Study protocol for evaluating the efficacy of early pulmonary rehabilitation combined with an internet-based patient management model in patients with COPD: a practical, multicentre, randomised controlled study from China

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Study protocol for evaluating the efficacy of early pulmonary rehabilitation combined with an internet-based patient management model in patients with COPD: a practical, multicentre, randomised controlled study from China https://bit.ly/4aFLxkk

Cite this article as: Ye W, Danye L, Jingjing C, *et al*. Study protocol for evaluating the efficacy of early pulmonary rehabilitation combined with an internet-based patient management model in patients with COPD: a practical, multicentre, randomised controlled study from China. *ERJ Open Res* 2024; 10: 00995-2023 [DOI: 10.1183/23120541.00995-2023].

Received: 10 Dec 2023
Accepted: 12 May 2024

Abstract

Background COPD, a preventable and treatable disease, is characterised by persistent respiratory symptoms and airflow limitations, with high incidence, disability, mortality and disease burden. Currently, drug treatments mainly include bronchodilators and glucocorticoids, which are used to alleviate symptoms and improve lung function. Traditional medical care models and patients' lack of understanding of the disease result in regular and long-term hospitalisations, affect patients' quality of life and cause a need to explore more effective comprehensive intervention plans.

Methods This study is designed as a multicentre, randomised controlled trial consisting of three parallel groups. Group A will receive early pulmonary rehabilitation in the hospital and remote internet pulmonary rehabilitation after discharge. Group B will receive the same early pulmonary rehabilitation in the hospital but outpatient pulmonary rehabilitation after discharge for 8 weeks and routine follow-up management. Group C will receive outpatient pulmonary rehabilitation during a stable period of 3–4 weeks after discharge and routine follow-up management. 1482 patients will be enrolled from 10 centres in China. The primary outcome measures will be the readmission rate due to acute exacerbation at 90 days and the 12-month readmission rate due to acute exacerbation. The secondary outcomes will mainly include differences in all-cause mortality; the number of acute exacerbations; COPD Assessment Test, modified Medical Research Council scale and St George's Respiratory Questionnaire scores; the pulmonary rehabilitation treatment completion rate; patient compliance; and patient and physician satisfaction scores among the three groups at 3, 6 and 12 months after the different interventions. In addition, the proportion of people with ⩾2 acute exacerbations within 12 months and the time of the first acute exacerbation will also be included.

Conclusions This study aims to further verify the substitutability of remote internet pulmonary rehabilitation for outpatient rehabilitation and its short-term and long-term effects in patients, providing comprehensive interventional evidence for the treatment of COPD.

Background

COPD is a heterogeneous lung condition characterised by chronic respiratory symptoms (dyspnoea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction [1]. Acute exacerbation of COPD (AECOPD) is defined as an event characterised by dyspnoea and/or cough and sputum that worsens over <14 days. Exacerbations of COPD are often associated with increased local and systemic inflammation caused by airway infection, pollution or other insults to the lungs [2]. A national epidemiological survey in 2018 showed that the prevalence of COPD among people older than 40 years of age in China was as high as 13.6%. The prevalence of COPD varies by region, with the highest prevalence in Southwest China (20.2%, 95% CI 14.7–25.8%) and the lowest in Central China (10.2%, 95% CI 8.2–12%) [3]. COPD has become the third most common chronic disease after hypertension and diabetes in China. It not only leads to a decline in patients' quality of life or even death but also results in frequent hospitalisation or emergency treatment, thus imposing a heavy social and economic burden on individuals and society.

The treatment goal of COPD is to alleviate acute exacerbation and prevent the occurrence of further acute exacerbation. At present, the main therapeutic drugs include bronchodilators and glucocorticoids, which are used to alleviate symptoms and improve lung function. However, some patients are prone to recurrent and prolonged illness, and traditional medical care models and patients' lack of understanding of the disease lead to regular and long-term hospitalisation, which increases the burden of disease on patients and affects their quality of life. Therefore, more effective comprehensive intervention plans need to be explored [4].

Pulmonary rehabilitation is an individualised treatment plan based on the evaluation of the condition of patients with COPD, including but not limited to comprehensive intervention measures such as exercise training, health education and self-management, aimed at improving the physiological and psychological status of patients with chronic respiratory disease and promoting long-term adherence to promote health [5]. For stable COPD and AECOPD patients, pulmonary rehabilitation as a comprehensive intervention has shown clear benefits; it can significantly reduce hospitalisation rates and improve survival rates. Despite these important clinical benefits, pulmonary rehabilitation has not been fully utilised worldwide, with data from the USA and Canada indicating that <5% of suitable populations have received pulmonary rehabilitation programmes [6]. Both the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2022 and GOLD 2023 mention that remote rehabilitation can serve as an alternative to traditional rehabilitation, but there is a lack of important research evidence, and the timing of pulmonary rehabilitation interventions has always been highly controversial. Whether pulmonary rehabilitation combined with remote rehabilitation can be initiated in AECOPD remains to be confirmed through research.

Methods

Trial objectives

The main purpose of this study is as follows: 1) to evaluate the number of acute exacerbations or readmission rates within 90 days in hospitalised patients with AECOPD using early pulmonary rehabilitation programmes; and 2) to determine whether, compared to traditional pulmonary rehabilitation, internet-based pulmonary rehabilitation interventions are more effective in improving the long-term prognosis of patients with COPD.

