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Article

Impact of Smoking Cessation and Charlson Comorbidity Index on Influenza Vaccination Efficacy in COPD Patients

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Abstract: Chronic obstructive pulmonary disease (COPD) patients are particularly susceptible to respiratory infections like influenza, which exacerbate symptoms and increase healthcare utilization. While smoking cessation and influenza vaccination are recommended preventive measures, their combined impact on healthcare resource utilization is underexplored. The Charlson Comorbidity Index (CCI) assesses comorbidity burden in COPD patients and may influence healthcare outcomes. We conducted a retrospective analysis of 357 COPD patients, evaluating smoking cessation success over one year and influenza vaccination receipt, stratifying patients by CCI scores. Healthcare utilization outcomes included emergency room visits, hospitalizations, and medical expenses. Results showed that 51.82% of patients quit smoking and 59.66% received influenza vaccination, with higher comorbidity prevalence in advanced COPD stages ($p=0.002$). Both smoking cessation and influenza vaccination independently correlated with decreased emergency room visits, hospital admissions, days, and costs. Patients who both quit smoking and received influenza vaccination exhibited the lowest healthcare utilization rates. In conclusion, smoking cessation and influenza vaccination significantly reduce healthcare resource utilization in COPD patients, with the combination yielding synergistic benefits, particularly in those with lower CCI scores. Integrating these interventions and comorbidity management in COPD strategies is essential for optimizing patient outcomes and healthcare efficiency.

Keywords: chronic obstructive pulmonary disease; influenza vaccination; charlson comorbidity index; smoking cessation

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a complex respiratory disorder marked by enduring airflow limitation, typically coupled with chronic bronchitis and emphysema [1]. It plays a substantial role in global health, contributing significantly to worldwide morbidity and mortality rates [2]. COPD patients grapple with a range of symptoms, including persistent coughing, wheezing, breathlessness, and diminished exercise tolerance, all of which severely impact their quality of life [3].

Of particular concern for COPD patients is their amplified susceptibility to respiratory infections like influenza [4]. Such infections can incite COPD exacerbations characterized by exacerbating symptoms and deteriorating lung function, culminating in hospital admissions and potentially even death [5]. Influenza poses a particular threat given its capacity to cause severe respiratory illness and complications, further undermining respiratory function in an already susceptible population [6].

Considering the increased risk of influenza-related morbidity and mortality amongst COPD patients, influenza immunization is heavily advocated as a preventive measure[7]. Influenza

vaccination has demonstrated effectiveness in reducing the incidence of influenza infection, hospitalizations, and mortality amongst COPD patients[8]. However, the efficiency of influenza vaccination in this group may be moderated by various factors including personal attributes and coexisting health conditions.

One such influential factor is smoking cessation, which is pivotal in managing COPD [9]. Smoking is the primary origin of COPD, and continuous smoking exacerbates disease progression and respiratory symptoms [10]. Ceasing smoking not only decelerates the decline in lung function but also lessens the likelihood of exacerbations and enhances overall health outcomes in COPD patients [11]. Nonetheless, the impact of smoking cessation on the efficacy of influenza vaccination is a topic of ongoing study.

Comorbidities that frequently coexist with COPD may also affect the outcomes of vaccination [12]. The Charlson Comorbidity Index (CCI) is a recognized tool for evaluating the burden of comorbidity, covering conditions like cardiovascular disease, diabetes, and renal dysfunction, among others [13]. These comorbidities may influence immune responses to vaccination, thereby predisposing COPD patients to a higher likelihood of influenza-related complications.

Grasping the interactions between smoking cessation, comorbidities as captured by the CCI, and the effectiveness of influenza vaccination is essential for enhancing preventive strategies in COPD patients. Personalised vaccination strategies based on individual patient profiles and addressing modifiable risk factors like smoking and comorbidities could increase vaccine effectiveness and better health outcomes in this vulnerable group [14]. Therefore, additional research is needed to clarify these relationships and guide evidence-based guidelines for influenza vaccination in individuals with COPD.

