Original Article

First booster dose uptake of COVID-19 vaccine and disease-related factors in chronic obstructive pulmonary disease—a cross-sectional survey in Hungary

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Background: In chronic obstructive pulmonary disease (COPD), uptake of the coronavirus disease 2019 (COVID-19) booster vaccine is important, as they are more likely to develop serious complications. Our aim was to investigate the uptake rate of first booster vaccination against COVID-19 among COPD patients and to identify other related factors of vaccine uptake.

Methods: We conducted a multicenter survey of COPD patients in Hungary by region: eastern, western and central ones from 15 November 2021. Respiratory function test results, anthropometric data and vaccination status were recorded for 1,510 randomly selected patients over 35 years of age. Multiple logistic regression analysis was used to determine factors associated with uptake of COVID-19 first booster dose vaccines.

Results: The average age was 67 [61–72] years, for men it was: 67 [62–73] and 66 [60–72] years for women, with a sample of 47.95% men and 52.05% women. The uptake rate of the COVID-19 first booster vaccine during the study period was 62.45%. Comparing patients who received the 3rd vaccine with those who did not receive the 3rd vaccine, the difference was significant in quality of life: COPD Assessment Test (CAT): 16 [11–21] *vs.* 14 [10–19], P<0.001, modified Medical Research Council (mMRC) dyspnea scale: 2 [2–2] *vs.* 2 [1–2], P=0.01 and in the number of moderate exacerbations: 1 [0–1] *vs.* 0 [0–1], P=0.04. In addition, who did not take the third vaccination significantly more people were hospitalized for acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (16 *vs.* 0, P<0.001) and almost the same proportion (n=14) required pulmonary outpatient rehabilitation for post-COVID symptoms. The factors that were most associated with higher COVID-19 vaccine first booster dose uptake were older age [odds ratio (OR): 1.06; 95% confidence interval (CI): 1.04–1.08], male gender (OR: 0.74; 95% CI: 0.57–0.96), absence of previous COVID-19 infection (OR: 0.34; 95% CI: 0.23-0.51).

Conclusions: The uptake rate of the COVID-19 booster vaccine among COPD patients in Hungary is lower than the target, and is associated with disease-related factors, and age, sex, previous COVID infection. The global COVID-19 vaccination target is 70% and 100% for elderly, vulnerable patients. Highlighting the importance of taking booster vaccine(s) should be a priority for health workers.

Keywords: Chronic obstructive pulmonary disease (COPD); coronavirus disease 2019 (COVID-19); vaccine uptake; COVID-19 vaccine first booster

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Introduction

The coronavirus disease 2019 (COVID-19) is an acute respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is currently causing a pandemic (1). Slowing the spread of the global epidemic remains a paramount importance to everyone, with many segments of society working to reduce the number of new infections (2). The disease has mild to moderately severe symptoms in most infected individuals, where the recovery can happen without hospitalization (3). However, people with chronic diseases such as chronic obstructive pulmonary disease (COPD) and older people are at a higher risk of developing serious complications (4). Primary prevention, including basic and booster vaccination(s) against the virus, is paramount (5).

Studies have described that the COVID-19 booster vaccines uptake significantly reduce the transmission and severity of COVID-19 infection, while increasing the titer of antibodies against different types of coronavirus variants (6-8). Therefore, the Centers for Disease Control and Prevention (CDC), World Health Organization (WHO) and the European Medicines Agency (EMA) all unanimously recommend the inclusion of booster vaccine(s), especially for at-risk groups (6,7). CDC data show that those who have been vaccinated in time for the full series are 13 times less likely to die from COVID infection than those who have not been vaccinated, and three times less likely to die than those who have not received the first booster vaccine. In addition, the COVID-19 booster vaccines can be given at the same time as the seasonal annual flu inoculation, with no waiting period between vaccinations (8).

