Supervised Pulmonary Hypertension Exercise REhabilitation (SPHERe) trial

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
13/03/2019		[X] Protocol		
Registration date	Overall study status	[X] Statistical analysis plan		
18/03/2019	Completed Condition category	Results		
Last Edited		Individual participant data		
22/07/2024	Circulatory System	Record updated in last year		

Plain English summary of protocol

Background and study aims

Pulmonary hypertension is a disabling long-term condition that can greatly reduce quality of life. Blood vessels supplying the lungs become thick and stiff, restricting blood flow. Blood pressure is increased in these vessels meaning the heart must work harder to pump blood to the lungs. Over time, the heart may begin to fail. Breathlessness, fatigue and dizziness are the most common symptoms. People with pulmonary hypertension are often anxious about carrying out normal daily activities. There are five types of pulmonary hypertension with different causes. Medical treatment is different for each type, and may help to improve symptoms. Little is known about whether exercise rehabilitation may help people living with pulmonary hypertension. Supervised exercise rehabilitation is a common treatment for many heart and lung conditions. It can improve fitness, breathlessness, anxiety, depression, and quality of life. Some research has shown that exercise rehabilitation may be helpful for people with certain types of pulmonary hypertension: pulmonary arterial hypertension, and pulmonary hypertension due to blood clots in the lungs. Most of these exercise programmes included three weeks of intensive exercise as a hospital in-patient. This is not feasible in the NHS, where exercise rehabilitation is an outpatient service, typically lasting an hour, twice a week for eight weeks. It is not known whether outpatient/home-based exercise rehabilitation can help improve the lives of people with pulmonary hypertension. The aim of this study is to find out whether outpatient exercise rehabilitation, combined with psychological and motivational support, can improve fitness and quality of life for people living with pulmonary hypertension, particularly people whose pulmonary hypertension is secondary to heart or lung disease, because exercise rehabilitation has not been researched in these groups. The study will be run in specialist rehabilitation centres by staff experienced in treating people with heart and lung problems.

COVID-19 update (29/03/2021):

In light of the COVID-19 pandemic, exercise rehabilitation will move to an online home-based delivery model. We have drawn on existing resources and data from home-based rehabilitation programmes aimed at breathless, fatigued and anxious clinical populations, where data supports the potential efficacy of home-based vs centre-based programmes. SPHERe will now be resource-based (manual, online content) using functional (body weight or chair-based) exercise and a structured home-based exercise bike programme, remotely supervised and facilitated online by trained practitioners.

Who can participate?

Patients with pulmonary hypertension who live near one of at least 10 rehabilitation centres mainly in the East and West Midlands

What does the study involve?

Participants will be randomly allocated to either remotely supervised exercise with psychological and motivational support, or best-practice usual care (general physical activity advice). The 8-week intervention includes:

- 1. An online individual assessment and exercise familiarisation session
- 2. Once-weekly live online remotely supervised group home exercise programme
- 3. Twice-weekly guided home exercise bike and functional fitness programme
- 4. Weekly group online psychosocial and motivational support and education session (for 6 weeks).

People in the usual care group will receive a single (online) session of 1:1 advice on safe and effective lifestyle physical activity. A walking test and quality of life questionnaires will be used over 1 year to measure if the intervention can help people with pulmonary hypertension, and represents good value for the NHS.

What are the possible benefits and risks of participating?

This study may not offer people any direct benefit, but the results will help people with pulmonary hypertension in the future. If any of the assessments find anything unusual with participants' health, they will receive prompt and appropriate medical care and attention. Exercise carries a very small risk of complications for people with pulmonary hypertension. If it is likely that certain people will have a problem during exercise, their medical team will not ask them to take part. For people who do take part, remote supervision will be provided by specialist staff. Exercise is likely to cause some tiredness, breathlessness and sore muscles, but this should get a bit easier over time. The researchers do not anticipate any serious risk to participants.

