International Journal of Chronic Obstructive Pulmonary Disease Dovepress
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ORIGINAL RESEARCH

Exploring the Relationship Between Education, Living Environment, and Anxiety/Depression Among Stable Patients: Insights from the COPD-AD China Registry Study

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Background: Education and living environment are related to mental health. But the independent and combined effects of them on mental health among patients with chronic obstructive pulmonary disease (COPD) are uncertain.

Methods: The independent and combined effects of education and living environment on mental health were assessed by binary logistic regression in 1064 COPD patients. Additive interaction was assessed with the relative excess risk ratio (RERI), attribution percentage (AP), and synergy index (SI).

Results: Our results shown that low education level and urban living environment were independently associated with higher risks for anxiety (odds ratio [OR]: 1.56, 95% confidence interval [CI] 1.06–2.29 and OR:2.15, 95% CI 1.51–2.05) or depression (OR:1.62, 95% CI 1.17–2.27 and OR: 2.01, 95% CI 1.46–2.75) among COPD patients. The combination effect of them was also associated with higher risks for anxiety (OR: 7.90, 95% CI 3.83–16.29, $P < 0.001$) or depression (OR: 11.79, 95% CI 5.77–24.10, $P < 0.001$) among these patients. Furthermore, we observed strong synergistic additive interactions between them for anxiety (SI: 11.57, 95% CI 1.41–95.27; RERI: 6.31, 95% CI 1.60–11.01; AP: 0.8, 95% CI 0.66–0.94) and depression (SI: 31.31, 95% CI 1.59–617.04; RERI: 10.44, 95% CI 2.66–18.23; AP: 0.89, 95% CI 0.8–0.97).

Conclusion: Low education levels and living in urban areas had an independent and synergistic effects on mental health among COPD patients.

Keywords: anxiety, China, COPD, depression, education, living environment

Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent chronic airway disease that often co-occurs with anxiety and depression.[1] Our previous research showed that 13.93% of patients with stable COPD reported symptoms of anxiety, and 23.37% experienced depression.[2] Moreover, patients with COPD that had a history of anxiety or depression exhibited poor physical function, impaired health status, and frequent acute exacerbations.[3,4] Therefore, identifying potentially modifiable risk factors that may improve mental health among patients with COPD is important.

Education and urban living environment are important factors that affect an individual's mental health.[5,6] Education can positively impact mental health by enabling individuals to succeed and pursue fundamental goals,[6] and a low education level can contribute to poor mental health. In addition, an urban living environment directly and indirectly

Received: 11 March 2024
Accepted: 6 September 2024
Published: 23 September 2024

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affects residents' mental health through factors such as congestion, crime, high-rise housing, noise pollution, air pollution, traffic congestion, poor housing, and heightened competition.[7] Therefore, it is necessary to consider education and living environment when addressing mental health issues in different populations. Importantly, education has complex interactions with a person's living environment.[8] For example, a previous study found that migrant residents with a tertiary education had a higher incidence of depressive symptoms compared with Italian-born residents.[9] This suggested the protective effect of education against anxiety and depression may be influenced by other social-contextual variables. Although researches have suggested that systemic inflammation, gender, smoking, acute exacerbation of COPD, hypoxemia, and disease knowledge level were risk factors for anxiety and depression symptoms among patients with COPD.[1,10,11] However, few studies have examined the independent and combined effects of education and living environment on mental health among patients with COPD.

When we collated the Chronic Obstructive Pulmonary Disease with Anxiety and Depression in China (COPD-AD China Registry) study database, we found that patients participating in that study originated from diverse urban and rural regions, had varied educational backgrounds, and some suffered from symptoms of anxiety and depression. Therefore, this paper aimed to evaluate the independent effects of education and living environment on mental health among patients with COPD and determine whether the impact of education on mental health differed between rural and urban living environments. This information will support a better understanding of factors that contribute to mental health issues in patients with COPD and facilitate development of targeted interventions to improve their mental well-being.

