Title

Feasibility trial of an adapted pulmonary rehabilitation programme in Georgia

Short title

Pulmonary Rehabilitation service set up in Georgia

Trial registration

The study will be registered on ISRCTN registry.

Protocol version

Version 2.0

Funding

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Roles and responsibilities

Names, affiliations and responsibilities

Lead investigators

Maka Maglakelidze (MM) will supervise the study, in conjunction with KJ and other collaborators from the University of Birmingham.

Research team collaborators

Tamaz Maglakelidze (TM) will be the main researcher on the study and will be responsible for delivery of the study.

Ivane Chkhaidze (IC). IC will be the lead advisory clinician on the study, providing support as required.

Nino Maglakelidze (NM). NM will be an adviser on the study, providing support as required.

Ruska Kurua. RK will be the research administrator, providing support for the study (administrative support)

Naniko Gonjilashvili (NG) will be the research administrator, providing support for the study (data management)

Keti Gogvadze (KG) will be the research administrator, providing support for the study (interviews)

Natia Chkhaidze (NC) will be the research administrator, providing support for the study (administrative support)

Prof Kate Jolly; University of Birmingham. KJ will supervise the study, in conjunction with MM and other collaborators from the University of Birmingham.

Dr Kiran Rai; University of Birmingham. KR will supervise the study in conjunction with MM, KJ and other collaborators from the University of Birmingham.

Study sponsor

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Summary

Research question What is the feasibility of an RCT to determine the effectiveness of a PR programme adapted to the Georgian context compared to usual care for patients with symptomatic COPD of MRC grade 2+?

Phase 1 Focus group discussion with key stakeholders to inform the adaptation of a pulmonary rehabilitation programme to the Georgian context. To recruit people with COPD (group 1), primary care doctors and respiratory physicians (group 2) and rehabilitation specialists (group 3). Six to eight participants in each group, with a range of characteristics. Data will be analysed using the framework approach.

Phase 2

Population Symptomatic COPD patients with MRC grade $\geq$ 2, from secondary care (Chapidze Emergency Cardiology Center) or referred from primary care.

Intervention Culturally adapted pulmonary rehabilitation programme, individually tailored

Control Two to three hour educational and exercise session after six-months follow-up

Outcome Feasibility outcome measures: fidelity, acceptability, recruitment rates, follow-up rates, adherence and patient-incurred costs. Outcome measures to inform a future trial: HRQoL, exercise capacity, smoking status, CAT, physical activity, anxiety, depression, exacerbations and health service utilisation

Study design Randomised controlled feasibility trial

Introduction

Background and rationale

COPD burden and health system in Georgia

Chronic Obstructive Pulmonary Disease (COPD) is a long-term incapacitating respiratory condition, responsible for substantial ill health (4th leading cause of death worldwide) (1, 2). The burden of chronic respiratory diseases (CRD) is growing in Georgia and age standardized mortality indicator during last 20 years shifted from 7th place to 3rd (from year 1990 to 2013).

The main risk factors for chronic respiratory diseases (CRDs) in Georgia are smoking, indoor air pollution and outdoor air pollution. 33% of Georgian population are smokers (Male – 58%, Female - 6%) (3). There is no comprehensive and integrated tobacco dependence and cessation program (3) and availability of pharmacotherapy is limited in practice.

Since 2013 the government of Georgia has launched a Universal Healthcare Program, which ensured universal coverage of healthcare services for Georgia's population (4). More than 90% of the Georgian population are beneficiaries; the rest are covered through private insurance services (5). The program covers planned and emergency outpatient and inpatient services and basic medication for vulnerable populations (5). Although the Universal Healthcare Programme covers all health care service costs and part of the cost of medicines few COPD patients receive medication because medications are only reimbursed for hospital inpatients and some vulnerable groups; most people have to pay for their medication.

Pulmonary rehabilitation (PR)

International scientific evidence suggests that pulmonary rehabilitation (PR) has physiological and psychosocial benefits (6), when delivered post-admission for an exacerbation PR reduces hospital admissions and may reduce mortality (7). PR has been shown to be cost-effective in high income country settings (8). A systematic review of trials showed that PR helps with fatigue and breathlessness, and improves quality of life and exercise capacity of patients, with evidence that at least 4 weeks of exercise training were needed for benefits to be observed (6), whilst the ATS/ERS Statement on PR recommend a minimum of 6 weeks of exercise training (9) and more recent guidance recommends a minimum of 8 weeks of exercise (10). Exercise is recommended to be 2-3 times per week and is often delivered in two supervised or monitored sessions, with a third unsupervised session. The most effective components within PR, its length and location, degree of supervision and intensity of training required is not clear (6), although exercise is considered to be the most important component (11). Recent recommendations from The ATS/ERS state that "to qualify as PR, programs must include, at a minimum: a structured and supervised exercise program for patients with a variety of respiratory conditions, a patient education/behavioural program intended to foster health enhancing behaviour, patient assessment and outcomes measures, and provision of recommendations for home-based exercise and physical activity" (10).

Rationale for the study

There are currently no PR services offered to the patients in Georgia. In this context, where resources are limited, yet COPD is a major burden, research is needed to evaluate whether offering PR is feasible and to assess whether the intervention would have similar effects to those observed in other settings. Using a short supervised course, and/or unsupervised home-based exercise is likely to

more economically viable. With limited availability of pharmacotherapy, there is also an opportunity to test the effectiveness of different components of PR or to evaluate a tiered approach tailored to patient need. The findings could have implications for other similar settings.

