Factors influencing acceptance of influenza and pneumococcal vaccinations for patients with chronic obstructive pulmonary disease

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ABSTRACT

Chronic obstructive pulmonary disease (COPD), often complicated by influenza or pneumococcus, is a leading cause of mortality worldwide. Vaccinations against influenza and pneumococcus are, but vaccination coverage in Thailand has not been ascertained. This study aimed to determine the determinants of influenza and pneumococcal vaccination acceptance in COPD patients. A cross-sectional study of 210 COPD patients was conducted. Demographics, vaccinations, clinical outcomes (exacerbations and hospitalizations), and pulmonary functions were collected. A total of 134 COPD patients (91.0% male) were eligible for final analysis. Of these, 102 (76.1%) and 59 (44.0%) were vaccinated against influenza and pneumococcus, respectively. The influenza-vaccinated group had a higher rate of pneumococcal vaccination than the influenza-unvaccinated group (57.8% vs 0%, P < .001). Rates of influenza and pneumococcal vaccinations were higher in the pulmonologist group than in the non-pulmonologist group (71.6% vs 31.3%, P < .001 and 91.5% vs 38.7%, P < .001, respectively). By multivariable logistic regression analysis, influenza vaccination coverage was significantly higher among patients with bronchodilator response on pulmonary function testing. Pneumococcal vaccination coverage was significantly higher among patients who were seeing pulmonologists. Reasons for not getting influenza vaccination or pneumococcal vaccination were lack of recommendation, lack of knowledge, and misunderstanding, and in the case of pneumococcal vaccine, the expense. In conclusion, the influenza vaccination coverage in our COPD patients was considered high while the pneumococcal vaccination coverage was considered low. Physicians are advised to recommend and promote pneumococcal vaccination.

Introduction

Chronic obstructive pulmonary disease (COPD) is the world’s third leading cause of mortality, often aggravated by influenza or pneumococcus.1 About 35% of COPD deaths occurred due to respiratory failure.2 The Global Initiative for Chronic Obstructive Lung Disease (GOLD)3 recommends vaccination against influenza and pneumococcus. They particularly recommend pneumococcal vaccination for patients with impaired pulmonary function or with comorbid disease, especially cardiac diseases, and for all patients aged 65 years or older.1 The Centers for Disease Control and Prevention of the United States recommends pneumococcal vaccination for anyone older than 65 years or for anyone between 19–64 years with comorbidities, such as lung disease, heart disease, liver disease, or smoking.4 The World Health Organization also recommends influenza vaccination for COPD patients, to reduce the burden of disease.5

Wongsurakiat P and colleagues found that influenza vaccination significantly lowered incidence of influenza-related acute respiratory illness in COPD patients, and that influenza vaccination for COPD patients reduced hospital costs, particularly costs of hospitalizations and mechanical ventilations.5,6 It was most cost-effective and cost-beneficial in patients with more severe airflow obstruction.7

Despite several studies and national guidelines which demonstrated that vaccinations are beneficial in COPD patients, vaccination coverage has not been one hundred percent complete. In England, the influenza vaccination coverage in COPD patients increased from <30% before 1995 to >70% in 2005 aged ≥60 years while the pneumococcal vaccination coverage in patients aged ≥70 years increased from 0 to 70%.8 A Turkish study in 2014, the influenza vaccination coverage in COPD patients was 36.5% and the pneumococcal vaccination coverage was 14.6%.9 In Thailand the influenza vaccination coverage was 35% in 2011 and 41% in 2012 and 201310; however, there was no data on pneumococcal vaccination, or on factors affecting receipt of vaccinations.

This study aimed to determine the determinants affecting acceptance of influenza and pneumococcal vaccinations in COPD patients in Thailand.

Materials and methods

Study design and participants

This was a cross-sectional study at Thammasat University Hospital, Thailand between March 2020 and January 2022. Study participants were recruited at 2 medical outpatient clinics in this hospital. The inclusion criteria were COPD...
patients aged ≥40 years with smoking history ≥10 pack-years and ratio of forced expiratory volume in one second (FEV₁) to forced vital capacity (FVC) <0.7. Patients who could not answer questions reliably, e.g. patients with dementia, were excluded. Questionnaires designed by the investigators, standardized by research assistants in a pre-study trial with COPD patients, and finalized by the investigators, were administered to the study participants. Data regarding demographics, comorbidities, type of physician, functional performance (assessed by modified Medical Research Council (mMRC) and COPD Assessment Test (CAT)), influenza vaccine, type of pneumococcal vaccine (13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23)), reasons for vaccinations, hospitalizations, exacerbations, and pulmonary functions (FEV₁ and FVC) with bronchodilator (BD) test were collected.