Methods

Data Source

The COPD-AD China Registry study comprises a comprehensive database. This database was a key national research and development project focused on COPD in China, and involved a national clinical registration study that was initiated in June 2017 and lasted for 3.5 years (Clinical Trials ID: NCT03187236). The registry was approved by the institutional review boards of all contributing hospitals and the study was conducted in accordance with the Declaration of Helsinki.

Study Cohort

Patients that were selected for this analysis were from the respiratory medicine outpatient departments in nine Chinese hospitals (Liangxiang Hospital of Fangshan District, Beijing; Affiliated Hospital of Binzhou Medical College; Ordos Central Hospital; Guangdong Provincial People's Hospital; Affiliated Hospital of Guangdong Medical College; the First Affiliated Hospital of Nanchang University; Qilu Hospital of Shandong University; Beijing Chaoyang Hospital of Capital Medical University; and the People's Hospital of Wuhan University). All patients were aged over 40 years and diagnosed with COPD via a lung function test following the 2017 Global Initiative Chronic Obstructive Lung Disease (GOLD): Global Strategy for the Diagnosis, Management, and Prevention of COPD.[12] None of the included patients were pregnant. Patients were informed about the purpose of the study and signed a consent form. Between 2017 and 2021, 1366 participants were enrolled in the COPD-AD China Registry Study. Patients with incomplete data (n=233) were excluded from this analysis. Further exclusion criteria were: severe cognitive disorder; suicide attempt or psychiatric hospitalization in the past year; current suicidal ideation with plan or intent; mental illness, such as dementia, autism, schizophrenia (n=3), or bipolar disorder; alcohol or drug abuse (n=10); bronchial asthma (n=24); bronchiectasis (n=12); pulmonary fibrosis (n=2); tuberculosis (n=8); neuromuscular disease (n=2); and cancer (n=8). After applying the exclusion criteria, 1064 participants were included in the final baseline study sample.

Measures

Clinical Measurements and Spirometry

Demographic characteristics (age, sex, height, weight, body mass index [BMI], smoking history, education, living environment) and clinical characteristics, including oxygen therapy status, Charlson Comorbidity Index (CCI), COPD Assessment Test (CAT) score, and modified Medical Research Council (mMRC) score, were collected from the data management network (mzf.fwncpc.com). We performed spirometry according to the guidelines for lung function tests

formulated by the Chinese Thoracic Society. We measured the percentage predicted forced expiratory volume in 1 second (FEV_1% predicted) for all participating patients.

Urban-Rural Classification

The Chinese administrative system has six levels: national, provincial, prefectural, county, township, and village levels. Each county-level unit (county or district) usually includes two types of township level units: townships and subdistricts. The former comprises a town center and dozens of surrounding villages. The latter comprises urban communities or suburbs. We defined the rural population as people living in townships, and the urban population as people living in subdistricts.[13] There were no rural townships in 17 of the studied urban districts; therefore, only an urban population was defined in these districts. Data for subdistrict populations were unavailable for five counties with predominantly rural populations, and we treated the population of these entire counties as rural populations. Therefore, we defined 655 sub-county level units for assessment overall: 97 urban units and 558 rural units. There were 32 units with small populations, including seven urban units and 25 rural units.

Education Classification

Education level was classified by years of formal education received: illiteracy (0 years), primary school (1–6 years), junior secondary school (7–9 years), senior secondary school (10–12 years), and university (≥ 13 years). We used 9 years as the cut-off value to categorize participants as having a low (≤ 9 years) or a high (> 9 years) education level because China has free compulsory education for 9 years.

