

The feasibility of early pulmonary rehabilitation and activity after COPD exacerbations: external pilot randomised controlled trial, qualitative case study and exploratory economic evaluation

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Scientific summary

The PRACTICE trial

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Scientific summary

Background

Chronic obstructive pulmonary disease (COPD) is estimated to affect > 3 million people in the UK and 210 million worldwide. Acute exacerbation of COPD (AECOPD) is defined as a sustained worsening of the patient's symptoms from his or her usual stable state that is acute in onset. Exacerbations often require hospital admission and AECOPD is the second most common reason for emergency hospital admission in the UK. AECOPD is associated with accelerated disease progression and increased mortality and patients with frequent episodes have a more rapid decline in lung function and quality of life and decreased exercise performance.

Pulmonary rehabilitation (PR) incorporating interval training or continuous exercise following AECOPD increases exercise capacity and improves symptoms; PR has become a cornerstone in the management of patients with COPD. UK and international guidelines recommend referral for PR following hospitalisation for AECOPD, commencing within 1 month of discharge. Systematic reviews have demonstrated large and important clinical effects of PR and benefits for patients in terms of quality of life and daily functioning, but only when they adhere to the programme. Despite the established benefits and widespread availability of PR, many patients are reluctant to attend because of misconceptions about the nature of the exercise training, social isolation or transportation difficulties.

Detrimental effects of the acute episode on physical fitness and skeletal muscle function occur rapidly during hospital admission, suggesting that an exercise and rehabilitation intervention delivered at the time of the acute illness might have a role in preserving muscle strength and maintaining physical function. Delivery of PR at this stage is often referred to as early PR (EPR). EPR also includes PR delivered at home after discharge following AECOPD.

This pilot trial aimed to test whether or not a full-scale randomised controlled trial (RCT) of usual care compared with EPR is feasible.

Objectives

Primary objective

The primary objective was to assess the feasibility of carrying out a definitive RCT to test the hypothesis that, compared with current practice, EPR is more clinically effective and cost-effective in AECOPD.

Secondary objectives

- Carry out an external pilot RCT to determine:
 - the availability of eligible patients and the likely rates of participant recruitment and attrition
 - whether or not data of acceptable quality can be collected
 - whether or not the research interventions can be delivered per protocol
 - key design features including the best primary end point and the sample size for the main trial.

- Carry out qualitative research to determine:
 - potential barriers to recruiting participating centres in the main trial
 - the reasons for patient refusal of consent and to collect data on whether or not the baseline characteristics and adherence to routine treatment of non-recruiters differs from those of consenting participants
 - the reasons for participant attrition
 - the acceptability of the research and intervention procedures to participants and health professionals.
- Carry out health economic modelling to:
 - identify key drivers of NHS and social care costs
 - pilot data collection strategies in advance of the definitive trial
 - quantify the potential benefit of carrying out a definitive trial.

Design

This was a parallel-group, randomised pilot 2 × 2 factorial trial (with an equal allocation ratio for each of the four groups) comparing hospital EPR, home EPR, both interventions and usual care alone (delayed community-based group rehabilitation). Integrated qualitative research and an economic analysis were also conducted.

Setting

The setting was two acute hospital trusts in the UK.

Participants

Between 28 September 2015 and 30 April 2016, 449 patients with AECOPD were screened for eligibility. Inclusion criteria were age ≥ 35 years, known COPD and admitted with AECOPD, non-acidotic and maintaining the blood oxygen saturation level (SpO_2) within a prescribed range. Exclusion criteria included the presence of comorbidities that would affect patients' ability to undertake the interventions. Sixty-one patients gave consent to participate in the trial and 58 were randomised.

Interventions

- *Manualised hospital EPR.* A cycle ergometer ('bike') was used to deliver exercises at the hospital bedside. The prescription (cycle workload) was set by a physiotherapist at session 1; further sessions could be delivered by another physiotherapist/physiotherapy assistant. The patient completed 16 revolutions of the bike on both set of limbs, three times a day for 5 consecutive days. Adjustments to the workload could be made to ensure completion of 16 revolutions.
- *Manualised home EPR.* The intervention consisted of eight exercises that could be adapted to account for participants' capability. Four sessions over 2 weeks were delivered by a physiotherapist in the patient's home.

Main outcome measures

Feasibility outcomes

The primary feasibility outcome was the feasibility of recruitment, defined as the recruitment of 76 participants in a 7-month recruitment window at two centres.

Other feasibility outcomes

- Recruitment and attrition rates.
- Number of missing values/incomplete cases.
- Intervention adherence.
- Participant views on intervention/research protocol acceptability.
- Therapist views on intervention/research protocol acceptability.
- Feasibility of recruiting participating centres.
- Decision on the primary end point for the main trial.

