

Comparison of a Supervised Home-Based Tele-Rehabilitation with Center-Based Pulmonary Rehabilitation: Protocol for a Randomized Non-Inferiority Multicenter Study in Ningxia

Hongxia Xin^{1,2,*}, Shuoshuo Wei^{1,3,*}, Hao Zheng^{4,*}, Yanchao Qi^{5,*}, Shuping Xu^{6,*},
Bei Wang², Wangshu Jiang⁷, Ning Deng^{7,*}, Juan Chen^{1,2,*}

¹Department of Key Laboratory of Ningxia Stem Cell and Regenerative Medicine, Institute of Medical Sciences, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, People's Republic of China; ²Department of Pulmonary and Critical Care Medicine, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, People's Republic of China; ³Department of Pulmonary and Critical Care Medicine, Affiliated Yijishan Hospital, Wannan Medical College, Wuhu, Anhui, People's Republic of China; ⁴Department of Pulmonary and Critical Care Medicine, Yanchi County People's Hospital, Wuzhong, Ningxia, People's Republic of China; ⁵Department of Pulmonary and Critical Care Medicine, Second People's Hospital of Shizuishan, Shizuishan, Ningxia, People's Republic of China; ⁶Department of Pulmonary and Critical Care Medicine II, Wuzhong People's Hospital, Wuzhong, Ningxia, People's Republic of China; ⁷Ministry of Education Key Laboratory of Biomedical Engineering, College of Biomedical Engineering and Instrument Science, Zhejiang University, Hangzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Ning Deng, Ministry of Education Key Laboratory of Biomedical Engineering, College of Biomedical Engineering and Instrument Science, Zhejiang University, Hangzhou, 310058, People's Republic of China, Email zju.dengning@gmail.com; Juan Chen, Department of Pulmonary and Critical Care Medicine, General Hospital of Ningxia Medical University, Yongan Lane, Xingqing District, Yinchuan, Ningxia, 750004, People's Republic of China, Email chenjuan7419@163.com

Background: Pulmonary rehabilitation (PR) is an effective intervention for people with chronic obstructive pulmonary disease (COPD). However, fewer than 5% of eligible individuals receive pulmonary rehabilitation, largely due to limited by the accessibility of rehabilitation and difficulties associated with travel and transport. Supervised home-based tele-rehabilitation (SHTR) is an alternative model to center-based pulmonary rehabilitation. We will determine whether supervised home-based tele-rehabilitation is non-inferior to center-based pulmonary rehabilitation.

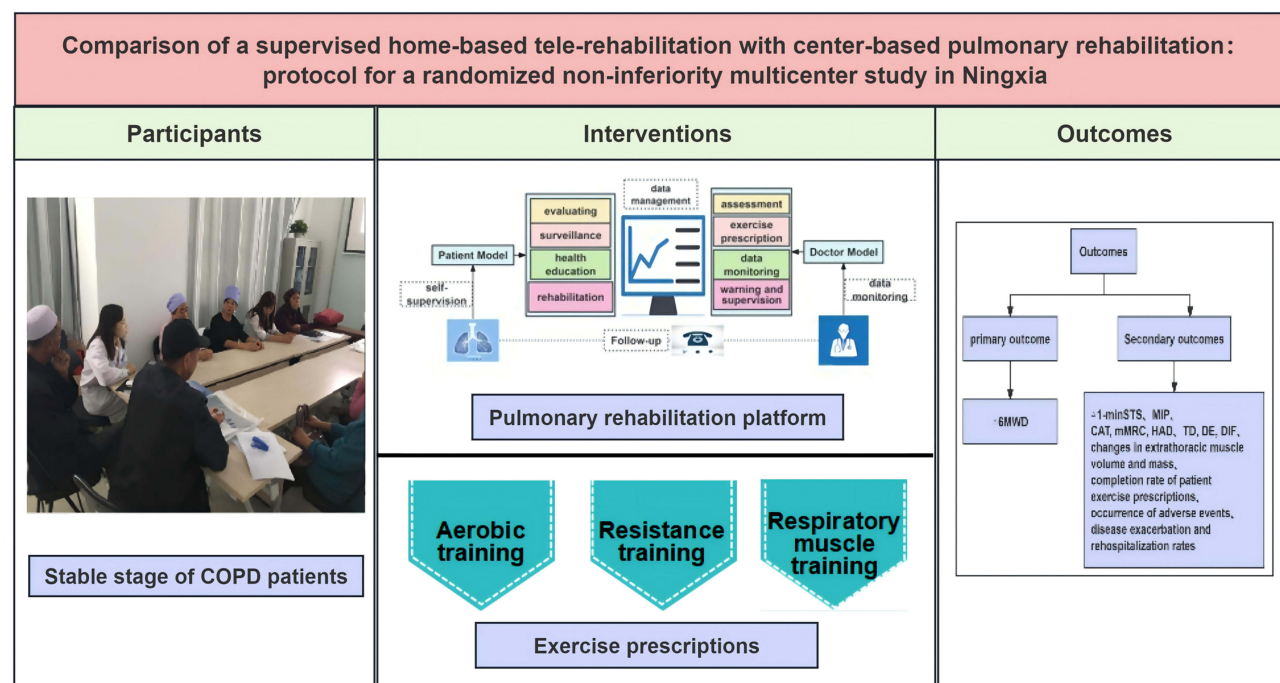
Methods: The participants will undergo an 8-week rehabilitation program. Pulmonary rehabilitation comprises four main modules: exercise training, education, nutritional support, and psychological and behavioral interventions. We mainly focus on the module of exercise training and education. The education module includes information on exercise training, nutrition, and psychology, which are presented in an educational booklet provided to each participant. Blinded assessors will evaluate the outcomes at baseline, post-intervention, and 6 months after the intervention. The primary outcome is the change in the 6-minute walking distance. Secondary outcomes will assess changes in the patients' 1-minute sit-to-stand test, maximal inspiratory pressure (MIP), scales (CAT, mMRC, HAD), diaphragm ultrasound (TD, DE, DIF), changes in extrathoracic muscle volume and mass, completion rate of patient exercise prescriptions, occurrence of adverse events, as well as disease exacerbation and rehospitalization rates after rehabilitation and during the 6-month follow-up.

Discussion: In order to improve the accessibility of pulmonary rehabilitation and patient-related outcomes, it is necessary to propose an alternative model of pulmonary rehabilitation. This trial will establish whether a supervised home-based tele-rehabilitation is not inferior to traditional center-based pulmonary rehabilitation.