Determination of Anxiety and Depression

Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS). The HADS comprises 14 items that detect anxiety and depression in patients with chronic diseases. There are seven anxiety items and seven depression items; each item is rated on a Likert scale from 0 to 3. The total scores for the anxiety and depression items are calculated separately, with scores of 0–7 indicating no anxiety/depression, 8–10 indicating mild anxiety/depression, 11–14 indicating moderate anxiety/depression, and 15–21 indicating severe anxiety/depression.[14]

Statistical Analysis

All statistical analyses were performed with SPSS version 25.0 (IBM Corp., Armonk, NY, USA), with the level of statistical significance set at $P<0.05$. Categorical data were reported as number (percentage), and continuous variables were presented as mean ± standard deviation (SD) for normally distributed data. Chi-square tests were used for comparisons of categorical variables, and independent *t*-tests were used for comparisons of normally distributed continuous variables. Binary logistic regression was used to analyze the effects of education and living environment (individually or in combination) on the risk for anxiety and depression among patients with COPD. To investigate the additive interaction of education and living environment on the risk for anxiety and depression among patients with COPD, the Microsoft Excel table compiled by Andersson et al was used to calculate the relative excess risk (RERI), attributive ratio (AP), and synergy index (SI) for the additive interactions.[15] Two models were used in this regression analysis. Model 1 was unadjusted, and Model 2 was adjusted for confounder variables, including age, sex, smoking history, BMI, CAT, FEV_1% predicted, oxygen therapy, mMRC score, and CCI score. We adjusted for these variables because we considered they were related to anxiety and depression.

Results

Participants' Characteristics

In total, 1064 patients with COPD were included in our analyses: 211 (19.8%) were complicated with anxiety and 319 (30.0%) were complicated with depression. Patients mean age was 69.97 years (SD: 8.68 years, range: 60–88 years). We observed significant differences in CAT scores, CCI scores, oxygen intake, education, and living environment between participants with and without anxiety. There were significant differences in CAT scores, FEV_1% predicted, CCI scores, oxygen intake, education, and living environment between patients with and without depression (Table 1).

Table 1 Characteristics of Study Participants

Variables	COPD (N=1064)		*P*	COPD (N=1064)		*P*
	No Anxiety n=853 (80.2)	Anxiety n =211 (19.8)		No Depression n =745 (70.0)	Depression n =319 (30.0)	
Age (years), mean ± SD	70.07 ± 8.50	69.58 ± 9.36	0.466	69.98 ± 8.61	69.96 ± 8.84	0.974
Male, n (%)	677 (80.0)	169 (20.0)	0.815	592 (70.0)	254 (30.0)	0.953
BMI (kg/m^2), mean ± SD	21.84 ± 4.08	22.10 ± 4.09	0.399	21.74 ± 3.97	22.24 ± 4.32	0.068
CAT, mean ± SD	14.17 ± 6.83	17.67 ± 7.66	< 0.01	13.97 ± 6.97	16.98 ±7.19	< 0.01
FEV_1% predicted, mean ± SD	51.13 ± 21.30	53.95 ± 22.42	0.089	50.67 ± 21.09	54.07 ± 22.43	0.018
CCI, mean ± SD	3.14 ± 1.22	2.88 ± 1.13	0.005	3.14 ± 1.24	2.96 ± 1.14	0.027
mMRC, n (%)			0.252			0.998
0–1	359 (78.6)	98 (21.4)		320 (70.0)	137 (30.0)	
2–4	494 (81.4)	113 (18.6)		425 (70.0)	182 (30.0)	
Oxygen therapy, n (%)			< 0.01			0.001
No	758 (82.5)	161 (17.5)		661 (71.9)	258 (28.1)	
Yes	95 (65.5)	50 (34.5)		84 (57.9)	61 (42.1)	
Smoker, n (%)	619 (79.3)	162 (20.7)	0.215	541 (69.3)	240 (30.7)	0.376
Education level, n (%)			0.021			0.004
High education level	241 (84.9)	43 (15.1)		218 (76.8)	66 (23.2)	
Low education level	612 (78.5)	168 (21.5)		527 (67.6)	253 (32.4)	
Living environment, n (%)			< 0.01			< 0.01
Rural living environment	673 (83.5)	133 (16.5)		596 (73.9)	210 (26.1)	
Urban living environment	180 (69.8)	78 (30.2)		149 (57.8)	109 (42.2)	

Abbreviations: BMI, body mass index; FEV_1% predicted, percentage predicted forced expiratory volume in 1 second; CAT, COPD Assessment Test; CCI, Charlson Comorbidity Index; mMRC, modified Medical Research Council; SD, standard deviation.

