Global Health Research

EQUI-RESP-AFRICA Study Protocol

Respiratory Medicine and Pulmonary Rehabilitation Feasibility Study and Randomised Controlled Trial in Nigeria, South Africa and Cameroon

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LIST OF ABBREVIATIONS:

6-MWT	Six Minute Walk Test
ACCORD	Academic and Clinical Central Office for Research & Development - Joint office for The University of Edinburgh and Lothian Health Board
COPM	Canadian Occupational Performance Measure
CAT	COPD Assessment Test
CCQ	Clinical COPD Questionnaire
CHAI	Clinton Health Access Initiative
CI	Chief Investigator
COPD	Chronic Obstructive Pulmonary Disease
CRD	Chronic Respiratory Disease
CRQ	Chronic Respiratory Questionnaire
ESWT	Endurance Shuttle Walking Test
FEV1	Forced expiratory volume in first second
FVC	Forced Vital Capacity
GCP	Good Clinical Practice
HADS	Hospital Anxiety and Depression Scale
HICs	High Income Countries
HRQoL	Health-Related Quality of Life
ILD	Interstitial Lung Disease
ISWT	Incremental Shuttle Walking Test
LMICs	Low- and Middle-Income Countries
mMRC	Modified Medical Research Council
NMES	Neuromuscular Electrical Stimulation
PHQ-9	Patient Health Questionnaire-9
PIAT	Pulmonary Impairment After Tuberculosis
PR	Pulmonary Rehabilitation
RCT	Randomised Controlled Trial
SGRQ	St. George's Respiratory Questionnaire
UoL	University of Lagos
UoW	University of Witwatersrand

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1. SUMMARY

Chronic Respiratory Diseases (CRDs) are common disabling conditions worldwide with high prevalence, morbidity and mortality. More than half of the CRD patients live in low- and middle-income countries (LMICs) where resources for identifying the condition, understanding the disease status of individual patients, and overall management are often poor. CRDs in high-income countries (HICs) are dominated by chronic obstructive pulmonary disease (COPD) and asthma, whereas in LMICs, post-tuberculosis (TB) lung disorders, bronchiectasis, and other (often unidentified) respiratory conditions contribute to a significant proportion of CRDs. Pulmonary rehabilitation (PR) is an essential component of evidence-based clinical management guidelines for CRDs, though most of the evidence on PR is disease-specific and generated from HICs. A recent systematic review by the RESPIRE group, with whom we collaborate, revealed that 12 out of 13 studies suggested that PR for patients with CRDs in LMICs was an effective intervention, though the studies were typically at high risk of bias. This highlighted the need for further high-quality large-scale studies in LMICs to assess the enablers and barriers, effectiveness, components, and mode of delivery of PR for CRDs.[1]

In our feasibility study, we will assess the resource infrastructure, optimal components of the PR programme, relevant CRDs eligibility, and model of service delivery for providing PR in Nigeria, South Africa and Cameroon, and then conduct a pilot randomised controlled trial (RCT). We will also assess potential outcomes, including before and after intervention measurement of functional exercise capacity and relevant patient-reported outcomes. In qualitative interviews, we will explore the barriers and enablers, and stakeholders' opinions on implementing PR in each country.

We will recruit (Nigeria - 30, South Africa - 30 and Cameroon - 30) clinically eligible patients and provide them with 8 weeks of either a centre- or community-based PR incorporating components derived from global PR guidelines and informed by the prior RESPIRE's systematic review and adapted to be deliverable in a low-resource setting. We will assess the patients at baseline, end of the program (8 weeks) and then at 6 months follow up to assess sustainability. Moreover, along with the quantitative assessment of outcomes (functional exercise capacity, health-related quality of life, dyspnoea severity and other secondary parameters), we will conduct a qualitative interview with a purposive sample of patients, providers, and other health care professionals, e.g., GPs, pulmonologists, physiotherapists. We will synthesise our findings for conference presentations, peer review publications, and advocate for PR with stakeholders.

2. INTRODUCTION

2.1 BURDEN OF CRDs

Chronic Respiratory Diseases (CRDs) are long-term disorders of the airways and other structures of the lung[2] and may be associated with other systemic disorders[3,4]. CRDs are not yet curable; however, with a better understanding of the pathophysiology, effective management strategies have been developed for the care of people with CRDs[5]. Our group assessed the global prevalence of ever having asthma (9.8%, translating to 645.2 million people in people aged 5-69 years)[6], and chronic obstructive pulmonary disease (COPD) (10.3%, translating to 391.9 million people in adults aged 30-79 years)[7]. These are the commonest chronic conditions of the lung responsible for substantial mortality and morbidity globally[6,7]. In their report, the World Health Organisation included post-tuberculosis lung disorder, bronchiectasis and other (often undiagnosed) conditions under the umbrella of CRDs[8-11].

With better control of infectious diseases, CRDs are emerging as imposing a double burden in low- and middle-income countries (LMICs)[12]. More than half of patients with CRDs live in LMICs[5], where healthcare infrastructure and management systems are not optimal to address the challenge[13]. Despite these global concerns, CRDs are not a prioritised healthcare issue in LMICs[14], including in Nigeria, South Africa, and Cameroon, where the prevalence of CRDs is increasing substantially. For example, the overall prevalence of current wheezing among people aged 5-69 years was the highest in the African Region at 13.2% compared to the 10% in the Americas Region in 2019[6], while the pooled prevalence of COPD in sub-Saharan Africa showed an increasing trend, ranging from 1.7% to 24.8% compared to other regions[15-17].

2.2 REDUCING THE BURDEN OF CRDs THROUGH PULMONARY REHABILITATION

CRDs, particularly COPD, are associated with breathlessness and fatigue, which, together with muscle dysfunction/wasting, contribute to reduced exercise capacity and physical activity levels[2,18]. This functional impairment is associated with reduced Health-Related Quality-of-Life (HRQoL), increased exacerbation rates and mortality independent of the degree of airway obstruction[2,18-21]. The increasing disability, reduced productivity, and associated anxiety and depression result in social isolation and economic hardship for patients and their families[22,23]. Along with evidence-based pharmacotherapy, lifestyle

modification, regular physical activities, patient involvement and empowerment are the key strategies of CRD management[24-26].

Pulmonary rehabilitation (PR) is a guideline-recommended multidisciplinary and multifaceted intervention that reduces the burden of chronic respiratory symptoms for people with CRDs[27,28]. The evidence is particularly strong for COPD, but the evidence is also emerging for asthma[29], post-TB lung disorder[30,31], bronchiectasis[32-34], lung fibrosis[35-37], occupational lung diseases[38-40], and pulmonary arterial hypertension[41-43]. PR improves shortness of breath, exercise tolerance, muscular reconditioning, psychosocial state and HRQoL[28], and reduces the number[44] and duration of hospital admissions due to exacerbations[45].

2.3 THE PULMONARY REHABILITATION PROGRAMME

Although programmes vary, core components of PR are exercise training, occupational therapy, dietary intervention, psychosocial counselling, exacerbation management, patient education, and empowerment of patients to manage their condition following a thorough assessment. Physical exercise training is the cornerstone of PR and may include treadmill walking, stationary cycling, strength, functional training, balance/ flexibility training, general physical exercise for lower and upper extremities (gym exercises), supervised outdoor walks, and/or neuromuscular electrical stimulation[46-48] (see Table 5 for the core components of the PR programme).

Generally, PR is delivered by a multidisciplinary team of healthcare professionals within a centre. Nevertheless, individual programs tend to differ in overall organisation and content across centres due to regional variation in healthcare systems, different patient populations, available professional and space resources, and varying approaches. Notwithstanding, programs staffed by 4 or 5 team members, with a duration of 8–12 weeks, consisting of two or three sessions per week, have been reported to be effective.

Furthermore, the use of home/community -based PR programme has been shown to be equally effective, including programs that use minimal equipment[4,5,10,68]. The advantages of a home/community -based PR program include reduced hospital costs, shortened travel time and distance from hospital, requires minimal equipment and adaptable[9,10]. The potential challenge to utilising home/community -based PR programme in LMICs is that most patients may not fully adhere to the intervention prescribed for them[11,12].

Also, the use of telemedicine, a telecommunication technology to deliver medical interventions and information, is increasingly gaining grounds[13]. Specifically, telerehabilitation (an extension of telemedicine) involves the use of information technologies and communication strategies remotely to provide rehabilitation services to individuals at home or in community settings [14,15]. Telerehabilitation is fast becoming a more permanent fixture in CRDs management, with growing interest in how it compares clinically and

economically to traditional centre-based pulmonary rehabilitation. Beside the differences in the cost-effectiveness of these two approaches, which influence long-term sustainability, access, and outcomes, for patients, convenience, adherence, and perception of care quality may play equally significant roles.

Moreover, community-based telerehabilitation saves the requirement for additional skilled staff and infrastructure, promotes task shifting and capacity building with lower equipment requirement and its maintenance. It also reduces patient load in tertiary-level centres and greater utilisation of community-level and primary care infrastructure. Telerehabilitation is possible in communities of LMICs due to the potentially high penetration of internet-enabled smart mobile devices in most communities and availability of community health extension workers (CHEWs) who support National TB programs and other primary health care delivery services.

2.4 CHALLENGES TO IMPLEMENTING PULMONARY REHABILITATION

PR is a relatively new intervention in LMICs; most LMICs have few, if any structured PR services. It is a new concept for patients, clinicians, healthcare managers and policymakers, and accordingly, there are many barriers such as lack of awareness, poor acceptance, limited-service availability, scarce skilled manpower, and problems with the financial capability of the patient to take up the service. Recent stakeholder engagement meetings in NIHR RESPIRE Global Health Unit and NIHR EQUI-RESP Global Health Group recommended a range of initiatives to implement PR in LMICS[49]. These included providing an economically viable service, using public places for generalised exercise, and promotion via widespread media coverage. More generic policy recommendations relevant to respiratory disease included banning tobacco cultivation and strict embargoes on tobacco use. There is a lack of knowledge on PR among health care professionals, which deters the initiation of programmes at their institutions due in part to a lack of formal training to deliver PR effectively, also lack of a structured PR programme or guidelines for care and referral[50].

2.5 PREVIOUS WORK AND GAPS IN EVIDENCE

There is strong evidence from High-Income Countries (HICs) that PR is effective, although most of the studies are disease-specific. The few trials in LMICs generated weak evidence due to the high risk of bias in the included studies in a recently conducted systematic review. This review identified 13 trials from LMICs, of which 11 were at high risk of bias, and moderate risk in the other two studies[51]. Feasibility studies within RESPIRE Global Health Unit – conducted in Bangladesh (Khulna), India (Pune, and Vellore) and Malaysia - used different approaches to delivering PR in their diverse contexts. Despite the highlighted

barriers, in general, pre-post outcomes demonstrated benefits typically greater than the minimum clinically important difference (MCID). These previous pilot studies emphasise the importance of adapting the core programme to different diverse contexts and highlight the need for feasibility work in different contexts.

2.6 RATIONALE FOR FEASIBILITY STUDIES AND A RANDOMIZED CONTROLLED TRIAL OF PR IN AFRICAN COUNTRIES

There is thus a need for centres working in new contexts to assess the feasibility of delivering PR in their setting, to adapt accordingly, and to conduct a pilot randomised controlled trial (RCT) to assess effectiveness of the intervention. This protocol relates to a feasibility study, which will assess the deliverability of PR in Nigeria, South Africa and Cameroon, and a pilot RCT of PR in the three settings. Specific questions for the studies in the three different settings include:

- What is the acceptability and uptake of PR in these African settings?
- What are the practicalities of delivering PR with the resources available in these settings?
- What trainings and skills are required to set up and deliver the PR programme in these settings?
- What is the potential effectiveness of the PR programme in patients with CRDs (COPD and post TB lung diseases) occurring in different contexts?

We will build on the experiences of the NIHR RESPIRE Global Health Unit. Table 1 summarises learnings from previous RESPIRE feasibility studies.

Table 1: Learnings from previous RESPIRE feasibility studies

Centre; population	**PR centre**	**Model**	**Outcomes and findings**
Bangladesh, Khulna; Urban/rural	Community	Centre-PR interrupted by COVID pandemic. Home-PR was thus instituted.	Difficulty accessing Centre-PR is a major barrier. Patients in Home-PR felt well supported by regular calls, though therapists felt that remote support was not sufficient. Pre/post data from Home-PR (n=51) showed improvement >MCID in exercise capacity and quality of life.
India, Pune; Rural	Rural hospital	Rural Centre-PR in Vadu linked to the urban setting in Pune	Rural service not maintained because of the pandemic. Women struggled to attend the urban service

India, Vellore; Rural	Outreach centre	Community-based Centre-PR using peer-led trainers to support healthcare professionals (HCPs)	Groups had social benefits, but difficulty missing work to attend Centre-PR. Pre/post data showed improvement >MCID in exercise capacity
Malaysia, Kuala Lumpur; Urban	Tertiary hospital	Centre-based in central Kuala Lumpur	Access to the tertiary hospital centre was a major barrier: completion only 22%.

Taken with previous feasibility studies within the RESPIRE, the studies in EQUI-RESP-AFRICA will not only inform the local provision of PR, but add to the understanding of the feasibility of delivering PR in low-resource settings of the African continent, and help to identify common factors potentially generalisable to other LMICs.

2.7. STUDY TEAM AND PARTNERSHIPS

Table 2: Study management

*S*ub-contractual arrangements between partners and local sites where studies will be conducted are pending the advice of Edinburgh Research Office. We will amend existing Collaboration Agreements to delegate local activities to local academic partners, ensuring the requisite local site agreements with hospitals/clinics and all local approvals are in place.

