 Jan 10]. Available from: URL:www.cdc.gov/ncidod/global/ieip/pdf/flu-nih_iceid04.pdf

Zimmerman RK. Lowering the age for routine influenza vaccination to 50 years: AAFP leads the nation in influenza vaccine policy, *American Family Physician* 1999;60:2061-70.