Trial Registration: Chinese Clinical Trial Registry ChiCTR2300076969. Registered on October 25, 2023.

Keywords: COPD, tele-rehabilitation, protocol, randomized non-inferiority trial

Graphical Abstract



Background

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by persistent respiratory symptoms and progressive airflow obstruction.¹ This chronic progressive respiratory disease can lead to reduced physical activity, muscle degeneration, worsening breathing difficulties, and decreased quality of life.² Research indicates that COPD is one of the common chronic disease that has steadily increased over the past 50 years. Currently, it is the third leading cause of death, surpassed only by cardiovascular diseases and stroke.^{3–5}

Pulmonary rehabilitation (PR) can improve symptoms, activity limitations, and enhance health-related quality of life.⁶ It is a core, non-pharmacological intervention in the management of COPD with strong evidence of effectiveness.^{7,8} Despite the numerous benefits of pulmonary rehabilitation, fewer than half of the eligible patients have completed the program. Traditional center-based pulmonary rehabilitation programs face established barriers related to referral practices, travel, transportation and disabilities.^{9,10} These barriers affect the opportunities for rural and community patients to engage in PR.¹¹ Given such difficulties, alternative approaches are needed to provide PR program, aiming to improve equal access and patient-related outcomes for individuals with COPD.¹²

A home-based pulmonary rehabilitation program has been proposed to improve the availability and accessibility of PR.^{13–15} Recent studies have shown that home-based pulmonary rehabilitation has comparable clinical outcomes to center-based rehabilitation.¹³ Tele-rehabilitation has the potential to improve access to healthcare and provide options for PR, particularly for geographically or socially isolated individuals, as well as those with travel difficulties.¹⁶ The Ningxia Hui Autonomous Region is a relatively remote area in China with a population of over 6 million people. The prevalence of COPD in Ningxia is 8.9% among individuals aged 40 years and older.¹⁷ There is evidence that tele-rehabilitation is effective, we now want to explore the effectiveness of tele-rehabilitation in the Ningxia region.

Our previous observational study demonstrated the safety and positive impact of tele-rehabilitation on the psychological well-being and quality of life of patients in the Ningxia region.¹⁸ However, in the above study, the effectiveness of home-based tele-rehabilitation compared to center-based pulmonary rehabilitation remained unclear. Therefore, the main objective of this study is to determine the non-inferiority of supervised home-based tele-rehabilitation compared to

center-based pulmonary rehabilitation, including: 1) evaluating whether the benefits of supervised home-based tele-rehabilitation, including improvements in exercise capacity, psychological well-being, respiratory symptoms, diaphragm function, respiratory muscle function, etc. are comparable to those of center-based pulmonary rehabilitation; 2) comparing the completion rate of exercise prescriptions and the incidence of adverse events between the two groups; 3) comparing the occurrence of acute exacerbation of the disease and rehospitalization in the two groups.

Methods

Trial Design

A randomized, controlled, evaluator-blind non-inferiority trial will be conducted in the Ningxia region of China. This study has obtained approval from the ethics committees of all participating centers (General Hospital of Ningxia Medical University, People's Hospital of Wuzhong City, Second People's Hospital of Shizuishan, and People's Hospital of Yanchi County). The trial was registered on October 25, 2023, in the Chinese Clinical Trial Registry (ChiCTR2300076969). We used the Additional file 1: SPIRIT checklist¹⁹ when writing our manuscript. Study procedures are illustrated in Figure 1

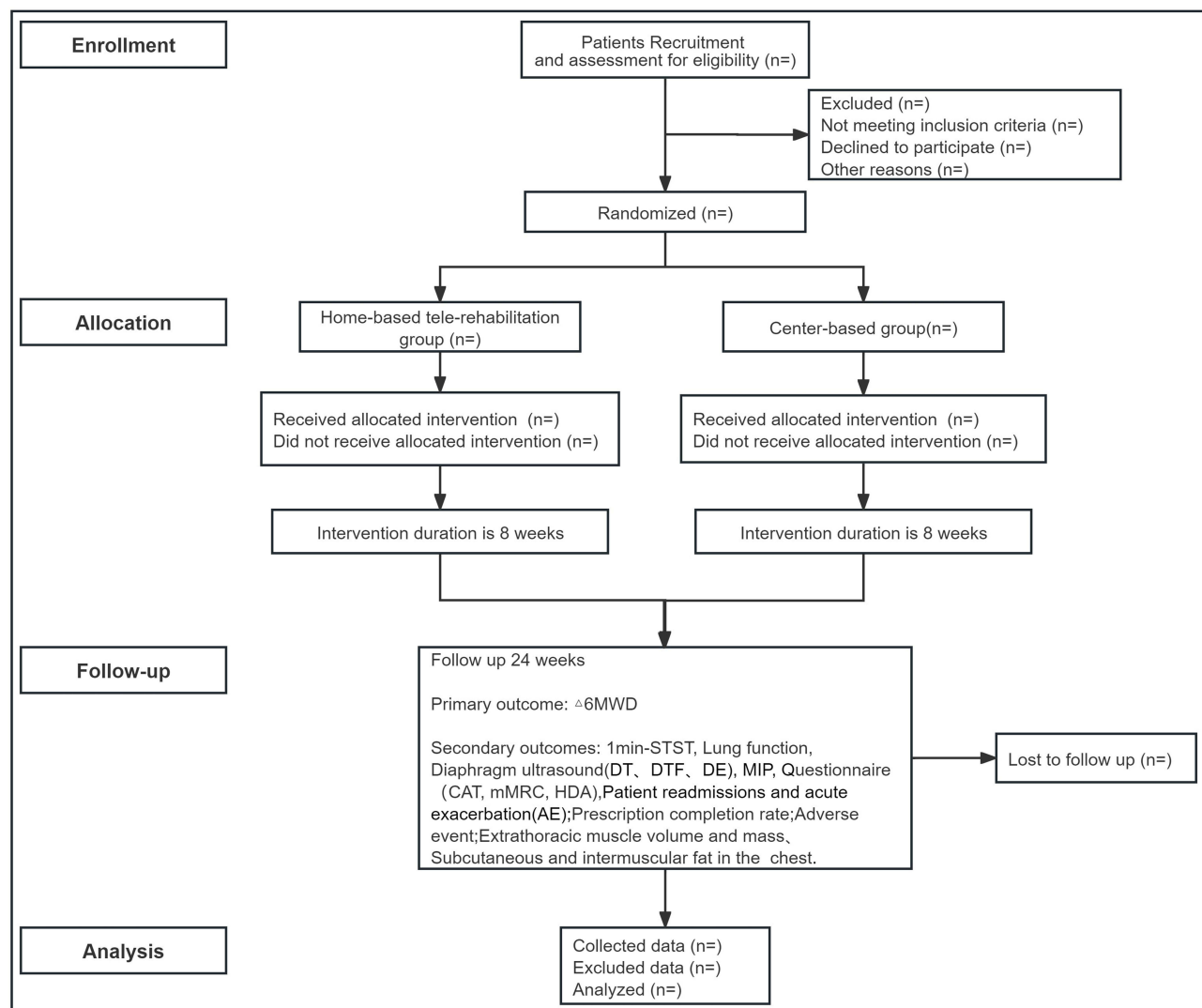


Figure 1 Design Flowchart.