Country	Name/Organisation	Role
Nigeria	Prof Obianuju Ozoh, University of Lagos	Principal investigator and leading pulmonologist
	Prof Jibril Mohammed, Bayero University Kano	Physiotherapist; Trainer for exercise-based assessment and PR delivery in Nigeria and across other sites (virtually)
	Prof Happiness Aweto, University of Lagos	Physiotherapist; supervising exercise-based PR delivery in the centre in Nigeria
	Dr. Temitope Fapohunda, University of Lagos	Pulmonologist; offer medical management and refer the right patients
	Two Respiratory physiotherapists: Lagos University Teaching Hospital	Conduct all exercise-based interventions for the patients undergoing PR in the centre
	One Respiratory physiologist: Lagos University Teaching Hospital	Conduct spirometry, exercise test, one RM and 6MWT assessment for all patients in the study
	One Clinical psychologist: Lagos University Teaching Hospital	Conduct psychological screening for all patients in the study and plan management (if applicable)

	One Occupational therapist: Lagos University Teaching Hospital	Assess for the occupational performance for all patients in the study and provide management at the centre PR (if applicable)
	One Dietician/nutritionist: Lagos University Teaching Hospital	Nutritional assessment of for all patients in the study and provide case by cases intervention
	One record officer: Lagos University Teaching Hospital	Responsible for randomising the participants in the centre or community arm of the study
	One Master of Science student trained on qualitative data collection: University of Lagos	Responsible for interviewing study participants during the qualitative studies
	One to three primary health centres in metropolitan Lagos will receive patients randomised for the community PR arm	The staff in these centres will be trained to provide the community-based PR under the supervision of the researchers above
South Africa	Ziyaad Dangor University of the Witwatersrand	Principal investigator
	Vicky Bailie University of the Witwatersrand	Principal scientist
	Alex Van Blydenstein University of the Witwatersrand	Pulmonologist; offer medical management and refer the right patients
	Ismail Kalla University of the Witwatersrand	Pulmonologist; offer medical management and refers the right patients
	Two Respiratory physiotherapist: Chris Hani Baragwanath Academic Hospital, Soweto	Conduct all exercise-based interventions for the patients
	One Respiratory physiologist: Chris Hani Baragwanath Academic Hospital, Soweto	Conduct spirometry, exercise test, one RM and 6MWT assessment for all patients in the study
	One Clinical psychologist: Chris Hani Baragwanath Academic Hospital, Soweto Chris Hani Baragwanath Academic Hospital, Soweto	Conduct psychological screening for all patients in the study and plan management (if applicable)
	One Occupational therapist: Chris Hani Baragwanath Academic Hospital, Soweto	Assess the occupational performance for all patients in the study and provide management at the centre PR (if applicable)

	One Dietician/nutritionist: Chris Hani Baragwanath Academic Hospital, Soweto	Nutritional assessment of for all patients in the study and provide case by cases intervention
	One record officer: Chris Hani Baragwanath Academic Hospital, Soweto	Responsible for randomising the participants in the centre or community arm of the study
	One Master of Science student trained on qualitative data collection: University of the Witwatersrand	Responsible for interviewing study participants during the qualitative studies
	One to three primary health centres in Soweto, South Africa will receive patients randomised for the community PR arm	The staff in these centres will be trained to provide the community-based PR under the supervision of the researchers above
Cameroon	Dr Yauba Saidu Clinton Health Access Initiative, Cameroon.	Principal Investigator — Provides overall scientific leadership, stakeholder engagement, and oversight for the Cameroon site
	Dr Michael Budzi Clinton Health Access Initiative, Cameroon.	Research Coordinator — Manages daily study operations, logistics, data processes, and reporting across the Cameroon site.
	Ismaila Karimu Faculty of Health Sciences, University of Buea.	PhD Student / Research Assistant — Supports data collection, patient follow-up, and implementation of PR activities
	Dr Arreyneke Nyenti	Co-PI, Oversees site operations.
	One Pulmonologist, Regional Hospital Limbe	Site Coordinator — Leads site-level implementation, patient evaluation, and coordination with hospital services.
	Two Physiotherapists: Regional Hospital Limbe	Physiotherapist — Conducts PR interventions and monitors patient progress.
	One Respiratory physiologist: Regional Hospital Limbe	Conduct spirometry, exercise test, one RM and 6MWT assessment for all patients in the study
	One Clinical psychologist: Regional Hospital Limbe	Conduct psychological screening for all patients in the study and plan management (if applicable)
	One Occupational therapist: Regional Hospital Limbe	Assess the occupational performance for all patients in the study and provide management at the centre PR (if applicable)
	One Dietician/nutritionist: Regional Hospital Limbe	Nutritional assessment of for all patients in the study and provide case by cases intervention
	One record officer: Regional Hospital Limbe	Responsible for randomising the participants in the centre or community arm of the study

	One Master of Science student trained on qualitative data collection: Faculty of Health Sciences, University of Buea	Responsible for interviewing study participants during the qualitative studies
	One to three (3) primary/community health centres in Limbe, Cameroon: Will receive patients randomised for the community PR arm	The staff in these centres will be trained to provide the community-based PR under the supervision of the researchers above
UK	Prof Igor Rudan, University of Edinburgh, UK	Co-lead EQUI-RESP-AFRICA
	Dr Richard Osei-Yeboah University of Edinburgh, Edinburgh, UK	Research Fellow
	Dr Davies Adeloye	Research Manager, training lead and coordinator between the Edinburgh-based team and the African partners, and the CEI NGOs.
	Prof Harry Campbell, University of Edinburgh, UK	Expert and consultant

3. STUDY OBJECTIVES

3.1 AIM

This study aims to assess the feasibility of delivering PR to people with CRDs (COPD and post TB lung disease) in Nigeria, South Africa and Cameroon, and to conduct a multi-country pilot RCT of PR to establish the effectiveness of the intervention.

3.2 OBJECTIVES

Objective 1: To explore stakeholder's (community leaders, patients, healthcare professionals, healthcare managers, and policymakers) attitudes toward PR as a part of CRD management

Objective 2: To determine the feasibility of delivering PR in study sites in Nigeria, South Africa and Cameroon specifically to inform the optimal resource infrastructure, components of the PR programme, relevant CRDs eligibility, and model of service delivery in providing PR.

Objective 3: To deliver a multi-country community-based and facility-based PR programme and conduct a pilot randomised controlled trial (RCT) with a 6-month follow-up to evaluate the effectiveness and completion rates of PR in adults with COPD and post-TB lung disease.
Objective 4: To identify and understand the barriers and facilitators to taking up PR in individuals with CRDs in these countries

3.3 ENDPOINTS

ENDPOINTS and KEY QUESTIONS FOR THESE FEASIBILITY STUDIES AND PILOT RCT AND HOW THE STUDIES WILL ANSWER THEM

This proposed research is a feasibility study, which will include a pilot (RCT) of PR. The key feasibility questions for the studies are shown in Table 2, while outcomes measured before and after the pilot PR RCT are in Tables 8 & 9. Answers to these questions are the endpoints of the feasibility studies and of the RCT.

Table 3: Key questions for the feasibility studies and RCT

Question	How the study will answer them
1. Feasibility of delivering PR in Nigeria, Cameroon, and South Africa	
What are the barriers to delivering PR?	Qualitative interviews with patients, providers and healthcare professionals.
What is the attendance and dropout rate of participants?	We will keep records of attendance and drop-out of participants with reasons (if provided)
How suitable are the adapted components and models of PR?	Staff logs about practical challenges, qualitative interviews with patients and healthcare providers will answer this.
What would be the optimal space, frequency, duration and time for delivering PR?	Qualitative interviews with providers and other healthcare professionals will answer this.
2. Potential outcomes	
How feasible is it to perform the measurements in low resource settings?	We will log any practical observations about undertaking the physiological measurements (e.g., equipment/space required) and questionnaire completion (e.g., clarity of questions/ability to complete)

What are the baseline measurements and magnitude of change?	We will use the spirometry, six- minute walk test (6MWT), Saint Georges Respiratory Questionnaire (SGRQ), COPD assessment Test (CAT), modified Medical Research Council Dyspnea scale (mMRC), Canadian occupational performance measure (COPM), psychological assessment using hospital anxiety and depression scale (HADS), peripheral muscle strength tests (using microfet dynamometer), nutritional assessment, laboratory assessment (liver function test, albumin, Hb, kidney), electrocardiography, medical status/medication use and functional test (short physical performance battery) as outcome measurement tools at 0 and 8 weeks (Baseline and at the end of PR).
How sustainable is the effect of PR to patient?	Follow-up assessment of patients at 6 months (from start of the PR intervention) will answer the sustainability of changes
3. Barriers and facilitators for the patient	
What proportion of clinically eligible patients agree to participate?	Recruitment logs will keep a record of COPD and post-TB lung disease patients identified in clinical practice as being potentially eligible for PR, whether they agreed to participate and subsequently attend
What are the challenges of attending at a PR centre and maintaining PR prescribed interventions at the community?	Attendance logs and qualitative interviews with patients and providers will answer this.
4. Stakeholder perceptions	
How acceptable is the PR? How may it be improved?	Qualitative interviews with patients, providers, healthcare professionals and other stakeholders will explore this
5. Effectiveness through the pilot RCT	
How effective is the PR in real-life setting on improving functional capacity, exercise tolerance, breathlessness, anxiety or depression?	Descriptive statistics of referral, attendance and completion rates with change in study outcomes. All data in the pilot RCT will be analysed by intention-to-treat analysis to assess non-inferiority of community-based versus facility-based models. Differences between groups for change over time will be analysed with linear mixed models. The relative risk of non-completion will be determined. We will conduct costing analysis and cost-effectiveness analysis.

4. STUDY DESIGN

The feasibility study will be a 'before and after' study with outcomes assessed at baseline, post-PR (8 weeks), and 6-month follow-up, and an embedded qualitative and quantitative process evaluation, including an RCT. See **Figure 1** for overview of the study design per country. For the non-RCT part of the study, we will employ a mixed-method approach – cross-sectional study and qualitative study using in-depth interviews.

Overview of study design per country. This study will recruit 30-50 cases in each of the three countries: Nigeria, South Africa, and Cameroon, who would benefit from PR because of their symptoms as per treatment guidelines.

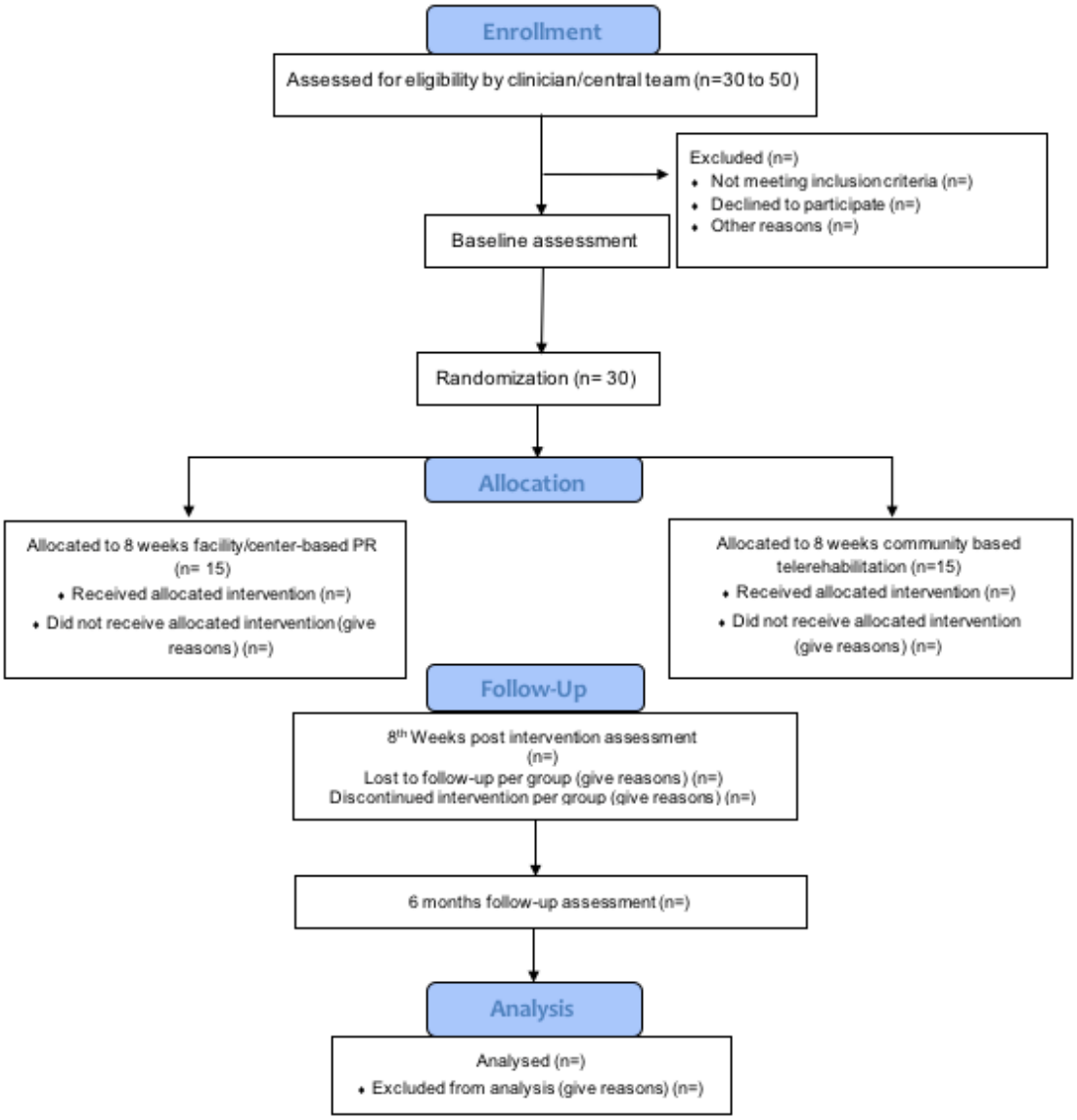

Figure 1: CONSORT flow diagram of the overview of the study design per site

4.1. STUDY TIMELINE

Figure 1: Proposed study timeline

Activities	MONTHS														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Protocol writing															
Sponsorship and Ethical approval															
Staff recruitment and training															
Study site preparation															
Participant recruitment															
Initial assessment															
PR intervention															
Post PR assessment															
Follow-up assessment															
Qualitative interviews															
Qualitative data analysis															
Quantitative data analysis															
Manuscript writing															
Dissemination															

4.2. STUDY SETTING

Whilst the feasibility studies will be conducted with the same overall protocol, there will be some minor variations highlighted in the table 3 below.