According to a CDC study, booster vaccines from Pfizer and Moderna's COVID-19 inoculations are highly effective in preventing hospitalizations due to the Omicron variant (9). Booster vaccines can put a stop to the need for hospitalization after infection in 90% of cases and prevent the need for emergency department admission in 82% of patients who are infected and hospitalized (10). Data show that unvaccinated adults over the age of 65 who are infected with COVID-19 are 49 times more likely to be hospitalized than those who are vaccinated and have received the booster vaccine, too. The unvaccinated adults over the age of 50 years are 45 times more likely to be hospitalized than those who have been vaccinated and have received the booster dose, too (11-13).

Song *et al.*'s study found out that the actual uptake rate of COVID-19 vaccination was relatively low (39.0%) among COPD patients, although the majority of them would be willing to accept the COVID-19 vaccine (14). Surprisingly, nearly half of the patients who were not vaccinated against this disease were not recommended by their doctors to be even vaccinated against COVID-19, which was probably the main reason for the low vaccination rates among them. In addition, their data have shown that a significant proportion of them have a lack of the necessary knowledge about the inoculation and lack confidence in the efficiency and safety of COVID-19 vaccination, which also acts as a barrier to the uptake (14). Another Chinese study described the COVID-19 vaccination rate among postoperative breast cancer patients was only 36.0% and a significant proportion of patients believed that COVID-19 vaccination could have a negative impact on the chemotherapy they received, i.e., that their recovery would be set back by receiving the vaccine(s), and were also concerned about the side effects of the vaccine (15). The role of healthcare staff (doctors, nurses) is therefore indisputable in promoting any vaccination, including COVID-19, raising awareness, dispelling misinformation and providing patients with comprehensive information. Unfortunately, misconceptions and misinformation about vaccination remains a major barrier to the uptake and to achieve an optimal vaccination coverage as well as to herd immunity in Hungary for various vaccines, e.g., seasonal influenza, pneumococcal vaccines, COVID-19 vaccine (16). A recently published meta-analysis described an association between people's gender, place

Highlight box

Key findings

- In COPD, uptake of the COVID-19 booster vaccine is important, as they are more likely to develop serious complications.

What is known and what is new?

- The WHO recommends the uptake of COVID-19 booster vaccine for long-term protection, especially for high-risk populations.
- The uptake rate of the COVID-19 first booster vaccine during the study period was 62.45%. The factors that were most associated with higher COVID-19 vaccine booster dose uptake were the following: older age, male gender, region of residence, better quality of life, lower number of exacerbations and emergency hospital visits, absence of previous COVID-19 infection.

What is the implication, and what should change now?

- Health personnel should make it a priority to promote vaccination, to raise awareness of the efficacy and safety of them, to educate patients as well as to highlight the importance of taking booster vaccine(s).

of residence, sociodemographic characteristics and their willingness to be vaccinated against COVID-19 (17). This study showed that Chinese men are 1.48 times more likely to be vaccinated against COVID-19 than women are (17). No similar study specifically for COPD patients was found in the international and national literature, the uptake of the first booster vaccine COVID-19 among COPD patients in Hungary and its related factors have not been investigated yet. Therefore, the aim of our study was to assess the uptake rate among them and to describe the related factors of first booster vaccine uptake in relation to disease-related factors such as quality of life, presence of comorbidities, smoking status, gender, age, previous COVID-19 infection, number of hospital visits. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-1256/rc).

Methods

Study design and population

A cross-sectional study was conducted in COPD patients from the eastern, western and central regions of Hungary from November 15, 2021. Patients were recruited from outpatient pulmonary clinics from community hospital, and their data were collected according to routine clinical practice. A total of 1,511 patients were included who were informed of the survey verbally and in writing before signing a consent statement. The exact dates of the COVID-19 vaccinations were obtained from the National eHealth Infrastructure (abbreviated EESZT). For one patient, the fact of revaccination could not be verified with certainty due to his employment abroad in the meantime, and he was excluded from the study, so 1,510 patients were included in the analysis. The study was approved by the Hungarian National Institute of Pharmacy and Nutrition (document No. IV/7743-1/2021/EKU) based on a positive review by the Hungarian National Research Ethics Committee (registration No. CHMED_2021/01), and the study complies with the Declaration of Helsinki (as revised in 2013). Inclusion criteria for the study were age over 35 years, patients with known COPD [forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) <70% after bronchodilator] (18), specialist diagnosis and inhalation therapy at least 1 year earlier. Exclusion criteria were the followings: if the patient did not meet any of the above expectations, or if the patient was unable to complete the portion of the questionnaire applicable to him/her. Anthropometric measurements, respiratory function test results, COVID infection history and post-COVID symptoms were recorded for the visiting patients. Our current study protocol and details of the conduct of the study were described in detail in our previous article (19).

