

# The Efficacy and Effectiveness of Influenza Vaccination among Thai Elderly Persons Living in the Community<sup>+</sup>

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+ This study was financially supported by the National Research Council of Thailand. Influenza vaccines used in this study were supported by Aventis Pasteur (Thailand) Ltd.

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**Objective:** To determine the efficacy and cost-effectiveness of influenza vaccination in the Thai elderly living in an urban community.

**Material and Method:** The study design was a stratified, randomized, double blind, placebo-controlled trial. A total of 635 participants aged 60 years and older living in an urban community was randomized to receive an influenza vaccine or tetanus toxoid as a placebo injection. All participants were followed up 4-6 weeks in the community for influenza-like illness and treatment received, hospitalization and death for one year. A hemagglutination inhibition (HI) test for influenza virus antibody of all participants was done on the day of vaccination as well as 1 month, 5 months, and 12 months after the vaccination. Main outcome measures were immune response rate and protective titer, influenza-like illness, serological influenza, treatment received for influenza-like illness and their expenses, hospitalization and death during the study period.

**Results:** The immune response rate of vaccinations was 97.1% and protective titer for A (H1N1) and A (H3N2) strains were 96.4 and 98.6%, respectively. The incidence of influenza-like illness was 4.83% in the vaccine group compared with 10.88% in the placebo group. The relative risk reduction was 56% (95%CI = 14 to 77%). The survival analysis also showed that vaccinations significantly reduced the incidence of influenza ( $p = 0.009$ ). The number needed to prevent one episode was 17 persons (95%CI = 9 to 71 persons). The adverse reactions of vaccinations were mild and tolerable. However, the number of treatments received for influenza-like illness and their cost were not significantly different between the two groups. None of the subjects had pneumonia nor needed hospitalization during the study period. Seven participants died during the year of follow up, but not from influenza.

**Conclusion:** In Thai elderly living in the community, influenza vaccination reduced the incidence of influenza-like illness by half, but not the number of treatments received for influenza-like illness, their cost, and its serious complications. In the year of the study, considering the cost of vaccines and the numbers needed to prevent one episode of infection from the provider's viewpoint, it may not be cost-effective to recommend that all Thai older persons living in the community should receive influenza vaccination annually. Vaccination recommendation for the elderly should be promptly implemented in expectation of a severe epidemic in Thailand.

**Keywords:** Influenza, Vaccine, Elderly, Efficacy, Cost-effectiveness

**J Med Assoc Thai 2005; 88(2): 256-64**

**Full text. e-Journal:** <http://www.medassocthai.org/journal>

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Influenza is one of the major causes of illness, suffering, and death in the elderly. Individuals aged 65 years or older are particularly susceptible to the complications of influenza such as pneumonia and the exacerbation of underlying medical conditions such as chronic heart and lung diseases<sup>(1,2)</sup>. However, influenza vaccines have been consistently found to be safe and effective in preventing influenza in Western countries. For example, a randomized double-blind placebo-controlled trial<sup>(3)</sup> showed that influenza vaccination reduced the incidence of influenza in elderly persons living in the community by 50%. Another three-year cohort study<sup>(4)</sup> revealed that vaccination against influenza reduced the rate and cost of hospitalization and deaths from influenza and its complications in the elderly citizens. A meta-analysis of influenza vaccination in older persons<sup>(5)</sup> showed similar findings. From the above evidence, annual influenza vaccination for the elderly has long been recommended by the Advisory Committee on Immunization Practices of the US Public Health Service<sup>(6)</sup> and the American College of Physicians<sup>(7)</sup>. The World Health Organization<sup>(8)</sup> has also suggested that elderly individuals be targeted for immunization.