5. STUDY POPULATION

Community leaders, patients, healthcare professionals, healthcare managers, and policymakers who work and oversee the services at the participating hospitals, including policymakers from the Ministries of Health and representatives of professional organisations such as the Thoracic societies, physiotherapy societies.

For the pilot RCT, COPD and post TB lung disease patients will be determined by managing clinicians as candidates for pulmonary rehabilitation from the participating hospitals.

5.1.1.NUMBER OF PARTICIPANTS / SAMPLE SIZE

For the pilot RCT, no sample size calculation is required. A total of 30 patients from each of the three countries will be enrolled to receive PR in this study, which is a sufficient sample size to assess feasibility within the available resources. This will offer enough opportunities to observe the process, assess the feasibility and identify problems. Fifteen stakeholders will be included in in-depth interviews.

5.1.2 .INCLUSION CRITERIA

Patients:

i. Male and female adults (>= 18 years) with specified clinical diagnosis (typically by detailed clinical history [persistent symptoms for ≥6 months] plus spirometry and/or other available tests e.g., chest X-ray]
ii. Individuals with CRDs specifically COPD, asthma or post tuberculosis lung disorder,
iii. Patients with CRDs who have an indication for PR (specifically, these are patients with moderate to severe staged disease who present with reduced exercise/functional capacity, poor quality of life, high disease symptoms particularly dyspnea) and medically fit to undergo exercise training (which is to be determined by pre-exercise screening and field tests).
iv. Patients with CRDs attending regular follow-up in the respiratory clinics of the selected centres.
v. Patients who are willing and able to provide written or oral (audio recorded) informed consent

Healthcare professionals and other stakeholders:

i. All level (primary, secondary, and tertiary) of healthcare professionals, including doctors, nurses, physiotherapists, respiratory therapists, medical assistants, healthcare administrators, pulmonologists, and other formal practitioners working in primary, secondary, and tertiary care settings, who provide services to the patients who may potentially require PR.

ii. Relevant stakeholders including policymakers, religious leaders, sports leaders, pharmaceutical industry, social workers, managers, and hospital/practice owners.
iii. Willing and able to provide written or oral (audio recorded) informed consent.

5.1.3. EXCLUSION CRITERIA

Patients:

i. Patients with other significant chronic co-morbidities such as heart failure, ischemic heart disease, DM, confusion/dementia
ii. pregnant women
iii. Co-morbidity that is a contraindication to PR (e.g., unstable angina, aortic aneurysm, recent myocardial infarction, acute infection etc.)
iv. Significant cognitive or physical impairment preventing participation in PR A
v. Active pulmonary tuberculosis
vi. Patient with current or recent disease exacerbations
vii. Non-respiratory cause for symptoms (e.g., breathlessness due to heart failure, anaemia)
viii. Unable to participate in exercise (e.g., due to severe arthritis, or paralysis)
ix. Undertaken PR within one year
x. Unwilling to participate in the study
xi. Unable to give written or oral (audio recorded) informed consent

Healthcare professionals and other stakeholders:

i. Healthcare professionals who are not involved in the care of patients who require PR e.g., midwives
ii. Having a conflict of interest that may influence the outcome
iii. Unable and unwilling to give written or oral (audio recorded) informed consent

5.2. CO-ENROLMENT

We will not enroll patients already participating in another research study.

6. PARTICIPANT SELECTION AND ENROLMENT

6.1 IDENTIFYING PATIENTS FOR THE STUDY (RCT)

Physicians working at the selected healthcare facilities in the respective centers namely Lagos University Teaching Hospital in Lagos Nigeria, Chris Hani Baragwanath Academic

Hospital in South Africa and General Hospital in Limbe Region in Cameroon, who are part of the participants direct clinical care team (who have exclusive access to health information of the patients), will identify eligible patients as described in **the inclusion and exclusion criteria** (above), who demonstrate the clinical need for PR. The eligible patients will then be referred/ directed to contact the study team for potential recruitment to participate in the study in each of the centres. Upon arrival of the patients, a designated team of researcher assistants who will mainly comprise physiotherapists in each of the three centres will start by obtaining consent of the participant before enrolling them in the study. The recruitment team will also perform a second layer of screening based on the inclusion and exclusion criteria to ensure that the patient is suitable for the study and has no contraindications to exercise training before commissioning an initial assessment as part of the baseline data for the study. A blinded member of the study assessment team will then randomise each recruited participant into one of the two study arms.

Ethical clearance will be obtained a priori from the ethical committees of these centres. To ensure accurate patient identification based on our inclusion and exclusion criteria, as well as indications and contraindications, a one-day virtual training program will be organised for potential referring physicians by the PR study leads (Jibril Mohammed and Obianuju Ozoh) and the teams conducting initial assessment. The training of the research team will be documented in a training log (CR007-T17 Study Specific Training Record v3.0_1). This training will be funded by our designated training budget. **Table 3** shows organisations and centres that will be engaged in the identification and recruitment of patients.

Table 4: Study setting

Country	**Description of EQUI-RESP-AFRICA Partner Organisation**	**Centre-based PR venue**	**Community-based (telerehab) PR venue****
Nigeria	Lagos University Teaching Hospital, Lagos, Nigeria	The physiotherapy department of the Lagos University Teaching Hospital, Lagos, Nigeria	Purposively selected one to three community /primary health centers closest to where participants dwell

South Africa	Chris Hani Baragwanath Academic Hospital, Soweto, South Africa	The internal medicine and physiotherapy department of the Chris Hani Baragwanath Academic Hospital, Soweto, South Africa	Purposively selected one to three community /primary health centres closest to where participants dwell
Cameroon	The Clinton Health Access Initiative, Yaounde, Cameroon	The internal medicine and physiotherapy department of the Regional Hospital Limbe, Cameroon.	Purposively selected one to three community /primary health centres closest to where participants dwell

** Sub-contractual arrangements between partners and local sites where studies will be conducted are pending the advice of Edinburgh Research Office. We will amend existing Collaboration Agreements to delegate local activities to local academic partners, ensuring the requisite local site agreements with hospitals/clinics and all local approvals are in place.

Newly registered patients or previously registered patients (with COPD or post TB lung disease) who present with features that make them clinically eligible for PR as defined in guidelines[45], will be considered for this study. We will inform the healthcare professionals (usually a doctor) and other participants about PR and the feasibility study through separate information leaflets (Appendices). Dr Jibril Mohammed, who is a co-investigator on the EQUI-RESP-Africa project and is primarily affiliated with Bayero University Kano, Nigeria, has previously received training on PR delivery. He will train the healthcare professionals in the three countries on identifying eligible patients, outcome assessments (both initial and end tests) and prescribing patient-tailored physical exercise through a one-day virtual training for both centre-based PR and community-based (tele)PR interventions.

Table 5: Identification and recruitment of patients

Country	Organization with description	Facility based PR Settings	Community based PR Settings
Nigeria	University of Lagos will work in partnership with the named centres and the organisations working in the camps to provide medical care. The partner organisations will identify patients and refer interested patients to the PR project.	Centre-based PR will be provided at the physiotherapy departments of the Lagos University Teaching hospital in Lagos State	This will be facilitated by community health extension workers who work in PHC centres within the community where the patients live. This will be complemented with telerehabilitation.
South Africa	Patients visiting the Internal medicine outpatient clinics or admitted in the hospital with CRD will be recruited for the study.	PR will be provided at the physiotherapy department or respiratory clinic at the Chris Hani Baragwanath Academic Hospital	This will be facilitated by community health extension workers who work in PHC centres within the community where the patients live. This will be complemented by telerehabilitation
Cameroon	Patients visiting the outpatient departments or admitted in the medical or pulmonology wards, with a diagnosis of CRD (COPD, post TB fibrosis, bronchiectasis) will considered for inclusion in the study	PR will be provided at the physiotherapy department or respiratory clinic at the regional Hospital Limbe, Cameroon	This will be facilitated by community health extension workers who work in PHC centres within the community where the patients live. This will be complemented by telerehabilitation

To identify patients as participants for this study, we will follow these steps:

- In Nigeria, South Africa and Cameroon patients will rarely question a doctor's advice and we are concerned that this will put undue pressure on the patient to agree to participate. Potentially interested patients will therefore be referred via a flyer containing the contact details of the study team for appointment with a research assistant (RA) enabling them to have a more open conversation.
- The RAs will be trained on how to take informed consent. This training of the RAs will be documented in a training log (CR007-T17 Study Specific Training Record v3.0_1). After a potential participant – patient or control - has been identified as eligible by their physician, the RA will ensure that the participant understands what is written in the information leaflet and encourage the participant to ask questions about the implications of participating in the study. If the patient wishes to consider or consult with family or friends, the discussion will be postponed until at least 24 hours but not more than one week later when the patient is ready to make a decision. It will be

emphasised that participation is voluntary and the patient does not have to provide any reason for their decision.

- The purpose and importance of the study will be explained to both all patients regardless of the assigned group in the study. The expected commitment and benefits of participation to encourage their involvement will be clearly outlined.

By following these steps, we will identify and recruit patients and controls as participants for our RCT of PR.

6.2. RECRUITMENT OF PATIENTS FOR THE QUALITATIVE STUDIES

After completion of the PR programme, a purposive sample of participants will be invited by the research assistants (telephone call) to participate in one-to-one in-depth interviews. A purposive sampling strategy will be used to ensure that participants of different ages, gender, CRD conditions, and distance from the PR Rehabilitation Centre are recruited to reflect a broader context. This will be done using a consent process (see 6.4.2 and **Appendix 1, 2, 6A and 6B**- participant information sheet and consent form). Participation in PR places no obligation on the patient to participate in interviews. Recruitment will continue until data saturation is reached. We anticipate that there may be up to 15 patient interviews in each Centre.

6.3. IDENTIFYING HEALTHCARE PROFESSIONALS AND OTHER STAKEHOLDERS

The HCPs who were involved in delivering the PR (including the therapists in the PR team) will be interviewed to explore their views and opinions about the practicalities of delivering the service (see Appendix 5, 6C- participant information sheet and consent form). In addition, we will interview other stakeholders whose opinions and perceptions could facilitate or block the future implementation of PR in Nigeria, South Africa and Cameroon. For example, pulmonologists, primary care clinicians, healthcare administrators, as well as policymakers, religious leaders, sports leaders, pharmaceutical industry, and social workers, as appropriate in the different Centres. Recruitment of stakeholders will continue until data saturation is reached. We anticipate that there will be up to 15 interviews. Healthcare professionals and other stakeholders will be recruited purposively according to research questions and local context, considering the source of maximum information.

To identify healthcare professionals as participants, we will be following these steps to recruit healthcare professionals as participants for our qualitative aspect of this study, we will follow any of these steps:

- Define the criteria: Determine the specific characteristics and roles of healthcare professionals that are relevant to our study. For example, we will be interested in including doctors, nurses, physiotherapists, community health extension workers (and if available, occupational therapists, respiratory therapists, psychologists, dieticians, exercise physiologists) and other professionals involved in the delivery of pulmonary rehabilitation.
- Identify target healthcare facilities: Select healthcare facilities that offer or have the potential to refer patients for pulmonary rehabilitation. These may include hospitals, clinics, rehabilitation centres, or specialised respiratory care centres. These may be separate facilities from the hospital where the trial is being commissioned. Moreover, the list of these potential health facilities will be stated in the local ethics application of each country. The administrative permission from their centres will not be required.
- Seek recommendations: Consult with experts in the field or individuals familiar with the healthcare professionals involved in pulmonary rehabilitation by providing the contact details of the lead researcher in the study flyers (Participant Information Leaflet), both in electronic and paper forms, to recruit participants from the professional associations for their members to participate in the study. They can provide insights and recommend potential participants (snowball recruitment) who have experience and knowledge relevant to our study. The contact details of the lead researcher will be included in the Participant Information Leaflet to enable those interested to contact the PI for possible participation.
- Use professional networks: Utilise professional networks, conferences, or online communities specific to pulmonary rehabilitation or respiratory care, such as the professional association of nurses, physiotherapists, occupational therapists, etc., will be contacted via official email or telephone contact provided in order to reach out to potential participants. These platforms can connect us with healthcare professionals who have expertise in the area.
- Conduct purposive sampling: Utilise purposive sampling techniques to select participants who meet our specific criteria. This approach involves intentionally selecting individuals who have the desired expertise and experience in pulmonary rehabilitation.
- Recruit through discussion with the potential participants: Discuss with identified healthcare professionals, explaining the purpose and importance of our study. Clearly outline the expected commitment and benefits of participation to encourage their involvement.