Clinical outcomes

The primary clinical outcome was the 6-minute walk distance (6MWD), a validated objective evaluation of functional exercise capacity. The primary outcome was measured at 90 days post randomisation; the secondary outcomes were measured at 30 days post randomisation.

Secondary clinical outcomes

- London Chest Activity of Daily Living (LCADL) scale.
- EuroQol-5 Dimensions five-level version (EQ-5D-5L).
- COPD Assessment Test (CAT).
- Medical Research Council (MRC) Dyspnoea Scale.
- Activity monitor data.
- Written activity diary.
- Serious adverse events (SAEs).
- Health and social care resource use.
- Perceived Necessity and Concerns questionnaire.
- Exacerbations.
- Readmissions.

Qualitative study

The qualitative study had a multiple case design with the unit of analysis being variably at the participant level and at the level of the two experimental intervention programmes ($n = 11$ staff interviews). For the participant case studies ($n = 27$ participant interviews), the embedded units of analysis were (1) interviews at 7 days post discharge ($n = 17$), (2) interviews at 90 days post randomisation ($n = 18$) and (3) quantitative case report forms, especially the Perceived Necessity and Concerns questionnaire. Data were available for all three embedded units for eight participants. Barriers to trial and intervention implementation were assessed through review of e-mails and Trial Management Group minutes. The acceptability of the research protocol and EPR was assessed through semistructured interviews. Interviews were audio recorded and transcribed verbatim with transcripts coded in NVivo version 11 (QSR International, Warrington, UK) and analysed using framework analysis within the theoretical domains framework and normalisation process theory.

Optimisation

Co-applicant physiotherapists reviewed intervention case report forms to determine the extent to which treatment was optimised using predefined criteria for self-reported perceived exertion, the prescription and adherence to the prescription.

Economic evaluation

An exploratory economic evaluation was undertaken to compare the potential incremental cost per quality-adjusted life-year (QALY) of the three interventions (home EPR, hospital EPR and both interventions) compared with usual care over the 90-day trial time horizon to (1) determine if the interventions have the potential to be cost-effective, which could be further assessed in a future larger trial; (2) assess the uncertainty around the cost and effect (QALY) estimates and the incremental cost-effectiveness ratios (ICERs) produced; and (3) quantify the expected value of perfect information (EVPI) from obtaining more information from a larger study in the future. A NHS and social care perspective was used.

Results

Over 7 months, 449 patients with COPD were screened in two NHS hospitals; most of these patients were not eligible for the trial.

Feasibility outcomes

Primary feasibility outcome

In total, 76% of the recruitment target was met as 58 participants were randomised; 61 patients consented to take part in the study.

Recruitment and attrition rates

Recruitment and attrition rates varied over the recruitment period because of changing and removing the exclusion criterion related to length of stay. The overall recruitment rate was 4.1 participants per centre per month, but in the last 3 months the recruitment rate was 5.1 participants per centre per month. In total, 17 participants withdrew from the trial: three withdrew prior to randomisation, five withdrew post randomisation and prior to discharge and nine withdrew during the follow-up period.

Number of missing values/incomplete cases

In total, 40 participants (69.0%) provided data at the 90-day follow-up time point. Completion of expected self-report measures ranged from 41.7% to 100% and varied considerably across time points and measures. Data collection forms completed by participants had a completion rate ranging from 97.1% (LCADL) to 100% (MRC Dyspnoea Scale). The 6MWD outcome was the measure that was missed most at each relevant time point.

Intervention adherence

Delivery of the hospital EPR intervention was difficult, with only 34.1% of sessions overall taking place, the main barrier being patient discharge. Of the sessions that were started, all were completed, showing 100% adherence to individual sessions.

The home EPR intervention had a better level of adherence, with 78.3% of the expected sessions taking place overall. The main reason for sessions not taking place was participant choice.

Participant views on intervention/research protocol acceptability

In general, the interviewed participants indicated that both interventions were acceptable, with higher acceptability found for the home EPR intervention. No concerns were raised about either intervention, but some participants did feel too unwell to undertake the exercise sessions in both interventions.

Therapist views on intervention/research protocol acceptability

The interventions were acceptable and understood by the majority of those delivering them.

Feasibility of recruiting participating centres

Other consultants were interested and willing to take part in a full-scale trial.

Decision on the primary end point for the main trial

The 6MWD outcome was not found to be an appropriate primary end point for the main trial; readmission was suggested as a suitable primary outcome.

Clinical outcomes

The proposed primary clinical outcome (6MWD) was poorly completed at all time points, with 21 (36.2%) patients completing it at the 90-day time point (primary outcome), 33 (56.9%) completing it at 30 days and 20 (34.5%) completing it prior to discharge.

