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# Effectiveness of the influenza vaccination program for the elderly in Taiwan

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#### ABSTRACT

Background and objectives: Since 1998, an influenza vaccination program has been implemented by the Taiwan government targeting people aged ≥65 years. However, the evidence of the effectiveness of this program in preventing influenza, which is based on the nation-wide database, is lacking. This study attempted to estimate the effectiveness of the influenza vaccination program in preventing influenza-and pneumonia-associated outpatient visits and hospitalization in the elderly.

Methods: Randomly sampled data of 1 million claims from the National Health Insurance Research Database compiled into seven consecutive cohorts were used to perform this analysis. Elderly claimants aged  $\geq$ 65 years were included in each cohort. To decrease potential bias between vaccinated and unvaccinated subjects, the propensity score method was applied. Logistic regression and zero-inflated negative binominal regression were used to examine the effectiveness of vaccination in preventing influenza- and pneumonia-associated outpatient visits and hospitalization.

Results: A significant decrease in both the risk and frequency of hospitalization was observed in elderly people who received influenza vaccination compared with those who did not. No similar decrease was observed in the risk and frequency of outpatient visits for influenza and pneumonia.

Conclusion: Vaccination against influenza reduced hospitalization for influenza and pneumonia in elderly Taiwanese people. These results are meaningful for the promotion of vaccination policy. Annual influenza vaccination of the elderly should be encouraged.

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#### 1. Introduction

Annual outbreaks of influenza result in substantial costs in terms of hospitalization and mortality [1,2]. Elderly patients aged ≥65 years are most vulnerable to the complications caused by influenza-related diseases, and mortality due to influenza is highest in this population group [1,3,4]. In view of the seriousness of this disease among elderly people, the World Health Organization (WHO) has recommended annual influenza vaccination for this age group. Consequently, vaccination programs for the elderly have been implemented in most high-income countries, and policies on influenza vaccination specifically target the elderly [5,6].

In Taiwan, as the cases in other causes of death, the majority of pneumonia and influenza mortality occurs in the elderly. To reduce the disease burden caused by influenza in the elderly, the Taiwan government initiated a pilot program in 1998 providing government-funded influenza vaccines for citizens with comorbidities who were aged  $\geq$ 65 years. The program gradually expanded to include all people aged  $\geq$ 65 years as of 2001.

The influenza vaccine is not perfect in terms of the level of protection from the disease due to the mismatch of vaccine strains and fickle circulating strains. Adding that people always confuses about influenza and common cold therefore expecting that the influenza vaccine protects all the acute respiratory infections. Thus, at times, it is difficult to persuade the elderly who experienced influenza or cold after taking the shot to receive this vaccine. Evaluation of the effectiveness of influenza vaccination is also subject to influence by the degree of match between the vaccine strain and the circulating strain and various epidemic situations in different years. Influenza is a highly respiratory infectious disease and the elderly patients are particularly vulnerable to the complications of influenza including the pneumonia [3]. Many studies have suggested that influenza vaccination for elderly people effectively aids in avoidance of hospitalization or death resulting from influenza or pneumonia [3,7–9]. Some studies that focused on Taiwanese elders from different localities also showed the effectiveness of vaccination, but the data are fragmented [10,11]. Furthermore, no data are available regarding the estimation of influenza vaccination benefits

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in elderly Taiwanese citizens at the national level and over a long period in order to promote this vaccination among the elderly.

The influenza vaccination program has been implemented in Taiwan for more than 10 years. Concern for the health of the elderly necessitates the evaluation of the effectiveness of this program. Using a longitudinal, nationwide database, this study estimated the effectiveness of the influenza vaccination program in elderly Taiwanese in terms of the reduction in influenza- and pneumonia-associated outpatient visits and hospitalizations.

#### 2. Methods

#### 2.1. Data sources and setting

Health care services in Taiwan have operated under the National Health Insurance (NHI) policy since 1995. Data for this analysis were obtained from a longitudinal health insurance database assembled for the year 2005 (LHID2005) from the National Health Insurance Research Database (NHIRD), which was provided by the Bureau of National Health Insurance, Department of Health and managed by the National Health Research Institutes in Taiwan. The LHID2005 contained data of 1 million subjects, who were enrolled in the year 2005 and randomly sampled from the registry of NHIRD for that year. A representative sample was tested, and no significant difference was found in results for that sample compared with those of the total population in terms of major demographic and socio-economic characteristics [12].