There has been scarce information regarding influenza in Thailand. Thawatsupha, et al<sup>(9)</sup> surveyed adult patients with acute respiratory infection in Bangkok between 1988-1995, which showed 588 influenza isolates from 2,733 throat swab specimens collected. They also found that influenza occurred mostly in the rainy season, compared with winter in Western countries. No data to date has been reported regarding the prevalence and severity of influenza in Thailand as well as the efficacy of vaccination in the Thai elderly. In addition, influenza vaccines have been launched in this country and promoted to be prescribed for the older persons since 1997; therefore, it is important to know the efficacy and cost-effectiveness of vaccinations among Thai elderly.

The authors conducted a randomized double-blind placebo-controlled trial to determine the efficacy and cost-effectiveness of influenza vaccination among Thai elderly living in the community. The authors also took particular interest in the adverse reactions and immune responses after vaccination, using both clinical and serological outcome parameters.

#### **Material and Method**

A stratified randomized double-blind placebo-controlled study was conducted from February 1998 to May 1999. All persons aged 60 years or older (n =

635), living in 6 urban communities within 10 km around Siriraj Hospital, Bangkok, who were capable of self-care and could walk outside their houses, were invited to enter the trial. Exclusion criteria included previous adverse reactions to influenza vaccination, allergy to eggs or egg protein, known cancer or other immunocompromised states such as regularly taking corticosteroids or chemotherapeutic agents. The demographic data such as age, sex, educational level, income, body mass index (body weight in kg/height in m<sup>2</sup>) of all participants were collected prior to the vaccinations. Informed consents were explained and signed. The protocol was approved by the Ethics Committee on Human Rights involving Human Research, Faculty of Medicine, Siriraj Hospital, Mahidol University.

#### **Randomization and vaccination**

All participants were stratified based on their ages as young-old (age 60-69) and old-old (age 70 or older), and their health status as low risk (no underlying disease) and high risk (history and physical examination by an experienced geriatrician (RP) compatible with chronic heart disease, chronic pulmonary disease, diabetes mellitus or chronic renal disease). Hence, the participants were divided into the following 4 categories: young-old/low risk, young-old/high risk, old-old/low risk, and old-old/high risk. In each stratum, each individual was numbered consecutively. These numbers had been previously randomized to the vaccine group or placebo group equally. At the vaccination session, from April to May, 1998, the name and number of each participant were identified. Then, the participant received an intramuscular injection of influenza vaccine or placebo in the deltoid muscle according to the previously randomized identification number. The processes of checking the identification number and vaccine or placebo were performed solely by a nurse who did not participate in the follow-up of these participants.

The vaccine used was the purified trivalent split-virus vaccine (Vaxigrip<sup>R</sup>) manufactured by Pasteur Merieux, Lyon, France. Each dose (0.5 ml) contained influenza A/Johannesburg/82/96(H<sub>1</sub>N<sub>1</sub>), A/Nanchang/993/95(H<sub>3</sub>N<sub>2</sub>), and B/Harbin/7/94, all with 15 µg of hemagglutinin. These vaccine antigens were in accordance with the recommendation of the World Health Organization. A 0.5 ml of tetanus toxoid was used as the placebo.

After the vaccine or placebo injection, each participant was provided a pre-stamped mailing card

to record adverse reactions to the vaccine or placebo injected. These cards were returned to the researchers by mail one week after injection.

### **Follow-up**

Upper respiratory tract infection (URI) was defined as a mild fever with upper respiratory tract symptoms. The diagnostic criteria for influenza-like illness modified from the Dutch Sentinel included an acute onset, high fever severe enough to cause the participant to rest in bed for more than 24 hours and at least three of the following symptoms: coughing, coryza, sorethroat, frontal headache or myalgia. A questionnaire regarding possible influenza episodes and the upper respiratory tract symptoms experienced was sent to each participant every 6 weeks. Participants were asked to fill out and return these questionnaires. The researchers went to visit all the participants in their communities at 4 weeks, 5 months and one year after vaccination. On these visits, relevant symptoms of respiratory illness, their treatments and outcomes during the past period also were rechecked. This information was analyzed by researchers blinded to vaccination status.