2. Method

This study conducted a retrospective analysis to explore the individual analysis of the Charlson Comorbidity Index for smoking cessation in patients with chronic obstructive pulmonary disease (COPD) after receiving influenza vaccination. Patient data were collected from the database of Kaohsiung Chang Gung Medical Center, which ranks first in the application for medical service points in the Nanping area. From January to October 2018, patients diagnosed with COPD in outpatient clinics were selected based on the main diagnosis of ICD-10 J44 appearing five times or more. According to a study published in 2017 in an international journal, early COPD patients were observed continuously for six years, with an average of 4.5 outpatient visits per year. In 2012, the average number of outpatient visits was 4.9 ± 5.2 times [5]. Considering that COPD patients need to use bronchodilator drugs for approximately two months, and they require regular follow-up visits to outpatient clinics to monitor their condition, the subjects of this study were selected based on the main diagnosis of ICD-10 J44 appearing five times or more in outpatient diagnosis records. The impact of smoking cessation for one year on the hospitalization days, emergency room visits, medical expenses, and occurrences of respiratory failure in COPD patients after receiving influenza vaccination was observed due to diagnoses of acute respiratory tract infections, pneumonia, and influenza.

2.1. COPD Severity

The severity of COPD was categorized as A, B, C, or D in accordance with GOLD 2020 guidelines [6], taking into account mMRC dyspnea score (< 2 or ≥ 2), the severity of airflow limitation, and the frequency of exacerbations per year.

2.2. Charlson Comorbidity Index (CCI)

Subjects were further stratified into three groups based on their Charlson Comorbidity Index (CCI) scores [7], which serves to adjust for comorbidity status. A higher CCI score indicates a greater burden of comorbid health conditions. Analyzing the distribution of subjects across different CCI

scores, we focused on those with scores of 0, 1, and 2 or higher. This study aims to evaluate the effectiveness of the Charlson index in predicting healthcare resource utilization in each group.

2.3. Statistical Analysis

Descriptive statistics were employed to analyze various study variables related to the severity of chronic obstructive pulmonary disease (COPD) across four major groups. The distribution of observed characteristics such as gender, age, Charlson Comorbidity Index, smoking status, influenza vaccination status, emergency room visits, hospitalization days, and medical expenses was examined within each group.

Inferential statistics included chi-square tests for categorical variables and independent samples t-tests for continuous variables. The independent variable in this study was the receipt of influenza vaccination. Multiple linear regression analysis was conducted to explore the relationship between age, gender, smoking status, Charlson Comorbidity Index, hospitalization days, hospitalization medical expenses, and influenza vaccination status.

Furthermore, negative binomial regression analysis was used to assess the impact of Charlson Comorbidity Index on the frequency of emergency room visits and hospitalizations.

3. Results

Table 1 and Figure 1 illustrates the distribution of the study sample. Participants aged 50-59 accounted for 13.73%, those aged 60-69 for 30.53%, those aged 70-79 for 35.85%, and those over 80 for 19.89%. Males comprised 92.44% of the sample, while females accounted for 7.56%, totaling 27 individuals. The Charlson Comorbidity Index, adjusted for COPD as the primary condition, deducted one point. Since COPD was the primary focus of this study, its weight in the Charlson Comorbidity Index was one point. In GOLD stage 1, 33.33% had a Charlson Comorbidity Index score of 0, 26.88% scored 1, and 39.78% scored 2 or higher. In GOLD stage 2, these proportions were 27.78%, 30.95%, and 41.27%, respectively. In GOLD stage 3, they were 20.00%, 19.05%, and 60.95%, and in GOLD stage 4, they were 9.09%, 18.18%, and 72.73%, respectively. Overall, 21.18% scored 0, 23.76% scored 1, and 55.06% scored 2 or higher on the Charlson Comorbidity Index, as shown in Table 1, depicting the distribution of the study sample.