All original claims of 1 million Taiwanese citizens for the period 2002–2009 in the LHID2005 were included in the analysis. Claims of citizens aged  $\geq$ 65 years in each respective year were analyzed to determine the effectiveness of influenza vaccination. Seven study periods were included: 2002–2003, 2003–2004, 2004–2005, 2005–2006, 2006–2007, 2007–2008 and 2008–2009.

Before conducting the analyses, we had to take notice of the difference in the health status of vaccinated and unvaccinated elderly people that might influence the outcomes. On one hand, some studies have indicated that patients with poorer health conditions were more likely to engage in preventive health behaviors because they experienced the illness more or had higher risk perception about the diseases [13,14]. On the other hand, elderly people who received influenza vaccination were healthier than those who did not, and limitations in health function might restrict the possibility of receiving vaccination [15,16]. In any study, if the selected cohort is affected by these characteristics, underestimation or overestimation of the effectiveness of vaccination may occur. Therefore, the propensity score method, a powerful statistical technique to adjust for observed confounders [17], was used in this study to decrease this possible bias. This method tries to simulate the experimental design by comparing individuals with similar characteristics. The propensity score, which is calculated using logistic regression, represents a kind of conditional probability (between 0 and 1) and illustrates the relationship between multiple characteristics and the treatment by a single value. Before the analysis, the subjects who have received the treatment and those without getting the treatment will be matched based on the similar propensity score to reduce the foregoing bias. In this study, the propensity score was regarded as the predicted probability of getting influenza vaccination given a set of observed variables that may influence their decision and the result was applied to enable matching of subjects with similar propensity scores in a hierarchical sequence until no more matching could be performed.

From 2002 to 2008, the policy of influenza vaccination in Taiwan was to make government-funded influenza vaccines available to all elderly citizens from 1st October in most years. Most elderly people who were willing to receive influenza vaccination were

vaccinated before 31st December. Thus, in this study, the vaccination status of each subject was defined according to the records from the claims data between 1st October and 31st December of each year. To control the confounding variables that might affect the results, the gender and age were identified and controlled in the analyses according to the past researches [9–11]. Moreover, the factors including the status of elders' household income, the level of hospital/clinic (such as district hospital, regional hospital and medical center) they visited most frequently each year, physician density of the region that the individual sought care mostly and coexisting chronic disease which might influence the probability of receiving influenza vaccination and the pneumonia-associated outpatient visits and hospitalizations were also included in the analytical model. Morbidity from chronic diseases was included to facilitate comparison of health status. To quantify this factor, the Chronic Condition Indicator (CCI) from the Healthcare Cost and Utilization Project (HCUP) sponsored by the U.S. Agency for Healthcare Research and Quality (AHRQ) [18,19] were used to divide the elderly claimants into groups with and without chronic diseases and to calculate the number of chronic diseases for each individual according to the diagnostic records (International Classification of Diseases, 9th revision, Clinical Modification Codes, ICD-9-CM).

According to the influenza surveillance data from the Centers for Disease Control in Taiwan, the epidemic of influenza usually began near the end of the year and peaked during February and March of the next year during the study period, although it occasionally persisted until the middle of the year. To be consistent with the analyses in each cohort, the outcome period was set between 1st January and 30th June for each year. Influenza- and pneumonia-associated outpatient visits and hospitalizations (ICD-9-CM 480 through 487) were used as dependent variables in multivariate models. Data of claimants who passed away during the study period were not included in the analyses. In addition, to ensure the timing of causality between vaccination and medical care utilization, those subjects with vaccination records after 31st December were excluded each year.

## 2.2. Statistical analyses

For analysing the differences in health status between elderly people with and without influenza vaccination, the chi-square test was employed to examine the distribution of chronic diseases among subjects using their vaccination records. In multivariate analyses, a logistic regression model was used to identify the association between influenza vaccination and the risk of influenza-and pneumonia-associated outpatient visits and hospitalizations. Furthermore, zero-inflated negative binominal regression was employed to determine significant reductions in the frequency of influenza- and pneumonia-associated outpatient visits and hospitalizations after vaccination. The analytical outcome of each cohort was presented depending on whether the outcome was matched by the propensity score. All analyses were performed using SAS software version 9.2 (SAS Institute Inc, Cary, NC, USA).

## 3. Results

Table 1 shows vaccination and chronic disease distributions for all cohorts. Before the 2005–2006 season, influenza vaccination rates exceeded 50% in all cohorts, and subsequently, the rates declined and fluctuated to approximately 40%. In a comparison of health status and morbidity from chronic diseases, vaccine recipients had a higher proportion of chronic diseases than non-recipients. All differences were significant (chi-square test). Outcome descriptions are presented in Table 2. Regarding outpatient visits, a consistently higher number of outpatient visits

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