Ethic approval was obtained from the Human Research Ethics Committee of Thammasat University No.1 (Faculty of Medicine), Thailand (IRB No. MTU-EC-IM-0-254/62, COA No. 061/2020), in compliance with Declaration of Helsinki, The Belmont Report, CIOMS Guidelines and The International Practice (ICH-GCP). All methods were performed in accordance with these guidelines and regulations. All participants provided written informed consent.

**Statistical analysis**

Based on our observation in the clinical practice, the influenza vaccination coverage in our COPD patients was approximately 50%. We hypothesized that the estimated coverage rate of influenza vaccination in our study was 50% using 80% power and 5% type I error. Thus, the estimated sample size would be 106. Data is expressed as number (%) and mean ± standard deviation. The chi-squared test and Fischer’s exact tests were used to compare categorical data between the vaccinated groups and the unvaccinated groups. Student’s t-test was used to compare continuous data between two groups. To determine the set of variables associated with the vaccination, we used the multivariable logistic regression model with the vaccination set as dependent variable. All significant independent variables were entered into the regression model simultaneously. We report odds ratio (OR), their 95% confidence interval and corresponding P-values. A two-sided p-value <.05 was considered statistically significant. Statistical analyses were performed using SPSS version 23.0 software (IBM Corp., Armonk, NY, USA).

**Results**

Two hundred and ten COPD patients were screened. Of these, 76 patients were excluded due to incomplete data (Figure 1). A total of 134 COPD patients (91% male) were included in the final analysis. Mean age was 75.40 ± 8.71 years. The majority of patients had quit smoking (91%). The main comorbidities were hypertension (62.7%), diabetes (25.4%), and heart disease (25.4%). Mean post-BD FEV₁/FVC was 56.74 ± 12.27%. The severity of airflow limitation was moderate (post-BD FEV₁ in 65%). The influenza vaccination coverage was 76.1%. The pneumococcal vaccination coverage was 44.0% (42.5% for PCV13 and 26.1% for PPSV23) (Table 1).

Regarding influenza vaccination, the vaccinated group had higher rate of pneumococcal vaccination (57.8% vs 0%, P <.001), rate of follow-up by pulmonologist (71.6% vs 31.3%, P <.001), and FEV₁ change after BD test (8.29 ± 11.24% vs 3.57 ± 7.64%, P = .029) than those unvaccinated for influenza (Table 2).

When compared to the pneumococcal unvaccinated group, the vaccinated group had higher proportion of heart disease (39.0% vs 14.7%, P = .001), proportion of lung disease (6.8% Vs 0%, P = .035), influenza vaccination rate (100.0% vs 57.3%, P <.001), rate of follow-up by pulmonologist (91.5% vs 38.7%, P <.001), and mMRC score (2.08 ± 1.12 points vs 1.67 ± 1.25 points, P = .046), but lower post-BD FVC (78.41 ± 22.16% predicted vs 86.34 ± 18.87% predicted, P = .037), post-BD FEV₁ (1.30 ± 0.48 L vs 1.52 ± 0.55 L, P = .024), and pre-BD FEV₁/FVC (54.22 ± 12.96% vs 59.00 ± 12.22%, P = .037) (Table 3).

By the multivariable logistic regression analysis, FEV₁ change after BD test was the only factor associated with influenza vaccination (OR 1.07 for every 1% increase in FEV₁ after BD test). Follow-up by pulmonologist was the only factor associated with pneumococcal vaccination (OR 23.22) (Table 4).

**Figure 1.** Flowchart of COPD patient recruitment to the study.
Table 1. Baseline characteristics of patients with chronic obstructive pulmonary disease.

| Characteristics          | N = 134 |
|-------------------------|---------|
| Age, years              | 75.40 ± 8.71 |
| Male                    | 122 (91.0) |
| BMI, kg/m²              | 22.58 ± 4.20 |
| Ex-smoking              | 122 (91.0) |
| Smoking, pack-years     | 27.27 ± 20.08 |
| Comorbidity             |         |
| Hypertension            | 84 (62.7) |
| Diabetes                | 34 (25.4) |
| Heart disease           | 34 (25.4) |
| Renal disease           | 12 (9.0) |
| Stroke                  | 7 (5.2) |
| Liver disease           | 4 (3.0) |
| Lung disease            | 4 (3.0) |
| Pneumococcal vaccination| 59 (44.0) |
| PCV13                   | 57 (42.5) |
| PPSV23                  | 35 (26.1) |
| Influenza vaccination   | 102 (76.1) |
| Physician               | 83 (61.9) |
| Pulmonologist           | 51 (38.1) |
| Internists              |         |
| Exacerbation in the past year, events | 1.20 ± 2.74 |
| Hospitalization in the past year, events | 0.65 ± 1.74 |
| Spirometry data         |         |
| Post-BD FVC, L          | 2.48 ± 0.72 |
| Post-BD FVC, % predicted| 82.74 ± 20.72 |
| Post-BD FEV₁, L         | 1.42 ± 0.53 |
| Post-BD FEV₁, %predicted| 65.05 ± 25.21 |
| FEV, change after BD, % | 7.14 ± 10.65 |
| Pre-BD FEV/FVC, %       | 56.92 ± 12.72 |
| Post-BD FEV/FVC, %      | 56.74 ± 12.27 |
| Functional performance  |         |
| mMRC, points            | 1.85 ± 1.20 |
| CAT score, points       | 9.51 ± 6.96 |

