ISRCTN10608766 https://doi.org/10.1186/ISRCTN10608766

# Supervised Pulmonary Hypertension Exercise REhabilitation (SPHERe) trial

**Submission date**
13/03/2019

**Recruitment status**
No longer recruiting

**Registration date**
18/03/2019

**Overall study status**
Completed

**Last Edited**
22/07/2024

**Condition category**
Circulatory System

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] 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

Clydebank
United Kingdom
G81 4DY

# 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

| 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<br>Protocol update | 01/05/2024 | 12/07/2024 | No | No |

| | | | | |
|---|---|---|---|---|
| Protocol article | 20/07/2024 | 22/07/2024 | Yes | No |