The secondary objectives of this study are as follows: 1) to evaluate the improvement effect of early pulmonary rehabilitation programmes on the quality of life of AECOPD patients; 2) to analyse the differences in patient compliance and economics between the early pulmonary rehabilitation plus remote internet pulmonary rehabilitation management model for AECOPD patients and the conventional pulmonary rehabilitation management model and provide information for medical and health system decision-making.

The exploratory purpose of this study was to analyse the impact of early pulmonary rehabilitation on proteomic biomarkers.

Trial design

This study is a pragmatic, multicentre, prospective, randomised controlled study that will be conducted simultaneously in multiple clinical trial institutions. The research subjects will be randomly assigned to three groups for corresponding treatment and follow-up (the detailed information for each group is described in figure 1).

Trial setting

The selection of hospitals is mainly based on the six major geographical regions in China, all of which are classified as Grade III Grade A hospitals: East China (Zhongshan Hospital Affiliated to Shanghai Fudan

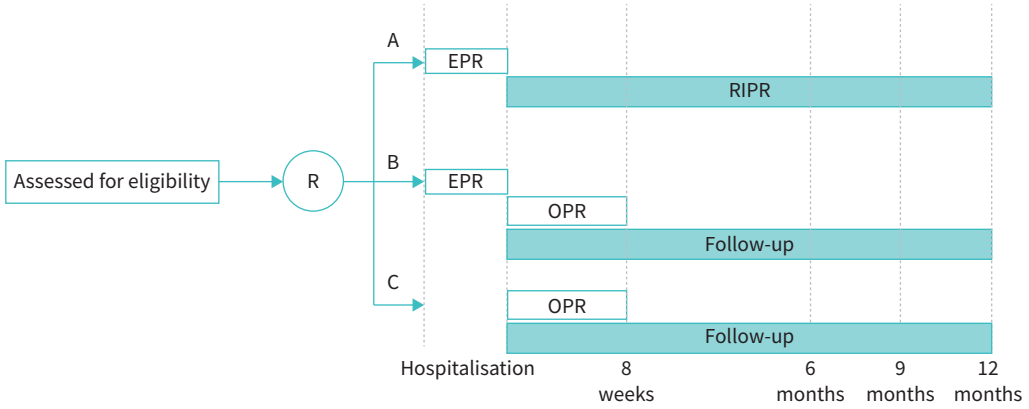

FIGURE 1 Schematic diagram of the research grouping. EPR: early pulmonary rehabilitation; OPR: outpatient pulmonary rehabilitation; RIPR: remote internet pulmonary rehabilitation; Follow-up: routine follow-up management.

University); North China (China-Japanese Friendship Hospital, National Respiratory Medicine Center; Qingdao Municipal Hospital; Inner Mongolia Autonomous Region People's Hospital; The First Hospital of Shanxi Medical University); Central China (Xiang ya Second Hospital of Central South University); Southwest region (Guizhou Provincial People's Hospital; Chengdu First People's Hospital); Northwest region (Xi'an Jiao tong University Affiliated First Hospital); and Northeast region (China Medical University Affiliated First Hospital).

Eligibility and exclusion criteria

The local responsible personnel will screen the daily list of patients with AECOPD and will recruit eligible patients from participating hospitals' outpatient and emergency departments. The study population will consist of moderate-to-severe COPD patients aged 40–75 years who are admitted for acute exacerbation treatment. The inclusion criteria are as follows: 1) age ⩾40 years and ⩽75 years; 2) conformed to the diagnostic criteria of the 2022 GOLD Global Initiative for AECOPD, with GOLD levels 2–4; 3) within 1 week of routine or emergency admission; 4) residing at the location of the research centre, with no planned relocation during the research period; 5) having volunteered to participate in the research and having signed an informed consent form; and 6) possessing a mobile phone that can download Android application platform software and can operate it. The exclusion criteria are as follows: 1) pregnant or lactating women; 2) patients who are participating in clinical trials or intervention studies of other drugs; 3) patients with a history of active pulmonary tuberculosis or partial, lobar or total pneumonectomy; 4) individuals with an expected survival period of <6 months, such as those with uncontrolled advanced malignant tumours, a history of acute myocardial infarction, unstable angina, acute stroke or acute heart failure within 6 months; 5) patients with liver or kidney failure who require dialysis treatment; 6) patients with severe uncontrolled mental illness with a tendency to harm others or oneself; 7) patients with severe cognitive impairment; and 8) patients determined by the researcher to have other conditions not suitable for inclusion in this study. Patients can stop participating in the study at any time during the study period. In addition, they may withdraw from the study if: 1) the patient or his or her representative is unwilling to continue participating in the study; 2) the investigator believes that there are serious concerns about patient safety; and 3) the study is terminated early (the details are shown in figure 2).