Abbreviations: 6MWD, 6-Minute walking test; 1-minSTST, 1 minute sit-to-stand test; CAT, COPD Assessment Test; mMRC, modified Medical Research Council; HAD, Hospital anxiety and depression; MIP, Maximum inspiratory pressure; DT, Thickness of the diaphragm; DTF, Diaphragm thickening fraction; DE, Diaphragmatic excursion; AE, Acute exacerbation.

Study Setting

The study will be conducted in Ningxia, China, which is located in the northwest part of the country. Ningxia is considered a remote region with a relatively underdeveloped economy. Due to its dry climate, strong winds, and abundant sand, the incidence of chronic obstructive pulmonary disease (COPD) was 8.9% (360/4055) in people 40 years of age or older.¹⁷ The diagnosis and management of COPD in this region were unsatisfactory. Both patients and healthcare workers have insufficient knowledge and utilization of pulmonary rehabilitation. Therefore, this study will be conducted in four hospitals of varying levels in different areas of Ningxia.

Participants

The study will recruit patients with a confirmed diagnosis of stable COPD, which mean the presence of a post-bronchodilator FEV1/FVC <0.70 confirms the presence of persistent airflow limitation. For patients with acute exacerbations, they will be included in the trial 4 weeks after discharge. Inclusion and exclusion criteria are detailed in Table 1.

A clinician or researcher will provide written and verbal information to all eligible participants at the first day of evaluation. Written informed consent will be provided by all individuals who agree to participate. Participating in the trial will not change the routine management of chronic obstructive pulmonary disease.

Recruitment and Randomization

Participants will be randomly assigned (2:1) to the supervised home-based tele-rehabilitation group and the center-based rehabilitation group. A computer-generated randomization scheme will be used, stratifying the samples based on modified Medical Research Council (mMRC score ≥ 2 or < 2) and recruitment location. The sequence generation will be conducted by individuals independent of the research team and random allocation will be done using an online database, keeping the random assignment sequence confidential from the researchers. Due to the nature of the intervention, participants will not be able to be blinded to the intervention, but all outcomes will be assessed by independent evaluators blinded to group allocation. The participants' flow in the study will be reported following the

Table 1 Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Patients aged 40–80 years old, male or female, with or without smoking history, from the community, receiving or not receiving oxygen therapy, outpatient or hospitalized settings	Unstable angina or arrhythmia, as well as unstable fractures
Modified Medical Research Council (mMRC) greater than or equal to one	Clinical diagnosis of lung cancer, asthma, bronchiectasis, pneumoconiosis, or other chronic respiratory diseases
Patients who were able to communicate effectively in either language or text and have the capability to complete any necessary ancillary examinations	Hematological diseases or malignant tumors that could hinder the completion of the research
Patients who have obtained informed consent and received approval from the Ethics Committee	Infectious diseases that pose a risk to others and have no isolation measures in place
Patients or their family members who have access to smartphones and are capable of interacting effectively with doctors through smartphones	Severe cognitive impairment
Patients who have not experienced an acute exacerbation of the disease within the previous month	Unwillingness of either the patient or their family members to participate in the study
	Current participation in or previous participation in any form of pulmonary rehabilitation within the past 6 months
	Lack of access to a smartphone

Table 2 The Summary of the Study Schedule

Timepoint	Baseline	1 Week	2 Weeks	3 Weeks	4 Weeks	5 Weeks	6 Weeks	7 Weeks	8 Weeks	24 Weeks Follow-up
Enrollment										
Eligibility screen	x									
Informed consent	x									
Demographics	x									
Comorbidities	x									
AE in the previous year	x									
Medication	x	x	x	x	x	x	x	x	x	x
Assessment										
6MWT	x								x	x
1 min-STST	x								x	x
Pulmonary function	x								x	x
Diaphragm ultrasound	x								x	x
MIP	x								x	x
Quality of Life (CAT)	x	x	x	x	x	x	x	x	x	x
Dyspnea (mMRC)	x	x	x	x	x	x	x	x	x	x
Mental state (HAD)	x	x	x	x	x	x	x	x	x	x
Extrathoracic muscle volume and mass	x								x	x
AE		x	x	x	x	x	x	x	x	x
Readmission rate		x	x	x	x	x	x	x	x	x
Safety monitoring										
Adverse event		x	x	x	x	x	x	x	x	x
Vital signs		x	x	x	x	x	x	x	x	x

Abbreviations: COPD, chronic obstructive pulmonary disease; 6MWT, 6-Minute walking test; FEV1pred%, Percentage of forced expiratory volume in the first second predicted value; MIP, Maximum inspiratory pressure; HADS, Hospital Anxiety and Depression Scale; mMRC, Modified Medical Research Council; 1ST, 1--minute sit-to-stand; CAT, COPD Assessment Test; AE Acute exacerbation.

recommendations of the Consolidated Standards of Reporting Trials (CONSORT).²⁰ Baseline information and follow-up information are shown in Table 2.

Interventions

Pulmonary rehabilitation comprises four main modules: exercise training, education, nutritional support, and psychological and behavioral interventions. We mainly focus on the module of exercise training and education. The education module includes information on exercise training, nutrition, and psychology, which are presented in an educational booklet provided to each participant. Besides, the supervised home-based rehabilitation group will receive a pedometer, a pulse oximeter, and the rehabilitation mobile application installed on their smartphones. Meeting the rehabilitation requirements involves completing at least 70% of the planned rehabilitation training.

