



Prevalence of influenza and pneumococcal vaccination in chronic obstructive pulmonary disease patients in association with the occurrence of acute exacerbations

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Background: Based on current evidence, vaccination is recommended against the influenza virus and pneumococcus to avoid serious acute exacerbations in patients with chronic obstructive pulmonary disease (COPD), but the rate of their vaccination coverage is still suboptimal. To determine the prevalence and effectiveness of influenza and pneumococcal vaccination in COPD patients, and to prove its hypothetical association with the decreasing number of acute exacerbations.

Methods: We conducted a retrospective, population-based cohort study. Influenza and pneumococcal vaccination history were collected from 250 patients selected by simple random sampling from all COPD patients in Budapest at the Department of Pulmonary Rehabilitation of the National Koranyi Institute of Pulmonology between 01 January 2019 and 01 June 2019. Inclusion criteria were the following: age 40 years and diagnosis of COPD. Odds ratios (ORs) were evaluated based on the occurrence of acute exacerbations during the preceding year.

Results: The average age was 66.62 (± 8.34) years, 67.30 (± 8.54) for males, and 66.09 (± 8.16) for females. Man:woman ratio: 43.6%:56.4% in total. Overall prevalence of influenza vaccination was 23.6%, and the pneumococcal vaccination rate was 10.8% among COPD patients. Influenza and pneumococcal vaccination showed a significant protective effect and reduced the occurrence of exacerbations in the following year, influenza vaccination OR: 2.11 (95% CI: 0.88–5.02), pneumococcal vaccination OR: 1.06 (95% CI: 0.84–1.34), when taking both vaccination: OR: 2.37 (95% CI: 1.39–4.08).

Conclusions: We found association between influenza and pneumococcal vaccination and the reduced risk of hospitalization due to exacerbations in the ensuing year. The prevalence of vaccination is significantly below the optimal level.

Keywords: Chronic obstructive pulmonary disease (COPD); acute exacerbation; vaccination; flu; pneumococcal infection

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Introduction

Chronic obstructive pulmonary disease (COPD) can be described as a chronic inflammatory disease. It is associated with an irreversible airflow limitation and causes a progressive deterioration of pulmonary functions, accompanied by symptoms including regular sputum production, chronic cough, breathlessness and reduced physical activity (1). Patients have a higher risk for respiratory tract infection, therefore a growth in the frequency of acute exacerbations of the disease can be observed. As a consequence of acute exacerbations, morbidity and mortality increase (2). Although mostly rhinovirus causes exacerbations, influenza is also known as an important factor in triggering exacerbations of COPD that lead to hospitalization in most cases, and it can contribute, as a major factor, to mortality and morbidity in COPD (3). Based on the various mechanisms, an increased production of specific cell adhesion molecules and impaired mucociliary clearance can mediate the attachments of viruses and bacteria to the airway epithelium (4), and because of these processes, patients with COPD are more likely to develop influenza (5) and pneumococcal pneumonia (6).

Currently, the annual influenza vaccination of COPD patients is a top priority and pneumococcal vaccination is recommended in 5 years (7). Kopsaftis *et al.* reviewed six randomised controlled trials about the efficiency of influenza vaccination in patients with chronic bronchitis or COPD. The studies included 2,562 patients. Based on their reports, influenza vaccine reduced the number of exacerbations compared to placebo in patients with COPD (8).

Schembri *et al.* found association between influenza vaccination and a 41% reduction in the risk of all-cause mortality (9). Although most international consensus guidelines advocate vaccination, and the positive effects of vaccinating patients with COPD have been proven, a significant percentage of patients still remain unvaccinated (10). A considerable effect of multiple psychosocial factors and preexisting health beliefs must be taken into account in the decision to accept vaccination (11). A great opportunity was provided to explore the reasons behind the advancement of the “anti-vaccine movement” during the swine flu pandemic in 2009. They analyzed interviews with public critics of the pandemic flu vaccine, and identified several common motivating factors. These included concerns over safety stemming from the belief that the vaccine and its side

effects had not been properly investigated, as seemingly the product was released onto the market in a short time, and the belief that pharmaceutical companies make a big impact on this process because of their financial interest. Another belief was that the vaccine may contain other “dangerous” ingredients, so by receiving the vaccine, their chance to develop other “serious diseases” may increase. The contrasting opinion was that pandemic influenza did not pose “a serious threat to the health of most individuals” meaning that the risks of vaccination outweighed those of influenza infection (12). Public health initiatives are necessary to emphasize the importance of influenza and pneumococcal vaccination, and to facilitate the increase of vaccination rates in this patient population. The purpose of this study was to determine the prevalence of influenza and pneumococcal vaccination in the population of COPD patients, and to investigate the effectiveness of vaccines in terms of reduction of the risk of severe, acute exacerbations of COPD.