Measurements

The uptake of the first booster dose (3rd vaccination) of COVID-19 vaccine was the outcome variable of the study. We have asked the participants if they had received a first booster dose of the vaccine, with the response options of yes/no. The gender was bivariate: male or female, and the place of residence was divided into three regions: Western, Eastern and Central Hungary. Our questionnaire asked about smoking habits: current heavy smoker, never smoked or quit smoking with response options. We also asked about co-morbidities, medications used for COPD, and the number of exacerbations (severe and moderate) in the past year. We also asked about the number of visits to healthcare facilities in the past year: visits to general practitioners (GPs), emergency departments, pulmonary departments and pulmonary outpatient services. When recording the COVID-19 vaccination history, we asked for vaccination status. Yes = vaccinated/no = not vaccinated. In the case of vaccinated patients, we also asked for the exact date of all three vaccinations and checked in EESZT, then recorded in the Excel spreadsheet of the survey. We asked whether the patient had SARS-CoV-2 infection, if so when, and whether he had required hospitalization for the acute COVID-19 infection. We also asked whether they had required pulmonary outpatient care for post-COVID symptoms, the response options were yes/no.

Examination of respiratory function

All patients underwent respiratory function testing with an automated computerized spirometer. Dynamic lung volume is defined as FEV_1, the degree of airway obstruction (ratio of FEV1/FVC) and the inspiratory vital capacity (IVC). Global Lung Function Initiative (GLI)—defined normal spirometry stratifies patients into Global Initiative for Chronic Obstructive Lung Disease (GOLD) A–D stages based on current and future risk parameters such as associated symptoms, quality of life [COPD Assessment Test (CAT)/modified Medical Research Council (mMRC)] and exacerbation numbers (20).

Quality of life examination

The CAT is used to measure quality of life. Patients answered eight questions and rated symptoms on a scale from 0 to 5, with 0 being healthy and 5 being severe symptoms. Subjective assessments of cough, sputum production, hyperinflation, resilience and energy levels while climbing stairs, and whether the patient dared to leave the house or whether the illness interfered with sleep (21).

mMRC dyspnea questionnaire

The mMRC questionnaire stratifies the severity of dyspnea and consists of five items; it almost completely covers the entire spectrum of shortness of breath, from no problems (grade 0) to complete respiratory failure (grade 5). Patient-rated on a scale of 0–5, all questions are relevant to daily activities and easy for the patient to understand. A score can be calculated in seconds and is the number that best matches the patient's condition (22).

Definition of exacerbation

COPD exacerbations were defined according to the current GOLD definition. Moderate exacerbations require a prescription for antibiotics or systemic corticosteroids, whereas severe exacerbations require admission to the emergency department or hospital (18,20).

Definition of COVID-19 infection

Any subject, who was asymptomatic or developed at least one of the following symptoms during the study period: cough, increased body temperature, fever, dyspnea, sudden loss of smell, loss of taste, or dysgeusia, and had detectable SARS-CoV-2 nucleic acid or antigen.

Body mass index (BMI)

BMI (kg/m^2) is calculated by dividing weight in kilograms (kg) by the square of height in meters (m^2).

