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CLINICAL TRIAL REPORT

Real-World COPD Management Over 3 Years at the Community Health Service Center of Shanghai During the COVID-19 Pandemic in China

Ting-Ting Wu[1,*], Yi Qun Jiang[2,*], Bang-Feng Zhao[1,*], Feng-Li Si[1], Peng Wu[1], Huan-Ying Wang[1], Chun-Feng Sheng[1], Xun Xu[1], Fan Li[1], Jing Zhang[3]

[1]Songjiang Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (Preparatory Stage), Shanghai, People's Republic of China; [2]General Practice/International Medical Care Center, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, People's Republic of China; [3]Department of Pulmonary and Critical Care Medicine, Zhongshan Hospital, Shanghai Medical College, Fudan University, Shanghai, People's Republic of China

*These authors contributed equally to this work

Correspondence: Fan Li; Jing Zhang, Email lifanking2015@163.com; jingatlas@outlook.com

Objective: To evaluate the real-world situation for the management of chronic obstructive pulmonary disease (COPD) and poorly controlled disease risk factors in the Chinese community.

Methods: This retrospective multicentre study analysed data from COPDMICand MICHC in Shanghai Songjiang District, Shanghai, China. The differences in COPD Assessment Test (CAT), the modified Medical Research Council (mMRC) dyspnea scale, and the number of emergency cases, emergency visits, inpatient cases, and hospitalisations from January 2018 to December 2020 were analysed. The impact of coronavirus disease 2019 (COVID-19) on COPD management was also assessed.

Results: For 2020 versus 2018, analysis of 468 COPD cases from COPDMIC matched with MICHC data showed significantly more patients with improved mMRC grades, significantly fewer emergency cases and emergency visits, and significantly fewer hospitalisation cases and hospitalisations. Differences in the number of emergency visits and hospitalisations per capita were statistically significant. Compared to GOLD 3–4, GOLD 1–2 patients showed significant improvements in CAT score, mMRC grade, the number of emergency visits and hospitalisations per capita. Treatment adherence from 2018 to 2020 was 25%, 29.1%, and 6.8%, and the proportion of medication regimens consistent with guidelines was 43.44%, 50.98%, and 71.87%, respectively. Higher treatment adherence resulted in significantly improved CAT scores and mMRC grades and fewer emergency department visits and hospitalisations per capita.

Conclusion: Combined with remote management tools, patients with COPD achieved continuous improvement in symptoms and exacerbations over 3 years. In the context of COVID-19 prevention/control measures, improvements were significant for patients with GOLD 1–2 COPD but limited with GOLD 3–4. Pharmacologic treatment significantly improved clinical symptoms and reduced emergency visits and hospitalisations. Severe airflow limitation and poor adherence to pharmacologic treatment were important risk factors for lack of disease remission.

Keywords: chronic obstructive, lung disease, COVID-19, family physician, management information center

Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease globally. In China, the prevalence of COPD for individuals older than 40 years has increased in less than a decade, from 8.6% in 2007 to 13.7% in 2018,[1,2] resulting in COPD becoming the third leading cause of disability and the fourth leading cause of mortality in China.[3] Despite this high prevalence and poor outcomes, however, numerous studies have shown that the rate of early diagnosis,

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standardisation of initial treatment regimens (ie consistency of drug regimens with guidelines), and adherence to drug therapy are generally low in patients with COPD in China. For example, Wang Chen et al reported[2] that only 9.7% of patients with COPD in China were diagnosed based on pulmonary function, and only 3.2% of patients with COPD had a medication regimen consistent with guidelines. A national cross-sectional survey of individuals aged 40 years and older showed a diagnosis rate of 5.9% and a treatment rate of 11.7% among those with COPD.[4] In terms of treatment adherence over 1 year among patients with stable COPD in two studies, 30% were adherent for more than 50% of the year, whereas 10% were adherent for more than 80% of the year.[5,6] Therefore, improving the rate of early diagnosis, treatment standardisation, and treatment adherence of patients with COPD in China is an important issue to improve the treatment outcomes in this population.

To address this issue, we developed COPD Management Information Center (COPDMIC), which went online in 2017 (Figure 1).[7] The COPDMIC is a regional COPD patient management platform established through the mobile Internet and Internet of Things, which unites family physicians from 21 community health service centres and respiratory specialists from three general hospitals in Songjiang District, Shanghai, China. Family physicians are responsible for screening high-risk groups for COPD, managing patients with stable disease and after treatment, referral for COPD acute exacerbations, and patient health education, among other services. Respiratory specialists are responsible for the diagnosis of COPD, treatment plan formulation, two-way referral for patients with acute exacerbations, and addressing challenges encountered by family physicians in the diagnosis and treatment of COPD. Since the platform began operating