Objectives

1. To tailor the content and delivery of pulmonary rehabilitation to fit the Georgian health service and setting

2. Conduct a randomised controlled trial to assess the feasibility of delivering a culturally tailored PR intervention

Study design

A qualitative study and randomised controlled feasibility trial

Methods: Participants, interventions, and outcomes

Phase 1: Tailoring pulmonary rehabilitation to the Georgian context

Study setting

This phase of the project will involve carrying out a qualitative study. The aim will be to carry out three separate focus groups with the following key stakeholders: group 1: COPD patients; group 2: clinicians; and group 3: rehabilitation specialists. Participants will be identified from the following settings: Chapidize Clinic in Tbilisi (COPD patients), Chapidze Emergency Cardiology Center (rehabilitation specialists) and primary and secondary care (clinicians). The focus groups will be carried out in the Chapidze Emergency Cardiology Center.

Participant timeline

Participants will be invited to take part in a single focus group session, which will last between 2.5 – 3.0.

Sample size

Each focus group will include 6 – 8 participants; this is considered as the optimum sample size for focus groups to enable effective and meaningful discussion to be generated among the participants (12), and achieve data saturation (13).

Recruitment

Recruitment of COPD patients A sample of patients from the Chapidze Emergency Cardiology Center will be identified and invited (via telephone) to take part in the qualitative study. Those interested will be sent an invitation by e-mail which will include an invitation letter, information sheet and a reply slip to indicate their interest in participating. Participants will be contacted by the research team to arrange a date for the focus groups. Participants will receive a reminder call three days prior to the focus group.

Recruitment of healthcare professionals Primary care doctors and respiratory physicians, who are known to the Georgian Respiratory Association (GRA), and rehabilitation specialists based at Chapidze Emergency Cardiology Center, will be invited to take part in the qualitative study. These individuals will be initially contacted by the telephone, and/or through the information meetings (primary care doctors attend information meetings). Those interested will be sent an email, which will include an invitation letter, information sheet and a reply slip to indicate their interest in participating. Participants will receive a reminder call three days prior to the focus group.

Focus group sessions

Preparation for the focus group As there are currently no pulmonary rehabilitation (PR) services being offered in Georgia, both patients and the healthcare professionals will be familiarised with the PR programme, 2-weeks prior to the focus group sessions. A UK-based PR video will be provided to the participants; this will include PR exercises and education on the management of COPD. Handouts, containing details of other PR programme components in high income settings, will also be provided.

Focus group discussion A discussion guide (appendix 1) will be used in all three focus groups to consider which are the essential elements of a PR programme for delivery, and the components that would be tailored to meet the needs of COPD patients in Georgia. For example, this will include assessing the need for: training on inhaler technique, medication adherence, action planning (managing COPD flare-ups)) and how or who should provide the education/information (for example, education on smoking cessation as part of the PR or whether there should be referral to a specialist smoking cessation programme). The discussion guide will also explore the appropriate and acceptable delivery methods of the PR programme for example, the setting (e.g. hospital vs. home), equipment (e.g. treadmill vs. outdoor walking), length of the programme (for example, 6-weeks vs. 8-weeks) and the duration of each PR session. The discussions will use the APEASE criteria - affordability, practicability, effectiveness (and cost-effectiveness), acceptability, side-effects (and safety), and equity (14).

Phase 2: Randomised controlled feasibility trial

Study setting

The study will primarily recruit participants from the Chapidze Emergency Cardiology Center, Tbilisi. This will be supplemented by recruiting for primary care (GP practices), if necessary.

Eligibility criteria

Inclusion:

- MRC 2+
- Confirmed COPD diagnosis based on spirometry (predicted ratio of FEV_1/FVC of 0.70)
- Patient must be able to walk 10 meters independently
- Patient able to exercise with some degree of independence, and within a group setting

Exclusion:

- Musculoskeletal or neurological conditions that prevent exercise
- Unstable CVD (e.g. unstable angina, aortic valve disease, unstable pulmonary hypertension)
- Severe cognitive impairment
- Severe psychotic disturbance
- Contagious infectious disease
- Very poor balance

Randomisation

Randomisation to one of the two groups will be performed using an electronic database (REDcap); allocation will be based on a 1:1 ratio.

Subsequent to randomisation, patients will be asked to complete all baseline measures and questionnaires.

Intervention: pulmonary rehabilitation programme

A pre-rehabilitation one-to-one assessment will be booked at a time convenient for the patient. The aim of this assessment will be to orientate the patient to the PR intervention and tailor their exercise programme. For this, the ISWT, perceived exertion and breathlessness scale will be used to prescribe the intensity of the exercise component of the PR programme. Patients will be prescribed 65 – 85% of their maximal baseline ISWT performance (can be lower in deconditioned patients) (15).

The adapted PR programme will consist of two main components: exercise and education on the management of COPD. The description, content and frequency of these components will be determined during phase 1 of this project (cultural tailoring).

Control group

Participants randomised to the control group will be offered to attend a 2 – 3 hour educational session. This will be carried out by the rehabilitations specialists 6-months after study enrolment, once follow-up is complete.

Outcome measures

Data will be collected from patients at the end of the PR programme (6 – 8 weeks) and at six-months.