Methods

Study design and population

The study involved 250 COPD patients hospitalized at the Pulmonary Rehabilitation Department. Inclusion criteria were age over 40 and the diagnosis of COPD based on the clinical feature and lung function (post-bronchodilation FEV₁/FVC <70%). Patients were selected by simple randomized sampling according to the data of respiratory functions, comorbidities and anthropometric details, which had been retrieved from the electronic health record system. As relevant comorbidities, we included congestive heart failure, coronary artery disease, hypertension, malignancy, diabetes, osteoporosis, metabolic syndrome, anxiety, and mood disorder. The study was approved by the Ethical Committee of the National Koranyi Institute for Pulmonology, Budapest, Hungary, under the registration number of 25/2017. All patients enrolled completed the informed consent form. The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013).

Collected characteristics

We collected the sociodemographic characteristics for each patient, including age, gender, alcohol consumption, smoking, years since their COPD diagnosis, treatments, the number and severity of COPD exacerbations, and the

history of 23 pneumococcal and influenza vaccination cases (seasons 2017–2018). In our questionnaire, we asked the patients' opinion about vaccination and whether they have been informed about the pathogens and vaccines by their physician. COPD exacerbation was defined as a significant change of the patient's initial symptoms (dyspnea, cough, sputum production), or if at least two of the following four symptoms exist (Anthonisen criteria): (I) an increase in purulent sputum, (II) deterioration in lung function, worsening of respiratory complaints, (III) fever, or (IV) leukocytosis. In the case of moderate exacerbation, the prescription of an antibiotic or systemic corticosteroid was required, while the definition of severe exacerbation when the patient had to be hospitalized for more than 24 hours, and received non-invasive or mechanical ventilation. Based on whether they had received influenza vaccination or not in the 2017–2018 campaign, patients were classified in two cohorts. Participants were also categorized into four groups according to their degree of bronchial obstruction, based on FEV₁ data defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines; mild: FEV₁ ≥80%; moderate: 50% FEV₁ <80%; severe: 30% FEV₁ <50%; very severe: FEV₁ <30% (GOLD stages 1–4). Body mass index (BMI) was used as the independent variable. It is calculated as weight divided by height squared (kg/m²). All participants were classified into four subgroups, underweight patients had a BMI under 18.5 (BMI <18.5), the BMI of average weight patients were between 18.5 and 25 (18.5 ≤ BMI <25), overweight participants had their BMI between 25 and 30 (25 ≤ BMI <30) and obese patients' BMI values were over 30 (BMI ≥30). The categorization was based on the standard of World Health Organization (WHO).

Statistical analysis

Shapiro-Wilk test was used to confirm the quantitative variables normal distribution which was followed by Student's *t*-test for comparisons. Chi-squared test was used for comparisons of the proportions of categorical and discrete variables. We estimated odds ratios (OR) using unconditional logistic regression with 95% confidence intervals (95% CIs). According to COPD severity (GOLD stages 1–2 versus GOLD stages 3–4), associations for a history of influenza and pneumococcal vaccination were stratified. Factors influencing vaccine uptake (age, gender, smoking status, comorbidities, and COPD GOLD stage) were analyzed by logistic regression. The

study was registered in the ISRCTN registry with the ID ISRCTN13019180, and before the statistical analysis was performed, data were anonymised. A value of *P*<0.05 was accepted for significance.

Results

The prevalence of influenza and pneumococcal vaccination coverage with principal clinical and sociodemographic characteristics is presented in *Table 1*. In total, we examined the data of 250 patients with chronic obstructive pulmonary disease, the sample consisted of 109 male patients (43.6%) and 141 female patients (56.4%). The average age of the observed population was 66.62 years (±8.34), 67.30 (±8.54) years for men, 66.09 (±8.16) years for women. Seven point two percent (n=18) of the patients were non-smoking. The observed patients had been smoking an average of 19.9 cigarettes a day for 37.16 years. One third of them (30.4%) (n=76) are still active smokers. COPD had been diagnosed approximately 8 years ago on average, and they had taken inhaled medications for 7.7 years. Patients who had successfully quit smoking had smoked their last cigarette 5 years before the study was conducted, on average.