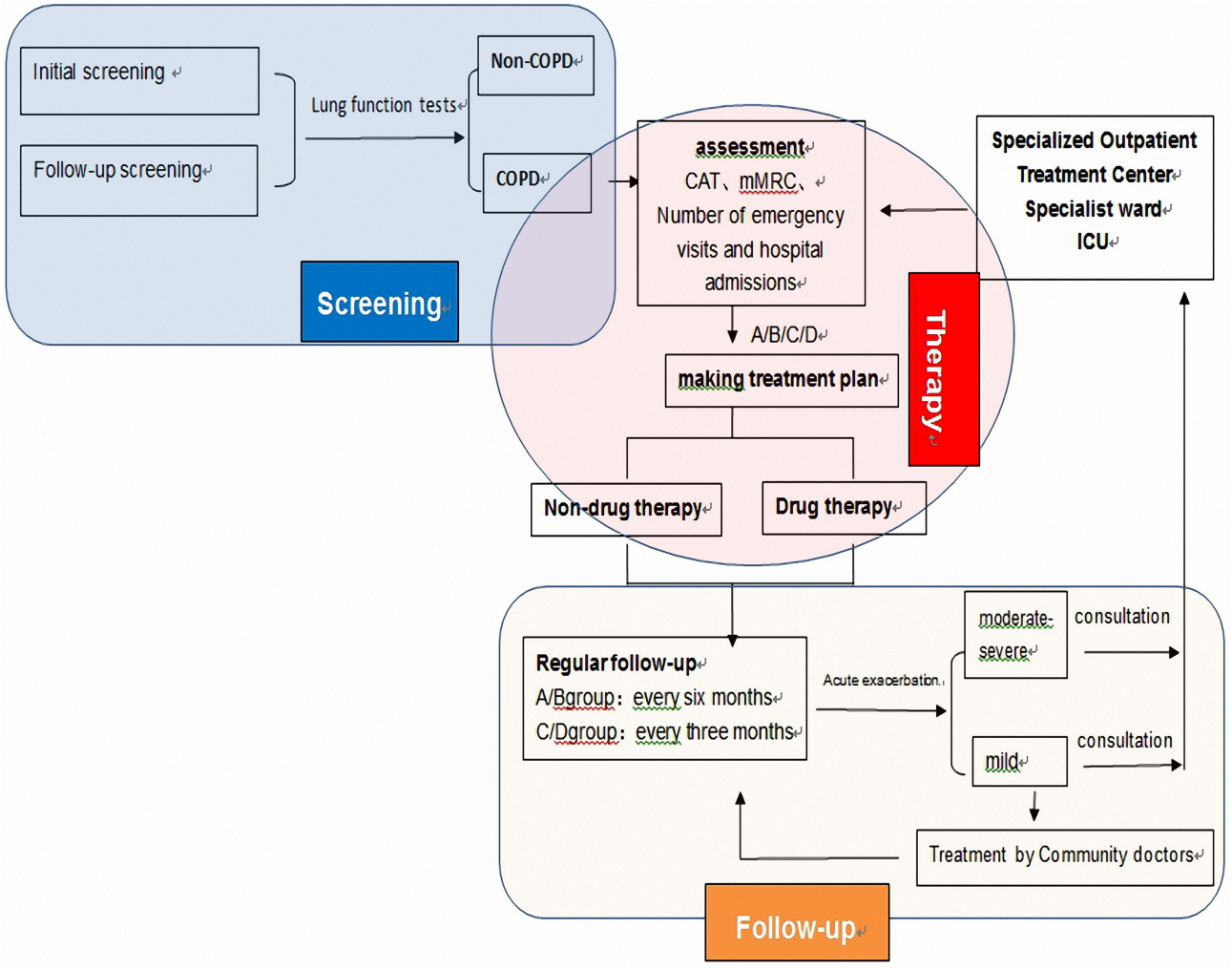

Figure 1 Flow chart of COPDMIC operations.

in 2017, we have sought to understand the real-world situation of COPD management in the community. To this end, our current study is a retrospective analysis of the platform data over 3 years, from 2018 to 2020.

During our study period, the global outbreak of coronavirus disease 2019 (COVID-19) began in December 2019, and this pandemic led to a greatly increased risk of acute exacerbations in patients with COPD.[8] To prevent the spread of the novel coronavirus in the population, countries internationally have taken prevention and control measures, such as

> wearing masks in hospitals, supermarkets, public transportation and other indoor places, maintaining a certain social distance, and strengthening hand disinfection.[9]

These measures also reduce the possibility of infection by other viruses in patients with COPD, thus reducing the occurrence of acute exacerbation of COPD (AECOPD).[10,11] However, another comorbidity for patients with COPD arose during the pandemic—restriction of social activities led to longer periods remaining at home, which worsened the original anxious and depressed psychological mood and subsequently triggered disease aggravation.[8] In addition to these effects of the pandemic, many healthcare institutions experienced medical staff infections during this time and temporarily suspended outpatient or inpatient services for closed-loop management. Moreover, some patients with COPD were concerned about the potential for COVID-19 infection during their visits to healthcare institutions.Epidemic prevention / control measures limit the number of visits to specialist outpatient clinics or community-based family doctor clinics to dispense medication for patients with COPD.

Against this background, important questions arise for patients with COPD. How do these factors affect COPD management? Is there any difference in the influence of COVID-19 on patients with COPD with different degrees of disease?To date, the real-world situation of patients with COPD in the Chinese community has not been well reported. To address these issues, our current study sought to compare the differences in symptom scores, dyspnoea ratings, and the number of emergency department visits and hospitalisations over the 3-year period from January 2018 to December 2020 for patients with COPD managed by family physicians.

Materials and Methods

Study Design

This retrospective, multicentre, self-controlled study collected data from the COPD Management Information Center (COPDMIC) and the Medical Information Center of Health Management Commission (MICHC) in Shanghai Songjiang District, Shanghai, China. The MICHC data were used to verify the authenticity of COPDMIC data by case matching.

Information Platforms

COPD Management Information Center (COPDMIC)

The COPDMIC is a mobile internet management system for patients with COPD that involves family physicians from 16 community health service centres and respiratory specialists from 5 general hospitals in Shanghai Songjiang District. The system is divided into three key domains: *Physician*, which includes management by specialists and family physicians, *Nurses–Pharmacists*, and *patients with COPD*. The platform was set up with a powerful COPD diagnosis and treatment information database to achieve a closed-loop management system for the early screening of high-risk groups, diagnosis and treatment planning, and follow-up of stable patients.The platform was interfaced with the Medical Information Center of Health Management Commission (MICHC), allowing for real-time, comprehensive information on patient visits while establishing a referral pathway to medical institutions in the region to ensure timely treatment for patients with acute exacerbations.

The COPDMIC platform content includes COPD screening scales; lung function data upload and automatic analysis; COPD Assessment Test (CAT) scores; modified Medical Research Council (mMRC) assessment; emergency and hospitalisation registry; COPD severity assessment (ABCD); treatment plan recommendation based on the 2017 Global Initiative for Chronic Obstructive Lung Disease (GOLD); medication records; determination of follow-up schedule; and teleconsultation and referral system for specialists and family physicians.[2] The COPD screening scale uses the symptom-based COPD screening questionnaire (COQ) recommended by the International Airways Organization

(IAPA).[12,13] The questionnaire includes 8 items, namely age, smoking history, body mass index, effect of weather on cough, cough not caused by the cold, presence of cough in the early morning, frequent wheezing, and history of allergy. The total score is 38, and a score of ≥17 is considered a high-risk group for COPD.The scale has been tested for reliability and validity in China and has been revised according to the characteristics of the Chinese, which can be used for the screening of the Chinese COPD population.[14]

Family doctors conducted proactive screening of individuals at high risk of COPD through the COQ screening questionnaire, including initial screening of patients in the community and re-screening of previously undiagnosed patients in the COPDMIC database; regular follow-up and health education for patients with confirmed COPD; and immediate management or referral of patients with exacerbations of COPD to ensure acute healthcare.

The responsibility of the specialist is to diagnose COPD, determine the initial treatment plan, provide solutions to challenges encountered by family physicians in the management of patients with COPD, and schedule hospitalisations.[2]

Data available in COPDMIC include the following: 1) *basic information*: name, sex, age, home address, contact phone number, identification number, health insurance number, smoking history, lung function at enrollment, lung function classification, CAT scores, and mMRC grades; 2) *medication information*: drug name, dosage, prescription time, and medication course; and 3) *family physician follow-up record*s: pulmonary function measured by forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), and FEV_1/projected value); pulmonary function classification; CAT scores; mMRC grades; the number of emergency visits; the number of hospitalisations; and actual medication use. The higher the CAT and mMRC values, the more severe the COPD symptoms or dyspnoea.

Medical Information Center of Health Management Commission (MICHC)

As the information management centre of the health administration authority, MICHC is in charge of all patient consultation and treatment information of medical institutions at all levels in Songjiang District. This centre is linked with Shanghai and National Health Insurance Information Center for real-time data exchange.

Inclusion and Exclusion Criteria

Inclusion criteria were the following: 1) pulmonary function tests that meet the GOLD 2017 COPD diagnostic criteria;[15] diagnosis of COPD was defined by the presence of a postbronchodilator $FEV_1/FVC < 0.70$ in patients with appropriate symptoms and significant exposure to noxious stimuli, according to the GOLD 2017 report; 2) complete follow-up record of the family physician from 1 January 2018 to 31 December 2020, and the last follow-up visit occurring in the period from October–December 2020; 3) clear follow-up indicators and no missing evaluation indicators at each follow-up visit.

Exclusion criteria were the following: 1) incomplete information on drug use, 2) follow-up not performed at the required time or with missing assessment indicators in the follow-up records, and 3) death during the study cycle.