Feasibility study outcomes will include: delivery with fidelity, acceptability to participants, recruitment rate, follow-up rate at 6 months, adherence to intervention, ability to carry out trial procedures, feasibility of methods to measure costs of PR, other COPD-related health care utilisation and patient-incurred costs

Outcome measures to inform a future trial to evaluate clinical and cost effectiveness: HRQoL (SGRQ and EQ-5D-5L); exercise capacity measured by the ISWT; smoking status validated by cotinine; COPD Assessment Test (CAT); self-reported physical activity (IPAQ); self-efficacy; anxiety and depression

(PHQ-9 and GAD-7); self-reported exacerbations; health care utilisation including hospital admissions; and costs/resource use incurred by patients.

Participant timeline

Participants randomised to the intervention group will be invited to a baseline visit/one-to-one pre-rehabilitation assessment. The number of PR intervention visits per week, and the total length of the PR programme will determined after phase 1 of the project (focus group discussions).

Participants randomised to the control group will be invited to four visits: baseline visit, follow-up visits (end of programme and 6-months) and a 2-3 hour educational and exercise session (6 months).

Sample size

Data from literature suggests that pilot studies that aim to inform larger trials should include ≥30 participants to estimate a parameter (16). Based on this, 30 patients will be included in each arm of the trial (total: n=60).

Recruitment

Eligible COPD patients, attending the Chapidze Emergency Cardiology Center, will be invited to take part in the feasibility trial. Those who work in the clinic (e.g. respiratory consultant, or consultant's assistant) will either phone existing clinic patients to provide information about the study, or inform those who are attending their clinic appointment. To encourage recruitment of a range of socioeconomic groups, patients will be recruited from primary care and other hospitals within Tbilisi.

Patients who are interested will be provided with the study invitation documents (including participant information sheet and reply slip) via email or post (through the DHL service, as the national postal service is unreliable). These documents will be provided at the time of the clinic appointment, for those who indicate an interest in-person.

Methods: Data collection, management, and analysis

Data collection methods

Phase 1: Tailoring pulmonary rehabilitation to the Georgian context

Three focus group discussions will be carried out, lasting up to 2 hours each, and will be audio-recorded. Informed consent will be gained at the time of the focus group session. No other research visits will be involved in the phase of the study.

Phase 2: Randomised controlled feasibility trial

Study assessment 1

The baseline research assessment is likely to last approximately 90 – 120 minutes, and include the following components:

1. Eligibility check: this will be assessed based on the inclusion/exclusion criteria above. Spirometry will be carried out by the respiratory team at the Chapidze clinic, who will confirm COPD diagnosis.

2. Informed consent: Participants will have the opportunity to ask any questions before completing the consent form with the researcher. As well as consenting to the main study, participants will asked to consent to being contacted and take part in the qualitative interviews linked to this study.

3. Completion of the case report form (CRF), which will include the following:

    a. Documenting patient details (initials, age, sex, ethnicity and employment status)

    b. Conducting the Incremental Shuttle Walking Test (ISWT): to be carried out twice; distance walked to be documented in meters; collect various measures pre and post each test (blood pressure, heart rate, oxygen saturations, Borg dyspnoea and RPE scores); record reason for cessation (e.g. breathless, dizziness, painful legs).

    c. Self-administered participant questionnaire booklet: sociodemographic data (age, sex, ethnicity, education level, marital status, number of dependents; number of adults in the household; and employment); comorbidities; medications; level of dyspnoea (MRC score); smoking status; quality of life and disease specific questionnaires (EQ-5D-5L; St George's Respiratory Questionnaire [SGRQ]; and COPD Assessment Test [CAT]); anxiety and depression (GAD 7 and PHQ-9); self-reported physical activity levels (International Physical Activity Questionnaire [IPAQ]); and health service use (hospitalisations).

    d. Measuring height and weight to calculate body mass index (BMI)

    e. Saliva or urine sample to measure cotinine (nicotine levels)

4. Randomisation to the treatment or control group

The baseline assessment will be carried out by a member of the research team (exception: the ISWT will be carried out by the trained rehabilitation specialist(s)). The researcher will record all study data on CRFs to ensure standardised data collection/recording. On completion, the researcher will enter the data on to the secure REDcap electronic database.

Study assessment 2

At the end of the PR programme, participants will be invited to a second study assessment. This will include collecting similar data as the baseline assessment:

1. Conducting the ISWT (once), and collecting all pre and post-test measures (as detailed above), by the rehabilitation specialist

2. Self-administered participant questionnaire including the following: level of dyspnoea (MRC score); smoking status; quality of life and disease specific questionnaires (EQ-5D-5L; St George's Respiratory Questionnaire [SGRQ]; and COPD Assessment Test [CAT]); anxiety and depression (GAD 7 and PHQ-9); self-reported physical activity levels (International Physical Activity Questionnaire [IPAQ]); health service use (hospitalisations); patients costs (for those attending the PR programme); and injuries or health issues as a result of the PR programme.

3. Saliva or urine sample to measure cotinine (nicotine levels)

Study assessment 3

Patients will be invited to attend a final follow-up assessment, after 6 months, to collect the following data:

1. The ISWT (once), and collecting all pre and post-test measures (as detailed above, and to carried out by a rehabilitation specialist)

2. Self-administered participant questionnaire including the following: level of dyspnoea (MRC score); smoking status; quality of life and disease specific questionnaires (EQ-5D-5L; St George's Respiratory Questionnaire [SGRQ]; and COPD Assessment Test [CAT]); anxiety and depression (GAD 7 and PHQ-9); self-reported physical activity levels (International Physical Activity Questionnaire [IPAQ]); and health service use (hospitalisations)

3. Saliva or urine sample to measure cotinine (nicotine levels)

Study assessments 2 and 3 will be carried out by a member of the research team.