Four point eight percent (n=12) of the 250 patients were classified as GOLD I (mild) stage, 35.6% (n=89) as GOLD II (moderate) stage, 46.4% (n=116) as GOLD III (severe) stage and, 13.2% (n=33) as GOLD IV (very severe) stage. The average values of FEV₁%pred, registered after bronchodilatation were GOLD I: 93.50%, GOLD II: 61.98%, GOLD III: 41.24%, GOLD IV: 20.11%.

The vaccination rates were 23.6% for influenza, and 10.8% for pneumococcus, only 6% of patients received both vaccinations. The vaccination rate was higher for more severe forms of COPD in both vaccinations (*Table 2*). Influenza vaccination coverage was 26.6% in men and 21.2% in women, the pneumococcal vaccination rate was 13.7% in male patients and 8.5% in female patients, and the vaccination rate was higher in elderly patients, and in patients with comorbidities. Thirteen point two percent of smokers were vaccinated against influenza and 5.2% against pneumococcus. The influenza vaccination rate among non-smokers was 28.2%, and it was significantly different from the pneumococcal vaccination rate (13.2%) (*P*<0.05).

We found statistically significant association between influenza and pneumococcal vaccination and the reduced risk of severe exacerbations, influenza vaccination OR: 2.11 (95% CI: 0.88–5.02) and pneumococcal vaccination OR: 1.06 (95% CI: 0.84–1.34) were detected (*Table 2*) and

Table 1 Influenza vaccination prevalence by principal clinical and sociodemographic features

Variables	Vaccinated		Unvaccinated		Total		P
	N=59	% Row	N=191	% Row	N=250	% Column	
Sex							
Men	29	26.61	80	73.39	109	43.60	0.325
Women	30	21.28	111	78.72	141	56.40	
Age, mean (SD)	67.90 (6.63)		66.23 (8.78)		66.62 (8.34)		0.111
BMI, kg/m ²							
Mean (SD)	27.65 (6.31)		26.05 (6.15)		26.42 (6.25)		0.112
Underweight	2	9.09	20	90.91	22	8.80	0.108
Normal weight	21	24.14	66	75.86	87	34.80	
Overweight	19	26.39	53	73.61	72	28.80	
Obesity	17	24.64	52	75.36	69	27.60	
Smoking habit							
Active	10	13.16	66	86.84	76	30.4	0.010
Non-smoker	49	28.16	125	71.84	174	69.6	
Former smoker	51	23.39	167	76.61	218	87.2	
Alcohol use							
Drinker	10	29.41	24	70.59	34	13.6	0.385
Non-drinker	47	22.60	161	77.40	208	83.2	
Unknown	2	25.00	6	75.00	8	3.2	
FEV ₁ ,ref%, mean (SD)	53.08 (17.21)		45.23 (17.55)		47.37 (17.73)		0.014
GOLD stage							
Mild	3	25.00	9	75.00	12	4.8	0.006
Moderate	32	35.96	57	64.04	89	35.6	
Severe	20	17.24	96	82.76	116	46.4	
Very severe	4	12.12	29	87.88	33	13.2	
Comorbidity							
Hypertonia	39	23.21	129	76.79	168	67.2	0.203
Diabetes mellitus	25	32.89	51	67.11	76	30.4	
Heart failure	8	16.67	40	83.33	48	19.2	
Ischemic heart disease	7	17.07	34	82.93	41	16.4	
Metabolic syndrome	2	15.38	11	84.62	13	5.2	
Osteoporosis	6	16.67	30	83.33	36	14.4	
Lung cancer	2	33.33	4	66.67	6	2.4	
Psychiatric history	32	30.19	74	69.81	106	42.4	

Table 1 (continued)

Table 1 (continued)

Variables	Vaccinated		Unvaccinated		Total		P
	N=59	% Row	N=191	% Row	N=250	% Column	
23-valent pneumococcal vaccination							
Yes	22	81.48	5	18.52	27	10.8	<0.001
No	37	16.59	186	83.41	223	89.2	
Exacerbations							
Mean (SD)	0.95 (0.52)		1.91 (1.76)		1.62 (1.74)		0.003
N	25	42.37	34	57.63	59	23.6	–

P<0.05 means the two indicators were significantly correlated. GOLD, Global Initiative for Chronic Obstructive Lung Disease; BMI, body mass index; FEV₁, forced expiratory volume in the first second; SD, standard deviation.