Statistical analysis

All statistical analyses were conducted in SPSS 28.0.0. Non-parametric statistical techniques were utilized because the majority of the continuous data did not conform to the normal distribution, as demonstrated by the Shapiro-Wilk test. Medians and interquartile ranges (IQRs) were used to interpret and represent continuous variables. Case numbers and ratios were used to present categorical data. Continuous variables were compared between the two groups using Mann-Whitney tests; Kruskal-Wallis tests were used when there were more than two groups. Fisher's exact test was used to investigate categorical variable frequency differences. The data were described using multiple logistic regression analysis to explain the relationship between various variables and unvaccinated and triple-vaccinated patients. Odds ratios (ORs) are presented with 95% confidence intervals (95% CIs), the significance level was $P<0.05$. In the logistic regression analysis, ORs are presented for sex (female/male), age, region of living (central/eastern/western), number of moderate/severe exacerbations (<1/≥1), GP care and emergency/pulmonary hospitalization (yes/no), CAT score, mMRC score, GOLD stage (CD/AB), currently smoking status (yes/no), number of comorbidities (<2/≥2), previous history of COVID-19 infection (yes/no), and participation in COVID-19 rehabilitation (yes/no). All statistical tests were two-sided, took into account a 95% CI, and the significance level was set at $P<0.05$.

Results

Sociodemographic and functional features

A total of 1,510 COPD patients took part in the study, 52.05% of whom were female and 47.95% male. The observed patients had been smoking an average of 17.5 cigarettes a day for 35.5 years. Almost half of the patients (46.49%) (n=702) were still active smokers, while 14.7% of patients (n=222) had never smoked. Demographic and anthropometric characteristics of the patients are presented in *Table 1*.

Overall, 943 (62.45%) participants received a booster dose of COVID-19 vaccine. The median age of the patients was 67 [61–72] years, older age can be associated with a higher proportion of COVID-19 booster vaccine administration 68 [63–73] *vs.* 64 [57–70], $P<0.001$. The booster dose was used significantly more in the western regions of the country (42.42%) than in the eastern (30.54%) or central (27.04%) regions. Significantly more men (51.64%) received the booster dose than women (48.36%). Patients who quit smoking and those who never smoked were significantly more likely to take the first booster dose of COVID-19 vaccine ($P<0.001$) (*Table 1*).

Table 1 Socio-demographic and functional characteristics of the study's respondents (got COVID-19 booster dose)

Characteristics	No (n=567, 37.55%)		Yes (n=943, 62.45%)		Total (n=1,510, 100.00%)		P value
	N/median	%/IQR	N/median	%/IQR	N/median	%/IQR	
Sex							
Men	237	41.80	487	51.64	724	47.95	<0.001
Women	330	58.20	456	48.36	786	52.05	
Age (years)	64	57–70	68	63–73	67	61–72	<0.001
BMI (kg/m^2)	27.3	24–31	27.6	24–31	27.5	24–31	0.92
Smoking habit							
Active	305	53.79	396	41.99	701	46.42	<0.001
Non-smoker	75	13.23	147	15.59	222	14.70	<0.001
Former smoker	187	32.98	400	42.42	587	38.87	<0.001
Region of living							
Western	204	35.98	400	42.42	604	40.00	0.01
Eastern	227	40.04	288	30.54	515	34.11	<0.001
Central	136	23.99	255	27.04	391	25.89	0.18
FEV_1 (% pred)	57	45–72	60	46–74	59	45–74	0.19
GOLD stage							
A	68	11.99	116	12.30	184	12.19	0.85
B	386	68.08	696	73.81	1082	71.66	0.01
C	3	0.53	7	0.74	10	0.66	0.62
D	110	19.40	124	13.15	234	15.50	<0.001
CAT	16	11–21	14	10–19	15	11–20	<0.001
mMRC dyspnoea scale	2	2–2	2	1–2	2	1–2	0.01
Severe exacerbation	0	0–0	0	0–0	0	0–0	0.94
Moderate exacerbation	1	0–1	0	0–1	0	0–1	0.04
Previous history of COVID infection	65	11.46	0	0.00	65	4.30	<0.001
Hospital treatment	16	2.82	0	0.00	16	1.06	<0.001
Post-COVID hospitalization	14	2.47	0	0.00	14	0.93	<0.001

P<0.05 means the two indicators were significantly correlated. COVID-19, coronavirus disease 2019; IQR, interquartile range; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; % pred, % of predicted value; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD Assessment Test; mMRC, modified Medical Research Council; COPD, chronic obstructive pulmonary disease.

