ISRCTN96143888 https://doi.org/10.1186/ISRCTN96143888

The development of an asthma-tailored pulmonary rehabilitation programme for individuals with severe asthma

Submission date 18/11/2013	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 30/01/2014	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 26/02/2020	**Condition category** Respiratory	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Asthma is a common condition that can cause coughing, wheezing, chest tightness and breathlessness. About 1 in 10 people with asthma have difficult to control symptoms and are described as having severe asthma. They need more healthcare support than milder disease. We know regular physical activity has important health benefits, but many patients with severe asthma avoid exercise. GPs and nurses may also be worried that exercise might worsen asthma symptoms. Physical training through short structured supervised programmes (pulmonary rehabilitation [PR]) leads to improved symptoms, quality of life and fitness in other chronic lung diseases. They are good value for money and lead to less healthcare use. However, few patients with severe asthma have access to such programmes. Our local PR service has accepted these patients, but patients said they would prefer to attend a specific programme for asthma. The aim of this study is to find out whether people with severe asthma would benefit from a PR programme specifically for asthma.

Who can participate?
Patients with severe asthma.

What does the study involve?
Participants are randomly allocated to one of two groups. One group attends a PR programme specifically for asthma. The other group receives usual care (disease education and exercise advice from asthma nurses).

A group of healthy volunteers were also recruited. This group received no care but undertook the same assessments as the participants with asthma.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Glenfield Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2013 to September 2018

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Dr Rachael Evans

Contact information

Type(s)
Scientific

Contact name
Dr Rachael Evans

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Additional identifiers

EudraCT/CTIS number

IRAS number
127552

ClinicalTrials.gov number

Secondary identifying numbers
CLRN 127552, IRAS 127552

Study information

Scientific Title
A feasibility study to inform the development of a multicentre randomised controlled trial of an asthma-tailored pulmonary rehabilitation programme versus usual care for individuals with severe asthma

Study objectives
Patients with severe asthma have a high morbidity and healthcare cost despite currently available therapies. Activity limitation is common, leading to reduced health-related quality of life (HRQoL). Cardiorespiratory fitness (CRF) is a strong predictor of mortality and asthma has a strong inverse association with CRF. Despite this, patients with severe asthma are often

excluded from exercise schemes due to perceived higher risks. Pulmonary rehabilitation (PR), with core components of exercise training and multi-professional education, is an integral part of the management of patients with chronic lung disease, with grade A evidence for improvements in dyspnoea, exercise tolerance and HRQoL. International guidance suggests inclusion of patients with asthma, but there is little published evidence evaluating either existing or tailored regimens in severe asthma, leading to few patients being referred. Our patients stated a preference for a PR programme specifically for their disease. We propose a feasibility study to inform the study design of a large multicentre randomised controlled trial (RCT) of asthma-tailored PR (AT-PR) for individuals with severe asthma compared to usual care (UC).

The aims of the proposed study are, in patients with severe asthma, to:
1. Understand the facilitators and barriers to regular physical activity and exercise
2. Understand healthcare professionals attitudes to exercise for this group
3. Perform a small scale version of the eventual RCT to:
3.1. Provide information on recruitment rate, retention rate, adverse events, accessibility and acceptability of the AT-PR programme, to assess the feasibility of the proposed study protocol, and to design and pilot a suitable patient cost questionnaire to be used in the proposed cost-effectiveness economic evaluation in the subsequent RCT
3.2. Identify further barriers or facilitators to participation in a AT-PR programme
4. To facilitate patient involvement in the design, conduct and dissemination for the multicentre trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East Midlands - Leicester, 17/10/2013, ref: 13/EM/0323

Study design
Qualitative study and small scale feasibility study of a randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Severe asthma

Interventions

Current interventions as of 26/02/2020:
This feasibility project uses the Medical Research Council (MRC) guidelines on developing a complex intervention. It will have four stages and adopts a mixed-methods approach. Recruitment for each stage will be separate.

The project will be conducted as stages:
1. A qualitative study involving semi-structured interviews will explore attitudes to exercise
2. A qualitative study involving focus groups of healthcare professionals will explore attitudes to exercise for severe asthma
3. A small scale feasibility study of an RCT of AT-PR versus UC will be performed. A qualitative approach will be used to explore the facilitators and barriers to participation in a AT-PR and the study protocol. AT-PR, modelled on our local successful PR programme for chronic obstructive pulmonary disease (COPD), will be exclusively for severe asthma and further modified according to the findings from stage 1 and 2. Usual care (DAC) will include disease education and exercise advice from asthma nurses. We plan to randomise 40 patients to the intervention arm and 20 patients to usual care. We estimate conservatively that we will recruit 30% of those invited to estimate the recruitment rate with a precision of at least +/- 7%. We suggest a conservative dropout rate of 25% (our local PR dropout rate is approximately 15%); recruiting 40 patients to the AT-PR programme, the precision of the estimated retention rate would be at least +/- 14%. From experience to date, we are expecting very few serious adverse events relating to the exercise programme. Based on a rate of 2.5%, the rate would be estimated to be less than 13%. All precisions are based on two-sided 95% confidence intervals.
4. The patient involvement during the project will be assessed to make any necessary adaptations for the multicentre trial

Healthy volunteers were recruited to
1. Provide age gender match controls for adults with severe asthma to compare daily physical activity patterns and levels
2. Build a healthy control cohort for other studies

They were not randomized to an intervention and did not receive an intervention. They were asked to participate in two study visits. The first visit was to provide consent, medical history and collection of physical activity monitor. On the second visit the participants returned the monitors and the study team downloaded the data.