Process measures

To be able to assess the feasibility of delivering the PR intervention, the following will be measured:

1. Fidelity of delivery of the programme by the rehabilitation specialists: the aim will be to assess whether patients are achieving their prescribed exercise goals which have been set by the rehabilitation specialist. For this, a member of the research team will examine the following patient data over six PR sessions: attendance to all PR sessions (noting number of missed sessions); completion of all prescribed exercises; achieved all sets/repetitions/exercise duration prescribed for each exercise; achieved the recommended exertion score (Borg score); and exercise prescription review (changes by physios based on patient progress). This data will be completed by the patient at each visit, and stored in their research file.

2. Participant adherence to the intervention: number of sessions attended; completion of the PR programme; where sessions were carried out (home/clinic) and how many session within each setting; consistent achievement of prescribed goals (e.g. sets/reps/exertion); and education session attendance. This data will be extracted for the patient's research file.

3. Ability to carry out trial procedures: baseline data (% complete); follow-up rates (end of programme and 6-months); recruitment rate, and comparison of the characteristics with those who declined to take part; and completeness of data entry.

4. Reach: characteristics of the participants; ability to recruit the more socio-economically disadvantaged members of the population; and assessment of geographical reach

5. Intervention acceptability – rehabilitation specialists: to conduct qualitative interviews with staff who delivered the PR programme about training, confidence with delivery and how PR fits with the rest of health care for people with COPD.

6. Intervention acceptability and experience – participants. To also conduct qualitative interviews with intervention group participants to explore their experience of the PR programme (n: 15-20). It is likely that all 30 intervention group participants will need to be invited for up to 20 to be interviewed. If acceptance rates are high then purposive sampling

will be used to ensure participants with a mix of socio-demographic characteristics, severity of COPD and differing levels of engagement with the PR programme. All participants who drop-out of the PR programme before completion will be invited to be interviewed to explore barriers to continuing with the PR programme. Semi-structured interview schedules based on the research literature, discussion within the team and input from PPI will be devised. All interviews will be recorded and transcribed verbatim. Reflective notes will be made following each interview.

Data management

Data will be collected on case report forms which will be kept by the Ivane Chkhaidze in a locked cabinet in a secure room at the Chapidze Emergency Cardiology Center, Tbilisi. The research team will enter data from case report forms into a bespoke REDCap online database. All electronic data held by the research team will be password protected and stored on encrypted study laptops. The research team will conduct monitoring visits during the recruitment period to ensure data are being collected, entered and stored according to pre-specified study working instructions.

Data analysis

Statistical methods

We will report recruitment and follow-up rates, with 95% confidence intervals, as a measure of feasibility of the trial. Although the trial will not be powered to detect a difference between intervention and wait-list control, we will calculate the HRQoL at PR end and 6 months for those allocated to each group; 95% confidence intervals will be provided for estimates obtained. The economic analysis will report questionnaire completion rates, and a cost-consequences analysis. This will include a descriptive analysis of health care costs and EQ-5D-5L scores and an initial estimate of the cost of PR, taking into account the duration of the intervention, format of sessions and number of sessions attended by each participant.

Qualitative data

The Framework approach to data management and analysis will be used for the interviews and focus groups (17).

Methods: Monitoring

Data monitoring

The study will be overseen by a Study Steering Committee, consisting of one representative from each of the following stakeholder groups: patient, clinician/policy maker, research team and, the Breathe Well executive committee. In addition there will be two representatives from the International Scientific Advisory Committee, one of whom will act as chairperson. The Study Steering Committee will meet on a 6-12 monthly basis, as required.

The research team will hold monthly meeting with the Breathe Well executive committee, to discuss current progress and any issues arising.

Harms

The focus group discussions, physiological and questionnaire-based measures pose no risk to the participants.

Non-serious adverse events

The risk of harm associated with study procedures and the intervention are considered to be very low. To further minimise the risk of events, we will:

1. Ensure patients meet the eligibility criteria
2. Carry out a risk assessment (e.g. of the venue, risks to patients and staff) – see appendix 2
3. Staff will be trained to manage any risks that are identified in the assessment

Due to the low risk in this study, only the following non-serious adverse events will be collected which will form part of the study outcomes:

- Musculoskeletal injury as a result of the intervention
- Other minor injuries as a result of the intervention
- Non-serious medical events during the rehabilitation that do not require admission to hospital, e.g. participant had to stop due to angina attack that resolved with medication.

Data on these occurrences will be collected on the participant CRF, and documented on an incident log (appendix 3) during each session. This information will be periodically assessed a member of the research team to identify any further training needs for the rehabilitation specialists.

Patients who are identified to have any suicidal thoughts (according to the PHQ-9 questionnaire at baseline) will be managed according to standard clinical practice in Georgia e.g. referral to a psychologist or primary care doctor.

Serious adverse events

Serious adverse events (SAEs) will be defined as an untoward medical occurrence that results in death, is life-threatening, requires hospitalisation, results in persistent or significant disability or incapacity, or is considered medically significant by the study investigator.

There are some potential SAEs which could be expected to occur during the exercise components of the PR programme, although assessing the eligibility of the participants according to the exclusion criteria will minimise this risk e.g. people with unstable cardiovascular disease, musculoskeletal or neurological conditions the prevent exercise and those with very poor balance.