### **Blood tests**

A 10 ml of venous blood was taken from each participant at the time of the vaccine or placebo injection ( $B_1$ ), at 4 weeks ( $B_2$ ), 5 months ( $B_3$ ) and one year after the injection. These blood samples were tested for influenza antibody titer by means of the hemagglutination inhibition (HI) test. The influenza virus strains of the vaccine were used for the titrations. The titer was defined as the reciprocity of the highest dilution which gave a positive reaction. A fourfold titer increase in convalescent serum compared with acute serum was considered as the criteria of serological influenza. The response rate was defined as the percentage of participants who showed at least fourfold HI titer increase of  $B_2$  compared with  $B_1$ . Protective titer was defined as HI titer of each influenza strain  $\geq 40$ . The protection rate meant the percentage of participants whose HI titer of any blood samples  $\geq 40$  after vaccination was compared with vaccinated participants.

### **Statistical analysis**

The authors estimated that a sample of 500 people would give an 85 percent chance of detecting a reduction of 50% in outcome events among influenza-vaccine recipients. From these calculations, it

was assumed that the prevalence of influenza was 20 percent of all upper respiratory infections, an event rate of once yearly among unvaccinated participants, and a two-sided alpha level of 0.05.

Students' t-test and chi-square test were used to conduct bivariate analyses of continuous and categorical data. The efficacy of vaccination against influenza was expressed in terms of relative risk (RR) and was tested by chi-square test. The reduction of relative risk among vaccinated participants was calculated as follows: relative risk reduction =  $(1 - \text{relative risk} \times 100 \text{ percent})^{(12)}$ . Kaplan-Meier's survival analysis was used to analyze the study outcome with control for potential biases from loss to follow-up data. Cost savings associated with vaccinations were calculated from the real cost of treatment for respiratory illnesses.

### **Results**

The characteristics of the study population are shown in Table 1. The vaccine and placebo groups were statistically similar regarding age, sex, education, income, body mass index (BMI), underlying diseases, and protective antibody titer before vaccination. Serological data were incomplete for 87 participants due to unavailability for follow-up, especially at 4 weeks after vaccination. The number of dropouts was also similar between the vaccine and placebo groups. Participants with incomplete samples were retained in the analysis whenever possible. The participants returned 605 questionnaires regarding adverse effects (95.28%) at 1 week, 507 questionnaires (79.84%) at 4 weeks, 508 questionnaires (80.0%) at 5 months, and 511 questionnaires (80.47%) at 12 months.

The response rate at 4 weeks after vaccination (Table 2) was significantly higher in the vaccine group than in the placebo group. The response rate did not change when comparing the two groups for variables, such as age, sex, educational level, income, body mass index (BMI), underlying diseases, age-health status categories and protective antibody titer before vaccination.

Protective titer (HI titer at least 40) of participants in the vaccine group throughout the study period is shown in Table 3. The protective titers for influenza A/Nanchang and A/Johannesburg were persistently high, 88.1% and 80.6%, respectively, at one year after vaccination; however, the titer for influenza B/Harbin dropped faster. The protective titer of four groups of participants stratified according to age-health status categories were also in the statistically similar pattern.