Both the tele-rehabilitation group and the center-based rehabilitation group underwent assessment and education at the hospital before enrollment. Each participant was provided with an educational booklet and informed about the program's goals, which include improving their exercise capacity, alleviating symptoms, and enhancing overall health. Therapists and doctors have face-to-face communication with the patients to introduce the rehabilitation plan, ensure patient understanding and compliance, teach the use of respiratory training devices, establish rehabilitation records, and instruct them on how to use the equipment. For the supervised home-based rehabilitation group, patients are also educated on how to use the rehabilitation mobile application. Therapists and doctors conduct weekly phone follow-ups with the patients, and the rehabilitation mobile application allows communication with the patients at any time.

For center-based rehabilitation patients, a weekly 40-minute face-to-face meeting is scheduled. During this meeting, doctors will repeatedly explain the content of the four modules of pulmonary rehabilitation to the patients and inquire about their execution progress. In addition, doctors and therapists provided personalized advice to patients, including recommendations on diet, sleep, and mental health, to help them recover to their optimal state more quickly. Therapists and doctors also conduct weekly phone follow-ups with these patients.

Participants in both groups are required to record their unsupervised training. Patients in the tele-rehabilitation group communicate their unsupervised training activities with therapists during weekly phone follow-ups, while patients in the center-based rehabilitation group share their unsupervised training during the weekly 40-minute face-to-face meeting.

Centre-Based Pulmonary Rehabilitation

Center-based rehabilitation participants will undergo a standard outpatient pulmonary rehabilitation program. This involves 8 weeks of twice-weekly sessions, supervised by a health professional experienced in the delivery of pulmonary rehabilitation (eg, physiotherapist, exercise physiologist). Each session includes at least 30 minutes of walking exercise (on a treadmill). If continuous training is limited by symptoms, the training time can be shortened (eg, 3×10 minutes or 2×15 minutes). The initial intensity of walking exercise is set at 60% of the walking speed during the 6-minute walk test. The training intensity is adjusted once a week, with the goal of maintaining the Borg dyspnea score between 3–5. Resistance training will be performed using elastic bands. The initial intensity is set at 60% of the maximum weight that can be lifted for 3 repetitions. Each training session includes 2–3 sets with 8–12 repetitions per set. When the patient completes the current exercise volume in two consecutive sessions and reaches the target number of repetitions, the load of resistance exercise will be adjusted by increasing the number of repetitions per set and the number of sets. Inspiratory muscle training will be conducted using the S2 respiratory training device. The initial intensity of inspiratory muscle training is set at 30% of the maximum inspiratory mouth pressure (MIP). The intensity is adjusted based on the Borg scale, with the goal of maintaining the Borg dyspnea score between 3–5. In tele-rehabilitation, the supervised sessions are conducted in the home environment, so it may be easier to transition to unsupervised sessions, so participants are encouraged to engage in 1–3 additional unsupervised training sessions per week.

Supervised Home-Based Tele-Rehabilitation

Establish a Pulmonary Rehabilitation Platform

A pulmonary rehabilitation mobile APP will be implemented, which consists of 3 parts: patient model, doctor model, and server model (Figure 2).

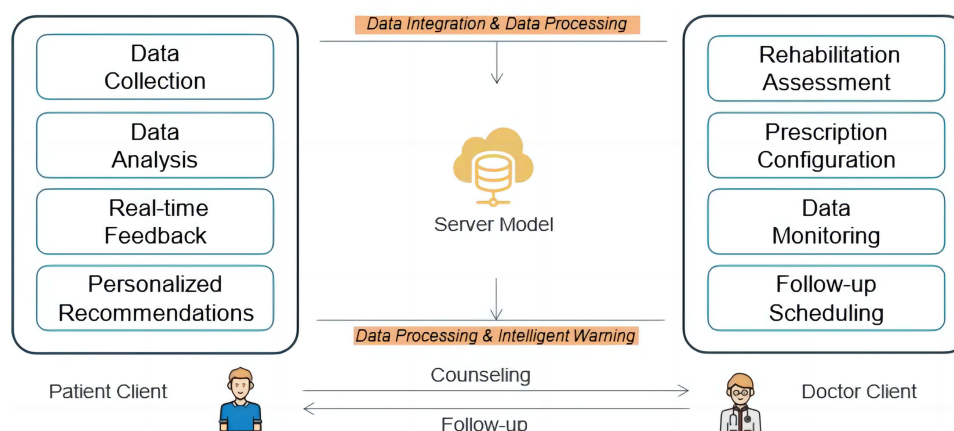


Figure 2 The mobile APP.

- 1) Patient Model: The patient terminal plays a pivotal role in mobile healthcare. It can be accessed via smartphone applications compatible with both Android and Apple platforms. It encompasses four primary modules: data collection, data analysis, real-time feedback, and personalized recommendations. The data collection module accepts manually input physiological parameters from patients or collects real-time physiological data, such as heart rate, respiratory rate, and blood oxygen saturation, by connecting to various biomedical devices. The data analysis module utilizes data mining techniques, combined with the patient clinical data gathered by the data collection module, to analyze and design the most suitable exercise regimen for each patient. The real-time feedback module provides a user-friendly interface for patients to monitor their exercise progress, rehabilitation status, and real-time physiological data. Additionally, the platform automatically adjusts exercise prescriptions based on the patient's actual condition, ensuring each exercise session is the most effective. The personalized recommendation module offers a series of tailored rehabilitation suggestions based on the specific conditions of each patient, including advice on diet, sleep, and mental health, to help patients recover to their best state more quickly.
- 2) Doctor Model: The doctor end of the system provides physicians and rehabilitation teams with a comprehensive toolkit. The scale assessment module allows doctors to use various scales to evaluate the health status and rehabilitation progress of patients, such as the 6-minute walk test and respiratory function tests. The rehabilitation assessment module provides a comprehensive report on a patient's rehabilitation status based on their biomedical data and clinical records. The prescription configuration module enables doctors to adjust the exercise prescriptions automatically generated in the patient model, tailoring exercise and rehabilitation plans to better suit each patient's individual conditions. The data monitoring module allows doctors to view in real time the physiological data, exercise progress, and rehabilitation status of patients. The follow-up scheduling interface provides doctors with a convenient interface to arrange and schedule subsequent rehabilitation plans for patients.
- 3) Server Model: Responsible for data integration and processing, this software plays a crucial role in managing the pulmonary rehabilitation project. The data integration and processing functionality enables the server to automatically gather and consolidate data from various biomedical devices, medical systems, and doctor-end applications. This data includes not only physiological data of patients but also their medical history, medication usage, treatment processes, and rehabilitation progress. Through its built-in data processing module, the real-time data analysis module can analyze consolidated data on-the-fly, identifying key health indicators and rehabilitation trends, offering real-time feedback and suggestions to doctors and patients. The alert system, an embedded intelligent warning system in the server, can send warning messages to doctors and patients in a timely manner when patient data shows abnormalities or reaches preset alert criteria, ensuring the patient's rehabilitation process remains on a safe and effective track.