6.4. CONSENTING PARTICIPANTS

Obtaining informed consent is a crucial and essential step in research. To ensure accuracy and compliance, we will approach the consent-taking process with the utmost caution, adhering to the recommended methods. We will provide comprehensive training to the designated consent taker(s) to ensure proficiency in conducting the consent process. The training of the consent taker(s) will be documented in a training log (CR007-T17 Study Specific Training Record v3.0_1). The following steps will be followed meticulously to ensure proper and ethical consent-taking:

- Preparation: Develop a thorough understanding of the study and the trial protocol and the information that needs to be conveyed to the potential participants. Prepare the informed consent document that includes all necessary details about the trial.
- Discussion: Engage in a comprehensive discussion with the potential participant, providing a clear explanation of the study's purpose, procedures, and their rights as a participant. Address any concerns or doubts they may have and ensure their understanding of the research.
- Voluntary Participation: Emphasise the voluntary nature of participation, Emphasising that they have the right to refuse or withdraw from the study or the trial at any point without repercussions.
- Documentation: If the potential participant agrees to participate, ensure they sign the informed consent document or provide verbal (oral) consent. Document their consent appropriately, providing them with a copy for their records.
- Ongoing communication: Maintain open and continuous communication with participants throughout the study, providing updates and addressing any new information or changes that may affect their continued participation.
- Ethical considerations: Adhere to ethical guidelines, regulations, and local laws governing the consent-taking process. Protect the rights, privacy, and confidentiality of participants throughout the trial.

By meticulously following these steps and ensuring proper training of consent takers, we will uphold the ethical principles of informed consent in the clinical trial process.

There are three potential outcomes from this discussion:

- agrees to participate in the study, written or audio-recorded oral informed consent will be taken, and the participant will be booked for their baseline assessment.
- If the patient does not want to participate in the study but does wish to attend PR, the research assistant will note any reason offered for not participating in the study and refer the patient to PR in the usual way (if available).

- If the patient does not want to participate in the study and does not want to accept PR, the research assistant will note any reason offered for not participating in the study and not accepting PR.

OPTIONS: All participants will be offered one of three options during the process of obtaining consent. The aim is to accommodate different preferences and ensure that participants are comfortable with their chosen method of providing consent:

i. Signed consent (paper)/ thumb print (accompanied by a witness signature): Participants will be given a copy of the Participant Information Sheet to consider in their own time. After reading the information, if they decide to participate, they will be asked to sign the paper consent form before enrolment, indicating their agreement to participate in the study. For participants who, due to low literacy, are unable to sign the consent form, the PIS will be read to the participant, and they will have the option of using a thumbprint or fingerprint on the consent form, in which case a witness signature must be provided by a legal representative of the participant.
ii. Verbal consent: In some cases, participants may agree to participate, but are unable to sign a paper document due to low literacy or may want to make further consultations with relatives, which is common in these countries. In such instances, the participants will be given a copy of the Information Sheet for someone to read out to them at their own time, or will have the Information Script read out to them by the research assistant. If they later decide to participate, verbal (oral) consent will be obtained remotely over the phone (Appendix 7). The remote consent over the telephone will be conducted only for participants who agree to participate after returning home. Their oral consent will be audio-recorded using a tape recorder. The participant will provide their name, age or month/year or year of birth and indicate they have been provided with information about the study and wish to participate. The participant will indicate understanding of their rights throughout the study, including the right to opt out without any implications. The tape recorder, such as a smartphone (that is compliant with UoE requirements) and the recordings will be transferred to a secure data storage location prior to transcription and analysis, and once the data is securely transmitted, the recordings will be deleted both on the device and the recycle bin by the research assistant concerned.

The consent-taking process for participants in the different categories of the study will be conducted as follows:

6.4.1 CONSENT PROCEDURE FOR PATIENTS PARTICIPATING IN THE RCT

- The patients who will be in the RCT study will be identified by their direct clinical care team, who will direct them to the research assistants, who will also ensure eligibility.
- The RAs are also responsible for providing a paper copy of the PISCF (Appendix 1, 2) for all the patients who are to participate in the RCT study to read.
- The consent of the patient will be obtained (using signed, verbal or remote consent options described above) after the participants have been satisfied with the PIS and are willing to participate in the study.
- Only specifically trained RAs in each of the centres will take the consent of the participants
- The participants will be given up to one week to consider participation in the RCT study between the period of receiving PIS and consent being taken
- For participants in the RCT, if they will be provided with the phone number of the PI, and also an independent authority in the institution (research/administration office staffer of the institution), should they have questions to ask about the study, whilst considering participation.

6.4.2 CONSENT PROCEDURE FOR PATIENTS PARTICIPATING IN THE STUDY INTERVIEWS

- The patients who will participate in the post RCT interviews will be purposively identified by the research assistant based on the study aims.
- The RAs will then contact the selected participants by telephone and explain the aims of the study interviews to them
- The participant who shows interest will then be invited to the centre and provided with the relevant paper version of the PISCF for the interviews (Appendix 3) to read
- The consent of the patient will then be obtained (using any of the three options above) after the participants report being satisfied with the PIS and are willing to participate in the study interview
- Only specifically trained RAs in each of the centres will take the consent of the participants
- The patient will be given up to one week to consider participation in the study interview between the period of receiving PIS and consent being taken
- For participants in the interview, the patient will be asked to contact the RAs, or the PI or an independent authority should they have questions to ask about this aspect of the study, whilst considering participation

6.4.3 CONSENT PROCEDURE FOR HCPs PARTICIPATING IN THE STUDY INTERVIEWS

- The HCPs that will participate in the post RCT interviews will be purposively identified by the central study teams in each country from the professional association of HCPs that are relevant to the topic area, namely, pulmonologists, doctors (family physicians), physiotherapists, and nurses.

- The executive council or secretariat of each professional association will be contacted to provide contact details (phone numbers) of their members working in the study area (for easy accessibility to attend the interview).
- The RAs will then contact the selected/eligible participants by telephone and explain the aims of the study interviews to them
- The participants who show interest to participate will be provided with the relevant PISCF for the interviews (Appendix 4) via email for them to read and have a good understanding of the study
- The consent of the participant will then be obtained (using any of the three options above) after the participants report being satisfied with the PIS and willing to participate in the study interview.
- Only specifically trained RAs in each of the centres will take consent from the participants
- The participants will be given up to two weeks to consider participation in the HCP interviews study between the period of receiving PIS and consent being taken
- The eligible HCPs will be provided with the phone number of the PI, and also an independent authority in the institution (research/administration office staffer of the institution), should they have questions to ask about the study whilst considering participation

6.5. WITHDRAWAL OF STUDY PARTICIPANTS

Participants are free to withdraw from the study at any point. For patients, if withdrawal occurs, the primary reason for withdrawal will be documented in the patient's case report form, if offered by the patient. For all participants, they will have the option of withdrawing from:

(i) all aspects of the trial, with no further contact, but the study will use the data collected up to that point

(ii) all aspects of the trial, including data collected up to that point, where it is possible to delete this data e.g., this data will not be used in the final data analysis. To safeguard rights, the minimum personally identifiable information possible will be retained e.g., consent form. Anonymised data will not be able to be withdrawn.
Those withdrawn can continue PR without participating in the study.

A change in clinical status, such that they are no longer eligible (e.g., a stroke, an injury, heart attack, or diagnosis of cancer affecting their ability to participate), would result in withdrawal from the PR, but not the study. Any physiological measures that were contraindicated or unacceptable to the patient would be omitted, but (if appropriate) we will request the completion of relevant outcome questionnaires.

7. RANDOMISED CONTROLLED TRIAL:

After providing consent, participants will be allocated to one of the PR groups (30 in Nigeria, 30 in South Africa and 30 in Cameroon), and provided with a schedule of three times weekly supervised PR sessions in the hospital or community centre for 8 weeks (i.e., a total of 24

sessions) The PR service will follow adapted guideline-recommended procedures[46,47,52]
Table 5 shows the components of the 8-week, (24-sessions) programme.

7.1. RANDOMISATION

Participants who meet our study eligibility criteria will be randomly allocated to either centre-based (PR) or Community-based (plus telerehabilitation) group using block randomisation (based on gender and disease condition). The randomisation sequence will be done using computer-generated numbers, and allocation of participants will be concealed by using consecutive numbered, sealed, and opaque envelopes. The randomisation will be performed by a third party (record officer at each of the study sites), who will be blinded to the study protocol.

7.2. BLINDING (SINGLE BLINDED PILOT RCT):

The outcome assessors will comprise different healthcare professionals, who will conduct the baseline and end of intervention assessment in this study. They will also be blinded to the group allocation and will not be involved in other procedural aspects of the study. However, due to the nature of the study intervention, clinicians and therapists providing treatment to the patients will not be blinded.

7.3. VARIABLES

INTERVENTION/EXPOSURE

Centre-based PR Programme: Participants in the intervention group will receive 24 supervised centre-based pulmonary rehabilitation. The application of treatments to each patient will be based on his/her pre-PR assessment status. The interventions will include physical exercise training (treadmill walking, stationary cycling, strength training. The participants will also receive group general physical exercise for lower and upper extremities, supervised outdoor walks, balance/flexibility exercises, group educational sessions and group relaxation training (and neuromuscular electrical stimulation, if applicable). For those who have an indication (and if applicable), occupational therapy, dietary intervention, psychosocial counselling, and exacerbation management will be offered (see Table 2 for details).

Community-based PR: The participants in the community-based PR groups will also be prescribed a patient tailored pulmonary rehabilitation. These exercise interventions will be delivered by trained community health extension workers using simple and affordable equipment in the community. The interventions will include endurance exercise training, strength training, physical exercise for lower and upper extremities, supervised outdoor walks,

balance/flexibility exercises, group educational sessions and group relaxation training. The trained community extension workers will be supervised by therapists via telerehabilitation. For those who have indication, occupational therapy, dietary intervention, psychosocial counselling, and exacerbation management will be provided at the community centre by the relevant professionals.

OUTCOMES

For this study, the following outcomes of patients with CRDs will be collected-

i. Patient characteristics: gender, age and body mass index (BMI)
ii. Disease-related data: spirometry, laboratory assessment
iii. Peripheral muscle function: isokinetic quadriceps muscle strength and muscle endurance as measured with the 1RM or dynamometer –
iv. Patient-reported outcome measures (PROMs): St. George's Respiratory Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS), Canadian Occupational Performance Measure (COPM), COPD Assessment Test (CAT) and modified Medical Research Council (mMRC) dyspnea scale.

Primary Outcomes: Exercise/functional capacity: 6-minute walk test and clinical status.

Secondary outcomes:

PROMs: HADS, SGRQ, isokinetic quadriceps muscle strength, spirometry (FEV_1), COPM and mMRC dyspnea scale and CAT.

The 6-minute walk distance was considered the primary outcome in the study based on earlier recommendations [16,17].

8. STUDY ASSESSMENTS

Table 6: Study assessments

Assessment	Screening	Day 1 Baseline	Day 2 Baseline	60 days	180 days
Assessment of Eligibility Criteria	X	X			
Written informed consent		X			
Demographic data, contact details,		X			
Study questionnaires administration (CAT, mMRC, SGRQ, HADS, COPM)		X		X	X
Anthropometric measures (weight and height)		X		X	X
Spirometry/		X		X	X

Functional exercise capacity (6MWT, sit-to-stand test)			X	X	X
Cycle test (to determine exercise parameters)			X	X	X
Peripheral muscle function (1RM)			X	X	X

8.1 LONG TERM FOLLOW UP ASSESSMENTS

We will conduct an assessment at 6 months of the study period to find the long-term effect of PR. This assessment will encompass all the elements covered in the evaluation conducted at the end of the 2-month intervention period. By comparing these components, we aim to ascertain the sustainability of the effects after the intervention. Before this long-term follow-up assessment, a baseline assessment will be conducted, and an assessment will also be carried out at the conclusion of the intervention. In total, this study has a schedule of three assessments, taking place at 0 months, 2 months, and 6 months (follow-up).

8.2. TRANSCRIPTION AND TRANSLATION

8.2.1 TRANSLATION

Translation Services

The study documents will be in English in Nigeria, South Africa, and Cameroon without translations.

9. DATA COLLECTION

9.1 QUANTITATIVE DATA COLLECTION

DATA COLLECTION AND QUALITY CONTROL METHODS:

Participants for the RCT study will be recruited by a team of qualified healthcare professionals (pulmonologists, nurses and physiotherapists) specially trained as research assistants for the study in each centre. The same group of research assistants will also partake in conducting the baseline, end of intervention and follow-up assessment for all participants.

For each participant, all data collection will be scheduled at a convenient time stated by the participants. The data collection for all participants, irrespective of study arm, will take place at the PR centre where recruitment was done in each of the respective study sites during the

working hours of the centre. The data will be collected by trained research assistants/team members as indicated in Table 2 (above).

We envisage that the baseline assessments will be completed within 5 hours across two days (each visit lasting between 2 to 3 hours). For the end assessment and follow-up, this will be completed within 3 hours within a day (See Table 7A for details). Data will be directly entered into a tablet provided, containing the electronic version of all the study questionnaires and tools (Appendix 8, 9, 10, 11, 12 & 14). The tablet will not be connected to any server.