**Table 1.** Baseline characteristics of the study participants

Subgroup	Vaccine group (n = 330) No. (%)	Placebo group (n = 305) No. (%)	p-value
Age (years):			
mean $\pm$ SD	68.22 $\pm$ 6.38	68.09 $\pm$ 6.89	0.78
median (range)	67 (60-89)	66 (60-87)	
Sex,			
male:female	124:206	113:192	0.72
Education:			
none	82 (24.8)	59 (19.3)	0.92
1-7 years	216 (65.5)	212 (69.6)	
8-13 years	15 (4.5)	16 (5.3)	
>13 years	4 (1.2)	3 (1.0)	
Income:			
insufficient	87 (26.4)	92 (30.2)	0.41
sufficient-rich	228 (69.1)	198 (65.0)	
no data	15 (4.5)	15 (4.9)	
Body mass index <sup>†</sup> : mean $\pm$ SD	23.88 $\pm$ 4.45	23.94 $\pm$ 4.88	0.88
Age-health status categories:			0.994
young-old/low risk	166 (50.3)	148 (48.5)	
young-old/high risk	60 (18.2)	56 (18.4)	
old-old/low risk	78 (23.6)	74 (24.3)	
old-old/high risk	26 (7.9)	27 (8.8)	
Diseases:			
chronic heart disease	33 (10.0)	19 (6.2)	0.11
chronic pulmonary disease	20 (6.1)	18 (5.9)	1.00
diabetes mellitus	40 (12.1)	49 (16.1)	0.19
chronic renal disease	3 (0.9)	5 (1.6)	0.49
Prevaccinated protective titer against*	n = 269	n = 239	
A/Johannesburg/82/96 (H <sub>1</sub> N <sub>1</sub> )	127/269 (47.2)	126/239 (52.7)	0.73
A/Nanchang/993/95 (H <sub>3</sub> N <sub>2</sub> )	109/269 (40.5)	95/239 (39.7)	0.48
B/Harbin/7/94	11/269 (4.1)	10/239 (4.2)	1.00

<sup>†</sup> BMI = Weight/(Height in Metre)<sup>2</sup>, \* total number of serological data available at 4 weeks and 5 months of study

**Table 2.** Response rate at 4 weeks after vaccination

Subgroup	Vaccine group (n = 277)* No. (%)	Placebo group (n = 261)* No. (%)	p-value
No response to any antigens	8 (2.9)	245 (93.9)	0.00
Response to 1 strain of antigens	148 (53.4)	12 (4.6)	0.00
Response to all 3 strains of antigens	121 (43.7)	4 (1.5)	0.00

\* total number of data available participants

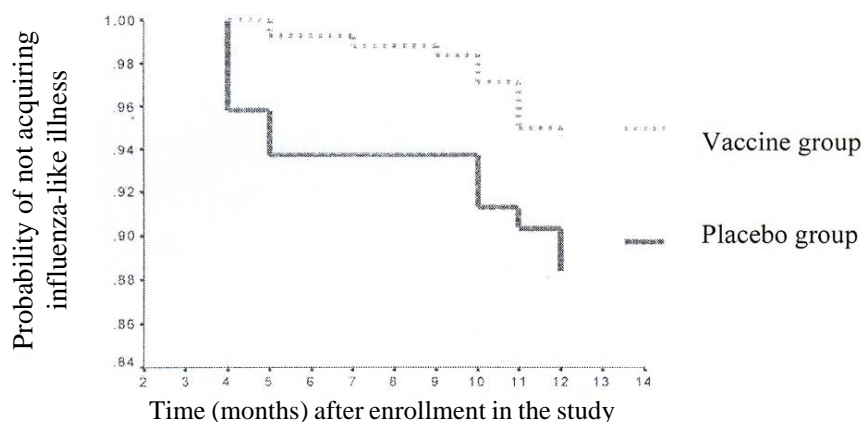
**Table 3.** Protective titer of participants in the vaccine group during the study period

	Baseline HI titer $\geq$ 40 (n = 282)* No. (%)	4 weeks HI titer $\geq$ 40 (n = 277)* No. (%)	5 month HI titer $\geq$ 40 (n = 268)* No. (%)	1 year HI titer $\geq$ 40 (n = 252)* No. (%)
A/Johannesburg (H <sub>1</sub> N <sub>1</sub> )	127 (45.0)	273 (98.6)	255 (95.1)	222 (88.1)
A/Nanchang (H <sub>3</sub> N <sub>2</sub> )	109 (38.7)	267 (96.4)	238 (88.8)	203 (80.6)
B/Harbin	11 (3.9)	134 (48.4)	70 (26.1)	39 (15.5)

\* total number of data available participants

Influenza-like illness diagnosed according to the modified Dutch Sentinel Stations had a statistically significant lower incidence in the vaccine group than in the placebo group between 1 and 5 months

after vaccination. Kaplan-Meier survival analysis confirmed the difference of influenza-like illness between the two groups in the same period ( $p = 0.009$ ) as shown in Fig. 1.