The mean 6MWD at 90 days was 267.4 m [standard deviation (SD) 160.90 m] in the hospital EPR group, 328.7 m (SD 108.02 m) in the home EPR group, 310.0 m (SD 194.29 m) in the hospital EPR and home EPR group and 199.6 m (SD 146.80 m) in the control group.

Limitation in activities of daily living

The mean LCADL score at 90 days was 41.3 (SD 16.93) in the hospital EPR group, 41.9 (SD 16.62) in the home EPR group, 37.6 (SD 13.43) in the hospital EPR and home EPR group and 40.6 (SD 15.87) in the control group.

Health-related quality of life

The mean EQ-5D-5L score at 90 days was 0.5 (SD 0.49) in the hospital EPR group, 0.6 (SD 0.29) in the home EPR group, 0.7 (SD 0.23) in the hospital EPR and home EPR group and 0.6 (SD 0.36) in the control group.

COPD Assessment Test

The mean CAT score at 90 days was 27.8 (SD 9.74) in the hospital EPR group, 26.4 (SD 6.91) in the home EPR group, 22.0 (SD 6.16) in the hospital EPR and home EPR group and 22.6 (SD 12.66) in the control group.

Serious adverse events

Overall, 26 participants (45%) experienced at least one SAE, six in the hospital EPR group, nine in the home EPR group, three in the hospital EPR and home EPR group and eight in the control group. None of these events was related to the interventions.

Exacerbations

In total, 25 participants experienced a COPD exacerbation (mild to severe), six in the hospital EPR group, eight in the home EPR group, five in the hospital EPR and home EPR group and six in the control group. The overall mean number of exacerbations reported by participants was 1.1 (SD 1.43), with a mean of 1.2 (SD 1.40) in the hospital EPR group, 1.5 (SD 1.96) in the home EPR group, 0.7 (SD 1.01) in the hospital EPR and home EPR group and 0.9 (SD 0.88) in the control group.

Readmissions

Overall, 18 (38%) patients experienced at least one COPD readmission during the trial, six out of 12 (50%) in the hospital EPR group, four out of 15 (27%) in the home EPR group, three out of 11 (27%) in the hospital EPR and home EPR group and five out of 10 (50%) in the control group. In total, there were 34 readmissions for COPD during the trial period, nine in the hospital EPR group, 10 in the home EPR group, five in the hospital EPR and home EPR group and 10 in the control group.

Activity monitor data

Activity monitor data were collected and three measures [metabolic equivalent of task (MET), sedentary MET and steps] were reported.

Medical Research Council Dyspnoea Scale

The MRC Dyspnoea Scale was analysed only with regard to feasibility (data collection results).

Other outcomes

The activity diary data were used to assess optimisation of home EPR, the health and resource use data were used in the economic analysis and the Perceived Necessity and Concerns questionnaire data are reported alongside the qualitative case studies.

Optimisation

In total, 106 out of 131 sessions that started were optimised. Half of the sessions that were not optimised could have been optimised with enhanced training of physiotherapists but half were not optimised because of the limitations of the equipment.

Clinical reasoning led to suboptimal aerobic exercise assessment in the first session and gradual introduction to exercise in the three subsequent sessions. Optimisation was hampered by inappropriate scoring and inadequate documentation of the Borg rating of perceived exertion values for resistance exercises.

Qualitative findings

Barriers to EPR were participants' concerns about breathlessness, participants believing that they were too ill and did not have the skills to undertake exercise or participants not believing that the exercises were beneficial. However, most participants were capable of undertaking the interventions and the acceptability of both interventions was high for participants and physiotherapists.

In relation to the trial protocol, participants found most aspects acceptable, with mixed views around burden and outcome measures. The Borg score was difficult to complete and study documentation and training may not have been sufficient for physiotherapists. Some aspects of organising the participant pathway were challenging. Resources were not sufficient to deliver both interventions without affecting existing services.

Health economics

In the exploratory cost-effectiveness analysis, all three interventions dominated usual care (less costly and more effective). The 'both' interventions trial arm had the highest probability of being cost-effective (87% and 88% for willingness-to-pay per QALY thresholds of £20,000 and £30,000 respectively), cost saving (78%) and more effective based on QALYs gained (83%) than any other intervention relative to usual care. The results suggest that there would be value in carrying out a larger trial to assess the cost-effectiveness of the hospital EPR and 'both' trial arms and collect more information to inform the hospital cost and QALY parameters.

Conclusions

This pilot study attempted to assess the feasibility of undertaking EPR in patients with AECOPD in hospital and immediately post discharge. The primary feasibility target of recruiting 76 patients was not met and a trial using the same protocol to test two interventions would not be feasible. Data from the trial can be used to design a full-scale trial of EPR following AECOPD.

Trial registration

This trial is registered as ISRCTN18634494, UKCRN 19145 and IRAS 163228.

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