Rehabilitation initiation criteria

- Respiratory system: 1) oxygen saturation ⩾90%; 2) respiratory rate ⩽40 breaths·min^{-1}
- Cardiovascular system: 1) systolic blood pressure ⩾90 mmHg and ⩽180 mmHg; 2) mean arterial pressure ⩾65 mmHg and ⩽110 mmHg; 3) heart rate: ⩾40 beats·min^{-1} and ⩽120 beats·min^{-1}; 4) no new arrhythmias or myocardial ischaemia; 5) no suspicious aortic stenosis; 6) no new unstable deep vein thrombosis or pulmonary embolism
- Other: 1) no unstable limb or spinal fractures; 2) no serious liver and kidney basic diseases or newly developed progressive liver and kidney function damage; 3) no active bleeding; 4) body temperature ⩽38.5°C

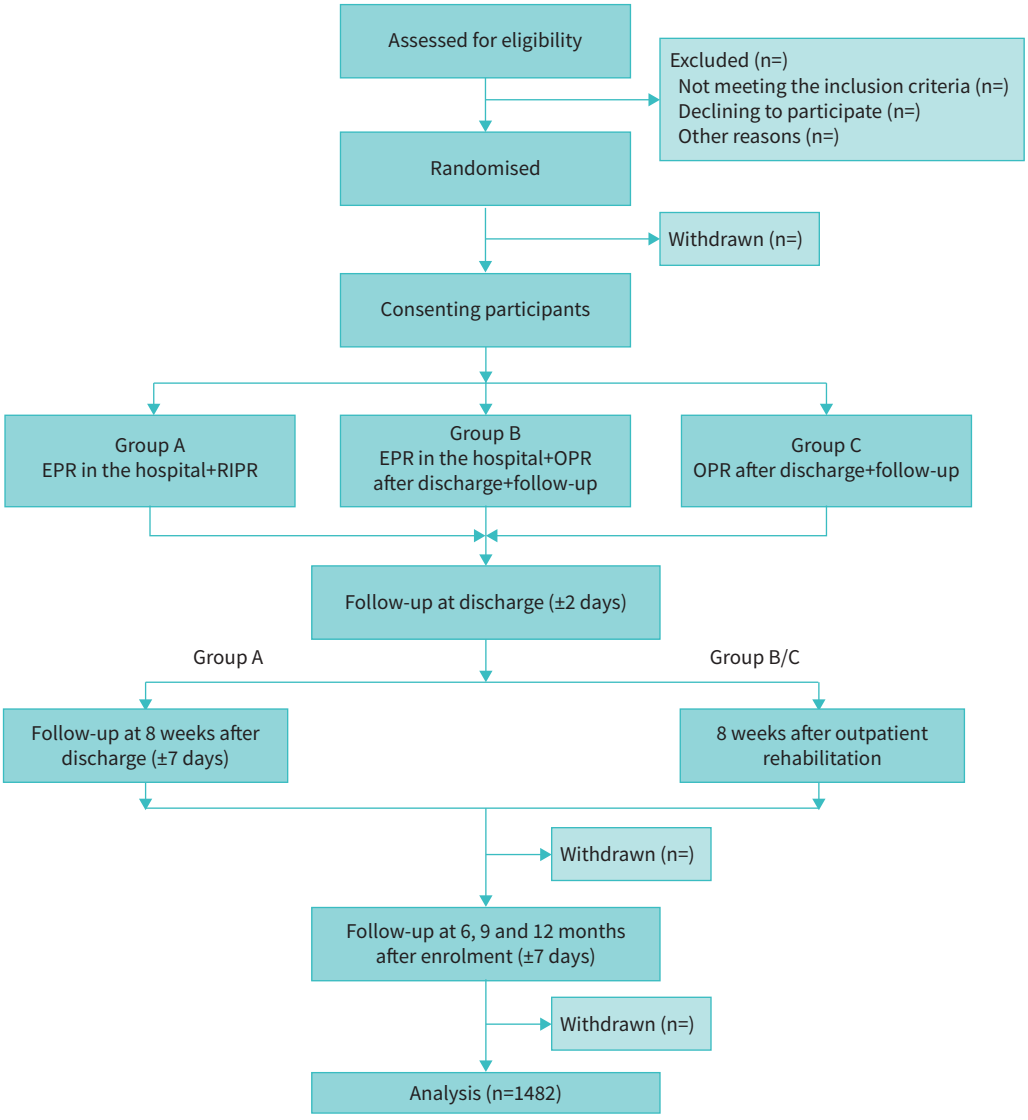

FIGURE 2 Study content for the schedule of enrolment, intervention and assessment. EPR: early pulmonary rehabilitation; OPR: outpatient pulmonary rehabilitation; RIPR: remote internet pulmonary rehabilitation; Follow-up: routine follow-up management.

Rehabilitation termination criteria

- Fluctuations in body temperature >37.2°C
- Dyspnoea index: Borg Dyspnoea Score >3 (total score: 10 points)
- Presence of the following symptoms (with the patients instructed to immediately stop activity and consult a doctor): chest tightness, chest pain, dyspnoea, severe cough, dizziness, headache, unclear vision, palpitations, sweating, unstable standing and other symptoms
- Situations determined by clinical doctors not to be suitable for activity

Randomisation and allocation

For patients who meet the inclusion and exclusion criteria and provide informed consent, each study centre will strictly assign random codes in order. The random grouping results will be generated by the central randomisation system according to the central hierarchical dynamic randomisation (minimisation method) after the randomisation form is submitted by the Electronic Data Capture System (EDCS) after enrolment to ensure close balance between groups. In principle, the number of centres enrolled should be evenly distributed as much as possible to ensure sufficient centre representation. Considering the feasibility and selection progress, the number of enrolled units will be adjusted according to the actual situation.