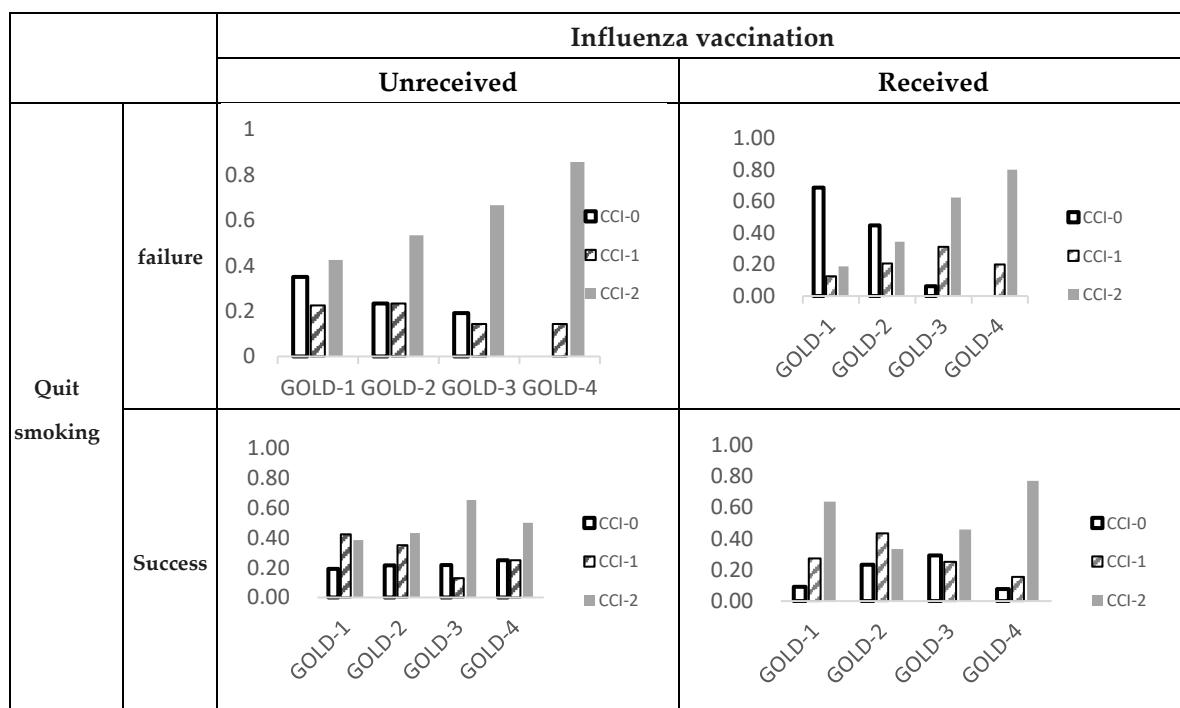


Figure 1. the comorbidity distribution between smoking cessation and influenza vaccination.

Table 1. The demographic characteristics of enrolled 357 patients with COPD.

Variables (N=357)	N(%)	p value			
Age					
50-59	49 (13.73%)				
60-69	109(30.53%)				
70-79	128(35.85%)				
>80	71(19.89%)				
Gender					
women	27 (7.56%)				
man	330(92.44%)				
Quit smoking					
success	185(51.82%)				
failure	172(48.18%)				
Influenza vaccination					
Received	213(59.66%)				
Unreceived	144(40.34%)				
	GOLD 1 (N=119)	GOLD 2 (N=66)	GOLD 3 (N=94)	GOLD 4 (N=78)	P=0.002
CCI 0	31(33.33%)	35(27.78%)	21(20.00%)	3(9.09%)	
CCI 1	25(26.88%)	39(30.95%)	20(19.05%)	6(18.18%)	
CCI ≥2	37(39.78%)	52(41.27%)	64(60.95%)	24(72.73%)	
Quit smoking >1 year					
success	56(60.22%)	59(46.83%)	58(55.24%)	12(36.36%)	P=0.057
failure	37(39.78%)	67(53.17%)	47(44.76%)	21(63.64%)	
Influenza vaccination					P=0.017
Received	66(70.97%)	67(53.17%)	65(61.90%)	15(45.45%)	
Unreceived	27(29.03%)	59(46.83%)	40(38.10%)	18(54.55%)	

CCI: Charlson Comorbidity Index.

Table 2 presents the analysis of healthcare resource utilization among patients based on smoking cessation and influenza vaccination status. Regarding emergency room visits, patients who quit smoking and did not receive influenza vaccination had an average of 2.72 ± 3.43 visits, whereas those who both quit smoking and received influenza vaccination had an average of 0.66 ± 1.24 visits, significantly fewer than the former group ($p = .001^{**}$). In terms of hospitalizations, patients who quit smoking and did not receive influenza vaccination had an average of 1.60 ± 1.58 hospitalizations, while those who both quit smoking and received influenza vaccination had an average of 0.26 ± 0.56 hospitalizations, significantly fewer than the former group ($p = .001^{**}$). Across hospitalization days, hospitalization expenses, and occurrences of respiratory failure, the group that both quit smoking and received influenza vaccination consistently showed lower values compared to the group that did not quit smoking and did not receive influenza vaccination, with all differences being statistically significant.

Table 2. Analysis of healthcare resource utilization among patients based on smoking cessation and influenza vaccination status.