Primary Analysis

Relationship Between Education and Risk for Anxiety/Depression Among Patients with COPD

Patients with COPD with a low education level had an increased risk for anxiety and depression compared with those with a high education level. This effect remained after adjustment for potential confounding factors (odds ratio [OR] 1.56, 95% confidence interval [CI] 1.06–2.29 and OR 1.62, 95% CI 1.17–2.27, respectively) (Table 2).

Relationship Between Living Environment and Risk for Anxiety/Depression Among Patients with COPD

Patients with COPD living in urban areas had an increased risk for anxiety and depression compared with those living in rural areas. This effect remained after adjustment for potential confounding factors (OR 2.15, 95% CI 1.51–3.05 and OR 2.01, 95% CI 1.46–2.75, respectively) (Table 2).

Table 2 Risk for Anxiety or Depression Among Patients with COPD by Education Level and Living Environment

Education Level and Living Environment	Anxiety		Depression	
	Model 1	Model 2	Model 1	Model 2
Education level				
High education level	1	1	1	1
Low education level	1.54 (1.07–2.22) *	1.56 (1.06–2.29) *	1.59 (1.16–2.17) **	1.62 (1.17–2.27) *
Living environment				
Rural living Environment	1	1	1	1
Urban living environment	2.19 (1.59–3.03) **	2.15 (1.51–3.05) **	2.08 (1.55–2.78) **	2.01 (1.46–2.75) **

Notes: Model 1: non-adjusted. Model 2: adjusted for age, sex, smoking history, body mass index, COPD Assessment Test, percentage predicted forced expiratory volume in 1 second; oxygen therapy, modified Medical Research Council score, and Charlson Comorbidity Index. * *P*<0.05, ***P*<0.01.

Table 3 Combined Effect of Education Level (High Vs Low) and Living Environment (Rural Vs Urban) Used to Calculate Interactions

Combined Effect (Educational Level and Living Environment)		Anxiety		Depression	
		Model 1	Model 2	Model 1	Model 2
High educational level	Rural living environment	1	1	1	1
Low educational level	Rural living environment	1.31 (0.73–2.34)	1.34 (0.74–2.42)	1.25 (0.78–2.01)	1.28 (0.78–2.09)
High educational level	Urban living environment	1.24 (0.63–2.44)	1.26 (0.62–2.55)	1.07 (0.61–1.88)	1.07 (0.59–1.93)
Low educational level	Urban living environment	9.14 (4.56–18.32) **	7.90 (3.83–16.29) **	13.76 (6.88–27.53) **	11.79 (5.77–24.10) **

Notes: Model 1: non-adjusted. Model 2: adjusted for age, sex, smoking history, body mass index, COPD Assessment Test, percentage predicted forced expiratory volume in 1 second, oxygen therapy, modified Medical Research Council score, and Charlson Comorbidity Index. **$P<0.01$.

Secondary Analysis

We used the binary educational level indicator (high education level vs low education level) and living environment indicator (rural living environment vs urban living environment) to examine the combined interaction. As expected, the combination group of low education level and urban living environment showed the highest and significantly elevated risk for anxiety or depression among patients with COPD (OR 9.14, 95% CI 4.56–18.32, $P<0.001$ and OR 13.76, 95% CI 6.88–27.53, respectively; $P<0.001$). The relationship was only slightly weakened after adjusting for potential confounding factors (OR 7.90, 95% CI 3.83–16.29, $P<0.001$ and OR 11.79, 95% CI 5.77–24.10, respectively; $P<0.001$) (Table 3).