Table 7A: Components of the 8-week (24 sessions) Centre-based PR programme

Component	Description	Participant time commitment	Timeline
Optimisation of pharmacotherapy	All participants: The study physician will undertake a review of the medications and medical management of each participant by interacting with them, with the aim of deciding whether the current line of management is optimal or whether there is a need to make a revision. This shall be done within any local prescribing constraints. Optimisation of pharmacotherapy involves review of current respiratory medications and assessment of inhaler technique using a standard checklist. This involves education regarding dose timing, adherence and recognition of side effects. Medication regimens will not be altered by the research team. Any clinical concerns identified will be referred to the participant's usual physician.	15 minutes per session	Time-point: 0 week, 4th week and 8th week
Baseline, assessment	**All participants:** Trained healthcare professionals (physiotherapists, occupational therapists, psychologists, dieticians, respiratory physiologists and laboratory scientists) at each of the centres will undertake a thorough clinical assessment for all patients using the study tools and assessment tests mentioned above. Measurements will include	5 hours across two days. 3 hours on Day 1 for the measurements as follows: exercise/functional capacity/6 MWT (30 mins), study questionnaires in	Time-point: 0 week, (Day and 2)

	exercise/functional capacity, symptom score, body composition, spirometry, quadricep muscle strength. All participants will have psychological, nutritional and occupational assessment by relevant professionals	terms of breathlessness (mMRC) health status (CAT), Quality of life (SGRQ), psychological (HADS), nutritional (SGA) and occupational (COPM) administration (1 hour 30 mins), quadricep muscle strength (30 mins), Rest interval (30 mins) 2 hours on Day 2 as follows: Spirometry (1 hour), Anthropometric measurements (30 mins)	
Prescription of exercise training and other support	**All participants:** Tailored PR interventions comprising endurance exercise training and education will be prescribed by trained therapists based on each patient's pre-assessment status during the 6MWT or a cycle test (conducted using heart rate, O_2 saturation and fatigue as thresholds [breathlessness score of 5-6 on the 10-point modified Borg scale]). Psychological, nutritional and occupational treatment will be provided based on individual needs (by telerehab).	Not applicable	Time-point: 0 week, and revised on a weekly basis
Supervision and support	**All participants:** Thrice weekly 2 hour supervised group sessions for 8 weeks (24 sessions) including exercise, motivation, and education at the hospital or community centre	2 hours/session, thrice weekly	Time-point: 0 week to 8th week

Aerobic / Endurance exercise	**Centre-based PR participants**: 30 mins supervised exercise training (3 times a week) Aerobic exercise: conducted at 75% of peak work rate established with 6 MWT or cycle test. Depending on the facilities available, aerobic training will be delivered on a treadmill or stationary cycle ergometer. Intensity of training will progress weekly by 5–10% of initial workload targeting a load that triggers a breathlessness score of 5-6 on the 10-point modified Borg scale. Endurance exercise training will be done using interval training modes (either interval intensive and/or interval extensive on alternate days of the week). As a general rule, we will consider: Cycle ergometer or Treadmill walk: (Interval intensive training =12*1 (with 1 min rest interval; Interval Extensive training=5*4 (with 1 min rest). **Warm-up**: At least 2 minutes before prescribed exercise using 50% of prescribe endurance training peak work rate	30 mins of exercise training /session, thrice weekly	Time-point: 0 week to 8th week
	Community-based PR participants: The participants will receive a 1 hour CHEW supervised aerobic exercise such as over ground brisk walking conducted at 75% of peak work rate determined from the 6 MWT. Step bench exercises will also be administered using similar exercise parameters (interval mode) under the supervision (3 times a week)	30 mins of exercise training /session, thrice weekly	Time-point: 0 week to 8th week
Strengthening exercise	**Centre-based PR participants**: Resistance training, prescribed at 70% of assessed maximal muscle strength per muscle group (quadriceps, biceps, triceps,	30 mins of strength training /session, thrice weekly	Time-point: 0 week to 8th week

	trunk, deltoid and calf muscles). We will use standard equipment (e.g. quadriceps chair; multi-gym [chest press, leg press, shoulder press, bicep curls, quadricep curls and other machines], dumbbells weights). Each strength training session will comprise a warm up (at 50% of prescribed loading for 8 repetitions). This is then followed three sets of the prescribed loading of 8 repetitions each, with up to 2 minutes of rest in between sets.		
	Community-based PR participants: Resistance training, prescribed at 70% of assessed maximal muscle strength per muscle group (quadriceps, biceps, triceps, trunk, deltoid and calf muscles). We will use available and improvised equipment (weights). Each strength training session will comprise a warm up (at 50% of prescribed loading for 8 repetitions). This is then followed three sets of the prescribed loading of 8 repetitions each with up to 2 minutes of rest in between sets.	30 mins of strength training /session, thrice weekly	Time-point: 0 week to 8th week
Motivating physical activity	**Centre-based PR participants**: Promotion of active lifestyle using *Group session* led by PR staff (physiotherapist), using behaviour change techniques to encourage an active lifestyle, supported by resources in the PuRe pack*. This will be a 30 mins of group outdoor therapist supervised walks in designated areas within the center/facility	30 mins group promotion of active lifestyle /session, thrice weekly	Time-point: 0 week to 8th week
	Community-based PR participants: 30 mins of group outdoor activities by community health extension worker supervised walks in designated areas within the community	30 mins of group outdoor/session, thrice weekly	Time-point: 0 week to 8th week

Mindfulness	**Centre-based PR participants**: Relaxation training will be offered Group *session* led by PR staff (physiotherapist), using different relaxation exercise techniques in groups	30 mins of group mindfulness/relaxation sessions, once weekly	Time-point: 0 week to 8th week
Occupational therapy	**Centre-based PR participants**: Energy conservation techniques will be taught to participants using Group *session* led by PR staff (occupational therapist), using different approaches	30 mins of occupational therapy intervention sessions once weekly	Time-point: 0 week to 8th week
Educational intervention	**Centre-based PR participants.** Educational sessions with Detailed education-based information will be provided in allocated teachings during PR sessions. One-to-one education will cover topics flexibly according to the concerns/questions of the patients. The therapist will log topics discussed to ensure all are covered. Topics will be reinforced by resources in the 'PuRe pack'* **The** education sessions will last for about 30 minutes audio-visual and hands-on training provided by trained healthcare professionals, depending on the topic. This may include inhaler technique, e.g., https://www.youtube.com/watch?v=bRhZz-q-u-s&ab_channel=HamiltonHealthSciences **Specific educational topics delivered during PR sessions and following above approach:** • Inhaler technique checked • Breathing techniques taught one-to-one • Coping strategies reinforced • Disease appropriate self-management explained one-to-one and personalised plan provided	30 mins of group educational intervention sessions once weekly	Time-point: 0 week to 8th week

	• General nutritional advice in group sessions and tailored one-to-one advice • Smoking/biomass as risk factors for CRD explained in groups and one-to-one. • Current smokers offered cessation support according to local services (trained nurse) • Group advice on managing psychological impact of CRD reinforced one-to-one **Community based PR participants**: A similar training will be provided by trained community health extension workers, with additional support by telehealth means (e.g. videos)		
Nutritional intervention	**Centre-based PR participants**: This will be provided by a nutritionist for patients requiring such intervention by means of physical assessment of their nutritional status needs and providing advice and nutritional prescription, as appropriate	30 mins of nutritional intervention/review once a week for those requiring the intervention	Timepoint: 0 week to 8th week
Psychological support	**Centre-based PR participants:** Cognitive Behaviour Therapy (CBT) for the participants if needed, will be provided by a psychologist in person.	30 mins once a week of psychological support for those requiring the intervention	Timepoint: 0 week to 8th week
Individual smoking cessation support	**All participants**: Assessment of dependency and structured cessation programme using the 5 A's principle. These interventions will be provided by telehealth means (e.g. videos)	Telehealth resources will be made available for those requiring the intervention to use at their own time	Timepoint: 0 week to 8th week
Post-PR assessment (and follow-up assessment)	**All participants:** The same trained healthcare professionals at each of the centres will undertake the post-PR clinical assessment as was done during the baseline assessment.	3 hours for the measurements as follows: exercise/functional capacity/6 MWT (30 mins), study	Timepoint: 8th week and 24th week

		questionnaires in terms of breathlessness (mMRC) health status (CAT), Quality of life (SGRQ), psychological (HADS), nutritional (SGA) and occupational (COPM) administration (1 hour), quadricep muscle strength (30 mins), Spirometry (30 mis), Anthropometric measurements (30 mins),	

* *Personalised resource packs (Pulmonary Rehabilitation 'PuRe pack') will be customised based on an individual's specific disease, its severity, prescribed exercises, and relevant educational materials. These packs will be accessible online or through a USB stick, compatible with TVs or computers. The PuRe pack will consist of video, audio, and written resources related to CRD, PR exercise demonstrations, and educational content support. With the individual's consent, therapists will create a video clip featuring the person performing key exercises, which will be included in their pack. This personalised approach aims to provide tailored advice and enhance motivation. The development of the PuRe pack will take place after conducting baseline assessments of patients. It will be exclusively designed based on the specific needs of individual patients during the assessment, exercise training, and education program. Typically, a PuRe pack will include various elements such as*

- *A video of the patient's 6-minute walk test, their completed exercises, discussions with the therapist, demonstrations of drug delivery or other manoeuvres,*
- *An exercise booklet, and a booklet containing information about the disease, among other components*
- *Any individual recommendation tailored to the patient's needs*

The participant-facing content for these personalized resource packs (e.g. exercise booklet, booklet about disease and any other relevant video/audio/written educational content) will be provided to the sponsor and to ethics at a later date as a study amendment.

INITIAL AND END ASSESSMENT

Before commencing PR (at week 0), all enrolled RCT participants will be assessed by spirometry and COPD Assessment Test (CAT), Six Minute Walk Test (6MWT), Saint George Respiratory Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS), Canadian Occupational Performance Measures (COPM), and modified Medical Research Council (mMRC) dyspnoea scale. Laboratory records, dietary assessment, body composition, occupational therapy assessment and psychological status will also be assessed. These are all standard assessments recommended by PR guidelines. The pharmacotherapy will be optimised in line with relevant disease-specific guidelines, and the patient advised accordingly. Healthcare professionals with relevant respiratory expertise will be trained to perform the assessment and provide clinical advice.

STUDY QUANTITATIVE OUTCOMES

PRIMARY AND SECONDARY OUTCOMES

We will include a number of quantitative outcomes in the feasibility study and the randomised controlled trial in order to assess the change after PR. These will be assessed at baseline, post-PR and 6-months. See Tables 8 & 9 for details.

Table 2: Primary outcomes

Domain	Test	Description
Functional Exercise Capacity	Six-minute Walk Test (**6MWT**)	The 6-min walk test (6MWT) is a simple and standardised test that is used to assess functional capacity in patients with COPD[57]. The test involves walking as far as possible for six minutes on a flat, hard surface.

Table 9: Secondary outcomes

Breathless-ness	Modified MRC Dyspnoea score (**mMRC**)	The mMRC Dyspnea Scale quantifies disability attributable to breathlessness on a scale of 0 to 4 (see Appendix 3). It is widely used for assessing perceptions of 41dyspnea in patients with respiratory diseases[59]. We will develop a French version of the mMRC with back-translation, and Yoruba version, if necessary.

Health-status	https://www.catestonline.org/patient-site-test-page-english.html	The CAT is a questionnaire assessing the impact of respiratory disease on health status on a scale of 0 to 40 (see **Appendix**). It is a quick and easy test for patients to complete[58]. It is available in English and Yoruba for Nigeria, English for South Africa, and French for Cameroon.
Psychological morbidity	Hospital Anxiety and Depression Scale (**HADs**)	The HADS measures symptoms of anxiety (HADS Anxiety) and depression (HADS Depression) in a combined questionnaire (see Appendix 3). HADS Anxiety and HADS Depression have acceptable internal consistency[60] and have been validated for use in CRD[61,62]. We will use the authorised translated version of HADS (GL Assessment Ltd. Email: permissions@gl-assessment.co.uk)
Health related quality of Life	Saint George Respiratory Questionnaire (SGRQ)	The St. George's Respiratory Questionnaire (SGRQ) is a tool used to assess the impact of respiratory diseases, particularly COPD (Chronic Obstructive Pulmonary Disease), on a patient's quality of life. It's a self-administered questionnaire that measures how symptoms, activity limitations, and social and emotional impacts of the disease affect the individual
Peripheral muscle strength	1 repetition maximum, microfet/dynamometer	A 1 repetition maximum (1RM) is the maximum amount of weight an individual can lift for a single, complete repetition of a specific exercise. It's a common measure of strength used in fitness and athletic training to gauge an individual's current strength level and to design personalised workout programs. The handheld dynamometry is an objective method in detecting **minimum muscle strength change**, which has an impact on the physical function in patients
Functional test	Short physical performance battery (SPPB)	Comprises the sit to stand test, 4m gait speed test, and balance test to assess the functional fitness of individuals
Nutritional state	Subjective Global Assessment (SGA),	Subjective Global Assessment (SGA), which uses a patient's medical history and physical exam, the Malnutrition Universal Screening Tool (MUST), which is a five-step screening for adults based on BMI, weight loss, and acute illness, and the Mini Nutritional Assessment (MNA)

Occupational performance	Canadian Occupational Performance Measure (COPM)	The Canadian Occupational Performance Measure (COPM) is the most widely used outcome measure in occupational therapy in the world. The COPM is a client-centred outcome measure for individuals to identify and prioritise everyday issues that restrict their participation in everyday living.
Anthropometric measures	Height, weight and Body mass index measures	-The height and weight will be measured using standard equipment and protocol. BMI will be calculated using the Weight *height^2 formular.

OTHER QUANTITATIVE PROCESS DATA

We will also collect data on the percentage of patients assessed for eligibility, fulfilling inclusion criteria, and ultimately included (of the total number identified), the number of missing sessions, the rate of intervention dropout and the rate of study withdrawal.

9.2. QUALITATIVE DATA COLLECTION

Patients

One-to-one interviews (usually face-to-face at the PR centre, by telephone call using MS Teams, where available, if more convenient and acceptable to the participant) will be conducted by the Masters students in the EQUI-RESP Africa project who will be trained in each of the participating country. This will be done with up to 15 patient participants for each country after completion of the PR at a time convenient to the participant and at a suitable venue. The discussion, which will be digitally audio-recorded using a smartphone compliant with UoE requirements and transcribed verbatim in the local language by experienced transcribers (members of the research team) and will last about 45 minutes and cover the following topics. The topic guide for the interview as provided in Appendix 6 is provided below:

- Acceptability of PR combining out-patient classes and home-based exercise
- What benefits (if any) did they notice from the PR?
- What challenges and barriers did they face, and how did they overcome them?
- How did they feel about PR before and after participating in the programme?
- What changes would they recommend for future rehabilitation?
- Would they recommend PR to other CRD patients in their community?

