



# Cost-effectiveness Analysis of Influenza and Pneumococcal Vaccinations among Elderly People in Japan

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【 150 】

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【 学位論文題目 】

Cost-effectiveness Analysis of Influenza and Pneumococcal  
Vaccinations among Elderly People in Japan  
(日本における高齢者へのインフルエンザワクチンと  
肺炎球菌ワクチンに関する費用効果分析)

審 査 委 員

主 査	教 授	西尾	久英
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	教 授	川端	眞人

## INTRODUCTION

Pneumonia and influenza are two of the common causes of mortality, morbidity, and economic loss among the elderly in Japan. During the rampancy of influenza in 1999, about 90 percent or 1,039 cases, of the total of 1,154 influenza-related mortalities including that from pneumonia, were among elderly people. It is momentous to realize that about 24 or 25 percent of the elderly who get infected with influenza subsequently develop a complication with pneumonia. Even in 2003, pneumonia was the fourth leading cause of deaths and the number of deaths resultant of pneumonia among the elderly reached as high as 90,757. Seen from an epidemiological perspective, it is mainly the elderly people who are at risk.

Generally, in Japan, the economic benefit, from a societal perspective, not to mention the clinical effectiveness of influenza vaccine particularly for the elderly population, is better recognized and accepted than that of pneumonia. Since November 2001, part of the cost for inoculating the elderly with influenza vaccine has been shared and is assisted by the Ministry of Health, Labour, and Welfare. In addition, it is noteworthy that the proportion of inoculation with influenza vaccines keeps rising in the country. It reached 45 percent in 2003 and 2004. Nevertheless, the proportion of inoculation with pneumococcal vaccine, in contrast, remains low. It was only 0.1 percent. In contrast, according to the data from the Centers for Disease Control (CDC) in the United States, the proportion of inoculation with pneumococcal vaccine in the USA was 45 percent.

A vaccine activates the immune system for a specific disease through introduction of an antigen to the body. Preventive effects of vaccines against some viral diseases, such as smallpox, measles, mumps, rubella, and chickenpox, are without any doubt substantial. As for influenza vaccines, previous studies also clearly indicate a firm effectiveness of the vaccines in reducing not only the number of deaths, but also the period of hospitalization. However, there have been controversies regarding the cost-effectiveness of pneumococcal vaccines. Moreover,

in 2004, Christenson et al., in their large cohort studies (N=258,754), found that utilization of influenza and pneumococcal vaccines jointly among the elderly population had additive preventive effect in reducing hospital admissions for influenza and pneumonia.

## MATERIALS AND METHODS

In order to estimate the social costs and benefits, we envisaged three vaccination strategies for 100,000 elderly persons: (i) no vaccination, (ii) influenza vaccine only, and (iii) influenza and pneumococcal vaccines combined.

In this study, the diagnoses of influenza and pneumonia, respectively, were made according to the end-point diagnoses before being administered to a hospital.

The following formulas materializing two concepts, a ratio and an incremental ratio, were employed to evaluate the cost-effectiveness of vaccination:

a) Cost-effectiveness ratio (CER) (a comparison with non-vaccinated strategy)

$$CER_{\text{vaccinated}} = \frac{C_{\text{vaccinated}} - C_{\text{non}}}{YOLS_{\text{vaccinated}}} \quad (A),$$

In the context of this study, CER is the amount of Japanese yen, which is required to obtain a unit of health effect, which, in this case, is one year of life saved (YOLS).

b) Incremental cost-effectiveness ratio (ICER) (a comparison of influenza-vaccination-only with the combined approach of both influenza and pneumococcal vaccines)

$$ICER_{\text{combined}} = \frac{C_{\text{combined}} - C_{\text{influenza}}}{YOLS_{\text{combined}} - YOLS_{\text{influenza}}} \quad (B).$$

The "C" denotes the total costs of the strategies. Health outcomes of effectiveness are measured by years of life saved, which refers to the total number of life years gained through avoidance of deaths, which, in turn, resulted from receiving vaccinations.

In the above-mentioned three scenarios (i), (ii), and (iii), it is important to note that if the formula (A) is used to estimate the first scenario (i), both the numerator and the denominator would be equal to zero, thereby making it impossible to have a CER.

Hence, the formula (A) is applied to calculate the CERs of the scenarios (ii) and (iii): the former is to evaluate the influenza-vaccine-only approach and the latter for the combined approach of influenza and pneumococcal vaccines. The formula (B), on the other hand, is employed to estimate ICER of the combined vaccination in comparison with the influenza-vaccine-only approach.

#### **Simulation analysis**

In order to assess the probable range of outcomes, computing simulations were conducted. Using the software called Crystal Ball 2000 Professional Edition (v5.2), which enables various computing simulations, the above-mentioned algorithms and the estimates were applied to carry out the Monte Carlo simulation, through which pseudo random numbers for multiple scenarios were generated. It allowed for the quantification of uncertain variables. The simulation was repeated with the trials of 10,000 times. Utilizing the Monte Carlo simulation, a sensitivity analysis was also conducted.