Figure 1 shows the excess risks due to low education level, urban living environment, and their interactions in an analysis of the risk for anxiety (A) or depression (B) among patients with COPD after adjusting for all confounders. The STROBE Statement advises reporting interaction analyses using an additive and multiplicative scale when evaluating the joint effect of exposures.[16] This is because an additive interaction model is closer to the nature of biological interaction and has more relevant public health significance than a multiplication model.[17] Therefore, as recommended in a previous study, we used an excel sheet to calculate the additive interaction.[15] As shown in Table 4, the estimated RERI values were 6.31 (95% CI 1.60–11.01) for anxiety and 10.44 (95% CI 2.66–18.23) for depression, indicating that of the additive interaction between low education level and urban living environment resulted in 6.31 relative excess risks for anxiety and 10.44 relative excess risks for depression. The AP revealed that 80% of the total odds of anxiety and 89% of the total odds of depression were attributable to the interaction between low education level and urban living environment. In addition, SI values were 11.57 (95% CI 1.41–95.27) and 31.31 (95% CI 1.59–617.04), suggesting that the risks for anxiety or depression in patients with both low education level and an urban living environment were 11.57 and 31.31 times as high as the sum of risks for patients presenting with a single factor.

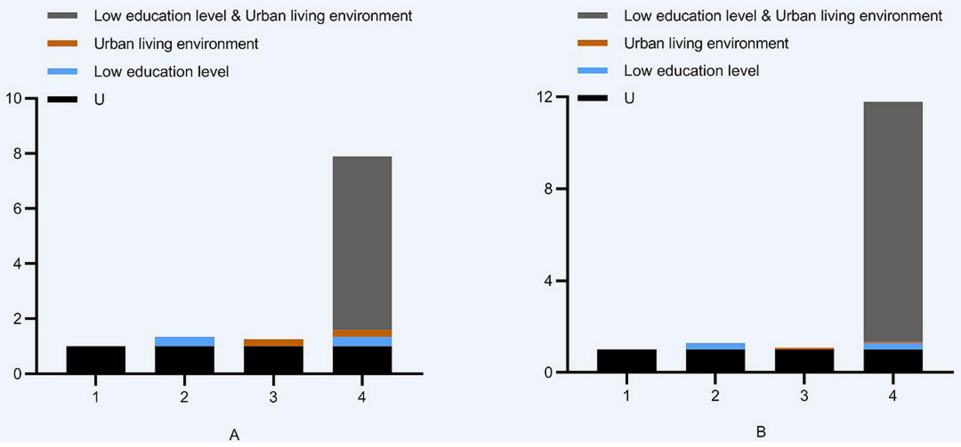

Figure 1 Relative risk with contributions from low education level, urban living environment, or a combination of both factors for anxiety (**A**) and depression (**B**). Multiple confounder adjustment included age, sex, smoking history, body mass index, COPD Assessment Test, percentage predicted forced expiratory volume in 1 second, oxygen therapy, modified Medical Research Council score, and Charlson Comorbidity Index.
Note: U means the odds ratio was equal to 1.

Table 4 Measures for Estimation of Biological Interaction Between Low Education Level and Urban Living Environment for the Risk for Anxiety or Depression Among Patients with COPD

Measures of Biological Interaction	Anxiety		Depression	
	Model 1	Model 2	Model 1	Model 2
RERI (95% CI)	7.60 (1.91–13.29)	6.31 (1.60–11.01)	12.45 (3.25–21.64)	10.44 (2.66–18.23)
AP (95% CI)	0.83 (0.72–0.95)	0.80 (0.66–0.94)	0.90 (0.84–0.97)	0.89 (0.80–0.97)
SI (95% CI)	14.95 (2.21–101.16)	11.57 (1.41–95.27)	40.45 (1.57–1043.07)	31.31 (1.59–617.04)

Notes: Model 1: non-adjusted. Model 2: adjusted for age, sex, smoking history, body mass index, COPD Assessment Test, percentage predicted forced expiratory volume in 1 second, oxygen therapy, modified Medical Research Council score, and Charlson Comorbidity Index. If there was no biological interaction the 95% CI for RERI and AP would include 0 and that for SI would include 1.
Abbreviations: RERI, relative excess risk due to interaction; AP, attribution ratio; SI, synergy index; CI, confidence interval.