Co-morbidities, quality of life, acute SARS-CoV-2 infection and post-COVID symptoms

Among the comorbidities the presence of hypertension (P=0.04) and acute myocardial infarction (MI) (P=0.008) were significantly associated with first booster vaccine uptake (*Table 2*). The quality of life: CAT: 16 [11–21] *vs.* 14 [10–19], P <0.001, mMRC dyspnoea scale points: 2 [2–2] *vs.* 2 [1–2], P=0.01, the severity of the disease (GOLD stage) and the number of moderate exacerbations in the previous year: 1 [0–1] *vs.* 0 [0–1], P=0.04 were also significantly associated with the uptake of the 3rd COVID-19 vaccination (*Table 1*). None of the three vaccine recipients had developed COVID-19 acute infection, while 11.46% of those who did not receive

Table 2 Comorbidities in COPD patients (got COVID-19 booster dose)

Comorbidity	No (n=567, 37.55%)		Yes (n=943, 62.45%)		Total (n=1,510, 100.00%)		P value
	N	%	N	%	N	%	
Hypertension	378	66.67	676	71.69	1,054	69.76	0.04
GERD	199	35.1	306	32.45	505	33.44	0.31
Asthma bronchiale	114	12.09	186	12.32	186	12.32	0.74
Ischaemic heart disease	114	20.11	229	24.28	343	22.7	0.06
Allergies	107	18.87	167	17.71	274	18.13	0.58
Sleep disorder	98	17.28	158	16.76	256	16.95	0.83
Diabetes mellitus	98	17.28	172	18.24	270	17.87	0.38
Anxiety	92	16.23	122	12.94	214	14.17	0.08
Osteoporosis	84	14.81	132	14.00	216	14.29	0.45
Depression	59	10.41	87	9.23	146	9.66	0.47
Heart failure	58	10.23	83	8.80	141	9.34	0.36
Cerebrovascular history	43	7.58	67	7.10	110	7.28	0.75
Other cancer	40	7.05	86	9.12	126	8.34	0.17
Prostata hyperplasia	39	16.46	95	19.47	134	18.48	0.35
Pre-diabetes	30	5.29	51	5.41	81	5.36	1.00
Chronic atrial fibrillation	25	4.41	54	5.73	79	5.23	0.28
Acute myocardial infarction	23	4.06	70	7.42	93	6.16	0.008
Sinusitis	23	4.06	37	3.92	60	3.97	0.89
Bronchiectasis	19	3.35	30	3.18	49	3.25	0.88
Lung cancer	15	2.65	37	3.92	52	3.44	0.24
Glaucoma	13	2.29	29	3.08	42	2.78	0.42
Sleep apnoea	7	1.23	19	2.01	26	1.72	0.31

P<0.05 means the two indicators were significantly correlated. COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; GERD, gastroesophageal reflux disease.

the first booster vaccination developed one (P<0.001). One-fifth (n=16) also required hospitalization for acute SARS-CoV-2 infection, and almost the same proportion (n=14) required pulmonary outpatient rehabilitation for post-COVID symptoms (*Table 1*).

Patients' inhaled medication use and number of hospital visits

Table 3 presents the medications used by our patients, showing that those who took the third vaccination (first booster), required significantly fewer short-acting beta-agonists (SABAs) (P<0.001), so there were fewer exacerbations during the study period. Significantly, fewer used a combination of inhaled corticosteroid (ICS) and long-acting beta-agonist (LABA) (P=0.01), and a combination of LABA, long-acting muscarinic antagonist (LAMA) and ICS or "triple therapy" (P=0.04). Patients who received three vaccinations used LAMA significantly more, than those who did not receive the third vaccination (P=0.04). No significant difference was found for the other combinations. The number of visits to healthcare facilities by COPD patients in the past year can be seen in *Table 4*. Patients receiving the COVID-19 first booster dose had a significantly lower rate of emergency department visits, which is associated with disease severity: 0 [0–0] *vs.* 0 [0–0], P=0.01.