Follow-Up Schedule

According to the GOLD 2017 comprehensive disease assessment criteria, A–B was classified as the low-risk group and C–D as the high-risk group. Those in groups A and B were followed up once every 6 months; those in groups C and D were followed up once every 3 months. Patients hospitalised for AECOPD were required to have their first follow-up visit within 1 month after discharge, and then follow-up visits were scheduled based on the results of the comprehensive disease assessment.

Measures of Disease

COPD Assessment Test Scores

The CAT scores were obtained by an 8-item questionnaire, with 6 subjective disease indicators (cough, sputum, chest tightness, sleep, energy, and mood) and 3 tolerance evaluation indicators (exercise endurance and daily exercise). Each item has a score of 0–5; total score ranges were 0–40. A score of 0–10 was rated as a *mild impact*, 11–20 as a *moderate impact*, 21–30 as a *severe impact*, and 31–40 as a *very serious impact* of COPD.

Modified Medical Research Council Grades

The MICHC grades were as follows: *grade 0*—respiratory distress after strenuous activity; *grade 1*—respiratory distress after walking fast on flat ground/climbing gentle slopes; *grade 2*—walking fast on flat ground/climbing gentle slopes slower than peers and needing rest; *grade 3*—needing to stop and catch their breath after walking 100 metres or several minutes on a flat ground; and *grade 4*—inability to leave home due to severe respiratory distress or respiratory distress that occurs when putting on and taking off clothes.

Acute Exacerbations of COPD

The definition of AECOPD is an acute worsening of respiratory symptoms that results in additional therapy and requires hospitalisation or visiting the emergency department.

Assessment of COPD Severity

Classification of Severity of Flow Limitation

The severity of flow limitation was assessed by investigators at Songjiang Hospital Affiliated with Shanghai Jiaotong University School of Medicine (preparatory stage). Spirometry data provided by the GPs were interpreted based on the GOLD Committee criteria, with airflow limitation defined as post-bronchodilator FEV_1/FVC ratio <0.7 (or 70%).[15] The COPD severity was classified as follows: GOLD 1 (mild)—FEV_1/FVC <0.70; $FEV_1 \geq 80\%$ predicted; GOLD II (*moderate*)—FEV_1/FVC <0.70; $50\% \leq FEV_1 < 80\%$ predicted; GOLD III (*severe*)—FEV_1/FVC <0.70; $30\% \leq FEV_1 < 50\%$ predicted; GOLD IV (*very severe*): $FEV_1/FVC < 0.70$; $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure. GOLD 1–2 is the mild to moderate group, and GOLD 3–4 is the severe to very severe group.

Spirometry

We performed spirometry to assess lung function by measuring FEV_1, FVC, and the FEV_1/FVC ratio. The device used was U-BREATH (PF680, China).[16] Before beginning the study, GPs were instructed on how to perform spirometry using the American Thoracic Society guidelines[17] by representatives of the spirometer sales company. During spirometry, the patient was seated with elbows bent and mouth firmly attached to the mouthpiece; a nose clip was also used to prevent air leaks. The FVC manoeuvres were performed 5 times; the best 3 results were considered, and the highest of these 3 results was selected if it did not exceed the second-largest value by more than 10%.[18]

ABCD Assessment

Participants were also investigated by questionnaires, including CAT scores and mMRC grades. The grouping thresholds were the number of exacerbations in the previous year, CAT score ≥ 10, mMRC grade ≥ 2, and whether frequent exacerbation occurred. The mMRC grade was used if it was inconsistent with the CAT score. According to the 2017 GOLD criteria, all participants were divided into A, B, C, and D categories.[12]

Pharmacotherapeutic Approaches

Drug treatment recommendations based on GOLD 2017 criteria were as follows. Group A preferred treatment was with a bronchodilator, and an efficacy evaluation was performed to decide whether to continue, stop, or replace the drug. Group B preferred treatment was with a long-acting bronchodilator, either a long-acting beta-agonist (LABA) or long-acting muscarinic antagonist (LAMA); combination therapy with LAMA plus LABA could be used for persistent symptoms. Group C treatment was with LAMA as the first choice; or, if symptoms continued to worsen, LAMA plus LABA or LABA plus inhaled corticosteroids (ICS) could be used. Group D preferred treatment was with LABA plus LAMA or LABA plus ICS, or LABA plus LAMA plus ICS could be used if the symptoms continued to worsen. Also, roflumilast or macrolide antibiotics could be added if the symptoms continue to worsen. Consistent or inconsistent guideline recommendations were determined in this study based on whether the patients' actual medication regimens were consistent with the GOLD 2017 recommendations for the COPD medication regimen.

Statistical Analysis

All statistical data were processed using SPSS (version 23, IBM, Armonk, NY, USA). All baseline data were presented only descriptively. For the overall population, data were presented either as mean and standard deviation (SD) or number and percentage. Subgroups were defined by COPD severity (GOLD grade 1–2 vs GOLD 3–4) and by medication use (Yes/No). In this study, the differences in CAT, mMRC, number of emergency visits per capita, and number of hospitalisations per capita were compared by analysis of variance. The Welch test was used when the variance was not equal. A value of $p < 0.05$ was considered statistically significant.

Ethics and Informed Consent

The study was approved by the Ethics Committee of Shanghai Songjiang District Central Hospital in accordance with the ethical requirements of the Declaration of Helsinki (China Clinical Trials Registry registration number: ChiCTR2000031092). We ensured the confidentiality of the personal information of the participants in this study. Because the study was retrospective and observational, informed consent was not required to be signed by the participants.

Results

Patient Characteristics

Data retrieval from COPDMIC yielded a total of 592 patients with COPD, 124 of whom were excluded because of nonadherence with the follow-up time or missing follow-up data. The final 468 patients were included in the analysis. Of these 468 patients, 306 (65.4%) were male. The mean age (SD) was 75.3 ± 8.8 years. Baseline pulmonary data were mean FEV_1(L ± SD)1.62 (0.88), mean FVC (L ± SD) 2.18 (0.99), the mean FEV_1/FVC (% ± SD) 51.6 ± 11.8.

Of the 468 participants at baseline, 50.4% were classified as GOLD 2 and 36.3% as GOLD 3, whereas GOLD 1 and GOLD 4 represented a small percentage (6.6% vs 6.6%). Disease severity assessed during the initial visit based on combined GOLD 2017 criteria revealed these rates from A to D categories: 13.2%, 47.9%, 0.6%, and 38.2%, respectively. The current smoker rate was 40.6%, and all smokers were men. The baseline demographics of the overall population are shown in Table 1.

Table 1 Baseline Demographics and Disease Characteristics of the Overall Population

Overall Population = 468		**Baseline Data**
Age (years), mean (SD)		75.3 ± 8.8
Male, No. (%)		306 (65.4)
Lung function	FEV1(L), mean (SD)	1.62 ± 0.88
	FEV1,% predicted	
	GOLD 1, No. (%)	31 (6.6)
	GOLD 2, No. (%)	236 (50.4)
	GOLD 3, No. (%)	170 (36.3)
	GOLD 4, No. (%)	31 (6.6)
	FVC(L), mean (SD)	2.18 ± 0.99
	FEV1/FVC, %(SD)	51.6 ± 11.8
ABCD assessment	A, No. (%)	62 (13.2)
	B, No. (%)	224 (47.9)
	C, No. (%)	3 (0.6)
	D, No. (%)	179 (38.2)
Smoking status, No. (%)		190 (40.6)

Notes: GOLD1: FEV1 >80% predicted, GOLD 2:50% ≤ FEV1 <80% predicted.GOLD3: 30%≤ FEV1 <50% predicted, GOLD4:FEV <30% predicted. All values refer to post-bronchodilator.