Healthcare professionals, managers and other stakeholders

One-to-one interviews (either face-to-face at the professional's place of work or by telephone/video call using MS Teams if available on the mobile phone according to convenience and preference of the participant) will be conducted with the members of the PR team; and up to 15 additional interviews with professionals, health service managers, policymakers and other stakeholders. Interviews will be arranged at a time convenient to the participant. The discussion, which will be digitally audio-recorded and transcribed verbatim in local languages, will last about 30-45 minutes and cover the topics detailed below:
The interviews with the PR providers:

- Did they feel the PR was feasible/effective and why?
- What factors/strategies made the PR more/less feasible/effective?
- What were the challenges and barriers they faced, how did they overcome?
- Did they feel able to offer support to the patients?
- What were the practical advantages /disadvantages?
- What changes would they make to future rehabilitation?

The interviews with healthcare professionals, managers and other stakeholders:

- What do they think about the effectiveness of PR?
- How do they consider PR as management for CRD?
- Would they refer a patient to a PR Centre?
- What are the barriers to referral to a PR Centre?
- How could they contribute to promoting PR?

9.3. Source Data Documentation

Data from the observation will first be documented in the printed paper copy case report form Appendix 14 which will be entered in the electronic worksheet (Excel) later on. Other source data to be documented will include all the is the data collected during the assessments (at baseline and at the end and follow-up) as indicated in Tables 8 and 9, the interview recordings, the interview transcriptions, and the consent forms.

9.4. Case Report Forms

We developed a case report form where the relevant clinical information will be recorded on a printed sheet (see **Appendix 14**).

10. DATA MANAGEMENT

10.1. PERSONAL DATA

The participants will be recruited from the sources as shown in the table below, and the assessments will be performed within the designated Centre. These assessments will be conducted for clinical purposes, specifically to provide PR. The assessments will include recording personal information such as names, addresses, and contact details, which are necessary for the provision of PR. It's important to note that these personal data will be treated as part of the clinical record and will be securely stored according to standard clinical practices. They will not be disclosed or shared outside of the practice for any reason. It is essential to clarify that the clinical record refers specifically to the relevant data required for providing PR and does not encompass the patient's entire medical record.

Personally identifiable data (for patients)

- Name:
- Date of birth
- Age and sex
- Medical records (data relevant for PR)
- Present and permanent address, including postal address
- Contact number: (Mobile or land phone)
- Occupation
- Name, address, contact number, postal and email address of a person for emergency contact
- Financial status
- Education level
- Consent form
- Audio recordings of verbal consent
- Audio/video recordings of interviews

Personally identifiable data (for healthcare professionals)

- Name
- Contact details (email and telephone/mobile number)
- Age and sex
- Occupation/Exact role in healthcare
- Workplace

- consent form
- Audio recordings of verbal consent
- Audio/video recordings of the interview

Table 10: Number of recruited participants at different centres

	N	Source of recruitment	Centre
Nigeria	30-50	Lagos University Teaching Hospital, Lagos, Nigeria	Lagos University Teaching Hospital, Lagos, Nigeria
South Africa	30	Chris Hani Baragwanath Academic Hospital	Department of internal medicine and physiotherapy
Cameroon	30	Regional Hospital Limbe.	The internal medicine and physiotherapy department

Paper consent forms will be kept in a locked filing cabinet located in the office of the National Principal Investigator at each partnering institution (UoL, UoW, and CHAI). Access to these forms will be restricted to the PI or the designated individual assigned by the PI. It is important to retain these documents for a minimum period of 3 years following the end of the study. Audio recordings of verbal consent will be stored in encrypted files on password-protected computers on institutional servers at UoL, UoW, and CHAI respectively. Audio recordings of verbal consent will be stored for a minimum of 3 years following the end of the study. After this time, paper consent forms will be shredded and disposed in secure bins, and audio recorded verbal consent will be deleted.

The electronic data collected for the study will be de-identified by a study ID and stored in a separate secured computer locally at the partner institution. The code identifying that render the de-identified data will be stored in a separate container at the partner institution. The following steps will be followed during the de-identification process:

(a) conduct a thorough review of the data to ensure any personally identifiable information (PII) such as names, addresses, or social security numbers are removed;
(b) develop a plan for de-identifying the data, which may involve the removal of PII or substitution with unique identifiers;
(c) test the de-identification process to ensure accuracy and consistency;
(d) document the de-identification process and incorporate it into the data handling plan.

The electronic data will be stored at UoL, UoW, and CHAI, which are the respective addresses mentioned below. To ensure security, the collected data will be stored in encrypted files on password-protected computers on institutional servers at UoL, UoW, and CHAI.

For data collected on recording devices (e.g. Dictaphone, smartphone), we will follow the procedure below:

i. All data will be stored on a secure smartphone or Dictaphone recording device that is password-protected. The device will only be accessible to authorised personnel.
ii. To transfer the data from the device to secure storage, the following steps will be followed:
    a. Connect the device to a secure computer with a USB cable.
    b. Copy the data from the device to the computer.
    c. Verify that the data has been transferred accurately.
    d. Store the data on a secure institutional server with access restricted to authorised personnel.
    e. Data stored in the device will be deleted once the data is transferred to the computer.

At the end of the study, anonymised data will be transferred from Nigeria, South Africa and Cameroon to University of Edinburgh in the UK via a secure, password-protected online platform using DataSync and then stored on DataStore a secure, password-protected data storage at University of Edinburgh for a minimum of 3 years following the end of the study. The archived de-identified data might be used for possible secondary analysis in the future. Participants will be asked to give their consent to share their de-identified data with other investigators for future use.

Qualitative interviews will be recorded on an encrypted digital recorder or using MS Teams and transferred securely to each institutional platforms to be accessed by a local language-speaking transcriber who is one of the research team members employed by the country-specific organisations. If any unwanted personal information is revealed accidentally during the interviews, it will be removed from the transcripts to maintain participant confidentiality. The audio recording will be destroyed once the transcription is complete and cross-checked. Transcripts will be anonymised and checked by the qualitative researchers who are native language speakers before the analysis and report. The interview transcripts for healthcare providers, healthcare professionals and other stakeholders will be kept in encrypted files on the password-protected computer at UoL (Nigeria), UoW (South Africa), and CHAI (Cameroon), at the addresses above. Access to this data will be limited to members of the research team at each participating centre. The data will be stored for at least three years after the end of the study.

10.2. Data Information Flow

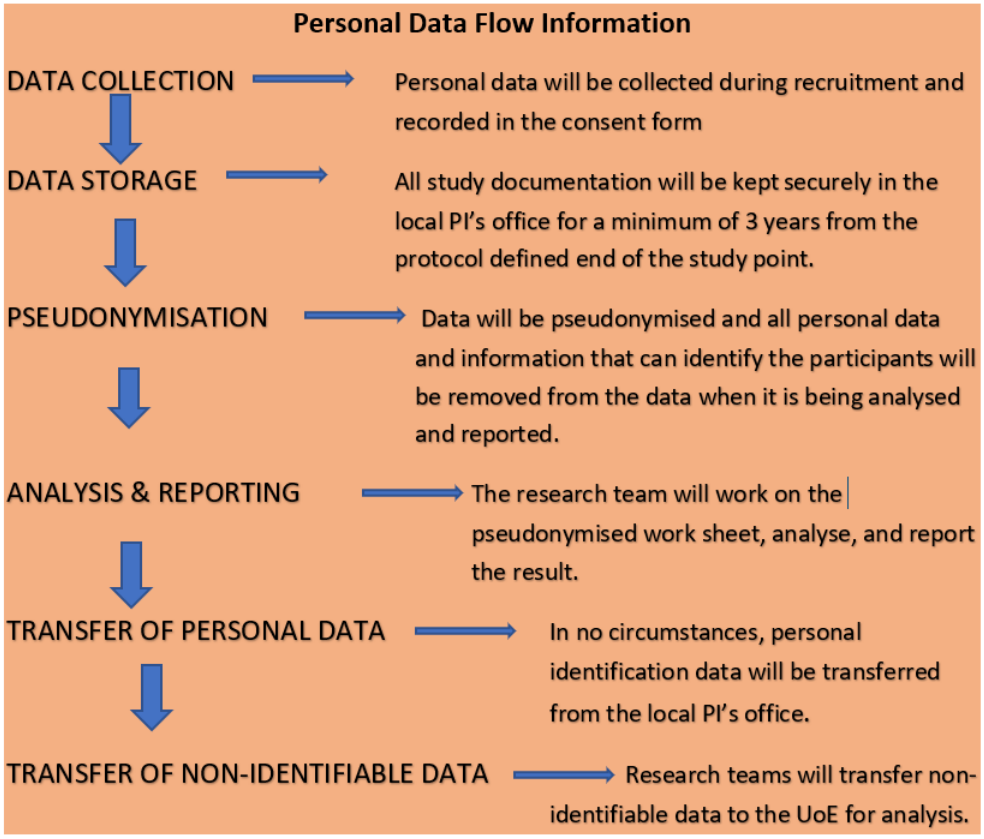

Figure 3: Personal data flow information

We will keep the personal data including contact details that we collect during the consent process until we have published results. This will be a minimum of 3 years after the study has ended. We will archive de-identified data generated from this study for up to 5 years after the study is finished. Archiving of research data will be performed in line with the requirements of the study sponsor (the University of Edinburgh) and in accordance with ACCORD's SOP Archiving Essential Study Documentation. Any transfer of data for archiving will be through the University of Edinburgh Virtual Private Network (VPN) service and files will be encrypted for secure international transfer for archiving. If archiving in Edinburgh is not possible, data will be archived locally on encrypted containers at all times and only accessed by authorised project personnel.

10.3. TRANSFER OF DATA

No personal data will be transferred out of the country where the data has been collected. All personal data will be managed locally by the respective participating centre. To prevent accidental or deliberate access, amendment, or deletion, we will utilise password-protected devices and secure data storage in data handling procedures. For secure data transfer, we ensure that all our data is encrypted during the transfer process using UoE DataSync**.** At the end of the study, the data will be transferred to a data repository (DataVault or DataShare) at the University of Edinburgh via a secure, password protected online platform e.g DataSync. Any transfer of data (NOT including personally identifiable data) to any external individuals or organisations outside of the hosting institutions will be governed by the rules and regulations of the University of Edinburgh and the agreement signed between them**.** Only anonymised data will be transferred from Nigeria, South Africa and Cameroon to the University of Edinburgh secure servers.

8.4. DATA CONTROLLER

The University of Edinburgh, College of Medicine of the University of Lagos, Wits Health Consult in Johannesburg, and the Clinton Health Access Initiative in Yaounde, Cameroon, are the data controllers. Any data breaches will be reported to the University of Edinburgh Data Protection Officer (dpo@ed.ac.uk), who will report to the relevant authority according to the appropriate timelines if required. Data breaches will also be reported to the relevant local research ethics committee:

The study protocol and consent forms will be submitted to the relevant approval (ethical clearance) will be obtained prior to commencing the study from all the centres accordingly:

NIGERIA

i. Health Research Ethics Committee of the Lagos University Teaching Hospital, Lagos, Nigeria.

SOUTH AFRICA

i. Human Research Ethics Committee, University of the Witwatersrand, Johannesburg, South Africa

CAMEROON

i. National Ethics Committee for Research in Human Health/Comité National d'Ethique de la Recherche pour la Santé Humaine (CNERSH), Yaounde, Cameroon

The University of Edinburgh, College of Medicine of the University of Lagos, Wits Health Consortium in Johannesburg, and the Clinton Health Access Initiative in Yaounde, Cameroon, are the joint data controllers.

8.5. DATA BREACHES

Any data breaches will be reported to the University of Edinburgh Data Protection Officer (dpo@ed.ac.uk), who will report to the relevant authority according to the appropriate timelines if required. Data breaches will also be reported to the relevant local research ethics committee:

- **Nigeria:** Health Research Ethics Committee of the Lagos University Teaching Hospital, Lagos, Nigeria. Chairperson: Dr Celestine U Odum. Email: cmd@luthnigeria.org; Alternate Contact: Dr Sakirat Y. Eweje, Email: syeweje@yahoo.com. Phone: +234 805 657 0994 Fax: +234 15 850 737. Address: Lagos State University Teaching Hospital, Idi-Araba, Lagos State, Nigeria.
- **South Africa:** Human Research Ethics Committee, University of the Witwatersrand, Johannesburg, South Africa. Email: HREC-Medical.ResearchOffice@wits.ac.za. Phone: +27 11 274 9200. Fax +27 11 274 9281. Address: Suite 189, Private Bag x2600, Houghton 2041, Johannesburg, South Africa.
- **Cameroon**: National Ethics Committee for Research in Human Health/Comité National d'Ethique de la Recherche pour la Santé Humaine (CNERSH), Yaounde, Cameroon. Chairperson: Prof Lazare Kaptue. Email: prkaptue@yahoo.fr. Telephone: +237 000 2221 1284. Administrator: Dr Marceline Djuidje Ngounoue Email: cnecprot@yahoo.fr. Address: Clinique Bastos, face Lycée Nkoléton, Yaoundé, Cameroon. Postal address: P.O. Box 1937, Yaoundé, Cameroon.

11. STATISTICS AND DATA ANALYSIS

11.1 SAMPLE SIZE CALCULATION

For the feasibility part of the study, no sample size calculation is required. A total of 90 (30 per study site) CRD patients will be enrolled in this study, which is a sufficient sample size to assess feasibility within the availability of resources. We anticipate recruiting over the course of approximately 3 to 4 months.