Smoking/ Non-influenza vaccine	Smoking /influenza vaccine	Quit Smoking / Non-influenza vaccine	Quit Smoking/ influenza vaccine	P Value
emergency room visits 2.74(3.43) ##+&&	1.40(1.88) **&	1.23(1.88) **&	0.66(1.24) **#+	0.000
hospitalizations 1.60(1.58) ##+&&	0.81(1.04) **&&	0.75(1.01) **&&	0.26(0.56) ** ##+	0.000
hospitalization days 10.95(15.53) ##+&&	3.97(5.89) **&	6.27(13.41) **&&	2.58(7.37) **#+	0.000
hospitalization expenses 77201(177342) ##+&&	39193(99960) **	31942(63771) **&	10543(31278) **	0.0012

* vs. neither quit smoking nor received influenza vaccination, * <0.05 ** $P<0.01$. # vs. not quit smoking and received influenza vaccination, # <0.05 ## $P<0.01$. + vs. quit smoking and not received influenza vaccination, + <0.05 ++ $P<0.01$. & vs. quit smoking and received influenza vaccination, & <0.05 && $P<0.01$.

Table 3 compares outcomes between success and failure smoking cessation groups, and between those who received and those who did not receive influenza vaccination. For the success smoking cessation group versus the failure smoking cessation group, significant decreases were observed in emergency department utilization (coefficient -0.61, 95%CI -0.85 to -0.367), hospital utilization (coefficient -0.54, 95%CI -0.77 to -0.31), hospital days (coefficient -2.14, 95%CI -4.19 to 0.083), and cost (coefficient -15684, 95%CI -37446 to 6078). In the group that received influenza vaccination compared to the group that did not, significant decreases were found in emergency department utilization (coefficient -0.56, 95%CI -0.81 to -0.32), hospital utilization (coefficient -0.71, 95%CI -0.95 to -0.47), hospital days (coefficient -4.14, 95%CI -6.11 to -2.17), and cost (coefficient -37417, 95%CI -58277 to -16557).

Table 3. Comparison of medical utilizations between success and failure smoking cessation groups, and between received and did not receive influenza vaccination.

variable	department utilization			hospital utilization			hospitalization days			hospitalization expenses		
	coefficient	95%CI	p Value	coefficient	95%CI	p Value	coefficient	95%CI	p Value	coefficient	95%CI	p Value
Quit smoking												
NO	-0.61	-0.85~-0.367	0.000**	-0.54	-0.77~-0.31	0.000**	-2.14	-4.19~-0.083	0.041*	-15684	-37446~6078	.0.157
YES *												
Influenza vaccine												
YES	-0.56	-0.81~-0.32	0.000	-0.71	-0.95~-0.47	0.000	-4.14	-6.11~-2.17	0.000	-37417	-58277~-16557	0.000
NO *												
CCI												
≥2	1.34	0.98~1.71	0.000	1.06	0.70~1.42	0.000	5.24	2.75~7.73	0.000	49620	-23189~38457	0.000
1	0.94	0.53~1.36	0.001	0.68	0.26~1.09	0.001	1.97	-0.93~4.87	0.183	7634	23282~75958	0.627
0*												

Comparing CCI ≥ 2 to CCI=0 group, significant increases were observed in emergency department utilization (coefficient -1.34, 95%CI 0.98 to 1.71), hospital utilization (coefficient 1.06, 95%CI -0.70 to 1.42), hospital days (coefficient 5.24, 95%CI 2.75 to 7.73), and cost (coefficient 49620, 95%CI -23189 to 38457). For CCI=1 compared to CCI=0 group, there was a significant increase in emergency department utilization (coefficient 0.94, 95%CI 0.53 to 1.36), and hospital utilization (coefficient 0.68, 95%CI -0.26 to 1.09). However, there were no significant differences in hospital days (coefficient 1.97, 95%CI -0.93 to 4.87) and cost (coefficient 7634, 95%CI 23282 to 75958).

Figure 2 presents the following findings: Successful smoking cessation groups exhibited a significant reduction in emergency visits ($p < 0.001$) and hospitalization frequencies ($p < 0.001$) compared to failed smoking cessation groups, both with and without influenza vaccination (Group III vs. Group I and Group IV vs. Group II). Additionally, successful smoking cessation groups demonstrated a significant reduction in hospitalization days ($p < 0.001$) and hospitalization costs ($p < 0.001$) compared to failed smoking cessation groups without influenza vaccination (Group III vs.