Aerobic Training (Walking on Flat Ground)

- a, Accurate exercise prescription: The patient's speed of exercise on flat ground can be determined using the following formula: $\text{Exercise Speed (Km/h)} = 6\text{MWD} \times 10/1000$, the initial exercise speed will be selected as 60% of calculating speed.
- b, To measure the patient's step distance and calculate their stride frequency per minute, we can use the following formula: $\text{Stride frequency per minute} = \text{Exercise speed} / \text{Step distance}$. If we consider the patient starting to exercise at an initial speed of 1.8 Km/h (30m/min) and their stride distance is 0.6 meters, the calculation would be as follows: $\text{Stride frequency per minute} = 30 \text{ m/min} / 0.6 \text{ m} = 50 \text{ steps per minute}$.
- c, Set the corresponding cadence for patients (ie, 50 steps/minute) in the metronome embedded in the mobile APP. The initial exercise duration is 15 minutes. Engage in walking exercise 2 times per day, 3–5 days per week. Wear the pedometer (iVOLE) during the walking process to record the daily step count and upload it to the mobile APP. Prior to walking exercise, warm up for 3–5 minutes, and during the exercise, keep the head up, chest out, and swing the upper limbs approximately 45 degrees. After the walking exercise, cool down for 3–5 minutes.

Resistance Training

The initial intensity is set at 60% of the maximum weight that can be lifted for 3 repetitions. Resistance training primarily utilizes elastic bands to train the upper and lower body. The exercise frequency is 2–3 times per week, with 2–3 sets of 8–12 repetitions per set. If the patient completes the current volume in two consecutive training sessions and reaches the target number of repetitions, the load of resistance exercise can be adjusted by increasing the number of repetitions per set and the number of training sets.

Respiratory Muscle Training

Inspiratory muscle training will be conducted using the S2 respiratory trainer (Xiamen SEEK Medical Equipment Co., Ltd in China). The S2 Respiratory Trainer utilizes dynamic valve technology, with diaphragmatic breathing and pursed-lip breathing as the physiological basis. By progressively increasing resistance, it aims to achieve full lung expansion and gradual increase in lung capacity. The initial intensity for inspiratory muscle training is set at 30% of the maximum pressure. To prevent inspiratory muscle fatigue, patients will be instructed to assess their level of dyspnea using the Borg scale after each breathing training session. The training regimen consists six sessions of inspiratory muscle training, with each session comprising five sets, conducting twice a day, three to five days a week.

Safety Supervision

During tele-rehabilitation program, the patient should monitor Pulse Oximeter Oxygen Saturation (SPO2) and heart rate (HR) by finger pulse oximeter. After performing the training session, the data of SPO2 and HR will be fill in mobile APP and transfer to pulmonary rehabilitation platform. If the patient experiences discomfort during training, such as chest pain, intolerable dyspnea, sweating, paleness, or if the transcutaneous oxygen saturation decreases by $\geq 4\%$ from the baseline value (measured after at least 10 minutes without oxygen inhalation), or if the transcutaneous oxygen saturation is below 85%, or if the heart rate exceeds the maximum limit of the target heart rate ($[(220-\text{age}) - \text{resting heart rate}] * 60\% + \text{resting heart rate}$), are recommendation for cessation exercise, if the patient has previously used oxygen, oxygen is recommended. If the above warning occurs for 2 consecutive days, it is necessary to adjust the intensity and duration of the training.

Compliance Monitoring

For patients in the center-based rehabilitation group, compliance is assessed based on their punctuality and attendance at scheduled appointments and training sessions. Attendance records are meticulously maintained for each participant. In contrast, for patients in the home-based tele-rehabilitation group, compliance is measured through a mobile application, where patients are required to log their daily exercise completion. While attendance and exercise logging are direct indicators of compliance, we acknowledge that they do not fully capture the actual effectiveness of the interventions. Therefore, a multifaceted approach will be employed to comprehensively assess the intervention outcomes, including regular follow-ups.

Regardless of whether patients are in the center-based or home-based rehabilitation groups, therapists and physicians will conduct detailed inquiries into the patients' rehabilitation progress during weekly follow-ups. These follow-ups will encompass discussions about the specific content of the exercises performed and the patients' subjective experiences. The mobile application is equipped with a daily reminder function to prompt patients to perform and record their exercises punctually. During the weekly phone follow-ups or face-to-face meetings, therapists will verify the exercise logs and delve into any difficulties encountered by the patients.

Outcomes

The baseline participant characteristics, including age, gender, height, weight, smoking history, medication use, previous year's acute exacerbation events, comorbidities, will be collected from participants and medical records. Clinical outcome measures (Table 3) will be assessed at baseline, intervention completion (week 8), and at the end of the 6-month follow-up. Participants are required to visit the recruiting hospital for evaluation. The completion rate is pre-defined as completing at least 70% of the planned sessions in the pulmonary rehabilitation process.