Previous interventions:
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Intervention Type
Behavioural

Primary outcome measure
To establish the practicality of a definitive multicentre RCT, the primary outcomes for the feasibility study are:
1. Recruitment rate
2. Retention rate
3. Incidence of adverse events

Secondary outcome measures
The outcome measures proposed for the multicentre trial will be included to assess patient acceptability of the tests, study protocol and data completion. The outcome measures to assess the intervention will be collected at baseline, 12 weeks and 6 months by a blinded investigator. We have experience in using all proposed outcome measures. Baseline demographics will be recorded including body mass index and spirometry.

Safety
1. Any adverse events directly or indirectly related to the exercise measurements and training sessions will be recorded. Any severe adverse event will be reported to our Research and Development office immediately. An external respiratory physician has agreed to independently assess any adverse events and stop the trial if necessary.
2. A full cardiopulmonary exercise test with expiratory gas analysis will be performed on a treadmill. Exercise-induced bronchoconstriction will be assessed by a flow-volume loop, before and after the treadmill test, before and after 12 weeks. All patients will be included in the programme and excluded only if they have an adverse event. This data will used as an outcome measure not just for safety.
3. Asthma control and disease activity will be assessed by:
3.1. The Juniper Asthma Control Score
3.2. Measuring airway inflammation by induced sputum count before and after the intervention
3.3. By comparing the preceeding 9 months unscheduled healthcare visits for asthma with 9 months after and including the intervention, including GP, accident and emergency attendance and hospital admissions.

Cost effectiveness
The Euroqol (EQ-5D) questionnaire will be used to assess quality-adjusted life-years (QALYs) at baseline, 12 weeks and 6 months. Costs will be calculated using NHS tariffs. All treatment including medication, adverse events and any over the counter medication will be recorded. Cost effectiveness will be assessed with the help of a health economist using methodology previously described.

The usual outcome measures for PR will be assessed to ensure acceptability of the protocol for the multicentre trial. As exercise rehabilitation is a complex medical intervention there are a number of different outcomes to assess including:
1. Asthma-specific health-related quality of life (HRQoL) using the asthma quality of life questionnaire (AQLQ) and Chronic Respiratory Questionnaire
2. Hospital Anxiety and Depression Scale
3. Incremental treatmill test (ITM)
4. Incremental shuttle walking test (ISWT)
5. Endurance shuttle walk test (ESWT)
6. Compliance with the supervised and home training programme

Acceptability and feasibility of other outcome measures that may be used for the multicentre RCT:
1. Domestic physical activity measured by tri-axial accelerometers (Sensewear pro 3). This is a valid measurement of daily activity to assess behaviour change
2. Quadriceps strength assessed by an adapted chair with a strain gauge
3. Venous blood sampling
4. Dual-energy X-ray absorptiometry (DEXA) scanning

Exacerbations of asthma
Patients will be asked to keep a diary of their exacerbations, treatment and unscheduled healthcare visits. Participants in both groups, along with their GPs, will receive a personalised management plan with guidance about initiating steroids for exacerbations. If participants present to the investigating team they will be reviewed by an independent clinician with the decision to commence treatment with oral prednisolone based on standard clinical guidelines. The patients will be asked to stop coming to the AT-PR sessions for any exacerbation requiring steroid treatment. If they are not recovered enough to start participation within 2 weeks they will be classified as a dropout. Similarly they will be excluded from the UC limb if they are not back to normal within 2 weeks to avoid bias.

Overall study start date
18/12/2013

Completion date
13/09/2018

Eligibility

Key inclusion criteria
Patients with severe asthma (defined as asthma which remains symptomatic at steps 4-5 of the British Thoracic Society asthma guidelines), despite management for >6 months in the Glenfield Difficult Asthma Clinic (DAC), will be recruited. All patients will have a thorough diagnostic work up and a treatment strategy targeting eosinophillic airway inflammation to optimise control; exercise-induced asthma is often a reflection of poor control.

Participant type(s)
Patient

Age group
Not Specified

Sex
Not Specified

Target number of participants
Stage 1: 2-30 patients; Stage 2: 6-8 focus groups of 6-10 healthcare professionals; Stage 3: 60 patients; Stage 4: patient representatives and the steering group commitee

Total final enrolment
273

Key exclusion criteria
1. Severe exacerbation within a month of entry
2. Inability to exercise e.g. due to significant musculoskeletal or neurological abnormalities

Date of first enrolment
18/12/2013

Date of final enrolment
05/09/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Glenfield Hospital
Leicester
United Kingdom
LE3 9QP

Sponsor information

Organisation
University Hospitals of Leicester NHS Trust (UK)

Sponsor details
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Sponsor type
University/education

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ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research, Research for Patient Benefit Grant, PB-PG-0712-28063

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
01/12/2020

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	23/03/2016		Yes	No
HRA research summary			28/06/2023	No	No