Variability in CAT Scores, mMRC Grades, Emergency and Inpatient Cases, Emergency and Inpatient Visits

We specifically analysed the variability of each study indicator over 3 years from 2018–2020; the results are shown in Figures 2 and 3 and Table 2. Because the emergency and hospitalisation conditions in COPDMIC were recorded during the family physician follow-up visit and obtained from the patient's self-report, memory errors may have occurred, so the MICHC platform data were matched by the patient identification number to verify the data authenticity.

CAT Scores and mMRC Grades

An annual decreasing trend in CAT scores and mMRC grades was observed for all patients with COPD over the 3 years. Patients with CAT <10 gradually improved from 26.5% in 2018 to 38.5% in 2020. Patients with mMRC grades 0–1 increased from 58.9% in 2018 to 64% in 2020, showing a significant improvement, but only mMRC had statistical significance.

Emergency Cases and Emergency Visits

Both COPDMIC and MICHC showed that the number of COPD emergency cases showed a downward trend each year from 2018 to 2020. In COPDMIC, the number of emergency cases in 2020 was 70, a decrease of 42.6% compared with 2018. In MICHC, the number of emergency cases in 2020 was 102, a decrease of 12.8% compared with 2018. In terms of the number of emergency episodes, the COPDMIC data showed a slight increase in 2019 (166) compared with 2018 (156) but a significant decrease of 41.02% in 2020 (92). The MICHC data curve was the same, with a slight increase in 2019 and a significant decrease in 2020 by 25.60%. Further statistical comparison in terms of cases per capita using MICHC data showed a statistically significant difference in 2020 compared with 2019.

Inpatients and Hospitalisations

The findings for the number of cases and hospitalisations echoed those for the emergency cases and emergency visits. The number of hospitalised cases of COPDMIC was 138, which was 23.3% lower than in 2018. The number of

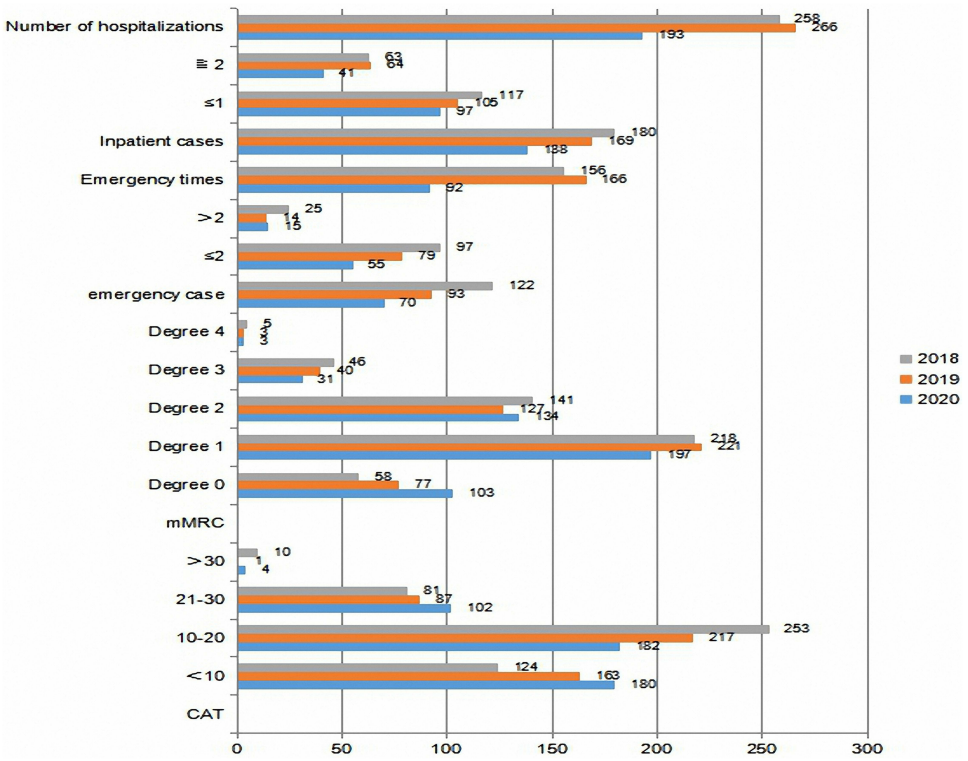

Figure 2 COPDMIC 2018–2020 overview of CAT, mMRC, emergency and hospitalisation of COPD patients.

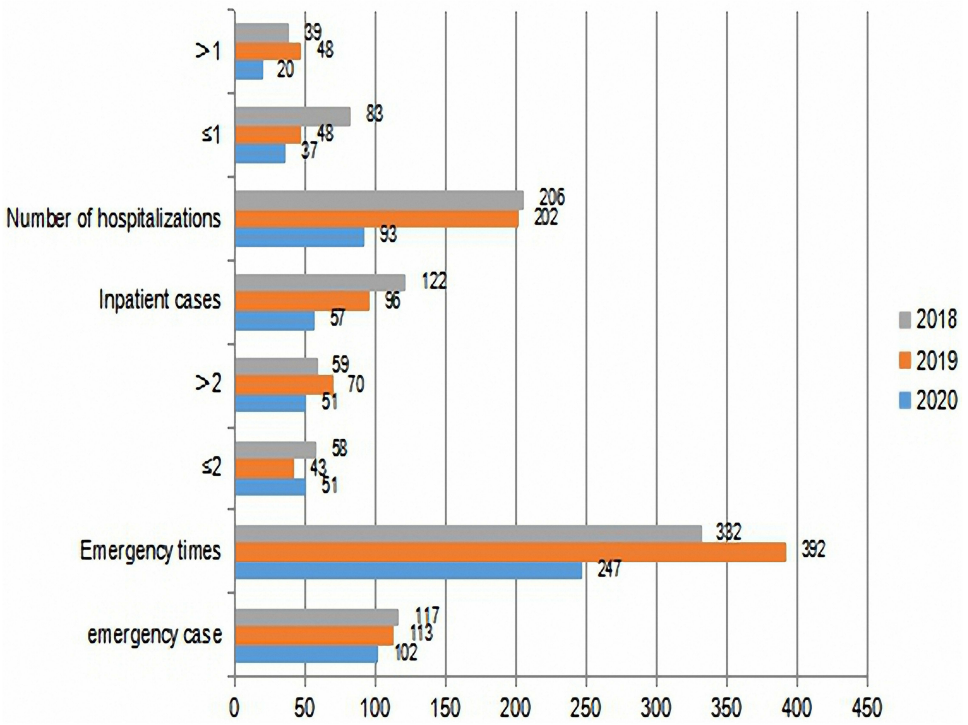

Figure 3 MICHC2018–2020 overview of CAT, mMRC, emergency and hospitalisation of COPD patients.

hospitalised cases in MICHC in 2020 was 57, which was 53.27% lower than in 2018. Regarding the number of hospitalisations, the COPDMIC data showed a slight increase in 2019 (266) compared with 2018 (258) but a significant decrease in 2020 (193) by 25.19%. The MICHC data curve was slightly different, showing a decreasing trend year by year by 54.85%. Both groups in the platforms showed statistically significant differences.