Where is the study run from?
University Hospitals Coventry & Warwickshire NHS Trust (UK)

When is the study starting and how long is it expected to run for? June 2019 to August 2024

Who is funding the study? Health Technology Assessment Programme (UK)

Who is the main contact?
Dr Gordon McGregor
gordon.mcgregor@uhcw.nhs.uk

Study website

https://www.warwick.ac.uk/SPHERE

Contact information

Type(s)

Scientific

Contact name

Dr Gordon McGregor

ORCID ID

http://orcid.org/0000-0001-8963-9107

Contact details

University Hospital Clifford Bridge Road Coventry United Kingdom CV22DX +44 (0)2476234570 gordon.mcgregor@uhcw.nhs.uk

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

261218

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

HTA 17/129/02

Study information

Scientific Title

Supervised Pulmonary Hypertension Exercise REhabilitation (SPHERe): a multi-centre randomized controlled trial

Acronym

SPHERe

Study objectives

The SPHERE intervention will improve clinical and patient-reported outcomes when compared to best practice usual care.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 13/07/2019, West Midlands - Coventry & Warwickshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)2071048101; nrescommittee.westmidlands-coventryandwarwick@nhs.net), REC ref: 19/WM/0155

Study design

Randomized controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Quality of life

Participant information sheet

Patient information material can be found at https://www.warwick.ac.uk/SPHERE

Health condition(s) or problem(s) studied

Pulmonary hypertension

Interventions

Current interventions as of 29/03/2021:

Participants will be randomly allocated to either remotely supervised exercise with psychological and motivational support, or best-practice usual care (general physical activity advice).

The intervention group will be invited to complete 8 weeks of once-weekly remotely supervised exercise rehabilitation, alongside a home exercise bike programme (twice-weekly). The researchers have developed an exercise programme suitable for people with all types of pulmonary hypertension that can be delivered virtually from existing NHS exercise rehabilitation services. The study will be run from specialist rehabilitation centres by staff experienced in treating people with heart and lung problems. Weekly psychological and motivational support aims to reduce anxiety and improve exercise adherence.

People in the usual care group will receive a single (online) session of 1:1 advice on safe and effective lifestyle physical activity, but not take part in the exercise programme.

Previous interventions:

Participants are randomly allocated to either supervised exercise with psychological and motivational support, or to continue with usual care (general physical activity advice).

The intervention group will be invited to complete 8 weeks of twice-weekly supervised outpatient exercise rehabilitation. The researchers have developed an exercise programme suitable for people with all types of pulmonary hypertension that can be delivered within existing NHS exercise rehabilitation services. They have tested, evaluated, and refined this over a six-month period. The study will be run in specialist rehabilitation centres by staff experienced in treating people with heart and lung problems. Psychological and motivational support will help reduce anxiety and improve exercise adherence.

People in the usual care group will receive general physical activity advice, but not supervised exercise.

Intervention Type

Behavioural

Primary outcome measure

Exercise capacity measured with incremental shuttle walk test (ISWT) at 4 months.

Secondary outcome measures

Current secondary outcome measures as of 24/02/2023:

- 1. Disease-specific health-related quality of life (HR-QoL) measured with Cambridge Pulmonary Hypertension Outcome Review at 4 and 12 months
- 2. Health utility measured with EQ-5D-5L at 4 and 12 months
- 3. Emotional well-being measured with the Hospital Anxiety and Depression Scale at 4 and 12 months
- 4. Generalised self-efficacy measured with a psychometric scale at 4 and 12 months
- 5. Fatigue measured with the Fatigue Severity Scale at 4 and 12 months
- 6. Functional status measured using WHO functional class at 4 and 12 months
- 7. Self-reported medication use at 4 and 12 months
- 8. Time to clinical worsening measured by medical notes and discussion with a clinician at 4 and 12 months
- 9. Health and social care resource use measured by participant self-report and NHS data at 4 and 12 months
- 10. All-cause hospital admissions from GP records at 12 months
- 11. Adverse events measured with NHS data at 4 and 12 months
- 12. All-cause mortality