**Fig. 1** Probability of not acquiring influenza-like illness over the study year estimated by the Kaplan-Meier survival analysis. Significant difference ( $p = 0.009$  by log-rank test) comparing this probability between the vaccine and placebo groups

The total number of influenza-like illnesses in the study period (Table 4) was 13 episodes in 269 data available participants of the vaccine group (risk of influenza-like illness with vaccination was 4.83%), compared with 26 episodes in 239 data available participants of the placebo group (risk without vaccination was 10.88%).

Absolute risk reduction between the two groups was calculated at 10.88-4.83% or 6.05%. Relative risk (RR) or risk with vaccination divided by risk without vaccination calculated was 4.83/10.88 or 0.44. Relative risk reduction (RRR) or  $(1 - \text{relative risk}) \times 100\%$  was 56% (95% CI, 14-77%). The number needed to treat (NNT) was calculated at 17 participants (95% CI, 9-71 participants).

**Table 4.** Episodes of influenza-like illness and total upper respiratory tract infection (URI) after vaccination during the study period

	Vaccine group (n = 269)* No. (%)	Placebo group (n = 239)* No. (%)	p-value
<b>At 4 weeks:</b>			
Influenza-like illness	0	0	-
Total URI	1 (0.4)	2 (0.8)	0.49
<b>Between 1-5 months:</b>			
Influenza-like illness	2 (0.7)	16 (6.7)	0.001
Total URI	75 (27.9)	43 (18.0)	0.019
<b>Between 5-12 months:</b>			
Influenza-like illness	11 (4.1)	11 (4.6)	0.97
Total URI	65 (24.2)	57 (23.8)	0.79

\* total number of data available participants

Subgroup analysis according to age-health status categories showed that only participants of the vaccine group in young-old/low risk category, but not those of the other categories, developed less influenza-like illnesses than those of the placebo group in the study period significantly (6 vs 16 episodes,  $p=0.009$ ).

The number of treatments participants received or influenza-like illnesses from the medical clinics and hospitals during the study period was not different between the two groups. The total expenses of influenza-like illnesses were 4,660 and 4,650 Baht for the vaccine and placebo groups, respectively. The total expenses of total URI were 12,885 and 9,060 baht for the vaccine and placebo groups, respectively. Both total expenses for influenza-like illnesses and total URI were not statistically different between the two groups. None of the participants had pneumonia nor needed hospitalization during the study period. Four participants from the vaccine group and three participants from placebo group died with symptoms not related to influenza.

The total number of serological influenza was 7 episodes from 277 data available specimens of the vaccine group, compared with 19 episodes from 265 data available specimens of the placebo group.

The risks of serological influenza with and without vaccination were 2.5% and 7.2%, respectively. The relative risk reduction calculated by the same method was 65% (95% CI, 16-85%)

The adverse reactions of vaccination (Table 5) were not different between the two groups. The number of reactions was small and the adverse events were mild.

**Table 5.** Adverse reactions of vaccination

	Vaccine group (n = 315)* No. (%)	Placebo group (n = 290)* No. (%)	p-value
Systemic reactions			
Fever	16 (5.1)	20 (6.9)	0.46
Generalized rash	14 (4.4)	13 (4.5)	1.00
Local reactions			
Localized swelling	11 (3.5)	22 (7.6)	0.44
Pain	13 (4.1)	15 (5.2)	0.69
Itching	7 (2.2)	13 (4.5)	0.19

\* total number of data available participants

## Discussion

In this stratified, randomized, placebo-controlled study the authors found that among the Thai elderly people living in the community, vaccination against influenza was associated with a high serological response rate and less frequent influenza-like illness. However, the cost of treatment for the illness was not different between the two groups. None of the participants had pneumonia nor needed hospitalization during the period of study.