Table 2 Variability in CAT, mMRC, Emergency and Inpatient Visits in COPD Patients, 2018–2020

N = 468	Year	Average Value (95% Confidence Interval)	ANOVA			Welch	
			Sum of Squares	F price	p value	Levene Statistic	p value
COPDMIC							
CAT questionnaire*mean (SD)	2018	14.02 (13.34–14.71)	196.557	1.644	0.194	0.295	0.181
	2019	13.27 (12.60–1.95)					
	2020	13.19 (12.45–13.94)					
mMRC score, mean(SD)[c]	2018	1.41 (1.33–1.48)	8.343	5.481	0.004	5.447	0.004
	2019	1.30 (1.22–1.38)					
	2020	1.22 (1.14–1.30)					
Emergencies, mean (SD) (times)	2018	1.28 (1.14–1.42)	15.554	0.783	0.458	0.568	0.568
	2019	1.79 (0.68–2.89)					
	2020	1.31 (1.13–1.50)					
Number of hospitalisation, mean (SD) (times)	2018	1.43 (1.33–1.53)	14.311	2.36	0.096	7.524	0.001
	2019	1.78 (1.35–2.20)					
	2020	1.40 (1.27–1.52)					
MICHC							
Emergencies, means (SD) (times)*[b]	2018	2.84 (2.32–3.36)	60.189	3.594	0.029	3.578	0.03
	2019	3.47 (2.83–4.10)					
	2020	2.42 (1.97–2.87)					

(*Continued*)

Table 2 (Continued).

N = 468	Year	Average Value (95% Confidence Interval)	ANOVA			Welch	
			Sum of Squares	F price	p value	Levene Statistic	p value
Number of hospitalisation per capita, mean (SD) (times)[a,b]	2018 2019 2020	1.69 (1.46–1.92) 2.10 (1.80–2.41) 1.63 (1.33–1.93)	11.884	3.378	0.036	3.048	0.05

Notes: *Indicates uneven variance, subject to Welch test correction value. [a]Indicates the difference between 2018 and 2019, [b]Indicates the difference between 2019 and 2020, and [c]Indicates the difference between 2018 and 2020.

Comparison of CAT Scores, mMRC Grades, Number of Emergency Patients and Number of Emergency Visits, Number of Inpatients and Number of Hospitalisations Inpatients with GOLD 1–2 and GOLD 3–4

This study divided participants into two groups based on 2017 GOLD criteria for the severity grading of pulmonary function—GOLD 1–2 for the mild to the moderate group and GOLD 3–4 for the severe to the very severe group. The differences in each index of CAT score, mMRC grade, number of emergency visits per capita and number of hospitalisations per capita were then compared between the two groups. Results are shown in Table 3 and Table 4. For the mild to moderate group, the CAT score and mMRC grade were lower in 2020 than in 2018 and 2019, indicating that the symptoms and dyspnoea for patients with COPD improved in 2020 compared with the previous 2 years. The number of emergency department visits per capita and hospitalisations per capita in COPDMIC and MICHC also showed a decreasing trend year by year, and the difference was statistically significant. However, these differences were not reflected in the very severe group.

Table 3 Comparison of Study Indicators in (GOLD1–2)

N = 201	Years	Average Value (95% Confidence Interval)	ANOVA			Welch	
			Sum of Squares	F price	p value	Levene Statistic	p value
COPDMIC							
Emergencies, mean (SD)	2018 2019 2020	1. 33 (1.07–1.58) 1.21 (1.09–1.33) 1.20 (0.99–1.41)	0.444	0.509	0.602	0.47	0.628
Hospital stay per capita, mean (SD)*[b]	2018 2019[a] 2020	1.57 (1.41–1.73) 1.46 (1.31–1.61) 1.27 (1.15–1.39)	3.764	3.788	0.024	5.424	0.006
CAT*	2018 2019 2020	13.30 (12.42–14.18) 14.14 (13.23–15.04) 13.04 (12.01–14.06)	176.287	1.456	0.234	3.689	0.026
mMRC[a,c]	2018 2019 2020	1.26 (1.16–1.36) 1.45 (1.34–1.55) 1.22 (1.11–1.33)	7.74	5.207	0.006	3.491	0.031
MICHC							
Emergencies, mean (SD)*[a,b]	2018 2019[b] 2020	3.36 (2.62–4.09) 2.30 (1.85–2.74) 2.39 (1.73–3.05)	45.353	3.628	0.029	3.116	0.048
Hospital stays per capita, mean (SD)*,[a,b]	2018[b] 2019[a] 2020	2.16 (1.74–2.57) 1.61 (1.34–1.87) 1.33 (1.12–1.54)	15.584	5.599	0.004	6.354	0.008

Notes: *Indicates uneven variance, subject to Welch test correction value. [a]Indicates the difference between 2018 and 2019, [b]Indicates the difference between 2019 and 2020, and [c]Indicates the difference between 2018 and 2020.

Table 4 Comparison of Study Indicators in (GOLD 3–4)

N = 267	Years	Average Value (95% Confidence Interval)	ANOVA			Welch	
			Sum of Squares	F price	p value	Levene Statistic	p value
COPDMIC							
Emergencies, mean (SD)	2018	1.36 (1.08–1.63)	1.632	1.175	0.312	2.086	0.131
	2019	1.14 (1.01–1.26)					
	2020	1.38 (1.11–1.64)					
Hospital stay per capita, mean (SD)	2018	1.40 (1.27–1.54)	1.5	1.033	0.358	1.212	0.301
	2019	1.58 (1.35–1.81)					
	2020	1.56 (1.32–1.79)					
CAT	2018	13.87 (12.81–14.94)	43.944	0.372	0.689	0.375	0.687
	2019	13.23 (12.18–14.29)					
	2020	13.40 (12.31–14.48)					
mMRC	2018	1.35 (1.24–1.47)	2.511	1.598	0.203	1.604	0.202
	2019	1.35 (1.22–1.48)					
	2020	1.21 (1.09–1.34)					
MICHC							
Emergencies, mean (SD)	2018	3.49 (2.49–4.49)	41.761	1.911	0.152	2.512	0.087
	2019	3.65 (2.45–4.85)					
	2020	2.45 (1.82–3.08)					
Hospital stays per capita, mean (SD)	2018	1.81 (1.39–2.23)	1.51	0.339	0.713	1.51	0.339
	2019	2.04 (1.58–2.51)					
	2020	2.04 (1.40–2.68)					

Comparison of Drug Treatment Profiles and Outcomes

This study evaluated the consistency of patients' actual medication regimens with the guidelines by referring to the 2017 GOLD drug treatment recommendations. Based on patient medication data for 2018–2020 from COPDMIC, the number of cases adhering to medication was 122, 153, and 32, accounting for 26.06%, 32.69.%, and 6.84% of the total study population. Bronchodilators were the main treatment drug, and the percentage of bronchodilator use among patients adhering to medication was 95.90%, 91.5% and 100% in 2018–2020. The duration of bronchodilator treatment ranged from a minimum of 5 months to a maximum of 3 years, with 80 cases on continuous medication in 2018 and 2019, 17 cases on continuous medication in 2019 and 2020, and 13 cases on continuous medication over 3 years. Among drug treatment cases, the agreement between the drug regimens and the guidelines increased each year by 43.44% in 2018, 50.98% in 2019, and 71.87% in 2020 (Table 5).