Table 2 Influenza and pneumococcal vaccination rate and odds ratio in patients with COPD (total n=250)

Variable	Vaccination rate (%)	Severe exacerbations, at least 1, n=59	
		OR	95% CI
Influenza vaccination (n=59)		2.11	0.88–5.02
GOLD I-II (n=101)	21.62	–	–
GOLD III-IV (n=149)	25.71	–	–
Pneumococcal vaccination (n=27)		1.06	0.84–1.34
GOLD I-II (n=101)	10.23	–	–
GOLD III-IV (n=149)	11.44	–	–

COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio; CI, confidence interval.

patients (15/250) with both vaccination (influenza and pneumococcal vaccine) OR: 2.37 (95% CI: 1.39–4.08). Logistic regression analysis of demographic and functional parameters influencing influenza and pneumococcal uptake are in Table 3. It describes how more advanced age (≥ 65 years), the presence of comorbidities, and more severe COPD disease were related positively with both influenza and pneumococcal uptake, while the presence of active smoking was associated with lower influenza and pneumococcal vaccination rates (Table 3).

Only 28.4% (n=71) of the patients were informed by their physician about the necessity of vaccination because of their chronic illness. Thirty-six percent (n=90) of the patients found vaccination against influenza beneficial, while 26.0% (n=65) considered pneumococcal vaccination as useful. According to 31.2% (n=78) of the patients, the influenza virus causes only mild illness and 54.0%

(n=135) of them had never heard about the Pneumococcus bacteria. Only 10.0% (n=25) of the observed patients had received treatment with bacterial lysate medicines (OM85-BV, Broncho-Vaxom), none of them had received other immunomodulators (Ribomunyl, Isoprinosine). Sixty-nine point six percent (n=174) of the patients had taken antibiotics in the preceding year, twice a year on average. Fifty-six point eight percent (n=142) of them received oral steroid cure, twice a year on average. Due to the deterioration of their condition, 36.8% (n=92) of the patients needed non-invasive or mechanical ventilation, twice a year on average.

Discussion

In our study, the influenza vaccination rate of the observed Hungarian COPD patients, aged 40 years or above was

Table 3 Logistic regression analysis of demographic and functional parameters influencing influenza and pneumococcal vaccination

Variables	Influenza vaccinated		Pneumococcal vaccinated	
	OR	95% CI	OR	95% CI
Age (≥ 65 year) (n=250)	2.27	1.39–4.01	2.13	0.95–4.77
Sex (men/women)	1.65	0.41–2.03	1.32	0.71–1.94
Smoking habit				
Active-smoker	0.20	0.03–1.49	0.72	0.36–1.42
Non-smoker				
Comorbidity	1.13	1.07–1.40	1.01	0.47–1.92
GOLD stage (III, IV/I, II)	1.17	1.02–1.34	1.09	0.77–1.65

OR, odds ratio; CI, confidence interval; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 4 Influenza and pneumococcal vaccination rates and recommendation among people with COPD

Country	Vaccination rates		
	Influenza vaccination in past 12 months (%)	Pneumococcal vaccination in past 5 years (%)	Recommended by WHO (%)
Hungary	23.6	10.8	75
USA	0.0	49.9	90
UK	36.1	16.8	75
Spain	49.4	32.5	75
Germany	46.5	14.6	75
France	73.0	53.0	75
Italy	30.5	13.3	75
Turkey	36.5	14.1	75

Apart from the indicators describing the vaccination rate of elderly (age ≥ 65), currently there is no available data of influenza and pneumococcal vaccination rates in other high-risk populations, so there is no accurate data or any available database of the vaccination coverage of patients with COPD. Source: (10,13-21). COPD, chronic obstructive pulmonary disease.

23.6%, which is below the internationally targeted 75% set by the WHO. The pneumococcal vaccination rate was 10.8%. Studies from other countries reported similar conditions as well (Table 4). According to the UK primary care consultation database, the influenza vaccination coverage rate of the COPD patients in the country was 36.1% (13) and the PPV23 vaccination rate was 16.8% (14). The influenza vaccination rate was 30.5%, while the pneumococcal vaccination rate was 13.3% in Italy in an epidemiological study (15). The rates were 36.5% for influenza and 14.1% for pneumococcus in Turkey (16). A clinical study observed 46.5% influenza and 14.6% pneumococcal vaccination in Germany (17). Influenza and pneumococcal vaccination were higher in the elderly, more

severe COPD population with comorbidities and who quit smoking in our research, which are similar to other previous studies (18,19).