We do not anticipate SAEs to occur in this study, but this is a group of patients with comorbidities doing an exercise intervention. With suitable monitoring by the rehabilitation specialists, we would expect SAEs to be minimised. But if they do occur, all SAEs will be recorded in the CRF and the database. SAEs will be reported to the chief investigator immediately and within 2 working days of being made aware of the event. If, in the opinion of the local doctor or chief investigator, the event was: ‘related’ (resulted from the administration of any of the research procedures) and ‘unexpected’

(not in our list of expected events), and also occurred within 24h of the study assessment, these will be reported to the lead and local in-country ethics committees, sponsor, UoB team and UoB ethics committee (appendix 4).

Auditing

The study may be subject to inspection and audit by the Chapidze Emergency Cardiology Center, under their remit as sponsor, and other regulatory bodies, to ensure adherence to agreed and relevant principles of GCP and local regulatory frameworks.

Research sites will receive study-specific training before recruitment commences, and all sites will be monitored by the research team throughout the study period.

Patient, clinician and policy maker involvement

Patients, clinicians and policy makers participated in a research prioritisation process (Oct 2017), to discuss this and other potential research studies; the proposed PR study was a highly prioritised research study.

An advisory group will be formed, including relevant patients, clinicians and policy makers. The advisory group will meet 3-4 times per year as required during the Breathe Well programme. Patient members of the advisory group will meet before the study begins to pilot the study assessment measures.

Policy makers will be engaged through a variety of means. 1) Involved in priority setting meeting; 2) short communications (and meetings as required) throughout the project to keep them informed of findings; 3) inclusion of health economic data to inform policy decisions; 4) framing findings of research in terms of policy solution; 5) preparing short briefing with policy solutions for dissemination at the end of the study.

Patients, clinicians and policy makers who are involved as above, will receive study updates twice a year during the study, and all stakeholders will be consulted at the end of the study for advice on appropriate means of disseminating study findings.

Ethics and dissemination

Research ethics approval

The ethics application will be submitted to Chapidze Emergency Cardiology Center, Tbilisi.

Consent or assent

Details of how participant informed consent will be obtained are provided in the 'Data collection methods' section above.

Confidentiality

All members the research team are healthcare professionals. For the research project, the team have taken part in good clinical practice (GCP), which includes training on the confidentiality.

For the purposes of the research study, only members of the research team will have access to identifiable participant data (e.g. name, contact details), which will be stored separately from study data. Study data and identifiable participant data will also be stored on a REDCap database, hosted on a University of Birmingham encrypted server.

Paper-based data (case report forms and/or consent forms) will be stored in locked filing cabinets at Chapidze Emergency Cardiology Center. Electronic data will be held securely on encrypted study laptops. Collaborators from University of Birmingham will have restricted access to the REDCap study database, and will not see identifiable data fields. The research team will not share identifiable data with external parties.

Declaration of interests

The principal investigators have no competing interests in relation to the study described in this protocol.

Access to data

Access to the study dataset will be restricted to the research team and relevant collaborators from University of Birmingham e.g. statistician, executive committee. As the data will be stored on University of Birmingham servers, contracts state that the data will be owned by University of Birmingham and the research team will have irrevocable, royalty-free, non-exclusive license to use the data.

Ancillary and post-trial care

Due to the low risk posed by this study, no ancillary and post-trial care is necessary.

Dissemination policy

Results of the study will be disseminated through academic peer-reviewed publications and at relevant national/international academic conferences. All publications will be open-access, with links provided on the Breathe Well website (https://www.birmingham.ac.uk/breathewell).

At the end of the study, a printed report will be produced and disseminated among stakeholders. A stakeholder meeting will be held to inform the study results, recommendations and discuss policy options.

In addition, COPD patient group capacity building will be provided to strengthen advocacy efforts on COPD in Georgia and in the regions. Necessary factsheets, policy briefs and infographics will be developed for communication reasons.

Timetable

Please refer to Gantt chart in the attached MS Excel document

Appendix 1

Tailoring of Pulmonary Rehabilitation to the Georgian context

Approach

The first stage of the project will be to 'tailor' pulmonary rehabilitation to take account of the local context, health care services and cultural norms and beliefs.

Issues to explore:

Health care service factors

1. Cost of the programme – would co-payments be acceptable?

2. Pathway of care

    a. Identification of people with COPD who are eligible for pulmonary rehabilitation - how?
    b. How would they be referred into the programme?

3. Programme length and frequency
    a. What duration of programme is feasible and affordable?
    b. What frequency would be acceptable? (e.g. once or twice a week)

4. Location of PR programme – hospital/clinic setting – appropriate?
    a. Culturally? Patients familiar with environment? Any emotional barriers identified by implementing PR in this setting?

5. Pulmonary rehabilitation equipment
    NOTE: to show video to group demonstrating parts of PR

    a. What is currently available?
    b. Does the exercise need to be adapted to use low cost elements e.g. walking, sandbags/bean bags and bottles for weights?
    c. Are there any culturally preferred exercises?
    d. Aerobic exercises – preferred with or without equipment? (e.g. treadmill/bicycle vs. walking aerobic training)

6. Physical activity homework
    NOTE: to show a potential homework booklet to the group (with pictures)

    a. Would a homework book be completed (information about exercises to be done at home)?
    b. Would pictures help?

c. Would patients mind completing filling a workbook for assessment at next visit? (culturally intrusive?)

7. Preparing the group for the PR programme as a way of increasing programme engagement and retention
   NOTE: feedback needed on video/clips of PR
   a. Should the first PR session educate the participants on what to expect and develop social cohesion among group members?
   b. Will video/video clips help in preparing the participants?
   c. Language of video?

8. What self-management components should be included and how?
   E.g. should smoking be integral or cessation support from a specialist service?