Comparing the drug and non-drug treatment groups (Table 6 and Table 7), COPDMIC data showed that the CAT score ($p < 0.05$), mMRC grade ($p < 0.05$), and the number of hospitalisations per capita ($p < 0.05$) were significantly lower in the drug treatment group in 2020 compared with previous years; however, the number of emergency visits per capita increased slightly but was not statistically significant. After data matching with MICHC, results showed that the

Table 5 Overview of Drug Treatment from 2018 to 2020

Years	Receive drug Treatment (N)	Proportion of the total Study Population (%)	Use of Branching Agent (N)	Proportion of Total Drug Treatment (%)	Consistent with the Guideline Recommendations (N)	Proportion of the Total (%)
2018	122	26.06	117	95.90	53	43.44
2019	153	32.69	140	91.50	78	50.08
2020	32	6.84	32	100	23	71.87

Table 6 Comparison of Study Indicators in the Bronchodilator Group

N = 204	Years	Average Value (95% Confidence Interval)	ANOVA			Welch	
			Sum of Squares	F price	p value	Levene Statistic	p value
COPDMIC							
Emergencies, mean (SD)	2018	1.19 (1.10–1.29)	0.648	0.775	0.463	0.47	0.628
	2019	1.25 (1.06–1.44)					
	2020	1.38 (0.91–1.84)					
Hospital stay per capita, mean (SD)	2018	1.44 (1.30–1.58)	8.107	4.054	0.003	5.424	0.006
	2019	1.77 (1.51–2.03)					
	2020	1.26 (1.09–1.43)					
CAT	2018	14.59 (13.55–15.63)	444.337	3.747	0.024	3.689	0.026
	2019	13.20 (12.18–14.22)					
	2020	12.54 (11.41–13.67)					
mMRC	2018	1.47 (1.35–1.59)	5.218	3.445	0.033	3.491	0.031
	2019	1.50 (1.38–1.62)					
	2020	1.29 (1.17–1.41)					
MICHC							
Emergencies, mean (SD)	2018	2.86 (2.14–3.58)	36.648	3.142	0.046	4.2	0.018
	2019	3.24 (2.46–4.02)					
	2020	2.08 (1.65–2.50)					
Hospital stays per capita, mean (SD)	2018	1.83 (1.48–2.19)	12.514	3.257	0.042	3.3	0.042
	2019	2.41 (1.87–2.95)					
	2020	1.59 (1.24–1.94)					

Table 7 Comparison of Study Indicators in the Non-Bronchodilator Group

N = 264	Years	Average Value (95% Confidence Interval)	ANOVA			Welch	
			Sum of Squares	F price	p value	Levene Statistic	p value
COPDMIC							
Emergencies, mean (SD)	2018	1.40 (1.11–1.70)	27.96	0.743	0.478	0.666	0.516
	2019	2.26 (0.17–4.35)					
	2020	1.28 (1.12–1.44)					
Hospital stay per capita, mean (SD)	2018	1.42 (1.28–1.56)	7.269	0.755	0.471	0.577	0.563
	2019	1.78 (1.09–2.48)					
	2020	1.28 (1.12–1.44)					
CAT	2018	13.64 (12.72–14.55)	19.131	0.166	0.847	0.156	0.855
	2019	13.75 (12.86–14.63)					
	2020	14.01 (13.03–14.99)					
mMRC	2018	1.54 (1.45–1.64)	1.703	1.666	0.19	1.724	0.18
	2019	1.42 (1.33–1.52)					
	2020	1.51 (1.41–1.61)					
MICHC							
Emergencies, mean (SD)	2018	2.82 (2.06–3.58)	28.414	1.318	0.27	1.13	0.327
	2019	3.65 (2.68–4.62)					
	2020	2.80 (1.98–3.61)					
Hospital stays per capita, mean (SD)	2018	1.55 (1.26–1.84)	3.617	1.131	0.325	1.119	0.332
	2019	1.89 (1.54–2.25)					
	2020	1.67 (1.17–2.16)					

number of emergency visits per capita ($p < 0.05$) and hospitalisations per capita ($p < 0.05$) were significantly reduced in 2020. The non-drug treatment group did not show these results.

Discussion

As a common preventable and treatable disease characterised by persistent respiratory symptoms and airflow limitation, COPD is usually associated with airway and/or alveolar abnormalities caused by significant exposure to toxic particles or gases. Despite the high prevalence of COPD, the diagnosis and treatment rates are low.[19] In one regard, because the disease progresses slowly and patients can tolerate cough, sputum, and even mild dyspnoea better in mild to moderate cases, the disease is usually difficult to detect, and the diagnosis is thus delayed; in another regard, delayed diagnosis may result from a lack of awareness of COPD among health care providers and patients. In 2017, we created a COPD management platform and established a regional COPD prevention and treatment alliance of *general practitioners–specialists–patient*s to explore a new strategy of *early screening–treatment–follow-up* for COPD management by focusing on screening groups at high risk for COPD, managing patients with COPD in the stable phase of the disease, managing acute exacerbations, and providing health education for patients.

In the closed-loop management of COPD based on early screening–treatment–follow-up, specialists and general practitioners work together to ensure the consistency and effective implementation of drug treatment plans. In this context, general practitioners conduct disease assessment, health education, problem identification, and adjustment of treatment plans during regular follow-up visits and provide timely treatment for AECOPD, all of which can benefit patients. The establishment of the COPD management platform has contributed to more standardised medication treatment, and the percentage of medication regimens that are consistent with guideline recommendations has increased yearly and is significantly higher than the previously reported 5%.[20] Long-term standardised drug therapy has contributed to a year-by-year decreasing trend in CAT scores and mMRC grades and the number of emergency cases and hospitalisations in patients with COPD over 3 years from 2018–2020, indicating that remote management is an effective and innovative model with positive implications for patients with COPD.

Meanwhile, in the middle of the study period, the worldwide outbreak of COVID-19 occurred in December 2019. Shanghai responded to the spread of COVID-19 by strengthening the protection of susceptible populations and defensive measures in medical institutions.[21] Defensive measures for susceptible populations included

> wearing masks in all indoor public places such as hospitals, public transport or supermarkets, maintaining a certain social distance between people, and strengthening hand disinfection.[22]

The defensive measures of medical institutions required people attending the clinic to take their temperature and report whether they had a history of travel and residence in a pandemic area and, for patients with fever, to first undergo COVID-19 nucleic acid testing to rule out infection before entering routine outpatient and inpatient treatment. Measures such as wearing masks and maintaining social distancing not only play an important role in the prevention and control of novel coronaviruses but also reduce the risk of other respiratory diseases, including COPD, to some extent. Many studies have confirmed this view.[10,23]