#### **RESULTS**

According to the results of the simulations, for per 100,000 elderly people, the CER of influenza vaccine only was about 516,332 JPY/YOLS. For the combined vaccine strategy, on the other hand, the CER was about 459,874 JPY/YOLS for the same number of elderly people. The smaller CER obtained for the combined strategy in comparison with the influenza-vaccine-only approach indicates the better cost-effectiveness of the combined strategy.

Moreover, the ICER of the combined vaccinations versus the influenza-vaccination-only was 426,698 JPY / YOLS per 100,000 elderly people. The results indicated superior health economic impacts of the combined vaccination over the other alternatives.

#### **DISCUSSION**

One of the critical challenges that Japan faces is to deal effectively with the low inoculation of pneumococcal vaccine among the elderly. The high cost of the vaccine, particularly from the standpoint of the consumers, is certainly one of the

factors that play a role in the low inoculation rate. One of the reasons for the high cost may be that there has been no public assistance for the expenses needed to implement a pneumococcal vaccination program. In turn, one possible explanation for the lack of funding may be that, in some previous studies, the questions with regard to the preventive effects of pneumococcal vaccines remain inconclusive. In response, this makes policy/decision-makers reluctant to mobilize public funding. As the Swedish study established the evidence of effectiveness and also, our studies indicate the cost-effectiveness of the combined strategy, it becomes important to increase the inoculation rate for pneumococcal diseases along with that for influenza, while also informing the public about the diseases and the cost-effective approach to tackle the diseases.

Sisk et al. found that pneumococcal vaccination against pneumococcal bacteremia among the elderly was cost-effective. Since there were no data on pneumococcal bacteremia available in Japan, this study is not inclusive of the possible health-economic outcomes of the disease. Moreover, although the potency of pneumococcal vaccine may last for five years, the analytical span of this study is set to the period of one year due to the limitation of data availability. Despite these limitations, it is possible to conjecture that given the cost-effectiveness of pneumococcal vaccination against pneumococcal bacteremia, the inclusion would have beneficial increment to the cost-effectiveness of the combined approach as investigated in this study.

As the results of this study suggest the cost-effectiveness of a joint-vaccination to protect the elderly from influenza and pneumonia, and reaching the decision for allocating funds to launch the joint-vaccination program are the foremost steps to be taken in Japan at this point. After such an achievement is made, it will be necessary to address the questions as to how it would be possible to promote and encourage the elderly to take the vaccines. These questions have been addressed by some researchers in other countries. For instance, While et al. indicated that tactics such as flyers, personal invitations, and doctors' recommendations were efficient to enhance

the proportion of receiving inoculation with the vaccination. In addition, one randomized controlled study conducted by Berg et al. in the USA found that direct mail-marketing, encouraging the recipients to receive vaccinations for influenza and pneumococcal disease, worked successfully and increased the vaccination rate as compared to the control group. It is also important not only for physicians or professionals in the field of healthcare, but also for policy/decision-makers to be sensitive to the specific needs of the elderly, taking into account such factors as their socio-economic status, psychosocial needs, their opinions or beliefs about their own lives as well as health. The health and well-being of the elderly and cost-effectiveness are not mutually exclusive. It is important also to note that cost-effectiveness, as described in this paper, is different from cost-saving. In particular, the strategy (iii) will be more costly as compared to the strategy (ii). Nevertheless, the effectiveness obtained from the strategy (iii) is more beneficial than that of the strategy (ii) despite the cost constraint required to implement (iii).

Our study, of course, has limitations which include the structure of decision tree for analysis, limited availability of data assigned to the decision tree, availability and reliability of clinical/epidemiological data for pneumococcal vaccination in Japan, and so on. The Monte Carlo simulation is one of the therapeutic treatments and methods to overcome the limitations of data including cost measurement.

In Japan, it is estimated that the number of people over the age of 65 will reach 31,880,000 by the year 2015. At the current rate, it is evident that social as well as economic needs for this population group will be enormous. In particular, health care costs related to influenza and pneumonia for this specific population in the future will be more demanding and certainly require a cost-effective, as well as efficient, approach. In conclusion, it was suggested that the combined use of influenza and pneumococcal vaccines should be adopted for the elderly with respect to increasing the benefit in public health.

## 論文審査の結果の要旨

受付番号	甲 第 1773 号	氏 名	蔡 立
論文題目 Title of Dissertation	Cost-effectiveness Analysis of Influenza and Pneumococcal Vaccinations among Elderly People in Japan 日本における高齢者へのインフルエンザワクチンと肺炎球菌ワクチンに関する費用効果分析		
審査委員 Examiner	主 査 西尾久英 Chief Examiner 副 査 秋田 龍牙 Vice-examiner 副 査 川端 聖人 Vice-examiner		
審査終了日	平成 18 年 4 月 19 日		

(要旨は1, 000字～2, 000字程度)

## INTRODUCTION

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## RESULTS

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The candidate, having completed studies on cost-effectiveness analysis of influenza and pneumococcal vaccination in Japan, with a specialty in the medical expenses among the elderly people, and having advanced the field of knowledge in the area of public health in an aging society, is hereby recognized as having qualified for the degree of Ph.D. (Medicine).