See table to explore the various self-management components

Self-management components

	Should this be included?	Face to face	Electronic material	Signposting to another professional	Priority? Y/N
Disease knowledge: anatomy, physiology, pathology in health and chronic respiratory disease					
Medication use and adherence					
Inhaler technique and use					
Smoking cessation					
Breathlessness or symptom management					
Action planning: managing exacerbations, coping plan, management of COPD symptoms, recognising when to call a doctor					
Breathing techniques					
Bronchial hygiene and techniques					
Energy conservation					
Nutritional advice					

Managing travel					
Psychological intervention					
Preventative actions					
The benefits of physical exercise					
Identifying and changing beliefs about exercise and health related behaviours					
Opportunities to exercise after pulmonary rehabilitation					
Confidence, self-efficacy and self-management					
Loving relationship/sexuality					
Goal setting and rewards					

9. Who would be best placed to deliver the PR programme (who has the skill-set)?
    a. The exercise sessions
    b. The educational sessions

10. Involvement of other persons or professionals in the delivery of the PR programme (other than the rehabilitation specialist)?

11. Forms of social support during the programme?
    a. Internet blogs or groups?
        i. Internet access available for most?
    b. Meetings/events with other COPD patients (e.g. support groups)?

Cognitive adaptations

NOTE: when exploring cognitive adaptations, to also assess whether any cross-culture differences (people in other parts of Georgia)

12. Language(s)?
    a. Group sessions
    b. Material (handouts, leaflets etc)
    c. Electronic material

13. Reading level adjustments?
    NOTE: share PR information/handouts/videos with the groups
    a. Literacy levels
    b. Literal translation practical?

14. Technological components (videos/PowerPoint slides/support groups)
    a. IT access and literate?

15. Use of non-offensive language
    NOTE: video clip about encouragement during PR programme
    a. Would patients be comfortable with such encouragement?
    b. Using the Borg scale as a method of assessing exercise intensity

Physical barriers

16. Travel
    a. Would this be an issue?
    b. Access from rural areas?
    c. What would patients think about a home-based element?

17. Employment?
    a. Timing of the programme

Outcome measures

1. Outcome measures to be assessed?
    a. Any culturally appropriate outcomes to assess intervention effectiveness?
    b. Current proposed measurement tools appropriate? (shuttle walk, MRC dyspnoea, Hospital Anxiety and Depression Scale, SGRQ, CAT, health service use, exacerbations, cotinine test, self-reported physical activity)

Other issues

- Other social and cultural issues
- Beliefs about breathlessness and exercise
- Gender issues?
- Form of relaxation?
- Cohort or rolling programme?
- Outside a trial setting, what are the facilities for assessments to ensure a diagnosis of COPD and of exercise capacity to tailor the physical activity to the individual
- Can national audit be built into the system? Assessments at baseline and follow-up with standard assessments to enable comparison between programmes.

Appendix 2

Pulmonary rehabilitation feasibility trial risk assessment

Possible Risk Design and methods	Describe the risk	Can the risks be reduced? What would you do?	How would you monitor the study to address concerns?
Risks to participant safety from clinical procedures specified by the protocol	• Musculoskeletal injury • Cardiovascular event	Eligibility criteria: exclusion of contraindicated/high risk patients Staff training on individualised exercise programmes, accounting for patient capacity and current injuries (e.g. strains and sprains) Patients will be orientated to the intervention equipment Collect and record adverse events in the patient research files, and an incident log.	Monitor serious adverse events Researchers to periodically monitor incident/adverse event log to identify further training needs for those delivering the intervention (rehabilitation specialists)
Risks to participant rights from failure to obtain appropriate consent	Risk that consent is not obtained prior to trial entry.	The Patient Information Leaflet (PIL) has been REC approved Patients will be provided with the information for the trial and given time to consider.	With the patient's explicit consent, the consent will be documented in the database and a proportion of these will be checked.

Possible Risk Design and methods	Describe the risk	Can the risks be reduced? What would you do?	How would you monitor the study to address concerns?
Risks to participant rights from failure to protect their personal data	Personal data including the patient's full name, address, date of birth, and ethnicity will be collected. Copies of signed Informed Consent Forms will be collected and stored with the patient's explicit consent.	Personal data recorded on all documents will be regarded as confidential and will be handled and stored in a secure environment and in accordance with UK and local Data Protection laws. Patients will be identified using only their unique trial number and initials on the Case Report Forms and correspondence between the Coordinating Office and the participating site.	All (n=60) signed informed consent forms will be checked to verify that patients have given explicit consent for their personal data.
Eligibility criteria- possibility that participants may be recruited that do not match the eligibility criteria (or include patients with exclusions criteria)	Recruit high risk patients, or those that do not have spirometry confirmed COPD.	Site training and use of an eligibility form will contain tick boxes containing individual statements regarding the inclusion/exclusion criteria. Spirometry will be carried out at the baseline visit to confirm COPD diagnosis.	Central monitoring will verify that eligibility was assessed prior to trial entry, on a proportion of patients