Trial withdrawal

If the study is withdrawn during the study period, the EDCS should record the withdrawal date and reason. If a patient withdraws from the study for any reason, researchers should strive to ensure that the patient follows the procedures outlined at the end of the study visit plan. Regulatory agencies or ethics committees may require patients to withdraw from the study.

Trial interventions

Implementation of pulmonary rehabilitation

The entire pulmonary rehabilitation study consists of four parts: patient evaluation, programme component, method of delivery and quality assurance. Patient evaluation is done using the Intelligent Pulmonary Rehabilitation Management System (IPRMS) developed by the researchers in the early stage of this study. The patient's training risk level (high, medium and low) will be comprehensively ascertained through intelligent algorithms based on multidimensional evaluation indicators such as anxiety and depression, nutrition, dyspnoea symptoms, sex, age, body mass index (BMI), GOLD lung function grading, ABE grouping, respiratory muscle strength, the 6-min walk distance (6MWD), maximal inspiratory pressure (MIP), one-repetition maximum (1RM) and comorbidities. The IPRMS system will first provide a rehabilitation prescription based on the evaluation results, which mainly includes aerobic exercise, resistance training, respiratory muscle training, breathing exercises and airway clearance techniques (active cycle of breathing techniques (ACBT)). Healthcare professionals can consider individualised factors based on the overall patient's condition, modify the treatment plan, promote continuous learning and upgrading of the system, and better meet clinical needs (for the basic rehabilitation plan that constitutes the algorithm see supplementary material). The rehabilitation prescription for patients is evaluated and decided by a multidisciplinary team composed of professional respiratory doctors, rehabilitation therapists and nurses, and is adjusted according to the patient's condition at any time. The intensity of aerobic exercise is determined by 6MWD, the intensity of respiratory muscle training is determined by MIP, and the intensity of resistance exercise is determined by 1RM. Each healthcare professional in the subcentre has received strict training, with monthly on-site quality control and online communication to ensure consistency and accuracy of research.

Early pulmonary rehabilitation in the hospital of group A/B

All participants will receive at least five pulmonary rehabilitation interventions during hospitalisation, including aerobic exercise, resistance exercise, inspiratory muscle strength training and airway clearance guidance. When necessary, patients will be given oxygen therapy or high-flow nasal cannula and noninvasive ventilation. Nutritional intervention at the level of 30 $kcal \cdot kg^{-1} \cdot day^{-1}$ and 1.2 $g \cdot kg^{-1} \cdot day^{-1}$ protein will be provided to individuals with nutritional risks [7].

Home-based pulmonary rehabilitation plan of group A

After discharge, Group A will continue the intensity of in-hospital training, with aerobic exercise lasting 20–40 min each time, conducted 3–5 times a week (completion of three times is considered to meet the standard). Every 2 weeks, according to the interview results and the data analysis of the pulmonary rehabilitation management platform, the exercise intensity should be adjusted to no more than 80% of 6MWD after evaluation by the doctor–rehabilitation therapist–nurse team. The form can be continuous or intermittent. The maximum intensity of resistance exercise will increase to 80% of the 1RM of the retest, and the maximum intensity of inspiratory muscle training will reach 70% MIP. ACBT can be increased or decreased depending on the situation.

Outpatient rehabilitation plan of group B/C

Group B. After discharge, pulmonary rehabilitation treatment will be carried out in the outpatient department for 8 weeks, with continuous training intensity in the hospital. Aerobic exercise will last for 20–40 min each time, and aerobic training will be conducted twice a week at the hospital (rehabilitation centre). In addition to attending the hospital twice a week for treatment, at least one aerobic exercise of the same intensity at home per week will be performed. The exercise intensity will be adjusted weekly based on the patient's condition and exercise status.

Group C. After 3–4 weeks of stable discharge, the patient will undergo a rehabilitation evaluation again at the outpatient clinic. Based on the evaluation results, a rehabilitation prescription will be formulated through the IPRMS. Aerobic exercise will be performed for 20–40 min each time, and aerobic training will be performed at the hospital (rehabilitation centre) twice a week. In addition to attending the hospital twice a week for treatment, at least one aerobic exercise of the same intensity will be performed at home per week. The exercise intensity will be adjusted weekly based on the patient's condition and exercise status.

Remote data collection

In this study, Group A patients will adopt an internet-based intelligent pulmonary rehabilitation follow-up management plan at home. The follow-up will be based on the following wearable and wireless transmission devices to collect relevant parameters: Huawei Watch GT2/Huawei Band (Huawei Technologies Co., Ltd., Shenzhen, China) (the collected parameters are detailed in the supplementary material); respiratory trainer for in-hospital use (Respiratory Pressure Test Module TA, Hong xiang Technologies Co., Ltd., Guangzhou, China); and respiratory trainer for use outside of the hospital (Respiratory Exerciser T1, Hong xiang Technologies Co., Ltd.; for collection of patient training frequency). The parameters collected using the above equipment and the respiratory trainer will be transmitted to the IPRMS for data storage and management. For parameters beyond the warning range, the platform will automatically send a report to the researchers, reminding them to make adjustment plans.