Discussion

The COPD-AD China Registry is a nationwide registration study in China that has a comprehensive database that tracks patients with COPD who also suffer from anxiety or depression. Its goal is to screen for the prevalence of anxiety and depression among patients with COPD at an early stage and track how these conditions impact the overall progression and prognosis of COPD. In this cross-sectional study, we investigated a sample of 1064 patients with COPD to evaluate the independent and combined effects of education level and living environment on their mental health.

Our results showed that the incidences of anxiety and depression were associated with education and living environment. After adjustment for potential confounding factors, binary logistic regression analyses showed that a lower education level and an urban living environment were independently associated with higher risks for anxiety and depression among patients with COPD. This suggested that lower education level and urban living environment were stable factors predicting the risk for anxiety and depression among patients with COPD. Education is a comprehensive reflection of a person's knowledge, skills, and values, and has a profound impact on that individual's cognition, behavior, and emotions.[18,19] Patients with COPD with a lower education level may lack relevant health knowledge, lack understanding and confidence about their disease and treatment methods, and feel helpless and fearful. They may also be more dependent on the advice of doctors and lack the ability and willingness to self-manage than patients with a higher education level.[20–23] In addition, they may face social barriers and discrimination and feel lonely and lost. These factors may lead to them being more susceptible to symptoms of anxiety and depression. Living environment refers to the conditions in which a person lives, and includes social, economic, and cultural aspects. An urban living environment has previously been considered an important factor affecting mental health.[24] Urban living environments have serious air pollution that impacts patients with COPD. Exhaust from cars, industrial waste gases, and dust from construction sites and other sources of pollution are constantly emitted into the atmosphere, causing concentrations of harmful substances such as PM2.5 in the air.[25,26] The respiratory system of patients with COPD has been damaged, and air pollution can therefore aggravate respiratory difficulties and symptoms.[27] Moreover, there is serious noise pollution in urban living environments.[28] Traffic, industrial, and community noise sources continuously interfere with the lives of patients with COPD. These noises may reduce the quality of patients' sleep and affect their emotional and mental state.[29,30] Finally, there may also be social problems in urban living environments such as tense interpersonal relationships.[31] The pace of urban life is fast, and interpersonal relationships are complex and many patients with COPD may feel lonely. All of these factors may cause patients to feel lost and helpless, further exacerbating their anxiety and depression. Therefore, we believed that a low education level and an urban living environment may increase the risks for anxiety and depression in patients with COPD.

We also examined the combined effect of a low education level and an urban living environment on the risks for anxiety and depression in patients with COPD. Our findings indicated that the combination of these two factors was statistically significant and exhibited a positive interactive effect. Specifically, the risk for anxiety or depression in patients with COPD was higher when they had a low education level and lived in urban areas, with this interactive effect being greater than the sum of their individual effects (11.57 times for anxiety and 31.31 times for depression). There are several possible explanations for the synergistic interaction between a low education level and an urban living