The response rate of influenza vaccines in the present study was very high (97.1%) compared with the rate of 16-85% from the study by Beyer et al<sup>(13)</sup>. The authors also found that the degree of serological response for A (H<sub>1</sub>N<sub>1</sub> and H<sub>3</sub>N<sub>2</sub>) and B subtypes was correlated with the prevaccination antibody levels, which was different from the previous study<sup>(13)</sup>. The high protective titers of influenza A (H<sub>1</sub>N<sub>1</sub> and H<sub>3</sub>N<sub>2</sub>) at 1 month in this study (98.6% and 96.4% respectively) were comparable to the findings from previous studies<sup>(13,14)</sup>. The authors also found that the response rate of the B/Harbin antigen was significantly lower than those of influenza type A. The probable explanation for this result is the lower prevaccination antibodies and the intrinsic properties of the B/Harbin antigen in the vaccine. The seroprotection persisted at a high rate (88.1% and 80.6% for influenza A subtype H<sub>1</sub>N<sub>1</sub> and H<sub>3</sub>N<sub>2</sub>, respectively) 1 year after vaccination. It could be concluded from the results of the present study that the immune response after an influenza vaccination once a year (at least for influenza type A) is satisfactory in the elderly, which is consistent with the recommendation from Western countries<sup>(6,7)</sup>.

From the present study, the response rate of influenza vaccination did not correlate with age nor

nutritional status, which was different from previous reports<sup>(15-18)</sup>. However, the finding of a high response rate to vaccines which was not affected by chronic disease, such as chronic heart, pulmonary and renal disease or diabetes mellitus, was similar to the study by Gross, et al<sup>(19)</sup>.

The present study showed that participants in the vaccine group had significantly fewer influenza-like illnesses than those in the placebo group, especially during 1-5 months after vaccination. This finding was confirmed by a significant difference between the two groups in Kaplan-Meier's survival analysis. Relative risk reduction of the vaccine group in this study was 56%, which was rather high compared with previous studies in which the efficacy in the elderly ranged from 30 to 50%<sup>(3,4,20)</sup>. The result of relative risk reduction of serological influenza confirmed the high efficacy of vaccinations. This high efficacy is most likely explained by the good immune response of these participants after vaccination and the close relation between the endemic viruses and the strains of viruses used in vaccines. Although the reported influenza-like illnesses in the present study largely depended on the cooperativeness and recall of elderly participants on events during past months and the diagnoses were not confirmed by throat swab cultures, the rigid clinical diagnostic criteria and the process of randomization made this statistical difference likely.

The present study could not demonstrate the benefit of vaccinations in the reduction of influenza complications, such as pneumonia, congestive heart failure, hospitalizations, and mortality rate, which was different from the previous studies<sup>(4,21-24)</sup>. These findings could be explained by the fact that the study year was not during an epidemic influenza period and the severity of influenza infection was low in Bangkok during the study period. The similar average expenses of treatment between the two groups in the present study may also be explained by the fact above.

The adverse reactions to influenza vaccines in the present study were mild and comparable to those tetanus toxoids used as placebo. These findings were different from previous works<sup>(25,26)</sup>, which reported local and systemic side effects as high as 17.5-20% and 5.7-11%, respectively. The low reactions may be partly explained by the method of data gathering from mailing cards, in which participants tended to ignore mild reactions and report only severe ones.

From the present findings, the number needed to treat was calculated at 17 persons (95% CI = 9-71 persons). In 1998, the estimated annual vaccination

cost of each participant was 248.40 baht. Thus, the authors need to spend 4,222.80 baht to reduce one episode of infection, which is higher than the average expense of each participant in the present study. In addition, if all participants in the placebo group were vaccinated, the total vaccination cost would be 75,762 baht. Compared with the total expense of the placebo group in the present study (4,650 baht), it may not be cost-effective to recommend that all older persons living in the community have influenza vaccinations annually.