Follow-up management

The routine follow-up will be completed by nurses. Within 8 weeks after Group A discharge, nurses will conduct a weekly phone/WeChat follow-up to inquire about the problems encountered by patients during rehabilitation, supervise patients in following medical advice and completing the rehabilitation treatment on time, and promptly provide feedback to doctors when problems are discovered. Therapists will provide exercise guidance to patients in the form of videos every 2 weeks. After the 9th week, phone or WeChat visits will be conducted every 2 weeks. If data are not uploaded for 3 consecutive days, WeChat/phone visits will be conducted. After completing 8 weeks of outpatient rehabilitation, Group B and Group C will undergo routine follow-up according to the follow-up schedule.

Patient education

A total of 22 fixed courses will be set up, and one to two specific teaching modules will be arranged according to the on-site questioning. The fixed courses will include disease awareness of COPD, identification and response of acute exacerbation, correct use of inhaled drugs, pulmonary rehabilitation knowledge and technical training, nutrition education, use of patient education manuals, *etc*. Each class will be 20 min long and will occur once a month, with a fixed time and provided links, and online questioning will be set up for live courses. Groups A, B and C will conduct patient education once a month through the WeChat group (the three groups will not cross).

Outcome measures

Primary outcomes

The primary outcomes of this study include the following:

- Readmission rate due to acute exacerbation at 90 days
- 12-month readmission rate due to acute exacerbation

Secondary outcomes

Secondary outcome measures will include the following:

- All-cause mortality rates at 3, 6 and 12 months
- Number of acute exacerbations at 3, 6 and 12 months
- The proportion of people with acute exacerbations occurring ⩾2 times within 12 months
- The time of the first acute exacerbation attack
- Self-assessment test (COPD Assessment Test (CAT) score), dyspnoea score (modified Medical Research Council (mMRC) score) and quality of life evaluation (St George's Respiratory Questionnaire (SGRQ) score) for patients with COPD at 3, 6 and 12 months
- The completion rate of pulmonary rehabilitation treatment at 3, 6 and 12 months
- 3, 6 and 12 months of patient treatment compliance
- Patient and doctor satisfaction scores at 12 months
- The incidence of adverse events (possible adverse events include symptoms such as palpitations, dizziness and hand tremors during lung function examinations, as well as muscle soreness, fatigue and fatigue during early rehabilitation exercises)

Exploratory outcomes

- Change in the levels of proteomic markers at 8 weeks after pulmonary rehabilitation compared with baseline
- Use of proteomics to verify the prediction targets of different proteins, followed by enrichment and analysis of effective targets; exploration of the possible mechanism of pulmonary rehabilitation in COPD patients

Combination medication and treatment

This study will not limit the specific plans for hospitalisation and long-term drug treatment of COPD, and researchers will develop treatment plans based on the patient's condition. The treatment of COPD with

medications can refer to the Chinese guidelines for the diagnosis and treatment of COPD, the Chinese expert consensus on the diagnosis and treatment of AECOPD and the American Thoracic Society (ATS) COPD medication treatment guidelines. For other comorbidities, symptomatic medications can be used without affecting the efficacy evaluation of the experimental drug. All combined drugs used must be recorded (drug name, medication reason, medication method, dosage and medication time) in the original medical record and case report form. If other medications are used due to unavoidable reasons or if there is a change in dosage, the name (common name) of the medication, reason for use, method of use, dosage and treatment time must be recorded on the original medical record.

Demographic data

The demographic data will include: sex, date of birth, place of residence (urban/rural), ethnicity, educational level, height, weight, *etc*.; informed consent form; screening for inclusion criteria; exposure history/exposure conditions including smoking history and occupational exposure (dust, asbestos, coal tar, heavy metals, rubber, *etc*.).

Medical history

The medical history will include: the timepoint of the first diagnosis of COPD, GOLD grade and acute exacerbation history in the past year; previous history of lung diseases, including asthma, pulmonary heart disease, tuberculosis and history of malignant tumours in the chest; other complications, such as hypertension, diabetes, cardiovascular disease, *etc.*

Chest imaging

Radiograph examination from 28 days before enrolment can be accepted, excluding other lung diseases.

Laboratory examination

Laboratory tests will include: routine blood counts (eosinophils), rapid C-reactive protein, liver function tests (alanine transaminase and aspartate transaminase), renal function analysis (serum creatinine and blood urea nitrogen), blood gas analysis and measurement of 12 cytokines (biological samples collected by designated research centres for examination, not required by other research centres). Data from the first 3 days of enrolment are acceptable.

Pulmonary function examination

Pulmonary function examination will include: vital capacity, forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), FEV_1/FVC ratio, maximum expiratory flow; acceptable inspection data within the past 7 days (whichever is the most recent).