Recruitment to the qualitative study

Recruitment will continue until data saturation is reached. We anticipate that this will be up to 15 patient interviews, and up to 15 additional interviews with professionals, health service managers and other stakeholders.

11.2. PROPOSED ANALYSES

Analytic approach: Independent samples t-test or Mann Whitney U test (if data is not normally distributed) will be used to determine group differences (centre-based vs. community-based). A multivariate linear regression analyses will be used to determine the influence of the study's independent variables on the measured variables. All statistical analyses will be conducted using the IBM SPSS v29 on windows software. Alpha probability level was significant at 0.05.

Quantitative analysis

In the feasibility study, summary statistics will be calculated as means, proportions and measures with standard parametric methods as needed. We will compare pre-post and follow-up assessment data using paired t-tests or nonparametric tests, though are aware that we cannot demonstrate causality in a before and after study.

In the RCT, descriptive statistics of referral, attendance and completion rates with change in 6MWD and SGRQ and other outcomes. All data in a RCT will be analysed by intention-to-treat analysis to assess non-inferiority of home-based versus facility-based models. Differences between groups for change over time will be analysed with linear mixed models. The relative risk of non-completion will be determined. We will conduct costing analysis and cost-effectiveness analysis.

Qualitative analysis

The interviews will be in the local language and the analysis will be carried out in the local language to retain the nuances of the data. Salient text will be translated into English for inclusion in publications or for discussion with UK colleagues. Transcripts from participants will be analysed using a framework analysis[63] and grounded theory[64] approaches if the data are rich and the local teams want to explore emerging themes. The analysis will comprise familiarisation with the data achieved by reading each transcript, and the generation of preliminary codes, which will be used to answer the research questions. Data from study participants and providers will initially be analysed separately, and then synthesised to give an overarching perspective on pulmonary rehabilitation.

Mixed methods synthesis

We will triangulate the findings from the quantitative and qualitative data. Interpretation of the qualitative data from the framework analysis will be used to corroborate or provide context for the quantitative findings. For example, improved functional exercise capacity (ESWT) may be related to a theme about the perception of being able to increase day-to-day activity. Barriers to acceptance of PR may be explained by attitudes explored in the qualitative interviews.

MIXED METHOD ANALYSES RELATED TO OBJECTIVES

Our analysis will address the study objectives:

Objective 1: To determine the feasibility of delivering PR in Nigeria, South Africa and Cameroon, specifically to inform the optimal resource infrastructure, components of the PR programme, relevant CRD eligibility, and model of service delivery in delivering PR

We will provide descriptive statistics on the detailed records of the study procedures such as identification, eligibility assessment, recruitment rates, data collection, attrition, resources needed to complete the intervention, and patient's adherence to the PR programme. We will log problems that arise at any stage in the process and identify troubleshooting/practical solutions. Additional insights will be obtained from the qualitative interviews.

Objective 2: To assess potential outcomes (specifically baseline and potential change in functional exercise capacity and HRQoL)

We will observe the ease (or otherwise) with which participants complete the exercise tests and whether they need help to complete the questionnaires. Summary statistics will be calculated as means, proportions and measures with standard parametric methods as needed. We will compare pre-post and follow-up assessment data using paired t-tests to inform the degree of change.

Objective 3: To identify and understand the barriers and facilitators to the uptake of PR in individuals with CRDs

The thematic analysis of the patient (and PR provider) interviews will answer this objective. Researcher notes of reasons for withdrawals may provide further evidence.

Objective 4: To explore stakeholders (community leaders, professionals, healthcare managers, and policymakers) attitudes toward PR as a part of CRD management

The thematic analysis of the interviews from the healthcare professionals and other stakeholders will answer this objective

Objective 5: To assess how effective is the PR in real-life setting on improving functional capacity, exercise tolerance, breathlessness, anxiety or depression?

Descriptive statistics of referral, attendance and completion rates with change in ISWT, ESWT and SGRQ and other outcomes. All data in a RCT will be analysed by intention-to-treat analysis to assess non-inferiority of home-based versus facility-based models. Differences between groups for change over time will be analysed with linear mixed models. The relative risk of non-completion will be determined. We will conduct costing analysis and cost-effectiveness analysis.

12. ADVERSE EVENTS

PR is an evidence-based intervention which is proven to improve exercise tolerance and quality of life. We will follow the recommendations of the ATS/ERS[47], BTS[46], Australia-New Zealand PR guidelines[52] and other recognised PR guidelines. From all these guidelines and the finding of our systematic review we will develop a protocol which will be deliverable and

applicable in our settings. Accordingly, we will deliver high-quality and safe PR[65] in the context of our low-resource settings.

We, therefore, do not expect a risk of harm due to the intervention. Furthermore, an experienced clinician will supervise the programme in each of the three sites. The PR training centre is attached to the clinical practice, which is equipped with the local standard of emergency care. Cardiorespiratory events such as new or worsening arrhythmia, Dizziness/hypotension during or after sessions, hypertensive crisis, oxygen desaturation, acute respiratory deterioration, and acute heart failure, exercise-related events such as falls, musculoskeletal injuries, unconsciousness, and psychological events such as panic attacks and severe anxiety episodes will be considered adverse events (AE). Post-intervention deaths within 30 days will be considered severe adverse events (SAEs). AEs/SAEs will be reported to the scientific advisory committee for this study to determine if they are related to the intervention. Related and non-related AEs/SAEs will be reported to the study scientific advisory committee and the relevant ethics committees within 24 hours of the site team becoming aware of the event. Adverse events and other safety events will not be reported to the sponsor for this study.

13. DISSEMINATION

We will present our findings at conferences and publish them in peer-reviewed journals. In addition, we will use the innovative media strategies developed by the NIHR RESPIRE Global Health Unit in EQUI-RESP-AFRICA. We will also disseminate through social media and national TV channels of Nigeria, South Africa and Cameroon and engage stakeholders to increase the impact.

RESEARCH ENVIRONMENT AND AVAILABLE EXPERTISE

PULMONARY REHABILITATION CENTRE

Table 11: Short description of study centres

Country	Organisation with description

Nigeria	Lagos University Teaching Hospital is the largest tertiary institution in Nigeria with over 700 beds. It has several departments and tuns a specialized clinic for COPD and other respiratory diseases. It also has a physiotherapy Department where the PR will be delivered.
South Africa	Chris Hani Baragwanath Academic Hospital plays a vital role in addressing the general medical needs of adult patients in Soweto, one of South Africa's most densely populated urban areas. It provides comprehensive internal medicine services, catering to patients with chronic conditions such as diabetes, hypertension, cardiovascular diseases, tuberculosis, and HIV/AIDS, which are prevalent in the region. The hospital's adult medical wards are organised into specialist units, including nephrology, pulmonology, endocrinology, infectious diseases, and oncology. Its HIV/AIDS and TB treatment programs are among the largest and most advanced in the country, integrating patient care with cutting-edge research and public health outreach. The outpatient clinics manage vast volumes of adult patients daily, offering follow-up care, chronic medication dispensing, and health education services that are key to disease management and prevention. This tertiary-level hospital is affiliated with the University of the Witwatersrand.
Cameroon	The Regional Hospital Limbe (RHL) is a 200-bed tertiary referral facility located in the coastal city of Limbe in Cameroon's South-West Region, serving a catchment population of more than one million people. Affiliated with the University of Buea Faculty of Health Sciences, RHL provides comprehensive medical, surgical, pediatric, obstetric, and emergency services, as well as specialised units for internal medicine and physiotherapy, where pulmonary rehabilitation services are currently offered. In 2025, the hospital became the first in Central Africa to install a liquid medical oxygen (LMO) tank, establishing a regional hub-and-spoke model for sustainable oxygen generation and respiratory care. This combination of advanced infrastructure, clinical expertise, and academic collaboration positions RHL as a strategic centre for pulmonary rehabilitation research and the expansion of oxygen-dependent care systems in Cameroon.

PR PROVIDERS

Each Centre will appoint PR providers, assessors, and research assistants. Training will be provided for clinical personnel from each site according to their convenience and capacity. Training will be delegated by the local PIs with filled up delegation form by the trainees once the process starts after the local REC's permission. Training will be documented on the ACCORD Study Specific Training Record.

USHER INSTITUTE

The Usher Institute works with people, populations and their data to understand and advance the health of individuals and populations through innovative collaborations in a global community. It sits within the Edinburgh Medical School in the College of Medicine and Veterinary Medicine at the University of Edinburgh[66]. EQUI-RESP-AFRICA, along with the RESPIRE, are two of the projects of the Usher Institute working for the reduction of morbidity and mortality from respiratory diseases in five low- and middle-income countries in Africa (EQUI-RESP-AFRICA) and seven in South-East Asia (RESPIRE) [67]. This feasibility study and RCT are funded by EQUI-RESP-AFRICA project.

EXPERTISE AVAILABLE

EDINBURGH, UK

- **Prof Igor Rudan**, the UK Co-PI, has been a co-founder and co-leader of both the CGH and WHO CC since 2014. He led the capacity building platform in four South-East Asian countries within the NIHR RESPIRE Global Health Unit, leading to 12 PhDs, 5 MPHs, and 4 Massive Open Online Courses (MOOCs) developed. He now seeks to extend this experience to Africa. He is Clarivate/ISI Highly Cited scientists who authored and co-authored >700 papers and >15 books, with H-index >200, with >270,000 citations (Google Scholar), and >GBP 40 million in grants received as PI or co-PI over the research career. He is the founder and co-Editor-in-Chief of the Journal of Global Health (JoGH) and the President of the International Society of Global Health (ISoGH), with a wide international network of collaborators. He is the leading epidemiologist in global and regional respiratory health, which is his particular interest, including landmark global epidemiological estimates on childhood pneumonia, COPD, asthma and COVID-19. He developed the CHNRI, EQUIST and PATHS tools. He received >30 awards and

recognitions for his work and is a member of the Royal Society of Edinburgh (FRSE), Academia Europaea (MAE) and European Academy of Sciences and Arts (MEASA).

- **Dr Richard Osei-Yeboah** based at the Centre for Global Health, UoE, is an infectious disease epidemiologist. Recent respiratory disease research include:

1. An EU IMI programme (led by the University of Edinburgh) focusing on RSV disease in children and adults [completed in 2024]
2. An AstraZeneca Externally Sponsored Research focusing on hMPV and RSV disease in children and adults [completed in 2025]

He will serve as the Research Fellow, co-training lead and coordinator between the Edinburgh-based team and the African partners. He will co-lead the Global Health Epidemiology Research Group.

- **Prof Harry Campbell** is Professor of Genetic Epidemiology and Public Health at the University of Edinburgh. His most important contributions include the control of childhood diseases in the economically developing world. He started the pneumonia research programme in MRC Gambia and then moved to WHO Geneva where he published the first estimates of the global burden of childhood pneumonia raising awareness that it is the most important cause of child death. He is a regular advisor to the WHO where he has helped develop global clinical guidelines, action plans and training materials. Recent contributions include a manual on influenza surveillance used in more than 50 countries. He has long standing experience in many aspects of global child health with a long-term interest in many aspects of childhood respiratory infections. Recent projects have explored global burden of disease, disease surveillance, use of linked routine heath datasets, risk factors and case management guidelines. He was a founding member then deputy chair of the WHO / UNICEF Child Health Epidemiology Group [CHERG] for about 20 years. He has served as an advisor to WHO and other UN agencies on ~100 occasions and is currently active in 2 WHO advisory groups. Recent respiratory disease research include:

    1. An EU IMI programme (led by the University of Edinburgh) focusing on RSV disease in children and adults [completed in 2024]
    2. An NIHR Global Health Unit on Respiratory Health [RESPIRE] (where his role is joint co-Director 2017-2026; 2017-2022 with Aziz Sheikh). RESPIRE was one of 5 UK research programmes which won an inaugural NIHR Impact Prize in 2025.

- **Dr Davies Adeloye**, based at the CGH UoE, is a physician and a leading NCD epidemiologist for Africa. He will serve as the Research Manager, training lead and coordinator between the Edinburgh-based team and the African partners, and the CEI NGOs.

LAGOS, NIGERIA

- **Prof Obianuju B. Ozoh** is a consultant pulmonologist at the Lagos University Teaching Hospital. She coordinates PATS MECOR initiative, which trained >300 students from 22 African countries over 15 years, many of whom have become regional research leaders and policymakers. She is currently working to develop Respiratory Disease Observatory for Africa. She was the Editor-in-Chief of the Journal of the Pan African Thoracic Society and a prolific researcher. In 2023, she became the winner of the World Lung Health Award from the American Thoracic Society.
- **Dr Jibril Mohammed** is a physiotherapist (and academic staff/researcher) affiliated to both Bayero University Kano/Aminu Kano Teaching Hospital, Kano, Nigeria. Over the last 15 years, he has taught and mentored both undergraduate and post graduate level students of physiotherapy, especially those majoring in chronic respiratory disease rehabilitation. HE has also supervised to completion; 44 Bachelors projects, 8 Master of Science Dissertations and one PhD Thesis. Dr Mohammed attended all three levels of the PATS MECOR Courses. He is a recipient of the 6-month European Respiratory Society Fellowship on Guideline Methodology, and another 6-month European Respiratory Society Clinical Training Fellowship, which was focused entirely on how to acquire relevant skills in ***pulmonary rehabilitation*** for patients with chronic respiratory diseases (at the CIRO institute in Horn, The Netherlands). I have attended several national and international conferences, workshops and courses relevant to pulmonary rehabilitation.