environment in terms of anxiety and depression. First, these risk factors are associated with increased stress. Living in an urban area can be stressful because of noise pollution, traffic congestion, and overcrowding. In addition, a low education level may be associated with lower socioeconomic status, which can lead to stress related to financial difficulties and inadequate access to healthcare.[32–34] Second, a low education level and an urban living environment may impact patient's social support network and social activities. A low education level may limit individuals' access to resources and opportunities, which in turn may impact their social support networks and social activities. In addition, the fast-paced, busy lifestyle of an urban living environment often leaves people without sufficient time and opportunities to connect with others and participate in social activities.[35,36] Third, a low education level may lead to a lack of necessary health knowledge and behaviors when facing health problems, resulting in a deterioration of health conditions. This situation can leave patients feeling frustrated and helpless, and in combination with the fast-paced, high-pressure, and competitive urban living environment, may also make individuals feel lonely, anxious, and even more helpless, meaning they feel unable to cope with the challenges of their illness and life.[37,38] Therefore, it is crucial for healthcare professionals to consider multiple risk factors when assessing risks for anxiety and depression among patients with COPD, especially those with low education levels that live in urban areas. Health policymakers should develop targeted interventions to reduce the risk for anxiety and depression in patients with COPD by increasing the greening rate in urban areas, strengthening governance of noise and pollution, providing regular health services and cultural activities, and offering economic and psychological support.

There were certain limitations in our study that should be noted. First, this study was conducted among patients from nine hospitals in China, which may limit the generalizability of the findings to other settings. Second, this study used a cross-sectional design, which limited our ability to establish causal relationships between urban living environment, low education level, and anxiety and depression among patients with COPD. Longitudinal studies are needed to further explore these relationships. Finally, we did not assess other potential confounding variables, such as socioeconomic status and medication complexity, which may affect our results.

In conclusion, our study provides evidence that the mental health of patients with COPD is influenced by their education and living environment. Patients with low education levels that live in urban areas may experience more anxiety and depression than better educated, rural dwelling patients, which can be compounded by their interactive effects. It is crucial to consider educational and environmental factors for patients with COPD, offer them optimal medical care and social support, and help them manage psychological distress. These efforts can enhance their quality of life and treatment outcomes.

Abbreviations

COPD, Chronic obstructive pulmonary disease; GOLD, Global Strategy for the Diagnosis; BMI, Body mass index; CCI, Charlson Comorbidity Index; CAT, COPD Assessment Test; mMRC, modified Medical Research Council; FEV_1% predicted, percentage predicted forced expiratory volume in 1 second; HADS, Hospital Anxiety and Depression Scale; SD, Standard deviation; RERI, Relative excess risk ratio; AP, Attribution percentage (AP); SI, Synergy index; OR, Odds Ratio; 95% CI, 95% Confidence Interval.

Data Sharing Statement

The data analyzed are available upon reasonable request to the corresponding author (Dr XN Zhao).

Ethical Standards

Our research has passed the ethical review and approval of the Ethics Review Committee of Liangxiang Hospital of Fangshan District, Beijing, the Ethics Review Committee of Affiliated Hospital of Binzhou Medical College, the Ethics Review Committee of Ordos Central Hospital, the Ethics Review Committee of Guangdong Provincial People's Hospital, the Ethics Review Committee of Affiliated Hospital of Guangdong Medical University, the Ethics Review Committee of the First Affiliated Hospital of Nanchang University, the Ethics Review Committee of Qilu Hospital of Shandong University, the Ethics Review Committee of Beijing Chaoyang Hospital of Capital Medical University, and the Ethics Review Committee of the People's Hospital of Wuhan University. The authors assert that all procedures contributing to

this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Acknowledgment

We thank Analisa Avila, MPH, ELS, of Liwen Bianji (Edanz) (www.liwenbianji.cn) for editing the language of a draft of this manuscript, all the patients participating in the study and all the staff involved at the hospital. This paper was presented at the Research Square as a preprint with interim findings: [http://dx.doi.org/10.21203/rs.3.rs-2877766/v1].

Funding

This research was supported by the National Key Research and Development Program of China (grant number: 2016YFC1304404), the Guangdong Medical Science and Technology Research Fund Project (grant number: B2021294), the Discipline Construction Project of Guangdong Medical University (grant number: 4SG21231G), the Clinical Research Project of Affiliated Hospital of Guangdong Medical University (grant numbers: LCYT2017A003, LCYJ2020B008, LCYJ2021B007), and the Project of Zhanjiang City (grant numbers: 2021A05052, 2021A05077).

Disclosure

The authors report no conflicts of interest in this work.

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