Our findings have proven that influenza and pneumococcal vaccination is associated with a decreased risk of acute exacerbations among patients with COPD, including severe exacerbations requiring hospitalisation. Similar results were found by Garrastazu *et al.* Their retrospective cohort study included 899 COPD patients from Spain. They reported that in the year following immunization, influenza vaccination significantly reduced the risk of severe exacerbations requiring hospitalization [OR 0.54 (95% CI: 0.35–0.84)], a better effect was found in patients with more severe COPD (22). A randomized

controlled trial (RCT), including 596 patients showed a significant efficacy of 76% (95% CI: 20–93%, $P=0.013$) of PPV23 against community-acquired pneumonia (CAP) in patients less than 65 years of age. It proved to be nearly significant at 48% (95% CI: 27–80%, $P=0.076$) in patients with severe airflow obstruction, and showed the best results when both characteristics were present (23).

Influenza and pneumococcal vaccination rates have been shown to be suboptimal among COPD patients in our study. Vandenbos *et al.* (24) found negative attitudes against influenza vaccinations and lack of recommendation from general practitioners or other doctors as main reasons for refusing. Patients do not believe in the effectiveness of vaccines, do not believe that they are exposed to this risk, and patients are also concerned about the undesirable side effects of vaccines in the study of Ciblak *et al.* (25).

The WHO also reports vaccine insecurity and non-vaccination among the top 10 threats to the world (20). Only one third (36.0%) of patients considered the influenza vaccine useful, while only a quarter (26.0%) thought that pneumococcal vaccine is beneficial, more than half of the patients (54.0%) had never heard of *Pneumococcus* bacteria in our present study in the Hungarian population similarly to other countries. In addition, in recent decades, anti-vax movements have taken root in many countries (26). Members of these movements most often live in developed countries, where the incidence of vaccine-preventable diseases is typically low. They spread their false and misleading information about the composition, side effects and harmful consequences of vaccines on a variety of Internet interfaces, social media sites and among themselves, causing great harm.

COPD patients are advised to receive influenza vaccination annually, but it is also recommended to other populations at risk, such as anybody over the age of 65, patients with chronic illnesses, health care workers, caregivers, or others at a higher risk of complications. Pneumococcal vaccination is recommended to everybody over 50, smokers (regardless of their age and comorbidities), patients under immunosuppressive therapy, patients with cochlear implants or cranial injury, to patients of any age with chronic diseases (such as diabetes, respiratory, renal, liver, heart diseases), and patients with asplenia, as they are more susceptible to severe pneumococcal infections (21,27).

A meta-analysis of influenza vaccination in the elderly (≥ 65 years) population found that respiratory disease was reduced by 56%, pneumonia by 53%, hospitalization by 50%, and all-cause mortality by up to 68% with vaccination

at the time of an influenza pandemic. Most studies showed that vaccination is clearly effective (28), yet vaccination is very low. After 1 year of follow-up, RCT studies reported that influenza-vaccinated patients experienced significantly ($P=0.005$) reduced exacerbations and influenza-like illnesses (ILIs) compared to the non-vaccinated population (29).

About 40% of CAP requiring hospital admission in adults is caused by *Streptococcus pneumoniae* (pneumococcus) (30). In Europe, the incidence of CAP was dramatically higher in persons with severe COPD. In the general population, 1.07–1.2/1,000 person-years incidence was found, while the number of cases in the population of COPD patients were 20-fold higher (22.4/1,000 person-year) (30). Despite accessible and adequate antimicrobial therapy in the past 60 years, severe pneumococcal infections with bacteraemia are still responsible for approximately 12% of the mortality (31). In addition to the fact that usually pneumonia has a poor outcome for COPD patients, healthcare systems also have to deal with its serious consequences. With COPD patients, productivity costs and direct medical costs associated with hospitalization for CAP are twice as high as with patients with no comorbidities. Substantial benefits could be provided to patients and the society as well by preventing pneumonia in patients with COPD (32). The effectiveness of antibiotic therapy is limited, and as a result of antibiotic resistance, it is becoming more significant, while the number of individuals at a high risk of infection is increasing in the population. The importance of prevention must be emphasized based on these observations (33).