Group I). However, there was no significant reduction in hospitalization days ($p=0.157$) and hospitalization costs ($p=0.126$) compared to failed smoking cessation groups without influenza vaccination (Group IV vs. Group II). Influenza vaccination groups displayed significant reductions in hospitalization frequency ($p < 0.05$), hospitalization days ($p < 0.05$), and hospitalization costs ($p < 0.05$) compared to non-influenza vaccination groups, both with and without successful smoking cessation (Group II vs. Group I and Group IV vs. Group III). Nevertheless, for influenza vaccination groups, there was no significant reduction in emergency visits ($p=0.169$) compared to the non-influenza vaccination groups, even with successful smoking cessation (Group IV vs. Group III).

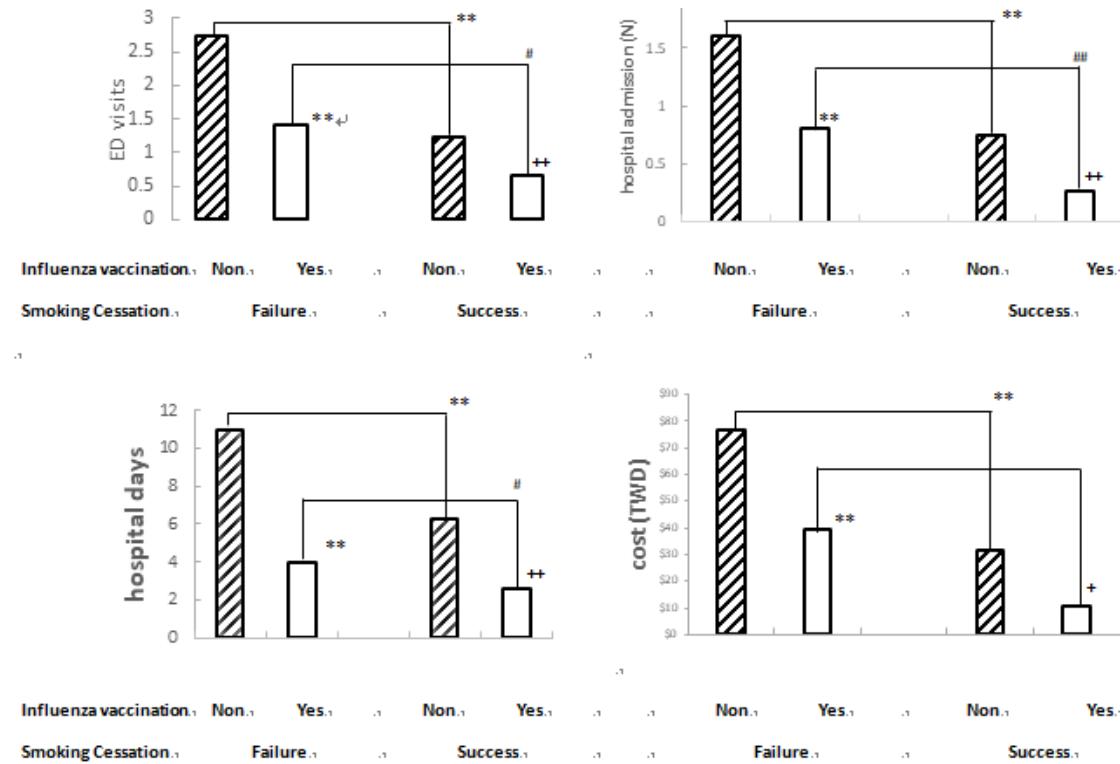


Figure 2. Analysis of healthcare resource utilization among patients based on their and influenza vaccination and smoking cessation status.

Figure 3 analyzes the negative binomial regression of emergency department visits by smoking cessation and influenza vaccination status among the study samples grouped by CCI=0, CCI=1, and CCI \geq 2. Separate analyses by CCI groups show that both the vaccinated and smoking cessation groups have fewer emergency department visits and hospitalizations, with significant differences observed in all groups except for the CCI=0 group ($p=.000**$). In terms of emergency department visits and hospitalizations, the CCI=0 group shows fewer visits and hospitalizations regardless of influenza vaccination, smoking cessation, or both, although the differences are not statistically significant. The CCI=1 group also shows fewer emergency department visits and hospitalizations regardless of influenza vaccination, smoking cessation, or both, except for the smoking cessation-only group, which does not show significant differences. However, in the CCI=2 group, all subgroups, whether vaccinated, quit smoking, or both, exhibit significantly fewer emergency department visits and hospitalizations.