CAT

The CAT score is an 8-item questionnaire aimed at evaluating and quantifying the health-related quality of life and symptom burden of COPD patients. Each item in the questionnaire is presented at six levels (0–5 points), with a total score of 40 points. Scores of 0–10, 11–20, 21–30 and 31–40 represent mild, moderate, severe or very severe clinical conditions, respectively. Evidence suggests that CAT can objectively evaluate the ability of intervention measures to reduce the severity of AECOPD [8] and is an effective tool for evaluating the therapeutic efficacy of acute exacerbation of COPD [9].

mMRC

The mMRC Respiratory Difficulty Scale score will be used to assess breathing difficulties. Research has shown that the mMRC can predict future mortality risks [10].

SGRQ

The SGRQ is a widely used quality of life assessment scale for COPD patients in China. Its Chinese version has been validated for reliability and validity in the Chinese patient population, demonstrating good internal consistency and retest reliability [11].

EQ-5D-5L

The EQ-5D-5L [12] is a widely used general questionnaire for assessing health status that consists of two parts. The first part (describing the system) evaluates health using five dimensions (action ability, self-care, daily activities, pain/discomfort, anxiety/depression), with each dimension containing five levels (not difficult, slightly difficult, moderately difficult, severely difficult and unusually difficult/unable to be performed). The second part of the questionnaire includes a visual analogue scale, on which patients will mark their perceived health level. The range is from 0 (the worst imaginable health state) to 100 (the best imaginable health state). The EQ-5D-5L survey questionnaire does not require high levels of cognitive

proficiency from respondents and can be completed in just a few minutes. Instructions for respondents are also included in the questionnaire.

6MWD

The 6MWD has been widely used to evaluate patients' exercise tolerance, medical intervention effectiveness and disease prognosis, with good practicality and effectiveness. It is best to perform the test indoors, to choose a straight corridor with a length of 30 m and few people passing through, and to mark the corridor every 3 m. The starting point should be marked on the floor with brightly coloured tape. The turning points at both ends can be marked with cones (such as orange cones).

Wearable device for monitoring data

Data collected by Group A patients will include the heart rate, oxygen saturation, R wave interval, daily exercise volume and daily sleep.

Combined medication history

The name, purpose, dosage, unit, route of administration, and start and stop dates of medication administered within 4 weeks prior to the screening visit will be recorded.

Combined treatment

The drug name, medication reason, usage and dosage, medication duration and medication purpose will be recorded. For COPD treatment drugs such as bronchodilators and glucocorticoids, the proportion of covered days will be recorded, and the medication compliance will be evaluated.

Hospitalisation status

This will include outpatient and inpatient visits, the reason for the visit, the visit time and the length of stay.

Acute exacerbation events

Whether there has been an acute exacerbation and the time and frequency of exacerbation will be recorded, as will the reason for the visit, whether the hospitalisation was due to acute exacerbation and the number of days of hospitalisation.

Medical expenses incurred during the follow-up period due to medical treatment

These will include total outpatient or inpatient expenses, drug expenses, medical service fees, examination fees, adverse reaction expenses, material fees, *etc*. (obtained through outpatient or hospital hospitalisation documents of the diagnosis and treatment institution).

Application status of the rehabilitation plan

The application status of the rehabilitation plan will include the completion frequency and time (completion record). The completion status of aerobic and resistance exercise, and inspiratory muscle training for Group A patients is automatically recorded by the respiratory rehabilitation management system, while Group B and C are recorded through patient diary cards.

Completion rate of pulmonary rehabilitation treatment

After completing each pulmonary rehabilitation treatment, all patients should register the completion time and status in a timely manner. Patients who have followed at least 75% of the designated pulmonary rehabilitation plan and have undergone subsequent follow-up evaluations will be defined as those who have completed treatment. The proportion of patients who have completed the rehabilitation treatment plan according to medical advice should be calculated [13].

Patient treatment compliance

After completing each pulmonary rehabilitation treatment, the patient should promptly register the completion time and status, summarise the number of completion times during the entire follow-up period and calculate the ratio of the actual number of completed rehabilitation times to the specified number of rehabilitation times [14].

Patient satisfaction score

A 5-point Likert scale will be used to assess the overall satisfaction of patients with the pulmonary rehabilitation treatment, with 1 point indicating "completely dissatisfied" and 5 points indicating "very satisfied" [15].

Adverse event occurrence rate

Adverse events refer to all adverse medical events that occur after a patient receives the experimental intervention, which can manifest as symptoms, signs, diseases or laboratory abnormalities but may not necessarily have a causal relationship with the experimental intervention factors.

Data collection and management

This study will use the IPRMS to formulate rehabilitation prescriptions for rehabilitation patients, monitor and manage remote rehabilitation, and achieve a fully intelligent, refined, personalised and digital management mode for pulmonary rehabilitation (the IPRMS detailed information is described in figure 3). The EDCS will be used for patient follow-up data management. Two types of data will be collected: 1) baseline data and 2) annual follow-up data (detailed information is described in the supplementary material).

Statistical analysis

The short-term outcome will be the readmission rate due to acute exacerbation at 90 days. According to the study by Lainscak *et al.* [16], it is estimated that the readmission rates for acute exacerbation at 90 days with and without early pulmonary rehabilitation are 10% and 20%, respectively. The PASS 15.0 software Logrank (Lakatos) test will be used, α=0.05, power=0.80, case enrolment time of 6 months, default enrolment mode of uniform rate, follow-up time of 3 months, total trial time (enrolment time plus follow-up time) of 9 months, estimated dropout rate of 10% within 3 months, sample size of 142 cases in each group.