Previous secondary outcome measures as of 29/03/2021 to 24/02/2023:

- 1. Exercise capacity measured with incremental shuttle walk test at 12 months
- 2. Disease-specific health-related quality of life (HR-QoL) measured with Cambridge Pulmonary Hypertension Outcome Review at 4 and 12 months
- 3. Emotional well-being measured with the Hospital Anxiety and Depression Scale at 4 and 12 months
- 4. Self-efficacy measured with the Generalised self-efficacy scale at 4 and 12 months
- 5. Fatigue measured with the Fatigue Severity Scale at 4 and 12 months
- 6. Functional status measured using WHO functional class at 4 and 12 months
- 7. Self-reported medication use at 4 and 12 months
- 8. Time to clinical worsening measured by medical notes and discussion with clinician at 4 and 12 months
- 9. Hospital admissions measured with NHS data at 4 and 12 months
- 10. Adverse events measured with NHS data at 4 and 12 months
- 11. All-cause mortality measured with NHS data at 4 and 12 months
- 12. Heath utility measured with EQ-5D-5L at 4 and 12 months
- 13. Health and care resource use measured by participant self-report and NHS records at 4 and 12 months.

Previous secondary outcome measures:

- 1. Exercise capacity measured with incremental shuttle walk test at 12 months
- 2. Exercise capacity measured with six-minute walk test at 4 and 12 months
- 3. Disease-specific health-related quality of life (HR-QoL) measured with Cambridge Pulmonary Hypertension Outcome Review at 4 and 12 months
- 4. Emotional well-being measured with the Hospital Anxiety and Depression Scale at 4 and 12 months

- 5. Self-efficacy measured with the Generalised self-efficacy scale at 4 and 12 months
- 6. Fatigue measured with the Fatigue Severity Scale at 4 and 12 months
- 7. Functional status measured using WHO functional class at 4 and 12 months
- 8. Medication use measured by self-report case report form at 4 and 12 months
- 9. Time to clinical worsening measured by medical notes and discussion with clinician at 4 and 12 months
- 10. Hospital admissions measured with NHS data at 4 and 12 months
- 11. Adverse events measured with NHS data at 4 and 12 months
- 12. All-cause mortality measured with NHS data at 4 and 12 months
- 13. Heath utility measured with EQ-5D-5L at 4 and 12 months
- 14. Health and care resource use measured by participant self-report and NHS records at 4 and 12 months

Overall study start date

01/06/2019

Completion date

31/08/2024

Eligibility

Key inclusion criteria

Current inclusion criteria as of 29/03/2021:

- 1. Adults with confirmed PH (groups 1 to 5) as detailed in ESC/ERS guidelines
- 2. Clinically stable
- 3. World Health Organisation (WHO) functional class II, III or IV
- 4. Fluent in spoken English to allow engagement with intervention and physical outcome measures
- 5. Live within reasonable travelling distance (as defined by the participant) of a SPHERE exercise rehabilitation centre (outcome assessments only)
- 6. Ability to provide informed consent
- 7. Access to appropriate IT infrastructure (computer, laptop, tablet, smart phone, email and internet connection)
- 8. Ability to make suitable travel arrangements to attend clinic (outcome assessments only)

Previous inclusion criteria:

- 1. Adults with confirmed PH (groups 1 to 5) as detailed in ESC/ERS guidelines
- 2. Clinically stable
- 3. World Health Organisation (WHO) functional class II, III or IV
- 4. Fluent in spoken English to allow engagement with intervention and physical outcome measures
- 5. Live within reasonable travelling distance (as defined by the participant) of a SPHERE exercise rehabilitation centre
- 6. Ability to provide informed consent

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

200

Total final enrolment

153

Key exclusion criteria

Current exclusion criteria as of 29/03/2021:

- 1. Absolute contraindications to exercise as per international clinical guidelines
- 2. PH related complications, or comorbidities severe enough to prevent attendance at a SPHERE centre, or participation in exercise rehabilitation
- 3. Any mental health issue that will prevent engagement with study procedures
- 4. Previous randomisation in the present trial
- 5. Pregnancy at the time of recruitment

Previous exclusion criteria:

- 1. Absolute contraindications to exercise as per international clinical guidelines
- 2. PH related complications, or comorbidities severe enough to prevent attendance at a SPHERE centre, or participation in exercise rehabilitation
- 3. Any mental health issue that will prevent engagement with study procedures
- 4. Unable to make suitable travel arrangements
- 5. Previous randomisation in the present trial
- 6. Pregnancy

Date of first enrolment

16/06/2021

Date of final enrolment

31/08/2023

Locations

Countries of recruitment

England

Scotland

United Kingdom

Wales

Study participating centre
University Hospitals Coventry & Warwickshire NHS Trust
Clifford Bridge Road

Coventry United Kingdom CV2 2DX

Study participating centre Walsall Healthcare NHS Trust

Manor Hospital Moat Road Walsall United Kingdom WS2 9PS

Study participating centre Royal United Hospitals Bath NHS Foundation Trust

Combe Park Bath United Kingdom BA1 3NG

Study participating centre

University Hospitals Birmingham NHS Foundation Trust

Queen Elizabeth Hospital Mindelsohn Way Edgbaston Birmingham United Kingdom B15 2GW

Study participating centre Broomfield Hospital

Court Road Broomfield Chelmsford United Kingdom CM1 7ET

Study participating centre Golden Jubilee National Hospital

Agamemnon Street

Sponsor information

Organisation

University Hospitals Coventry & Warwickshire NHS Trust

Sponsor details

University Hospital Clifford Bridge Road Coventry England United Kingdom CV2 2DX +44 (0)2476 966195 R&DSponsorship@uhcw.nhs.uk

Sponsor type

Hospital/treatment centre

Website

https://www.uhcw.nhs.uk

ROR

https://ror.org/025n38288

Funder(s)

Funder type

Government

Funder Name

Health Technology Assessment Programme

Alternative Name(s)

NIHR Health Technology Assessment Programme, HTA

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

The publication of a trial protocol, trial results and trial data will be in line with the NIHR standard terms: The protocol and other information will be available online here: https://www.journalslibrary.nihr.ac.uk/programmes/hta/1712902/#/

Results of the trial will be prepared by the research team and lay partners, and submitted to funders as a final report. Findings will be submitted to peer-reviewed journals and disseminated to the medical and exercise rehabilitation communities. Papers will be published in open-access journals describing the development of the SPHERe intervention, the trial protocol, and results and data, in accordance with recommended guidance for transparent reporting, the Consolidated Standards of Reporting Trials (CONSORT) guidelines (www.consort-statement.org) and the NIHR standard terms. Abstracts will be submitted to national and international conferences e.g. British Thoracic Society, British Cardiology Society, European Respiratory Society, American College of Cardiology.

The SPHERe intervention will be fully manualised and available for public access once the trial has been completed. If appropriate, a practitioner training programme will be developed to support the implementation of SPHERe.

If the SPHERe intervention is successful, work will be undertaken with national governing bodies (BACPR, BTS), charities (PHA-UK, BHF, BLF) and service audit providers (National Audit of Cardiac Rehabilitation [NACR], National Asthma and COPD Audit Programme [NACAP], NHS Digital PH audit), to promote the inclusion of people with PH in cardio-pulmonary rehabilitation programmes.

Intention to publish date

31/03/2025

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request after publication of the main study results. Requests for data sharing will be managed in accordance with University of Warwick policy on data sharing.

IPD sharing plan summary

Available on request

Study outputs

occes occasion					
Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	19/05/2020	26/05/2020	Yes	No
HRA research summary			28/06/2023	No	No
Statistical Analysis Plan	version 1.1	01/05/2024	12/07/2024	No	No

Protocol update

<u>Protocol article</u> 20/07/2024 22/07/2024 Yes No