The strengths of the present study include the use of the stratified, randomized, double-blinded, placebo-controlled method, which resulted in comparable baseline characteristics and the findings of immune response and the incidence of influenza-like illnesses between the vaccinated and unvaccinated participants. Moreover, the authors chose the months of April and May, which were prior to the rainy season, to have all older participants vaccinated. This period of the year would be the best time to induce an immune response from the vaccinated participants before they were infected<sup>(6)</sup>.

The limitation of the present report includes firstly, the design to study the older participants in urban areas, where many of them were unavailable to follow-up, resulting in incomplete information. However, the number of participants recruited in the present study was 20% more than the sample size calculated. In addition, the number of dropouts and their baseline characteristics in the two groups were not significantly different. Secondly, the process of data collection needed the cooperation and recall of events during the past months from the older participants. However, in the present study the authors chose to collect information by mailing questionnaires and telephone calls every 6 weeks, which would overcome this problem. Thirdly, the lack of throat swab culture to confirm diagnosis of influenza-like illness may result in both false-positive and false-negative diagnoses. However, the rigid clinical diagnostic criteria may reduce this flaw, at least partly.

In conclusion, influenza vaccination is highly efficacious for Thai elderly living in the community in terms of immune response induction and reduction of the incidence of infection by half. However, influenza infection in the older people during the period studied did not cause serious complications or death. Considering the cost of vaccines and the number needed to prevent one episode of infection from the provider's point of view, it may not be cost-effective to recom-

mend that every Thai elderly living in the community should have an influenza vaccination annually. Vaccination recommendation for the elderly should be promptly implemented in expectation of a severe epidemic in Thailand.

#### Acknowledgements

The authors wish to thank the people in Taling Chan, Bangkok Noi, Bangkok Yai, Bang Phlat, Phasi Charoen, and Khlongsan who wholeheartedly participated in the present study, all the elderly people and their relatives as well as the heads and secretaries of the communities.

The authors wish to thank Dr. Wichai Chattanavaree and Ms. Anjana Klangkaew for their assistance in performing the present study, Mr. Suthipol Udompanturak for the statistical analysis, and Ms. Pichavadee Sae-ung for preparation of this manuscript. We also thank the Dean of the Faculty of Medicine, Siriraj Hospital, and especially Prof. Dr. Khun Nanta Maranetra who continually gave invaluable support, and finally to all who are not mentioned here, but contributed in both small and large ways to the success of the present study.

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## ประสิทธิภาพและประสิทธิผลของการฉีดวัคซีนป้องกันโรคไขหวัดใหญ่ในผู้สูงอายุไทยในชุมชน

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**วัตถุประสงค์:** เพื่อศึกษาประสิทธิภาพ ประสิทธิผล และผลข้างเคียงของการฉีดวัคซีนป้องกันโรคไขหวัดใหญ่ให้แก่ผู้สูงอายุในชุมชน

**วัสดุและวิธีการ:** การศึกษานี้เป็นแบบ stratified, randomized, double-blind, placebo-controlled study โดยทำการศึกษาในผู้สูงอายุไทยในชุมชนรอบ รพ.ศิริราช จำนวน 635 คน แบ่งเป็น 2 กลุ่ม คือ กลุ่มศึกษา 330 คน ได้รับวัคซีนป้องกันโรคไขหวัดใหญ่ และกลุ่มควบคุม 305 คน ได้รับ tetanus toxoid ได้ทำการเจาะเลือดตรวจหา influenza antibody ก่อนฉีดวัคซีน และติดตามเจาะเลือดตรวจหา influenza antibody หลังฉีดวัคซีนครบ 1, 5 และ 12 เดือน โดยวิธี haemagglutination inhibition (HI) test ได้ติดตามสอบถามอาการของโรคไขหวัดใหญ่ตามเกณฑ์ทางคลินิก การรักษาที่ได้รับ การรับไว้รักษาในโรงพยาบาลและค่าใช้จ่ายที่เกี่ยวข้องกับการรักษาทางจดหมาย และโทรศัพท์ โดยผู้สอบถามซึ่งไม่ทราบถึงชนิดของวัคซีนทุก 4-6 สัปดาห์