For long-term outcomes, according to the follow-up studies of Stefan *et al.* [17] and Benzo *et al.* [18] on patients admitted with acute exacerbation of COPD, the readmission rate of patients with acute exacerbation at 12 months is approximately 30−43.7%. A total of 1482 cases are needed.

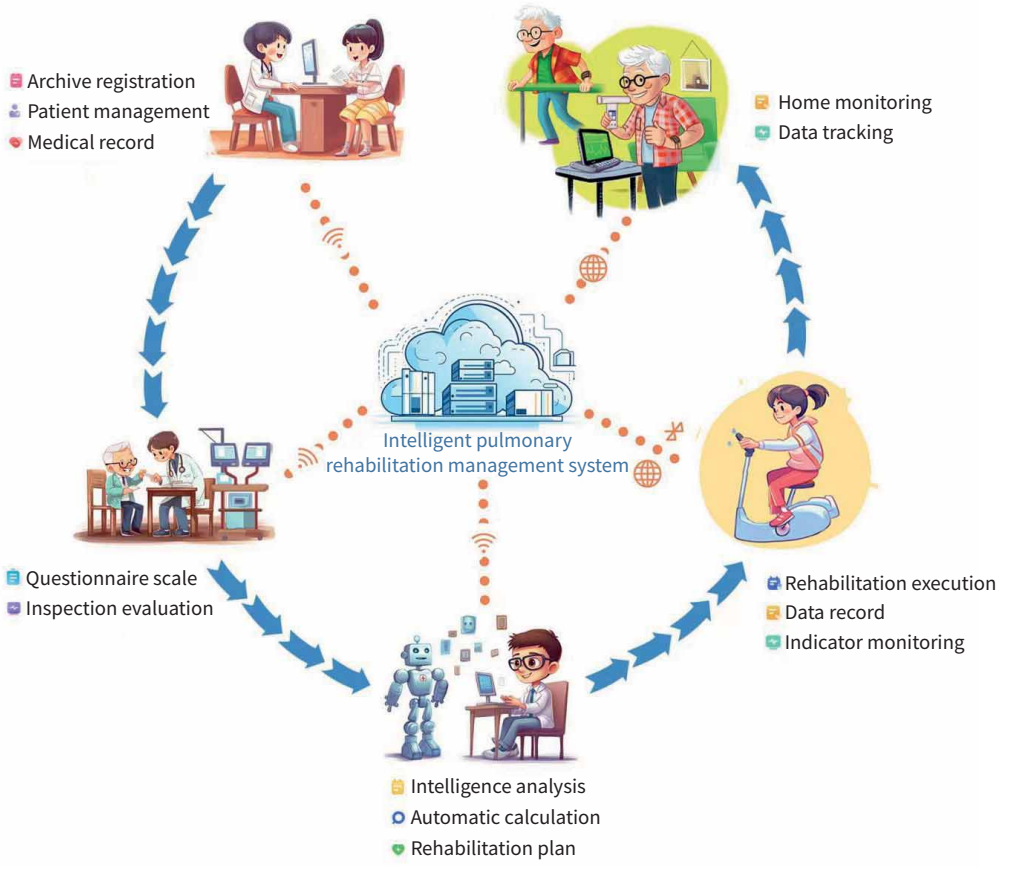

FIGURE 3 Intelligent pulmonary rehabilitation management system.

Discussion

According to GOLD, pulmonary rehabilitation is the most effective treatment intervention and respiratory disease management strategy for reducing breathing difficulties and improving physical function and quality of life. Compared to drug therapy, such treatment has significant cost-effectiveness advantages. Multiple studies have shown that pulmonary rehabilitation can effectively improve motor ability, muscle strength, functional ability and health-related quality of life in stable COPD patients, reduce symptoms, hospitalisation and unplanned medical visits, and enhance patients' self-efficacy [7]. However, for patients with acute exacerbations, a meta-analysis of 13 randomised trials was conducted in the 2017 European Respiratory Society (ERS)/ATS guidelines, and it was found that lung rehabilitation for admission to AECOPD may reduce readmission rates, improve quality of life and enhance motor ability. However, the project team conducted a stratified analysis based on the start time of rehabilitation and found that early pulmonary rehabilitation during hospitalisation may increase the risk of death [19]. Owing to the different rehabilitation plans used in the studies included in the analysis, the reference value of the meta-analysis results is limited.

Another 2020 systematic review included 42 studies for network meta-analysis, showing that 57% of pulmonary rehabilitation studies were conducted among hospitalised patients, and 24% of studies began pulmonary rehabilitation within 24–48 h after admission [20]. The meta-analysis results showed that pulmonary rehabilitation is a safe intervention measure during acute exacerbation of COPD. The rehabilitation programme of exercise training combined with pulmonary rehabilitation technology improved motor function, quality of life and breathing difficulties, but there was no difference in mortality at 6 or 12 months. In addition, the study by Chou *et al*. [21] also suggests that patients who underwent early pulmonary rehabilitation 3 days before mechanical ventilation had a significantly shorter duration of mechanical ventilation compared to matched control groups who did not receive early rehabilitation treatment.