The study analysis of COPDMIC data revealed a slight increase in the number of emergency visits while the number of emergency cases decreased in 2019, but the difference was not significant. The number of COPDMIC emergencies and hospitalisations was provided by the patient through recall during the GP follow-up assessment, and memory bias may be present, leading to discrepancies, which may correlate with the determination of emergency episodes. An acute worsening of respiratory symptoms that leads to additional treatment was considered AECOPD.[19] These COPD exacerbations usually alternate with stabilisation, and, in the real world, approximately 50% of AECOPD cases are unreported.[24] There is no uniform method for determining AECOPD.[25] It has been suggested that the determination of AECOPD should be based on a comprehensive assessment of the patient's symptoms, symptom severity, and an increase in the drug type due to symptom exacerbation.[26] However, the sensitivity and specificity of this judgement of AECOPD vary widely due to the influence of patient age, culture, and symptom assessment. If the symptoms of AECOPD and an increase in the drug type are used as judgement factors, the accessibility of medication, the physician's choice of medication, and the accuracy of the patient's record of medication review may lead to different results in the

determination of AECOPD[27–29] ultimately leading to *over-assessment* or *under-assessment* of AECOPD severity. For example, exacerbations are usually classified as *mild* if only short-acting bronchodilator therapy is chosen, *moderate* if short-acting bronchodilator plus antibiotic and/or oral corticosteroid therapy is chosen, and *severe* if the patient seeks help at the emergency department or requires hospitalisation.[19,30] Therefore, it is difficult to be precise in the clinical judgement to determine AECOPD. In this study, we verified the authenticity of the COPDMIC data by matching MICHC data when assessing the number of patient emergency department visits versus hospital admissions to minimise the impact of patient recall bias and differences in AECOPD determination on the study results, and the number of emergency visits per capita and the number of hospitalisations per capita were used to compare statistical differences.

Many causes may precipitate AECOPD, including respiratory infections, the severity of airflow limitation, anxiety, cold and flu season, and medications.[31] Therefore, we compared the differences in study metrics between GOLD 1–2 and GOLD 3–4 cohorts and found that patients with GOLD 1–2 in 2020 had significantly lower CAT scores, mMRC grades, and the number of emergency visits and hospitalisations than in 2018 and 2019; however, these results were not found in the patient with GOLD 3–4 COPD cohort.

Severe airflow obstruction may be one of the influencing factors leading to ineffective disease control. In one regard, patients with GOLD 1–2 classification are less restricted by the disease and have frequent contact with the external environment. During the COVID-19 pandemic, prevention and control measures have a protective effect on patients by reducing the chance of their contact with the external environment. In contrast, patients with GOLD grades 3–4 have significant activity restriction due to the disease itself and low exposure to the external environment, so the impact of the COVID-19 pandemic prevention and control measures on patients with GOLD grades 3–4 is not significant. In another regard, patients with GOLD grade 1–2 may have poor medication adherence due to insignificant clinical symptoms such as cough, sputum, and dyspnoea, but after these patients were included in the COPD management platform, their medication adherence improved significantly through regular follow-up and health education by family physicians, and medication adherence was closely related to disease control, medical cost expenditure, and risk of death[32,33] In contrast, the severity of disease in patients with GOLD grade 3–4 leads to a higher dependence on medication, and this medication adherence did not differ before and after the establishment of the COPD management platform, whereas this group has a disease more difficult to control and a higher risk of emergency and hospitalisation. Studies have reported that the risk of AECOPD in patients with GOLD 4 is 17 times higher than that for patients with GOLD 1 and 5 times higher than patients with GOLD 3 compared with GOLD 1 patients.[34] In sum, these combined factors may be contributors to the significant improvement in CAT scores and mMRC grades and the significant decrease in the number of emergency visits and hospitalisations among patients with COPD in GOLD grades 1–2, whereas patients in GOLD grades 3–4 did not show the same results.

We also focused on patient treatment rates and medication adherence, and this community-based patient management data showed 122 and 153 cases of patient medication use in 2018 and 2019, respectively, representing 26.06% and 32.69% of the study population, which is higher than the 11.7% reported in other studies,[4] suggesting that the role of COPD management platforms in increasing the proportion of patients treated in the community is affirmable. At the same time, however, another worrisome phenomenon has been identified. Among the 204 patients who used medication, only 13 could adhere to 3 years of continuous medication, and the medication adherence decreased year by year over time; most patients did not use bronchodilator therapy for a long time, and some only maintained bronchodilator therapy for a period after discharge and then stopped using medication after symptom relief or only used medication when the symptoms were aggravated—all of which suggest that the challenges of medication adherence among patients with COPD should not be overlooked. The importance of adherence assessment should be increased in COPD management, and methods to improve adherence should be actively explored, such as enhancing patient adherence education, optimising inhalation drug and device selection, and building an adherence support and monitoring system.[26] Another point of concern is the relatively low proportion of drug use in 2020 in our study. This finding may be attributed to patients' concerns about the pandemic or the inconvenience of active or passive drug access due to prevention and control measures during the pandemic. In addition, this finding suggests that we should optimise the functional modules in the COPD management platform and recognise that internet drug purchasing and provision of patient education about medication with the help of information technology may better serve patients during public health emergencies.

Conclusions

Since the establishment of the specialist–family physician–patient COPD prevention and treatment consortium in 2017, the consistency of drug treatment regimens with guidelines has increased each year. Patients with COPD had significantly improved CAT scores and mMRC grades and a significantly decreased number of emergency and hospitalisation cases and the number per capita. Preventive measures for COVID-19 were a contributor to the reduction in CAT scores and mMRC grades and the decrease in the number of emergency and hospitalisation cases in GOLD 1–2 patients with COPD, but these measures were relatively limited for patients with GOLD 3–4. In addition, severe airflow limitation and poor medication adherence are possible factors contributing to the lack of effective disease control.

This study has several important limitations. First, the sample size was small, which may bias the judgement of some results; Due to the limited study sample size, this study was not able to stratify medication and lung function classifications. Second, the data of this study were obtained from two data platforms—COPDMIC and MICHC. The number of COPD emergency and hospitalisation cases recorded by COPDMIC was within the year prior to the date of follow-up, which may span years, whereas the MICHC data were recorded from 1 January to 31 December of each year, so the data recorded by both systems for the same patient were not completely consistent, which may have an impact on the study results. Third, the patient demographic information, such as educational attainment or socioeconomic status, was not available for the assessment of medication adherence, so the analysis of medication adherence may be one-sided.

Abbreviations

AECOPD, acute exacerbations of chronic obstructive pulmonary disease; CAT, chronic obstructive pulmonary disease assessment test; COPD, chronic obstructive pulmonary disease; COPDMIC, Chronic Obstructive Pulmonary Disease Management Information Center; COVID-19, coronavirus disease 2019; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroids; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; MICHC, Medical Information Center of Health Management Commission; mMRC, modified Medical Research Council.

Data Sharing Statement

The datasets generated and/or analysed during the current study are not publicly available because this database is being used in another work as part of a doctoral thesis, so we would prefer that, before its completion, it was not for public use. Dr. García-Sanz is the guarantor of the paper and all information about this (database and informed consent signed by patients). Access to this information could be provided in the future, duly justifying it, since there is another study pending completion based on these data.