Possible Risk Design and methods	Describe the risk	Can the risks be reduced? What would you do?	How would you monitor the study to address concerns?
Patient visits	Participants colliding with each other Tripping over equipment Participants misusing equipment Participant experiences a negative response to physical activity – excessive breathlessness or fatigue or dizziness	Participants will be familiarised with the environment, and informed of safe areas as well as areas where there may be obstacles or equipment. Appropriate distances will be maintained between participants so that exercises can be carried out safely. Participants will be trained on how to use the equipment safely. Rehabilitation specialists will carry out a pre-rehabilitation session with each participant to prescribe an individualised and safe exercise programme which is based on the patient's exercise capacity. Participants will be informed of how to respond if they experience a negative response to the exercise programme. A rehabilitation specialist will be available at each exercise session, and will observe all patients.	Adverse events will be documented in the patient file and on an incident log. Rehabilitation specialists will receive additional training if safety issues are identified Patients will be re-trained on how to use equipment. Rehabilitation specialists will re-assess on the patient's exercise prescription, and consider the need for changes. Researchers to assess incident logs to identify training needs of rehabilitation specialists.
Data collection methods	The risk of incomplete data is low as most CRFs will be completed face to face with the participant. There may be a small risk of incomplete data due to the length of the questionnaires.	The CRFs have been kept to a minimum and have been well reviewed, so complexity is reduced.	Early monitoring of data return may identify any issues
Database systems • System complexity • User training	Risk of transcription errors from paper to database.	Some data validation is built into the database so range, date and logic checks are performed for some of the entries.	Data entry quality checks will be performed on a sample of CRFs.

Risks Assessment Report Review (Main Coordinator/Chief Investigator)

Name	Signature	Date

Appendix 3

Incident log

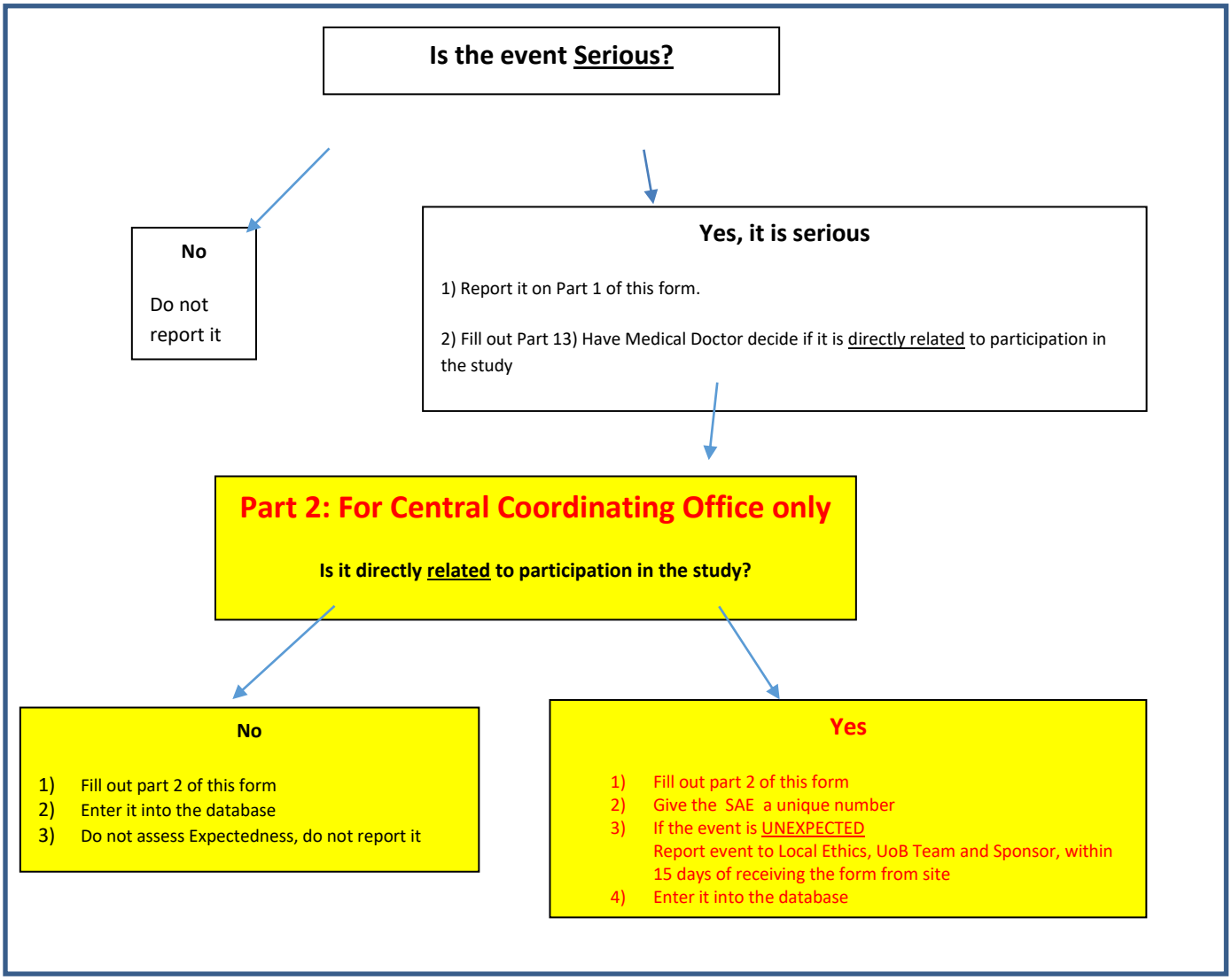
Date	Participant ID	Incident details	Action taken	Follow-up action (if applicable)	Outcome (with date)	Rehabilitation specialist details	Signature

Appendix 4 Serious adverse event guidance and form

Guidance How to use this form to report a serious adverse event	
Definitions	
Related Event	An event which directly resulted from any of the study procedures.
Serious Adverse Event (SAE)	An untoward occurrence that: • Results in death • Is life-threatening • Requires hospitalisation or prolongation of existing hospitalisation* • Results in persistent or significant disability or incapacity • Or is otherwise considered medically significant by the Study Doctor or CI *Hospitalisation for elective procedures are not regarded as a SAE.