	CCI=0 (N=90)				CCI=1 (N=90)				CCI≥2 (N=177)					
number of emergency department														
Vaccine	-	+	-	+	Vaccine	-	+	-	+	Vaccine	-	+	-	+
Quit	-	-	+	+	Quit	-	-	+	+	Quit	-	-	+	+
P value	0.145	0.470	0.452		P value	0.011*	0.054	0.000**		P value	0.094	0.000**	0.000**	
number of hospital admission														
Vaccine	-	+	-	+	Vaccine	-	+	-	+	Vaccine	-	+	-	+
Quit	-	-	+	+	Quit	-	-	+	+	Quit	-	-	+	+
P value	0.062	0.204	0.218		P value	0.006**	0.096	0.000**		P value	0.033*	0.000**	0.000**	

Figure 3. analyzes the negative binomial regression of emergency department visits by smoking cessation and influenza vaccination status.

4. Discussion

Our study's findings emphatically highlight the significance of smoking cessation, influenza vaccination, and the Charlson Comorbidity Index (CCI) in lessening COPD's burden and refining usage of healthcare resources among affected patients. In analyzing these interventions' implications on COPD outcomes and patterns of healthcare utility, we gleaned several decisive insights.

Primarily, we discerned a prominent correlation between smoking cessation and a decline in healthcare resources among COPD patients. Individuals who successfully relinquished smoking exhibited fewer emergency department consultations, hospital admissions, and related costs compared to persistent smokers [11, 15]. This observation harmonizes with current evidence proposing that smoking cessation not just decelerates the advance of COPD but also curtails the regularity and severity of exacerbations, consequently reducing healthcare dependency.

Secondly, influenza vaccination revealed itself as a safeguard against unfavorable COPD outcomes and consumption of healthcare resources [16]. Patients who were immunized against influenza had lower rates of emergency department visits, hospital admissions, and related costs compared with their unvaccinated counterparts [5]. These data accentuate vaccination's necessity in averting influenza-related exacerbations and complications in COPD patients, hence alleviating the strain on healthcare provision.

Our analysis additionally examined the impact of comorbidities, as reflected by the Charlson Comorbidity Index (CCI), on COPD outcomes and healthcare consumption [17]. We discovered that elevated CCI scores, signaling a greater burden of comorbidity, were linked with intensified use of healthcare resources across all examined groups. Notwithstanding, even when comorbidities were present, smoking cessation, and influenza vaccination remained operative in diminishing healthcare reliance among COPD patients.

By incorporating CCI in our evaluation, we've gleaned invaluable insights into the effects of comorbidities on the management of COPD and the usage of healthcare resources. COPD patients with higher CCI scores may present more complex healthcare needs and increased susceptibility to adverse results, underscoring the requirement for customized interventions to refine their care [18]. Despite the hurdles imposed by comorbidities, our observations imply that both smoking cessation and influenza vaccination continue to confer substantial advantages in limiting healthcare consumption in this group.

Crucially, our research revealed reciprocated benefits when smoking cessation, influenza immunization, and management of comorbidities were amalgamated into COPD care. COPD patients who quit smoking, received influenza vaccinations, and had lower CCI scores registered the least frequented emergency department visits, hospitalizations, and corresponding costs. This finding underscores adopting a comprehensive approach to managing COPD, tackling modifiable risk factors, precluding exacerbations, and efficiently managing comorbidities.

5. Conclusions

To conclude, our study underlines the profound influence of smoking cessation, influenza vaccination, and management of comorbidities in decreasing the reliance on healthcare resources in COPD patients. These interventions collaboratively play crucial roles in perfecting COPD outcomes, averting exacerbations, and augmenting healthcare effectiveness. By addressing modifiable risk factors like smoking, advocating preventive measures like vaccination, and managing comorbidities effectively, we can lessen the burdens COPD imposes on healthcare systems and enhance patient outcomes. Additional research is necessitated to elucidate the mechanisms underpinning these interventions' effects and to refine their implementation in clinical practice.

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Data Availability Statement: Data can be obtained from Hui-Chuan Chang (elaine11142@cgmh.org.tw).

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Conflicts of Interest: The author declared no conflicts of interest.

Abbreviations

COPD	Chronic Obstructive Pulmonary Disease
GOLD	Global Initiative for Chronic Obstructive Lung Disease
FEV1	Forced expiratory volume during the first second
FVC	Forced Vital Capacity

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