Table 3 Inhaled medications taken by chronic obstructive pulmonary disease patients (got COVID-19 booster dose)

Medication	No (n=567, 37.55%)		Yes (n=943, 62.45%)		Total (n=1,510, 100.00%)		P value
	N	%	N	%	N	%	
SABA	466	82.19	707	74.97	1,173	77.68	<0.001
LAMA	49	8.64	112	11.88	161	10.66	0.04
LABA	16	2.82	44	4.67	60	3.97	0.07
LABA and LAMA	166	29.28	300	31.81	466	30.86	0.30
ICS and LABA	76	13.40	89	9.44	165	10.93	0.01
LABA and LAMA and ICS	251	44.27	368	39.02	619	40.99	0.04
Rare combination	7	1.23	23	2.44	30	1.99	0.10
No data available	8	1.41	4	0.42	12	0.79	–

P<0.05 means the two indicators were significantly correlated. COVID-19, coronavirus disease 2019; SABA, short-acting beta-agonist; LAMA, long-acting muscarinic antagonist; LABA, long-acting beta-agonist; ICS, inhaled corticosteroids.

Table 4 Number of visits to healthcare facilities by COPD patients in the past year (got COVID-19 booster dose)

Number of visits to health care facilities in the last year	No (n=567, 37.55%)		Yes (n=943, 62.45%)		Total (n=1,510, 100.00%)		P value
	Median	IQR	Median	IQR	Median	IQR	
GP care	2	1–3	2	0–3	2	0–3	0.69
Attendance at an emergency care center	0	0–0	0	0–0	0	0–0	0.01
Outpatient pulmonary care	1	0–2	1	0–2	1	0–2	0.82
Care in the pulmonary ward	0	0–0	0	0–0	0	0–0	0.75

P<0.05 means the two indicators were significantly correlated. COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; IQR, interquartile range; GP, general practitioner.

Multiple logistic regression analysis

Multiple logistic regression analysis showed that male gender (OR: 0.74; 95% CI: 0.57–0.96; P=0.02), older age (OR: 1.06; 95% CI: 1.04–1.08; P<0.001), absence of previous COVID-19 infection (OR: 0.34; 95% CI: 0.23–0.51; P<0.001) significantly influenced the uptake of first booster vaccination and were predictive factors for uptake of the third COVID-19 vaccine. Those who had sought emergency care in the past year were less likely to receive a third vaccination (OR: 0.54; 95% CI: 0.37–0.79; P=0.002) (*Table 5*).

Discussion

The aim of our study was to investigate the uptake rate of the first booster vaccine against COVID-19 and to identify predictors of vaccine uptake. Our results suggest that the coverage of COVID-19 first booster vaccination among patients is suboptimal (62.45%), i.e., lower than the target. Patients vaccinated three times compared to those who did not receive a third vaccination, the difference between their quality of life (CAT), severity of dyspnea (mMRC) and the number of moderate exacerbations were all significant. In terms of post-COVID symptoms, there were significantly fewer outpatient hospital admissions among patients who had been vaccinated three times. The factors that were most associated with higher COVID-19 vaccine booster dose uptake were the following: older age, male sex, place of residence (western regions of Hungary), quality of life (CAT, mMRC), absence of previous COVID-19 infection and lower rates of exacerbations and emergency hospital visits.

In Hungary, large quantities of vaccines of all types are available, but unfortunately, the vaccination coverage rate is very low, with just over one third of people having received

Table 5 Multiple logistic regression analysis for estimates of predictors associated with getting COVID-19 vaccine booster dose

Variables	OR	95% CI	P value
Gender (female *vs*. male)	0.74	0.57–0.96	0.02
Age (years)	1.06	1.04–1.08	<0.001
Region of living			
Central	Ref.		
Eastern	0.81	0.57–1.16	0.26
Western	0.93	0.67–1.30	0.70
Currently smoking (yes *vs.* no)	0.89	0.68–1.18	0.43
Number of comorbidities (<2 *vs.* ≥2)	0.99	0.74–1.33	0.95
Number of severe exacerbation (<1 *vs*. ≥1)	1.81	0.91–3.59	0.08
Number of moderate exacerbation (>1 *vs*. ≤1)	0.89	0.63–1.24	0.48
GOLD (CD *vs.* AB)	0.79	0.46–1.33	0.37
CAT (points)	0.99	0.97–1.01	0.61
mMRC dyspnea scale (points)	0.88	0.74–1.04	0.14
COVID-19 infection (yes *vs*. no)	0.34	0.23–0.51	<0.001
GP care	0.87	0.63–1.21	0.42
Emergency care	0.54	0.37–0.79	0.002
Outpatient pulmonary care	1.29	0.95–1.74	0.09
Care in pulmonary ward	0.93	0.48–1.79	0.82

COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; mMRC, modified Medical Research Council; GP, general practitioner.

the first booster vaccine (39.7%) (23). The WHO target is at least 70% and 100% for elderly, vulnerable people and health workers (24). In Hungary, there has been strong social and health action to increase the vaccination coverage rate, with a target of at least 80%. Governmental measures to protect the population are also very strong, e.g., formal, valid proof of COVID immunity or a recent negative COVID-19 antigen test/negative PCR result is required in public enclosed spaces that are visited daily (e.g., health care facilities) and there was a 10-day official quarantine during the study period in case of COVID-19 infection (19). In the present study, the vaccination coverage of COPD patients is below the desired target but better than the Hungarian average population (62.45% *vs.* 39.70%). Those who have not yet received a first booster vaccine should definitely consider receiving one, as this new vaccine offers hope of mitigating the effects of future potential new waves of COVID-19 (25). New generation vaccines are already available, in the hope that these will not only increase the number of antibodies more potently, thus providing stronger protection, but hopefully this protection will also be longer and more durable, so that fewer booster vaccines will be needed in the future. Vaccines are also the best way to prevent serious infections, hospitalizations and death (26,27). It is therefore a priority for health workers to promote vaccination, raise awareness about the efficacy and safety of vaccines, and highlight the importance of taking booster vaccine(s), especially for at-risk groups e.g., elderly, chronically ill, health workers at risk, but all in all for the general public.

The presence of COPD does not necessarily mean a higher risk of developing COVID-19, but patients treated with multiple drugs, some of which affect the immune system, such as high-dose systemic steroids given in exacerbation, have a more severe outcome. COVID-19 affects the respiratory system, so COPD increases the chance of developing more serious complications. In

COPD, on the one hand, the body's defence system does not function properly and on the other hand, the respiratory surface area is reduced, as well as the respiratory reserve, which in the case of pneumonia, quickly leads to respiratory failure (28). Some patients already need oxygen therapy on a daily basis, and for them, coronavirus infection can be particularly dangerous. Active smokers and patients with COPD have increased expression of the angiotensin converting enzyme-2 (ACE-2) receptor in the lower airways, which may partly explain why COVID-19 poses an increased risk among them (29). In the case of other respiratory viruses, such as respiratory syncytial virus, inhaled tobacco smoke has been described to increase both the speed and severity of transmission of viral respiratory infection (30). However, the specific mechanisms by which COVID-19 infection increases COPD severity and mortality through specific pathomechanisms are not yet known.

COPD exacerbation is a very important event in the natural course of the disease, which is associated with worsening of symptoms, often resulting in hospitalization and a rather poor prognosis. Causes include various bacteria, other pathogenic factors such as increased air pollution, stress, etc., but viral infections, including coronaviruses, remain the main trigger (31). The reduction in the number of potentially fatal exacerbations also justifies effective preventive measures, including vaccination, to reduce the risk of COVID-19 infection in COPD patients and current smokers. There are gender differences in vaccine uptake in COPD patients, e.g., lower uptake of influenza vaccine among women (32) and lower uptake of COVID-19 vaccine, than men (33). This is confirmed by our present study. Studies have also described that vaccine uptake increases with age, which also correlates positively with our study (33-36).

However, vaccine hesitancy and misinformation remains a major barrier to achieving optimal vaccination coverage around the world, including Hungary. Previous studies have described that the willingness to receive booster doses of COVID-19 vaccine is based primarily on the benefits of information and communication (37,38). While the National Immunisation Programme in Hungary—thanks to the National Immunisation Programme—is an example of an almost 100% vaccination rate in children, the adult immunisation programme is still on hold. The benefits, both social and economic, of launching an effective lifelong vaccination programme for adulthood could bring very significant results. On the one hand, it is an effective protection against serious infectious diseases and, on the other hand, the widespread use of vaccination can indirectly reduce the use of antibiotics, thus contributing to the reduction of antibiotic resistance (39).