Data shown as mean ± SD or n (%).
BD = bronchodilator, BMI=body mass index, CAT=COPD assessment test, FEV₁ = forced expiratory volume in 1 second, FVC = forced vital capacity, kg = kilogram, L = liters, m = meters, mMRC = modified Medical Research Council, PCV13 = 13-valent pneumococcal conjugate vaccine, PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

The main reasons that study participants didn’t get influenza and pneumococcal vaccinations were because their doctors didn’t recommend it (81.3% and 92.0%), they didn’t know how to get it (68.8% and 85.3%), they didn’t know when to get it (59.4% and 70.7%), and they didn’t know how to access it (50.0% and 60.0%). Also, the pneumococcal vaccine was too expensive for average Thai wage earners (18.7%) (Table 5). Those who did get vaccinated did so because of their doctor’s advice (89.2% and 98.3%), or because of information from friends (24.5% and 3.4%), hospital posters (18.6% and 1.7%) or television (16.7 and 1.7%) (Table 6).

Discussion
This is the first study of vaccination rates in COPD patients in developing countries, including Thailand. Our study showed that the influenza vaccination coverage in COPD patients was 76.1%, and the pneumococcal vaccination coverage was 44.0%. These findings correspond to a previous observational study in Thailand by Saiphoklang N and colleagues. They showed that the coverage rate of influenza vaccination was 71.4%, and the coverage rate of pneumococcal vaccination was 50.6%.

In Thailand, free influenza vaccination is provided annually from May-September to 7 high-risk groups; 1) children aged 6 months to 2 years, 2) pregnant women, 3) obese persons, 4) persons with cerebral palsy, 5) persons with thalassemia or immune suppressive state including symptomatic human immunodeficiency virus (HIV), 6) persons aged 65 years or older, and 7) persons with chronic illness including COPD, asthma, heart disease, stroke, chronic kidney disease, diabetes, and cancer with chemotherapy. Influenza vaccination coverage for these targeted groups in Thailand in 2020 is 82.8%, which is slightly higher than our study.

Pneumococcal vaccinations are not free for all people in Thailand because they are not part of Thailand’s national immunization program. However, they are recommended by the Infectious Disease Association of Thailand for adults aged 65 years or older and persons with COPD, heart disease, chronic kidney disease, diabetes, cirrhosis, asplenia, HIV infection, severe immune suppressive state, and organ or bone marrow transplantation. PCV13 or PPSV23 are recommended as pneumococcal vaccinations for COPD patients in Thailand and are considered for revaccination depending on vaccine types. There is no national data on the pneumococcal vaccination coverage in Thailand. Pneumococcal vaccination coverage in Thai patients with diabetes in 2010–2018 was relatively stable at less than 20%, which is approximately half of coverage rates of COPD patients in our study.

Table 2. Comparison of associated factors between influenza vaccinated group and non-vaccinated group in patients with chronic obstructive pulmonary disease.

| Influenza vaccination |
|-----------------------|
| Characteristics       | Vaccinated | Unvaccinated | P-value |
| Age, years            | 75.44 ± 8.85 | 75.25 ± 8.38 | .914 |
| Male                  | 92 (90.2) | 30 (93.8) | .730 |
| Ex-smoking            | 95 (93.1) | 27 (84.4) | .157 |
| Smoking, pack-years   | 27.66 ± 20.52 | 26.04 ± 18.90 | .692 |
| Comorbidity           |         |
| Hypertension          | 66 (64.7) | 18 (56.3) | .338 |
| Diabetes              | 27 (26.5) | 7 (21.9) | .602 |
| Heart disease         | 30 (29.4) | 4 (12.5) | .055 |
| Renal disease         | 11 (10.8) | 1 (3.1) | .292 |
| Lung disease          | 4 (3.9) | 0 (0) | .572 |
| Pneumococcal vaccination | 59 (57.8) | 0 (0) | <.001 |