JOHANNESBURG, SOUTH AFRICA

- **Prof Ziyaad Dangor** is the key adviser in clinical pulmonology, and director clinical research director at the world-renowned Vaccines and Infectious Diseases Analytics Research Unit (VIDA) at the University of the Witwatersrand. Ziyaad has undertaken investigator-initiated, original research using a range of clinical, epidemiological, and laboratory-based research techniques to establish a successful research output, including the publication of papers in high-impact factor journals in the field. Ziyaad also serves on a number of local and international committees including the WHO and Ministerial Advisory Committees.
- **Dr Sarah Alexandra van Blydenstein** is an Adult Pulmonologist, Specialist Physician, working at Chris Hani Baragwanath Academic Hospital (CHBAH), and is also affiliated with the University of Witwatersrand. Alex has submitted her PhD which

explored various clinical perspectives of hypoxaemic pneumonia during the COVID-19 pandemic. Alex serves on the CHBAH research committee, is Chair of the University of Witwatersrand School of Clinical Medicine, Department of Internal Medicine MMed Protocol Committee, and is a member of the Graduate Studies and Research Committee for the University. She has supervised 18 Master of Medicine Research Reports, and has received the following prizes, amongst others: SA Heart best abstract presentation 2021; Early Career Academic Development 2022; Wits Clinician Research PhD award 2023; Ken Huddle role model award 2024; and the best poster for PhD at the University Research Day 2025.

- **Dr Ismail Kalla** is the Academic Head of Department for Internal Medicine at WITS. He holds dual board certifications in Pulmonology and Critical Care Medicine. As Principal Investigator, he has overseen multiple large-scale international research projects involving COVID-19, including the WHO Solidarity, REMAP-CAP, ACCCOS, and RECOVERY trials, while leading a COVID-19 research unit recognized for its extensive publications on the pandemic's impact in South Africa. He represents Southern Africa on the Middle East and Africa Asthma Steering Committee, dedicated to improving asthma management and outcomes in low- and middle-income nations. He is a Fellow at both the Infectious Disease and Oncology Research Institute (IDORI) and the Wits Machine Intelligence and Neural Discovery Institute (MIND). Recently, his interests have expanded to artificial intelligence applications in medical research and education, where he leads several Gates Foundation–funded innovation projects that harness AI's potential across the clinical and educational spectrum.

YAOUNDE, CAMEROON

- **Dr Yauba Saidu** is a public health leader and researcher with extensive experience in health systems strengthening and oxygen ecosystem development across Cameroon. As Country Representative of CHAI, he has spearheaded national efforts to expand access to medical oxygen, including coordinating the establishment of the National Oxygen Taskforce, conducting nationwide assessments of oxygen capacity and needs, and leading the development of Cameroon's National Oxygen Strategy. He has also played a pivotal role in conceptualising and overseeing the installation of a liquid medical oxygen (LMO) tank at the Regional Hospital Limbe — the first of its kind in Central Africa — designed to serve as a hub-and-spoke model for sustainable oxygen production and distribution across the South-West and neighboring regions.
- **Dr Michael Budz**i is a public health physician and implementation researcher with expertise in chronic disease care, health systems strengthening, and essential

medicines access. As CHAI Cameroon's Program Lead for NCDs and Essential Medicines, he collaborates closely with the National Sub-Directorate for NCDs within the Ministry of Public Health to advance national strategies for the prevention and management of chronic respiratory and cardiovascular diseases. He has supported multiple health systems assessments and interventions aimed at improving health system strengthening, ; oxygen access, clinical readiness, and service delivery in secondary and tertiary care facilities, including in the Regional Hospital Limbe.

14. COMMUNITY ENGAGEMENT AND INVOLVEMENT

CEI is the global equivalent of Patient and Public Involvement. Patients are key stakeholders and we will establish CEI groups in each centre. We will seek the advice of patient colleagues before commencing the study which will give us valuable insight into improving our study design. We will feedback our preliminary findings to gather their perspectives and assist with interpreting the findings and formulating recommendations. In a parallel process, we will also conduct a stakeholder meeting with professional advisors on the delivery of PR, study design and how to implement and promote PR in Nigeria, South Africa, and Cameroon.

15. OVERSIGHT ARRANGEMENTS

15.1. INSPECTION OF RECORDS

Investigators and institutions involved in the study will permit study-related monitoring and audits on behalf of the sponsor, ethics committee review, and regulatory inspection(s). In the event of audit or monitoring, the Investigator agrees to allow the representatives of the sponsor direct access to all study records and source documentation. In the event of regulatory inspection, the Investigator agrees to allow inspectors direct access to all study records and source documentation.

15.2. STUDY MONITORING AND AUDIT

The ACCORD Sponsor Representative will assess the study to determine if an independent risk assessment is required. If required, the independent risk assessment will be carried out by the ACCORD Quality Assurance Group to determine if an audit should be performed before/during/after the study and, if so, at what frequency. Risk assessment, if required, will determine if an audit by the ACCORD quality assurance group is required. Should an audit be required, details will be captured in an audit plan. Audit of Investigator sites, study

management activities, and study collaborative units, facilities and 3rd parties may be performed.

16. GOOD CLINICAL PRACTICE

16.1. ETHICAL CONDUCT

The study will be conducted by the principles of the International Conference on Harmonisation Tripartite Guideline for Good Clinical Practice (International Conference on Harmonisation GCP). Before the study can commence, all required approvals will be obtained and any conditions of approvals will be met.

16.2. PRINCIPAL INVESTIGATOR RESPONSIBILITIES

The Principal Investigators of EQUI-RESP (IR and OO) are responsible for the overall conduct of the study. National Principal Investigators (OO, ZD, YS) are responsible for at the site and compliance with the protocol and any protocol amendments. In accordance with the principles of ICH GCP, the following areas listed in this section are also the responsibility of the Principal Investigator. Responsibilities may be delegated to an appropriate member of study site staff.

Informed Consent

The National Principal Investigators are responsible for ensuring informed consent is obtained before any protocol-specific procedures are carried out. The decision of a participant to participate in clinical research is voluntary and should be based on a clear understanding of what is involved.

Participants must receive adequate oral and written information – appropriate Participant Information and Informed Consent Forms will be provided. The oral explanation to the participant will be performed by the Investigator or a qualified delegated person and must cover all the elements specified in the Participant Information Sheet and Consent Form (please see the **Appendix 1-5 and Appendix 6A, 6B, and 6C**)

The participant must be given every opportunity to clarify any points they do not understand and ask for more information. The participant must be given sufficient time to consider the information provided. It should be emphasised that the participant may withdraw their

consent to participate at any time without loss of benefits to which they otherwise would be entitled.

The participant will be informed and agree to their medical records being inspected by regulatory authorities and representatives of the sponsor(s).

The National Principal Investigator or delegated member of the trial team and the participant will sign and date the Informed Consent Form(s) to confirm that consent has been obtained. The participant will receive a copy of this document and a copy filed in the Investigator Site File (ISF) and the participant's medical notes (if applicable).

Study Site Staff

The National Principal Investigators developed the protocol and are thus familiar with the study requirements. It is the National PI Investigators' responsibility to ensure that all staff assisting with the study are adequately informed about the protocol and their trial-related duties.

Data Recording

The National Principal Investigators are responsible for the quality of the data recorded in the case reporting form at each Principal Investigator Site.

Principal Investigator Documentation

The National Principal Investigators will ensure that the required documentation is available in the local investigator site files.

GCP Training

For non-CTIMP (i.e., non-drug) studies all researchers are encouraged to undertake GCP training to understand the principles of GCP. However, this is not a mandatory requirement unless deemed so by the sponsor. GCP training status for all investigators should be indicated in their respective CVs.

16.3. Data Protection Training

All University of Edinburgh employed researchers, students and study staff will complete the Data Protection Training through Learn.

16.4. Information Security Training

All University of Edinburgh employed researchers, students and study staff will complete the Information Security Essentials modules through Learn and will have read the minimum and required reading setting out ground rules to be complied with.

GCP Confidentiality

All evaluation forms, reports, and other records must be identified in a manner designed to maintain participant confidentiality. All records must be kept in a secure storage area with limited access. Clinical information will not be released without the written permission of the participant. The Principal Investigator and study site staff involved with this study may not disclose or use for any purpose other than the performance of the study, any data, record, or other unpublished information, which is confidential or identifiable and has been disclosed to those individuals for the study. Prior written agreement from the sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

Data Protection

All Investigators and study site staff involved with this study must comply with the requirements of the appropriate data protection legislation (including the European Union General Data Protection Regulation, the Data Protection Act 2018 in the UK and any relevant Data Protection laws in the country where the study is being conducted: Nigeria, South Africa and Cameroon, with regard to the collection, storage, processing and disclosure of personal information.

Computers used to collate the data will have limited access measures via usernames and passwords. Published results will not contain any personal data and be of a form where individuals are not identified and re-identification is not likely to take place

STUDY CONDUCT RESPONSIBILITIES

16.5. PROTOCOL AMENDMENTS

Any changes in research activity, except those necessary to remove an apparent, immediate hazard to the participant in the case of an urgent safety measure, must be reviewed and approved by the Principal Investigators.

Amendments will be submitted to a sponsor representative for review and authorisation before being submitted in writing to the appropriate Research Ethical Committee, and local institutional review board for approval before participants are enrolled into an amended protocol.

16.6. MANAGEMENT OF PROTOCOL NON-COMPLIANCE

Prospective protocol deviations, i.e., protocol waivers, will not be approved by the sponsors and therefore will not be implemented, except where necessary to eliminate an immediate hazard to study participants. If this necessitates a subsequent protocol amendment, this should be submitted to the REC, and local R&D for review and approval if appropriate.
Protocol deviations will be recorded in a protocol deviation log and logs will be submitted to the sponsors every 3 months. Each protocol violation will be reported to the sponsor within 3 days of becoming aware of the violation. All protocol deviation logs and violation forms should be emailed to QA@accord.scot
Deviations and violations are non-compliance events discovered after the event has occurred. Deviation logs will be maintained for each site in multi-centre studies. An alternative frequency of deviation log submission to the sponsors may be agreed upon in writing by the sponsors.

16.7. SERIOUS BREACH REQUIREMENTS

A serious breach is a breach which is likely to affect a significant degree:
(a) the safety or physical or mental integrity of the participants of the trial; or
(b) the scientific value of the trial.
If a potential serious breach is identified by the Principal Investigators, National Principal Investigators, or delegates, the sponsors (seriousbreach@accord.scot) must be notified within 24 hours. It is the responsibility of the sponsors to assess the impact of the breach on the scientific value of the trial, to determine whether the incident constitutes a serious breach and to report to research ethics committees as necessary.

16.8. STUDY RECORD RETENTION

All study documentation will be kept for a minimum of 3 years from the protocol-defined end of the study point. When the minimum retention period has elapsed, study documentation will not be destroyed without permission from the sponsor.

16.9. END OF STUDY

The end of the study is defined as the last participant's last visit. The Principal Investigators or the sponsor(s) have the right at any time to terminate the study for clinical or administrative reasons. The end of the study will be reported to the Research Ethics Committee Office(s) and sponsors within 90 days, or 15 days if the study is terminated prematurely. The Investigators will inform participants of the premature study closure and ensure that the appropriate follow-up is arranged for all participants involved. End-of-study notification will be reported to the sponsors via email to resgov@accord.scot A summary report of the study will be provided to the REC within 1 year of the end of the study.

16.10. CONTINUATION OF TREATMENT FOLLOWING THE END OF THE STUDY

The patient will have completed the course of PR after 8 weeks. No further PR is required and the patient will return to usual care

16.11. INSURANCE AND INDEMNITY

The sponsors are responsible for ensuring proper provision has been made for insurance or indemnity to cover their liability and the liability of the Principal Investigators and staff.
The following arrangements are in place to fulfil the sponsor's responsibilities:

- The Protocol has been designed by the Principal Investigators and researchers employed by the University and collaborators. The University has insurance in place (which includes no-fault compensation) for negligent harm caused by poor protocol design by the Principal Investigators and researchers employed by the University.
- Sites participating in the study will be liable for clinical negligence and other negligent harm to individuals taking part in the study and covered by the duty of care owed to them by the sites concerned. The sponsors require individual sites participating in the study to arrange for their insurance or indemnity in respect of these liabilities.
- Sites outwith the United Kingdom will be responsible for arranging their indemnity or insurance for their participation in the study, as well as for compliance with local laws applicable to their participation in the study.

17. REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

17.1. REPORTING OF RESULTS

Results will be made available in the public register where the study was initially registered within 12 months of the end of study. Results will be summarised in the annual report and provided to the NHIR. Results of the study will be published in openly accessible peer-reviewed journals.

17.2. AUTHORSHIP POLICY

The Parties acknowledge that publication and knowledge dissemination for the public good is a core purpose of EQUI-RESP-AFRICA. All publications shall be in accordance with the terms of the EQUI-RESP-AFRICA Publication Policy. All publications shall comply with the NIHR Award Terms and shall acknowledge the funding made available for the Project by the NIHR. The NIHR Award Terms and the EQUI-RESP-AFRICA Publication Policy are intended to be read in harmony to the fullest extent possible. However, in the event of any material conflict between the EQUI-RESP-AFRICA Publication Policy and the NIHR Award Terms, the NIHR Award Terms shall govern. The provisions of this clause shall survive termination or expiry of this Agreement for a period of 5 years.

This Agreement shall not prevent or hinder registered students of any Party from submitting for degrees of that Party theses based on results obtained during the course of work undertaken as part of the Project; or from following that Party's procedures for examinations and for admission to postgraduate degree status.

In accordance with normal academic practice, all employees, students, agents or appointees of the Parties (including those who work on the Project) shall be permitted in pursuance of the Parties' academic functions, to discuss work undertaken as part of the Project in internal seminars and to give instruction within their organisation on questions related to such work.

No Party shall use the name or any trademark or logo of any other Party or the name of any of its staff or students in any press release or product advertising, or for any other commercial purpose, without the prior written consent of the Party(s).

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