Ethics Approval and Informed Consent

The study was approved by the Ethics Committee of Shanghai Songjiang District Central Hospital in accordance with the ethical requirements of the Declaration of Helsinki (China Clinical Trials Registry registration number: ChiCTR2000031092). We ensured the confidentiality of the personal information of the participants in this study. Because the study was retrospective and observational, informed consent was not required to be signed by the participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

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References

1. Zhong N, Wang C, Yao W, et al. Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. *Am J Respir Crit Care Med*. 2007;176(8):753–760. doi:10.1164/rccm.200612-1749OC
2. Wang C, Xu J, Yang L, et al.; China Pulmonary Health Study Group. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet*. 2018;391(10131):1706–1717. doi:10.1016/S0140-6736(18)30841-9
3. Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019;394(10204):1145–1158. doi:10.1016/S0140-6736(19)30427-1
4. Fang L, Gao P, Bao H, et al. Chronic obstructive pulmonary disease in China: a nationwide prevalence study. *Lancet Respir Med*. 2018;6(6):421–430.
5. Liang C, Mao X, Niu H, et al. Management and in-hospital clinical outcomes among inpatients with acute exacerbation of chronic obstructive pulmonary disease in China: results from the phase I data of ACURE study. *Int J Chron Obstruct Pulmon Dis*. 2021;16:451–465. doi:10.2147/COPD.S281957
6. Yang T, Cai B, Cao B, et al. REALizing and improving management of stable COPD in China: a multi-center, prospective, observational study to realize the current situation of COPD patients in China (REAL) - rationale, study design, and protocol. *BMC Pulm Med*. 2020;20(1):11. doi:10.1186/s12890-019-1000-x
7. Li F, Gao Z, Sheng CF, et al. Role of smartphone-based D2P-COPD platform in the hierarchical diagnosis and treatment of chronic obstructive pulmonary disease. *Chinese Gen Pract*. 2018;21(30):3730–3734.
8. McAuley H, Hadley K, Elneima O, et al. COPD in the time of COVID-19: an analysis of acute exacerbations and reported behavioural changes in patients with COPD. *ERJ Open Res*. 2021;7(1):718–2020. doi:10.1183/23120541.00718-2020
9. COVID-19 Map. Johns Hopkins coronavirus resource center. Johns Hopkins Coronavirus Resource Center. Available from: https://coronavirus.jhu.edu/map.html. Accessed January 6, 2022.
10. González J, Moncusí-Moix A, Benitez ID, et al. Clinical Consequences of COVID-19 lockdown in patients with COPD: results of a pre-post study in Spain. *Chest*. 2021;160(1):135–138. doi:10.1016/j.chest.2020.12.057
11. Hu W, Dong M, Xiong M, et al. Clinical courses and outcomes of patients with chronic obstructive pulmonary disease during the COVID-19 epidemic in Hubei, China. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2237–2248. doi:10.2147/COPD.S265004
12. Price DB, Tinkelman DG, Nordyke RJ, et al.; COPD Questionnaire Study Group. Scoring system and clinical application of COPD diagnostic questionnaires. *Chest*. 2006;129(6):1531–1539. doi:10.1378/chest.129.6.1531
13. International Primary Care Airway Group. Ipag diagnosis management handbook chronic airways disease A guide for primary care physician; 2016.
14. Juan W, Wenbing X, Xuejun Z, et al. Initial validation and evaluation on a Chinese version of chronic obstructive pulmonary disease screening questionnaireinSmokers. *Chin J Int Med*. 2012;51(4):311–312.
15. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med*. 2017;195(5):557–582. doi:10.1164/rccm.201701-0218PP
16. Wu Z, Huang R, Zhong L, et al. Technical performance analysis of different types of spirometers. *BMC Pulm Med*. 2022;22(1):23. doi:10.1186/s12890-021-01752-8
17. Standardization of Spirometry, 1994 Update. American thoracic Society. *Am J Respir Crit Care Med*. 1995;152(3):1107–1136. PMID: 7663792. doi:10.1164/ajrccm.152.3.7663792
18. Sarkar M, Srinivasa S, Madabhavi I, et al. Tuberculosis associated chronic obstructive pulmonary disease. *Clin Respir J*. 2017;11(3):285–295. doi:10.1111/crj.12621
19. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease 2020 report[EB/OL]; 2021. Available from: goldcopd.org/2022-gold-reports. Accessed March 8, 2023.
20. Kim JA, Lim MK, Kim K, et al. Adherence to inhaled medications and its effect on healthcare utilization and costs among high-grade chronic obstructive pulmonary disease patients. *Clin Drug Investig*. 2018;38(4):333–340. doi:10.1007/s40261-017-0612-2
21. Feng J, Xu J, Xu S, et al. Psychological impact during the first outbreak of COVID-19 on frontline health care workers in Shanghai. *Front Public Health*. 2021;9:646780. doi:10.3389/fpubh.2021.646780
22. Li ZY, Meng LY. Technical guidelines on prevention and control of novel coronavirus infec- tion in medical institutions (First edition). *Chin J Infect Control*. 2020;19(2):189–191.
23. Kaye L, Theye B, Smeenk I, et al. Changes in medication adherence among patients with asthma and COPD during the COVID-19 pandemic. *J Allergy Clin Immunol Pract*. 2020;8(7):2384–2385. doi:10.1016/j.jaip.2020.04.053
24. Seemungal TA, Donaldson GC, Paul EA, et al. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1998;157(5):1418–1422. doi:10.1164/ajrccm.157.5.9709032
25. Jenkins CR. Towards precision in defining COPD exacerbations. *Breathe*. 2021;17(3):210081. doi:10.1183/20734735.0081-2021
26. Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med*. 1987;106(2):196–204. doi:10.7326/0003-4819-106-2-196

27. Jenkins CR, Wen FQ, Martin A, et al. The effect of low-dose corticosteroids and theophylline on the risk of acute exacerbations of COPD: the TASCS randomised controlled trial. *Eur Respir J*. 2021;57(6):2003338. doi:10.1183/13993003.03338-2020
28. Linnell J, Hurst JR, Exacerbations: COPD, Patient A. Physician's Perspective. *Adv Ther*. 2020;37(1):10–16. doi:10.1007/s12325-019-01138-7
29. Howcroft M, Walters EH, Wood-Baker R, et al. Action plans with brief patient education for exacerbations in chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2016;12(12):CD005074. doi:10.1002/14651858.CD005074.pub4
30. Vestbo J, Leather D, Diar Bakerly N, et al. Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice. *N Engl J Med*. 2016;375(13):1253–1260. doi:10.1056/NEJMoa1608033
31. Textor J, van der Zander B, Gilthorpe MS, et al. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol*. 2016;45(6):1887–1894. doi:10.1093/ije/dyw341
32. Vestbo J, Anderson JA, Calverley PM, et al. Adherence to inhaled therapy, mortality and hospital admission in COPD. *Thorax*. 2009;64(11):939–943. doi:10.1136/thx.2009.113662
33. Jansen EM, van de Hei SJ, Dierick BJH, et al. Global burden of medication non-adherence in chronic obstructive pulmonary disease (COPD) and asthma: a narrative review of the clinical and economic case for smart inhalers. *J Thorac Dis*. 2021;13(6):3846–3864. doi:10.21037/jtd-20-2360
34. Chan KPF, Ma TF, Kwok WC, et al. Significant reduction in hospital admissions for acute exacerbation of chronic obstructive pulmonary disease in Hong Kong during coronavirus disease 2019 pandemic. *Respir Med*. 2020;171:106085. doi:10.1016/j.rmed.2020.106085