RELATED Category	Definition	Causality
Definitely	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out	Related
Probably	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely	
Possibly	There is some evidence to suggest a causal relationship. However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant events or medication)	
Unlikely	There is little evidence to suggest there is a causal relationship. There is another reasonable explanation for the event (e.g. the patient's clinical condition, other concomitant events or medication)	Unrelated
Not related	There is no evidence of any causal relationship	

- If the event is not serious, do not report it.
- **Part 1-** to be filled out by clinic site team. The diagnosis and decision of event being directly related, or not to the study activity, to be performed by the site Medical Doctor
- Have the Medical Doctor at site decide if the event is directly related to the study
- Enter the form on the database.
- **Send the form to the Central Coordinating office- they fill in Part 2.**


Is the event Serious?
No
Do not report it
Yes, it is serious
1) Report it on Part 1 of this form.
2) Fill out Part 13) Have Medical Doctor decide if it is directly related to participation in the study
Part 2: For Central Coordinating Office only
Is it directly related to participation in the study?
No
1) Fill out part 2 of this form
2) Enter it into the database
3) Do not assess Expectedness, do not report it
Yes
1) Fill out part 2 of this form
2) Give the SAE a unique number
3) If the event is UNEXPECTED
Report event to Local Ethics, UoB Team and Sponsor, within 15 days of receiving the form from site
4) Enter it into the database

Serious adverse event form

Part 1: To be completed at the patient clinic sites			
Study Name:			
Clinic Name:		Name of Lead Doctor	
Participant Details			
Participant ID Number:	☐☐☐☐☐☐	Participant Sex:	Male ☐ Female ☐
Participant Initials:	☐☐☐	Participant Date of Birth:	D D M M Y Y Y Y
Event Diagnosis-			
Event Information, **Describe what happened**			

	Yes	**No**	**Details**	
Death	☐	☐	Date of death:	D D M M Y Y Y Y
			Cause of death:	
In-patient hospitalisation or prolongation of existing hospitalisation	☐	☐	Initial	☐
			Prolonged	☐
			Date of discharge:	D D M M Y Y Y Y
Persistent or significant disability/incapacity	☐	☐		
Other:				
Details of Event				

Date of Onset	D D M M Y Y Y Y	Date became serious	D D M M Y Y Y Y
Date aware	D D M M Y Y Y Y	Date resolved **or** tick if ongoing ☐	D D M M Y Y Y Y

Causality Asssessment (performed by Medical Doctor)

Is the event directly related, or caused by participation in this study? Yes ☐ No ☐	

Person reporting

Name		Date reported
Signature of Lead Doctor or medically qualified delegate		D D M M Y Y Y Y

1. **Send this event to the Main Study Centre within 2 working Days**
   (Maka Maglakelidze or Tamaz Maglakelidze)

2. **Enter this form into the database:**

NAME OF PERSON ENTERING THIS FORM ON THE DATABASE:_____

DATE FORM WAS ENTERED D D M M Y Y Y Y

Part 2:

To be completed by the Main Coordinating

Centre Chief Investigator

(Kate Jolly; University of Birmingham; 0121 414 7552)

On receipt of an SAE Form, a unique SAE number will be issued. The CI or delegate will independently determine the **seriousness, relatedness and the expectedness** of the SAE. An SAE judged by the PI, CI or delegate to have a reasonable causal relationship with the study will be regarded as a related SAE. The causality assessment given by the PI will not be downgraded by the CI or delegate. If the CI or delegate disagrees with the PI's causality assessment, the opinion of both parties will be documented, and where the event requires further reporting, the opinion will be provided with the report to Local and UoB Ethics Committees, the Sponsor and the UoB Breathe Well Team, within 15 days of receipt.

Initial Report	☐ Unique SAE number ☐☐☐☐☐☐
Final Report	☐ Unique SAE number ☐☐☐☐☐☐

Review of relatedness to the study by Chief Investigator or delegate

Relateness to study	Unrelated ☐	Related ☐

If the event is related, fill in the Expectedness section, below.

If the event is not related, do not do not assess expectedness, and do not report the event.

Is the event expected, according to the protocol?	**Expected** ☐ **See list at end of this form**	Unexpected ☐

If event is related and unexpected, please report it to:

1) Local Ethics 2) UoB team 3) The Sponsor

1. Signatures - In signing this form the Investigator or delegate confirms the **Causality** of the event

Name of Chief Investigator or delegate	Signature of CI or delegate	Date of CI or delegate signature
		D D M M Y Y Y Y

Please enter form into the database

Date reported to UoB Team (c.b.jolly@bham.ac.uk)	D D M M Y Y Y Y
Date reported to Local Ethics committee	D D M M Y Y Y Y
Date reported to Sponsor	D D M M Y Y Y Y

Category	Definition of Expectedness
Expected	An adverse event that is classed in nature as serious and which is consistent with known information about the study related procedures. There are some absolute contraindications for performing pulmonary rehabilitation (listed below), but documented contraindications are screened for prior to testing. • Angina pectoris • Recent myocardial infarction • Severe pulmonary hypertension • Congestive heart failure • Musculoskeletal problems **DO NOT REPORT THE ABOVE EVENTS**
Unexpected	An adverse event that is classed in nature as serious and which is not listed above. **Report to Ethics, sponsor and UoB Team**

Protocol amendments

Not currently applicable.

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