Table 3 Clinical Outcome Measures and Assessment Time Points

Outcomes	Description	Assessment Point(s)	Time
Exercise capacity (Δ 6MWT)	The test assesses the distance covered by a participant in a 6-minute walk. Participants will receive standardized encouragement and will be instructed to walk as far as they can within a 6-minute timeframe. Two tests will be conducted during each session, and the maximum distance achieved will be recorded. ^{20,21} The final assessment measures the change in the patient's 6-minute walking distance.	Baseline End of intervention End of 6 months follow-up	Primary outcome
Exercise capacity (1-mSTS)	This is a practical, reliable, valid, and responsive alternative for measuring exercise capacity, particularly where space and time are limited ²²	Baseline End of intervention End of 6 months follow-up	Secondary outcomes
Pulmonary function tests (FEV1pred%)	COPD is diagnosed through a combination of clinical symptoms and physiological measurements via pulmonary function tests. ²³ Pulmonary function tests are performed by spirometry using the same machine and the same technician for all participants according to international recommendations ²⁴		
Respiratory muscle training (MIP)	Respiratory or ventilatory muscle training, aims to improve inspiratory muscle strength and endurance through a series of breathing exercises. ²⁵		
Dyspnoea (mMRC)	The mMRC scale measures functional breathlessness on a scale ranging from 0 to 4. A score of 0 indicates no limitations in activities due to breathlessness, while a score of 4 represents the highest level of impairment ²⁶		
Mental state (HADS)	Anxiety and depression are frequently observed as comorbidities in individuals with COPD. These conditions can be alleviated through pulmonary rehabilitation and will be assessed using the Hospital Anxiety and Depression Scale (HAD) ²⁷		
Quality of Life (CAT)	This self-assessment questionnaire consists of 8 items, evaluating various manifestations of COPD, with the aim of providing a simple quantitative measurement of quality of life ^{28,29} .		
Diaphragm ultrasound (TD, DTF, DE)	The diaphragm is the most important inspiratory muscle, and the diaphragm dysfunction directly leads to dyspnoea and respiratory failure. ³⁰ Rehabilitation could increase diaphragmatic endurance and strength, reduce airflow resistance and improve dyspnoea in patients with COPD ³¹		
AE and Readmission to hospital	Determination was made using hospital medical records and cross-validated through patient self-reports		
Extrathoracic muscle volume and mass; Subcutaneous and intermuscular fat in the chest.	Quantification of subcutaneous adipose tissue, intermuscular fat, and extrathoracic muscle volume and mass through chest CT is used to predict clinical outcomes. ^{32,33}		
Adverse event	Any adverse medical events that may occur during the intervention of a study, which may not necessarily have a causal relationship with the treatment intervention.		
Completion rate	Completing at least 70% of the planned sessions		

Abbreviations: COPD, chronic obstructive pulmonary disease; 6MWT, 6-Minute walking test; FEV1pred%, Percentage of forced expiratory volume in the first second predicted value; MIP, Maximum inspiratory pressure; MEP, Maximum expiratory pressure; HADS, Hospital Anxiety and Depression Scale; mMRC, Modified Medical Research Council; ISTS, 1--minute sit-to-stand; CAT, COPD Assessment Test; TD, Thickness of the diaphragm; DTF, Diaphragm thickening fraction; DE, Diaphragmatic excursion; AE, acute exacerbation.

Statistical Analysis

Sample Size Calculation

The sample size was estimated using a non-inferiority test (difference method) based on a single-sample mean. Previous research findings determined that the minimum clinically important difference (MCID) for the 6-minute walk test (6MWT) in COPD before and after rehabilitation is at least 26 meters^{34,35}. The non-inferiority margin was set at 50% of the known MCID, considering a dropout rate of 30%, $\alpha=0.025$ (one-sided) significance level, and a power (1- β) of 0.80. The sample ratio between the two groups was set at 2:1. Using PASS 11 software, the calculated sample sizes for the supervised home-based tele-pulmonary rehabilitation group and the traditional center-based pulmonary rehabilitation group were 80 and 40, respectively.

Data Collection and Management

Data collection will take place before the intervention, at the end of the 8-week intervention, and at the 6th month after the intervention. Detailed collection is shown in Table 3. In this trial, the part of data generated during the management process will be automatically recorded by the system and stored in the database. The assessment data will be electronically entered by an investigator. To ensure accuracy, a double data entry process will be conducted, and a different investigator will review and verify all data ranges. Each patient, physician, case manager (CM), and general practitioner (GP) will have unique IDs, and their login passwords will be encrypted and kept anonymous to the database administrator.

Data Monitoring

The Data Monitoring Committee consists of statisticians from the General Hospital of Ningxia Medical University. The committee operates independently from the sponsor and has no competing interests. It is responsible for auditing the trials to oversee the quality of research data. The committee charter is available from the corresponding author.

Statistical Analysis Plan

According to the CONSORT criteria for clinical trial reports, the primary and secondary outcomes of non-inferiority trials will be analyzed and reported.³⁶ Baseline characteristics will be described using descriptive statistics, with continuous variables presented as mean \pm standard deviation and categorical variables presented as frequencies and percentages. Treatment evaluation will follow the principle of intention-to-treat analysis. For missing data on primary outcomes, assuming the data are multivariate normally distributed and missing at random, multiple imputation methods will be employed. Sensitivity analysis will be conducted to assess the impact of missing data, as recommended for non-inferiority trials. Statistical tests for the primary non-inferiority outcomes will be one-sided with $\alpha=0.025$, while tests for secondary outcomes will be two-sided with $\alpha=0.05$. The non-inferiority hypotheses will be evaluated using non-inferiority confidence interval methods. The non-inferiority testing for both primary and secondary outcomes will be repeated at the 6-month follow-up using the same methods as described above.

Based on rehabilitation survival data, decision curve analysis (DCA) will be conducted using a single-model single-time-point approach. The dataset will consist of information from 120 patients, with each variable standardized before analysis. The DCA analysis will be performed using the `stdca()` R package³⁷ to evaluate the clinical benefits under different rehabilitation strategies.

Discussion

COPD is one of the most prevalent respiratory disease worldwide.⁵ Pulmonary rehabilitation is a proven treatment for people with COPD,⁸ yet limited access to programs prevents the widespread application. The home-based tele-rehabilitation model provides pulmonary rehabilitation to patients with COPD through a mobile App, eliminating issues such as transportation, travel, and weather.³⁸ This approach addresses the barriers of access for patients and the healthcare system. By improving accessibility, more patients have the opportunity to develop a wise and positive understanding of the benefits of PR.

Unlike previous studies,^{39,40} our studying for home-based tele-rehabilitation requires minimal technical support, and is very familiar to clinicians and patients, with the potential for easy application in clinical practice. Tele-rehabilitation

can be conducted at any time and any place, increasing access to PR for patients in remote areas. Supervised tele-exercise training is a key feature in this tele-rehabilitation model, allowing PR to be conducted in locations where specialized services are usually unavailable.⁴¹

The purpose of this study is in line with the policy statement encouraging the implementation of alternative models for PR to enhance access and delivery of pulmonary rehabilitation.¹² If this study demonstrates that the clinical effectiveness of supervised tele-rehabilitation is not inferior to center-based pulmonary rehabilitation, then this model has the potential to significantly improve the availability and accessibility of rehabilitation services.