An analysis of COPD patients aged 55 or above showed that in vaccinated participants, the hazard ratio of acute coronary syndrome requiring hospitalization was significantly lower than in unvaccinated participants. Sung *et al.* also reported the relevance of repeating influenza vaccinations in the same patient across several study seasons, as it has a significant benefit ($P<0.001$) (34). PCV13 and seasonal influenza vaccine can be given at the same time, as the vaccines have no effect on each other, however, it provides us a good opportunity to avoid missed occasions for vaccination (35). Moreover, applying the two vaccines together have an additive effect in reducing the mortality due to influenza or pneumonia and the risk of hospitalization for pneumonia (36). Effective pneumococcal vaccination could also be of great help in reducing the need for antibiotic treatments, which is an important aspect, as the reduction of antibiotic treatments could result in a delay or prevention in the colonization of the lungs by antibiotic-resistant bacteria (37).

A single-centre study of 187 COPD patients admitted

with an acute exacerbation (109 pre-intervention, 78 post-intervention) was performed by Bhatt *et al.* in Alabama, US. The aim of the study was to determine whether 30-day all-cause recurrence rates of COPD exacerbations and overall costs could be reduced by multimodal intervention. It included a rapid check-up in a COPD clinic in case of post-acute exacerbations, a pack of tutorials to educate patients, and regular follow-up phone calls by a practice nurse. The primary outcomes have not shown any differences in their study. However, the observed post-intervention influenza vaccination rates (31% *vs.* 51%, $P=0.011$) and pneumococcal vaccination rates (37% *vs.* 82%, $P<0.001$) were significantly increased. The results of their study suggest that greater patient engagement with evidence-based care including vaccination could be expected in case of an acute admission, due to an exacerbation of COPD, despite the study had the limitation of its small sample size. Furthermore, the conclusion of the study is that the greatest effect on vaccination rates could be achieved by combining clinician and patient-focused interventions, using multimodal intervention methods (38).

Based on research evidence, to optimize the care of COPD patients and to increase vaccination rates in high-risk populations, adopting a holistic approach may be more efficient, and so would be targeting several different aspects of care simultaneously. For instance, during smoking cessation, counseling vaccine recommendations and other aspects of evidence-based care should be highlighted as well (39). Patients who built trust with their physician are more likely accept and respect treatment recommendations, as trust is a key determinant of patient behaviour. Therefore, this factor must be kept in mind during vaccination consultations (40). Recent research has shown that focusing on cultivating “positive patient-doctor relationships based on listening and understanding” by applying a patient-centered, narrative medication method helps establish a good cooperation and can improve adherence to treatment recommendations in COPD patients (41,42). The importance of influenza vaccination cannot be stressed enough; annual immunization against influenza administered together with pneumococcal vaccination significantly decreases the number and severity of complications in older patients as well.

Limitations and strengths of the study

Several limitations of our study should be noted. First, sociodemographic variables, such as educational level

and marital status were not available. Second, we could only conclude the association between influenza and pneumococcal vaccination and the risk of occurrence of acute exacerbation. Third, in our study, we applied GOLD I–IV classification, because data [modified Medical Research Council (mMRC) or COPD assessment test (CAT) results] necessary for the current GOLD A–D classification were not available. Despite the listed limitations, we have to mention the important strengths of the study. The association between influenza and pneumococcal vaccination and the risk of acute exacerbation of COPD patients at the Department of Pulmonary Rehabilitation of the National Koranyi Institute of Pulmonology, Budapest had not been reported before.

Conclusions

In conclusion, along with the available evidence, the findings of this study support the association between influenza and pneumococcal vaccination and the decreasing risk of COPD exacerbations in the following year. The overall prevalence of influenza and pneumococcal vaccination was under the optimal level, despite the evidence for its protective effect. Therefore, these high-risk patients are recommended to receive annual influenza vaccination, pneumococcal vaccination every 5 years and should be informed about their vaccination opportunities by their physician during their treatment. Older age, the presence of comorbidities, and more severe GOLD stages had a positive effect on the uptake of both influenza and pneumococcal vaccinations. Further large-scale prospective studies are required to analyse the effectiveness of influenza and pneumococcal vaccination in patients with COPD.

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Footnote

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Conflicts of Interest: All authors have completed the

ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/jtd-20-814>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethical Committee of the National Koranyi Institute for Pulmonology, Budapest, Hungary, under the registration number of 25/2017. All patients enrolled completed the informed consent form. The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013).

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