Data shown as mean ± SD or n (%).
BD = bronchodilator, CAT = COPD assessment test, FEV₁ = forced expiratory volume in 1 second, FVC = forced vital capacity, kg = kilogram, L = liters, mMRC = modified Medical Research Council, PCV13 = 13-valent pneumococcal conjugate vaccine, PPSV23 = 23-valent pneumococcal polysaccharide vaccine.
A cross-sectional study in Turkey by Aka Akturk U and coworkers found that the proportion of patients vaccinated for influenza was 36.5% and for pneumococcus was 14.1%. A survey study in Italy by Chiatti C, et al showed that 30.5% of adults and 74.8% of older people with COPD reported influenza vaccination. The influenzavaccination coverage among COPD patients in a Spanish study by Santos-Sancho JM, et al was 49.4%. A cross-sectional study of a nationwide survey in the United States by Arabyat RM, et al demonstrated that the influenza vaccination rate was 53% among 36,433 COPD patients. The pneumococcal vaccination rate was extremely low (0.8%) in COPD patients aged ≥40 years in China by a study from Fan J, et al. Factors associated with influenza vaccination among COPD patients in Korea were older age, poor self-rated health status, regular health checkup, married marital status, and household income below average.

Our study found that a higher proportion of the pneumococcal vaccinated group saw a pulmonologist than did the non-vaccinated group. Perhaps, as specialists, pulmonologists provide more detailed care to COPD patients. Because doctors usually recommend both influenza and pneumococcal vaccines together unless the patient has a contraindication, the group of patients who received...
influenza vaccination had a higher rate of pneumococcal vaccination. Every patient who had received a pneumococcal vaccination had also received an influenza vaccination.

According to our findings, patients who didn’t get vaccinated didn’t do so because either their doctor didn’t recommend it, or they didn’t know how to get it, or they didn’t know when to get it, or they didn’t believe they were in a high-risk group. For pneumococcal vaccination, the expense also played a major role. Reasons that patients did get vaccinated were because their doctors advised it or because of information from friends, hospital posters, or television. These findings are similar to a Turkish study in which the main reasons were their doctor didn’t recommend it, and they didn’t need to get vaccinated.9

A pilot project in Singapore by Li A, et al showed that the influenza vaccination rate in COPD patients could be improved by multi-dimensional strategies including patient education posters, vaccination card reminders, a new electronic healthcare record system, and direct interventions by physicians or nurses.22 A study in Hong Kong by Hui MTE, et al showed that a clinical audit for COPD management in primary care clinics significantly enhanced the influenza vaccination rate from 46.9% to 57.0% and the pneumococcal vaccination rate from 40.7% to 59.6%.23

In accordance with GOLD 20201, we recommend influenza and pneumococcal vaccination; the benefits are confirmed by numerous studies.6,7,24,25,26,27,28,29,30,31 The Thai government should encourage vaccinations, and subsidize pneumococcal vaccine for COPD. Private hospitals should also promote vaccinations. Internists should update COPD treatment guidelines to advocate vaccination for their patients.

There are some limitations of this study. Firstly, because of the small population size and the selection bias of patients, some data were not collected and some results might not be obviously different between the vaccinated groups and the non-vaccinated groups. Secondly, the data was collected during a COVID-19 outbreak, when fewer patients underwent pulmonary function tests. Thirdly, this is a cross sectional study so it cannot explain associations between cause and result. Finally, we collected data in the single center which might not represent the entire country, because some hospitals didn’t have pneumococcal vaccine, and in some areas, vaccines were promoted in different ways.

In conclusion, the influenza vaccination coverage was high in Thailand, but the pneumococcal vaccination coverage was relatively low. Vaccination rates are increasing around the world, including in Thailand. Yet, patients still don’t know how necessary vaccinations are. Therefore, we recommend including in the national expanded programme on immunization both influenza and pneumococcal vaccinations, either PCV13 or PPSV23, for COPD patients.

In a future prospective cohort study, patients should get early vaccination before they have low pulmonary functions. Then we could compare the clinical outcomes in both groups.

**Abbreviations**

**COPD** Chronic obstructive pulmonary disease  
**GOLD** Global Initiative for Chronic Obstructive Lung Disease  
**FEV₁** Forced expiratory volume in 1 second  
**FVC** Forced vital capacity  
**mMRC** modified Medical Research Council  
**CAT** COPD Assessment Test  
**PCV13** 13-valent pneumococcal conjugate vaccine  
**PPSV23** 23-valent pneumococcal polysaccharide vaccine

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