In Hungary, people received the vaccination card after the second COVID vaccination, so they were not forced to take the first booster vaccination, except the workers in high-risk jobs, e.g., people working in health care and higher education institutions. Therefore, the uptake rate of the 3rd vaccination is much lower, than that of the second COVID-19 vaccination (63.2% *vs.* 39.7%) (23). Studies have described that the uptake rate of COVID-19 booster dose increased as the educational attainment increased (40,41). Comorbidities such as respiratory diseases (for example asthma, COPD), hypertension, diabetes mellitus, tumour and immunodeficiency diseases showed positive correlations with participation in booster vaccination (42). Our current research has reached a similar conclusion. Several studies have described younger age, female sex, lower education and lower income as being associated with lower vaccine uptake (43-45). In addition, the recommendation of doctors and health care staff is the primary factor driving vaccine uptake (46), which is also true for patients with chronic diseases (47). Doctor recommendation is also a well-known motivating factor for uptake of other infectious disease vaccines (48,49). A cross-sectional study made in Beijing (14) revealed that the actual uptake rate of the vaccine was relatively low (39.0%), although their research predicted that the majority of their patients would be willing to accept the COVID-19 vaccine. To their surprise, only 16.2% of patients (n=161) who had not received COVID-19 vaccination reported that clinicians had recommended the uptake, while 23.5% were unaware of the inoculation, probably the main reason for the low uptake rates among these patients. Educating patients that the benefits of vaccination outweigh the potential risks should be a very important task for healthcare workers. Revaccination, i.e., receiving three vaccines, provides long-lasting protection not only against acute COVID-19 infection, but also against respiratory failure, the development of post-COVID syndrome and death. These are very important because COPD patients are at higher risk of developing serious complications from COVID-19 (19).

There is currently no data available on the effectiveness of COVID-19 vaccines specifically for people with COPD. However, all approved vaccines show fully reliable and promising levels of efficacy (50). The humoral and cellular immune responses of COPD patients to COVID-19

vaccination were similar to those of healthy controls, ensuring that current vaccines elicit the desired immune response in COPD despite the presence of immune dysregulation (51). A preprint 2021 study suggests that those who receive the full vaccine series (i.e., 3 vaccines) are three times less likely to acquire a new COVID-19 infection (52). Our present research also supports the protection of vaccinated patients. For all these reasons, we would like to recommend that health organizations, the government and other authorities develop strategies to increase public knowledge and awareness in order to dispel myths and disinformation about the booster dose of COVID-19 vaccine as well as to achieve full vaccination coverage and herd immunity.

Limitation

Our cross-sectional survey is an observational study that should be interpreted with caution. First and foremost, a potential bias may be the fact that vaccinated patients are more likely to have access to health care, be more motivated to seek treatment and take other protective measures for themselves such as adherence to medication, avoiding tobacco smoke and people with active respiratory infections, using masks and washing hands regularly. Second, our patients were not longitudinally followed up over time; therefore, we do not know whether they subsequently received booster (third and fourth) vaccinations. Thirdly, our questionnaires, e.g., CAT, mMRC, might be validated, but they are subjective and symptom-based, as is the experience of moderate exacerbation. The symptoms were based on patient self-reported data, potentially leading to misclassification, and we did not ask about patients' attitudes, fears and knowledge about vaccines. Fourthly, and last, those who have taken the full series of vaccinations are more likely to be health conscious and in addition more cooperative with their doctor, which has a long-term impact on their quality of life.

Conclusions

Among COPD patients in Hungary, uptake of the COVID-19 booster vaccine is lower than the targeted value. The factors that were most associated with higher COVID-19 vaccine booster dose uptake were the following: older age, male sex, region of residence (western regions of Hungary), better quality of life, lower number of exacerbations and emergency hospital visits, and absence of prior COVID-19 infection. Health personnel should make it a priority to promote vaccination, to raise awareness of the efficacy and safety of them, to educate patients as well as to highlight the importance of taking booster vaccine(s).

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Footnote

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