The reason for the inconsistent research results may be the heterogeneity in the design of pulmonary rehabilitation plans. The previous studies have differences in the following aspects. 1) Research environment: involving pulmonary rehabilitation plans in different environments (such as hospitalisation, outpatient and home). 2) Composition of the rehabilitation programme: the programme components are composed of separate or combined modules, such as aerobic training, muscle strengthening, patient education, *etc*. 3) The start time of the pulmonary rehabilitation intervention: 2–3 weeks from admission to discharge, with multiple intervention time nodes in different studies. 4) The duration of rehabilitation varies, and there are also differences in training intensity and frequency [6]. These different research settings can all affect the efficacy evaluation of pulmonary rehabilitation.

In recent years, with the development of internet technology and mobile devices, internet plus medical or digital medicine has gradually highlighted its advantages in chronic disease treatment and management. Providing medical care through telemedicine, smartphone applications, wearable devices, artificial intelligence and other technologies can help identify health risks and assist in the diagnosis, treatment and monitoring of health and disease conditions to achieve various forms of chronic disease management services [22]. Previous studies have found that patient management based on "Internet plus" can improve the exercise endurance and quality of life of COPD patients, and some researchers have found that telemedicine can improve the lung function of COPD patients. Two systematic reviews by Cochrane in 2021 evaluated randomised trials in this field and found that respiratory distress symptoms can be improved after a longer period of digital intervention [23, 24]. However, compared to remote rehabilitation and on-site rehabilitation, there was little or no difference in exercise endurance and quality of life scores. Compared with the 70% completion rate of on-site pulmonary rehabilitation, subjects are more likely to complete remote rehabilitation, with a completion rate of 93% (95% CI 90–96%) [24], but there is still insufficient evidence to support the impact of the "Internet plus" management model on long-term outcomes.

A randomised controlled trial based on Chinese patients randomly divided stable COPD patients who completed 8 weeks of traditional pulmonary rehabilitation into three groups: Group A received nursing rehabilitation through home social media supervision (n=47), Group B received hospital-based pulmonary rehabilitation (n=44) and Group C received routine nursing (n=49). During a 12-month follow-up period, the frequency of AECOPD, 6MWD, CAT and mMRC scale were evaluated every 3 months. Compared with the conventional care group (n=49), the clinical improvement in 6MWD, CAT and mMRC scores in the home group (n=47) and the inpatient rehabilitation group (n=44) persisted ($p<0.001$), and no differences were observed between the two groups ($p>0.05$), indicating that the internet-based patient management model may replace the traditional inpatient management model [25].

Based on computer algorithms, IPRMS, as an internet management system, is an advanced intelligent pulmonary rehabilitation management system that integrates information collection, electronic medical record

entry, examination and evaluation, rehabilitation plan formulation, remote data monitoring and feedback. This system not only provides rehabilitation prescriptions quickly and intelligently but also continuously learns and improves during the period when doctors adjust plans based on individual patient conditions, making computer algorithms more advanced and rehabilitation plans more tailored to clinical needs. This advantage of the system will greatly compensate for the current lack of accessibility in pulmonary rehabilitation, further promote the popularisation of pulmonary rehabilitation and benefit more patients.

Based on the above evidence-based medical evidence, this study further verifies the substitutability of remote rehabilitation for outpatient rehabilitation and its short-term and long-term effects on patients, providing comprehensive intervention evidence for the treatment of COPD.

Conclusion

This study aims to further verify the substitutability of remote internet pulmonary rehabilitation for outpatient rehabilitation and its short-term and long-term effects in patients, providing comprehensive interventional evidence for the treatment of COPD. The combined application of IPRMS and EDCS can achieve intelligent, personalised and refined full process management of pulmonary rehabilitation for COPD patients.

Provenance: Submitted article, peer reviewed.

Acknowledgements: The authors would like to thank all eligible COPD patients for their participation and all the subcentre investigators for their excellent work.

Data availability: The data will be used for the analysis of the entire study. If a journal needs them, they can be used as supplementary materials according to regulations. After the study is completed, we will also conduct long-term follow-up for patients.

The protocol has been retrospectively registered at https://www.chictr.org.cn/ with identifier number ChiCTR2200065327.

Ethics statement: This study is approved by the Ethics Committee of the China–Japan Friendship Hospital (2022-KY-219). Informed consent will be obtained from all participants following a detailed description of the purpose, potential risks and benefits of the investigation. Participation will be voluntary and subjects will be offered the choice to withdraw from the study at any time without any obligations.

Author contributions: W. Ye and L. Danye drafted this manuscript; C. Jingjing and Z. Siyu were responsible for the nursing follow-up; W. Jiaxi and W. Siyuan were responsible for the rehabilitation guidance; Z. Hongmei and W. Chen participated in the design of the research plan and provided guidance.

Conflict of interest: All authors declare that there are no conflicts of interest.

Support statement: This study is supported by the Clinical Research and Achievement Transformation of Key Diagnostic and Treatment Technologies for Major Respiratory Diseases Project (2022-NHLHCRF-LX-01) and Key Technology Research Project of Medical Knowledge Management and Intelligent Knowledge Service of Chinese Academy of Medical Sciences (grant number 2021-I2M-1-056). Funding information for this article has been deposited with the Crossref Funder Registry.

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