**ผลการศึกษา:** การตอบสนองต่อวัคซีนป้องกันไขหวัดใหญ่ เมื่อได้รับการฉีดวัคซีนครบ 1 เดือนอยู่ในเกณฑ์สูงมาก ถึงร้อยละ 97.1 และระดับ protective titer ต่อเชื้อไวรัสสายพันธุ์ A (H<sub>1</sub>N<sub>1</sub>) และ A(H<sub>3</sub>N<sub>2</sub>) สูงถึงร้อยละ 96.4 และ 98.6 ตามลำดับ อุบัติการณ์ของโรคไขหวัดใหญ่ในผู้สูงอายุของกลุ่มควบคุมเท่ากับร้อยละ 10.88 ในขณะที่อุบัติการณ์ในกลุ่มศึกษามีเพียงร้อยละ 4.83 relative risk reduction เท่ากับ 56% (95% CI = 14-77%) และยืนยันจาก survival analysis ว่ากลุ่มศึกษามีอัตราการไม่เป็นไขหวัดใหญ่สูงกว่ากลุ่มควบคุมอย่างชัดเจน (p = 0.009) ผลข้างเคียงจากการฉีดวัคซีนป้องกันไขหวัดใหญ่ มีน้อยและไม่รุนแรง ซึ่งไม่ต่างจากกลุ่มควบคุม อย่างไรก็ตามไม่มีผู้สูงอายุรายใดเป็นโรคปอดอักเสบ หรือ เสียชีวิตเนื่องจากสาเหตุซึ่งเกี่ยวกับโรคไขหวัดใหญ่ รวมทั้งพบว่าจำนวนครั้งของการรักษาตนเองด้วยวิธีต่าง ๆ และค่าใช้จ่ายที่เกี่ยวข้องในผู้สูงอายุทั้ง 2 กลุ่มไม่แตกต่างกัน

**สรุป:** การฉีดวัคซีนป้องกันโรคไขหวัดใหญ่ ให้แก่ผู้สูงอายุไทยซึ่งอาศัยในชุมชน ช่วยลดอุบัติการณ์ของโรคไขหวัดใหญ่ได้ประมาณครึ่งหนึ่ง การติดเชื้อไขหวัดใหญ่ในผู้สูงอายุ ในปีที่ทำการศึกษาไม่รุนแรงจนเป็นเหตุให้เกิดโรคแทรกซ้อนหรือเสียชีวิต ซึ่งเมื่อคำนึงถึงค่าใช้จ่ายจากการฉีดวัคซีน และจำนวนผู้สูงอายุ ซึ่งต้องรับการฉีดวัคซีน เพื่อป้องกันการเกิดโรค 1 คน เทียบกับความรุนแรงของโรค สรุปจากมุมมองของผู้ให้บริการว่าหากอุบัติการณ์และความรุนแรงของโรคไขหวัดใหญ่ที่เกิดกับผู้สูงอายุในชุมชนเป็นดังปีการศึกษา การฉีดวัคซีนป้องกันโรคไขหวัดใหญ่ให้แก่ผู้สูงอายุในชุมชนทุกคนทุกปีอาจได้ผลไม่คุ้มค่า แต่ควรพิจารณาฉีดวัคซีนเมื่อเริ่มมีการระบาดในต่างประเทศ และคาดว่าจะมีการระบาดใหญ่เกิดขึ้นในประเทศไทย

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