Adverse Event Reporting

Adverse events will be recorded in Case Report Form (CRF). The protocol distinguishes between adverse events directly related to the study interventions and those unrelated to the study. Serious adverse events are reported within 24h to the principal investigator. The steering committee is composed of a pulmonologist and a respiratory nurse who will oversee the study procedures and assess serious adverse events. The steering group represents the trialists involved in this study.

Research Ethics Approval

Before the study, the researchers submitted the study protocol, informed consent form, and other necessary documents to the Ethics Committee of the General Hospital of Ningxia Medical University for review and approval. The ethics number for this clinical study is KYLL-2024-0342. I confirm that the test will comply with the provisions of the Declaration of Helsinki.

Patient and Public Involvement

The experiences of patients from our previous trials of home-based pulmonary rehabilitation⁴² and our pilot study of home-based pulmonary rehabilitation informed the development of the protocol, including the timing of recruitment, assessments, and intervention resources. 6MWT is chosen as the primary outcome of the trial due to its significant relevance to individuals with COPD.

Confidentiality

The researchers have the responsibility to maintain the anonymity of the participants. The case report forms or other participant-related documents should only use uppercase letters, numbers, and codes to identify the participants, rather than their names. The researchers must securely store and record the participant codes.

Dissemination

The results of this research will be fully disclosed in international peer-reviewed journals. The publication will include both positive and negative findings, and the results will be conveyed to people with COPD through lay publications and seminars.

Abbreviations

COPD, Chronic obstructive pulmonary disease; PR, Pulmonary rehabilitation; AE, Acute exacerbation; 6-MWT, 6-Minute walking test; CAT, COPD Assessment Test; FEV1pred%, Percentage of forced expiratory volume in the first second (FEV1) predicted value; MIP, Maximum inspiratory pressure; MEP, Maximum expiratory pressure; CRF, Case report form; 1-minSTS, 1 minute sit-to-stand test; mMRC, modified Medical Research Council; RCT, Randomized controlled trial; HADS, Hospital anxiety and depressions scale; SPIRIT, Standard protocol items recommendations for interventional trials; TD, Thickness of the diaphragm; DTF, Diaphragm thickening fraction; DE, Diaphragmatic excursion.

Funding

This work is supported by the Key Research and Development Program of Ningxia Hui Autonomous of China (No. 2023BEG02021).

Disclosure

The authors report no conflicts of interest in this work.

References

1. National Institute for Health and Care Excellence. National institute for health and care excellence: guidelines. In: *Chronic Obstructive Pulmonary Disease in Over 16s: Diagnosis and Management*. London: National Institute for Health and Care Excellence (NICE) Copyright © NICE 2018; 2019.
2. Ramon MA, Ter Riet G, Carsin AE, et al. The dyspnoea-inactivity vicious circle in COPD: development and external validation of a conceptual model. *Eur Respir J*. 2018;52(3):1800079. doi:10.1183/13993003.00079-2018
3. Thomashow BM, Walsh JW, Malanga EDF. The COPD Foundation: celebrating a Decade of Progress and Looking Ahead to a Cure. *Chronic Obstr Pulm Dis*. 2014;1(1):4–16. doi:10.15326/jcopdf.1.1.2014.0122
4. Chapman KR, Mannino DM, Soriano JB, et al. Epidemiology and costs of chronic obstructive pulmonary disease. *Eur Respir J*. 2006;27(1):188–207. doi:10.1183/09031936.06.00024505
5. Soriano JB, Kendrick PJ, Paulson KR. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet Respir Med*. 2020;8(6):585–596. doi:10.1016/S2213-2600(20)30105-3
6. Wagg K. Unravelling self-management for COPD: what next? *Chron Respir Dis*. 2012;9(1):5–7. doi:10.1177/1479972311435910
7. Alison JA, McKeough ZJ, Johnston K, et al. Australian and New Zealand Pulmonary Rehabilitation Guidelines. *Respirology*. 2017;22(4):800–819. doi:10.1111/resp.13025
8. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2015;2015(2):Cd003793. doi:10.1002/14651858.CD003793.pub3
9. Cox NS, Oliveira CC, Lahham A, Holland AE. Pulmonary rehabilitation referral and participation are commonly influenced by environment, knowledge, and beliefs about consequences: a systematic review using the Theoretical Domains Framework. *J Physiother*. 2017;63(2):84–93. doi:10.1016/j.jphys.2017.02.002
10. Keating A, Lee A, Holland AE. What prevents people with chronic obstructive pulmonary disease from attending pulmonary rehabilitation? A systematic review. *Chron Respir Dis*. 2011;8(2):89–99. doi:10.1177/1479972310393756
11. Johnston CL, Maxwell LJ, Maguire GP, Alison JA. How prepared are rural and remote health care practitioners to provide evidence-based management for people with chronic lung disease? *Aust J Rural Health*. 2012;20(4):200–207. doi:10.1111/j.1440-1584.2012.01288.x
12. Rochester CL, Vogiatzis I, Holland AE, et al. An Official American Thoracic Society/European Respiratory Society Policy Statement: enhancing Implementation, Use, and Delivery of Pulmonary Rehabilitation. *Am J Respir Crit Care Med*. 2015;192(11):1373–1386. doi:10.1164/rccm.201510-1966ST
13. Holland AE, Mahal A, Hill CJ, et al. Home-based rehabilitation for COPD using minimal resources: a randomised, controlled equivalence trial. *Thorax*. 2017;72(1):57–65. doi:10.1136/thoraxjnl-2016-208514
14. Puente-Maestu L, S  n ML, S  n P, Cubillo JM, Mayol J, Casaburi R. Comparison of effects of supervised versus self-monitored training programmes in patients with chronic obstructive pulmonary disease. *Eur Respir J*. 2000;15(3):517–525. doi:10.1034/j.1399-3003.2000.15.15.x
15. G  ell MR, de Lucas P, G  ldiz JB, et al. Home vs hospital-based pulmonary rehabilitation for patients with chronic obstructive pulmonary disease: a Spanish multicenter trial. *Arch Bronconeumol*. 2008;44(10):512–518. doi:10.1157/13126830
16. Zanaboni P, Dinesen B, Hoaas H, et al. Long-term telerehabilitation or unsupervised training at home for patients with chronic obstructive pulmonary disease: a randomized controlled trial. *Am J Respir Crit Care Med*. 2023;207(7):865–875. doi:10.1164/rccm.202204-0643OC
17. Qiu J, Zhang YN, Chen J, et al. 宁夏回族自治区慢性阻塞性肺疾病流行病学调查分析 [Prevalence of chronic obstructive pulmonary disease in Ningxia Hui Autonomous Region of China]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2013;36(4):265–268. Chinese.
18. Deng N, Chen J, Liu Y, et al. Using mobile health technology to deliver a community-based closed-loop management system for chronic obstructive pulmonary disease patients in remote areas of China: development and prospective observational study. *JMIR mHealth uHealth*. 2020;8(11):e15978. doi:10.2196/15978
19. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med*. 2013;158(3):200–207. doi:10.7326/0003-4819-158-3-201302050-00583
20. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *J Pharmacol Pharmacother*. 2010;1(2):100–107. doi:10.4103/0976-500X.72352
21. Holland AE, Spruit MA, Troosters T, et al. An official European respiratory society/American thoracic society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J*. 2014;44(6):1428–1446. doi:10.1183/09031936.00150314
22. Matos Casano HA, Anjum F. Six-minute walk test. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing Copyright © 2023, StatPearls Publishing LLC.; 2023.
23. Bohannon RW, Crouch R. 1-minute sit-to-stand test: systematic review of procedures, performance, and clinimetric properties. *J Cardiopulm Rehabil Prev*. 2019;39(1):2–8. doi:10.1097/HCR.0000000000000336
24. Press VG, Gershon A, Blagev DP. Predicting COPD and lung function decline among a general population: too good to be true? *Chest*. 2020;157(3):481–483. doi:10.1016/j.chest.2019.11.028
25. Bokov P, Delclaux C. Interpretation and use of routine pulmonary function tests: spirometry, static lung volumes, lung diffusion, arterial blood gas, methacholine challenge test and 6-minute walk test. *Rev Med Interne*. 2016;37(2):100–110. doi:10.1016/j.revmed.2015.10.356
26. Ammous O, Feki W, Lofli T, et al. Inspiratory muscle training, with or without concomitant pulmonary rehabilitation, for chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev*. 2023;1(1):Cd013778.
27. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the medical research council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999;54(7):581–586. doi:10.1136/thx.54.7.581
28. Brat  s O, Gr  nning K, Forbord T. Psychometric properties of the hospital anxiety and depression scale and the general health questionnaire-20 in COPD inpatients. *Scand J Caring Sci*. 2014;28(2):413–420. doi:10.1111/scs.12054
29. Jones P, Harding G, Wiklund I, Berry P, Leidy N. Improving the process and outcome of care in COPD: development of a standardised assessment tool. *Prim Care Respir J*. 2009;18(3):208–215. doi:10.4104/pcrj.2009.00053

30. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD assessment test. *Eur Respir J*. 2009;34(3):648–654. doi:10.1183/09031936.00102509
31. Elsayy SB. Impact of chronic obstructive pulmonary disease severity on diaphragm muscle thickness. *Egypt J Chest Dis Tuberculosis*. 2017;66(4):587–592. doi:10.1016/j.ejcdt.2017.08.002
32. Gosselink R, De Vos J, van den Heuvel SP, Segers J, Decramer M, Kwakkel G. Impact of inspiratory muscle training in patients with COPD: what is the evidence? *Eur Respir J*. 2011;37(2):416–425. doi:10.1183/09031936.00031810
33. McDonald ML, Diaz AA, Ross JC, et al. Quantitative computed tomography measures of pectoralis muscle area and disease severity in chronic obstructive pulmonary disease. A cross-sectional study. *Ann Am Thorac Soc*. 2014;11(3):326–334. doi:10.1513/AnnalsATS.201307-229OC
34. Puhan MA, Chandra D, Mosenifar Z, et al. The minimal important difference of exercise tests in severe COPD. *Eur Respir J*. 2011;37(4):784–790. doi:10.1183/09031936.00063810
35. Holland AE, Hill CJ, Rasekaba T, Lee A, Naughton MT, McDonald CF. Updating the minimal important difference for six-minute walk distance in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil*. 2010;91(2):221–225. doi:10.1016/j.apmr.2009.10.017
36. Piaggio G, Elbourne DR, Pocock SJ, Evans SJ, Altman DG, CONSORT Group FT. Reporting of noninferiority and equivalence randomized trials: extension of the CONSORT 2010 statement. *JAMA*. 2012;308(24):2594–2604. doi:10.1001/jama.2012.87802
37. Giorgi FM, Ceraolo C, Mercatelli D. The R language: an engine for bioinformatics and data science. *Life*. 2022;12(5):648. doi:10.3390/life12050648
38. Keating A, Lee AL, Holland AE. Lack of perceived benefit and inadequate transport influence uptake and completion of pulmonary rehabilitation in people with chronic obstructive pulmonary disease: a qualitative study. *J Physiother*. 2011;57(3):183–190. doi:10.1016/S1836-9553(11)70040-6
39. Barberan-Garcia A, Vogiatzis I, Solberg HS, et al. Effects and barriers to deployment of telehealth wellness programs for chronic patients across 3 European countries. *Respir Med*. 2014;108(4):628–637. doi:10.1016/j.rmed.2013.12.006
40. Tabak M, Vollenbroek-Hutten MM, van der Valk PD, van der Palen J, Hermens HJ. A telerehabilitation intervention for patients with chronic obstructive pulmonary disease: a randomized controlled pilot trial. *Clin Rehabil*. 2014;28(6):582–591. doi:10.1177/0269215513512495
41. Johnston CL, Maxwell LJ, Alison JA. Establishing and delivering pulmonary rehabilitation in rural and remote settings: the opinions, attitudes and concerns of health care professionals. *Aust J Rural Health*. 2016;24(2):106–114. doi:10.1111/ajr.12202
42. Deng N, Sheng L, Jiang W, et al. A home-based pulmonary rehabilitation mHealth system to enhance the exercise capacity of patients with COPD: development and evaluation. *BMC Med Inform Decis Mak*. 2021;21(1):325. doi:10.1186/s12911-021-01694-5

International Journal of Chronic Obstructive Pulmonary Disease

Dovepress

Publish your work in this journal

The International Journal of COPD is an international, peer-reviewed journal of therapeutics and pharmacology focusing on concise rapid reporting of clinical studies and reviews in COPD. Special focus is given to the pathophysiological processes underlying the disease, intervention programs, patient focused education, and self management protocols. This journal is indexed on PubMed Central, MedLine and CAS. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-chronic-obstructive-pulmonary-disease-journal>